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Palladium-catalyzed annulation of dienes and acetylenes

John Mathew Zenner
Iowa State University

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Palladium-catalyzed annulation of dienes and acetylenes

by

John Mathew Zenner

A dissertation submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of
DOCTOR OF PHILOSOPHY

Department: Chemistry
Major: Organic Chemistry
Major Professor: Richard C. Larock

Iowa State University
Ames, Iowa
1996

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Major Professor

Signature was redacted for privacy.

For the Major Department

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For the Graduate College

To all those who have supported me mentally, physically and financially in the completion of this degree. To those people who have seemingly passed from my life and to those who remain, my family and truest friends, I offer my most sincere thanks.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS vi

GENERAL INTRODUCTION 1

Dissertation Organization 1

CHAPTER 1: PALLADIUM-CATALYZED ENANTIOSELECTIVE HETERO- AND CARBOANNULATION OF 1,2-DIENES USING FUNCTIONALLY-SUBSTITUTED ARYL AND VINYLIC IODIDES 3

Abstract 3
Introduction 3
Results and Discussion 5
Conclusion 26
Experimental 26
Acknowledgement 39
References 39

CHAPTER 2: ENANTIOSELECTIVE PALLADIUM-CATALYZED HETEROANNULATION OF 1,3-DIENES USING ORTHO-FUNCTIONALIZED ARYL IODIDES. 43

Abstract 43
Introduction 43
Results and Discussion 46
Conclusion 57
Experimental 58
Acknowledgement 60
References 61

CHAPTER 3: PALLADIUM-CATALYZED CARBOANNULATION OF INTERNAL ACETYLENES USING BIARYLS 63

Abstract 63
Introduction 63
Results and Discussion 65
Conclusion 90
Experimental 90
Acknowledgement 115
References 116

GENERAL CONCLUSIONS 119

APPENDIX A: CHAPTER 1 ^{1}H AND ^{13}C NMR SPECTRA 122

APPENDIX B: CHAPTER 2 ^{1}H AND ^{13}C NMR SPECTRA 196

APPENDIX C: CHAPTER 3 ^{1}H AND ^{13}C NMR SPECTRA 202

GENERAL ACKNOWLEDGEMENTS 282

LIST OF ABBREVIATIONS

Ac	acetyl
aq	aqueous
Ar	aryl
BINAP	[1,1’-binaphthalene]-2,2’-diylbis[diphenylphosphine)
BPPFA	1-[1-(dimethylamino)ethyl]-1’,2-bis(diphenylphosphino)ferrocene
br	broad
Bu	butyl
concd.	concentrated
dba	dibenzylideneacetone
dd	doublet of doublets
ddd	double doublet of doublets
DMA	*N,N*-dimethylacetamide
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
dq	doublet of quartets
dt	doublet of triplets
ee	enantiomeric excess
eq	equation
equiv	equivalent(s)
Et	ethyl
h	hour(s)
hfc	3-(heptafluoropropylhydroxymethylene)-(+)-camphorato
HRMS	high resolution mass spectroscopy
Hz	Hertz

IR	infrared
L	ligand
Me	methyl
mL	milliliters
mol	mole(s)
mp	melting point
Ms	methanesulfonyl
n	normal
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
o	ortho
p	para
Ph	phenyl
Piv (Pv)	pivaloate
PPA	polyphosphoric acid
q	quartet
t	tertiary
s	singlet
t	triplet
TBAC	tetra-*n*-butylammonium chloride
TBDMS	*t*-butyl(dimethyl)silyl
Tf	trifluoromethanesulfonyl
TMS	trimethylsilyl
Ts	*p*-toluenesulfonyl
UV	ultraviolet

GENERAL INTRODUCTION

Palladium-catalyzed processes have proven to be extremely useful methods for the synthesis of a wide variety of hetero- and carbocycles. The continuing interest in and widespread research on palladium-catalyzed transformations stems from the fact that these reactions are remarkably general in scope, often proceed with a high degree of regio- and stereoselectivity and tolerate an extensive number of functional groups. In addition, most commonly used palladium catalysts are neither oxygen nor moisture sensitive, which contributes to the procedural ease with which these reactions can be carried out..

The Larock group has recently reported that aryl and vinylic iodides with nucleophilic substituents in the ortho or allylic position respectively react with a variety of dienes and internal acetylenes to afford a wide array of hetero- and carbocycles in high yield. This dissertation serves to expand the scope of some of that earlier work to include asymmetric versions of these annulations and also to further develop the annulation processes of internal acetylenes. The author of this manuscript was the primary investigator and author for each of the papers reported in this thesis.

Dissertation Organization

Chapter 1 concerns the development of an enantioselective annulation of allenes using functionally-substituted aryl and vinylic iodides. This methodology utilizes a palladium catalyst in the presence of a chiral bisoxazoline ligand to afford five- and six-membered ring hetero- and carbocycles in good yields and 46 to 88 % enantiomeric excess (ee). The methodology is extremely general, especially for terminal allenes, and includes the highest level of asymmetric induction yet reported for an intramolecular π-allylpalladium displacement of this kind.

Chapter 2 deals with asymmetric heteroannulation of 1,3-dienes. The main effort of this study was the annulation of 1,3-cyclohexadiene using 2-iodophenol. Asymmetric induction in this system is dependent upon an enantioselective Heck reaction. A number of acyclic 1,3-dienes were also annulated using *N*-tosyl-2-iodoaniline. The asymmetric annulation of acyclic dienes is formally an enantioselective π-allylpalladium displacement related to those discussed in Chapter 1. While the levels of asymmetric induction observed in this study are only moderate, the results have provided mechanistic insight into the types of substrates which may facilitate the formation of products of high enantiomeric excess.

Chapter 3 describes the palladium-catalyzed carboannulation of internal acetylenes using *o*-iodobiaryls. This methodology tolerates a wide array of functionality both on the biaryl and the acetylene and provides an exceptionally efficient route to a variety of substituted polycyclic aromatic hydrocarbons, including synthetic analogues of the antiviral natural product hypericin.

The general conclusion will discuss the current scope and limitations of this methodology and show common relationships between the three chapters.

Finally, appendices A-C will provide pertinent ^{1}H and ^{13}C NMR spectra for all new products of the palladium-catalyzed reactions described in Chapters 1-3 of this thesis. These same supplementary materials will be available through the American Chemical Society after publication in the *Journal of Organic Chemistry*.

CHAPTER 1: PALLADIUM-CATALYZED, ASYMMETRIC HETERO- AND CARBOANNULATION OF ALLENES USING FUNCTIONALLY-SUBSTITUTED ARYL AND VINYLIC IODIDES

A paper to be submitted to the *Journal of Organic Chemistry*

Richard C. Larock* and John M. Zenner
Department of Chemistry, Iowa State University, Ames, Iowa 50011

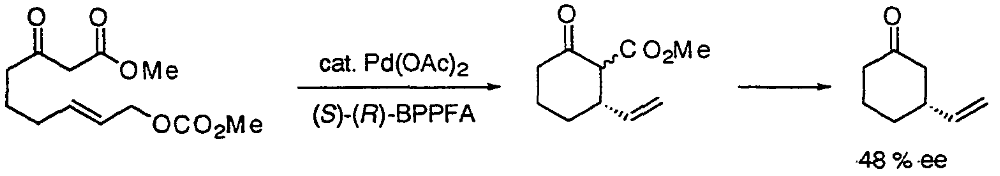
Abstract

Aryl and vinylic iodides with a nucleophilic substituent in the ortho or allylic position respectively, react with 1,2-dienes in the presence of a palladium catalyst and a chiral bisoxazoline ligand to afford five- and six-membered ring heterocycles and carbocycles in good yields and 46 to 88 % enantiomeric excess. The generality of this process has been demonstrated by the use of nucleophilic substituents as varied as tosylamides, alcohols, carboxylic acids and stabilized carbanions.

Introduction

Biologically active molecules, which are chiral, often exhibit significant variance in biological activity between the enantiomers.[1] For this reason, the development of asymmetric synthetic methodologies has been of prime importance to organic chemists. The enantioselective, palladium-catalyzed allylic substitution reaction has been shown to be a useful means of forming new chiral carbon-carbon,[2] carbon-nitrogen[3] and carbon-sulfur bonds.[4] Most work in this area has focused on intermolecular nucleophilic substitution of the symmetrical 1,3-diphenyl-π-allylpalladium system and the development of improved chiral ligands for use in this process.[5] Relatively little work has been done on more complicated unsymmetrical systems.[6]

Asymmetric induction in intramolecular π-allylpalladium displacements has received far less attention with only three examples of this type of process appearing in the literature.[7] Tsuji reported in 1982 an asymmetric cyclization of methyl (*E*)-3-oxo-9-phenoxy-7-nonenoate in the presence of a chiral diphosphine ligand to give the cyclized product in up to 48 % ee (eq 1).[7a] Genet and Grisoni synthesized an ergot alkaloid synthon in up to 70 % ee using a palladium-chiraphos catalyst (eq 2),[7b] and Shibasaki *et al* have recently reported the synthesis of a *cis*-decalin derivative in up to 83 % ee via an asymmetric π-allylpalladium displacement (eq 3).[7c]



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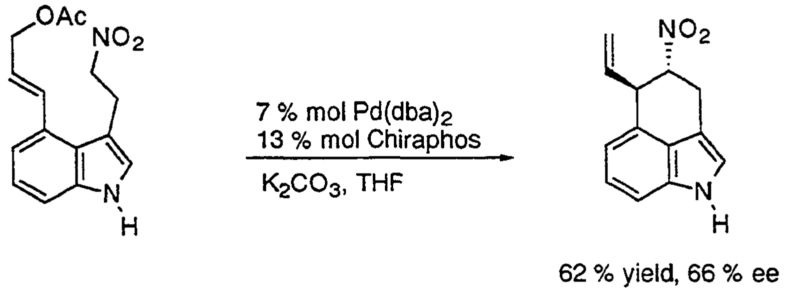

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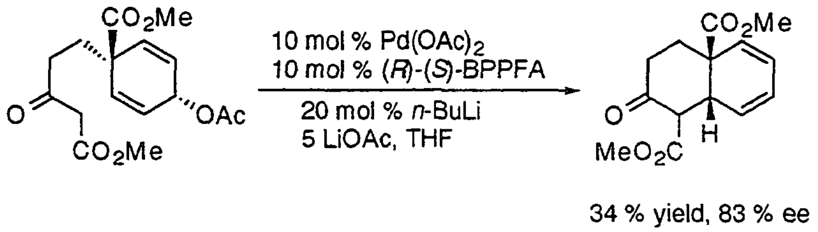
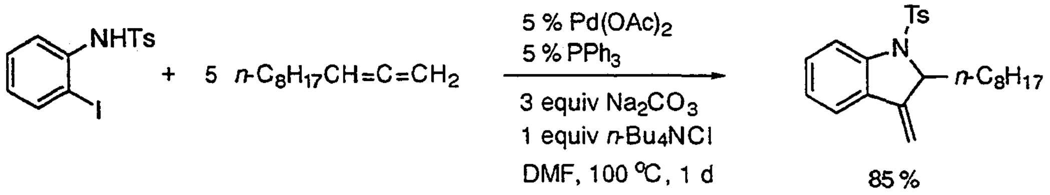


(3)

We have recently reported the regioselective, palladium-catalyzed hetero- and carboannulation of allenes using functionally-substituted aryl[8] and vinylic halides.[9] The nature of the π-allylpalladium intermediates involved encouraged us to examine asymmetric versions of these annulation processes. Preliminary results of this work have been published in the form of a communication.[10] We now wish to report, in greater detail, the results of our investigation.

Results and Discussion

The reaction of *N*-tosyl-2-iodoaniline with 1,2-undecadiene was chosen as a model system to optimize conditions for asymmetric induction. We have previously reported that using as reaction conditions 5 mol % $Pd(OAc)_2$, 5 mol % PPh_3, 3 molar equiv of Na_2CO_3, 1 equiv of n-Bu_4NCl (TBAC) in DMF at 100 °C for 1 day, the desired product was obtained in 85 % yield (eq 4).[8] Initial attempts at asymmetric induction utilized these same conditions, but replaced PPh_3 with (R)-BINAP. Under these conditions, the product was obtained in 87 % yield, but only 5 % ee (Table 1, entry 1). Removal of TBAC from the system did not lead to improved enantioselectivity (Table 1, entry 2).



(4)

Recent reports by Shibasaki *et al* have demonstrated that in the presence of silver salts, significantly enhanced levels of aymmetric induction can be achieved in chiral ligand mediated Heck-type reactions of aryl or vinylic halides.[11] It is thought that in the presence of Ag^+, I^- is precipitated as AgI, allowing stronger coordination of the chiral ligand to palladium.[11a] For this reason, reaction conditions were altered to include a silver base. Replacement of Na_2CO_3 with a silver salt led to enhanced levels of enantioselectivity (Table 1, entries 3 and 4), although the overall yield was reduced significantly. We hypothesized that a redox reaction between Pd(0) and Ag(I) could account for the lower yields and the observed mirror on the reaction vial. Since only 1 equiv of Ag^+ is theoretically needed, the amount of Ag_3PO_4 was reduced to 0.4 molar equiv (1.2 ion equiv) and under these conditions the product was obtained in 65 % yield and a slightly higher 30 % ee (Table 1, entry 5). Variation of the reaction temperature had a pronounced effect on the enantioselectivity (Table 1, entries 5-7). Raising or lowering the

Table 1. Optimization of Conditions for the Enantioselective Reaction of *N*-Tosyl-2-iodoaniline and 1,2-Undecadiene (eq 4).[a]

entry	base type	base mol/ArI	solvent	Temp (°C)	% yield	% ee
1[b]	Na_2CO_3	3.0	DMF	100	87	5
2	Na_2CO_3	3.0	DMF	100	78	4
3	Ag_2CO_3	1.0	DMF	100	36	25
4	Ag_3PO_4	1.0	DMF	100	36	25
5	Ag_3PO_4	0.4	DMF	100	65	30
6	Ag_3PO_4	0.4	DMF	120	44	16
7[c]	Ag_3PO_4	0.4	DMF	80	63	0
8	Ag_3PO_4	0.4	DMA	100	63	0
9	Ag_3PO_4	0.4	THF	100	56	13
10	Ag_3PO_4	0.4	DMSO	100	71	7
11	Ag_3PO_4	0.4	Toluene	100	15	20
12	Ag_3PO_4	0.4	CH_3CN	100	23	10

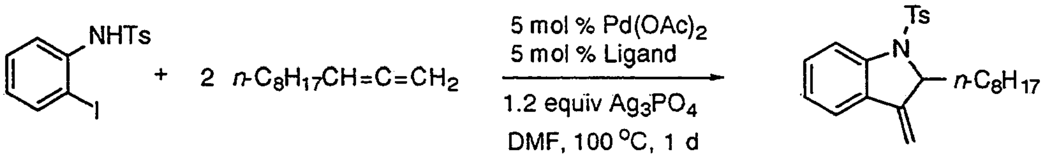
[a] 5 Mol % of $Pd(OAc)_2$ and 5 mol % of BINAP were used as the catalyst.

[b] 1 Equiv of TBAC was used in this reaction.

[c] Similar results were obtained using DiPAMP and MeO-BIPHEP as chiral ligands.

reaction temperature 20 °C caused a reduction in ee, to the extent of affording an essentially racemic product at 80 °C. Solvent effects were also very important both in terms of chemical yield and ee with the original solvent DMF giving the best results (Table 1, entries 8-12). There was no significant effect on enantioselectivity when $Pd(OAc)_2$ was replaced by either $Pd(dba)_2$ or $PdCl_2$ in this system.

The final variable examined was the chiral ligand itself. A variety of chiral ligands were purchased by or donated to this research group and used in the reaction of *N*-tosyl-2-iodoaniline with 1,2-undecadiene (eq 5). The results are summarized in Table 2.

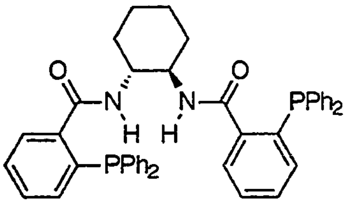
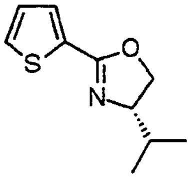
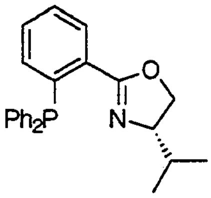
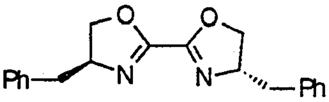
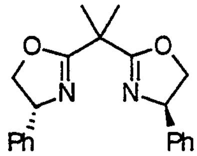
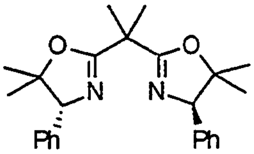
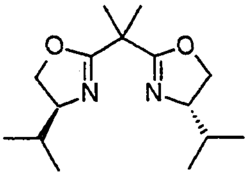
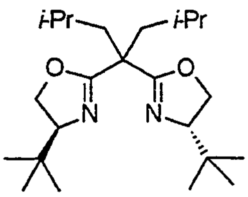


(5)

Table 2. Comparison of the Asymmetric Induction of Various Chiral Ligands in the Reaction of *N*-Tosyl-2-iodoaniline and 1,2-Undecadiene (eq 5).[a]

entry	chiral ligand	ref	% yield	% ee
1	BINAP	-	65	30
2	DIPAMP	5a	32	23
3	BIPHEMP	12	65	26
4	MeO-BIPHEP	12	63	53
5	DUPHOS	13	40	3
6	Chiraphos	-	58	0
7	Sparteine	-	73	3
8	MeO-MOP	14	85	31
9	Pybox	15	79	18

Table 2 (continued)

10		2f	84	27
11		5g	92	1
12		2e	52	50
13		5b	53	14
14		5f	79	39
15		16	80	50
16		5f	88	67
17		17	96	24

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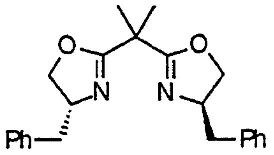
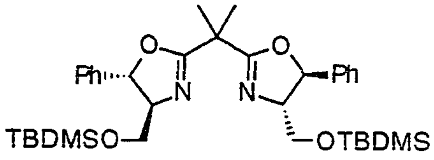
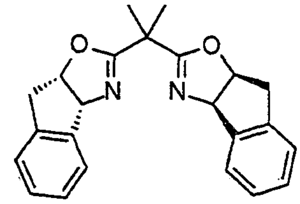
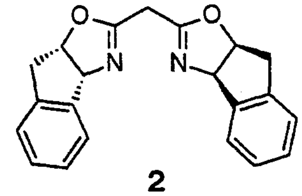
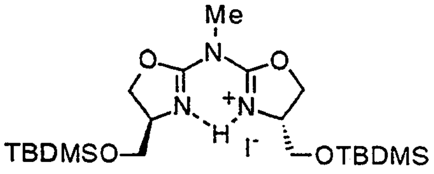
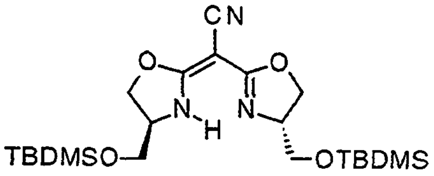
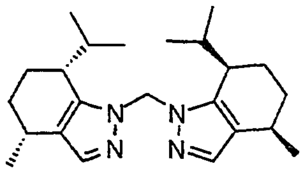
18	 **1**	5e,f	79	75
19		18	87	78
20		19	98	77
21	 **2**	19	90	86
22		5e	88	~0
23		5e	0	-
24		5i	76	20

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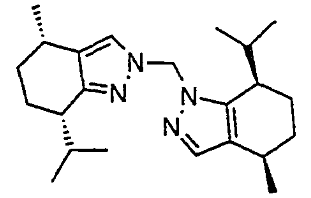
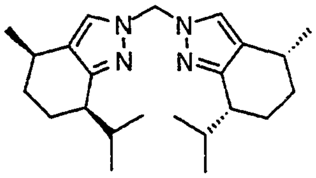
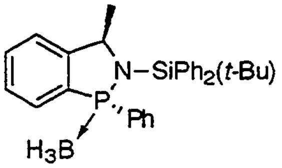
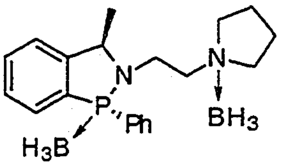
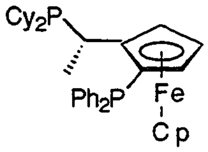
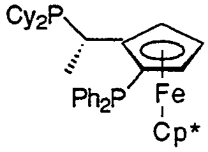
25		5i	88	29
26		5i	74	17
27		5j	76	<5
28		5j	62	<5
29		5k	40	7
30		5k	29	<5

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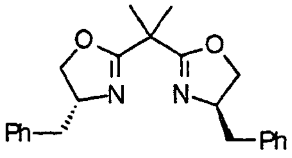
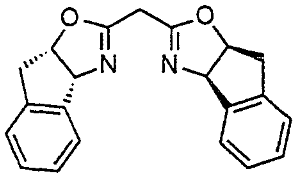
[a] All reactions were run in the presence of 5 mol % of $Pd(OAc)_2$, 5 mol % of the chiral ligand and 1.2 ion equiv of Ag_3PO_4 in DMF at 100 °C for 1 day.

The following observations have been made with regard to ligand structure. Those ligands which when coordinated to Pd form a 6-membered ring lead to products of higher ee than those which form a 5-membered ring, and more electron-rich ligands tend to give higher asymmetric induction. Best results were obtained using the bisoxazoline ligands developed by Pfaltz and others (Table 2, entries 14-17),[5b-d,18] particularly compound **1**. Further optimization



1



2

using **1** afforded the desired product in 94 % yield and 82 % ee (Table 3, entry 1). Only recently we have found that in the presence of chiral ligand **2**,[19] these same reaction conditions give the desired product in 84 % yield and an even higher enantiomeric excess of 88 %. However, subsequent results have suggested that **2** does not generally give higher levels of asymmetric induction than chiral ligand **1**. Reaction of *N*-tosyl-2-iodoaniline with the internal allenes 4,5-nonadiene and 1,2-cyclotridecadiene again gave the products in high yield and showed no change in the level of enantioselectivity (Table 3, entries 2 and 3).

Extension of this process to other nucleophilic substrates has been achieved, although, in general, not to the level of success attained in the model system. For all substrates, the highest enantiomeric excesses have been obtained using 1 equiv of the aryl or vinylic iodide, 2 equiv of the allene, 1.2 equiv of Ag_3PO_4 in DMF using a Pd/**1** catalyst, at a temperature low enough to achieve asymmetric induction, while still allowing the reaction to go to completion (Table 3).

Table 3. Palladium-Catalyzed, Asymmetric Annulation of Allenes Using Chiral Bisoxazoline Ligand 1.[a]

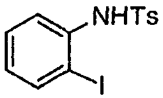
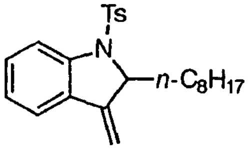
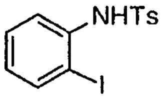
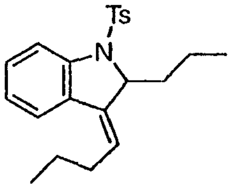
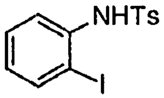
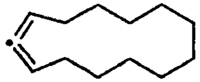
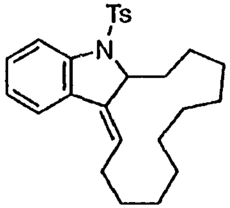
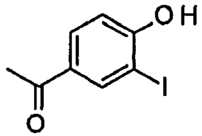
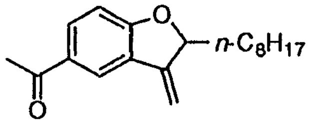
entry	organic iodide	allene	catalyst[b]	temp. (°C)	time (d)	product	% isolated yield	% ee	$[\alpha]_D$
1		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	A	90	1		94	82	-19.4°
2		$n\text{-}C_3H_7CH{=}C{=}CH\text{-}n\text{-}C_3H_7$	A	90	1		95	80	-32.5°
3			A	90	1		95	81	-37.0°
4		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	B	100	2		95	52	-61.2°

Table 3 (continued)

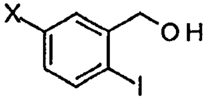
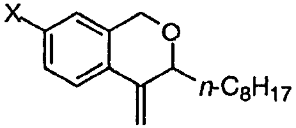
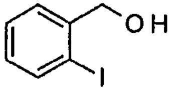
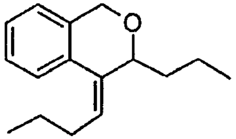
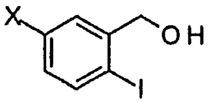
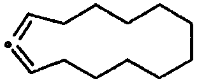
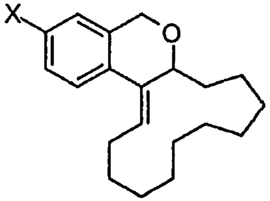
		n-C$_8$H$_{17}$CH=C=CH$_2$							
5			A	80	4	X = H	72	73	-15.6°
6			A	80	4	X = Me	56	67	-17.1°
7			A	80	4	X = Br	64	67	-8.7°
8		n-C$_3$H$_7$CH=C=CH-n-C$_3$H$_7$	A	80	3		73	55	-71.6°
									
9			A	80	3	X = H	29	77	-148.9°
10			A	80	3	X = Br	33	$-^c$	-118.0°

Table 3 (continued)

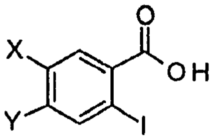
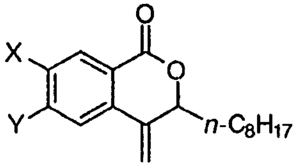
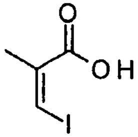
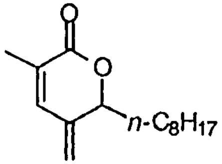
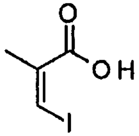
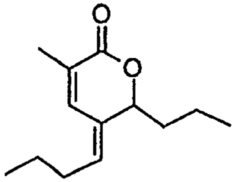
		n-$C_8H_{17}CH{=}C{=}CH_2$							
11			C	40	3	X = Y = H	50	67	-79.5°
12			C	40	6	X = Me, Y = H	69	63	-70.7°
13			C	40	6	X = Y = MeO	78	71	-52.6°
14			C	40	6	X = Br, Y = H	67	48	-47.1°
15		n-$C_8H_{17}CH{=}C{=}CH_2$	D	40	3		41	80	-93.5°
16		n-$C_3H_7CH{=}C{=}CH$-n-C_3H_7	D	40	5		59	46	-97.5°

Table 3 (continued)

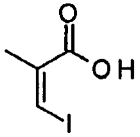
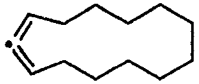
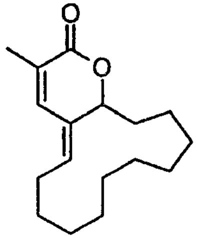
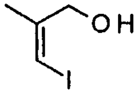
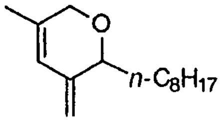
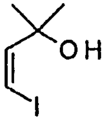
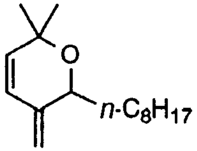
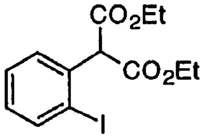
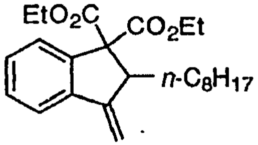
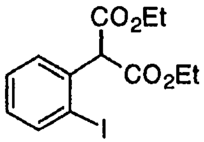
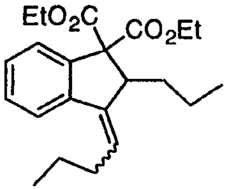
17			D	40	3		52	61	-202.6°
18		n-$C_8H_{17}CH=C=CH_2$	A	80	4		70	79	-11.5°
19			B	40	15		21	88	undet.
20		n-$C_8H_{17}CH=C=CH_2$	B	80	4		62	-[d]	+46.0°
21		n-$C_8H_{17}CH=C=CH_2$	E	90	3		67	75	+48.8°

Table 3 (continued)

22		n-$C_3H_7CH{=}C{=}CH$-n-C_3H_7	E	75	3		79 (*Z*:*E*=7:1)	47	+28.0°

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[a] All reactions were run in the presence of 1.2 silver ion equiv of Ag_3PO_4 in DMF (1.0 mL/0.50 mmol of organic iodide).

[b] Catalyst A: 5 mol % of $Pd(OAc)_2$, 10 mol % of ligand **1**. Catalyst B: 5 mol % of $Pd(OAc)_2$, 5 mol % of ligand **1**. Catalyst C: 5 mol % of $Pd(dba)_2$, 5 mol % of ligand **1**. Catalyst D: 5 mol % of $Pd(dba)_2$, 10 mol % of ligand **1**. Catalyst E: 10 mol % of $Pd(dba)_2$, 10 mol % of ligand **1**.

[c] Recrystallized product appeared to be >95 % ee ($[\alpha]_D$ = -211.0°).

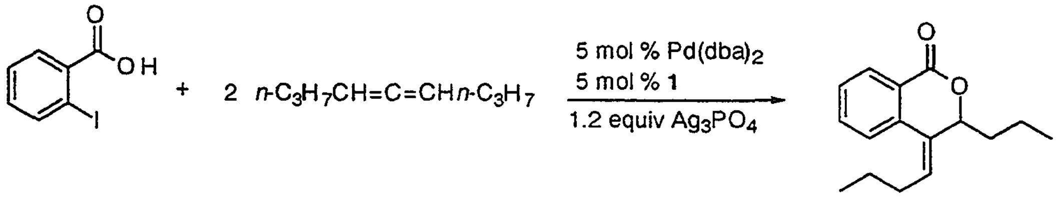
[d] The ee of this product has not been determined, since the ee could not be obtained using of $Eu(hfc)_3$.

Aryl and vinylic iodides containing oxygen nucleophiles have been used to form 6-membered ring heterocycles in fair to excellent ee's. The reaction of 2-iodo-4-acetylphenol and 1,2-undecadiene afforded the desired benzofuran derivative in excellent yield, but only 52 % ee (Table 3, entry 4). Experimental conditions for asymmetric induction were not optimized for this system. 2-Iodobenzyl alcohol reacts with 1,2-undecadiene to give the desired product in 72 % yield and 73 % ee (Table 3, entry 5). Substitution in the 5-position of 2-iodobenzyl alcohol had little effect on the enantioselectivity (Table 3, entries 6 and 7).

In general, for all functionalized aryl iodides, except *N*-tosyl-2-iodoaniline, internal allenes gave lower levels of enantioselectivity than terminal allenes. For example, the reaction of 2-iodobenzyl alcohol with 4,5-nonadiene gave the annulation product in 73 % yield, but only 55 % ee (Table 3, entry 8). Since chiral ligand **2** had performed better than **1** in the annulation of 1,2-undecadiene using *N*-tosyl-2-iodoaniline, it was tried in the reaction of 2-iodobenzyl alcohol with 4,5-nonadiene. However, in this case the reaction was much slower, lower yielding and afforded the product in the same 55 % ee. While the same aryl iodide reacted with 1,2-cyclotridecadiene to afford the desired product in 77 % ee, the yield was only 29 % (Table 3, entry 9).

The reaction of 2-iodobenzoic acid with the terminal allene 1,2-undecadiene gave good selectivity, but in this system substituents on the aromatic ring of the substrate did cause significant variation in the ee (Table 3, entries 11-14).

The reaction of 2-iodobenzoic acid and 4,5-nonadiene gave the desired product in only low yield, although the ee remained reasonably high (Table 4, entry 1) (eq 6). Due to



(6)

the low overall yield, further optimization of this reaction was attempted (Table 4). Solvent effects were found to be most crucial, both in terms of product yield and ee. Unfortunately, those solvents which facilitate product formation seem to do so at the expense of enantioselectivity.

Table 4. Effect of Solvent on Product Yield and Enantioselectivity in the Reaction of 2-Iodobenzoic Acid and 4,5-Nonadiene (eq 6).[a]

entry	solvent	temp. (°C)	time (d)	% yield[b]	% ee
1	DMF	40	3	16	69
2	CH_2Cl_2	40	2	61 (6:1)	35
3	CH_2Cl_2	r.t.	1	40 (6:1)	45
4	$ClCH_2CH_2Cl$	40	2	81 (7:1)	30
5	$CHCl_3$	40	3	84 (8:1)	36
6	THF	40	3	87	44
7	THF	r.t.	5	87	39
8	DMF/THF (1:1)	40	17	39	48
9	Toluene	40	3	71 (6:1)	30
10	Tetramethylurea	40	3	30	43
11	DMSO	40	3	0	-
12	CH_3CN	40	3	65	23
13	CH_3NO_2	40	3	45 (4:1)	38

[a] All reactions were run in the presence of 5 mol % of $Pd(OAc)_2$, 5 mol % of ligand **1** and 1.2 ion equiv of Ag_3PO_4.

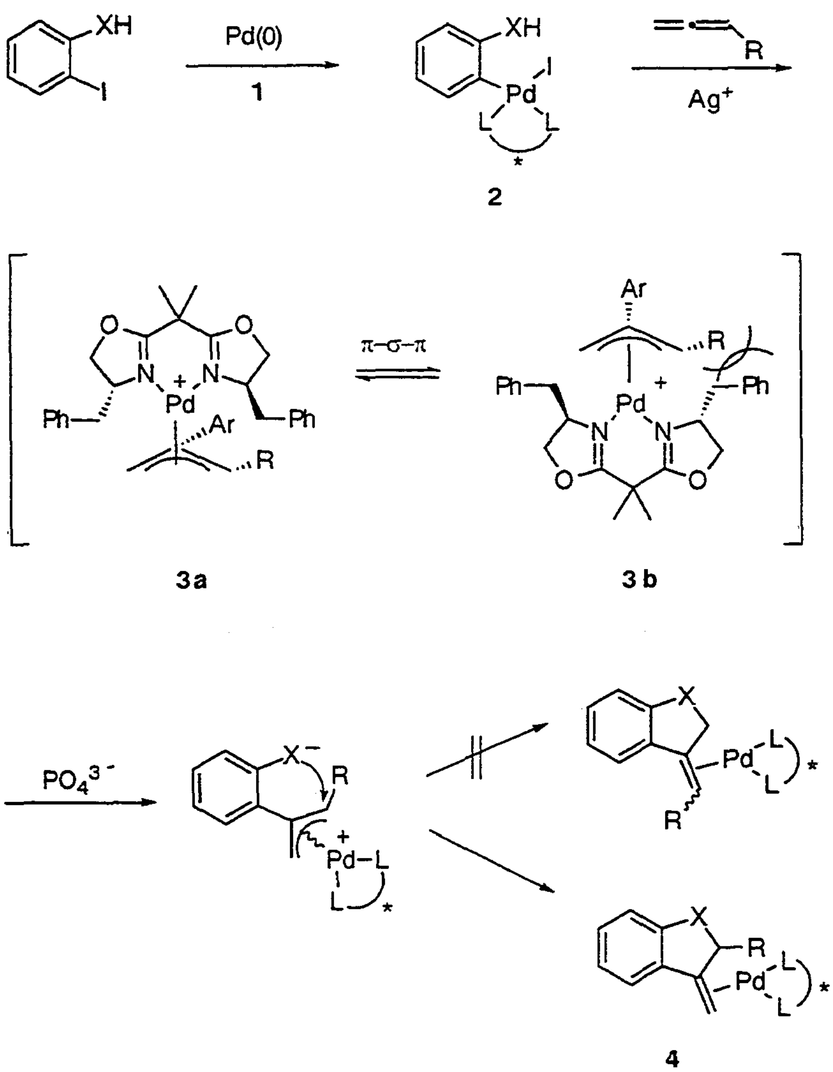
[b] Numbers in parenthesis indicate the ratio of *E*:*Z* isomers.

The formation of 6-membered ring heterocycles using vinylic iodides bearing alcohol or carboxylic acid functionality in the allylic position followed the same trends found with the aryl analogues (Table 3, entries 15-20). Entries 18 and 19 (Table 3) demonstrate a quite significant temperature effect in the reaction of *Z*-3-iodo-2-methyl-2-propen-1-ol and 1,2-undecadiene. This reaction at 40 °C afforded a product of 88 % ee; higher than we had observed in any other of our annulation processes. Unfortunately, at this lower temperature, the reaction was very sluggish and even after a reaction time of 15 days the product was isolated in only a 21 % yield.

Carboannulation has also been carried out enantioselectively using this methodology. Using as the substrate diethyl 2-iodophenylmalonate, it again was found that terminal allenes led to products of higher optical purity than internal symmetrical allenes (Table 3, entries 21 and 22).

The mechanism of this reaction has been outlined in our earlier publication and is reproduced in Scheme 1.[10] The first step is undoubtedly reduction of Pd(II) to Pd(0) followed by oxidative addition of the organic halide. The addition of aryl or vinylic palladium compounds to allenes is known to produce π-allylpalladium compounds, which readily undergo intramolecular nucleophilic substitution.[8,9,20] In the presence of Ag^+, the iodide is removed as AgI, allowing the formation of a 16 electron, positively-charged Pd intermediate to which the bidentate chiral ligand is coordinated.[11] This system then resembles those investigated by Bosnich in which interconversion between diastereomers is accomplished via a π-σ-π process.[6] This interconversion is known to occur rapidly in terminal π-allylpalladium species and this is no doubt of paramount importance to eventual enantio-discrimination.[6b] Bosnich's work has suggested that the major π-allylpalladium intermediate gives rise to the major enantiomer observed. In light of this, we speculate that steric interactions between the benzyl groups of the chiral ligand and the terminal alkyl substituent of the π-allylpalladium

Scheme 1



intermediate lead to a preference for one diastereomer **3a** over the other, which goes on to form the major observed enantiomer. Therefore, enantioselectivity is achieved due to minimization of steric interactions. Assuming backside nucleophilic displacement of **3a**, this mechanistic model predicts an (*S*) absolute configuration for the observed product. An X-ray crystal structure determination of 7-bromo-3,4-dihydro-4-methylene-3-*n*-octyl-1*H*-2-benzopyran (Table 3, entry 7) has confirmed the predicted (*S*) absolute configuration (Figure 1).

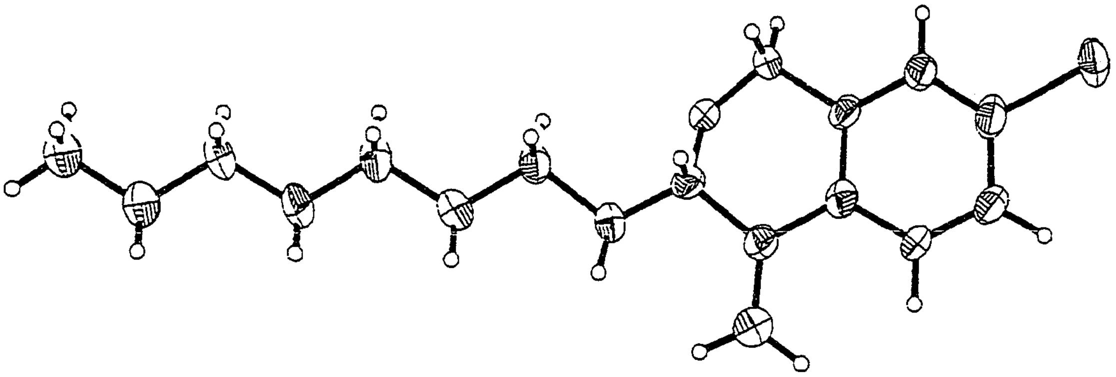
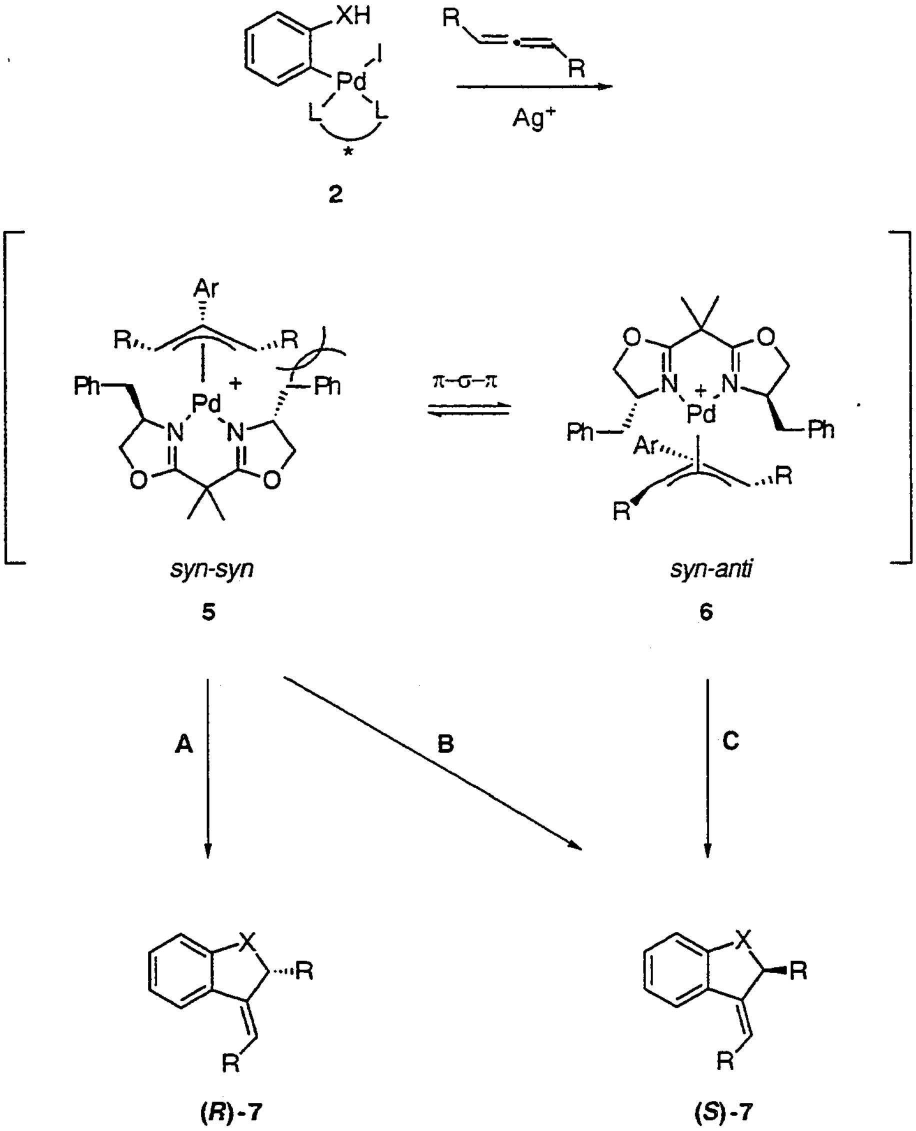


Figure 1. An ORTEP Drawing of the Crystal Structure of 7-Bromo-3,4-dihydro-4-methylene-3-*n*-octyl-1*H*-2-benzopyran.

In the case of internal allenes, if the π-allyl system maintains a *syn-syn* conformation, a symmetrical π-allylpalladium species is generated in which steric interactions cannot be minimized (Scheme 2). This system would then resemble a 1,3-disubstituted π-allylpalladium intermediate for which factors leading to enantioselectivity in the intermolecular nucleophilic attack have been well described elsewhere.[18,21] Those studies conclude that nucleophilic attack occurs at the end of the π-allyl system at which there exists steric interactions between the π-allyl substituent and the substituent on the oxazoline ring.[18] As the π-bound Pd(0)-alkene primary product is formed, this strain is alleviated (Scheme 2, path A). The above described mechanism of asymmetric induction would predict an (*R*) absolute configuration for the products of internal allene annulation. However, the optical rotations of the products we have obtained from internal allenes, as well as the ^{1}H NMR splitting patterns in the presence of a chiral lanthanide shift reagent, appear more consistent with the (*S*) configuration observed for

Scheme 2



products arising from the annulation of terminal allenes. A determination of the X-ray crystal structure of (*E*)-3-bromo-5,6a,7,8,9,10,11,12,13,14,15,16-dodecahydrobenzo[d]cyclotrideca[b]pyran (Table 3, entry 10) has shown the absolute configuration is in fact (*S*) (Figure 2). Therefore, we hypothesize that in the case of a 1,2,3-trisubstituted π-allylpalladium system, the steric bulk of the substituent in the 2-position may

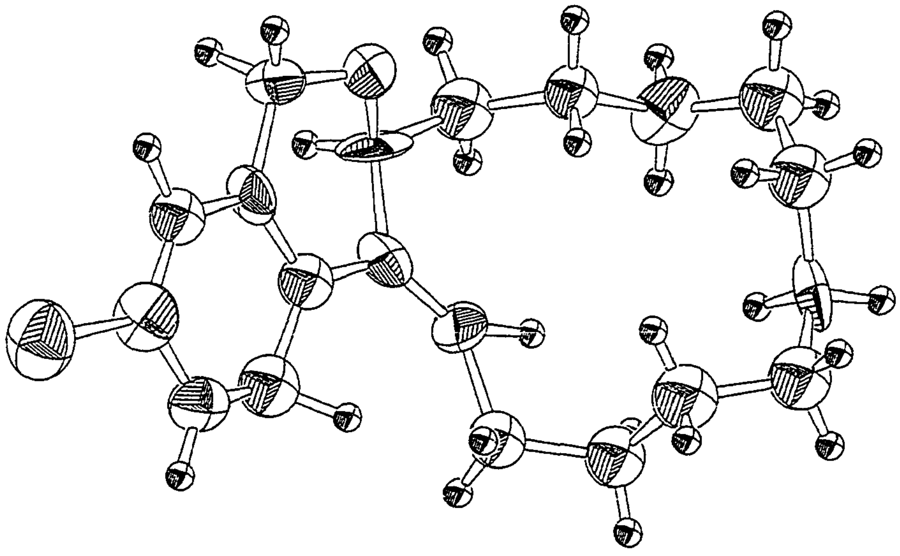
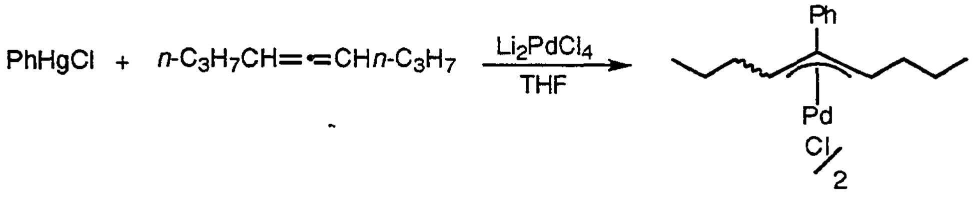


Figure 2. An ORTEP Drawing of the Crystal Structure of (*E*)-3-bromo-5,6a,7,8,9,10,11,12,13,14,15,16-dodecahydrobenzo[d]cyclotrideca[b]pyran.

lead to an equilibrium which favors the *syn-anti* (**6**) over the *syn-syn* conformer (**5**) (Scheme 2).[22] To confirm this suspicion, we have synthesized and isolated di-μ-chloro-di(η^3-5-phenylnon-4-enyl)dipalladium(II) (eq 7).[23] Proton and ^{13}CNMR spectroscopic analysis in chloroform has shown this to be a mixture of *syn-syn* and *syn-anti* conformers in an

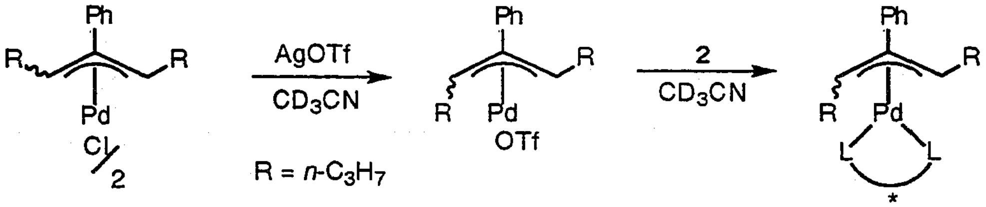


(7)

8 (2 : 1)
(*syn-syn*/*syn-anti*)

approximately 2 : 1 ratio. We hypothesize that coordination of the bisoxazoline chiral ligand may further shift this equilibrium towards the *syn-anti* conformer, since this conformer is relatively free of steric interactions between the benzyl substituents of the bound ligand and the substituents on the π-allyl system (**6**). To examine this possibility, we formed the (η^3-5-

phenylnon-4-enyl)palladium(II)-**2** complex in CD_3CN. Initial attempts to form this complex by stirring di-μ-chloro-di(η^3-5-phenylnon-4-enyl)dipalladium(II) and **2** in CD_3CN at 80 °C gave no evidence of coordination. Therefore, di-μ-chloro-di(η^3-5-phenylnon-4-enyl)dipalladium(II) was first stirred with AgOTf precipitating AgCl and leading to the formation of (η^3-5-phenylnon-4-enyl)palladium(II) triflate. This was then stirred with ligand **2** in CD_3CN at 80 °C (eq 8). Analysis of the resulting complex by ^{1}H NMR spectroscopy verified that in the ligand bound π-allylpalladium species this equilibrium is further shifted, favoring the *syn-anti* over the *syn-syn* conformer in a ratio of 3 : 1. This same experiment using ligand **1** resulted in a 3.8 : 1 mixture of *syn-anti* and *syn-syn* conformers. These results



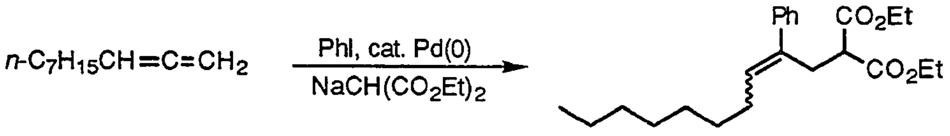
(8)

8 (2 : 1)
(*syn-syn*/*syn-anti*)

9 (1 : 1.4)

10(1 : 3)

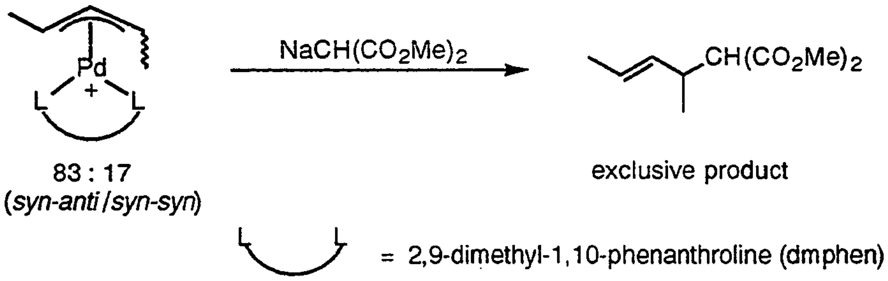
have precedent in the work of Gore and co-workers, who reported an 85:15 (*E*/*Z*) ratio of products for the intermolecular displacement of a 1-*n*-heptyl-2-phenyl-π-allylpalladium intermediate by sodium diethylmalonate (eq 9).[20a] Again, if as suggested by Bosnich[6] and others,[24] the major π-allylpalladium intermediate present in solution gives rise to the major enantiomer observed, backside nucleophilic attack must occur preferentially at the *anti* terminus



(9)

71 % yield
85 :15 (*E* : *Z*)

of the π-allyl system in order to give the observed productof (*S*)-absolute configuration at the stereogenic center and (*E*)-configuration about the double bond (Scheme 2, path C). The higher reactivity of the *anti*-substituted carbon, required by this mechanistic path, has precedent in work by Åkermark (eq 10).[22c] Di-μ-chloro-di(η^3-5-(2'-hydroxymethylphenyl)non-4-



(10)

enyl)dipalladium(II) has been prepared by the reaction of 2-(chloromercurio)benzyl alcohol, 4,5-nonadiene and Li_2PdCl_4,[23] but this π-allylpalladium compound rapidly decomposed at room temperature. Therefore, we were unable to attempt to correlate the ratio of *syn-syn* and *syn-anti* comformers to the ee of the annulation product (*E*)-4-*n*-butylidene-3,4-dihydro-3-*n*-propyl-1*H*-2-benzopyran. Alternatively, nucleophilic attack at the end of the π-allyl system which is relatively free of steric interactions in the *syn-syn* conformer (Scheme 2, path B), also leads to the observed (*S*) isomer. We have as yet been unable to determine the precise mechanism at work in these systems.

The regioselectivity of this annulation process is generally quite high, often better than that observed under our previously reported conditions using PPh_3 as the ligand.[8,9] The reaction of aryl or vinylic iodides and 1,2-undecadiene forms five- or six-membered ring products by nucleophilic attack exclusively at the more substituted end of the π-allylpalladium intermediate (Table 3; entries 1, 4, 5 and 7). The regioselectivity of attack at the more sterically-congested π-allyl terminus may be explained on the basis of two electronic factors: (1) the net positive charge on the π-allylpalladium species being more localized at the alkyl-substituted terminus,[25] and (2) the observation that electron-rich palladium(0)-ligand complexes favor coordination to the more electron-deficient, less-substituted double bond of the observed product.[6,26] For these reasons, the transition state leading to the observed product may be favored.

Conclusion

The palladium-catalyzed, asymmetric hetero- and carboannulation of allenes using functionally-substituted aryl and vinylic iodides has been achieved in moderate to high levels of enantiomeric excess. The generality of this process has been demonstrated by the use of a wide variety of aryl and vinylic iodides, internal nucleophiles and allenes. This generality, combined with the procedural ease with which these reactions are carried out, make this an attractive route to enantiomerically enriched hetero- and carbocycles. The results of this study include the highest ee's reported for a palladium-catalyzed intramolecular allylic substitution reaction.

Experimental

General. All ^1H and ^{13}C NMR spectra were recorded at 30 and 75.5 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) or basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O]. All melting points are uncorrected.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. All palladium reagents were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co., Ltd. 2-Iodoaniline, 2-iodobenzyl alcohol, 2-iodobenzoic acid, 2-iodobenzyl chloride, propargyl alcohol, *p*-toluenesulfonyl chloride, diethyl malonate, 1-decene, 4-octene, cyclododecene, bromoform, MeLi, Et_3N, PCC and $Eu(hfc)_3$ were purchased from Aldrich

Chemical Co., Inc. 5-Bromo-2-iodobenzoic acid, 2-iodo-5-methylbenzoic acid and 2-iodo-4,5-dimethoxybenzoic acid were obtained from Trans World Chemicals, Inc.

Allenes. 1,2-Undecadiene, 4,5-nonadiene and 1,2-cyclotridecadiene were prepared by treating the corresponding 1,1-dibromocyclopropanes with methyllithium according to a literature procedure.[27] The appropriate 1,1-dibromocyclopropanes were prepared from the corresponding alkenes using a literature procedure.[28]

***N*-Tosyl-2-iodoaniline.** Tosylation of 2-iodoaniline (25 mmol) was carried out by treating 2-iodoaniline with tosyl chloride (25 mmol) in pyridine (8 mL) and heating for 3 h at 80 °C.[29] The product was purified by recrystallization from ethanol, followed by washing several times with hexanes: ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3 H), 6.95 (ddd, 1 H, J = 7.5, 7.5, 1.5 Hz), 7.34 (d, 2 H, J = 7.8 Hz), 7.37 (ddd, 1 H, J = 8.1, 7.5, 1.5 Hz), 7.47 (dd, 1 H, J = 8.1, 1.5 Hz), 7.65 (d, 2 H, J = 8.1 Hz), 7.79 (dd, 1 H, J = 8.1, 1.5 Hz), 8.0 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 122.4, 126.8, 127.4, 129.4, 129.6, 135.8, 137.4, 139.1, 144.2 (one sp^2 signal missing due to overlap); IR ($CHCl_3$) 3300, 2950, 1285, 1233 cm^{-1}. Anal. calcd for $C_{13}H_{12}INO_2S$: C, 41.82: H, 3.22 Found: C, 41.77; H, 3.47.

5-Bromo-2-iodobenzyl alcohol. Prepared in 55 % yield by borane reduction of the corresponding benzoic acid following a literature procedure:[30] ^{1}H NMR ($CDCl_3$) δ 2.25 (bs, 1 H), 4.62 (s, 2 H), 7.13 (dd, 1 H, J = 8.1, 2.1 Hz), 7.61 (d, 1 H, J = 2.1 Hz), 7.64 (d, 1 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 68.7, 94.6, 123.0, 131.1, 132.2, 140.3, 144.6; IR ($CHCl_3$) 3250, 1111, 733, 479 cm^{-1}.

2-Iodo-5-methylbenzyl alcohol. Prepared in 83 % yield by borane reduction of the corresponding benzoic acid following a literature procedure:[30] ^{1}H NMR ($CDCl_3$) δ 2.02 (bs, 1 H), 2.26 (s, 3 H), 4.58 (s, 2 H), 6.76 (dd, 1 H, J = 8.1, 1.5 Hz), 7.21 (d, 1 H, J = 1.5 Hz), 7.61 (d, 1 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.0, 69.1, 93.3, 129.3, 130.2, 138.5, 138.8, 142.2; IR ($CHCl_3$) 3230, 1232, 482 cm^{-1}.

Diethyl 2-iodophenylmalonate. Prepared by treatment of ethyl 2-iodophenylacetate with NaH and diethyl carbonate according to a literature procedure:[31] ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 6 H, J = 7.2 Hz), 4.25 (dq, 4 H, J = 7.2, 1.5 Hz), 5.12 (s, 1 H), 7.01 (dt, 1 H, J = 7.8, 1.5 Hz), 7.37 (dq, 1 H, J = 7.8, 1.2 Hz), 7.47 (dd, 1 H, J = 7.8, 1.5 Hz), 7.87 (dd, 1 H, J = 7.8, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 29.4, 62.0, 101.6, 128.5, 129.6, 129.7, 136.4, 139.6, 167.7; IR (neat) 2955, 2924, 1736, 1217, 1175, 1030 cm^{-1}; HRMS for $C_{13}H_{15}IO_4$: calcd 362.0015, found 362.0013.

***Z*-3-Iodo-2-methylpropen-1-ol.** Prepared in 42 % yield from propargyl alcohol by treating with MeMgI and CuI in THF/Et_2O and subsequent addition of I_2 according to a literature procedure:[32] ^{1}H NMR ($CDCl_3$) δ 1.80 (t, 1 H, J = 6.3 Hz), 1.98 (s, 3 H), 4.24 (d, 2 H, J = 6.3 Hz), 5.98 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.5, 67.6, 74.7, 145.8; IR (neat) 3354, 2919, 1436, 1134, 489 cm^{-1}.

***Z*-3-Iodo-2-methylpropenoic acid.** Prepared from *Z*-3-iodo-methylpropen-1-ol by first oxidizing with PCC to give *Z*-3-iodo-2-methylpropenal. This compound was not characterized due to its rapid decomposition. *Z*-3-Iodo-2-methylpropenal was immediately converted to the acid by $NaClO_2/H_2O_2$ mediated oxidation according to a literature procedure:[33] ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 3 H), 7.10 (s, 1 H), 11.3 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.46, 86.67, 137.6, 172.0; IR ($CHCl_3$) 2980, 1693, 1593, 492 cm^{-1}.

General Procedure for the Enantioselective, Palladium-catalyzed Annulation of Allenes. To a 1 dram vial is added the palladium reagent (0.019 mmol), the appropriate organic iodide (0.375 mmol), Ag_3PO_4 (0.150 mmol), the appropriate allene (0.750 mmol) and 0.75 mL of a DMF/chiral ligand stock solution containing the desired amount of bisoxazoline ligand **1** (0.019 or 0.038 mmol). The vial is then flushed with N_2, capped with a screw cap containing a teflon liner, and placed in an oil bath at the desired temperature for the specified period of time (see Table 1). The vial was then removed from the oil bath and the reaction mixture columned directly on silica gel using hexanes/EtOAc as eluents. Determination of the enantiomeric excess of the products was accomplished using the chiral NMR shift reagent Eu(hfc)$_3$. Optical rotations were determined using a Jasco DIP-370 digital polarimeter.

Spectral Data

***N*-Tosyl-2,3-dihydro-3-methylene-2-*n*-octylindole** (Table 3, entry 1). Obtained as a pale yellow oil in 94 % yield from the reaction of *N*-tosyl-2-iodoaniline and 1,2-undecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -19.4°, C = 0.040, dichloroethane [82 % ee, based on integration of two aromatic peaks corresponding to H-7 and Ts in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.86 (t, 3 H, J = 6.9 Hz), 1.1-1.5 (m, 12 H), 1.70-1.85 (m, 1 H), 1.95-2.15 (m, 1 H), 2.32 (s, 3 H), 4.55-4.67 (m, 1 H), 4.85 (d, 1 H, J = 2.0 Hz), 5.34 (d, 1 H, J = 2.0 Hz), 7.03 (ddd, 1 H, J = 7.5, 7.5, 0.6 Hz), 7.13 (d, 2 H, J = 8.1 Hz), 7.27 (t, 1 H, J = 7.8 Hz), 7.29 (d, 1 H, J = 7.8 Hz), 7.53 (d, 2 H, J = 8.1 Hz), 7.74, (d, 1 H, J = 7.8 Hz). The other spectral properties match those previously reported.[8]

(*E*)-*N*-Tosyl-3-*n*-butylidene-2,3-dihydro-2-*n*-propylindole (Table 3, entry 2). Obtained as a clear, colorless oil in 95 % yield from the reaction of *N*-tosyl-2-iodoaniline and 4,5-nonadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -32.5°, C = 0.045, dichloroethane [80 % ee, based on integration of two aromatic peaks corresponding to H-7 and Ts in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.84 (t, 3 H, J = 7.5 Hz), 0.89 (t, 3 H, J = 7.5 Hz), 1.31-1.45 (m, 4 H), 1.60-1.74 (m, 1 H), 1.78-1.92 (m, 1 H), 2.21-2.27 (m, 2 H), 2.30 (s, 3 H) 4.53 (td, 1 H, J = 5.4, 1.5 Hz), 5.28 (td, 1 H, J = 7.4, 1.5 Hz), 7.04 (td, 1 H, J = 7.7, 0.9 Hz), 7.10 (d, 2 H, J = 8.4 Hz), 7.22 (td, 1 H, J = 7.5, 0.9 Hz), 7.38 (d, 1 H, J = 7.5 Hz), 7.47 (d, 2 H, J = 8.4 Hz), 7.72 (d, 1 H, J = 8.1 Hz); ^{13}C NMR (CDCl$_3$) δ 13.6, 14.0, 16.8, 21.4, 22.6, 30.0, 40.2, 67.4, 117.6, 124.5, 127.0, 128.5, 129.3, 130.9, 134.6, 143.5, 144.2 (three sp^2 signals missing due to overlap);

IR (neat) 3060, 3030, 2950, 2920, 2860, 1592, 1490, 1450, 1353, 1168 cm^{-1}; HRMS for $C_{22}H_{27}NO_2S$: calcd 369.1763, found 369.1766. Anal. Calcd for $C_{22}H_{27}NO_2S$: C, 71.51; H, 7.37. Found: C, 70.02; H, 7.40.

(*E*)-5-Tosyl-5,5a,6,7,8,9,10,11,12,13,14,15-undecahydrocyclotridec[*b*]indole (Table 3, entry 3). Obtained as a white solid in 95 % yield from the reaction of *N*-tosyl-2-iodoaniline and 1,2-cyclotridecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: mp 144-147 °C; $[\alpha]_D$ = -37.0° [81 % ee, based on integration of two aromatic peaks corresponding to H-7 and Ts in the presence of Eu(hfc)$_3$]; ^{1}H NMR ($CDCl_3$) δ 1.0-1.35 (m, 16 H), 1.63-1.77 (m, 2 H), 2.08-2.23 (m, 1 H), 2.27 (s, 3 H), 2.52-2.68 (m, 1 H), 4.63 (m, 1 H), 5.37 (dd, 1 H, *J* = 10.4, 5.1 Hz), 6.99 (t, 1 H, *J* = 8.0 Hz), 7.10 (d, 2 H, *J* = 8.1 Hz), 7.19 (t, 1 H, *J* = 8.0 Hz), 7.51 (d, 1 H, *J* = 8.0 Hz), 7.56 (d, 2 H, *J* = 8.1 Hz), 7.76 (d, 1 H, *J* = 8.0 Hz). The other spectral properties match those previously reported.[8]

5-Acetyl-2,3-dihydro-3-methylene-2-*n*-octylbenzofuran (Table 3, entry 4). Obtained as a pale yellow oil in 95 % yield from the reaction of 2-iodo-4-acetylphenol and 1,2-undecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -61.2° (52 % ee, chiral HPLC), *C* = 0.30, chloroform; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3 H, *J* = 6.0 Hz), 1.20-1.60 (m, 12 H), 1.70-1.90 (m, 2 H), 2.57 (s, 3 H), 4.98 (d, 1 H, *J* = 3.0 Hz), 5.25 (m, 1 H), 5.54 (d, 1 H, *J* = 3.0 Hz), 6.84 (d, 1 H, *J* = 9.0 Hz), 7.86 (dd, 1 H, *J* = 9.0, 2.1 Hz), 8.01 (d, 1 H, *J* = 2.1 Hz). The other spectral properties match those previously reported.[8]

3,4-Dihydro-4-methylene-3-*n*-octyl-1*H*-2-benzopyran (Table 3, entry 5). Obtained as a clear, colorless oil in 72 % yield from the reaction of 2-iodobenzyl alcohol and 1,2-undecadiene after purification by column chromatography using 30:1 hexanes/EtOAc: $[\alpha]_D$ = -15.6°, *C* = 0.30, dichloroethane [73 % ee, based on integration of the methylene hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H, *J* = 7.0 Hz), 1.20-1.40 (m, 12

H), 1.70-1.80 (m, 2 H), 4.27 (dd, 1 H, J = 7.2, 6.6 Hz), 4.71 (d, 1 H, J = 15.3 Hz), 4.82 (d, 1 H, J = 15.3 Hz), 5.02 (s, 1 H), 5.59 (s, 1 H), 6.98-7.03 (m, 1 H), 7.18-7.24 (m, 2 H), 7.61-7.65 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.7, 25.6, 29.3, 29.5, 29.6, 31.9, 65.7, 77.2, 106.9, 123.9, 124.3, 126.8, 127.6, 131.6, 134.4, 142.0 (one sp^3 carbon missing due to overlap); IR (neat) 2926, 2854, 1634, 1103 cm^{-1}; HRMS for $C_{18}H_{26}O$: calcd 258.1984, found 258.1980.

3,4-Dihydro-7-methyl-4-methylene-3-*n*-octyl-1*H*-2-benzopyran (Table 3, entry 6). Obtained as a clear, colorless oil in 56 % yield from the reaction of 2-iodo-5-methylbenzyl alcohol and 1,2-undecadiene after purification by column chromatography using 30:1 hexanes/EtOAc: $[\alpha]_D$ = -17.1°, C = 0.026, EtOAc [67 % ee, based on integration of the methylene hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, 3 H, J = 6.9 Hz), 1.20-1.60 (m, 12 H), 1.70-1.80 (m, 2 H), 2.32 (s, 3 H), 4.25 (dd, 1 H, J = 7.5, 6.3 Hz), 4.64 (d, 1 H, J = 15.0 Hz), 4.72 (d, 1 H, J = 15.0 Hz), 4.97 (d, 1 H, J = 1.2 Hz), 5.54 (s, 1 H), 6.83 (s, 1 H), 7.03 (d, 1 H, J = 8.4 Hz), 7.53 (d, 1 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.6, 21.7, 23.2, 26.1, 29.8, 30.1, 30.1, 32.4, 33.0, 66.1, 77.8, 106.3, 124.3, 125.2, 128.3, 129.3, 134.8, 138.0, 142.4; IR (neat) 2923, 2853, 1635, 1615, 1106 cm^{-1}; HRMS for $C_{19}H_{28}O$: calcd 272.2140, found 272.2138.

7-Bromo-3,4-dihydro-4-methylene-3-*n*-octyl-1*H*-2-benzopyran (Table 3, entry 7). Obtained as a clear, colorless oil in 64 % yield from the reaction of 5-bromo-2-iodobenzyl alcohol and 1,2-undecadiene after purification by column chromatography using 30:1 hexanes/EtOAc: $[\alpha]_D$ = -8.7°, C = 0.034, EtOAc [67 % ee, based on integration of the methylene hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 6.9 Hz), 1.22-1.59 (m, 12 H), 1.69-1.78 (m, 2 H), 4.25 (t, 1 H, J = 6.6 Hz), 4.60 (d, 1 H, J = 15.3 Hz), 4.68 (d, 1 H, J = 15.3 Hz), 5.05 (s, 1 H), 5.58 (s, 1 H), 7.17 (d, 1 H, J = 1.2), 7.32 (dd, 1 H, J = 8.4, 1.8 Hz), 7.48 (d, 1 H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2, 22.7, 25.5, 29.3, 29.6, 31.9, 32.5, 65.2, 77.2, 107.5, 121.6, 125.7, 127.3, 130.1, 130.7, 136.4, 141.2 (one sp^3 carbon missing due to overlap); IR (neat) 2925, 2853, 1634, 1591, 1111 cm^{-1}; HRMS for $C_{18}H_{25}BrO$: calcd 336.1089, found 336.1091.

(*E*)- 4-*n*-Butylidene-3,4-dihydro-3-*n*-propyl-1*H*-2-benzopyran (Table 3, entry 8). Obtained as a clear, colorless oil in 73 % yield from the reaction of 2-iodobenzyl alcohol and 4,5-nonadiene after purification by column chromatography using 30:1 hexanes/EtOAc: $[\alpha]_D = -71.6°$, $C = 0.030$, dichloroethane [55 % ee, based on integration of the vinylic hydrogen in the presence of $Eu(hfc)_3$]; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 7.8 Hz), 0.95 (t, 3 H, J = 7.8 Hz), 1.30-1.65 (m, 6 H), 2.36 (dq, 2 H, J = 7.5, 2.1 Hz), 4.28 (dd, 1 H, J = 6.9, 5.7 Hz), 4.64 (d, 1 H, J = 14.7 Hz), 4.70 (d, 1 H, J = 14.7 Hz), 5.51 (t, 1 H, J = 6.9), 7.06 (dd, 1 H, J = 6.9, 1.5 Hz), 7.18-7.28 (m, 2 H), 7.41 (dd, 1 H, J = 6.9, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 14.1, 19.0, 23.5, 31.0, 36.3, 65.4, 79.4, 124.2, 126.3, 126.8, 127.9, 128.1, 132.6, 133.7, 136.3; IR (neat) 3019, 2958, 2930, 2870, 1082 cm^{-1}; HRMS for $C_{16}H_{22}O$: calcd 230.1671, found 230.1672.

(*E*)-5,6a,7,8,9,10,11,12,13,14,15,16-Dodecahydrobenzo[d]cyclotrideca[b]pyran (Table 3, entry 9). Obtained as a clear, colorless oil in 29 % yield along with a trace of an unknown impurity from the reaction of 2-iodobenzyl alcohol and 1,2-cyclotridecadiene after purification using 30:1 hexanes/EtOAc: $[\alpha]_D = -148.9°$, $C = 0.017$, dichloroethane [77 % ee, based on integration of the vinylic hydrogen in the presence of $Eu(hfc)_3$]; ^1H NMR ($CDCl_3$) δ 1.20-1.60 (m, 16 H), 1.62-1.75 (m, 2 H), 2.10-2.25 (m, 1 H), 2.55-2.70 (m, 1 H), 4.38 (dd, 1 H, J = 8.7, 3.6 Hz), 4.60 (d, 1 H, J = 14.1 Hz), 4.68 (d, 1 H, J = 14.1 Hz), 5.64 (dd, 1 H, J = 11.1, 5.1 Hz), 7.09 (d, 1 H, J = 6.3 Hz), 7.19-7.30 (m, 2 H), 7.53 (d, 1 H , J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 22.4, 24.6, 24.8, 25.3, 26.0, 26.1, 27.3, 27.8, 28.7, 33.1, 66.1, 80.1, 124.5, 126.6, 126.7, 127.2, 129.4, 132.6, 133.1, 136.8; IR (neat) 3063, 2930, 2857, 1458, 1081 cm^{-1}; HRMS for $C_{20}H_{28}O$: calcd 284.2140, found 284.2138.

(*S*)-(*E*)-3-Bromo-5,6a,7,8,9,10,11,12,13,14,15,16-dodecahydrobenzo[d]cyclotrideca[b]pyran (Table 3, entry 10). Obtained as a pale yellow oil in 33 % yield along with a trace of an unknown impurity from the reaction of 5-bromo-2-iodobenzyl alcohol and 1,2-cyclotridecadiene after purification using 30:1 hexanes/EtOAc: $[\alpha]_D$ = -118.0°, C = 0.021, $CDCl_3$. This oil was crystallized from hexane to give white needles: $[\alpha]_D$ = - 211.0°, C = 0.008, $CDCl_3$ [>95 % ee, no resolution of the vinylic hydrogen was observed in the presence of $Eu(hfc)_3$]; ^1H NMR δ 1.2-1.6 (m, 16 H), 1.62-1.80 (m, 2 H), 2.12-2.25 (m, 1 H), 2.48-2.62 (m, 1 H), 4.35 (dd, 1 H, J = 8.4, 3.3 Hz), 4.56 (d, 1 H, J = 14.7 Hz), 4.64 (d, 1 H, J = 14.7 Hz), (5.64 (ddd, 1 H, J = 10.8, 5.1, 0.3 Hz), 7.26 (s, 1 H), 7.39 (d, 2 H, J = 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 22.2, 24.6, 24.8, 25.3, 25.9, 26.1, 27.2, 27.8, 28.6, 32.9, 65.5, 80.0, 120.6, 127.6, 128.9, 129.8, 130.1, 131.6, 132.3, 138.9; IR ($CHCl_3$) 2932, 2858, 1478, 1465 cm^{-1}; HRMS for $C_{20}H_{27}OBr^{79}$: calcd 362.1245, found 362.1245; $C_{20}H_{27}OBr^{81}$: calcd 364.1226, found 364.1223.

4-Methylene-3-*n*-octyl-1-isochromanone (Table 3, entry 11). Obtained as a clear, colorless oil in 50 % yield from the reaction of 2-iodobenzoic acid and 1,2-undecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -79.5°, C = 0.068, dichloroethane [67 % ee, based on integration of aromatic H-8 in the presence of $Eu(hfc)_3$]; ^1H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 6.9 Hz), 1.20-1.55 (m, 12 H), 1.60-1.75 (m, 1 H), 1.80-2.00 (m, 1 H), 5.00 (t, 1 H, J = 7.2 Hz), 5.33 (s, 1 H), 5.71 (s, 1 H), 7.42-7.48 (dq, 1 H, J = 8.1, 2.4 Hz), 7.57-7.61 (m, 2 H), 8.11 (d, 1 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 25.2, 29.1, 29.3, 31.7, 34.6, 81.9, 113.3, 123.5, 123.8, 129.0, 129.9, 133.9, 136.2, 138.6, 164.1 (one sp^3 signal missing due to overlap); IR ($CHCl_3$) 2952, 2854, 1720, 1114 cm^{-1}; HRMS for $C_{18}H_{24}O_2$: calcd 272.1776, found, 272.1771.

7-Methyl-4-methylene-3-*n*-octyl-1-isochromanone (Table 3, entry 12). Obtained as a clear, colorless oil in 69 % yield from the reaction of 2-iodo-5-methylbenzoic acid and 1,2-undecadiene after purification by column chromatography using 10:1

hexanes/EtOAc: $[\alpha]_D$ = -70.7°, C = 0.033, dichloroethane [63 % ee, based on integration of aromatic H-8 in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.87 (t, 3 H, J = 6.6 Hz), 1.20-1.55 (m, 12 H), 1.66 (m, 1 H), 1.92 (m, 1 H), 2.43 (s, 3 H), 4.99 (t, 1 H, J = 6.9 Hz), 5.28 (s, 1 H), 5.66 (s, 1 H), 7.42 (dd, 1 H, J = 8.1, 0.9 Hz), 7.49 (d, 1 H, J = 8.1 Hz), 7.94 (s, 1 H); ^{13}C NMR (CDCl$_3$) δ 14.1, 21.2, 22.6, 25.3, 29.2, 29.3, 29.4, 31.8, 34.8, 82.1, 112.4, 123.3, 123.8, 130.2, 133.6, 134.9, 138.6, 139.3, 164.5; IR (CHCl$_3$) 2960, 2856, 1715, 1183 cm^{-1}; HRMS for $C_{19}H_{26}O_2$: calcd 286.1933, found 286.1939.

6,7-Dimethoxy-4-methylene-3-*n*-octyl-1-isochromanone (Table 3, entry 13). Obtained as a clear, colorless oil in 78 % yield from the reaction of 2-iodo-4,5-dimethoxybenzoic acid and 1,2-undecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -52.6°, C = 0.027, dichloroethane [71 % ee, based on integration of the methylene hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.87 (t, 3 H, J = 6.9 Hz), 1.20-1.55 (m, 12 H), 1.60-1.75 (m, 1 H), 1.85-1.95 (m, 1 H), 3.95 (s, 3 H), 4.00 (s, 3 H), 4.98 (t, 1 H, J = 6.9 Hz)), 5.25 (s, 1 H), 5.59 (s, 1 H), 6.97 (s, 1 H), 7.55 (s, 1 H); ^{13}C NMR (CDCl$_3$) δ 14.1, 22.7, 25.4, 29.2, 29.4, 31.9, 35.0, 56.2, 56.3, 82.2, 105.3, 111.2, 111.6, 116.4, 130.7, 138.8, 150.0, 154.0, 164.3 (one sp^3 signal missing due to overlap); IR (neat) 2925, 2854, 1714, 1653, 1140, 1061 cm^{-1}; HRMS for $C_{20}H_{28}O_4$: calcd 332.1988, found 332.1997.

7-Bromo-4-methylene-3-*n*-octyl-1-isochromanone (Table 3, entry 14). Obtained as a clear, colorless oil in 67 % yield from the reaction of 5-bromo-2-iodobenzoic acid and 1,2-undecadiene after purification by column chromatography using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -47.1°, C = 0.024, dichoroethane [48 % ee, based on integration of aromatic H-8 in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.87 (t, 3 H, J = 6.9 Hz), 1.15-1.45 (m, 12 H), 1.60-1.70 (m, 1 H), 1.80-1.95 (m, 1 H), 5.00 (t, 1 H, J = 6.9 Hz), 5.37 (s, 1 H), 5.72 (s, 1 H), 7.46 (d, 1 H, J = 8.4 Hz), 7.72 (dd, 1 H, J = 8.4, 2.1 Hz), 8.25 (d, 1 H, J = 2.1 Hz); ^{13}C NMR (CDCl$_3$) δ 14.1, 22.6, 25.3, 29.1, 29.3, 31.8, 34.7, 82.0, 114.1, 123.1, 125.1, 125.7, 132.8, 135.0, 137.0, 137.8, 162.9 (one sp^3 signal missing due to overlap); IR ($CHCl_3$) 2960, 2850, 1710, 1150 cm^{-1}; HRMS for $C_{18}H_{23}BrO_2$: calcd 350.0881, found 350.0890.

5,6-Dihydro-3-methyl-5-methylene-6-*n*-octyl-2*H*-pyran-2-one (Table 3, entry 15). Obtained as a clear, colorless oil in 41 % yield from the reaction of (*Z*)-3-iodo-2-methyl-2-propenoic acid and 1,2-undecadiene after purification using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -93.5°, C = 0.014, dichloroethane [80 % ee, based on integration of the methyl hydrogens in the presence of $Eu(hfc)_3$]; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 6.6 Hz), 1.22-1.55 (m, 12 H), 1.66-1.79 (m, 1 H), 1.80-1.93 (m, 1 H), 1.99 (s, 3 H), 4.99 (dd, 1 H, J = 8.1, 5.7 Hz), 5.13 (s, 1 H), 5.22 (s, 1 H), 6.77 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.1, 17.1, 22.7, 24.8, 29.3, 29.5, 31.9, 36.1, 80.8, 115.9, 127.2, 138.7, 139.5, 164.7 (one sp^3 carbon missing due to overlap); IR (neat) 2926, 2856, 1716, 1655, 1110 cm^{-1}; HRMS for $C_{15}H_{24}O_2$: calcd 236.1776, found 236.1770.

(*E*)- 5-*n*-Butylidene-5,6-dihydro-3-methyl-6-*n*-propyl-2*H*-pyran-2-one (Table 3, entry 16). Obtained as a clear, colorless oil in 59 % yield (96:4 *E/Z*) from the reaction of (*Z*)-3-iodo-2-methyl-2-propenoic acid and 4,5-nonadiene after purification using 10:1 hexanes/EtOAc: $[\alpha]_D$ = -97.5°, C = 0.027, dichloroethane [46 % ee, based on integration of the methyl hydrogens in the presence of $Eu(hfc)_3$]; ^{1}H NMR ($CDCl_3$) δ 0.93 (t, 3 H, J = 6.9 Hz), 0.94 (t, 3 H, J = 7.2 Hz), 1.30-1.52 (m, 4 H), 1.58-1.72 (m, 1 H), 1.78-1.90 (m, 1 H), 2.00 (s, 3 H), 2.19 (qt, 2 H, J = 7.5 Hz), 4.84 (t, 1 H, J = 6.9 Hz), 5.55 (t, 1 H, J = 7.8 Hz), 7.03 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.7, 13.9, 17.5, 18.4, 22.6, 29.4, 38.1, 81.9, 126.1, 130.4, 132.3, 133.7, 165.3; IR (neat) 2959, 2872, 1714, 1647, 1463, 1105 cm^{-1}; HRMS for $C_{13}H_{20}O_2$: calcd 208.1463, found 208.1467.

(*E*)-2,6,7,8,9,10,11,12,13,14,15,15a-Undecahydro-3-methylcyclotrideca[*b*]pyran-2-one (Table 3, entry 17). Obtained as a clear, colorless oil in 52 % yield (98:2 *E/Z*) from the reaction of (*Z*)-3-iodo-2-methyl-2-propenoic acid and

1,2-cyclotridecadiene after purification using 10:1 hexanes/EtOAc: $[\alpha]_D = -202.6°$, $C = 0.022$, dichloroethane [61 % ee, based on integration of the methyl hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 1.18–1.66 (m, 16 H), 1.80 (qt, 2 H, J = 6.3 Hz), 2.01 (s, 3 H), 2.07-2.22 (m, 1 H), 2.28-2.42 (m, 1 H), 4.91 (t, 1 H, J = 5.1 Hz), 5.56 (dd, 1 H, J = 11.1, 6.0 Hz), 7.02 (s, 1 H); ^{13}C NMR (CDCl$_3$) δ 17.6, 21.4, 24.7, 24.8, 26.2, 26.4, 26.6, 28.0, 35.5, 82.4, 126.2, 130.0, 133.3, 133.6, 165.1 (two sp^3 carbons missing due to overlap); IR (neat) 2929, 2858, 1714, 1645, 1614, 1449, 1125 cm^{-1}; HRMS for $C_{17}H_{26}O_2$: calcd 262.1933, found 262.1932.

5,6-Dihydro-3-methyl-5-methylene-6-*n*-octyl-2*H*-pyran (Table 3, entry 18). Obtained as a clear, colorless oil in 70 % yield from the reaction of (*Z*)-3-iodo-2-methyl-2-propen-1-ol and 1,2-undecadiene after purification using 30:1 hexanes/EtOAc: $[\alpha]_D = -11.5°$, $C = 0.031$, dichloroethane 79 % ee, based on integration of the methyl hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.88 (t, 3 H, J = 6.9 Hz), 1.15-1.45 (m, 12 H), 1.45-1.55 (m, 1 H), 1.65-1.75 (m, 1 H), 1.71 (s, 3 H), 3.95-4.15 (m, 3 H), 4.72 (s, 1 H), 4.73 (s, 1 H), 5.97 (s, 1 H); ^{13}C NMR (CDCl$_3$) δ 14.3, 18.8, 22.7, 25.6, 29.4, 29.7, 29.7, 32.0, 32.1, 66.4, 75.4, 107.3, 122.4, 136.1, 142.9; IR (CHCl$_3$) 2958, 2929, 2870, 1653, 1616, 1102 cm^{-1}; HRMS for $C_{13}H_{22}O$: calcd 194.1471, found 194.1468.

5,6-Dihydro-2,2-dimethyl-5-methylene-6-*n*-octyl-2*H*-pyran (Table 3, entry 20). Obtained as a clear, colorless oil in 62 % yield from the reaction of (*Z*)-4-iodo-2-methyl-3-buten-2-ol and 1,2-undecadiene after purification using 30:1 hexanes/EtOAc: $[\alpha]_D = +46.0°$, $C = 0.036$, CHCl$_3$ (ee undetermined); ^{1}H NMR (CDCl$_3$) δ 0.88 (t, 3 H, J = 7.2 Hz), 1.20-1.45 (m, 18 H), 1.50-1.70 (m, 1 H), 1.75-1.90 (m, 1 H), 4.22 (m, 1 H), 4.83 (d, 2 H, J = 9.6 Hz), 5.69 (d, 1 H, J = 9.9 Hz), 6.07 (d, 1 H, J = 9.9 Hz); ^{13}C NMR (CDCl$_3$) δ 14.2, 22.7, 24.6, 25.4, 29.4, 29.6, 29.7, 29.7, 31.9, 32.0, 69.6, 72.3, 108.7, 125.5, 136.6, 143.0; IR (neat) 3090, 3028, 2925, 2854, 1603, 1177, 1089 cm^{-1}; HRMS for $C_{16}H_{28}O$: calcd 236.2140, found 236.2139.

Diethyl 3-methylene-2-*n*-octyl-1,1-indanedicarboxylate (Table 3, entry 21). Obtained as a pale yellow oil in 67 % yield from the reaction of diethyl 2-iodophenylmalonate and 1,2-undecadiene after purification using 10:1 hexanes/EtOAc: $[\alpha]_D = 48.8°$, $C = 0.29$, dichloroethane [75 % ee, based on integration of the methylene hydrogens in the presence of Eu(hfc)$_3$]; ^{1}H NMR (CDCl$_3$) δ 0.87 (t, 3 H, $J = 6.9$ Hz), 1.22 (t, 3 H, $J = 7.2$ Hz), 1.29 (t, 3 H, $J = 6.9$ Hz), 1.21-1.52 (m, 14 H), 3.62-3.72 (m, 1 H), 4.02-4.34 (m, 4 H), 5.11 (d, 1 H, $J = 1.2$ Hz), 5.52 (d, 1 H, $J = 1.8$ Hz), 7.25-7.33 (m, 2 H), 7.45-7.48 (m, 1 H), 7.59-7.63 (m, 1 H); ^{13}C NMR (CDCl$_3$) δ 14.0, 14.2, 14.2, 22.7, 27.1, 29.3, 29.5, 29.7, 30.4, 31.9, 50.8, 61.3, 61.7, 68.1, 105.0, 120.8, 127.4, 128.5, 128.8, 140.3, 140.8, 149.8, 169.3, 169.6; IR (neat) 2926, 2855, 1734, 1615, 1456, 1239, 1190 cm^{-1}; HRMS for $C_{24}H_{34}O_4$: calcd 386.2457, found 386.2448.

Diethyl 3-*n*-butylidene-2-*n*-propyl-1,1-indanedicarboxylate (Table 3, entry 22). Obtained as a pale yellow oil in 79 % yield (7:1 *Z*/*E*) from the reaction of diethyl 2-iodophenylmalonate and 4,5-nonadiene after purification using 10:1 hexanes/EtOAc: $[\alpha]_D = 28.0°$, $C = 0.037$, dichloroethane [47 % ee, based on integration of the vinylic hydrogen in the presence of Eu(hfc)$_3$]; ^{1}H NMR (***Z* isomer**) (CDCl$_3$) δ 0.86 (t, 3 H, $J = 6.9$ Hz), 0.98 (t, 3 H, $J = 7.2$ Hz), 1.19 (t, 3 H, $J = 7.2$ Hz), 1.29 (t, 3 H, $J = 6.9$ Hz), 1.15-1.50 (m, 4 H), 1.55 (qt, 2 H, $J = 7.2$ Hz), 2.36-2.47 (m, 2 H), 3.54 (dd, 1 H, $J = 8.4, 4.8$ Hz), 4.0-4.4 (m, 4 H), 5.59 (t, 1 H, $J = 7.5$ Hz), 7.21-7.33 (m, 2 H), 7.51 (d, 1 H, $J = 7.2$ Hz), 7.63 (dd, 1 H, $J = 6.9, 1.8$ Hz); ^{1}H NMR (***E* isomer**) (CDCl$_3$) δ 0.79 (t, 3 H, $J = 6.9$ Hz), 1.00 (t, 3 H, $J = 7.2$ Hz), 1.16 (t, 3 H, $J = 7.2$ Hz), 1.31 (t, 3 H, $J = 6.9$ Hz), 1.15-1.50 (m, 4 H), 1.51 (m, 2 H), 2.15-2.35 (m, 2 H), 3.92 (m, 1 H), 4.0-4.4 (m, 4 H), 5.93 (t, 1 H, $J = 7.5$ Hz), 7.21-7.33 (m, 2 H), 7.37 (dd, 1 H, $J = 6.6, 2.1$ Hz), 7.59 (dd, 1 H, $J = 7.2, 1.5$ Hz). The other spectral properties match those previously reported.[8]

Di-μ-chloro-di(η^3-5-phenyl-non-4-enyl)dipalladium(II) (8). Obtained as a 2 : 1 mixture of the *syn-syn* and *syn-anti* conformers from the reaction of 4,5-nonadiene,

Li_2PdCl_4 and PhHgCl in CH_3CN according to a literature procedure:[22] *(syn-syn)* ^{1}H NMR ($CDCl_3$) δ 0.78 (t, 6 H, *J* = 6.9 Hz), 1.20-1.40 (m, 4 H), 1.40-1.58 (m, 4 H), 3.73 (m, 2 H), 7.36-7.43 (m, 3 H), 7.63-7.65 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.0, 31.5, 81.7, 127.4, 127.8, 128.3, 130.0, 133.6; *(syn-anti)* ^{1}H NMR ($CDCl_3$) δ 0.78 (t, 3 H, *J* = 6.9 Hz), 0.99 (t, 3 H, *J* = 7.2 Hz), 1.20-1.40 (m, 2 H), 1.40-1.58 (m, 2 H), 1.58-1.70 (m, 2 H), 1.80-1.92 (m, 2 H), 3.73 (m, 2 H), 7.36-7.43 (m, 3 H), 7.63-7.65 (m, 2 H).

(η^3-5-Phenyl-non-4-enyl)palladium(II) trifluoromethanesulfonate (9). A 1 : 2 ratio of di-μ-chloro-di(η^3-5-phenyl-non-4-enyl)dipalladium(II) and AgOTf were stirred at 80 °C in CD_3CN for 0.25 h. The starting π-allylpalladium chloride dimer was a 1 : 1 ratio of *syn-anti* to *syn-syn* conformers. A white precipitate of AgCl was observed immediately upon mixing. ^{1}H NMR spectral analysis of an aliquot of the resultant solution indicated it was a 1.4 : 1 mixture of *syn-anti* and *syn-syn* conformers based on integration of the methyl peaks. For the two conformers all three *syn*-methyl groups are found at 0.78 ppm, while the *anti*-methyl group is found at 1.02 ppm. Spectral data for the product mixture: ^{1}H NMR (CD_3CN) δ ^{1}H NMR ($CDCl_3$) δ 0.78 (t, 9 H, *J* = 6.9 Hz), 1.02 (t, 3 H, *J* = 7.2 Hz), 1.27-1.54 (m, 12 H), 1.55-1.70 (m, 2 H), 1.80-1.90 (m, 2 H), 3.99 (m, 2 H), 7.44-7.49 (m, 5 H).

(η^3-5-Phenylnon-4-enyl)palladium(II) trifluoromethanesulfonate-ligand 2 (10). (η^3-5-Phenylnon-4-enyl)palladium(II) trifluoromethanesulfonate and **2** were stirred in CD_3CN at 80 °C for 16 h. The mixture was cooled to room temperature and an aliquot removed and analyzed by ^{1}H NMR spectroscopy. Determination of the ratio of *syn-anti* and *syn-syn* isomers was based upon integration of the methyl peaks. See Appendix 1 for a ^{1}H NMR spectrum of this complex.

(η^3-5-Phenylnon-4-enyl)palladium(II) trifluoromethanesulfonate-ligand 1. This complex was formed as described for the preparation of (η^3-5-phenylnon-4-enyl)palladium-**2**. The ^{1}H NMR spectral data was recorded at 65 °C to eliminate peak broadening. See Appendix 1 for a ^{1}H NMR spectrum of this complex.

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CHAPTER 2: ENANTIOSELECTIVE PALLADIUM-CATALYZED HETEROANNULATION OF 1,3-DIENES USING ORTHO-FUNCTIONALIZED ARYL IODIDES

A paper to be submitted to the *Journal of Organic Chemistry*

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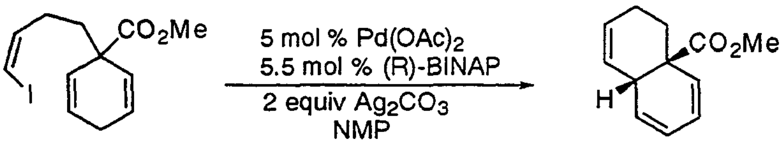
Abstract

Aryl iodides with a nucleophilic substituent in the ortho position react with 1,3-dienes in the presence of a palladium catalyst and a chiral ligand to afford five- and six-membered ring heterocycles in moderate enantiomeric excess. The enantioselective annulation of cyclic dienes occurs via an asymmetric arylpalladium addition, while acyclic dienes proceed by way of an asymmetric π-allylpalladium displacement.

Introduction

Since its discovery in the late 1960's, the Heck reaction has emerged as a powerful means of generating carbon-carbon bonds.[1] Though the scope and limitations of this methodology have been to a great extent determined, one of the major areas of current research is the development of conditions to carry out this type of reaction asymmetrically.

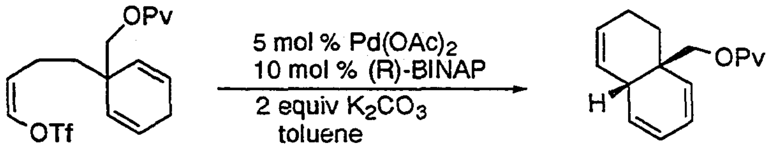
The first example of an asymmetric Heck reaction was reported by Shibasaki in 1989.[2] Using as a chiral ligand (R)-BINAP, he synthesized *cis*-decalin derivatives in up to 46 % enantiomeric excess (ee) by means of an intramolecular cyclization of prochiral alkenyl iodides (eq 1). In subsequent work this group extended the methodology to include the



74 % yield, 46 % ee

(1)

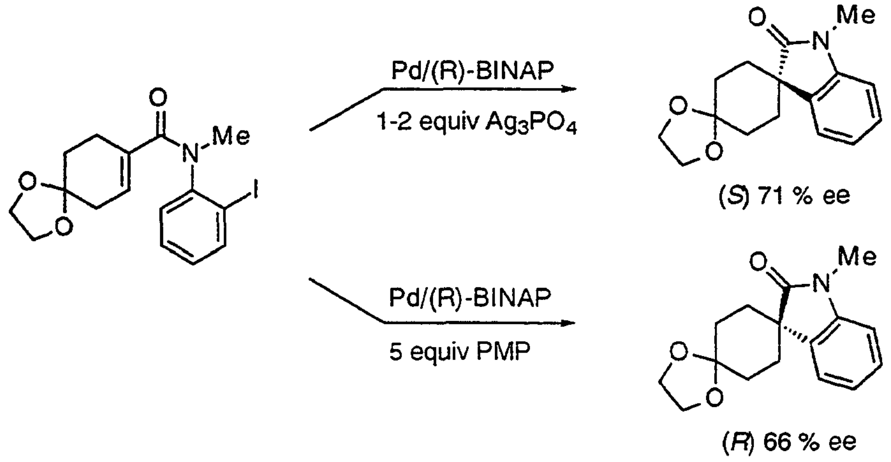
enantioselective synthesis of 5-membered rings,[3] and in competition studies showed the 6-exo ring closure occurs in preference to the 5-exo ring closure.[4] Shibasaki was also the first to systematically study the importance of Ag salts in the asymmetric addition of aryl and vinylic halides to double bonds,[5] and to note that utilization of vinylic triflates eliminated the need for the addition of Ag$^+$ to the system, giving the *cis*-decalin products in up to 91 % ee (eq 2).[6]



60 % yield, 91 % ee

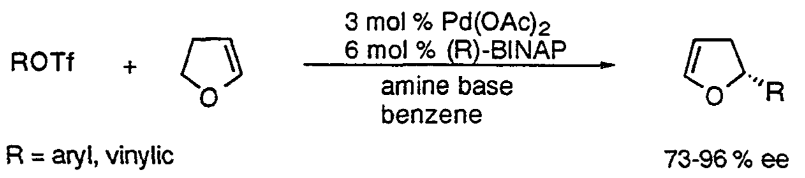
(2)

Overman reported in 1992 the asymmetric synthesis of spirocycles in good enantiomeric excess by the intramolecular cyclization of aryl iodides.[7] Using (R)-BINAP as the chiral ligand, aryl iodides could be cyclized, in the presence of Ag$_3$PO$_4$, to give the (*S*)-isomer in up to 71 % ee, while in the presence of the hindered amine base 1,2,2,6,6,-pentamethylpiperidine (PMP), the same aryl iodide gave the (*R*)-optical isomer in up to 66 % ee, even in the absence of Ag salts (eq 3).



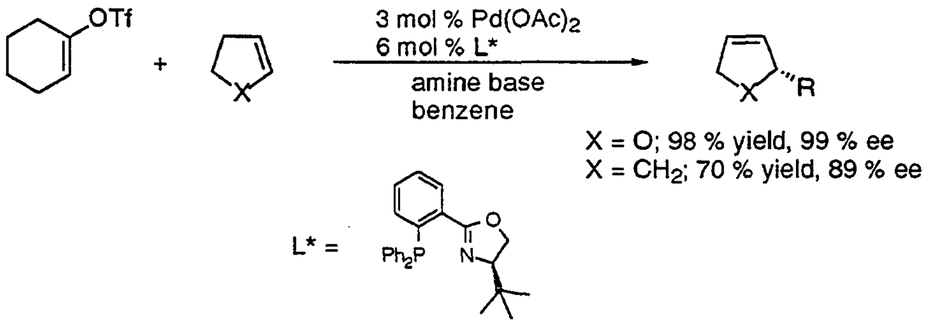
(3)

Hayashi and co-workers were the first to demonstrate an asymmetric intermolecular reaction of this type.[8] The palladium/(R)-BINAP-catalyzed addition of aryl or vinylic triflates to 2,3-dihydrofuran was achieved in 73 to 96 % ee (eq 4). The analogous reaction of aryl triflates with *N*-substituted 2-pyrrolines gave the 5-aryl-2-pyrrolines in 68 to 83 % ee.[9]



(4)

A recent report by Pfaltz and co-workers has demonstrated the use of phosphanyldihydrooxazoles in this same intermolecular reaction (eq 5).[10] In contrast to Hayashi's work, under Pfaltz's conditions double bond isomerization was not observed. The 2,5-dihydrofuran derivative was isolated exclusively. The low tendency of the (phosphanyldihydrooxazole)palladium catalyst to promote C=C double bond migration also allows the use of cyclopentene as a substrate, as shown in eq 5.



X = O; 98 % yield, 99 % ee
X = CH_2; 70 % yield, 89 % ee

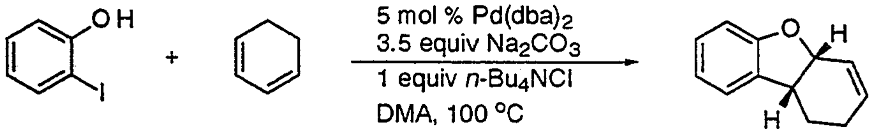
(5)

Continued research in this area has focused on the extension of this methodology to other systems[11] and its application to the total synthesis of natural products or to the synthesis of important precursors to biologically active molecules.[12] While these reports demonstrate the promise of this methodology, the full potential of this reaction in asymmetric synthesis has yet to be realized.

We recently reported that aryl halides with heteroatom-bearing functional groups in the ortho position react with 1,3-dienes in the presence of a palladium catalyst to afford oxygen- and nitrogen-containing heterocycles.[13] As an extension of these earlier results, and encouraged by Hayashi's success, we decided to examine asymmetric versions of these heteroannulations. Here we report the details of that study.

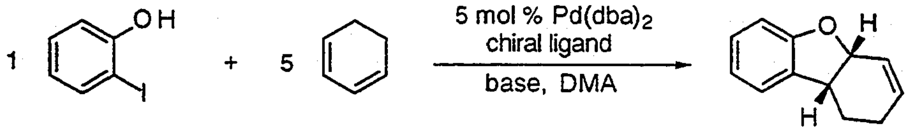
Results and Discussion

We chose as a model system for this study the reaction of 2-iodophenol and 1,3-cyclohexadiene. Previously, we reported that in the presence of 5 mol % $Pd(dba)_2$, 3.5 equiv of Na_2CO_3, and 1 equiv of n-Bu_4NCl (TBAC), using DMF as a solvent the desired tetrahydrodibenzofuran was obtained in 44 % yield (eq 6).[13] This reaction was chosen despite the moderate chemical yield, because it was felt that the relative rigidity of the 1,3-cyclohexadiene would aid the enantiodiscrimination process.



(6)

(R)-BINAP was used as the chiral ligand in the optimization work due to the success using this ligand in asymmetric Heck-type reactions described in the introduction (eq 7). Initial attempts to achieve asymmetric induction in this system involved the simple addition of a chiral diphosphine ligand to the earlier developed optimum conditions. Addition of 5 mol % of (R)-BINAP to the system afforded the desired product in 37 % yield, but determination of the enantiomeric excess of this product, using the chiral lanthanide shift reagent Eu(hfc)$_3$, revealed only a slight asymmetric induction of 4 % ee (Table 1, entry 1).



(7)

Recent reports in the literature have demonstrated the importance of the addition of silver salts to the reaction mixture in palladium-catalyzed enantioselective additions of aryl iodides.[5] It is thought that Ag$^+$ acts as a halide scavenger, precipitating iodide from the reaction mixture as AgI. This leads to the formation of a 16 electron, positively-charged organopalladium intermediate to which the bidentate chiral ligand is more strongly coordinated.[5a] Altering the reaction conditions to include a silver salt necessitated the removal of TBAC from the system, and when this was done the chemical yield of the reaction was dramatically reduced. Using 1 molar equiv of Ag$_3$PO$_4$ as the base, the product was obtained in only 12 % yield, but this addition did improve the enantioselectivity to 33 % ee (Table 1, entry 2). Due to this result, a variety of other silver salts were employed in this reaction, but without exception the chemical yields were lower than that obtained with Ag$_3$PO$_4$, often less than 10 %

(Table 1, entries 3-6). The small amount of product obtained made the determination of the enantiomeric excess nearly impossible. Since Overman and co-workers had reported relatively high asymmetric induction in the absence of silver salts using highly hindered organic amines as the base, PMP was tried in our model system (Table 1, entry 7).

Table 1. The Palladium-Catalyzed Reaction of 2-Iodophenol and 1,3-Cyclohexadiene in the Presence of a Chiral Ligand (eq 7).

entry	ligand (mol %)	base (equiv)	TBAC	temp. (°C)	time (d)	% yield	% ee
1	BINAP (5)	Na_2CO_3 (3.5)	+	100	1	37	4
2		Ag_3PO_4 (1.0)	-	100	1	20	33
3		Ag_2CO_3 (1.0)	-	100	1	<10	
4		AgOAc (1.0)	-	100	2	0	
5		Ag_2O (1.0)	-	100	2	<10	
6		AgOTf (2.0)	-	80	3	0	
7		PMP (1.0)	+	100	3	<10	
8		Ag_3PO_4 (2.0) PMP (1.0)	-	80	3	0	
9		Ag_3PO_4 (2.0) *i*-Pr_2NEt (1.0)	-	80	3	<10	
10		Ag_3PO_4 (2.0) Ph_3N (2.0)	-	80	3	23	38
11		Ag_3PO_4 (2.0) H^+ sp (1.0)[a]	-	80	3	7	
12		Ag_3PO_4 (1.0)	-	120	2	17	33
13		Ag_3PO_4 (1.0)	-	80	3	14	~33

Table 1 (continued)

14		Ag_3PO_4 (2.0)	-	80	3	19	46
15		Ag_3PO_4 (3.0)	-	80	3	12	44
16		Ag_3PO_4 (0.4)	-	80	3	21	56
17		Ag_3PO_4 (1.0)	-	60	5	<10	
18	BINAP (10)	Ag_3PO_4 (2.0)	-	100	2	<10	
19	BINAP (2.5)	Ag_3PO_4 (2.0)	-	80	3	16	~35
20[b]	MeO-BIPHEP (5)	Ag_3PO_4 (0.4)	-	80	3	20	55

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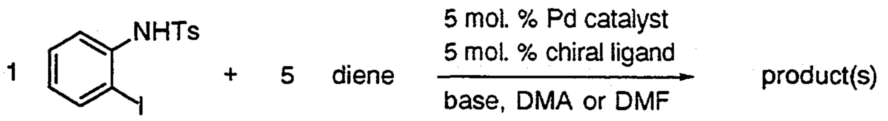
[a] H^+sp is *N,N,N,N*-tetramethyl-1,8-diaminonaphthalene (proton sponge).
[b] DMF used as the solvent.

In general, only low asymmetric induction could be achieve without the addition of a silver ion source. When a Ag^+ source was used in tandem with an organic amine (Table 1, entries 8-11), ee's were found to be slightly higher than those with Ag^+ alone.

The reaction temperature and the stoichiometry of the silver salt were investigated as variables in the model system (Table 1, entries 12-16)). The reaction run in the presence of 2 molar equiv of Ag_3PO_4 at 80 °C for 3 days gave the optimum results with a product yield of 19 % and a 46 % ee (entry 14). During the course of this optimization work, it was observed that in some cases a silver mirror was found on the reaction vial. A redox reaction between Ag^+ and Pd(0) could explain this reduction to Ag(0) which would thus hinder palladium catalysis. For this reason, the amount of Ag_3PO_4 was reduced to 0.4 molar equiv (1.2 ion equiv) and in this case the product was obtained in a slightly higher 21 % yield and 56 % ee (Table 1, entry 16).

The chiral ligand was also investigated as a variable in this reaction. Increasing the amount of (R)-BINAP to 10 mol % actually lowered the yield of the desired product to the extent that no determination of ee was carried out (Table 1, entry 18). Reducing the amount of the chiral ligand to 2.5 mol % afforded the product in 16 % yield and approximately 35 % ee (entry 19). MeO-BIPHEP, a chiral (diphenylphosphino)biphenyl ligand with methoxy substituents in the 6- and 6'-positions,[14] was employed in this reaction. Although a significantly more electron-rich ligand, this ligand gave results nearly identical to those obtained with BINAP (Table 1, entry 20).

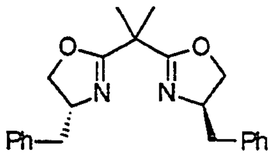
With work on this system at a standstill, the reaction of *N*-tosyl-2-iodoaniline and 1,3-cyclohexadiene was investigated. Again, upon addition of a diphosphine chiral ligand, the chemical yields were reduced significantly from an 88 % yield under our earlier conditions[13] to a 13 % yield (eq 8) (Table 2, entries 1-6). Using our optimum conditions for enantioselective



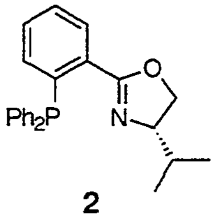
(8)

synthesis developed for the reaction of 2-iodophenol and 1,3-cyclohexadiene, the product was obtained in only a very low yield and determination of the ee was hindered by baseline distortions leading to inconsistencies from one peak integration to another. The values for the ee, determined by integration of several different peaks, ranged from 30-77 %.

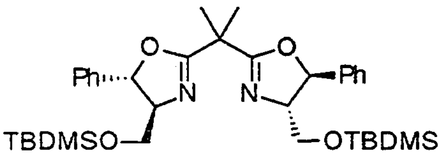
Since determination of the ee of the carbazole product presented difficulties, other dienes were investigated as substrates in this annulation process. Using chiral ligands **1-3**, a



1



2



3

Table 2. The Palladium-Catalyzed Reaction of *N*-Tosyl-2-iodoaniline and 1,3-Dienes in the Presence of a Chiral Ligand (eq 8).

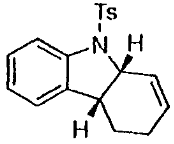
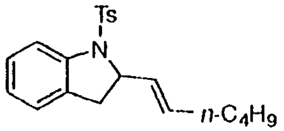
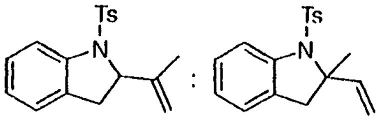
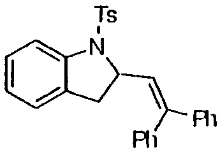
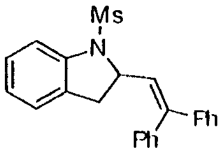
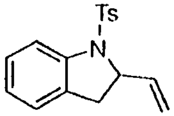
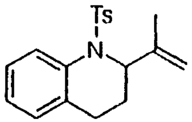
entry	diene	Pd catalyst	ligand (5 mol %)	base (equiv)	temp. (°C)	time (d)	product(s)	% yield (ratio)	% ee
1	1,3-cyclohexadiene	Pd(dba)$_2$	PPh$_3$	Na$_2$CO$_3$ (3.5)	100	2		88	0
2		Pd(dba)$_2$	BINAP	Na$_2$CO$_3$ (3.5)	100	2		13	33
3		Pd(dba)$_2$	BINAP	Ag$_3$PO$_4$ (2.0)	100	1		5	-
4		Pd(dba)$_2$	BINAP	Ag$_3$PO$_4$ (1.0)	100	2		4	-
5		Pd(dba)$_2$	BINAP	Ag$_3$PO$_4$ (3.0)	80	4		14	30-77
6		PdCl$_2$	BINAP	Ag$_3$PO$_4$ (3.0)	80	4		16	15-60
7		Pd(OAc)$_2$	**1**	Ag$_3$PO$_4$ (0.4)	90	1		37	0
8		Pd(OAc)$_2$	**2**	Ag$_3$PO$_4$ (0.4)	90	1		24	0
9	1,3-octadiene	Pd(OAc)$_2$	**1**	Ag$_3$PO$_4$ (0.4)	90	1		90	10
10			**3**	Ag$_3$PO$_4$ (0.4)	90	1		84	10

Table 2 (continued)

11	isoprene	Pd(OAc)$_2$	1	Ag$_3$PO$_4$ (0.4)	90	1		56 (7:1)	20:26
12		Pd(OAc)$_2$	1	Ag$_3$PO$_4$ (0.4)	60	5		undet. (3:2)	23 (maj)
13	1,1-diphenyl- 1,3-butadiene	Pd(dba)$_2$	1	Ag$_3$PO$_4$ (0.4)	100	1		89 $[\alpha]_D$ = 19.1°	[a]
14[b]	1,1-diphenyl- 1,3-butadiene	Pd(OAc)$_2$	1	Ag$_3$PO$_4$ (0.4)	100	2		~40	15
15	1,3-butadiene	Pd(OAc)$_2$	1	Ag$_3$PO$_4$ (0.4)	80	1		0	-
16	5-methyl-1,4- hexadiene	Pd(OAc)$_2$	MeO- BiPHEP	Ag$_3$PO$_4$ (0.4)	90	1		0	-

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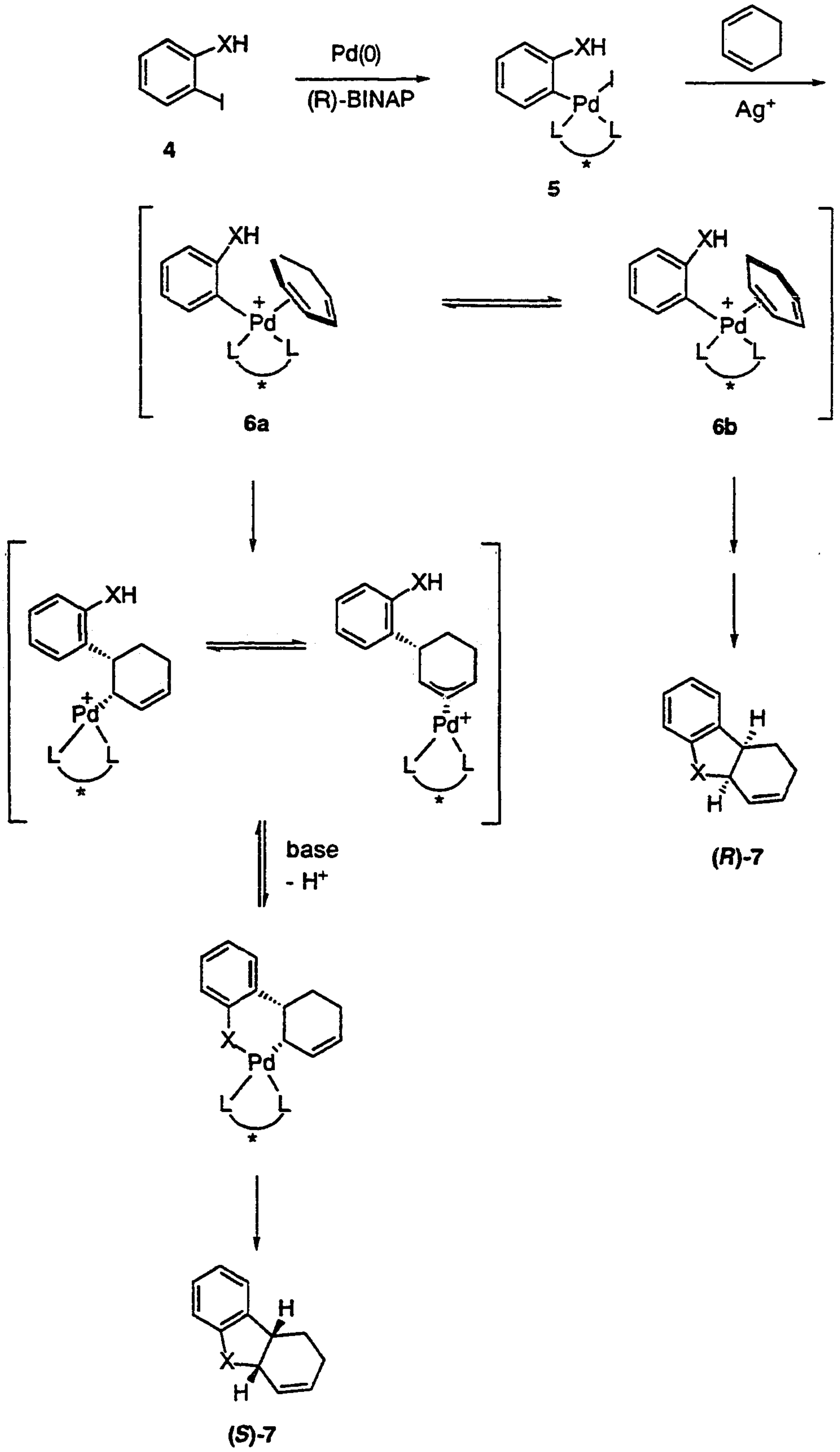
[a] Determination of the ee of this product was not possible using Eu(hfc)$_3$.

[b] *N*-Mesyl-2-iodoaniline was used as the starting ArI for this reaction.

variety of 1,3-dienes were annulated using *N*-tosyl-2-iodoaniline. The reaction of *N*-tosyl-2-iodoaniline and 1,3-octadiene gave the desired product in a high yield, but a very low enantiomeric excess (Table 2, entries 9 and 10). The annulation of isoprene by this same aryl iodide proceeds via a terminal π-allylpalladium intermediate. As expected the ee increased, though only slightly (Table 2, entries 11 and 12). The reaction of *N*-tosyl-2-iodoaniline and 1,1-diphenyl-1,3-butadiene gave an optically active product in high yield, but determination of the ee was not possible using the chiral lanthanide shift reagent $Eu(hfc)_3$ (Table 2, entry 13). Determination of the enantiomeric excess of the analogous *N*-mesyl product was possible using $Eu(hfc)_3$, but it was found to be only 15 % ee (Table 2, entry 14). The reaction of *N*-tosyl-2-iodoaniline and 1,3-butadiene afforded none of the desired product (Table 2, entry 15). We have previously reported the annulation of 1,4-dienes using ortho-functionalized aryl iodides via a π-allylpalladium intermediate. Despite this earlier result, the reaction of 5-methyl-1,4-hexadiene and *N*-tosyl-2-iodoaniline in the presence of chiral ligand **1** afforded none of the desired product (Table 2, entry 16).

The mechanism of this heterocyclization process, described in our earlier publication,[13] may be used to explain the dramatic drop in product yield with the addition of a chiral ligand and perhaps also the only moderate asymmetric induction (Scheme 1). Oxidative addition of the aryl halide to Pd(0) leads to the formation of an arylpalladium intermediate **5** to which the chiral ligand is chelated. Coordination of the diene and precipitation of AgI generates a 16 electron, positively-charged palladium intermediate to which the chiral ligand is presumably more strongly chelated. In this chiral environment, the faces of the diene become diastereotopic **(6a,b)** with selective addition to one of these faces of the molecule leading to the eventual excess of one enantiomer over the other. Addition of the arylpalladium intermediate to the diene leads to the formation of a σ-allylpalladium intermediate, which subsequently collapses to a π-allylpalladium intermediate. In the case of 1,3-cyclohexadiene, frontside

Scheme 1



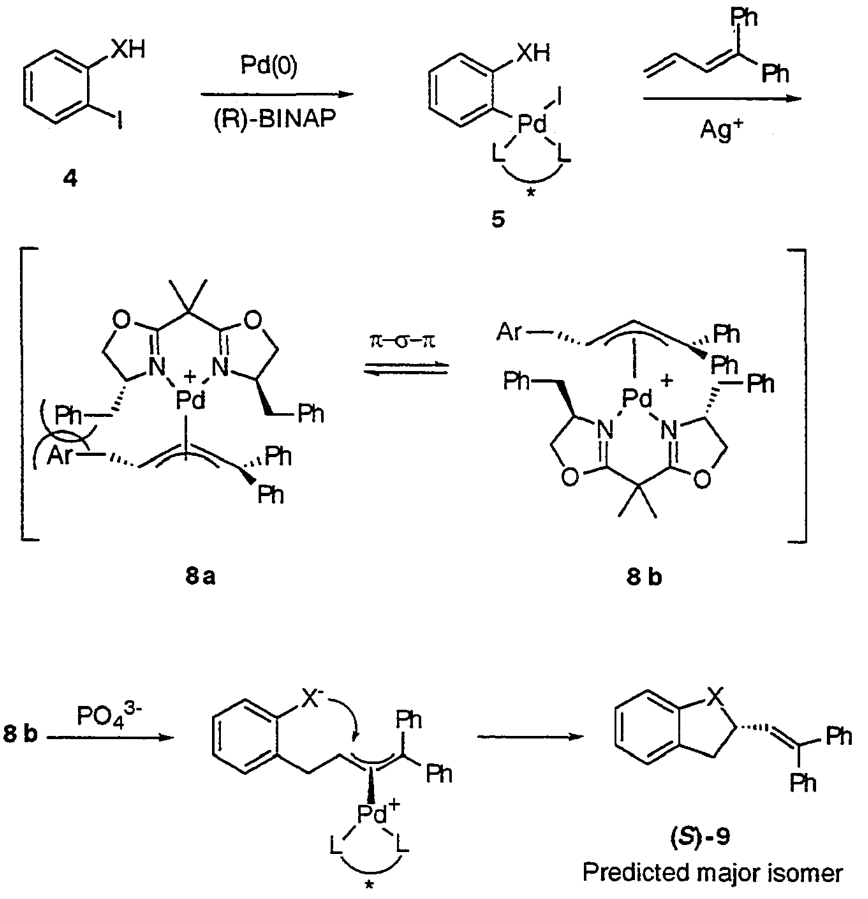
coordination of the deprotonated nucleophile, followed by reductive elimination of the five-membered ring product regenerates Pd(0), which reenters the catalytic cycle.

This mechanism can be used to explain the significant reduction in product yield in the presence of a bidentate chiral ligand. It isknown that prior to reductive elimination palladium must open a coordination site.[15] Stille has shown that rates of reductive elimination are reduced significantly in the presence of a diphosphine ligand relative to the rate in the presence of PPh_3.[16] The strength of chelation of the bidentate ligand hinders the opening of a coordination site on the palladium needed to facilitatereductive elimination. Thus, this becomes the rate determining step and leads to low product yields.

In the case of acyclic dienes and most heteroatom nucleophiles, the nucleophile is thought to attack via direct backside displacement of the palladium in the π-allylpalladium intermediate; thus, rates for these substrates would be little effected by chelation of the chiral ligand. In this type of reaction, the initial addition of the arylpalladium species to the double bond does not form a chiral center. Instead, the chiral center is generated during nucleophilic attack on the π-allylpalladium intermediate. For this reason, a diene substrate must be chosen which allows for rapid equilibration of the diasteriotopic π-allylpalladium intermediates. With this in mind, several dienes which lead to the formation of a terminally disubstituted π-allylpalladium system in which both of the substituents are the same, were annulated using *N*-tosyl-2-iodoaniline in the presence of a variety of chiral ligands. The reaction of isoprene with *N*-tosyl -2-iodoaniline leads to a terminal π-allylpalladium intermediate which would be expected to undergo rapid equilibration. Unfortunately, this reaction gave the product as a mixture of regioisomers with the major isomer being derived from the addition of **5** to the terminus of the monosubstituted double bond (Table 2, entries 12 and 13). The ratio of isomers seems dependent upon the reaction temperature. The asymmetric induction in this reaction was also disappointing. Determination of the ee of both isomers showed them to range from 20-26 % ee.

Bosnich has shown that a chiral ligand bound to 1,1,3-triphenyl-π-allylpalladium intermediates undergoes equilibration between diastereomers quite rapidly[17] and for this reason 1,1-diphenyl-1,3-butadiene was reacted with *N*-tosyl-2-iodoaniline (Table 2, entry 14). The resultant π-allylpalladium intermediate is similar to Bosnich's chiral ligand bound 1,1,3-triphenyl-π-allylpalladium, since the π-σ-π equilibration mechanism can occur at the diphenyl-substituted end of the π-allyl system. The addition of the arylpalladium intermediate to 1,1-diphenyl-1,3-butadiene leads to the formation of two π-allylpalladium intermediates **8a** and **8b** (Scheme 2). In this system steric interactions will always exist at the diphenyl-substituted end

Scheme 2



of the π-allylpalladium intermediate between the benzyl substituent on the chiral ligand and one of the phenyl rings. In **8a**, there exists an additional interaction between the benzyl substituent on the ligand and the Ar substituent on the π-allyl system and for this reason it is expected that **8b** will be the favored intermediate. Unfortunately, determination of the ee of this product was hampered by the steric hindrance of the Lewis basic site on the molecule preventing coordination to the chiral lanthanide shift reagent. Our best estimate of the ee is approximately 35 %, suggesting that equilibration between these π-allylpalladium intermediates is not occurring rapidly enough relative to nucleophilic attack to allow for high levels of enantiodifferentiation. An unsubstituted terminal π-allyl intermediate would be expected to undergo this equilibration much faster than the diphenyl-substituted system, but reaction of *N*-tosyl-2-iodoaniline with 1,3-butadiene gave none of the desired product (Table 2, entry 15). Likewise, the annulation of 5-methyl-1,4-hexadiene by *N*-tosyl-2-iodoaniline is expected to proceed via an unsubstituted terminal π-allylpalladium intermediate, but this reaction afforded none of the annulation product (Table 2, entry 16).

Thus, fundamentally different mechanisms are at work in these cyclic and acyclic systems. While the asymmetric annulation of 1,3-cyclohexadiene involves an asymmetric arylpalladium addition, the analogous annulation of 1,1-diphenyl-1,3-butadiene and other acyclic dienes involves an intramolecular asymmetric π-allylpalladium displacement.

Conclusion

The development of palladium-catalyzed, enantioselective annulations of 1,3-dienes has in many cases been hindered by the poor yields of the desired products. At present, the low levels of asymmetric induction observed in the annulation of 1,3-dienes are probably not synthetically useful, but the principles learned in this study, as well as in the asymmetric annulation of allenes described in Chapter 1, allow a rationalization of the observed results. In addition, the mechanistic considerations needed to design systems more likely to facilitate high enantioselectivities have been to some extent elucidated.

Experimental

General. All ^{1}H and ^{13}C NMR were recorded at 300 and 75.5 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) or basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O]. All melting points are uncorrected.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. All palladium reagents were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co., Ltd. 2-Iodoaniline, *p*-toluenesulfonyl chloride, methanesulfonyl chloride, 1,3-cyclohexadiene, β-phenylcinnamaldehyde, (*R*)-BINAP and Eu(hfc)$_3$ were purchased from Aldrich Chemical Co., Inc. 2-Iodophenol was purchased from Lancaster Synthesis, Inc. 1,3-Octadiene and 5-methyl-1,4-hexadiene were purchased from Wiley Organics. Isoprene was purchased from Fluka Chemie.

***N*-Tosyl-2-iodoaniline.** Tosylation of 2-iodoaniline (25 mmol) was carried out by treating 2-iodoaniline with tosyl chloride (25 mmol) in pyridine (8 mL) and heating for 3 h at 80 °C.[18] The product was purified by recrystallization from ethanol, followed by washing several times with hexanes. ^{1}H NMR ($CDCl_3$) δ 2.4 (s, 3 H), 6.95 (ddd, 1 H, J = 7.5, 7.5, 1.5 Hz), 7.34 (d, 2 H, J = 7.8 Hz), 7.37 (ddd, 1 H, J = 8.1, 7.5, 1.5 Hz), 7.47 (dd, 1 H, J = 8.1, 1.5 Hz), 7.65 (d, 2 H, J = 8.1 Hz), 7.79 (dd, 1 H, J = 8.1, 1.5 Hz), 8.0 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.6, 122.4, 126.8, 127.4, 129.4, 129.6, 135.8, 137.4, 139.1, 144.2 (one sp^2 signal missing due to overlap); IR 3300 (C-N), 2950 (C-H), 1285, 1233 (S=O) cm^{-1}. Anal. calcd for $C_{13}H_{12}INO_2S$: C, 41.82: H, 3.22 Found: C, 41.77; H, 3.47.

1,1-Diphenyl-1,3-butadiene. Prepared by treatment of β-phenylcinnamaldehyde with methylene triphenylphosphorane according to a literature procedure.[19] ^{1}H NMR ($CDCl_3$) δ 5.11 (d, 1 H, J = 10.2 Hz), 5.36 (d, 1 H, J = 15.3 Hz), 6.37-6.50 (m, 1 H), 6.70 (d, 1 H, J = 11.1 Hz), 7.20-7.45 (m, 10 H).

General Procedure for the Enantioselective, Palladium-catalyzed Annulation of 1,3-Dienes. To a 1 dram vial is added the palladium reagent (0.025 mmol), the appropriate organic iodide (0.50 mmol), Ag_3PO_4 (0.20 mmol), the appropriate diene (2.5 or 1.0 mmol) and 1.0 mL of a solvent/chiral ligand stock solution containing the desired amount of the chiral ligand (0.025 or 0.050 mmol). The vial is then flushed with N_2, capped with a screw cap containing a teflon liner, and placed in an oil bath at the desired temperature for the specified period of time (see Table 1). The vial was then removed from the oil bath, diluted with ether, washed with sat'd NH_4Cl and water, dried over $MgSO_4$, and concentrated. The resulting residue was purified by column chromatography (silica gel) using hexanes/EtOAc as eluents. Determination of the enantiomeric excess of the products was accomplished using the chiral NMR shift reagent Eu(hfc)$_3$. Optical rotations were determined using a Jasco DIP-370 digital polarimeter.

Spectral Data

3,4,4a,9a-Tetrahydrodibenzofuran. Obtained as a pale yellow oil from the reaction of 2-iodophenol and 1,3-cyclohexadiene. Spectral data matched those reported by Berrios-Peña.[13]

***N*-Tosyl-3,4,4a,9a-tetrahydrocarbazole.** Obtained as a white solid from the reaction of *N*-tosyl-2-iodoaniline and 1,3-cyclohexadiene: mp 135-136 °C (EtOH); ^{1}H NMR ($CDCl_3$) δ 1.8-2.0 (m, 4 H), 2.35 (s, 3 H), 3.05 (m, 1 H), 4.71 (dd, 1 H, J = 8.1, 1.8 Hz), 5.87 (s, 2 H), 7.0 (d, 1 H, J = 6.9 Hz), 7.06 (ddd, 1 H, J = 7.2, 7.2, 1.0 Hz), 7.16 (d, 2 H, J = 8.1 Hz), 7.21 (dd, 1 H, J = 7.5, 7.5 Hz), 7.57 (d, 2 H, J = 8.4 Hz), 7.64 (d, 1 H, J = 8.1 Hz). Additional spectral data matched those reported by Berrios-Peña.[13]

***N*-Tosyl-2-isopropenyl-2,3-dihydroindole and *N*-tosyl-2-ethenyl-2-methyl-2,3-dihydroindole.** Obtained as a clear, colorless oil as a 7:1 mixture of isomers in 56 % yield from the reaction of *N*-tosyl-2-iodoaniline and isoprene. The spectral properties matched those reported by Berrios-Peña.[13]

***N*-Tosyl-2-(2,2-diphenylethenyl)-2,3-dihydroindole.** Obtained as a yellow solid in 89 % yield from the reaction of *N*-tosyl-2-iodoaniline and 1,1-diphenyl-1,3-butadiene. Determination of the ee of this product was not possible using Eu(hfc)$_3$: $[\alpha]_D = 19.1°$, $C = 0.053$, $CHCl_3$; ^{1}H NMR ($CDCl_3$) δ 2.72 (s, 3 H), 2.82 (dd, 1 H, J = 15.0, 6.0 Hz), 3.02 (dd, 1 H, J = 15.0, 9.9 Hz), 4.64 (m, 1 H), 6.28 (d, 1 H, J = 9.3 Hz), 6.93-7.04 (m, 2 H), 6.94 (d, 2 H, J = 7.8 Hz), 7.16-7.35 (m, 10 H), 7.40 (m, 3 H), 7.69 (d, 1 H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 21.5, 36.6, 61.1, 115.8, 123.9, 124.9, 127.3, 127.5, 127.6, 127.8, 128.1, 128.3, 128.4, 128.8, 129.0, 130.0, 130.3, 134.3, 139.3, 141.4, 141.9, 142.0, 143.7; IR ($CHCl_3$) 3100, 3050, 2910, 2856, 1621, 1598, 1358 cm^{-1}; HRMS for $C_{29}H_{25}NO_2S$: calcd 451.1606, found 451.1606.

***N*-Mesyl-2-(2,2-diphenylethenyl)-2,3-dihydroindole.** Obtained as a yellow solid from the reaction of *N*-mesyl-2-iodoaniline and 1,1-diphenyl-1,3-butadiene: 15 % ee; ^{1}H NMR ($CDCl_3$) δ 2.80 (s, 3 H), 2.98 (dd, 1 H, J = 15.9, 5.1 Hz), 3.38 (dd, 1 H, J = 15.9, 9.6 Hz), 4.84 (ddd, 1 H, J = 9.6, 9.3, 4.5 Hz), 6.27 (d, 1 H, J = 9.3 Hz), 7.02 (dt, 1 H, J = 7.5, 0.6 Hz), 7.10-7.42 (m, 13 H); ^{13}C NMR ($CDCl_3$) δ 36.7, 36.8, 62.1, 114.3, 123.8, 125.4, 127.4, 127.7, 127.8, 128.0, 128.2, 128.3, 128.5, 129.7, 130.0, 139.0, 141.1, 141.7, 142.7; IR ($CHCl_3$) 3079, 3020, 1610, 1520, 1352 cm^{-1}; HRMS for $C_{23}H_{21}NO_2S$: calcd 375.1293, found 375.1297.

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CHAPTER 3: PALLADIUM-CATALYZED CARBOANNULATION OF ACETYLENES USING 2-IODOBIARYLS

A paper to be submitted to the *Journal of Organic Chemistry*

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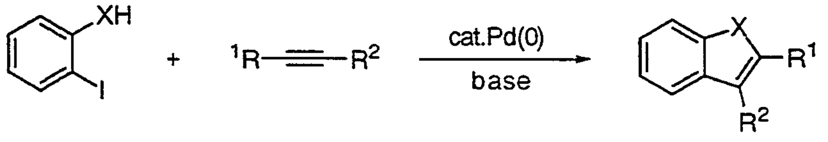
Abstract

A variety of 2-iodobiaryls react with internal acetylenes in the presence of a palladium catalyst to afford carboannulation products in moderate to excellent yields. This methodology provides an exceptionally efficient route to a variety of substituted polycyclic aromatic hydrocarbons, including synthetic analogues of the antiviral natural product hypericin.

Introduction

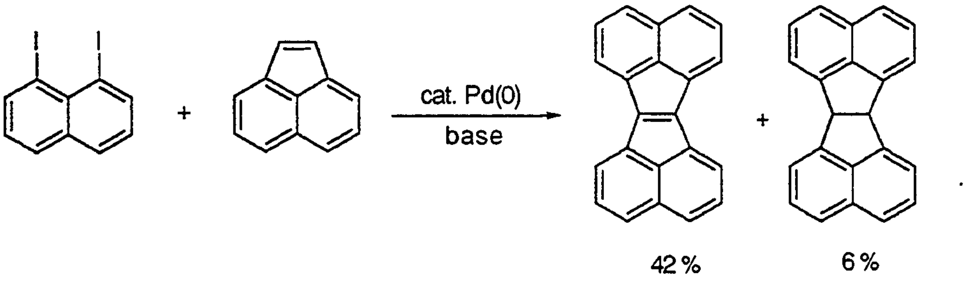
Palladium-catalyzed annulation processes have received a great deal of recent attention. In our own laboratories, it has been demonstrated that aryl iodides with functionality in the ortho position react with internal acetylenes to give a wide variety of hetero- and carbocycles, including indoles,[1] benzofurans,[2] benzopyrans,[2] isocoumarins,[2] indenones[3] and indanes[4] (eq 1).



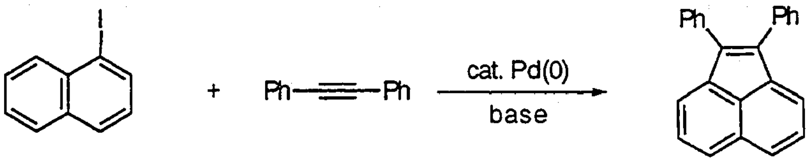
(1)

X = O, CR_2O, NR, CO_2, CO, $C(CO_2Et)_2$

Recent reports in the literature have demonstrated the use of palladium-catalyzed methodologies as a means of forming polycyclic aromatic hydrocarbons. Dyker[5] has synthesized disubsituted acenaphthylene derivatives from 1,8-diiodonaphthalene and alkenes in the presence of a palladium catalyst (eq 2), while Grigg[6] has formed 7,8-diphenylacenaphthylene by the palladium-catalyzed reaction of 1-iodonaphthalene and diphenylacetylene (eq 3).

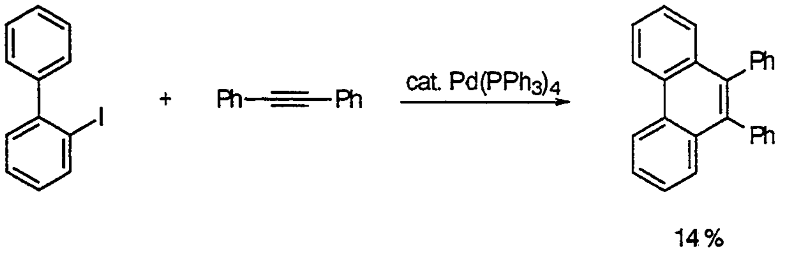


(2)



(3)

Substituted phenanthrenes have also been synthesized using palladium-mediated methods.[7] Heck[7b] reported in 1987 the formation of 9,10-diphenylphenanthrene in 14 % yield in the palladium-catalyzed reaction of 2-iodobiphenyl and diphenylacetylene (eq 4). Our own

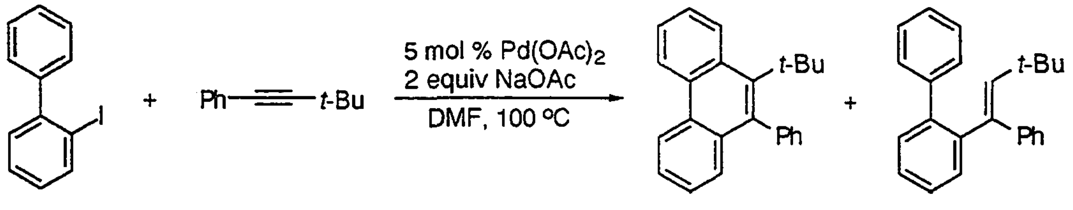


(4)

interest in the annulation of internal acetylenes led us to further investigate this reaction. Here we report improved reaction conditions, which extend this process to include the annulation of a wide variety of internal acetylenes with structurally and functionally diverse biaryls in moderate to excellent yields.

Results and Discussion

Initial work was performed by Mark Doty[8] in which he found that some internal acetylenes reacted with 2-iodobiphenyl to form 9,10-substituted phenanthrenes under conditions similar to those utilized in his palladium-catalyzed synthesis of substituted isocoumarins.[2] Doty's work,[8] along with investigation of the annulation of 1-phenyl-2-(trimethylsilyl)acetylene, showed that the highest product yields were obtained using Pd(OAc)$_2$ as the catalyst, NaOAc as the base, and DMF as the solvent. Further optimization of this process was performed using as a model system the reaction of 2-iodobiphenyl and 3,3-dimethyl-1-phenyl-1-butyne (eq 5).



(5)

1 **2**

Under earlier developed conditions, the desired 9-*t*-butyl-10-phenylphenanthrene (**1**) was obtained along with (*E*)-3,3-dimethyl-1-phenyl-1-(2'-biphenyl)-1-butene (**2**) in a 2 : 1 ratio (Table 1, entry 2). Investigation of this system revealed the importance of the chloride ion source on the ratio of products; thus, when LiCl was removed entirely from the system, products **1** and **2** were obtained in a 95 % yield in a ratio of 3 : 1 (Table 1, entry 1). The use of n-Bu$_4$NCl (TBAC) as the halide source further improved the product ratio (Table 1, entries 4-7). In the presence of 1 equiv of TBAC, the product ratio improved to 4 : 1. Two equivs. of

Table 1. Optimization of Conditions for the Reaction of 2-Iodobiphenyl with 3,3-Dimethyl-1-phenyl-1-butyne (eq 5).

entry	Cl source (equiv)	reaction time (d)	% isolated yield	ratio **1** : **2**
1	none	1	95	3 : 1
2	LiCl (0.5)	1	90	2 : 1
3	LiCl (1.25)	1	98	2.3 : 1
4	*n*-Bu_4NCl (1.0)	1	97	4 : 1
5	*n*-Bu_4NCl (2.0)	2	97	7 : 1
6	*n*-Bu_4NCl (3.0)	4	95	11 : 1
7	*n*-Bu_4NCl (4.0)	7	80	11 : 1

TBAC increased this ratio to 7 : 1 and 3 equiv afforded the products in an 11 : 1 ratio in 95 % yield. Each additional equiv of TBAC led to a reduction in the reaction rate and therefore a point of diminishing returns was reached at 4 equiv of TBAC. The 11 : 1 mixture of products from Table 1, entry 6 could be further purified by recrystallization to give pure 9-*t*-butyl-10-phenylphenanthrene in 80 % isolated yield.

These results led to the development of two general reaction procedures - Procedure A: 1 equiv. of the ArI, 1.2 or 2.0 equiv of the acetylene, 5 mol % of $Pd(OAc)_2$, 2 equiv of NaOAc, 1 equiv of LiCl in DMF at 100 °C, and Procedure B: 1 equiv of the ArI, 1.2 or 2.0 equiv of the acetylene, 5 mol % of $Pd(OAc)_2$, 2 equiv of NaOAc, 3 equiv of TBAC in DMF at 100 °C. The procedure used for these reactions is strongly influenced by the structure of the alkyne. In general, Procedure A works better for diarylacetylenes and silylacetylenes, while Procedure B is more successful when alkyl-substituted acetylenes are used.

We next set out to determine the scope and limitations of this methodology by annulating acetylenes of varying structure with a number of unfunctionalized and functionalized biaryls. The results are summarized in Table 2.

Methyl-substituted internal acetylenes reacted with 2-iodobiphenyl using Procedure B to give the 9,10-disubstituted phenanthrenes in good yield (Table 2, entries 2 and 3). These same substrates gave a complex mixture of products when reacted using Procedure A.

Substituted 2-iodobiphenyls reacted with diarylacetylenes to give the desired products in high yields (Table 2, entries 4-8). There was, however, a significant reduction in reaction rate when the electron-withdrawing trifluoromethyl group was present in the 4'-position of the biphenyl (Table 2, entry 5). Functionalization of the aryl groups on the acetylene seemed to have little or no effect on the reaction rate or product yield (Table 2, entries 7-10).

Aryl bromides show much lower reactivity than the corresponding aryl iodides. 2-Bromobiphenyl reacted with diphenylacetylene to give 9,10-diphenylphenanthrene in only a 35 % yield after a reaction time of 5 days (Table 2, entry 11). This compares with an 89 % yield using an identical procedure and 2-iodobiphenyl as reported by Doty.[8] The reaction of 2-(trifluoromethanesulfonyloxy)biphenyl and diphenylacetylene yielded no 9,10-diphenylphenanthrene (Table 3, entry 1). 2-Iodobiphenyl was also reacted with 1-bromo-2-(phenylethynyl)benzene in the hopes that after formation of the phenanthrene, palladium insertion into the aryl bromide bond would be followed by further closure of the ring system. There was no evidence of this final ring closure and 9-phenyl-10-(2'-bromophenyl)phenanthrene was obtained in only 39 % yield (Table 2, entry 12). Photolytic ring closure of this product was also unsuccessful.

Silylacetylenes reacted with 2-iodobiphenyl to give the desired 9,10-disubstituted phenanthrenes in fair yield (Table 2, entries 13-16). The relatively low yields obtained using these substrates is most likely due to competing desilylation of the acetylene and subsequent

Table 2. Synthesis of Polycyclic Aromatics via Palladium-Catalyzed Carboannulation of Internal Acetylenes.

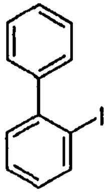
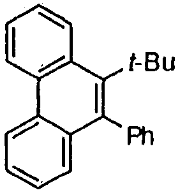
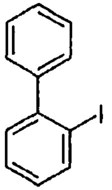
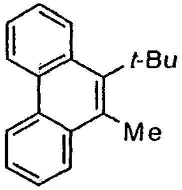
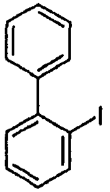
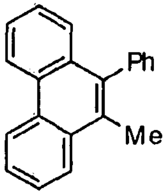
entry	aryl iodide	acetylene (equivs)	product[a]	procedure, rxn time[b]	% yield (isomer ratio)
1		Ph—≡—*t*-Bu (2.0)		B, 24 h	80
2		Me—≡—*t*-Bu (1.5)		B, 24 h	63
3		Me—≡—Ph (2.0)		B[c], 24 h	45

Table 2 (continued)

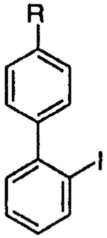
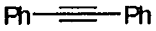
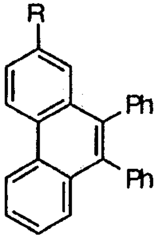
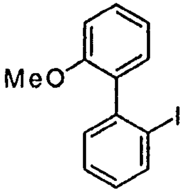
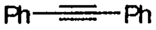
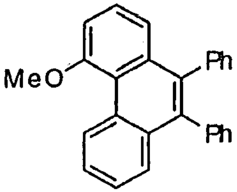
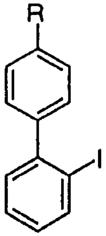
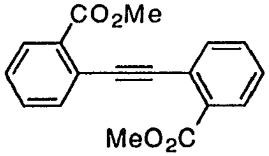
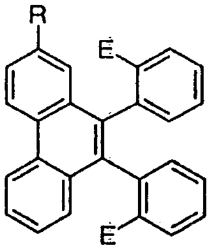
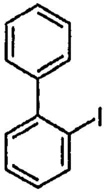
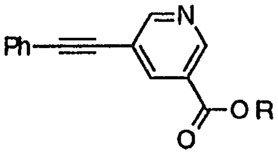
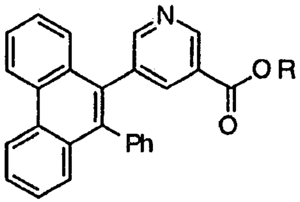
4 5		 (1.1)		R = OMe R = CF_3	B, 24 h A, 144 h	86 69
6		 (1.1)			A, 24 h	84
7 8		 (1.1)	 E = CO_2Me	R = OMe R = OH	A, 48 h A, 48 h	76 69
9 10		 (1.1)		R = H R = Me	A, 24 h A, 24 h	55 84

Table 2 (continued)

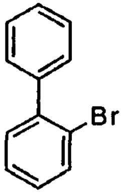
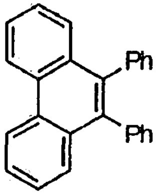
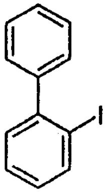
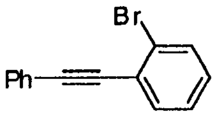
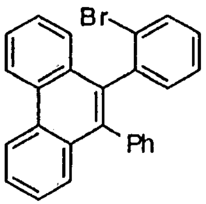
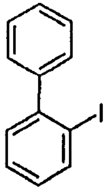
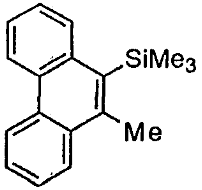
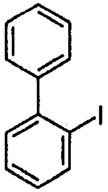
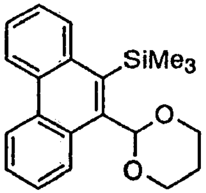
11		$Ph-\equiv-Ph$ (1.1)		A, 120 h	35
12		 (2.0)		A, 24 h	39
13		$Me-\equiv-SiMe_3$ (2.0)		A, 24 h	42
14		 (1.1)		A, 24 h	54

Table 2 (continued)

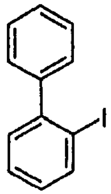
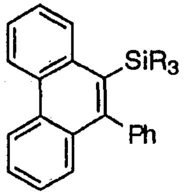
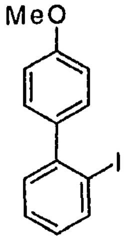
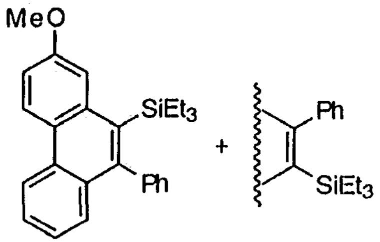
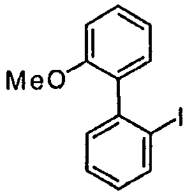
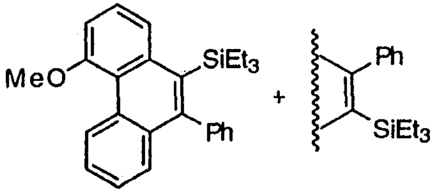
15		$\mathrm{Ph{-}{\equiv}{-}SiR_3}$ (2.0)		R = Me	A^d, 24 h	42
16				R = Et	A, 48 h	49
17		$\mathrm{Ph{-}{\equiv}{-}SiEt_3}$ (2.0)			A, 24 h	50 (1 : 1)
18		$\mathrm{Ph{-}{\equiv}{-}SiEt_3}$ (2.0)			A, 24 h	61 (3 : 1)

Table 2 (continued)

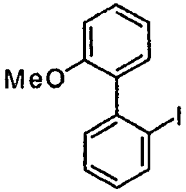
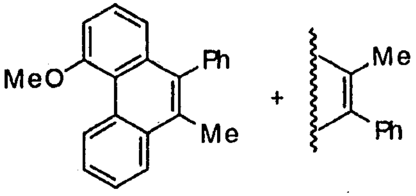
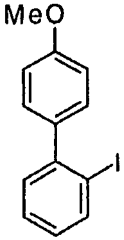
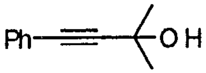
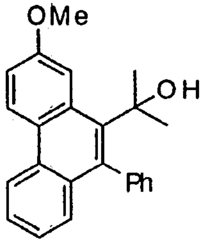
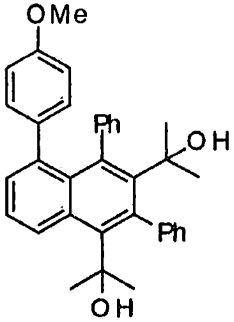
19		$\mathrm{Me{-}C{\equiv}C{-}Ph}$ (2.0)		A^c, 24 h	40 (2.4 : 1)
20		 (2.0)	 and	A, 18 h	41
					50

Table 2 (continued)

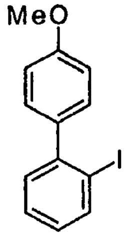
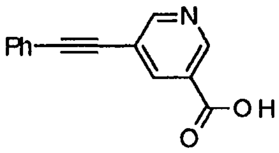
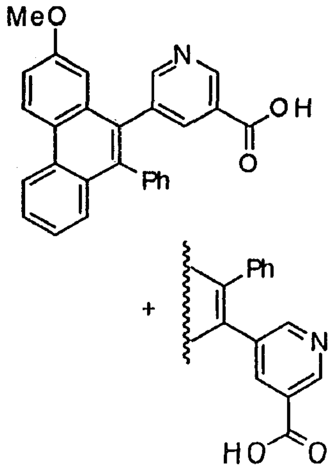
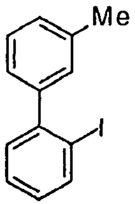
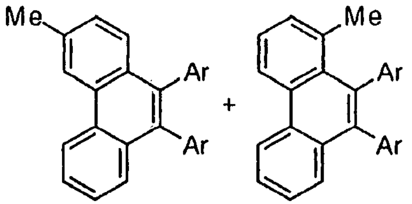
21		 (1.1)		A, 24 h	94 (1 : 1)
22		$\text{Ar}-\!\!\equiv\!\!-\text{Ar}$ (1.1) Ar = Ph		A, 24 h	83 (1 : 1)
23		Ar = 4-MeOC$_6$H$_4$		A, 24 h	51 (1 : 1)

Table 2 (continued)

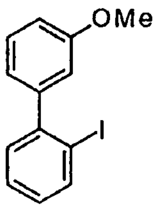
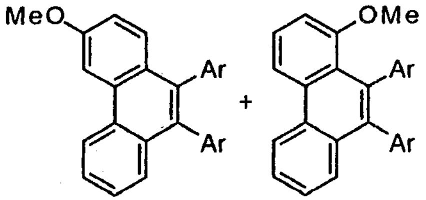
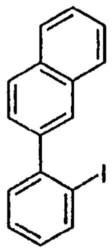
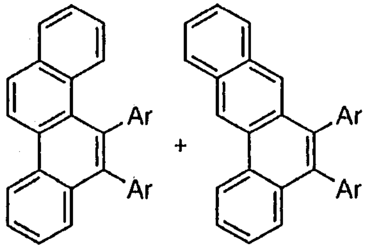
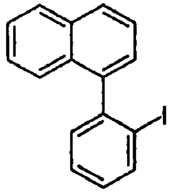
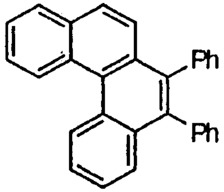
24		Ar—≡—Ar (1.1) Ar = Ph		A, 24 h	72 (2 : 1)
25		Ar = 4-MeOC$_6$H$_4$		A, 24 h	72 (2.3 : 1)
26		Ar—≡—Ar (1.1) Ar = Ph		A, 24 h	80 (1 : 1)
27		Ar = 4-MeOC$_6$H$_4$		A, 24 h	75 (5 : 1)
28		Ph—≡—Ph (1.1)		B, 12 h	78

Table 2 (continued)

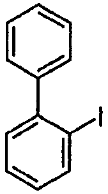
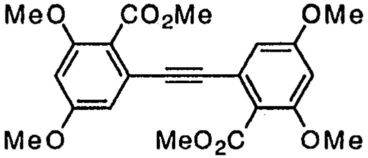
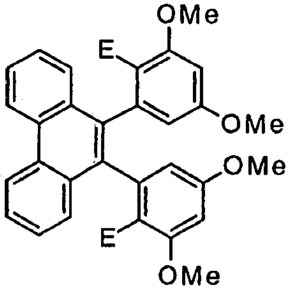
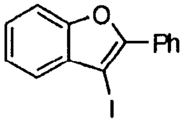
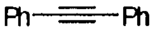
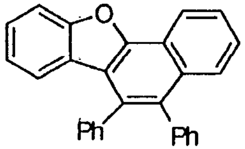
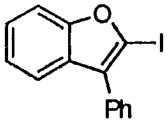
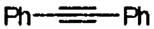
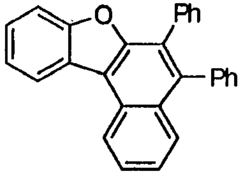
29		 (1.1)	 E = CO_2Me	A, 48 h	49
30		 (1.1)		B, 14 h	65
31		 (1.1)		B, 16 h	73

Table 2 (continued)

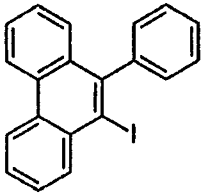
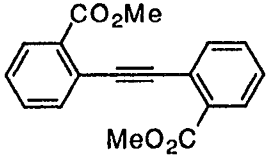
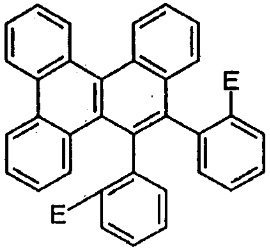
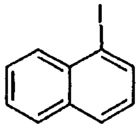
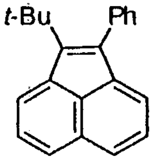
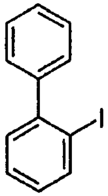
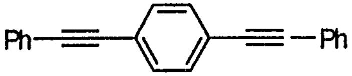
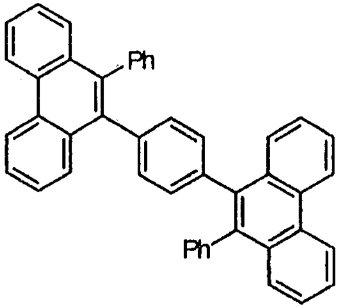
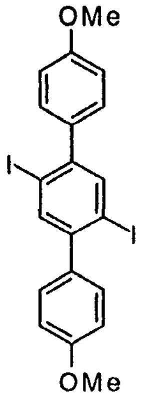
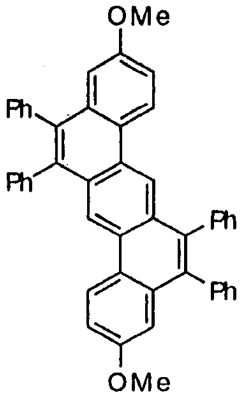
32		 (1.1)	 E = CO_2Me	A, 48 h	60
33		Ph—≡—*t*-Bu (2.0)		B, 24 h	89
34		 (0.5)		A, 24 h	77

Table 2 (continued)

35		Ph—≡—Ph (2.2)		A, 24 h	67

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[a] Where more than one product was observed, a "+" indicates an inseparable mixture, and an "*and*" indicates the products were separated by column chromatography.

[b] Procedure A: 5 mol % of $Pd(OAc)_2$, 2 equiv of NaOAc, 1 equiv of LiCl in DMF at 100 °C for the specified period of time. Procedure B: 5 mol % of $Pd(OAc)_2$, 2 equiv of NaOAc, 3 equiv of *n*-Bu_4NCl in DMF at 100 °C for the specified period of time.

[c] Reaction was diluted to 10 mL of solvent per 0.25 mmol of starting aryl iodide.

[d] Procedure A was altered to include 3 equiv of LiCl.

palladium-catalyzed coupling of the aryl iodide to the terminal acetylene to produce the aryl acetylene. This side product has been isolated in 30 % yield from the reaction of 2-iodobiphenyl and 1-phenyl-2-(trimethylsilyl)acetylene.[8] Past work in our research group has suggested that increasing the steric bulk of the silyl group can retard the rate of desilylation and lead to improved product yields. In these carboannulation reactions, this has not held true. Although not included in Table 2, 1-(triisopropylsilyl)propyne gave nearly the same yield as 1-(trimethylsilyl)propyne (Table 2, entry 13), but the reaction rate of the more hindered acetylene was much slower, requiring 6 days for completion and the product was inseparable from an unknown impurity. The rate of reaction of phenyl(trimethylsilyl)acetylene and 1-phenyl-2-(triethylsilyl)acetylene were nearly the same, although the yield for the triethylsilyl derivative was slightly higher and no significant desilylation-coupling product was observed (Table 2, entries 15 and 16).

We next investigated the regioselectivity of the acetylene insertion. Our earlier annulation work using aryl iodides with a Lewis basic functional group in the ortho position (see eq 1) gave high, and in many cases complete selectivity for addition of the arylpalladium species to the acetylene generating a vinylic palladium intermediate with the metal geminal to the more sterically demanding alkyne substituent.[1-4,8] In this carboannulation of internal acetylenes with biaryls, the acetylene insertion is much less regioselective. The reaction of 2-iodo-4'-methoxybiphenyl and 1-phenyl-2-(triethylsilyl)acetylene gave a 1:1 mixture of regioisomers in 50 % yield (Table 2, entry 17). Attempts to enhance the regioselectivity of the acetylene insertion by the addition of bidentate ligands were unsuccessful. In all cases the addition of a ligand led to significant desilylation of the acetylene. The subsequent coupling of this terminal acetylene to the aryl halide led to a reduction in the yield of the desired annulation products. In contrast, the reaction of 2-iodo-2'-methoxybiphenyl with this same acetylene afforded a 3:1 mixture of regioisomers in 61 % yield (Table 2, entry 18). Likewise, the reaction of 2-iodo-2'-methoxybiphenyl with 1-phenyl-1-propyne gave modest selectivity for aryl addition to the less hindered end of the acetylene (Table 2, entry 19). The greater selectivity of alkyne insertion demonstrated by 2-iodo-2'-methoxybiphenyl is consistent with reports noting the importance of intramolecular chelation of an arylpalladium intermediate in determining the regioselectivity of this kind of arylpalladium addition (Figure 1).[9] The reaction of 2-iodo-4'-methoxybiphenyl and 3-methyl-1- phenyl-1-butyn-3-ol did occur regiospecifically, perhaps due to chelation of the tertiary alcohol to the palladium, affording 2-methoxy-10-(1'-hydroxy-1'-methylethyl)-9-phenylphenanthrene in 41 % yield (Table 2, entry 20). Interestingly, this reaction also yielded the product resulting from double insertion of the acetylene, 1,3-di(1-hydroxy-1-methylethyl)-2,4-diphenyl-5-(4'-methoxyphenyl)naphthalene, in 50 % yield (Table 2, entry 20). This result has precedent in the work of Heck[7b,10] and others[11] in which the palladium-catalyzed reaction of aryl halides with 2 equiv of an acetylene afforded tetrasubstituted naphthalenes in high yield via double insertion of the acetylene, followed by cyclization onto the arene ring.

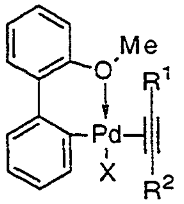
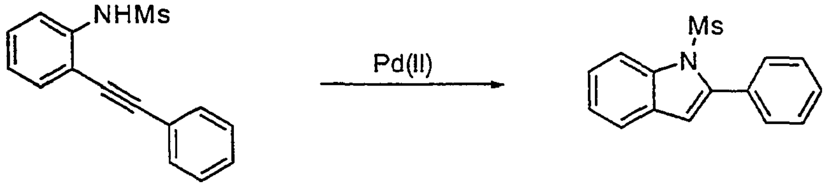


Figure 1. An arylpalladium-acetylene π-complex with the proposed intramolecular chelation.

In an investigation of possible electronic influences on the regioselectivity of attack on the acetylene, 2-iodo-4'-methoxybiphenyl was used to annulate 5-(phenylethynyl)pyridine-3-carboxylic acid. The desired product was obtained as a 1:1 mixture of regioisomers in 94 % yield (Table 2, entry 21). Thus, there seems to be little or no electronic influence on the regioselectivity of the acetylene insertion.

The structure of the biaryl was then altered to examine the effect of steric hindrance and electronic effects on the site of final ring closure. The reactions of 2-iodo-3'-methylbiphenyl with diphenylacetylene and di(4-methoxyphenyl)acetylene gave 1:1 mixtures of isomers in 83 and 55 % yields respectively (Table 2, entries 22 and 23). The selectivity was much better in the reaction of 2-iodo-3'-methoxybiphenyl with diphenylacetylene giving the products in 72 % yield as a 2:1 mixture of regioisomers (Table 2, entry 24). Approximately the same selectivity was achieved in the analogous reaction with di(4-methoxyphenyl)acetylene (Table 2 , entry 25). In the reaction of acetylenes with 2-(2'-iodophenyl)naphthalene, annulation via electrophilic aromatic substitution would be expected to favor attack at the 1-position of the naphthyl group. In the reaction of this iodobiaryl with diphenylacetylene, attack at the 1- and 3-positions occurred with no selectivity to give 5,6-diphenylchrysene and 3,4-diphenylbenz[a]anthracene in a 1:1 ratio in 80 % yield (Table 2, entry 26). Much better selectivity for annulation at the 1-position was achieved in the reaction of 2-(2'-iodophenyl)-naphthalene with di(4-methoxyphenyl)acetylene giving 5,6-di(4-methoxyphenyl)chrysene and 3,4-di(4-methoxyphenyl)benz[a]anthracene in a 5:1 ratio (Table 2, entry 27). The electron-releasing methoxy groups in this system presumably reduce the electrophilicity of the vinylic palladium intermediate, thus allowing greater selectivity for attack at the more electron-rich 1-position of the naphthalene ring.

More highly functionalized acetylenes have also been annulated using this methodology. In general, functionalization of the acetylene has little effect on the reaction rate or product yields with the following exceptions. Simple primary dialkyl-substituted acetylenes give no annulation product. Likewise, 2-iodo-4'-methoxybiphenyl gave none of the desired annulation product in its reaction with *N*-mesyl-2-(phenylethynyl)aniline. Instead, the Pd(II)-catalyzed cyclization of the acetylene to the indole derivative occurred in high yield (eq 6).

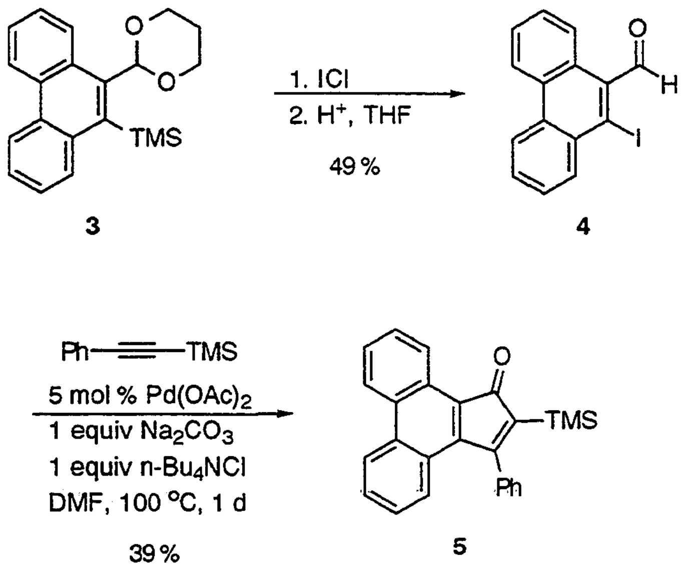


(6)

2-Iodobiphenyl reacted with bis(3,5-dimethoxy-2-methoxycarbonylphenyl)acetylene using Procedure A to give the desired product in only 49 % yield (Table 2, entry 29). The relatively low yield obtained with this acetylene may be further evidence in support of annulation via an electrophilic palladation mechanism, since in the vinylic palladium intermediate, the aryl methoxy groups can by resonance place more electron density on the metal making it less electrophilic. However, that effect may be cancelled out by the adjacent electron-withdrawing ester group. Alternatively, steric hindrance may be impeding cyclization here.

In most cases, varying the structure of the biaryl had little effect on the product yields. 3-Iodo-2-phenylbenzofuran reacted with diphenylacetylene to give 1,2-diphenylbenzo[c]dibenzofuran in 65 % yield using procedure B (Table 2, entry 30). Similarly, the reaction of 2-iodo-3-phenylbenzofuran and diphenylacetylene afforded 3,4-diphenylbenzo[a]dibenzofuran in 73 % yield, again using procedure B (Table 2, entry 31). 9-Iodo-10-phenylphenanthrene, prepared by iodination of 9-trimethylsilyl-10-phenylphenanthrene by ICl (Table 2, entry 15), reacted with di(2-methoxycarbonylphenyl)acetylene to afford the desired product in 60 % yield (Table 2, entry 32). We have previously reported the annulation of internal alkynes with 2-iodo arylaldehydes.[3] As an additional demonstration of the utility of this methodology, 9-(1,3-dioxan-2-yl)-10-(trimethylsilyl)phenanthrene **3**, readily available from our annulation chemistry (Table 2, entry 14), has been converted in two steps to 9-formyl-10-iodophenanthrene **4** (Scheme 1). The palladium-catalyzed reaction of this substrate with phenyl(trimethylsilyl)acetylene afforded 2'-(trimethylsilyl)-3'-phenyldibenzo[a,c]indenone **5** in 39 % yield (Scheme 1). This relatively low yield is nearly identical to that reported earlier for the reaction of 2-iodobenzaldehyde with the same acetylene.[3] This process of annulation of silylacetylenes, followed by iodination and subsequent further annulation, offers a rapid, stepwise route to large polycyclic aromatic hydrocarbons.

Scheme 1



Bis-annulation using this methodology has also been demonstrated. Two equiv of 2-iodobiphenyl react with 1,4-di(phenylethynyl)benzene to give bis-1,4-(10-phenyl-9-phenanthryl)benzene in 77 % yield (Table 2, entry 34). In a related double annulation process, 1,4-diiodo-2,5-di(*p*-methoxyphenyl)benzene reacted with 2 equiv of diphenylacetylene to give 3,10-dimethoxy-5,6,12,13-tetraphenyldibenz[a,h]anthracene in 67 % yield (Table 2, entry 35).

This process is not general for all iodo-substituted biaryls. A summary of functionalized biaryls which failed to annulate internal acetylenes can be found in Table 3. Aryl triflates and diazonium salts were inadequate substrates in this process (Table 3, entries 1 and 2). The reaction of diphenylacetylene and 2-iodo-3-phenylindole or *N*-mesyl-2-phenyl-3-iodoindole gave none of the expected annulation products (Table 3, entries 3 and 4). Likewise, diphenylacetylene, 3,3-dimethyl-1-phenyl-1-butyne and 3-methyl-1-phenyl-1-butyn-3-ol all failed to give discernable annulation products when reacted with 3-iodo-2-phenylfuran (Table 3, entries 5-7). While one example of an annulation using 1-iodonaphthalene is included in Table 2 (entry 33), reactions using this substrate have not proven to be general in scope.

Table 3. 2-Functionalized Biaryls Which Failed to Annulate Internal Acetylenes Under Standard Reaction Conditions.[a]

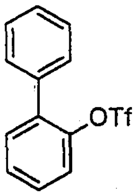
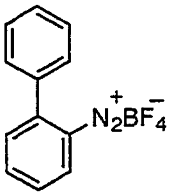
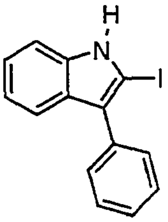
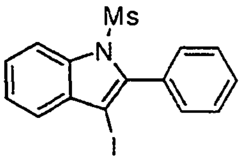
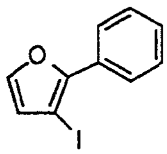
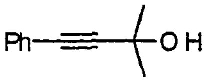
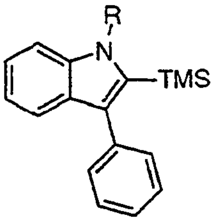
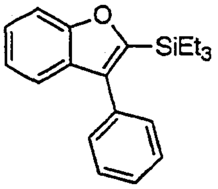
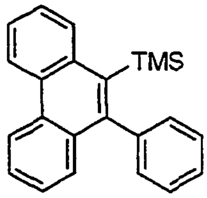
entry	functionalized biaryl	acetylene
1		Ph—≡—Ph
2		Ph—≡—Ph
3		Ph—≡—Ph
4		Ph—≡—Ph

Table 3 (continued)

5		Ph—≡—Ph
6		Ph—≡—*t*-Bu
7		 $Ph-\equiv-C(CH_3)_2OH$
8[b,c]	 R = H, Ac	Ph—≡—Ph
9[d]		Ph—≡—Ph
10[b]		Ph—≡—Ph

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[a] The following substrates gave either no annulation product or a complex mixture of products which could not be characterized.

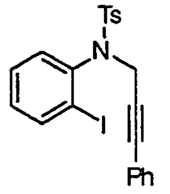
[b] Reactions run using Procedure A (see text and Table 2) and stoichiometric amounts of Pd(OAc)$_2$ and also using catalytic Pd(OAc)$_2$, DMSO, O$_2$ atmosphere.

[c] 3-Phenylindole was isolated from the reaction using 2-(trimethylsilyl)-3-phenylindole.

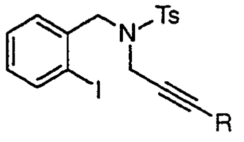
[d] Reaction run using a stoichiometric amount of Pd(OAc)$_2$ in DMF. No base or chloride salt were included.

The palladium-catalyzed annulation of internal acetylenes using arylsilanes has also been attempted. It was thought that the ipso electrophilic palladation of arylsilanes by $Pd(OAc)_2$ would lead directly to arylpalladium intermediates. These arylpalladium intermediates could then undergo acetylene insertion and subsequent annulation, generating a polycyclic aromatic and Pd(0). The feasibility of this type of process is supported by the addition of 3-methyl-2-(trimethylsilyl)indole to ethyl acrylate and methyl vinyl ketone in the presence of stoichiometric amounts of Pd(II).[12] In fact, reactions of this type might be carried out using either a stoichiometric amount of Pd(II) or using catalytic amounts of Pd(II) and a reoxidant. We have previously reported that many Pd(II)-catalyzed cyclization processes, including the cyclization of olefinic tosylamides,[13] acids[14] and alcohols,[15] can be carried out in DMSO using catalytic amounts of Pd(II) and only 1 atmosphere of O_2 as the reoxidant. Unfortunately, in practice arylsilanes were ineffective substrates for the annulation of internal acetylenes using either stoichiometric amounts of Pd(II) or the catalytic Pd(II)/O_2 procedure (Table 3, entries 8-10). The arylsilanes did not seem to undergo electrophilic palladation and were recovered unreacted from the reaction mixture.

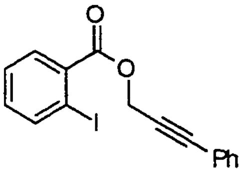
The palladium-catalyzed intramolecular cyclization of aryl iodides onto acetylenes with subsequent trapping of the vinylic palladium intermediate is well known in the literature.[16] Therefore, in a related project, the cyclization of aryl iodides bearing an acetylene group, followed by intermolecular acetylene addition and subsequent annulation onto the arene ring was attempted using several substrates (compounds **6-9**) with less than encouraging results. This cyclization-annulation process was attempted on compounds **6-9** using diphenylacetylene and procedure A, but, though the starting materials were consumed, no discernible products could be isolated. Under a variety of other reaction conditions, using



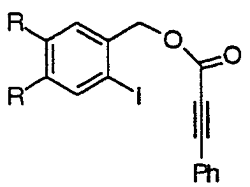
6



7a: R = TMS
7b: R = H

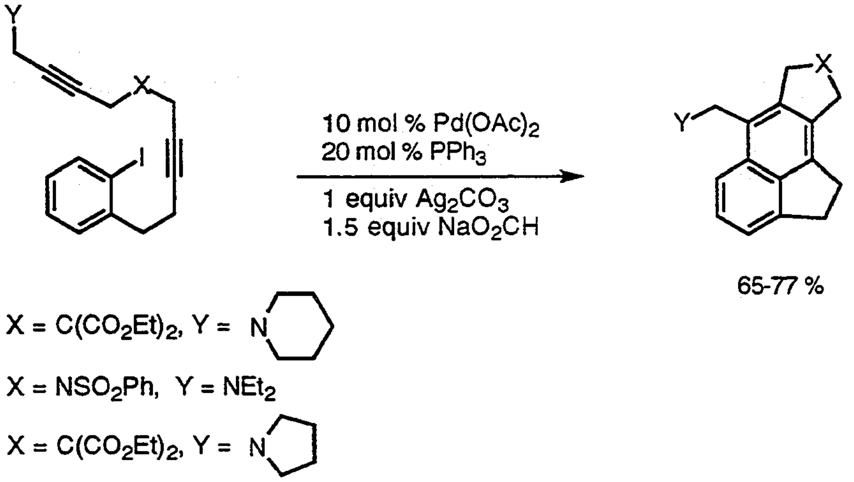


8



9a: R = H
9b: R = OCH_3

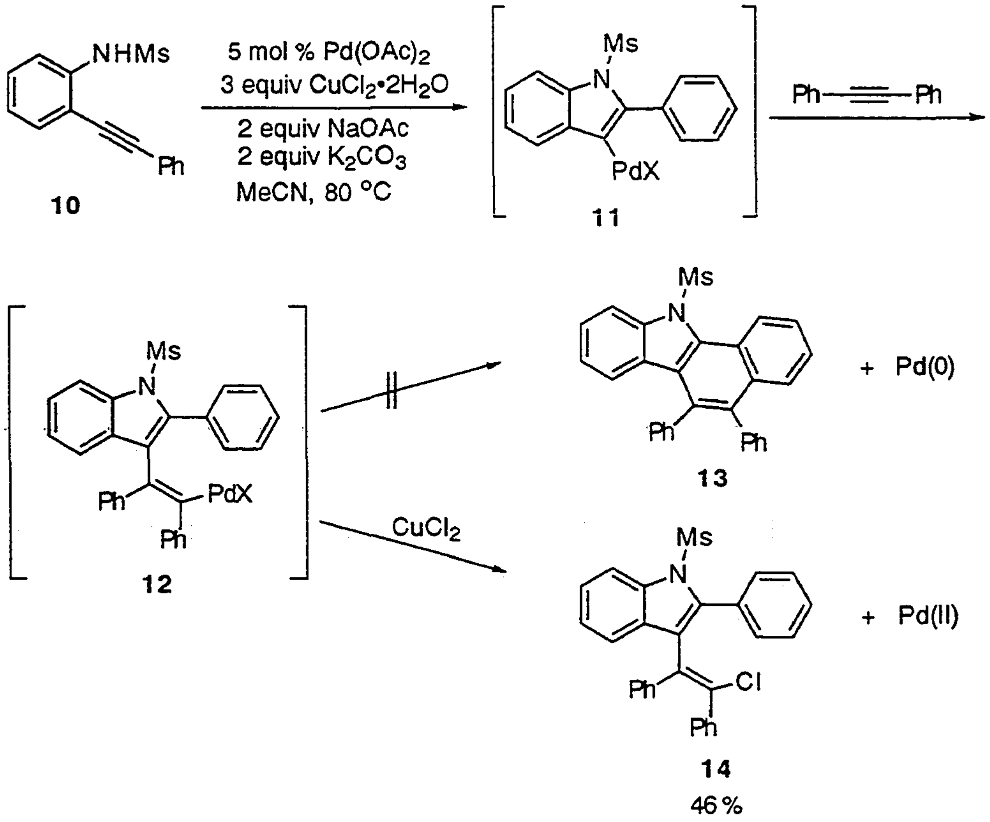
diphenylacetylene or 4,4-dimethyl-2-pentyne, no products resulting from external acetylene insertion were observed in reactions using substrates **6-9**. The failure of these substrates to undergo this cyclization-annulation process is curious, since Grigg has recently reported a similar process for the palladium-catalyzed synthesis of polyfused heterocycles (eq 7).[17]



(7)

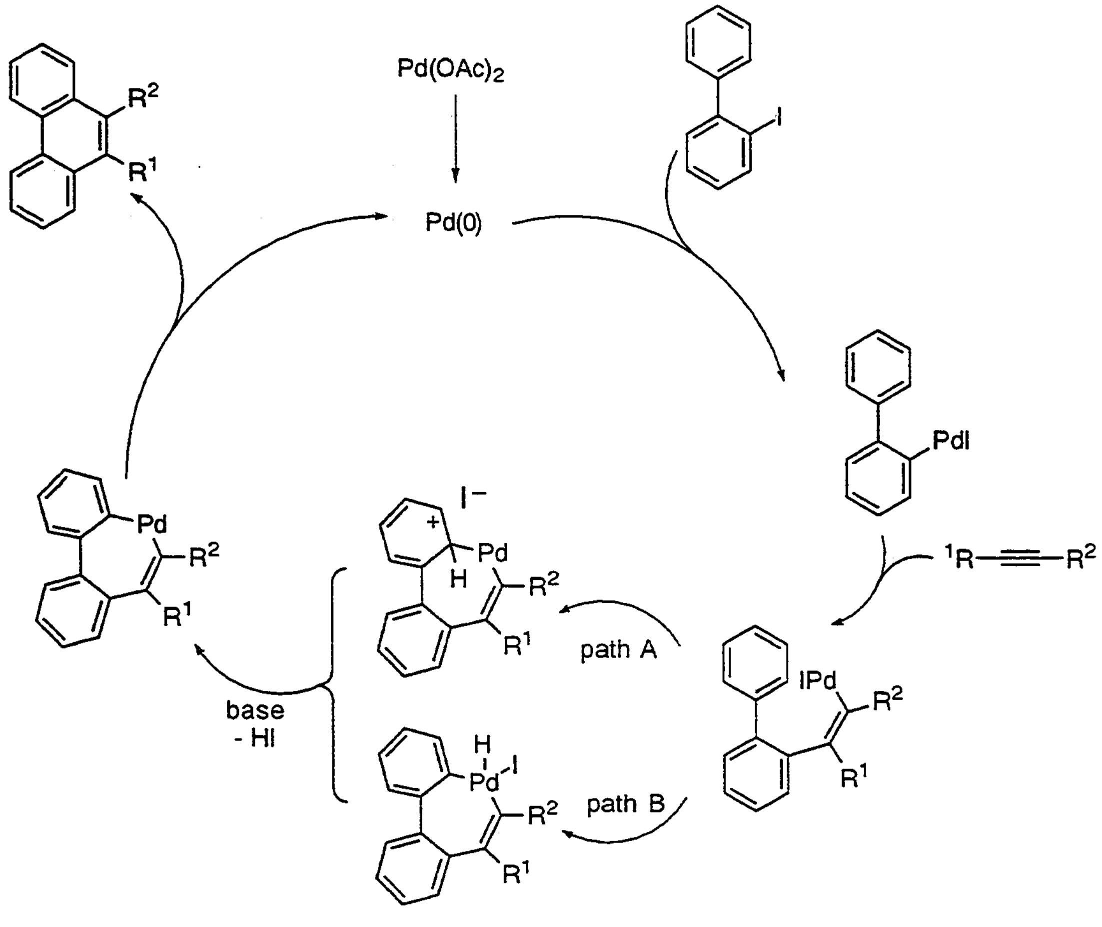
In addition, the tandem Pd(II)-catalyzed cyclization of *N*-mesyl-2-(phenylethynyl)aniline **10** with subsequent acetylene insertion and annulation was attempted.[18] Cyclization and acetylene insertion generated a vinylic palladium intermediate which failed to annulate onto the arene ring. Instead, under our conditions, this intermediate underwent chloride substitution giving the vinylic chloride product **14** in 46 % yield (Scheme 2).

Scheme 2

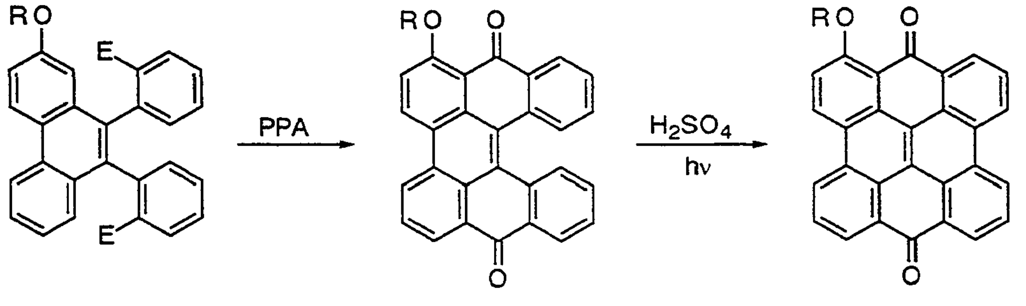


The mechanism of our carboannulation process has not yet been elucidated, but based upon the profound difference in the rate of annulation onto the MeO- versus the CF_3-substituted aromatic ring (Table 2, entries 4 and 5), as well as the preference of 2-(2'-iodophenyl)naphthalene for annulation in the 1-position (Table 2, entry 25), we tentatively propose a process involving oxidative addition of the aryl halide to produce an arylpalladium intermediate, which rapidly inserts the acetylene to produce a vinylic palladium species. This in turn undergoes electrophilic aromatic substitution, followed by reductive elimination of the observed product to regenerate Pd(0) (Scheme 3, path A). An alternative mechanistic route might involve oxidative addition of the neighboring aryl C-H bond to the vinylic palladium intermediate generating a Pd(IV) species, followed by reductive elimination of the product and HI, thus regenerating Pd(0) (Scheme 3, path B).

Scheme 3



Polycyclic aromatic hydrocarbons are ubiquitous pollutants formed in the combustion of organic matter.[19] Though many of these compounds are carcinogens of moderate potency, others possessing the phenanthrene and bianthrone skeletons possess interesting biological activity, including antiviral properties.[20] For example, hypericin is a natural product having the naphthodiathrone skeleton, which has demonstrated promising anti-HIV activity.[21] Our annulation process offers a general synthetic route to hypericin and a number of synthetic anologues of this molecule. 4-Methoxynaphthodianthrone **16a**, 4-hydroxynaphthodianthrone **16b** and 2,4,2',4'-tetramethoxynaphthodianthrone **17** have been synthesized in good yields from our readily available annulation products and will soon be submitted for biological testing (eqs 8 and 9). The sequential PPA catalyzed electrophilic cyclization, followed by the light induced ring closure in concd H_2SO_4 was necessary, since concd H_2SO_4 did not efficiently catalyze the acylation reaction. The purification of **15a** was difficult and for this reason the isolated yield of this synthetic intermediate was only 50 %. Due to the greater solubility of **15b** in organic solvents, the isolation and purification was much easier, affording the product in 90 % yield. Problems associated with the isolation and purification of **15a,b** could be avoided by directly treating the crude product mixture of the PPA reaction with concd H_2SO_4 and hv to afford the naphthodianthrones **16a,b** in 79 % and 85 % yields respectively.



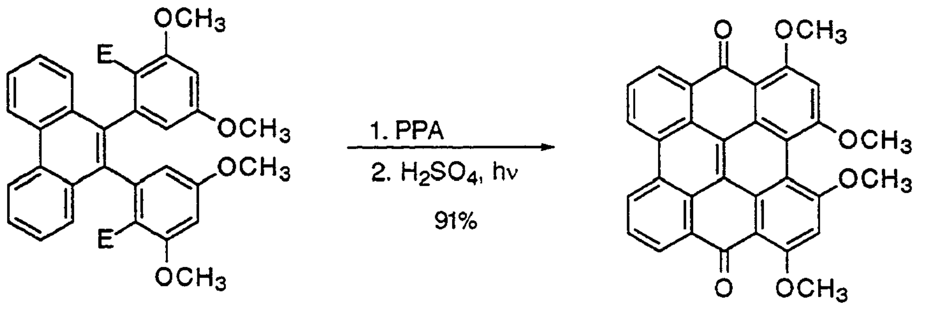
E = CO_2CH_3

15a,b

16a,b

(8)

a : R = Me, 79 % overall
b : R = H , 85 % overall



E = CO_2CH_3

17

(9)

Conclusion

The palladium-catalyzed carboannulation of internal acetylenes using biaryls has been shown to be a process which is quite general in scope. A wide variety of internal alkynes can be annulated using this chemistry, though the reaction is most general for aryl acetylenes or hindered alkyl or silyl acetylenes. Functionalization of the biaryl seems to have little effect on the product yields. The regiochemistry of the acetylene insertion, though generally not high, can be influenced by both the steric bulk of the acetylene substituents, as well as substituents on the biaryl. This methodology provides an exceptionally efficient route to a wide variety of substituted polycyclic aromatic hydrocarbons from readily available starting materials, affording the products in moderate to excellent yields.

Experimental

General. All ^1H and ^{13}C NMR spectra were recorded at 30 and 75.5 MHz respectively. Thin-layer chromatography was performed using commercially prepared 60-mesh silica gel plates (Whatman K6F), and visualization was effected with short wavelength UV light (254 nm) or basic $KMnO_4$ solution [3 g of $KMnO_4$ + 20 g of K_2CO_3 + 5 mL of NaOH (5%) + 300 mL of H_2O]. All melting points are uncorrected.

Reagents. All reagents were used directly as obtained commercially unless otherwise noted. All palladium reagents were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co., Ltd unless otherwise noted. 2-Iodoaniline, *p*-toluenesulfonyl chloride, methanesulfonyl chloride, diphenylacetylene, 1-phenyl-2-(trimethylsilyl)acetylene, 1-(trimethylsilyl)-1-propyne, 1-phenyl-1-propyne, 1-iodo-4-(trifluoromethyl)benzene, 4-bromoanisole, 3-bromoanisole, 2-bromoanisole, 3-iodotoluene, 4-(dimethylamino)pyridine, bis(triphenylphosphine)palladium(II)chloride, MeLi and 2,2,6,6-tetramethylpiperidine were purchased from Aldrich Chemical Co., Inc. 2-Iodobiphenyl, 2-iodonaphthalene, 4,4-dimethyl-2-butyne and 2-hydroxy-4,6-dimethoxybenzoic acid were purchased from Lancaster Synthesis, Inc. 1,4-Diiodobenzene, 1-bromo-2-iodobenzene and iodobenzene were purchased form Eastman Chemical. 3-Hydroxycarbonyl-5-(phenylethynyl)pyridine was purchased from Maybridge Chemical Co., Ltd.

Preparation of Alkynes.

3,3-Dimethyl-1-phenyl-1-butyne. Prepared from phenyl(trimethylsilyl)acetylene according to a literature procedure giving a clear, colorless liquid with spectral properties matching those in previous reports.[22]

Phenyl(triethylsilyl)acetylene. Prepared by reacting lithium phenylacetylide with chlorotriethylsilane as described in a literature procedure:[23] ^{1}H NMR ($CDCl_3$) δ 0.66 (q, 6 H, J = 7.8 Hz), 1.05 (t, 9 H, J = 7.8 Hz), 7.27-7.29 (m, 3 H), 7.46-7.48 (m, 2 H).

3-Methoxycarbonyl-5-(phenylethynyl)pyridine. Obtained as a white solid in 95 % yield by refluxing 3-hydroxycarbonyl-5-(phenylethynyl)pyridine in acidic methanol:[8] mp 91-92 °C; ^{1}H NMR ($CDCl_3$) δ 3.98 (s, 3 H), 7.35-7.41 (m, 3 H), 7.54-7.58 (m, 2 H), 8.41 (t, 1 H, J = 2.1 Hz), 8.90 (d, 1 H, J = 1.8 Hz), 9.14 (d, 1 H, J = 2.1 Hz).

1-Bromo-2-(phenylethynyl)benzene. Obtained as a clear, colorless oil from the palladium-catalyzed reaction of 1-bromo-2-iodobenzene with phenylacetylene according to a literature procedure:[24] ^{1}H NMR ($CDCl_3$) δ 7.14 (dt, 1 H, *J* = 7.5, 1.5 Hz), 7.25 (dt, 1 H, *J* = 7.8, 1.5 Hz), 7.33-7.40 (m, 3 H), 7.53-7.63 (m, 4 H).

Methyl 2-hydroxy-4,6-dimethoxybenzoate. Obtained as a white solid from 2-hydroxy-4,6-dimethoxybenzoic acid following a literature procedure:[25] ^{1}H NMR ($CDCl_3$) δ 3.80 (s, 3 H), 3.82 (s, 3 H), 3.91 (s, 3 H), 5.95 (d, 1 H, *J* = 3.0 Hz), 6.10 (d, 1 H, *J* = 3.0 Hz), did not find OH.

Methyl 2-(trifluoromethanesulfonyloxy)-4,6-dimethoxybenzoate. Obtained as a white solid in 70 % yield (overall yield for this and the previous step) from the reaction of methyl 2-hydroxy-4,6-dimethoxybenzoate with Tf_2O in pyridine at -10 °C and allowing it to stir while warming to room temperature:[26] mp 62-64 °C; ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3 H), 3.86 (s, 3 H), 3.91 (s, 3 H), 6.42 (d, 1 H, *J* = 3.0 Hz), 6.47 (d, 1 H, *J* = 3.0 Hz).

Methyl 2-(triethylsilylethynyl)-4,6-dimethoxybenzoate. Obtained as a white solid in 98 % yield from the reaction of methyl 2-(trifluoromethanesulfonyloxy)-4,6-dimethoxybenzoate with (triethylsilyl)acetylene and a palladium catalyst according to a literature procedure:[24] ^{1}H NMR ($CDCl_3$) δ 0.65 (q, 6 H, *J* = 7.5 Hz), 1.03 (t, 9 H, *J* = 7.5 Hz), 3.79 (s, 3 H), 3.80 (s, 3 H), 3.88 (s, 3 H), 6.44 (d, 1 H, *J* = 1.5 Hz), 6.59 (d, 1 H, *J* = 1.5 Hz).

Methyl 2-ethynyl-4,6-dimethoxybenzoate. Obtained as a white solid in 93 % yield by treating methyl 2-(triethylsilylethynyl)-4,6-dimethoxybenzoate with KF according to a literature procedure:[27] ^{1}H NMR ($CDCl_3$) δ 3.17 (s, 1 H), 3.80 (s, 6 H), 3.90 (s, 3 H), 6.47 (d, 1 H, *J* = 3.0 Hz), 6.63 (d, 1 H, *J* = 3.0 Hz).

Di(2-methoxycarbonylphenyl)acetylene. Obtained as a light yellow solid in 54 % yield from the palladium/copper-catalyzed reaction of methyl 2-iodobenzoate with acetylene according to a literature procedure:[24] mp 94.5-95.5 °C; ^{1}H NMR ($CDCl_3$) δ 3.96 (s, 6 H), 7.40 (dt, 2 H, J = 7.8, 1.5 Hz), 7.51 (dt, 2 H, *J* = 7.5, 1.2 Hz), 7.72 (dd, 2 H, *J* = 7.8, 0.9 Hz), 7.99 (dd, 2 H, *J* = 7.8, 1.2 Hz).

Di(3,5-dimethoxy-2-methoxycarbonylphenyl)acetylene. Obtained as a white solid from the palladium-catalyzed reaction of methyl 2-ethynyl-3,5-dimethoxybenzoate and methyl 2-(trifluoromethanesulfonyloxy)-3,5-dimethoxybenzoate:[28] mp 149 °C; ^{1}H NMR ($CDCl_3$) δ 3.82 (s, 12 H), 3.92 (s, 6 H), 6.48 (d, 2 H, J = 0.9 Hz), 6.62 (d, 2 H, J = 0.9 Hz).

1,4–Di(phenylethynyl)benzene. Obtained as a white solid in 94 % yield from the palladium-catalyzed reaction of 1,4-diiodobenzene with phenylacetylene according to a literature procedure:[24] mp 178-180 °C (lit. mp[29] 178-179, 181-182 °C); ^{1}H NMR ($CDCl_3$) δ 7.34–7.40 (m, 6 H), 7.50-7.57 (m, 8 H).

Preparation of Starting Biaryls.

2-Iodo-4'-methoxybiphenyl. Obtained as a white solid in 39 % yield following a procedure by Hart *et al.*:[30] mp 59-60 °C; ^{1}H NMR ($CDCl_3$) δ 3.86 (s, 3 H), 6.94 (d, 2 H, J = 8.7 Hz), 7.00 (dt, 1 H, J = 7.8, 1.8 Hz), 7.24-7.31 (m, 3 H), 7.36 (dt, 1 H, J = 7.5, 0.9 Hz), 7.93 (dd, 1 H, J = 7.8, 0.9 Hz).

2-Iodo-3'-methylbiphenyl. Obtained as a clear colorless oil in 51 % yield following a procedure by Hart *et al.*:[30] ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3 H), 7.00 (dt, 1 H, J = 7.8, 1.8 Hz), 7.10-7.42 (m, 6 H), 7.92 (d, 1 H, J = 7.8 Hz).

4'-Trifluoromethyl-2-iodobiphenyl. Obtained as a clear colorless oil following a procedure by Hart *et al.*:[30] ^{1}H NMR ($CDCl_3$) δ 7.06 (dt, 1 H, J = 7.5, 1.5 Hz), 7.26 (dd, 1 H, J = 9.8, 1.8 Hz), 7.39 (d, 1 H, J = 7.5 Hz), 7.44 (d, 2 H, J = 8.1 Hz), 7.68 (d, 2 H, J = 8.1 Hz), 7.96 (d, 1 H, J = 8.1 Hz).

4-(2'-Iodophenyl)phenol. Obtained as an off white solid in quantitative yield by treating 2-iodo-4'-methoxybiphenyl with BBr_3 according to a literature procedure:[31] ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 1 H), 6.87 (d, 2 H, J = 8.1 Hz), 7.00 (t, 1 H, J = 7.8 Hz), 7.22 (d, 2 H, J = 8.4 Hz), 7.24-7.39 (m, 2 H), 7.93 (d, 1 H, J = 8.1 Hz).

2-Iodo-2'-methoxybiphenyl. Obtained as a white solid in approximately 40 % yield following a procedure by Hart *et al.*:[30] m.p. 55-57 °C; ^{1}H NMR (CDCl$_3$) δ 3.77 (s, 3 H), 6.95 (d, 1 H, *J* = 6.0 Hz), 7.02 (dt, 2 H, *J* = 6.0, 0.9 Hz), 7.10 (dd, 1 H, *J* = 6.0, 1.5 Hz), 7.25 (dd, 1 H, *J* = 6.0, 1.5 Hz), 7.35-7.45 (m, 2 H), 7.91 (dd, 1 H, *J* = 6.0, 0.9 Hz).

2-Iodo-3'-methoxybiphenyl. Obtained as a clear, colorless oil following a procedure by Hart *et al.*.[30] The yield of this product was undetermined: ^{1}H NMR (CDCl$_3$) δ 3.83 (s, 3 H), 6.86-6.95 (m, 3 H), 7.01 (dt, 1 H, *J* = 9.0, 1.5 Hz), 7.28-7.35 (m, 3 H), 7.92 (dd, 1 H, *J* = 9.0, 0.9 Hz).

1-(2'-Iodophenyl)naphthalene. Obtained as a white solid in 47 % yield following a procedure by *Hart et al.*:[30] mp 109-111 °C; ^{1}H NMR (CDCl$_3$) δ 7.11 (dt, 1 H, *J* = 7.8, 1.5 Hz), 7.33 (t, 2 H, *J* = 7.8 Hz), 7.40-7.57 (m, 5 H), 7.90 (d, 2 H, *J* = 8.7 Hz), 8.00 (dd, 1 H, *J* = 8.1, 0.9 Hz).

2-(2'-Iodophenyl)naphthalene. Obtained as a white solid in 46 % yield following a procedure by *Hart et al.*:[30] mp 78-80 °C (lit. mp[30] 80-82 °C); ^{1}H NMR (CDCl$_3$) δ 7.02-7.09 (m, 1 H), 7.37-7.42 (m, 2 H), 7.47-7.54 (m, 3 H), 7.79 (s, 1 H), 7.85-7.91 (m, 3 H), 7.97 (dd, 1 H, *J* = 7.5, 0.9 Hz).

2-(Phenylethynyl)anisole. Prepared in 60 % yield from the palladium-catalyzed coupling of 2-iodoanisole and phenylacetylene according to a literature procedure:[24] ^{1}H NMR (CDCl$_3$) δ 3.89 (s, 3 H), 6.87 (d, 1 H, *J* = 8.4 Hz), 6.92 (dt, 1 H, *J* = 7.5, 0.9 Hz), 7.25-7.36 (m, 4 H), 7.48 (dd, 1 H, *J* = 7.8, 1.8 Hz), 7.54-7.58 (m, 2 H).

2-Phenyl-3-iodobenzofuran. Prepared by treating 2-(phenylethynyl)anisole with mercuric acetate in glacial acetic acid at rt. The resulting solution was stirred at rt for 30 min, then poured into a sat'd NaCl-ice mixture.[32] The solid 3-(chloromercurio)-2-phenylbenzofuran was collected by filtration and without further purification was iodinated by stirring with I_2 in chloroform at rt for 3 h. The solution was diluted with ether, washed with 10 % $NaHSO_3$ and water, concentrated and purified by column chromatography to give 2-phenyl-3-

iodobenzofuran as a white solid in 76 % overall yield:[32] mp 39.5-41.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.25-7.52 (m, 7 H), 8.14 (d, 1 H, *J* = 6.6 Hz), 8.15 (d, 1 H, *J* = 8.7 Hz).

2-Iodo-3-phenylbenzofuran. Prepared in 63 % overall yield from 2-(trimethylsilyl)-3-phenylbenzofuran. 2-(Trimethylsilyl)-3-phenylbenzofuran was desilylated using 3 equiv of $KF \cdot 2H_2O$ and 3 equiv of TBAC in CH_3CN at 80 °C for 4 h according to a literature procedure[27] and purified by column chromatography using hexanes as the eluant to give **3-phenylbenzofuran** as a clear, colorless oil in 100 % yield: ^{1}H NMR ($CDCl_3$) δ 7.28-7.36 (m, 3 H), 7.45 (m, 2 H), 7.53 (m, 1 H), 7.62 (m, 2 H), 7.76 (s, 1 H), 7.81 (dd, 1 H, *J* = 6.9 Hz, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 111.8, 120.4, 122.3, 123.0, 124.6, 126.5, 127.5, 127.5, 129.0, 132.1, 141.3, 155.8. 3-Phenylbenzofuran was then treated with ICl in CH_2Cl_2 at room temperature for 3 h in a foil covered vial.[33] The reaction was diluted with ether, washed with 10 % $NaHSO_3$ and water, concentrated and purified by column chromatography to give 2-iodo-3-phenylbenzofuran in 63 % yield as a white solid: ^{1}H NMR (CDCl3) δ 7.24-7.33 (d of quintets, 2 H, *J* = 7.8, 1.8 Hz), 7.37-7.41 (m, 1 H), 7.43-7.52 (m, 3 H), 7.59-7.66 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 111.1, 116.2, 119.7, 123.6, 124.7, 127.9, 127.9, 128.7, 128.8, 130.4, 137.7, 153.5.

9-Iodo-10-phenylphenanthrene. 9-Trimethylsilyl-10-phenylphenanthrene (0.5 mmol) was treated with ICl (0.6 mmol) in 1.0 mL of CH_2Cl_2 at room temperature and stirred for 2 h in an aluminum foil covered vial.[33] The reaction was then diluted with ether, washed with 10 % $NaHSO_3$ and water, concentrated and purified by column chromatography to give the product in 75 % yield as a pale yellow solid: ^{1}H NMR ($CDCl_3$) δ 7.26 (dd, 2 H, *J* = 7.8, 1.8 Hz), 7.36-7.40 (m, 2 H), 7.49-7.56 (m, 3 H), 7.60-7.69 (m, 3 H), 8.44-8.47 (m, 1 H), 8.64-8.66 (m, 1 H), 8.68 (d, 1 H, *J* = 8.1 Hz); GCMS for $C_{20}H_{13}I$: calcd 380, found 380.

1,4-Diiodo-2,5-di(4'-methoxyphenyl)benzene. Obtained as a white solid in very low yield following a procedure by *Hart et al.*:[30] mp 235-237 °C; ^{1}H NMR ($CDCl_3$) δ 5.87 (s, 6 H), 6.95 (d, 4 H, *J* = 9.0 Hz), 7.29 (d, 4 H, *J* = 8.7 Hz), 7.85 (s, 2 H).

9-(1,3-Dioxan-2-yl)-10-iodophenanthrene. Obtained as a yellow solid from the reaction of 9-(trimethylsilyl)-10-(1,3-dioxan-2-yl)phenanthrene (0.5 mmol) with ICl (0.6 mmol) in methylene chloride (1.0 mL) at room temperature for 2 h in an aluminum foil covered vial:[33] ^{1}H NMR (of crude mixture) ($CDCl_3$) δ 1.25 (d, 1 H, *J* = 13.8 Hz), 2.46-2.59 (m, 1 H), 4.18 (dt, 2 H, *J* = 12.3, 2.1 Hz), 4.38 (m, 2 H), 6.78 (s, 1 H), 7.59-7.70 (m, 4 H), 8.47 (dd, 1 H, *J* = 6.3, 2.1 Hz), 8.50 (dd, 1 H, *J* = 6.6, 2.4 Hz), 8.62 (dd, 1 H, *J* = 6.6, 2.1 Hz), 9.14 (dd, 1 H, *J* = 7.5, 2.1 Hz).

9-Formyl-10-iodophenanthrene. Obtained as a white solid by treating 9-iodo-10-(1,3-dioxan-2-yl)phenanthrene with acidic THF at room temperature for 8 h and purifying by column chromatography.[34] The yield for the two reaction sequence from 9-trimethylsilyl-10-(1,3-dioxan-2-yl)phenanthrene was 49 %: mp 143-144 °C; ^{1}H NMR ($CDCl_3$) δ 7.55-7.67 (m, 4 H), 8.36 (dd, 1 H, *J* = 8.4, 1.2 Hz), 8.42 (d, 1 H, *J* = 8.1 Hz), 8.53 (d, 1 H , *J* = 8.1 Hz), 8.56 (dd, 1 H, *J* = 6.9, 0.9 Hz), 10.39 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 111.4, 122.7, 122.7, 125.0, 127.8, 128.0, 128.2, 128.6, 129.9, 130.2, 130.9, 131.8, 133.6, 133.7, 199.1.

2-(Trifluoromethanesulfonyloxy)biphenyl. Obtained as a clear, colorless liquid in quantitative yield by treating 2-phenylphenol (5 mmol) with Tf_2O (5.5 mmol) and pyridine (5.0 mL) at -10 °C and allowing it to stir while warming to room temperature:[26] ^{1}H NMR ($CDCl_3$) δ 7.35-7.51 (m, 9 H).

General procedure for palladium-catalyzed carboannulation. To a 2 dram vial equipped with a stir bar is added $Pd(OAc)_2$ (0.125 mmol), NaOAc (0.50 mmol), either LiCl (0.25 mmol) or TBAC (0.75 mmol), the aryl iodide (0.25 mmol), the appropriate alkyne (0.25 or 0.50 mmol) and 5 mL of DMF. The vial is then flushed with N_2, capped with a screw cap containing a teflon liner and placed in an oil bath at 100 °C for the specified length of time (see tables). The vial is then removed from the oil bath, diluted with Et_2O and/or EtOAc, washed with sat'd NH_4Cl and water, dried over $MgSO_4$ and concentrated. This residue was then either purified by column chromatography or washed and/or recrystallized with MeOH and/or Et_2O.

Spectral Data

9-*t*-Butyl-10-phenylphenanthrene (Table 2, entry 1). Obtained as a white solid in 95 % yield as a 11:1 mixture of the desired product **1** and the vinylic biaryl **2** from the reaction of 2-iodobiphenyl and 1-phenyl-3,3-dimethyl-1-butyne using procedure B and purified by column chromatography using hexanes as eluent. After recrystallization from methanol, the pure product was obtained in 80 % yield: mp 168-170 °C (MeOH); ^1H NMR ($CDCl_3$) δ 1.42 (s, 9 H), 7.19-7.25 (m, 1 H), 7.30-7.36 (m, 3 H), 7.39-7.44 (m, 3 H), 7.49-7.61 (m, 3 H), 8.57 (dd, 1 H, J = 7.8, 2.1 Hz), 8.61 (d, 1 H, J = 8.4 Hz), 8.74 (dd, 1 H, J = 7.5, 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 35.12, 38.52, 121.81, 123.34, 124.53, 125.29, 125.96, 126.22, 126.96, 127.41, 127.68, 129.26, 129.42, 131.42, 131.62, 131.81, 133.42, 136.65, 141.13, 142.73; IR ($CHCl_3$) 2957, 1652, 1558, 1429, 1285, 1232 cm^{-1}; HRMS for $C_{24}H_{22}$: calcd 310.1722, found 310.1719.

9-*t*-Butyl-10-methylphenanthrene (Table 2, entry 2). Obtained as a clear, colorless oil in 63 % yield from the reaction of 2-iodobiphenyl with 4,4-dimethyl-2-butyne using procedure B and purified by column chromatography using hexanes as eluent: m.p. 60-61 °C (MeOH); ^1H NMR ($CDCl_3$) δ 1.71 (s, 9 H), 2.78 (s, 3 H), 7.40-7.51 (m, 2 H), 7.52-7.61 (m, 2 H), 8.03-8.06 (m, 1 H), 8.31 (dd, 1 H, J = 7.2, 1.5 Hz), 8.56 (d, 2 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 21.3, 33.6, 38.5, 122.3, 123.2, 123.8, 124.1, 124.4, 125.6, 126.6, 126.9, 129.3, 130.2, 130.9, 132.5, 134.0, 142.4; IR ($CHCl_3$) 3071, 3023 (sp^2 C-H), 2957, 2869, 1570, 1489, 1197 cm^{-1}; HRMS for $C_{19}H_{20}$: calcd 248.1565, found 248.1569.

9-Methyl-10-phenylphenanthrene (Table 2, entry 3). Obtained as a white solid in 45 % yield from the reaction of 2-iodobiphenyl and 1-phenyl-1-propyne using procedure B and purified by column chromatography using hexanes as eluent: mp 94-97 °C (~3:1 MeOH/Et_2O); ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 3 H), 7.29-7.70 (m, 10 H), 8.15 (dd, 1 H, J = 7.5, 4.5 Hz), 8.72 (d, 1 H, J = 8.4 Hz), 8.77 (dd, 1 H, J = 7.5, 4.5 Hz); ^{13}C NMR ($CDCl_3$) δ 17.4, 122.4, 122.9, 125.1, 125.6, 126.2, 126.4, 126.8, 127.0, 127.5, 128.4, 129.4, 129.8, 130.0, 130.4, 131.9, 132.3, 137.1, 140.7; IR ($CHCl_3$) 3074, 2954, 1558, 1489, 1442 cm^{-1}; HRMS for $C_{21}H_{16}$: calcd 268.1252, found 268.1248.

2-Methoxy-9,10-diphenylphenanthrene (Table 2, entry 4). Obtained as a pale yellow solid in 86 % yield from the reaction of 2-iodo-4'-methoxybiphenyl and diphenylacetylene using procedure A. After the normal workup, drying and concentrating, the resultant solid was washed with MeOH and Et_2O to give essentially pure product: mp 241-242 °C (toluene); ^{1}H NMR ($CDCl_3$) δ 3.71 (s, 3 H), 6.93 (d, 1 H, J = 2.7 Hz), 7.12-7.27 (m, 9 H), 7.27 (d, 1 H, J = 2.7 Hz), 7.31 (d, 1 H, J = 2.7 Hz), 7.41 (t, 1 H, J = 7.2 Hz), 7.51 (d, 1 H, J = 7.5 Hz), 7.63 (t, 1 H, J = 7.2 Hz), 8.70 (d, 1 H, J = 11.4 Hz), 8.71 (d, 1 H, J = 9.3 Hz); ^{13}C NMR ($CDCl_3$) δ 55.2, 109.1, 116.4, 122.1, 124.2, 124.6, 125.7, 126.5, 126.6, 127.6, 127.7, 128.0, 130.3, 131.1, 131.1, 133.5, 136.9, 137.9, 139.8, 139.8, 158.5 (two sp^2 C missing due to overlap); HRMS for $C_{27}H_{20}O$: calcd 368.1960, found 368.1965; Anal. Calcd for $C_{27}H_{20}O$: C, 89.96; H, 5.60. Found: C, 90.22; H, 5.67.

2-Trifluoromethyl-9,10-diphenylphenanthrene (Table 2, entry 5). Obtained as a white solid in 69 % yield from the reaction of 2-iodo-4'-(trifluoromethyl)biphenyl and diphenylacetylene using procedure A after purification by column chromatography using hexanes as eluent: mp 176-178 °C (hexanes); ^{1}H NMR ($CDCl_3$) δ 7.08-7.34 (m, 10 H), 7.50-7.59 (m, 2 H), 7.69 (dt, 1 H, J = 6.6, 1.5 Hz), 7.82-7.94 (m, 2 H), 8.79 (d, 1 H, J = 8.4 Hz), 8.87 (d, 1 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 122.2, 122.6, 122.9, 123.5, 125.1, 126.2, 126.8, 127.0, 127.0, 127.7, 127.9, 128.1, 128.6, 129.3, 130.9, 130.9, 131.5, 132.1, 132.6, 137.2, 138.5, 138.7, 139.0; IR ($CHCl_3$) 3061, 3019, 1575, 1480, 1335, 1216, 1128 cm^{-1}; HRMS for $C_{27}H_{17}F_3$: calcd 398.1282, found 398.1290.

4-Methoxy-9,10-diphenylphenanthrene (Table 2, entry 6). Obtained as a white solid in 84% yield using procedure A. After the normal workup, drying and concentrating, the resultant solid was washed with MeOH and Et_2O to give essentially pure product: mp 189-191 °C (toluene); ^1H NMR ($CDCl_3$) δ 4.14 (s, 3 H), 7.10-7.23 (m, 12 H), 7.36-7.47 (m, 2 H), 7.54 (dd, 1 H, *J* = 7.8, 1.5 Hz), 7.63 (dt, 1 H, *J* = 7.8, 1.5 Hz), 9.82 (d, 1 H, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0, 108.4, 120.7, 120.8, 125.9, 126.1, 126.3, 126.3, 126.4, 127.4, 127.6, 128.5, 130.0, 131.0, 131.0, 132.4, 134.4, 137.2, 138.1, 139.9, 140.3, 158.7; IR (nujol) 3056, 3018, 1216, 1081 cm^{-1}; HRMS for $C_{27}H_{20}O$: calcd 360.1514, found 360.1525.

2-Methoxy-9,10-di(2'-methoxycarbonylphenyl)phenanthrene (Table 2, entry 7). Obtained as an off-white solid in 76 % yield from the reaction of 2-iodo-4'-methoxybiphenyl and di(2'-methoxycarbonylphenyl)acetylene using procedure A. After the normal workup, drying and concentrating, the resulting solid was washed with MeOH and Et_2O to give essentially pure product: m.p. 239-241 °C (toluene); ^1H NMR ($CDCl_3$) δ 3.39 (s, 3 H), 3.42 (s, 3 H), 3.67 (s, 3 H), 6.69 (d, 1 H, *J* = 2.7 Hz), 7.09 (d, 2 H, *J* = 7.8 Hz), 7.10-7.38 (m, 7 H), 7.57 (dt, 1 H, *J* = 6.9, 1.2 Hz), 7.80 (d, 2 H, *J* = 7.8 Hz), 8.65 (d, 1 H, *J* = 8.1 Hz), 8.67 (d, 1 H, *J* = 9.3 Hz); ^{13}C NMR ($CDCl_3$) δ 51.6, 51.7, 55.22, 109.1, 115.7, 122.0, 124.1, 124.1, 125.4, 126.2, 127.1, 127.2, 127.7, 129.7, 130.3, 130.3, 131.0, 131.1, 131.2, 131.3, 131.4, 133.2, 133.2, 133.7, 135.6, 136.6, 140.4, 140.5, 158.1, 166.8, 166.9; HRMS for $C_{31}H_{24}O_5$: calcd 476.1624, found 476.1633; Anal. Calcd for $C_{31}H_{24}O_5$: C, 78.12; H, 5.08. Found: C, 78.16; H, 5.24.

2-Hydroxy-9,10-di(2'-methoxycarbonylphenyl)phenanthrene (Table 2, entry 8). Obtained as an off-white solid in 69 % yield from the reaction of 2-iodo-4'-hydroxybiphenyl and di(2'-methoxycarbonylphenyl)acetylene using procedure A. After the normal workup, drying and concentrating, the resultant solid was washed with MeOH and Et_2O to give essentially pure product: mp 234-237 °C (decomposed, $CHCl_3$/hexane); ^1H NMR

($CDCl_3$) δ 3.41 (s, 3 H), 3.44 (s, 3 H), 5.08 (broad s, 1 H), 6.64 (d, 1 H, *J* = 2.7 Hz), 7.09 (dd, 2 H, *J* = 7.2, 0.9 Hz), 7.21 (dd, 1 H, *J* = 9.0, 2.7 Hz), 7.20-7.40 (m, 6 H), 7.58 (dt, 1 H, *J* = 7.2, 1.2 Hz), 7.82 (d, 2 H, *J* = 7.8 Hz), 8.65 (d, 2 H, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 51.7, 51.8, 111.3, 116.2, 121.9, 124.1, 124.5, 125.5, 126.3, 127.2, 127.2, 127.7, 129.7, 130.3, 130.3, 131.0, 131.1, 131.2, 131.3, 133.1, 133.2, 133.9, 135.2, 136.7, 140.4, 154.1, 166.8, 166.9 (two sp^2 C missing due to overlap); IR ($CDCl_3$) 3208, 3061, 2950, 2842, 1724, 1714, 1293, 1256, 1128, 1077 cm^{-1}; HRMS for $C_{30}H_{22}O_5$: calcd 462.1472, found 462.1467.

3-(Hydroxycarbonyl)-5-(10'-phenylphenanthr-9'-yl)pyridine (Table 2, entry 9). A white solid obtained in 55 % yield from the reaction of 2-iodobiphenyl and 3-hydroxycarbonyl-5-(phenylethynyl)pyridine using procedure A. The product was purified by base extraction of the crude reaction mixture: mp 275-290 °C (decomposed, ether); ^1H NMR ($CDCl_3$) δ 3.34 (broad s, 1 H), 7.14-7.32 (m, 6 H), 7.38 (dd, 1 H, *J* = 9.0, 0.9 Hz), 7.56 (dt, 2 H, *J* = 7.8, 0.96 Hz), 7.65 (dt, 2 H, *J* = 9.0, 0.9 Hz), 8.05 (t, 1 H, *J* = 1.2 Hz), 8.58 (d, 1 H, *J* = 1.5 Hz), 8.91 (d, 1 H, *J* = 1.2 Hz), 8.98 (d, 1 H, *J* = 6.0 Hz), 9.00 (d, 1 H, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 123.1, 123.3, 125.7, 126.5, 127.1, 127.2, 127.3, 127.5, 128.0, 128.1, 129.6, 129.8, 130.6, 130.7, 130.7, 130.9, 132.2, 134.8, 138.1, 138.3, 138.6, 148.6, 154.6, 166.1; IR (nujol) 3000-2500, 1684, 1596, 1461 cm^{-1}; HRMS for $C_{26}H_{17}NO_2$: calcd 375.1259, found 375.1262.

3-(Methoxycarbonyl)-5-(10'-phenylphenanthr-9'-yl)pyridine (Table 2, entry 10). Obtained as an off-white solid in 84 % yield from the reaction of 2-iodobiphenyl and 3-methoxycarbonyl-5-(phenylethynyl)pyridine using procedure A. After the normal work-up, drying and concentrating, the resultant solid was washed with MeOH and Et_2O to give essentially pure product: mp 209-211 °C ($CHCl_3$/hexane); ^1H NMR ($CDCl_3$) δ 3.92 (s, 3 H), 7.09 (dd, 1 H, *J* = 9.0, 1.2 Hz), 7.20-7.29 (m, 4 H), 7.42 (d, 1 H, *J* = 7.8 Hz), 7.50-7.54 (m, 3 H), 7.69 (dt, 2 H, *J* = 9.0, 0.9 Hz), 8.14 (t, 1 H, *J* = 0.9 Hz), 8.57 (d, 1 H, *J* = 0.9

Hz), 8.84 (dd, 2 H, J = 9.0, 6.0 Hz), 9.07 (d, 1 H, J = 0.9 Hz); ^{13}C NMR ($CDCl_3$) δ 52.4, 122.6, 122.9, 125.1, 126.9, 127.0, 127.0, 127.1, 127.2, 128.1, 128.1, 128.2, 130.1, 130.4, 130.8, 130.9, 131.2, 131.5, 132.2, 135.4, 138.6, 138.8, 139.2, 148.9, 155.1, 165.7 (calc 27 C if free rotation of Ph is hindered, one sp^2 C missing due to overlap); IR (nujol) 3030, 2953, 2924, 2854, 1723, 1281, 1212 cm^{-1}; HRMS for $C_{27}H_{19}NO_2$: calcd 389.1416, found 389.1416.

9,10-Diphenylphenanthrene (Table 2, entry 11). Obtained as a white solid in 35 % yield from the reaction of 2-bromobiphenyl and diphenylacetylene using procedure A. The ^{1}H NMR spectral properties matched those reported by Doty.[9]

9-Phenyl-10-(2'-bromophenyl)phenanthrene (Table 2, entry 12). Obtained as an off-white solid in 39 % yield from the reaction of 2-iodobiphenyl and 1-bromo-2-(phenylethynyl)benzene using procedure A. After the normal work-up, drying and concentrating, the residue was purified by column chromatography using hexanes as eluent: mp 230-232 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 7.05-7.30 (m, 7 H), 7.37 (dt, 2 H, J = 7.8, 1.2 Hz), 7.45-7.58 (m, 4 H), 7.67 (dt, 2 H, J = 7.8, 1.2 Hz), 8.00 (d, 2 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 122.63, 122.7, 125.2, 126.6, 126.7, 126.7, 126.9, 126.9, 127.0, 127.1, 127.4, 128.0, 128.6, 129.6, 129.9, 130.4, 130.8, 131.9, 132.3, 132.9, 136.1, 137.2, 139.2, 140.6; IR ($CHCl_3$) 3040, 3019, 2000-1400, 756 cm^{-1}; HRMS for $C_{26}H_{17}Br$: (^{81}Br) calcd 410.0495, found 410.0497; (^{79}Br) calcd 408.0514, found 408.0519.

9-Methyl-10-(trimethylsilyl)phenanthrene (Table 2, entry 13). Obtained as a clear, colorless oil in 42 % yield from the reaction of 2-iodobiphenyl and 1-trimethylsilyl-1-propyne using procedure B and purified by column chromatography using hexanes as eluant: ^{1}H NMR ($CDCl_3$) δ 0.52 (s, 9 H), 2.82 (s, 3 H), 7.46-7.62 (m, 4 H), 8.06 (dd, 1 H, J = 7.5, 1.8 Hz), 8.12 (dd, 1 H, J = 7.5, 1.8 Hz), 8.61 (d, 2 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 4.2, 22.0, 122.7, 123.0, 124.6, 125.1, 125.5, 126.6, 126.8, 128.9, 129.4, 130.9, 132.0, 134.6, 135.5, 140.9; IR ($CHCl_3$) 3070, 3010, 2952, 2899, 1252 cm^{-1}; HRMS for $C_{18}H_{20}Si$: calcd 264.1334, found 264.1335.

9-(1,3-Dioxan-2-yl)-10-(trimethylsilyl)phenanthrene (Table 2, entry 14). Obtained as a white solid in 54 % yield from the reaction of (1,3-dioxan-2-ylethynyl)trimethylsilane and 2-iodobiphenyl using procedure A: mp 175-177 °C (hexane); ^1H NMR (CDCl3) δ 0.62 (s, 9 H), 1.51 (s, 1 H), 2.48-2.53 (m, 1 H), 4.04 (dt, 2 H, *J* = 10.2, 2.1 Hz), 4.33-4.39 (m, 2 H), 6.20 (s, 1 H), 7.49 (dt, 1 H, *J* = 7.8, 0.9 Hz), 7.56-7.65 (m, 3 H), 8.20 (dd, 1 H, *J* = 8.4, 0.6 Hz), 8.61 (dt, 2 H, *J* = 8.4, 1.2 Hz), 9.05 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 4.3, 25.9, 67.6, 104.5, 122.3, 123.1, 125.2. 126.0, 126.3, 126.9, 128.4, 129.1, 129.7, 130.6, 132.0, 134.8, 137.3, 140.5; IR ($CDCl_3$) 3017, 2954, 2859, 1216, 1120, 1099, 1070 cm^{-1}; HRMS for $C_{21}H_{24}O_2Si$: calcd 336.1546, found 336.1537.

9-Phenyl-10-(trimethylsilyl)phenanthrene (Table 2, entry 15). Obtained as a white solid in 42 % yield from the reaction of 2-iodobiphenyl and 1-phenyl-2-(trimethylsilyl)acetylene using a modification of procedure A, followed by purification by column chromatography using hexanes as eluant. The ^1H NMR spectral properties matched those reported by Doty.[9]

9-Phenyl-10-(triethylsilyl)phenanthrene (Table 2, entry 16). Obtained as a white solid in 49 % yield from the reaction of 2-iodobiphenyl and 1-phenyl-2-(triethylsilyl)acetylene using procedure A, followed by purification by column chromatography using hexanes as eluent: mp 134-136 °C (MeOH); ^1H NMR ($CDCl_3$) δ 0.57 (q, 6 H, *J* = 7.8 Hz), 0.79 (t, 9 H, *J* = 7.5 Hz), 7.26-7.52 (m, 6 H), 7.60 (d quintet, 4 H, *J* = 5.7, 1.5 Hz), 8.38 (dd, 1 H, *J* = 7.8, 1.5 Hz), 8.71 (d, 1 H, *J* = 8.4 Hz), 8.76 (dd, 1 H, *J* = 8.1, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 5.6, 8.3, 122.1, 123.0, 125.7, 125.8, 126.2, 126.8, 127.5, 127.7, 127.9, 128.9, 129.7, 130.8, 131.6, 132.1, 132.3, 135.3, 142.5, 148.3; IR ($CHCl_3$) 3064, 3017, 2955, 2873, 1545, 1485, 1215 cm^{-1}; HRMS for $C_{26}H_{28}Si$: calcd 368.1960, found 368.1965.

2-Methoxy-9-phenyl-10-(triethylsilyl)phenanthrene and 2-methoxy-10-phenyl-9-(triethylsilyl)phenanthrene (Table 2, entry 17). A white solid obtained in 50 % yield as an inseparable 1:1 mixture of regioisomers from the reaction of 2-iodo-4'-methoxybiphenyl and 1-phenyl-2-(triethylsilyl)acetylene using procedure A and purified by column chromatography using hexanes as eluent and then recrystallization from MeOH. Spectral data for product mixture: ^{1}H NMR ($CDCl_3$) δ 0.58 (q, 6 H, *J* = 7.8 Hz), 0.59 (q, 6 H, *J* = 7.8 Hz), 0.79 (t, 9 H, *J* = 7.8 Hz), 0.80 (t, 9 H, *J* = 7.8 Hz), 3.65 (s, 3 H), 3.98 (s, 3 H), 6.68 (d, 1 H, *J* = 3.0 Hz), 7.20-7.39 (m, 8 H), 7.41-7.67 (m, 9 H), 7.80 (d, 1 H, *J* = 3.0 Hz), 8.34 (dd, 1 H, *J* = 9.0, 1.2 Hz), 8.61 (d, 1 H, *J* = 9.0 Hz), 8.62 (d, 1 H, *J* = 9.0 Hz), 8.64 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.4, 5.5, 8.2, 8.3, 55.1, 55.5, 109.1, 110.4, 115.8, 116.6, 121.7, 122.5, 123.8, 124.0, 124.5, 124.7, 125.2, 125.3, 125.9, 126.9, 127.5, 127.5, 127.7, 127.8, 128.0, 129.0, 129.8, 131.0, 131.2, 131.4, 131.5, 131.6, 132.9, 133.6, 134.4, 136.8, 142.6, 147.7, 149.0, 157.4, 157.8 (one sp^2 C missing due to overlap); HRMS for $C_{27}H_{30}OSi$: calcd 398.2066, found 398.2070.

4-Methoxy-9-phenyl-10-(triethylsilyl)phenanthrene and 4-methoxy-10-phenyl-9-(triethylsilyl)phenanthrene (Table 2, entry 18). A white solid obtained in 61 % yield as a 3 : 1 mixture of isomers from the reaction of 2-iodo-2'-methoxybiphenyl and 1-phenyl-2-(triethylsilyl)acetylene using procedure A and purified by column chromatography using 30 : 1 hexanes/EtOAc. The nearly pure major isomer was obtained by column chromatography and therefore was fully characterized. For the minor isomer, only ^{1}H NMR spectral data were obtainable. **4-Methoxy-9-phenyl-10-(triethylsilyl)phenanthrene:** ^{1}H NMR ($CDCl_3$) δ 0.55 (q, 6 H, *J* = 7.8 Hz), 0.77 (t, 9 H, *J* = 7.5 Hz), 4.13, (s, 3 H), 7.15 (d, 1 H, *J* = 7.8 Hz), 7.33-7.38 (m, 5 H), 7.42-7.46 (m, 3 H), 7.49 (q, 1 H, *J* = 8.1 Hz), 7.99 (dd, 1 H, *J* = 8.1, 0.9 Hz), 9.68 (dd, 1 H, *J* = 8.4, 0.9 Hz); ^{13}C NMR ($CDCl_3$) δ 5.8, 8.3, 55.9, 108.0, 121.9, 125.2, 125.5, 125.8, 126.3, 127.3, 127.5, 127.6, 128.0, 130.6, 131.9, 132.4, 132.6, 138.0, 142.6, 149.0, 158.7; IR ($CDCl_3$) 3074, 3018, 2956, 2873, 1215, 1084 cm^{-1}; HRMS for $C_{27}H_{30}OSi$: calcd 398.2066, found 398.2070. **4-Methoxy-9-(triethylsilyl)-10-phenylphenanthrene:** ^1H NMR ($CDCl_3$) δ 0.55 (q, 6 H, *J* = 7.8 Hz), 0.77 (t, 9 H, *J* = 7.5 Hz), 4.12, (s, 3 H), 6.98 (dd, 1 H, *J* = 7.2, 1.2 Hz), 7.15 (d, 1 H, *J* = 7.2 Hz), 7.33-7.38 (m, 5 H), 7.42-7.46 (m, 1 H), 7.54-7.60 (m, 2 H), 8.35 (dd, 1 H, *J* = 7.2, 1.2 Hz), 9.72 (dd, 1 H, *J* = 7.8, 1.5 Hz).

4-Methoxy-9-methyl-10-phenylphenanthrene and 4-methoxy-10-methyl-9-phenylphenanthrene (Table 2, entry 19). Obtained as white solid in 40% yield (2.4 : 1 ratio of inseparable isomers) from the reaction of 2-iodo-2'methoxybiphenyl and 1-phenyl-1-propyne using a modification of procedure B (reaction diluted to 20 mL of solvent/0.5 mmol ArI) and purified by column chromatography using hexanes as eluant. **4-Methoxy-9-methyl-10-phenylphenanthrene** (major isomer): ^1H NMR ($CDCl_3$) δ 3.42 (s, 3 H), 4.12 (s, 3 H), 7.00 (dd, 1 H, *J* = 9.0, 1.5 Hz), 7.18 (d, 1 H, *J* = 9.0 Hz), 7.25-7.70 (m, 8 H), 8.17 (m, 1 H), 9.80 (m, 1 H). **4-Methoxy-10-methyl-9-phenylphenanthrene** (minor isomer): ^1H NMR ($CDCl_3$) δ 3.42 (s, 3 H), 4.14 (s, 3 H), 7.21 (d, 1 H, *J* = 7.8 Hz), 7.25-7.70 (m, 9 H), 7.79 (dd, 1 H, *J* = 7.8, 1.2 Hz), 9.72 (d, 1 H, *J* = 9.0 Hz). Additional spectral data for the mixture: ^{13}C NMR ($CDCl_3$) δ 17.7, 18.3, 55.9, 55.9, 107.8, 108.5, 117.8, 120.1, 120.6, 120.7, 120.7, 124.4, 125.3, 125.7, 125.9, 126.0, 126.1, 126.7, 126.9, 127.0, 127.1, 128.3, 128.4, 128.6, 128.8, 130.0, 130.3, 130.4, 130.7, 132.4, 132.8, 134.4, 134.8, 137.1, 138.0, 141.2, 141.6, 158.6, 159.0 (one sp^2 C missing due to overlap); IR ($CDCl_3$) 3055, 3015, 1248, 1215, 1068, 1047 cm^{-1}; HRMS for $C_{22}H_{18}O$: calcd 298.1258, found 298.1358.

1,3-Di(1-hydroxy-1-methylethyl)-2,4-diphenyl-5-(4'-methoxyphenyl)naphthalene (Table 2, entry 20). Obtained as a white solid in 50 % yield from the reaction of 2-iodo-4'-methoxybiphenyl and 2-methyl-4-phenyl-3-butyn-2-ol using procedure B after purification by column chromatography using 7:1 hexanes/EtOAc: mp = 177-178 °C ($CHCl_3/Et_2O$); ^1H NMR ($CDCl_3$) δ 1.61 (s, 6 H), 1.66 (s, 6 H), 1.80 (s, 1 H), 2.07 (s, 1 H), 3.98 (s, 3 H), 7.15 (d, 1 H, *J* = 8.7 Hz), 7.24 (d, 1 H, *J* = 0.9 Hz), 7.26-7.38 (m, 6 H), 7.39-7.48 (m, 5 H), 7.51 (t, 1 H, *J* = 7.2 Hz), 8.38 (s, 1 H), 8.56 (d, 1 H, *J* = 8.4 Hz), 8.66 (d, 1 H, *J* = 9.0 Hz); ^{13}C NMR ($CDCl_3$) δ 31.5, 33.6, 55.4, 65.6, 76.1, 82.1, 93.8, 111.5, 115.6, 121.5, 122.7, 124.4, 125.4, 125.8, 126.6, 127.2, 128.0, 128.0, 128.3, 129.9, 130.7, 131.6, 131.9, 136.1, 138.8, 142.3, 156.9 (7 sp^3 C due to hindered rotation, 2 sp^2 C missing due to overlap); IR (nujol) 3550, 1608, 1227, 1149, 1099, 1039 cm^{-1}; HRMS for $C_{35}H_{34}O_3$: calcd 502.2508, found 502.2498.

2-Methoxy-10-(1'-hydroxy-1'-methylethyl)-9-phenylphenanthrene (Table 2, entry 20). Obtained as a pale orange solid in 41 % yield from the reaction of 2-iodo-4'-methoxybiphenyl and 2-methyl-4-phenyl-3-butyn-2-ol using procedure B after purification by column chromatography using 7:1 hexanes/EtOAc: mp = 155-156 °C ($CHCl_3$/hexane); ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 6 H), 1.75 (broad s, 1 H), 3.61 (s, 3 H), 6.56 (d, 1 H, *J* = 2.7 Hz), 7.18 (dd, 1 H, *J* = 9.0, 2.7 Hz), 7.27-7.33 (m, 2 H), 7.40-7.63 (m, 5 H), 8.56 (d, 1 H, *J* = 9.0 Hz), 8.63 (dd, 1 H, *J* = 8.1, 1.5 Hz), 8.78 (dd, 1 H, *J* = 8.7, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 33.9, 55.0, 76.1, 109.2, 116.2, 122.6, 123.6, 124.2, 124.4, 125.9, 127.3, 128.1, 129.2, 129.3, 130.5, 131.5, 134.4, 135.0, 140.3, 142.4, 157.9; IR (nujol) 3550, 1614, 1289, 1229, 1172, 1101 cm^{-1}; HRMS for $C_{24}H_{22}O_2$: calcd 342.1620, found 342.1611.

3-(Hydroxycarbonyl)-5-(2'-Methoxy-9'-phenylphenanthr-10'-yl)pyridine and 3-(Hydroxycarbonyl)-5-(2'-methoxy-10'-phenylphenanthr-9'-yl)pyridine (Table 2, entry 21). A white solid obtained as a 1 : 1 mixture of regioisomers in 94 % yield from the reaction of 2-iodo-4'-methoxybiphenyl and 3-phenylethynyl-5-pyridinecarboxylic acid using procedure A. The product was purified by base extraction of the crude reaction mixture. Spectral data for the product mixture: ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 3 H), 3.65 (s, 3 H), 6.63 (d, 1 H, *J* = 2.7 Hz), 6.75 (d, 1 H, *J* = 2.7 Hz), 7.13 (d, 2 H, *J* = 7.2 Hz), 7.17-7.40 (m, 14 H), 7.44 (dt, 2 H, *J* = 7.2, 1.2 Hz), 7.67 (dt, 2 H, *J* = 7.8, 0.9 Hz), 8.05 (d, 2 H, *J* = 1.2 Hz), 8.53 (dd, 2 H, *J* = 1.2, 0.9), 8.83 (dt, 4 H, *J* = 12.0, 6.0

^{13}C NMR (CDCl$_3$) δ 55.0, 55.1, 108.0, 108.7, 116.3, 116.5, 122.5, 122.7, 123.9, 124.1, 124.9, 125.1, 126.1, 126.4, 126.5, 127.1, 127.1, 127.1, 127.2, 127.2, 127.3, 128.0, 128.0, 128.1, 129.7, 129.9, 130.0, 130.5, 130.7, 131.8, 132.2, 132.5, 132.8, 134.7, 134.8, 137.6, 138.4, 138.5, 138.6, 138.6, 138.7, 148.6, 148.7, 154.2, 154.2, 158.1, 158.2, 166.5 (one carbonyl C missing due to overlap); IR (nujol) 2900-2450, 2339, 1717, 1615, 1222, 1114, 1045; HRMS for $C_{27}H_{19}NO_3$: calcd 407.1345, found 407.1373.

1-Methyl-9,10-diphenylphenanthrene and 3-methyl-9,10-diphenylphenanthrene (Table 2, entry 22). Obtained as an inseparable 1:1 mixture of isomers in 83 % yield, as a white solid, from the reaction of 2-iodo-3'-methylbiphenyl and diphenylacetylene using procedure A after purification by column chromatography using hexanes as eluant: ^{1}H NMR (CDCl$_3$) (for mixture) δ 1.90 (s, 3 H), 2.61 (s, 3 H), 7.00-7.70 (m, 30 H), 8.58 (s, 1 H), 8.60 (d, 1 H, J = 10.2 Hz), 8.78 (d, 2 H, J = 9.0 Hz); ^{13}C NMR (CDCl$_3$) δ 22.0, 25.4, 121.3, 122.3, 122.5, 122.9, 126.1, 126.2, 126.4, 126.5, 126.5, 126.6, 127.0, 127.4, 127.6, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.3, 129.7, 129.8, 130.1, 130.3, 130.4, 131.1, 131.1, 131.2, 131.3, 131.5, 131.5, 132.0, 136.1, 136.3, 136.8, 136.9, 137.1, 138.9, 139.7, 139.8, 140.0, 143.1 (two sp^2 C missing due to overlap); HRMS for $C_{27}H_{20}$: calcd 344.1565, found 344.1566.

1-Methyl-9,10-di(4'-methoxyphenyl)phenanthrene and 3-methyl-9,10-di(4'-methoxyphenyl)phenanthrene (Table 2, entry 23). Obtained as a 1 : 1 mixture of isomers in 51 % yield from the reaction of 2-iodo-3'-methylbiphenyl and di(4'-methoxyphenyl)acetylene using procedure A. Spectral data for product mixture: ^{1}H NMR (CDCl^3) δ 1.92 (s, 3 H), 2.62 (s, 3 H), 3.76 (s, 3 H), 3.79 (s, 9 H), 6.65 (d, 2 H, J = 8.7 Hz), 6.74-6.80 (m, 7 H), 6.93-6.97 (m, 3 H), 7.02-7.07 (m, 4 H), 7.29 (t, 2 H, J = 6.9 Hz), 7.41-7.68 (m, 8 H), 8.57 (s, 1 H), 8.72 (m, 1 H), 8.76 (d, 2 H, J = 8.7 Hz); ^{13}C NMR (CDCl$_3$) δ 22.0, 25.5, 55.1 (2 C), 112.5, 112.9, 113.1, 113.1, 113.1, 121.3, 122.3, 122.5, 122.9, 126.0, 126.1, 126.3, 126.4, 126.6, 127.7, 127.8, 127.8, 127.9, 128.3, 129.7, 130.1, 130.3, 130.4, 130.9, 131.3, 131.4, 131.9, 132.1, 132.2, 132.2, 132.4, 132.4, 135.6, 136.0, 136.2, 136.9, 137.0, 137.1, 138.9, 157.8, 157.9, 157.9, 158.0 (three sp^3 C and one sp^2 C missing due to overlap); IR (nujol) 1609, 1284, 1244, 1178, 1106, 1032 cm^{-1}; HRMS for $C_{29}H_{24}O_2$: calcd 404.1776, found 404.1776.

3-Methoxy-9,10-diphenylphenanthrene and 1-methoxy-9,10-diphenylphenanthrene (Table 2, entry 24). Obtained as light brown solid in 72% yield as an inseparable 2 : 1 mixture of regioisomers from the reaction of 2-iodo-3'-methoxybiphenyl and diphenylacetylene using procedure A. After the normal workup, drying and concentrating, the resultant solid was washed with MeOH to give spectroscopically pure product. **4-Methoxy-9,10-diphenylphenanthrene** (major isomer based on chemical shift of the MeO): ^1H NMR ($CDCl_3$) δ 4.01 (s, 3 H), 6.99-7.24 (m, 11 H), 7.41-7.64 (m, 4 H), 8.17 (d, 1 H, J = 2.4 Hz), 8.70 (d, 1 H, J = 8.4 Hz). **1-Methoxy-9,10-diphenylphenanthrene** (minor isomer): ^1H NMR ($CDCl_3$) δ 3.32 (s, 3 H), 6.93 (d, 1 H, J = 7.8 Hz), 6.99-7.24 (m, 10 H), 7-41-7.64 (m, 4 H), 8.42 (d, 1 H, J = 8.4 Hz), 8.76 (d, 1 H, J = 8.7 Hz). Additional spectral data for the mixture of products: ^{13}C NMR ($CDCl_3$) δ 55.5, 55.9, 104.0, 109.2, 115.5, 116.4, 122.5, 123.0, 124.7, 126.0, 126.1, 126.2, 126.3, 126.4, 126.6, 126.7, 126.9, 126.9, 127.3, 127.6, 127.6, 127.7, 127.8, 127.9, 129.4, 129.5, 129.5, 129.7, 131.0, 131.1, 131.3, 131.4, 131.4, 132.0, 132.2, 132.3, 134.9, 137.1, 138.1, 139.7, 139.7, 139.7, 139.8, 144.1, 157.8, 158.3; IR (nujol) 3030, 3015, 1616, 1505, 1462, 1261, 1239, 1100, 1041 cm^{-1}; HRMS for $C_{27}H_{20}O$: calcd 360.1514, found 360.1508.

3-Methoxy-9,10-di(4'-methoxyphenyl)phenanthrene (A) **and 1-methoxy-9,10-di(4'-methoxyphenyl)phenanthrene** (B) (Table 2, entry 25). Obtained as light brown solid in 72 % yield as an inseparable 2.3 : 1 mixture of regioisomers from the reaction of 2-iodo-3'-methoxybiphenyl and di(4-methoxyphenyl)acetylene using procedure A. After the normal work-up, drying and concentrating, the resultant solid was washed with MeOH, ether and hexanes to give spectroscopically pure product. Assignment of the major isomer was based upon the doublet at δ 8.15 (*J* = 2.4 Hz) corresponding to the 4-H in 3-methoxy-9,10-di(4'-methoxyphenyl)phenanthrene. Spectral data for the product mixture: ^{1}H NMR (CDCl$_3$) δ (an asignment of the number of hydrogens has been omitted where ambiguous) 3.38 (s, 3 H, **B**), 3.75 (s, 3 H, **B**), 3.79 (s, 9 H, **A+B**), 4.03 (s, 3 H, **A**), 6.64 (d, *J* = 8.4 Hz), 6.74 (d, *J* = 8.4 Hz), 6.77 (d, *J* = 8.4 Hz), 6.90 (d, 2 H, *J* = 8.7 Hz, **B**), 6.94 (d, 1 H, *J* = 8.4 Hz, **A**), 7.02 (d, 4 H, *J* = 7.5 Hz, **A**), 7.13 (dd, 1 H, *J* = 9.0, 2.4 Hz, **A**), 7.43-7.65 (m, **A+B**), 8.15 (d, 1 H, *J* = 2.4 Hz, **A**), 8.42 (d, 1 H, *J* = 8.4 Hz, **B**), 8.69 (d, 1 H, *J* = 8.4 Hz, **A**), 8.73 (d, 1 H, *J* = 8.4 Hz, **B**); ^{13}C NMR (CDCl$_3$) δ 55.1, 55.5, 56.1, 104.0, 109.3, 111.7, 112.9, 113.1, 115.5, 115.5, 116.3, 122.5, 123.0, 123.0, 123.1, 125.9, 126.2, 126.7, 126.8, 126.8, 127.0, 127.8, 127.9, 127.9, 129.4, 129.5, 129.7, 130.4, 130.5, 131.4, 132.0, 132.1, 132.2, 132.2, 132.5, 132.8, 134.9, 135.1, 136.9, 137.0, 138.2, 156.8, 157.9, 158.0, 158.2 (5 carbons missing due to overlap); HRMS for $C_{29}H_{24}O_3$: calcd 420.1725, found 420.1735.

11,12-Diphenylbenzo[a]phenanthrene and 6,7-diphenylbenz[a]anthracene (Table 2, entry 26). Obtained as a 1 : 1 mixture of isomers in 80 % yield from the reaction of 1-(2'-iodophenyl)naphthalene and diphenylacetylene using procedure B. Spectral data for the product mixture: ^{1}H NMR (CDCl$_3$) δ 7.01-7.30 (m, 21 H), 7.37-7.60 (m, 8 H), 7.65 (dd, 2 H, *J* = 9.6, 5.1 Hz), 7.82 (d, 1 H, *J* = 9.0 Hz), 7.85 (dd, 1 H, *J* = 9.0, 1.2 Hz), 7.97 (d, 1 H, *J* = 9.0 Hz), 8.00 (s, 1 H), 8.12 (d, 1 H, *J* = 9.0 Hz), 8.81 (t, 2 H, *J* = 9.3 Hz), 8.91 (d, 1 H, *J* = 8.1 Hz), 9.25 (s, 1 H); ^{13}C NMR (CDCl$_3$) δ 121.1, 121.4, 122.8, 123.2, 124.7, 125.6, 125.7, 126.0, 126.2, 126.3, 126.5, 126.5, 126.6, 126.7, 126.8, 127.1, 127.5, 127.7, 127.7, 127.8, 127.9, 128.1, 128.1, 128.2, 128.3, 128.7, 128.7, 129.6, 130.0, 130.3, 130.9, 131.0, 131.1, 131.2, 131.2, 131.3, 131.6, 131.7, 131.9, 132.3, 133.7, 136.8, 137.1, 137.3, 139.4, 139.6, 139.6, 140.0, 143.5 (3 sp^3 C missing due to overlap); HRMS for $C_{30}H_{20}$: calcd 380.1565, found 380.1565.

3,4-Di(4'-methoxyphenyl)benz[a]anthracene and 5,6-di(4'-methoxyphenyl)chrysene (Table 2, entry 27). A light brown solid obtained as an inseparable, 5 : 1 mixture of isomers in 75 % yield from the reaction of 1-iodo-2-(2'-naphthyl) benzene and di(4-methoxyphenyl)acetylene using procedure A. The assignment of isomers is based on a singlet at 9.27 ppm for the minor isomer. **3,4-Di(4-methoxyphenyl)benz[a]anthracene** (major isomer): ^{1}H NMR ($CDCl_3$) δ 3.79 (s, 3 H), 3.82 (s, 3 H), 6.72 (d, 2 H, J = 8.4 Hz), 6.80 (d, 2 H, J = 9.3 Hz), 6.95-7.14 (m, 5 H), 7.51 (t, 1 H, J = 7.2 Hz), 7.54 (dd, 2 H, J = 7.8, 0.6 Hz), 7.60-7.70 (m, 2 H), 7.85 (d, 1 H, J = 8.1 Hz), 8.03 (d, 1 H, J = 9.0 Hz), 8.83 (t, 2 H, J = 9.0 Hz). **5,6-Di(4-methoxyphenyl)chrysene** (minor isomer): ^{1}H NMR ($CDCl_3$) δ 3.81 (s, 3 H), 3.83 (s, 3 H), 6.74 (d, 2 H, J = 8.4 Hz), 6.82 (d, 2 H, J = 9.3 Hz), 6.95-7.04 (m, 4 H), 7.51 (t, 1 H, J = 7.2 Hz), 7.54 (dd, 2 H, J = 7.8, 0.6 Hz), 7.60-7.70 (m, 2 H), 7.83 (d, 1 H, J = 8.7 Hz), 8.01 (s, 1 H), 8.12 (d, 1 H, J = 8.1 Hz), 8.92 (d, 1 H, J = 8.4 Hz), 9.27 (s, 1 H); Additional spectral data for the product mixture: ^{13}C NMR ($CDCl_3$) δ 55.2, 113.1, 113.7, 121.1, 123.2, 124.7, 125.5, 126.4, 126.5, 127.8, 128.1, 128.2, 128.3, 128.7, 129.5, 130.0, 131.4, 132.0, 132.2, 132.4, 133.7, 136.1, 136.8, 139.3, 157.9 (after 5000 scans these were the only peaks detected); HRMS for $C_{32}H_{24}O_2$: calcd 440.1776, found 440.1777.

11,12-Diphenylbenzo[c]phenanthrene (Table 2, entry 28). Obtained as a white solid in 78 % yield from the reaction of 1(2'-iodophenyl)naphthalene and diphenylacetylene using procedure B: mp 207-210 °C; ^{1}H NMR ($CDCl_3$) δ 7.20-7.32 (m, 10 H), 7.55 (d, 2 H, J = 9.0 Hz), 7.55-7.84 (m, 5 H), 8.02 (d, 1 H, J = 7.8 Hz), 9.17 (d, 2 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 125.3, 125.7, 126.0, 126.1, 126.1, 126.6, 127.1, 127.4, 127.5, 127.6, 127.6, 128.2, 128.3, 128.6, 129.8, 129.9, 130.2, 131.1, 131.3, 131.3, 132.8, 133.2, 137.2, 137.6, 139.5, 139.7; IR (nujol) 3061, 3027, 1585, 1479 cm^{-1}; HRMS for $C_{30}H_{20}$: calcd 380.1565, found 380.1563. Anal. Calcd for $C_{30}H_{20}$: C, 94.70; H, 5.30. Found: C, 94.60; H, 5.30.

9,10-Bis[(2'-methoxycarbonyl-3',5'-dimethoxy)phenyl]phenanthrene (Table 2, entry 29). Obtained as an orange solid in 49% yield from the reaction of 2-iodobiphenyl and di(3,5-dimethoxy-2-methoxycarbonylphenyl)acetylene using procedure A and purified by column chromatography using 4:1 hexanes/EtOAc: mp 210-212 °C (toluene); ^{1}H NMR ($CDCl_3$) δ 3.18 (s, 6 H), 3.63 (s, 6 H), 3.83 (s, 6 H), 6.39 (d, 2 H, *J* = 3.0 Hz), 6.81 (d, 2 H, *J* = 3.0 Hz), 7.50 (dt, 2 H, *J* = 7.8, 0.9 Hz), 7.62 (m, 4 H), 8.70 (d, 2 H, *J* = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 51.5, 55.6, 55.9, 98.5, 106.9, 117.2, 122.3, 126.3, 126.5, 127.8, 129.8, 130.5, 134.8, 141.0, 157.7, 161.5, 167.9; IR ($CDCl_3$) 3010, 1717, 1103, 1047 cm^{-1}; HRMS for $C_{34}H_{30}O_8$: calcd 566.1941, found 566.1952.

1,2-Diphenylbenzo[c]dibenzofuran (Table 2, entry 30). Obtained as a white solid in 65 % yield from the reaction of 3-iodo-2-phenylbenzofuran and diphenylacetylene using procedure B and purified by column chromatography using 30:1 (hexanes/EtOAc): mp 224-225 °C; ^{1}H NMR ($CDCl_3$) δ 6.78 (dd, 1 H, *J* = 8.1, 0.6 Hz), 7.07 (dt, 1 H, *J* = 7.8, 0.9 Hz), 7.19-7.35 (m, 10 H), 7.38 (dt, 1 H, *J* = 7.8, 1.5 Hz), 7.47 (dt, 1 H, *J* = 7.8, 1.5 Hz), 7.62-7.72 (m, 3 H), 8.54 (dd, 1 H, *J* = 7.5, 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 111.6, 118.3, 120.7, 120.9, 122.0, 122.6, 125.2, 126.0, 126.1, 126.4, 126.7, 127.1, 127.7, 127.7, 128.0, 130.2, 131.7, 132.5, 133.9, 133.9, 138.7, 139.0, 151.3, 156.2; IR (nujol) 2957, 1285, 1233 cm^{-1}; HRMS for $C_{28}H_{18}O$: calcd 370.1358, found 370.1365.

3,4-Diphenylbenzo[a]dibenzofuran (Table 2, entry 31). Obtained as a yellow solid in 73 % yield from the reaction of 2-iodo-3-phenylbenzofuran and diphenylacetylene using procedure B and purified by column chromatography using 30:1 (hexanes/EtOAc): mp 209-211 °C ($CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.22-7.35 (m, 10 H), 7.42-7.51 (m, 3 H), 7.62-7.65 (m, 1 H), 7.70 (dt, 1 H, *J* = 6.9, 1.2 Hz), 7.78 (dd, 1 H, *J* = 8.4, 0.9 Hz), 8.45-8.48 (m, 1 H), 8.71 (d, 1 H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 112.2, 116.9, 122.0, 123.2, 123.4, 124.6, 125.1, 125.9, 126.5, 126.9, 127.0, 127.1, 127.7, 127.8, 128.4, 128.7, 130.2, 131.0, 131.6, 135.5, 138.6, 138.9, 152.7, 156.0; IR (nujol) 2953, 1208 cm^{-1}; HRMS for $C_{28}H_{18}O$: calcd 370.1358, found 370.1365.

9,10-Bis(2'-methoxycarbonylphenyl)benzo[a]triphenylene (Table 2, entry 32). An off-white solid obtained in 60 % yield from the reaction of 9-iodo-10-phenylphenanthrene and di(2-methoxycarbonylphenyl)acetylene using procedure A: mp 265-275 °C (decomposed, $CHCl_3$/hexane); ^{1}H NMR ($CDCl_3$) δ 3.33 (s, 3 H), 3.36 (s, 3 H), 7.03-7.16 (m, 2 H), 7.16-7.20 (m, 2 H), 7.27-7.34 (m, 2 H), 7.40-7.46 (m, 3 H), 7.50-7.56 (m, 2 H), 7.64-7.70 (m, 4 H), 7.83 (dd, 1 H, J = 7.5, 1.2 Hz), 8.57 (d, 1 H, J = 8.1 Hz), 8.66 (dd, 1 H, J = 6.9, 1.2 Hz), 8.84 (t, 2 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 51.6, 51.7, 122.9, 123.5, 125.2, 125.8, 126.0, 126.1, 126.1, 126.4, 126.6, 126.9, 127.2, 127.9, 128.8, 129.6, 129.7, 129.9, 130.0, 130.2, 130.3, 130.8, 131.0, 131.1, 131.2, 131.5, 131.5, 132.0, 132.7, 134.0, 136.4, 140.6, 144.0, 167.0, 167.8 (3 sp^2 C missing due to overlap); IR (nujol) 2953, 2924, 2853, 1726, 1715, 1296, 1266, 1128, 1084 cm^{-1}; HRMS for $C_{38}H_{26}O_4$: calcd 546.1831, found 546.1831.

7-*t*-Butyl-8-phenylacenaphthylene (Table 2, entry 33). Obtained as a yellow solid in 89 % yield from the reaction of 1-iodonaphthalene and 1-phenyl-3,3-dimethyl-1-butyne using procedure B after purification by column chromatography using hexanes as eluent: mp 118-119 °C (hexane); ^{1}H NMR ($CDCl_3$) δ 1.55 (s, 9 H), 7.25-7.43 (m, 3 H), 7.50-7.57 (m, 2 H), 7.71-7.87 (m, 4 H), 8.05 (d, 1 H, J = 7.2 Hz), 8.52 (d, 1 H, J = 8.7 Hz); ^{13}C NMR ($CDCl_3$) δ 30.9, 33.3, 118.0, 119.3, 124.5, 125.9, 127.1, 127.4, 128.8, 129.4, 130.0, 134.4, 135.0, 136.3, 137.0, 138.4, 141.4, 148.5; IR ($CHCl_3$) 2958, 1652, 1558, 1429, 1232 cm^{-1}; HRMS for $C_{22}H_{20}$: calcd 284.1565, found 284.1564.

Bis-1,4-(10-phenylphenanthr-9-yl)benzene (Table 2, entry 34). Obtained as a white solid in 77 % yield from the reaction of 2-iodobiphenyl and 1,4-di(phenylethynyl)benzene: mp > 300 °C; ^{1}H NMR ($CDCl_3$) δ 7.00 (s, 2 H), 7.08 (m, 2 H), 7.20-7.40 (m, 10 H), 7.51 (dt, 4 H, J = 6.0, 1.2 Hz)), 7.62-7.76 (m, 8 H), 8.81 (dd, 4 H, J

= 9.0, 1.2 Hz); HRMS for $C_{46}H_{30}$: m/z calcd 582.2346, found 582.2378; Anal. Calcd for $C_{46}H_{30}$: C, 94.81; H, 5.19. Found: C, 94.28; H, 5.10.

3,10-Dimethoxy-5,6,12,13-tetraphenyldibenz[a,h]anthracene (Table 2, entry 35). Obtained as a white solid from the reaction of 1,4-diiodo-2,5-di(*p*-methoxyphenyl)benzene and diphenylacetylene. The product which precipitated from the reaction mixture was rinsed with MeOH and Et_2O, to give essentially pure product in 67 % yield. Trace amounts of palladium remained in this product; therefore, it was dissolved in hot anisole and filtered through a cotton plug into a test tube. A small amount of ether was added and crystallization of the product occurred as the solution cooled to room temperature. After further cooling in a freezer, the tube was centrifuged and the solvent drawn off using a Pasteur pipet. The precipitate was rinsed several times with ether, dried under vacuum and submitted for elemental analysis: m.p. > 300 °C; ^{1}H NMR ($CDCl_3$) δ 3.70 (s, 6 H), 6.93 (d, 2 H, J = 2.7 Hz), 7.14-7.40 (m, 22 H), 8.27 (d, 2 H, J = 9.0 Hz), 8.82 (s, 2 H); IR (nujol) 1610, 1238 cm^{-1}; HRMS for $C_{48}H_{34}O_2$: calcd 642.2559, found by visual peak match 642.2591. Anal. Calcd for $C_{48}H_{34}O_2$: C, 89.76; H, 5.30. Found: C, 88.78; H, 5.42. No ^{13}C NMR spectra was obtained due to the low solubility of this product.

2-(Trimethylsilyl)-3-phenyldibenzo[a,c]indenone (5). Obtained as a white solid in 39 % yield from the reaction of 9-formyl-10-iodophenanthrene with 1-(trimethylsilyl)-2-phenylacetylene using procedure C and purifying by column chromatography using 10 : 1 hexanes/EtOAc: ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9 H), 7.20-7.22 (m, 2 H), 7.38-7.42 (m, 2 H), 7.50-7.68 (m, 6 H), 8.58 (d, 1 H, J = 7.8 Hz), 8.64 (d, 1 H, J = 8.4 Hz), 9.08 (dd, 1 H, J = 7.8, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ -0.2, 122.5, 122.7, 123.6, 124.9, 125.8, 126.5, 126.6, 126.6, 126.7, 127.1, 127.8, 128.0, 128.2, 128.6, 131.6, 134.1, 134.2, 138.6, 145.2, 170.1, 204.8; IR ($CHCl_3$) 3070, 2960, 2854, 2361, 2336, 1697, 1248 cm^{-1}; HRMS for $C_{26}H_{22}OSi$: calcd 378.1440, found 378.1439.

(Z)-*N*-Mesyl-2-phenyl-3-(2'-chloro-1',2'-diphenylethenyl)indole (14). Obtained as a white solid in 46 % yield from the palladium-catalyzed reaction of *N*-mesyl-2-(phenylethynyl)aniline (0.25 mmol) and diphenylacetylene (0.275 mmol) using 5 mol % of $PdCl_2$, 3 equiv of $CuCl_2•2H_2O$, 1 equiv of NaOAc, 1 equiv of K_2CO_3 in CH_3CN (5.0 mL) at 80 °C for 20 h and purified by column chromatography using 5:1 (hexanes/EtOAc): mp 214-216 °C; ^{1}H NMR ($CDCl_3$) δ 2.83 (s, 3 H), 6.62 (dd, 2 H, *J* = 7.2, 1.5 Hz), 6.86 (t, 2 H, *J* = 7.2 Hz), 6.90-6.98 (m, 1 H), 7.16-7.22 (m, 3 H), 7.25-7.35 (m, 6 H), 7.37-7.46 (m, 3 H), 7.61 (dd, 1 H, *J* = 8.1, 2.4 Hz), 8.17 (dd, 1 H, *J* = 7.5, 1.8 Hz); ^{13}C NMR ($CDCl_3$) δ 39.9, 116.1, 120.4, 124.8, 125.5, 126.2, 127.0, 127.5, 127.7, 128.1, 128.6, 128.9, 129.4, 129.6, 130.0, 130.5, 131.1, 131.9, 134.9, 137.3, 137.9, 138.3, 139.0; HRMS for $C_{29}H_{22}NO_2SCl$: calcd 483.1060, found 483.1074.

Preparation of Naphthodianthrones

4-Methoxy-dibenz[a,o]-3,10-perylenedione (15a). Obtained as an yellow solid in 50 % isolated yield (actual yield is much higher) by treating 2-methoxy-9,10-di(2'-methoxycarbonylphenyl)phenanthrene with PPA for 24 h at 100 °C.[35] The PPA solution was quenched with water, extracted several times with $CHCl_3$ and the organic phase concentrated. This residue was then treated with concd H_2SO_4 for 24 h while excluding light. The resultant deep blue solution was poured over crushed ice and extracted with EtOAc, dried and concentrated. The residue was then purified by column chromatography using 1:2 hexanes/EtOAc: mp >300 °C; ^{1}H NMR ($CDCl_3$) δ 4.24 (s, 3 H), 7.26-7.36 (m, 2 H), 7.48 (t, 2 H, *J* = 7.2 Hz), 7.60 (d, 1 H, *J* = 8.7 Hz), 7.82 (d, 1 H, *J* = 7.8 Hz), 7.92 (t, 2 H, *J* = 7.8 Hz), 8.32 (dd, 1 H, *J* = 7.8, 1.2 Hz), 8.42 (dd, 1 H, *J* = 7.8, 1.2 Hz) 8.72 (dd, 1 H, *J* = 7.5, 0.9 Hz), 8.85 (d, 1 H, *J* = 8.1 Hz), 8.91 (d, 1 H, *J* = 9.3 Hz); HRMS for $C_{29}H_{16}O_3$: calcd 412.1099, found 412.1106.

4-Methoxynaphthodianthrone (16a). Obtained as a yellow solid by treating 4-methoxy-dibenz[a,o]-3,10-perylenedione (30 mg) with conc. H_2SO_4 (25 mL) and subjecting the solution to sunlight or lamp light at rt for ~20 h.[36] Under these conditions, the original deep blue solution turns to a bright red. The red acidic solution is then poured over crushed ice and neutralized. Attempts to extract this aqueous solution with a variety of organic solvents led to the formation of a yellow layer at the boundary of the aqueous and organic layers. This layer was isolated and found to have the following spectral data: mp >300 °C; ^{1}H NMR ($CDCl_3$) δ 4.24 (s, 3 H), 7.50 (d, 1 H, J = 1.2 Hz), 7.80-7.90 (m, 3 H), 8.60-8.95 (m, 7 H); HRMS for $C_{29}H_{14}O_3$: calcd 410.0943, found 410.0954; UV-Vis absorption λ_{max} ($CHCl_3$) 500, 545 nm; UV-Vis fluoresence excitation λ_{max} ($CHCl_3$) 500, 545 nm. This compound has not been further characterized due to its low solubility. Solid phase ^{13}C NMR is an available option for characterization. Please note that 2-methoxy-9,10-di(2'-methoxycarbonylphenyl)phenanthrene can be converted directly to 1-methoxybianthrone without isolation of the intermediate (eq 8). After treating with PPA as described above, the solution is quenched and extracted several times with $CHCl_3$. After drying and concentrating the resultant residue is dissolved in conc. H_2SO_4 and light excluded overnight. The deep blue solution is then exposed to sunlight at rt for 24 h and isolated as described above to give 1-methoxybianthrone in 79 % overall yield for the two steps.

4-Hydroxydibenzo[a,o]-3,10-perylenedione (15b). Obtained as an orange crystalline solid in 90 % yield by treating 2-hydroxy-9,10-di(2'-methoxycarbonylphenyl)phenanthrene (35 mg) with PPA (~ 5 g) at 100 °C[35] for 18 h and then conc. H_2SO_4 (~ 25 mL) at rt for 24 h while excluding light:[36] ^{1}H NMR ($CDCl_3$) δ 6.29-7.39 (m, 3 H), 7.48-7.58 (m, 3 H), 7.88 (d, 1 H, J = 8.1 Hz), 7.94 (t, 1 H, J = 8.1 Hz), 8.06 (d, 1 H, J = 8.4 Hz), 8.38 (d, 1 H, J = 7.5 Hz), 8.49 (d, 1 H, J = 7.5 Hz), 8.71 (d, 1 H, J = 7.2 Hz), 8.87 (t, 2 H, J = 8.1 Hz). HRMS for $C_{28}H_{14}O_3$: calcd 398.0943, found 398.0933.

Anal. Calcd for $C_{28}H_{14}O_3$: C, 84.41; H, 3.54. Found: C, 82.14; H, 3.59. Further characterization was not obtained due to the low solubility of this product.

4-Hydroxynaphthodianthrone (16b). Obtained as a orange-brown solid in 85 % yield as described for the preparation of **16a**. The very low solubility of this product has prevented characterization. Evidence that this is the actual product is the intense UV absorbance λ_{max} 500, 545 nm and UV fluoresence excitation λ_{max} 500, 545 nm, characteristic of naphthodianthrones with one or more free hydroxyl groups in the 1-position. The absorbance and emission spectra for **16b** are identical to **16a**, but much greater in their intensity.

2,4,2',4'-Tetramethoxynaphthodianthrone (17). Obtained as an orange-brown solid in 91 % yield by treatment of 9,10-bis(2'-methoxycarbonyl-3',5'-dimethoxyphenyl)phenanthrene with PPA[35] and then conc. H_2SO_4 and sunlight:[36] ^{1}H NMR ($HCCl_3$) δ 4.18 (s, 6 H), 4.26 (s, 6 H), 6.94 (s, 2 H), 7.90 (t, 2 H, J = 7.8 Hz), 8.77 (d, 2 H, *J* = 7.5 Hz), 8.93 (d, 2 H, *J* = 8.1 Hz). The HRMS for $C_{32}H_{20}O_6$ was not obtained due to limitations in the HRMS ionization techniques. Electrospray low resolution mass spectroscopy found 500.8 (m + 1); UV-Vis absorption λ_{max} (DMSO) 398, 419, 475, 503 nm; UV-Vis fluoresence excitation λ_{max} (DMSO) 396, 418, 474, 502 nm; UV-Vis emission λ_{max} (DMSO) 531, 559 nm. Further characterization was not obtained due to the low solubility of this product.

Acknowledgment

We gratefully acknowledge Procter & Gamble Corporation for financial support. In addition, we thank the U.S. Department of Education for support in the form of a GAANN (Graduate Assistance in Areas of National Need) Fellowship. Thanks is also expressed to Mike Fehr and Doug English for aid in characterization of the naphthodianthrone products.

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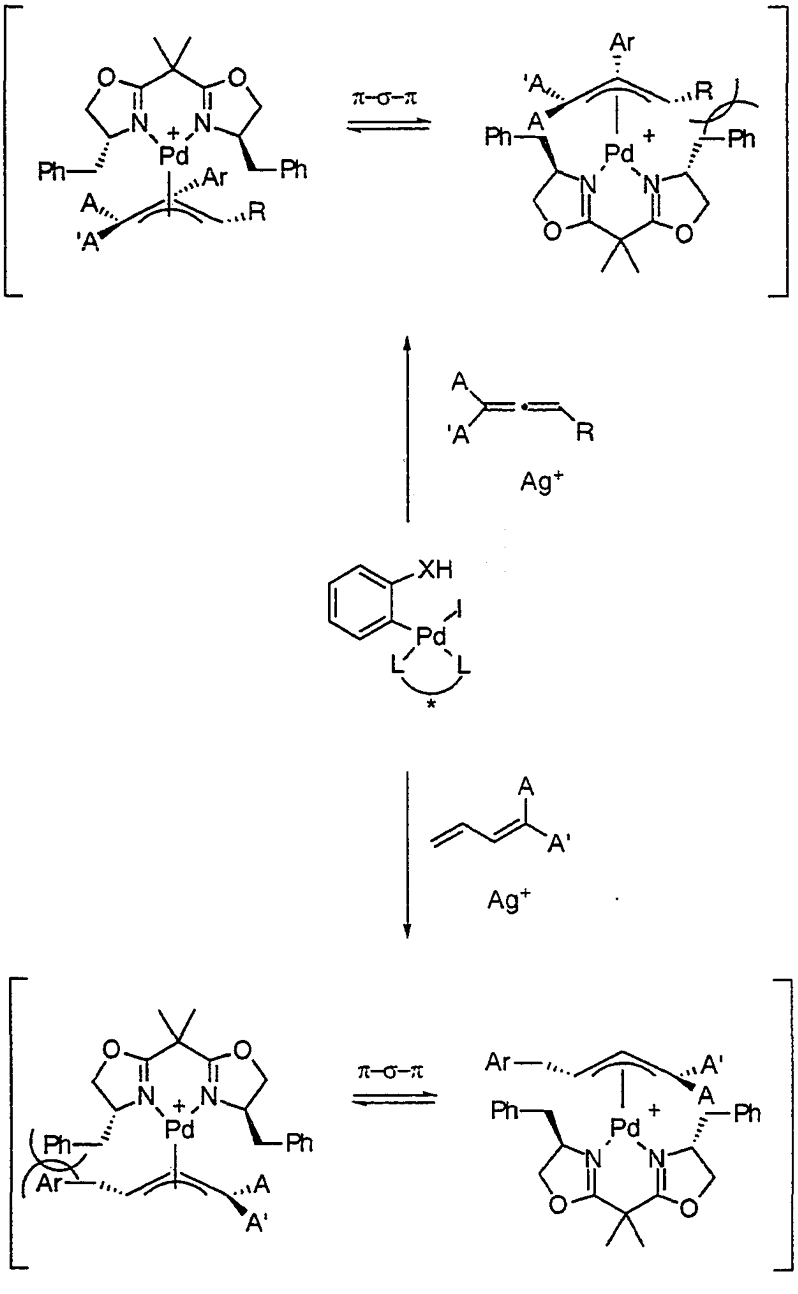
GENERAL CONCLUSIONS

In this dissertation, the enantioselective palladium-catalyzed annulation of dienes using a variety of functionalized aryl and vinylic iodides has been demonstrated. Although literature methodologies exist for the intermolecular asymmetric addition of nucleophiles to symmetrical, chiral ligand bound π-allylpalladium intermediates, this dissertation extends this process to include intramolecular enantioselective π-allylpalladium substitutions. In doing so, this provides for the synthesis of a wide variety of optically active heterocycles of potential biological significance.

Chapters 1 and 2 are clearly related in terms of the mechanistic considerations involved in the asymmetric induction processes. The enantioselective annulation of terminal 1,2- and acyclic 1,3-dienes depends upon the rapid interconversion of diastereomeric π-allylpalladium intermediates (Scheme 1). This interconversion proceeds via an η^3-η^1-η^3 mechanism. For this reason, substrates must be chosen which lead to a π-allylpalladium system in which this process does indeed lead to the formation of diastereomeric intermediates and not structural isomers. In Scheme 1, where $A \neq A'$, the π-allylpalladium intermediates are isomeric, not diastereomeric, and little or no asymmetric induction is expected. Where $A = A'$, this interconversion gives diastereomeric π-allylpalladium intermediates and if this is a rapidly occurring process, high levels of enantioselectivity may be observed. Herein lies the major problem to overcome in this type of reaction. The π-allyl substituents (A, A') must be chosen which facilitate the η^3-η^1-η^3 equilibration mechanism at a fast rate relative to intramolecular nucleophilic attack.

The palladium-catalyzed carboannulation of internal acetylenes using *o*-iodobiaryls described in this dissertation, provides an exceptionally efficient route to polycyclic aromatics. Although tolerant of a wide variety of substituted biaryls and functionalized alkynes, the

Scheme 1

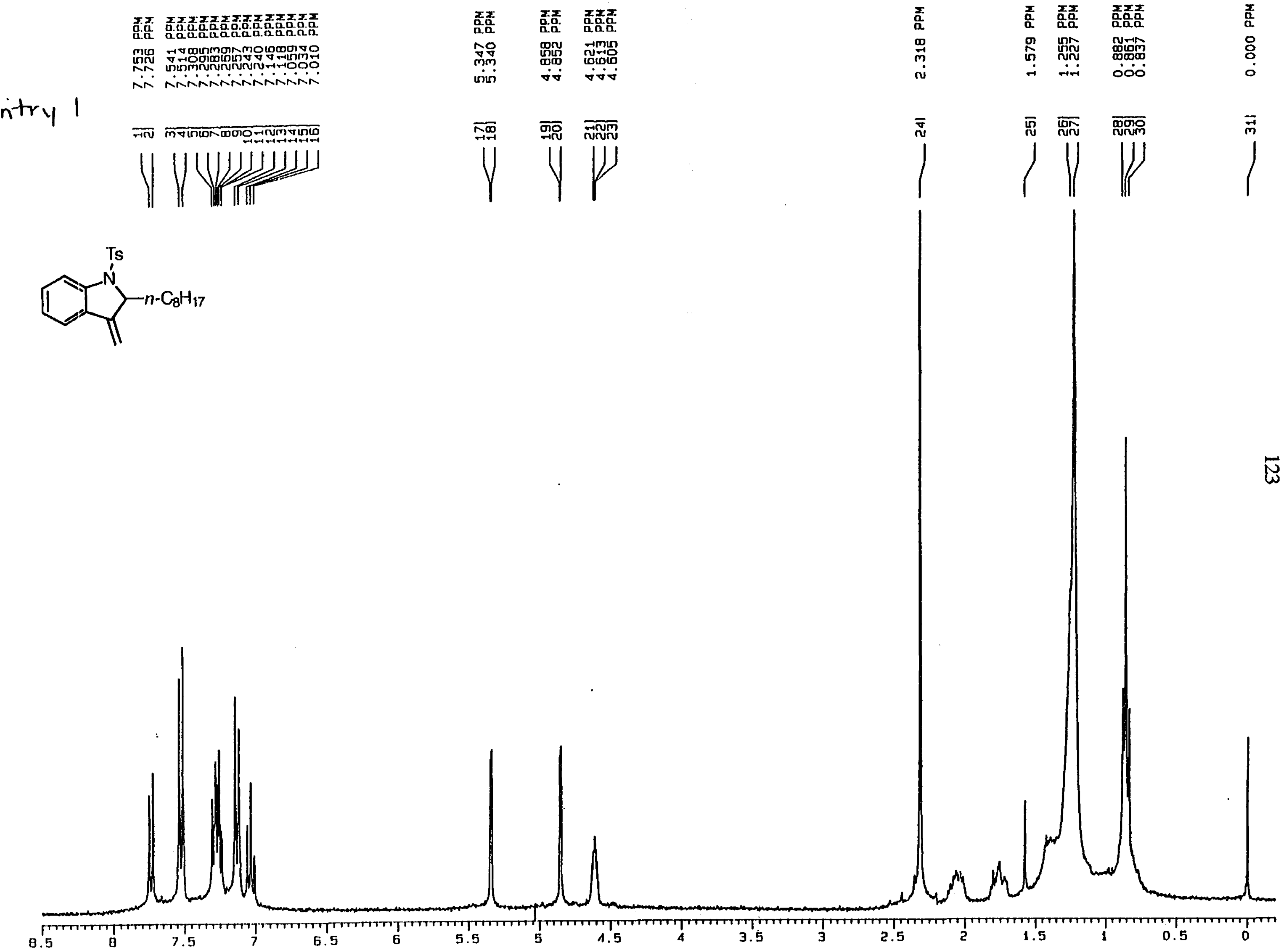


methodology is limited to some extent by the relatively poor regioselectivity of acetylene insertion observed for most biaryl substrates. Attempts to improve this selectivity by the addition of external ligands has had little effect on the regioselectivity of the insertion. The methodology, though quite general for aryl acetylenes or hindered alkyl or silyl acetylenes, does not appear to be useful in the annulation of most dialkyl-substituted acetylenes. While at present there are no obvious solutions to these problems, further study is warranted.

In summary, a general, palladium-catalyzed methodology has been developed for the asymmetric synthesis of hetero- and carbocycles. The generality of this process, as well as the procedural ease with which the reactions are run, make it a very synthetically attractive route to these ring systems. Likewise, the palladium-catalyzed annulation of internal acetylenes using biaryls proceeds under relatively mild conditions and utilizes readily accessible starting materials. The utility of the process has been demonstrated for a wide variety of biaryls and acetylenes with yields generally ranging from good to excellent.

APPENDIX A: CHAPTER 1 ^{1}H AND ^{13}C NMR SPECTRA

Entry 1



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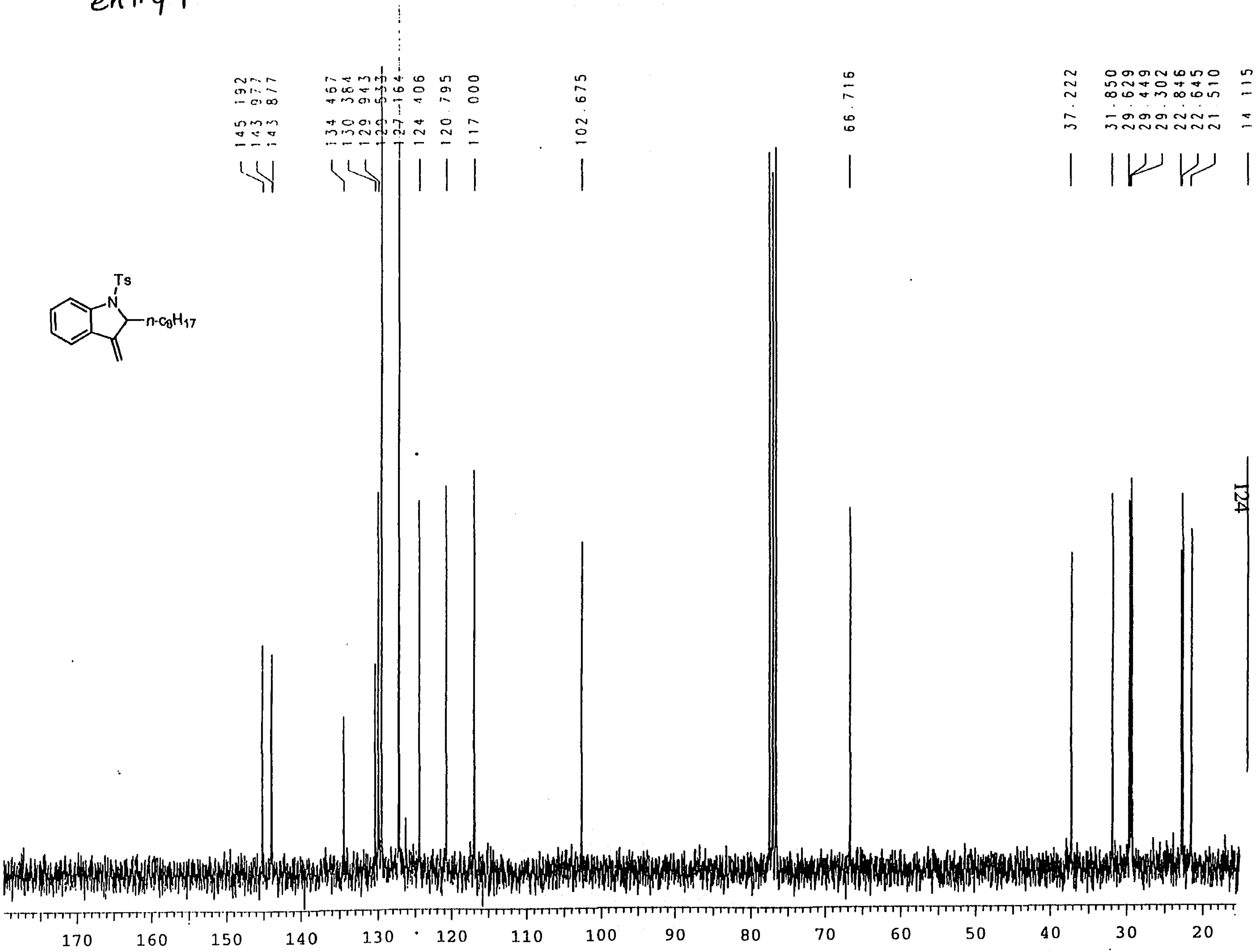

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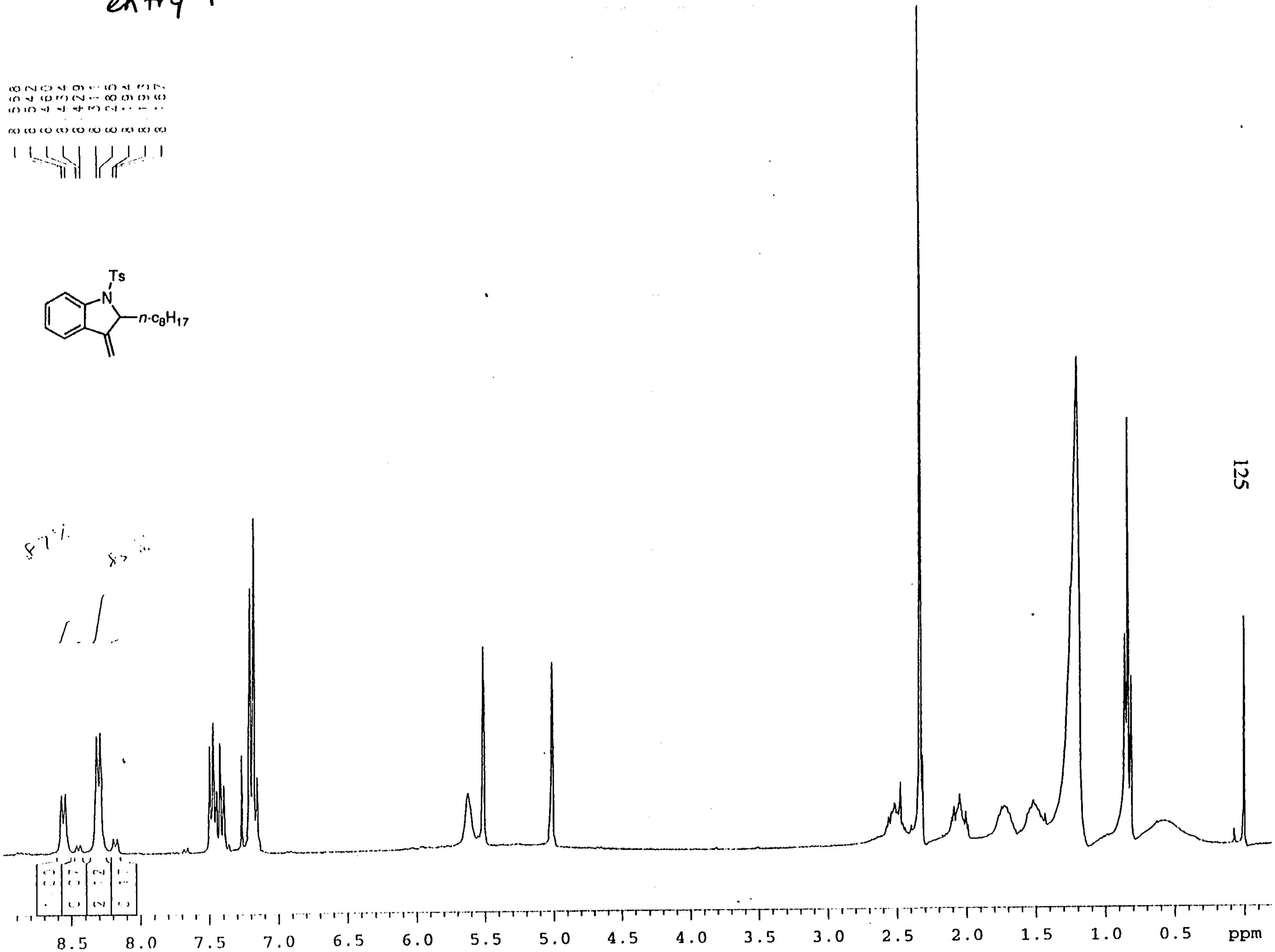

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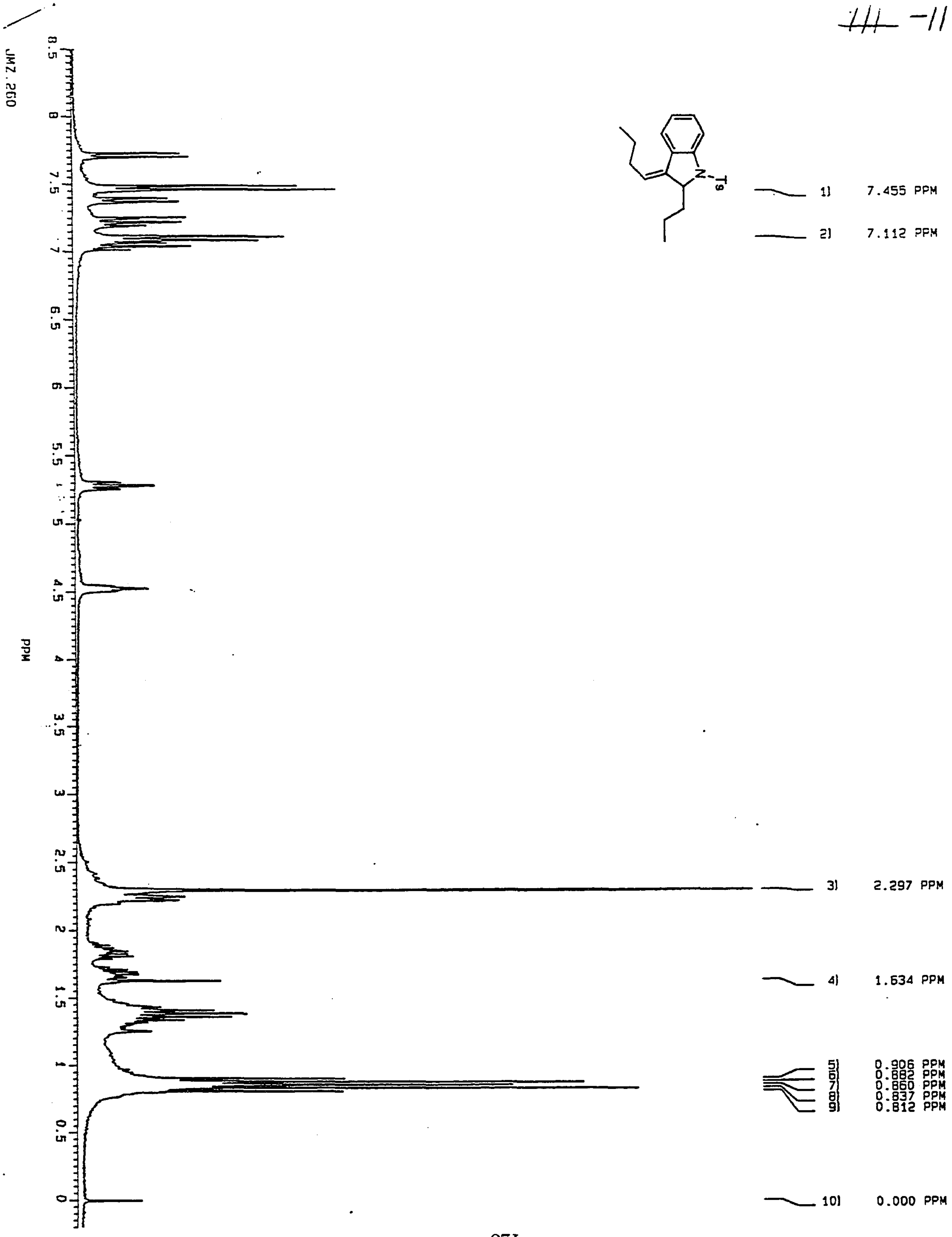
III -11



Entry 2

Entry 2

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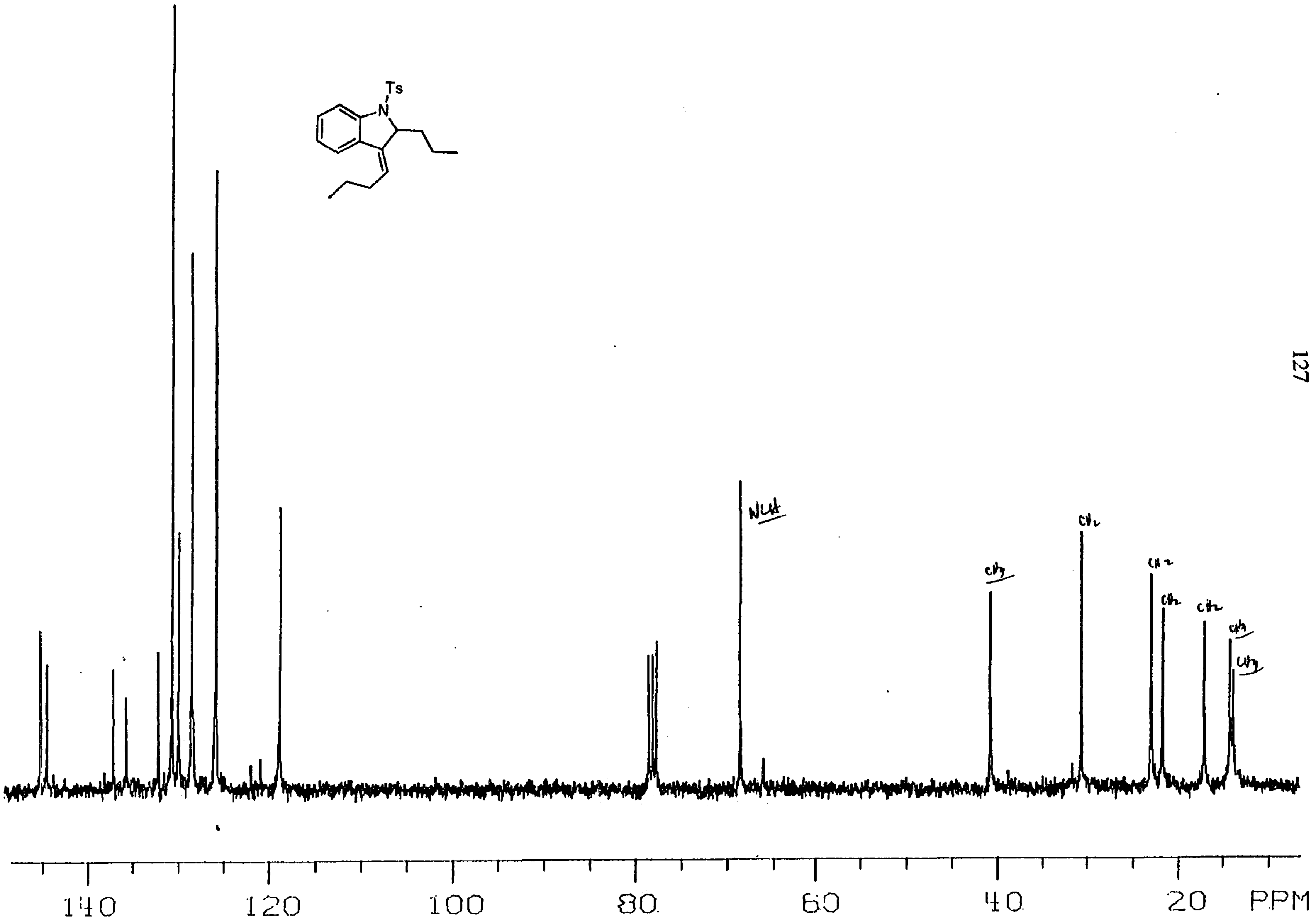

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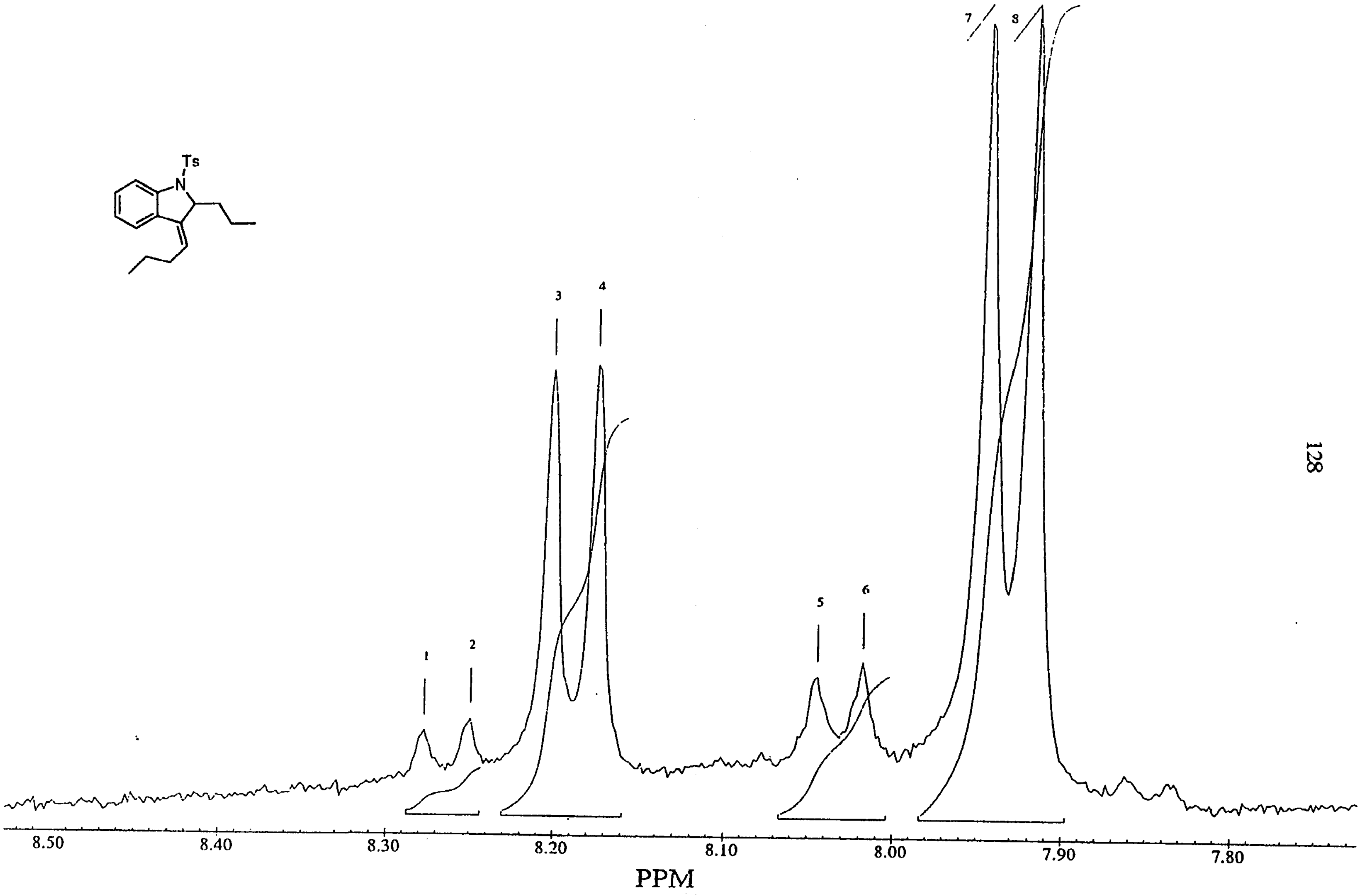

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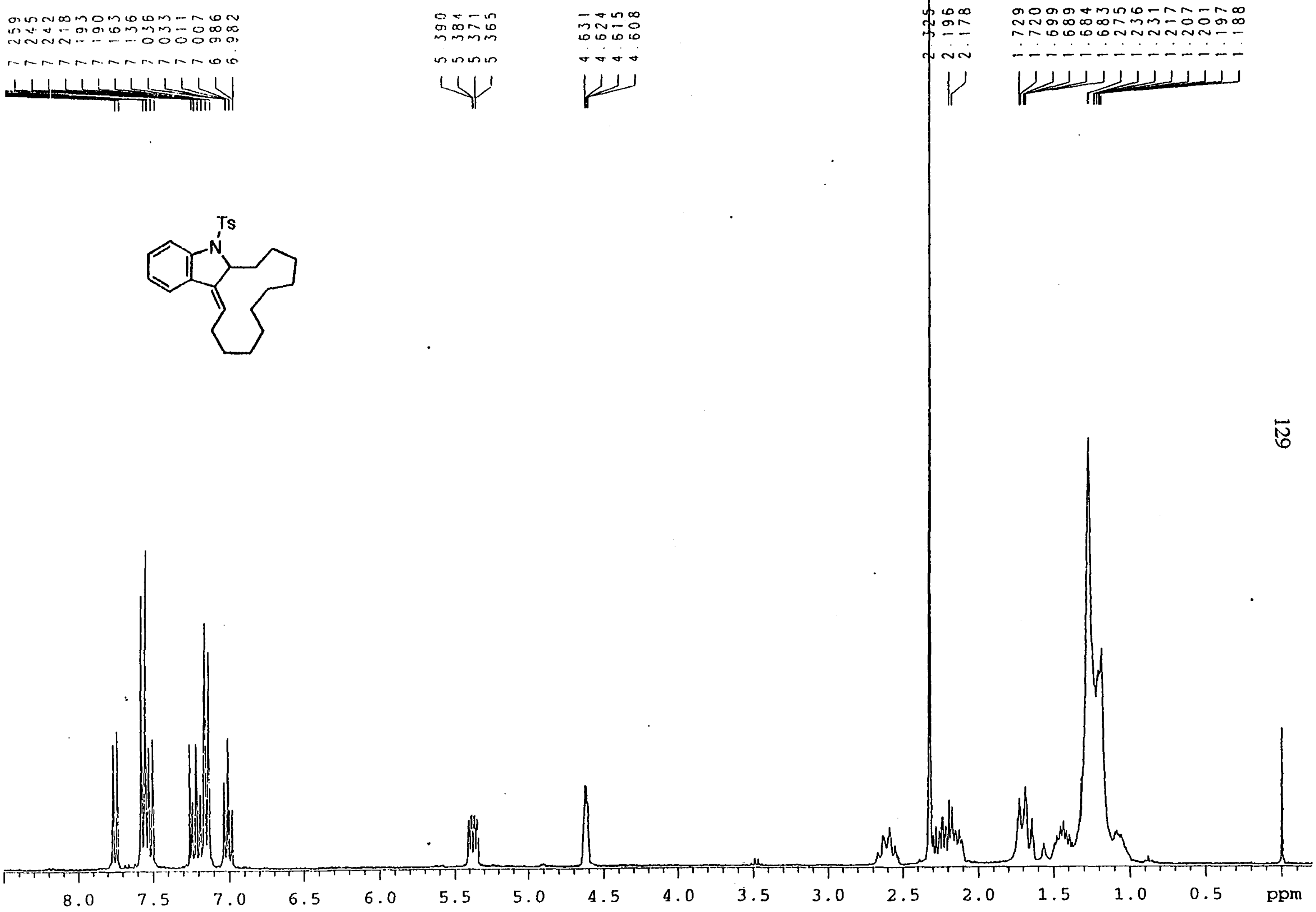

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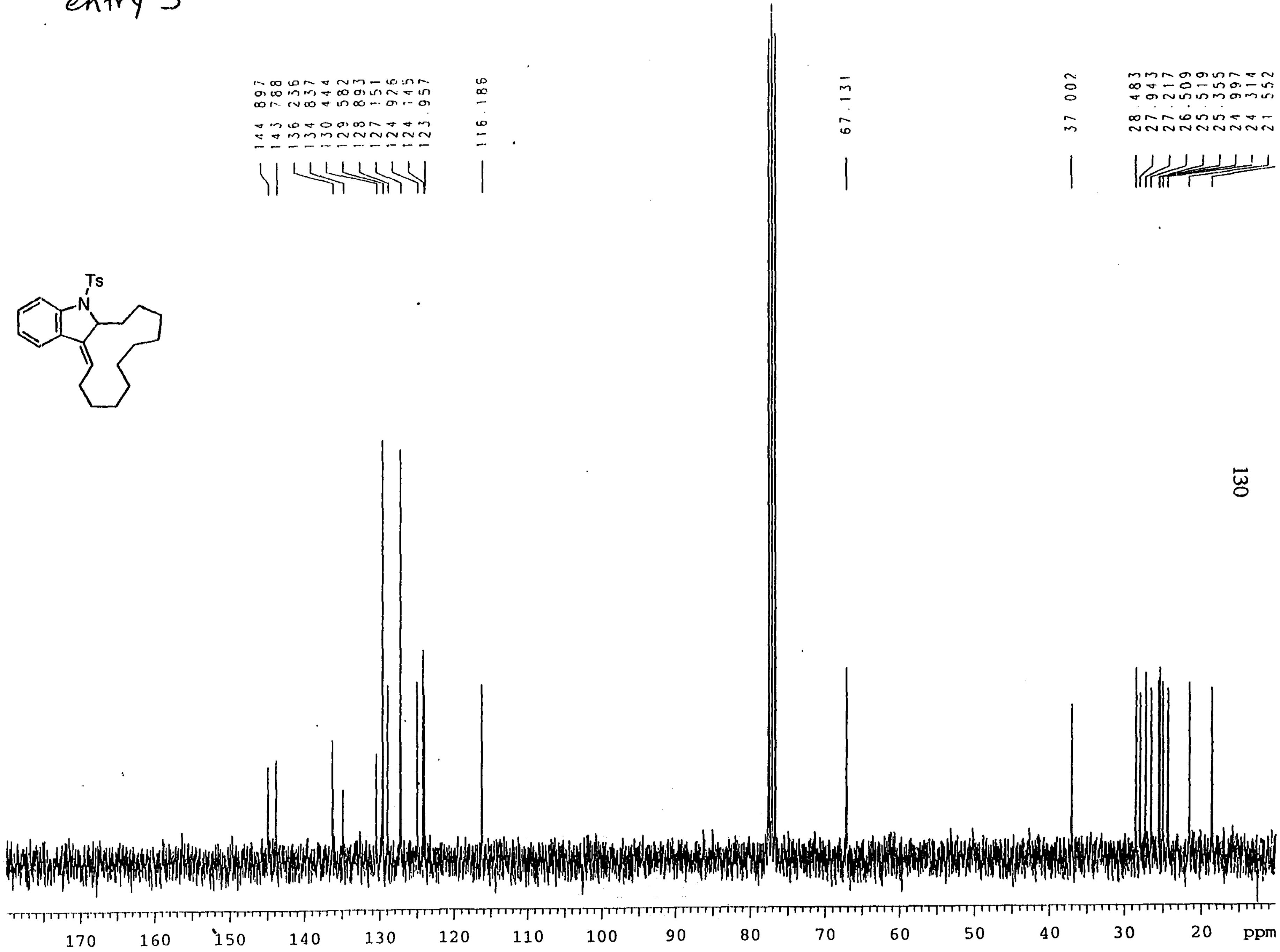

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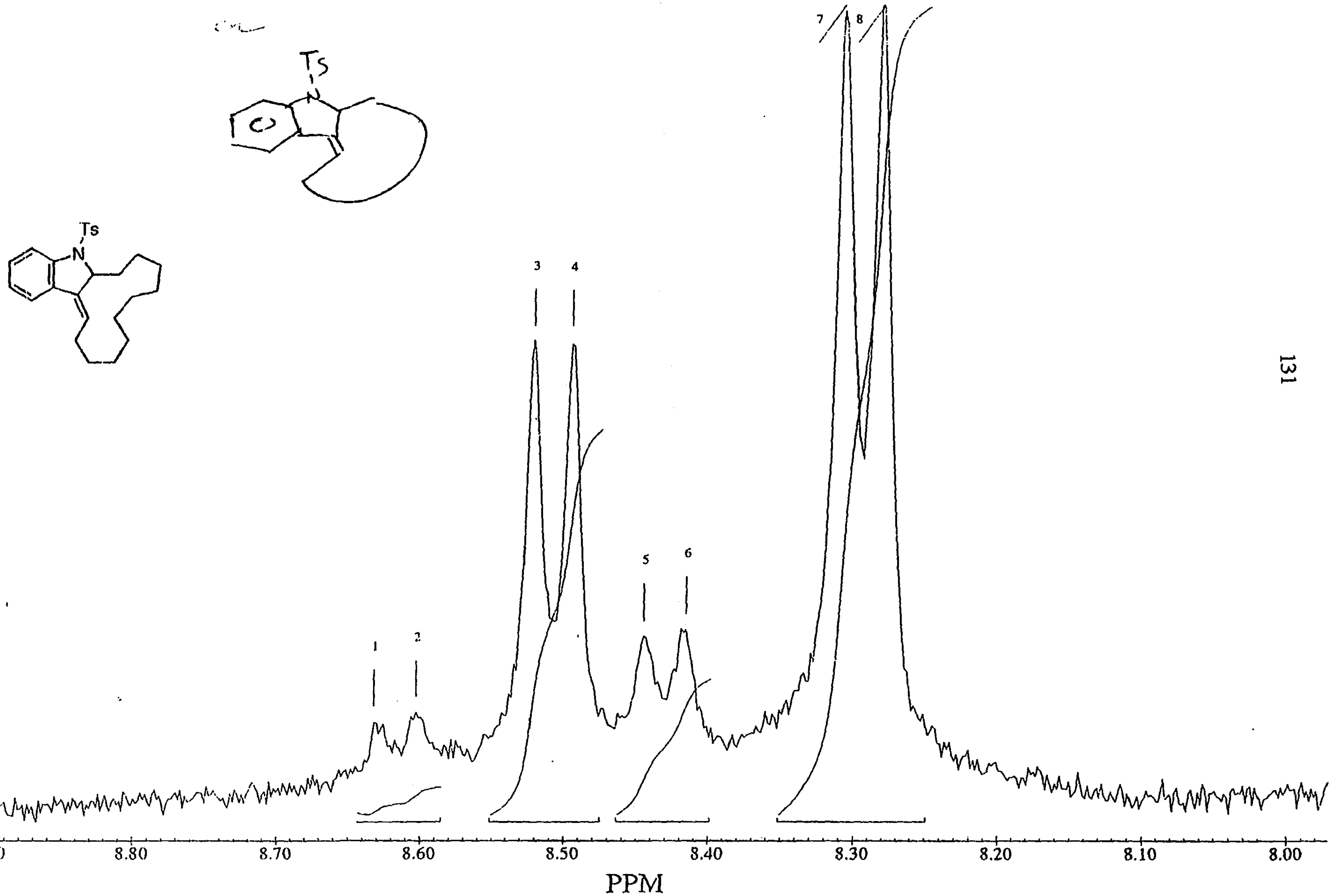
III-12

NMR1™



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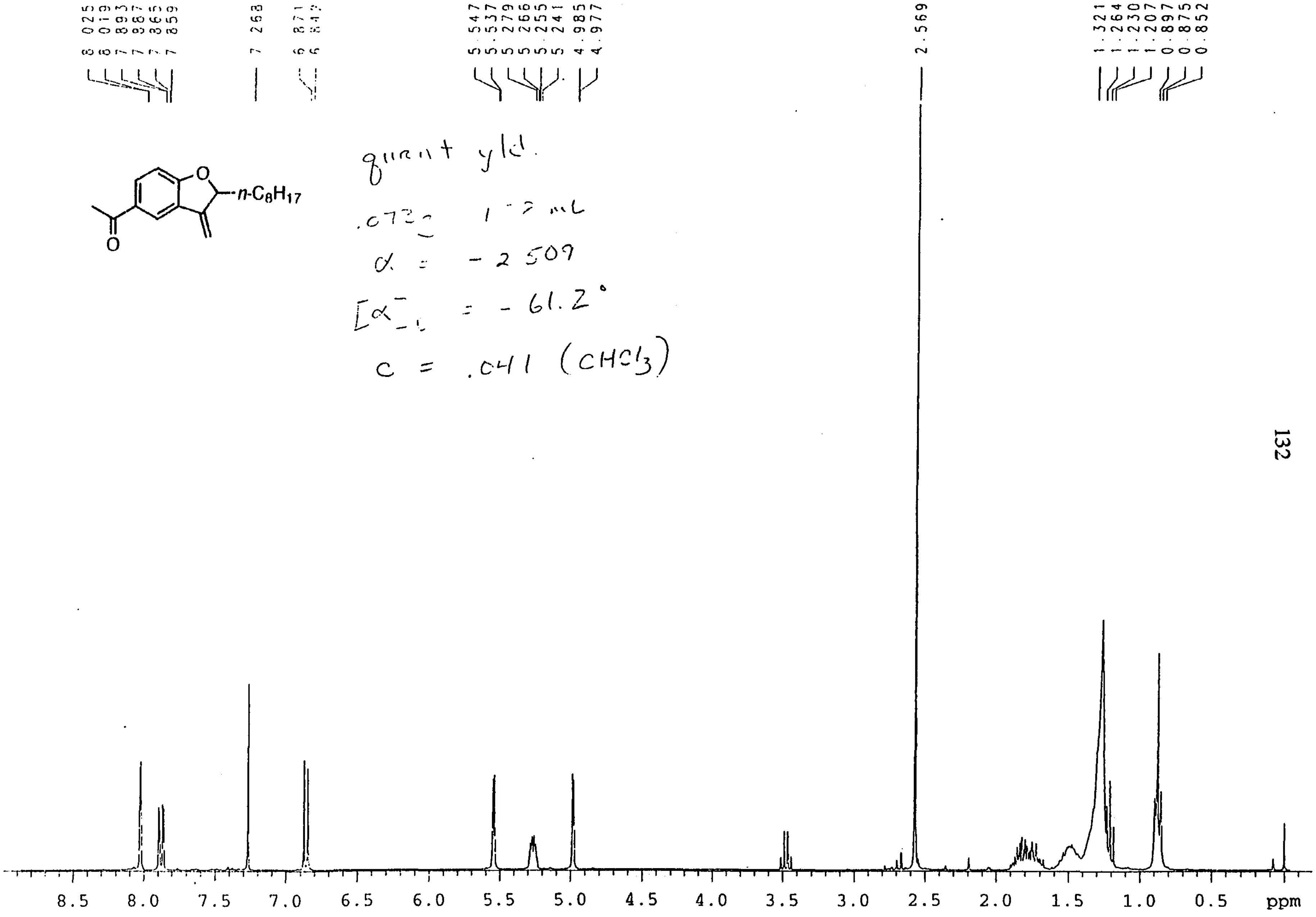

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.0732 g 1.[illegible] mL

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$[\alpha]_D = -61.2°$

c = .041 ($CHCl_3$)

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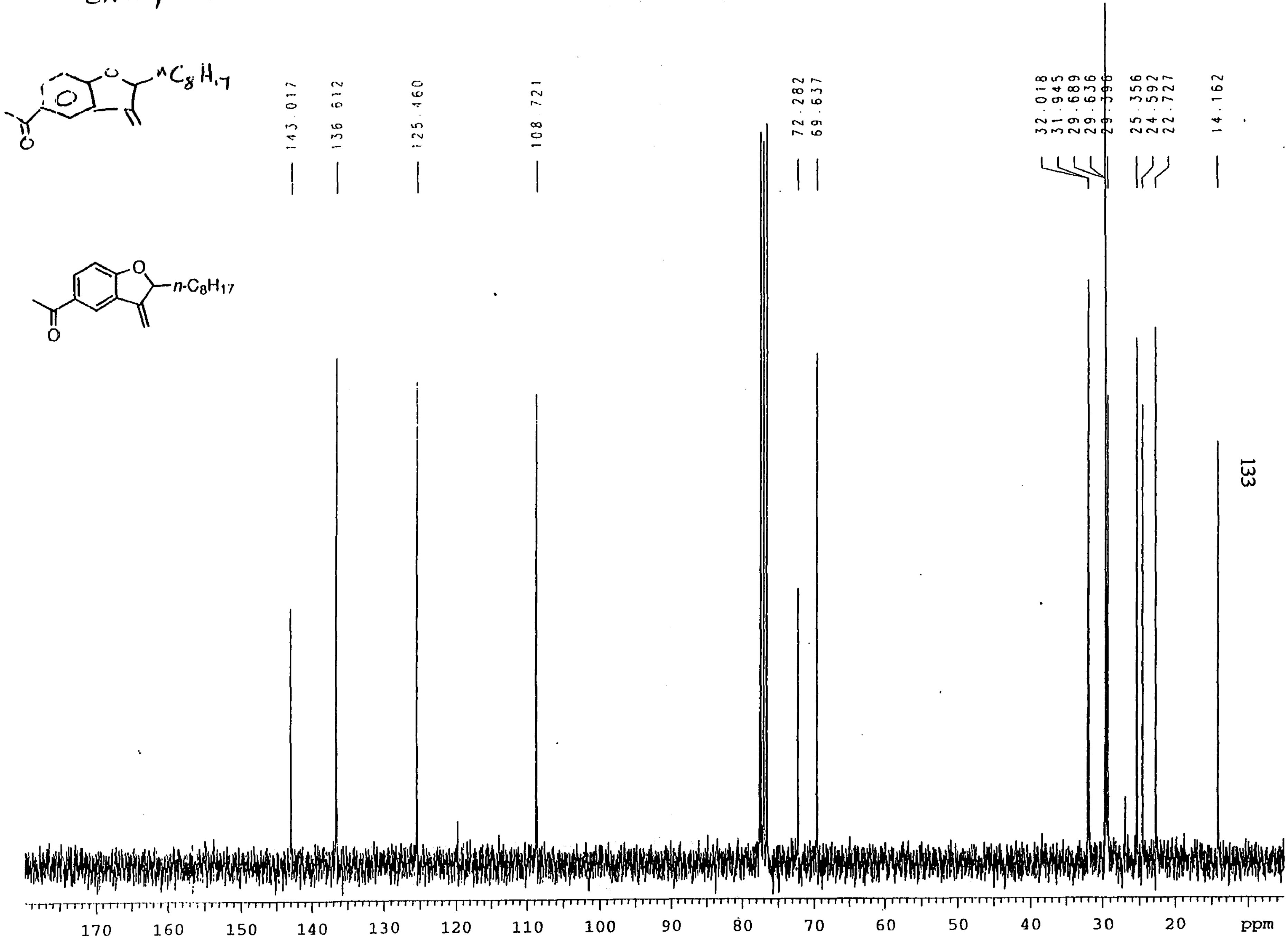

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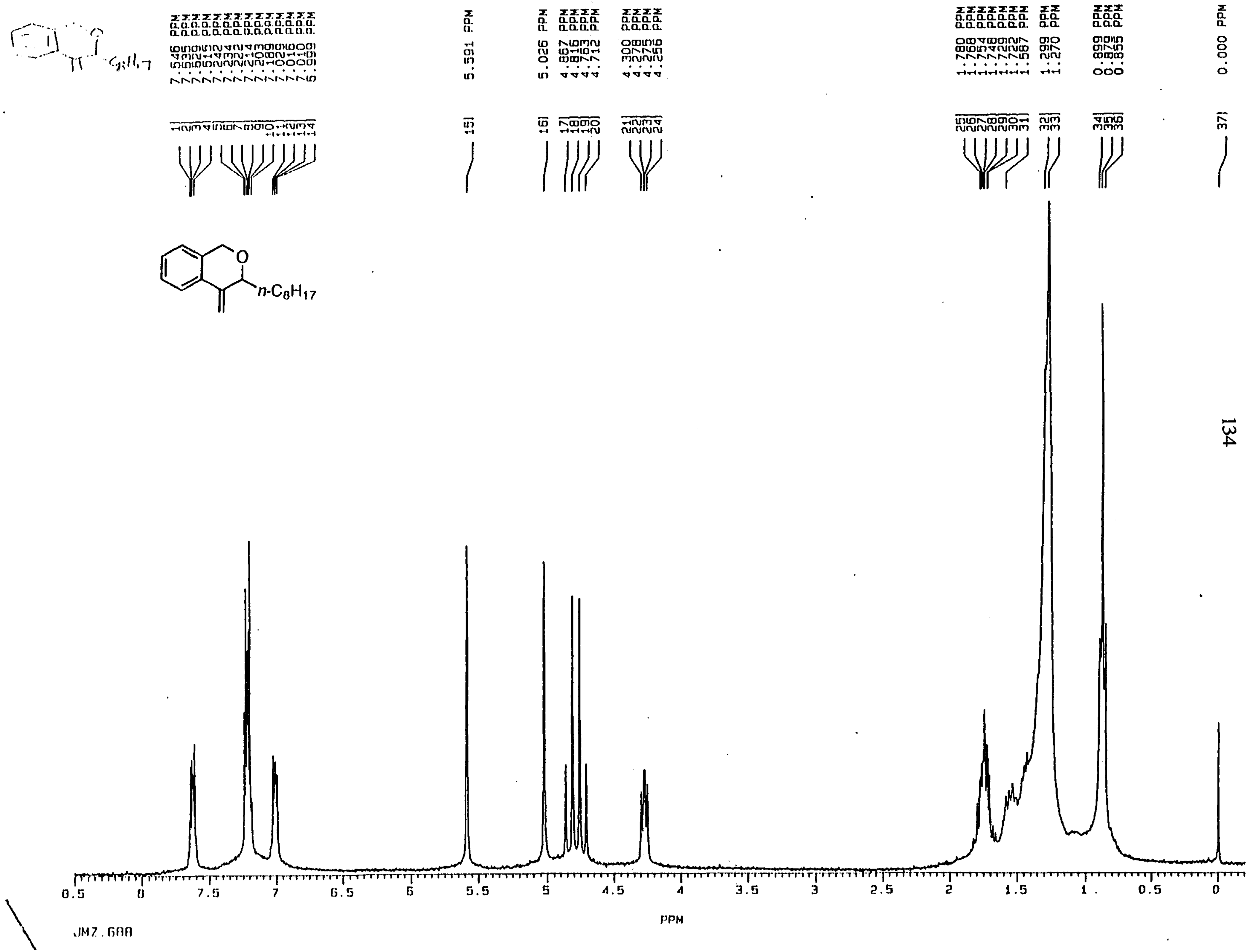

C_8H_{17}
7.546 PPM
7.535 PPM
7.529 PPM
7.515 PPM
7.242 PPM
7.234 PPM
7.222 PPM
7.214 PPM
7.203 PPM
7.189 PPM
7.029 PPM
7.016 PPM
7.010 PPM
6.999 PPM
5.591 PPM
5.026 PPM
4.867 PPM
4.816 PPM
4.763 PPM
4.712 PPM
4.300 PPM
4.278 PPM
4.275 PPM
4.256 PPM
1.780 PPM
1.768 PPM
1.754 PPM
1.748 PPM
1.729 PPM
1.722 PPM
1.587 PPM
1.299 PPM
1.270 PPM
0.899 PPM
0.879 PPM
0.855 PPM
0.000 PPM
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
O
n-C_8H_{17}
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1.
0.5
0
PPM
JMZ.688

Entry 5

ITEM	HEIGHT	PP HEIGHT(1)	FREQ(HZ)	PPM
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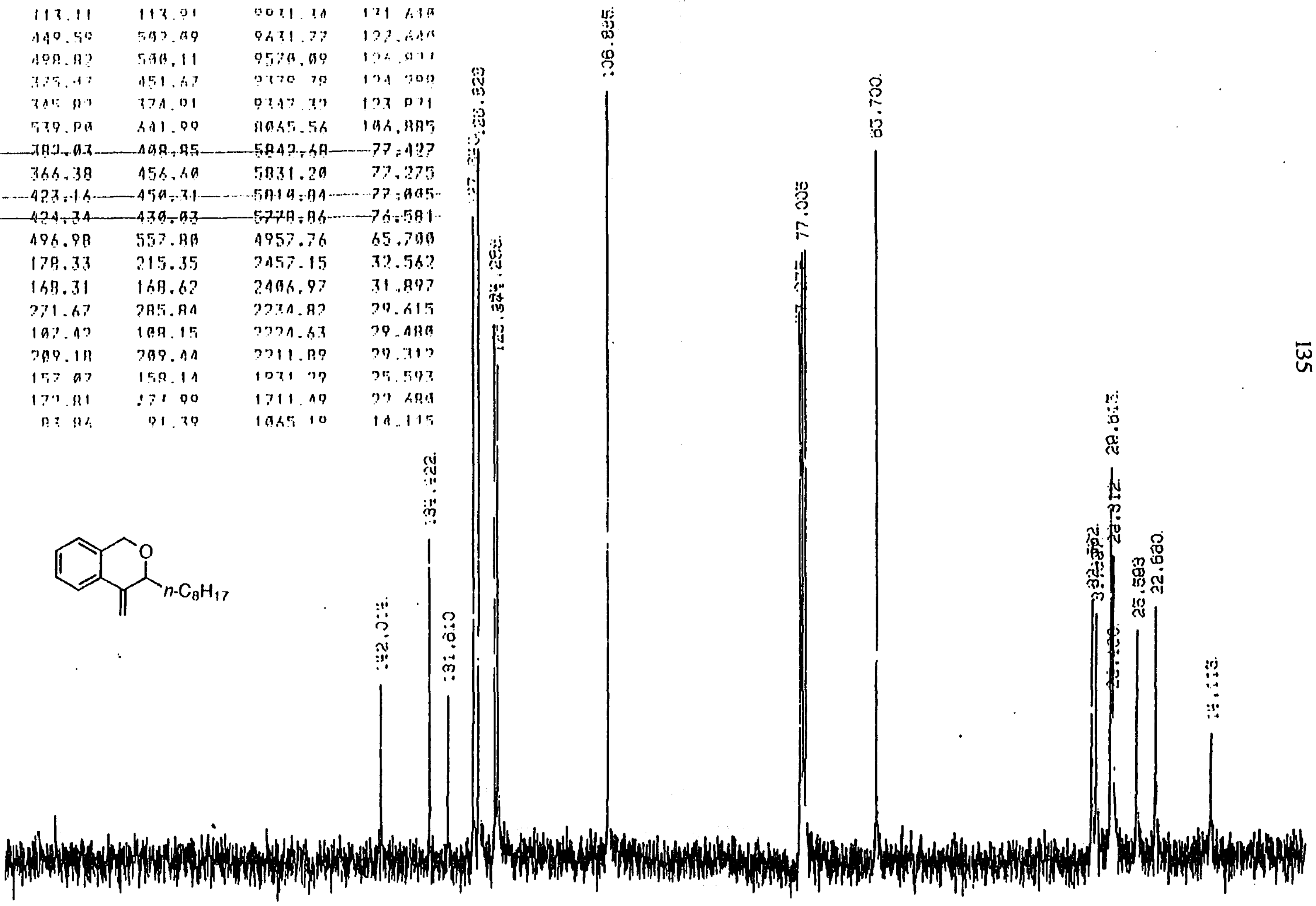
2	223.35	242.53	10143.51	134.422
3	113.11	113.91	9931.14	131.610
4	449.59	542.09	9631.77	127.640
5	498.82	580.11	9570.09	126.821
6	325.47	451.67	9370.78	124.209
7	345.02	374.01	9347.39	123.871
8	539.80	641.99	8065.56	106.885
~~9~~	~~389.03~~	~~408.85~~	~~5842.68~~	~~77.427~~
10	366.38	456.40	5831.20	77.275
~~11~~	~~423.16~~	~~450.31~~	~~5814.04~~	~~77.045~~
~~12~~	~~424.34~~	~~430.03~~	~~5778.86~~	~~76.581~~
13	496.98	557.80	4957.76	65.700
14	178.33	215.35	2457.15	32.562
15	168.31	168.62	2406.97	31.897
16	271.67	285.84	2234.82	29.615
17	107.42	108.15	2224.63	29.480
18	209.18	209.44	2211.89	29.312
19	157.07	158.14	1931.22	25.593
20	172.81	171.90	1711.49	22.680
21	83.84	91.39	1065.10	14.115



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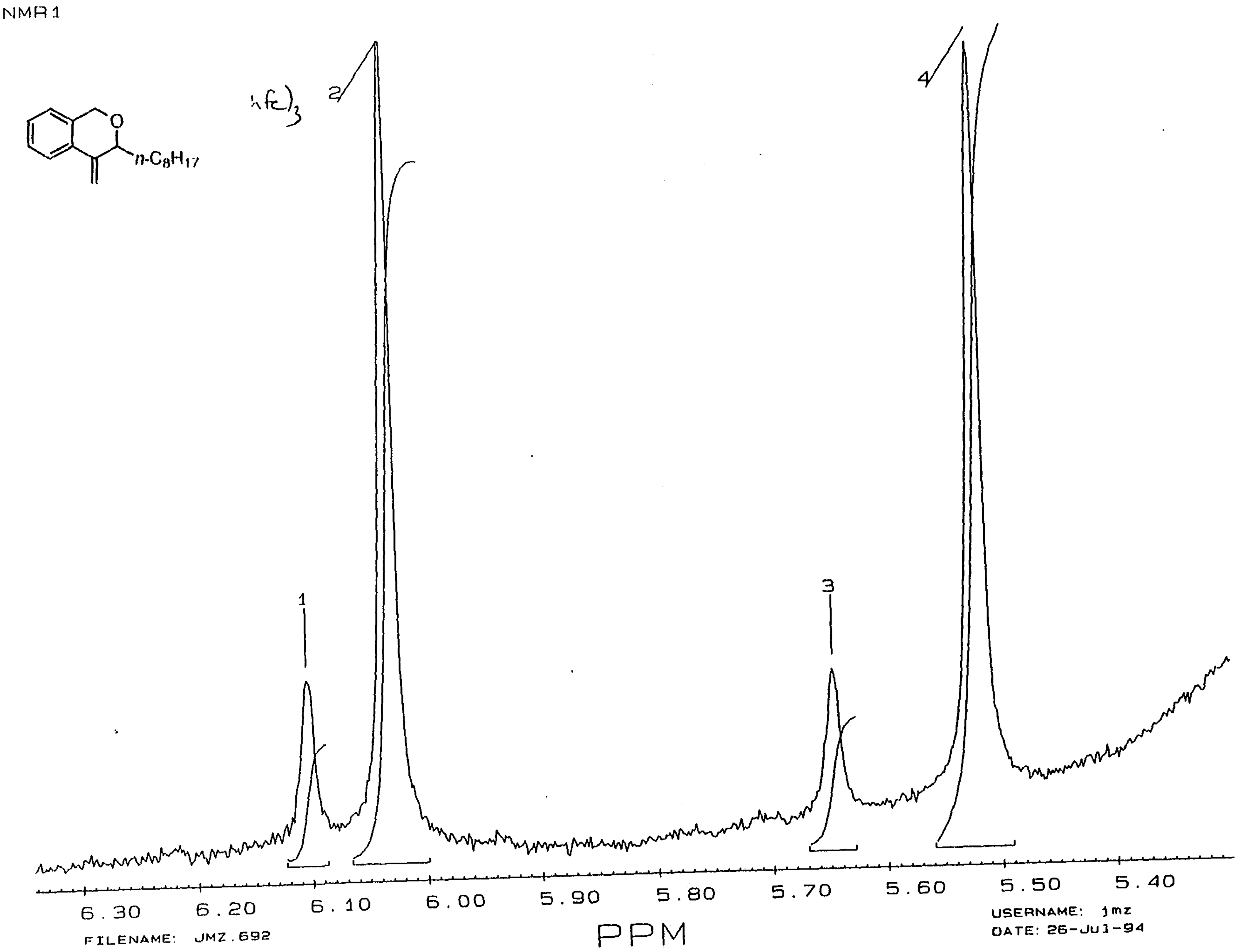
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O
n-C$_8$H$_{17}$
hfc)$_3$
1
2
3
4
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6.20
6.10
6.00
5.90
5.80
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5.60
5.50
5.40
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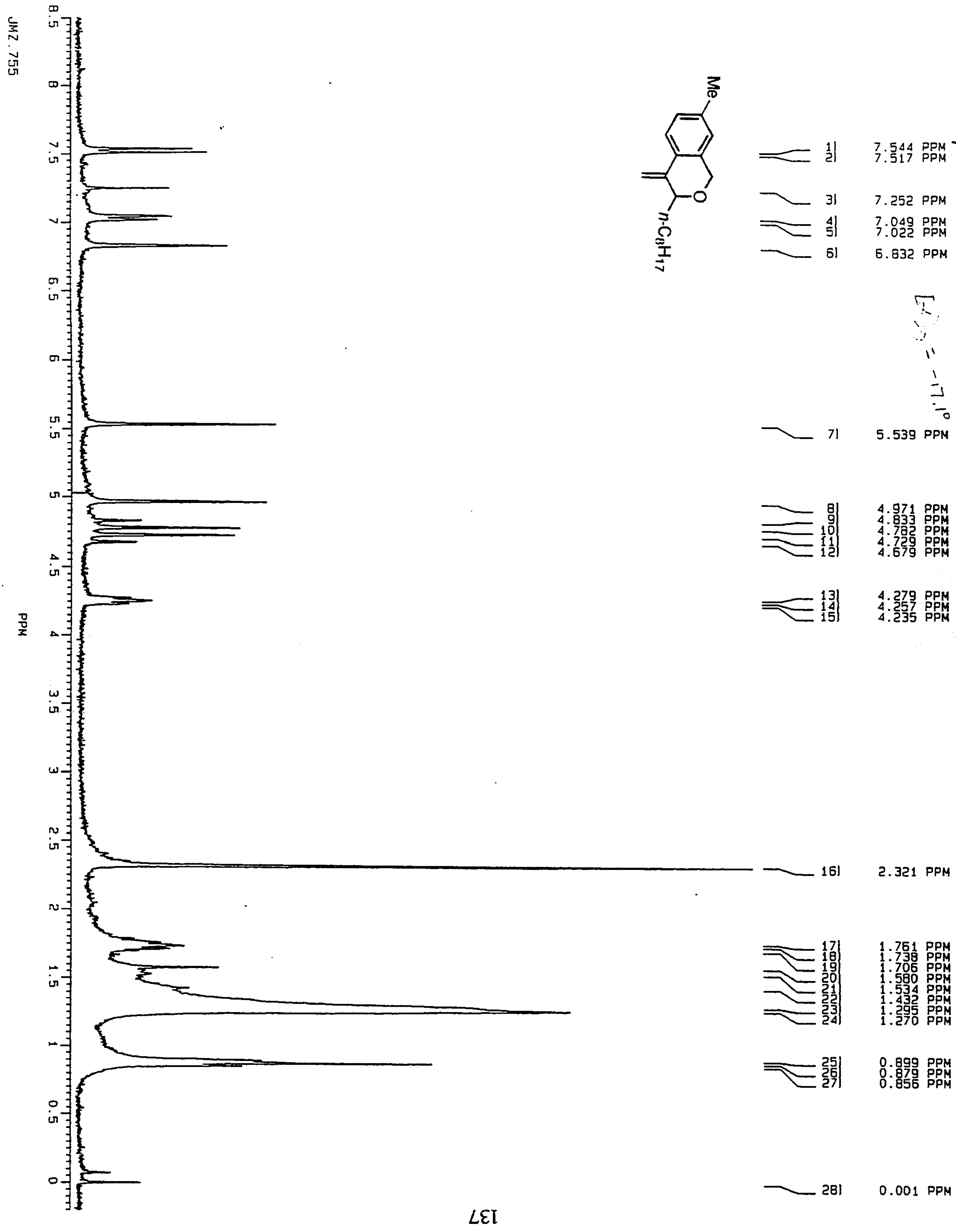

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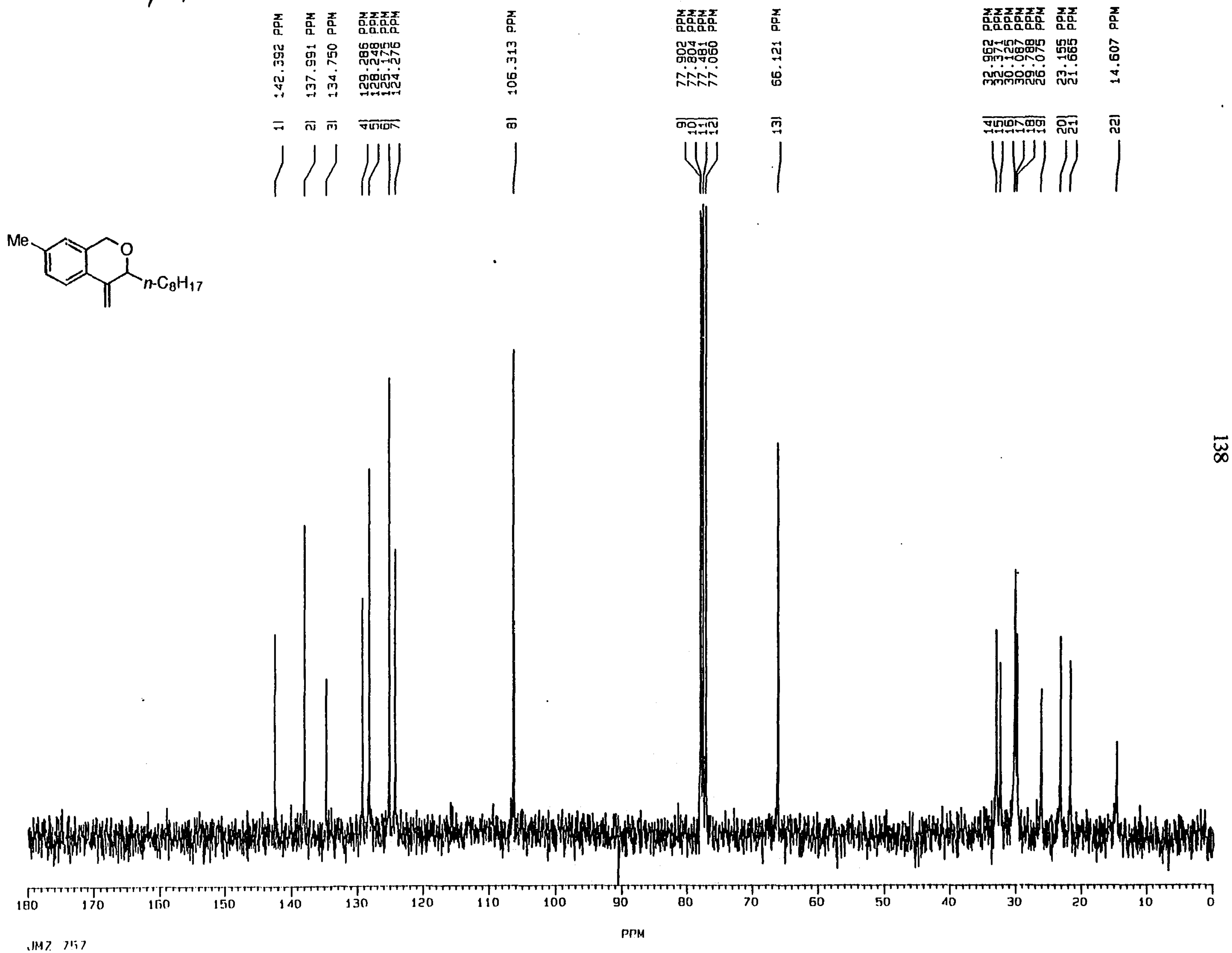
Entry 6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O
n-C8H17
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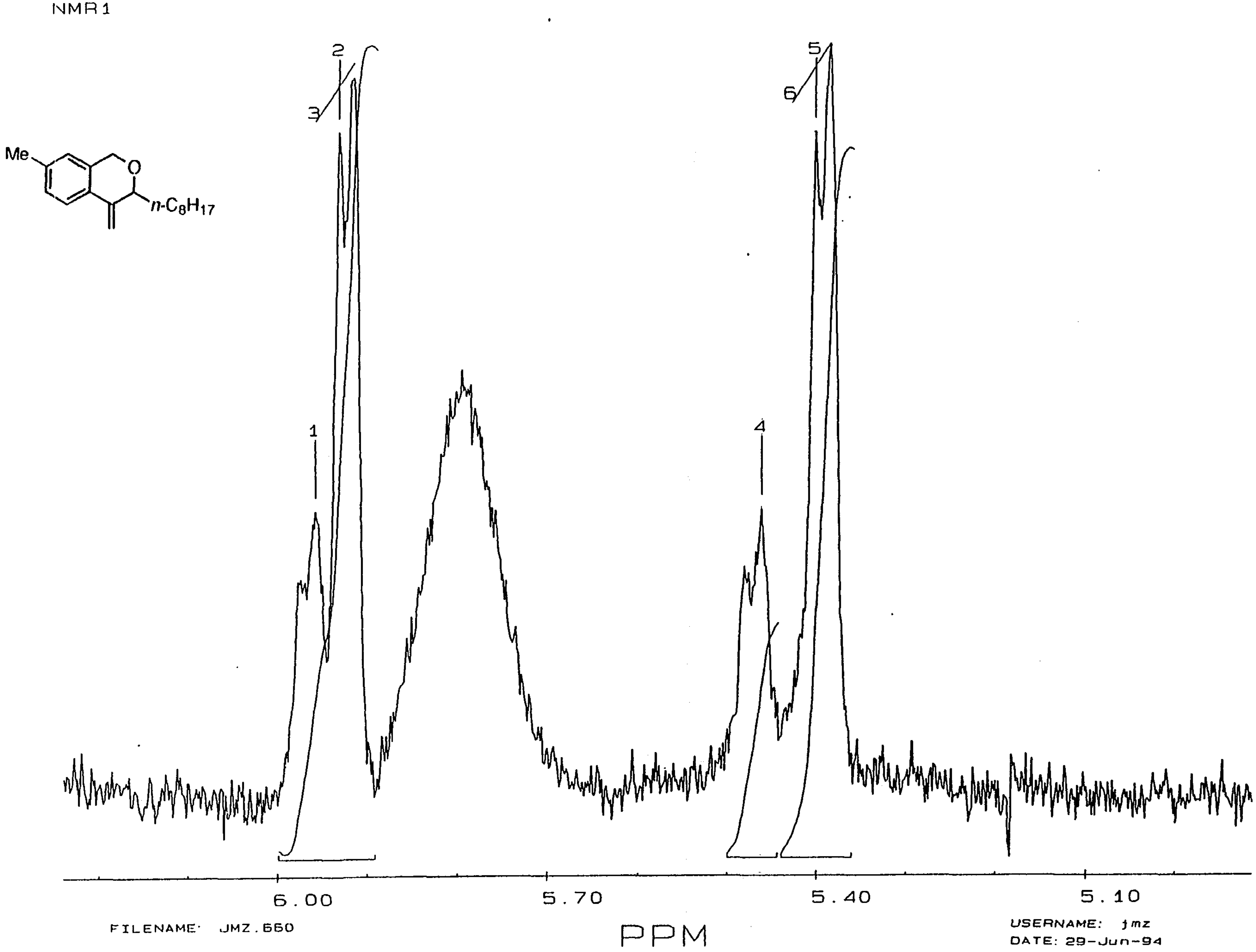
3| 134.750 PPM
4| 129.286 PPM
5| 128.248 PPM
6| 125.175 PPM
7| 124.276 PPM
8| 106.313 PPM
9| 77.902 PPM
10| 77.804 PPM
11| 77.481 PPM
12| 77.060 PPM
13| 66.121 PPM
14| 32.962 PPM
15| 32.371 PPM
16| 30.125 PPM
17| 30.087 PPM
18| 29.788 PPM
19| 26.075 PPM
20| 23.155 PPM
21| 21.665 PPM
22| 14.607 PPM
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JMZ 757

entry 6


NMR 1
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5.40
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entry 1

JMZ

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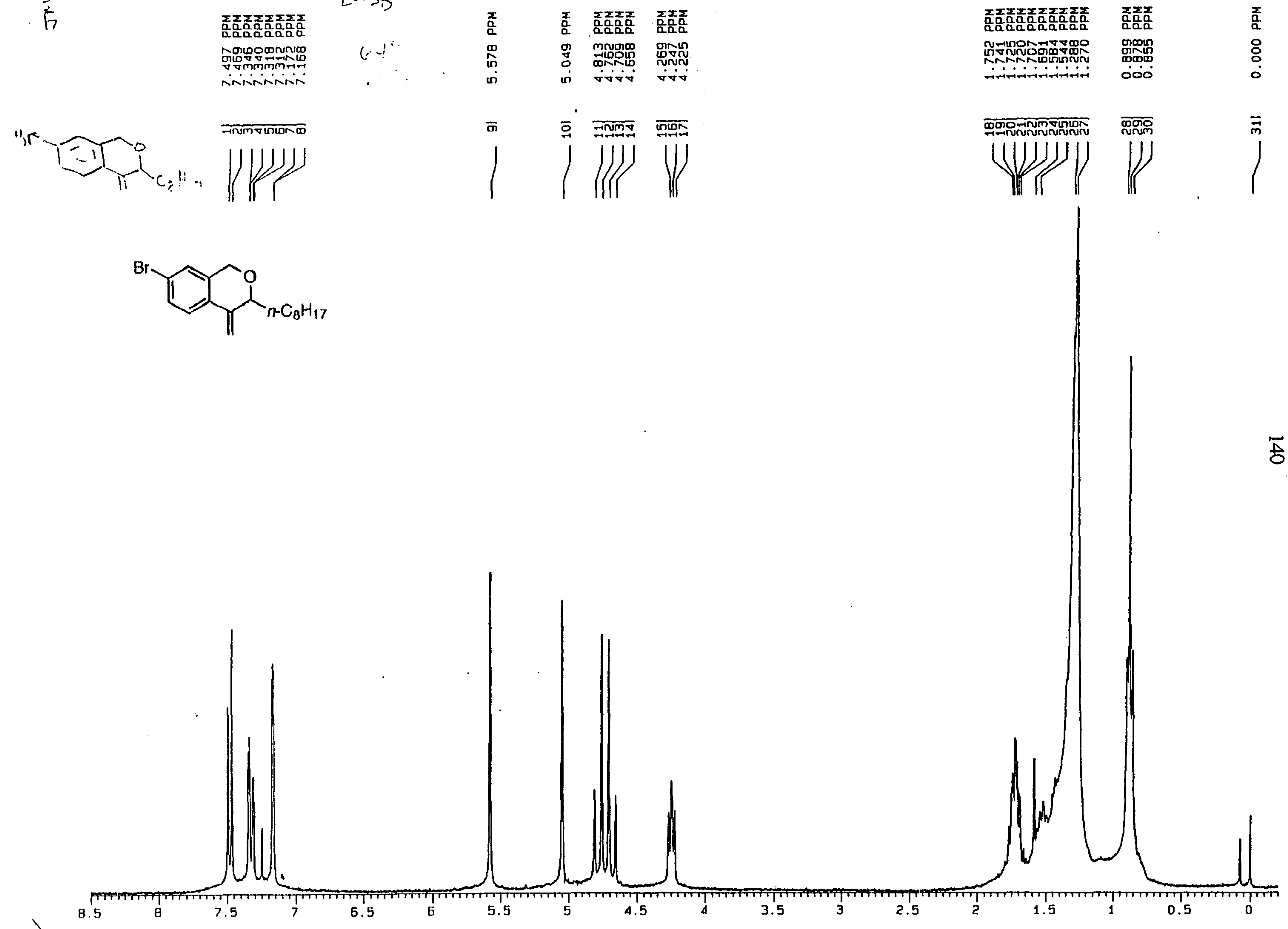

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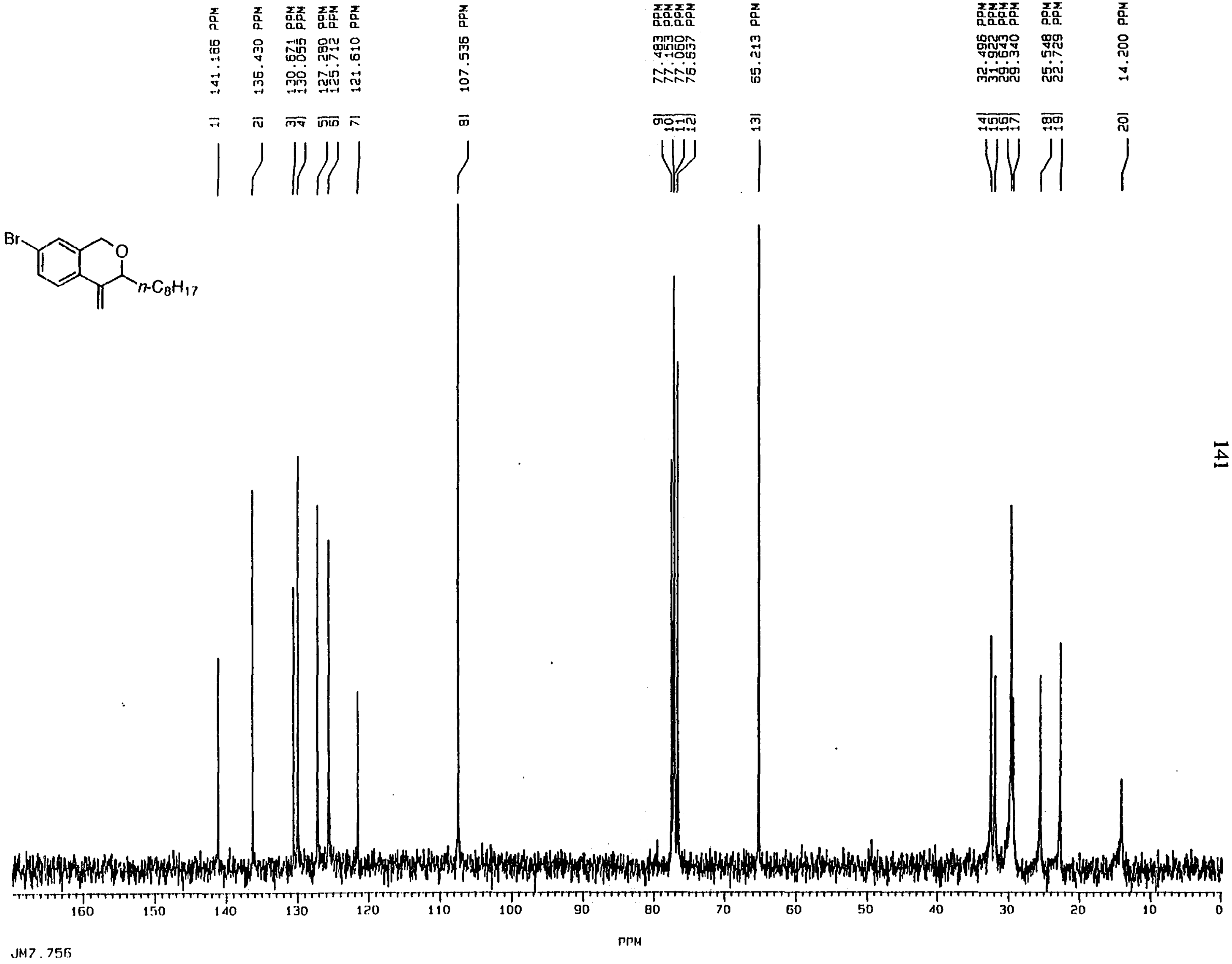
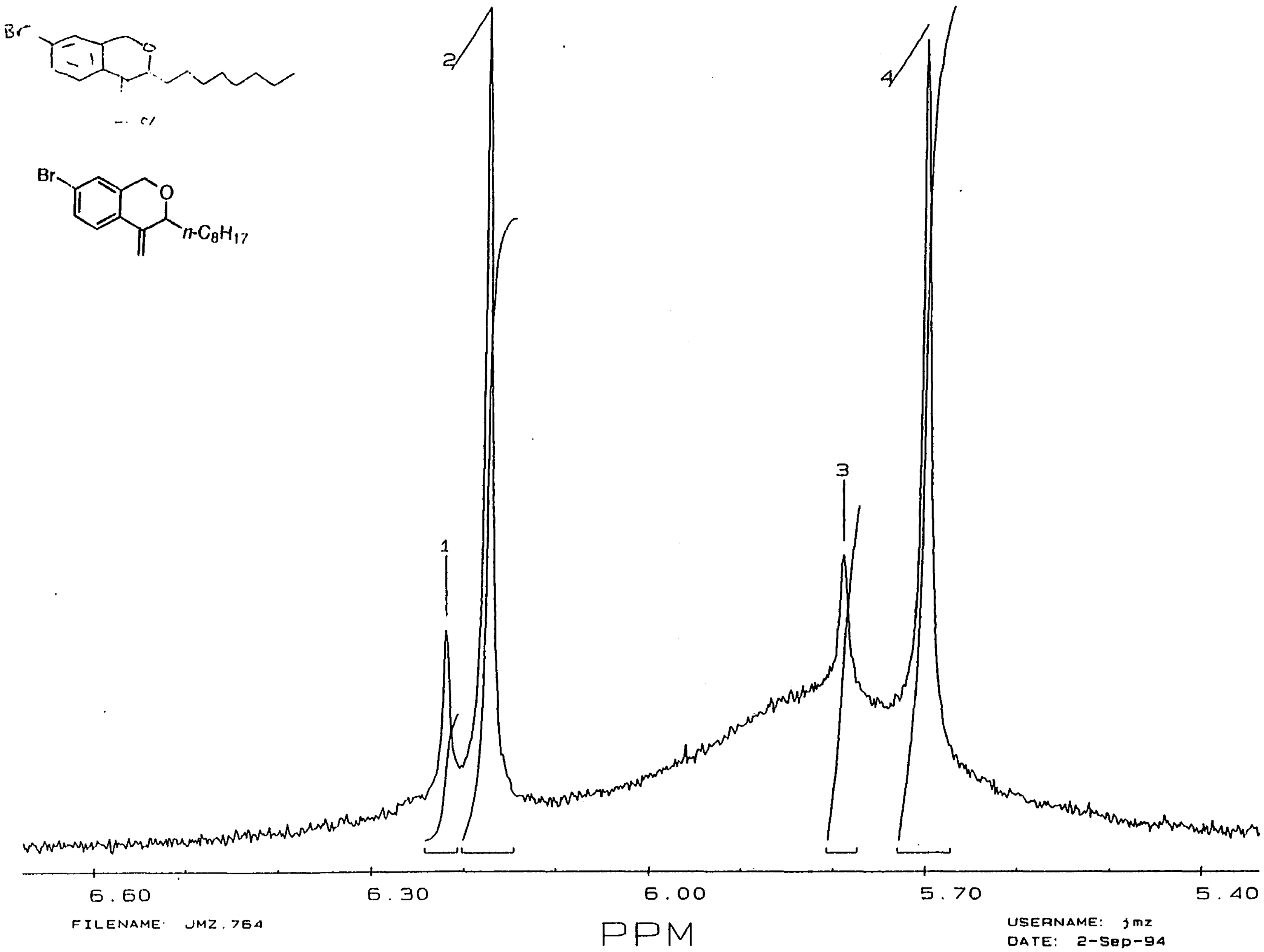
Entry ~~8~~ 7


Br
O
n-C8H17
1| 141.186 PPM
2| 136.430 PPM
3| 130.671 PPM
4| 130.055 PPM
5| 127.280 PPM
6| 125.712 PPM
7| 121.610 PPM
8| 107.536 PPM
9| 77.483 PPM
10| 77.153 PPM
11| 77.060 PPM
12| 76.637 PPM
13| 65.213 PPM
14| 32.496 PPM
15| 31.922 PPM
16| 29.643 PPM
17| 29.340 PPM
18| 25.548 PPM
19| 22.729 PPM
20| 14.200 PPM
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JM7.756

Entry 1

NMR 1



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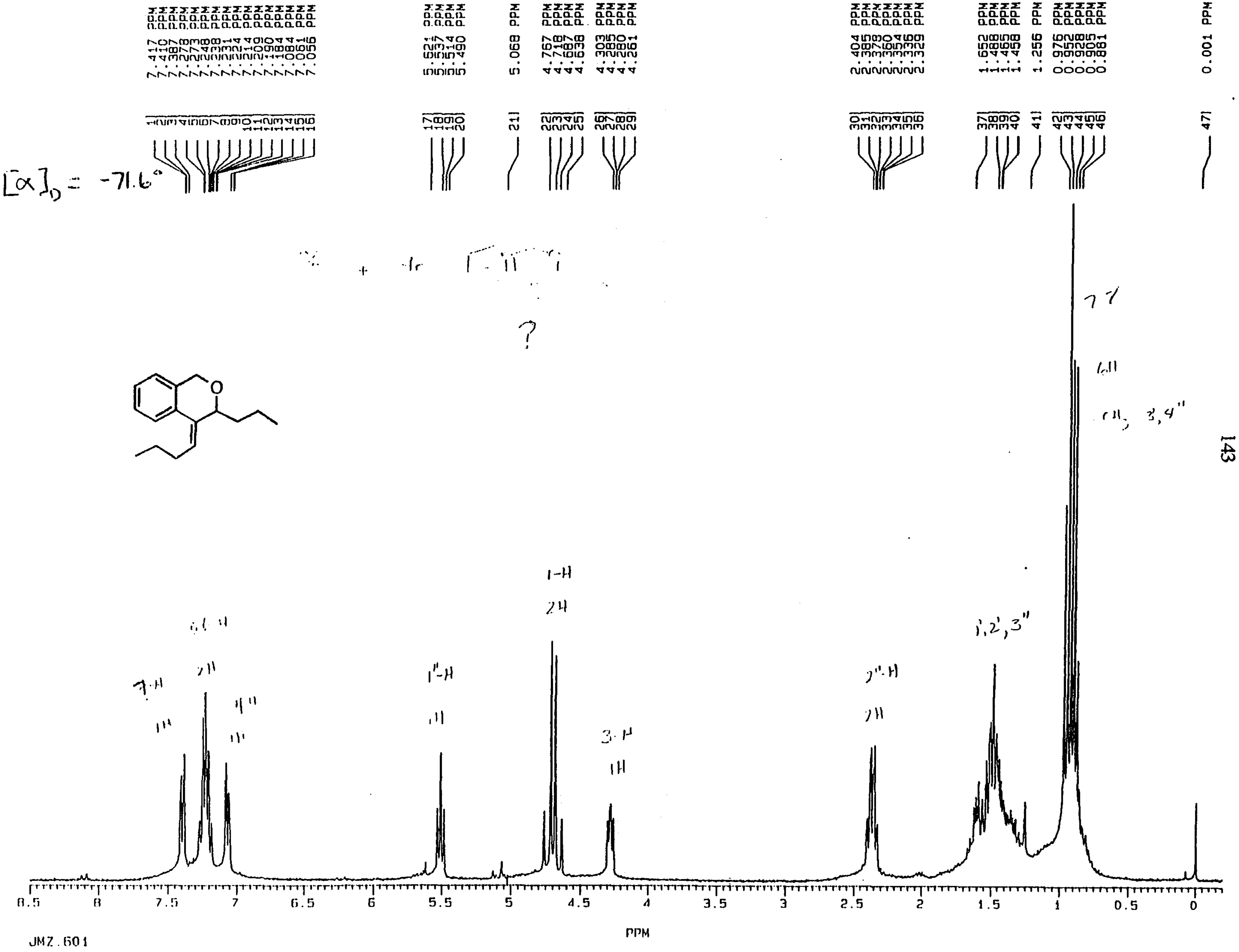
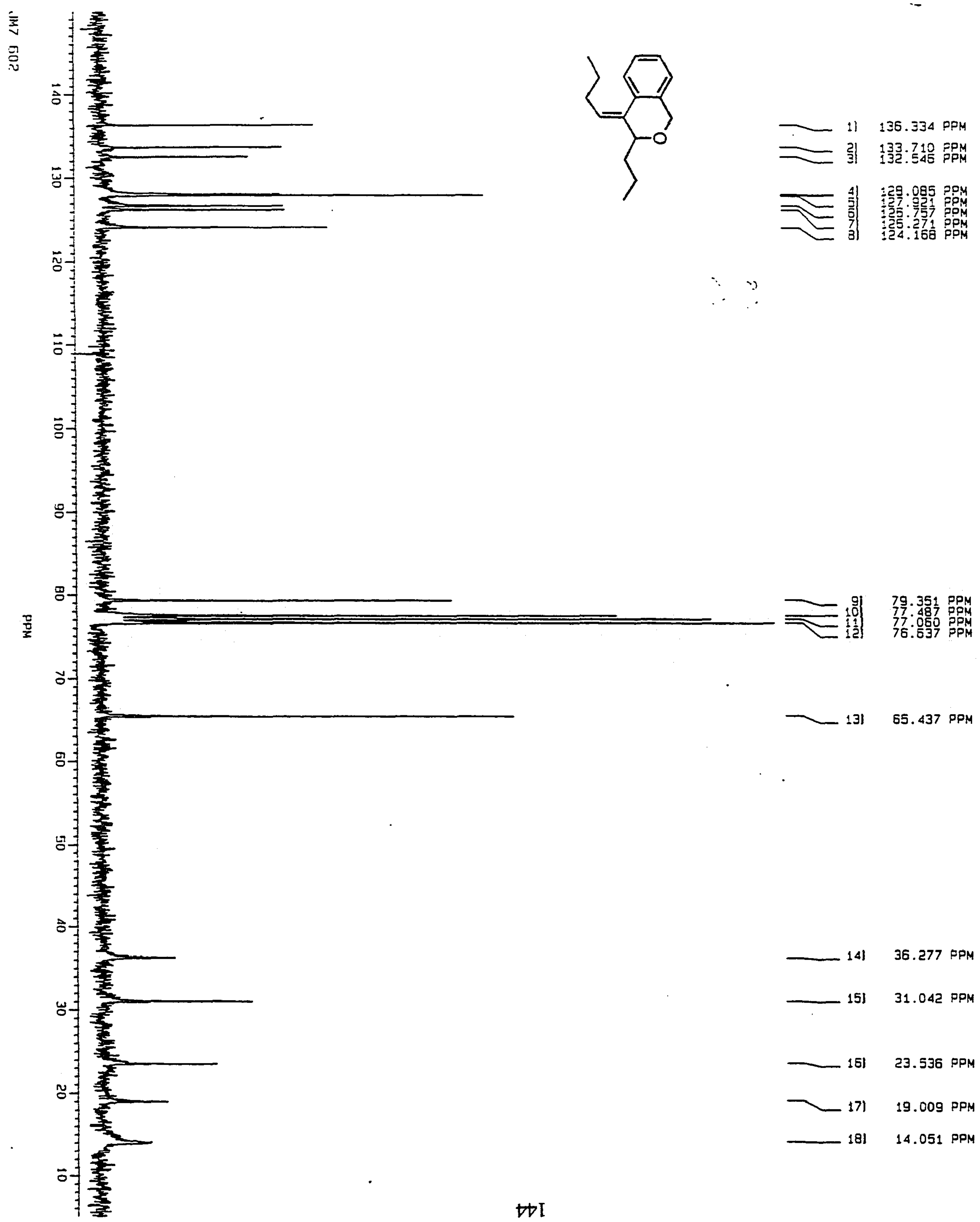
Entry 8 (8)

$[\alpha]_D = -71.6°$



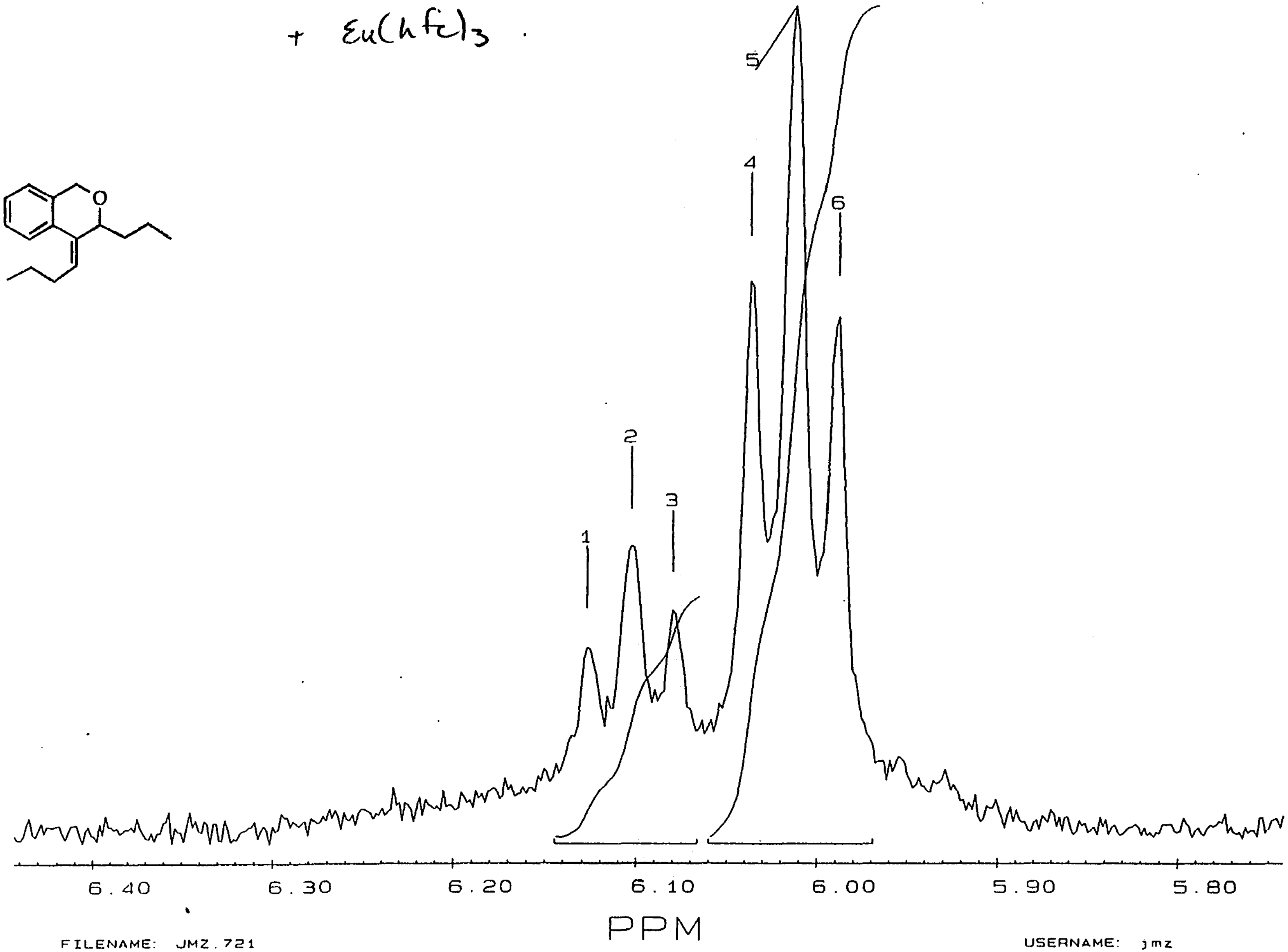

JM7 602
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
O
1) 136.334 PPM
2) 133.710 PPM
3) 132.546 PPM
4) 128.085 PPM
5) 127.921 PPM
6) 126.757 PPM
7) 126.271 PPM
8) 124.168 PPM
9) 79.351 PPM
10) 77.487 PPM
11) 77.060 PPM
12) 76.637 PPM
13) 65.437 PPM
14) 36.277 PPM
15) 31.042 PPM
16) 23.536 PPM
17) 19.009 PPM
18) 14.051 PPM

Entry 8

Entry 8

NMR 1

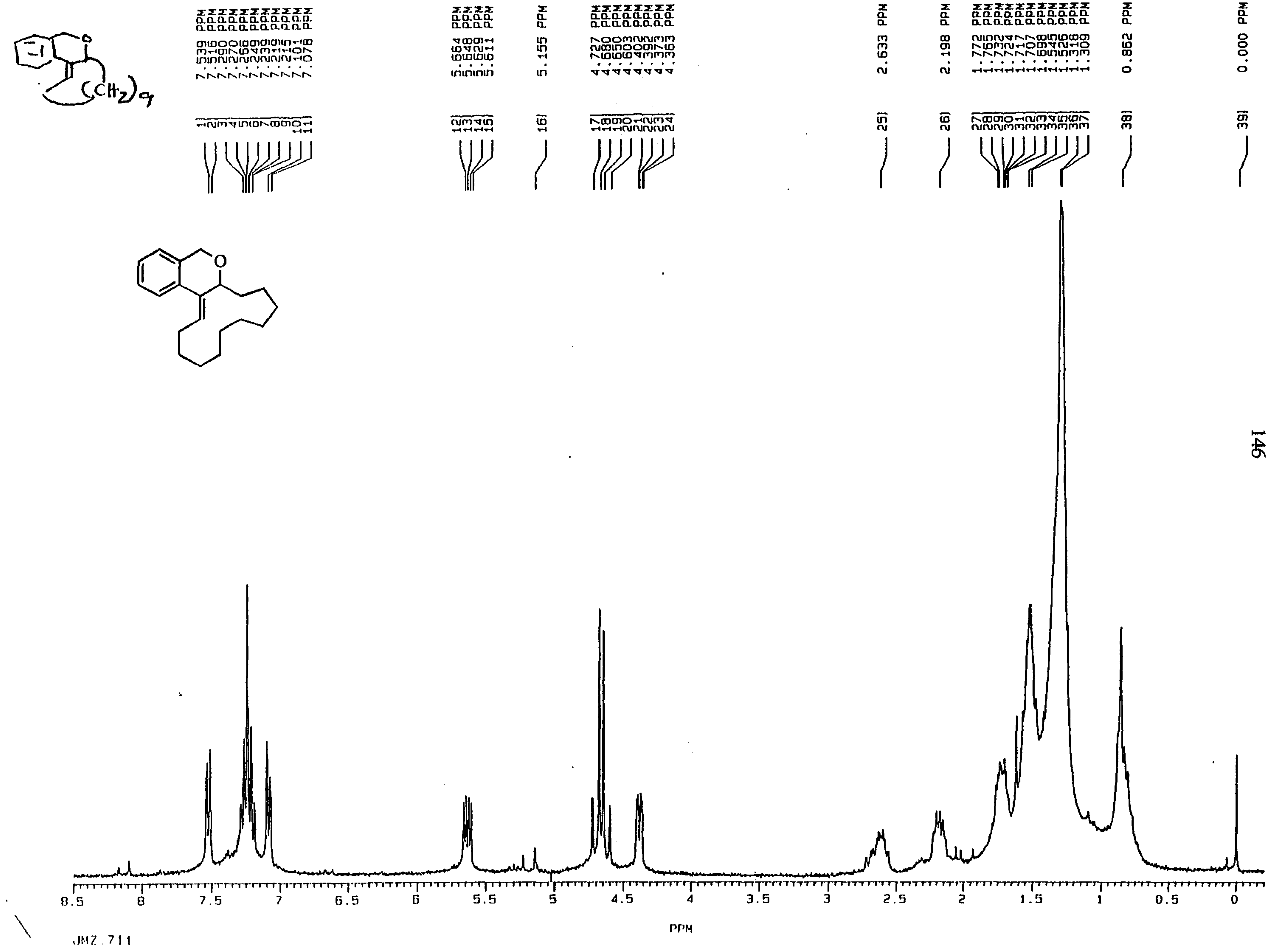
+ Eu(hfc)$_3$



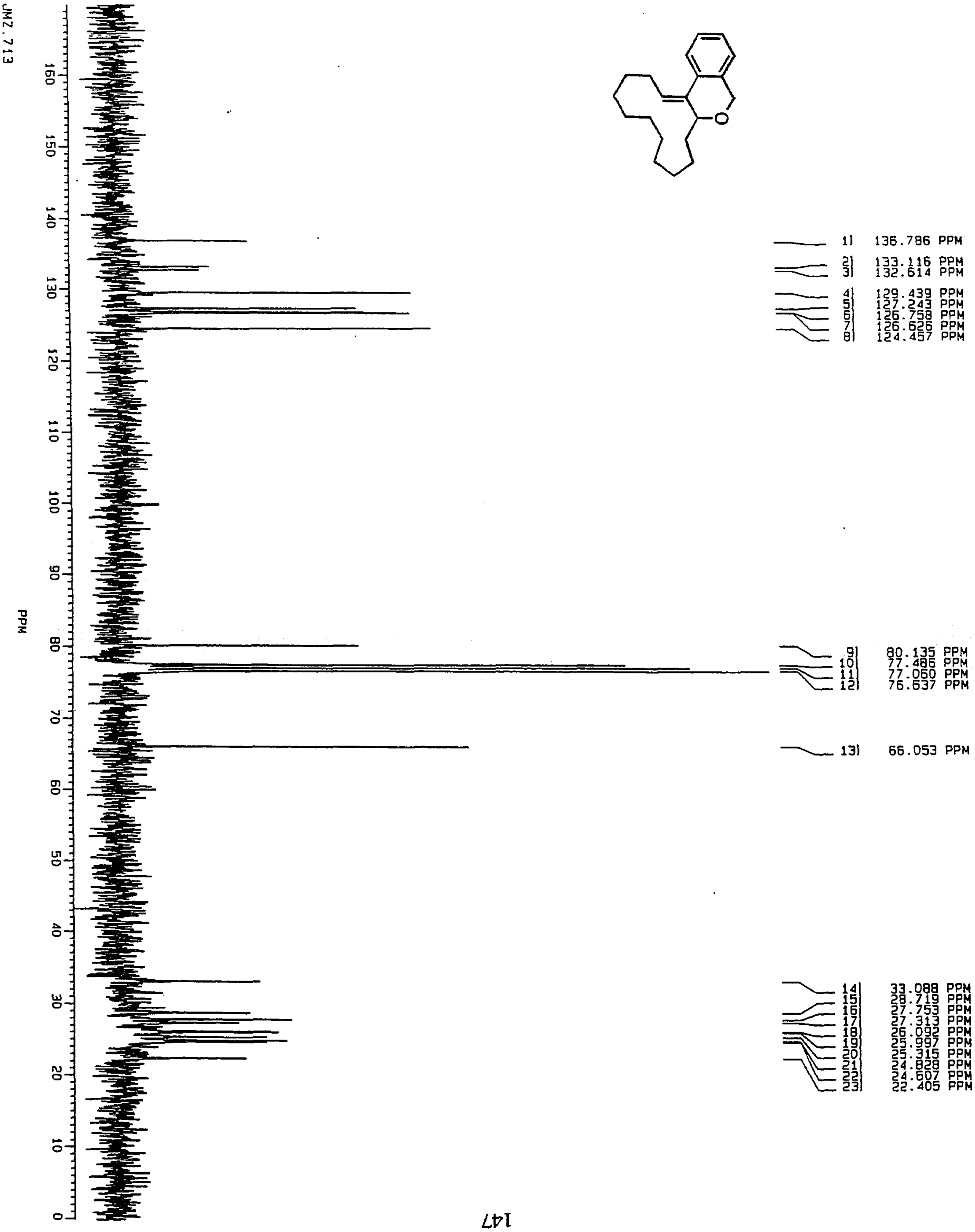
FILENAME: JMZ.721

USERNAME: jmz
DATE: 10-Aug-94

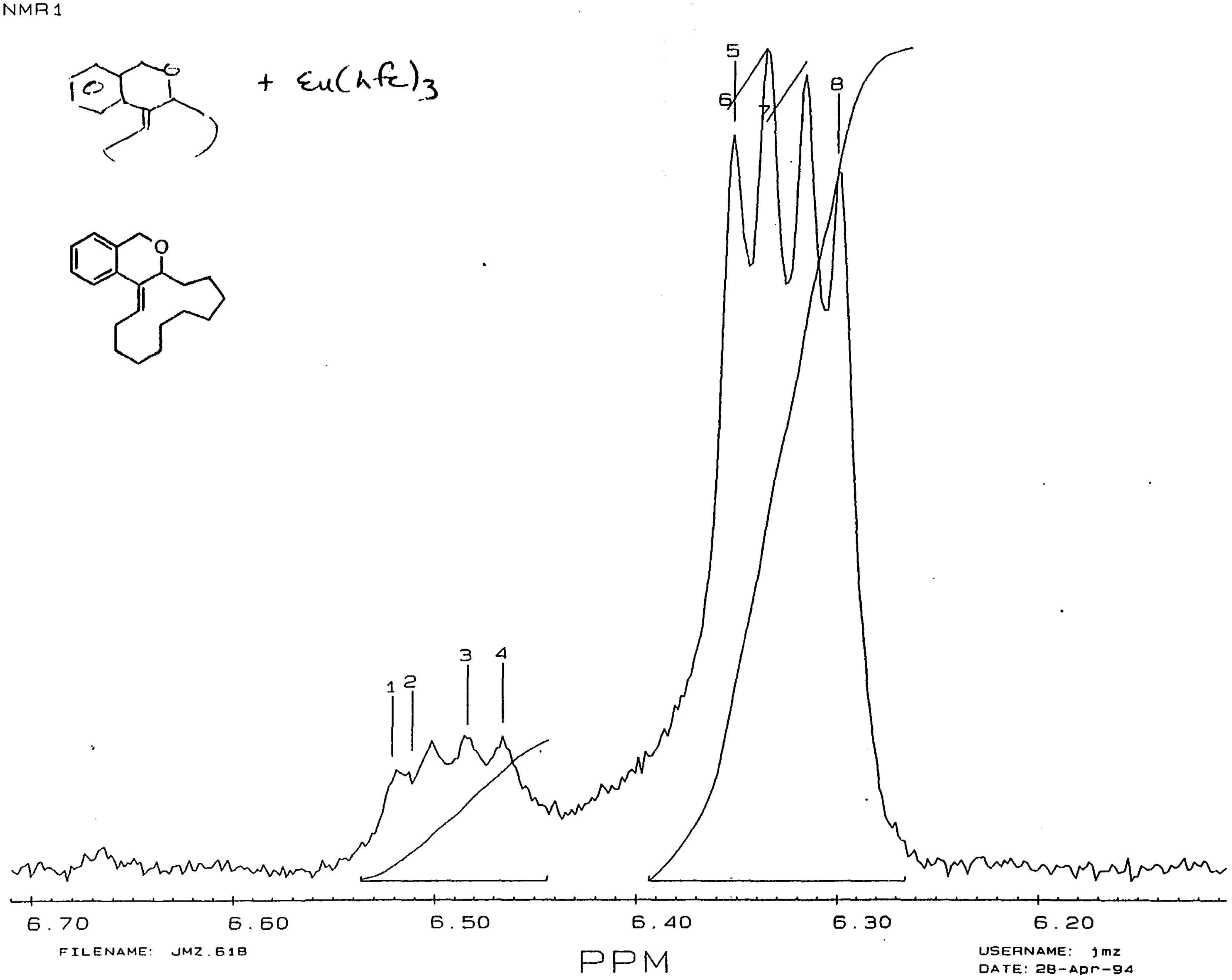
Entry ~~6~~ 9


(CH2)9
O
1) 7.539 PPM
2) 7.516 PPM
3) 7.290 PPM
4) 7.270 PPM
5) 7.266 PPM
6) 7.249 PPM
7) 7.239 PPM
8) 7.219 PPM
9) 7.215 PPM
10) 7.101 PPM
11) 7.078 PPM
12) 5.664 PPM
13) 5.648 PPM
14) 5.629 PPM
15) 5.611 PPM
16) 5.155 PPM
17) 4.727 PPM
18) 4.680 PPM
19) 4.650 PPM
20) 4.603 PPM
21) 4.402 PPM
22) 4.392 PPM
23) 4.373 PPM
24) 4.363 PPM
25) 2.633 PPM
26) 2.198 PPM
27) 1.772 PPM
28) 1.765 PPM
29) 1.732 PPM
30) 1.724 PPM
31) 1.717 PPM
32) 1.707 PPM
33) 1.698 PPM
34) 1.545 PPM
35) 1.526 PPM
36) 1.318 PPM
37) 1.309 PPM
38) 0.862 PPM
39) 0.000 PPM
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
JMZ.711

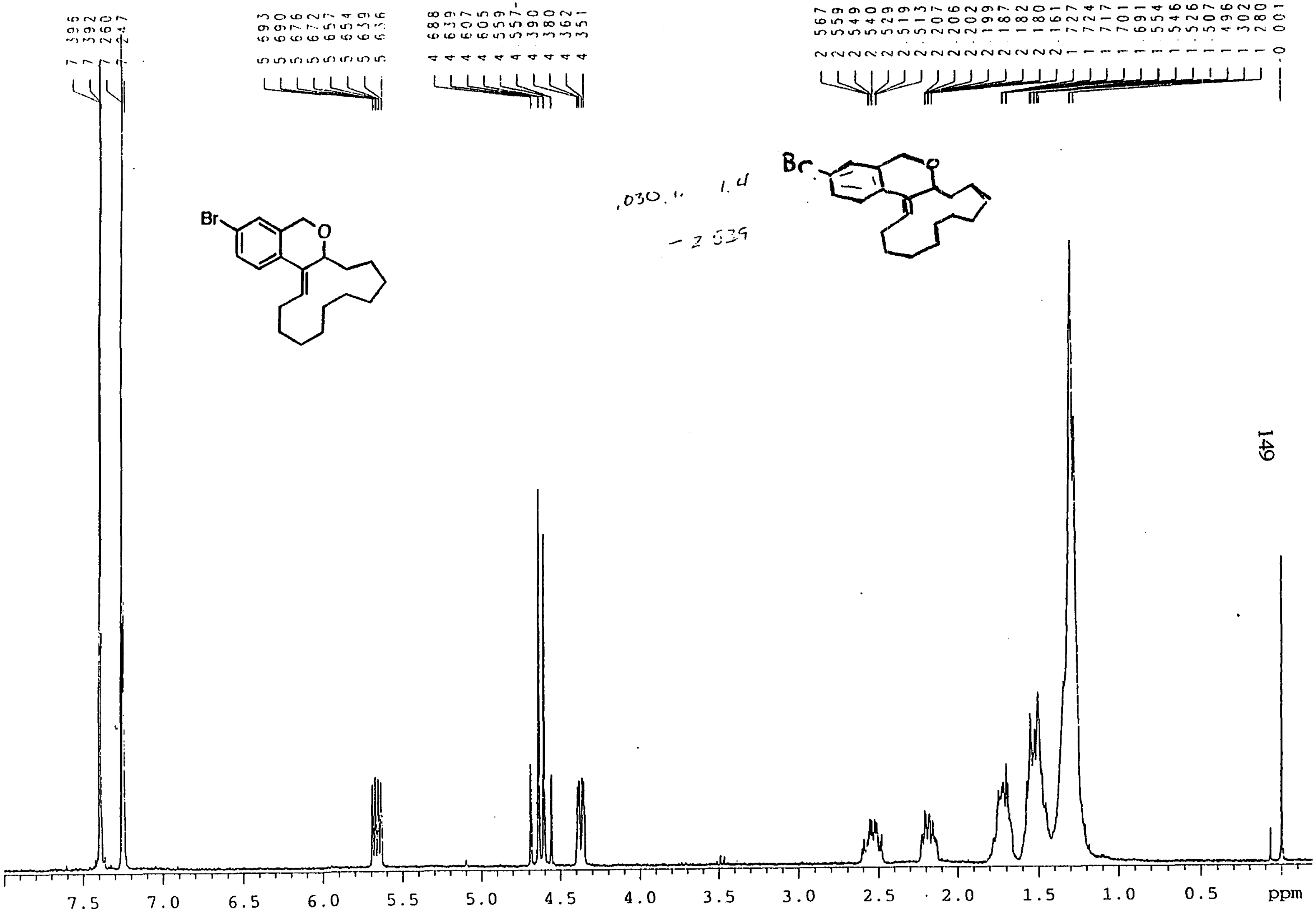
Entry 9


JMZ.713
PPM
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
1) 136.786 PPM
2) 133.116 PPM
3) 132.614 PPM
4) 129.439 PPM
5) 127.243 PPM
6) 126.758 PPM
7) 126.626 PPM
8) 124.457 PPM
9) 80.135 PPM
10) 77.486 PPM
11) 77.060 PPM
12) 76.637 PPM
13) 66.053 PPM
14) 33.088 PPM
15) 28.719 PPM
16) 27.753 PPM
17) 27.313 PPM
18) 26.092 PPM
19) 25.997 PPM
20) 25.315 PPM
21) 24.828 PPM
22) 24.607 PPM
23) 22.405 PPM
O

Entry 9


NMR1
+ Eu(hfc)3
1
2
3
4
5
6
7
8
6.70
6.60
6.50
6.40
6.30
6.20
PPM
FILENAME: JMZ.618
USERNAME: jmz
DATE: 28-Apr-94

Entry 10

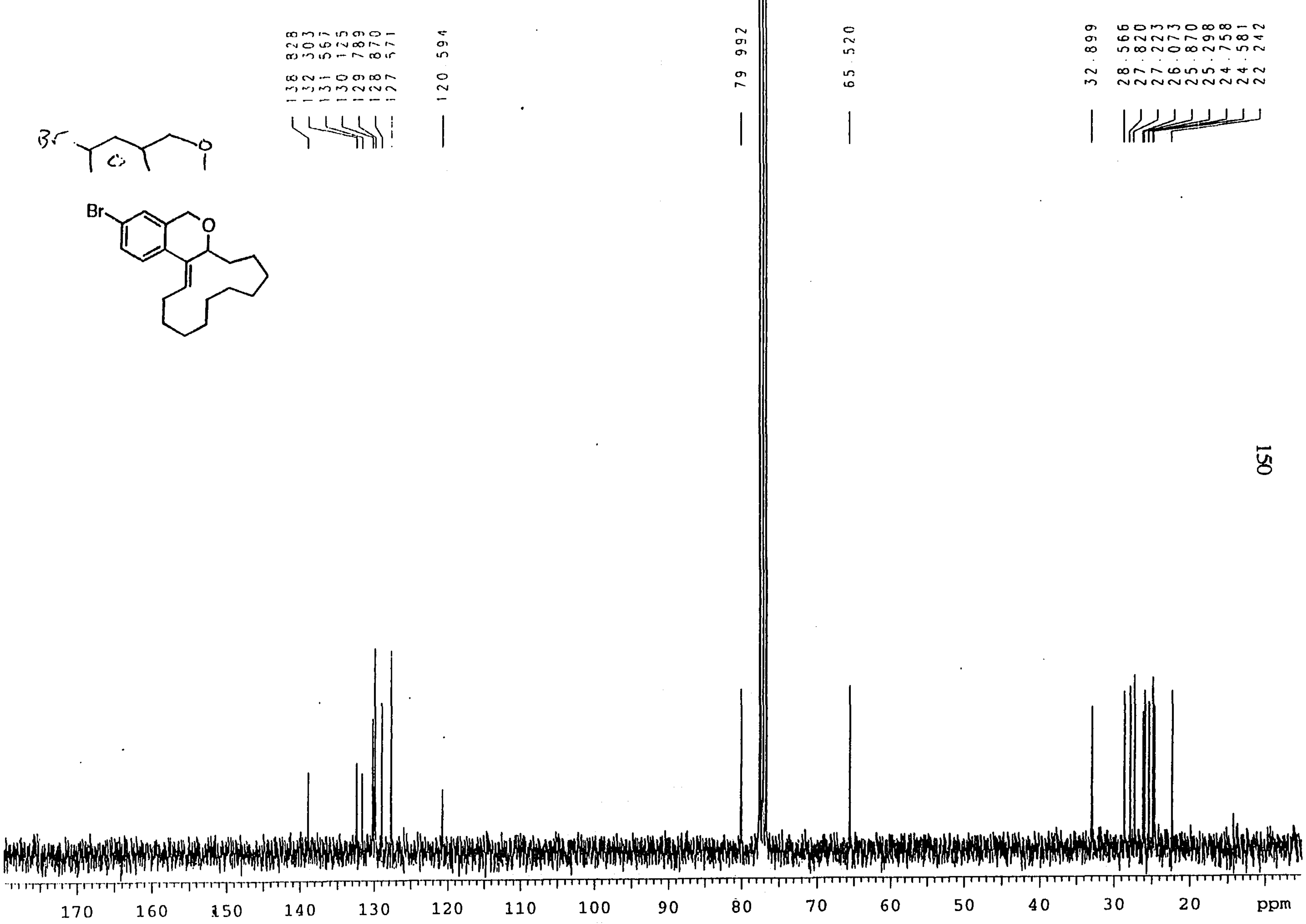


,030.‥ 1.4

– 2.539

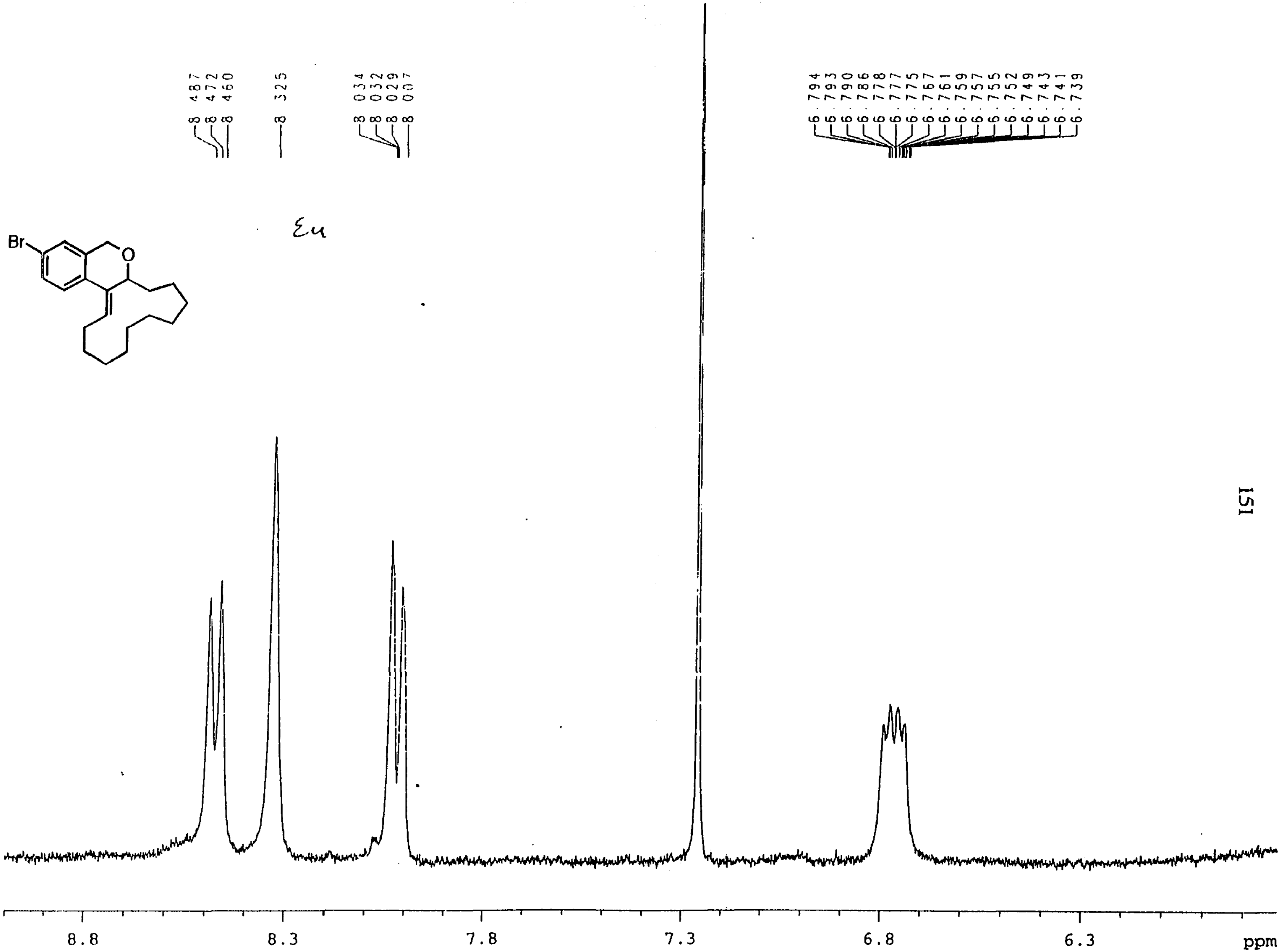
/giga/data/jmz/nmr/jmz.234.fid/1/pdata/1 unknown Wed Apr 17 18:05:41 1996

Entry 10



/giga/data/jmz/nmr/jmz.235.fid/1/pdata/1 unknown Wed Apr 17 18:16:01 1996

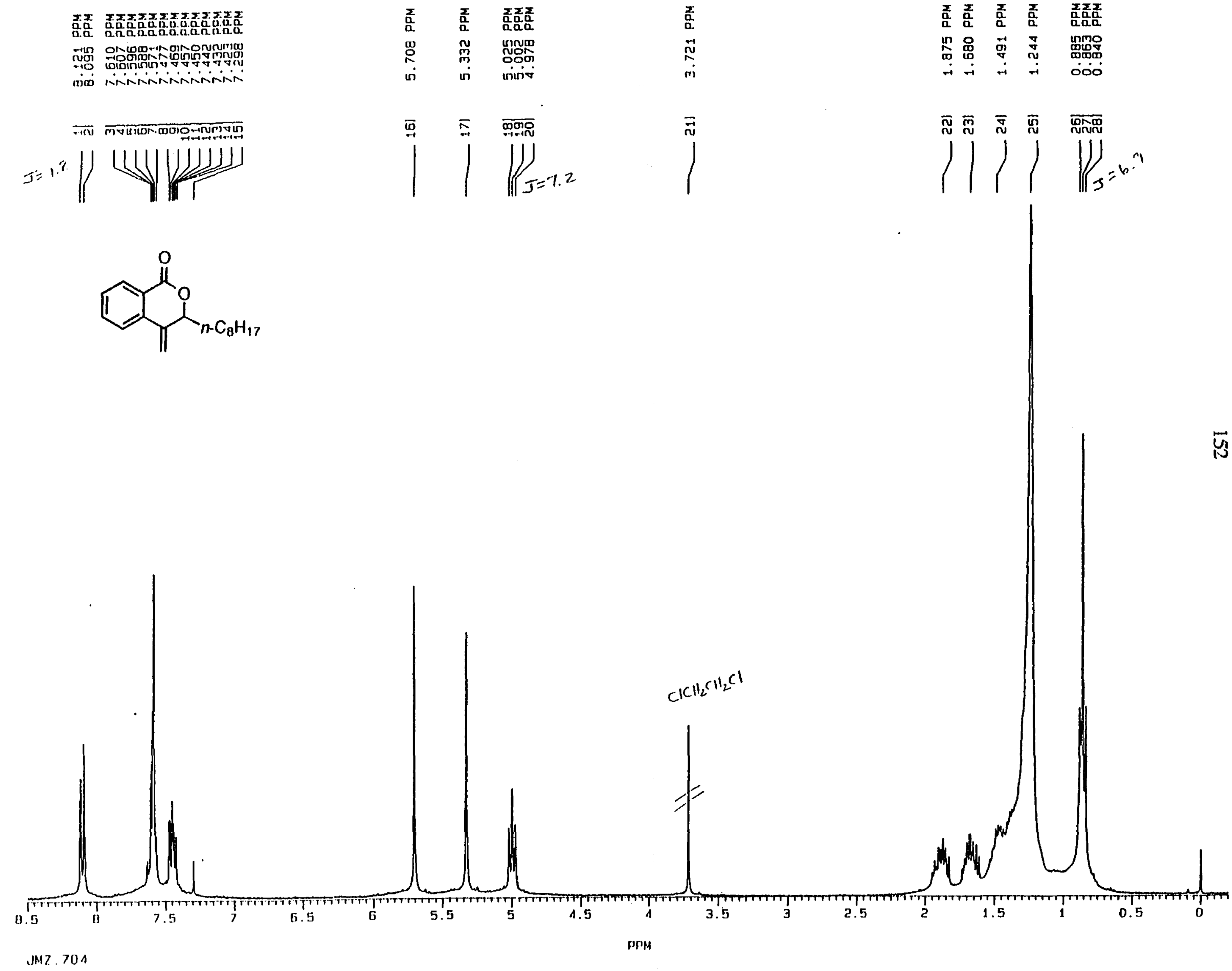
1 10.



Eu

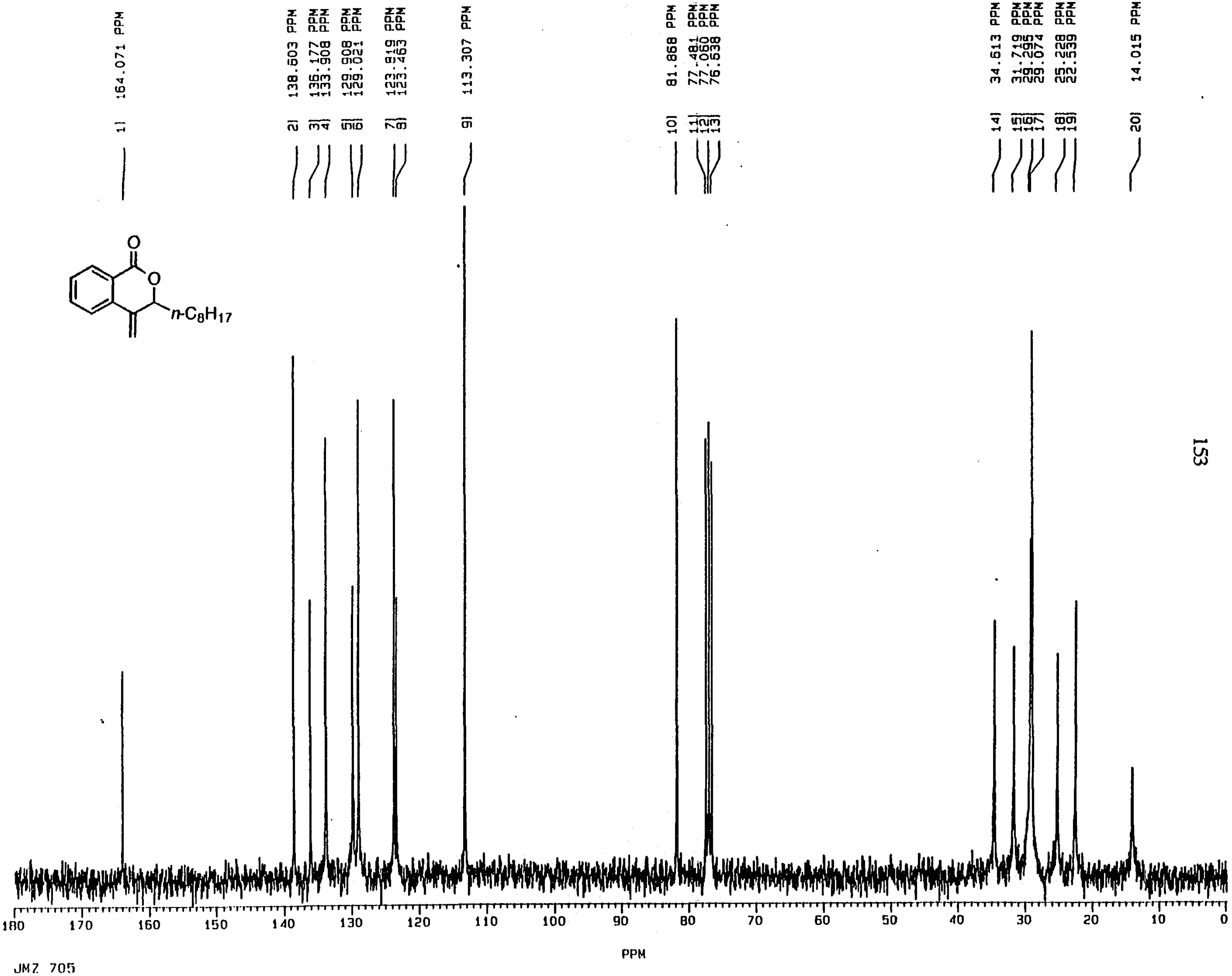
/giga/data/jmz/nmr/jmz.236.fid/1/pdata/1   unknown   Sat May 4 11:38:22 1996

Entry 11



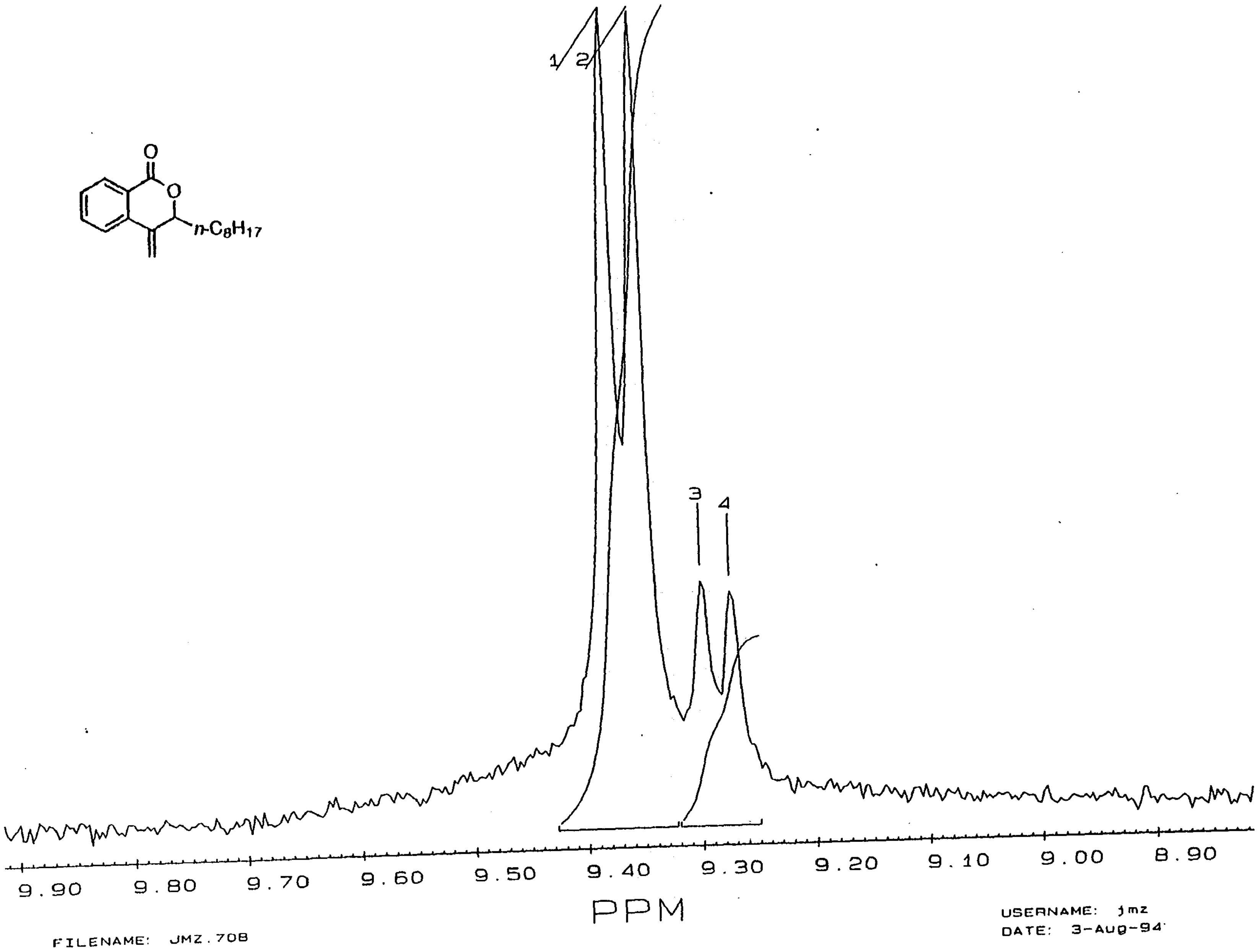
J= 1.2
1| 8.121 PPM
2| 8.095 PPM
3| 7.610 PPM
4| 7.607 PPM
5| 7.596 PPM
6| 7.588 PPM
7| 7.571 PPM
8| 7.477 PPM
9| 7.469 PPM
10| 7.457 PPM
11| 7.450 PPM
12| 7.442 PPM
13| 7.432 PPM
14| 7.423 PPM
15| 7.298 PPM
16| 5.708 PPM
17| 5.332 PPM
18| 5.025 PPM
19| 5.002 PPM
20| 4.978 PPM
J=7.2
21| 3.721 PPM
22| 1.875 PPM
23| 1.680 PPM
24| 1.491 PPM
25| 1.244 PPM
26| 0.885 PPM
27| 0.863 PPM
28| 0.840 PPM
J=6.7
O
O
n-C8H17
ClCH2CH2Cl
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
JMZ.704

Entry 11


n-C8H17
O
O
1) 164.071 PPM
2) 138.603 PPM
3) 136.177 PPM
4) 133.908 PPM
5) 129.908 PPM
6) 129.021 PPM
7) 123.819 PPM
8) 123.463 PPM
9) 113.307 PPM
10) 81.868 PPM
11) 77.481 PPM
12) 77.060 PPM
13) 76.638 PPM
14) 34.613 PPM
15) 31.719 PPM
16) 29.295 PPM
17) 29.074 PPM
18) 25.228 PPM
19) 22.539 PPM
20) 14.015 PPM
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JMZ 705

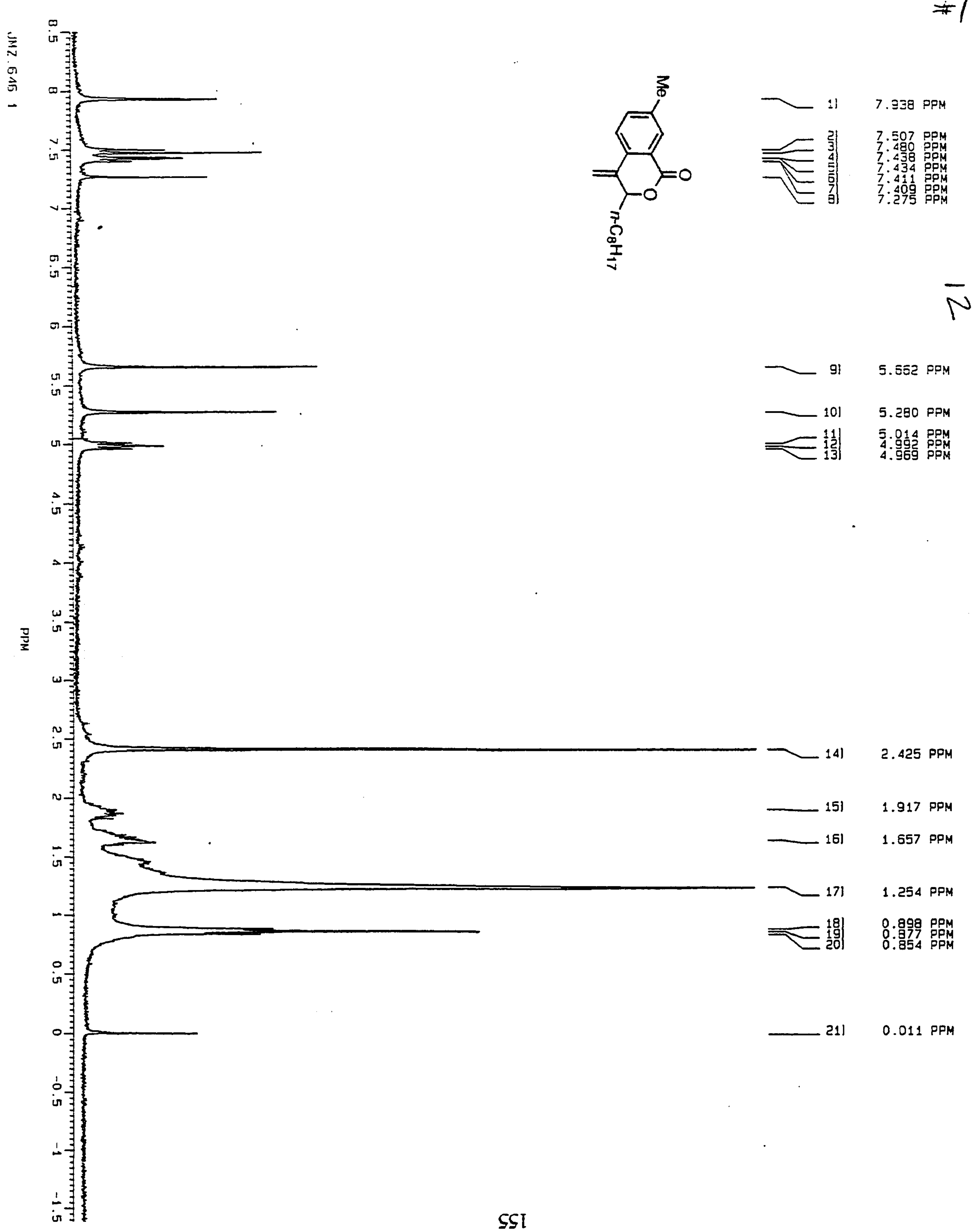
Entry 11

64%


O
O
n-C8H17
1
2
3
4
9.90
9.80
9.70
9.60
9.50
9.40
9.30
9.20
9.10
9.00
8.90
PPM
FILENAME: JMZ.708
USERNAME: jmz
DATE: 3-Aug-94

#1

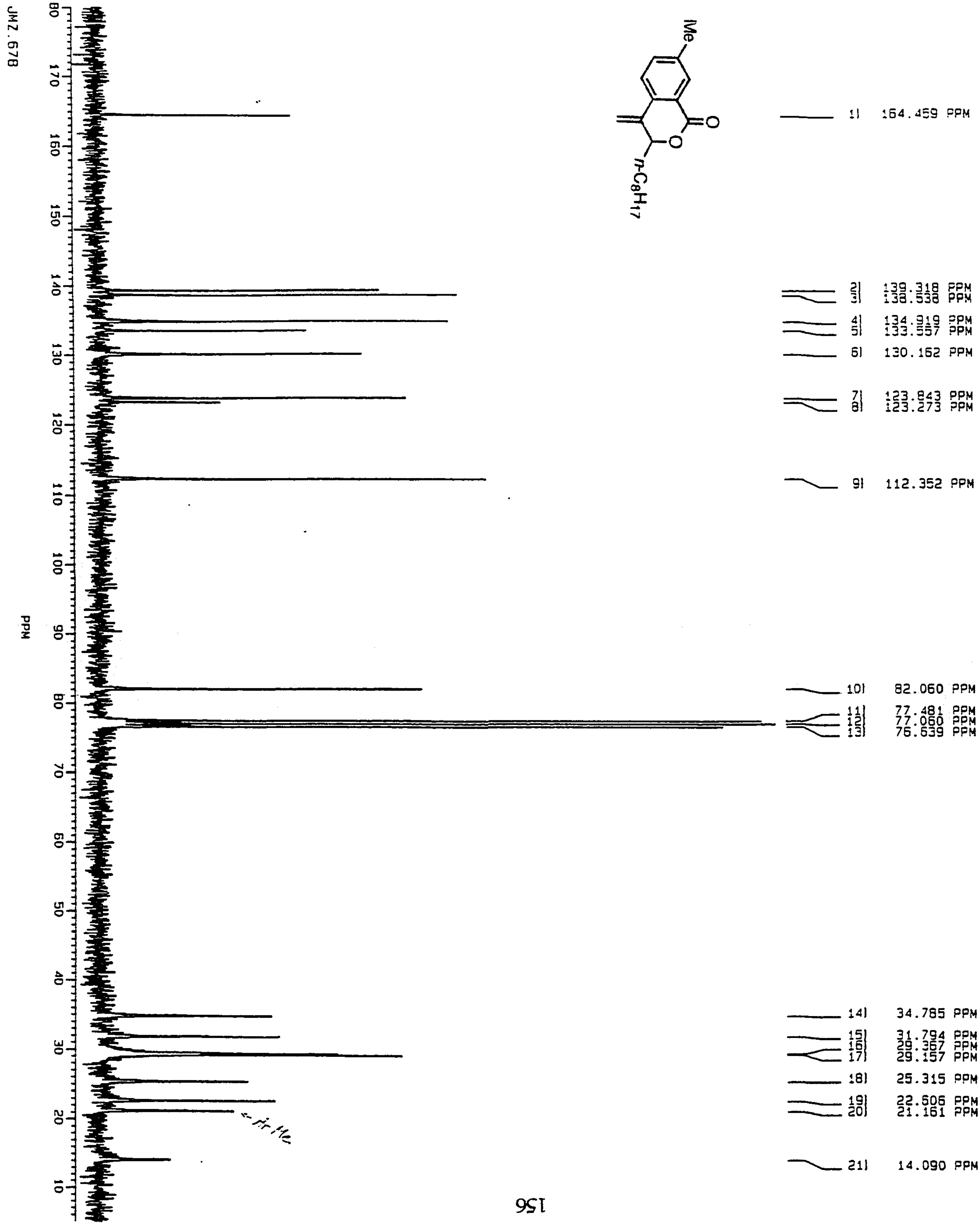
Entry ~~8~~ 12



1] 7.938 PPM
2] 7.507 PPM
3] 7.480 PPM
4] 7.438 PPM
5] 7.434 PPM
6] 7.411 PPM
7] 7.409 PPM
8] 7.275 PPM
9] 5.662 PPM
10] 5.280 PPM
11] 5.014 PPM
12] 4.992 PPM
13] 4.969 PPM
14] 2.425 PPM
15] 1.917 PPM
16] 1.657 PPM
17] 1.254 PPM
18] 0.898 PPM
19] 0.877 PPM
20] 0.854 PPM
21] 0.011 PPM

V - [illegible], #1

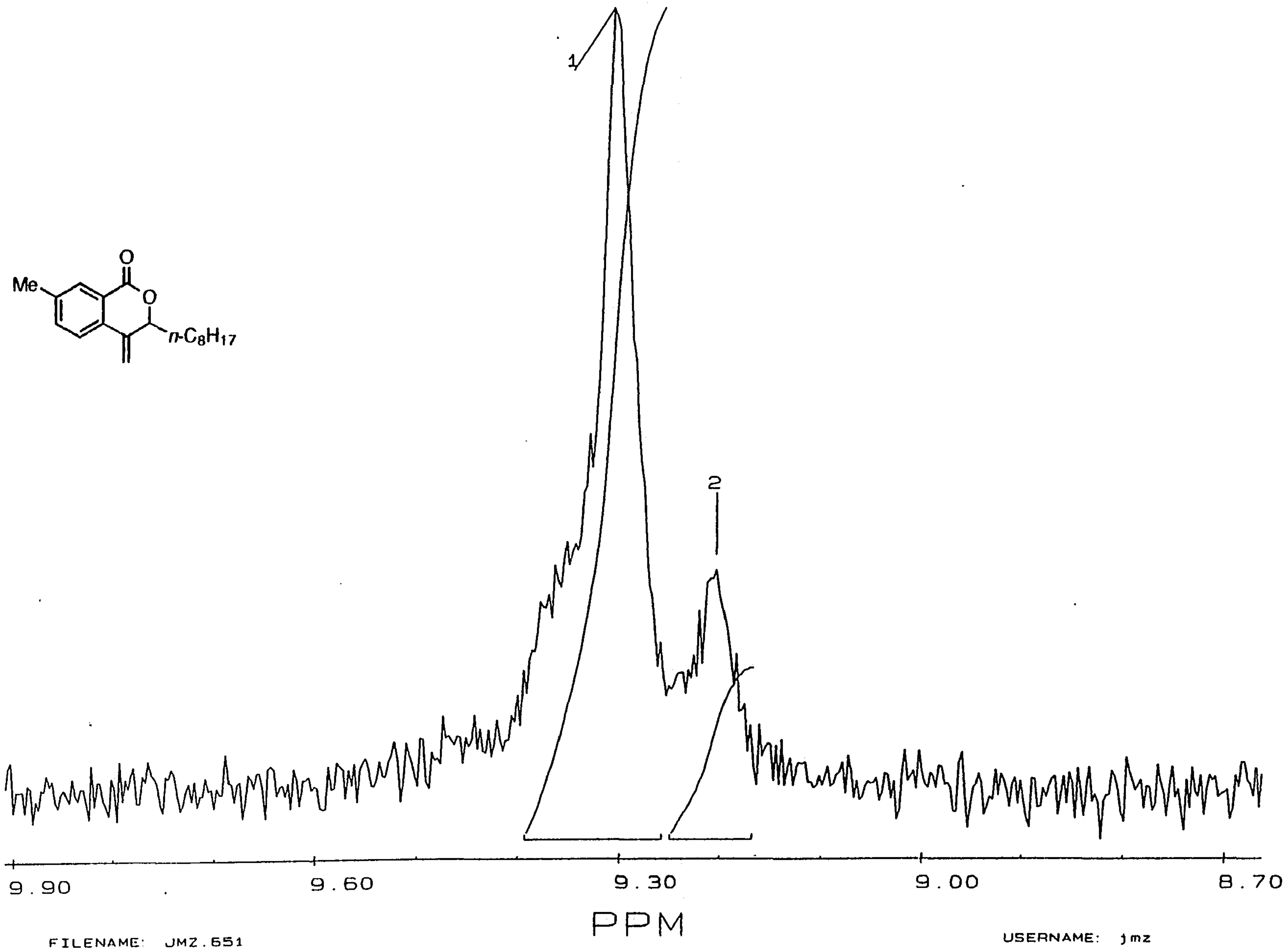
Entry 12


Me
O
O
n-C8H17
1| 164.459 PPM
2| 139.318 PPM
3| 138.538 PPM
4| 134.919 PPM
5| 133.557 PPM
6| 130.162 PPM
7| 123.843 PPM
8| 123.273 PPM
9| 112.352 PPM
10| 82.060 PPM
11| 77.481 PPM
12| 77.060 PPM
13| 76.639 PPM
14| 34.785 PPM
15| 31.794 PPM
16| 29.367 PPM
17| 29.157 PPM
18| 25.315 PPM
19| 22.606 PPM
20| 21.161 PPM
21| 14.090 PPM
← Ar-Me
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
JMZ.678

Entry 12

+ ~.0200 g Eu(hfc)$_3$

#7

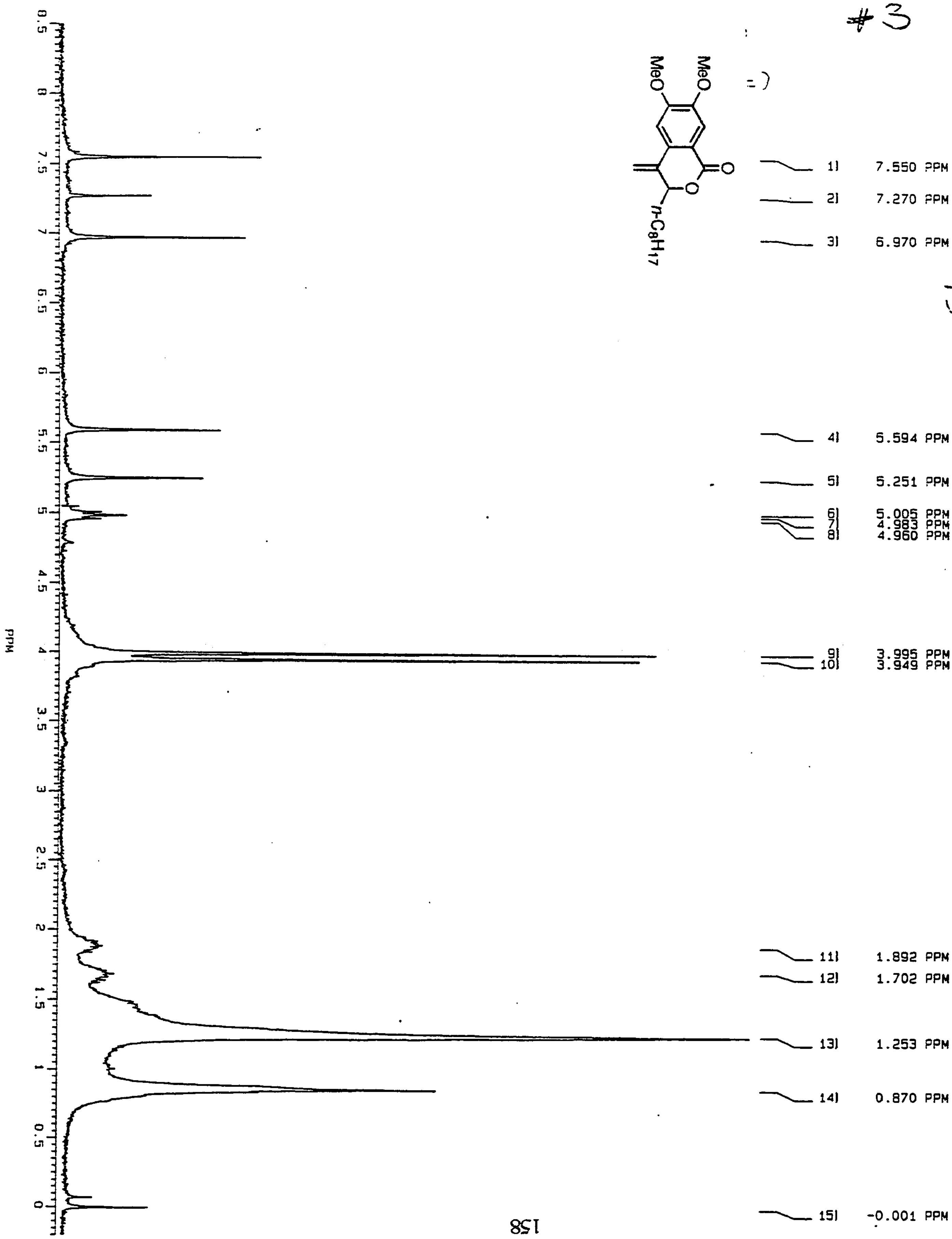


FILENAME: JMZ.651

USERNAME: jmz
DATE: 30-May-94

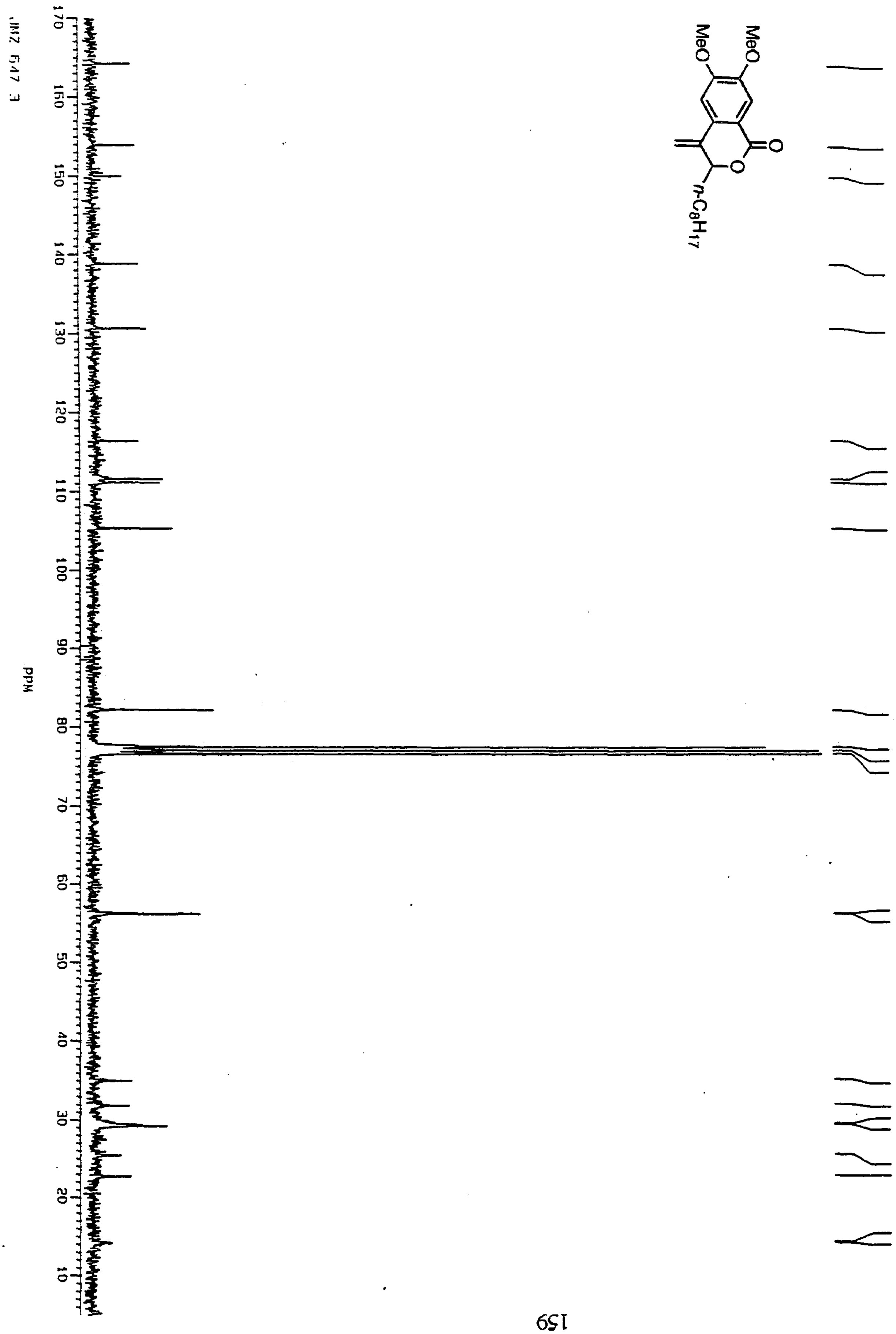
IV-74
#3

Entry 13



#3

Entry 13

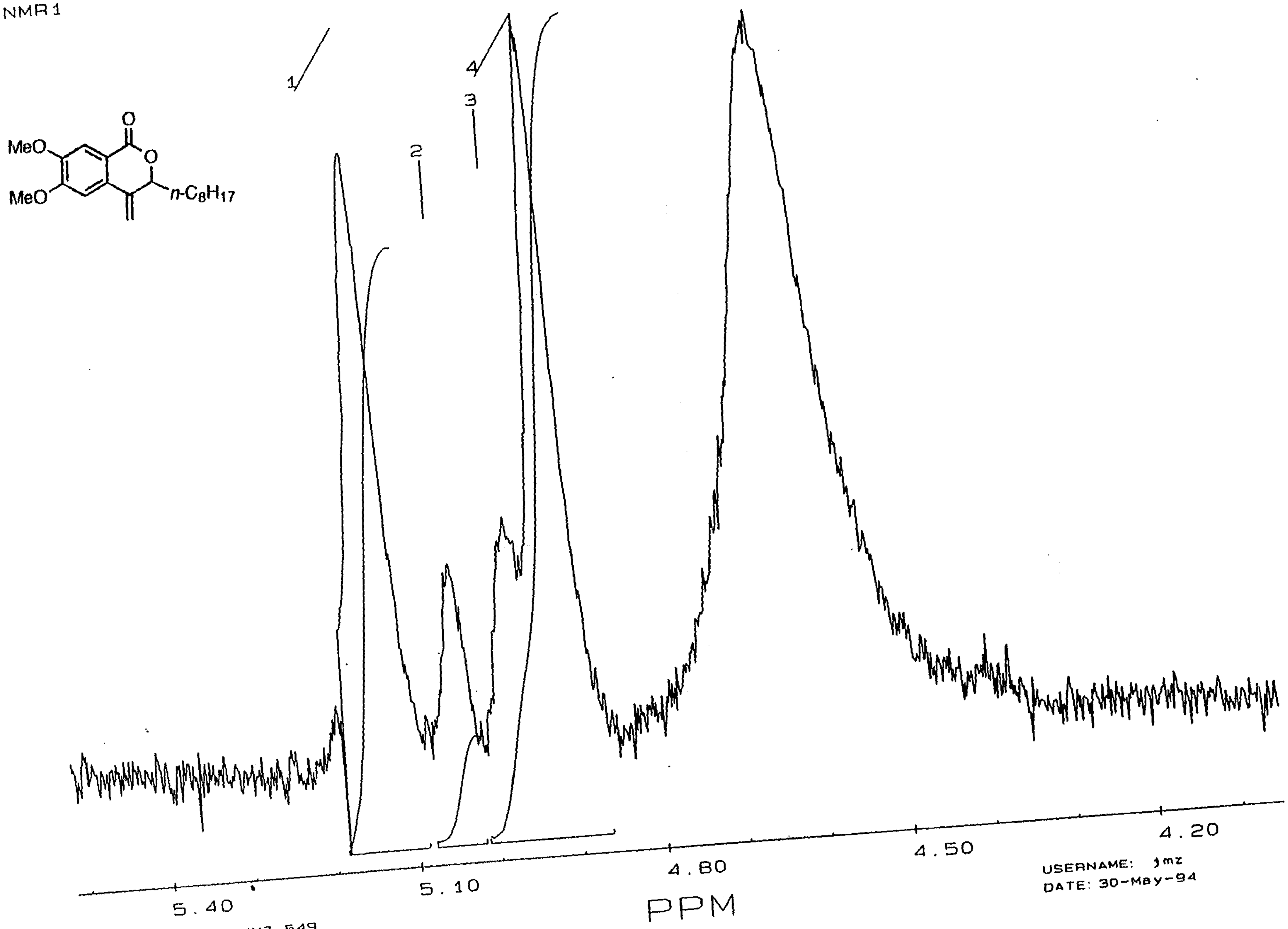


```
 1|  164.297 PPM
 2|  153.976 PPM
 3|  150.034 PPM
 4|  138.830 PPM
 5|  130.679 PPM
 6|  116.409 PPM
 7|  111.605 PPM
 8|  111.200 PPM
 9|  105.339 PPM
10|   82.172 PPM
11|   77.482 PPM
12|   77.060 PPM
13|   76.639 PPM
14|   56.281 PPM
15|   56.225 PPM
16|   35.026 PPM
17|   31.851 PPM
18|   29.440 PPM
19|   29.238 PPM
20|   25.412 PPM
21|   22.668 PPM
22|   14.213 PPM
23|   14.104 PPM
```

Entry 13

IV-74
#3

NMR1

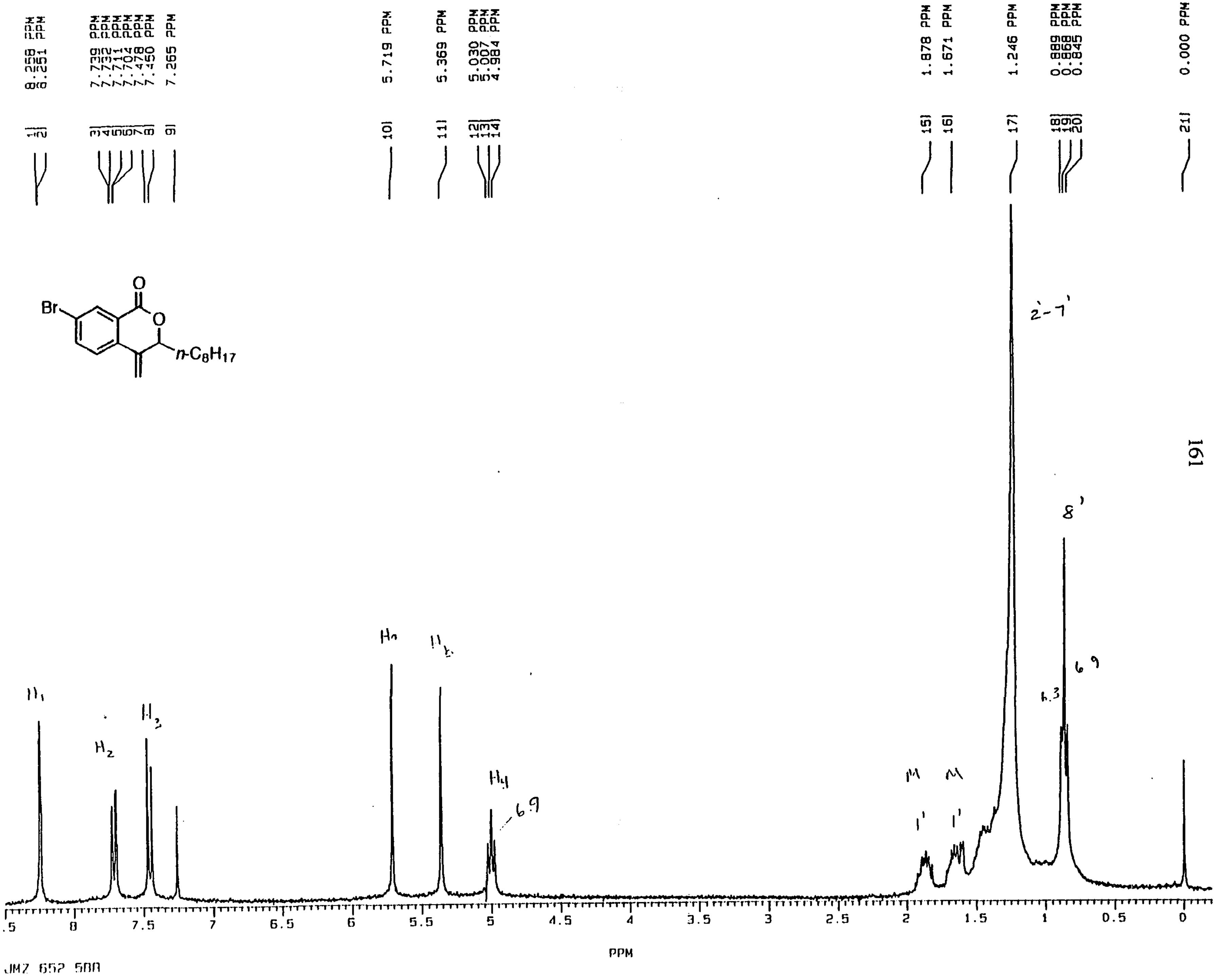


FILENAME: JMZ.649

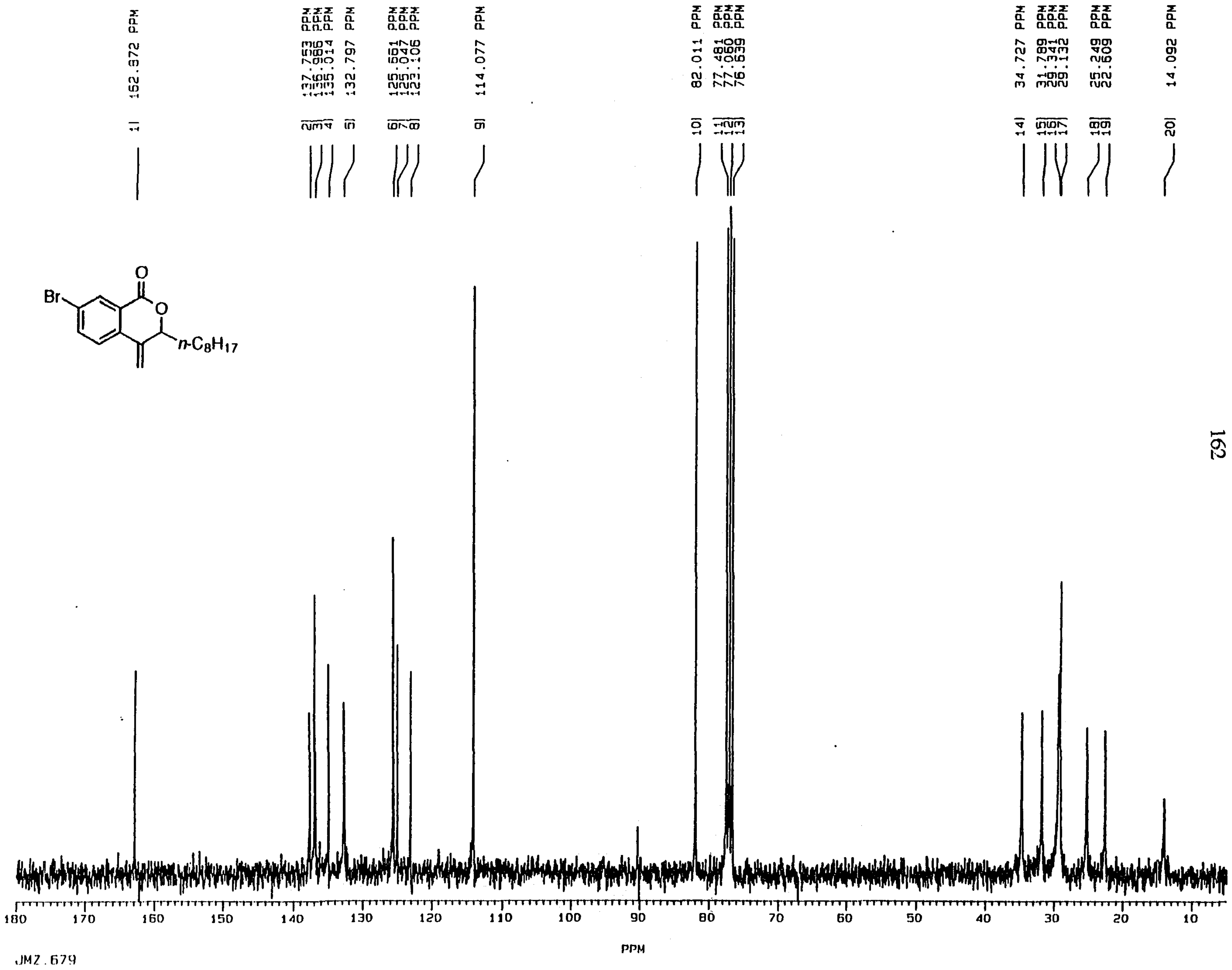
USERNAME: jmz
DATE: 30-May-94

IV-74 #2

Entry 14

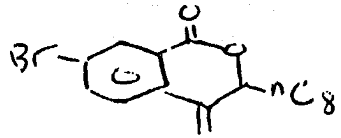


Entry 14



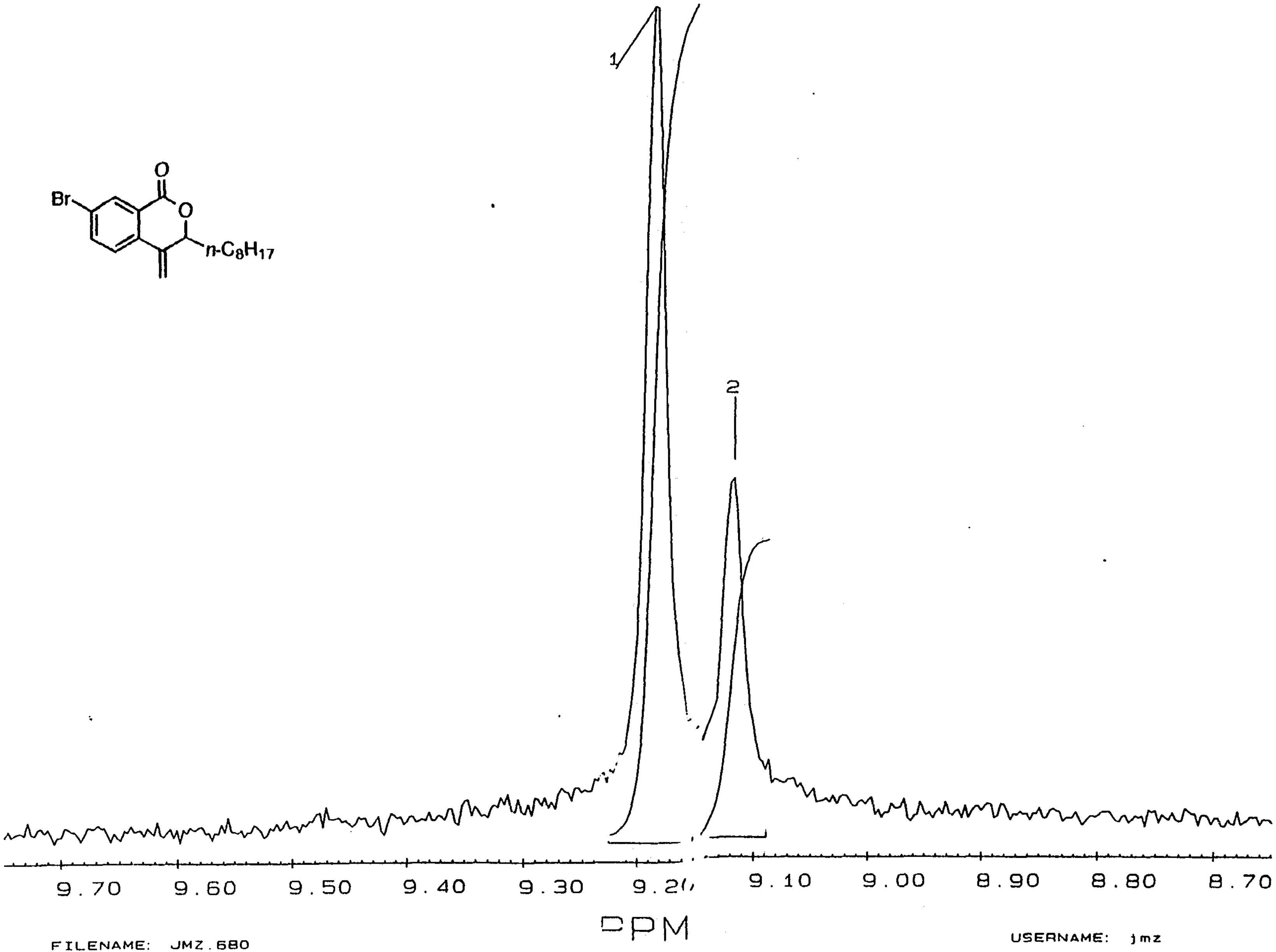
1| 162.872 PPM
2| 137.753 PPM
3| 136.986 PPM
4| 135.014 PPM
5| 132.797 PPM
6| 125.561 PPM
7| 125.047 PPM
8| 123.106 PPM
9| 114.077 PPM
10| 82.011 PPM
11| 77.481 PPM
12| 77.060 PPM
13| 76.639 PPM
14| 34.727 PPM
15| 31.789 PPM
16| 29.341 PPM
17| 29.132 PPM
18| 25.249 PPM
19| 22.609 PPM
20| 14.092 PPM
Br
O
O
n-C8H17
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
JMZ.679

Entry 14



+ Eu(hfc)3

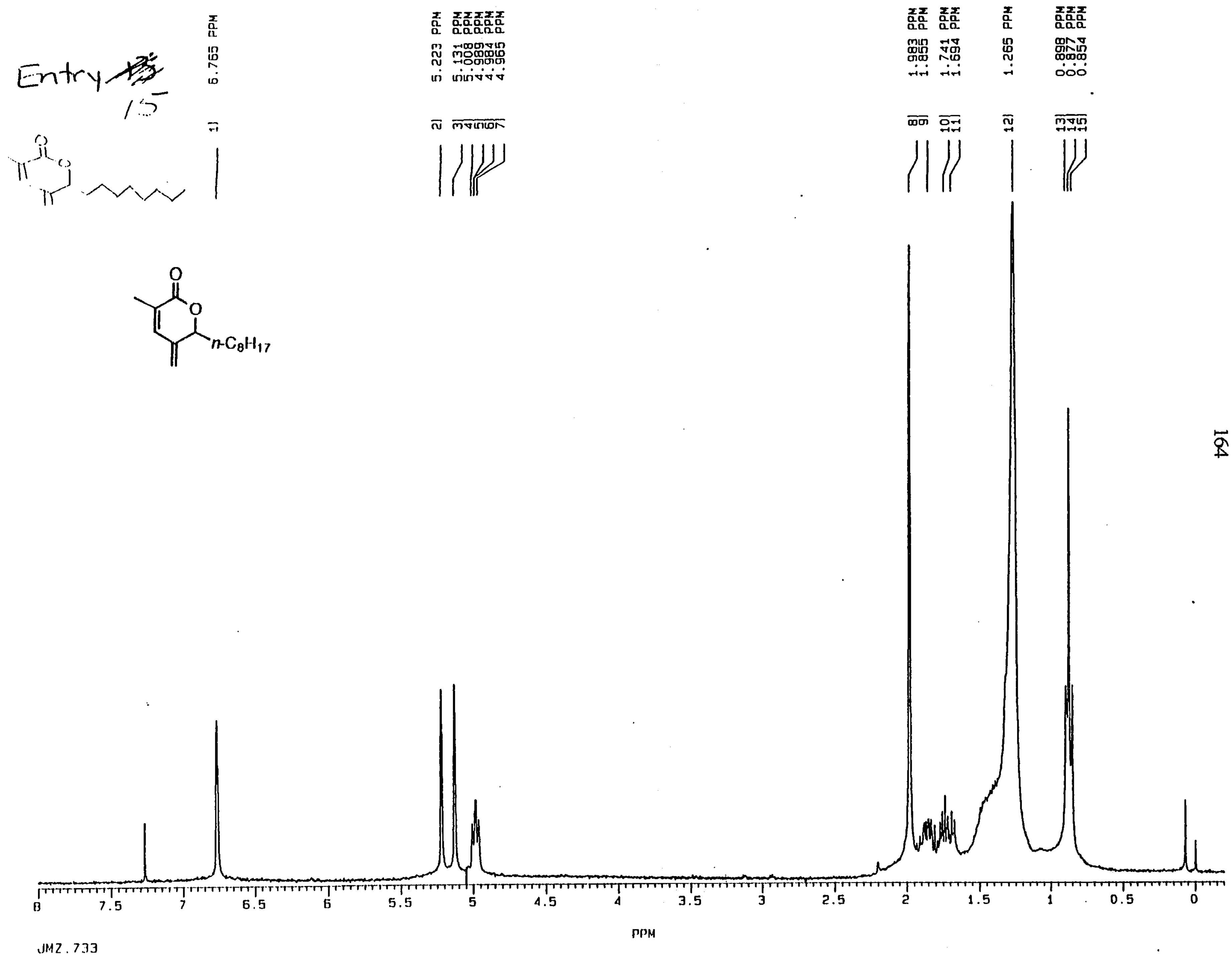
NMR 1



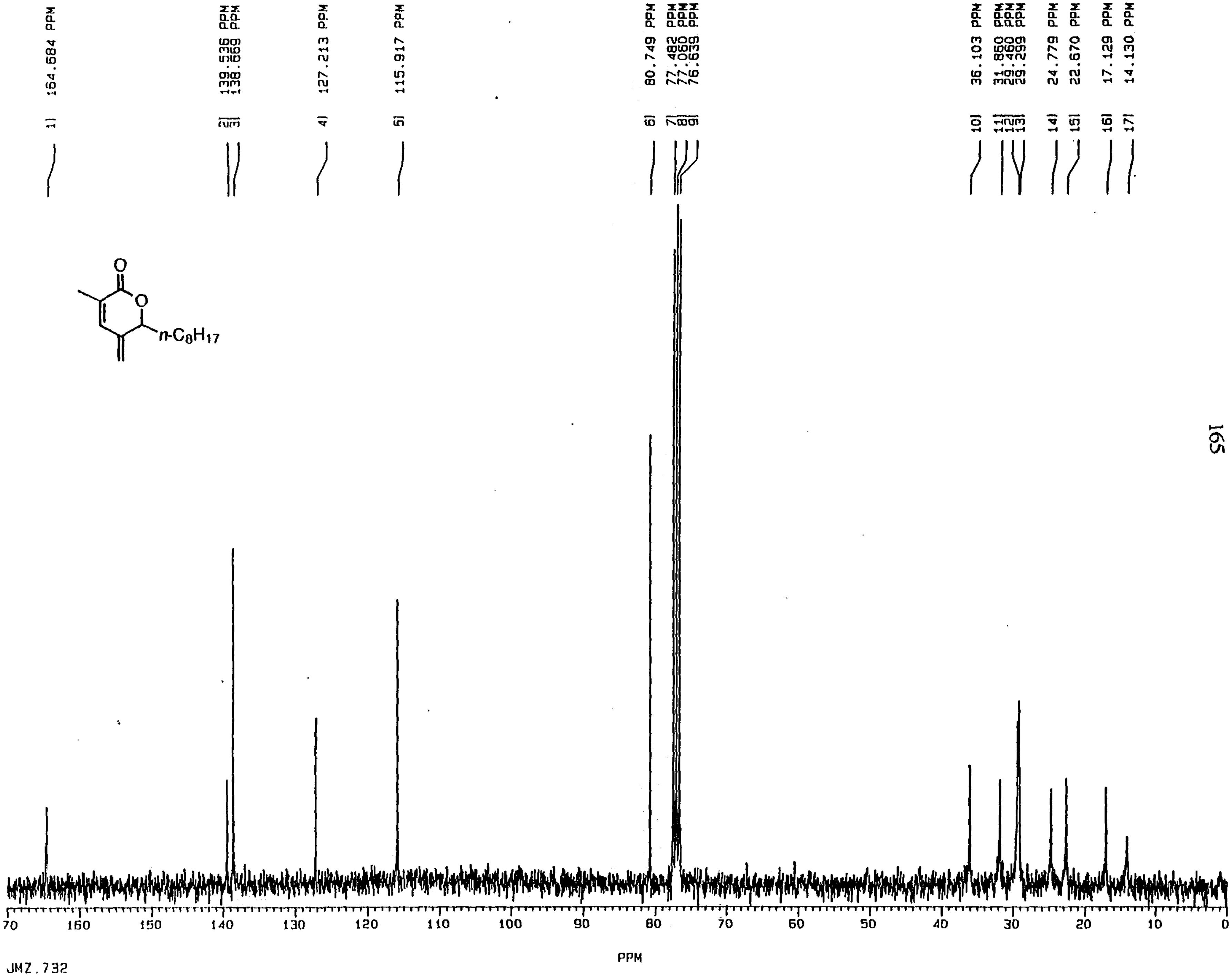
FILENAME: JMZ.680

USERNAME: jmz
DATE: 20-Jul-94

Entry ~~13~~ 15


1) 6.765 PPM
2) 5.223 PPM
3) 5.131 PPM
4) 5.008 PPM
5) 4.989 PPM
6) 4.984 PPM
7) 4.965 PPM
8) 1.983 PPM
9) 1.855 PPM
10) 1.741 PPM
11) 1.694 PPM
12) 1.265 PPM
13) 0.898 PPM
14) 0.877 PPM
15) 0.854 PPM
O
O
n-C8H17
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
JMZ.733

Entry 15

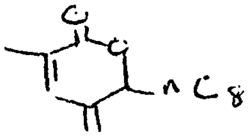


JMZ.732

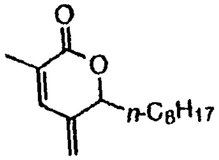
Entry 15

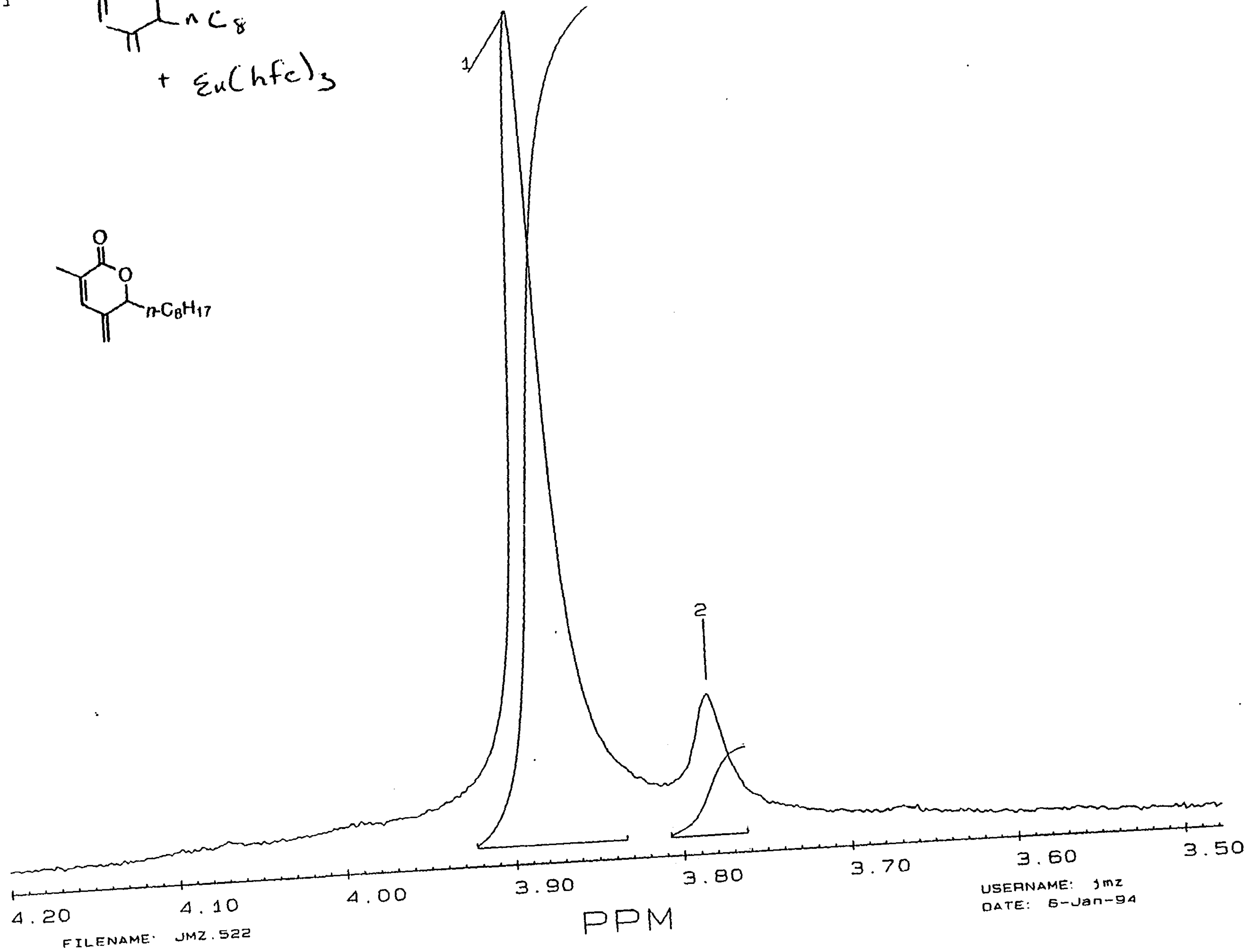
[illegible]

NMR1

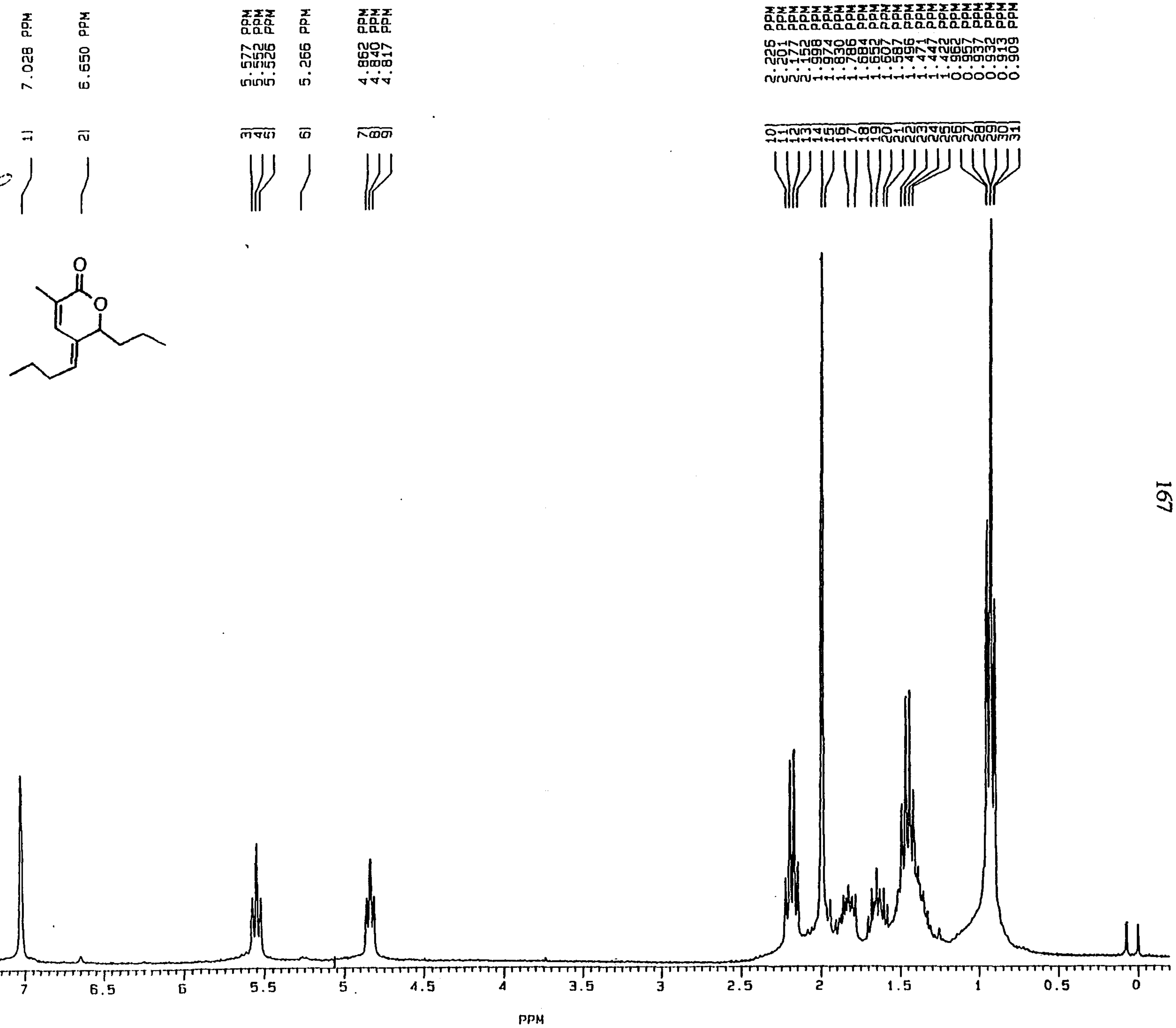


+ Eu(hfc)3



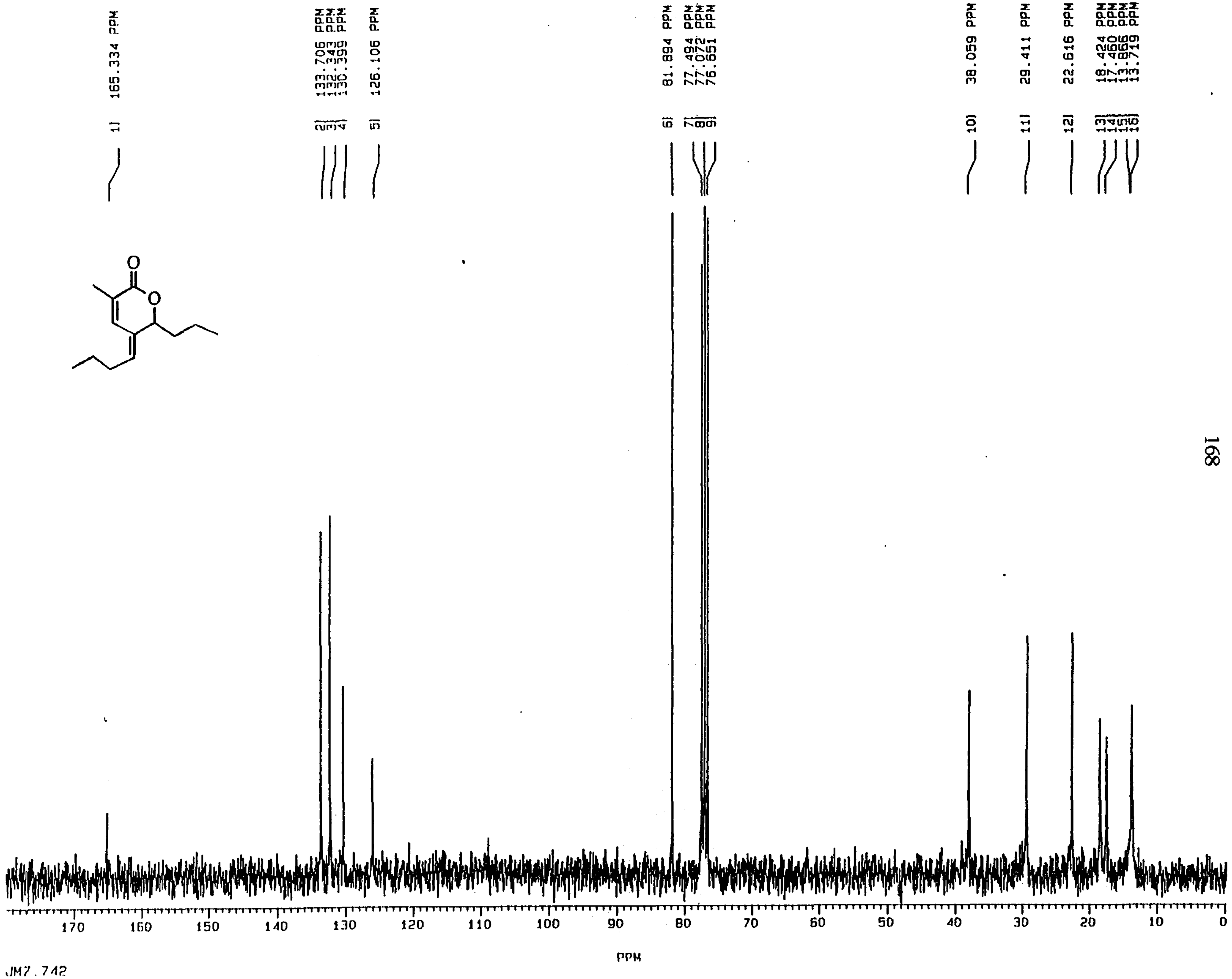


Entry 16



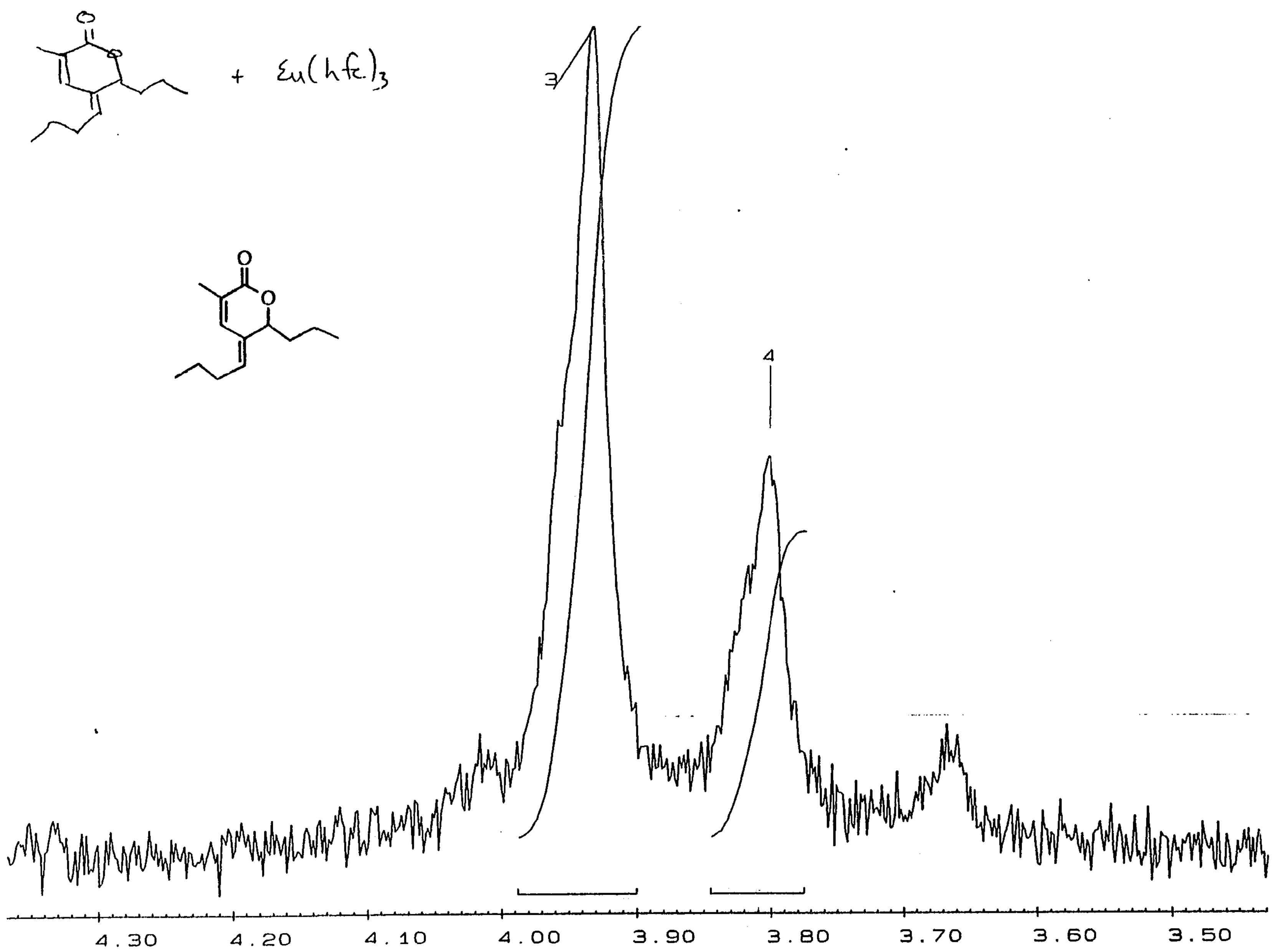
JMZ.738

Entry 16


1] 165.334 PPM
2] 133.706 PPM
3] 132.343 PPM
4] 130.399 PPM
5] 126.106 PPM
6] 81.894 PPM
7] 77.494 PPM
8] 77.072 PPM
9] 76.651 PPM
10] 38.059 PPM
11] 29.411 PPM
12] 22.616 PPM
13] 18.424 PPM
14] 17.460 PPM
15] 13.866 PPM
16] 13.719 PPM
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JM7.742

Entry 16

IV-32

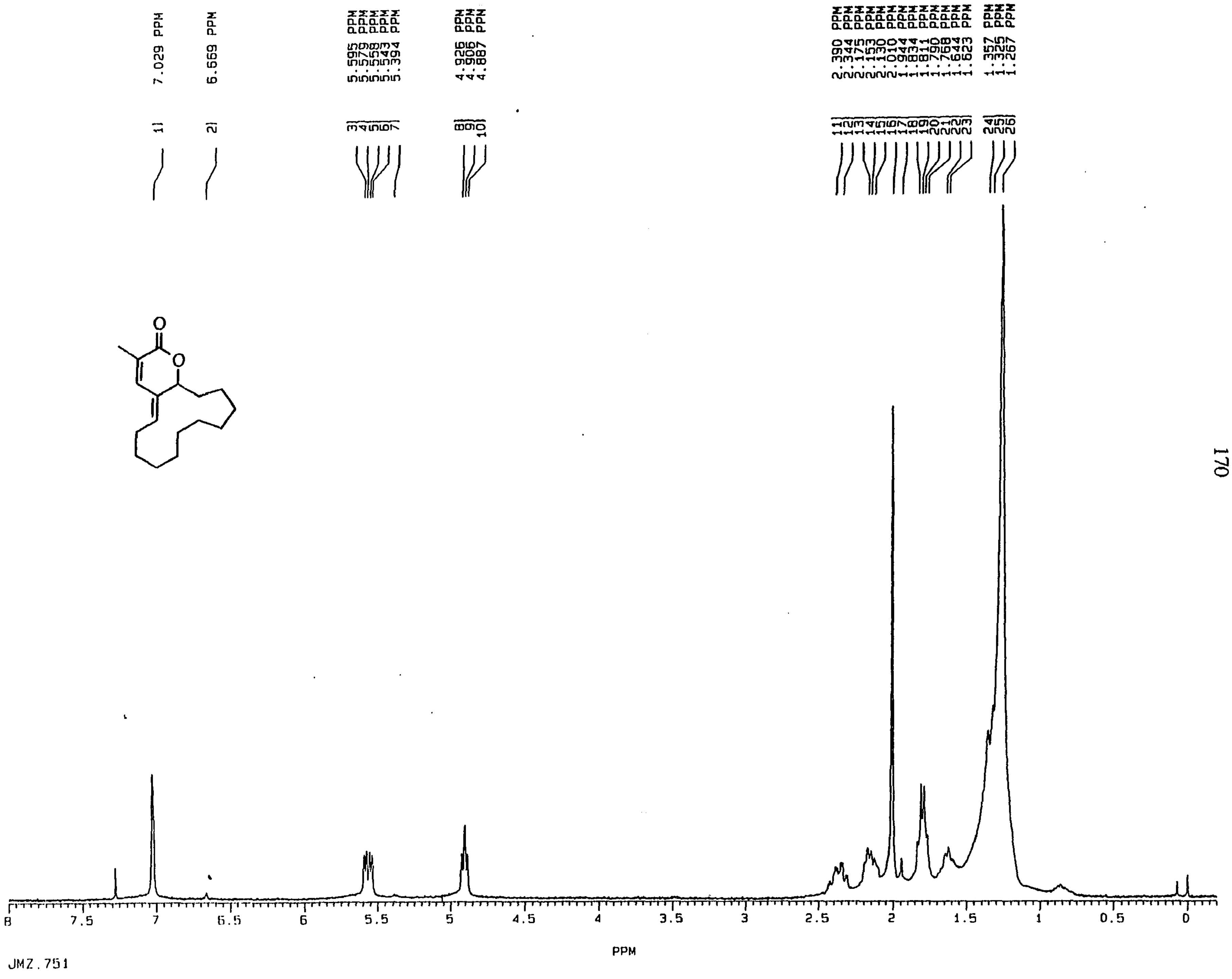


FILENAME: JMZ.519

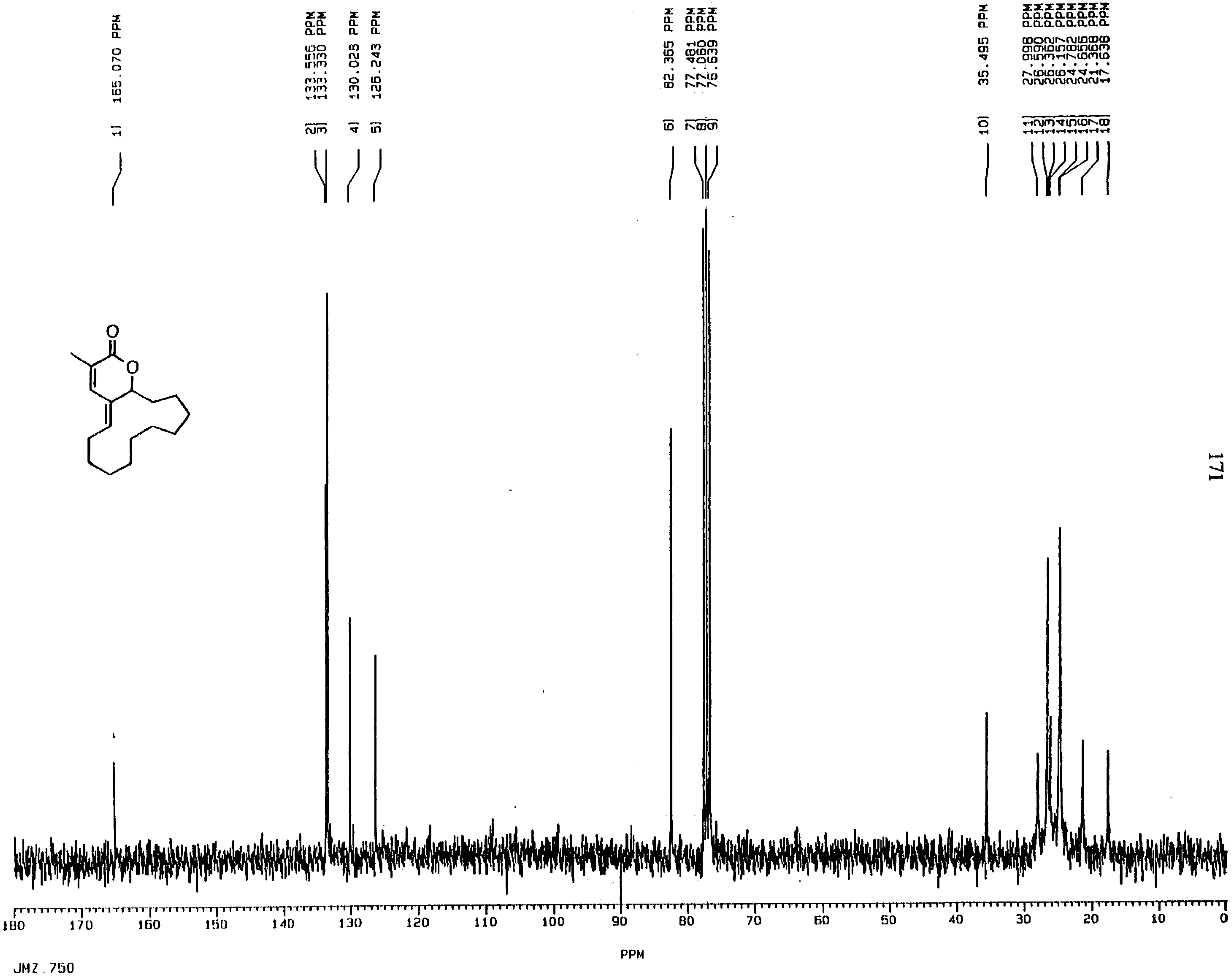
USERNAME: jmz

DATE: 3-Jan-94

Entry 17

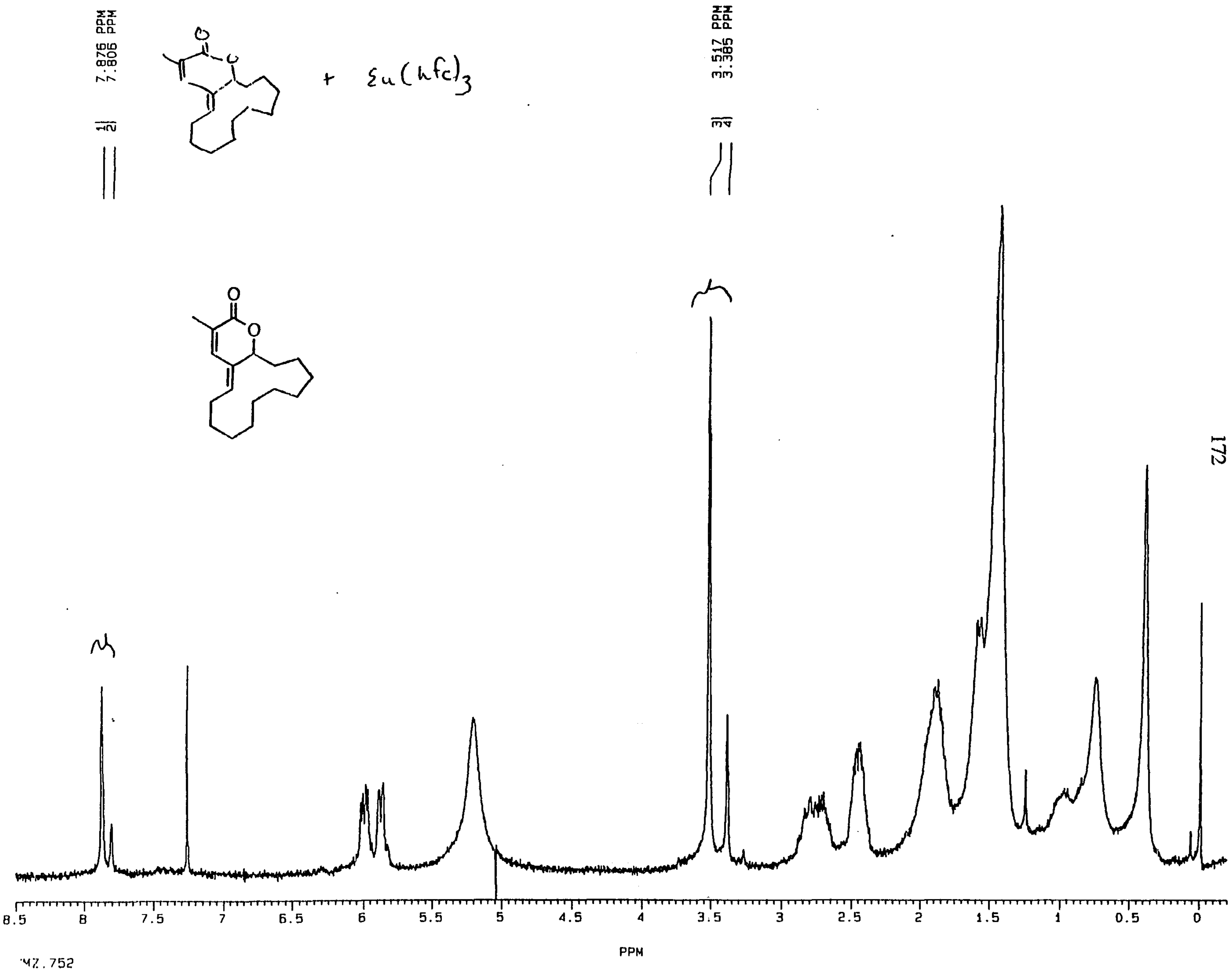

1] 7.029 PPM
2] 6.669 PPM
3] 5.595 PPM
4] 5.579 PPM
5] 5.559 PPM
6] 5.543 PPM
7] 5.394 PPM
8] 4.926 PPM
9] 4.906 PPM
10] 4.887 PPM
11] 2.390 PPM
12] 2.344 PPM
13] 2.175 PPM
14] 2.153 PPM
15] 2.130 PPM
16] 2.010 PPM
17] 1.944 PPM
18] 1.834 PPM
19] 1.811 PPM
20] 1.790 PPM
21] 1.768 PPM
22] 1.644 PPM
23] 1.623 PPM
24] 1.357 PPM
25] 1.325 PPM
26] 1.267 PPM
O
O
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
JMZ.751

Entry 17

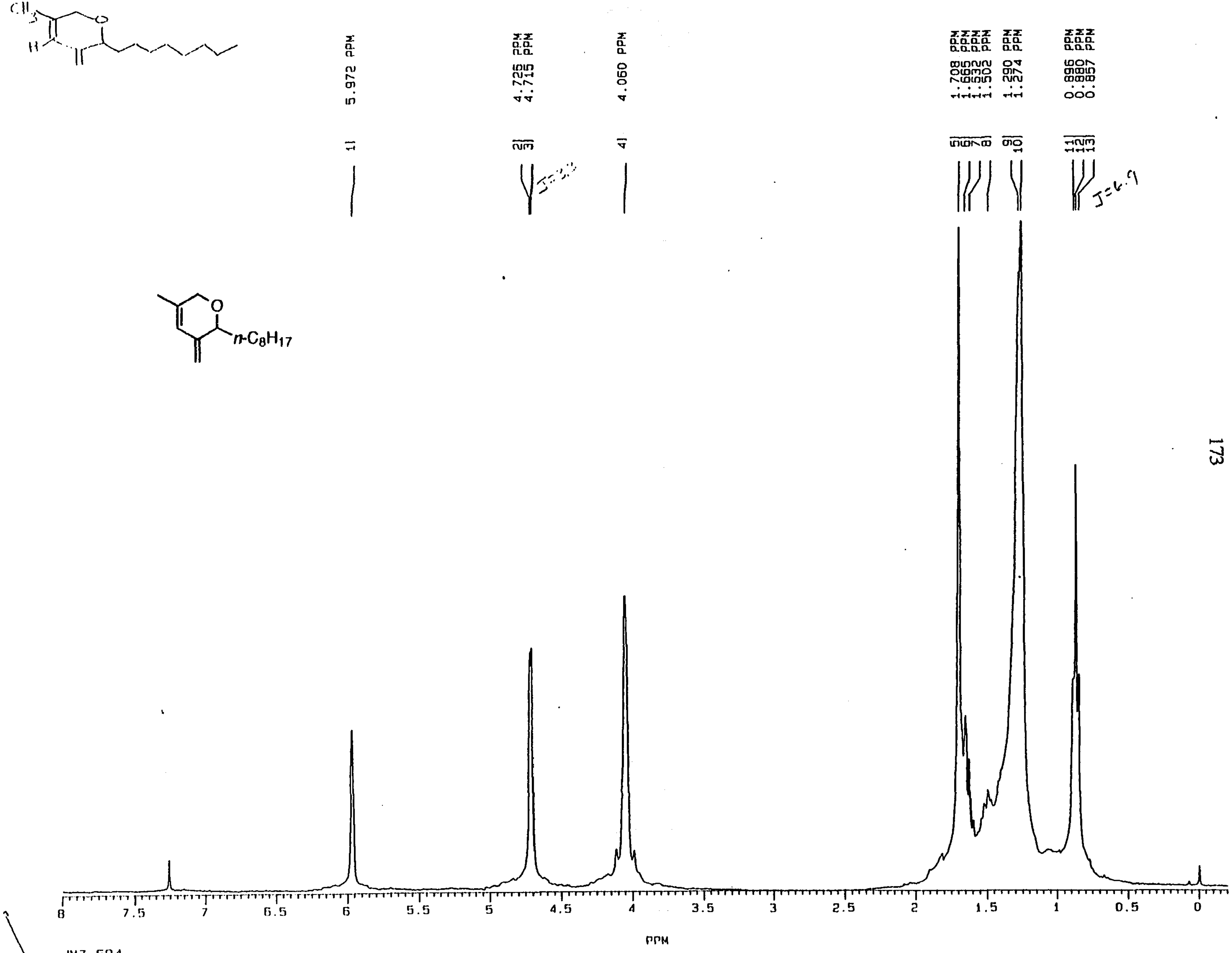


1) 165.070 PPM
2) 133.556 PPM
3) 133.330 PPM
4) 130.028 PPM
5) 126.243 PPM
6) 82.365 PPM
7) 77.481 PPM
8) 77.060 PPM
9) 76.639 PPM
10) 35.495 PPM
11) 27.998 PPM
12) 26.590 PPM
13) 26.362 PPM
14) 26.157 PPM
15) 24.782 PPM
16) 24.656 PPM
17) 21.368 PPM
18) 17.638 PPM
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JMZ.750

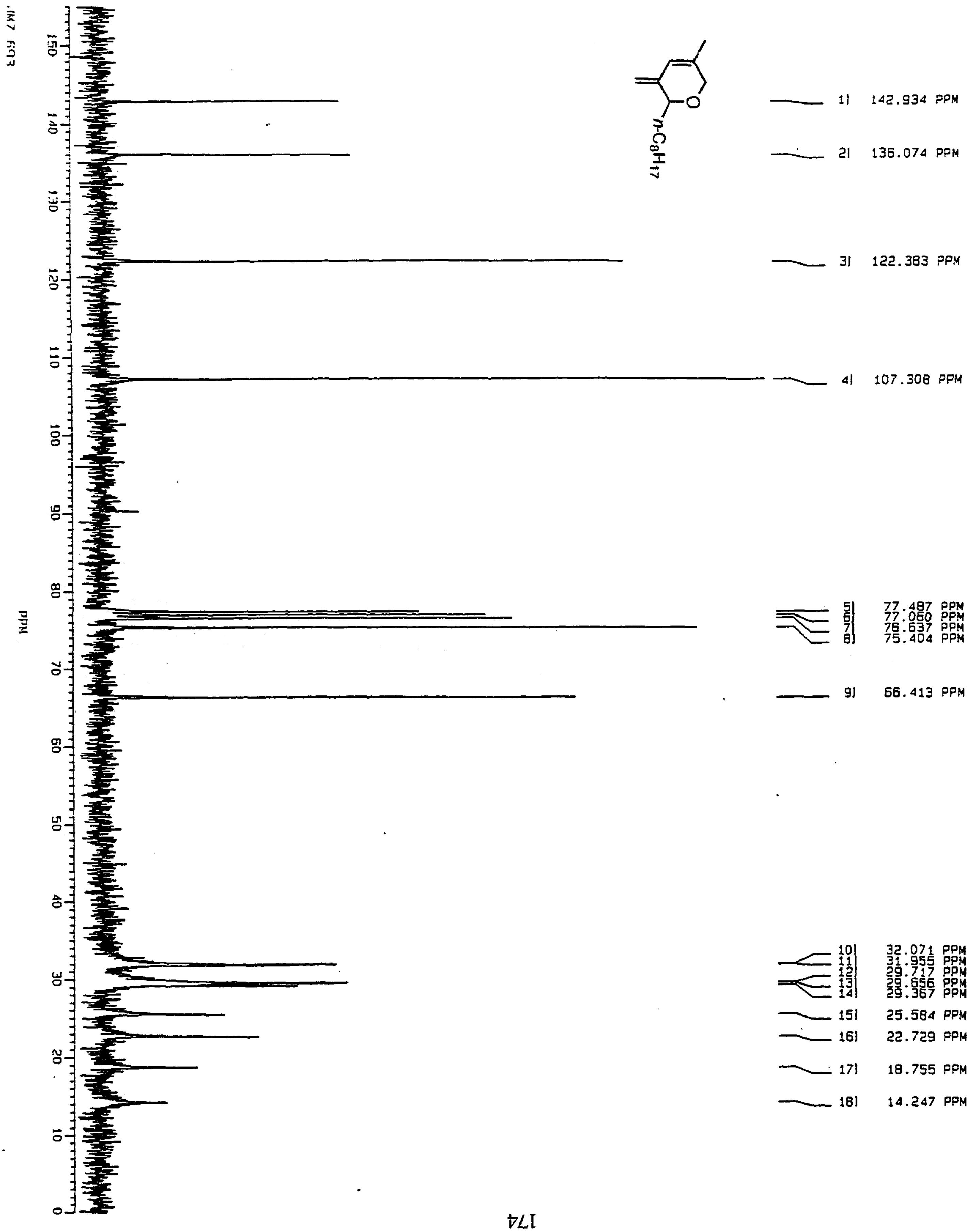
Entry 17


1| 7.876 PPM
2| 7.806 PPM
3| 3.517 PPM
4| 3.385 PPM
+ Eu(hfc)$_3$
O
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
MZ.752

Entry 18



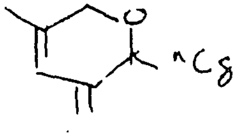
JMZ.694


n-C8H17
O
1) 142.934 PPM
2) 136.074 PPM
3) 122.383 PPM
4) 107.308 PPM
5) 77.487 PPM
6) 77.060 PPM
7) 76.637 PPM
8) 75.404 PPM
9) 66.413 PPM
10) 32.071 PPM
11) 31.955 PPM
12) 29.717 PPM
13) 29.656 PPM
14) 29.367 PPM
15) 25.584 PPM
16) 22.729 PPM
17) 18.755 PPM
18) 14.247 PPM
PPM
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

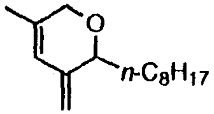
Entry 18

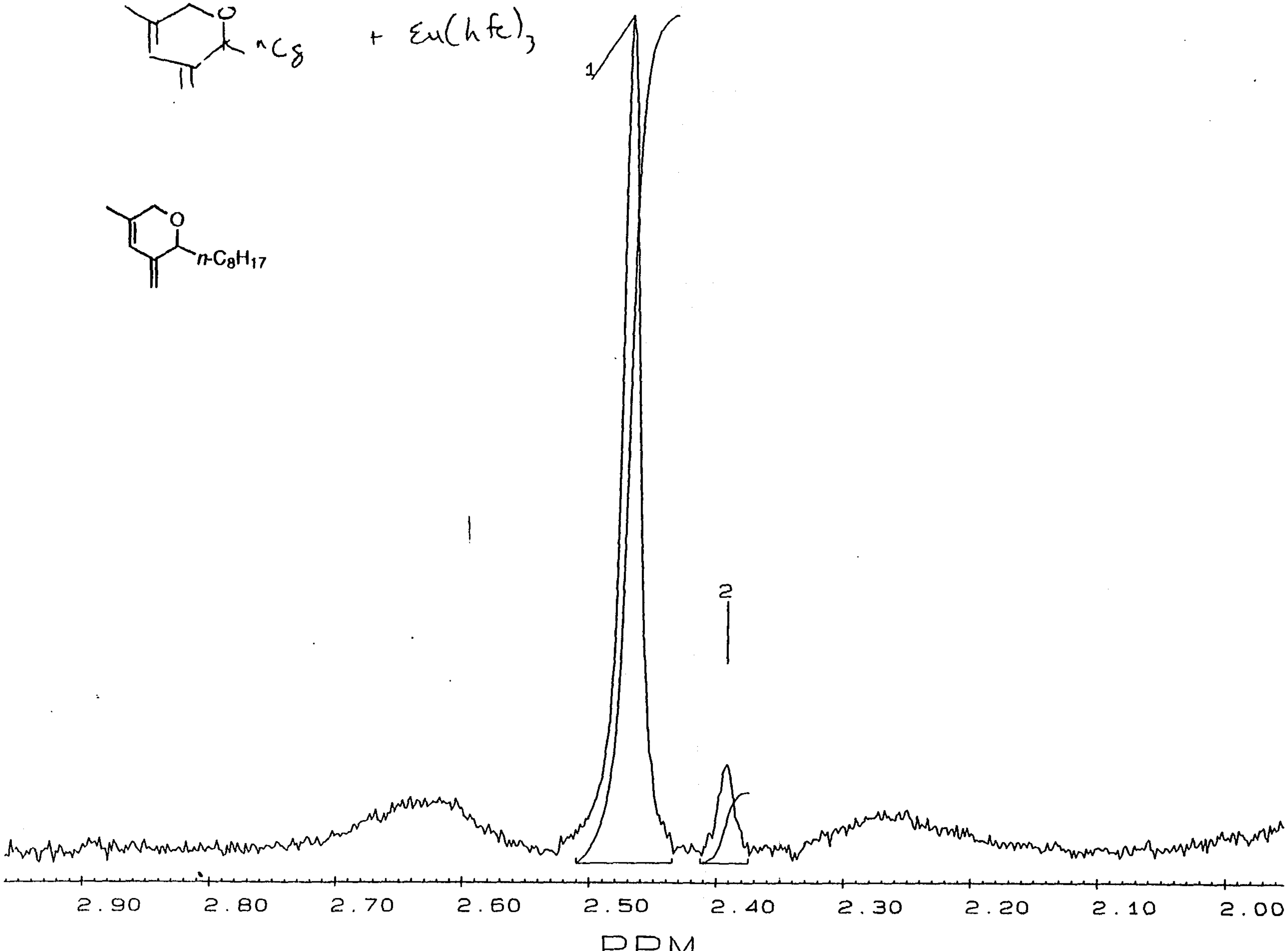
Entry 18

NMR 1



+ Eu(hfc)$_3$

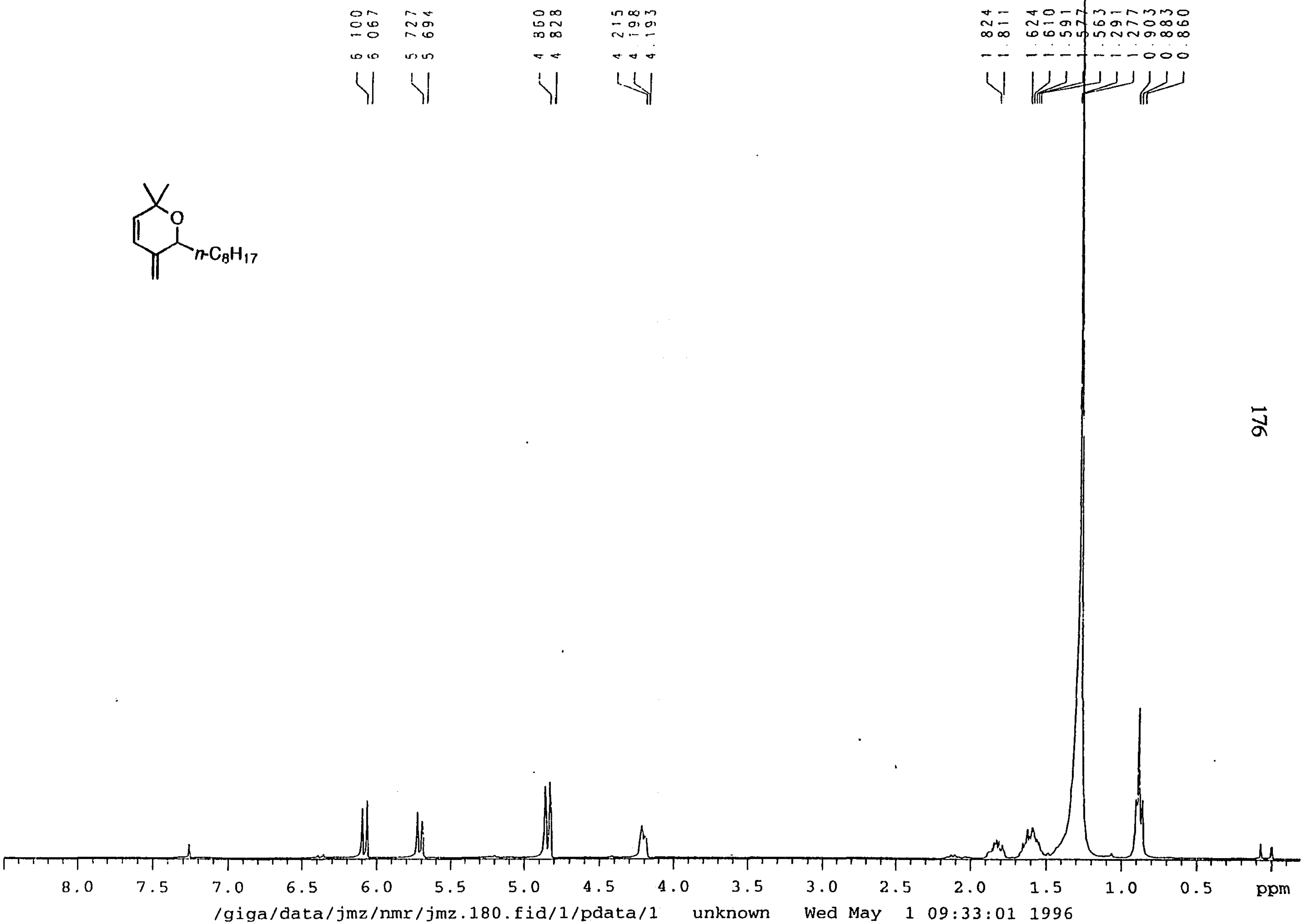




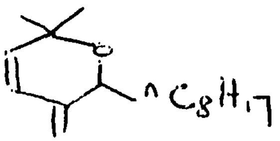
FILENAME: JMZ.696

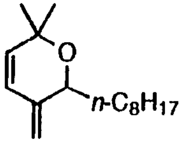
USERNAME: jmz

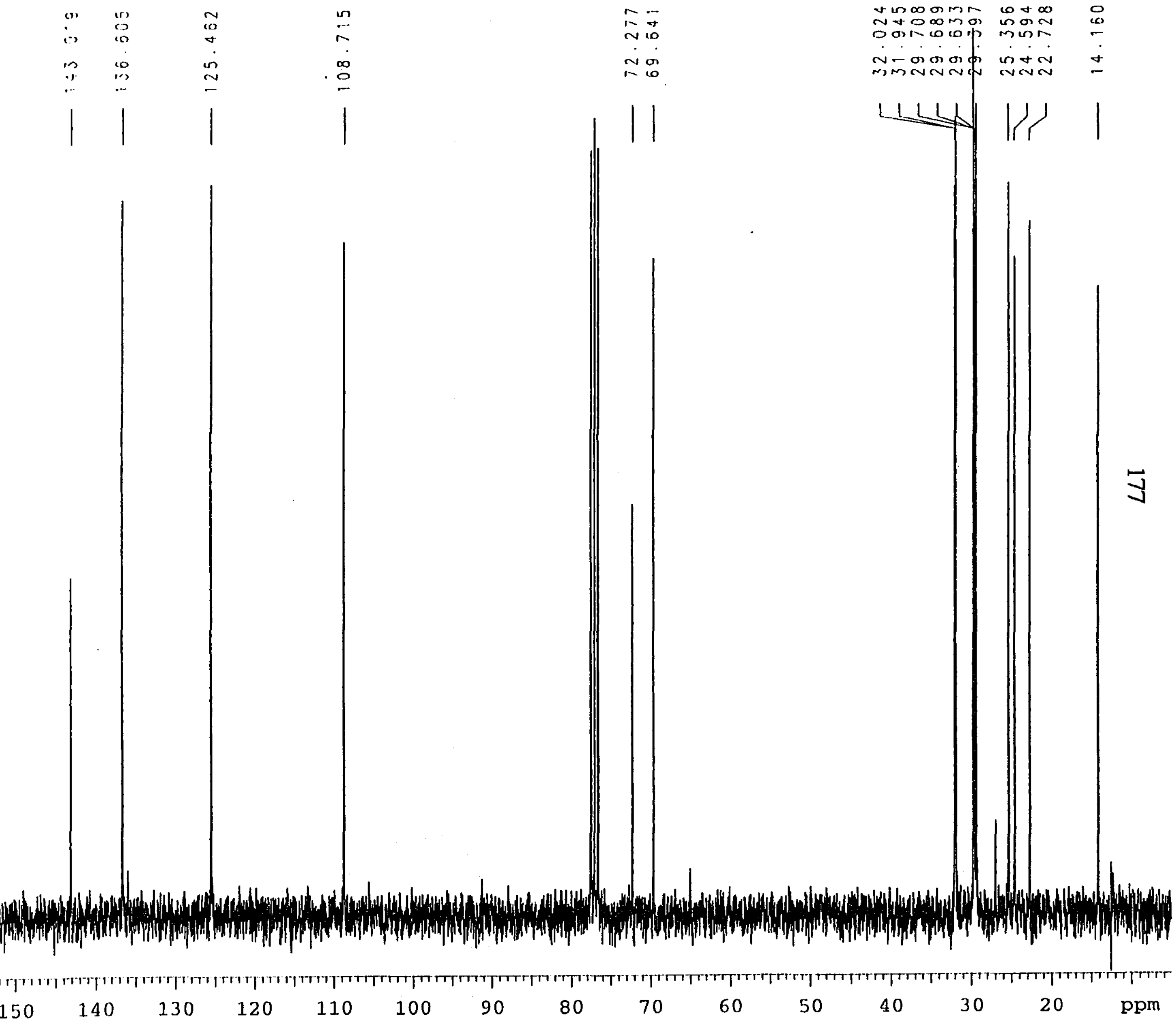
Entry 20


6.100
6.067
5.727
5.694
4.850
4.828
4.215
4.198
4.193
1.824
1.811
1.624
1.610
1.591
1.577
1.563
1.291
1.277
0.903
0.883
0.860
O
n-C8H17
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
/giga/data/jmz/nmr/jmz.180.fid/1/pdata/1 unknown Wed May 1 09:33:01 1996

Entry 20

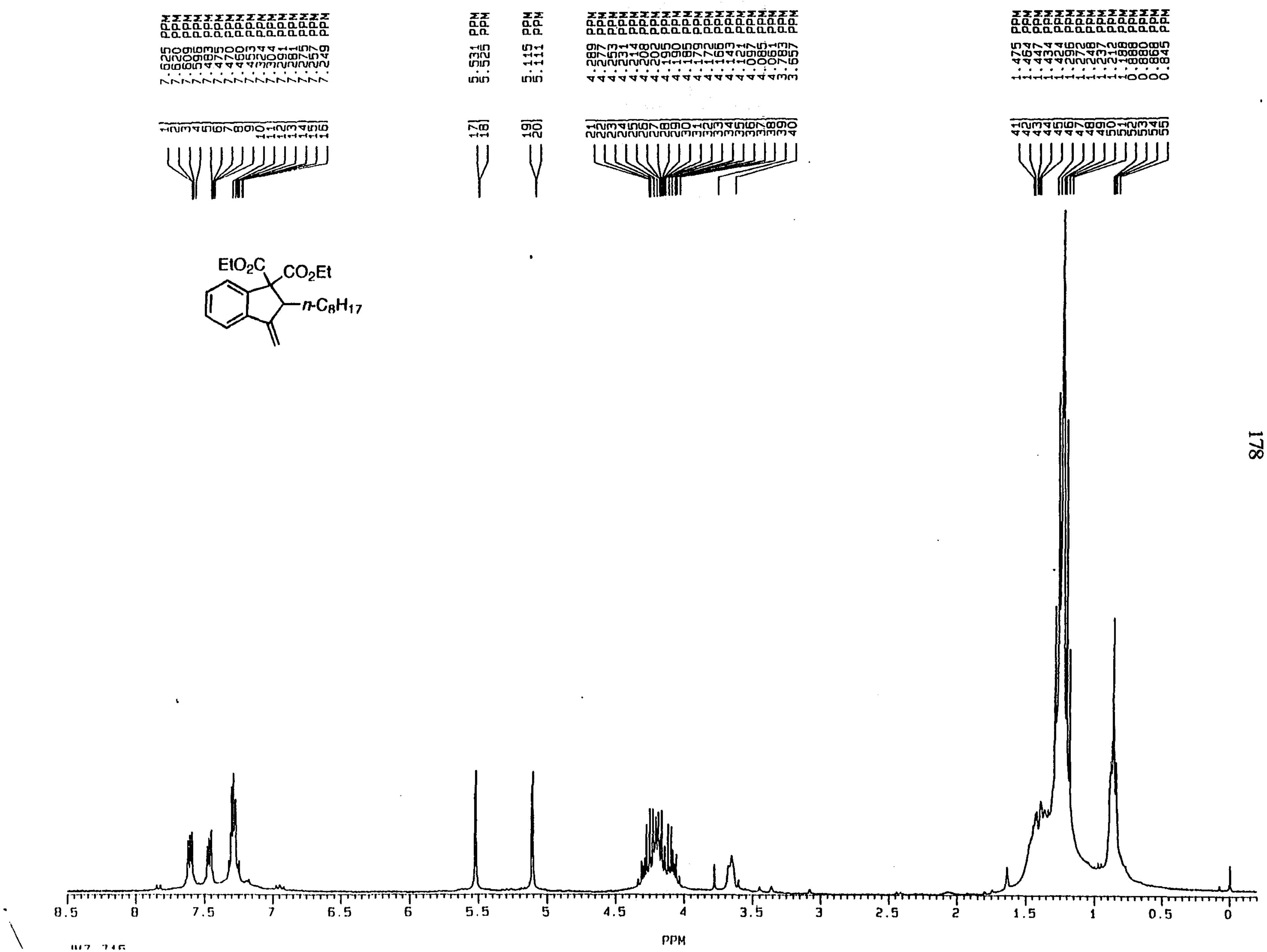






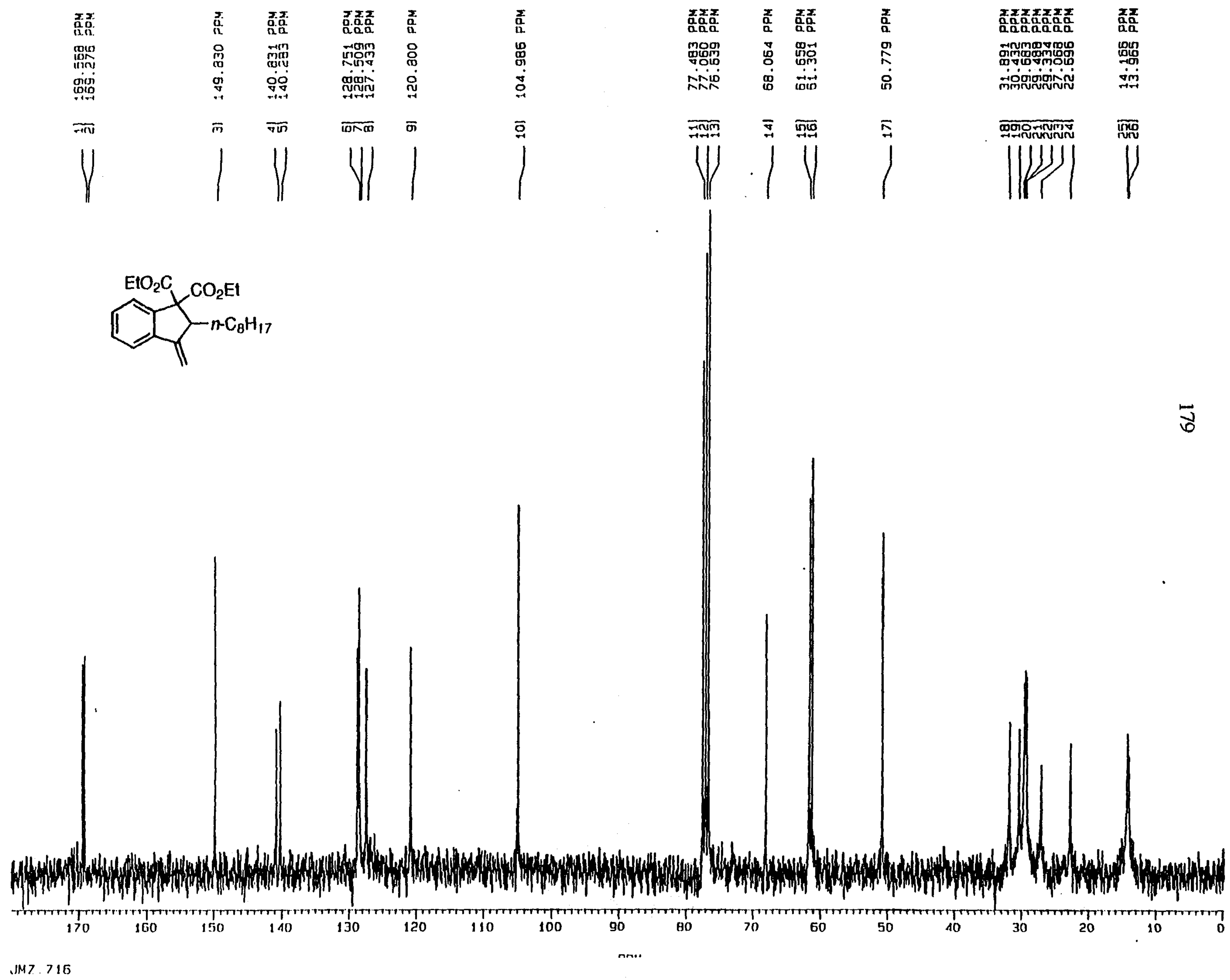
/giga/data/jmz/nmr/jmz.215.fid/1/pdata/1 unknown Tue Mar 19 14:02:05 1996

Entry # 21



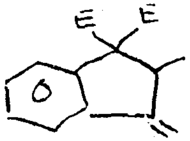
EtO2C
CO2Et
n-C8H17
1 7.625 PPM
2 7.620 PPM
3 7.609 PPM
4 7.596 PPM
5 7.483 PPM
6 7.475 PPM
7 7.470 PPM
8 7.460 PPM
9 7.453 PPM
10 7.324 PPM
11 7.304 PPM
12 7.291 PPM
13 7.281 PPM
14 7.275 PPM
15 7.257 PPM
16 7.249 PPM
17 5.531 PPM
18 5.525 PPM
19 5.115 PPM
20 5.111 PPM
21 4.289 PPM
22 4.277 PPM
23 4.253 PPM
24 4.231 PPM
25 4.214 PPM
26 4.208 PPM
27 4.202 PPM
28 4.195 PPM
29 4.190 PPM
30 4.185 PPM
31 4.179 PPM
32 4.172 PPM
33 4.166 PPM
34 4.143 PPM
35 4.121 PPM
36 4.097 PPM
37 4.085 PPM
38 4.061 PPM
39 3.783 PPM
40 3.657 PPM
41 1.475 PPM
42 1.464 PPM
43 1.447 PPM
44 1.434 PPM
45 1.424 PPM
46 1.296 PPM
47 1.272 PPM
48 1.248 PPM
49 1.237 PPM
50 1.212 PPM
51 1.188 PPM
52 0.888 PPM
53 0.880 PPM
54 0.868 PPM
55 0.845 PPM
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM

Entry 21

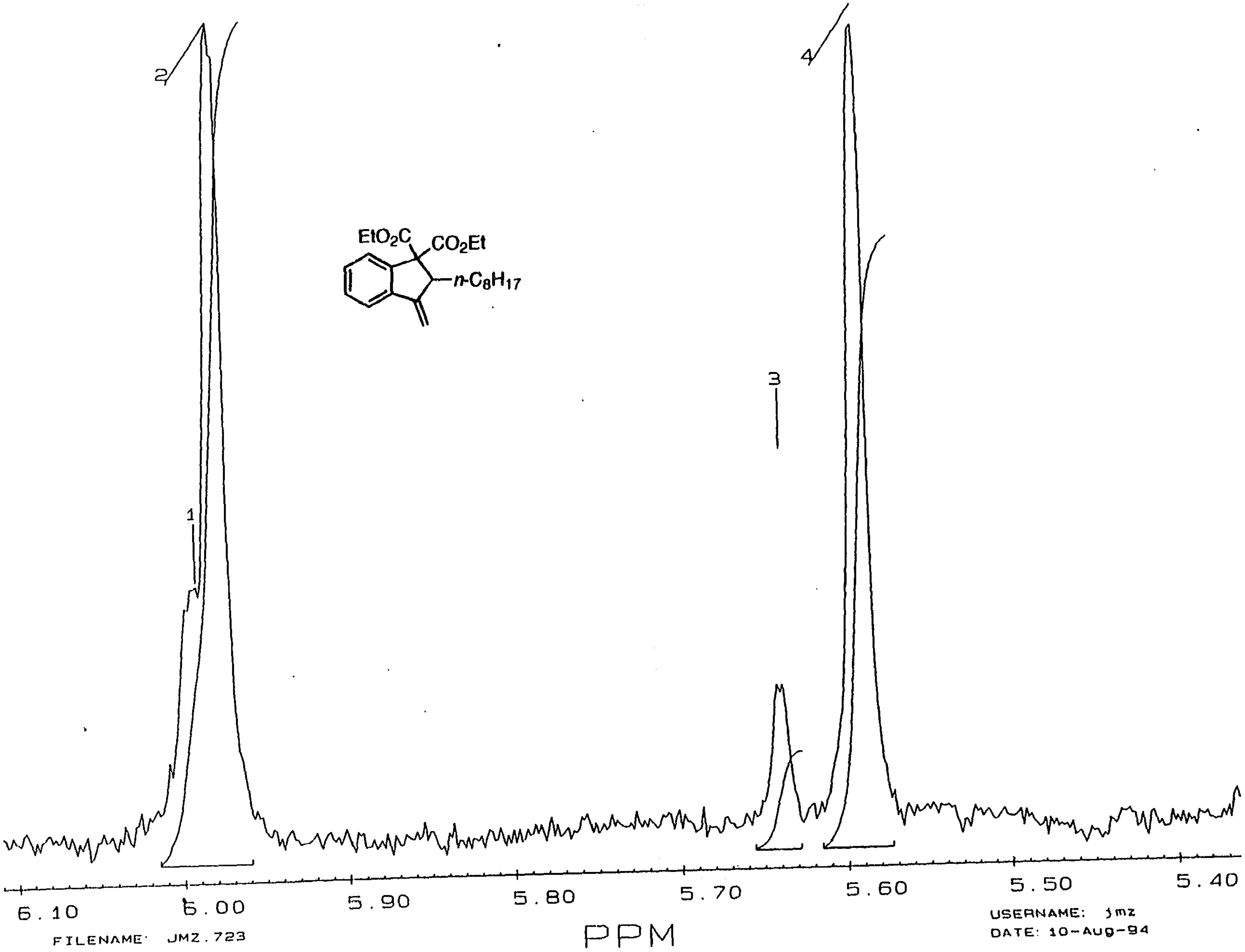

1) 169.568 PPM
2) 169.276 PPM
3) 149.830 PPM
4) 140.831 PPM
5) 140.283 PPM
6) 128.751 PPM
7) 128.509 PPM
8) 127.433 PPM
9) 120.800 PPM
10) 104.986 PPM
11) 77.483 PPM
12) 77.060 PPM
13) 76.639 PPM
14) 68.064 PPM
15) 61.658 PPM
16) 61.301 PPM
17) 50.779 PPM
18) 31.891 PPM
19) 30.432 PPM
20) 29.683 PPM
21) 29.488 PPM
22) 29.334 PPM
23) 27.068 PPM
24) 22.696 PPM
25) 14.166 PPM
26) 13.965 PPM
EtO2C
CO2Et
n-C8H17
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JMZ.716

Entry
21

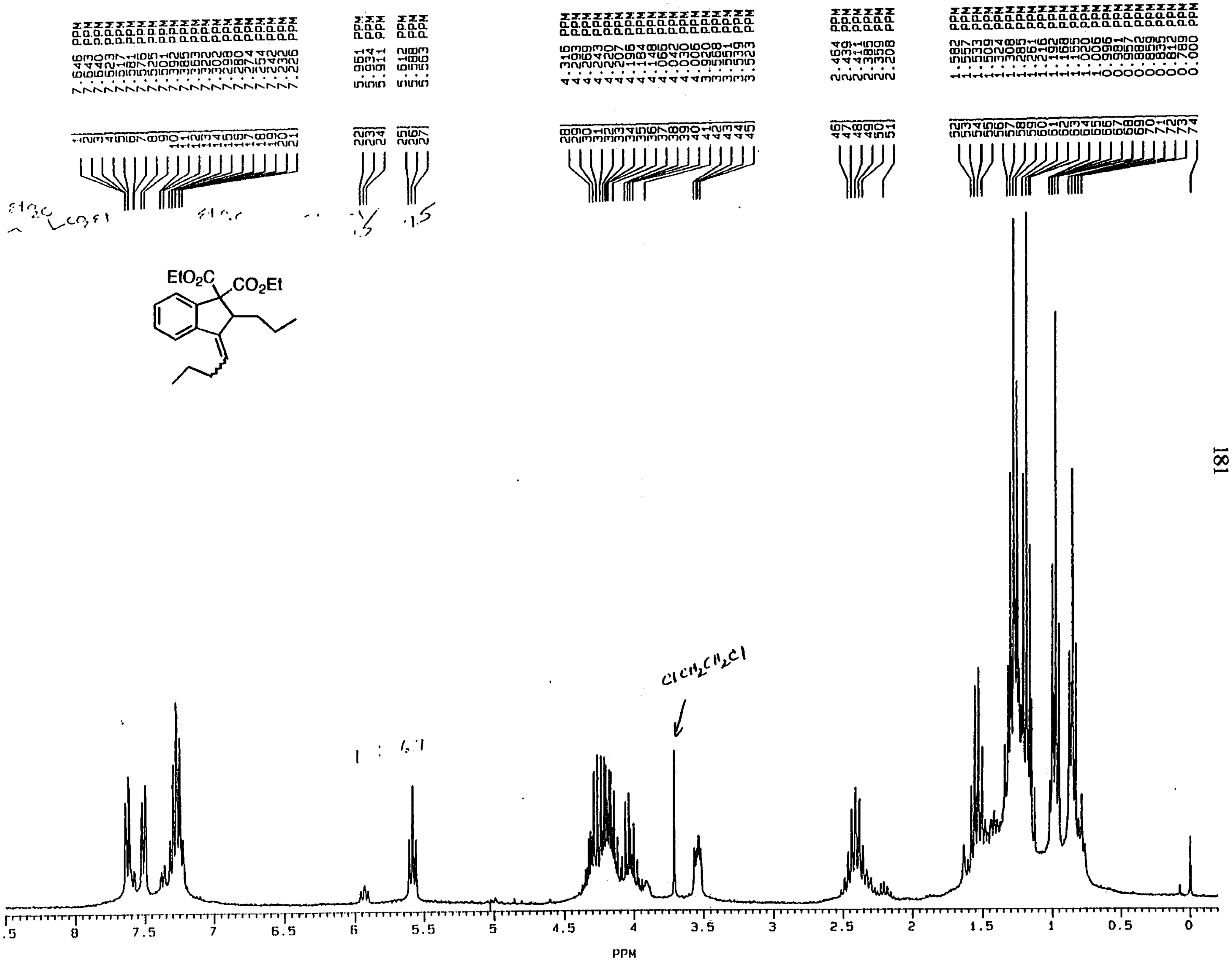
NMR1



+ Eu(hfc)3



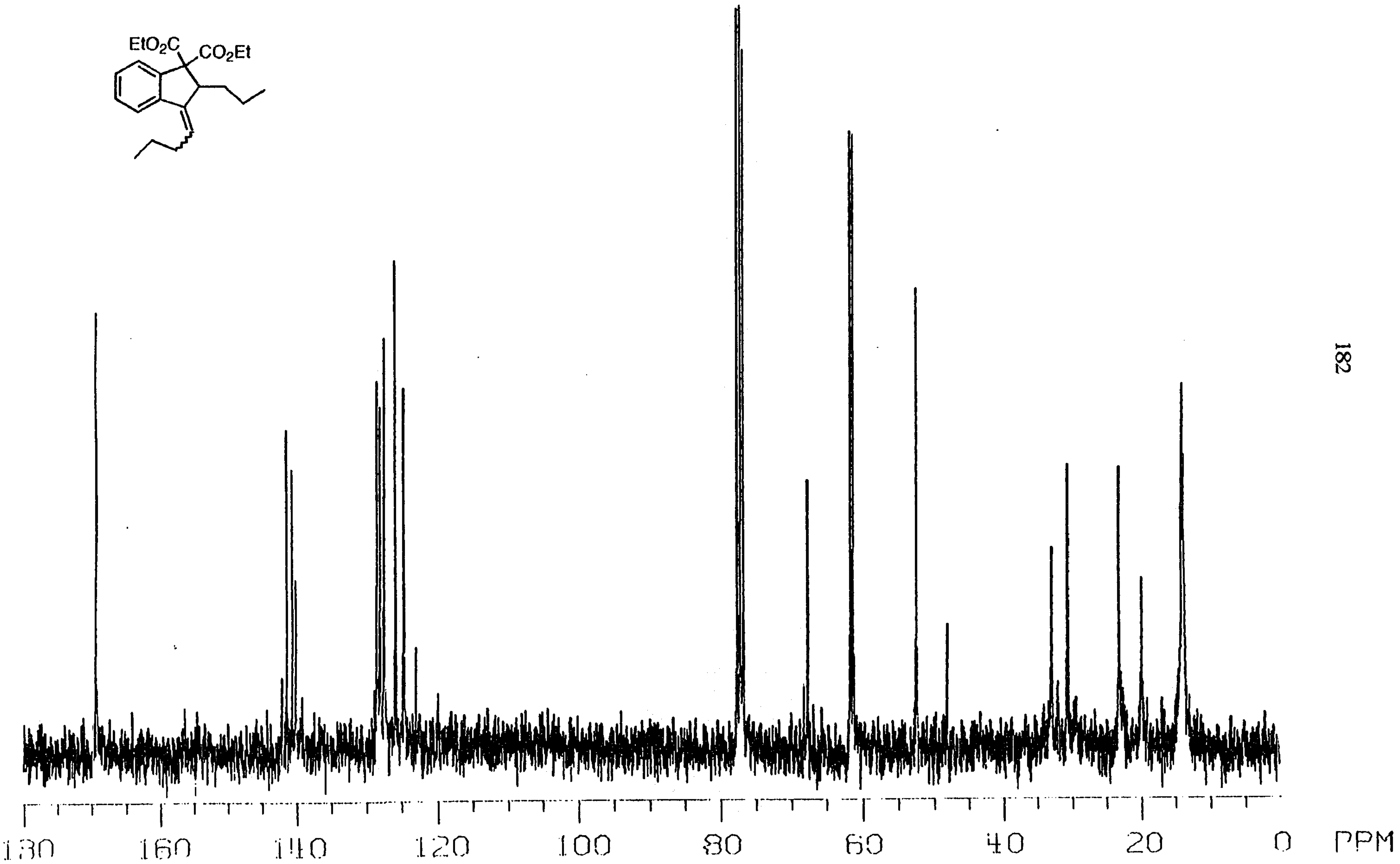
Entry 22



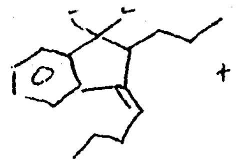
JMZ 245 ~~CMMAF-A-P-DBZL~~

Entry 22

CAF , 002 GF 13MAY89
CAF-VIII-41,A 13C

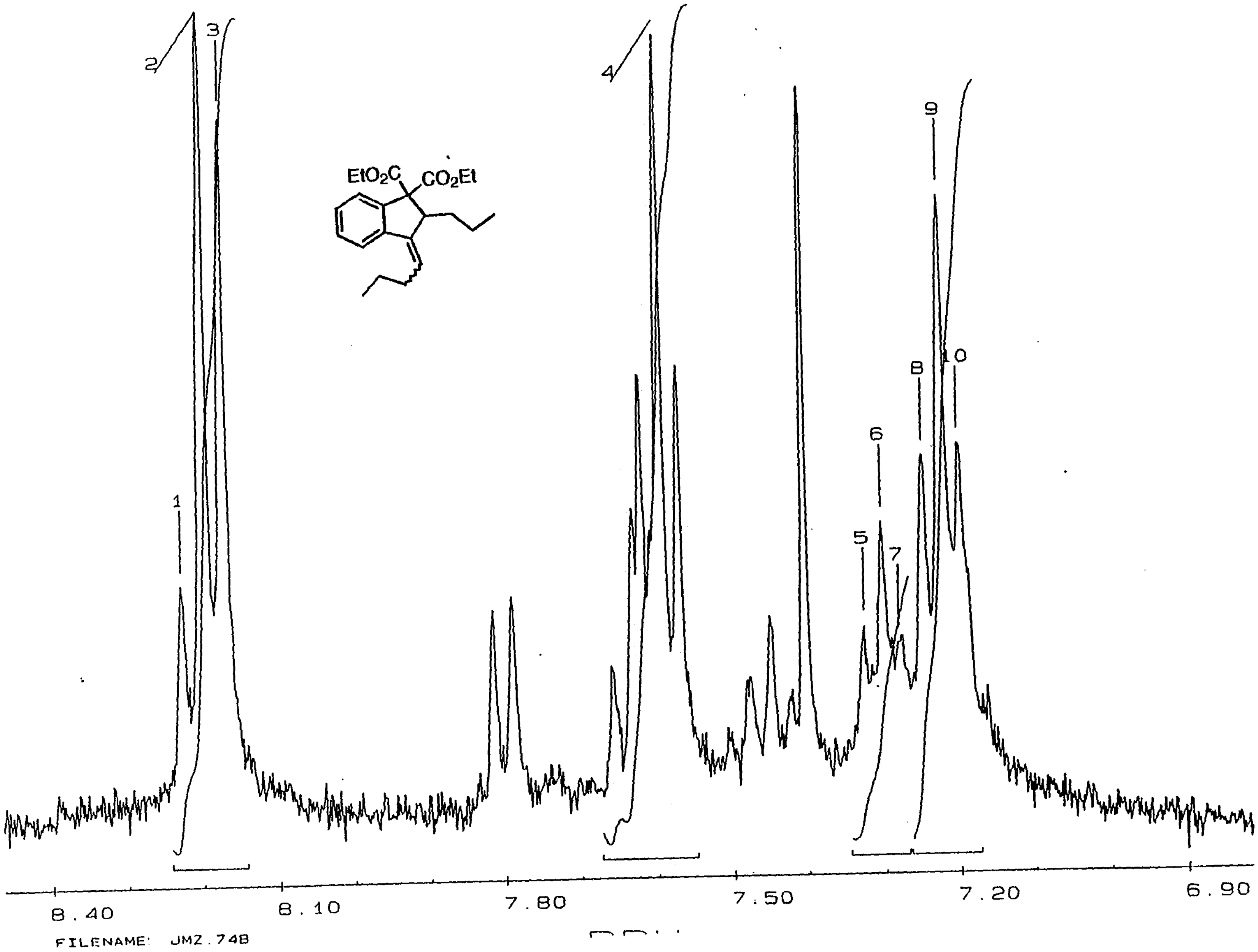


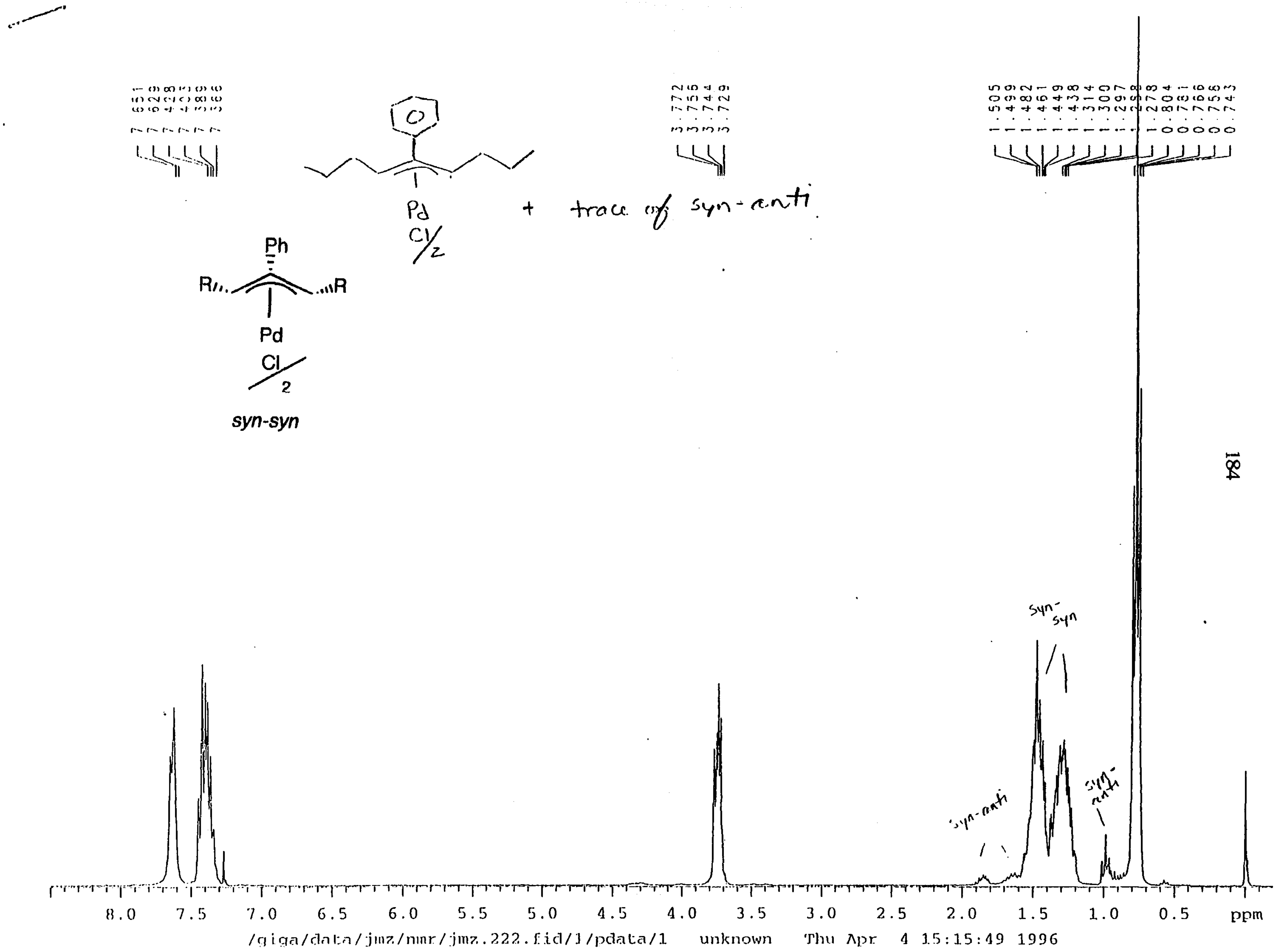
Entry 22



+ Eu(hfc)$_3$

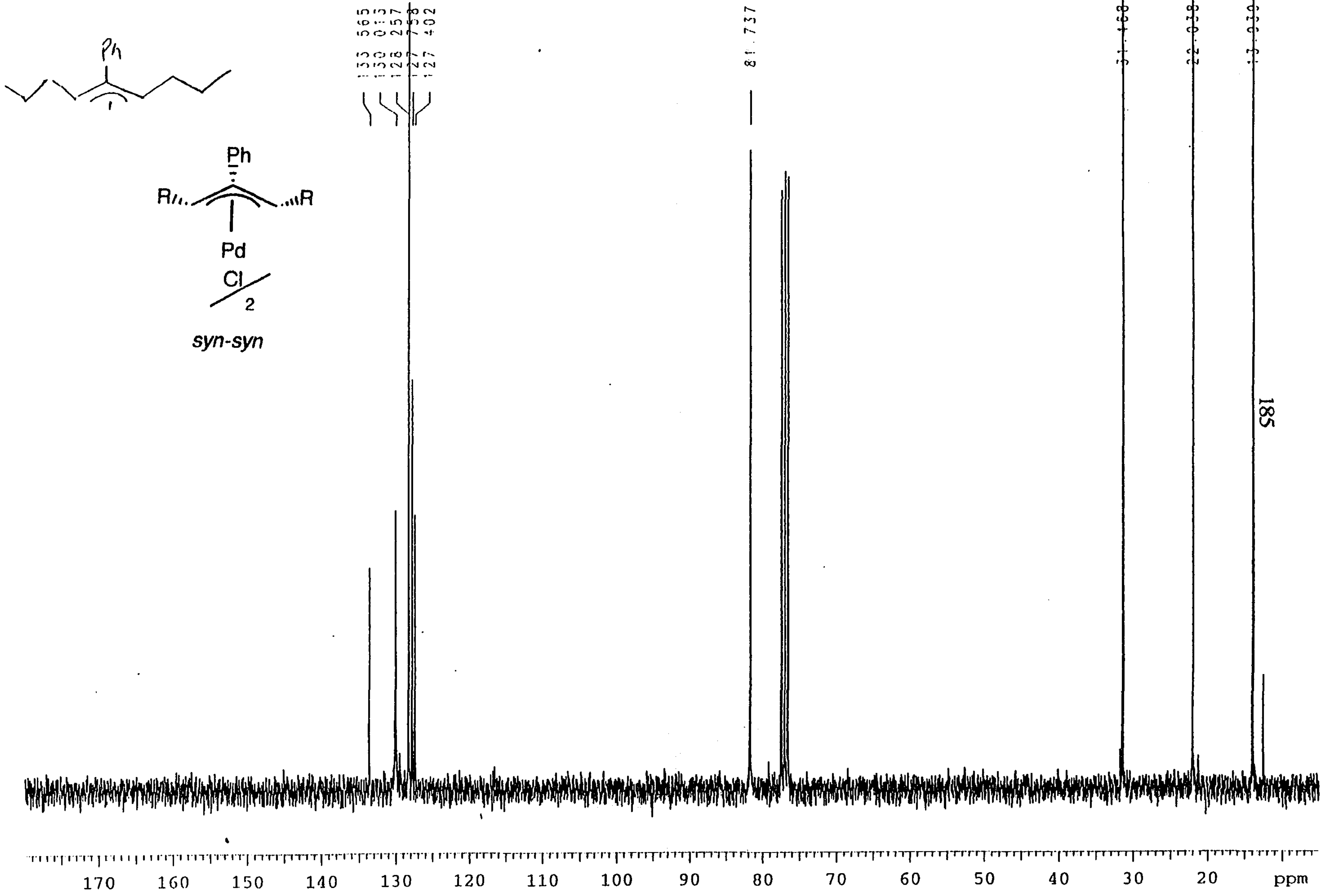
NMR1





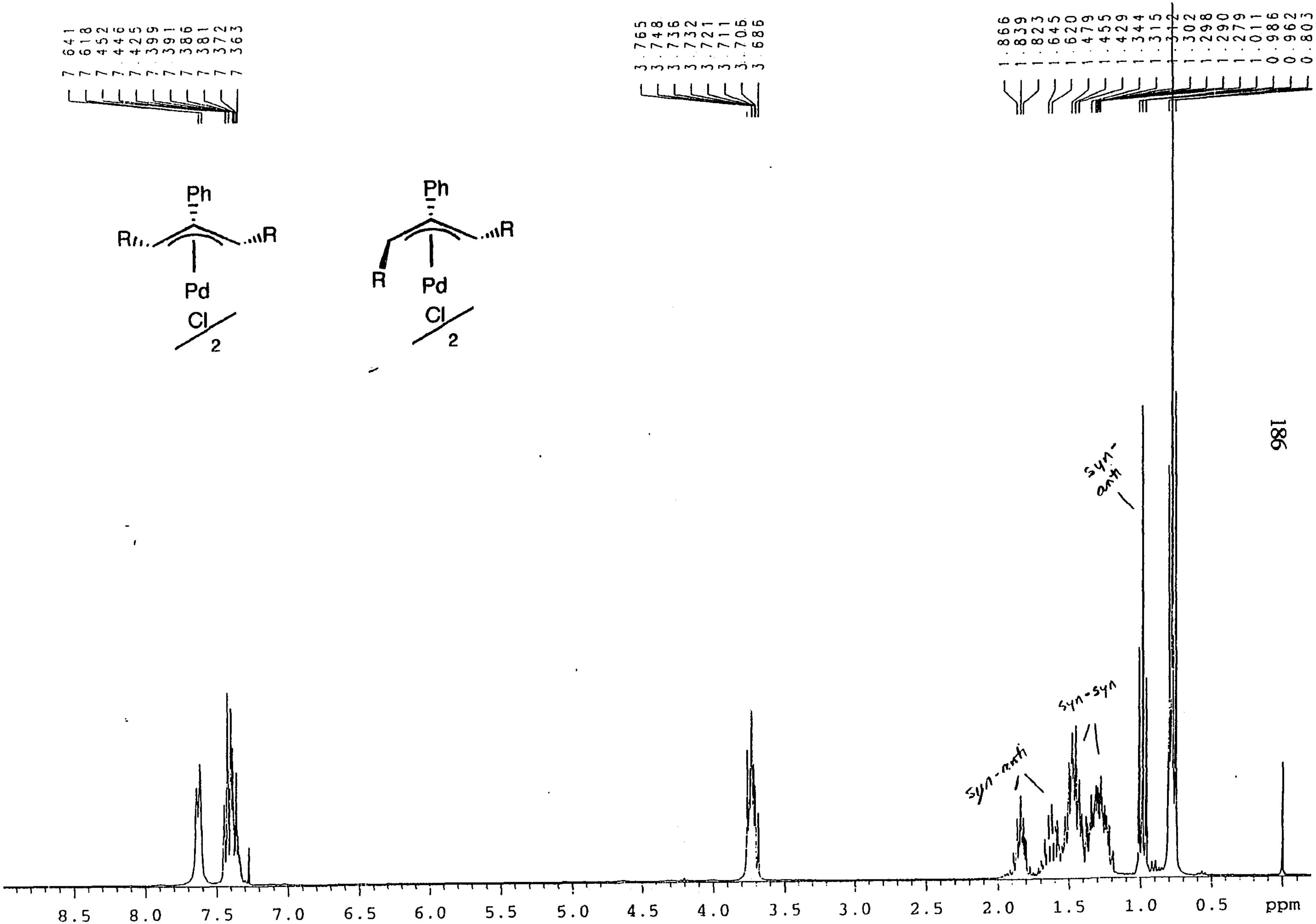
+ trace of syn-anti.

/giga/data/jmz/nmr/jmz.222.fid/1/pdata/1 unknown Thu Apr 4 15:15:49 1996

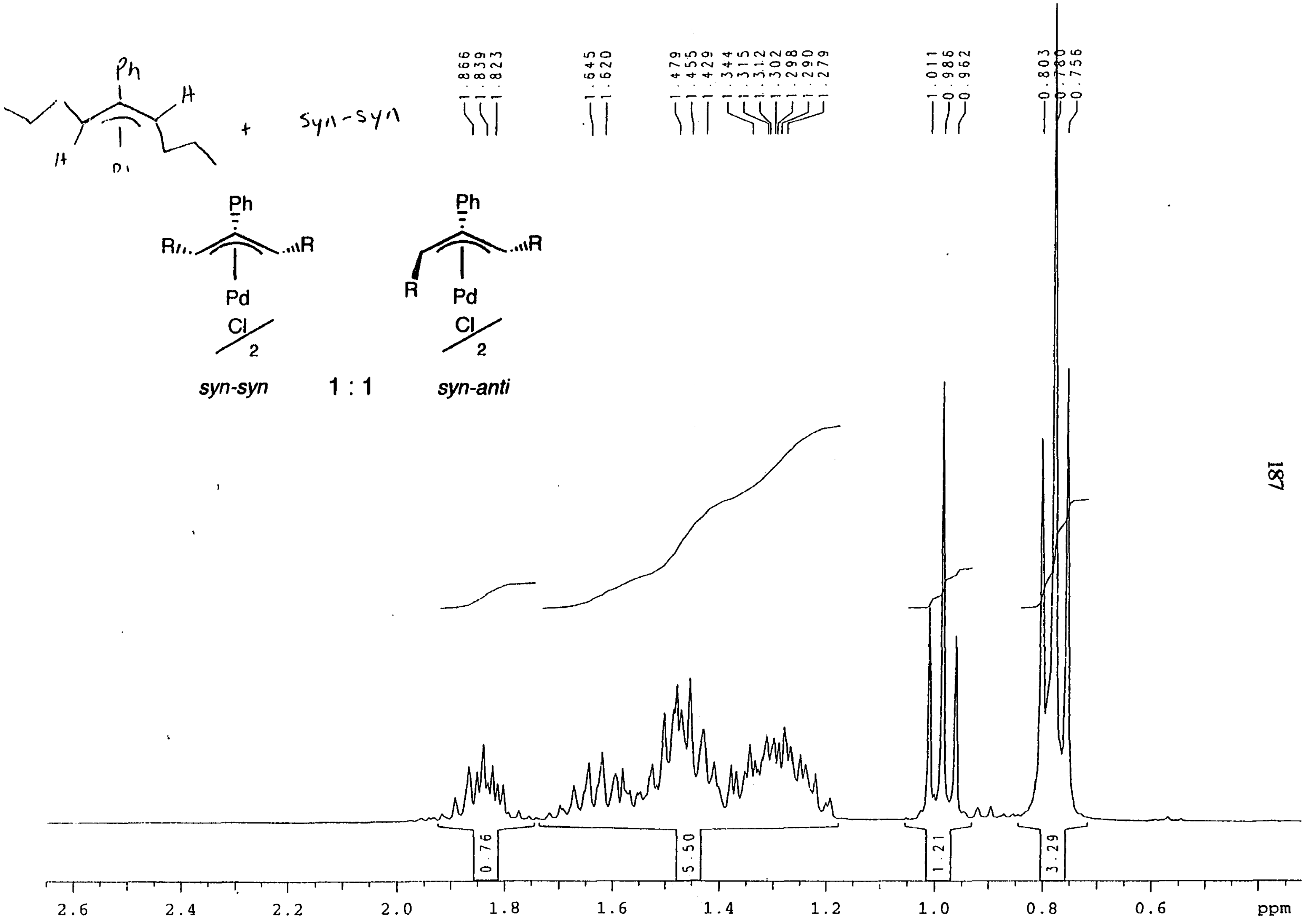


syn-syn

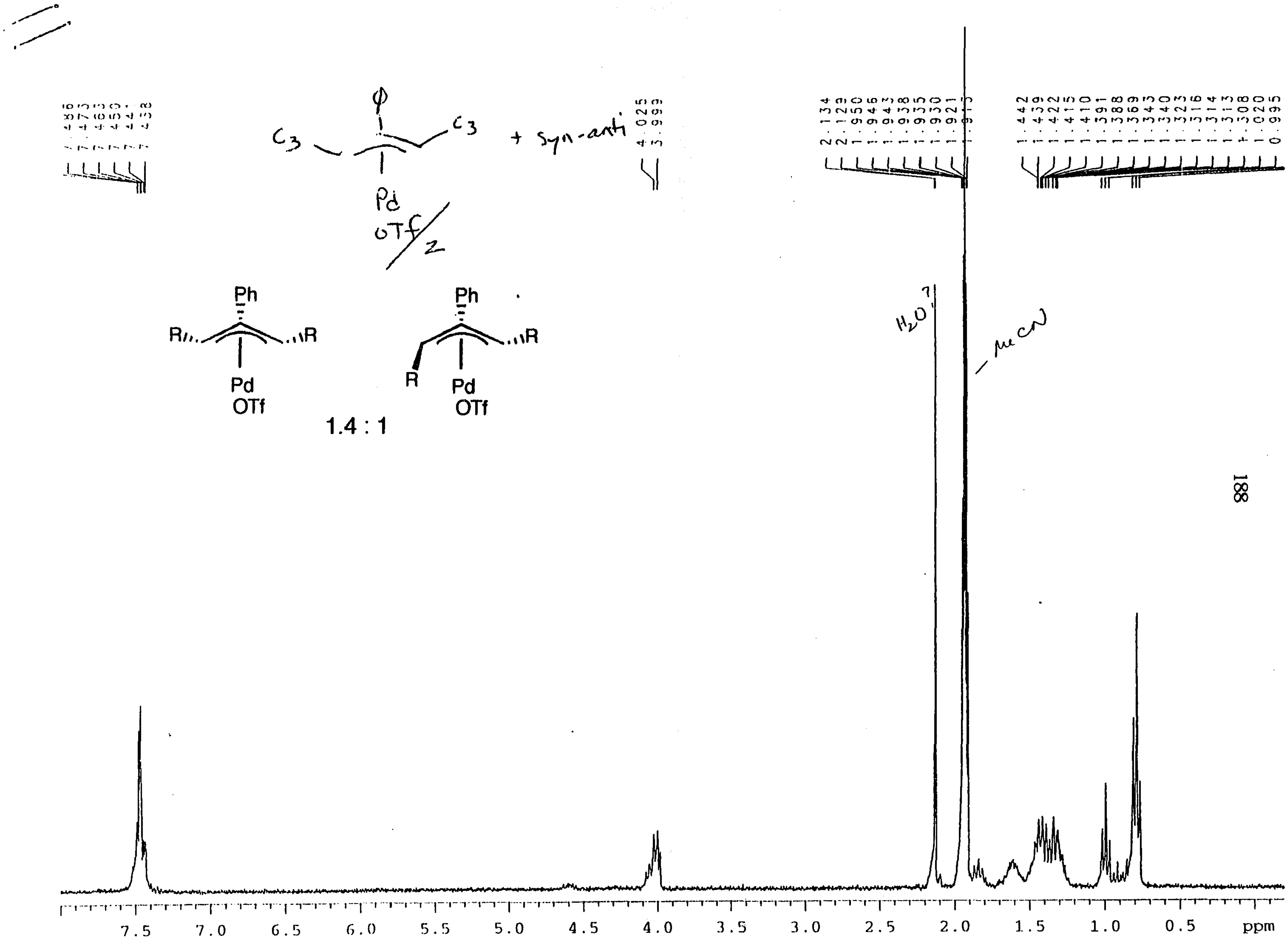
/giga/data/jmz/nmr/jmz.223.fid/1/pdata/1 unknown Thu Apr 4 15:20:13 1996 no sign of



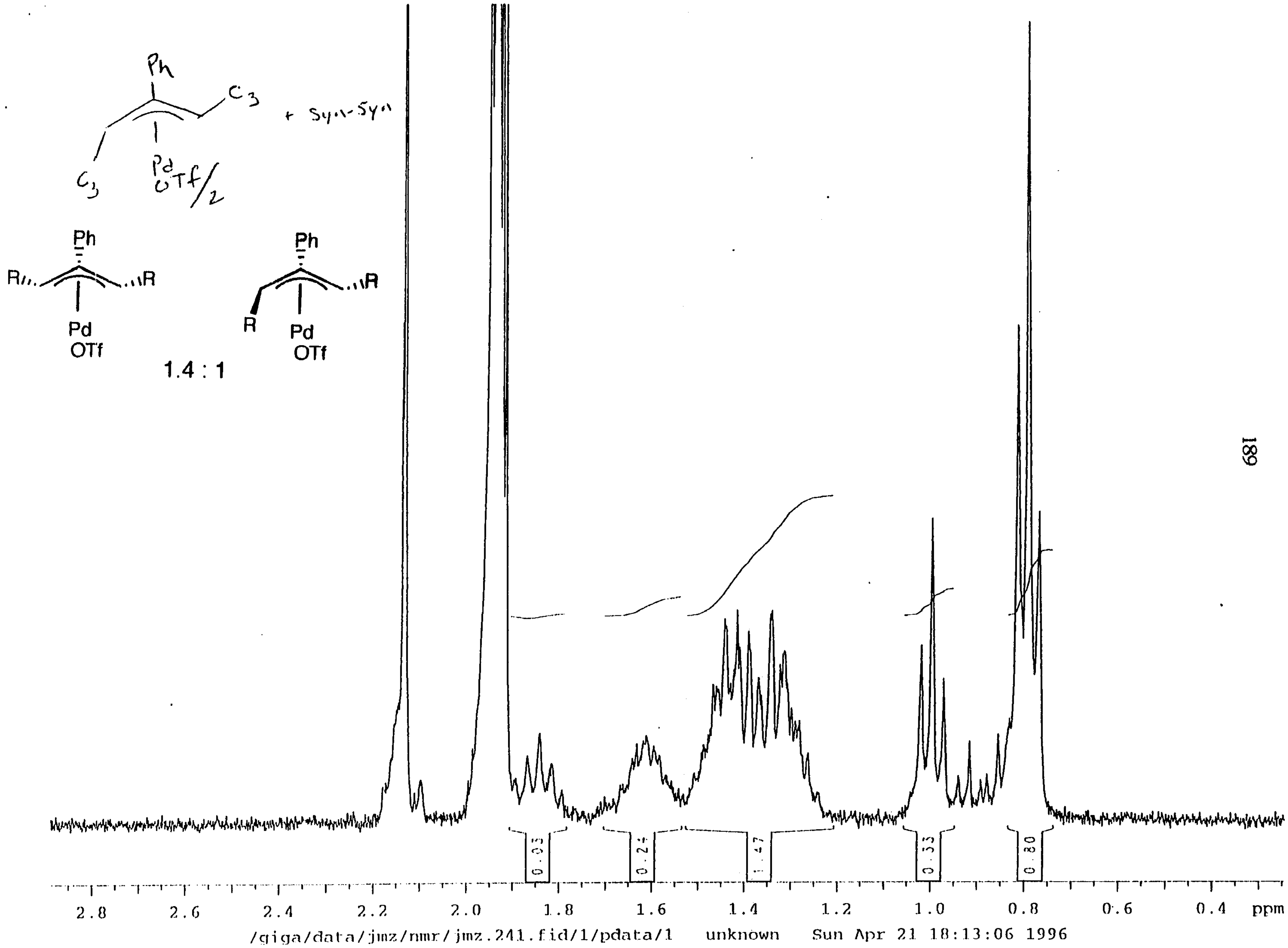
/giga/data/jmz/nmr/jmz.221.fid/1/pdata/1 unknown Wed Apr 3 14:32:48 1996

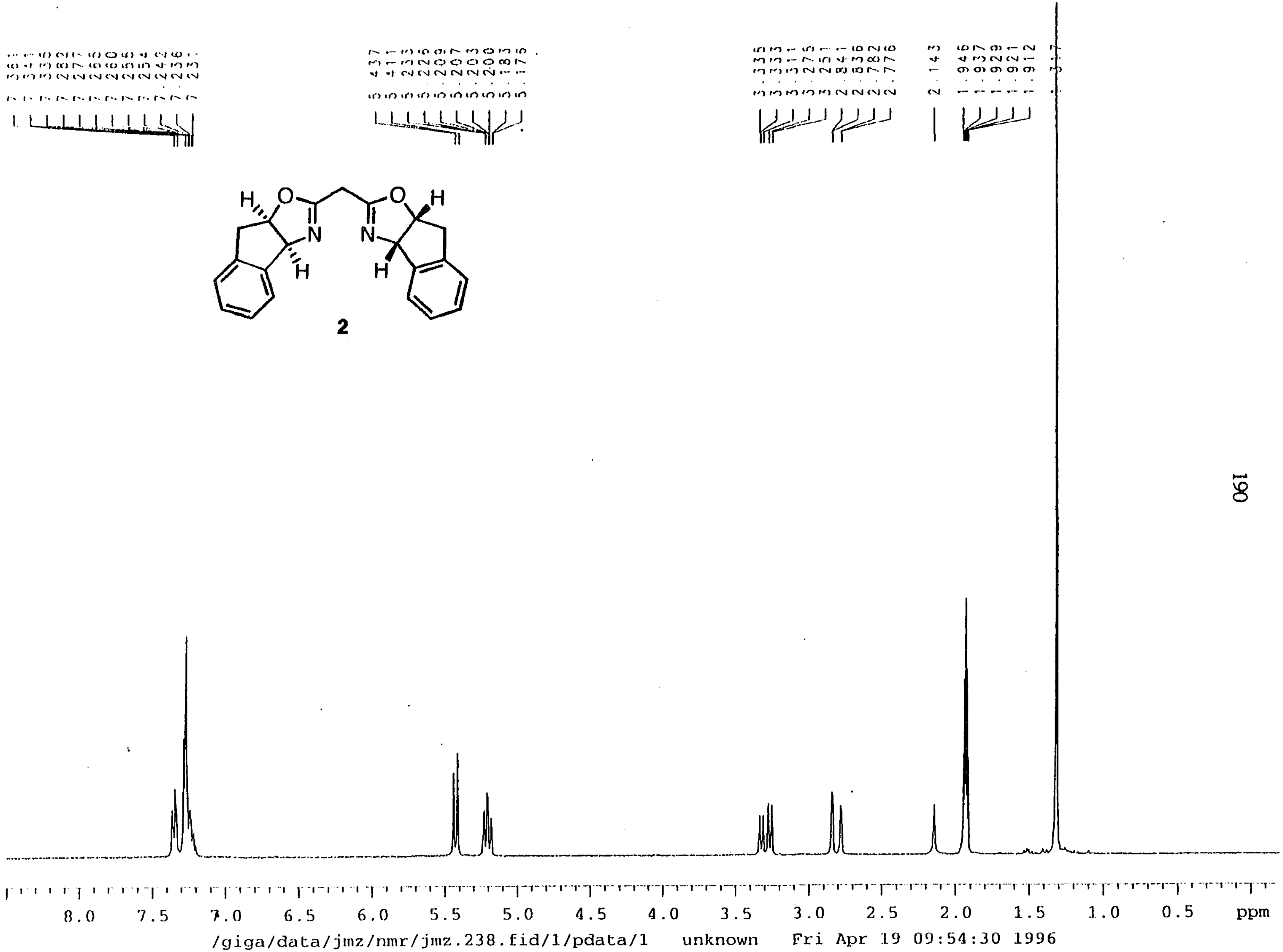


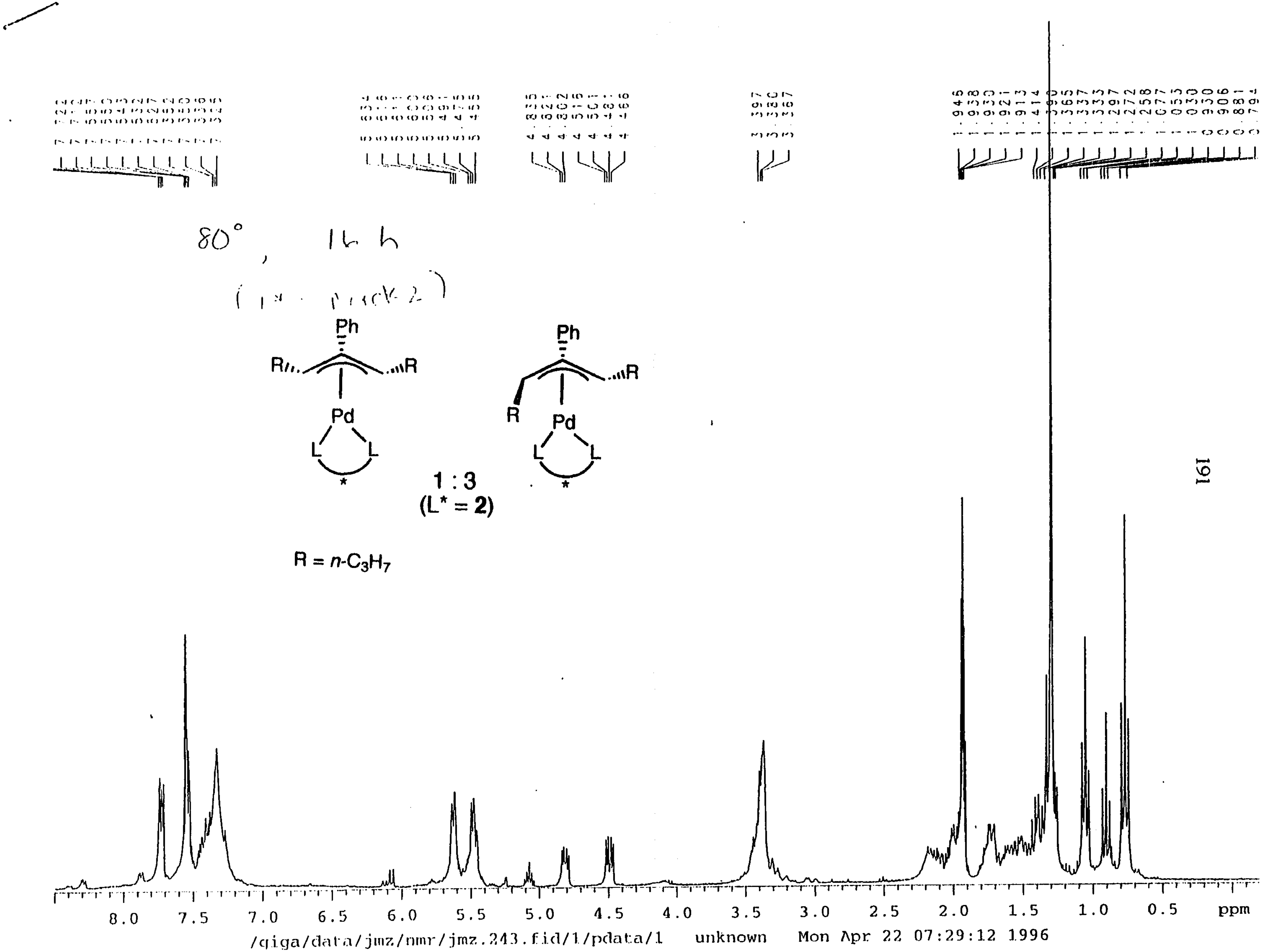
/giga/data/jmz/nmr/jmz.221.fid/1/pdata/1 unknown Wed Apr 3 14:34:34 1996



/giga/data/jmz/nmr/jmz.241.fid/1/pdata/1 unknown Sun Apr 21 14:55:54 1996


Ph
C3
C3
Pd
OTf/2
+ Syn-Syn
Ph
R
R
Pd
OTf
1.4 : 1
Ph
R
R
Pd
OTf
0.03
0.24
1.47
0.33
0.80
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
ppm
/giga/data/jmz/nmr/jmz.241.fid/1/pdata/1 unknown Sun Apr 21 18:13:06 1996


7.361
7.341
7.335
7.282
7.277
7.265
7.260
7.255
7.254
7.242
7.236
7.231
5.437
5.411
5.233
5.226
5.209
5.207
5.203
5.200
5.183
5.175
3.335
3.333
3.311
3.275
3.251
2.841
2.836
2.782
2.776
2.143
1.946
1.937
1.929
1.921
1.912
1.317
H
O
N
H
O
H
N
H
2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
/giga/data/jmz/nmr/jmz.238.fid/1/pdata/1 unknown Fri Apr 19 09:54:30 1996

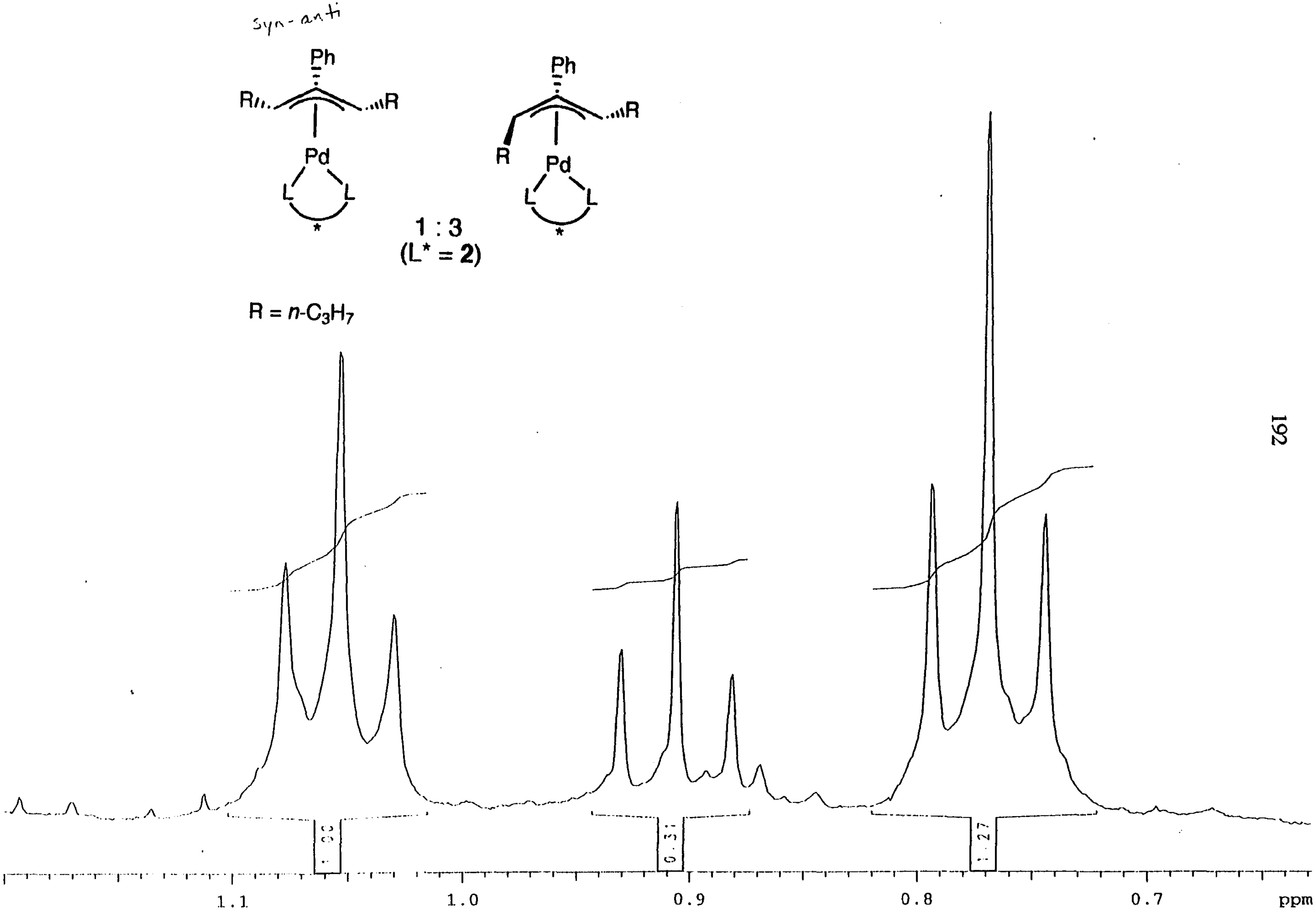


80°, 16 h

(1st - [illegible])

1 : 3
(L* = 2)

R = *n*-C_3H_7

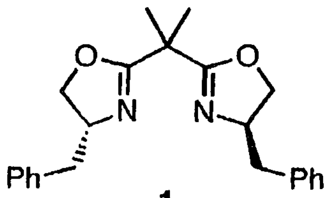


1 : 3
(L* = 2)

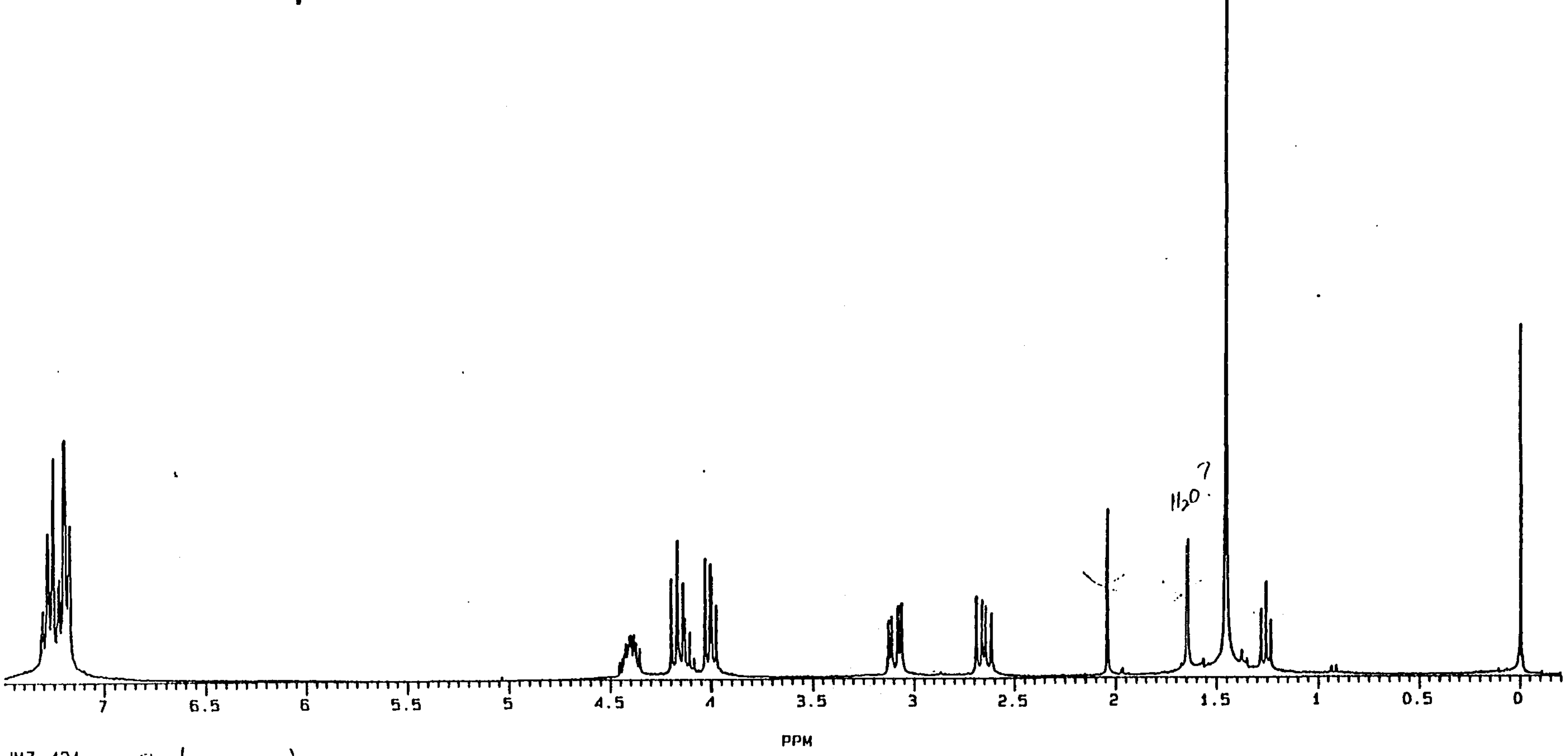
R = n-C_3H_7

/giga/data/jmz/nmr/jmz.243.fid/1/pdata/1   unknown   Mon Apr 22 07:35:10 1996

JMZ III-1.

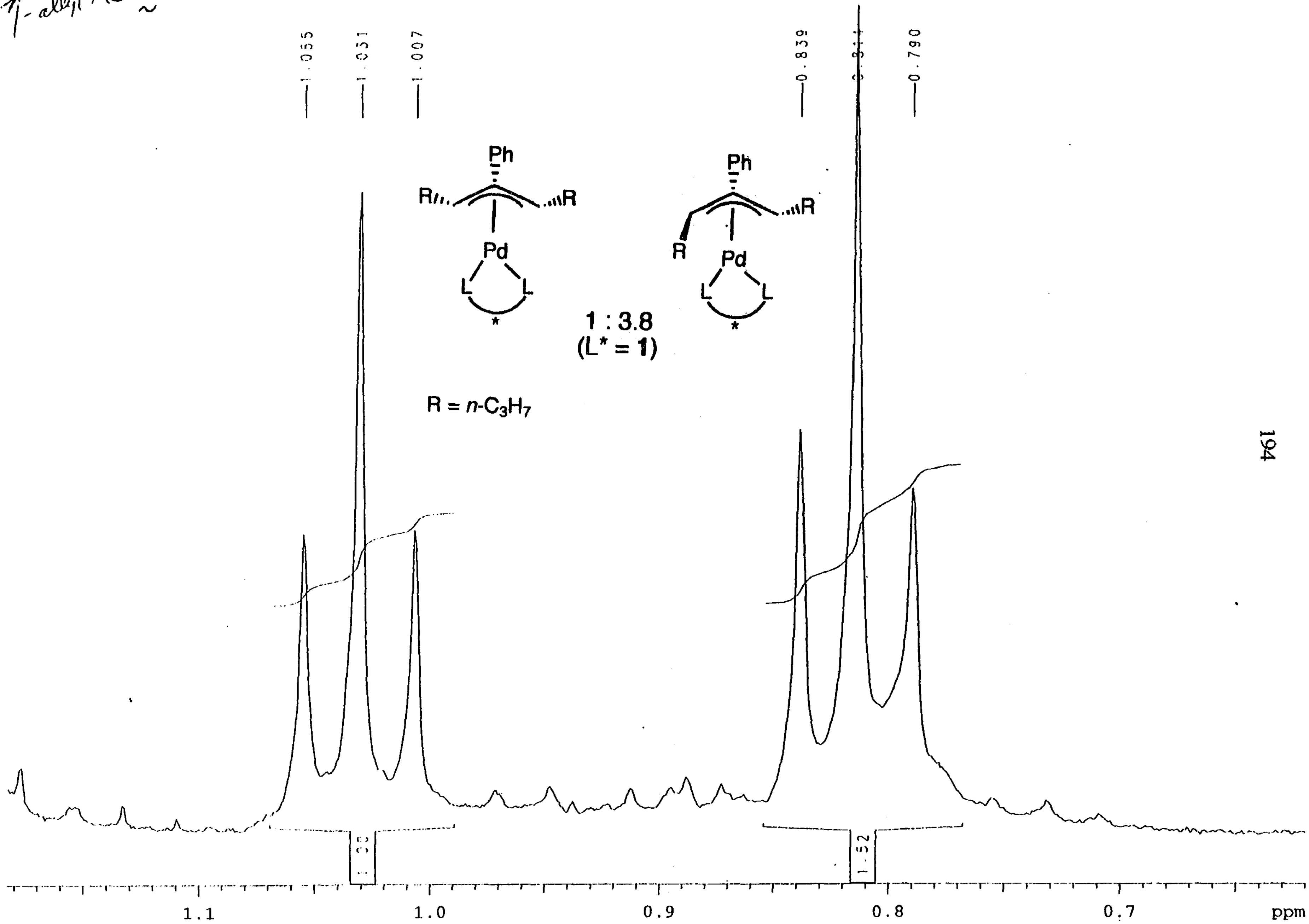


1

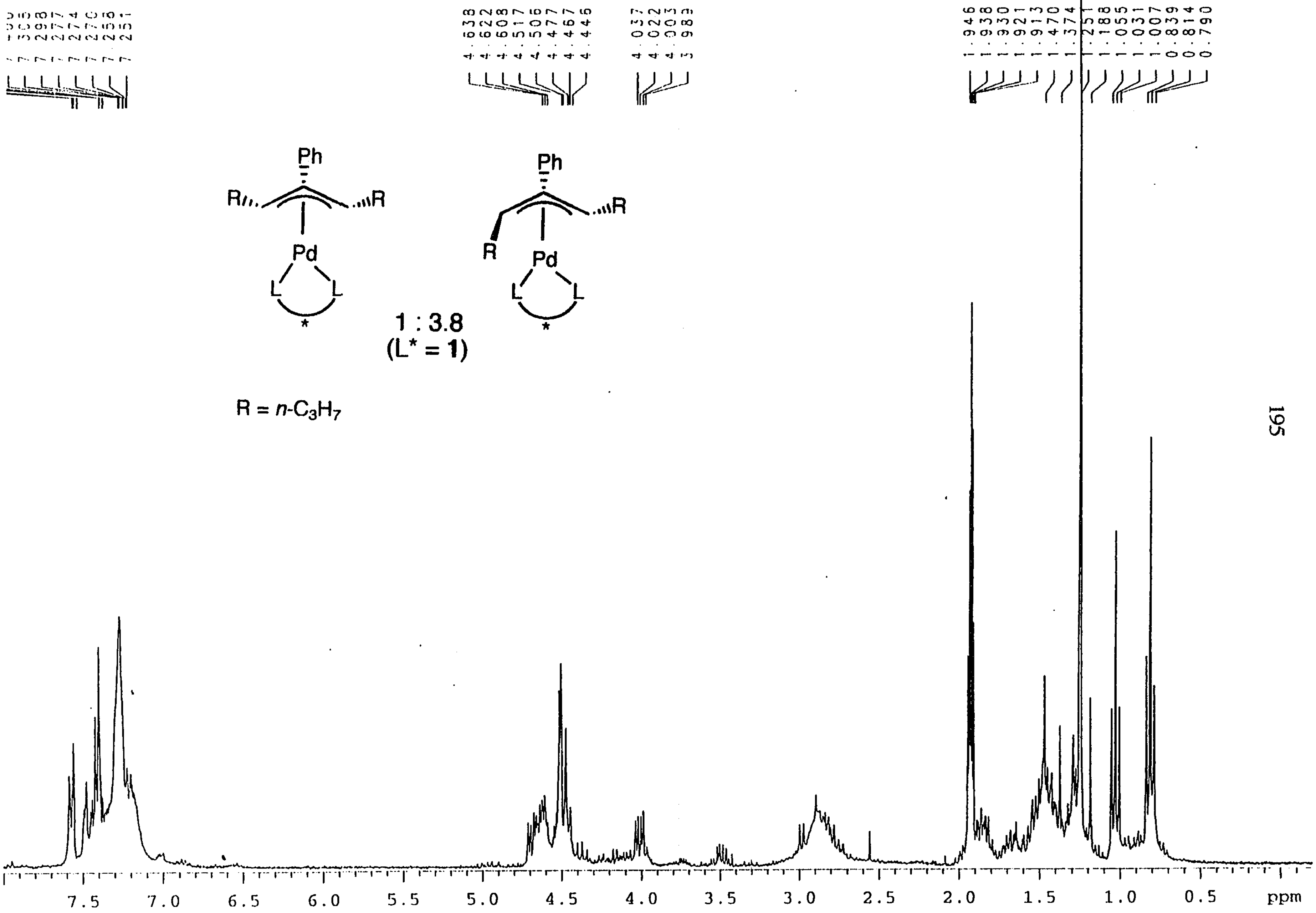


JMZ.421 Columned

(η^3-allyl) Pd $\underset{\sim}{1}$



/giga/data/jmz/nmr/jmz.251.fid/1/pdata/1 unknown Tue Apr 23 12:38:54 1996 nmr temp = 65°C



1 : 3.8
(L* = 1)

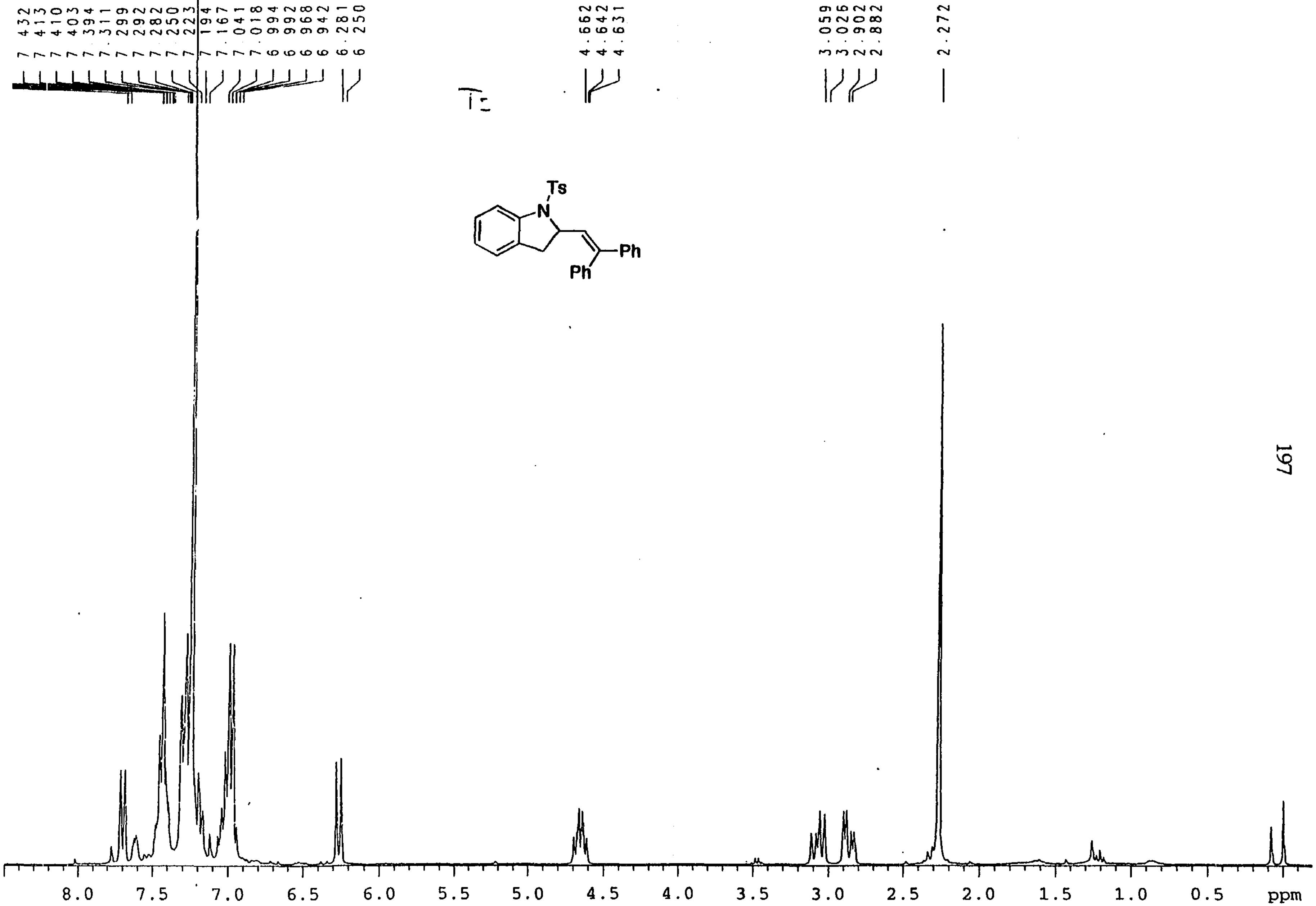
R = *n*-C_3H_7

/giga/data/jmz/nmr/jmz.251.fid/1/pdata/1 unknown Tue Apr 23 12:37:19 1996

APPENDIX B: CHAPTER 2 ^{1}H AND ^{13}C NMR SPECTRA

$[\alpha]_D = +19.1$

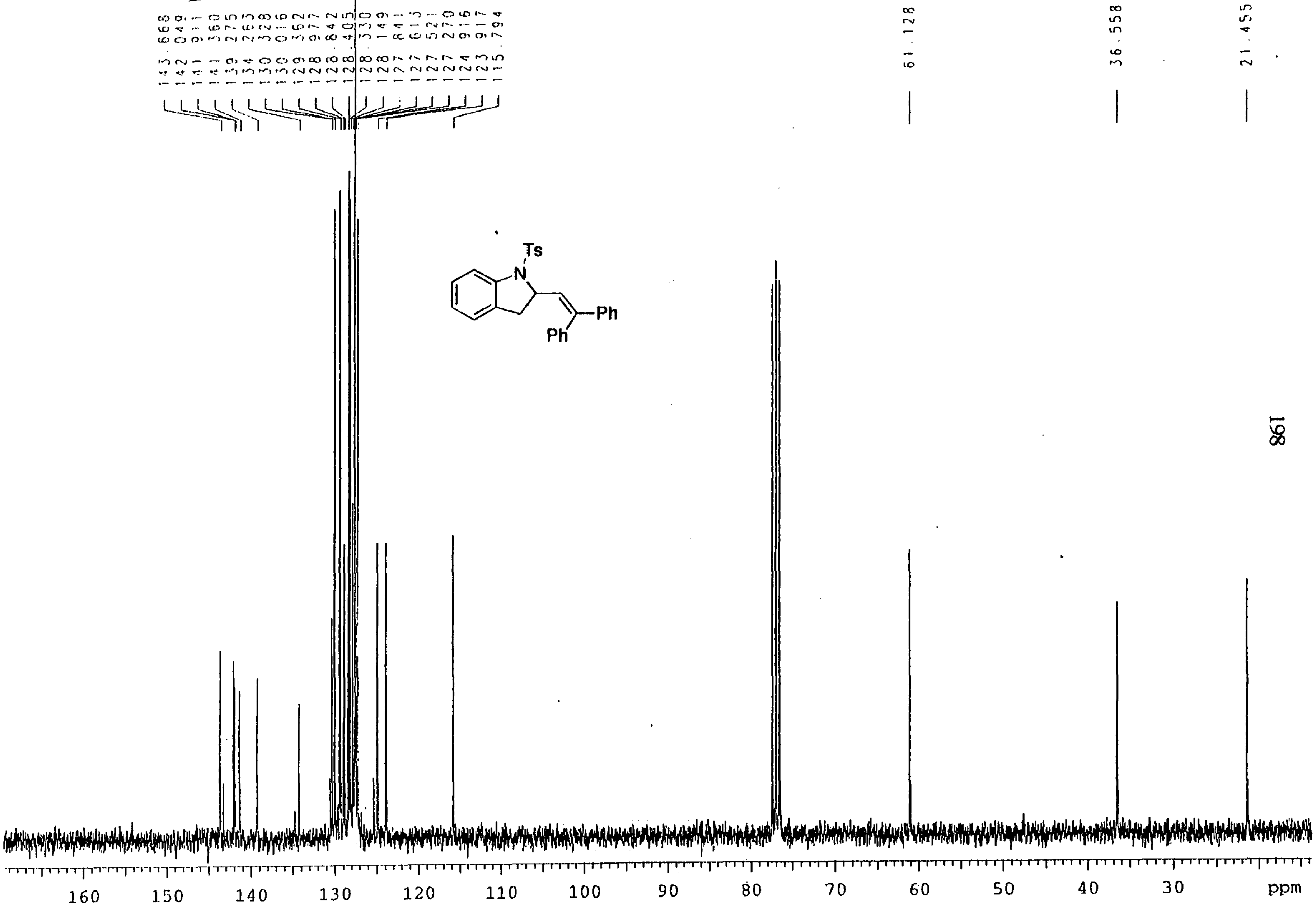
$c = .053$ $CHCl_3$



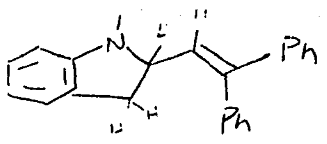
/giga/data/jmz/nmr/jmz.196.fid/1/pdata/1 unknown Sun Feb 25 13:15:31 1996

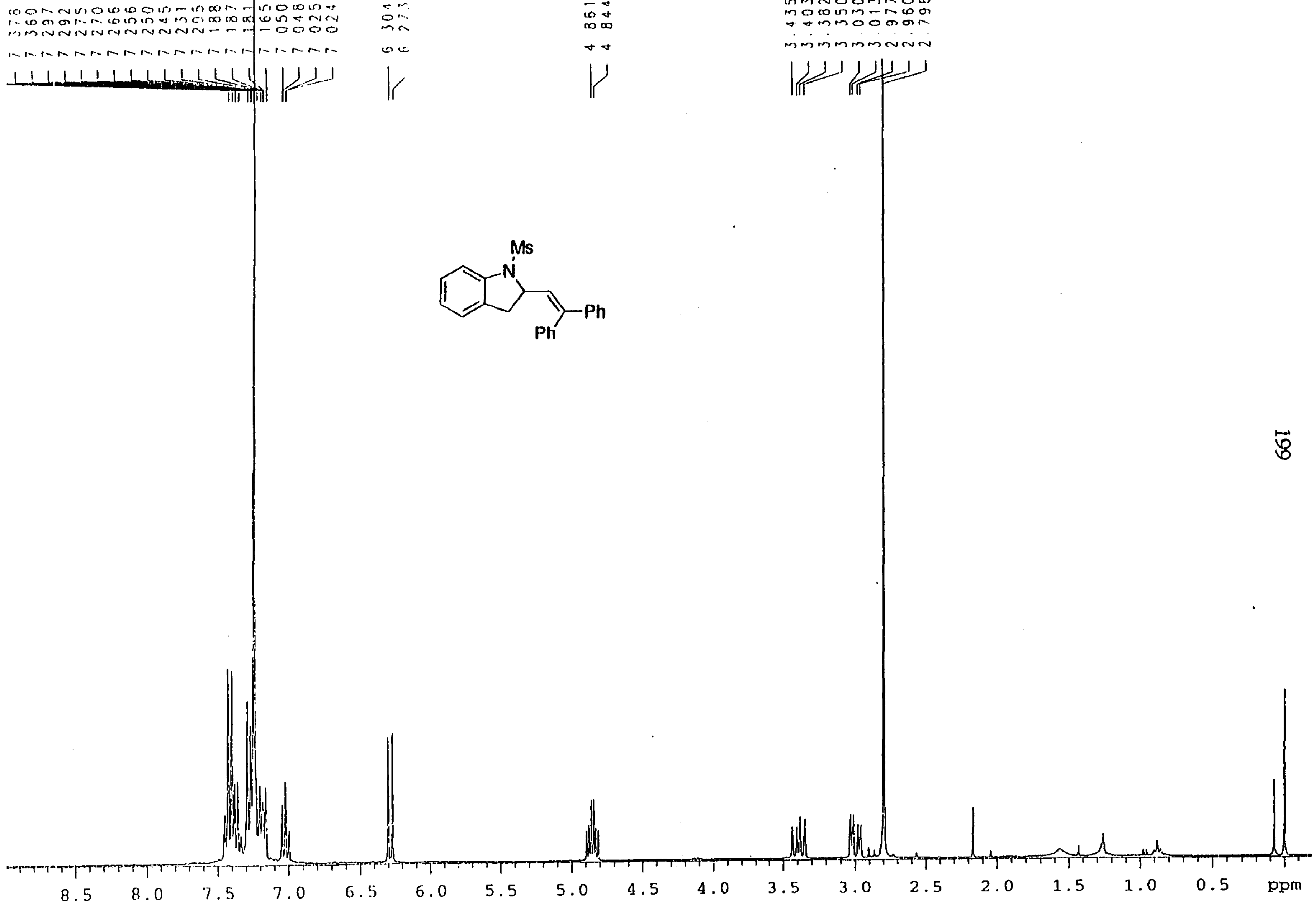
.199 g

198

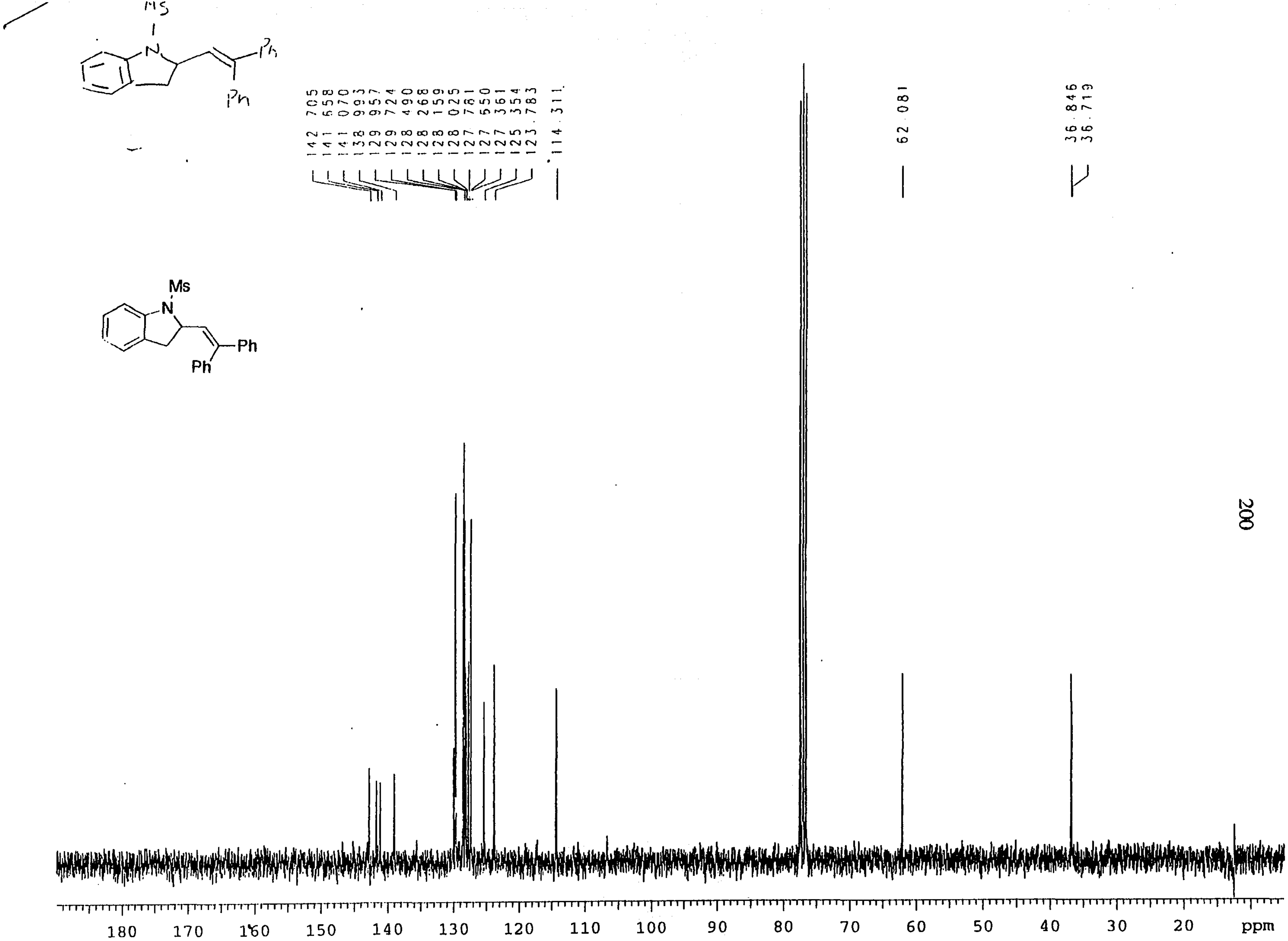


/giga/data/jmz/nmr/jmz.198.fid/1/pdata/1 unknown Sun Feb 25 14:40:48 1996

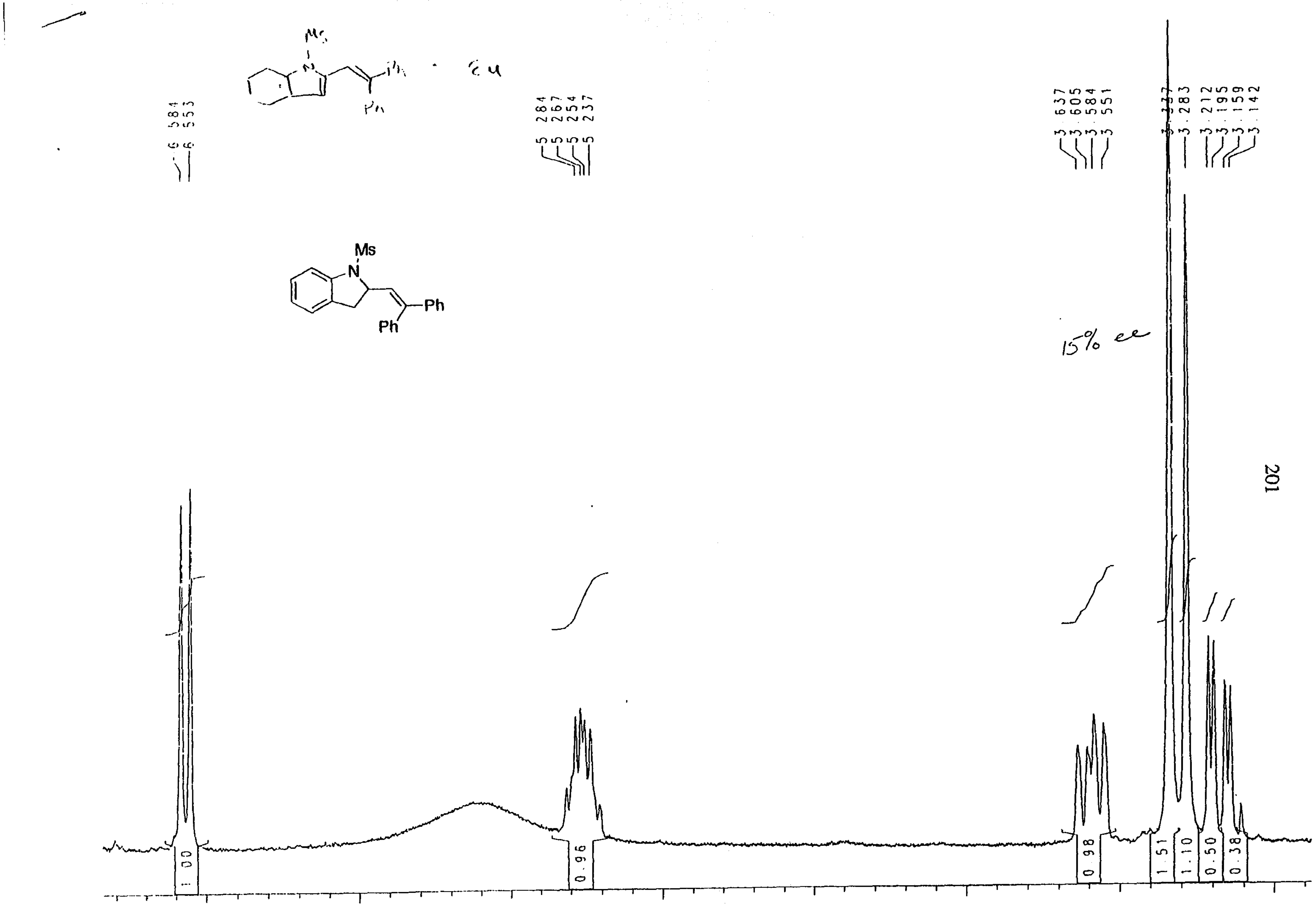




/giga/data/jmz/nmr/jmz.189.fid/1/pdata/1 unknown Tue Feb 20 08:12:34 1996



/giga/data/jmz/nmr/jmz.192.fid/1/pdata/1 unknown Tue Feb 20 18:27:58 1996



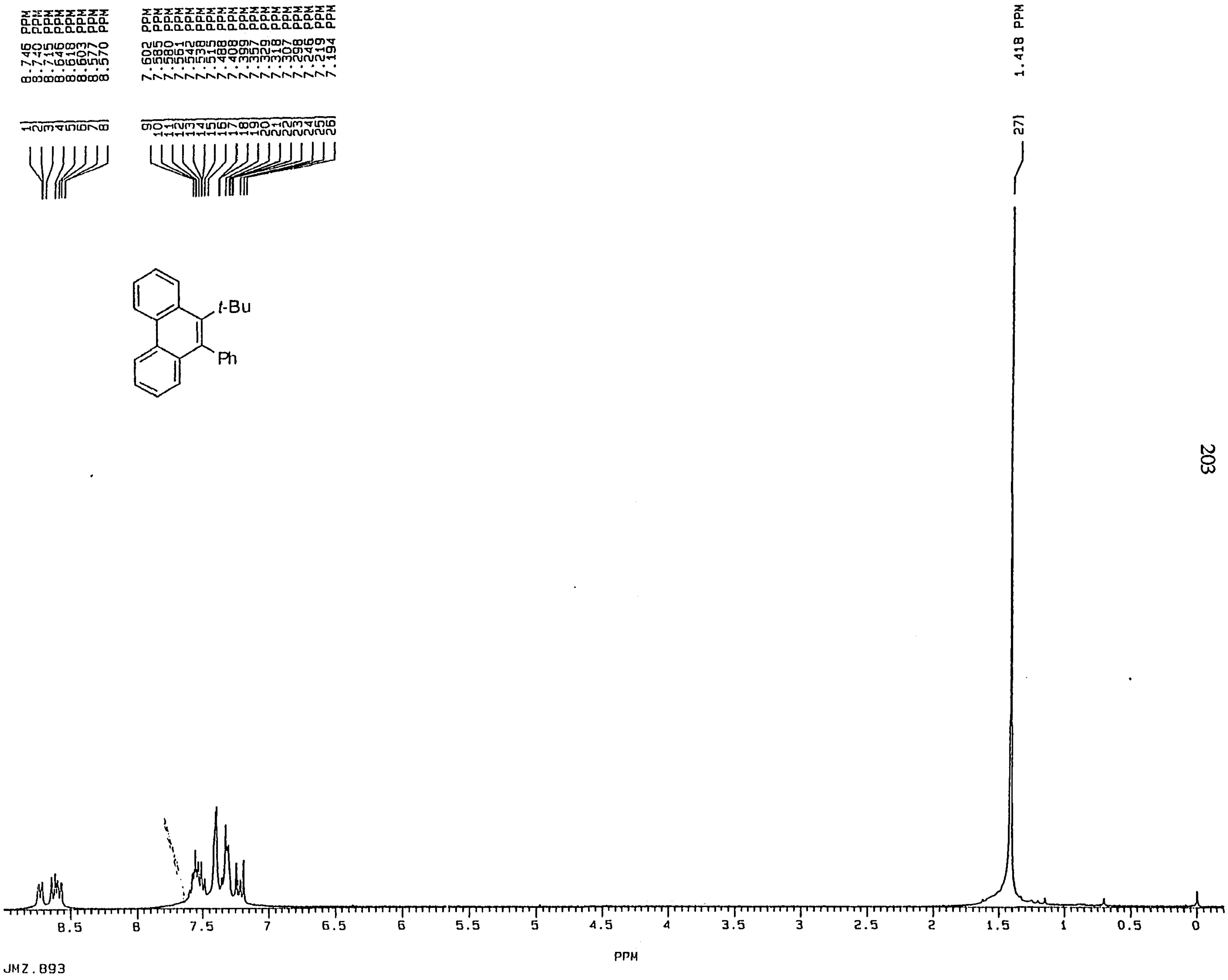
15% ee

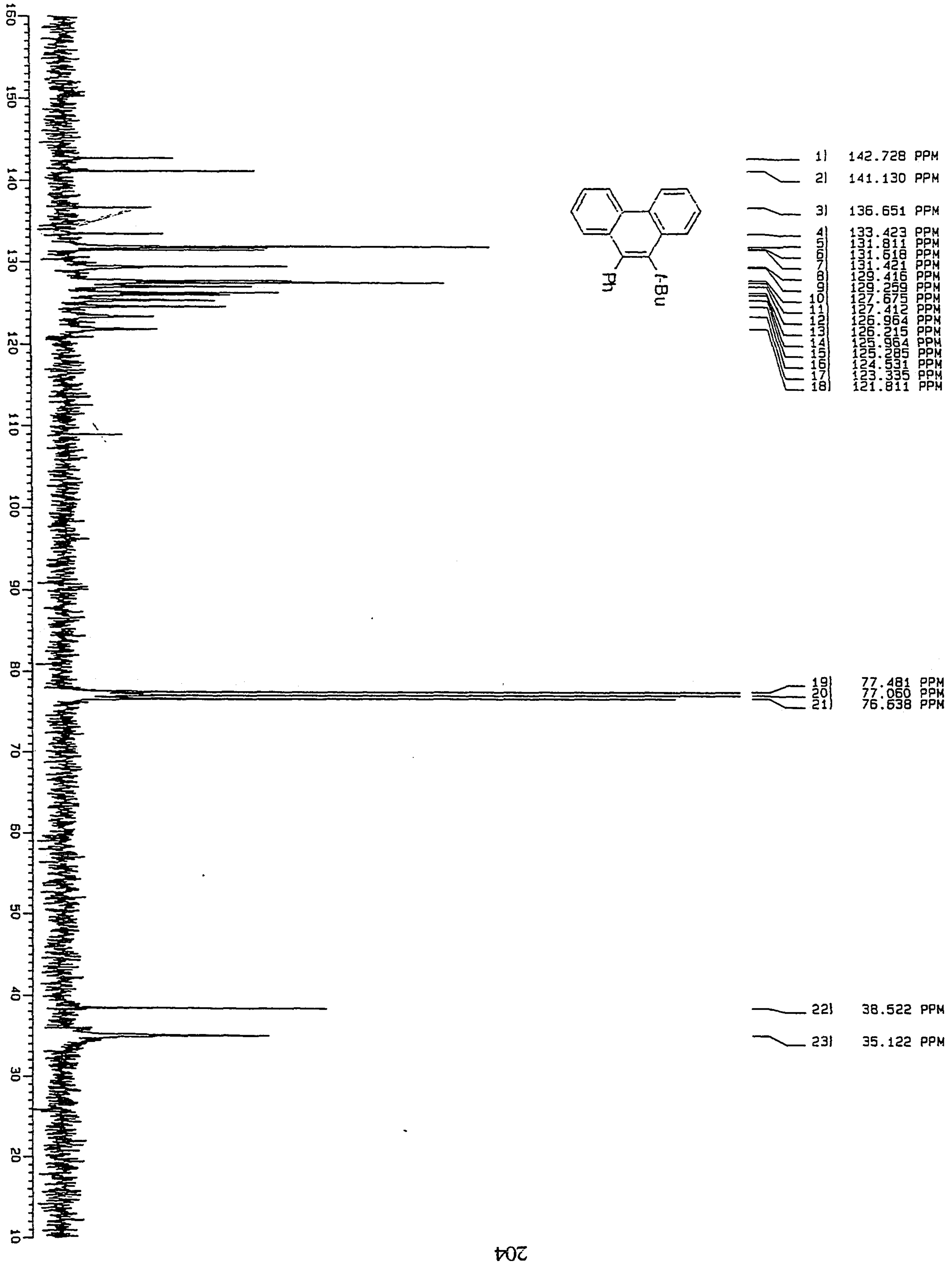
/giga/data/jmz/nmr/jmz.193.fid/1/pdata/1 unknown Tue Feb 20 18:48:28 1996

APPENDIX C: CHAPTER 3 ^{1}H AND ^{13}C NMR SPECTRA

VII - 13

Table 2, 1

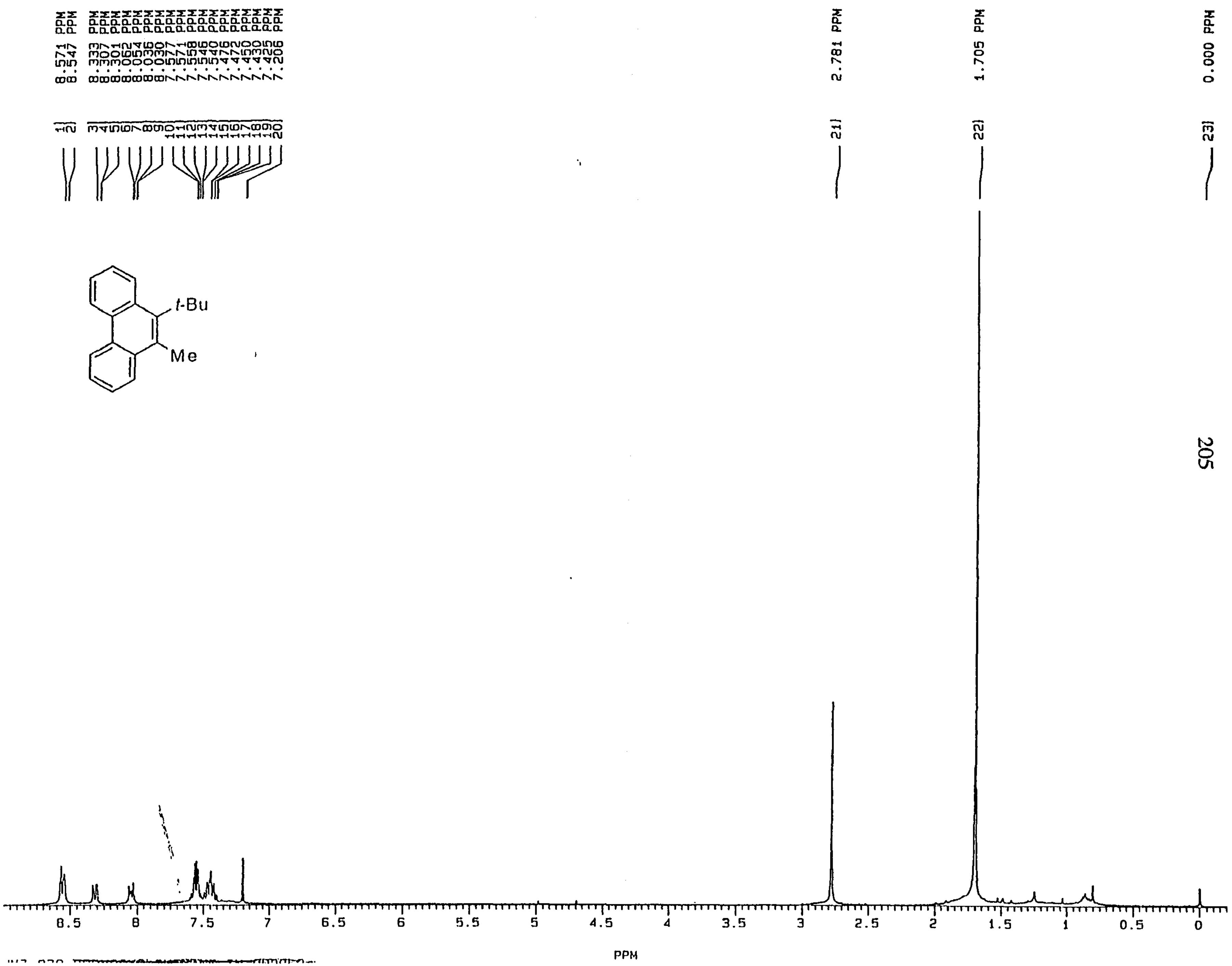



13C
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
t-Bu
Ph
1) 142.728 PPM
2) 141.130 PPM
3) 136.651 PPM
4) 133.423 PPM
5) 131.811 PPM
6) 131.618 PPM
7) 131.421 PPM
8) 129.416 PPM
9) 129.259 PPM
10) 127.675 PPM
11) 127.412 PPM
12) 126.964 PPM
13) 126.215 PPM
14) 125.964 PPM
15) 125.285 PPM
16) 124.531 PPM
17) 123.335 PPM
18) 121.811 PPM
19) 77.481 PPM
20) 77.060 PPM
21) 76.638 PPM
22) 38.522 PPM
23) 35.122 PPM

2,1

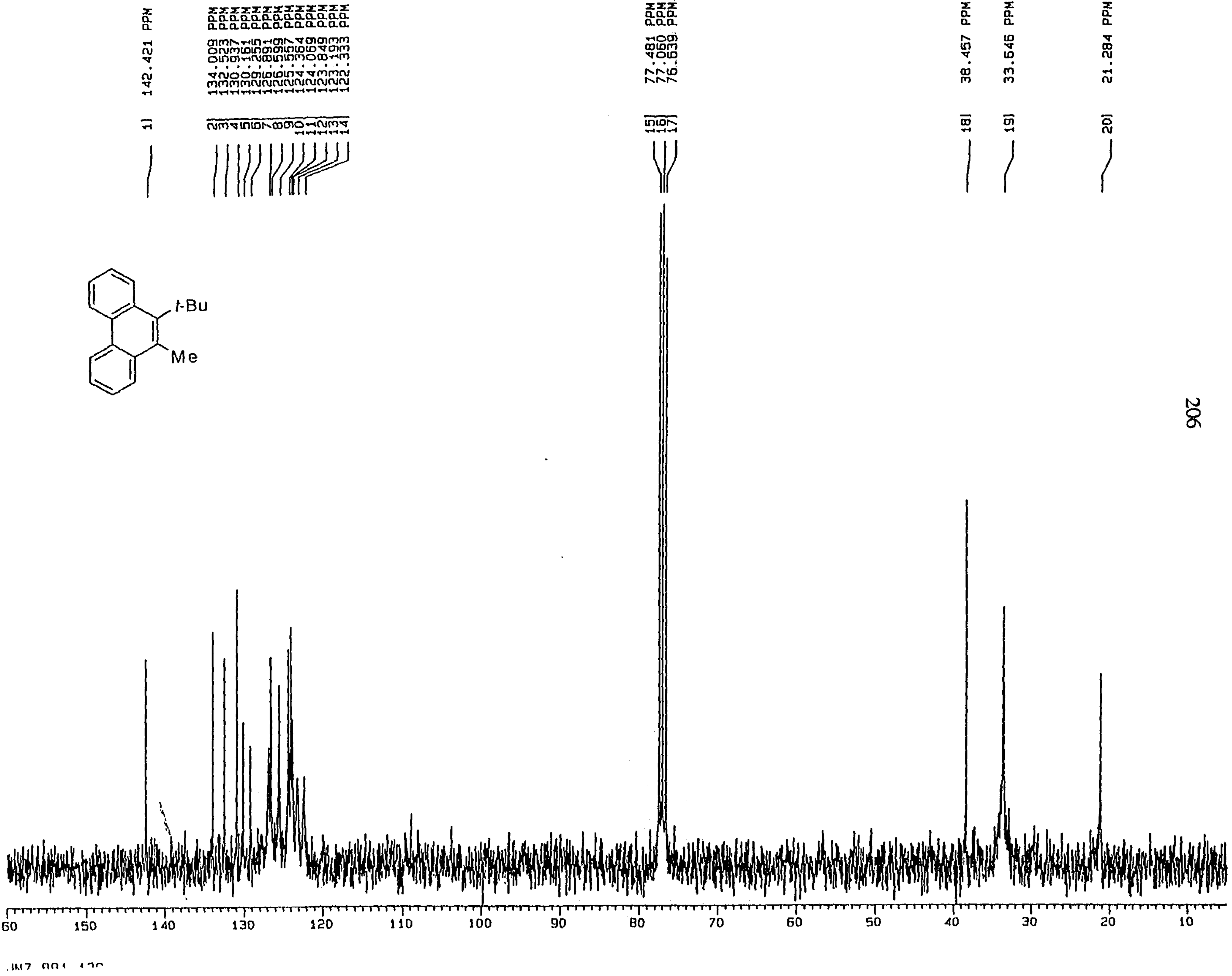
Table 2, [illegible]

TL-16



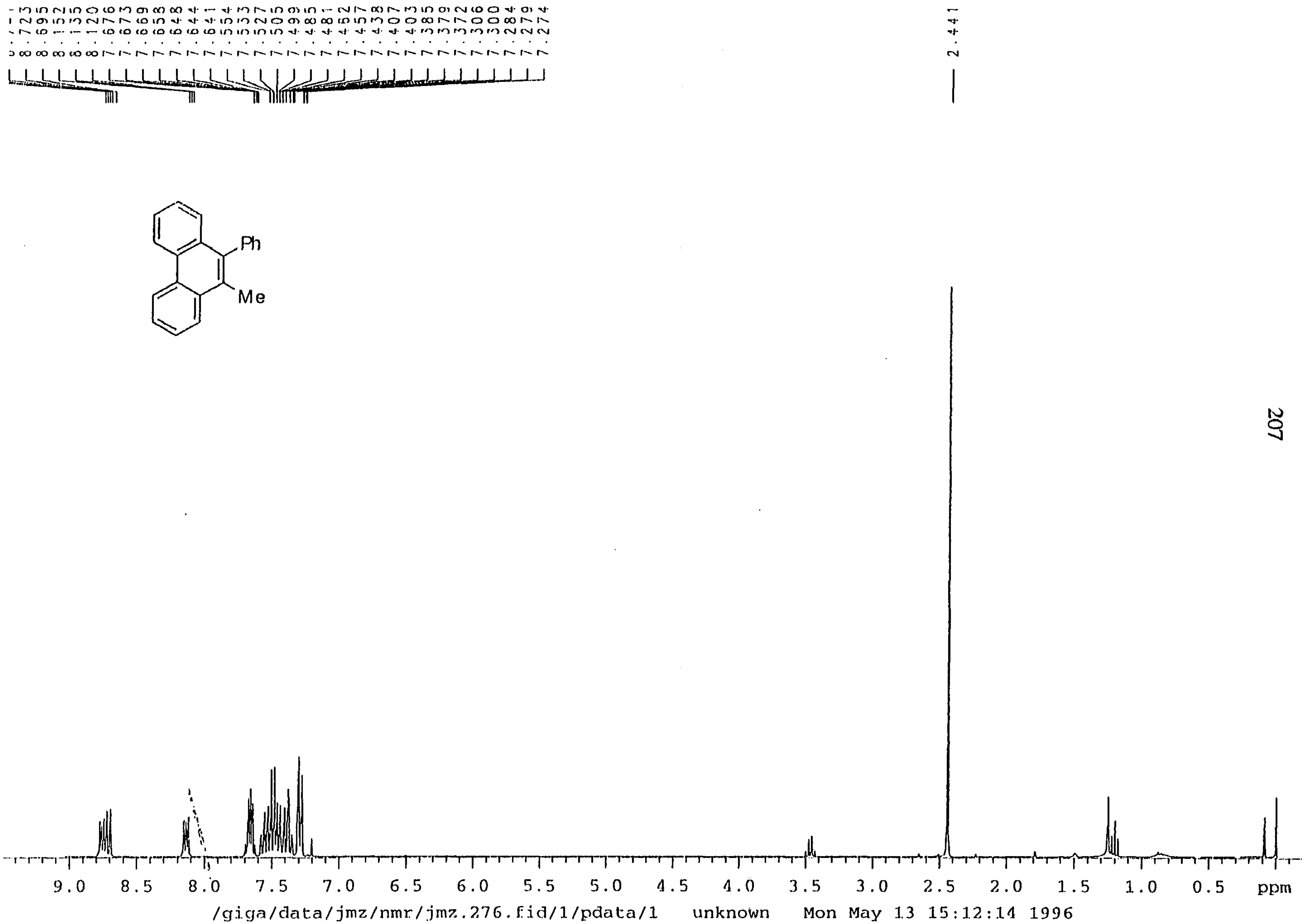
1) 8.571 PPM
2) 8.547 PPM
3) 8.333 PPM
4) 8.307 PPM
5) 8.301 PPM
6) 8.062 PPM
7) 8.054 PPM
8) 8.036 PPM
9) 8.030 PPM
10) 7.577 PPM
11) 7.571 PPM
12) 7.558 PPM
13) 7.546 PPM
14) 7.540 PPM
15) 7.476 PPM
16) 7.472 PPM
17) 7.450 PPM
18) 7.430 PPM
19) 7.425 PPM
20) 7.206 PPM
21) 2.781 PPM
22) 1.705 PPM
23) 0.000 PPM
t-Bu
Me
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM

Table 2, 2



t-Bu
Me
1) 142.421 PPM
2) 134.009 PPM
3) 132.523 PPM
4) 130.937 PPM
5) 130.161 PPM
6) 129.255 PPM
7) 126.891 PPM
8) 126.599 PPM
9) 125.557 PPM
10) 124.364 PPM
11) 124.069 PPM
12) 123.849 PPM
13) 123.193 PPM
14) 122.333 PPM
15) 77.481 PPM
16) 77.060 PPM
17) 76.639 PPM
18) 38.457 PPM
19) 33.646 PPM
20) 21.284 PPM
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

3


8.741
8.723
8.695
8.152
8.135
8.120
7.676
7.673
7.669
7.658
7.648
7.644
7.641
7.554
7.553
7.537
7.527
7.505
7.499
7.485
7.481
7.462
7.457
7.438
7.407
7.403
7.385
7.379
7.372
7.306
7.300
7.284
7.279
7.274
2.441
Ph
Me
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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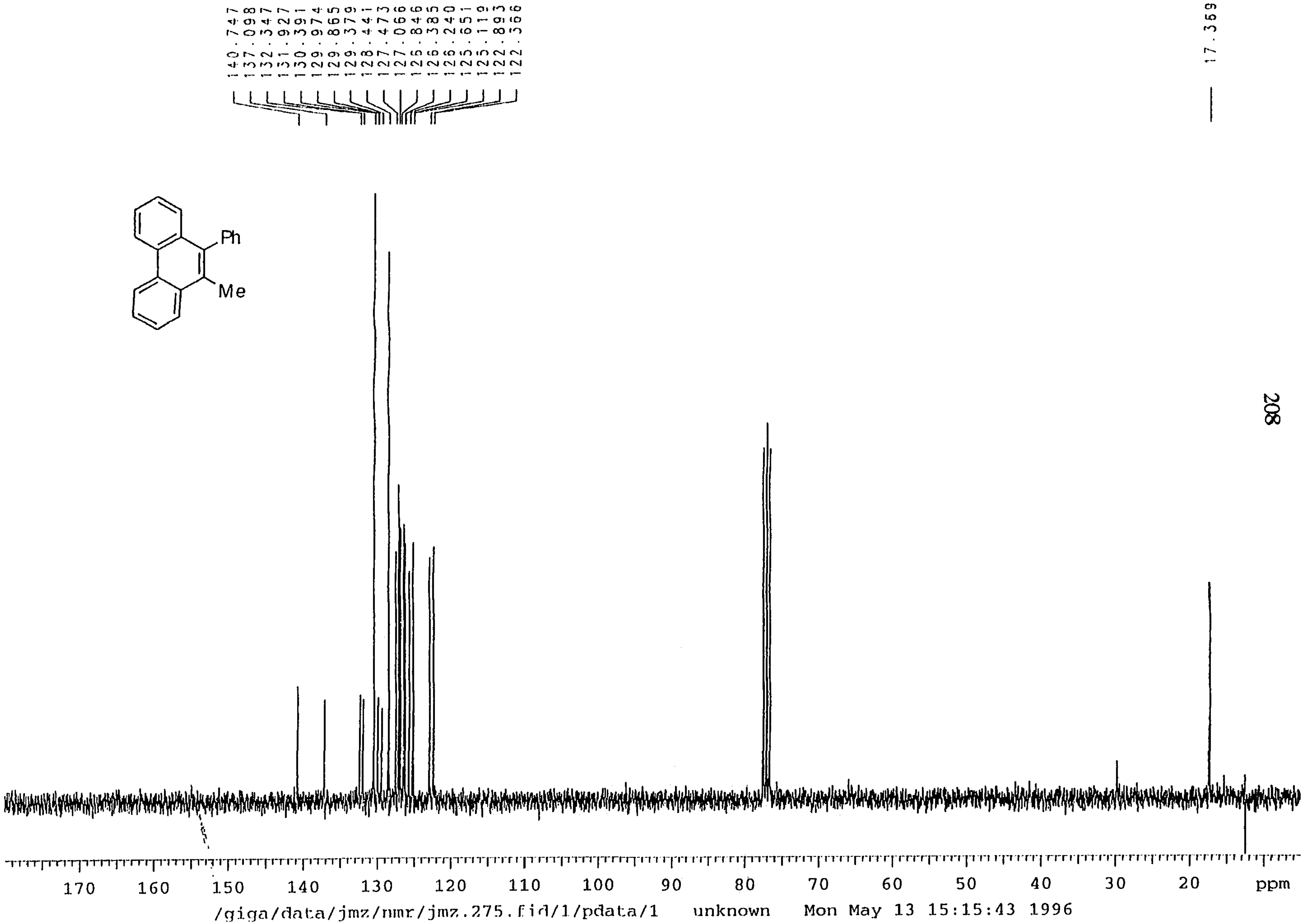
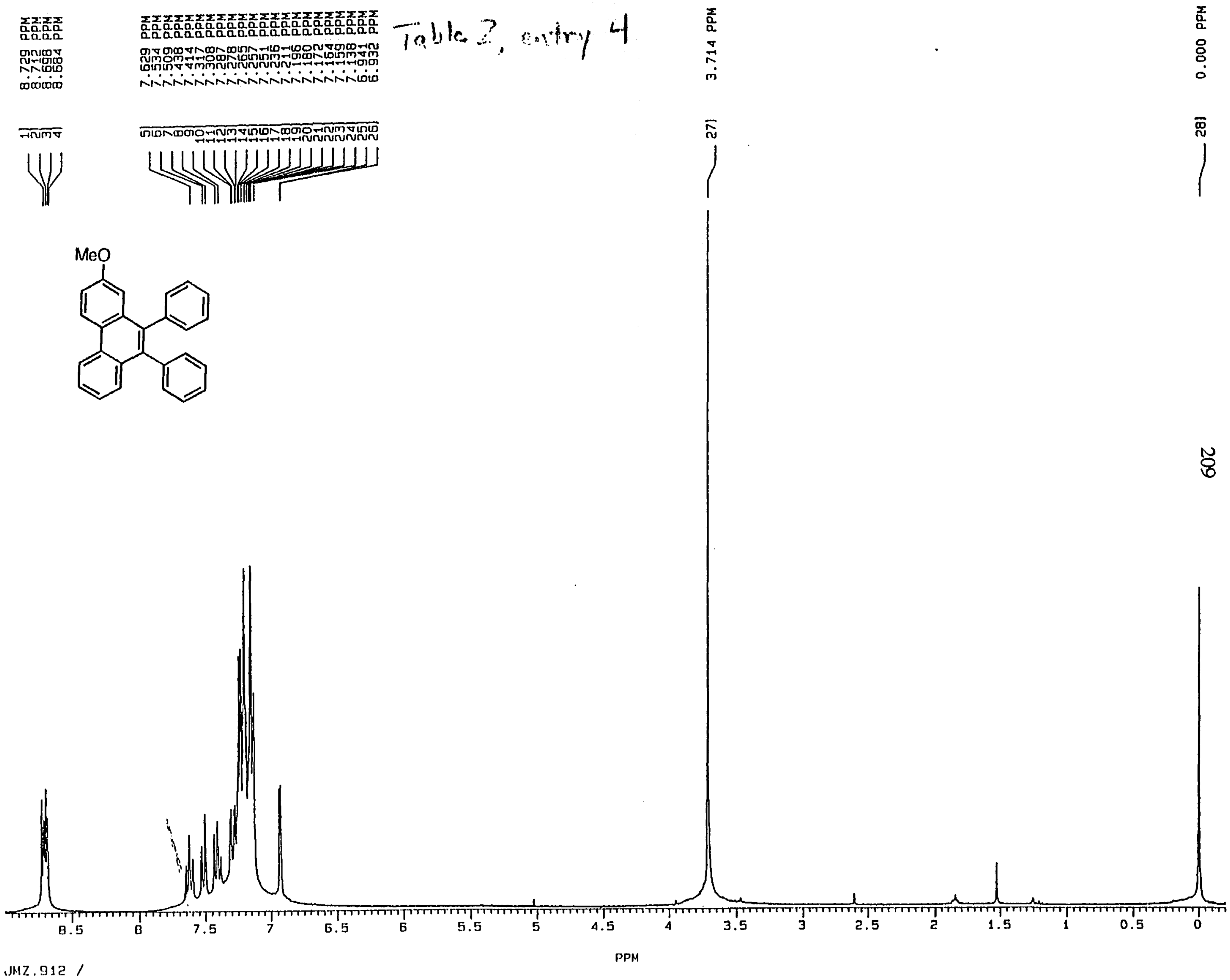

140.747
137.098
132.347
131.927
130.391
129.974
129.865
129.379
128.441
127.473
127.066
126.846
126.385
126.240
125.651
125.119
122.893
122.366
17.369
Ph
Me
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
/giga/data/jmz/nmr/jmz.275.fid/1/pdata/1 unknown Mon May 13 15:15:43 1996

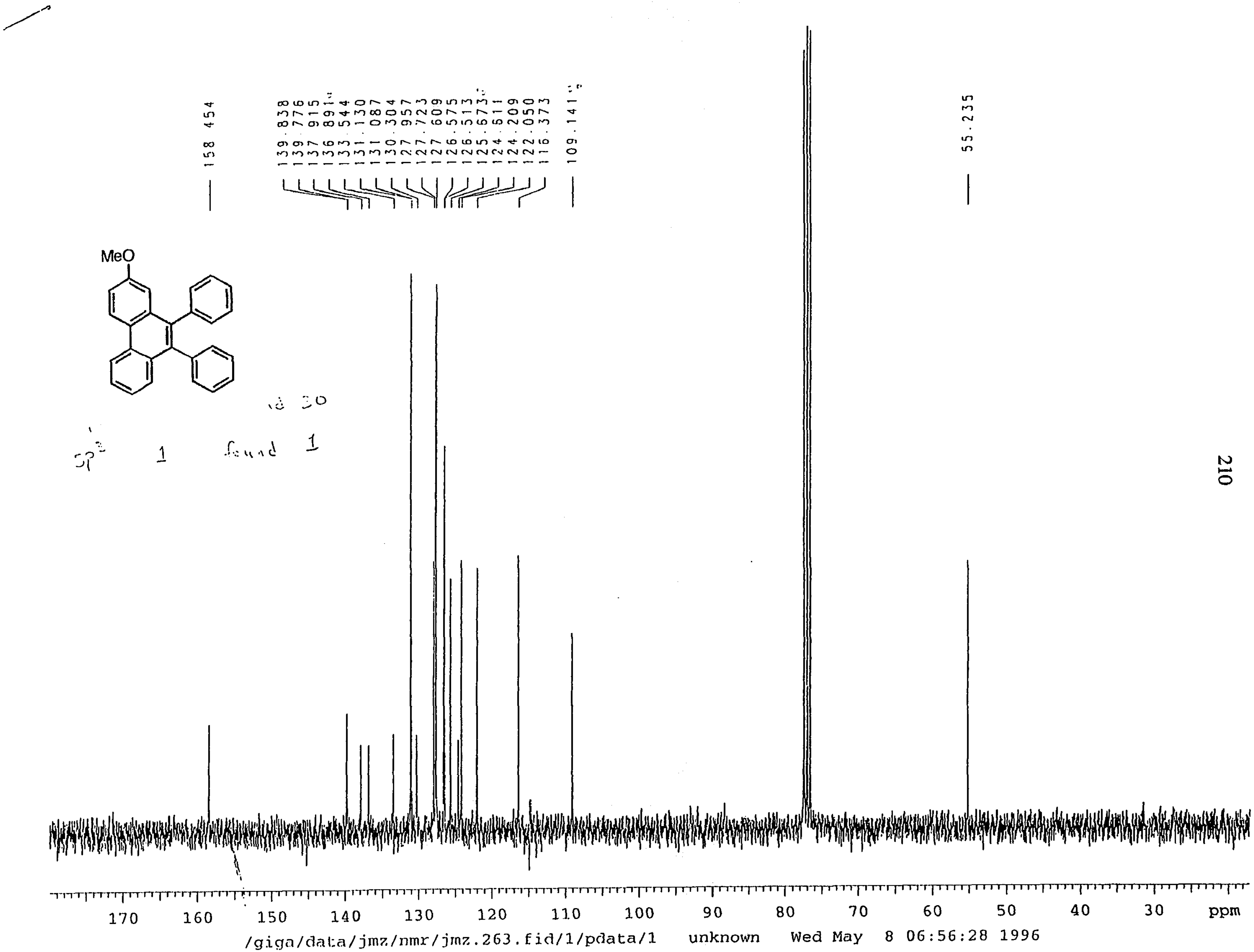
VI - 26

Also have elem. anal.

Table 2, entry 4



JMZ.912 /


MeO
158 454
139.838
139.776
137 915
136 891
133.544
131.130
131 087
130.304
127 957
127.723
127 609
126.575
126.513
125.673
124.611
124.209
122.050
116.373
109.141
55.235
sp3 1 found 1
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 ppm
/giga/data/jmz/nmr/jmz.263.fid/1/pdata/1 unknown Wed May 8 06:56:28 1996

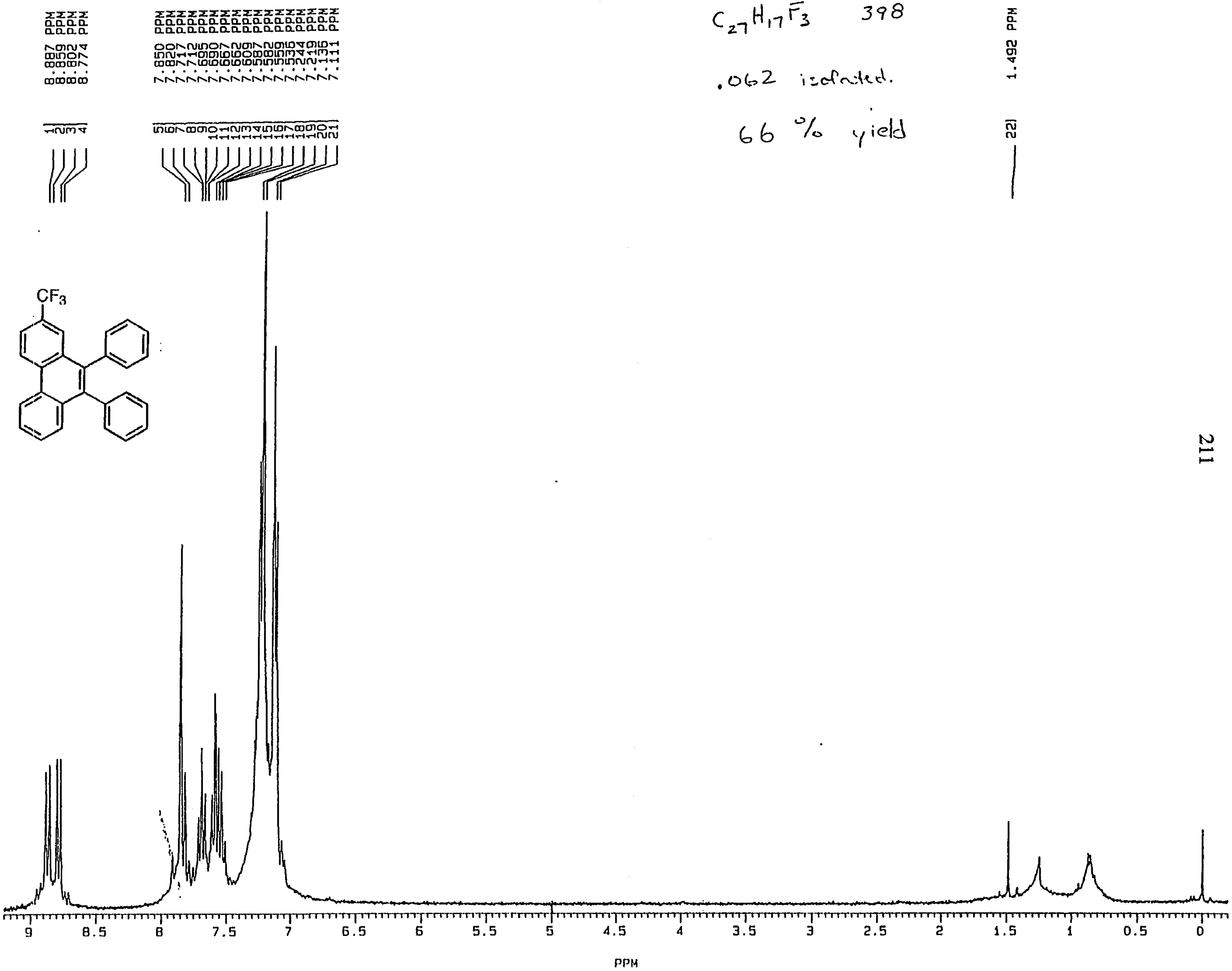
VI-41

Table 2, 5

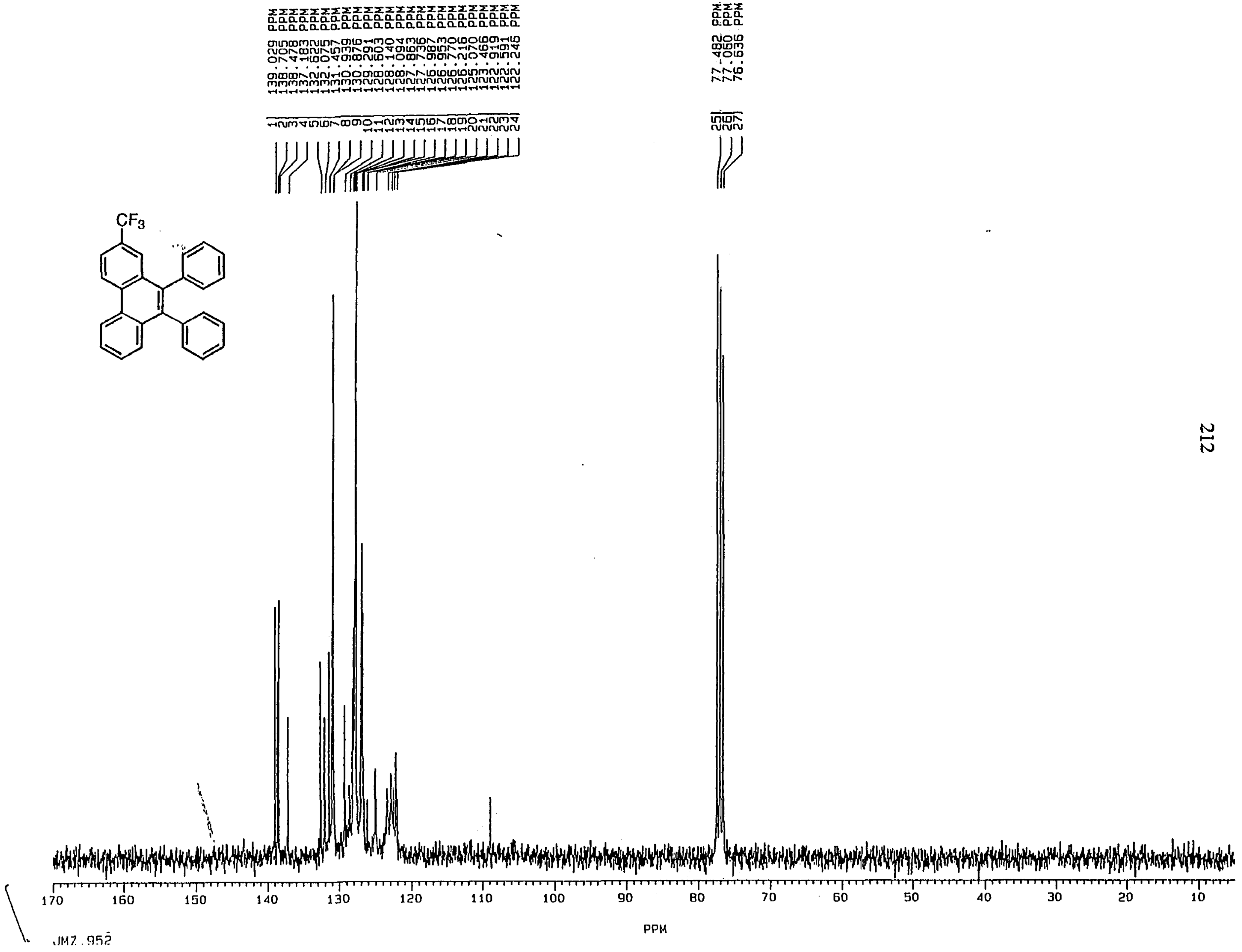
$C_{27}H_{17}F_3$ 398

.062 isolated.

66 % yield

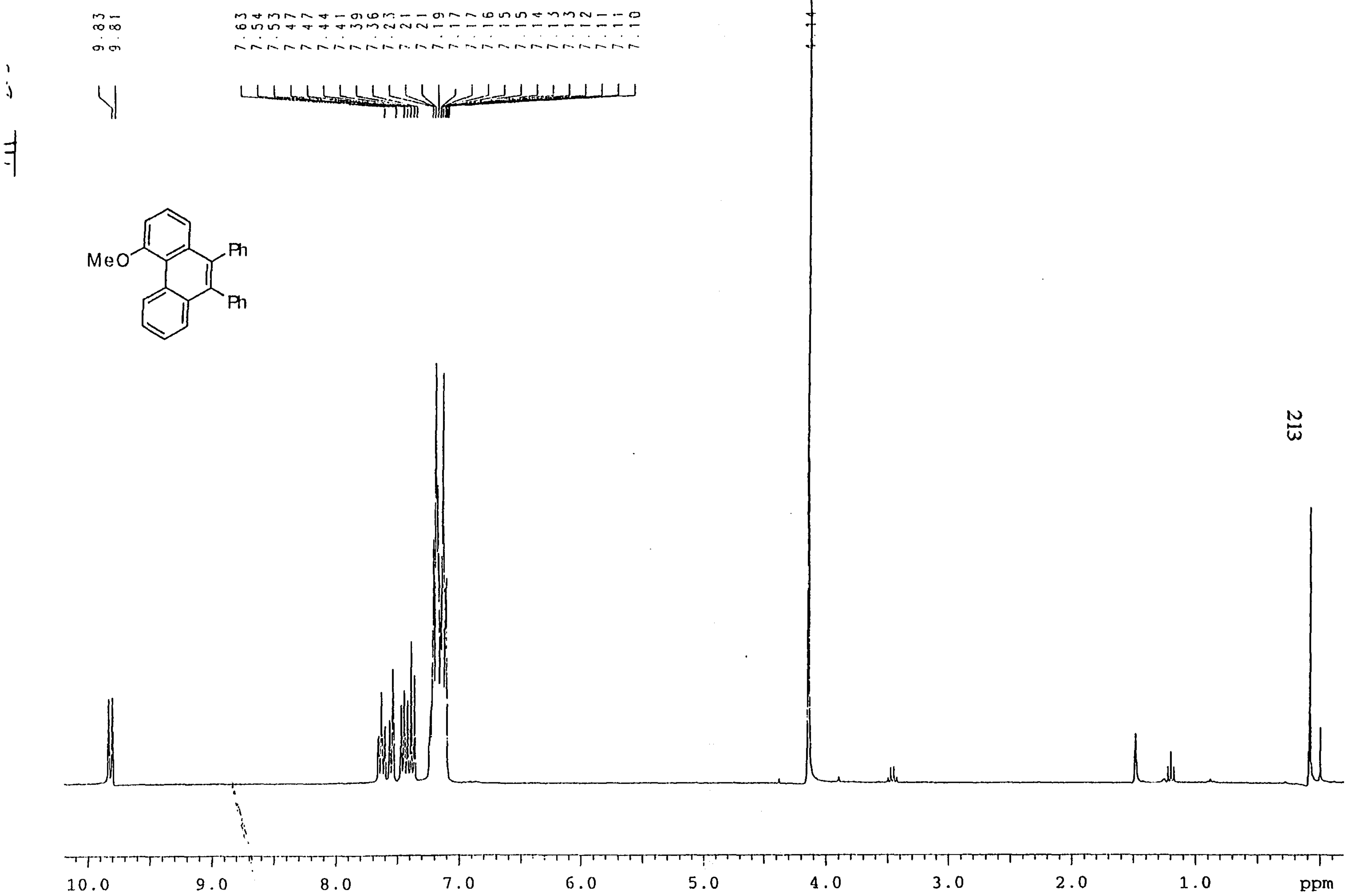


2, 3



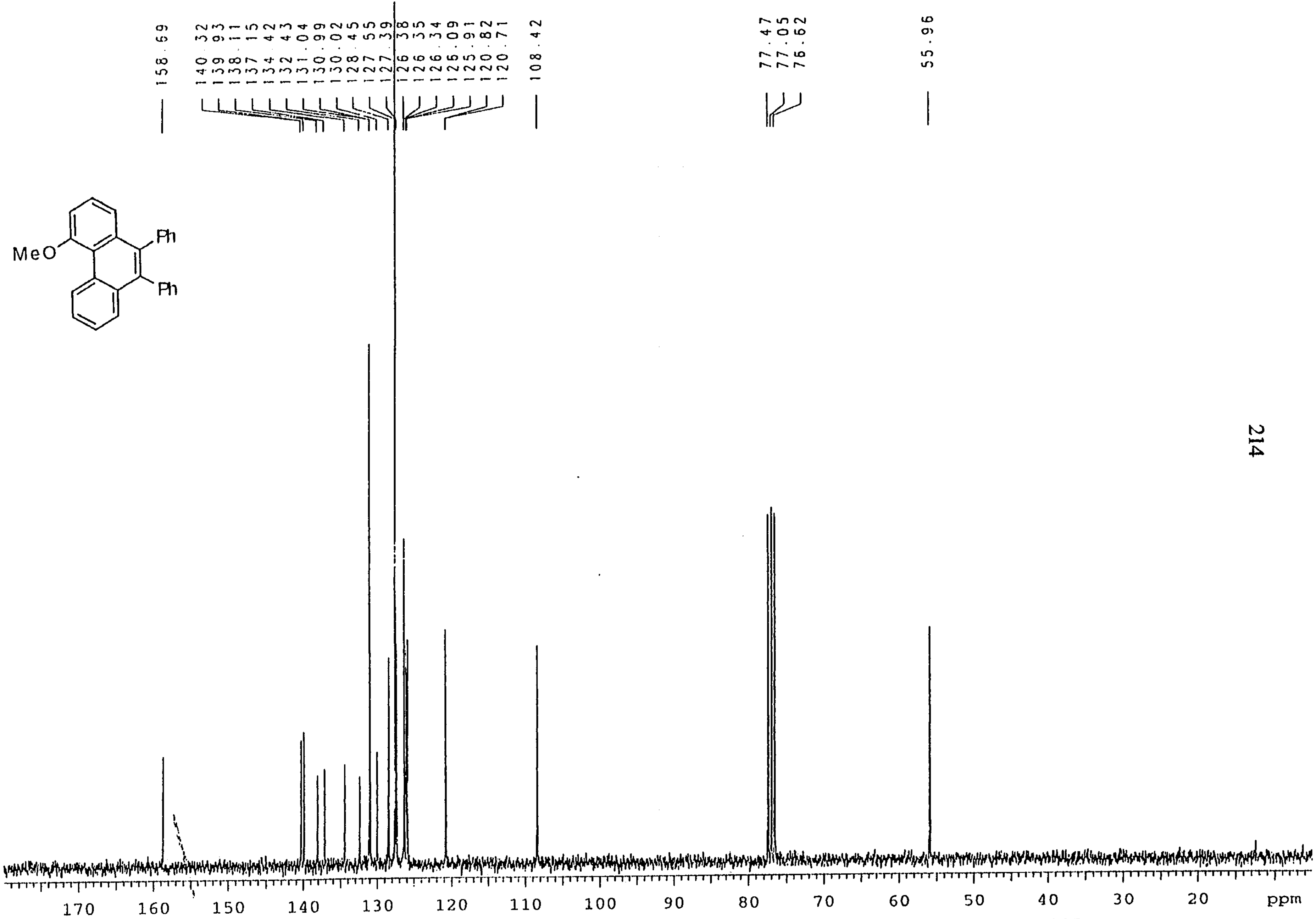
CF3
1) 139.029 PPM
2) 138.705 PPM
3) 138.478 PPM
4) 137.183 PPM
5) 132.622 PPM
6) 132.075 PPM
7) 131.457 PPM
8) 130.939 PPM
9) 130.876 PPM
10) 129.291 PPM
11) 128.603 PPM
12) 128.140 PPM
13) 128.094 PPM
14) 127.863 PPM
15) 127.736 PPM
16) 126.987 PPM
17) 126.953 PPM
18) 126.770 PPM
19) 126.216 PPM
20) 125.070 PPM
21) 123.466 PPM
22) 122.919 PPM
23) 122.591 PPM
24) 122.246 PPM
25) 77.482 PPM
26) 77.060 PPM
27) 76.636 PPM
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
JM7.952

Table 2, entry 6



/giga/data/jmz/nmr/jmz.030.fid/1/pdata/1 unknown Wed Jul 19 19:20:20 1995

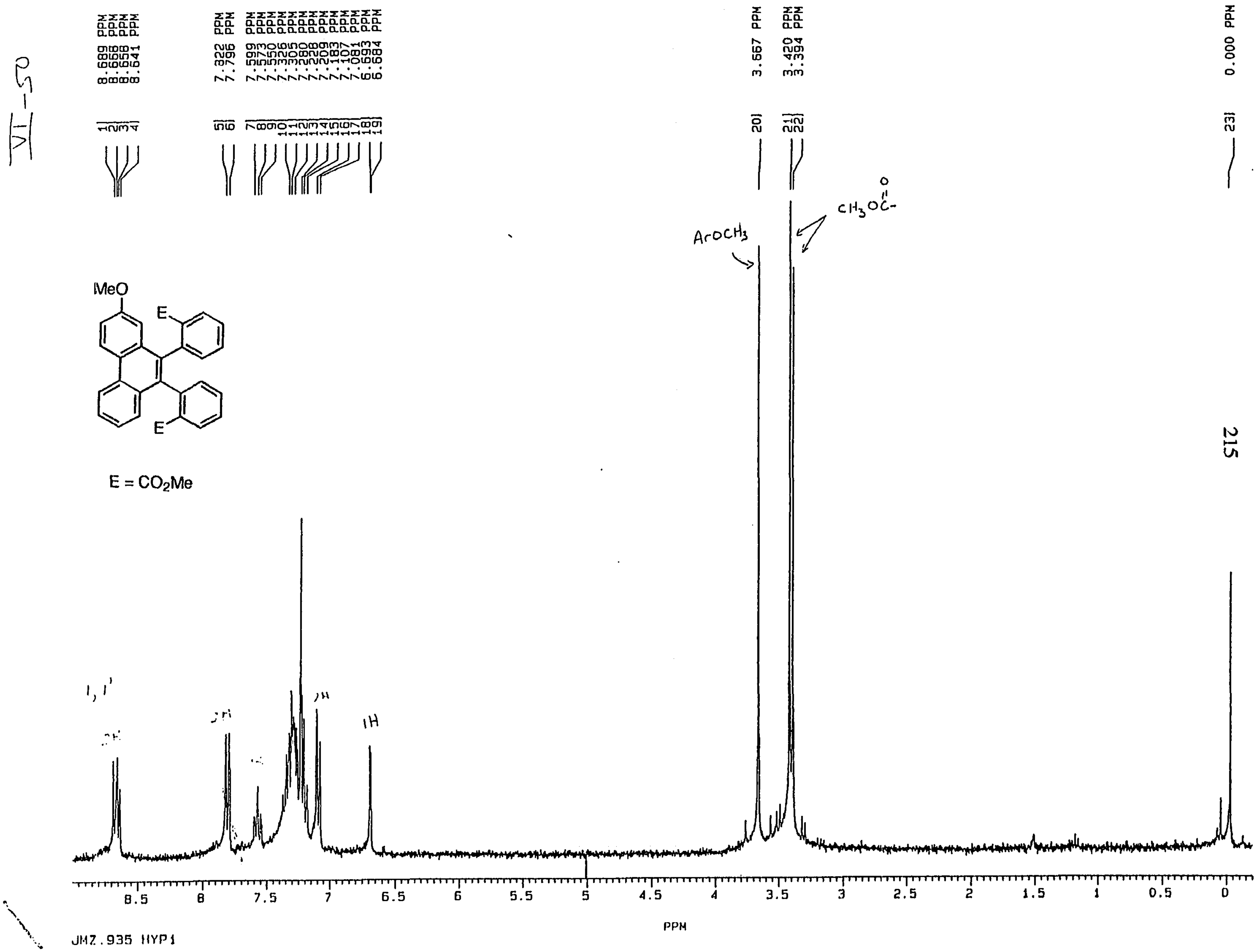
2,6



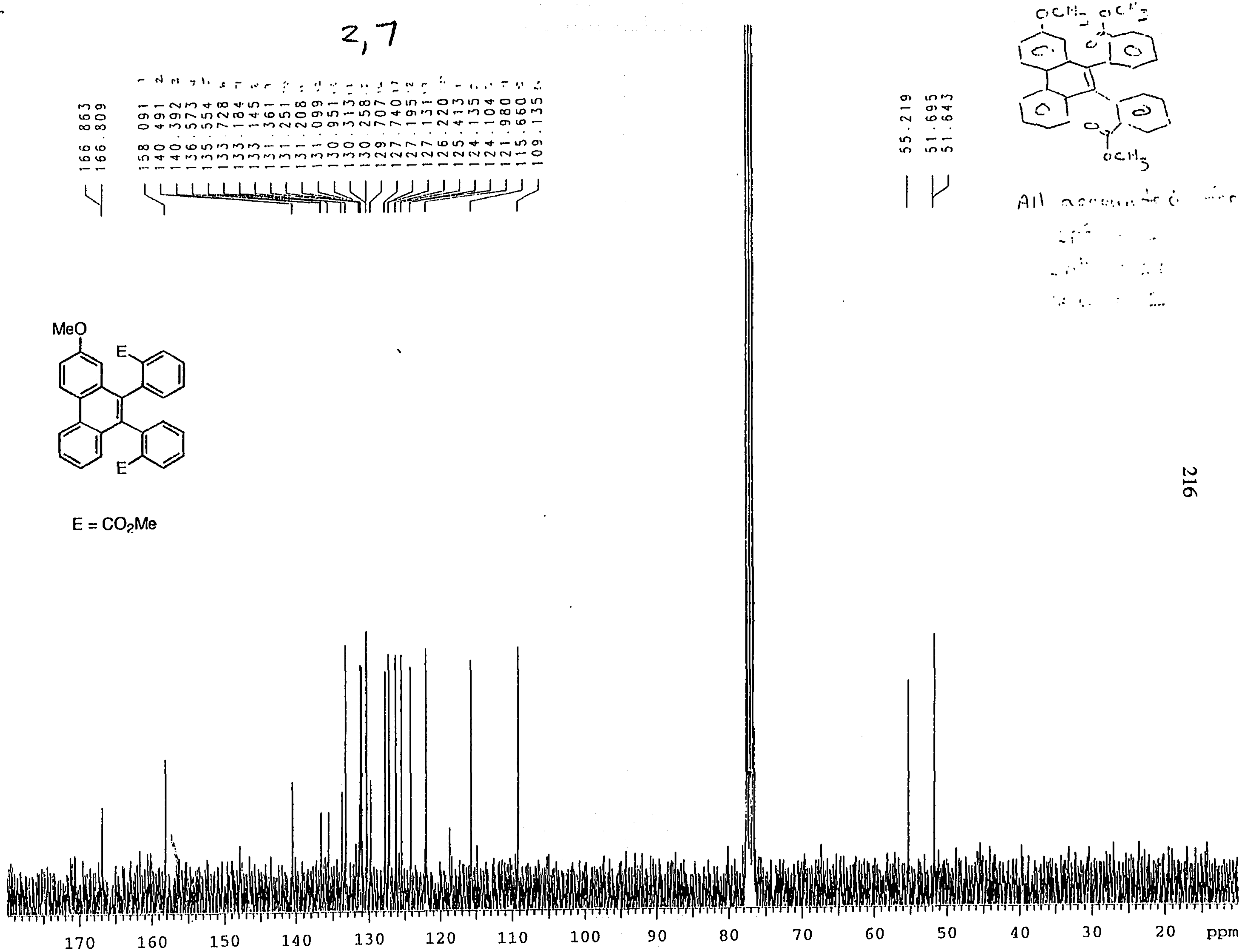
/giga/data/jmz/nmr/jmz.031.fid/1/pdata/1 unknown Wed Jul 19 19:34:42 1995

VI-50

15 H (Aromatic) [illegible]



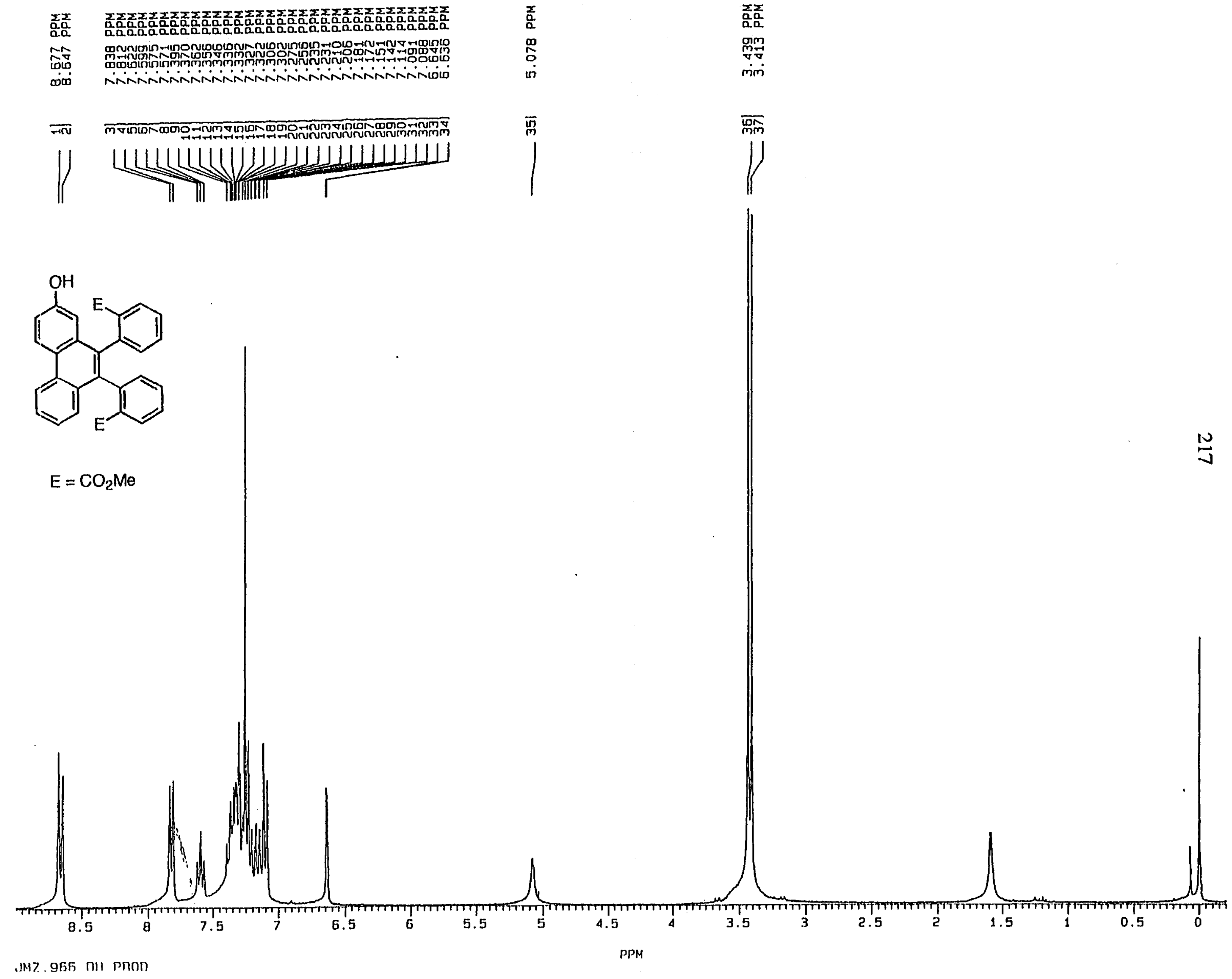
2,7



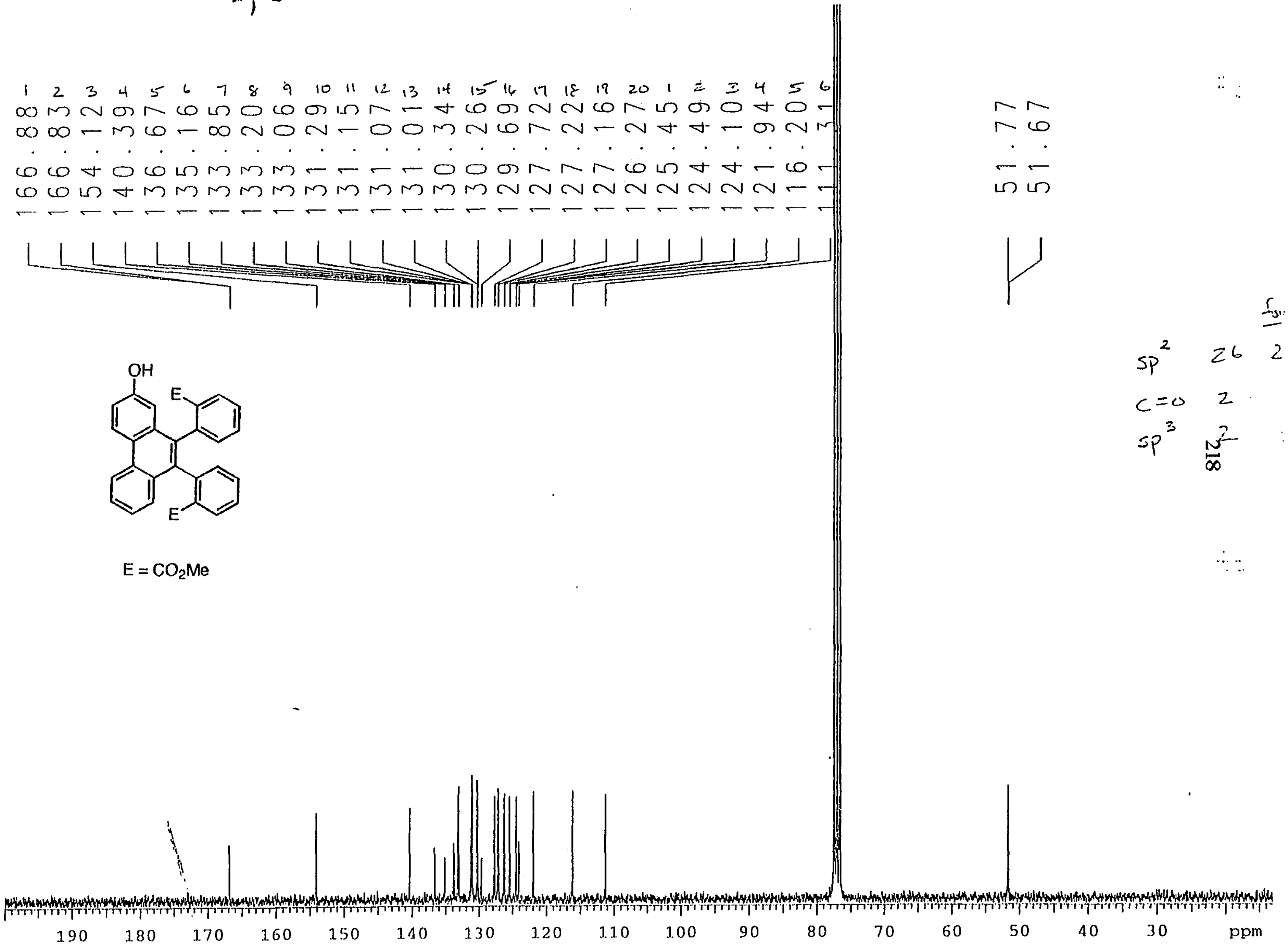
All [illegible]

/giga/data/jmz/nmr/jmz.078.fid/1/pdata/1 unknown Sun Sep 17 13:20:54 1995

Table 4, entry 8



2, 8



file:/gigb/data/jmz/nmr/jmz.138.fid/1/pdata/1/plotfile user:unknown date:Wed Dec 27 09:47:30 1995

sp^2 26 2

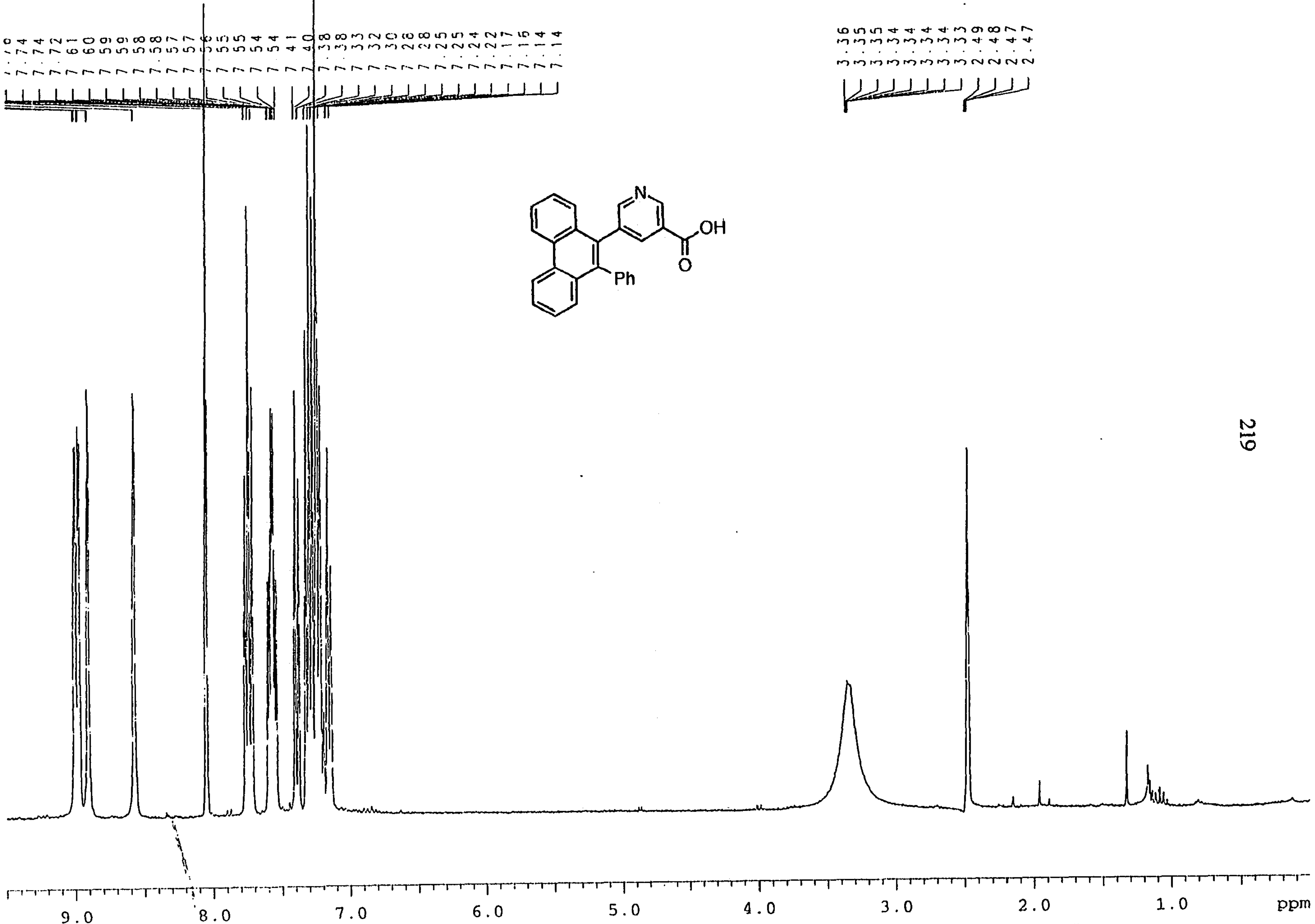
C=O 2

sp^3 2

218

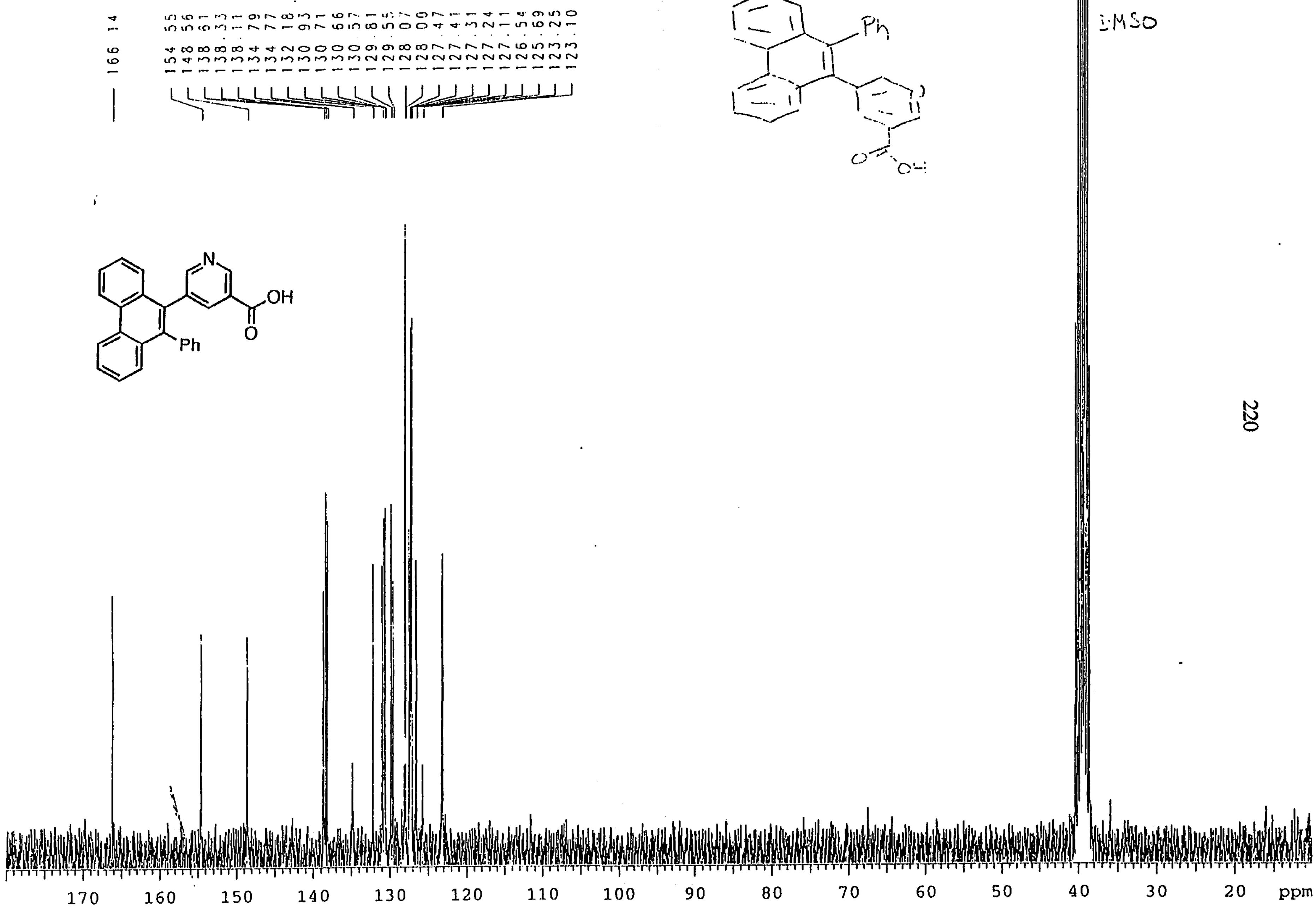
Table 4, entry 9

VIII-23



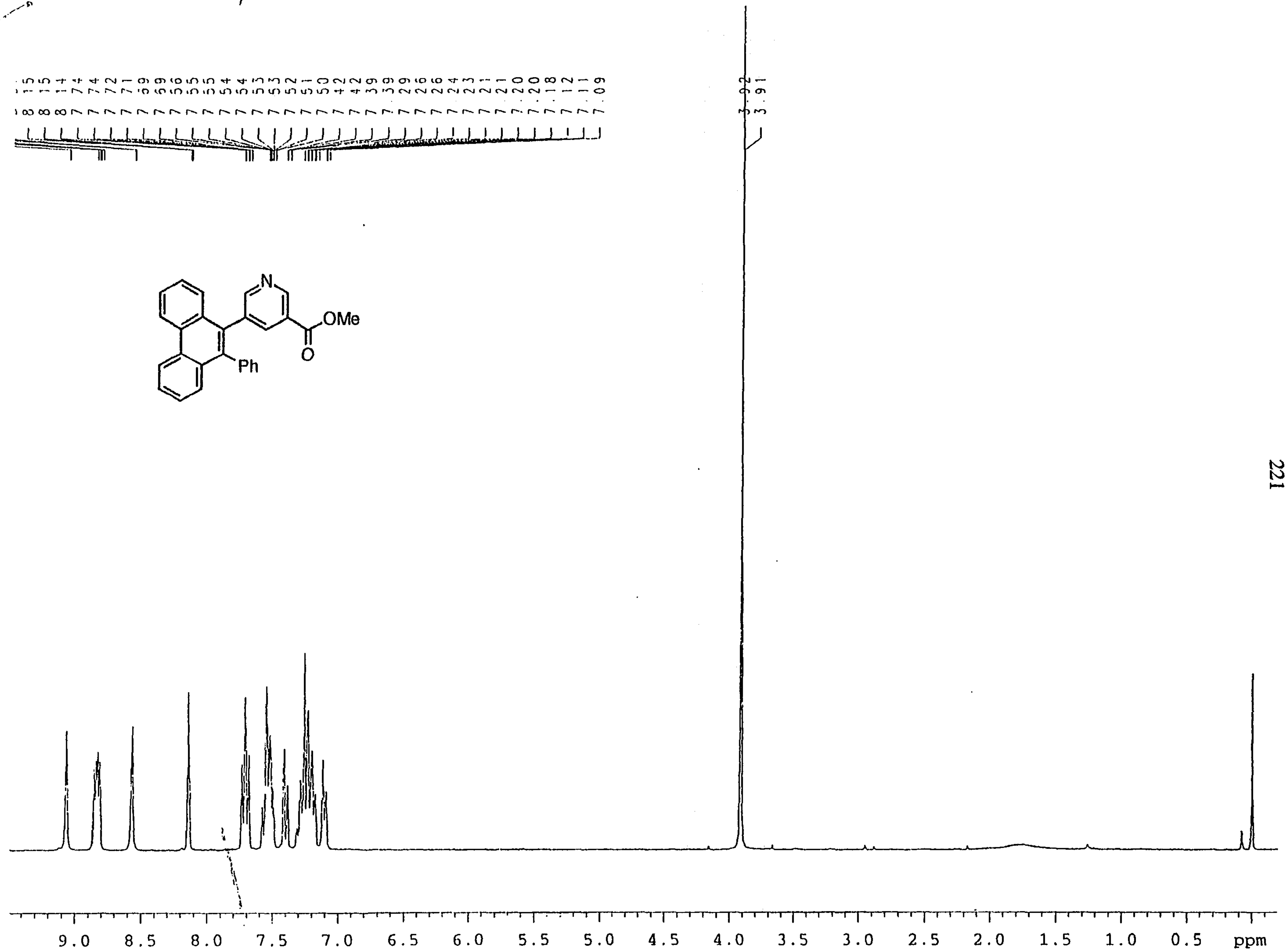
/giga/data/jmz/nmr/jmz.035.fid/1/pdata/1 unknown Fri Jul 21 10:58:33 1995

2,9



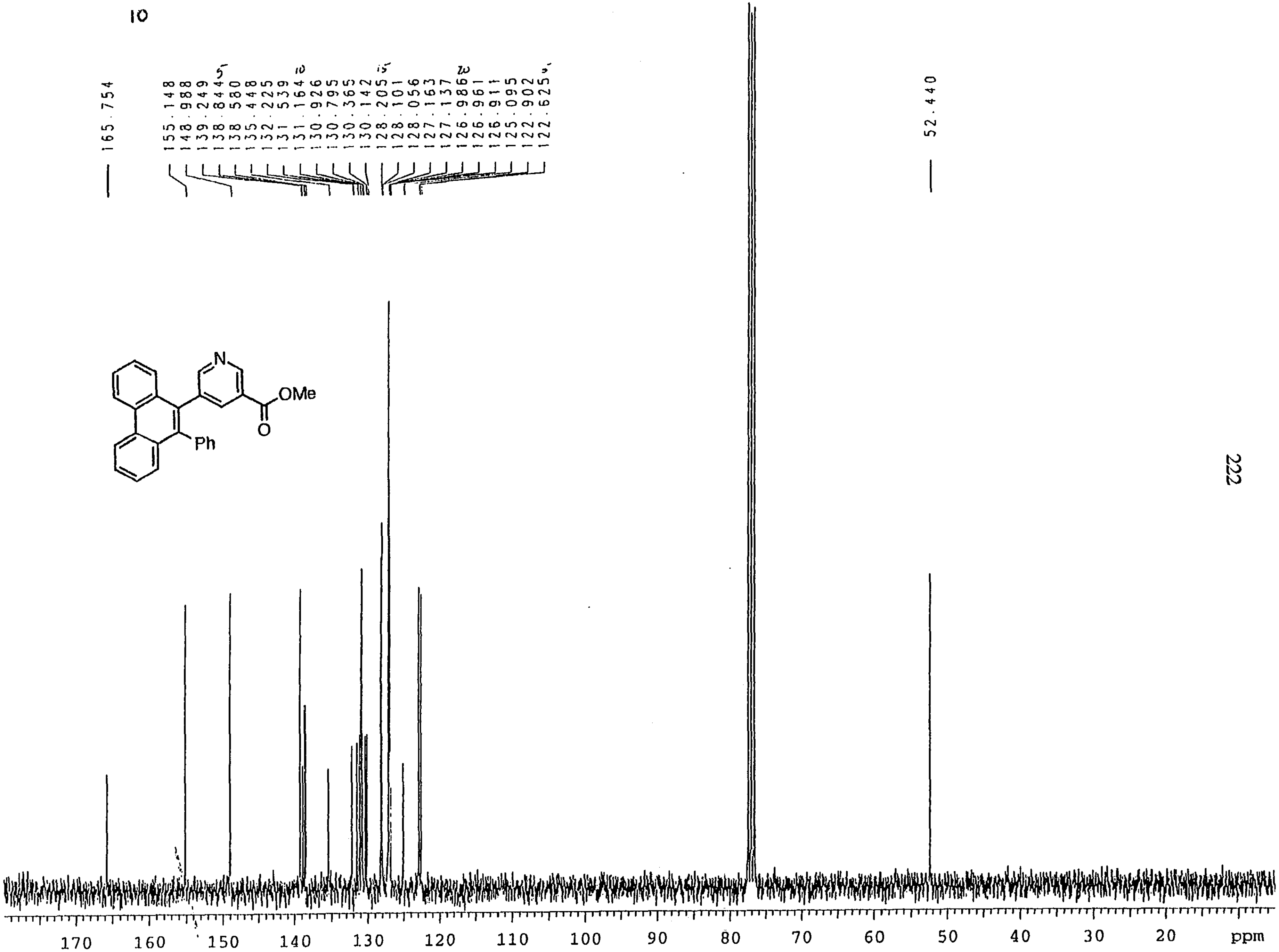
/giga/data/jmz/nmr/jmz.044.fid/1/pdata/1 unknown Tue Jul 25 19:31:57 1995

Table 2, entry 10

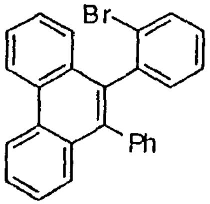


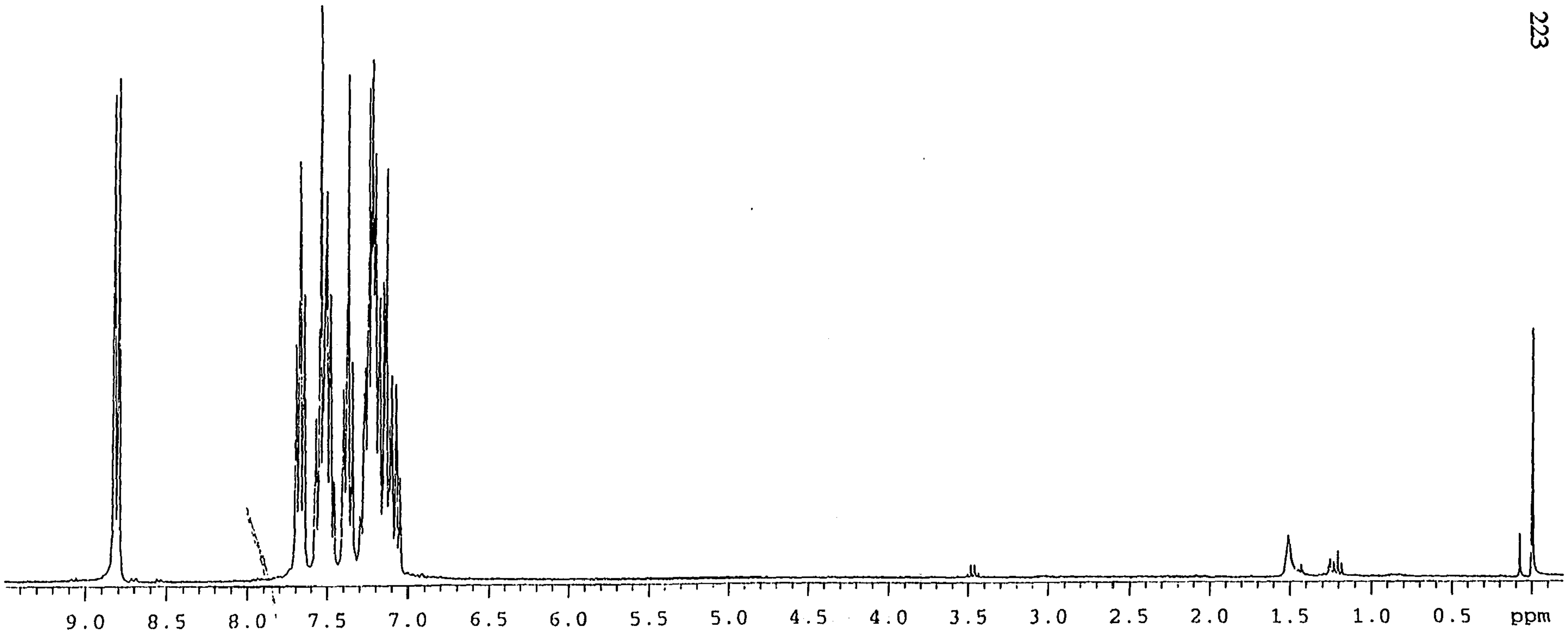
/giga/data/jmz/nmr/jmz.041.fid/1/pdata/1 unknown Mon Jul 24 12:47:37 1995

10


165.754
155.148
148.988
139.249
138.844
138.580
135.448
132.225
131.539
131.164
130.926
130.795
130.365
130.142
128.205
128.101
128.056
127.163
127.137
126.986
126.961
126.911
125.095
122.902
122.625
52.440
5
10
15
20
25
N
OMe
O
Ph
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm
/giga/data/jmz/nmr/jmz.266.fid/1/pdata/1 unknown Wed May 8 10:59:54 1996

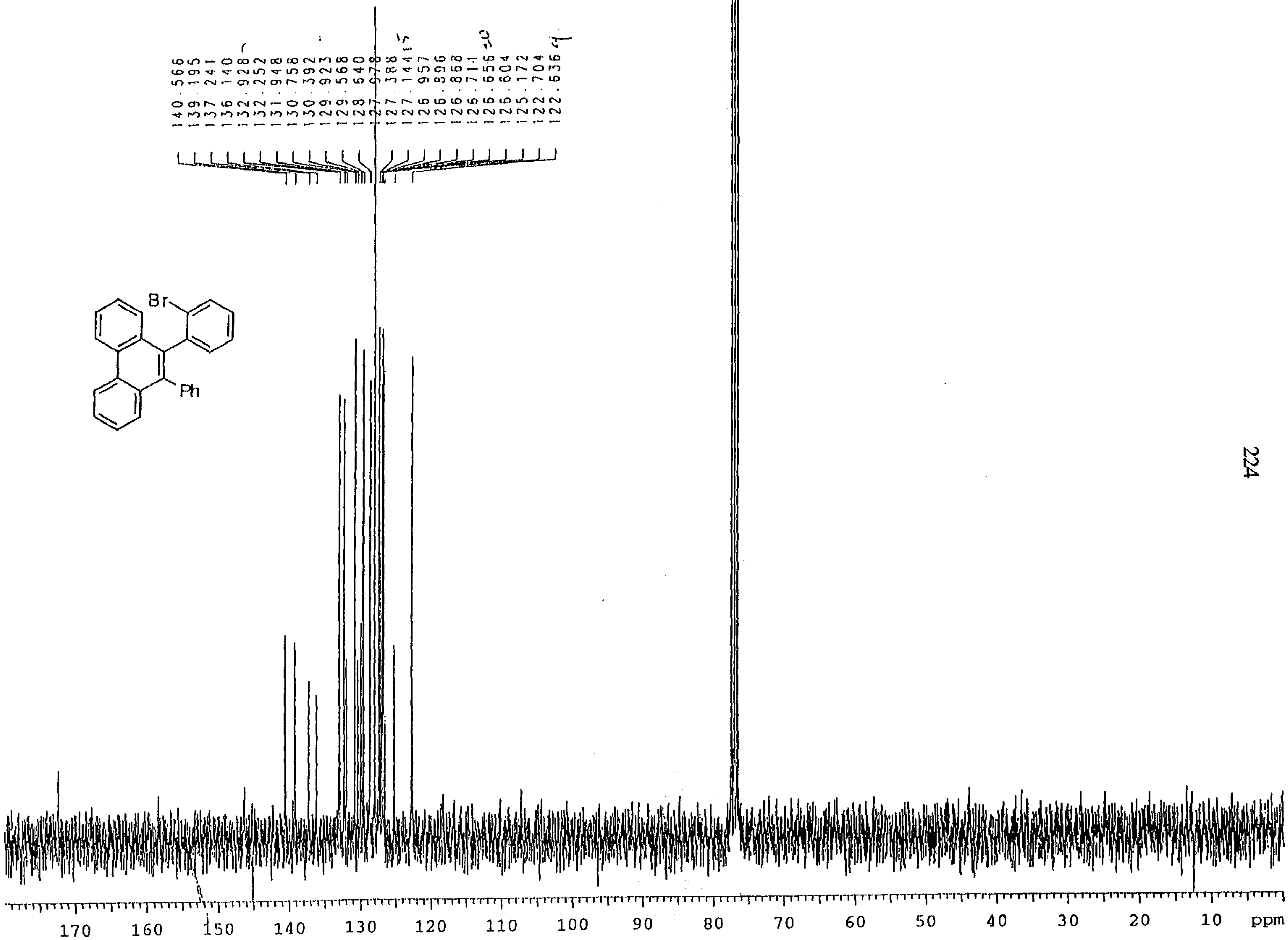
11





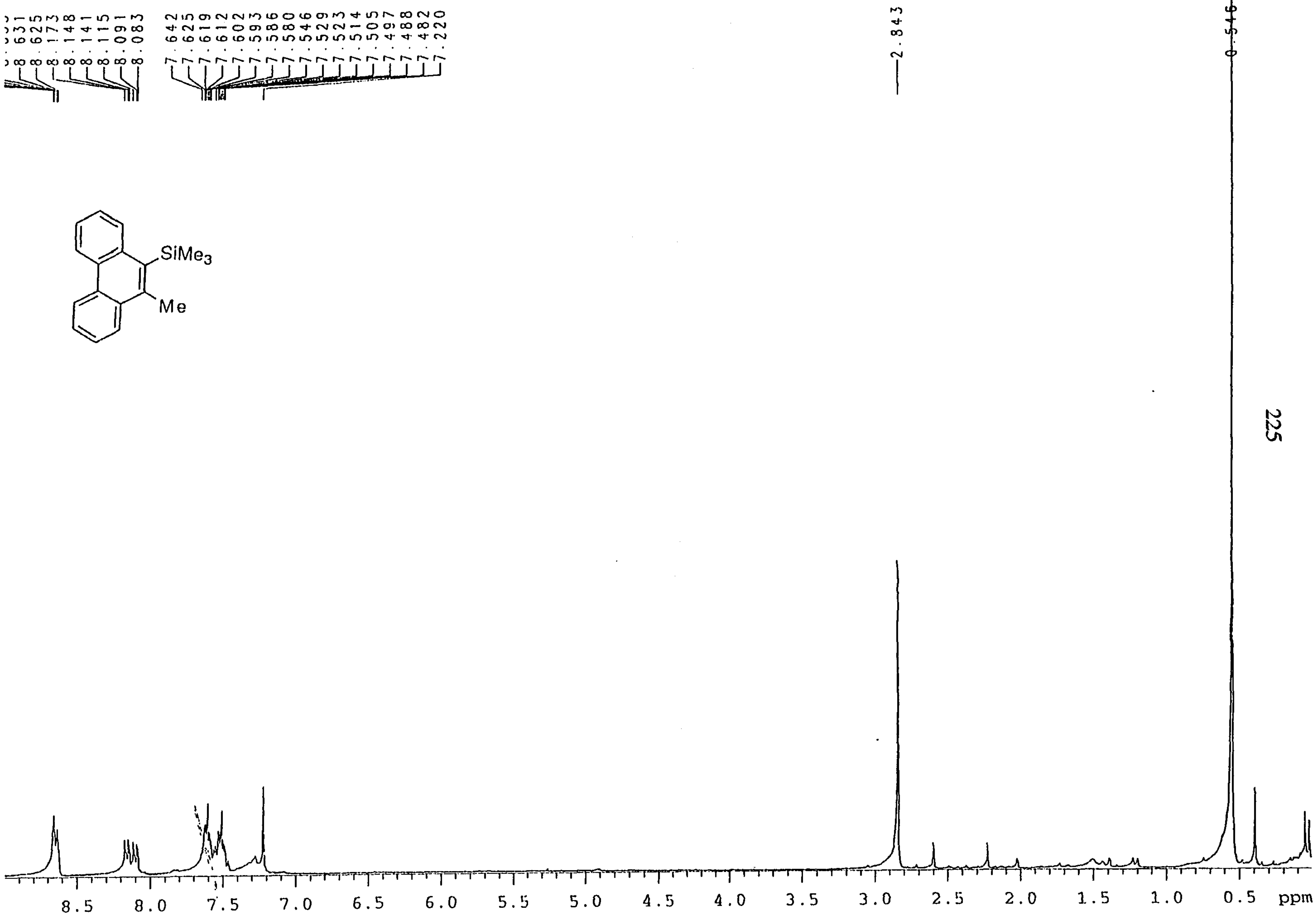
/giga/data/jmz/nmr/jmz.181.fid/1/pdata/1 unknown Thu Feb 8 09:18:03 1996

11



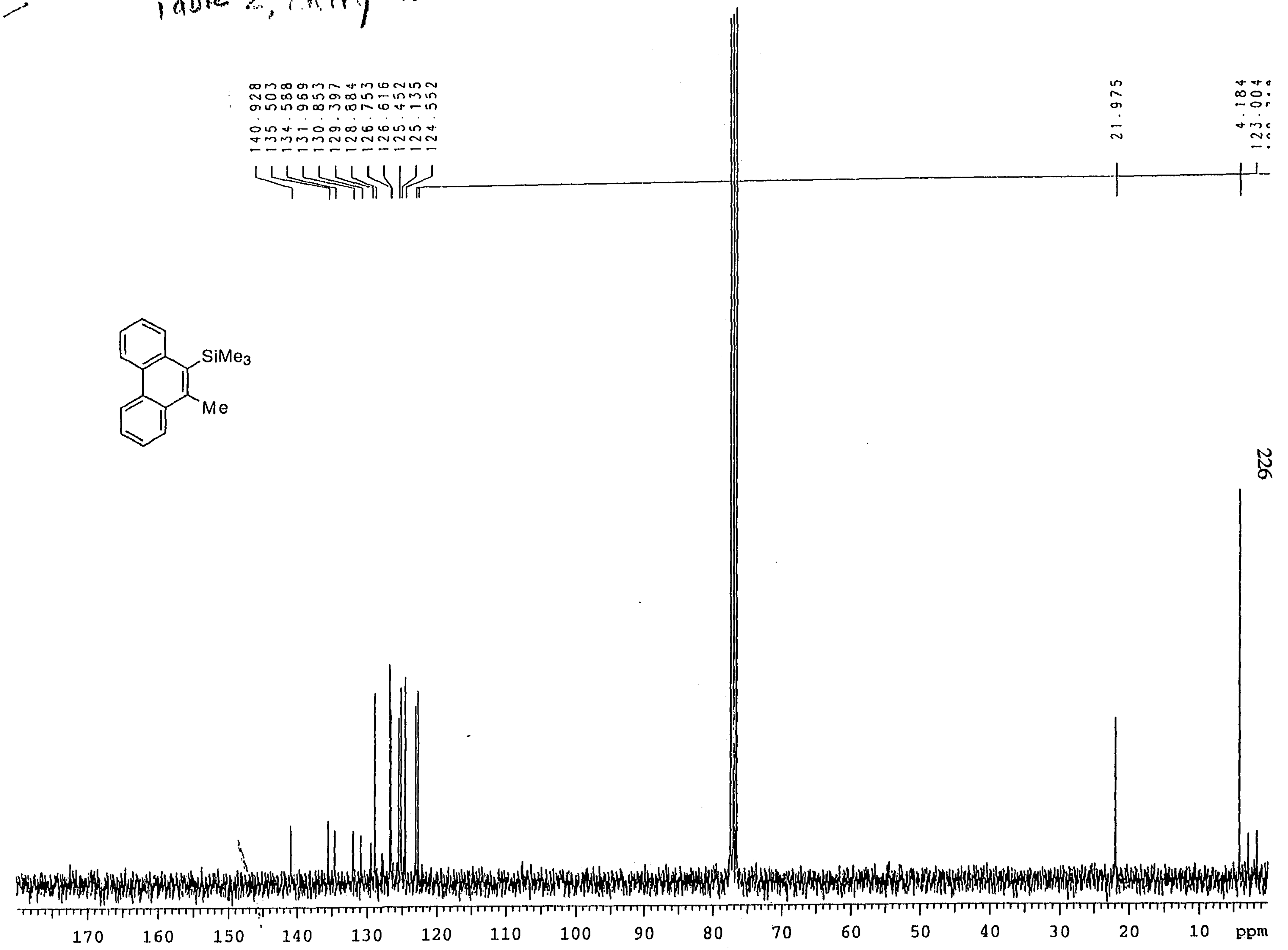
/giga/data/jmz/nmr/jmz.179.fid/1/pdata/1 unknown Wed Feb 7 14:45:30 1996

Table 2, entry 13



/giga/data/jmz/nmr/jmz.209.fid/1/pdata/1 unknown Tue Mar 12 13:58:56 1996

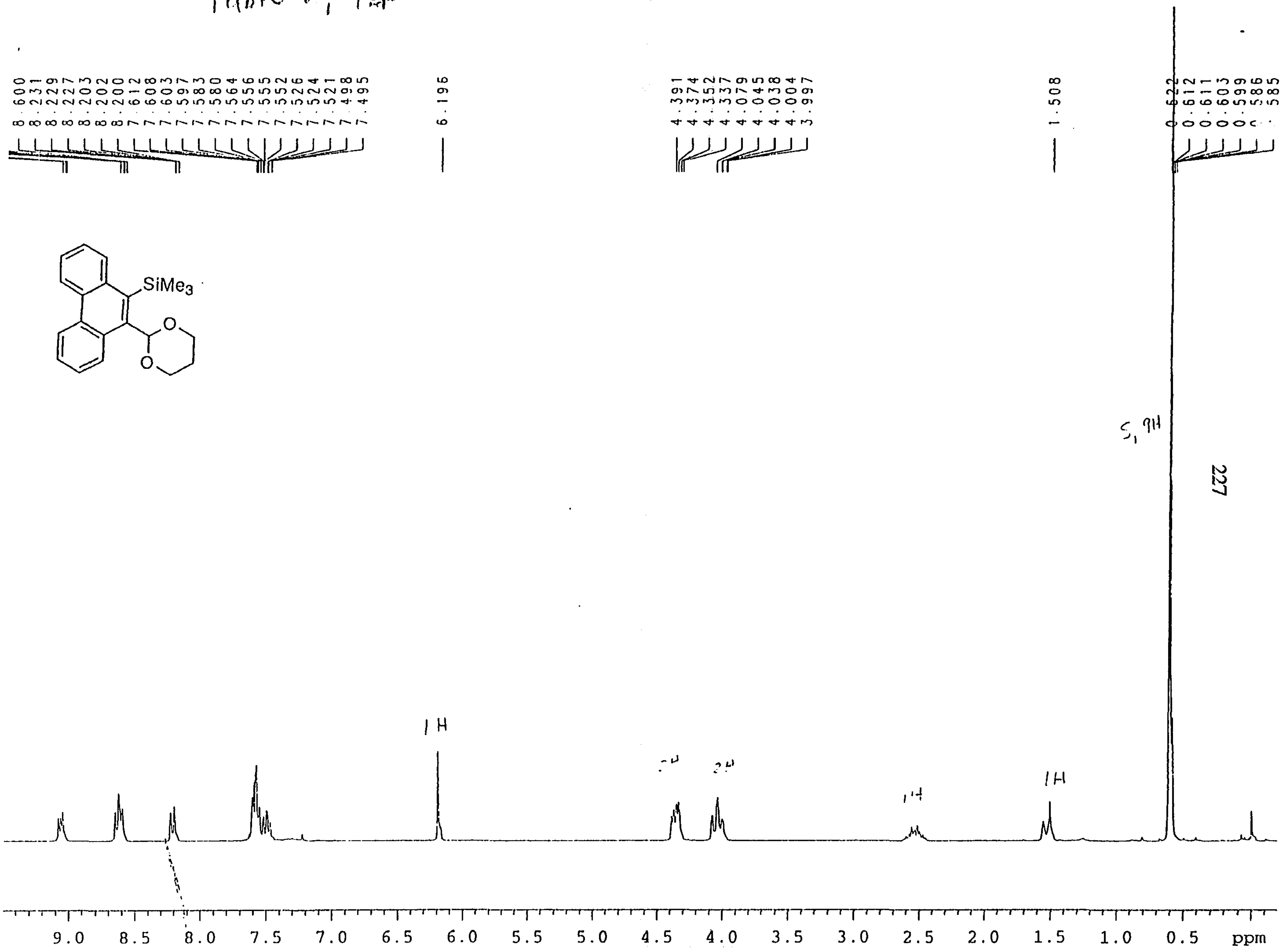
Table 2, entry 13



/giga/data/jmz/nmr/jmz.151.fid/1/pdata/1 unknown Mon Jan 15 10:17:31 1996

Table 2, 14

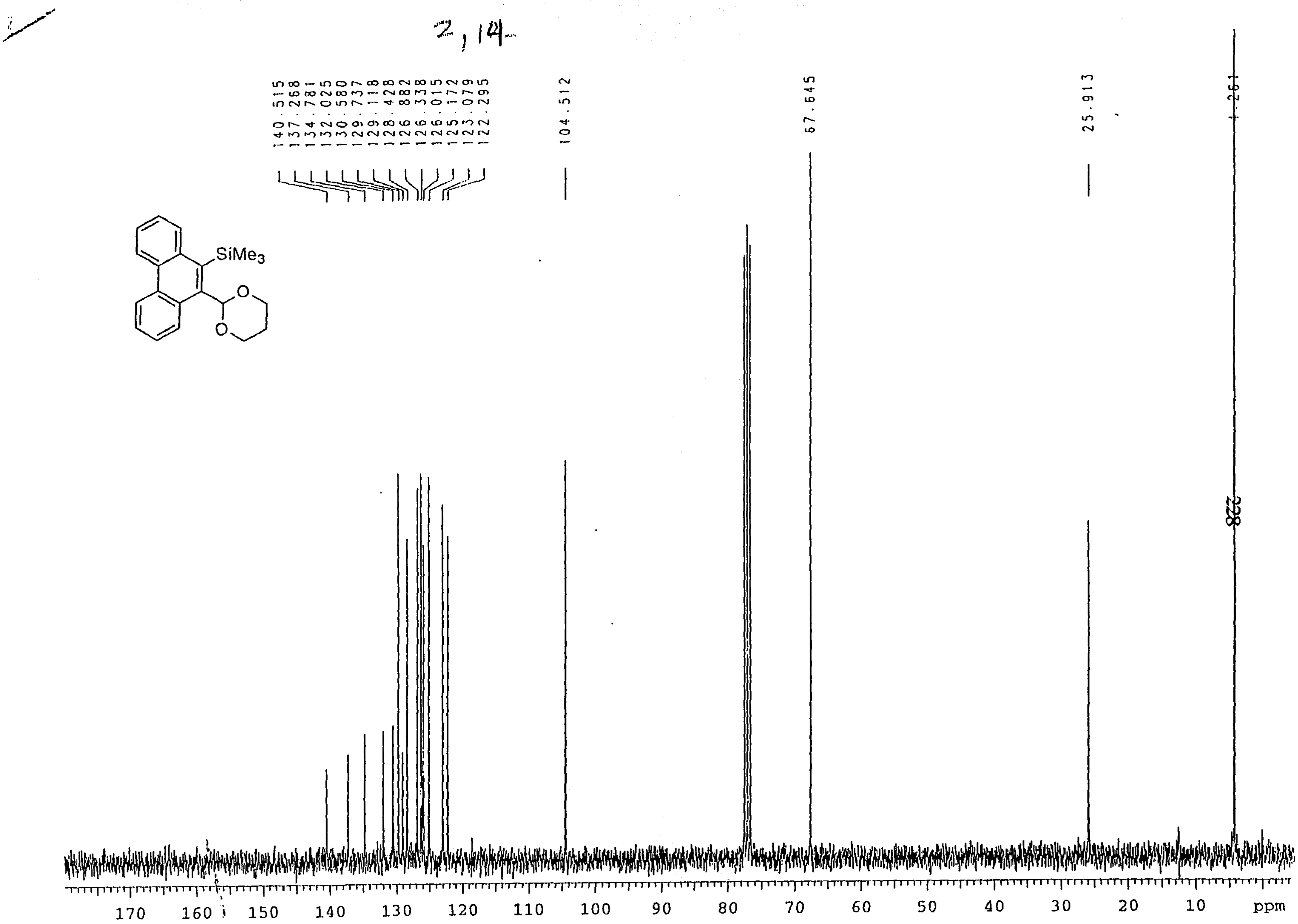
VII - 61
¹H + ¹³C



227

/giga/data/jmz/nmr/jmz.092.fid/1/pdata/1 unknown Fri Sep 29 14:57:24 1995

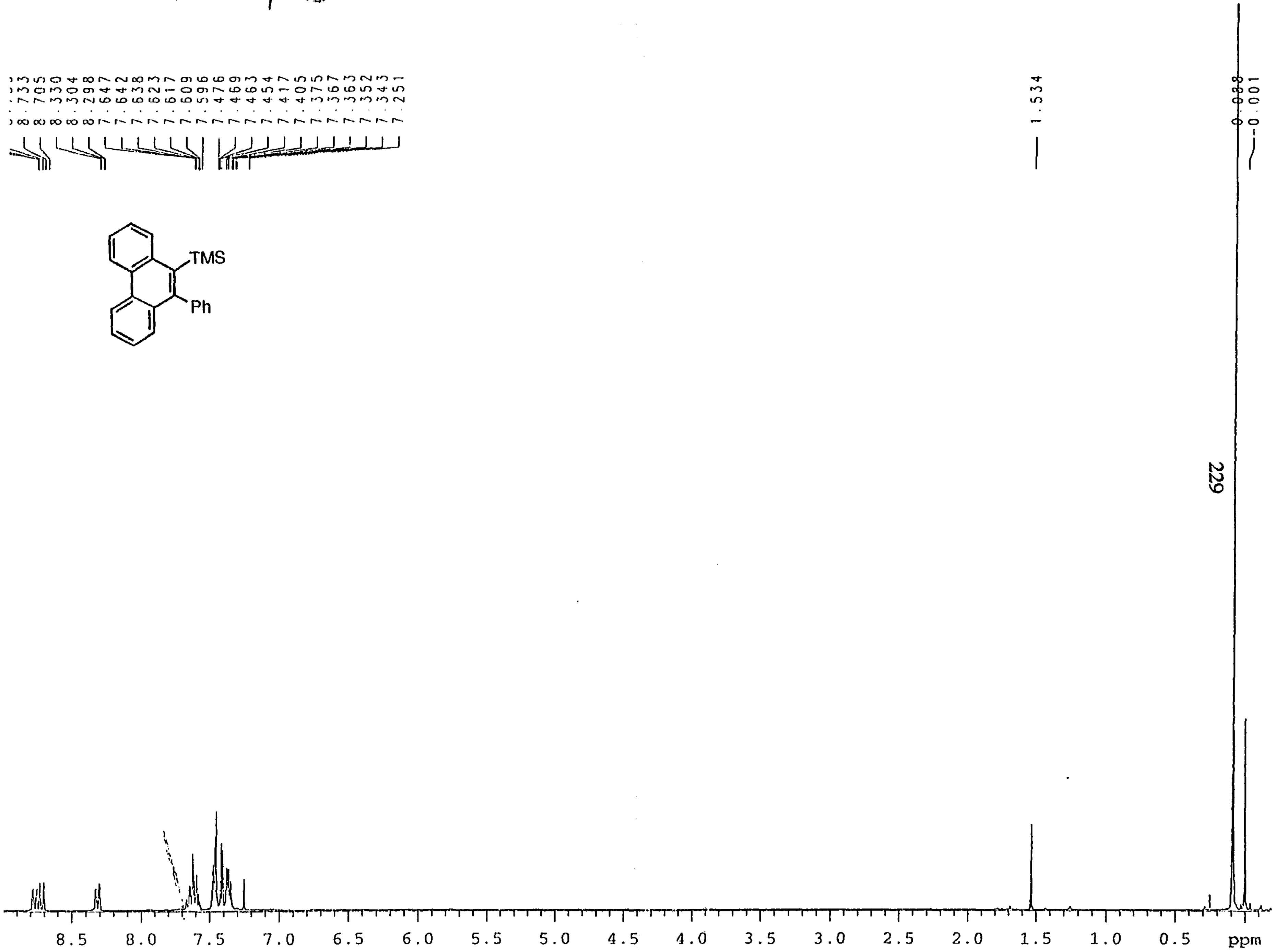
2, 14



/giga/data/jmz/nmr/jmz.096.fid/1/pdata/1 unknown Mon Oct 2 10:50:48 1995

Table 2, entry 15

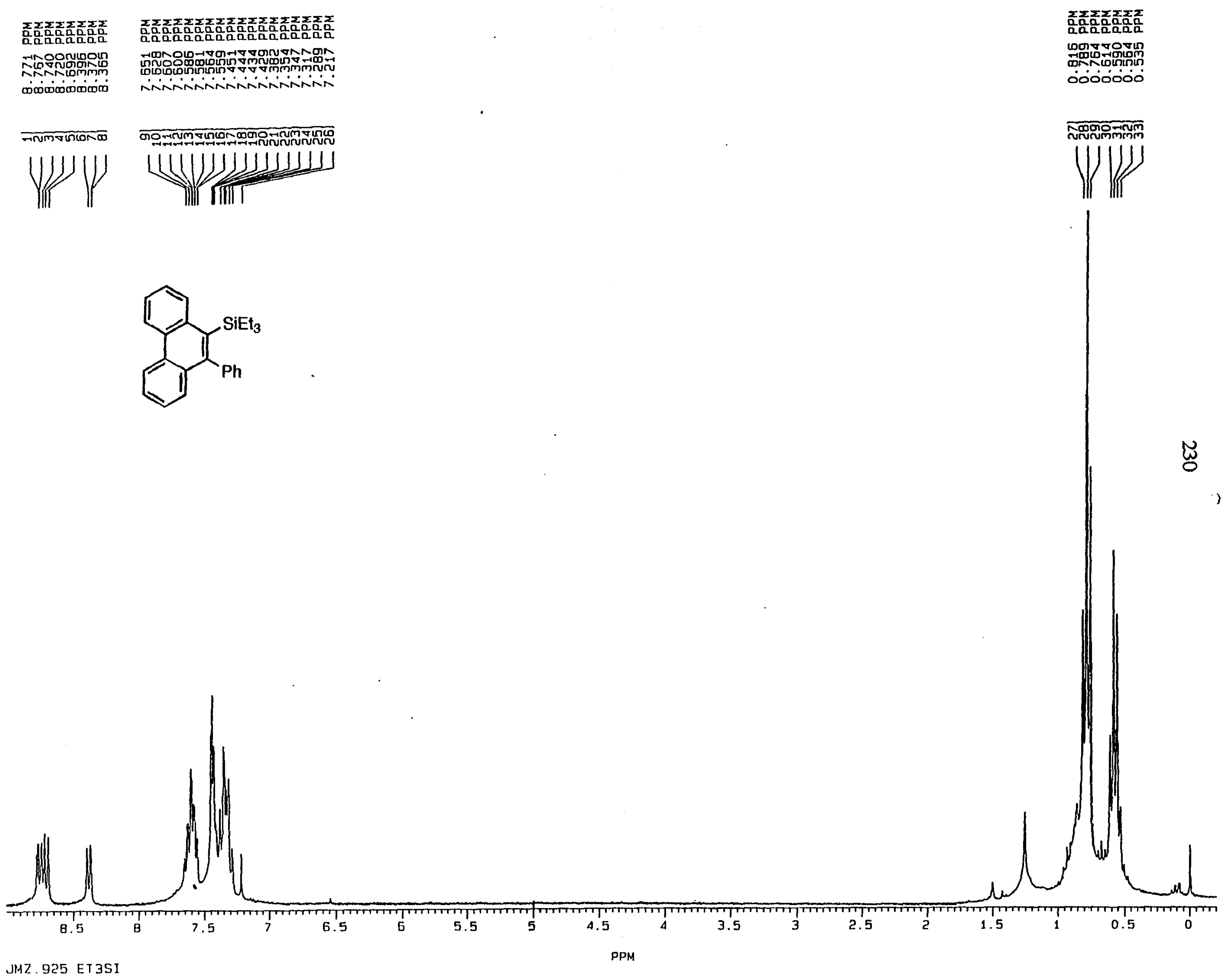
II-67



/giga/data/jmz/nmr/jmz.118.fid/1/pdata/1 unknown Wed Nov 15 11:14:06 1995

VI-39

Table 2, 19



JL - 27

2,19

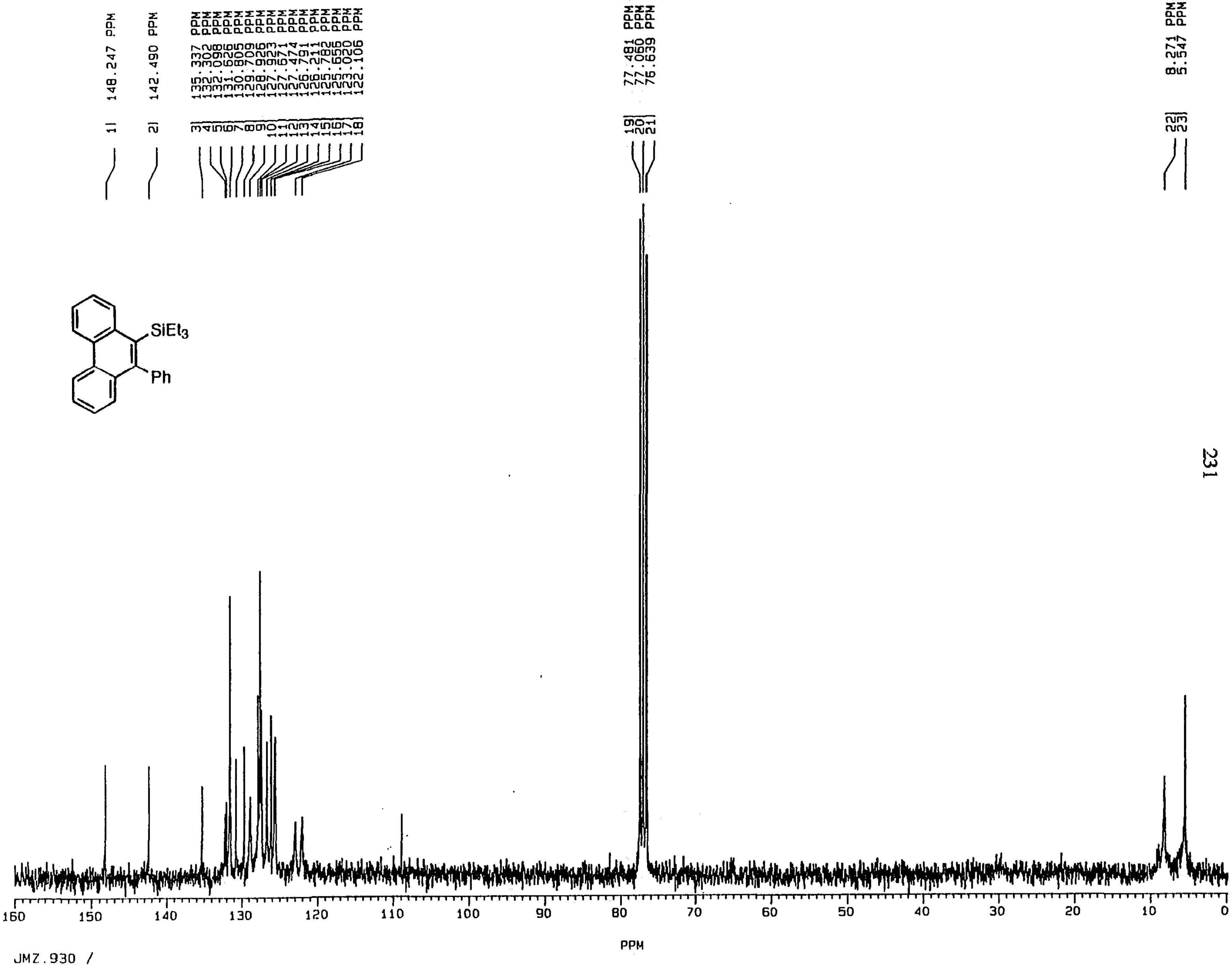
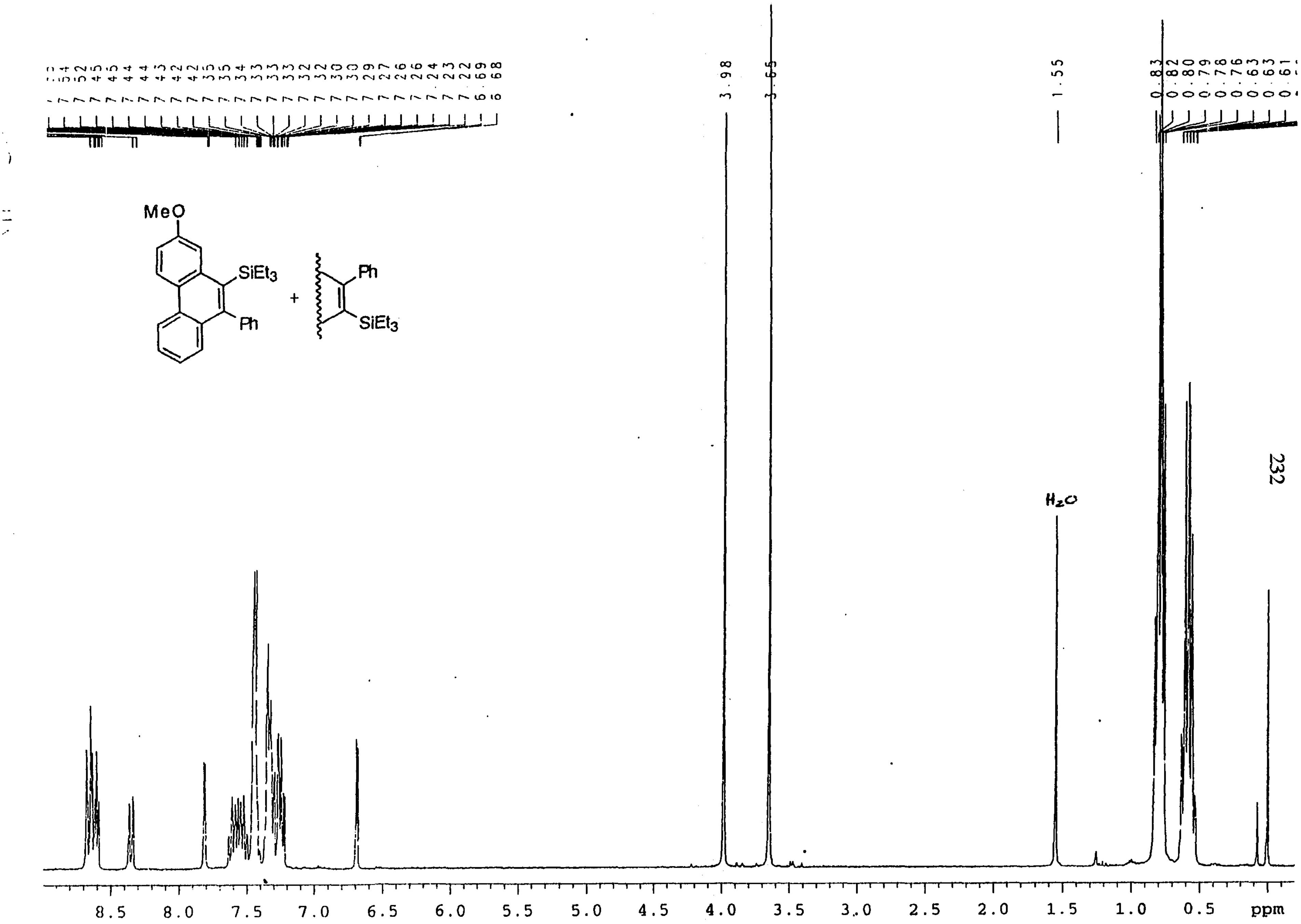
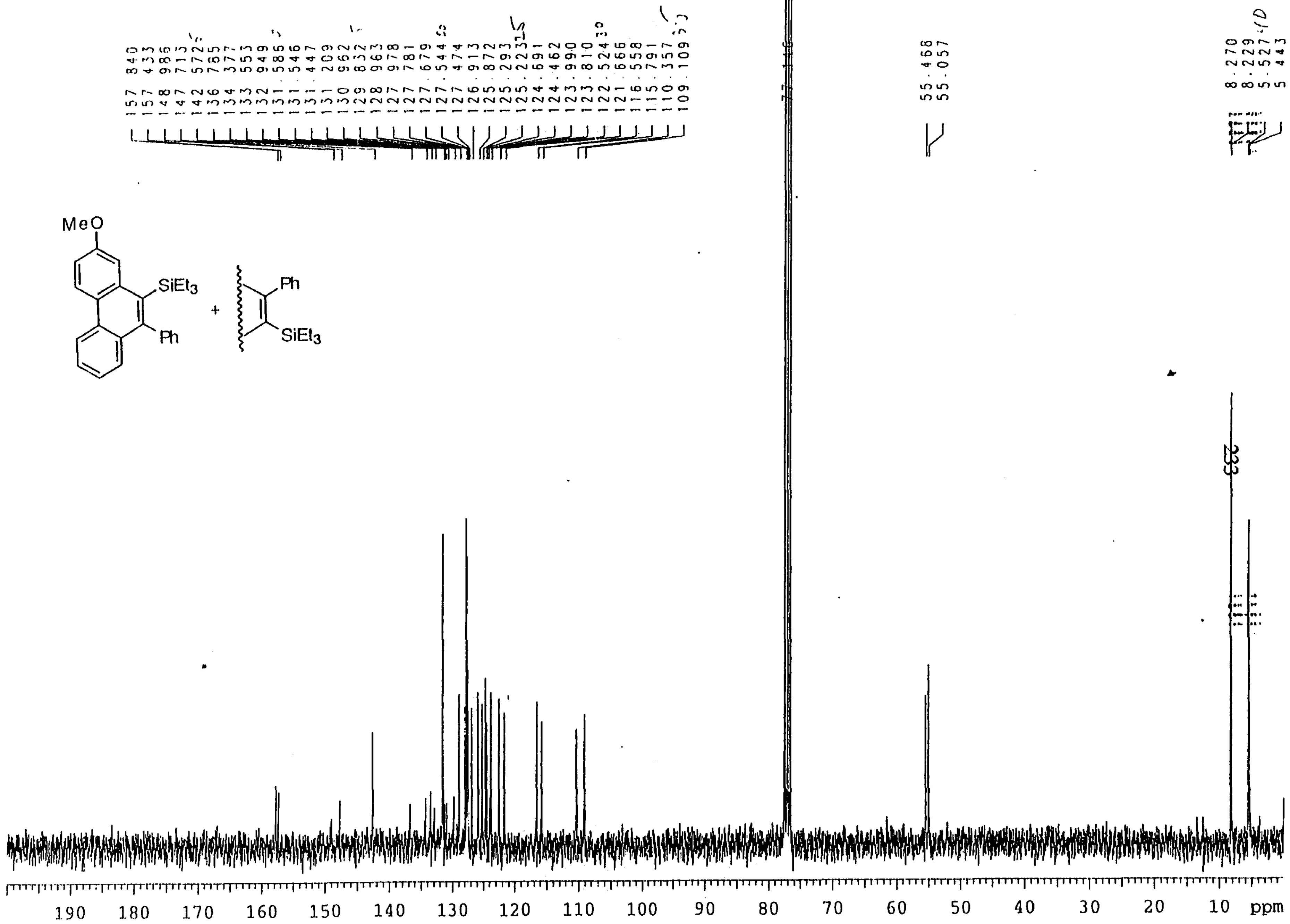

1| 148.247 PPM
2| 142.490 PPM
3| 135.337 PPM
4| 132.302 PPM
5| 132.098 PPM
6| 131.626 PPM
7| 130.805 PPM
8| 129.709 PPM
9| 128.926 PPM
10| 127.923 PPM
11| 127.671 PPM
12| 127.474 PPM
13| 126.791 PPM
14| 126.211 PPM
15| 125.782 PPM
16| 125.656 PPM
17| 123.020 PPM
18| 122.106 PPM
19| 77.481 PPM
20| 77.060 PPM
21| 76.639 PPM
22| 8.271 PPM
23| 5.547 PPM
SiEt3
Ph
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM
JMZ.930 /

Table 2, 15



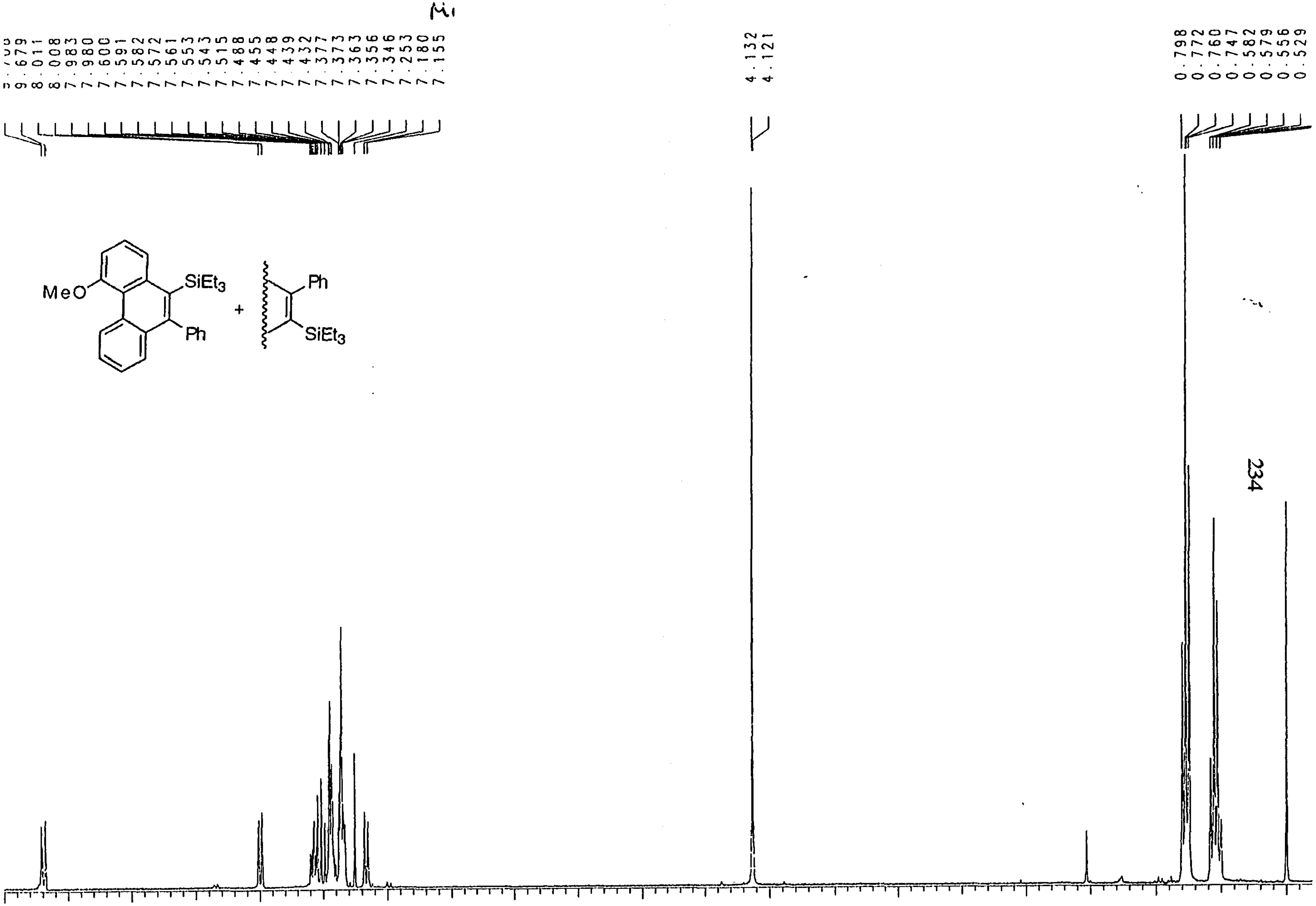
/giga/data/jmz/nmr/jmz.055.fid/1/pdata/1 unknown Wed Aug 2 11:23:22 1995

2, 157



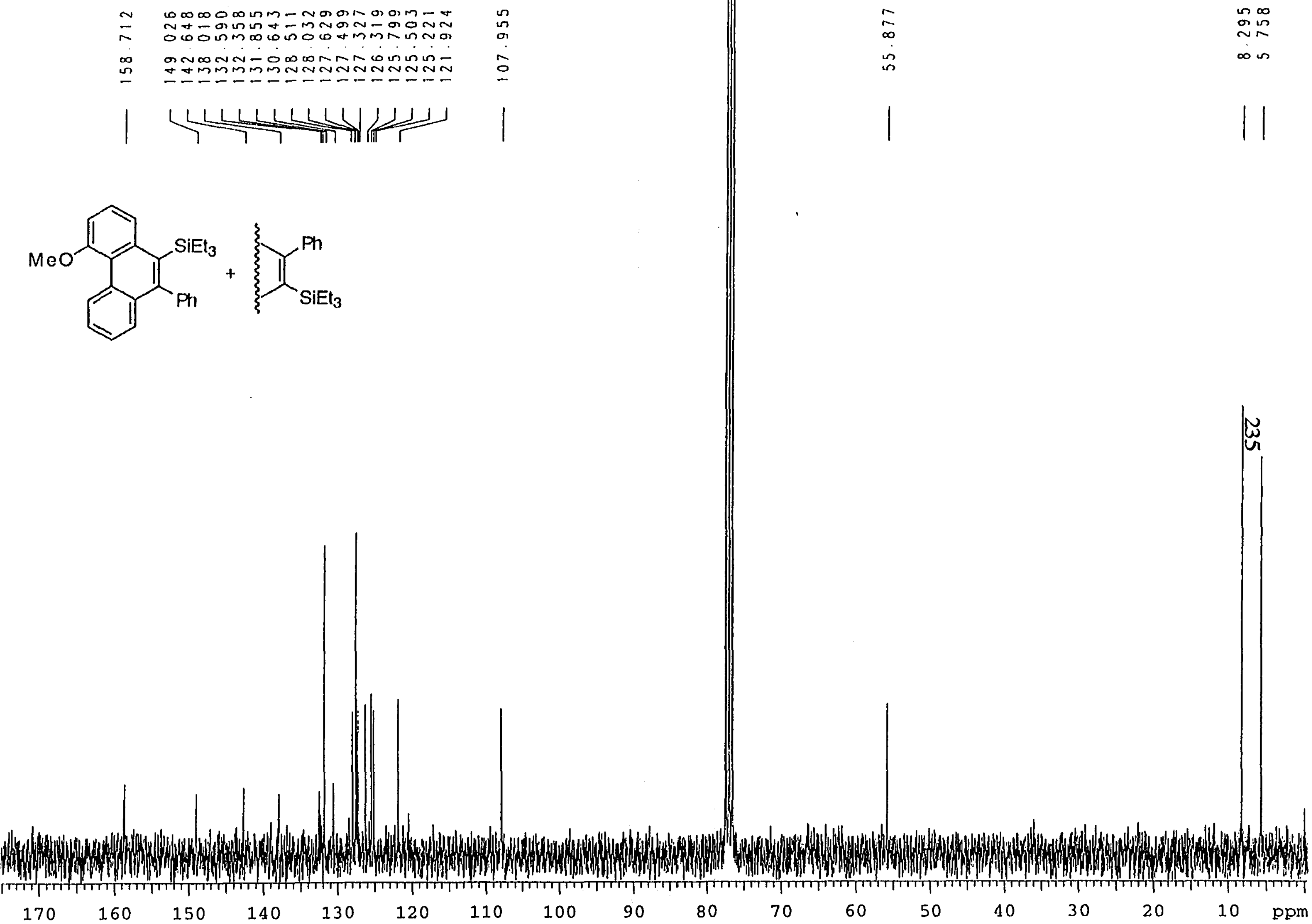
/giga/data/jmz/nmr/jmz.140.fid/1/pdata/1 unknown Thu Dec 28 12:41:17 1995

Table 2, entry 18



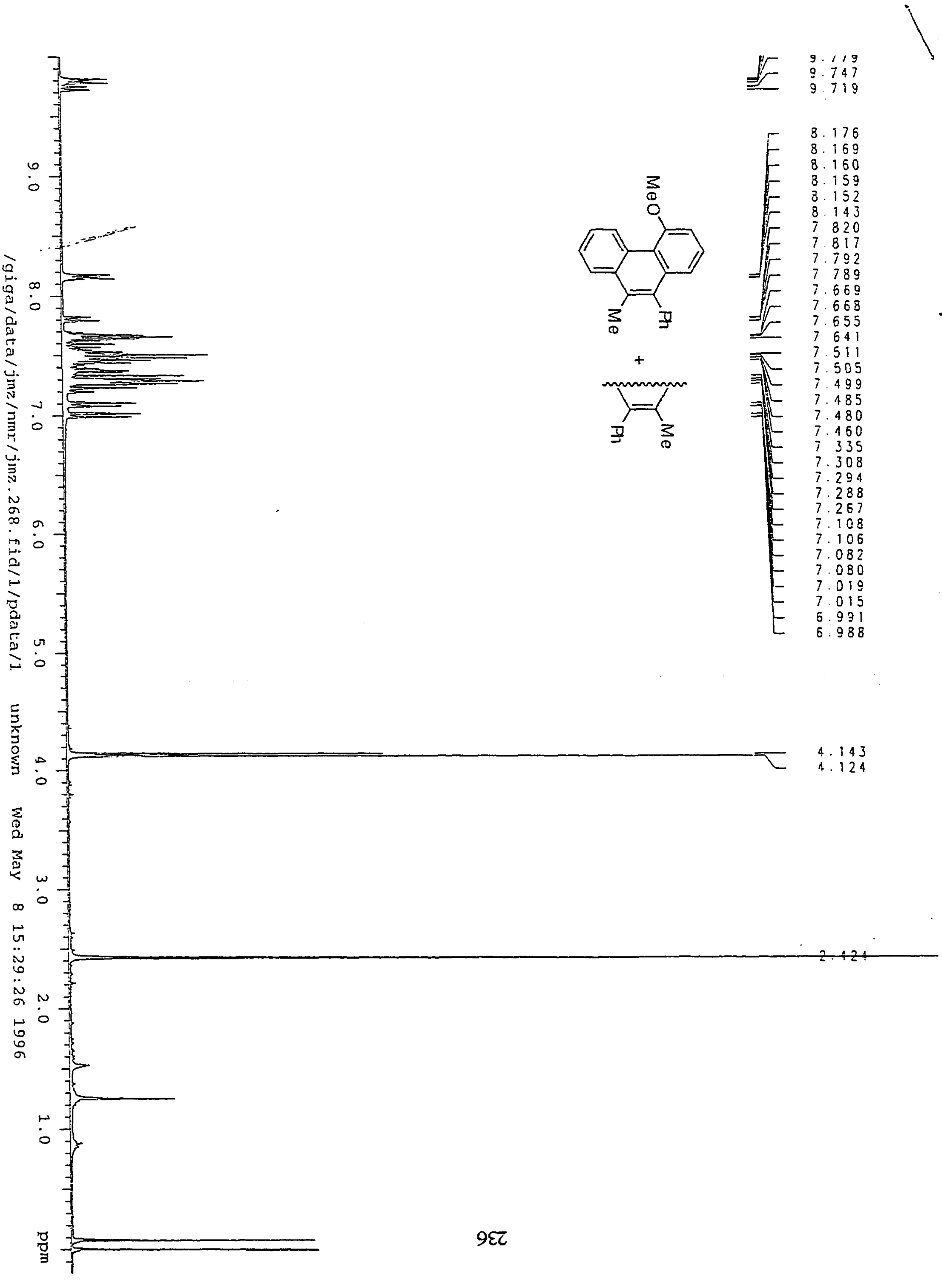
/giga/data/jmz/nmr/jmz.205.fid/1/pdata/1 unknown Wed Mar 6 08:57:29 1996

Table 2, entry 18

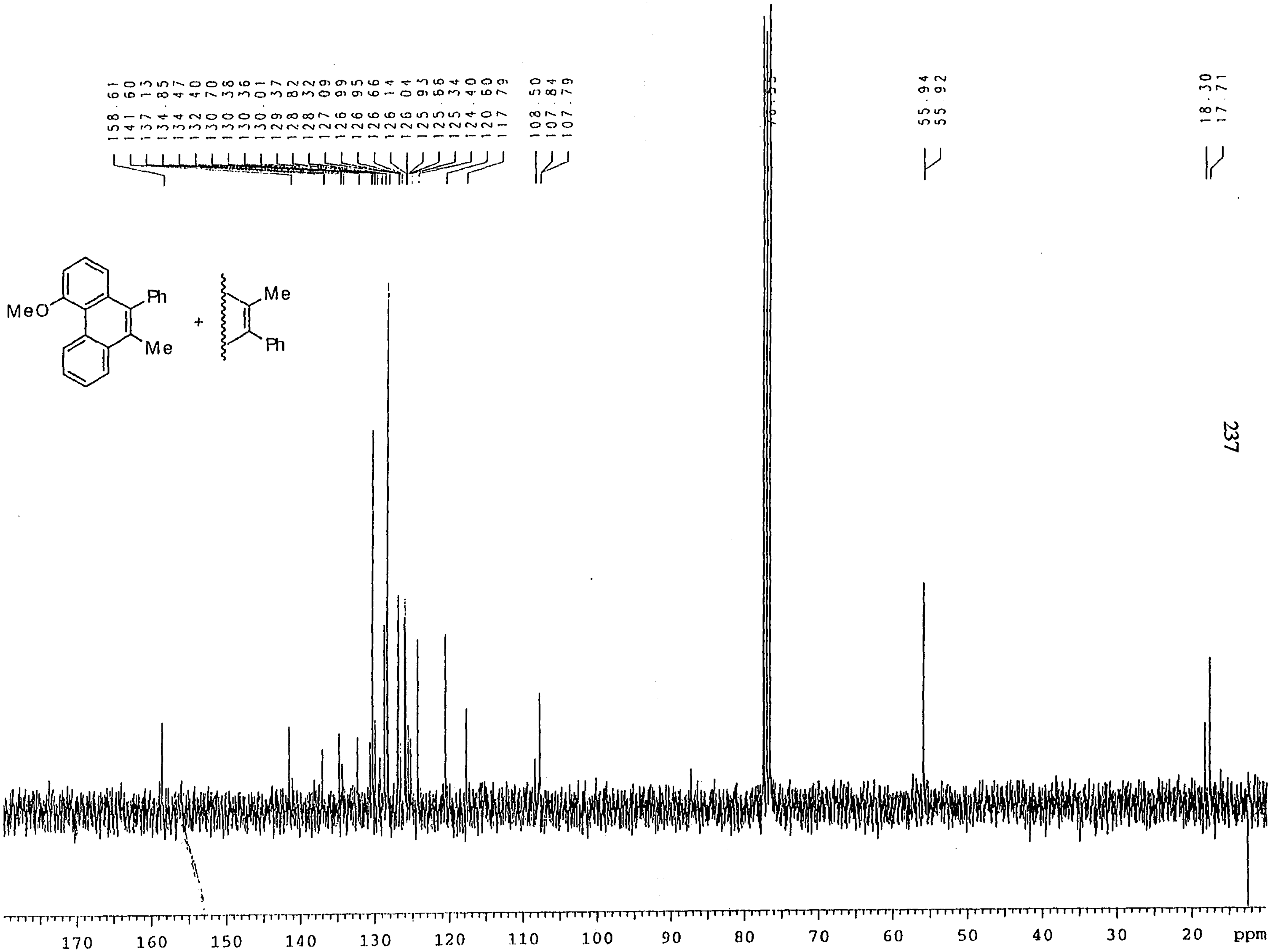


/giga/data/jmz/nmr/jmz.206.fid/1/pdata/1 unknown Wed Mar 6 11:19:13 1996

19

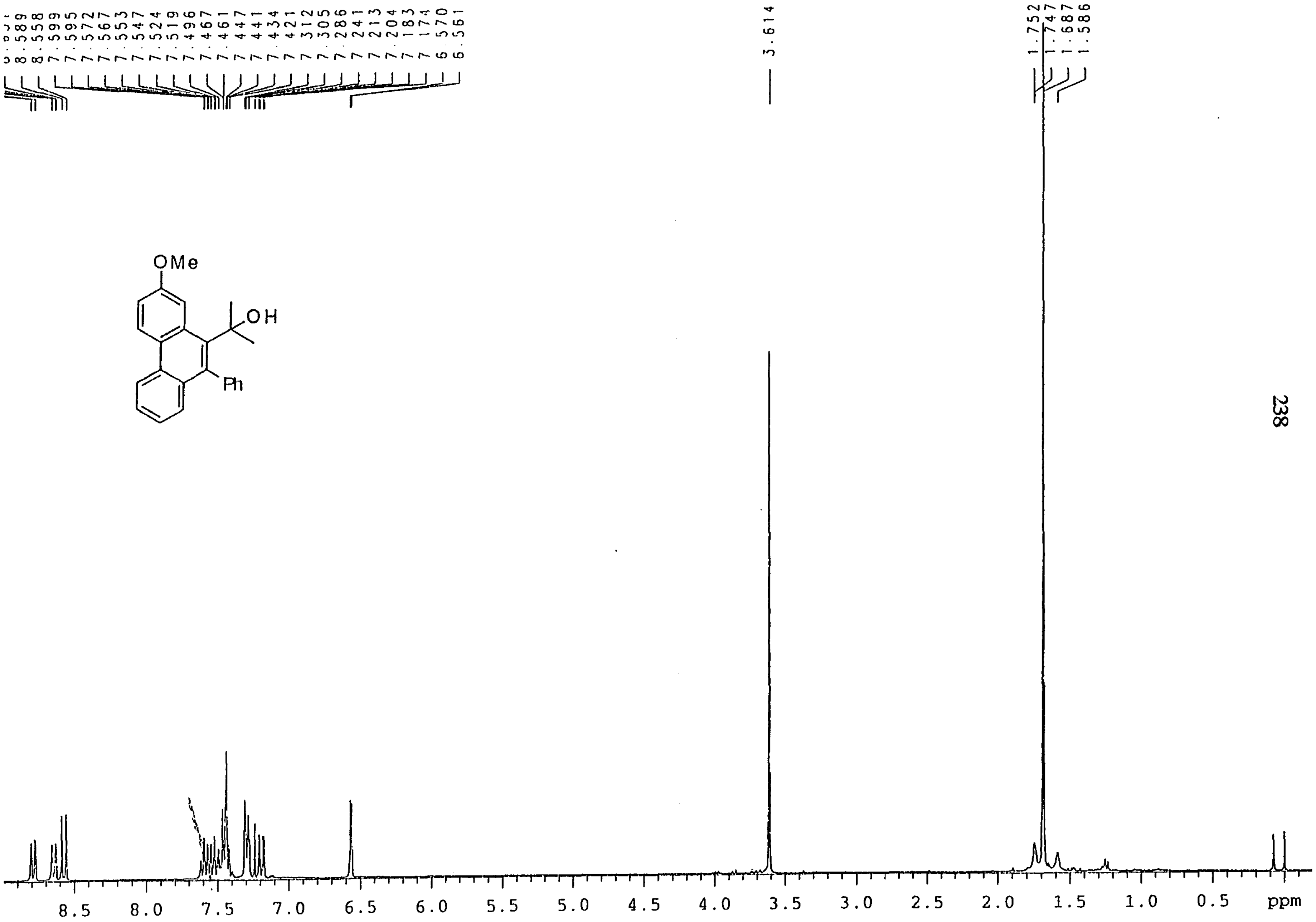

9.779
9.747
9.719
8.176
8.169
8.160
8.159
8.152
8.143
7.820
7.817
7.792
7.789
7.669
7.668
7.655
7.641
7.511
7.505
7.499
7.485
7.480
7.460
7.335
7.308
7.294
7.288
7.267
7.108
7.106
7.082
7.080
7.019
7.015
6.991
6.988
4.143
4.124
2.424
MeO
Ph
Me
+
Me
Ph
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm
/giga/data/jmz/nmr/jmz.268.fid/1/pdata/1 unknown Wed May 8 15:29:26 1996

19



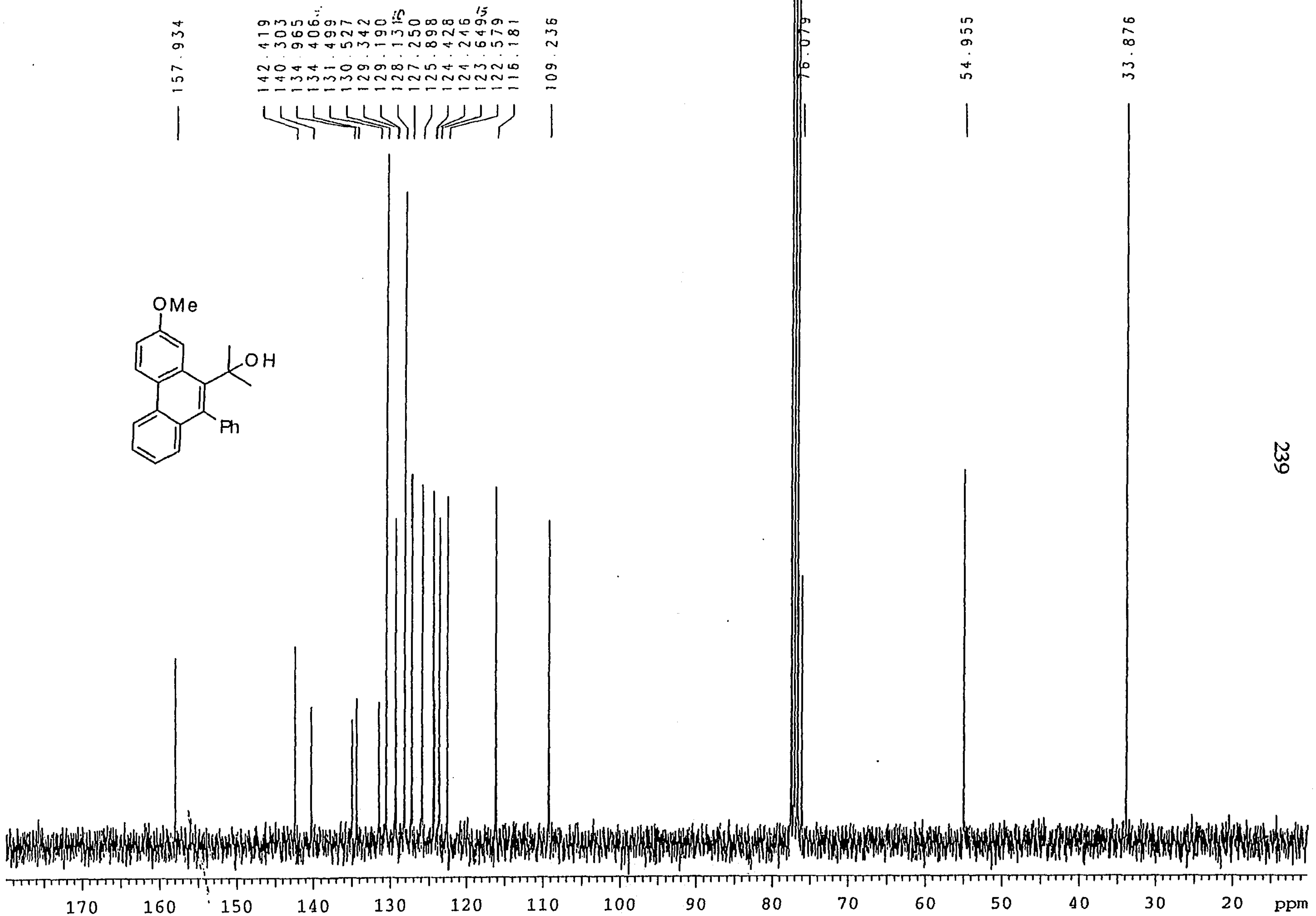
/giga/data/jmz/nmr/jmz.060.fid/1/pdata/1 unknown Fri Aug 4 14:14:37 1995

209



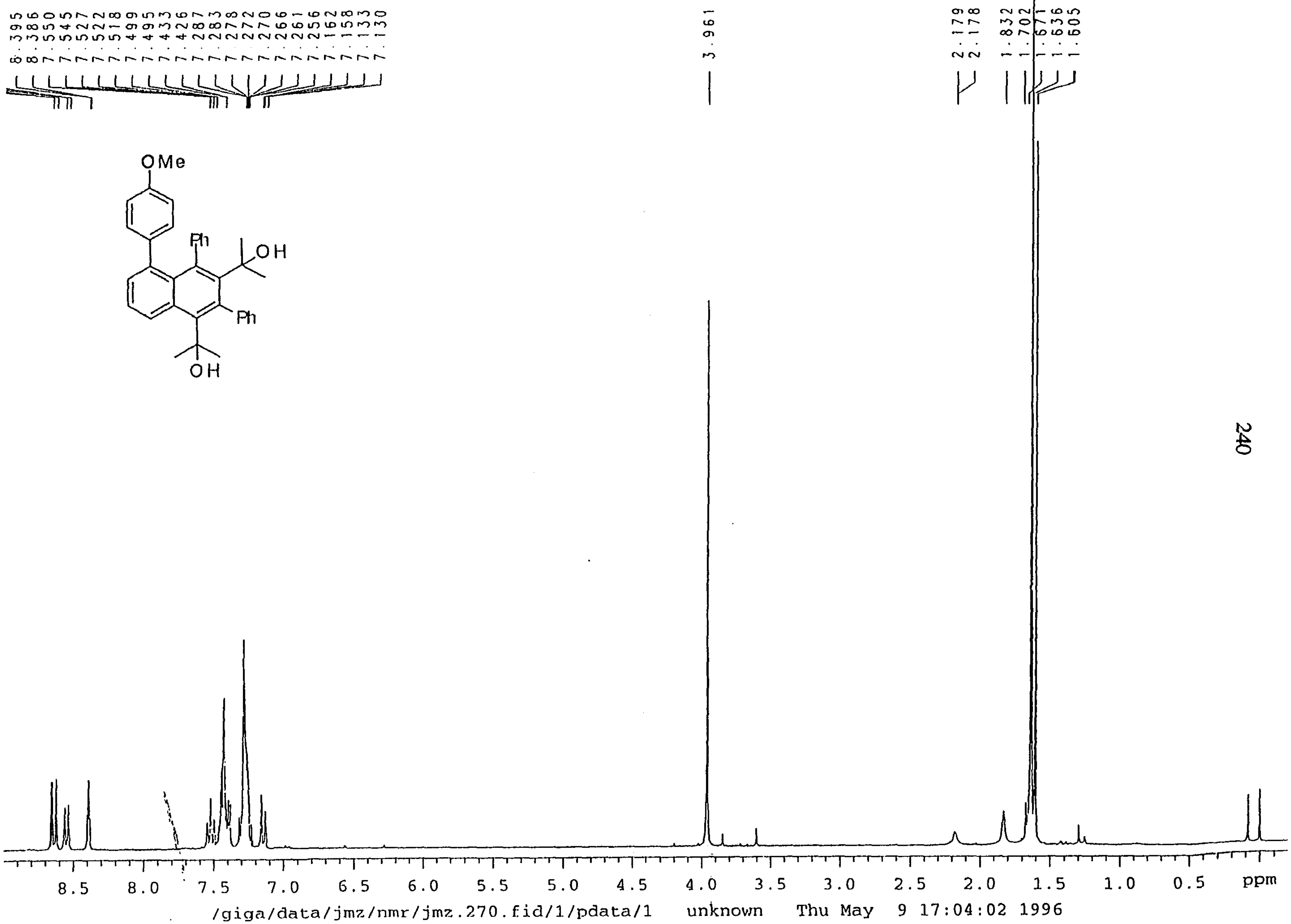
/giga/data/jmz/nmr/jmz.272.fid/1/pdata/1 unknown Thu May 9 17:18:19 1996

20a

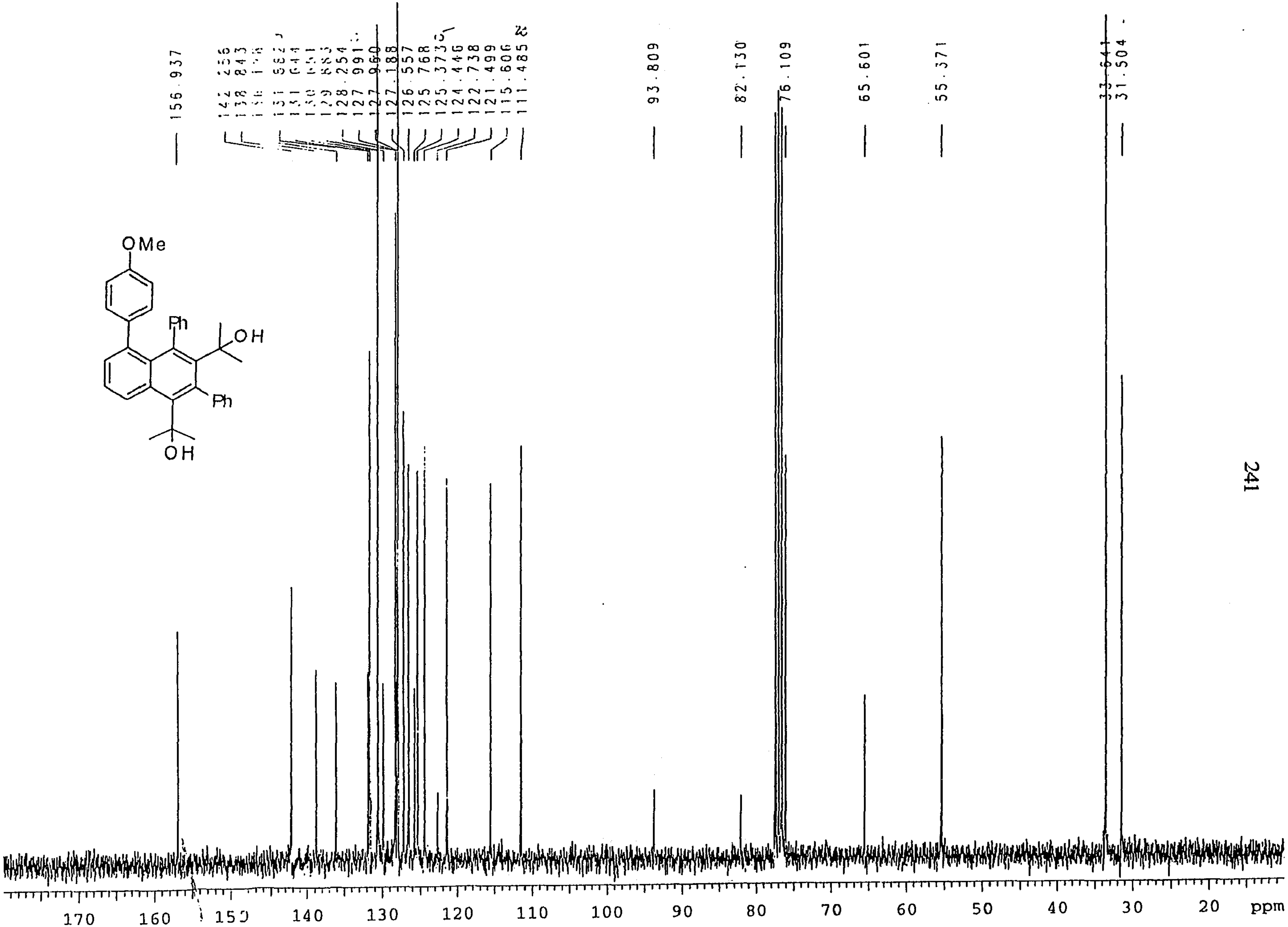


/giga/data/jmz/nmr/jmz.273.fid/1/pdata/1 unknown Thu May 9 17:29:28 1996

20b


8.395
8.386
7.550
7.545
7.527
7.522
7.518
7.499
7.495
7.433
7.426
7.287
7.283
7.278
7.272
7.270
7.266
7.261
7.256
7.162
7.158
7.133
7.130
3.961
2.179
2.178
1.832
1.702
1.671
1.636
1.605
OMe
Ph
OH
Ph
OH
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
/giga/data/jmz/nmr/jmz.270.fid/1/pdata/1 unknown Thu May 9 17:04:02 1996

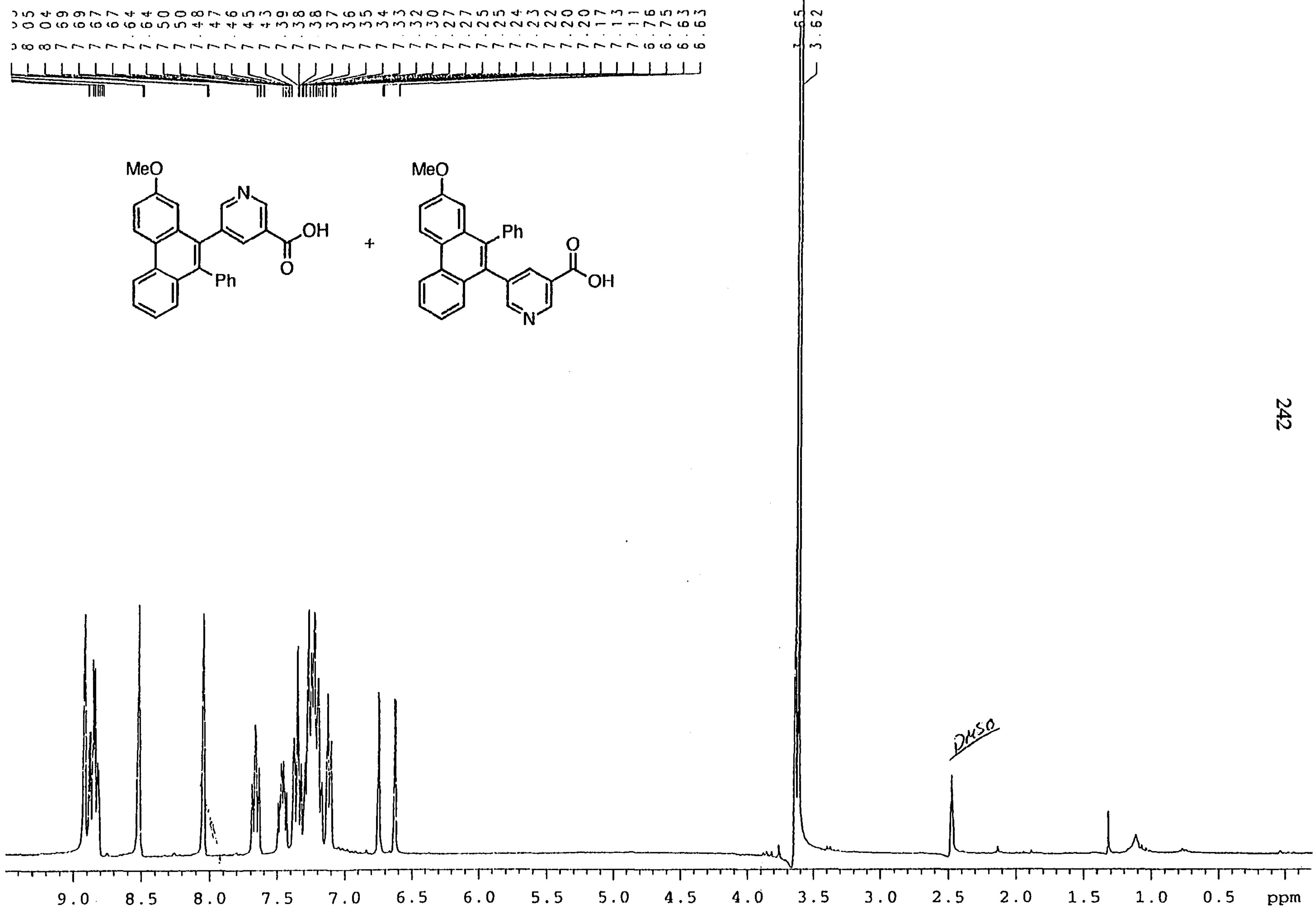
206



/giga/data/jmz/nmr/jmz.271.fid/1/pdata/1 unknown Thu May 9 17:14:33 1996

21

Table 2, entry 19

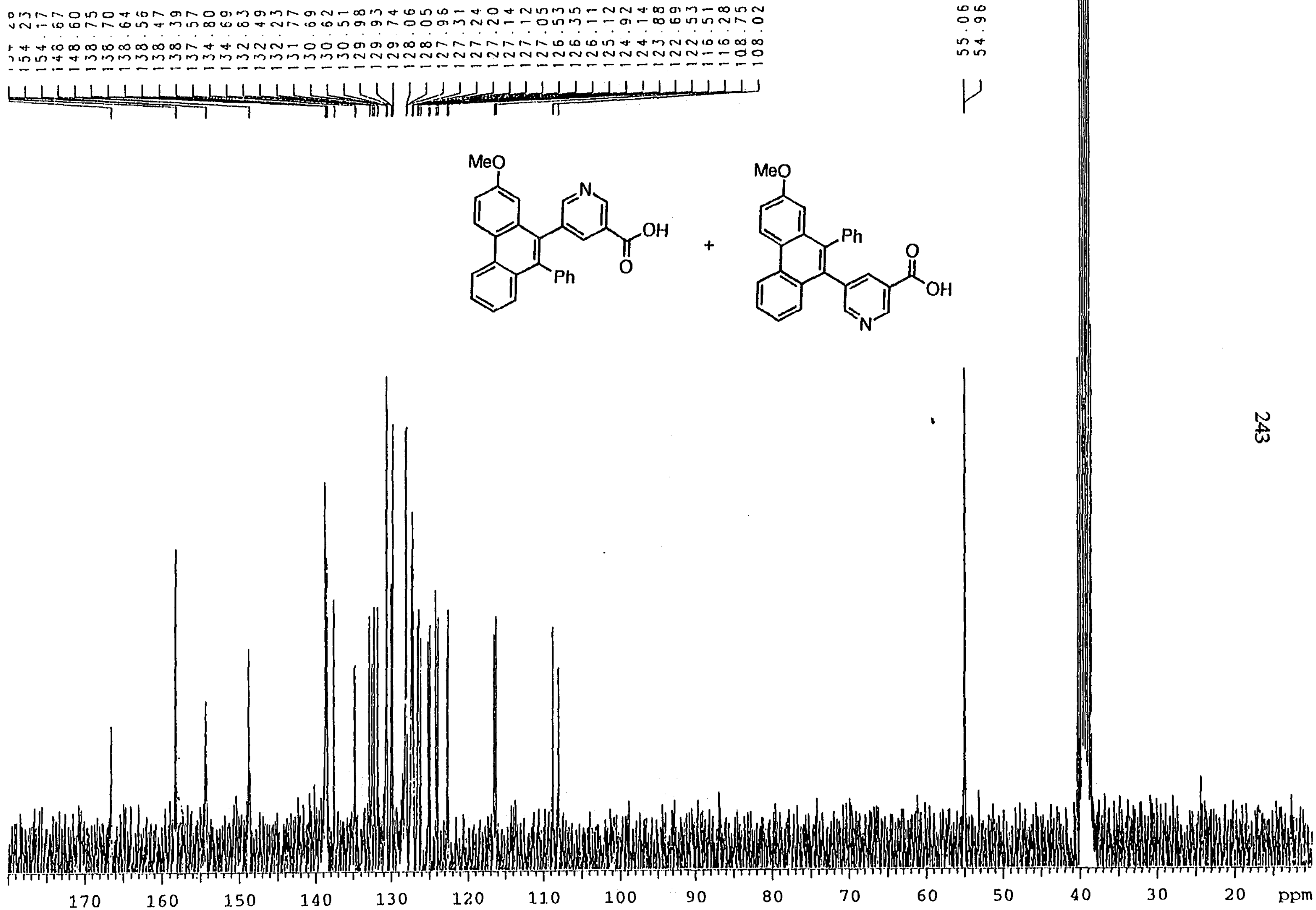


/giga/data/jmz/nmr/jmz.048.fid/1/pdata/1 unknown Sat Jul 29 13:02:52 1995

21

2, 19

VII - 51



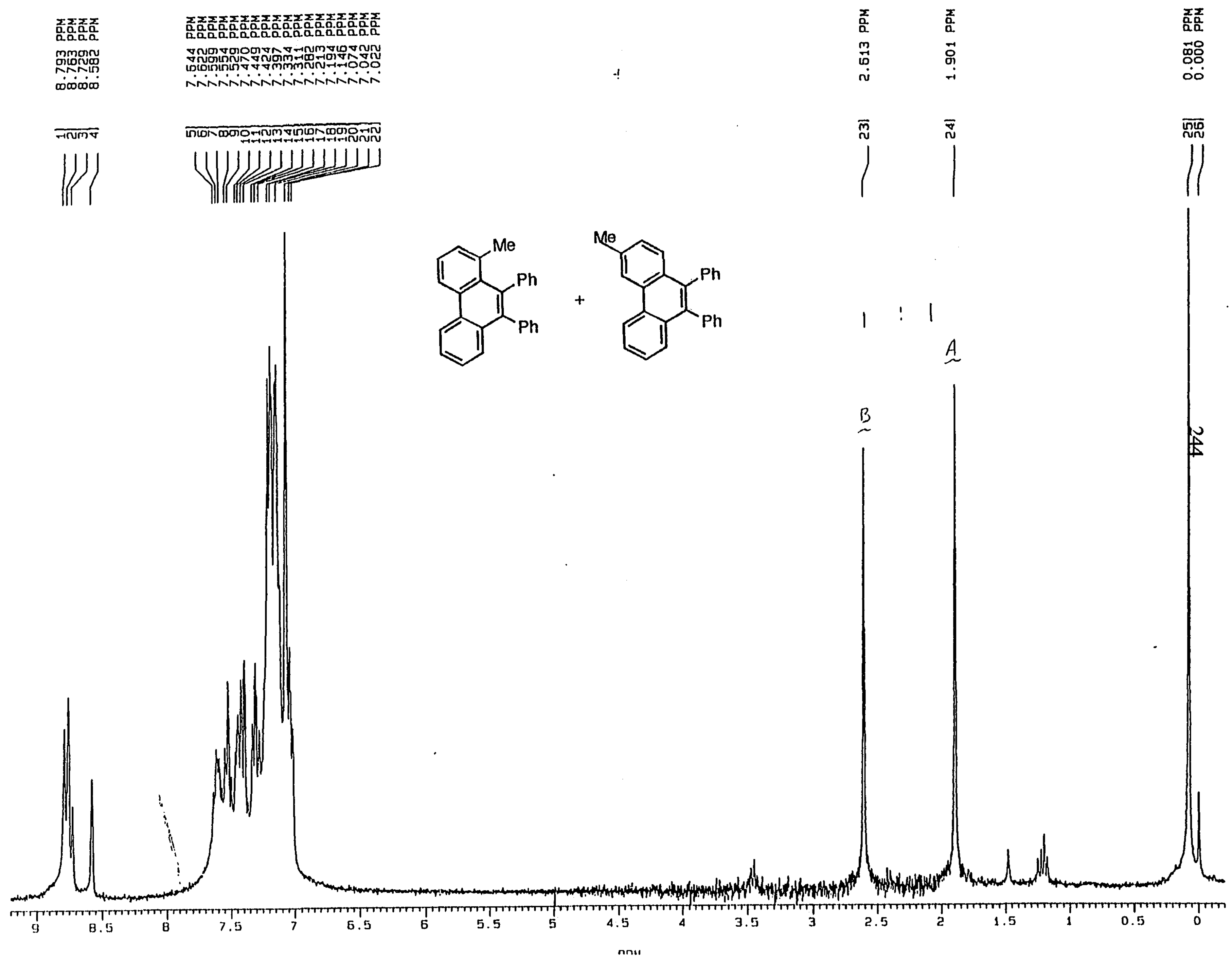
/giga/data/jmz/nmr/jmz.049.fid/1/pdata/1 unknown Sat Jul 29 13:25:29 1995

VII-58

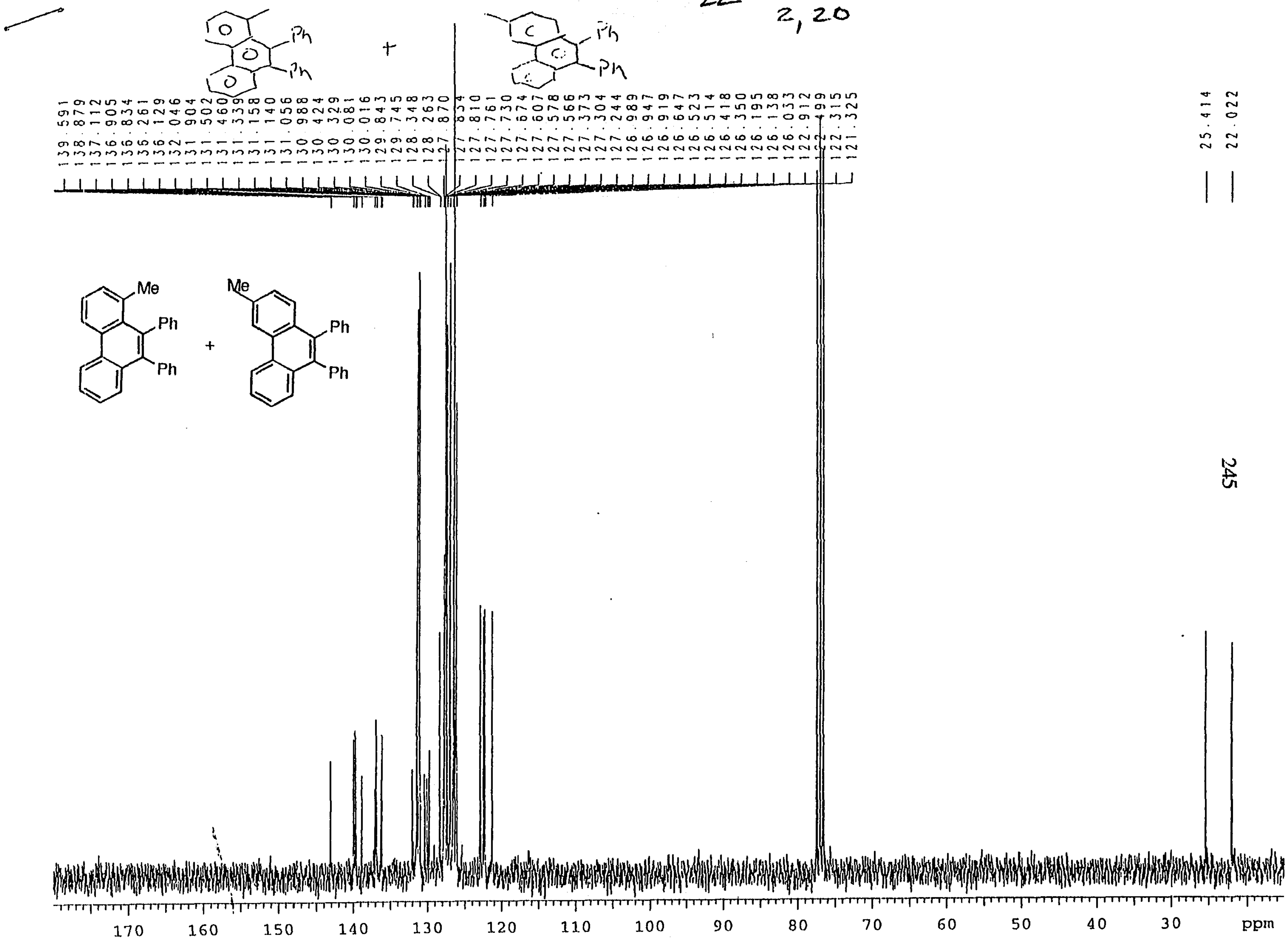
27

22

Table 2, entry 20



22 2,20

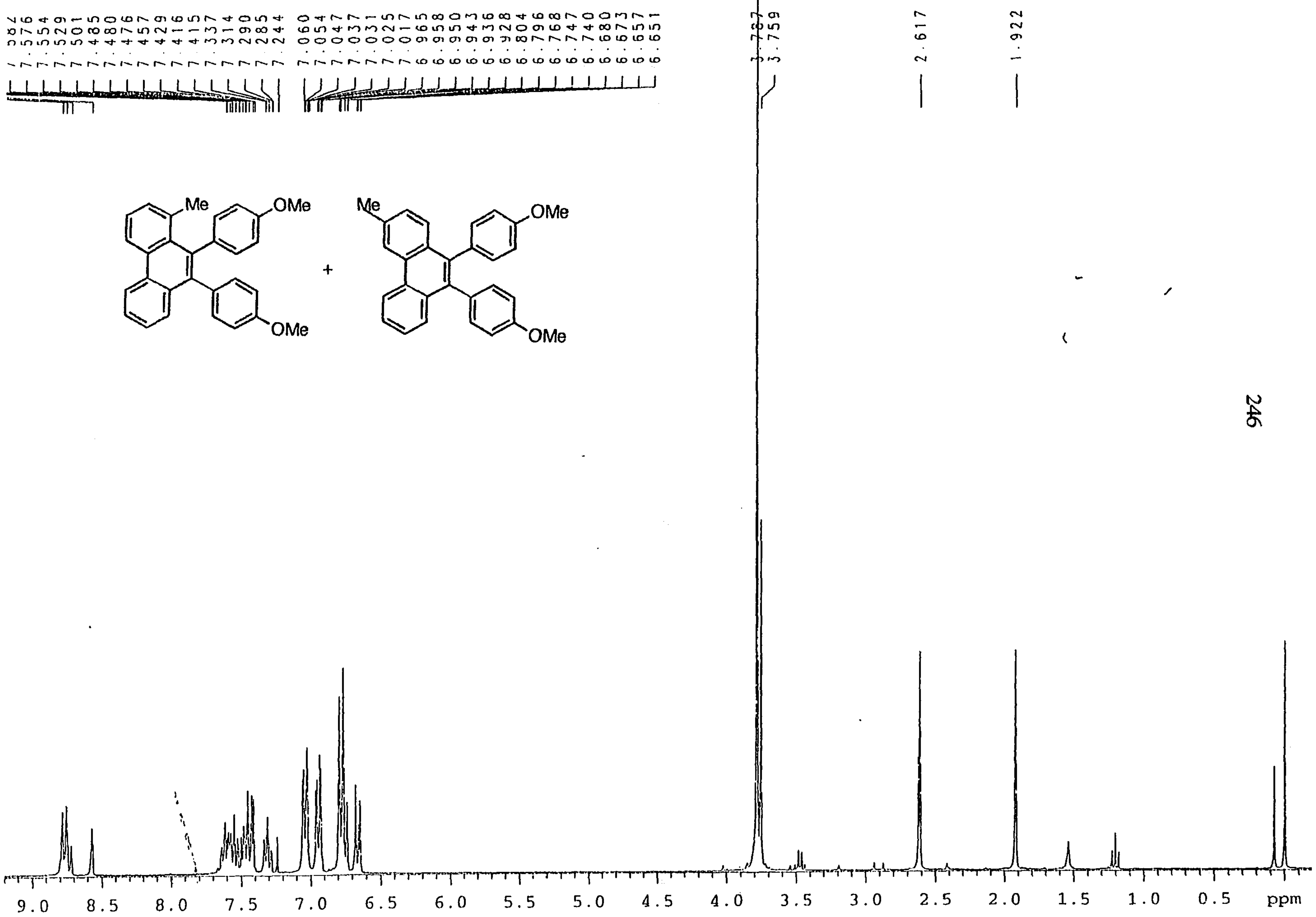


/giga/data/jmz/nmr/jmz.130.fid/1/pdata/1 unknown Fri Dec 15 11:31:02 1995

VII - 14

23

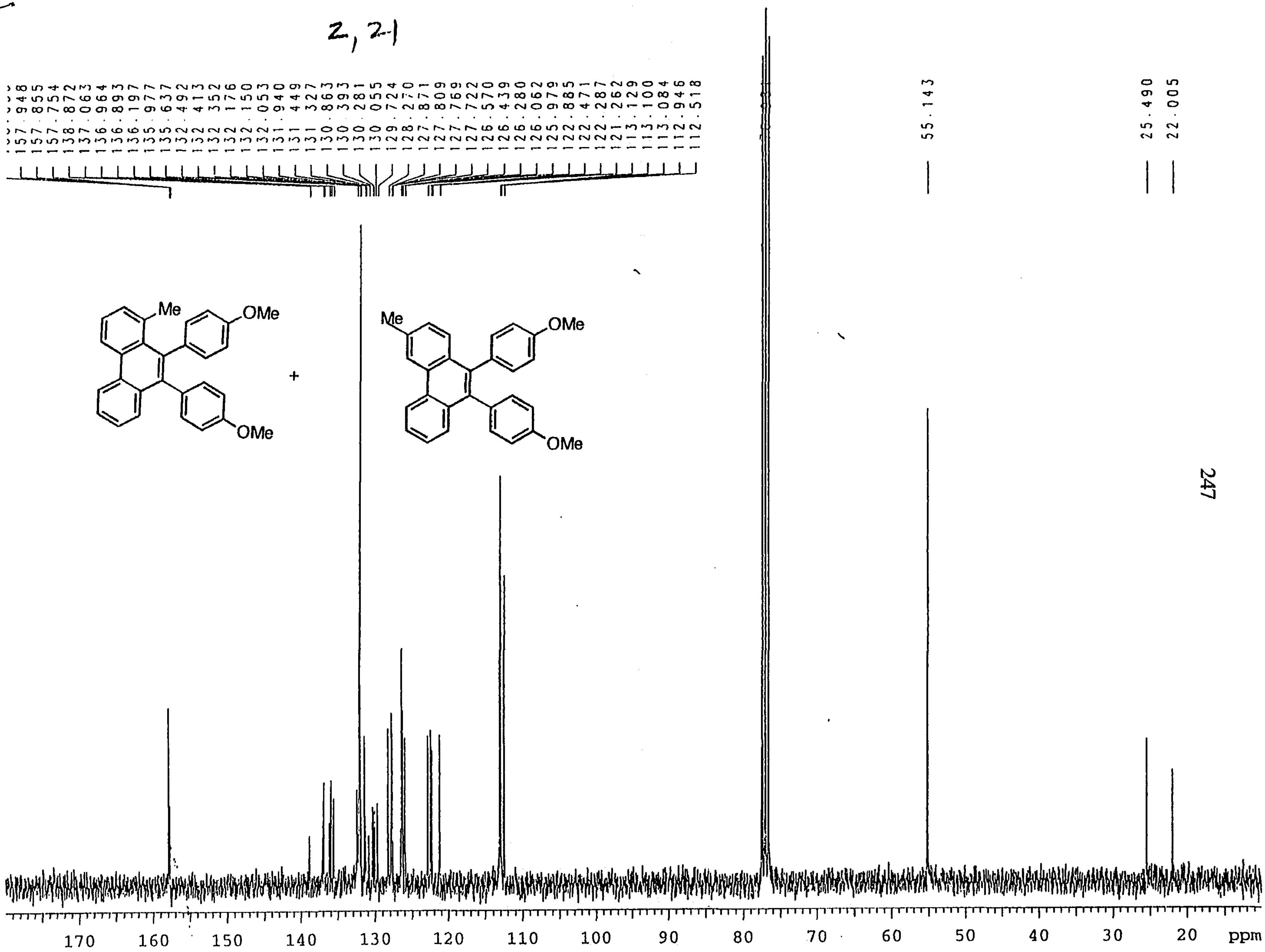
Table 2, 21



/giga/data/jmz/nmr/jmz.126.fid/1/pdata/1 unknown Thu Nov 30 11:27:08 1995

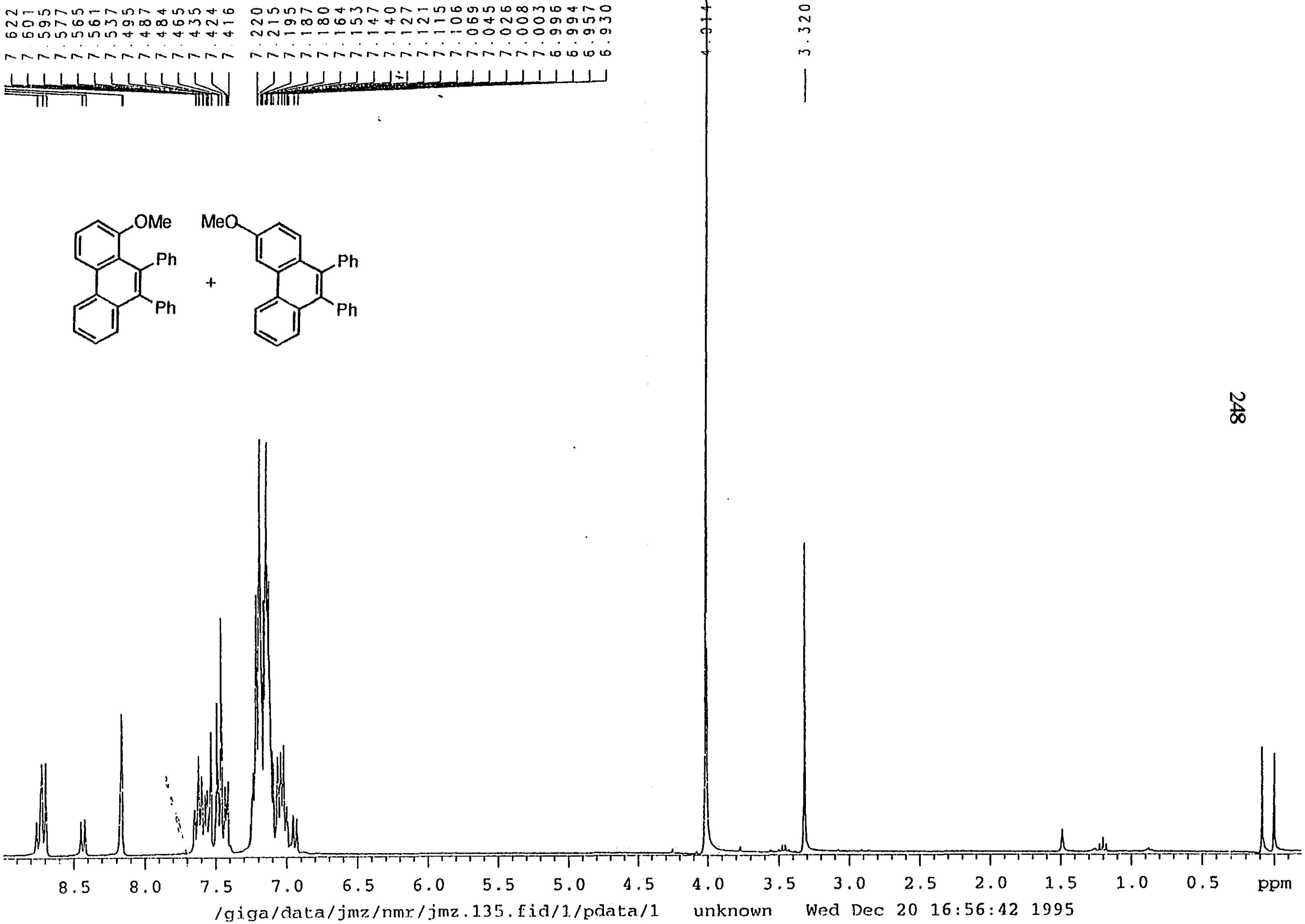
2.

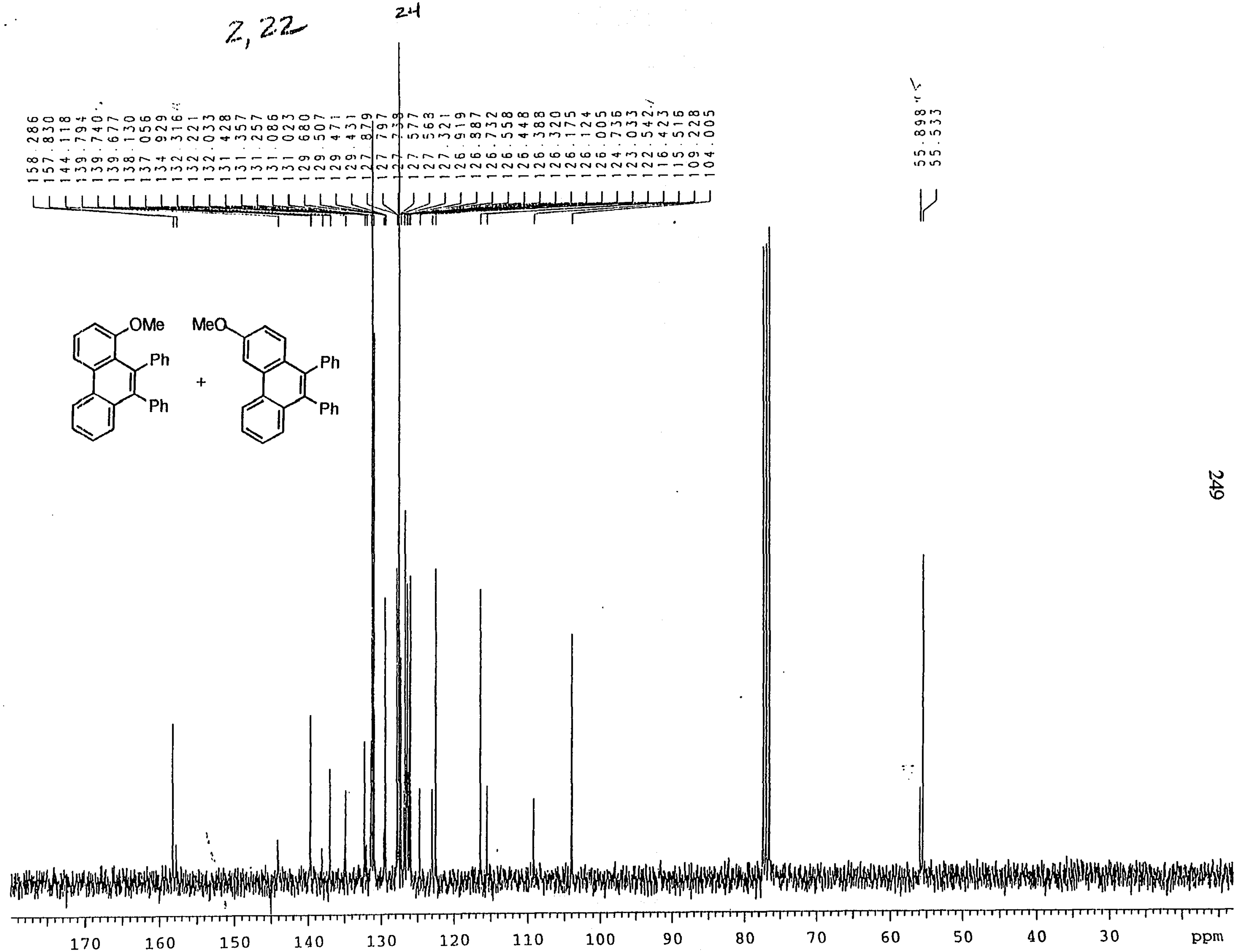
2, 21



/giga/data/jmz/nmr/jmz.132.fid/1/pdata/1 unknown Mon Dec 18 09:13:05 1995

Table 2, 22 24

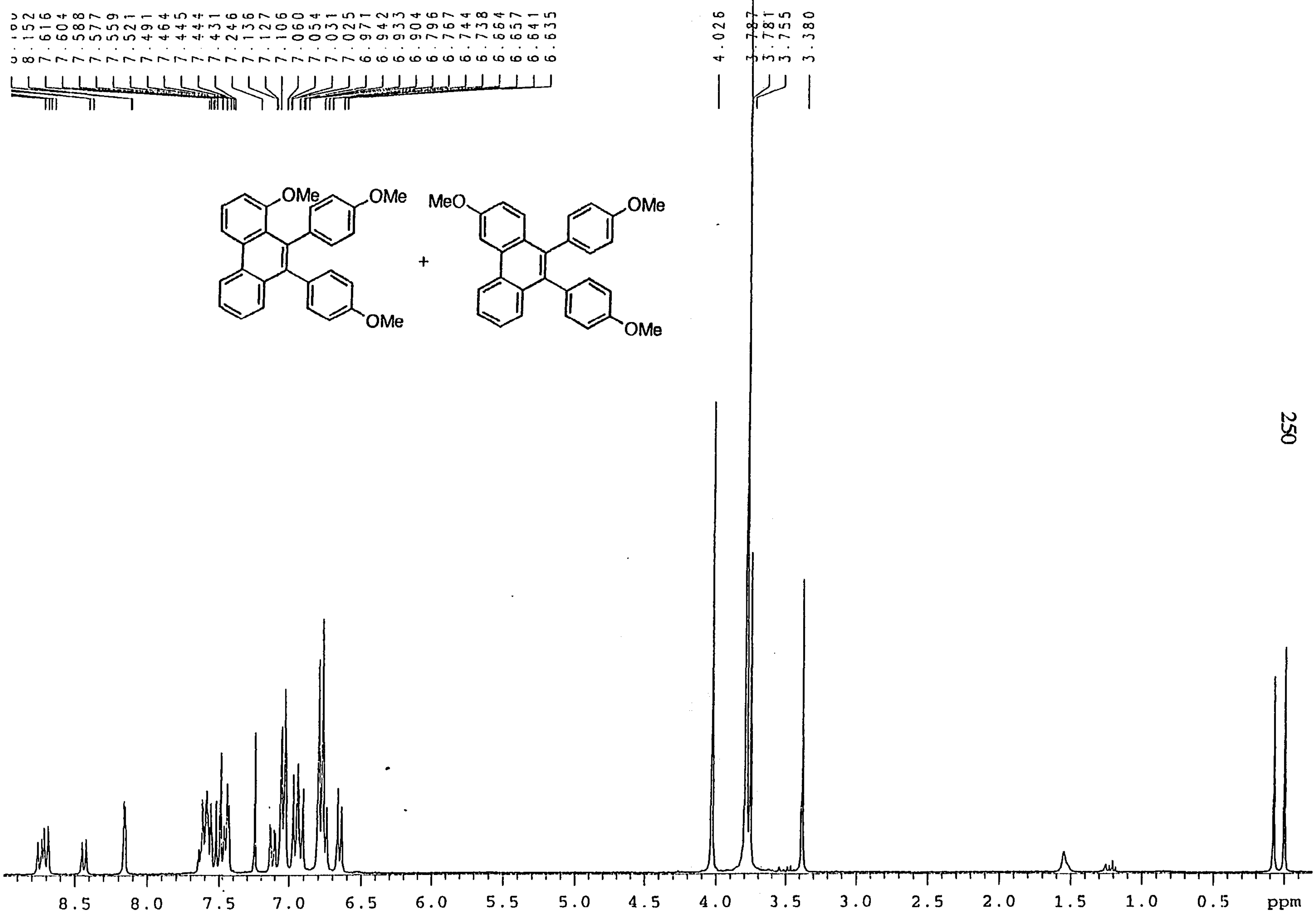

7.622
7.601
7.595
7.577
7.565
7.561
7.537
7.495
7.487
7.484
7.465
7.435
7.424
7.416
7.220
7.215
7.195
7.187
7.180
7.164
7.153
7.147
7.140
7.127
7.121
7.115
7.106
7.069
7.045
7.026
7.008
7.003
6.996
6.994
6.957
6.930
4.014
3.320
OMe
Ph
Ph
+
MeO
Ph
Ph
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
/giga/data/jmz/nmr/jmz.135.fid/1/pdata/1 unknown Wed Dec 20 16:56:42 1995



/giga/data/jmz/nmr/jmz.136.fid/1/pdata/1 unknown Wed Dec 20 17:03:19 1995

25

Table 2, entry 23



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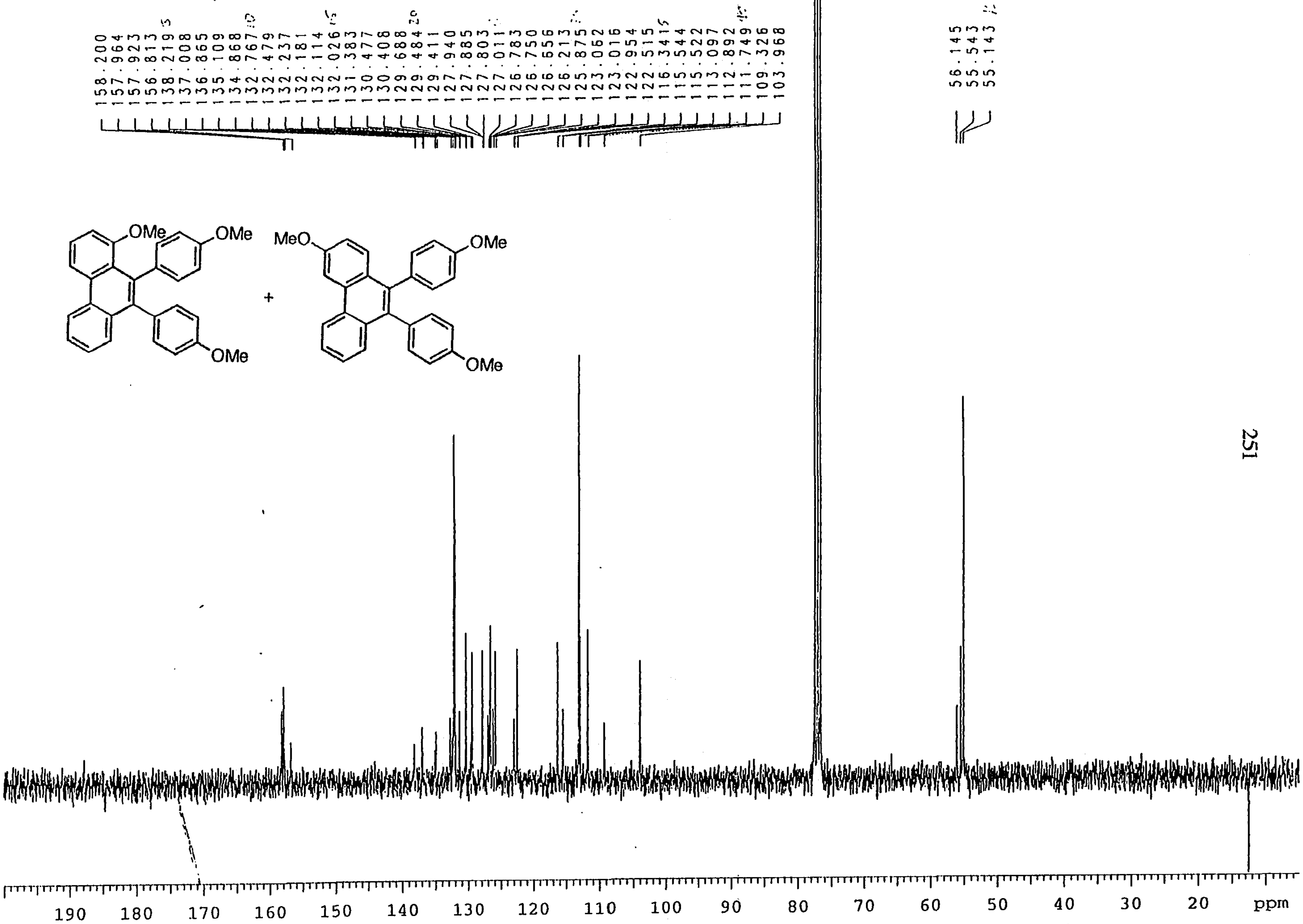
2, 23

23



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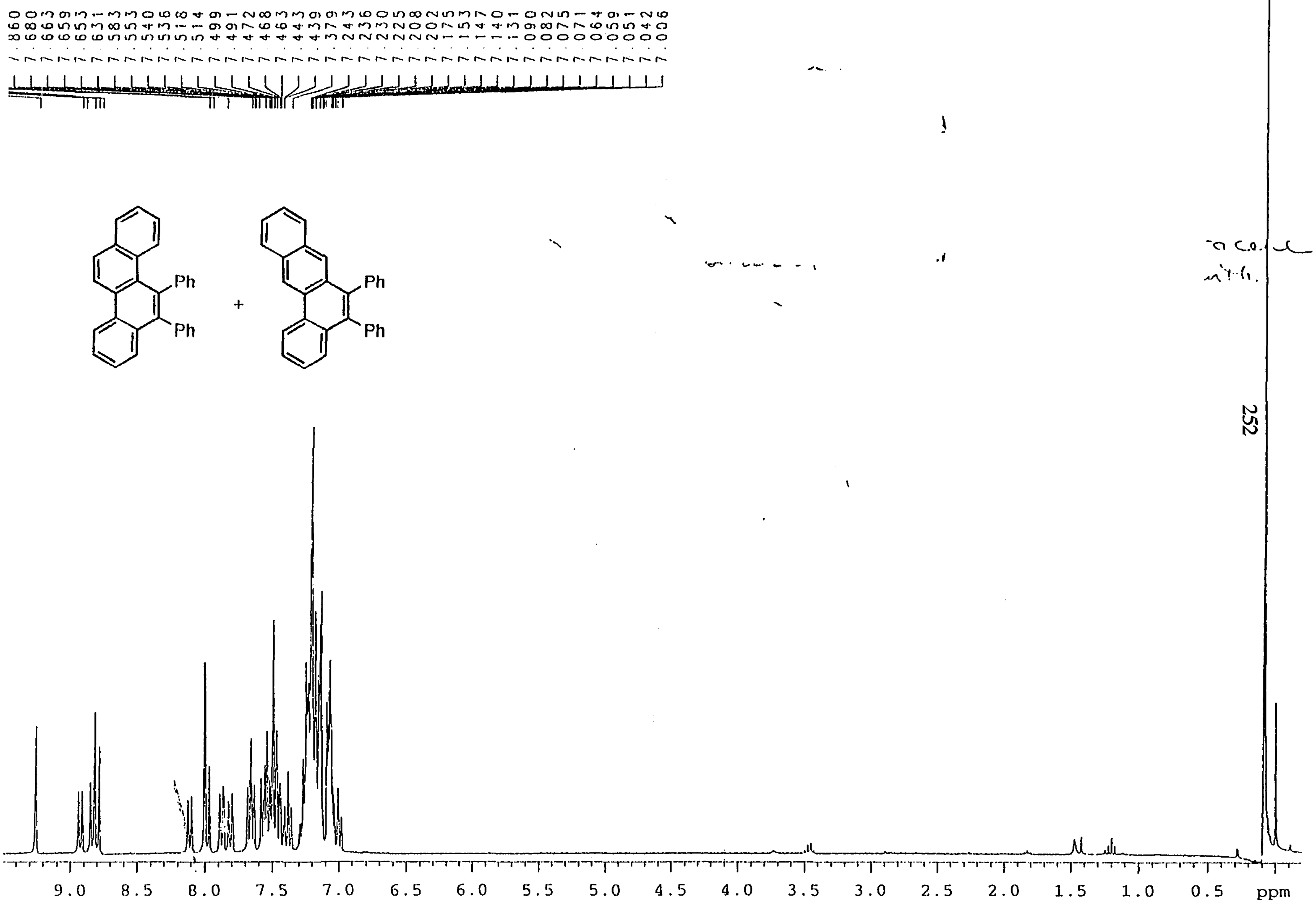
VII 70

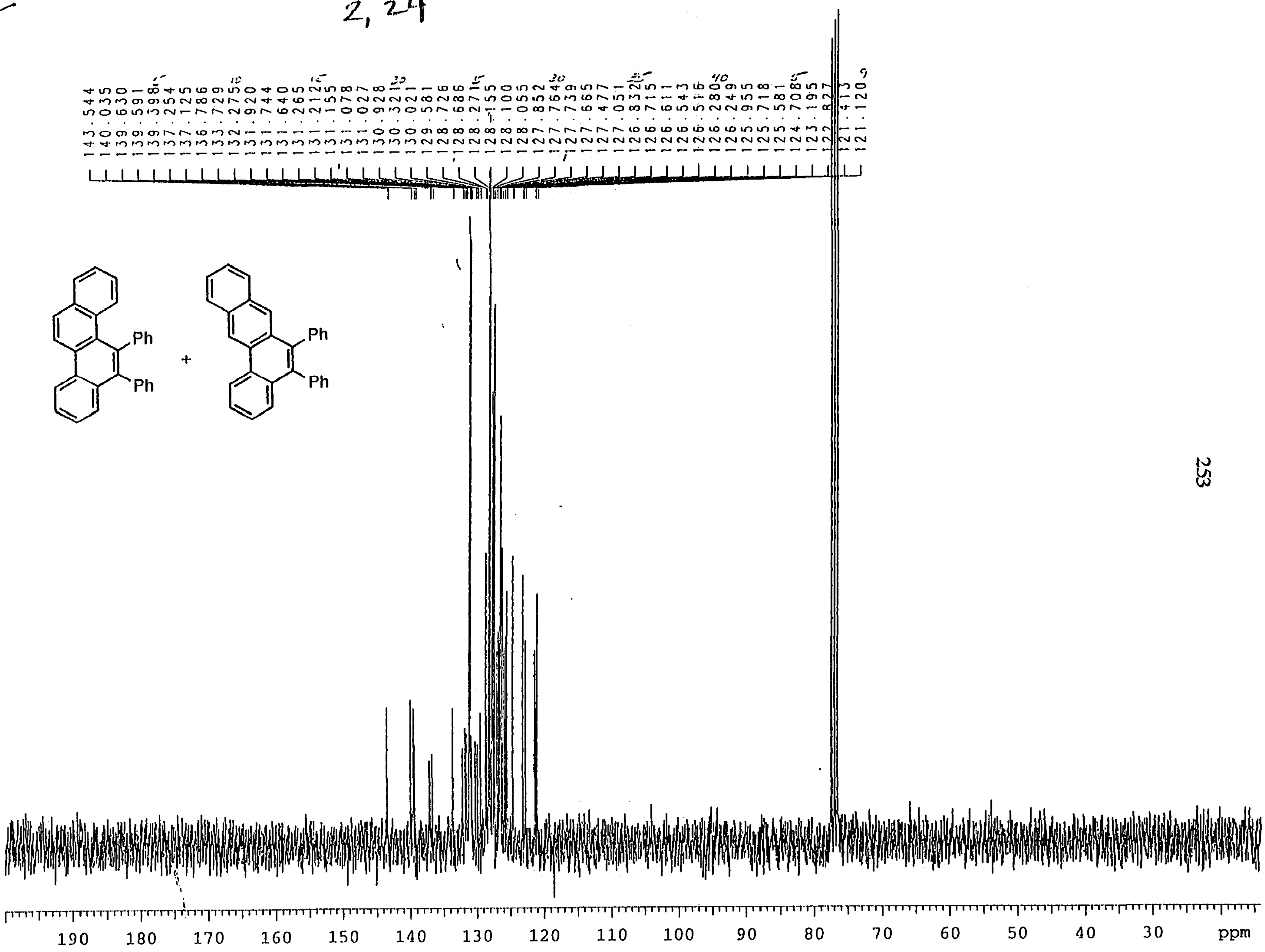
Table 2, 2.4

26



/giga/data/jmz/nmr/jmz.120.fid/1/pdata/1 unknown Thu Nov 16 15:57:20 1995

2, 24

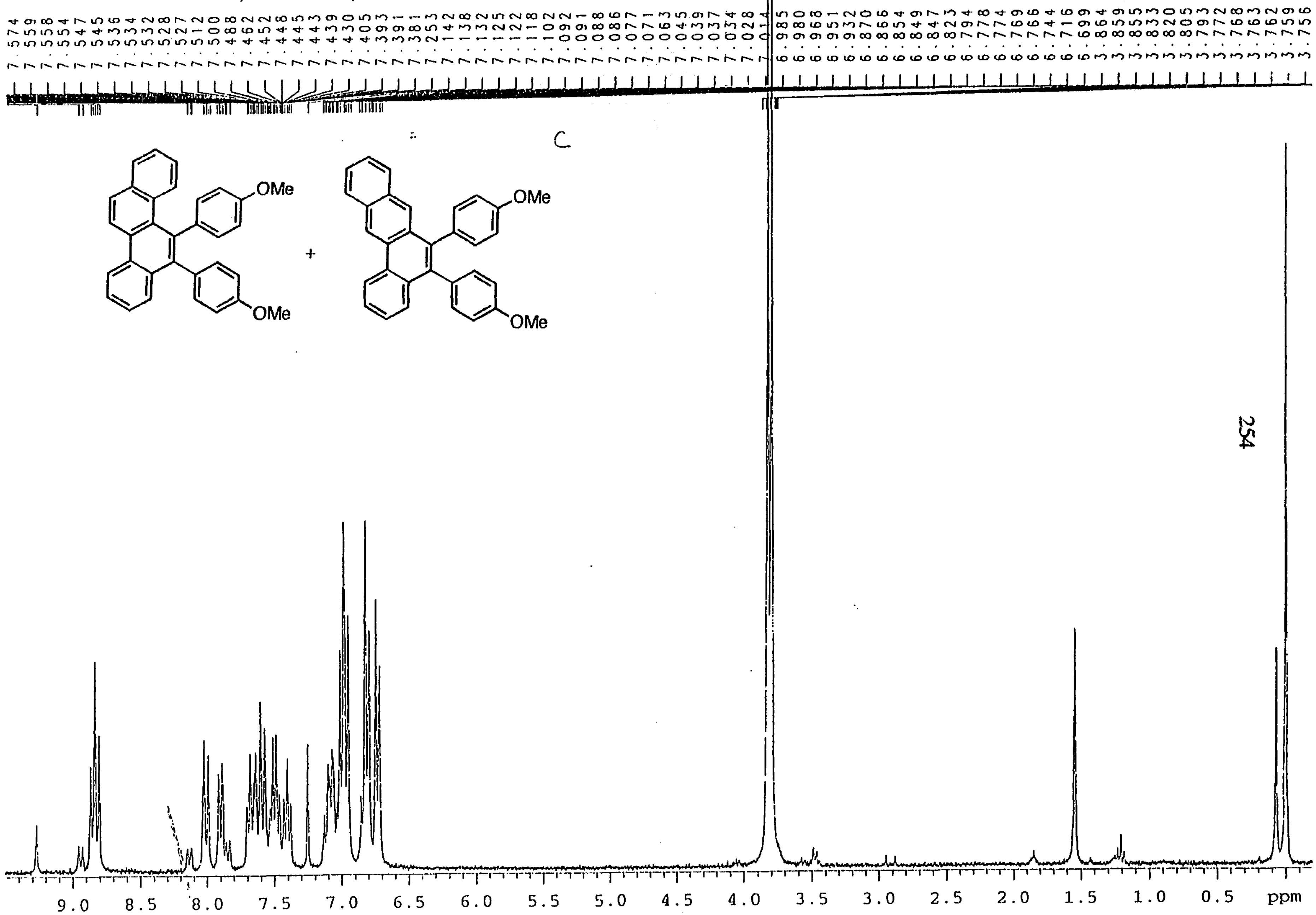


/giga/data/jmz/nmr/jmz.133.fid/1/pdata/1 unknown Mon Dec 18 15:42:43 1995

JM-117

27

Table 2, entry 25



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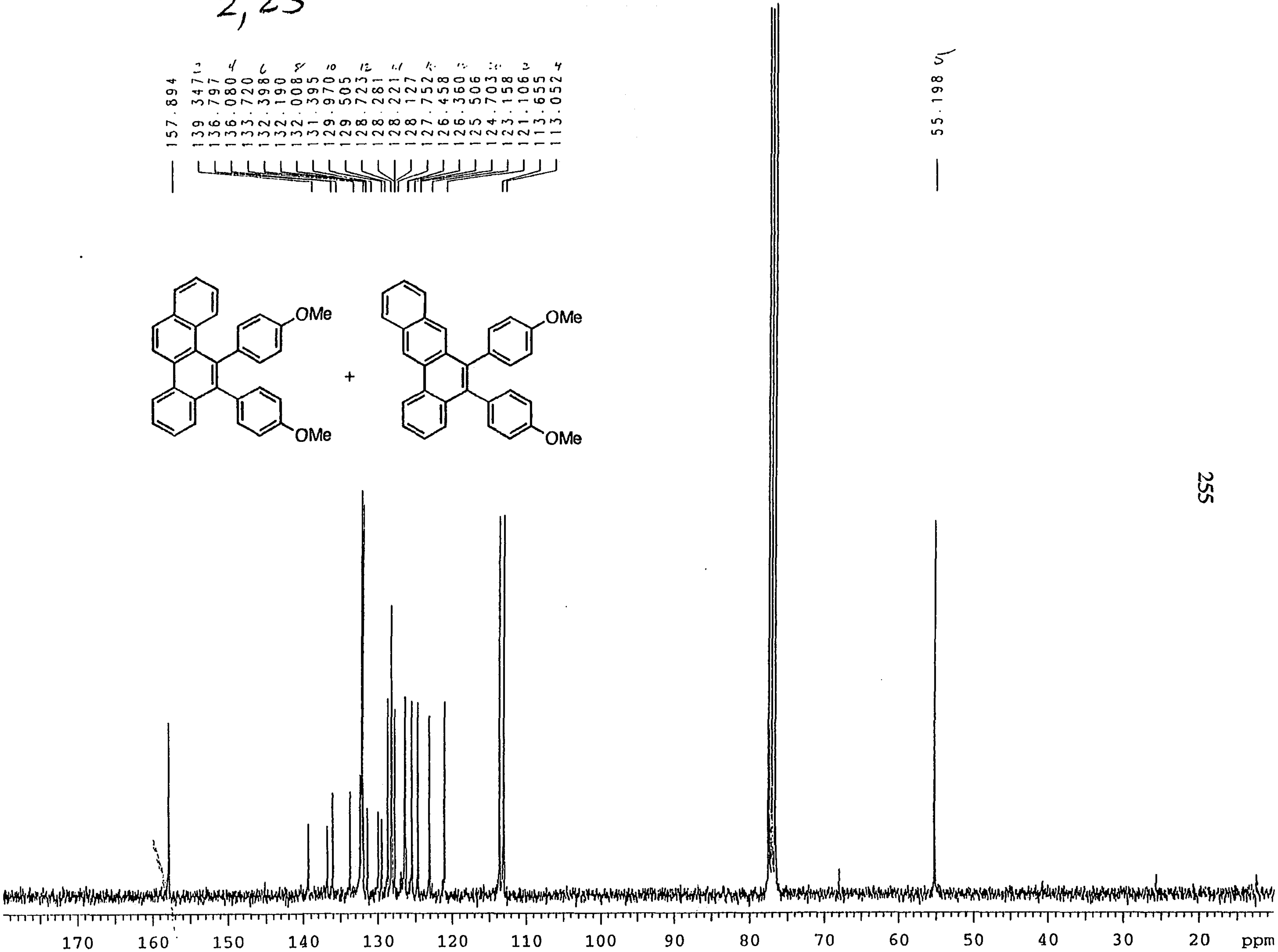
2,25 27

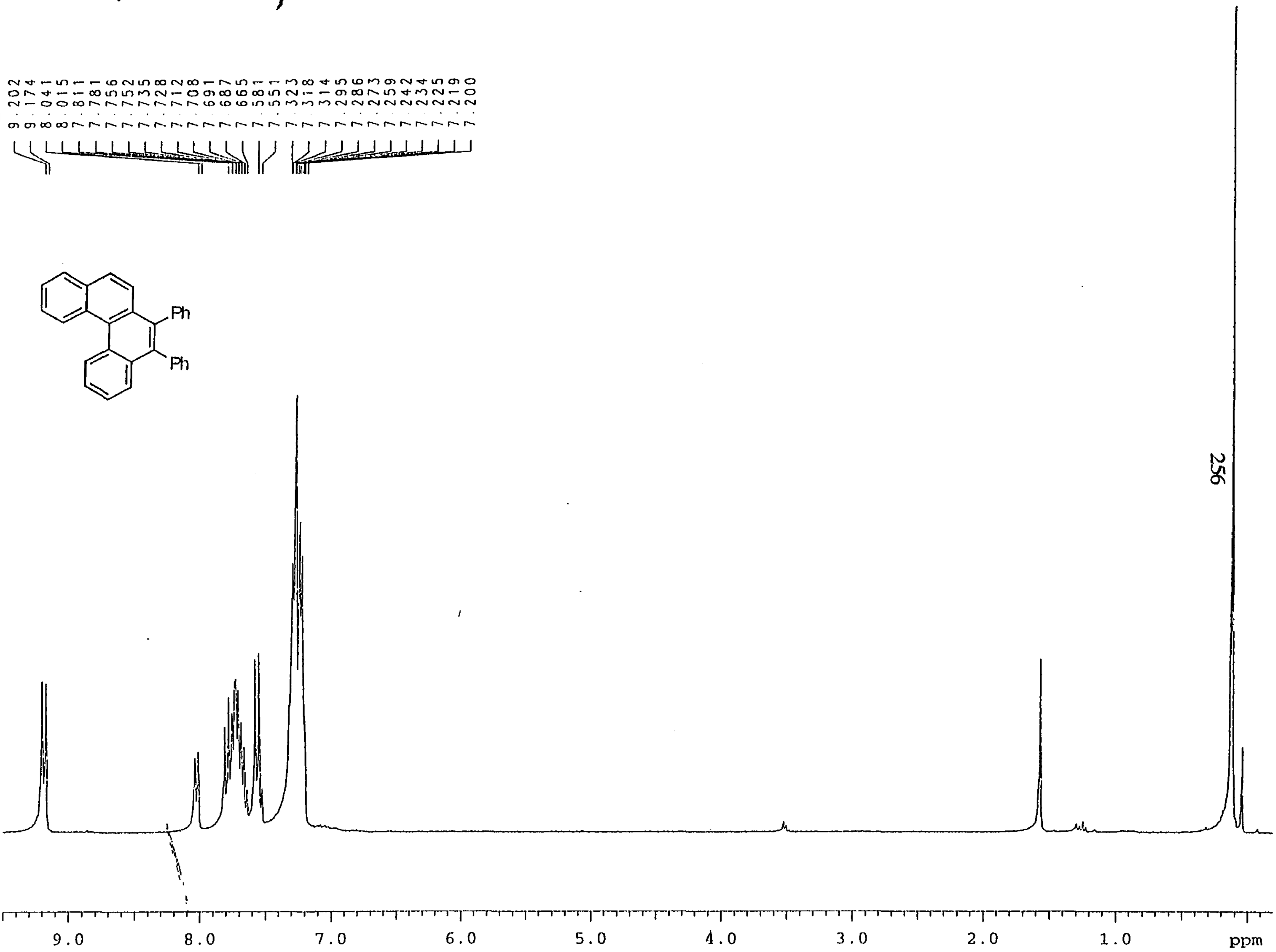


/giga/data/jmz/nmr/jmz.131.fid/1/pdata/1 unknown Sat Dec 16 01:35:02 1995

Table 2, 26 28

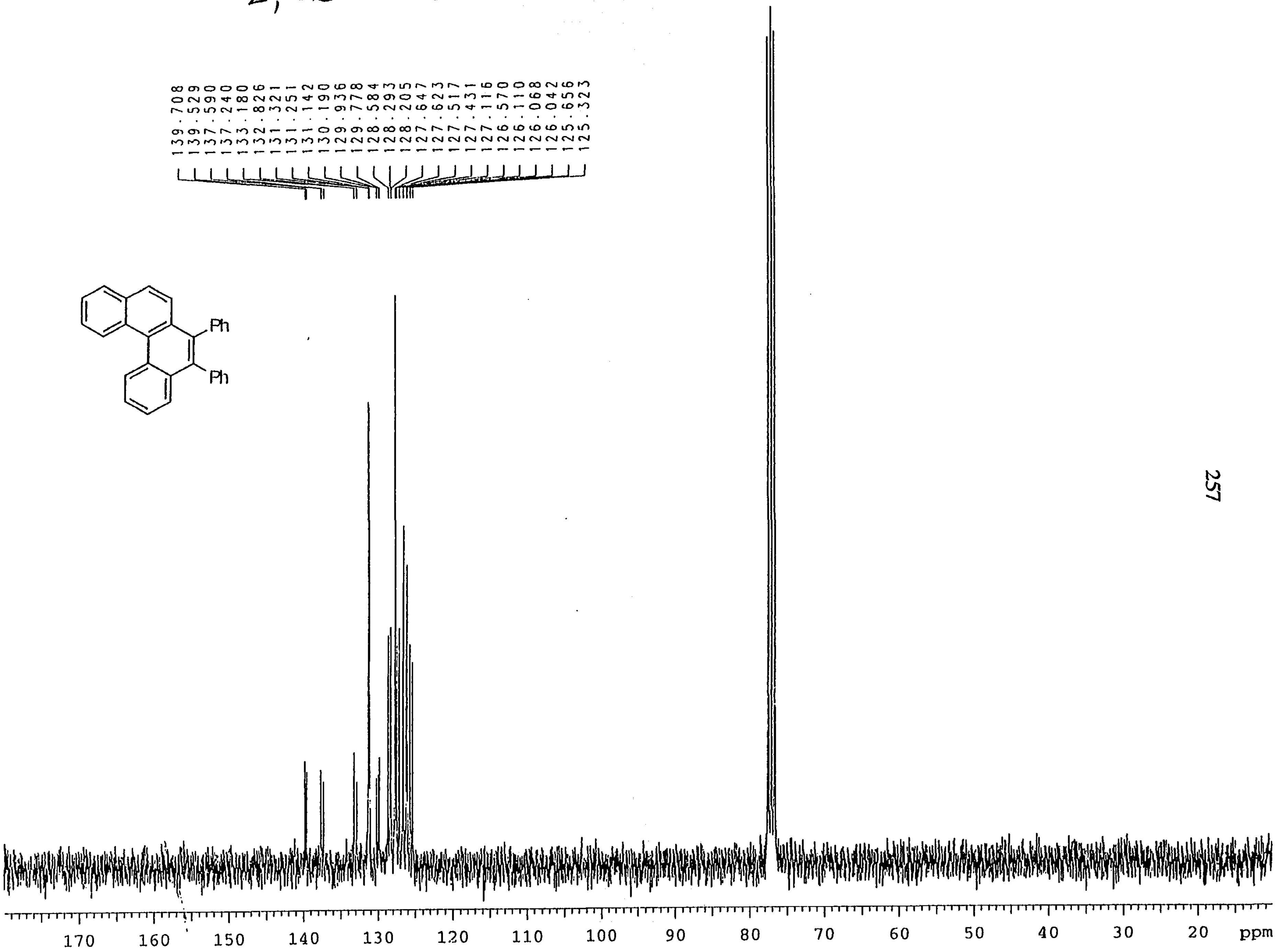
VIII – 46

^1H + ^{13}C



/giga/data/jmz/nmr/jmz.072.fid/1/pdata/1 unknown Sun Sep 3 11:43:56 1995

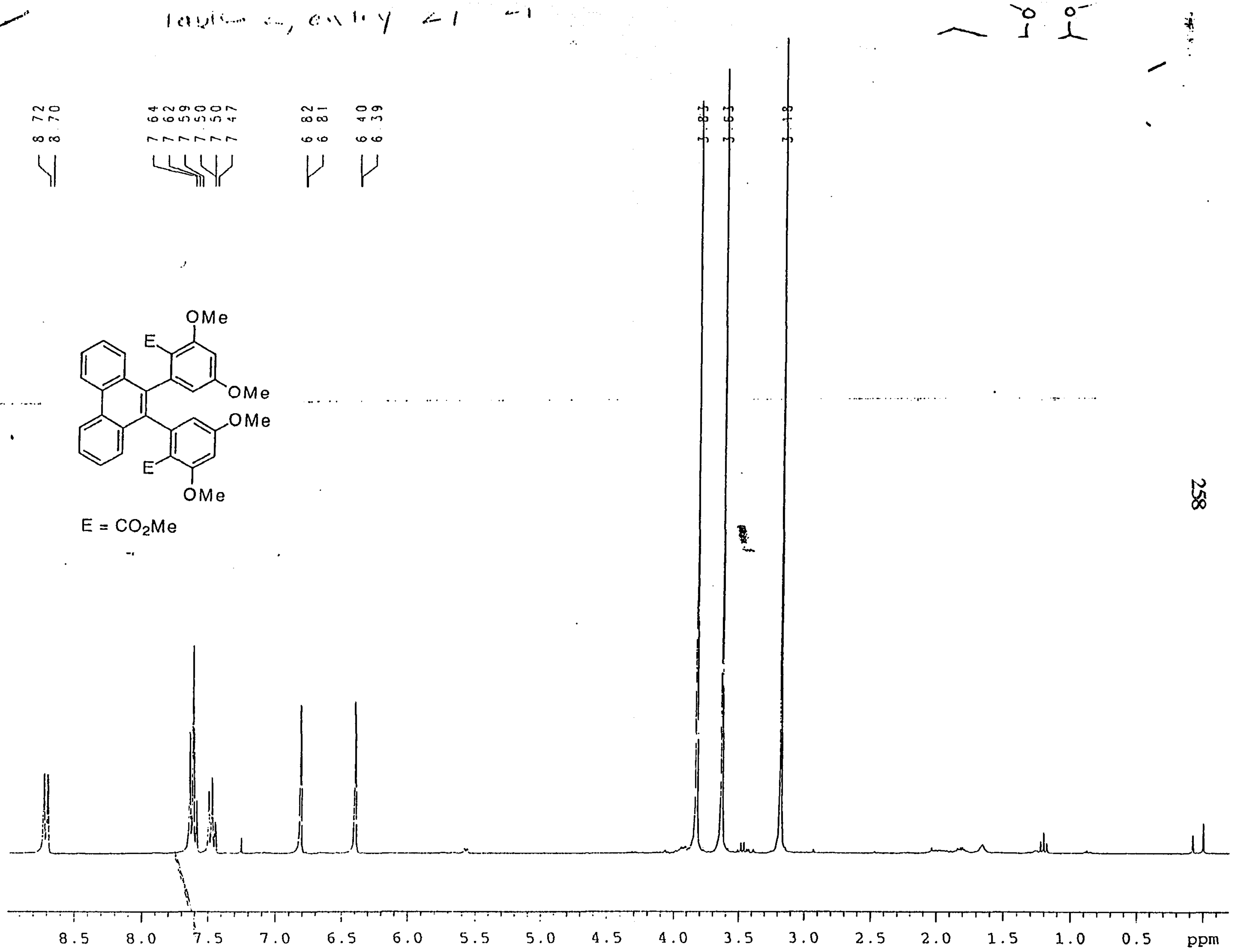
2, 26 28



/giga/data/jmz/nmr/jmz.073.fid/1/pdata/1 unknown Sun Sep 3 12:11:35 1995

VII-26

table 2, entry 21



/giga/data/jmz/nmr/jmz.039.fid/1/pdata/1 unknown Mon Jul 24 12:25:32 1995

VII-26

2, 21 21

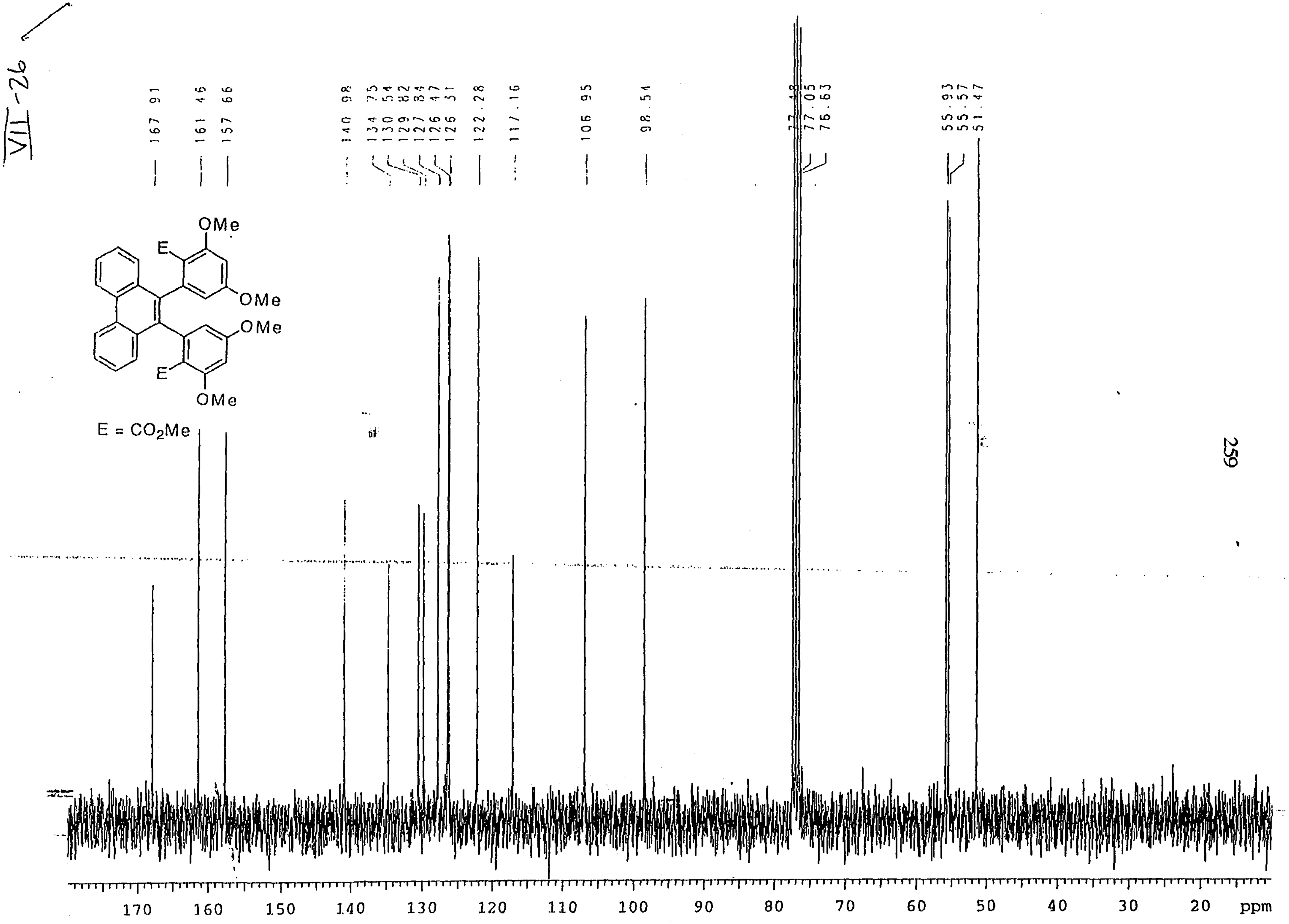


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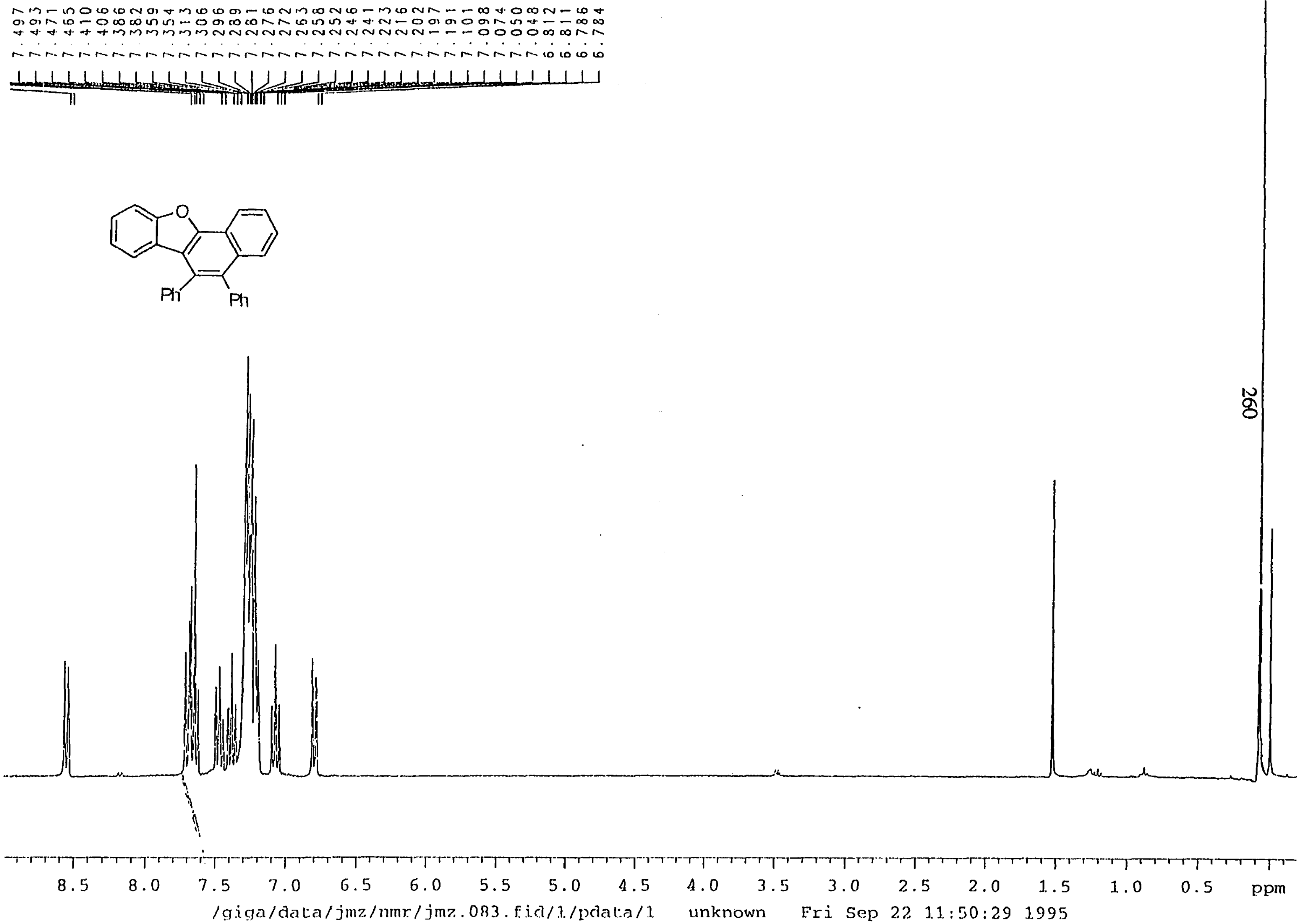
Table 2, entry 28

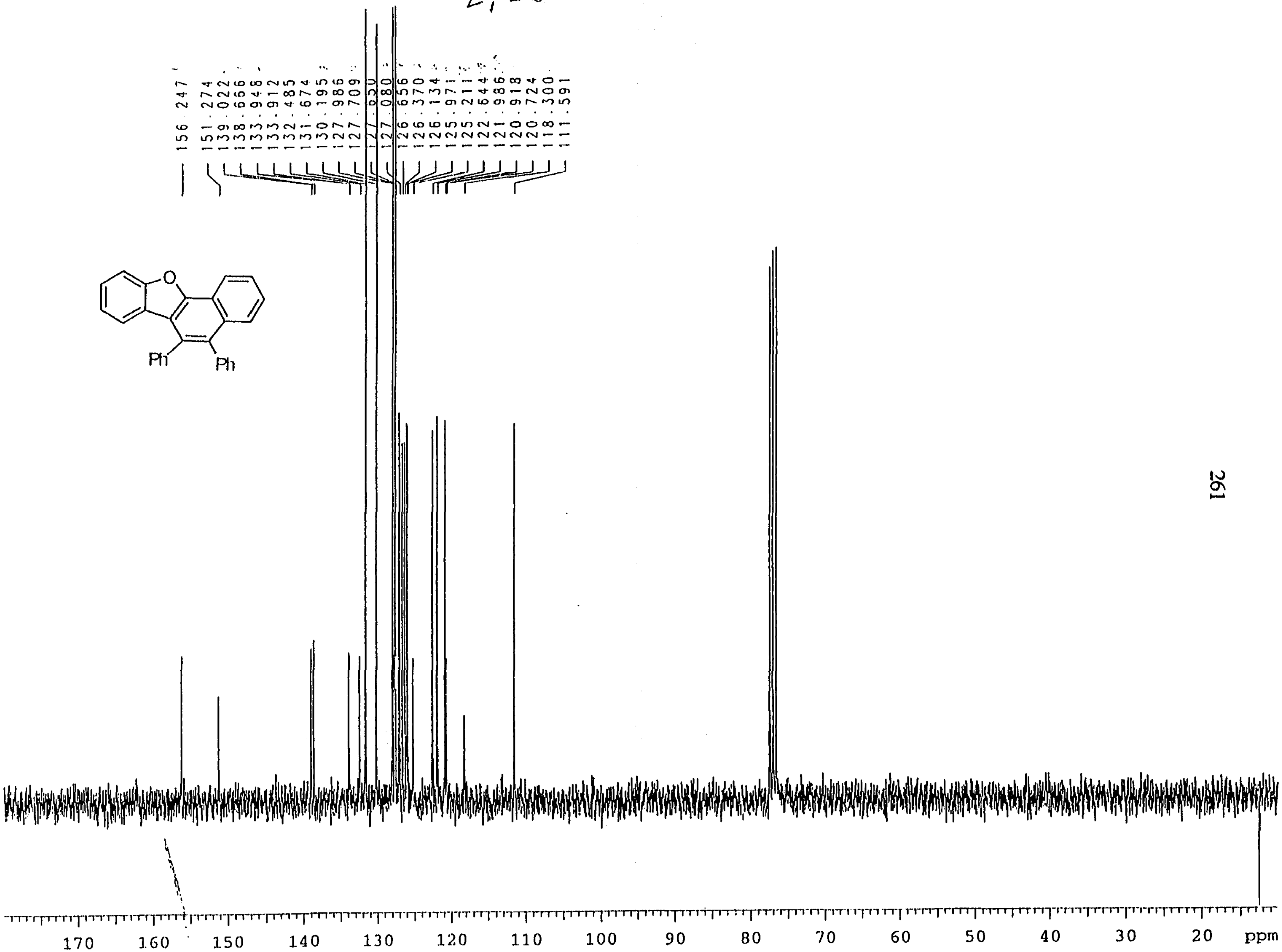
50

mp 224-225

VII - 28



2, 28 30



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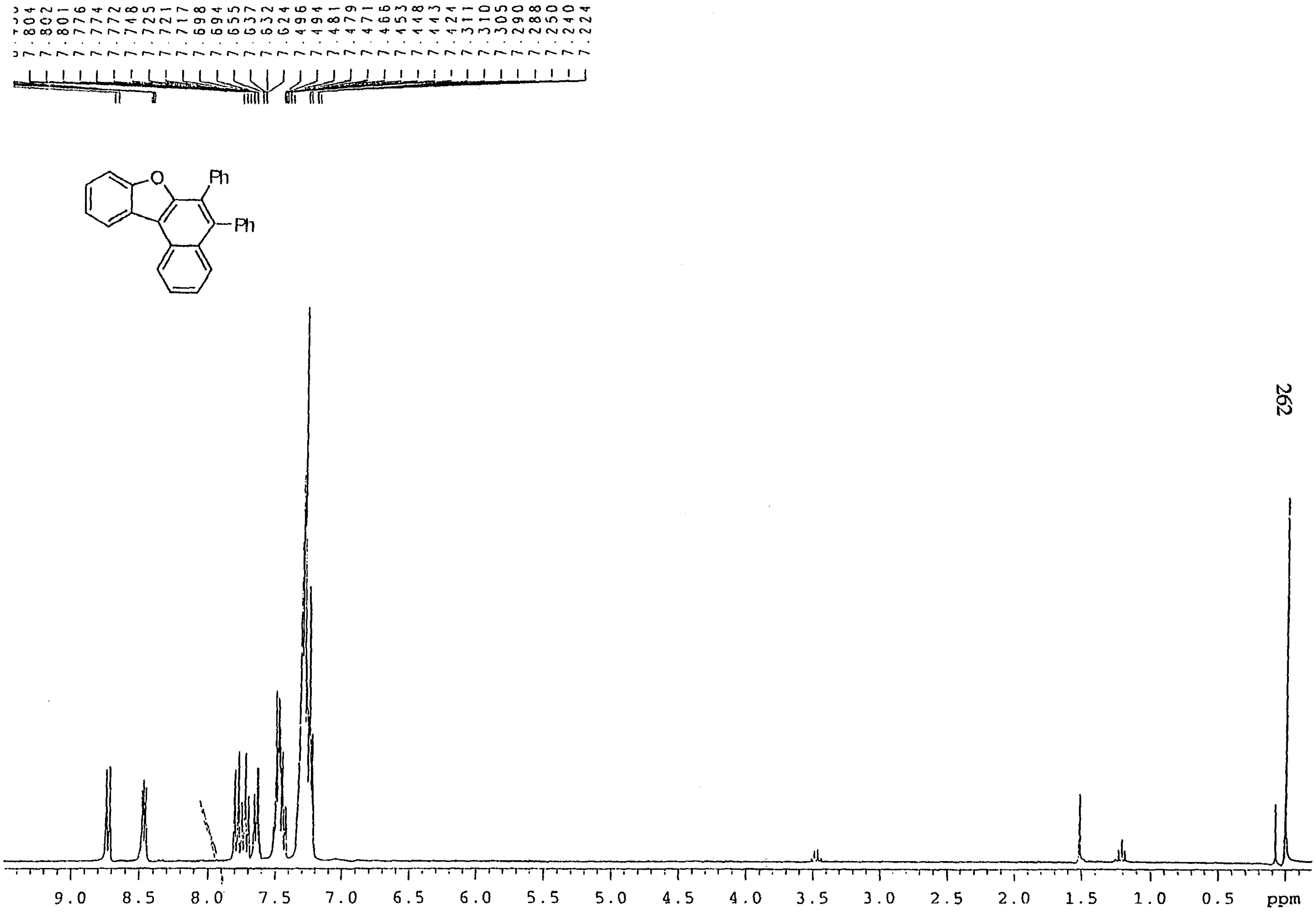
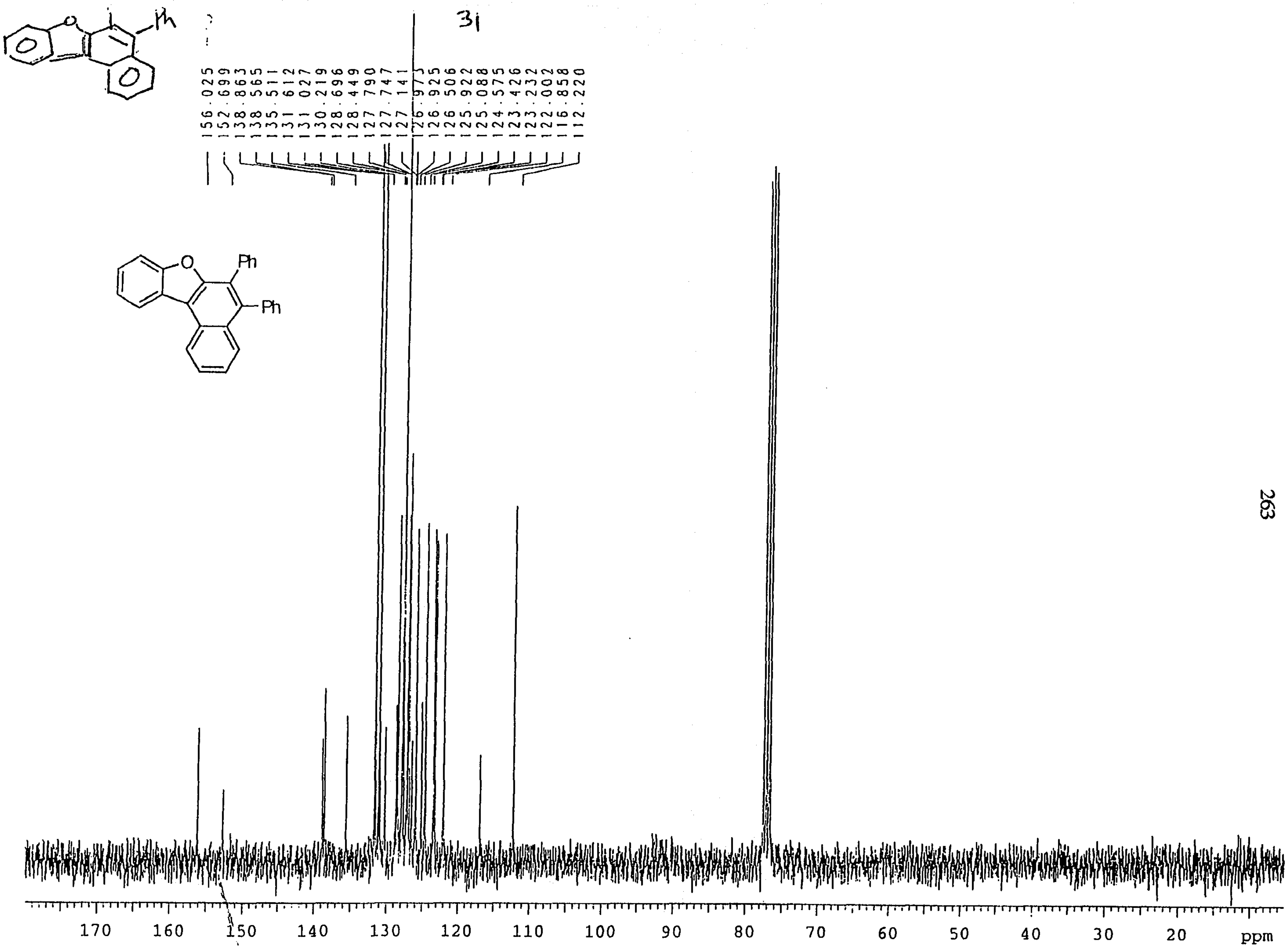
31



/giga/data/jmz/nmr/jmz.258.fid/1/pdata/1 unknown Mon Apr 29 10:15:35 1996

3l

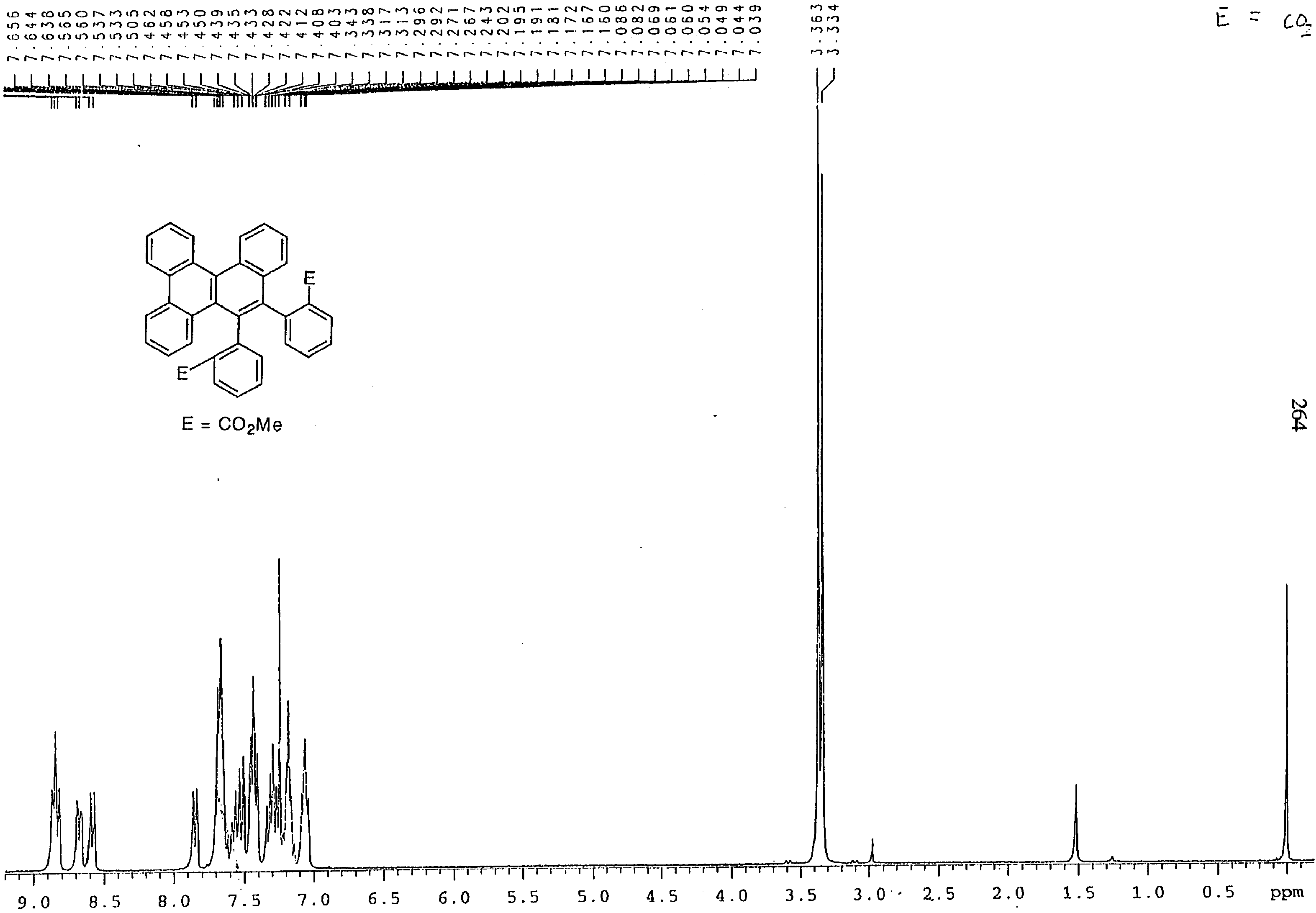


/giga/data/jmz/nmr/jmz.257.fid/1/pdata/1 unknown Fri Apr 26 10:29:14 1996

Table 2, 29 32

$C_{38}H_{26}O_4$

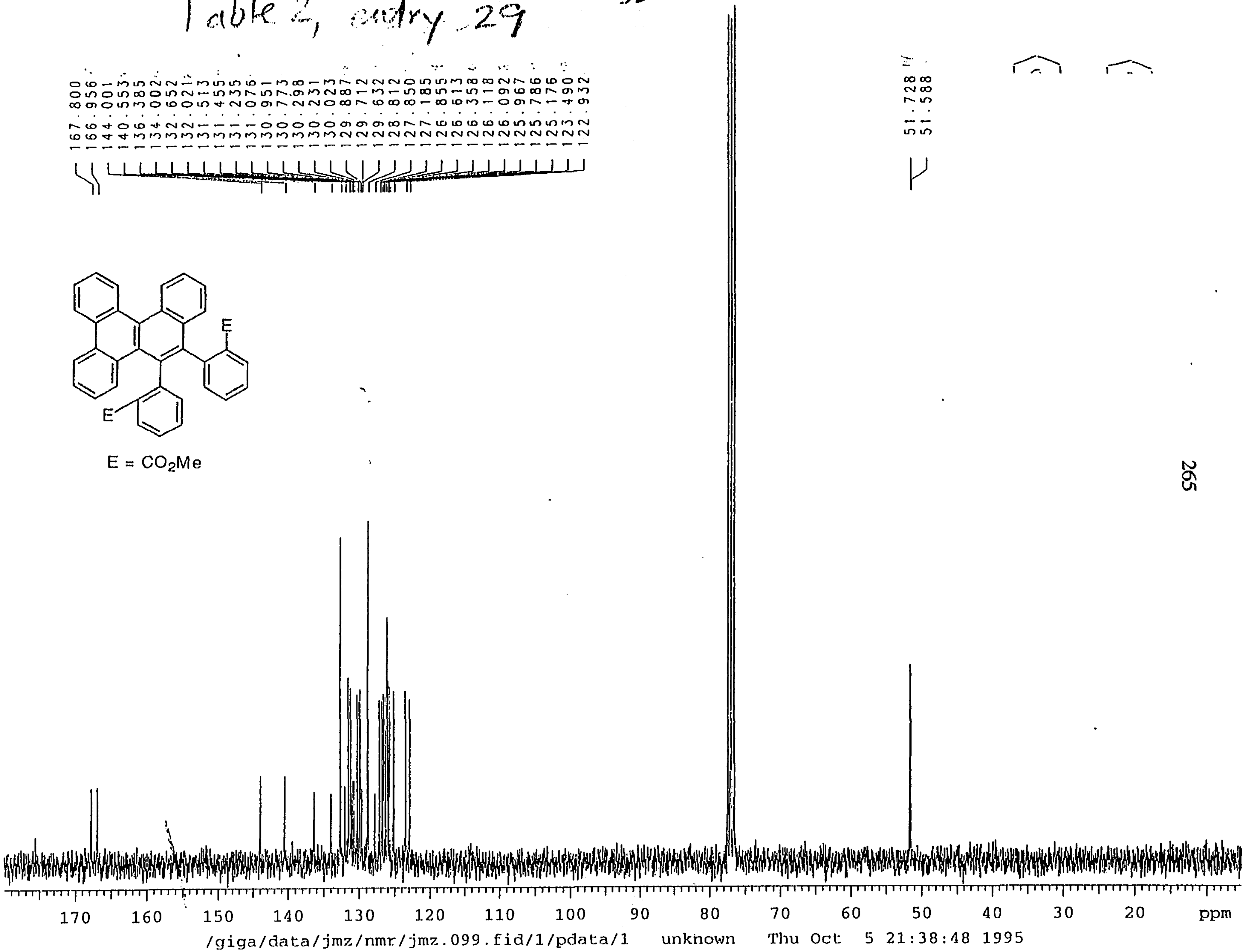
E = CO_2Me



/giga/data/jmz/nmr/jmz.098.fid/1/pdata/1 unknown Thu Oct 5 10:22:27 1995

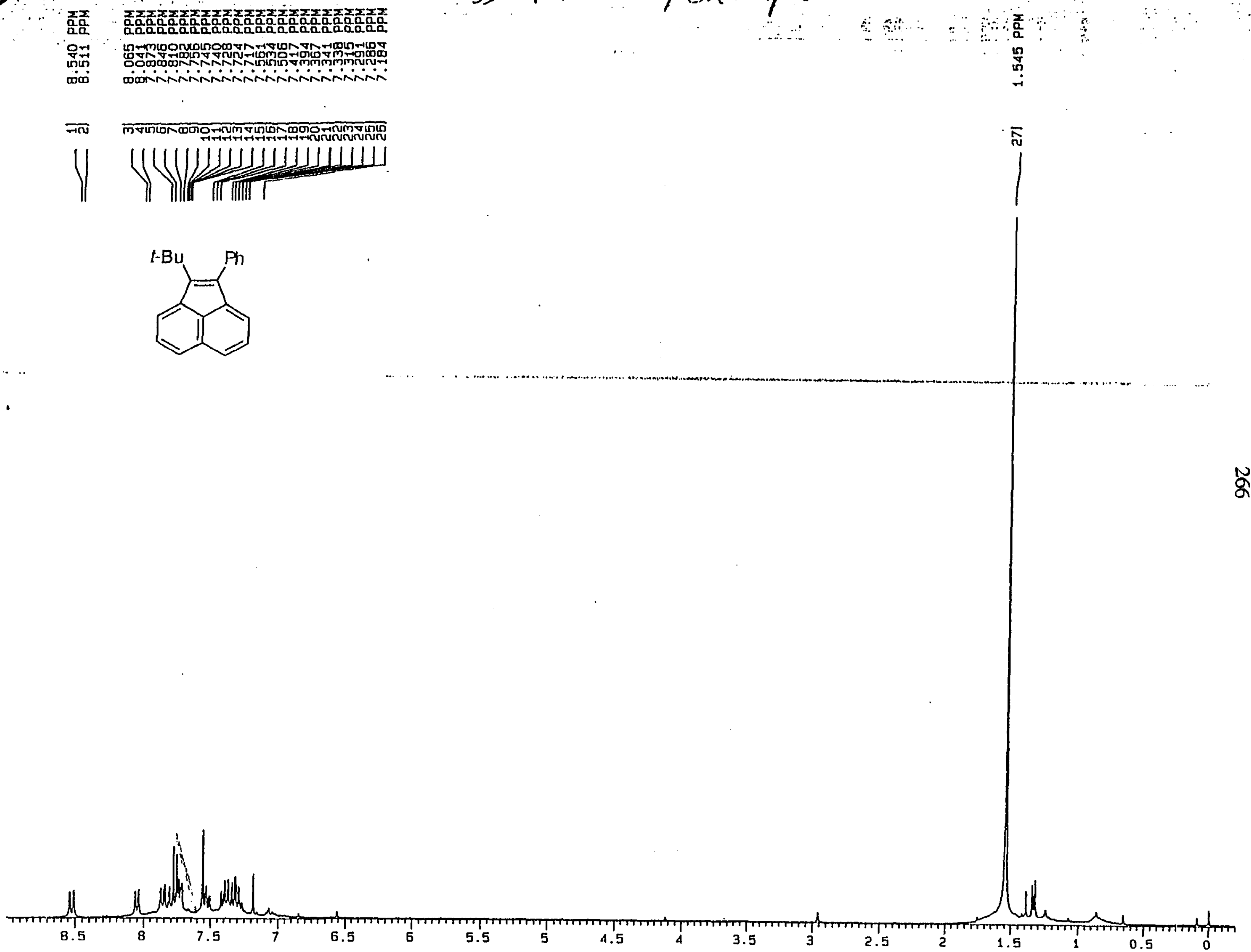
Table 2, entry 29

32



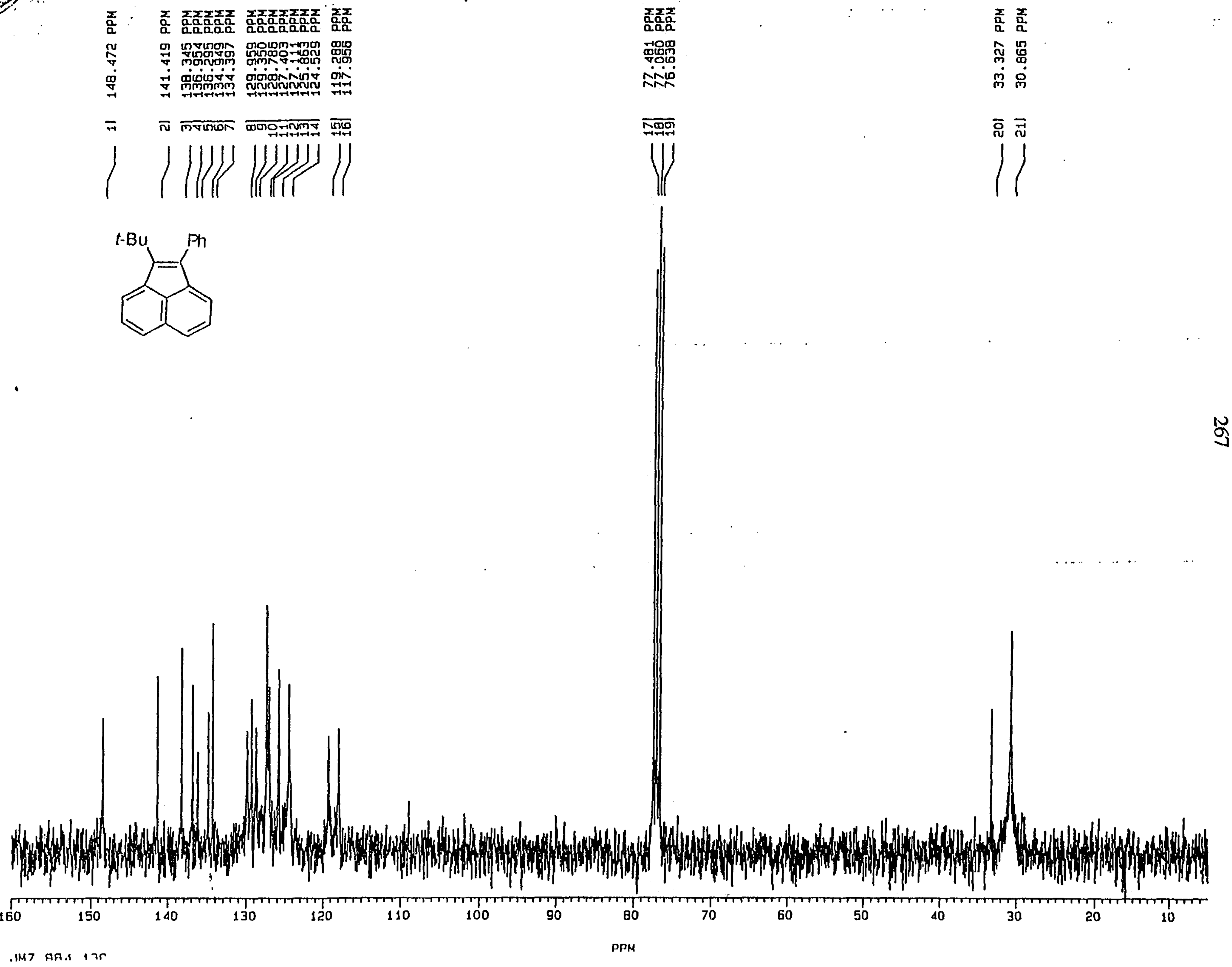
33 Table 2, entry 30

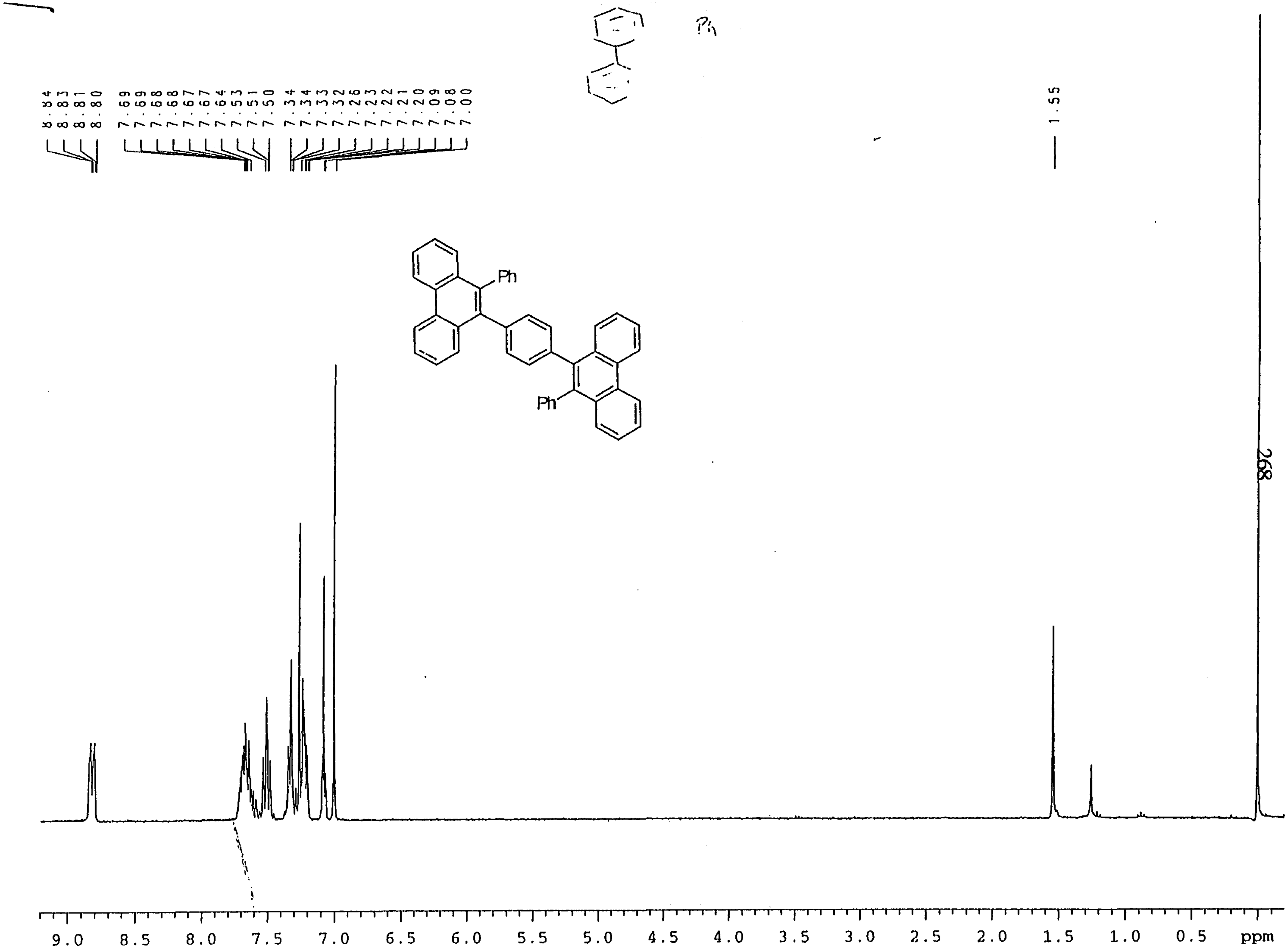
III-17



JMZ.880

2, 30 33


1] 148.472 PPM
2] 141.419 PPM
3] 138.345 PPM
4] 136.954 PPM
5] 136.295 PPM
6] 134.949 PPM
7] 134.397 PPM
8] 129.959 PPM
9] 129.350 PPM
10] 128.786 PPM
11] 127.403 PPM
12] 127.111 PPM
13] 125.863 PPM
14] 124.529 PPM
15] 119.288 PPM
16] 117.956 PPM
17] 77.481 PPM
18] 77.060 PPM
19] 76.638 PPM
20] 33.327 PPM
21] 30.865 PPM
t-Bu
Ph
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM
JM7 884 13C



file:/giga/data/jmz/nmr/jmz.006.fid/1/pdata/1/plotfile.3   user:unknown   date:Thu Jun 1 18:45:16 1995

Table 2, entry 32. 35

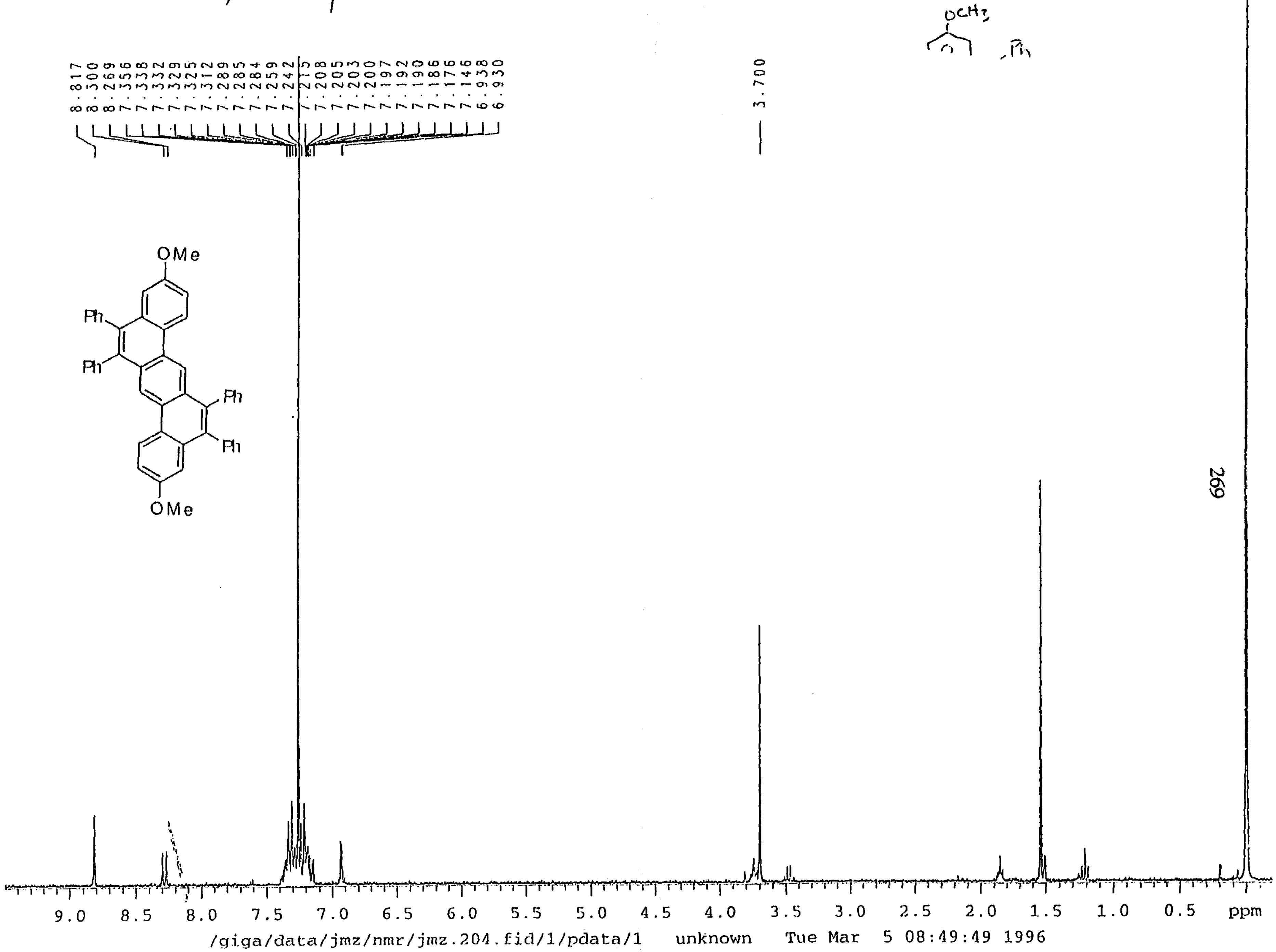
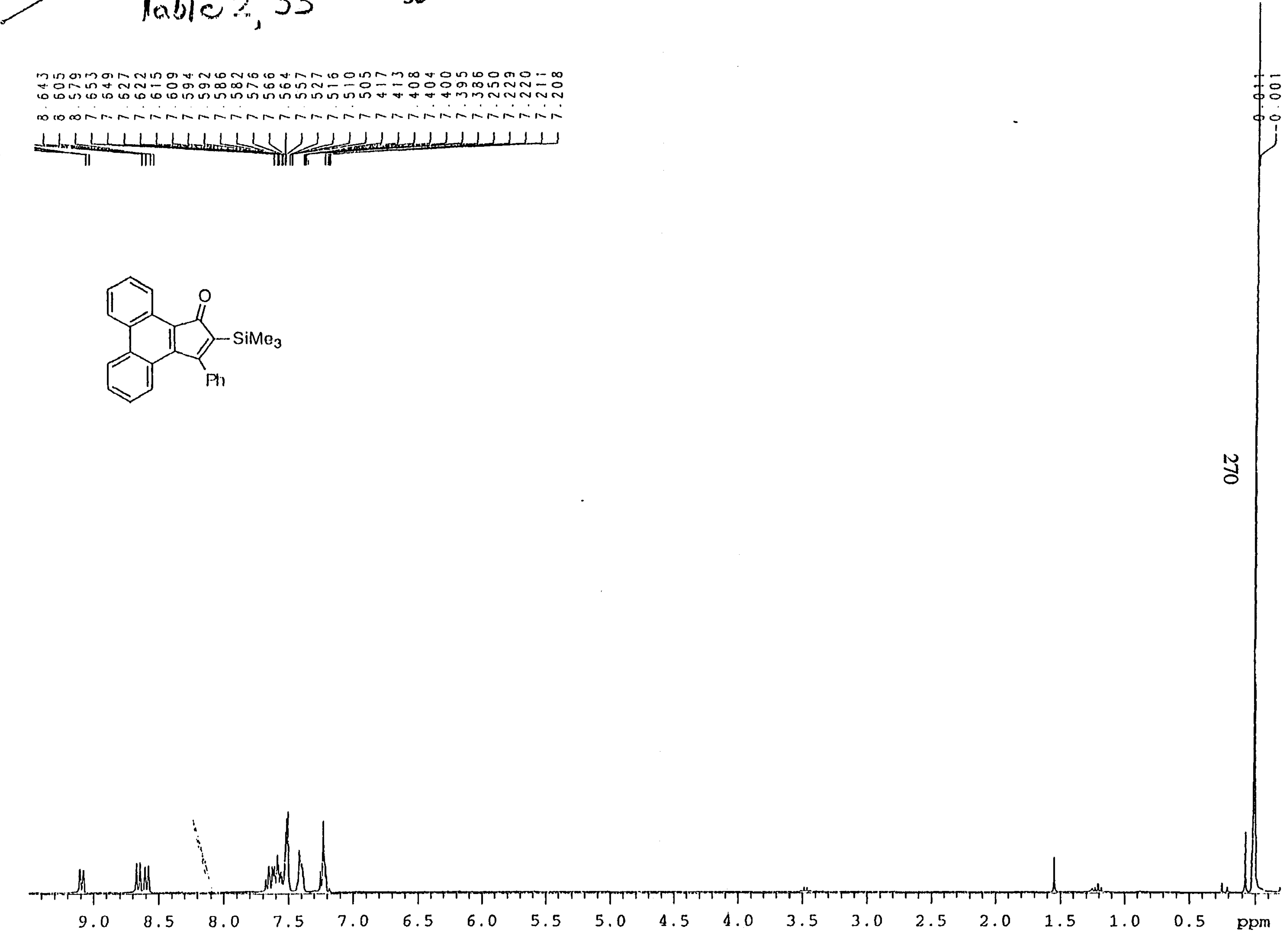


Table 2, 33

36

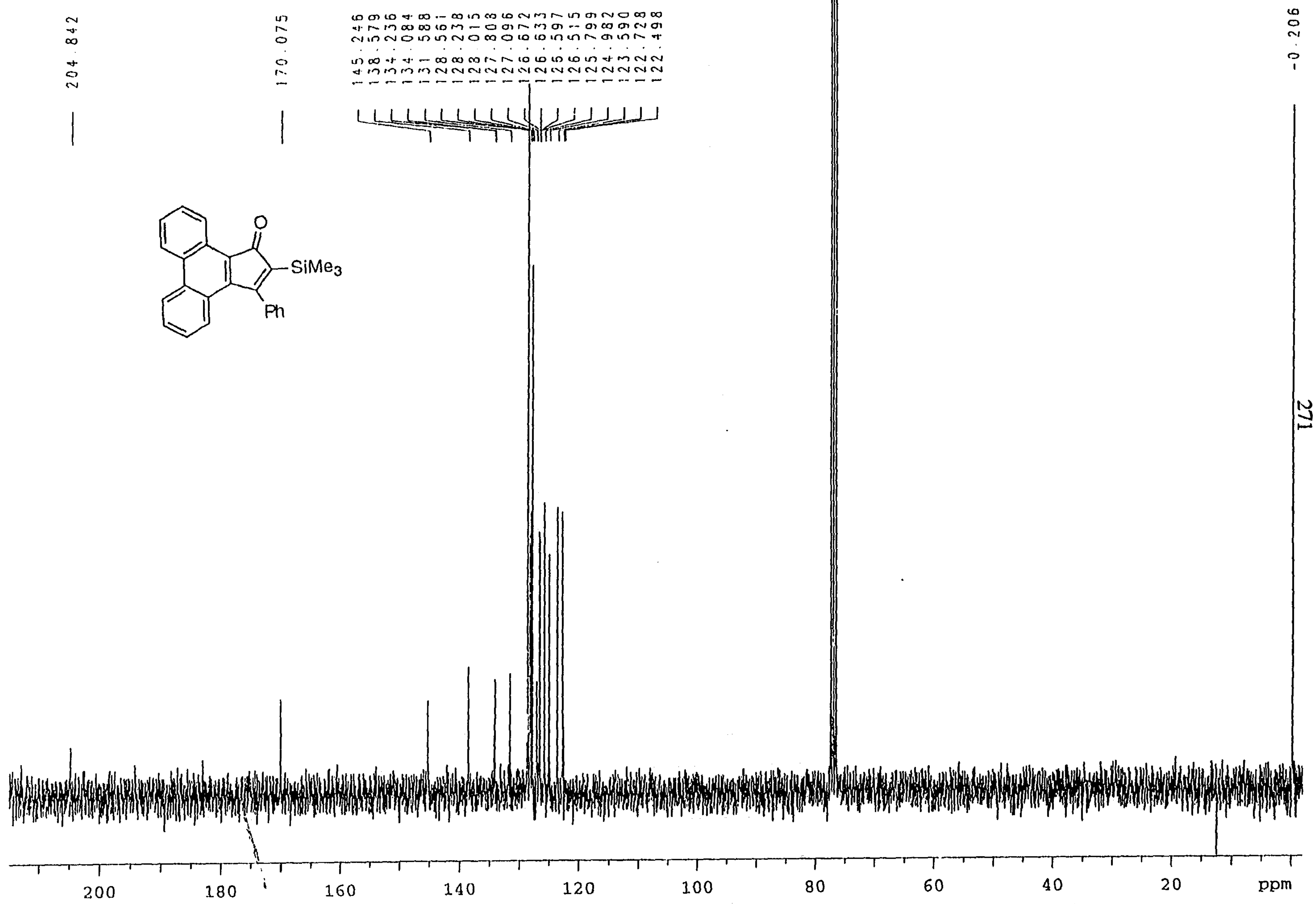
VII-66



/giga/data/jmz/nmr/jmz.111.fid/1/pdata/1 unknown Thu Oct 26 13:01:19 1995

30

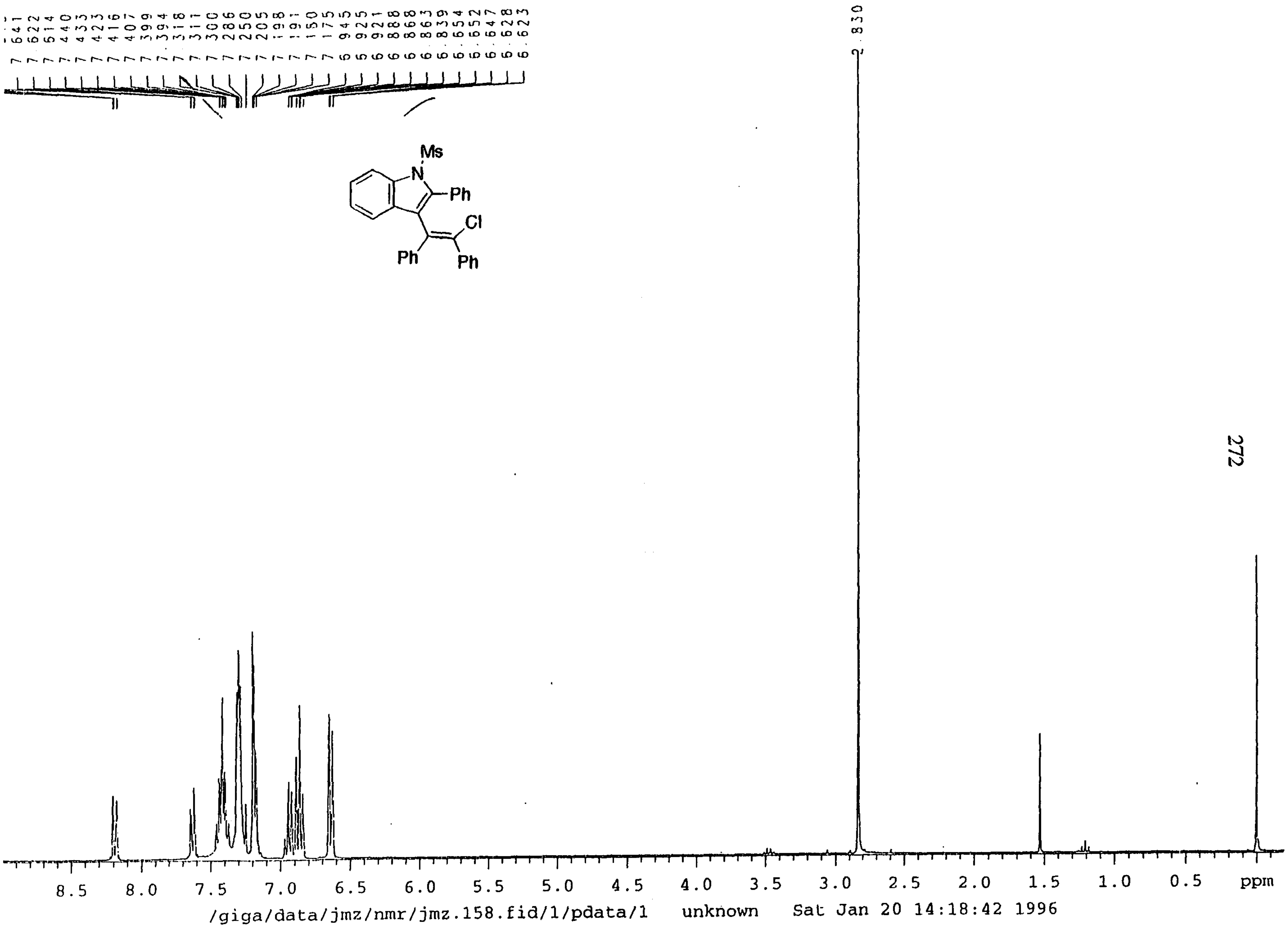
2,33

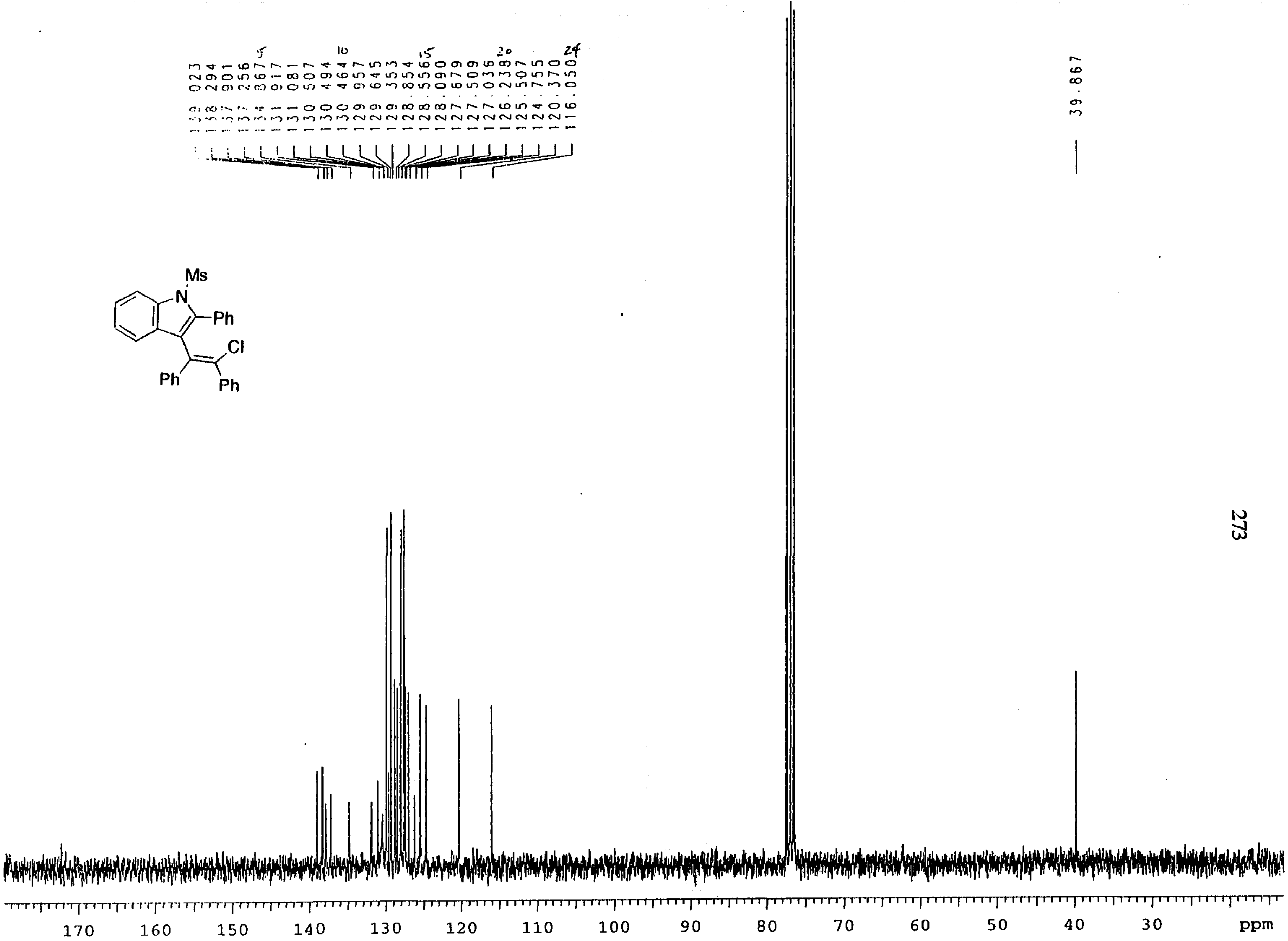


/giga/data/jmz/nmr/jmz.114.fid/1/pdata/1   unknown   Mon Oct 30 09:46:36 1995

271

^1H


7.641
7.622
7.614
7.440
7.433
7.423
7.416
7.407
7.399
7.394
7.318
7.311
7.300
7.286
7.250
7.205
7.198
7.191
7.150
7.175
6.945
6.925
6.921
6.888
6.868
6.863
6.839
6.654
6.652
6.647
6.628
6.623
2.830
Ms
N
Ph
Cl
Ph
Ph
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
/giga/data/jmz/nmr/jmz.158.fid/1/pdata/1 unknown Sat Jan 20 14:18:42 1996



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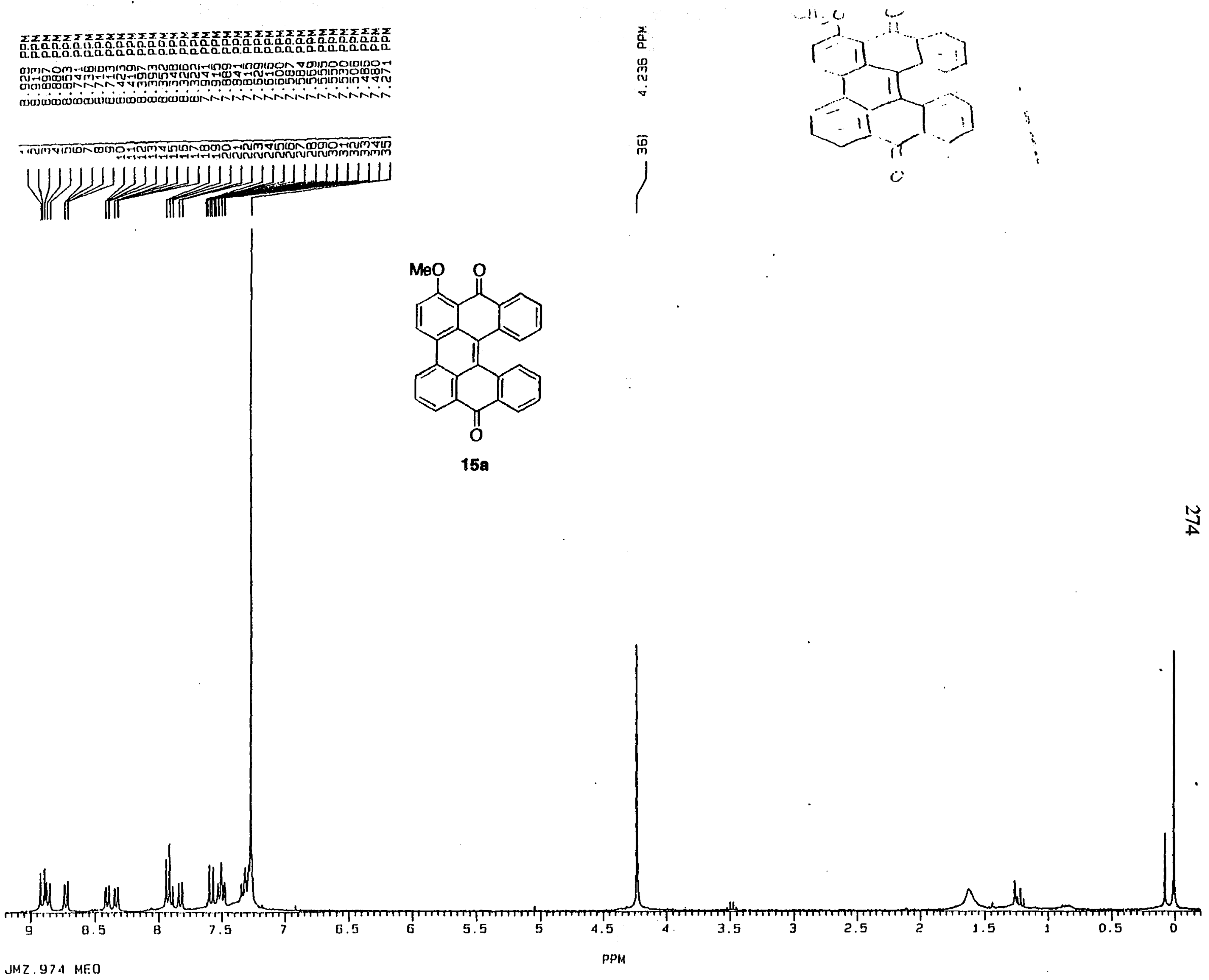
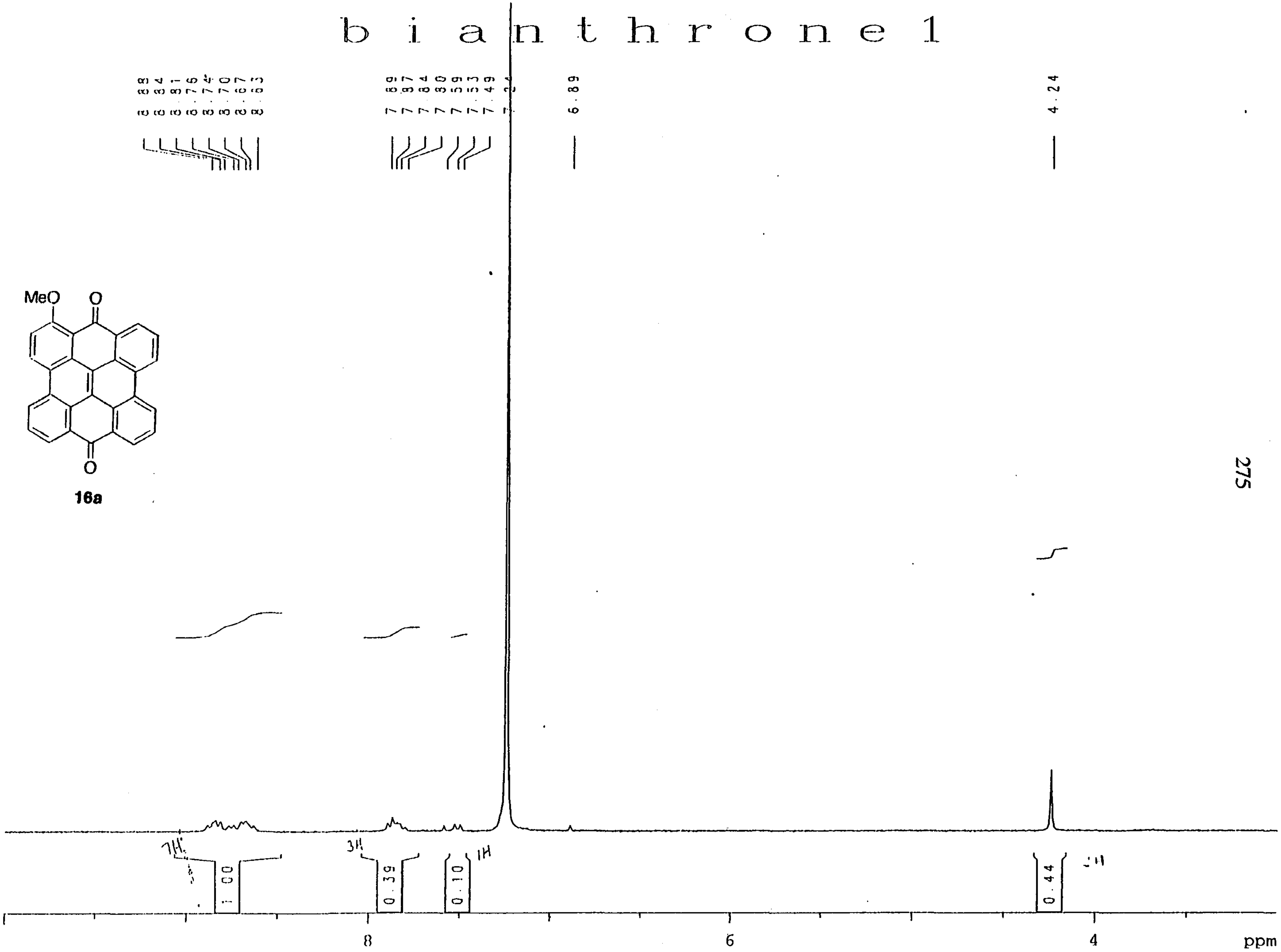
VI-5 1

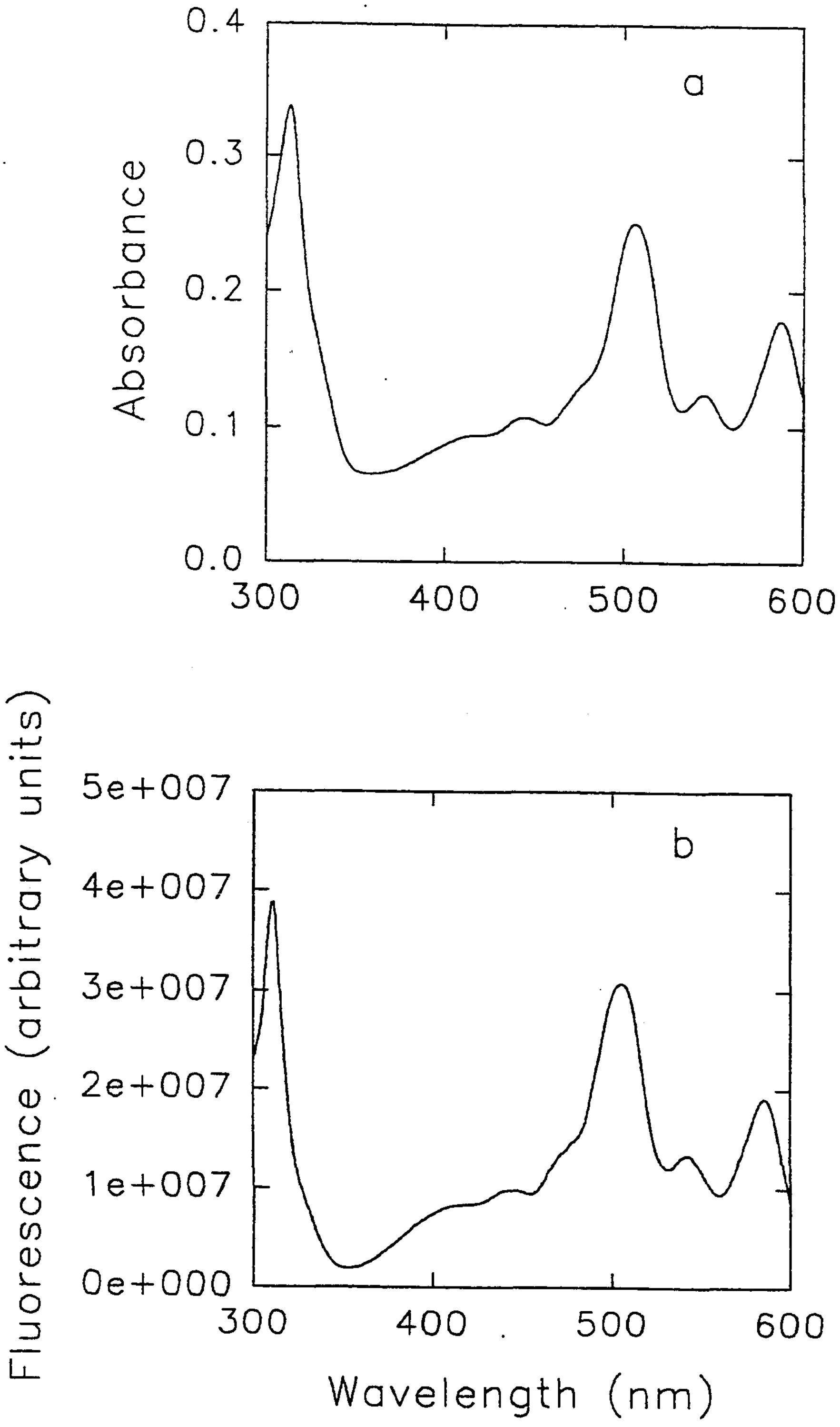


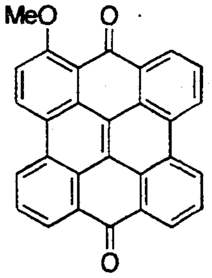
15a

JMZ.974 MEO



file:/giga/data/jmz/nmr/sajmz.002.fid/1/pdata/1/plotfile.2 user:unknown date:Mon May 15 23:37:16 1995

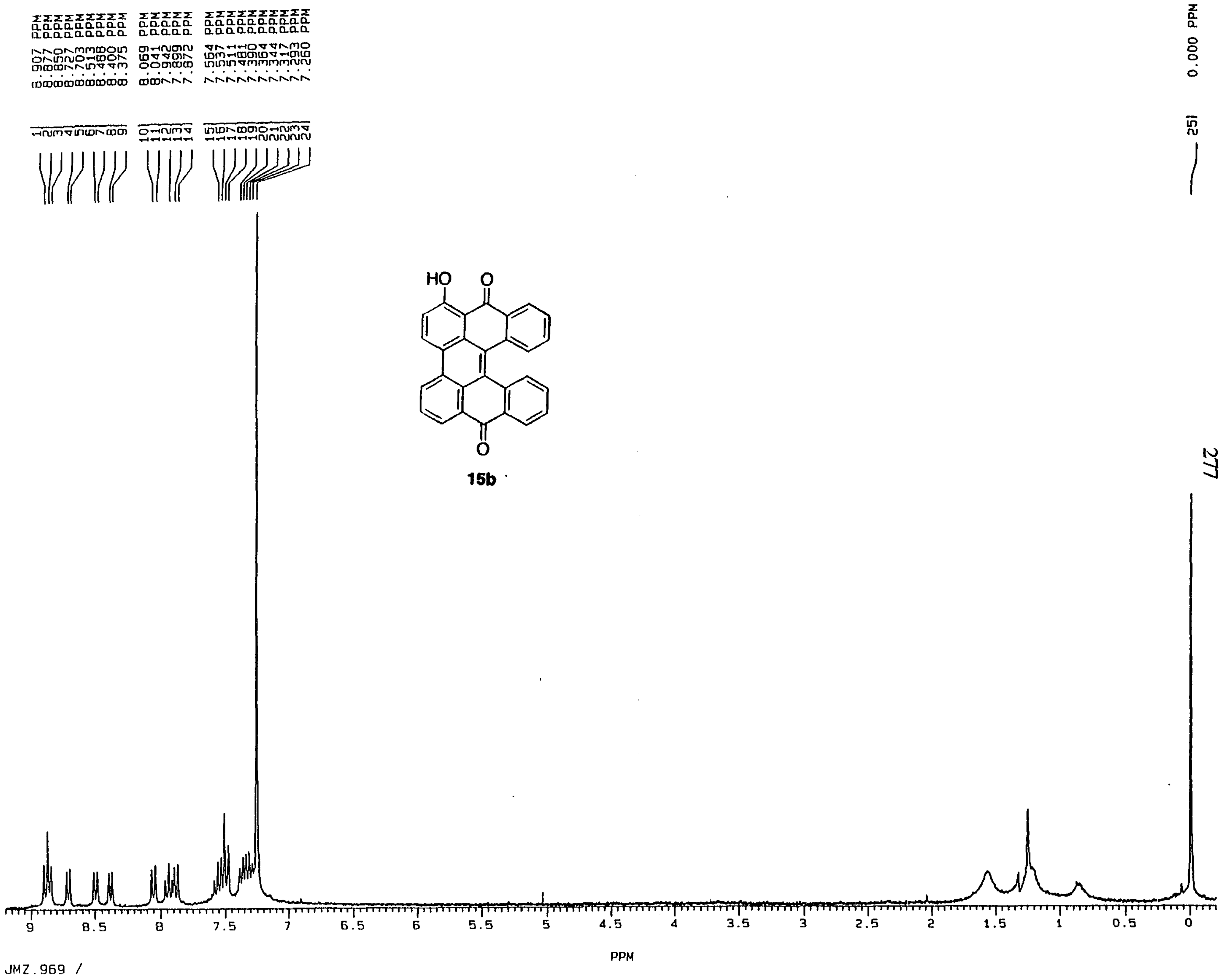




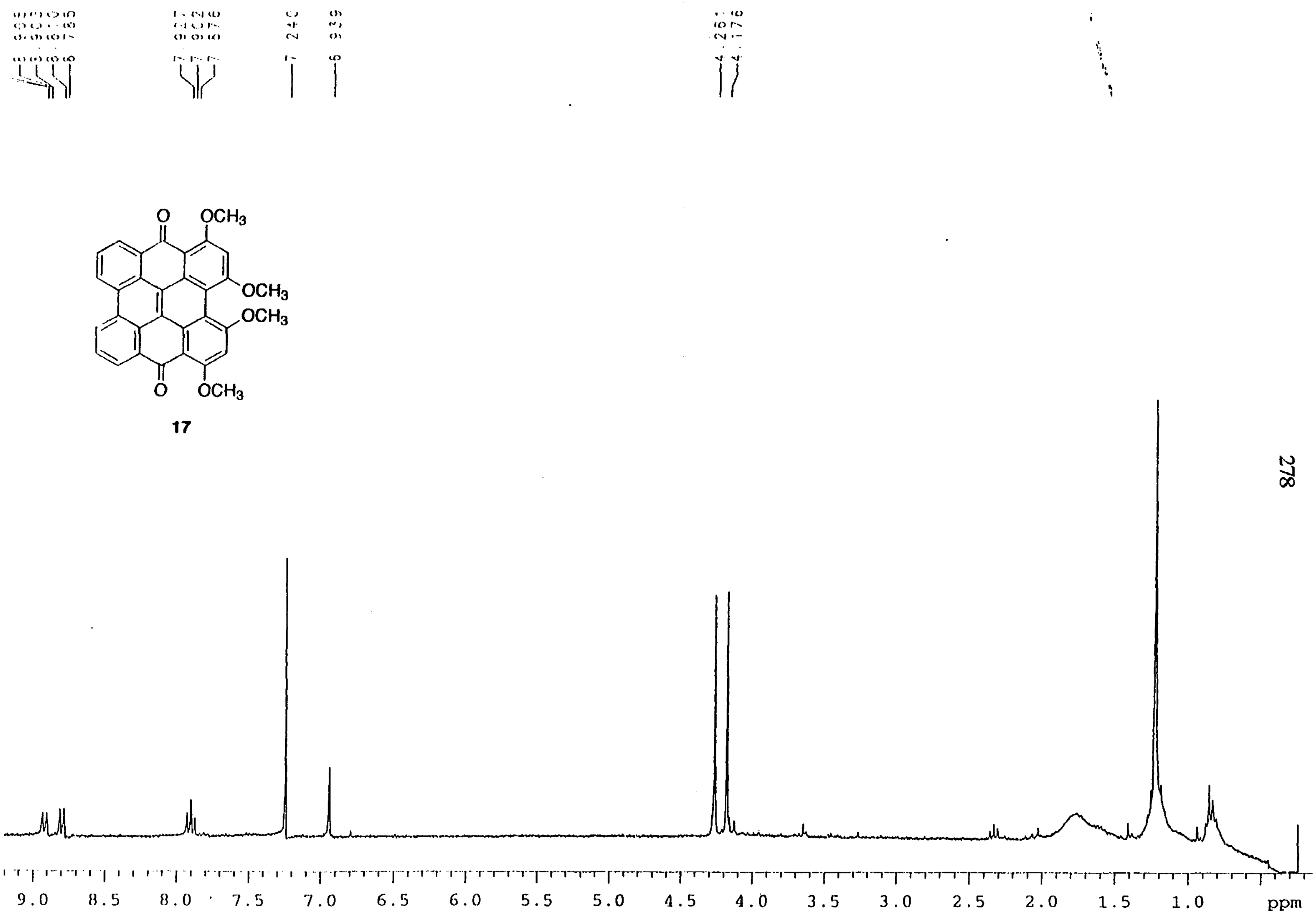
16a

UV-Vis absorption and fluoresence excitation in $CHCl_3$

VI -64.

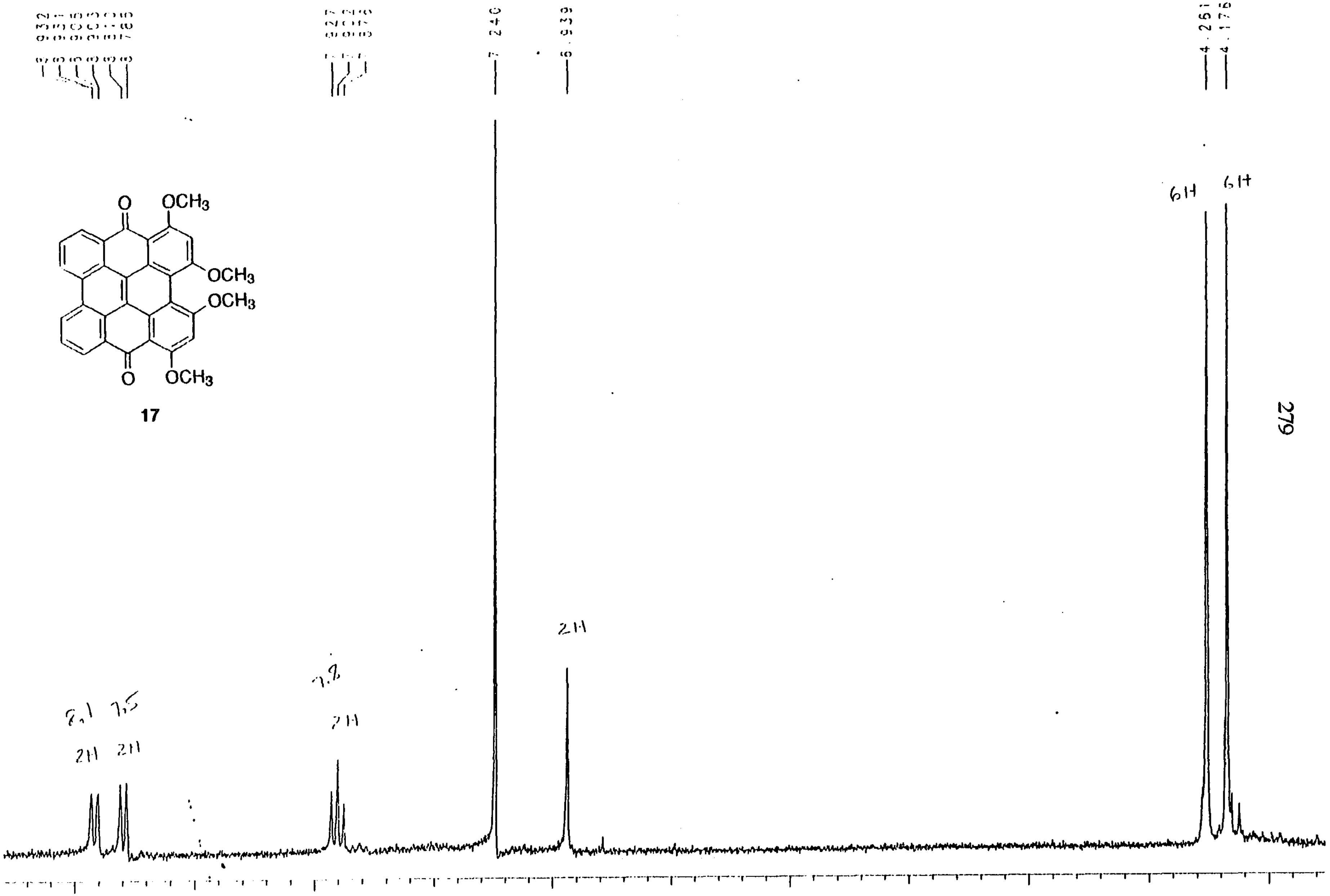

1 8.907 PPM
2 8.877 PPM
3 8.850 PPM
4 8.727 PPM
5 8.703 PPM
6 8.513 PPM
7 8.488 PPM
8 8.400 PPM
9 8.375 PPM
10 8.069 PPM
11 8.041 PPM
12 7.942 PPM
13 7.899 PPM
14 7.872 PPM
15 7.564 PPM
16 7.537 PPM
17 7.511 PPM
18 7.481 PPM
19 7.390 PPM
20 7.364 PPM
21 7.344 PPM
22 7.317 PPM
23 7.293 PPM
24 7.260 PPM
25 0.000 PPM
HO
O
O
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
PPM
JMZ.969 /

15b


7.240
6.939
4.251
4.176
O
OCH3
OCH3
OCH3
O
OCH3
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
/giga/data/jmz/nmr/jmz.065.fid/1/pdata/1 unknown Thu Aug 10 12:13:41 1995

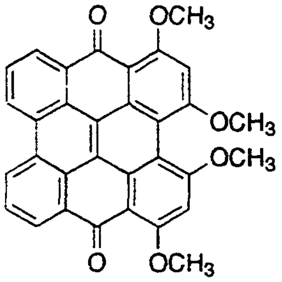
17

VII-54

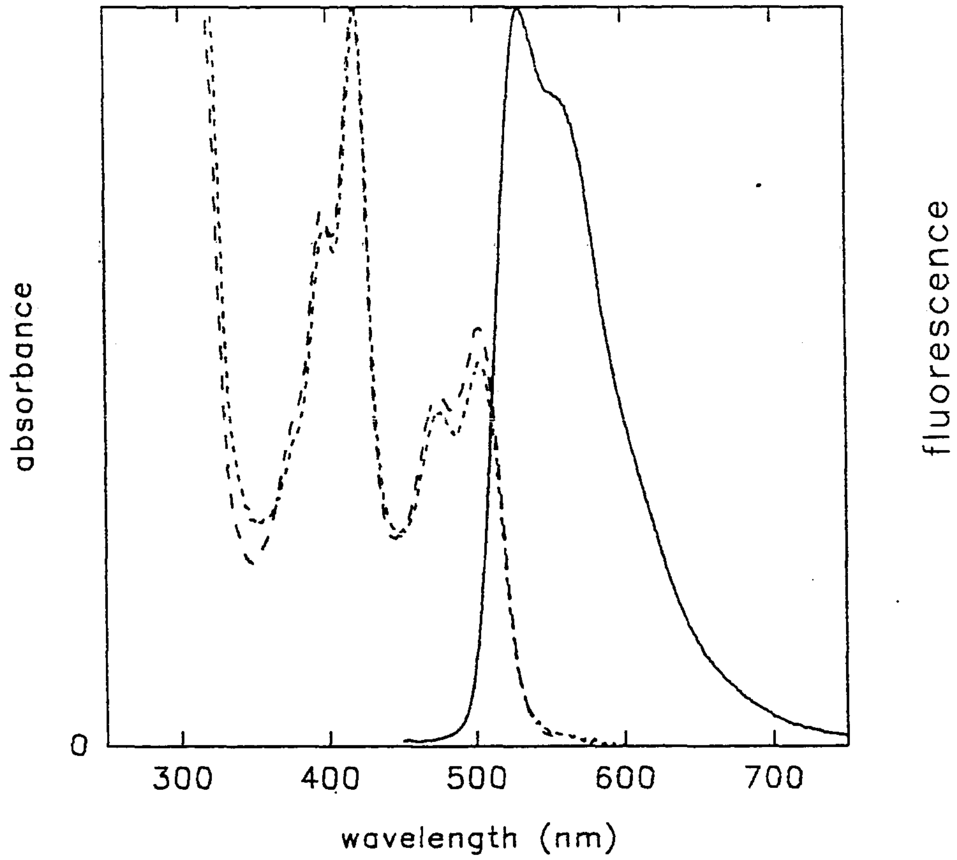


17

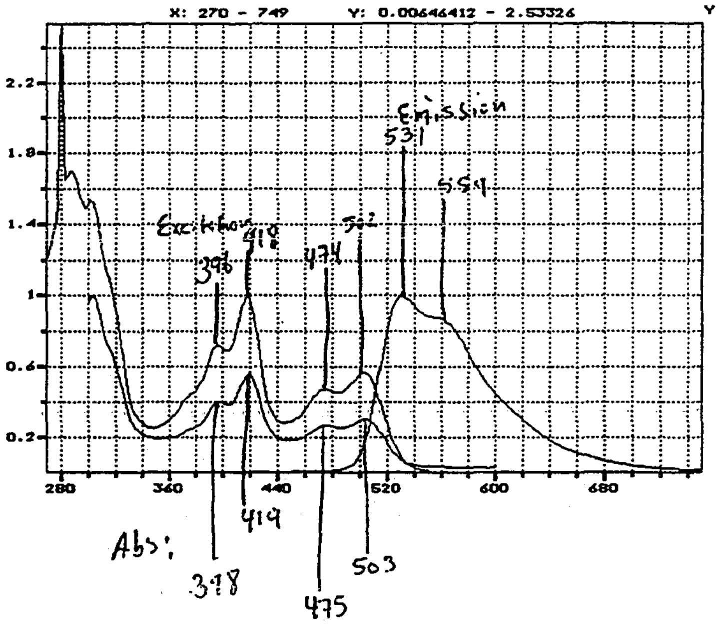
/giga/data/jmz/nmr/jmz.065.fid/1/pdata/1 unknown Thu Aug 10 12:13:11 1995

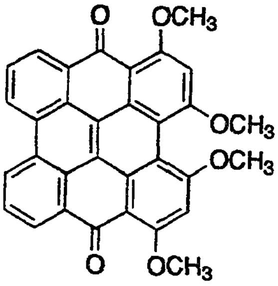


17



UV-Vis absorption and fluoresence excitation in DMSO





17

UV-Vis absorption and fluoresence excitation in DMSO

GENERAL ACKNOWLEDGMENTS

I would like to extend my thanks to Dr. Richard C. Larock, not only for all the chemistry which he has taught me, but for that which he has withheld. Under his guidance, I was allowed to learn through my own successes and failures in the laboratory and challenged to devise solutions to problems which arose in the development of the previously described methodology. I would also like to thank all members of the Larock group with whom I have worked. In particular, I would like to thank the following: Mark Doty for his insight into acetylene annulation chemistry and chemistry in general, Lisa Hasvold and Tim Hightower for all the chit chat and cheer, and Hoseok Yang and Kelvin Sham for teaching me how to do palladium chemistry in the early days.