I. as-OCTAHYDROANTHRACENES: SYNTHESIS AND STEREOCHEMICAL STUDIES

II. SYNTHESIS OF 1,8-DISUBSTITUTED NAPHTHALENES AND 1,2,3,4-TETRAHYDRONAPHTHALENES: STUDY OF PERI-INTERACTION USING ^{1}H AND ^{13}C NMR

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TABLE OF CONTENTS

CHAPTER Page

Part II

LIST OF TABLES

LIST OF FIGURES

LIST OF SPECTRA

SYMBOLS AND ABBREVIATIONS

ACOH	acetic acid
Anal.	analysis
as	asymmetric
bp	boiling point
^{o}C	degree centigrade
Calcd	calculated
conc.	concentrated
d	doublet
DIBAH	diisobutyl aluminum hydride
DMSO	dimethyl sulfoxide
FT	Fourier transform
g	gram
GC	gas chromatography
h	hour
Hz	Hertz
IR	infrared
Kcal	kilocalorie
Kg	kilogram
L	liter
LAH	lithium aluminum hydride
LC	liquid chromatography
lit.	literature
M	molar
m	multiplet
m/e	mass/electron charge
mg	milligram
MHz	megaHertz
min.	minute
mL	milliliter
mm	millimeter
mmol	millimole
mol	mole
mp	melting point
MS	mass spectrometry
NMR	nuclear magnetic resonance
PNA	polynuclear aromatic
PPA	polyphosphoric acid
ppm	parts per million
Py.	pyridine
q	quartet
rel.	relative
s	singlet
t	triplet
temp.	temperature
THF	tetrahydrofuran
TMS	tetramethylsilane
wt.	weight

INTRODUCTION

This dissertation is divided into two parts. The two problems are not related and entirely independent of each other. Each part contains its own introduction, historical, results and discussion, and experimental. However, the bibliography and appendices are combined.

PART I

as-OCTAHYDROANTHRACENES: SYNTHESIS AND STEREOCHEMICAL STUDIES

CHAPTER I

INTRODUCTION

Polynuclear aromatic (PNA) hydrocarbons and their hydrogenated derivatives have been subjected to considerable experimental and theoretical investigation for practical purposes and to learn about thermodynamic and spectral properties. Among these, anthracene and its hydrogenation products are important representatives of a large and interesting class of substances.

A special interest in hydrogenation products of anthracene was raised by a study of the catalytic hydrogenation of a multiring aromatic coal-tar constituent (anthracene) by Wiser, Singh, Quadar, and Hill,[1] who reported

> "bituminous coal is understood to consist primarily of fused ring structures joined by various types of linkages to form an extensive network. These ring structures are highly aromatic, although considerable quantities of hydroaromatic configurations are present. The size of these structures may vary from one to several rings, an average-sized configuration containing three or four rings". p. 350.

An understanding of the thermochemistry of coal and its hydrogenation products will guide strategies for the liquefaction of coal by thermodynamically determining most stable structures and most likely reaction paths.

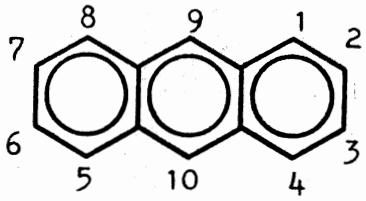
The object of this research is not only to study structural and stereochemical aspects of two isomeric as-octahydroanthracenes and

several intermediates involved in their synthesis, but also to provide hydrocarbons of high purity for thermochemical studies at the U.S. Department of Energy, Bartlesville Energy Technology Center in Bartlesville, Oklahoma.

CHAPTER II

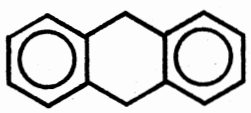
HISTORICAL

A variety of partially or fully hydrogenated anthracenes are obtained by direct hydrogenation of the parent hydrocarbon, anthracene (1), when it is subjected to different hydrogenation conditions.[2]



1

Anthracene is hydrogenated much more easily than benzene or naphthalene, e.g., by employing a copper chromite catalyst.[3] The initial product is 9,10-dihydroanthracene (2), which is also obtained by reducing anthracene with sodium and an alcohol.[4] Continued hydrogenation using nickel catalysts[5] affords first 1,2,3,4-tetrahydroanthracene (3), and then 1,2,3,4,5,6,7,8-octahydroanthracene (4).



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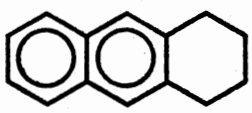

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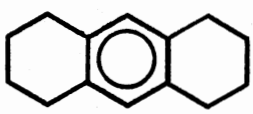

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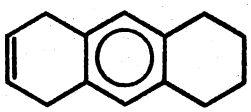
Birch reduction of 1,2,3,4,-tetrahydroanthracene (3) affords 1,2,3,4,5,8-hexahydroanthracene (5),[6] and 1,2,3,4,5,8,9,10-octahydroanthracene (6).



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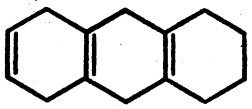

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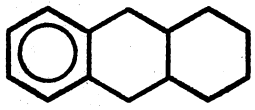
A decahydroanthracene and three perhydroanthracenes, $C_{14}H_{24}$, have also been obtained.[7] However, no as-octahydroanthracene (15) was found among the products under any hydrogenation condition.



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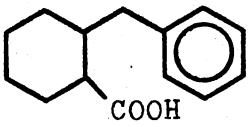
A simple method of synthesis of as-octahydroanthracene by cyclization of 2-benzylcyclohexanecarboxylic acid (11) to hexahydro-9-anthrone (12), followed by Clemmensen reduction, was worked out by Cook, McGinnis, and Mitchell[8] in 1944.



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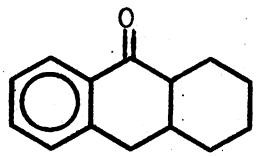
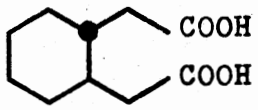


12

A study of the stereochemical relationships of hydroanthracenes was also commenced. Cook, Hewett, and Lawrence[9] described a synthesis of the two stereoisomeric 9-oxo-as-octahydroanthracenes (12) and suggested the trans configuration for the readily available higher-melting isomer (mp 109 °C). Clemmensen reduction of ketone 12b provided as-octahydroanthracene. Sulfonation, followed by fusion with potassium hydroxide, converted this hydrocarbon into a hydroxy derivative which was oxidized by alkaline permanganate to trans-cyclohexane-1,2-diacetic acid (7).



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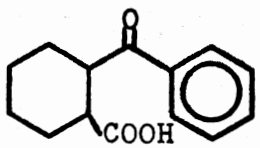
Based on the above information, it was concluded[8] that the octahydroanthracene obtained from ketone 12b is the trans isomer. Cook and his coworkers also attempted synthesis of cis-as-octahydroanthracene, but did not succeed.[8]

The Friedel-Crafts reaction of 1,2-cyclohexanedicarboxylic anhydride with benzene and isomerization of the resulting keto acid in alkaline solution was also studied by Scribner and Miller.[10] They reported Clemmensen reduction of keto acid 8 and cyclization of the re-



8

sulting desoxy acid in concentrated sulfuric acid. However, proof of the stereochemistry of products and isomeric purity of each compound remain uncertain.

The conformational behavior and stereochemistry of cyclohexane and its derivatives have been studied in great detail, and many more facts are available than on any other cyclic system.[11] Systems which contain fused cyclohexane rings can be studied conformationally in much the same way as cyclohexane. A detailed account of the stereochemistry of fused cycloalkanes containing two or more cyclohexane rings has been given by Eliel.[12] Among the fused six-membered-ring systems similar to as-octahydroanthracene, the stereochemistry of two decalins and five isomeric perhydroanthracenes have been studied.

W. Huckel[13] demonstrated that decalin may exist in cis and trans forms, of which the trans is the more stable. The counting of butane gauche interactions in the decalins reveals three such interactions in the cis isomer and none in the trans. Thus, the trans isomer should be lower in enthalpy than the cis isomer by about 11 KJ/mole. Experimental values from equilibration and heat of formation differences range from 11-12 KJ/mole.[11] trans-Decalin is a rigid molecule, whereas the cis isomer has two interconvertible conformations.

The first perhydroanthracene isomer was synthesized about the turn of the century.[14] It was soon recognized that other geometric isomers were possible and as many as 20 were suggested.[5] Fries and Schilling[7a] ultimately delineated the correct number as being five, the last of which was synthesized by Clarke[15] in 1961. Many workers contributed to the synthesis and characterization of the several isomers.[7a,8,16] X-ray[17] and electron-diffraction[18] work demonstrated that the individual

six-member rings in these compounds normally exist as chair forms, with the exception of the center ring of the trans-anti-trans compound, which is locked in a boat conformation.

During the last decade, conformation and configuration studies of substituted cyclic and polycyclic compounds have been facilitated to a great extent by employment of NMR spectroscopy. Although no NMR study of the two isomeric as-octahydroanthracenes and their precursors have been reported, the stereochemistry of some closely related compounds have been studied in great detail, utilizing carbon-13 and proton NMR spectroscopy. Examples of such investigations are: carbon-13 NMR studies of decalins,[19] methyldecalins,[20] and perhydroanthracenes[21] by Grant and Dalling, and proton and carbon-13 studies of perhydronaphthacenes by Pessemier, Vanhee, and Tavernier.[22]

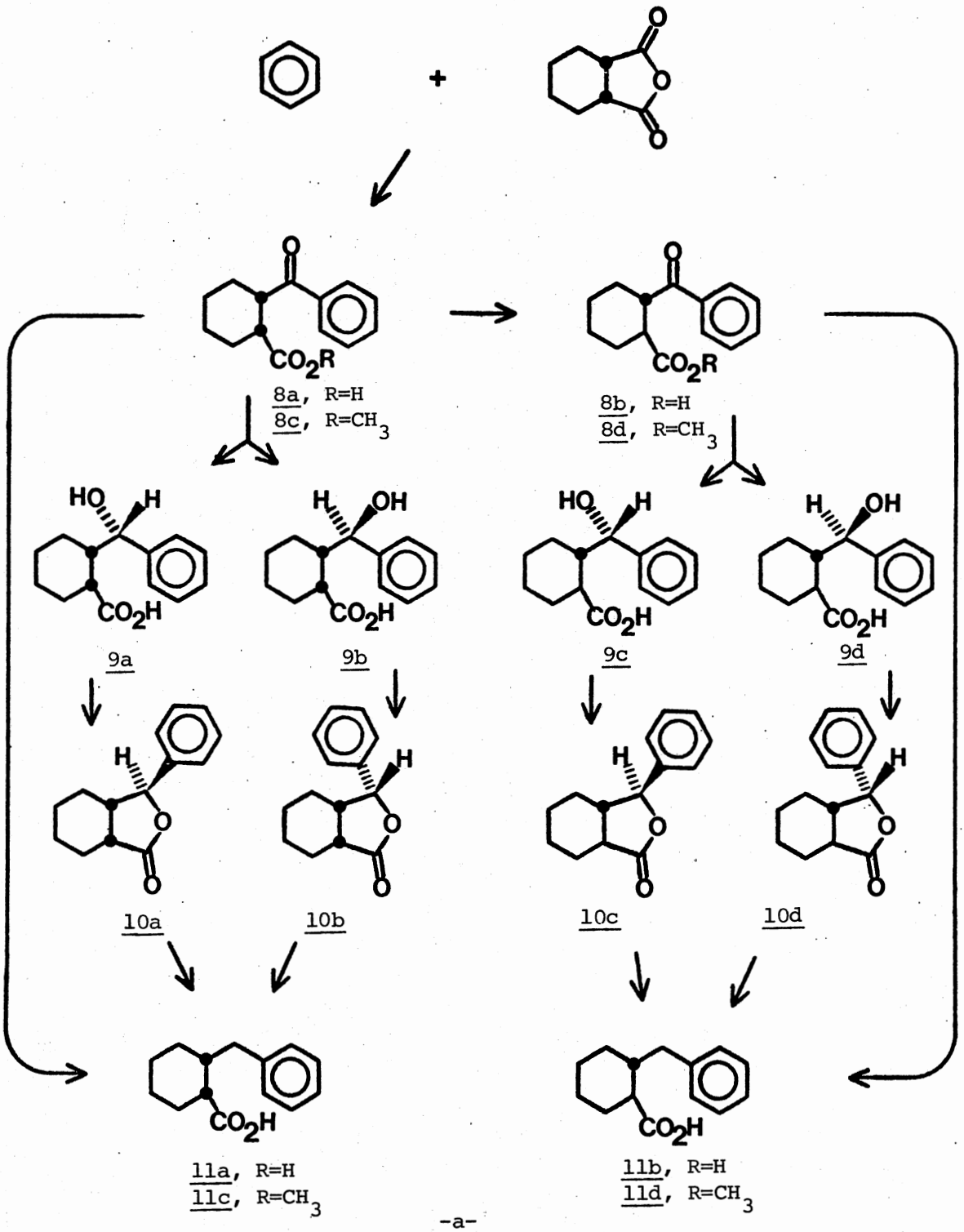
CHAPTER III

RESULTS AND DISCUSSION

The routes used for the synthesis of two isomeric octahydroanthracenes 15a and 15b are outlined in Figure 1.

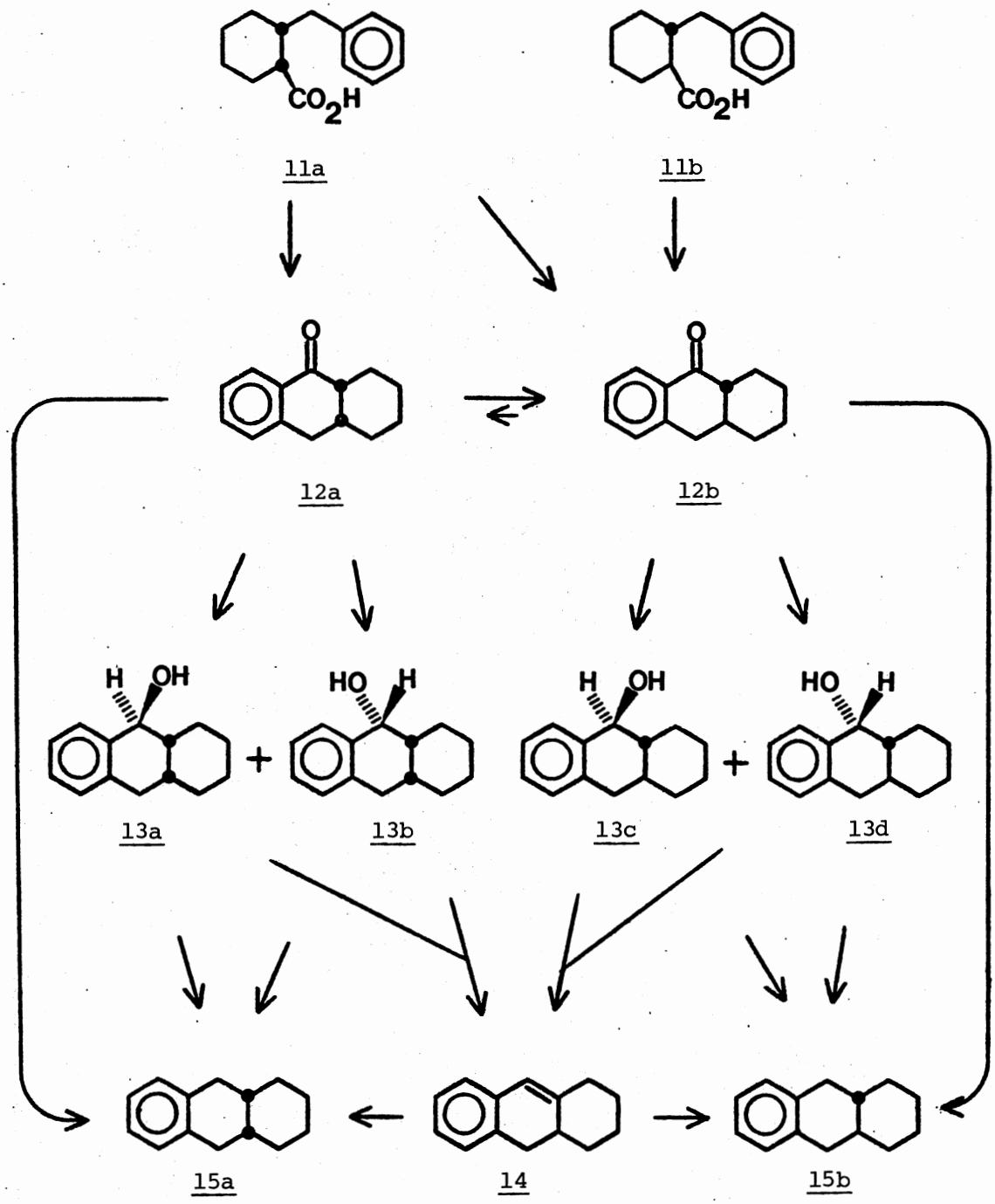
Friedel-Crafts reaction of cyclohexane-1,2-dicarboxylic anhydride with benzene was reported by Fieser and Novello,[23] and later by Scribner and Miller,[10] to give keto acid 8a in 90% yield. Conversion of acid 8a to 8b by heating in alkaline solution and Clemmensen reduction of keto acid 8b to 11b was also described by Scribner and Miller.[10] Cook and coworkers[9] prepared acid 11b by conversion of 2-benzylcyclohexanol into the corresponding 1-chloro-2-benzylcyclohexane and subsequent treatment of a Grignard solution prepared from the chloro-compound with carbon dioxide. A mixture of the two stereoisomeric 2-benzylcyclohexanecarboxylic acids 11a and 11b resulted from this procedure, from which acid 11b was isolated by recrystallization in a 20% yield. Cyclization of acid 11b in cold concentrated sulfuric acid to hexahydroanthrone 12b, and Clemmensen reduction of this ketone to trans-octahydroanthracene 15b was also reported by Cook, McGinnis, and Mitchell.[8]

We began by confirming the results described by Cook and by Scribner and Miller. The Scribner and Miller procedure was easily reproduced, and pure cis-keto acid 8a was isolated in 97% yield from a large scale Friedel-Crafts reaction of cis-hexahydrophthalic anhydride with benzene. Acid 8a was then converted into the trans isomer 8b by heating



-a-

Figure 1. Reaction Sequence for the Synthesis of cis, and trans-Octahydroanthracene 15a, and 15b



-b-

Figure 1. (Continued)

8a in 10% aqueous sodium hydroxide and treating the resulting reaction mixture with dilute hydrochloric acid. The purity of these two isomeric keto acids was studied by converting them to methyl esters with diazomethane and by subsequent analysis of the esters by gas chromatography. Each isomer was found to be 99.0% pure (proof of stereochemistry will be discussed later). Careful study of the IR spectra of these keto acids gave no evidence for presence of a lactol form in equilibrium with the keto acid.

Reduction of keto acids 8a and 8b to hydroxy acids 9a, 9b, 9c, and 9d was carried out with sodium borohydride; however, reduction was extremely slow. Even after three days of stirring the substrates with the reagent in ethanol, isopropyl alcohol, or methanol, the product was a mixture of keto acids and hydroxy acids. Because of the slow reduction of the keto acids using this method, epimerization occurred, and none of the four possible hydroxy acids could be isolated in a reasonable purity. From a search for a more powerful reducing reagent which would attack the keto function leaving carboxyl group untouched, lithium triethylborohydride (Super-Hydride) appeared promising.[24] Reduction of cis-keto acid 8a with Super-Hydride afforded a mixture of cis-lactones 10a and 10b in a 94:6 ratio and 82% yield. No hydroxy acid could be isolated from the reaction mixture. Similar reduction of the trans-keto acid 8b, however, when carefully worked up, afforded the trans-hydroxy acid in a 23% yield and a mixture of an equal amount of the trans-lactones 10c and 10d in a 76% yield. The two stereoisomeric lactones 10c and 10d (mp 78-80 ^{o}C and 80-81 ^{o}C) were separated by column chromatography (isomer 10d elutes first) and were identified by ^{13}C and proton NMR spectroscopy. This will be discussed later. The trans-

hydroxy acid isolated from this reaction shows only one set of peaks in its ^{13}C NMR spectrum and only one peak when analyzed by high-pressure LC. It is insoluble in most of the common organic solvents and lactonizes rapidly in an acidic media or upon heating of the neat sample to a melt at 150 °C. Lactonization by heating yielded a mixture of lactones 10c and 10d in a 4:96 ratio, respectively. This result suggested that the starting trans-hydroxy acid was 96% acid 9d. The author was not able to reproduce the result of Fieser and Novello[23] who reported the zinc and alkali reduction of the keto acid to a hydroxy acid with mp 145-147 °C.

Catalytic reduction of 10a and 10b to acid 11a, and 10c and 10d to acid 11b was carried out in acetic acid in the presence of Pd/C. Direct reduction of keto acid 8a to 11a and keto acid 8b to 11b was also successfully carried out in ethyl acetate using Pd/C, with less than 1% epimerization in each case. However, the Clemmensen reduction of both the cis- and trans-keto acids 8a and 8b yielded only the more stable trans-desoxcy acid 11b.

Conversion of the two isomeric acids 11a and 11b to the hexahydroanthrone 12a or 12b was probed with different reagents and reaction conditions; the results are summarized in Table I. These results indicate that epimerization is taking place in acidic media. When either ketone 12a or 12b was heated in an alkaline solution of ethanol, equilibrium was established in 90 min. at reflux temperature to give the mixture 12a:12b (16:84) respectively. The two isomeric ketones 12a and 12b were completely separated by preparative high-pressure LC. Their stereochemistry and proof of structure will be discussed later.

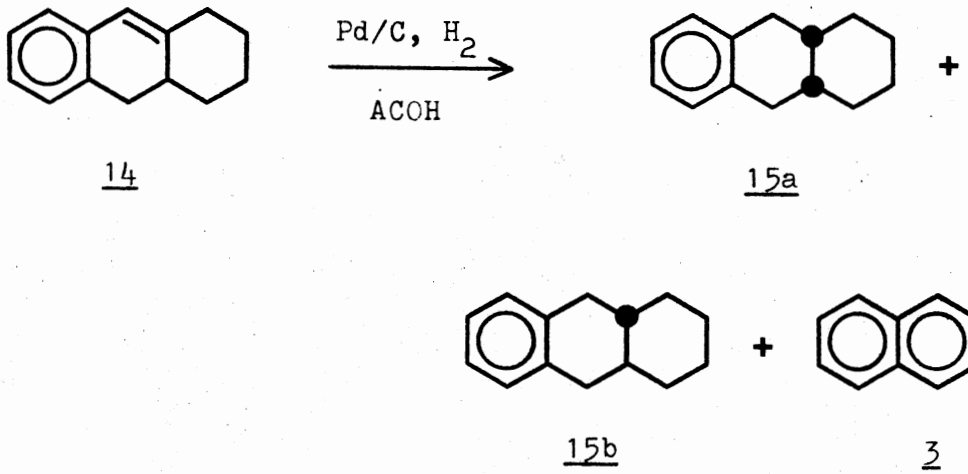
TABLE I

CYCLIZATION OF 2-BENZYLCYCLOHEXANECARBOXYLIC ACIDS UNDER VARIOUS CONDITIONS

Substrate	Reagent	Temp./Time	Total Yield	12a:12b
11a	Conc. H_2SO_4	25 °C/5 min.	86%	94:6
11a	Conc. H_2SO_4	100 °C/30 min.	94%	45:55
11b	Conc. H_2SO_4	25 °C/5 min.	90%	5:95
11b	Conc. H_2SO_4	100 °C/30 min.	96%	40:60
11b	PPA	80 °C/50 min.	91%	48:52

Diisobutylaluminum hydride (DIBAH) and lithium aluminum hydride (LAH) reduction of cis-ketone 12a was found to be stereospecific and afforded only the cis-alcohol 13b, while the DIBAH reduction of trans-ketone 12b gave a mixture of alcohols 13c and 13d in a ratio of 60:40. Alcohol 13c was isolated from the mixture in 98% purity by several recrystallizations from n-hexane. Column chromatography was carried out on the mixture remaining in the mother liquid, and alcohol 13d was isolated in a 90% purity. Stereospecificity of the reduction of the cis-ketone 12a, and stereochemistry of the three stereoisomeric alcohols will be considered later. Dehydration of all three alcohols gave hexahydroanthracene 14, which upon hydrogenation (Pd/C) yielded a mixture of hydrocarbons 15a, 15b, and 3 in a ratio 53:35:12. Tetrahydroanthracene 3 is assumed to form through disproportionation of hydrocarbon 14.

Clemmensen reduction of ketone 12b, previously reported by Cook,[8] was found to proceed slowly and for both ketones 12a and 12b resulted



14 15a

15b 3

in a mixture of the cis- and trans-hydrocarbons 15a and 15b in less than 60% total yield after 68 h of reaction. Wolff-Kishner reduction of ketones 12a and 12b also gave a mixture of 15a and 15b. For a more convenient and highly stereoselective conversion of ketone 12b to hydrocarbon 15a, or ketone 12b to hydrocarbon 15b, the catalytic hydrogenation in a neutral solvent (ethyl acetate) appears to be superior. This condition was also found suitable for synthesis of hydrocarbons 15a and 15b from alcohols 13b, 13c, and 13d. cis-Octahydroanthracene 15a was obtained from catalytic hydrogenation of cis-ketone 12a in a 98% isomeric purity while trans-ketone 12b was converted to trans-octahydroanthracene with a 100% stereospecificity.

Discussion of the Stereochemistry and ^{13}C NMR Assignments

The stereochemistry of most of the compounds discussed above was established through use of ^{1}H and ^{13}C NMR spectroscopy, and where necessary, chemical studies were also employed. Through the work of Grant and Dalling[27] and Perlin and Koch,[28] chemical-shift data for the

cyclohexane system have been established based on the conformational features found for this class of compounds. It is well known that an equatorial substituent provides lower field shifts for all the cyclohexane carbons as compared to the shift from the corresponding axial substituent. In the particular case of the γ-carbons, axial substituents produce a sizeable upfield shift (4-7 ppm), whereas the corresponding equatorial substituents have a much smaller upfield shift (0-3 ppm). This effect is due to γ-gauche interaction between an axial substituent and the 3- and 5-carbons of cyclohexane ring. Such interactions have proved valuable in conformational analysis.

The ^{13}C chemical shift values for compounds 8a, 8b, 10a, 10c, 10d, 11a, and 11b are given in Table II. Assignment of the chemical shifts will be presented in this order as the stereochemistry of each compound is being discussed. The assignments are made through the help of closely related model compounds or in some cases parametrically. The following numbering system is used for all compounds of Table II.

Carbons 1-6 are numbered on the cyclohexane ring starting from the carbon bearing the carboxyl substituent. Carbons 1'-6' are referred to carbons of the benzene ring starting from the substituted carbon. The benzylic position becomes carbon 9, and the carbonyl of the carboxyl group is numbered 10.

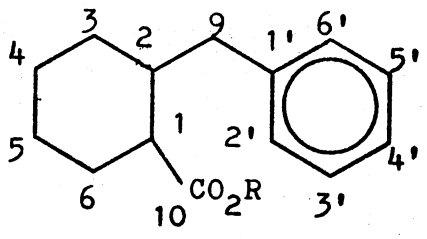


TABLE II

^{13}C CHEMICAL SHIFTS OF COMPOUNDS 8a, 8b, 10a, 10c, 10d, 11a, AND 11b[a]

	8a	8b	10a	10c	10d	11a	11b
C-1	42.70	44.20	42.95	51.85	46.69	44.85	49.60
C-2	44.06	46.60[b]	37.87	46.55	40.24	39.40	41.29[b]
C-3	25.03[b]	29.06[b]	26.82	27.08[b]	27.57[b]	27.50[b]	30.27[b]
C-4	24.40[b]	25.55[b]	22.87	24.75[b]	25.01[b]	23.80[b]	25.36
C-5	22.38[b]	25.44[b]	22.87	24.95[b]	25.13[b]	22.81[b]	25.36[b]
C-6	27.58	29.76[b]	22.97	25.24	25.27	25.75	30.11[b]
C-1'	136.36	135.80	138.41	137.12	135.52	140.65	139.75
C-2'	128.31	128.36	124.86	125.62	124.92	128.01	127.88
C-3'	127.98	128.18	128.37	128.40	128.19	128.90	129.15
C-4'	132.30	132.68	127.85	128.16	127.75	125.70	125.71
C-5'	127.98	128.18	128.37	128.40	128.19	128.90	129.15
C-6'	128.31	128.36	124.86	125.62	124.94	128.01	127.88
C-9	202.02	202.48	82.98	85.36	81.96	36.74	40.33
C-10	180.31	181.18	178.01	176.34	177.54	181.33	182.64

[a] In PPM from TMS. All samples at same molar concentration in $CDCl_3$.

[b] Uncertain assignment.

Proton-decoupled ^{13}C spectra of acids 8a and 8b show twelve lines, of which six appear in the aliphatic range. For the trans-isomer 8b a chair conformation of the cyclohexane ring with both substituents equatorial is the most feasible and the lowest energy structure. Any other conformer, e.g. axialy substituted conformers, will have higher energy, less likely to be present, and therefore should not contribute significantly to the ^{13}C spectrum of this molecule. For the cis-keto acid 8a, however, interconvertible conformations with two substituents being axial-equatorial to each other contribute to the ^{13}C spectrum of the molecule. The effect of a carboxyl substituent on ^{13}C chemical shifts of cyclohexane ring has been studied, and the chemical shift parameters for this substituent are known.[25,26] These parameters are the same for a methyl carboxylate substituent.[26] A carboxyl substituent in an axial position deshields the α position by 11.7 ppm, and the β position by 0.2 ppm, but shields the γ carbons by 4.4 ppm and the δ carbon by 1.0 ppm (chemical shift of the carbons of unsubstituted cyclohexane is 27.1 ppm). When the carboxyl group takes an equatorial position, it has a deshielding effect on both the α carbon (16.2 ppm) and the β carbons (1.7 ppm), but an equal shielding effect on γ and δ carbons (1.6 ppm). The effect of the benzoyl substituent can also be estimated since Pehk and Lippmaa[32] published the ^{13}C chemical shift values for an acetyl substituted cyclohexane. Correcting for the effect of substituting a phenyl group for methyl[29,30] α- and β-deshielding would be in the order of 22-25 for α, and 1-2 for β carbons (in ppm from cyclohexane), and a shielding of almost the same magnitude as for the carboxyl substituent for γ- and δ-carbons. Based on these literature data, the assignment of ^{13}C chemical shifts are made for acids 8a and 8b. In

each spectrum six lines are in the aliphatic range of which only two give a distinct doublet in the off-resonance decoupled spectrum. These are assigned to C-1, and C-2. The greatest downfield value is assigned to the carbon bearing the benzoyl substituent because of stronger α-deshielding effect of this substituent compared to a CO_2H group. Both substituents have almost the same β-effect. From the remaining four aliphatic carbon signals, the two at highest upfield are assigned to C-4 and C-5 because each of these carbons experiences one γ- and one δ-substituent effect which accumulate to shield these carbons. The remaining two lines are assigned to C-3, and C-6. Carbonyl signals are displaced downfield and their assignment are confidently made. Assignments of signals in the aromatic range are also straightforward. Four lines are observed, from which one is shifted downfield further than the other three and it is a singlet in the off-resonance decoupled spectrum. Thus it is assigned to C-1'. From the other three signals two are of double intensity and must be the ortho and meta carbons. Substitution of an alkyl carbonyl group (such as $COCHMe_2$) on benzene is known[33] to deshield the para position (~ 4 ppm), and shield the meta position (~ 0.5 ppm) while having no effect on the shielding of the ortho carbon. Based on these data, the chemical shift values are assigned as shown in Table II. Comparing the ^{13}C spectra of keto acids 8a, and 8b yields additional information about the stereochemistry of these compounds. C-1, and C-2 chemical shifts in 8b are downfield of corresponding carbon signals in 8a indicating more equatorial substituent effect for compound 8b which establishes the trans geometry of this compound. This effect also causes increased shielding of C-4 and C-5 in the cis isomer as compared to the trans isomer, due to the higher

contribution of γ-gauche interaction by an axial substituent in the cis isomer. Comparison of carbonyl signals of the two isomers 8a and 8b is also informative. The carbonyl of the benzoyl group gives a resonance line at 202.48 in compound 8b and 202.02 in 8a. The difference being 0.46 ppm. While the shift difference for carboxyl carbon in these two compounds is 0.87 ppm (181.18 in 8b compared to 180.31 in 8a). Thus the carboxyl group is shielded to a larger extent in the trans isomer, i.e., the carbonyl group experiences more γ-interaction than benzoyl group in the cis isomer. Therefore, the conformer in which the carboxyl group is in an axial position has more significant contribution to the spectrum of the molecule 8a.

The chemical shift assignments are made in the same way for acids 11a and 11b. Effect of a benzyl substituent on a cyclohexane ring was estimated by using methyl cyclohexane[34] and ethyl cyclohexane[32] as models and considering the parameters for substitution of phenyl group in aliphatic compounds.[29] The assignment of ^{13}C resonance lines of the aromatic carbons are easily made by considering some closely related compounds[33] as well as the observed line intensity and the splitting patterns in the off-resonance decoupled spectrum. Comparison of C-1, C-2, C-4, and C-5 chemical shifts in isomers 11a and 11b as discussed for acids 8a, and 8b establishes the stereochemistry of these compounds.

Three lactones were isolated from reduction of cis- and trans-keto acids and identified as follows. The cis geometry at the ring junction for 10a follows from its C-1, and C-2 ^{13}C chemical shifts (42.95 and 37.82) which are upfield from C-1, and C-2 in both trans-lactones 10c (51.85, 46.55) and 10d (46.69, 40.24). The same conclusion is reached

when chemical shift values for C-4, and C-5 in these lactones are compared. The ^{13}C proton-decoupled spectrum of the lactone 10a shows eleven lines which are assigned as follows: From seven lines in aliphatic range, three of them become doublets in off-resonance decoupled spectrum, and correspond to C-1, C-2, and C-9. The more downfield of these (82.98) is assigned to C-9 which is attached directly to oxygen. The value of 42.95 is assigned to C-1 which is attached to a carbonyl carbon and deshielded more than expected for C-2. Thus 37.87 is assigned to C-2. The highest upfield chemical shifts are assigned to the outermost carbons of 10a for the same reason discussed for cis-acid 8a. Accidently in lactone 10a these carbons are degenerate. Two remaining lines in the aliphatic range are assigned to C-3 and C-6. Examination of the Dreiding models of the molecule indicates a peri-type interaction between the carbonyl and C-6, which would cause a shielding of this carbon. Based on this speculation, the value of 22.97 is assigned to C-6 leaving the 28.82 line for C-3. Assignment of aromatic signals are made through help of the off-resonance decoupled spectrum, the line intensities, and data reported by Ewing[33] on model compounds. The ^{13}C line assignments for 10c, and 10d are also made in this manner.

The stereochemistry of these lactones at C-9 (benzylic position) was established through the study of their proton NMR spectra. A distinct doublet for benzylic proton is observed around 5.00 ppm. The coupling constant of this proton (vicinal coupling with proton on C-2) is a diagnostic feature in establishing the stereochemistry at C-9. The most important factor influending these couplings is the dihedral angle (ϕ) between the CH bonds.[31] The original theoretical predictions may be approximately written in the form of the following equation

$$J_{(CH.CH)} = 10 \cos^2\phi$$

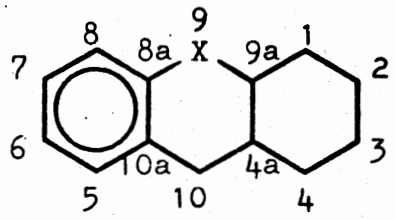
This prediction is generally obeyed;[31] however, other effects such as the substituent dependence of the couplings are present. Thus, a variation of about ± 2 Hz may be observed between theoretical and experimental values.

For trans-lactones 10c and 10d, the models of these compounds show an almost rigid geometry. For all these lactones, ϕ can be measured from their models. For lactone 10c the angle ϕ is 150° if a chair conformation is assumed for the cyclohexane ring and this angle increases to 160° when a boat conformation of cyclohexane ring is used. With lactone 10d, ϕ is 35° for cyclohexane chair model and 40° when cyclohexane takes a boat conformation. The cis-lactones 10a, and 10b have more flexible structures. Examination of conformations for cis-lactone 10a shows a variation of ϕ between 110° and 135°. Whereas ϕ varies from 10° to 20° for cis-lactone 10b. Substitution of these values in the above equation results in a theoretical value of $J_{(CH.CH)}$ for each compound and these are summarized in Table III.

For the two trans-lactones which were separated by column chromatography, we observed coupling constants of 9.0 Hz and 6.0 Hz which suggested structure assignment of 10c and 10d, respectively. Lactone 10d emerged first from a silica column using 4:1 mixture of methylene chloride and n-hexane. The third lactone exhibited a coupling constant of 3.0 Hz for the benzylic proton and as shown in Table III, 10a is suggested as the structure.

The stereochemistry of ketones 12a and 12b, alcohols 13a-d, and the hydrocarbons 15a and 15b were next considered. Chemical shift values

for these compounds are given in Table IV and the following numbering system was used.



12a-b, X=CO

13a-d, X=CHOH

15a-b, X=CH_2

TABLE III

EXPERIMENTAL AND THEORETICAL $^3J_{HH}$ COUPLING FOR BENZYLIC PROTONS OF LACTONES 10a-d

Lactone	ϕ	$^3J_{HH}$ Calcd[a]	$^3J_{HH}$ Observed
10a	110° - 135°	1.12 - 5.00	3.00
10b	20° - 10°	8.83 - 9.70	--
10c	150° - 160°	7.48 - 8.83	9.00
10d	40° - 35°	5.87 - 6.69	6.00

[a] In Hz.

Dreiding models of ketones 12a and 12b show that the trans isomer has a rigid structure with the middle ring locked in a skewed conformation and the outer cyclohexane ring favoring a chair conformation. Several interconvertible structures may be assumed for the mobile cis

TABLE IV

^{13}C CHEMICAL SHIFTS OF COMPOUNDS 12a, 12b, 13b, 13c, 13d, 15a, AND 15b[a]

	12a	12b	13b	13c	13d	15a	15b
C-1	25.35	25.91	25.56	30.32	28.07	28.86	33.76
C-2	23.87[b]	25.35[b]	19.02[b]	25.77	25.99[b]	23.31	26.26
C-3	23.34[b]	25.24[b]	20.34[b]	25.77	26.41[b]	23.31	26.26
C-4	28.80	33.91	28.57	33.62	30.96	28.86	33.76
C-4a	35.80	39.89	31.31	37.15	37.26	33.47	38.60
C-9a	48.12	51.76	42.01	47.24	43.51	33.47	38.60
C-9	199.62	199.33	71.96	74.85	71.23	32.48	37.38
C-10	33.31	37.12	30.55	36.62	33.97	32.48	37.38
C-5	129.01	128.34	128.25	127.90	129.79	128.89	128.33
C-6	133.09	132.89	126.46[b]	126.73[b]	128.54[b]	125.07	125.10
C-7	126.17[b]	126.24[b]	125.67[b]	126.59[b]	127.67[b]	125.07	125.10
C-8	126.87[b]	126.93[b]	125.53[b]	125.83	125.77	128.89	128.33
C-8a	131.55	132.01	137.79	139.22	138.38	135.34	136.48
C-10a	142.49	143.19	135.19	135.95	136.51	135.34	136.48

[a] PPM from TMS in $CDCl_3$.

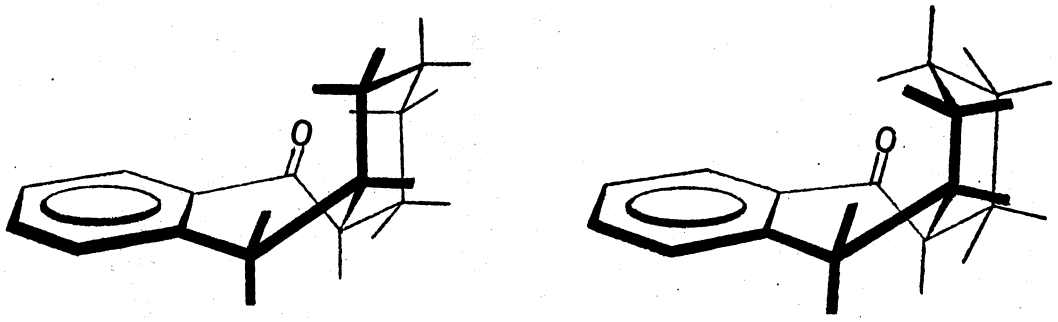
[b] Uncertain assignments.

isomer.

Fourteen lines appear in the ^{13}C proton-decoupled spectra of ketones 12a and 12b. Carbons at the ring fusion are easily distinguished by their splitting patterns in the off-resonance decoupled spectrum. The ultimate and penultimate upfield signals are assigned to the two outermost carbons of the cyclohexane ring because of the γ- and δ-shielding effects that each of these experiences. From three remaining lines, the one downfield of the other two is assigned to benzylic carbon. Carbon-1 is slightly shielded by a peri-type interaction with oxygen whereas C-4 is shielded by the β-effect of benzyl substituent. Therefore, two remaining signals are assigned such that C-1 is given the lower value. For aromatic carbons, two quaternary carbons are distinguished by single lines in the off-resonance decoupled spectrum. The lower field signal is assigned to C-10a because of a stronger ipso deshielding effect of an alkyl substituent compared to a carbonyl substituent[33] (for a comparison see ^{13}C chemical shifts of 8a, 8b, 11a, and 11b, Table II). The C-6 signal is strongly deshielded because of a para carbonyl substituent effect, and C-8 is shielded because of a peri-type interaction with oxygen. Cis and trans ring junctions are easily discriminated by comparison of ^{13}C chemical shifts of 12a, and 12b. The resonance of the bridgehead carbons of cis forms are upfield from those of the trans forms because of the γ upfield effect.

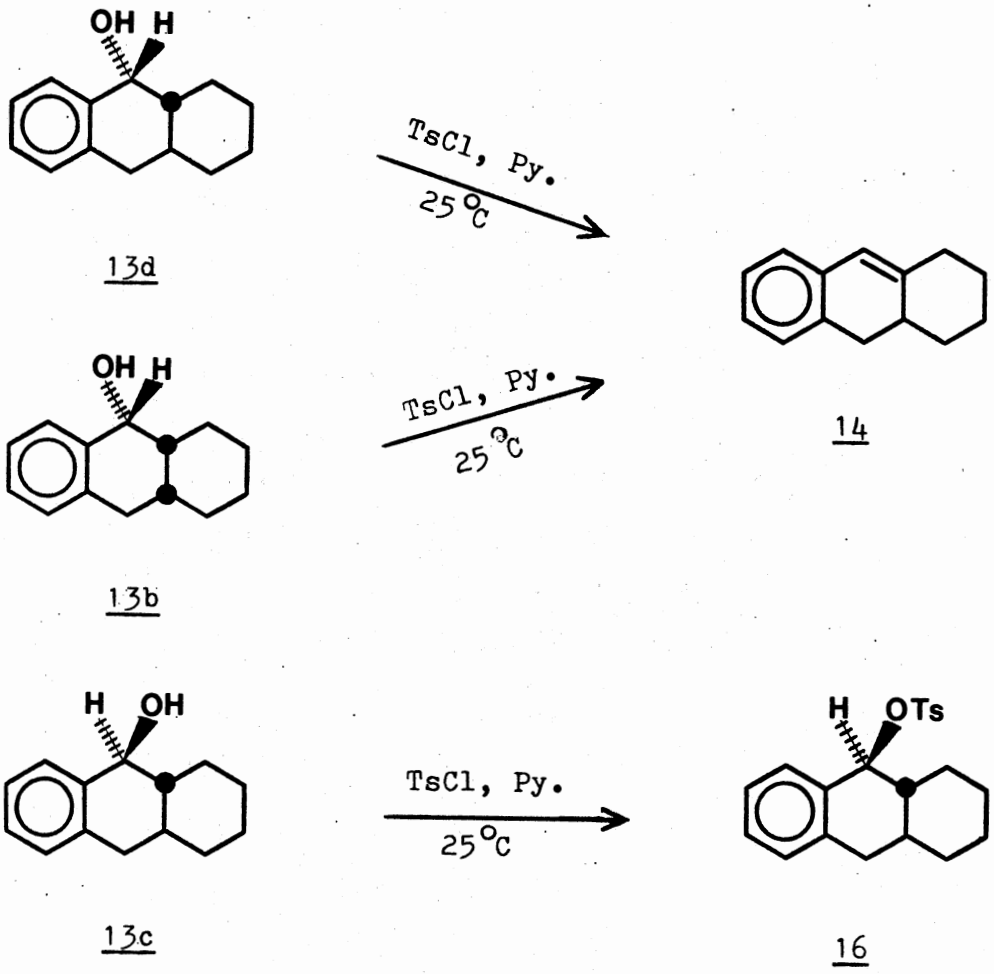
Because of the stereospecific reaction of cis-ketone 12a with DIBAH and LAH, the structure of this ketone deserved closer consideration. Dreiding models show that attack by hydride from the opposite side of the hydrogen adjacent to carbonyl is disfavored regardless of the conformation adopted by the terminal cyclohexane ring, as shown in

the following examples:



Therefore, the attacking hydride ion approaches from the hydrogen side, which is in agreement with the Cram's rule. If this postulate is true, the alcohol product that we obtain must be 13b, and this was indeed found to be the case. Treatment of 13b with tosyl chloride in pyridine at ambient temperature for three days gave only the alkene 14, which suggests an anti-coplanar arrangement of OH and the hydrogen at the adjacent carbon. This behavior is strong evidence to suggest the stereochemical assignment as shown for 13b. Structure 13a would not be expected to respond in this manner. DIBAH reduction of trans-ketone 12b gave alcohols 13c and 13d. Tosylation of alcohol 13c gave the stable tosylate 16 while the alcohol 13d afforded only olefin 14 upon tosylation.

The proton spectra of these alcohols are informative in identifying each stereoisomer. As was previously discussed, the vicinal proton coupling constant is indicitive of the dihedral angle between these protons. In a six membered ring system, $^{3}J_{aa}$ varies from 8-12 Hz, and $^{3}J_{ae}$ from 2-4 Hz, depending on the number of electronegative substituents present.[31] In the ^{1}H NMR spectrum of alcohols 13c and 13d, the

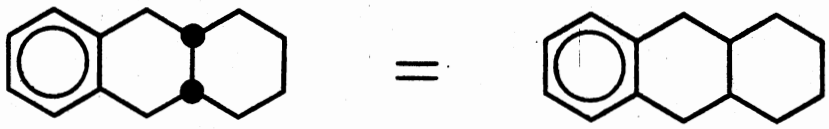


proton signal geminal to OH is mixed with OH signal itself and its coupling is somewhat effected by OH proton. However, when the alcohols are converted to their acetates, these signals move further downfield and a distinct doublet around 6 ppm appears with a $^{3}J_{HH}$ = 2 for 13c and $^{3}J_{HH}$ = 8 for 13d which further verifies the stereochemistry of these alcohols. In the alcohols with a cis ring juncture, because of an averaging of the proton on the ring junction between an axial and equatorial position, $^{3}J_{HH}$ may not be a reliable identification tool.

The stereochemistry of these alcohols (13b, 13c, 13d) at the ring

junction is established by their ^{13}C proton-decoupled spectra. Chemical shifts of carbons at the ring junction for the cis-isomer 13b are upfield of those of the trans isomers (see Table IV). Chemical shift assignments (^{13}C) were made by the help of the off-resonance decoupled spectrum and the spectra of the parent hydrocarbons 15a and 15b which will be discussed later. Substitution of an OH group at C-9 causes deshielding of C-9, C-8a, and C-9a (α,β-deshielding), while it has a shielding effect on C-1, C-4a, C-8, and C-10a because of a gauche-type interaction.

cis-Octahydroanthracene 15a has a plane of symmetry and is meso, while the trans-octahydroanthracene 15b has only a two-fold axis of symmetry and is a dl-pair.



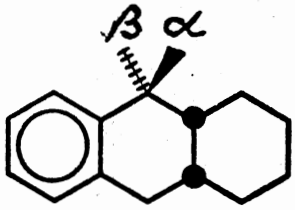
4a(R), 9a(S) 4a(S), 9a(R)

4a(S), 9a(S) 4a(R), 9a(R)

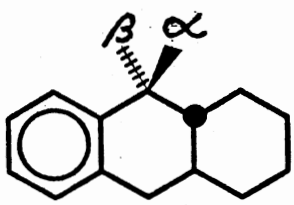
Examination of the gauche-butane interactions in the cis-and trans-hydrocarbons show three more such interactions in the former than in the latter. Computing the butane gauche interaction as 0.85 Kcal/mole in the liquid phase or 0.95 Kcal/mole in the vapor phase[35] leads to

a calculated difference in enthalpy between cis- and trans-hydrocarbon of 2.55 Kcal/mole (liquid state) or 2.85 Kcal/mole (vapor state), favoring the trans isomer.

Proton and ^{13}C proton-decoupled spectra of cis- and trans-hydrocarbon 15a, and 15b are given in the following pages. In the cis-hydrocarbon, the diastereotopic protons (α, and β) at the benzylic position are magnetically equivalent due to rapid interconversion at the ring junction which results in an averaging of the proton NMR signals. Thus a doublet of J=5 Hz at 2.74 ppm is observed for these four protons.

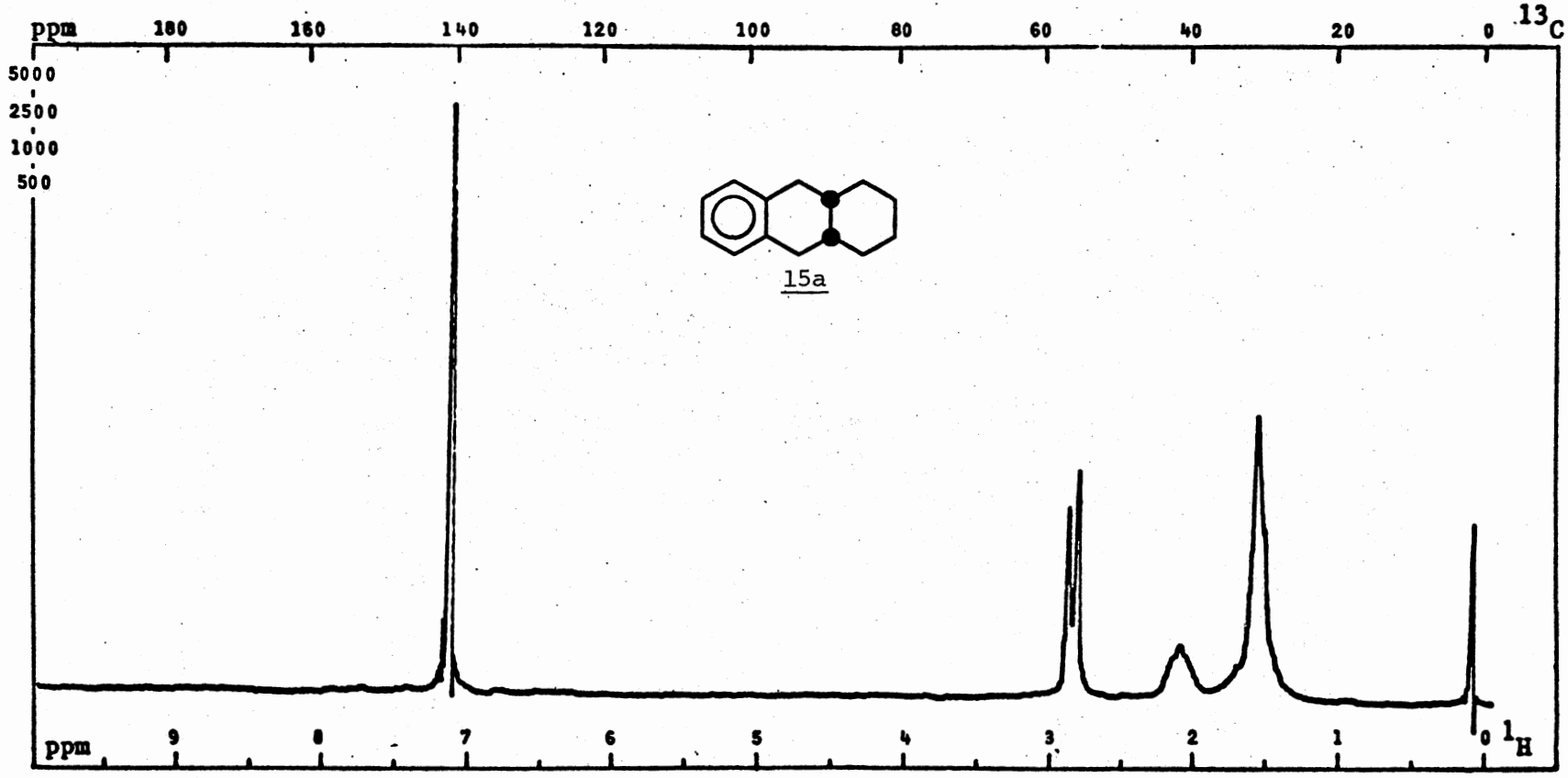


The trans-isomer 15b, however, because of a rigid geometry, does not undergo proton averaging and two different signals of equal intensity for α and β protons appear in the spectrum of the molecule, each signal as a doublet of doublet. Each signal is split by a geminal proton with a coupling constant of 16 Hz and then each doublet is further split by a vicinal proton. β-Protons are equatorial and their splitting

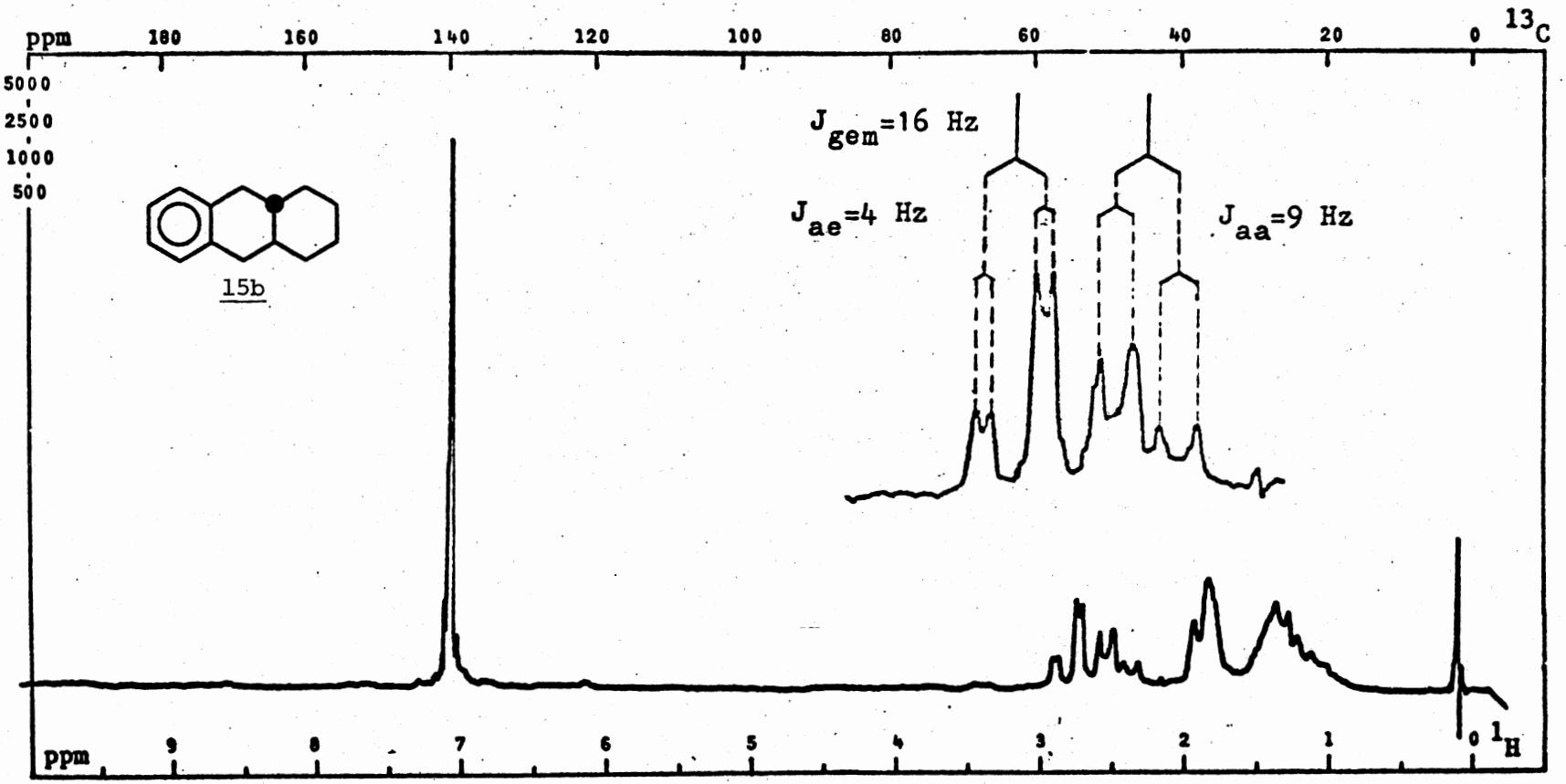


by the vicinal proton which is axial is smaller than coupling constant between α protons (axial) and vicinal axial protons ($J_{ae} < J_{aa}$).[31] Thus the signal centered at 2.75 ppm ($J_{vicinal}$ = 4 Hz) corresponds to β protons and the signal centered at 2.38 ppm ($J_{vicinal}$ = 9 Hz) is that of α protons.

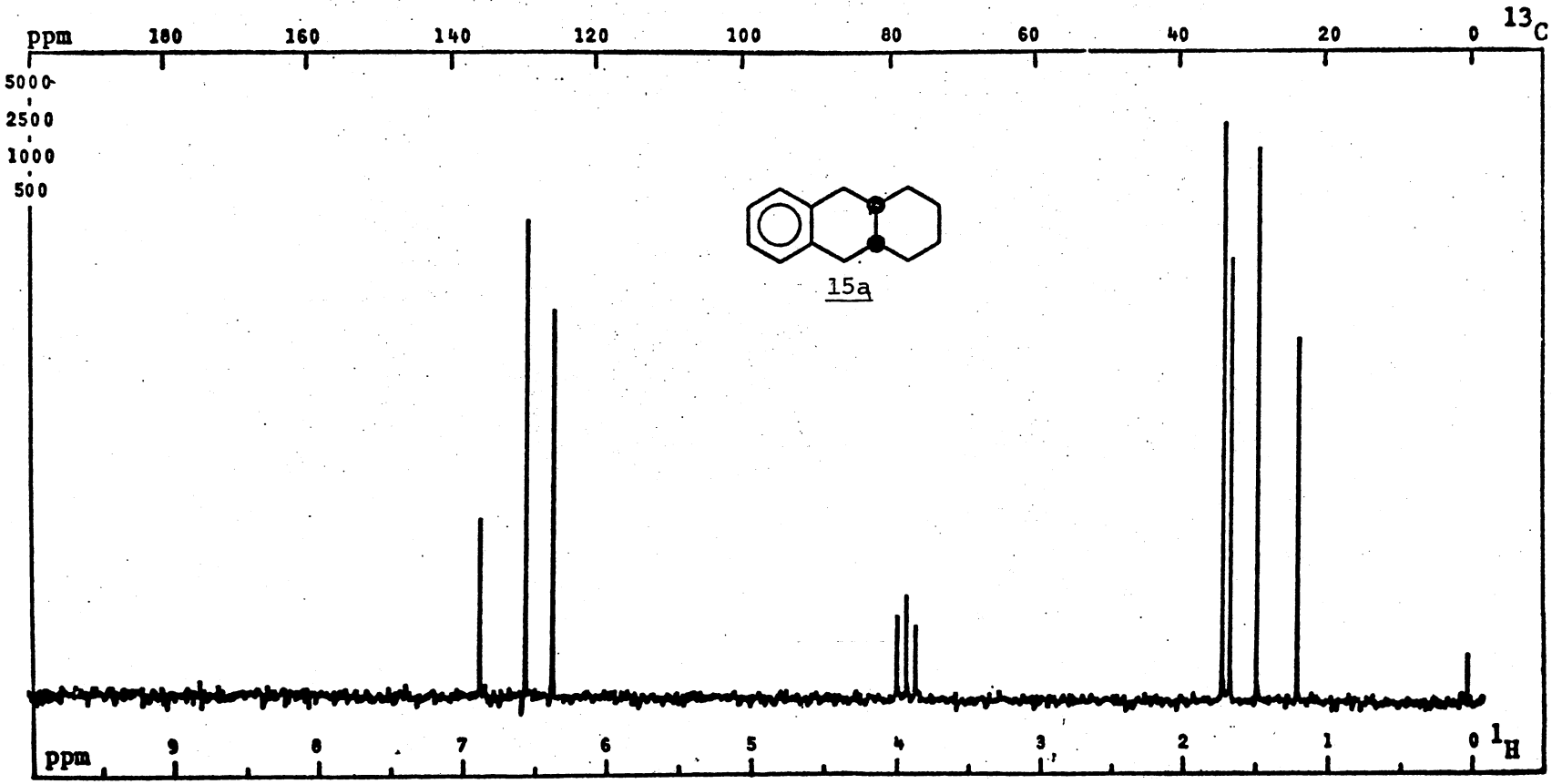
Because of the symmetry of 15a and 15b, only seven lines appear in ^{13}C proton-decoupled spectrum of each isomer, three in the aromatic and four in the aliphatic range (see Table IV). From the signals in the aromatic range, the one most downfield belongs to the quaternary carbons 8a, and 10a and these do not split in the off-resonance decoupled spectrum. The other two signals are assigned in the same way as in tetralin which has almost the same chemical shifts for aromatic carbons.[36] From four lines in the aliphatic range, the furtherest downfield is assigned to the carbons at ring junction by the help of off-resonance decoupled spectrum. The most upfield signal is assigned to C-2, and C-3 because of γ-upfield effect. From the remaining two aliphatic carbon signals, the downfield one is assigned to C-9, C-10 benzylic carbons and the other signal is then for C-1, and C-4. The cis geometry of hydrocarbon 15a is evident from its C-9a, and C-4a signals (carbons at the ring juncture) at 33.47 ppm which is upfield of the corresponding signals for trans isomer (38.60 ppm). The same conclusion is drawn from comparison of the ^{13}C chemical shift of the outermost carbon (C-2, and C-3) which is 23.31 ppm for the cis isomer and 26.26 ppm for the trans isomer.



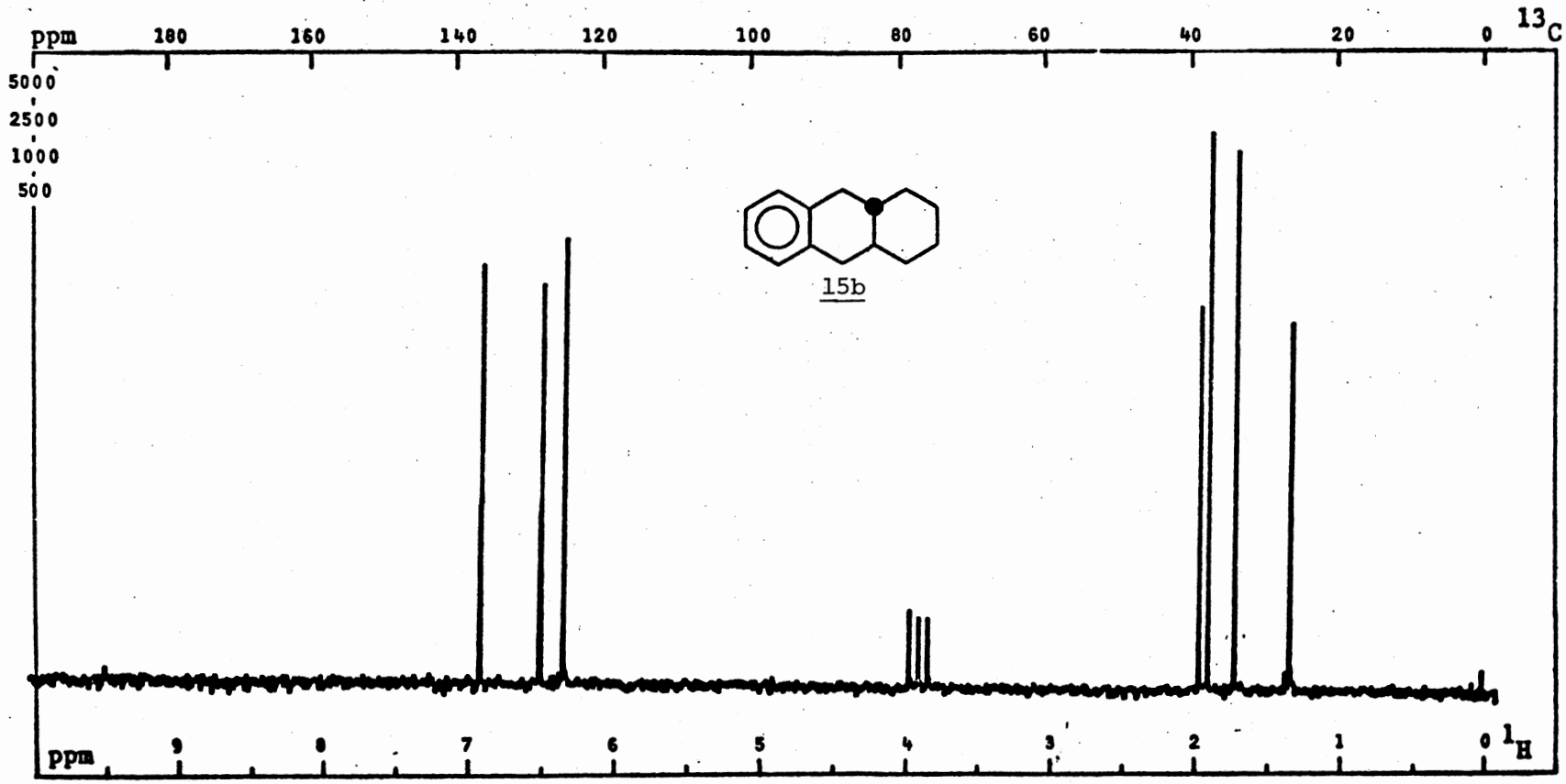
Spectrum 1. ^{1}H NMR of cis-as-Octahydroanthracene (15a)



Spectrum 2. ^{1}H NMR of trans-as-Octahydroanthracene (15b)



Spectrum 3. ^{13}C NMR of cis-as-Octahydroanthracene (15a)



Spectrum 4. ^{13}C NMR of trans-as-Octahydroanthracene (15b)

CHAPTER IV

EXPERIMENTAL

All melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 681 instrument. Proton NMR spectra were determined at 100.1 MHz on a Varian XL-100A using tetramethylsilane as internal standard in $CDCl_3$ or DMSO-d_6 solvent. The ^{13}C NMR spectra were obtained at 25.2 MHz in the FT mode on a Varian XL-100A interfaced with a 12 K Nicolet 1080 computer system. Chemical shifts are reported in ppm using tetramethylsilane as an internal standard. GC-MS spectra were provided by CONOCO Inc., Ponca City, Oklahoma, employing a Finnigan Model 4023 system with a 30 m SP-2100 glass capillary column. The spectra were scanned at 1.1 sec intervals with a head pressure of 30 psig programmed from 60-260 ^{o}C at 8 ^{o}C per minute; Probe temperature 140 ^{o}C. Gas chromatographic analyses were obtained with a Varian 3700 capillary gas chromatograph, and a Varian aerograph model 550. Analytical and preparative high pressure LC separations were performed on a Waters Associates system and Prep LC 500 system. Microanalyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tennessee.

cis-2-Benzoylcyclohexanecarboxylic Acid (8a)

A 775 g (5 mol) sample of cis-hexahydrophthalic anhydride and 6 L of benzene were mechanically stirred in a 12-L flask at 0-5 ^{o}C. To the resulting solution was added 1343 g (10.1 mol) $AlCl_3$ during 2 h.

The temperature was maintained below 10 °C during the addition. The yellow mixture was stirred for forty minutes, the cooling bath was drained, and the flask contents were then warmed to 40-50 °C by adding hot water to the tub surrounding the flask. The reaction mixture was decomposed by pouring onto 5 Kg of ice mixed with 2 L of concentrated hydrochloric acid. The resulting mixture was transferred to a 22 L separatory funnel and 4 L of ether were added. The organic layer was separated, washed with water, dried ($MgSO_4$), and concentrated to 5 L. The keto acid 8a crystallized upon cooling and 815 g were collected by filtration. Evaporation of solvent from mother liquid gave another 315 g of 8a. The overall yield was 1130 g (97%); mp 138-139 °C (lit.[10] mp 138.5 - 140 °C): IR (KBr) cm^{-1} 2850 (CO_2H), 1700 and 1685 (CO); ^1H NMR ($CDCl_3$) δ 7.9 - 7.2 (m, 5, ArH), 3.9 (m, 1), 2.7 (m, 1), 2.3 - 1.3 (m, 8); ^{13}C NMR ($CDCl_3$) ppm 202.02 (CO), 180.31 (CO_2H), 136.36, 132.30, 128.31 (x2), 127.98 (x2), 44.06, 42.70, 27.58, 25.03, 24.40, 22.38.

trans-2-Benzoylcyclohexanecarboxylic Acid (8b)

The cis-keto acid 8a was converted to the trans-isomer 8b in quantitative yield by heating in 10% aqueous sodium hydroxide for 1 h followed by acidification. The product was isolated by filtration and recrystallized from ethyl acetate to give 8b; mp 152-153 °C (lit.[10] mp 153.5-154 °C). The purity of keto acids 8a and 8b was studied by converting them to methyl esters with diazomethane and analyzing with gas chromatography (13' x 1/8" of 4% UCW-98 on Chm. G). Isomer 8b elutes first. Each isomer was found to be 99% pure and free of the other isomer. Spectral data for the trans-keto acid 8b: IR (KBr) cm^{-1} 2850 (CO_2H), 1700 and 1660 (CO); ^1H NMR ($CDCl_3$) δ 8.0-7.2 (m, 5, ArH), 3.5

(m, 1), 2.9 (m, 1), 2.3-1.2 (m, 8); ^{13}C NMR ($CDCl_3$) ppm 202.48 (CO), 181.18 (CO_2H), 135.80, 132.68, 128.36 (x2), 128.18 (x2), 46.60, 44.20, 29.76, 29.06, 25.55, 25.44.

cis-2-Benzylcyclohexanecarboxylic Acid (11a)

A 23.2 g (0.1 mol) sample of cis-2-benzylcyclohexanecarboxylic acid (8a), 2.5 g of 5% Pd/C and 500 mL of ethyl acetate were hydrogenated at 60 °C (45 psi) for 6 h. The mixture was cooled, filtered, and concentrated to give 21.5 g of crystalline product. Recrystallization from isohexane gave 19.9 g (92%) of cis-2-benzylcyclohexanecarboxylic acid (11a), mp 102-103 °C: ^1H NMR ($CDCl_3$) δ 11.18 (CO_2H), 7.18 (m, 5, ArH), 2.64 (d, 2, CH_2Ar), 2.62 (m, 1), 2.08 (m, 1), 1.80-1.20 (m, 8); ^{13}C NMR ($CDCl_3$) ppm 181.33 (CO), 140.65, 128.9 (x2), 128.01 (x2), 125.70, 44.85, 36.74, 27.50, 25.75, 23.80, 22.81.

Clemmensen reduction of cis-2-benzoylcyclohexanecarboxylic acid (8a) gave trans-2-benzylcyclohexanecarboxylic acid (11b). The purity of the two isomeric acids was established by conversion to methyl esters with diazomethane and their analysis by high-pressure LC. The methyl esters 11c and 11d were separated by high-pressure LC using silica column (methylene chloride: n-hexane; 2:1). Isomer 11d elutes first.

trans-2-Benzylcyclohexanecarboxylic Acid (11b)

a. Clemmensen Reduction of trans-2-Benzoylcyclohexanecarboxylic Acid (8b)

Mossy zinc (165 g), mercuric chloride (12 g), concentrated hydrochloric acid (10 mL), and water (170 mL) were swirled for 5 min. in a

1-L flask. The liquid was decanted and compound 8b (70 g, 0.3 mol), water (100 mL), toluene (140 mL), and concentrated hydrochloric acid (250 mL) were added. The mixture was refluxed vigorously for 36 h with additions of hydrochloric acid (70 mL) every 6 h. After removal of most of the toluene by rotary evaporation, the remainder of the organic phase was poured into n-hexane (500 mL). Acid 11b slowly crystallized, 46.0 g (70%); mp 132-133 °C (lit.[10] mp 133.5-134 °C): IR (KBr) cm^{-1} 2900 (CO_2H), 1690 (CO); ^1H NMR ($CDCl_3$) δ 7.20 (m, 5, ArH), 2.80, and 2.90 (d, 2), 2.40-1.00 (m, 10); ^{13}C NMR ($CDCl_3$) ppm 182.64 (CO_2H), 139.75, 129.15 (x2), 127.88 (x2), 125.71, 49.60, 41.29, 40.33, 30.27, 30.11, 25.36 (x2).

b. Catalytic Hydrogenation of trans-2-Benzoyl-cyclohexanecarboxylic Acid (8b)

Hydrogenation of trans-keto acid 8b in ethyl acetate using 5% Pd/C was accomplished as described for cis-keto acid 8a. A sample of the crude product was treated with diazomethane and analyzed by high-pressure LC (silica column, dichloromethane: n-hexane; 2:1), and found to be identical to 11d.

Lithium Triethylborohydride (Super-Hydride) Reduction of cis-Keto Acid (8a)

To a solution of 11.6 g (0.05 mol) acid 8a in 250 mL dry THF was added dropwise 150 mL (1M) solution of Super-Hydride in THF. The mixture was stirred at room temperature for 1 h, then poured into 1 L ice-water. Most of the THF was removed by rotary evaporation and the product was extracted with ether, washed with dilute HCl, water, and then with sodium bicarbonate. Neutralization of the bicarbonate

extract afforded no acidic product. The organic layer was washed with water, dried ($MgSO_4$), and concentrated to 8.9 g (82%) yellow oil, which was distilled (Kugelrohr; 140-142 °C, 0.05 mm) and proved to be a 94:6 mixture of cis-lactones 10a and 10b by capillary GC (SE-54, 30 m/0.25 mm): ^1H NMR ($CDCl_3$) δ 7.28 (m, 5, ArH), 5.16 (d, 1, J=3 Hz, ArCH), 2.60 (m, 3), 2.02-1.20 (m, 7); ^{13}C NMR ($CDCl_3$) ppm 178.01 (CO), 138.41, 128.37 (x2), 127.85, 124.86 (x2), 82.98, 42.95, 37.87, 26.82, 22.97, 22.87 (x2); Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.25; H, 7.41.

Lithium Triethylborohydride (Super-Hydride) Reduction of trans-Keto Acid 8b

A sample of trans-keto acid 8b (4 g, 17 mmol) in 75 mL dry THF was added dropwise to a cooled solution of Super-Hydride (50 mL, 1 M in THF). The mixture was stirred at room temperature for 1 h, then poured into 100 mL ice-water. Most of the THF was removed by rotary evaporation and the product was extracted with ether. The ether layer was washed three times with sodium bicarbonate. Combined bicarbonate extracts were neutralized, extracted with ether, washed with water and dried ($MgSO_4$). Removal of solvent afforded 0.95 g (23%) of crystalline trans-hydroxy acid which showed only one set of peaks in the ^{13}C NMR spectrum. The product lactonized when melted at 150-151 °C: IR (KBr) cm^{-1} 3590, 2930, 2860, 1690 (CO); ^1H NMR (DMSO-d_6) δ 7.26 (m, 5, ArH), 4.72 (s, 1, OH), 2.50 (m, 2), 2.10-0.90 (m, 9); ^{13}C NMR (DMSO-d_6) ppm 177.04, 145.15, 127.58, 127.58, 126.06, 125.50 (x2), 72.05, 45.70, 45.58, 30.15, 25.36, 25.12, 22.15.

The original ether layer was concentrated to 2.8 g (76%) of yellow

oil which was shown to be a mixture of trans-lactones 10c and 10d by high-pressure LC (silica column, methylene chloride: n-hexane; 4:1). Isomer 10d elutes first.

Column chromatography was performed using 100 g of Merk I, 70-230 mesh silica gel packed under n-hexane. A total of 2.5 g of crude lactone mixture in 5 mL of CH_2Cl_2 was applied to the column, and eluted with a 4:1 mixture of methylene chloride: n-hexane with 10-mL fractions collected. Lactone 10d was isolated from fractions between 880 and 950 mL in 90% purity (400 mg): IR (KBr) cm^{-1} 1770 (CO); ^1H NMR ($CDCl_3$) δ 7.42-7.04 (m, 5, ArH), 5.60 (d, 1, J=6 Hz, ArCH), 2.40-1.00 (m, 10); ^{13}C NMR ($CDCl_3$) ppm 177.54 (CO), 135.52, 128.19 (x2), 127.75, 124.92 (x2), 81.96, 46.69, 40.24, 27.57, 25.27, 25.13, 25.01.

Lactone 10c was obtained from fractions between 1120 and 1170 mL in 86% purity (250 mg): IR (KBr) cm^{-1} 1770 (CO); ^1H NMR ($CDCl_3$) δ 7.32 (m, 5, ArH), 4.96 (d, 1, J=9 Hz, ArCH), 2.30-2.00 (m, 2), 2.00-1.70 (m, 4), 2.46-1.12 (m, 4); ^{13}C NMR ($CDCl_3$) ppm 176.34, 137.12, 128.40 (x2), 128.16, 125.62 (x2), 85.36, 51.85, 46.55, 27.08, 25.24, 24.95, 24.75.

Lactonization of Hydroxy Acids 9c, and 9d

A 100 mg sample of hydroxy acid obtained from reduction of trans-keto acid 8b was heated to 150 ^oC. Lactonization takes place rapidly when the hydroxy acid melts. The product was shown to be a mixture of lactones 9c and 9d in a 4:96 ratio by high-pressure LC (silica column; methylene chloride: n-hexane, 4:1). Lactone 10d elutes first.

Reduction of Lactones 10a, and 10b to Acid 11a

A sample of 2.16 g (0.01 mol) mixture of lactones 10a and 10b was dissolved in 75 mL of acetic acid, 0.4 g 5% Pd/C was added and hydrogenation was carried out at 50 °C, 45 psi for 2 h. The mixture was filtered through Dicalite, concentrated to 10 mL by rotary evaporation, and poured in 100 mL water. The product was extracted with ether, washed several times with sodium bicarbonate and then with water. No unreacted lactone was found upon evaporation of solvent from the ether layer. Combined sodium bicarbonate extracts were neutralized, extracted with ether, washed with water, dried ($MgSO_4$), and concentrated to 1.95 g (89%) of cis-acid 11a; mp 102-103 °C.

Reduction of lactones 10c, and 10d in similar way yielded acid 11b in a 90% yield; mp 132-133 °C (lit.[10] mp 133-134 °C).

cis-1,2,3,4,4a,9,9a,10-Octahydro-anthracene-9-one (12a)

A sample of 11 g (0.05 mol) of cis-acid 11a (99% pure) was dissolved in 200 mL of cold concentrated sulfuric acid and poured onto ice. The crystalline product was extracted with ether, washed with water, then with sodium bicarbonate and water, dried ($MgSO_4$) and concentrated to 8.6 g (86%) of ketone 12a of 94% purity. Three successive recrystallization from n-hexane gave cis-ketone 12a of 99% purity (HPLC, silica column, CH_2Cl_2, trans-isomer 12b elutes first), mp 99-100 °C: IR (KBr) cm^{-1} 1670 (CO); ^1H NMR ($CDCl_3$) δ 8.02 (d, 1, ArH ortho to carbonyl), 7.50-7.10 (t, 3, ArH), 2.96 (q, 2, $ArCH_2$), 2.70 (m, 1), 2.50-2.00 (m, 3), 1.50 (m, 6); ^{13}C NMR ($CDCl_3$) ppm 199.62 (CO), 142.49, 133.09, 131.55, 129.01, 126.87, and 126.17 (aromatic), 48.12, 35.80, 33.31,

28.80, 25.35, 23.87, and 23.34 (aliphatic).

The 2,4-DNP derivative of ketone 12a was recrystallized from nitroethane to yield deep red crystals, mp 251-252 °C.

trans-1,2,3,4,4a,9,9a,10-Octahydroanthracene-9-one (12b)

A sample of 59 g (0.27 mol) of trans-acid 11b was dissolved in 500 mL of 98% sulfuric acid and slowly added to 2 Kg of ice. trans-Hexahydroanthrone 12b was extracted with ether, washed with water and then with sodium bicarbonate, dried ($MgSO_4$), and concentrated. The product 49 g (90%) was analyzed by high-pressure LC (silica column, methylene chloride) and found to be ketone 12b of 95% isomeric purity (trans-isomer 12b elutes first). This mixture was recrystallized twice from isopropyl alcohol to give 37.5 g (76%) of trans-hexahydroanthrone 12b of 99.9% purity; mp 110-111 °C (lit.[9] mp 109 °C): IR (KBr) cm^{-1} 1670 (CO); ^1H NMR ($CDCl_3$) δ 7.90 (d, 1, ArH ortho to carbonyl), 7.42-7.00 (m, 3, ArH), 2.70 (m, 2), 2.30 (m, 1), 1.80 (m, 5), 1.20 (m, 4); ^{13}C NMR ($CDCl_3$) ppm 199.33 (CO), 143.19, 132.89, 132.01, 128.34, 126.93, and 126.24 (aromatic), 51.76, 39.89, 37.12, 33.91, 25.91, 25.35, and 25.24 (aliphatic).

The 2,4-DNP derivative of ketone 12b was prepared and recrystallized from ethyl acetate to give orange fluffy crystals, mp 156-157 °C.

Diisobutylaluminum Hydride (DIBAH)

Reduction of cis-Ketone 12a

A solution of 4.4 g (22 mmol) of cis-ketone 12a in 60 mL of dry benzene was slowly added to 10 g (0.07 mol) of DIBAH in 100 mL of ben-

zene. The reaction temperature was maintained below 25 °C during addition. When addition was completed, the mixture was stirred for an additional 1 h, then poured in ice-water. Concentrated hydrochloric acid (50 mL) was added and the product was extracted with ether, washed with water, dried ($MgSO_4$), and concentrated. The product (4.0 g, 91%) gave only one peak on LC (silica column, methylene chloride: n-hexane, 4:1); mp 135-136 °C: ^1H NMR ($CDCl_3$) δ 7.58 (m, 1, ArH), 7.12 (m, 3, ArH), 4.86 (d, 1), 3.05-0.85 (m, 12); ^{13}C NMR ($CDCl_3$) ppm 137.79, 135.19, 128.25, 126.46, 125.67, 125.53, 71.96 (CHOH), 42.01, 31.31, 30.55, 28.57, 25.56, 20.34, 19.02.

Lithium aluminum hydride (LAH) reduction of cis-ketone 12a also gave the same product in a 90% yield.

Diisobutylaluminum Hydride (DIBAH)

Reduction of trans-Ketone 12b

To a solution of 21.3 g (0.15 mol) DIBAH in 150 mL dry benzene was slowly added a solution of trans-ketone 12b (10 g, 0.05 mol) in 100 mL of dry benzene. The temperature was maintained at 20-25 °C during addition. The mixture was stirred at room temperature for 30 min. then at 60 °C for 20 min., cooled and poured into ice-water, and 50 mL concentrated hydrochloric acid was added. The product was extracted with ether, and the combined ether-benzene layer was washed with water, dried ($MgSO_4$), and concentrated. The product (9.8 g, 98%) was analyzed by high-pressure LC (silica column, methylene chloride) and found to be a 60:40 mixture of alcohols 13c and 13d. Isomer 13d elutes first. Several recrystallizations from n-hexane yielded 13c of 98% purity; mp 136-137 °C: ^1H NMR ($CDCl_3$) δ 7.56 (m, 1), 7.40-6.90 (m, 3), 4.30

(d, 1), 2.90-0.86 (m, 12); ^{13}C NMR ($CDCl_3$) ppm 139.22, 135.95, 127.90, 126.59, and 125.83 (aromatic), 74.85 (CHOH), 47.24, 37.15, 36.62, 33.62, 30.32, and 25.77 (x2).

From the mother liquid was obtained a mixture rich in 13d which was then added to a chromatographic column containing 150 g Merck I, 70-230 mesh silica gel and then eluted with methylene chloride in 10 mL fractions. The fractions between 1220-1260 mL yielded 13d (800 mg) of 90% purity: ^{1}H NMR ($CDCl_3$) δ 7.30-6.90 (m, 4, ArH), 4.38 (d, 1), 2.90-0.80 (complex multiplet); ^{13}C NMR ($CDCl_3$) ppm 138.38, 136.51, 129.79, 128.54, 127.67, and 125.77 (aromatic), 71.23 (CHOH), 43.51, 37.26, 33.97, 30.96, 28.07, 26.41, and 25.94 (aliphatic).

Hexahydroanthracene 14

Azeotropic distillation of water from a magnetically stirred mixture of alcohols 13c and 13d (5 g, 25 mmol), 250 mL of toluene, and 2 g of oxalic acid was carried out during 3 h. The cooled mixture was washed with water, and dried ($MgSO_4$). The toluene was removed by rotary evaporation and the product was recrystallized from methanol to give white crystalline hexahydroanthracene 14 (3.8 g, 83%); mp 69-70 °C (lit.[8] 63-66 °C): IR (KBr) cm^{-1} 2850, and 1430; ^{1}H NMR ($CDCl_3$) δ 7.02 (m, 4, ArH), 6.10 (s, 1), 3.02-1.12 (m, 10); ^{13}C NMR ($CDCl_3$) ppm 143.28, 134.32, 133.74, 126.73, 125.97, 125.65, 124.81, 120.98, 36.33, 35.92, 35.07, 34.14, 26.93, 25.88.

Dehydrogenation of a mixture of cis-alcohols 13a and 13b in similar way afforded hexahydroanthracene 14 in a 85% yield.

cis-1,2,3,4,4a,9,9a,10-Octahydroanthracene (15a)

A sample of cis-ketone 12a (2 g, 10 mmol) was hydrogenated in 100 mL of 95% ethanol with 0.4 g of 5% Pd/C, for 8 h at 60 °C and 50 psi. The mixture was filtered through Dicalite, concentrated to 1.7 g, which was purified by passing through a column of silica gel using n-hexane as eluant. Evaporation of solvent afforded 1.30 g (70%) of cis-octahydroanthracene 15a, which was found to be 98% pure by glass capillary GC (SE-54, 30 m/0.25 mm); mp 54-55 °C: ^{1}H NMR ($CDCl_3$) δ 7.02 (s, 4, ArH), 2.74 (d, 4, J=5 Hz), 2.00 (m, 2), 1.48 (m, 8); ^{13}C NMR ($CDCl_3$) ppm 135.34 (x2), 128.89 (x2), 125.07 (x2), 33.47 (x2), 32.48 (x2), 28.86 (x2), 23.31 (x2); MS m/e (rel. intensity) 186 (31), 104 (100), 94 (15), 81 (21).

Hydrogenation of a 2 g mixture of cis-alcohols 13a, and 13b by the same procedure yielded hydrocarbon 15a in 68% yield.

trans-1,2,3,4,4a,9,9a,10-Octahydroanthracene (15b)

A solution of 10 g (0.05 mol) of trans-ketone 12b, in 500 mL of acetic acid containing 1 g of 5% Pd/C was hydrogenated at 60-65 °C at 40 psi. When hydrogen uptake ceased, the solution was filtered, concentrated, poured into water, extracted with ether, and dried ($MgSO_4$). Evaporation of solvent by rotary evaporation gave a 73% yield (6.8 g) of hydrocarbon, 15b. Recrystallization from methanol yielded 5.5 g (99% purity) of white crystals; mp 63-64 °C (lit.[8] mp 63-64 °C): ^{1}H NMR ($CDCl_3$) δ 7.00 (s, 4, ArH), 2.90-2.20 (m, 4), 1.90-1.68 (m, 2), 1.50-0.88 (m, 8); ^{13}C NMR ($CDCl_3$) ppm 136.48 (x2), 128.33 (x2), 125.10 (x2), 38.60 (x2), 37.38 (x2), 33.76 (x2), 26.26 (x2); MS m/e (rel. intensity) 186 (72), 143 (15), 129 (35), 117 (32), 104 (100), 95 (64), 41 (28).

Hydrogenation of a mixture of trans-alcohols 13c and 13d in the same way gave the hydrocarbon 15b in 70% yield.

Catalytic Hydrogenation of Hexahydroanthracene 14

Hydrocarbon 14 (5 g, 17.5 mmol) was hydrogenated in 200 mL of ethyl acetate containing 0.5 g of 5% Pd/C, at room temperature and 35 psi. Hydrogen uptake ceased in 20 min. The mixture was filtered through Dicalite and concentrated to a yellow oil which solidified by standing at room temperature. The mixture was found to be trans-octahydroanthracene 15b, cis-octahydroanthracene 15a, and tetrahydroanthracene 3 in the ratio 35:53:12, by GC-MS.

Wolff-Kishner Reduction of trans-Ketone 12b

Ketone 12b (20 g, 0.1 mol), hydrazine hydrate (20 mL, 85%), KOH (12 g, 0.216 mol), and diethylene glycol (250 mL) were added to a 500-mL stainless steel vessel and slowly heated to 250 ^{o}C. This temperature was maintained until the product codistilled with diethylene glycol. The distillate was poured into 500 mL of water and it was then extracted with n-hexane. The organic layer was washed with dilute HCl, water, dried ($MgSO_4$), and then concentrated to give 14.8 g (79%) of hydrocarbon product, which was found to be a 55:45 mixture of cis- and trans-octahydroanthracene, 15a, and 15b.

PART II

SYNTHESIS OF 1,8-DISUBSTITUTED NAPHTHALENES AND 1,2,3,4-TETRAHYDRONAPHTHALENES: STUDY OF *PERI*-INTERACTION USING ^{1}H AND ^{13}C NMR

CHAPTER V

INTRODUCTION AND HISTORICAL

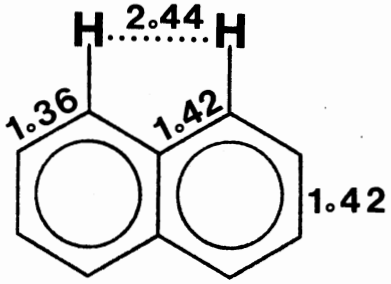
Substituents in the 1- and 8-positions (peri-position) of naphthalene are forced into close contact. The distance between such substituents is, in general, closer than the sums of their non-bonded (van der Waals) radii.[37] The close proximity of the substituents provides several unique properties for peri-substituted naphthalenes, which have received considerable attention.[38]

Relief of steric strain in these compounds may be accomplished by: (a) in-plane splaying of the substituents (Figure 2a); (b) out-of-plane bending of the substituents in opposite directions (Figure 2b); and (c) distortion or buckling of the aromatic nucleus itself.[40-49]

Figure 2. (a) In-Plane and (b) Out-of-Plane Deflection of the Substituents in peri-Substituted Naphthalenes

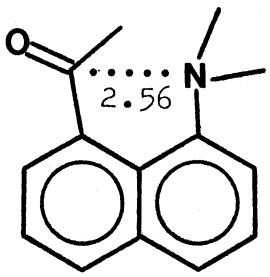
The structure of the unsubstituted naphthalene molecule is known to be planar[37,39] and the distance between the peri-hydrogens has been

established as 2.4-2.5 Å.



Considering that a normal nonbonded carbon-carbon distance in aromatic molecules is about 3.0 Å, it is reasonable to expect a sizeable steric interaction between substituents other than hydrogen at the peri-positions.

Most of the 1,8-disubstituted naphthalenes that have been studied by x-ray analysis,[40-49] show a distortion pattern consistent with a repulsion between the substituents. The exocyclic bonds are splayed outwards and the substituents are displaced to opposite sides of the naphthalene plane to make the internuclear distance between the substituents longer than it would be for an idealized naphthalene skeleton (2.45 Å). For example, d(C-C) = 2.93 Å in 1,8-dimethylnaphthalene[40] and 3-bromo-1,8-dimethylnaphthalene,[41] d(N-N) = 2.79 Å in 1,8-bis(dimethylamino)naphthalene,[42] and d(C-C) = 2.99 Å in 1,8-diphenylnaphthalene.[43] This internuclear distance is shortened when there is an intramolecular attraction between peri-substituents. Thus, the distance between nitrogen or oxygen and carbonyl carbons are reported[44] to be 2.56 Å in compound 17, and 2.61 Å in compound 18.



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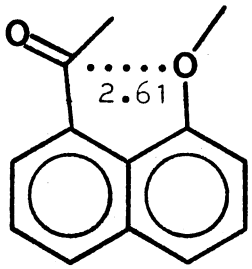
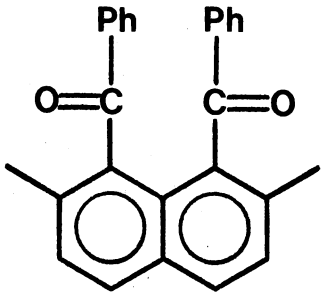


18

Distortion of the naphthalene nucleus is also observed in several instances. Gore and Henrick[45] reported a distortion of the molecular geometry in 1,8-dibenzoyl-2,7-dimethylnaphthalene (19), wherein the C atoms of the carbonyl substituents are splayed outwards (d_{C-C} = 2.85 Å),



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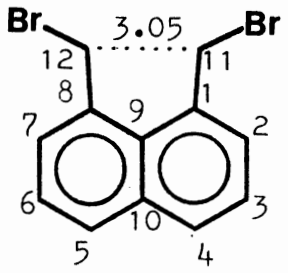
and partial relief of strain is achieved by non-planar distortion of the naphthalene nucleus, with maximum displacements of 0.03 Å from the mean plane for individual atoms.

In 1,8-di(bromomethyl)naphthalene (20)[46] overcrowding between the peri-CH_2Br groups, is relieved by in-plane bending of the C-1-C-11 and C-8-C-12 bonds, and out-of-plane distortions involving the entire molecule. The puckering of the naphthalene system is accomplished by a 4° twist about the central C-9-C-10 bond. This twist apparently results



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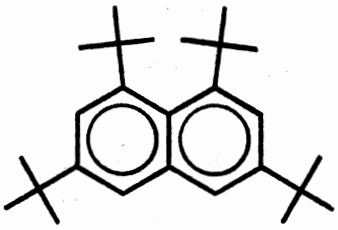
in a redistribution of electrons in the ring system, the C-9-C-10 bond is significantly longer than in naphthalene while the C-2-C-3 and C-6-C-7 bonds are marginally shorter.

In 1,3,6,8-tetra(t-butyl)naphthalene (21), the most extreme example that has been studied so far,[47] the distance between the t-butyl carbon



21

atoms bonded to the peri-positions is 3.86 Å. The nonplanarity of the naphthalene nucleus in this compound is quite marked, with each benzene ring distorted into a flattened half-chair shape. Owing to this distortion, there is no aromatic plane which can serve as a standard of comparison. The t-butyl carbons bonded to the peri-positions are twisted further from the mean plane, placing them 1.22 Å above and below the plane.

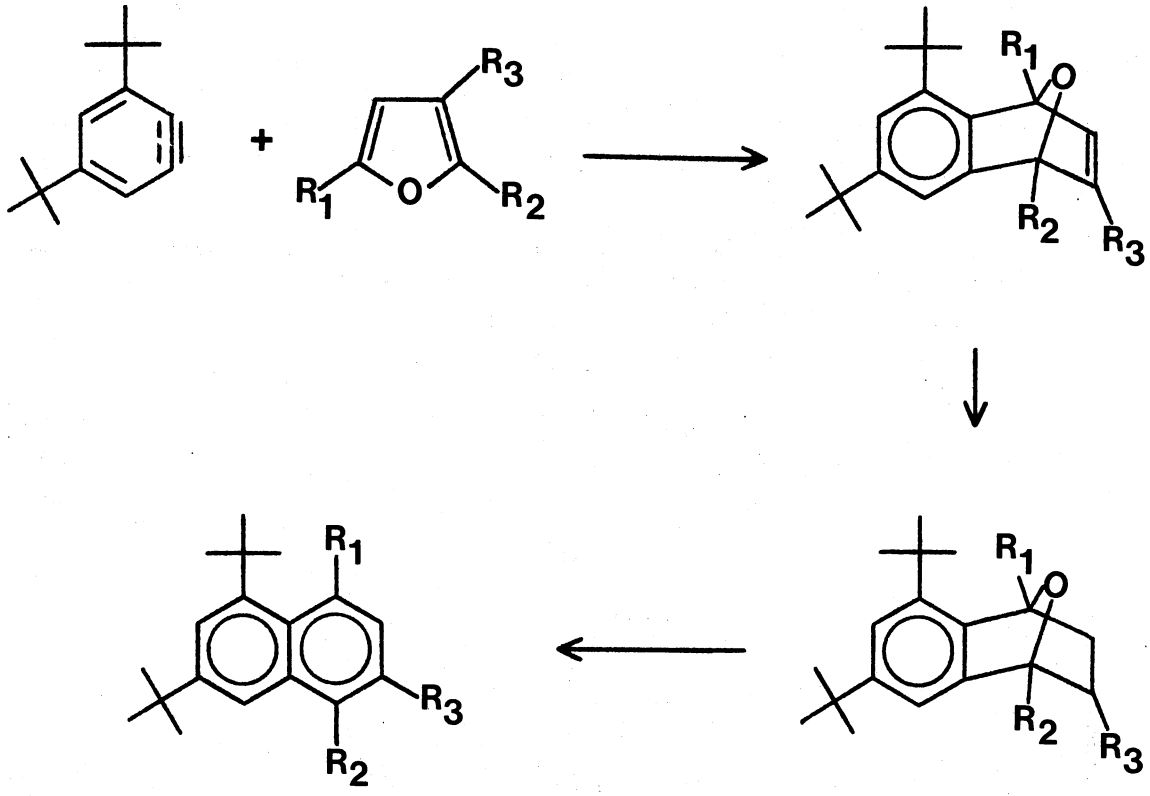
Similar results from x-ray diffraction studies of 1,8-bis(trimethyl

germyl)naphthalene and 1,8-bis(trimethyl stannyl)naphthalene have been reported.[48]

Interest in the study of the properties and structures of 1,8-disubstituted naphthalene derivatives remains active for a variety of reasons: the preparation of such molecules poses synthetic challenge, they provide exceptional insights into the effect of intramolecular strain on chemical properties of these compounds, and relatively few other simple molecules have the special feature of having the substituents close to one another and attached to a relatively rigid framework by essentially parallel bonds. Unlike the other disubstituted naphthalene derivatives, peri-substituted naphthalenes cannot be synthesized by a simple Friedel-Crafts condensation, since the substitution at the α-position prevents the introduction of another substituent at the peri-position. Mayer and Duswalt[50] prepared thirteen out of possible fourteen methylethylnaphthalene isomers by alkylating 1, and 2-methylnaphthalenes. Sterically hindered 1-methyl-8-ethylnaphthalene was not found among the products.

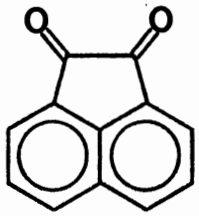
Roberts and coworkers[51] developed a general route for synthesis of the 1,8-diarylnaphthalenes. The key step in their procedure is the direct joining of two nonequivalent aromatic molecules by an organo-nickel-catalyzed Grignard-aryl halide coupling reaction at -15 ^{o}C. This route is limited to synthesis of diaryl naphthalenes. A synthetic route which provided the highly strained 1,3,6,8-tetra(t-butyl)naphthalene (21) was developed by Franck and Leser.[52,53] Their approach involves a Diels-Alder reaction of a benzyne (generated from 3,5-di-t-butylanthranilic acid) with an appropriate furan to form an endoxide which is converted to a dihydroendoxide via catalytic hydrogenation and then dehydrated in ethanolic HCl to afford a peri-substituted naph-

thalene.



This synthetic procedure suffers from many disadvantages. The yield is very low (5-10%) when R_1 and R_2 are any substituent other than hydrogen, the choice of starting substituted furan is very limited, and the resultant peri-substituted product contains at least two additional substituents (the same as peri-substituents) which further complicates study of the spectroscopy and the structural behavior of these compounds.

The most common synthetic routes to 1,8-disubstituted naphthalene derivatives originate from acenaphthenequinone (22),[54] or naphthalic anhydride (23).[55-59]



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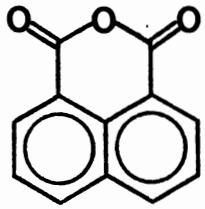
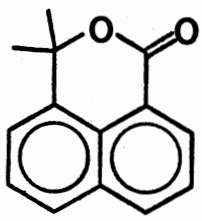


23

Naphthalic anhydride is a stable compound but insoluble in organic solvents. Because of its poor solubility even at elevated temperatures, common nucleophilic addition reactions with this compound are often troublesome and give a low yield. When a Grignard reaction was carried out with this anhydride in refluxing ether, or benzene, unreacted anhydride was recovered to the extent of 50-70%.[57] Reaction of the anhydride with two mole equivalents of methyllithium[55] yields 3,3-dimethyl-1,8-naphthalide (24) in a yield lower than 25%.



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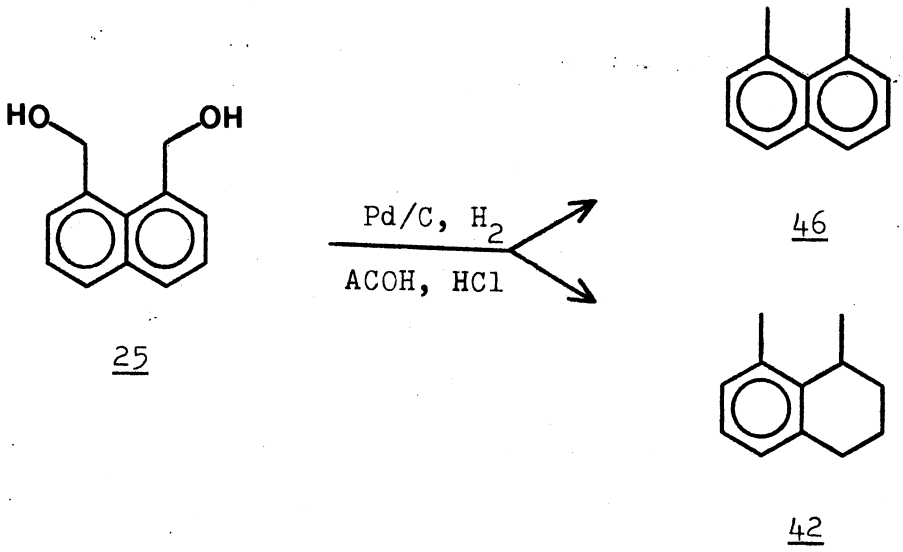
An improved method for reduction of naphthalic anhydride by DIBAH was reported by Burnham, et al. to yield 1,8-naphthalenedimethanol (25) in a 94% yield.[59]



25 46 42

1,8-Dimethylnaphthalene (46) and 1,8-dimethyl-1,2,3,4-tetrahydronaphthalene (42) were obtained by a catalytic hydrogenation (Pd/C) of diol 25 in acetic acid and hydrochloric acid.

The molecular interactions in peri-substituted naphthalenes and related derivatives have been studied through use of spectroscopic methods; among these nuclear magnetic resonance has become increasingly popular. Both proton and carbon-13 NMR studies of the naphthalene system examining the effect of a variety of substituents at different positions on the nucleus have been reported.[61-74] In the ^{1}H NMR spectrum of naphthalene, the α-proton resonance appears at 7.80 ppm and the β-proton resonance at 7.44 ppm.[60] The presence of substituents in the naphthalene nucleus affects the resonance positions of the ring protons. Proton NMR spectra of some substituted naphthalenes was studied by Lucchini and Wells.[61]

The striking advantages of ^{13}C NMR spectroscopy in characterization of hydrocarbons was discovered by Lauterbur.[62] Subsequently, Grant and his group examined a variety of aromatic systems in detail[63] to estab-

lish clearly the utility of ^{13}C shieldings for hydrocarbon identification and as a probe for assessing the electronic structure of aromatic compounds.[64]

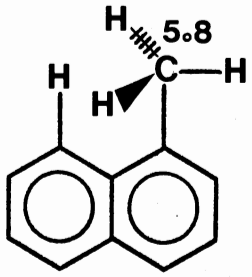
Proton-decoupled ^{13}C spectra of naphthalene compounds are relatively simple compared to the often very complex ^{1}H spectra. ^{13}C NMR has thus become a very important and useful tool in structure elucidations of naphthalene derivatives. The ^{13}C chemical shifts promise to be useful monitors of mesomerism, π-induction, steric effects and other factors affecting the electron distribution and consequently provide useful measures of substituent effects. Though ^{13}C NMR spectra are simple in appearance, the assignment problems are substantial. Among various techniques employed for carbon-13 assignments, deuterium substitution is found to be useful for naphthalene compounds.[65,70] Upon replacement of hydrogen by deuterium at specific carbon, the shielding of that carbon is increased by the deuterium isotope effect and its absorption is a triplet since $I_D = 1$.

Other useful techniques which are employed in carbon-13 chemical shift assignments of naphthalene derivatives are the use of fully proton-coupled (non-decoupled) spectra[67-69] and selective $^{13}C[^{1}H]$ decoupling.[68,69]

Although many structural characteristics of molecules are clearly revealed by the ^{13}C chemical shifts and coupling constants, additional structural information as well as insight into dynamic molecular processes can be gained from relaxation time measurements. The two characteristic times, T_1 for spin-lattice relaxation, and T_2 for spin-spin relaxation, describe different time-dependent processes occurring in the nuclear spin system.[77] Unlike chemical shifts and coupling

constants, T_1 values are dependent on molecular reorientation and can therefore act as powerful sources of information on both intermolecular and intramolecular motions.[103] This information can be used indirectly as an aid to spectral assignment[79] or more directly in studies of hindered rotation, axes of rotation, segmental motion, association, and complexation.[75,76,103]

An interesting case of the effect of hindered rotation on methyl ^{13}C T_1 values is found for 1-methylnaphthalene (45) and 9-methylanthracene (26), which give values of 5.8 and 14.0 sec., respectively.[78]



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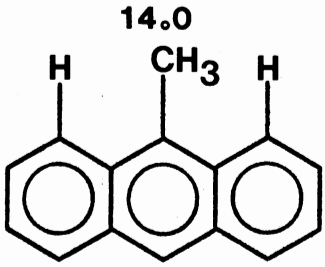


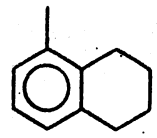
26

In 1-methylnaphthalene the interaction with the peri-proton causes the methyl group to adopt a staggered conformation, thereby hindering its rotation and leading to a smaller value of T_1, compared to T_1 values of the methyl group in 26. In 9-methylanthracene, however, the existence of two peri-hydrogens means that there is no longer any preferred conformation of the methyl group, thus decreasing the rotation barrier and facilitating free rotation which, in turn, leads to a marked increase in T_1, as observed.

CHAPTER VI

RESULTS AND DISCUSSION

Synthesis and NMR studies of the following series of alkylated naphthalenes and 1,2,3,4-tetrahydronaphthalenes were carried out to learn the effect of the proximity and the bulk of the substituents at peri-positions on the NMR spectra of 1,8-substituted naphthalene and related tetralin systems.



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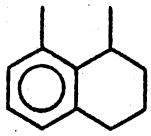

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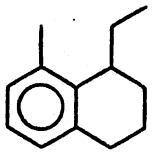

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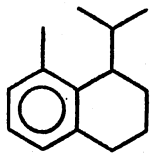

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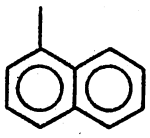

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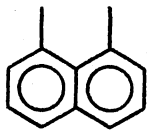

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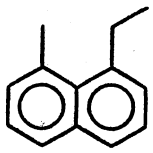

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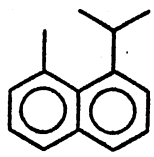

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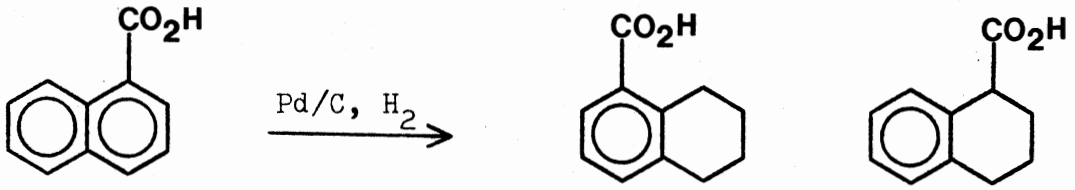
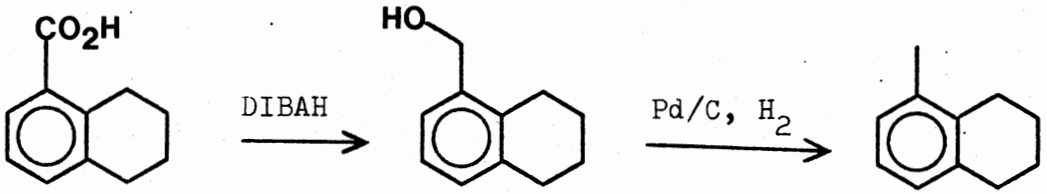
1,2,3,4-Tetrahydro-8-naphthoic acid (28) was available from a Pd/C catalyzed hydrogenation of 1-naphthoic acid (27) and subsequent separation of two isomeric acids 28, and 29.



27 28 29

DIBAH reduction of acid 28 in benzene and subsequent hydrogenolysis of alcohol 30 in the presence of Pd/C in acetic acid afforded hydrocarbon 41.



28 30 41

1-Methylnaphthalene (45) is commercially available. It was purified by distillation. 1,8-Dimethyl-1,2,3,4-tetrahydronaphthalene (42) and 1,8-Dimethylnaphthalene (46) were available from J. D. Burnham's[59] work.

The reaction sequence for synthesis of 1-ethyl-8-methyl-1,2,3,4-tetrahydronaphthalene (43) and 1-ethyl-8-methylnaphthalene (47) is shown in Figure 3. Reduction of naphthalic anhydride (23) with two molar

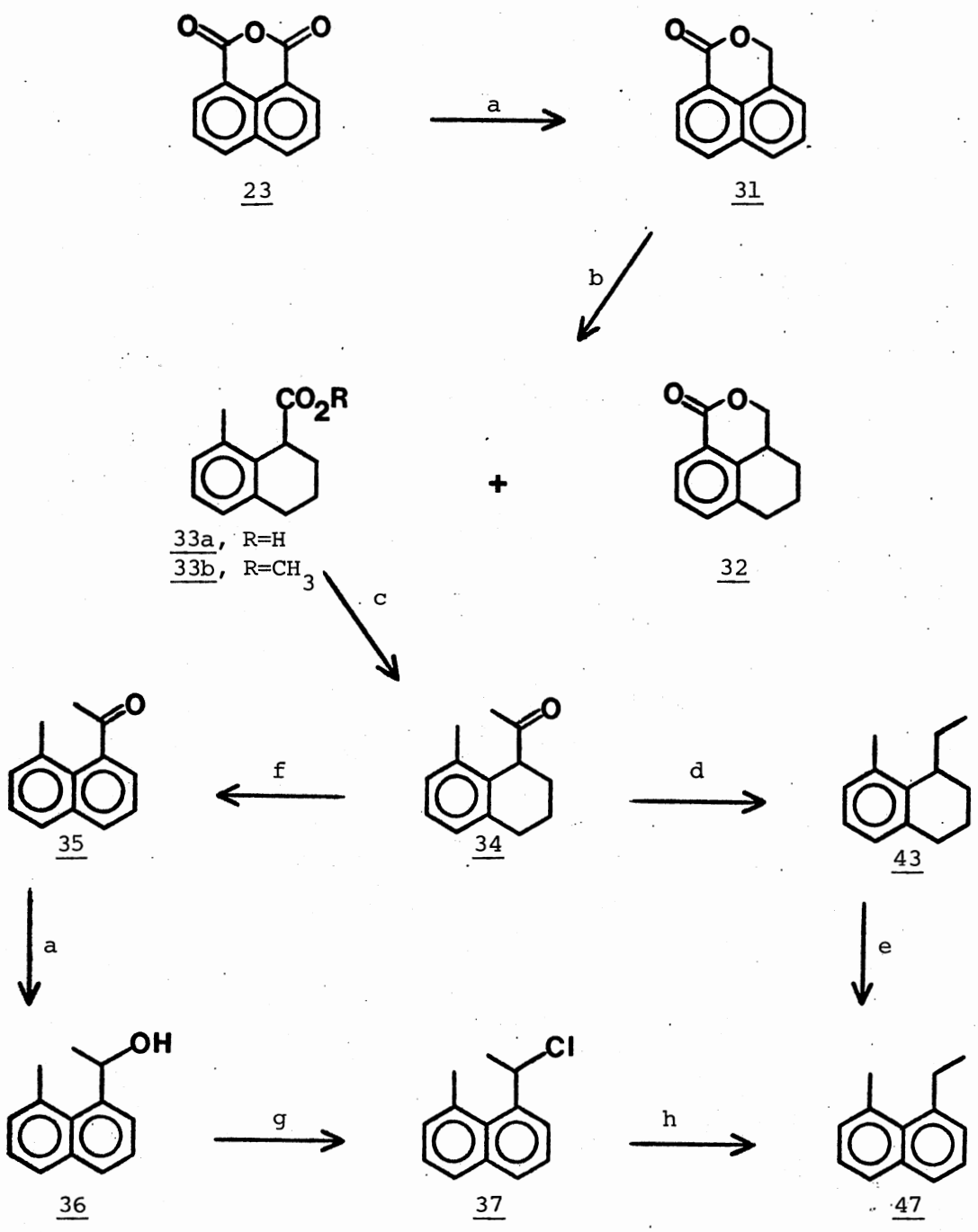
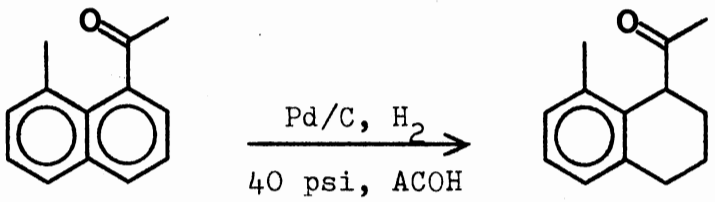


Figure 3. Synthesis of Hydrocarbons 43 and 47

[a]DIBAH, Toluene, 5-10°C. [b]Pd/C, ACOH, H_2. [c]SO_2Cl; $(CH_3)_2Cd$. [d]N_2H_4, KOH, DEG. [e]Pd/C, Δ, Cymene. [f]Pd/C, Δ. [g]Conc. HCl. [h]$Li(Et)_3BH$.

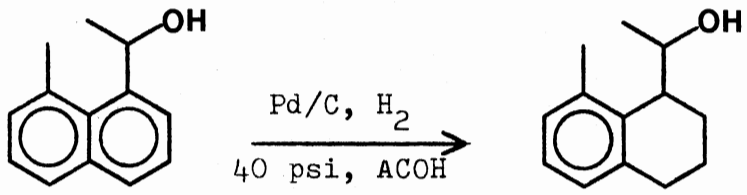
77% yield. Catalytic hydrogenation of lactone 31 in acetic acid in the presence of Pd/C afforded a mixture of acid 33a (71%) and lactone 32 (29%). The acid 33a was separated from the mixture by sodium bicarbonate extraction. Conversion of acid 33a to ketone 34 by the well known method[83] of treating with methyllithium failed, even when the acid was converted to the acid chloride and then treated with the reagent. This may be due to the steric hindrance from the peri-methyl substituent which renders attack at the carbonyl site difficult. However, when the acid was converted to the corresponding acid chloride and then treated with dimethyl cadmium (prepared from methyl magnesium bromide), ketone 34 was obtained in a 85% yield. Success of this reaction is probably the result of a higher reaction temperature (refluxing benzene), and also a different reaction mechanism[85] compared to that of the organolithium reaction.[83] Hydrocarbon 43 was obtained in a 42% yield from a Wolff-Kishner reduction of ketone 34. Aromatization of this hydrocarbon was carried out in refluxing cymene to give 1-ethyl-8-methylnaphthalene (47) in 67% yield. Thus the overall yield of conversion of ketone 34 to hydrocarbon 47 was 28%. An improved overall yield resulted when ketone 34 was aromatized by heating with Pd/C to give ketone 35, which in turn was converted to alcohol 36 in a quantitative yield by DIBAH reduction. Treatment of this alcohol with concentrated hydrochloric acid in olefin-free n-hexane and subsequent dehalogenation of resultant chloride 37 by Super-Hydride (lithium triethylborohydride), afforded hydrocarbon 47 in an overall yield of 52%. Several other methods were examined to convert ketone 35 to hydrocarbon 47, but all gave unsatisfactory results. Catalytic hydrogenation of ketone 35 by Pd/C resulted in reduction of naphthalene nucleus, and no reduction of

the carbonyl group was observed.



35 34

A similar result was observed when alcohol 36 was hydrogenated in the presence of Pd/C as shown below.

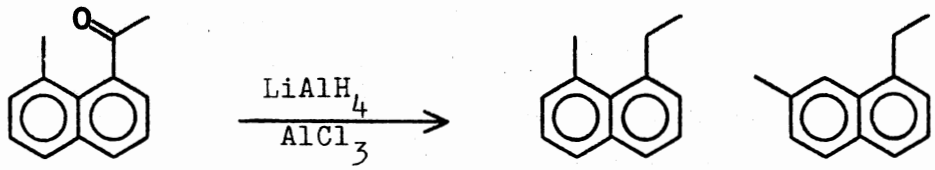


36 49

The peri-interaction between the substituents at 1 and 8 positions is responsible for the unusual behavior of these compounds. Possible distortion of the aromatic nucleus due to peri-interaction alters the activation energy of these systems, thereby decreasing the activation energy for hydrogenation of aromatic nucleus. On the other hand, in the transition state the peri-strain is released, at least partially, resulting in an increased reaction rate for hydrogenation.

Wolff-Kishner and Clemmensen reduction of ketone 35 was also unsuccessful, and most of the starting material was recovered from these

reactions. Use of mixed hydride reduction method described by Nystrom and Berger[80] resulted in the formation of by product 50 along with hydrocarbon 47.



35 47 50

Isomerization of hydrocarbon 47 to 50 is expected since Suld and Stuart[84] reported the isomerization of 1,8-dimethylnaphthalene to 1,7-dimethylnaphthalene in the presence of BF_3 and HF at room temperature.

Corey and Achiwa reported[81] a method for deoxygenation of benzylic alcohols using a pyridine-sulfur trioxide complex in tetrahydrofuran as the reagent for hydroxyl activation and carrying out the reduction by $LiAlH_4$. This method was tried to convert alcohol 36 to hydrocarbon 47, but the yield was low (~ 25%) and considerable (~ 15%) elimination product was formed as shown by GC analysis.

The reaction sequence for the synthesis of 1-isopropyl-8-methyl-1,2,3,4-tetrahydronaphthalene (44) and 1-isopropyl-8-methylnaphthalene (48) is shown in Figure 4. Aldohol 38 was obtained by methylation of ester 33b, or ketone 34. It was then dehydrated by azeotropic distillation of water from a solution of the alcohol in toluene containing 2% oxalic acid. The product of this reaction was found by GC-MS to be a mixture of alkenes 39, and 40. Hydrogenation of these olefins gave the hydrocarbon 44 which was then dehydrogenated in refluxing cymene for 55-60 h (Pd/C) to yield hydrocarbon 48. Both hydrocarbons 47 and 48 were puri-

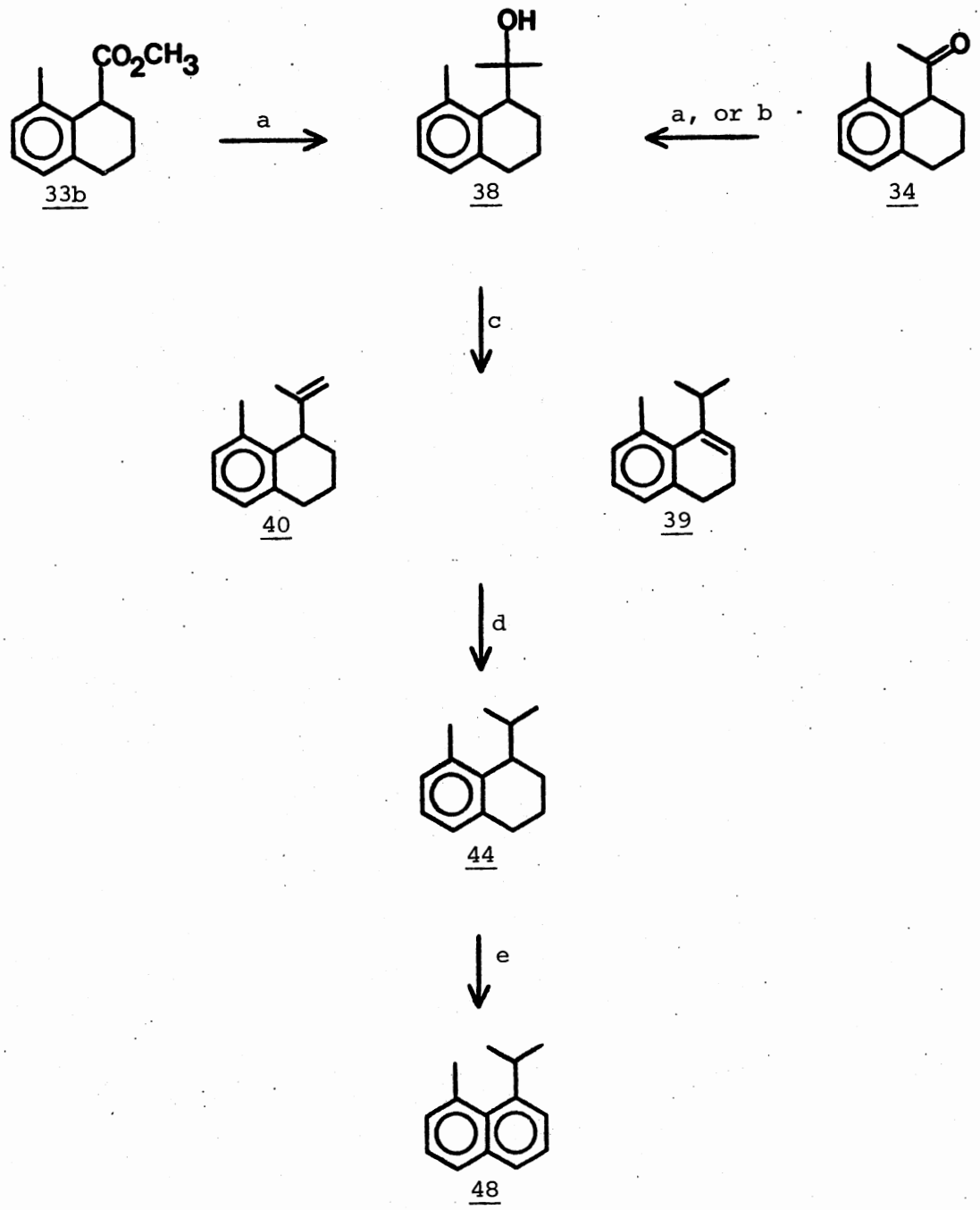
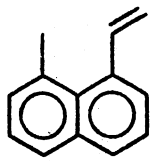


Figure 4. Synthesis of Hydrocarbons 44, and 48

[a] CH_3Li. [b] CH_3MgBr. [c] Toluene, oxalic acid, Δ. [d] Pd/C, H_2, ACOH. [e] Pd/C, cymene, Δ.

fied by picrate formation and decomposition of the picrate on a column of basic alumina.[82]

Attempts to convert the aromatic ketone 35 to 1-isopropyl-8-methylnaphthalene failed. The ketone 35 did not react with either methyl lithium or methyl magnesium bromide. When it was converted to chloride 37 and coupled with methyl Grignard reagent, the only product was the olefin 51 which slowly polymerized.



51

The coupling reaction of a Grignard reagent prepared from the chloride 37 with methyl iodide was also unsuccessful.

Discussion of the ^{1}H and ^{13}C NMR

It is well known that hydrogen atoms which are subject to significant steric compression, generally exhibit a downfield shift relative to TMS.[86] This effect is rationalized in terms of induced charge polarization in the C-H bond as a result of nonbonded hydrogen-hydrogen repulsive forces.[86,87] It also has been demonstrated that the same effect is responsible for an increase in the shielding experienced by the associated ^{13}C nuclei.[87] The magnitude of these shifts, however, exhibits a strong dependence upon the conformational geometry existing between the C-H bonds in the two interacting groups.[86]

Based on the above observations it is reasonable to expect that in

the series of compounds, 41-44 and 45-48, the downfield ^1H chemical shift of the methyl group at the peri-position will increase as the bulk of the other peri-substituent increases. ^1H NMR shifts for the methyl group in compounds 41-48 are presented in Table V.

TABLE V

^1H NMR SHIFTS OF THE METHYL GROUP IN 41-48

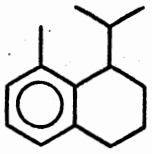
Compound	$\delta^a_{CH_3}$	$\Delta\delta$
41	2.16	0.00
42	2.24	0.08[b]
43	2.26	0.10[b]
44	2.27	0.11[b]
45	2.52	0.00
46	2.73	0.21[c]
47	2.78	0.26[c]
48	2.84	0.32[c]

[a] ppm from TMS in $CDCl_3$.
[b] Relative to 41.
[c] Relative to 45.

The results given in Table V show a deshielding effect on methyl proton signal by increase of peri-interaction for both series of tetralins 41-44, and naphthalenes 45-48. This proton deshielding effect by peri-interaction is more pronounced in the naphthalene series 45→48 as compared to the tetralins 41→44, because of the increased proximity of

peri-substituents in the former series.

The NMR spectrum of compound 44 is interesting since an unusual nonequivalence of isopropyl method signals were observed in this compound. In the ^{1}H NMR spectrum, these signals appear as a pair of doublets centered at 0.89 and 0.86 ppm



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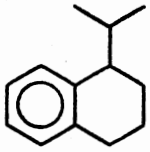


53

Compounds containing an isopropyl group adjacent to a chiral carbon are known to show a magnetic nonequivalence of geminal methyls in the NMR spectra.[88-91] However, the chemical shift difference ($\Delta\nu$) value of 3 Hz in compound 44 (given in Table VI) is unexpectedly small compared for example to a $\Delta\nu$ of 28.0 Hz for geminal methyl signals of 1-isopropyl tetralin 53. Variable temperature NMR studies of compound 44 (Table VI) show that two methyl signals approach each other with increase in temperature (Figure 5), and coincide at 85°C. Upon further increase in temperature, these methyl signals separate and $\Delta\nu$ increases with increase in temperature.

This unusual behavior is not observed in other compounds containing an isopropyl group attached to an asymmetric center. The chemical shift difference between the geminal groups in conformationally mobile systems may be partitioned into a "conformational" term $\Delta\delta_c$ depending on the differences of conformer populations and a temperature independent "intrinsic" term $\Delta\delta_i$ that is independent of these conformer popula-

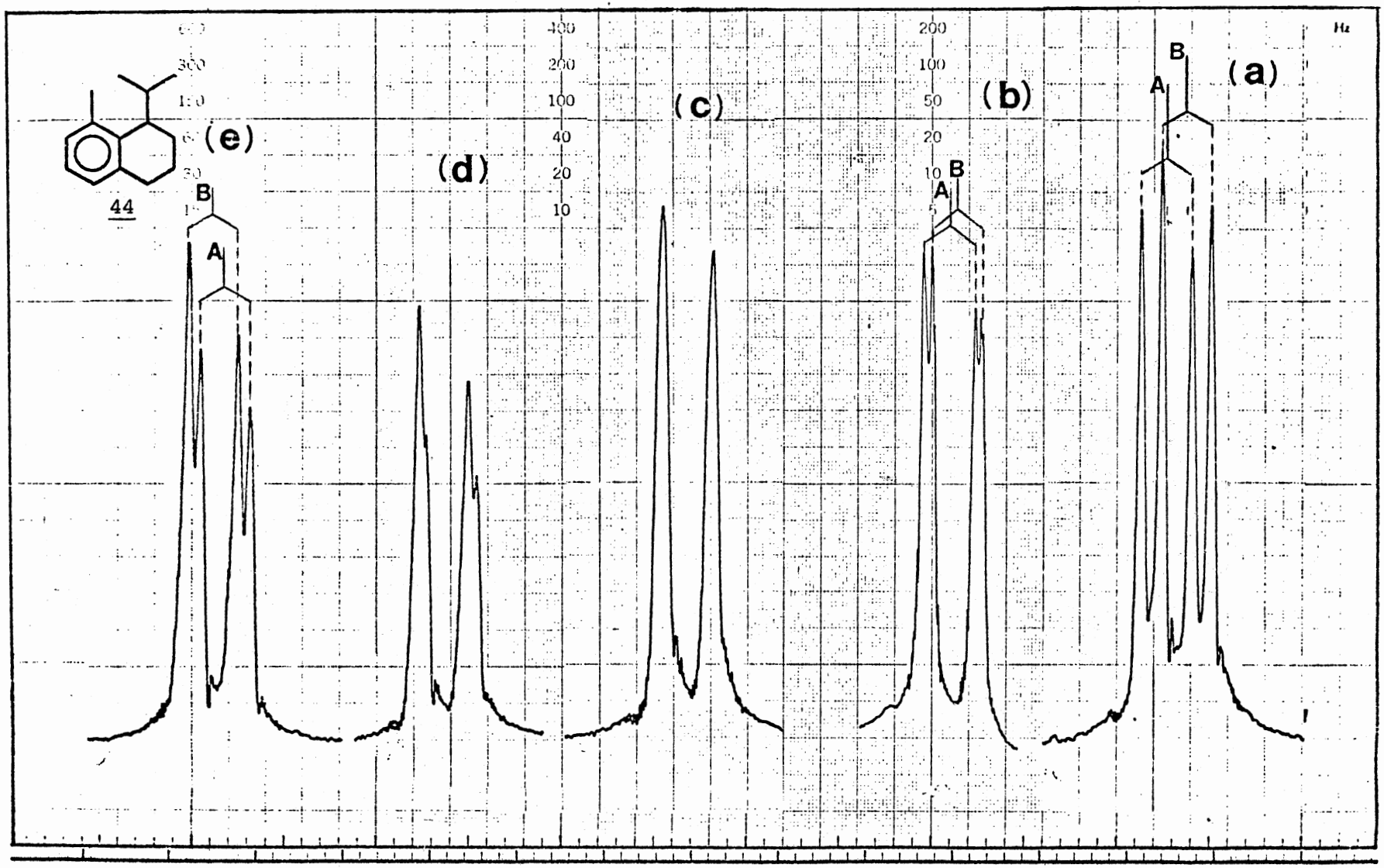


Figure 5. ^{1}H NMR Isopropyl Methyl Signals of 44 at (a) 30°C, (b) 65°C, (c) 85°C, (d) 120°C, and (e) 145°C

tions.[90,91]

$$\Delta\delta_{obs.} = \Delta\delta_c + \Delta\delta_i \quad (1)$$

TABLE VI

^{1}H NMR SHIFTS[a] FOR ISOPROPYL METHYL GROUPS IN 44

Temp.[b]	δ_A	δ_B	$\delta_A - \delta_B$
30	87.0	84.0	3.0
65	87.0	85.6	1.4
85	87.0	87.0	0.0
120	87.0	87.9	-0.9
145	87.0	88.6	-1.6

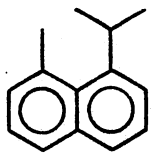
[a] In Hz from TMS in 1,2,4-trichlorobenzene.

[b] ^oC.

Binsch and Franzen[90] suggested that $\Delta\delta_c$ and $\Delta\delta_i$ may differ in relative sign. Thus, a possible explanation for unusual behavior of compound 44 is that $\Delta\delta_i$ term in Equation (1) has a contribution to $\Delta\delta_{obs.}$ which is opposite in sign to $\Delta\delta_c$, in this compound. As a result, the contributions from the terms $\Delta\delta_c$ and $\Delta\delta_i$ partially cancel each other at room temperature and completely cancel each other at 85^{o}C. Above 85^{o}C the contribution from $\Delta\delta_i$ term overcomes the $\Delta\delta_c$ term which results in increasing $\Delta\nu$ with raise in temperature. It is interesting to note that one methyl resonance remains uneffected by the changes of temperature, while the other methyl signal moves downfield. This may be due to the fact that at room temperature there is a favored conformation in

which one of the methyl groups is located in shielding zone of the aromatic ring and its doublet appears at higher field than the other methyl signal. With increase in temperature, the rate of conformational interchange increases, therefore the upfield methyl signal starts to move downfield as the time spent in shielding zone of the aromatic ring by the corresponding methyl group lessens.

Low-temperature NMR spectra of hydrocarbon 48 were examined with the expectation that a high degree of steric interference would lead to restricted rotation of the isopropyl group, a phenomenon which has been observed with 55 which has similar steric crowding.[73] Ernst and Mannschreck reported that below -63 °C compound 55 exists as two



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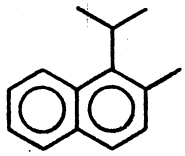


55

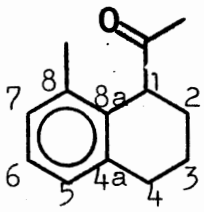
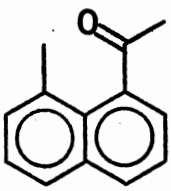
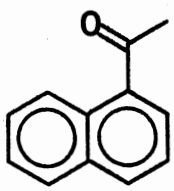
rotamers in the ratio 20:80. However, the low-temperature NMR spectra of hydrocarbon 48 indicate that the rotation of the peri-isopropyl group is fast on the NMR time scale even at -110 °C. Franck, et al. suggested[104] that steric interactions may occasionally produce low rather than high barriers to rotation. They reported a low rotation barrier of 6.5 Kcal/mole for 1,8-di-t-butylnaphthalenes and suggested that if the out-of-plane deflection of substituents in peri-substituted naphthalenes is sufficiently great, interaction of the substituents and, therefore, steric inhibition of rotation may be reduced. Thus, changes in the NMR spectrum associated with hindered rotation may be considerably reduced.

Before starting the discussion of ^{13}C spectra of hydrocarbons 41-48, it is convenient to consider the ^{13}C NMR spectra of two intermediate ketones 34, and 35. The ^{13}C chemical shifts for these ketones are given in Table VII. The ^{13}C chemical shifts for 1-acetonaphthone (54) are also given for comparison. Chemical shift assignments for 54 have been made by several workers.[68,69,70,71] Chemical shift assignments for ketone 34 were made with the help of model compound 41 (^{13}C NMR of this compound will be discussed later), and taking into consideration the substituent effect of acetyl group on a cyclohexane ring.[32] The off-resonance decoupled spectrum was also used to distinguish between primary, secondary, tertiary, and quaternary carbons. ^{13}C NMR shifts of compound 34 indicate considerable shielding of C-3 and C-8 which are γ to the carbonyl whereas C-8a which is also γ to the carbonyl remains unaffected (compared to compound 41). This effect can be understood by examination of a model of ketone 34. The cyclohexane ring in a tetralin system adopts a skewed conformation. When an acetyl group is placed at C-1 in an axial arrangement, it is in close proximity to C-3, whereas an equatorial conformation of this acetyl group brings it into the neighborhood of C-8. As a result, these two positions experience γ-gauche interactions with acetyl group and they are shielded.

The ^{13}C chemical shift assignments for ketone 35 were made through use of the off-resonance decoupled spectrum and a gated decoupling experiment. Resonance lines at 140.2, 134.4, 133.4, and 128.5 survived in the off-resonance decoupled spectrum and were assigned to quaternary carbons. An acetyl substituent at the α-position of naphthalene gives rise to a C-1 shift of 134.7 (see compound 54, Table VII), and its α-deshielding effect is enhanced[68,72] when there is steric interaction.

TABLE VII

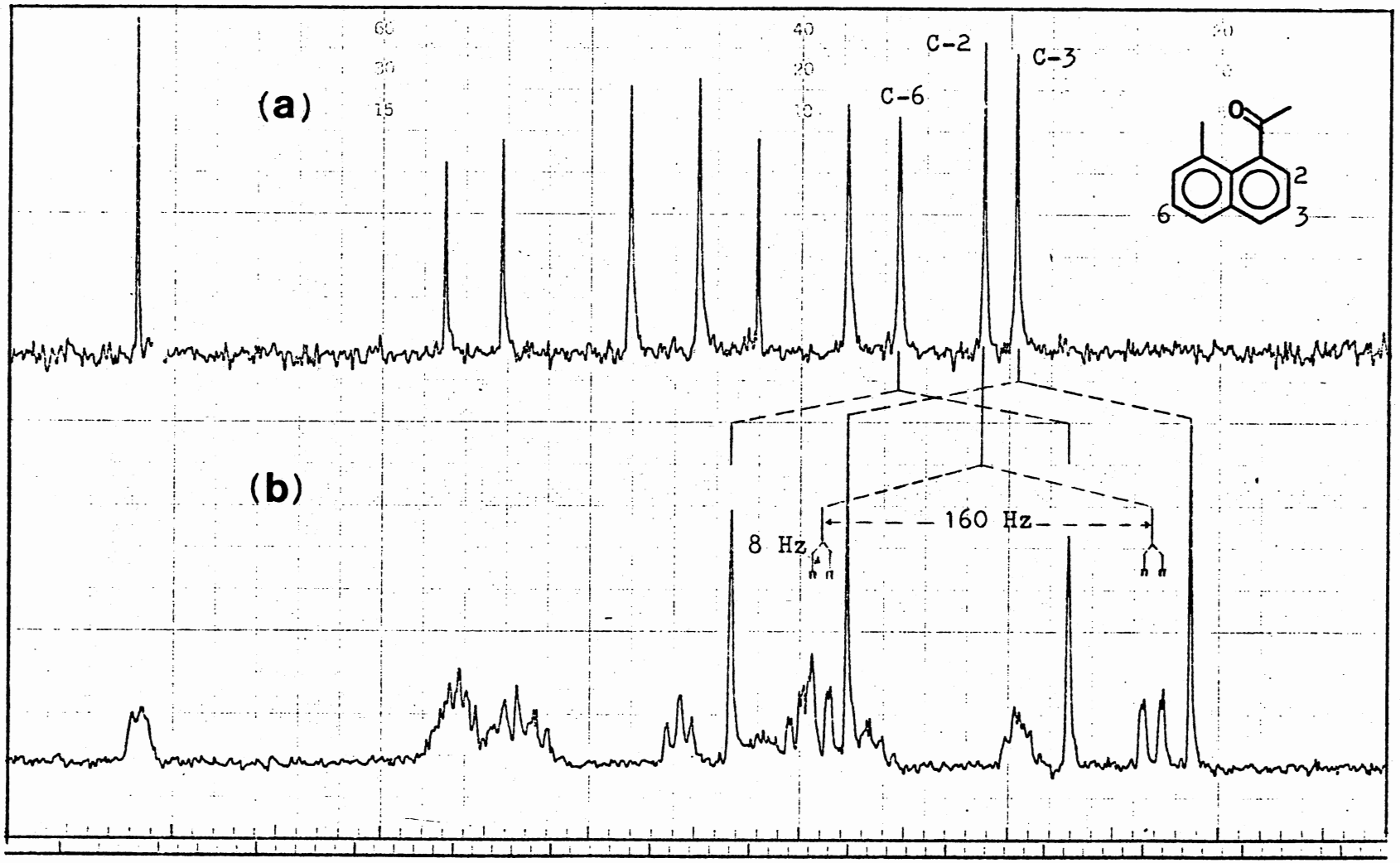
^{13}C CHEMICAL SHIFTS[a] OF KETONES 34, 35, AND 54

Carbon No.	 34	 35	 54
C-1	50.5	140.2	134.7
C-2	26.6	124.3	128.8
C-3	19.7	123.7	124.1
C-4	29.7	131.0	132.7
C-4a	136.4	133.4[b]	133.7
C-5	127.0[b]	126.8	128.2
C-6	126.4	125.9	126.1
C-7	127.6[b]	129.7	127.7
C-8	132.9	134.4[b]	126.0
C-8a	137.3	128.5	129.0
CO	209.9	205.8	200.8
$\underline{C}H_3CO$	28.0	31.8	29.4
CH_3Ar	19.6	23.6	---

[a] ppm from TMS. All samples at same molar concentration in $CDCl_3$.

[b] These assignments may be reversed.

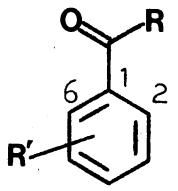
Thus the signal at 140.2 for 35 is assigned to C-1. The highest-field quaternary signal at 128.5 is assigned to C-8a based on comparison with model compound 54 and considering the shielding effect exerted on this carbon by a methyl substituent at C-8.[69-71,94,99] Assignments for C-2 (124.3), C-3 (123.7), and C-6 (125.9) are made by the help of the gated decoupled spectrum (Spectrum 5). Only the aromatic range (120-150 ppm) is shown in the spectrum. In aromatic compounds, the magnitudes not only of one-bond ($^1J_{CH}$) but also three-bond ($^3J_{CH}$) couplings are valuable in the assignment of spectra. In naphthalene compounds, three-bond couplings are fairly large, 4-10 Hz[71,74,100,101] compared to two-bond couplings of 0.5-2.0 Hz.[71,74,102] One-bond couplings are in the order of 120-160 Hz.[71,74,101] In 1,8-disubstituted naphthalenes, C-3 and C-6 do not experience any three-bond C-H coupling, and their splitting with two-bond hydrogens are often too small to be resolved. Therefore, in a proton-coupled spectrum (or gated-decoupled spectrum) these two carbons split only by directly bonded hydrogens, so their signals appear as a pair of sharp doublets, which can be distinguished from other signals. In the particular case of ketone 35, C-2 experiences only one three-bond splitting by H-4. Thus its signal in gated-decoupled spectrum is expected to appear as a doublet of doublet, ignoring two-bond coupling by H-3. Examination of Spectrum 5 reveals that the signal from C-2 is split by directly bonded hydrogen, ^1J(C-2, H-2) = 160 Hz, which is then split by H-4, ^3J(C-2, H-4) = 8 Hz. A very small splitting by H-3 is also observed, ^2J(C-2, H-2) ~1.5 Hz. From two meta carbons (C-3, and C-6), C-3 is more shielded due to stronger meta shielding effect of acetyl substituent than a methyl substituent.[68,69,71] The assignments for the remaining three aromatic carbons are made by the help of two model com-



Spectrum 5. The Aromatic Portion of (a) Full Decoupled, and (b) Gated-Decoupled ^{13}C NMR of Ketone (35) (Observed at SW = 1000 Hz)

pounds, 1-acetonaphthone (35), and 1-methylnaphthalene (45). Reported substituent chemical shift parameters for naphthalene compounds[68-72] do not give good results when applied to peri-substituted naphthalenes. An example of this is shown in Table VIII, wherein the calculated ^{13}C chemical shift values, using substituent chemical shift parameters[71] are compared with experimentally observed values. Except for a case of a few carbons, there is a strong deviation between calculated and observed values, possibly due to distortion of an idealized geometry of the molecule by peri-interaction.

Data from work of Drakenberg, et al.[92,93] on the barriers to internal rotation in benzaldehydes and acetophenones show that the carbon s-trans to the carbonyl oxygen (C-2, in the structure shown below) is



shifted to higher field. Thus, the signs of the substituent effects at the ortho carbons in 1-naphthoyl derivatives may be an indication of the orientation of the carbonyl group. This supports the view of the preferential orientation of the carbonyl oxygen towards C-8a (Figure 6). However, the symmetric methyl group in 1-methylnaphthalene also causes substituent effects, although smaller, at C-2 and C-8a, and these have the same signs, +0.90 and -0.95 ppm, respectively[94] of a carbonyl substituent. A comparison of the ^{13}C chemical shifts in 1-naphthaldehyde

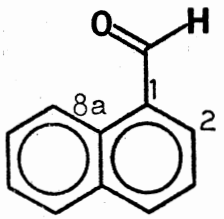
TABLE VIII

THEORETICAL AND EXPERIMENTAL ^{13}C SHIFTS FOR KETONE 35

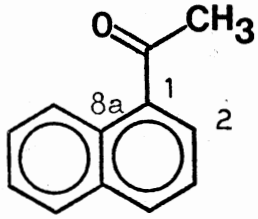
Carbon No.	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-8a	C-4a
Calcd. ^{13}C shift[a]	131.0	128.8	123.9	133.4	126.8	125.9	128.5	132.4	130.0	132.9
Observed ^{13}C shift	140.2	124.3	123.7	131.0	126.8	125.9	129.7	134.4	128.5	133.4
Deviation From Calcd.	+ 9.2	- 4.5	- 0.2	- 2.4	0.0	0.0	+ 1.2	+ 2.0	- 1.5	+ 0.5

[a]Substituent shift parameters from Ref. 71 are used.

with those in 1-acetonaphthone indicates[71] that the formyl and acetyl group adopt the same conformation, with the C=O bond trans to the C-1-C-2 bond (Figure 6). This deduction was based on the similarity in the C-9 chemical shifts as compared to the large difference in the C-2 chemical shifts.[71]



56



54

Figure 6. Preferred Conformations for 1-Naphthaldehyde (56) and 1-Acetonaphtone (54)

Comparison of C-2 and C-8a chemical shifts in compounds 35 and 54 (Table VI) reveals that C-2 is shielded by 4.3 ppm in 35 compared to C-2 in 54 (effect of peri-methyl substituent on this carbon is negligible), while C-8a shows a smaller change in comparing 54 to 35 (0.9 ppm shielding effect of the C-8 methyl group acting on C-8a must be considered). This result is an indication that in ketone 35 the C=O bond is forced out of planarity and the oxygen is rotated away from carbon 8a. Thus, the increased shielding of C-2, and C-4 (by 1.7 ppm) in 35 results from decreased conjugation of the carbonyl substituent with the aromatic system. This shielding effect is strong at C-2, probably because of the outward splaying of peri-substituents, which brings the acetyl methyl group closer to C-2 and results in an increased γ-shielding effect. For

C-8a, however, the shielding effect caused by a loss of conjugation is compensated by a reduced shielding effect as a result of increased distance between carbonyl oxygen and C-8a. Comparison of ^{13}C chemical shifts of the carbonyl carbons and acetyl methyl carbons, also supports the steric inhibition of conjugation. A ^{13}C NMR study of a large number of saturated and conjugated carbonyl compounds of both aliphatic and aromatic series clearly shows that the conjugated carbonyl carbon nuclei are shielded relative to the corresponding saturated derivatives,[95] an effect which is attributed to an increase in the electron density about that carbon, as in the aromatic series.[72,96,97] The electron withdrawing effect of the carbonyl group on the carbonyl methyl bond in methyl ketones is reduced in a conjugated system relative to its saturated analogue, leading to a reduced polarization of this bond which in effect increases the electron density at the methyl carbon nucleus. Thus the acetyl methyl carbons absorb ~4 ppm at higher field in the conjugated systems. It follows, therefore, that any factor which can reduce the degree of conjugation in an acetyl substituted aromatic system is expected to reduce the shielding at the carbonyl and acetyl methyl carbons. This is indeed the case for compound 35, since both carbonyl and acetyl methyl are deshielded by 5.0 ppm and 2.4 ppm respectively in this compound compared to less hindered analogue 54 (Table VII).

Stothers and Dhami[97,98] developed an empirical expression by which the angles of twist in conjugated systems may be calculated from degree of deshielding of the carbonyl carbon due to loss of conjugation. Unfortunately, this expression can not be applied to ketone 35, since the deshielding effect experienced by carbonyl carbon of this compound is partially due to a δ-syn-axial type interaction caused by introduc-

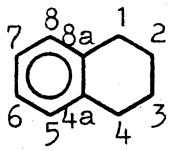
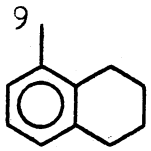
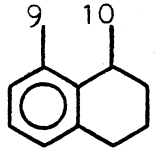
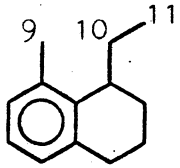
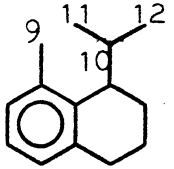
tion of the methyl group at peri-position (this effect will be further discussed later). It is difficult to extract this effect from a deshielding caused by the steric inhibition of conjugation.

We may now proceed with discussion of the ^{13}C NMR spectra of hydrocarbons 41-44 and 45-48. The ^{13}C chemical shifts for 41-44 are given in Table IX. To make the comparison easier, we use the numbering system as shown in the Table IX. The ^{13}C chemical shifts of tetralin are also given for comparison. Chemical shift assignments for tetralin, by Johnson and Jankowski[106] appear to be incorrect and were revised by several workers.[36,107-111] Our chemical shift assignment for 52 is in agreement with the recent literature. The NMR samples for these compounds were prepared in the same molar concentration (2 mmol/mL) for all samples, to eliminate any concentration effect on chemical shift difference. The ^{13}C chemical shift assignments were made with the help of the off-resonance decoupled spectra, and considering the substituent effects reported for cyclohexane[19,28] and benzene compounds.[33] Signals for C-6 in 41 and 42 were located by gated-decoupling experiment (Spectra 6 and 7). Since C-6 do not experience any three-bond CH coupling in 41 and 42, its signal in gated-decoupled spectra appears as a sharp doublet (split by directly bonded hydrogen only). Once the C-6 is located in 41 and 42, it can be easily distinguished from other signals in 43 and 44 too. The ^{13}C signals arising from the two methyl groups in 42 were distinguished from each other by deuterium substitution at C-10. Deuterated hydrocarbon 60 was prepared from acid 33a by the following route.

Placement of a deuterium at C-10 changes the ^{13}C signal of this carbon in the proton-decoupled spectrum to a triplet (Spectrum 21). Ambiguiety still remains in ^{13}C chemical shift assignments of some

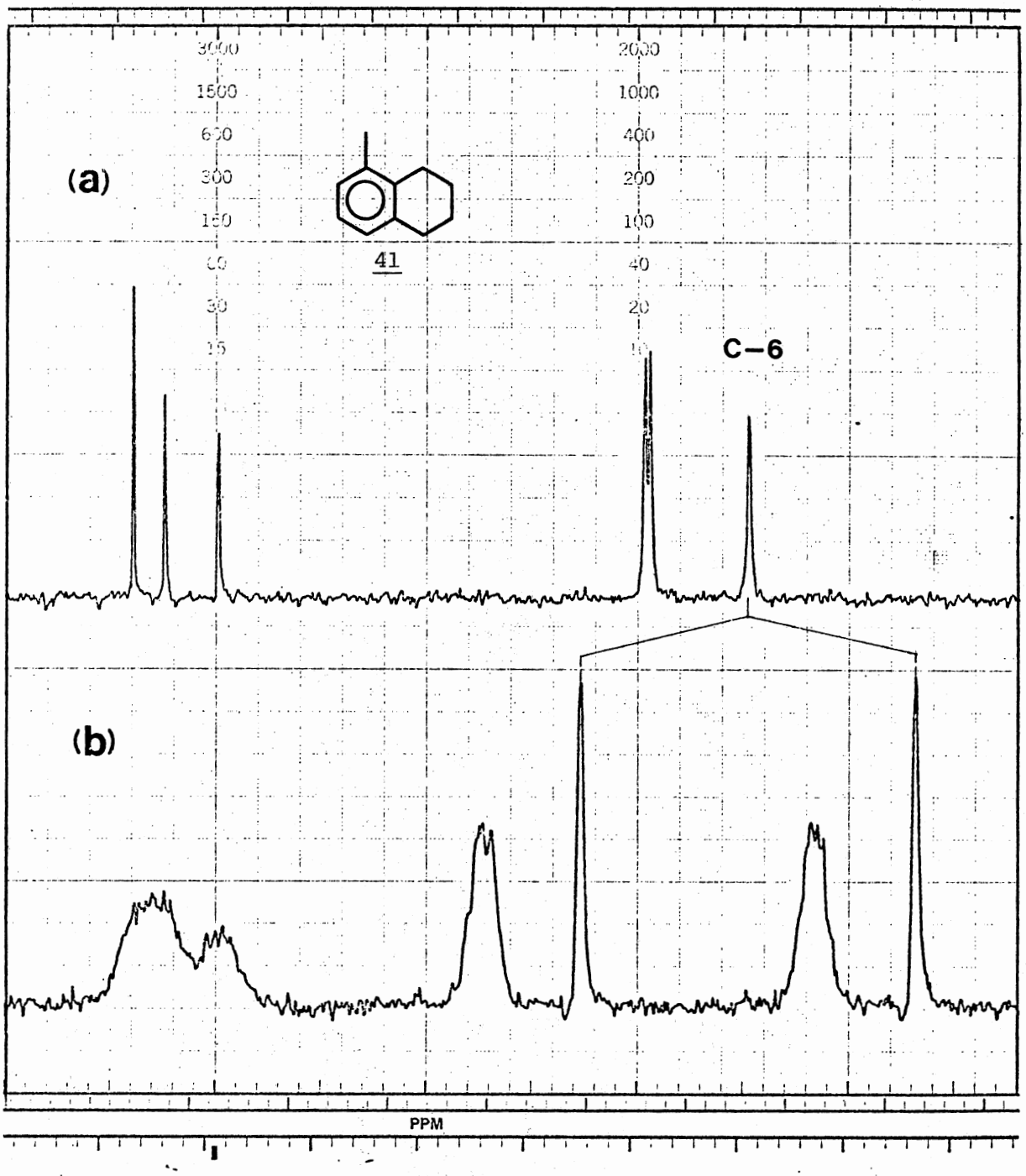
TABLE IX

^{13}C CHEMICAL SHIFTS OF PERI-SUBSTITUTED TETRALINS[a]

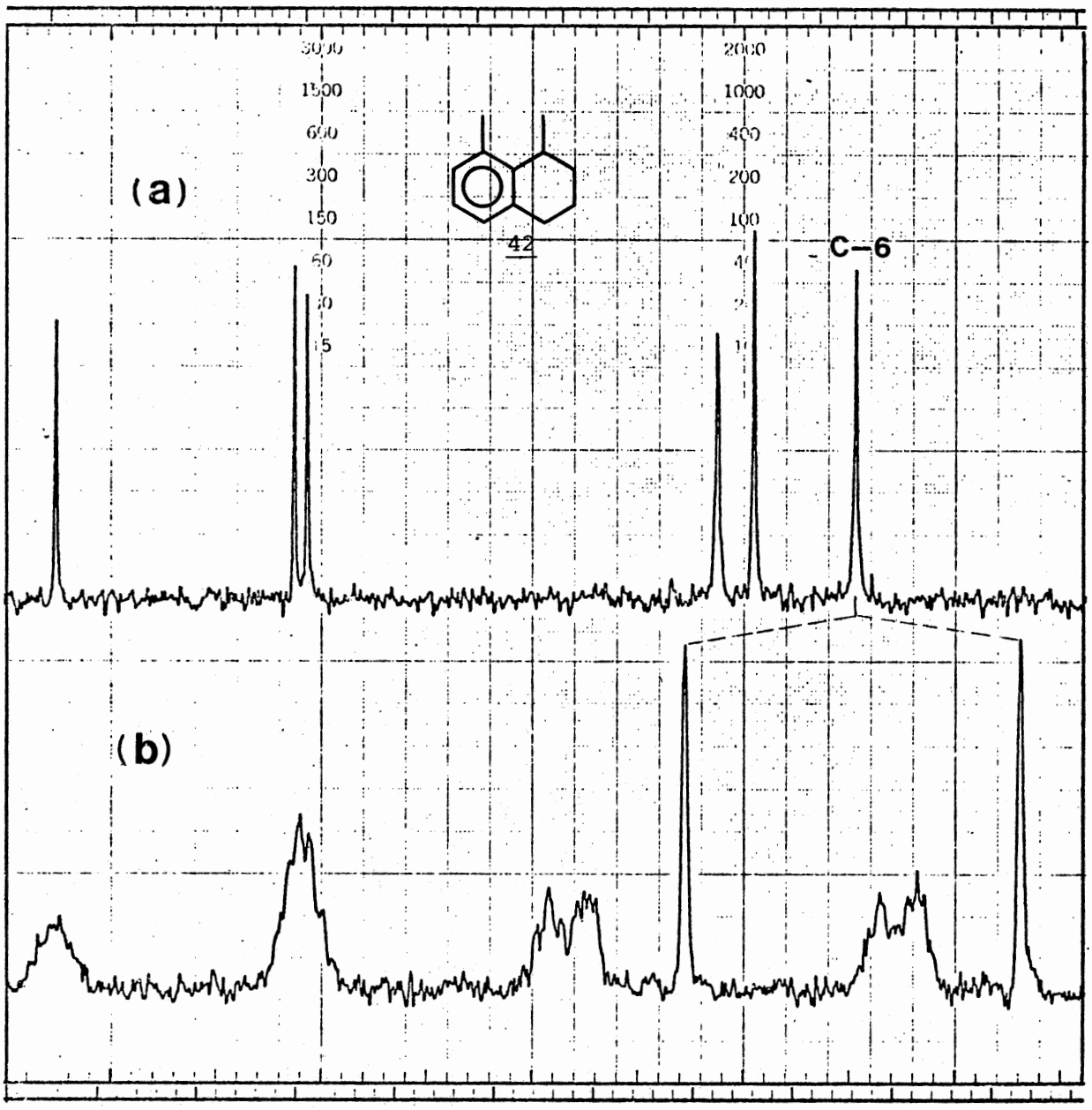
Carbon No.	 52	 41	 42	 43	 44
C-1	29.4	26.6	29.1	36.4	40.5
C-2	23.3	22.9	30.3	27.0	24.0
C-3	23.3	23.5	17.7	17.8	19.9
C-4	29.4	30.1	29.7	29.5	28.9
C-4a	136.8	136.7	135.9	136.0	137.9
C-5	128.9	126.8[b]	127.6[b]	127.6[b]	127.7[b]
C-6	125.2	124.9	125.1	125.0	124.9
C-7	125.2	126.7[b]	127.0[b]	126.8[b]	126.3[b]
C-8	128.9	135.2	135.6	135.7	135.5
C-8a	136.8	136.2	140.3	140.3	140.0
C-9	---	19.4	18.8	19.0	21.2
C-10	---	---	20.9	25.1	31.0
C-11	---	---	---	12.6	19.4
C-12	---	---	---	---	19.5

[a] ppm from TMS in $CDCl_3$.

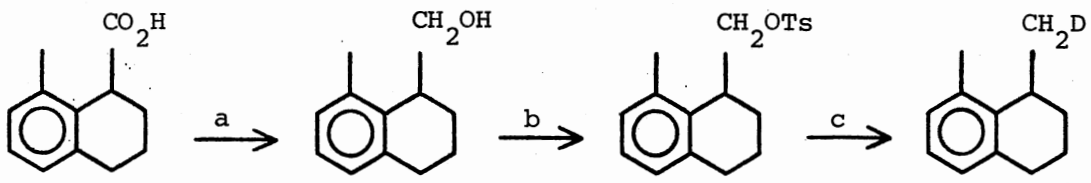
[b] These assignments may be reversed.



Spectrum 6. The Aromatic Portion of (a) Full-Decoupled, and (b) Gated-Decoupled ^{13}C NMR of 41



Spectrum 7. The Aromatic Portion of (a) Full-Decoupled, and (b) Gated-Decoupled ^{13}C NMR of 42



33a 58 59 60

[a] DIBAH
[b] TsCl,Py
[c] $LiAlD_4$

carbons which are denoted in Table IX. Our discussion will be mainly focused on those carbons for which chemical shift assignment is made with a higher degree of certainty.

Since the ^{13}C chemical shift effect arising from interactions of nuclei separated by more than three bonds is often small and variable, less attention has been given to their detailed examination although nuclei separated by four bonds can exist in orientations in which the nonbonded internuclear distances are comparable to or shorter than those for the γ-gauche arrangements. From the theory proposed by Grant and Cheney,[87] a general conclusion was drawn that ^{13}C shieldings increase as the extent of steric crowding increases, until Grover, et al.[112] reported that the substitution in cyclic compounds of hydroxyl having δ syn-axial steric interactions with methyl carbons produces downfield shifts ~3 ppm. This long-range δ-deshielding effect was further considered by Stothers, et al.[113] In cyclic compounds, different orientations are possible for carbons separated from each other by four bonds (Figure 7).

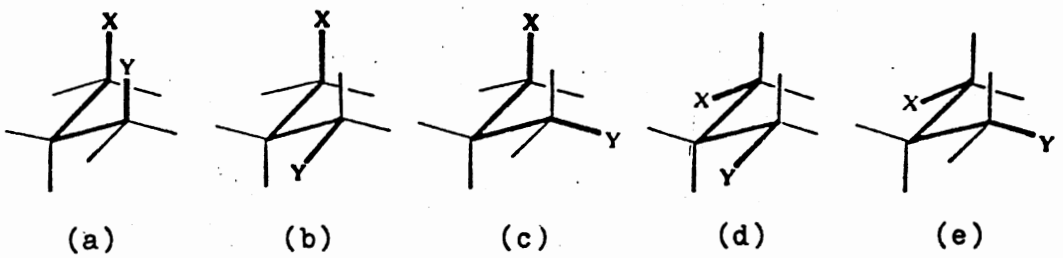
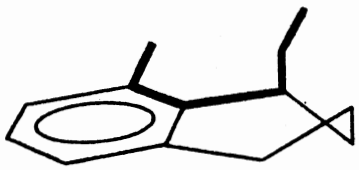


Figure 7. Possible Orientations of Four-bonded Nuclei in Cyclic System

It was found[112,113] that only syn-axial orientation (a) of neighboring δ-nuclei produces appreciable downfield shifts (δ effects) as large as 5 ppm while the other orientations (b-e) produce a small upfield shift. It was also shown[112] that the magnitude of these syn-axial interactions appear to be larger for those cases in which the interacting groups are less able to increase the non-bonded interatomic distances by splaying of the ring system. This kind of δ deshielding effect is found in acyclic systems too,[114] however, its magnitude is small due to a low population of g(+) g(-) orientation[114] (analogous orientation to syn-axial in cyclic compounds). The origin of this kind of δ-deshielding effect is not very well understood. Undoubtedly, the interpretation relating steric crowding with upfield shifts through steric polarization of the interacting bonds[87] is inadequate to account for these syn-axial effects. Batchelor suggested that a second contribution to ^{13}C steric shifts must be postulated.[114] This hypothetical mechanism must produce deshielding as the distance between the interacting groups decreases, the distance dependence being steeper than that of the shielding mechanism which dominates γ steric shifts. According to Batchelor, a possible deshielding mechanism is the second-order

electric field effect due to fluctuating molecular dipoles.

The ^{13}C chemical shift data given in Table IX show that C-9 is shielded in 42 compared to 41. Examination of model of hydrocarbon 42 shows a syn-axial type orientation of methyl groups when an equatorial arrangement is adopted by the methyl group on the cyclohexane ring (for identification purposes we will refer to this kind of parallel orientation of the substituents as "syn-axial type" orientation). However, when a methyl group on a cyclohexane ring is axial, a gauche type orientation (analogous to that in Figure 7c) exists between methyl groups which is expected to produce a shielding effect on C-9. On, the other hand, a strong shielding effect (5.8 ppm) is produced on C-3 (compound 42) by the same methyl group due to γ-gauche interaction. Since this kind of γ-shielding is only possible with an axial methyl substituent, it is concluded that a conformation with methyl group in axial position is highly favored in 42. A similar conclusion may be drawn from ^{13}C chemical shifts of C-9, and C-3 in compounds 43 and 44 (see Table IX for numbering), as they are compared to C-9, and C-3 chemical shifts in 41. It is interesting that the shielding of C-3 is reduced in 42→44, since introduction of a methyl group on C-10 provides a possibility of syn-axial type interaction between this methyl group and C-3, which causes a δ-deshielding effect, and consequently reduces the γ-shielding effect. Also, C-9 is deshielded (0.2 ppm) in 43, and (2.4 ppm) in 44, compared to 42. This result can not be explained by a δ-syn-axial type effect. It is shown in following conformational arrangement that an orientation similar to a syn-axial orientation is possible for nuclei separated by five bonds in peri-substituted tetralins 43 and 44. Assuming that the same shielding trend discussed for δ-effect is also

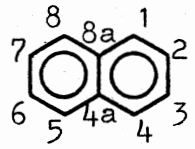
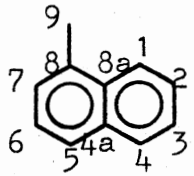
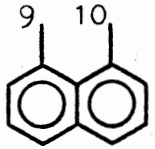
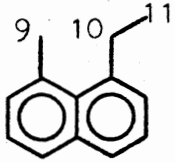
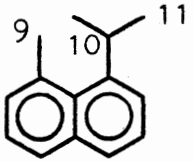


true for five-bonded nuclei, the observed chemical shifts of C-9 can be explained. Population of syn-axial type orientation in 43 is low compared to other possible orientations. As a result, C-9 is deshielded only by 0.2 ppm in 43 compared to 42. Introduction of another methyl group in 44 increases the possibility of syn-axial type orientation, therefore result in an increased deshielding of C-9 in 44 compared to 42. However, the effect in these cases are less pronounced since the distance between interacting nuclei is increased.

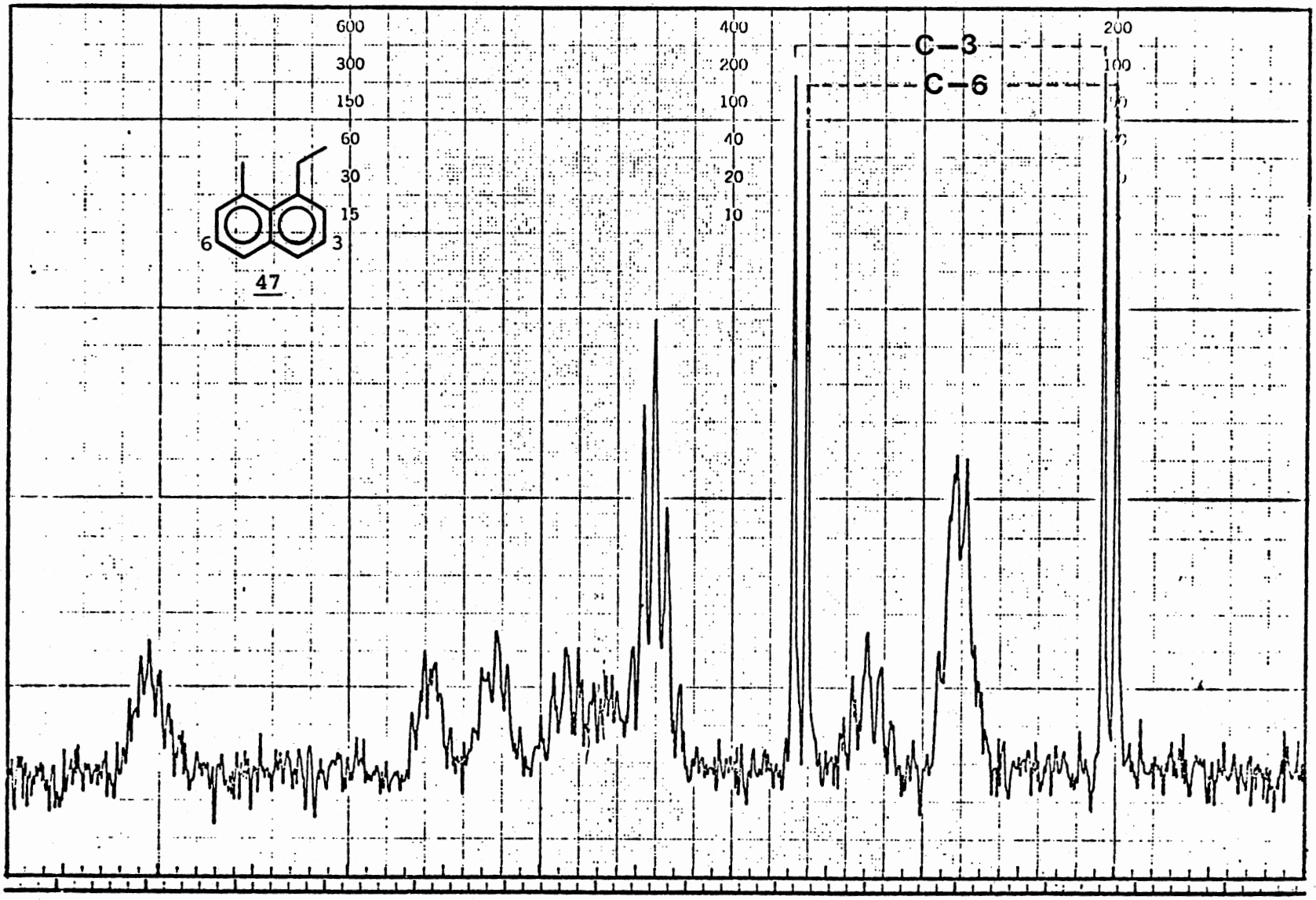
The ^{13}C chemical shifts for naphthalene (57) and alkylated naphthalenes 45-48 are shown in Table X. The numbering system used to represent the data is also shown (1-methylnaphthalene is numbered as 8-methylnaphthalene so that the changes in the chemical shift of each carbon can be easily followed). The ^{13}C chemical shift assignments for naphthalene, 1-methylnaphthalene, and 1,8-dimethylnaphthalene are known[65,66,70,71,74,105] (assignments made for 1,8-dimethylnaphthalene by Jones, et al.[64a] proved to be incorrect and were revised by other workers[65]). Our assignments for 45 and 46 are in accordance with the recent literature values. Although the chemical shift assignments for 45 and 46 are known, the complete assignment of compounds 47 and 48 could not be easily made without the aid of special experiments. A gated decoupling experiment was employed in making assignments for C-3 and C-6 (Spectra 8 and 9). When three-bond couplings are present in

TABLE X

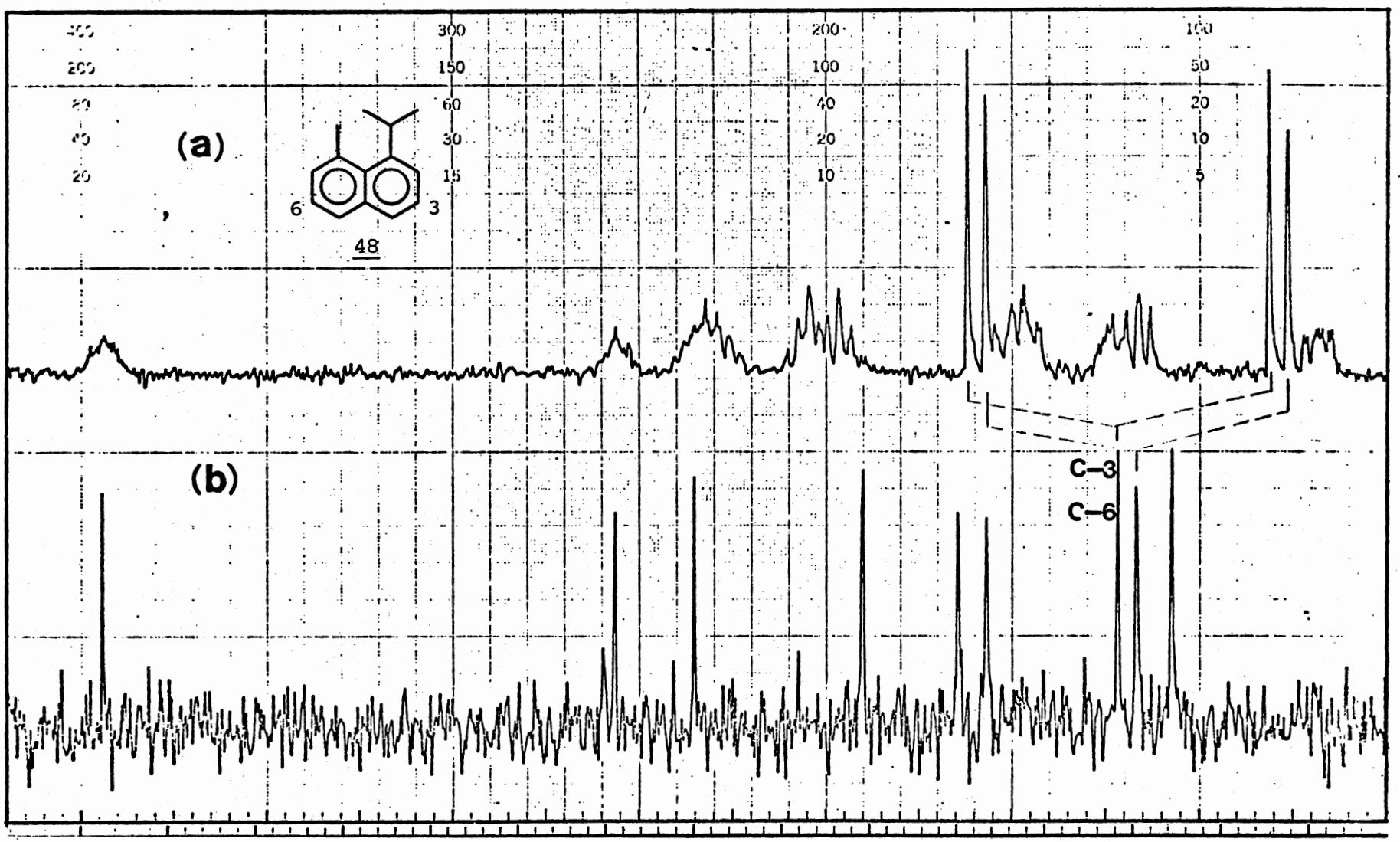
^{13}C CHEMICAL SHIFTS[a] OF NAPHTHALENE AND ITS PERI-SUBSTITUTED DERIVATIVES 45-48

Carbon No.	 57	 45	 46	 47	 48
C-1	127.7	123.8	135.1	141.4	146.3
C-2	125.6	125.3	129.1	127.7	123.6
C-3	125.6	125.2	124.3	124.8	124.8
C-4	127.7	128.2	127.6	128.0	128.2
C-4a	133.4	133.3	135.3	135.5	135.5
C-5	127.7	126.1	127.6	127.7	127.6
C-6	125.6	125.2	124.3	124.5	124.4
C-7	125.6	126.3	129.1	129.6	130.2
C-8	127.7	133.8	135.1	134.2	133.7
C-8a	133.4	132.4	132.8	131.8	131.6
C-9	--	19.1	25.7	25.3	26.2
C-10	--	--	25.7	29.6	29.7
C-11	--	--	--	13.3	25.2

[a] ppm from TMS in $CDCl_3$



Spectrum 8. The Aromatic Portion of Gated-Decoupled ^{13}C NMR of 47 in $CDCl_3$



Spectrum 9. The Aromatic Portion of (a) Gated-Decoupled, and (b) Full-Decoupled ^{13}C NMR of 48 in $CDCl_3$

compounds which have protons with chemical shifts different from those of the aromatic ones, they can be observed by irradiation of the aromatic protons.[115,116] This technique was used to pick out the ortho carbons. Distinction of C-2 from C-7, C-3 from C-6, and C-4 from C-5 is possible by comparison of their chemical shifts with corresponding chemical shifts in 45 and 46.

peri-Substituted naphthalenes appear to be the best examples among the organic compounds in which a non-bonded δ-syn-axial type interaction is observed. In monocyclic or conformationally mobile systems the interaction between syn-axial groups can be reduced to some extent by ring splaying. But in 1,8-disubstituted naphthalenes, having a more rigid structure, it is reasonable to expect a more enhanced deshielding effect be present by this type of interaction. Comparison of the ^{13}C chemical shift of the methyl group in 1-methylnaphthalene (19.1 ppm) and 1,8-dimethylnaphthalene (25.7) substantiates this prediction. The introduction of the second methyl group in the δ position causes a 6.6 ppm downfield shift, the strongest non-bonded δ-deshielding effect so far observed. However, the results given in Table X show that further increase in the size of peri-substituent (47 and 48) do not have a considerable effect on shielding of the methyl substitutent, even though the examination of models show a very enhanced steric interaction between peri-substitutents in 47 and 48. This observation further supports the idea that shielding effect due to non-bonded interactions between nuclei separated by more than three bonds strongly depends on the orientation of two interacting groups. These results also present another case in which explanation of steric effects on ^{13}C chemical shifts in terms of bond polarization fails.

Examination of models of 47 and 48 reveals that if an out-of-plane splaying of substituents takes place, methyl groups separated by five bonds in 47 and 48 can adopt arrangements from which only one orientation (pseudo-parallel) may have a deshielding effect, while the other orientations having a shielding effect, similar to what was previously discussed for the tetralin system. Low population of the pseudo-parallel arrangement in 47 and relatively higher probability of this kind of orientation in 48 may explain the observed chemical shifts for the methyl group (25.3, 26.2) in these compounds.

Comparison of ^{13}C chemical shifts of C-2 and C-8a in compounds 46-48 indicates an in-plane deflection of C-1-C-10 and C-8-C-9. This deduction is based on a stronger γ-shielding effect experienced by C-2, than C-8a in compounds 47 and 48, which suggests a bending of the ethyl and isopropyl groups in 47 and 48 toward C-2 and away from C-8a. An enhanced ortho deshielding effect experienced by C-7 in these series of compounds (45-48) also must be a result of bending of the methyl substituent toward this carbon.

Although quantitative information concerning dynamic molecular motions can be obtained from ^{13}C spin-lattice relaxation times T_1 values, these require a detail study of mechanism of this kind of relaxation. However, a qualitative idea may be drawn from comparison of T_1 values of identical substituents in similar environments, wherein major deviation in mechanism of the spin-lattice relaxation is not expected. T_1 values for methyl group (C-9) in compounds 45-48 are given in Table XI.

TABLE XI

SPIN-LATTICE RELAXATION TIMES (T_1) FOR METHYL SUBSTITUENT IN 45-48

	45	46	47	48
T_1	5.8 sec.	3.9 sec.	2.8 sec.	2.9 sec.

A higher rotation barrier for methyl group by increase in the size of peri-substituent results in a faster spin-lattice relaxation. Activation energies for internal rotation have been measured for 45 and 46 by proton spin-lattice relaxation methods[117,118] as well as ^{13}C spin-lattice relaxation.[119] The methyl interaction with a peri-proton prevents rapid rotation of the methyl group resulting in a reasonably large activation energy for 45 (2.1 Kcal/mole)[119] as compared to, for example, the methyl group in toluene (0.014 Kcal/mole).[120] In the case of 46 the steric interactions are further increased resulting in a larger barrier to rotation and a decrease in spin-lattice relaxation time. T_1 value of 2.8 sec. found for 47 suggests even larger rotation barrier for methyl group in this compound. However, no further change in T_1 of the methyl group is observed going from 47 to 48, probably because of in-plane and out-of-plane splaying of the substituents in 48, lowering the rotational barrier for methyl substituent.

CHAPTER VII

EXPERIMENTAL

Diisobutylaluminum Hydride (DIBAH)

Reduction of Acid 28

To a solution of 60 g (0.41 mol) DIBAH in 250 mL dry benzene was slowly added a solution of acid 28 (17.6 g, 0.1 mol) in 100 mL of dry benzene. The mixture was stirred at room temperature for 1 h, then at 70 °C for 30 min. Ethyl acetate (20 mL) was added to deactivate unreacted DIBAH. The reaction mixture was poured into ice-water, and 50 mL concentrated hydrochloric acid was added. The product was extracted with ether, and the combined ether-benzene layer was washed with water, dried ($MgSO_4$), and concentrated. The product (15.0 g, 92.5%) gave only one peak on LC (silica column, CH_2Cl_2): ^1H NMR ($CDCl_3$) δ 7.00 (m, 3, ArH), 4.40 (s, 2, CH_2OH), 3.22 (s, 1, OH), 2.65 (m, 4), 1.70 (m, 4); ^{13}C NMR ($CDCl_3$) ppm 138.23, 136.74, 134.34, 128.19, 124.86, and 124.24 (aromatic), 62.29 (CH_2OH), 29.75, 25.08, 22.93, and 22.61 (aliphatic).

5-Methyl-1,2,3,4-tetrahydronaphthalene (41)

A sample of alcohol 30 (8.1 g, 0.05 mol) was hydrogenated in 100 mL of acetic acid containing 1.6 g of 5% Pd/C, for 3 h at 60 °C and 45 psi. The mixture was filtered through Dicalite, concentrated, poured in water and extracted with ether. The ether layer was washed with

water, dried ($MgSO_4$) and concentrated to 6.8 g (93%) of hydrocarbon 41. Distillation (Kugelrohr, bp 68-69 °C/0.2 mm; lit.[121] bp 101-102 °C/11 mm gave 6.0 g of hydrocarbon 41 as a colorless liquid: ^1H NMR ($CDCl_3$) δ 6.90 (s, 3, ArH), 2.70 (t, 2), 2.58 (t, 2), 2.16 (s, 3, CH_3), 1.75 (m, 4); ^{13}C NMR ($CDCl_3$) ppm 136.74, 136.19, 135.17 126.79, 126.70, and 124.89 (aromatic), 30.09, 26.65, 23.46, 22.94, 19.41; MS m/e (rel. intensity) 146 (100), 143 (32), 131 (75), 118 (24), 59 (64).

Diisobutylaluminum Hydride (DIBAH) Reduction of Naphthalic Anhydride (23)

To a 22-L flask fitted with stirrer and a dropping funnel with side-bore Teflon stopcock and equalizing sidearm was added 8 L of dry toluene and 792 g (4 mol) of anhydride. The reaction mixture was cooled in an ice bath to 5-10° and held at this temperature range during addition of 1188 g (8.3 mol) of neat DIBAH over 3 h. The direct addition of DIBAH from 1-L storage bottles to the dropping funnel was readily accomplished through use of an adapter (Neoprene stopper fitted with 3/8" O.D. polyethylene tubing). The reaction mixture was then poured onto 5 kg of ice and water. The salts were decomposed with 2 L of concentrated hydrochloric acid. Three L of ethyl acetate were added and the resulting mixture was filtered through Dicalite to remove small amount of suspended material. A second 2 L of ethyl acetate extract was combined with the first extract and these were dried ($MgSO_4$), filtered, and concentrated to 580 g of crude, yellow lactone (79%). It was purified by dissolving in 10% sodium hydroxide and extracting with ether to remove neutral material. On acidification to pH 7-8, the lactone 31 solidified as 568 g (77%) of colorless crystals, mp 150-154

°C. Further purification by sublimation gave 485 g (66%) of white crystalline lactone 31, mp 154-156 °C (lit.[59] mp 154-157 °C): MS m/e (rel. intensity) 184 (66), 183 (38), 156 (19), 155 (100), 127 (70), 126 (22); ^{1}H NMR ($CDCl_3$) δ 8.30 (d, 1, ArH ortho to carbonyl), 8.13-7.21 (m, 5, ArH), 5.72 (s, 2, $ArCH_2$).

8-Methyl-1,2,3,4-tetrahydro-1-naphthoic Acid (33a)

Lactone 31 (300 g, 1.63 mol) was dissolved in 3 L of glacial acetic acid and added to the hydrogenation vessel. Pd/C (20 g 5%) was added and hydrogenation was carried out at 55-60 psi at 60 °C for 24 h. The solution was filtered and concentrated, poured into water and extracted with ether. The ether layer was extracted with sodium bicarbonate solution and evaporation of the solvent from the ether layer gave 87 g (29%) of lactone 32, mp 65-66 °C; ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 1, ArH ortho to carbonyl), 7.30 (m, 2, ArH), 4.40 and 4.00 (q, 1, CH_2OCO), 3.20-2.60 (m, 3, benzylic protons); ^{13}C NMR ($CDCl_3$) ppm 164.96 (carbonyl), 138.32, 135.05, 133.82, 127.34, 126.65, and 124.05 (aromatic), 71.64 (CH_2O), 33.35 (ArCH), 27.71 ($ArCH_2$), 23.72, and 21.56 (aliphatic). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.42; O, 17.00. Found: C, 76.73; H, 6.63; O, 16.51.

The bicarbonate extract was acidified, extracted with ether, dried ($MgSO_4$) and concentrated to give 218 g (72%) of acid 33a, mp 146-148 °C. This acid was purified by recrystallization from ethyl acetate, mp 148-149 °C: ^{1}H NMR ($CDCl_3$) δ 11.1 (s, 1, CO_2H), 7.20-6.90 (m, 3, ArH), 3.8 (t, 1, $ArCHCO_2H$), 2.8 (t, 2, $ArCH_2$), 2.2 (d, 3, $ArCH_3$), 1.8 (m, 4, CH_2); ^{13}C NMR ($CDCl_3$) ppm 181.35 (CO_2H), 137.15, 136.97, 131.43, 127.49, 127.02, and 126.73 (aromatic), 42.08, 29.44, 27.26, 19.61 and 19.38

(aliphatic).

8'-Methyl-1',2',3',4'-tetrahydro-1-aceto-

naphtone (34)

In a 2-L flask was placed 105 g (0.55 mol) of acid 33a in 1 L ether, a few drops of pyridine and 80 mL of thionyl chloride. The mixture was stirred at room temp. for 3 h, the ether was evaporated, 500 mL benzene were added and then evaporated under reduced pressure. Addition of benzene and evaporation was repeated 3 times to remove thionyl chloride.

To a dry 3-neck, 3-L flask equipped with mechanical stirrer and a reflux condenser, was added 2 mol of methylmagnesium bromide solution in ether (from Aldrich). Addition was done by means of an adaptor under nitrogen flow. The solution was cooled in ice bath and 240 g of dry $CdCl_2$ was added all at once. The ice bath was removed and 1 L of dry benzene was added to the flask. The ether was removed and distillation was continued until a dark semi-solid residue remained, then 1 L of dry benzene was added and the mixture was stirred and refluxed until the cake had been broken up and dispersed through the mixture. There was then added, during 1 h, a solution of the acid chloride (114 g, 0.54 mol) in 900 mL dry benzene. After the exothermic reaction had subsided, the mixture was refluxed with stirring for one hour and then cooled and poured into ice-cold dilute hydrochloric acid. The product was isolated by ether extraction and distilled (Kugelrohr; bp 129 ^{o}C, 0.05 mm). Recrystallization from pet. ether (bp 60^{o}) gave 34 as a white crystalline product melting at 37-38 ^{o}C, 86 g (85%): IR (CCl_4), 1720 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 7.10-6.90 (m, 3, ArH), 3.8 (t, 1,

ArCHCO), 2.8 (t, 2, $ArCH_2$), 2.15 (s, 3, $ArCH_3$), 2.10 (s, 3, CH_3CO), 2.00 (m, 2), and 1.6 (m, 3, ArH); ^{13}C NMR ($CDCl_3$) ppm 209.93 (CO), 137.33, 136.39, 132.86, 127.61, 126.96, and 126.38 (aromatic), 50.49, 29.71, 28.04, 26.50, 19.69, and 19.64 (aliphatic); MS m/e (rel. intensity) 188 (M^+, 15.9), 145 (100.0), 130 (30.0), 115 (20.0), 105 (24.4), 43 (26.9). Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.82; H, 8.78.

8'-Methyl-1-acetonaphthone (35)

Ketone 34 (56.5 g, 0.3 mol) was heated at 280-290 °C with 3 g 10% Pd/C for 12 h until H_2 evolution ceased. After cooling, the mixture was dissolved in ether and filtered through Dicalite. Concentration by rotary evaporation gave 48 g of yellow oil which was shown by high pressure LC (C-18 column, 4:1 acetonitrile:water) to be ketone 35 and 1-methylnaphthalene in 4:1 ratio. Addition of 100 mL of petroleum ether, refrigeration and filtration gave 36 g (65%) of ketone. A second recrystallization from isohexane gave 32.5 g (58%) of ketone 35 free of 1-methylnaphthalene, mp 39-40 °C: ^1H NMR ($CDCl_3$) δ 7.8-7.4 (m, 6, ArH), 2.65 (s, 3, $ArCH_3$), 2.50 (d, 3, CH_3CO); ^{13}C NMR ($CDCl_3$) ppm 205.81 (CO), 140.24, 134.43, 133.36, 131.03, 129.71, 128.51, 126.85, 125.92, 124.28, and 123.66 (aromatic), 31.80 ($\underline{C}H_3CO$), 23.64 ($ArCH_3$); IR (KBr) 1690 cm^{-1} (CO); Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.58. Found: C, 84.94; H, 6.65.

Diisobutylaluminum Hydride (DIBAH) Reduction of Ketone 35 to Alcohol 36

Ketone 35 (38.6 g, 0.21 mol) was dissolved in 250 mL of dry benzene

and then added dropwise to a solution of 72 g (0.5 mol) DIBAH in 500 mL benzene at room temp. When addition was complete, the mixture was stirred at room temp. for 2 h and then at 50° for 0.5 h. The reaction mixture was cooled and poured into ice water. Aluminum salts were broken up by addition of concentrated HCl and the product was extracted with ether. Evaporation of solvent gave 38.5 g (99%) of alcohol 36. Recrystallization from isohexane gave 36.0 g of white needles of 36, mp 78-79 °C: ^{1}H NMR ($CDCl_3$) δ 7.70-7.20 (m, 6, ArH), 5.8 (q, 1, OH), 2.7 (s, 3, $ArCH_3$), 2.6 (m, 1, ArCH), 1.2 (d, 3, CH_3CHOH); ^{13}C NMR ($CDCl_3$) ppm 143.42 (x2), 134.99, 133.15, 130.18, 128.87, 127.90, 124.66, 124.54, and 123.46 (aromatic), 66.30 (CHOH), 26.06 (CH_3CHOH), 25.65 ($ArCH_3$). Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.64; H, 7.51.

Conversion of Alcohol 36 to Chloride 37

Alcohol 36 (36.5 g, 0.194 mol), 2 L n-hexane and 100 mL concentrated HCl were placed in a 3-L Erlenmeyer flask and mixed thoroughly by vibromixer for 30 min. at room temp. The mixture was transferred to a separatory funnel, washed with 10% sodium bicarbonate, then several times with water, dried ($MgSO_4$) and concentrated to give 38 g (95%) of chloride 37: ^{1}H NMR ($CDCl_3$) δ 7.80-7.00 (m, 6, ArH), 6.20 (q, 1, ArCHCl), 2.80 (s, 3, $ArCH_3$), 1.80 (d, 3, CH_3CHCl); ^{13}C NMR ($CDCl_3$) ppm 139.28, 134.99, 132.63, 130.88, 130.07, 127.99, 125.80, 124.89, 124.78, and 124.46 (aromatic), 55.79, 26.88, and 25.24 (aliphatic).

1-Ethyl-8-methylnaphthalene (47) From Chloride 37

Chloride 37 (37 g, 0.18 mol) was dissolved in 500 mL dry THF and added dropwise to a solution of 0.3 mol Super-Hydride (lithium

triethylborohydride) in 300 mL of THF. The temperature was maintained below 30 °C during addition of chloride. The resulting mixture was stirred at room temperature for 2 h., then poured into 1 L ice water. The product was extracted with n-hexane, washed with dil. HCl and water, then dried ($MgSO_4$). Concentration of the solution gave 29.5 g (97%) of hydrocarbon 47, mp 5-7 °C, bp 104-105 °C (0.1 mm): ^{1}H NMR ($CDCl_3$) δ 7.64-7.10 (m, 6, ArH), 3.17 (q, 2, methylene), 2.76 (s, 3, $ArCH_3$), 1.20 (t, 3, CH_3CH_2); ^{13}C NMR ($CDCl_3$) ppm 141.35, 135.54, 134.14, 131.84, 129.59, 127.96, 127.72, 127.67, 124.81, and 124.54 (aromatic), 29.65, 25.33, and 17.34 (aliphatic); MS m/e (rel. intensity) 170 (64), 155 (100), 141 (10), 128 (12), 115 (14), 77 (20), 63 (8).

Purification of 1-Ethyl-8-methylnaphthalene (47)

To a beaker containing 200 mL methanol was added 28 g (0.165 mol) of 47 of approximately 99% purity, and 41.5 g (0.18 mol) of picric acid. The suspension was boiled until solution was complete. The solution was allowed to cool to room temperature and the picrate of 47 crystallized spontaneously as bright oragne needles. After several hours of refrigeration, the crystals were filtered and dried to give 52 g, mp 96-98 °C. Successive recrystallizations from 150-175 mL of methanol gave 43.5 (69%), 38 g (60%) based on dried weight of picrate which melted at 97-97.5 °C.

A dried 37 g sample of the purified picrate was passed through a column of basic alumina using n-hexane as eluant. The elution was continued until the orange color of the picrate had changed to the pale yellow color of anhydrous picric acid. The contents of the recovery flask were concentrated (rotary evaporation) to give 18.5 g (0.109

mol) of 47 (99.98% purity).

1-Ethyl-8-methyl-1,2,3,4-tetrahydro-naphthalene (43)

A sample of ketone 34 (3.5 g, 19 mmol), hydrazine hydrate (5 mL 85%), KOH (2.5 g, 45 mmol), and diethylene glycol (75 mL) were added to a 250-mL stainless steel reaction vessel and slowly heated to 250 °C. This temperature was maintained until the product codistilled with diethylene glycol. The distillate was poured into 100 mL of water and it was then extracted with ether. The ether layer was washed with dilute acid, water; then dried ($MgSO_4$) and concentrated to give 1.4 g (42%) hydrocarbon product, which was purified by passing through a column of alumina: ^{1}H NMR ($CDCl_3$) δ 6.90 (m, 3, ArH), 2.70 (m, 3, benzylic), 2.26 (s, 3, $ArCH_3$), 2.00-1.20 (m, 6), 1.00 (t, 3, CH_3CH_2); ^{13}C NMR ($CDCl_3$) ppm 140.29, 136.01, 135.66, 127.64, 126.79, and 125.04 (aromatic), 36.45, 29.53, 27.02, 25.08, 18.99, 17.85, and 12.63 (aliphatic).

Dehydrogenation of 1-Ethyl-8-methyl-1,2,3,4-tetrahydronaphthalene (43)

A sample of 1 g (5.7 mmol) hydrocarbon 43, and 150 mg 10% Pd/C in 5 mL of cymene was refluxed under nitrogen. Samples were taken every 12 h and analyzed by LC (silica column, n-hexane). Dehydrogenation almost stopped after 60 h with 80% of 43 aromatized. The mixture was filtered and most of the cymene was removed by fractional distillation under reduced pressure. 1-Ethyl-8-methylnaphthalene (47) was purified by formation of picrate, recrystallization and decomposition of picrate

by passing through a column of basic alumina, using n-hexane as eluant. Evaporation of n-hexane gave 0.65 g (67%) of pure 1-ethyl-8-methylnaphthalene.

Methyl(8'-methyl-1',2',3',4'-tetrahydro)-1'-naphthoate (33b)

To a solution of 19 g (0.1 mol) of acid 33a in 300 mL ether was added dropwise a solution of diazomethane in ether. Addition and stirring was continued at room temperature until evolution of gas ceased and the color of diazomethane persisted. Nitrogen was bubbled through the solution to remove excess of diazomethane. The solution was then washed with 10% sodium bicarbonate and water, dried ($MgSO_4$), and concentrated to 20 g (98%) of ester 33b, which was distilled (Kugelrohr, bp 125-126 ^{o}C, 0.1 mm): ^{1}H NMR ($CDCl_3$) δ 6.84-7.18 (m, 3, ArH), 3.82 (t, 1, ArCHCO), 3.64 (s, 3, CH_3O), 2.80 (t, 2, $ArCH_2$), 2.15 (s, 3, $ArCH_3$), 1.70-2.30 (m, 4, CH_2); ^{13}C NMR ($CDCl_3$) ppm 174.44 (CO), 136.65, 136.43, 131.75, 127.05, 126.58, and 126.06 (aromatic), 51.32, 41.96, 29.20, 27.13, 19.34, and 18.87 (aliphatic); MS m/e (rel. intensity) 204 (M^+, 9), 145 (100), 129 (8), 115 (4).

α, α, 8-Trimethyl-1,2,3,4-tetrahydro-1-naphthalenemethanol (38)

a. From Ester 33b

To a 80 mL (1.8 M) solution of methyllithium in ether at reflux temperature was added dropwise a solution of 9.2 g (0.045 mol) of ester 33b in 150 mL dry ether. The solution was stirred at room temperature

for 15 h, cooled in ice bath and 30 mL of dilute hydrochloric acid was added slowly. The mixture was transferred to a separatory funnel, the ether layer was washed with 10% hydrochloric acid, and then with water, dried ($MgSO_4$), and concentrated to 8.9 g crude product. The product was analyzed by high-pressure LC (silica column, methylene chloride), and GC-MS, and found to be a mixture of alcohol 38, ketone 34, and unreacted ester 33b; 58:25:17. Alcohol 38 was separated from the mixture on a silica column, using methylene chloride as eluant; ^1H NMR ($CDCl_3$) δ 7.00-6.80 (m, 3, ArH), 3.12 (q, 1, ArCH), 2.60-2.90 (m, 2, $ArCH_2$), 2.32 (s, 3, $ArCH_3$), 2.20-1.50 (m, 4, CH_2), 1.14, and 1.17 (s, 3, CH_3COH); ^{13}C NMR ($CDCl_3$) ppm 140.13, 137.09, 135.93, 127.58, 126.35, and 125.22 (aromatic), 75.23 (COH), 43.31, 29.47, 29.12, 26.78, 24.48, 20.57, and 20.19.

b. From Ketone 34

To a 15 mL solution of methylmagnesium bromide (Aldrich, 2.9 M in ether) was added dropwise at ice bath temperature a solution of 0.94 g (5 mmol) ketone 34 in 30 mL of anhydrous ether. The ice bath was removed and the mixture was stirred at room temperature for 6 h, then refluxed for 1 h. The mixture was poured into ice-water and concentrated hydrochloric acid (10 mL) was added. The ether layer was washed with water, dried ($MgSO_4$), and concentrated. The crude product was found to be alcohol 38, and unreacted ketone 34 in the ratio 68.32 by high-pressure LC (silica column, methylene chloride). Alcohol 38 was isolated using a silica column (methylene chloride), and found to be identical to that obtained from methylation of ester 33b.

Dehydration of Alcohol 38

The dehydration of 38 was carried out by azeotropic distillation of water from a magnetically stirred mixture of 4 g (19.6 mmol) of alcohol 38, 200 mL of toluene and 2 g of oxalic acid during 2 h. The mixture was washed with water, and dried ($MgSO_4$). The toluene was removed by rotary evaporation, and the product was distilled (Kugelrohr; bp 92-95 °C, 0.5 mm) to give 3.5 g (96%) product which was identified as a 29:71 mixture of alkenes 39 and 40 by GC-MS (alkene 40 elutes first). Attempts to separate the alkenes by column chromatography (silica), or fractional distillation were unsuccessful. MS data obtained by GC-MS are as follows: Alkene 39 (71%), MS m/e (rel. intensity) 186 (M^+, 100), 171 (78), 158 (40), 143 (48), 128 (36), 77 (23), 41 (20). Alkene 40 (29%); MS m/e (rel. intensity) 186 (M^+, 46), 171 (40), 145 (100), 130 (58), 117 (39), 79 (20), 39 (25). Anal. Calcd for $C_{14}H_{18}$ (mixture): C, 90.26; H, 9.74. Found: C, 90.39; H, 9.81.

1-Isopropyl-8-methyl-1,2,3,4-tetrahydro-naphthalene (44)

A mixture of alkenes 39 and 40 (3.5 g, 18.8 mmol) was hydrogenated in 100 mL of acetic acid, using 700 mg of 5% Pd/C, at 40 psi for 2 h. The mixture was filtered through Dicalite, concentrated to 25 mL and poured into 100 mL of water. The product was extracted with ether, washed with water, dried ($MgSO_4$), and concentrated to give 3.2 g (91%) of hydrocarbon 44. The hydrocarbon was further purified by passing through a column of silica, and distilling (Kugelrohr; bp 82 °C, 0.2 mm): ^1H NMR ($CDCl_3$) δ 6.95 (m, 3, ArH), 2.27 (s, 3, $ArCH_3$), 0.89 (d, 3,

CH_3CH), 0.86 (d, 3, CH_3CH); ^{13}C NMR ($CDCl_3$) ppm 140.01, 137.89, 135.54, 127.67, 126.33, and 124.87 (aromatic), 40.45, 31.02, 28.89, 23.99, 21.21, 19.90, 19.46, and 19.41 (aliphatic); MS m/e (rel. intensity) 188 (M^+, 4), 145 (100), 130, (6), 43 (5). Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.05; H, 10.57.

1-Isopropyl-8-methylnaphthalene (48)

A sample of 1.5 g (9 mmol) hydrocarbon 44, 5 mL cymene, and 150 mg 10% Pd/C were refluxed for 55 h. The mixture was filtered through Dicalite, and most of the cymene was removed by distillation under reduced pressure. The remaining mixture was poured in 15 mL 95% ethanol and 2.5 g picric acid was added. The mixture was heated until it became homogeneous. Upon cooling, picrate crystallized as orange-needles. The picrate crystals (3.2 g) were filtered, dried (mp 118 °C), and decomposed on a column of basic alumina by extraction with n-hexane. Evaporation of solvent from the eluted mixture gave 0.9 g (60%) of 48 which was found to be 97% pure by high-pressure LC (C-18 column, acetonitrile): ^1H NMR ($CDCl_3$) δ 7.65-7.10 (m, 6, ArH), 4.12 (m, 1, CH_3CH), 2.84 (s, 3, $ArCH_3$), 1.24 (d, 6, CH_3CH); ^{13}C NMR ($CDCl_3$) ppm 146.28, 135.46, 133.65, 131.58, 130.20, 128.16, 127.56, 124.75, 124.37, 123.61, 29.67, 26.18, 25.15 (x2); MS m/e (rel. intensity) 184 (M^+, 74), 169 (100), 154 (72), 141 (45), 115 (35), 83 (56), 76 (50); Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.41; H, 8.65.

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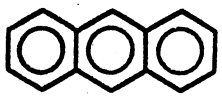
APPENDIX A

GLOSSARY OF STRUCTURES



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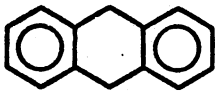

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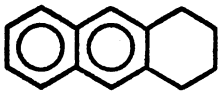

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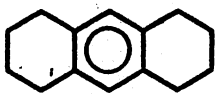

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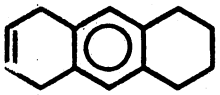

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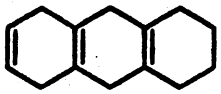

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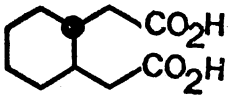

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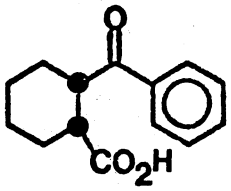

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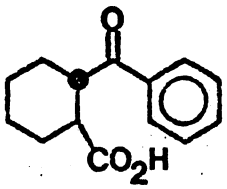

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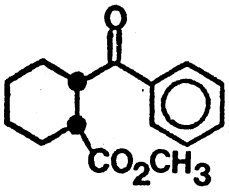

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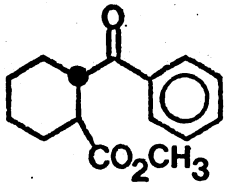

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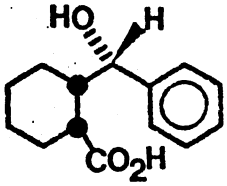

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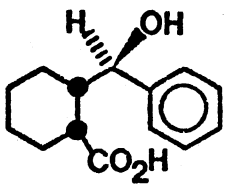

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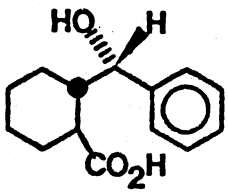

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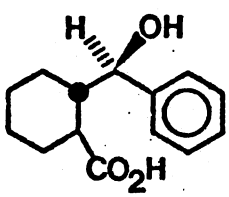

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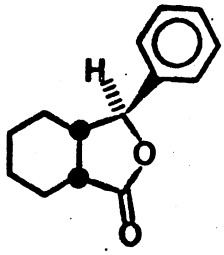

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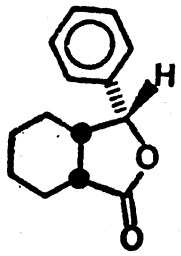

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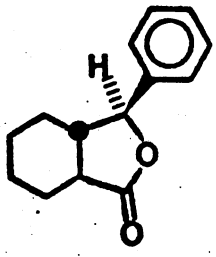

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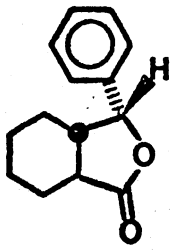

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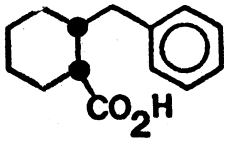

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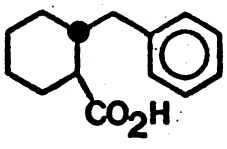

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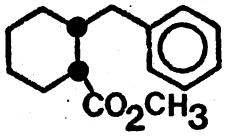

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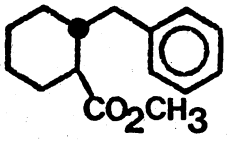

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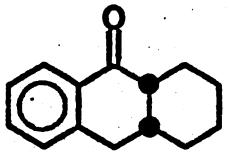

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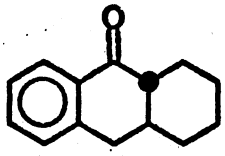

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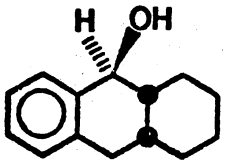

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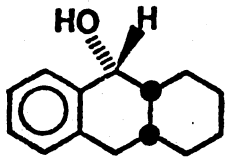

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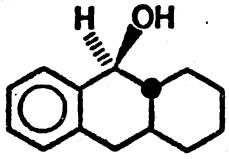

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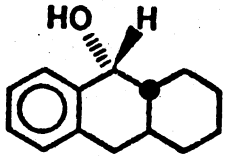

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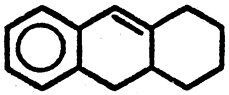

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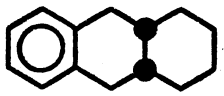

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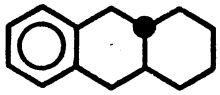

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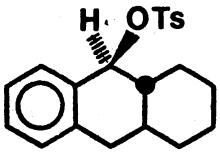

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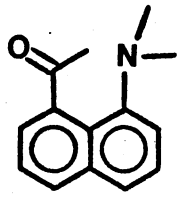

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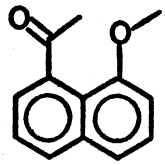

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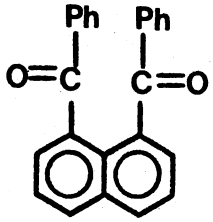

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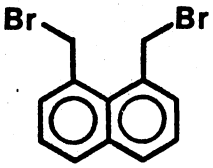

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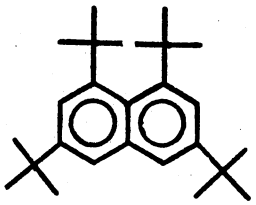

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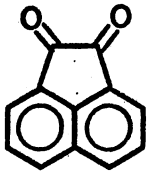

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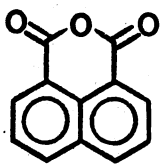

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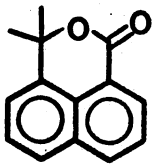

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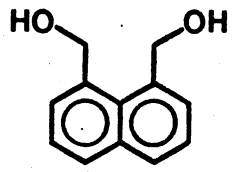

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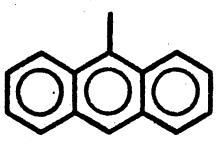

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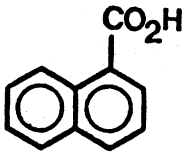

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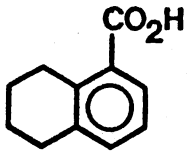

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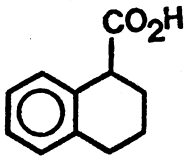

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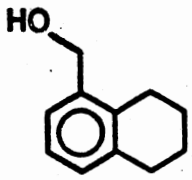

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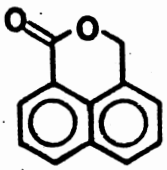

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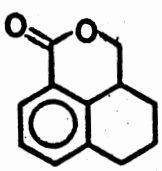

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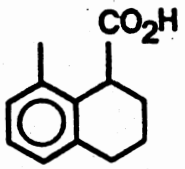

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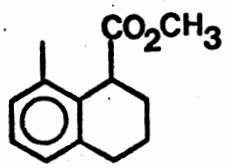

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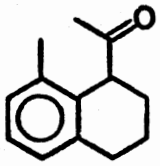

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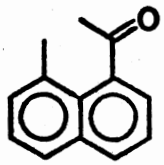

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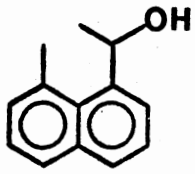

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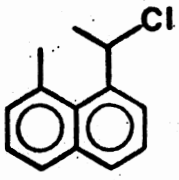

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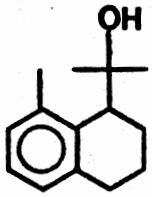

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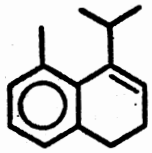

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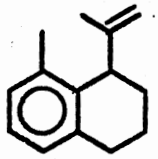

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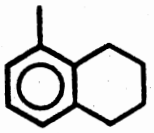

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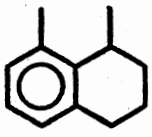

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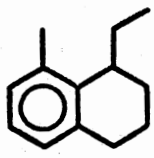

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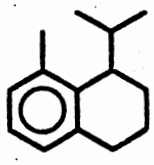

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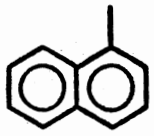

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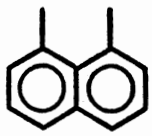

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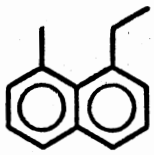

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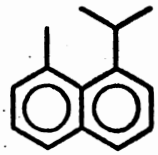

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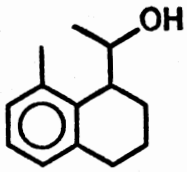

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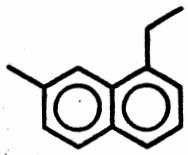

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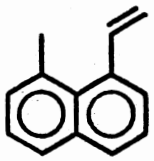

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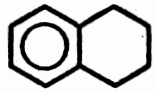

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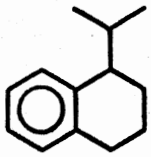

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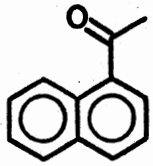

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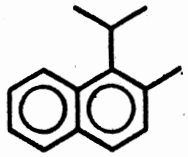

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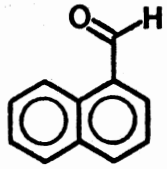

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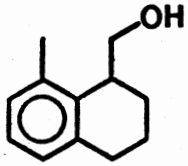

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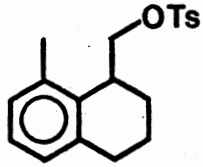

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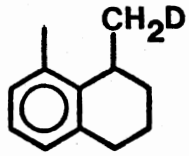

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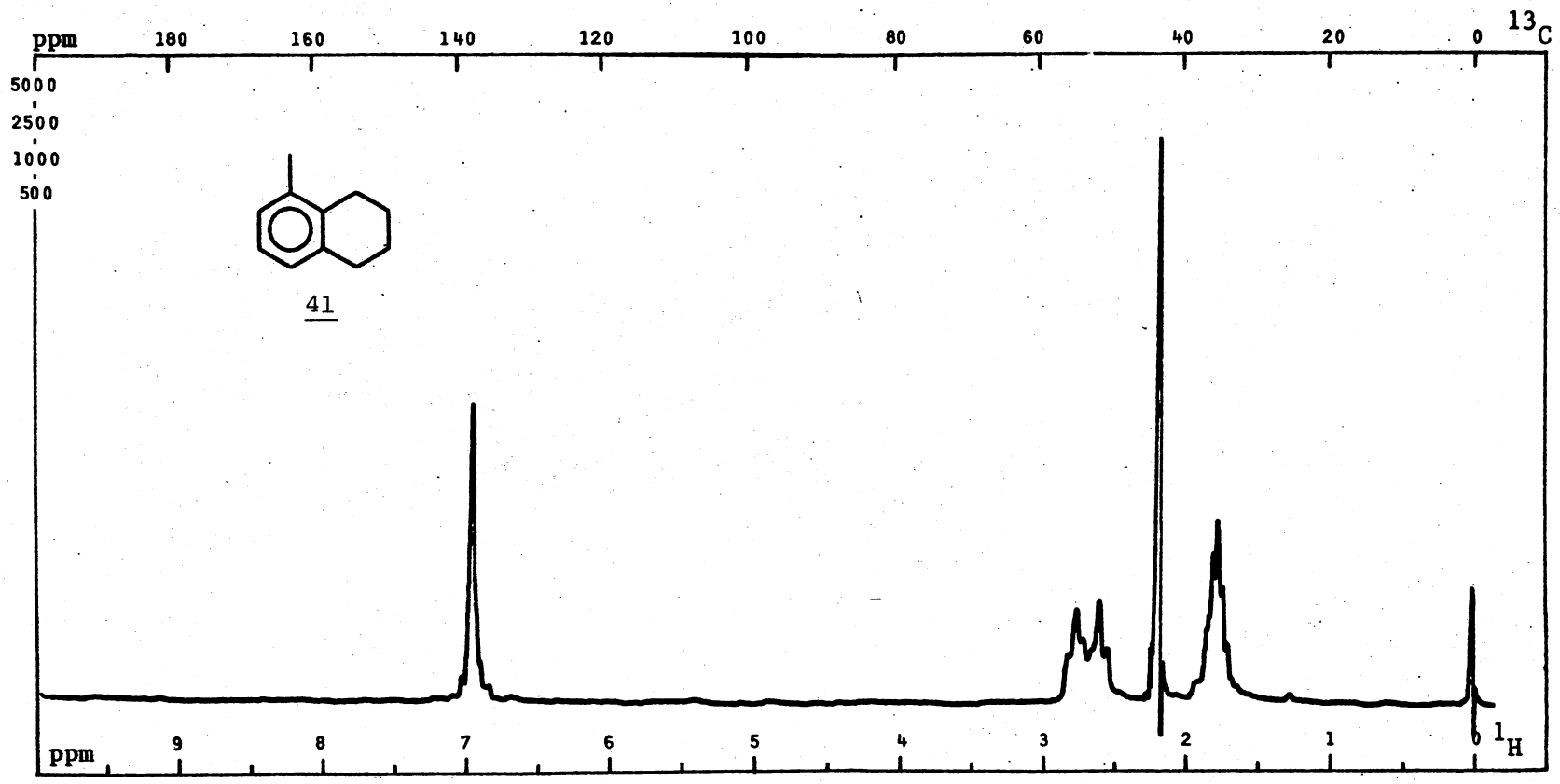
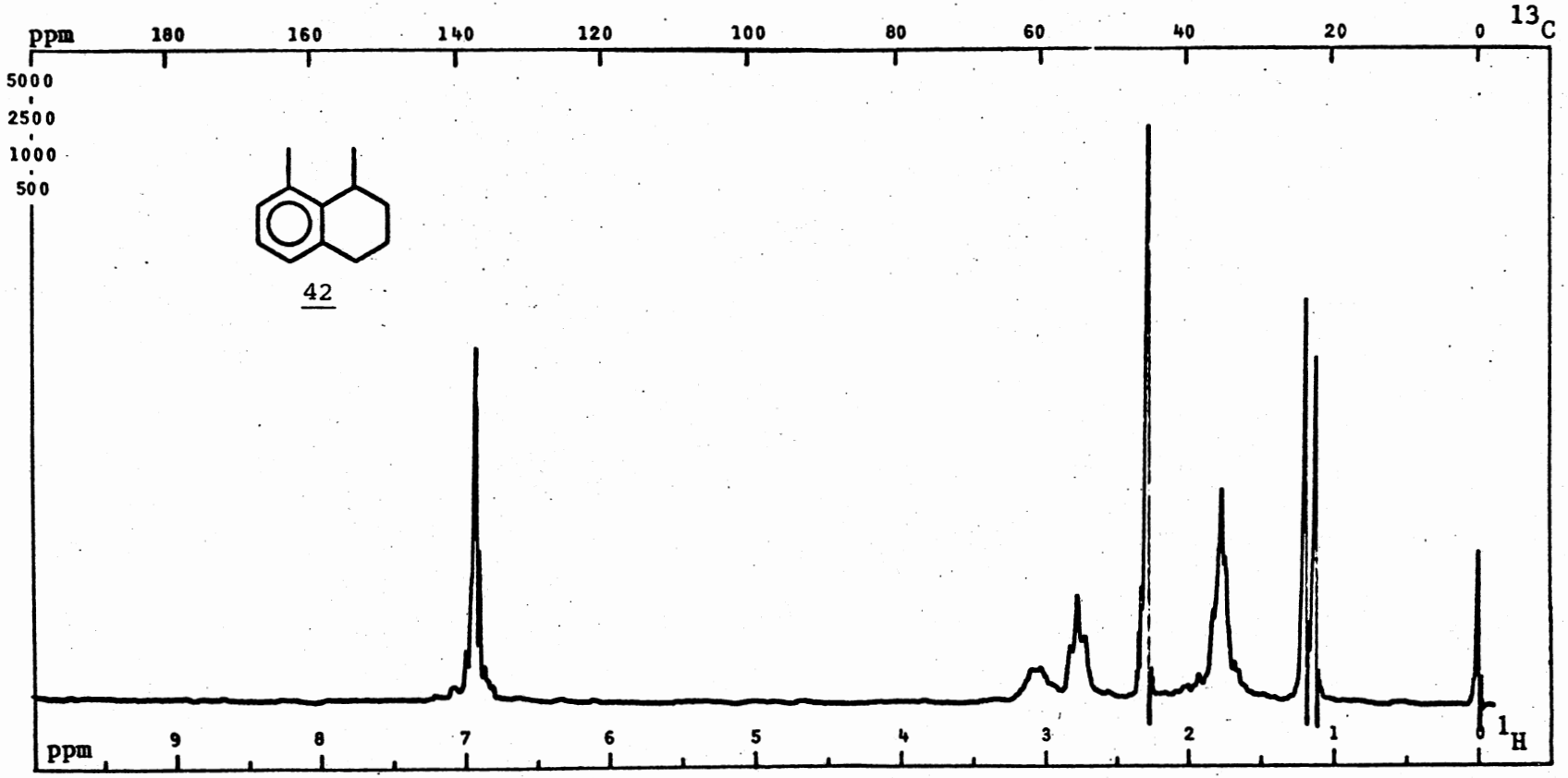
APPENDIX B

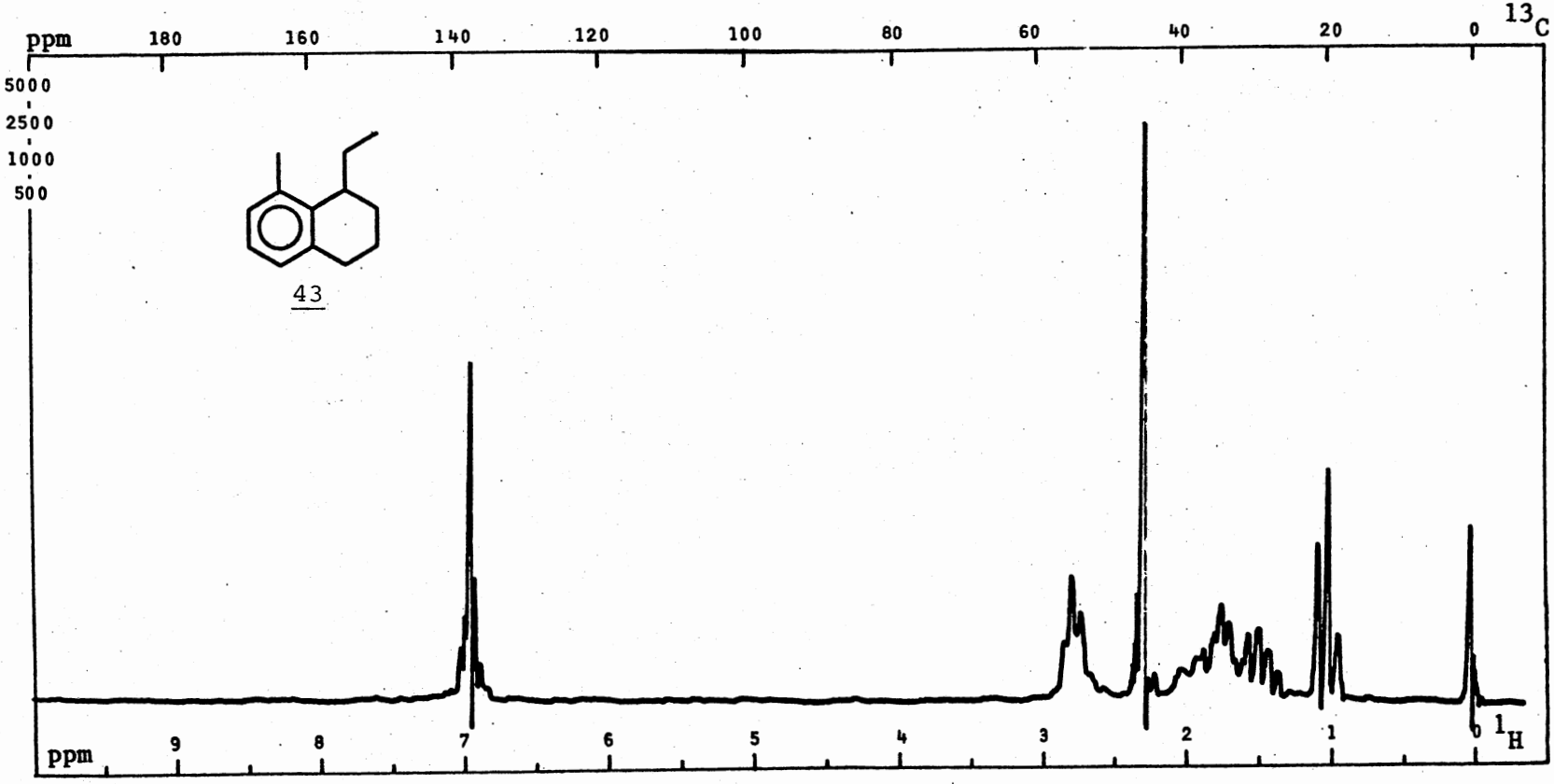
SELECTED SPECTRA



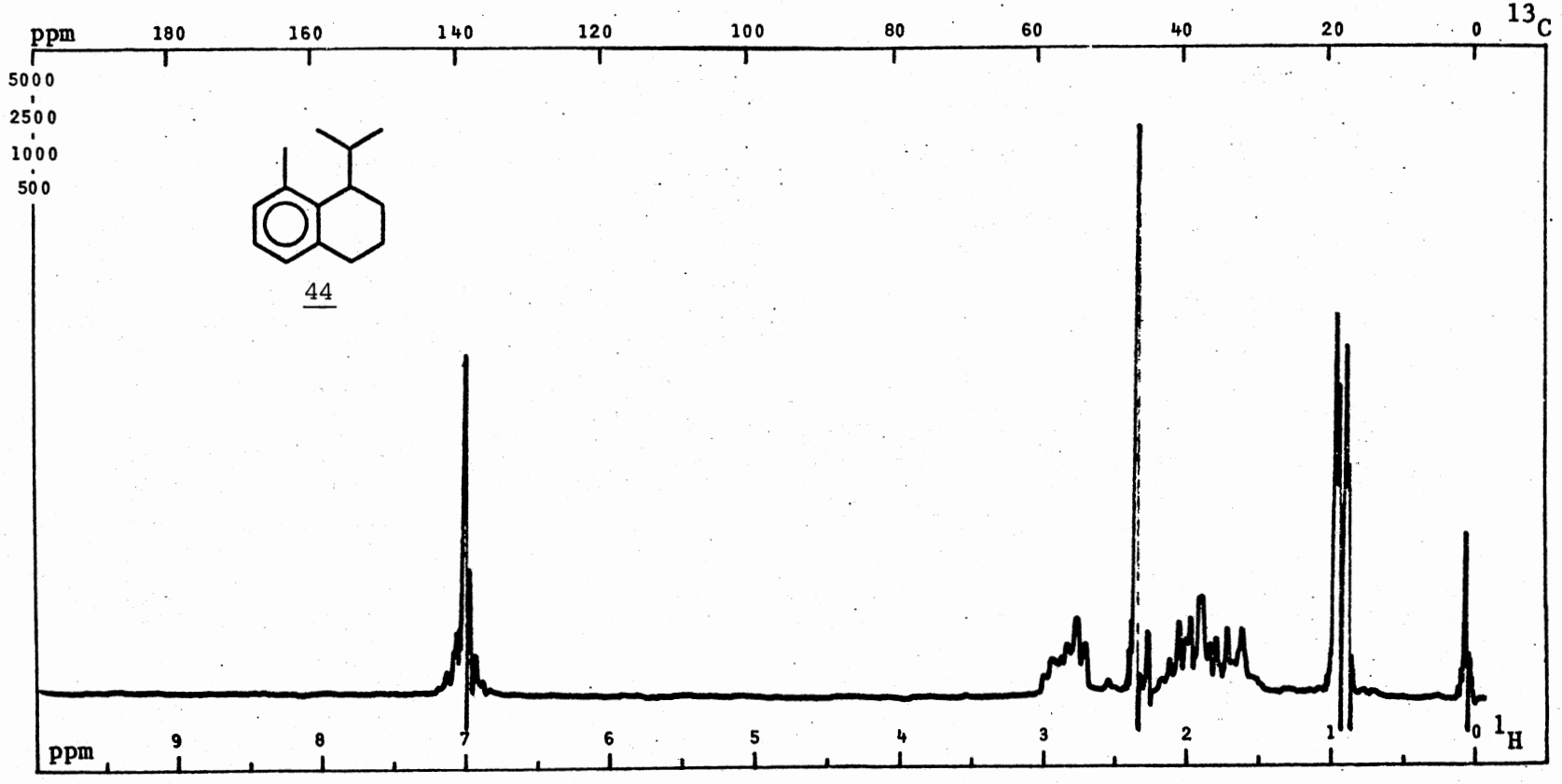
Spectrum 10. ^{1}H NMR of 5-Methyl-1,2,3,4-tetrahydronaphthalene (41)



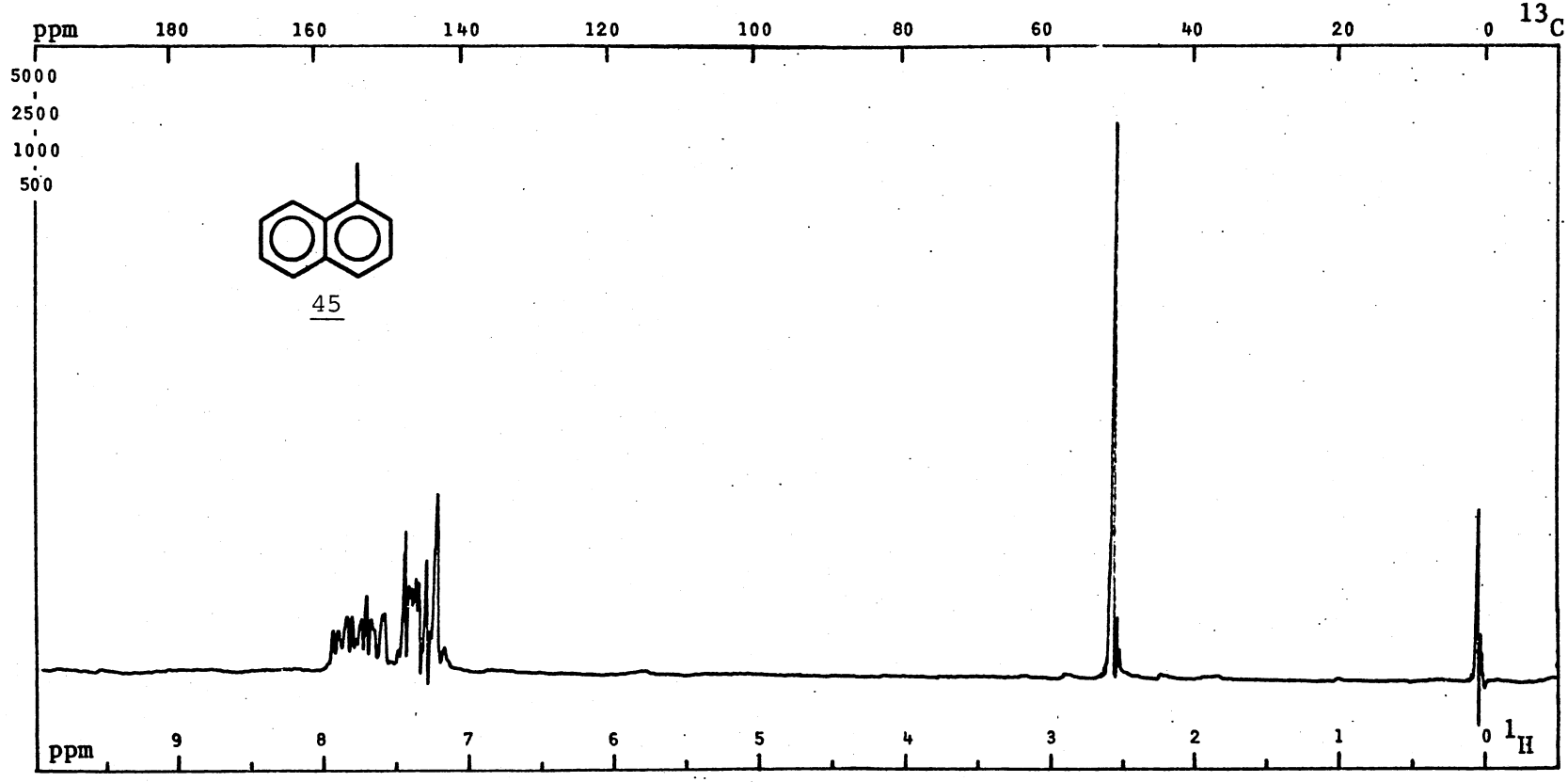
Spectrum 11. ^{1}H NMR of 1,8-Dimethyl-1,2,3,4-tetrahydronaphthalene (42)



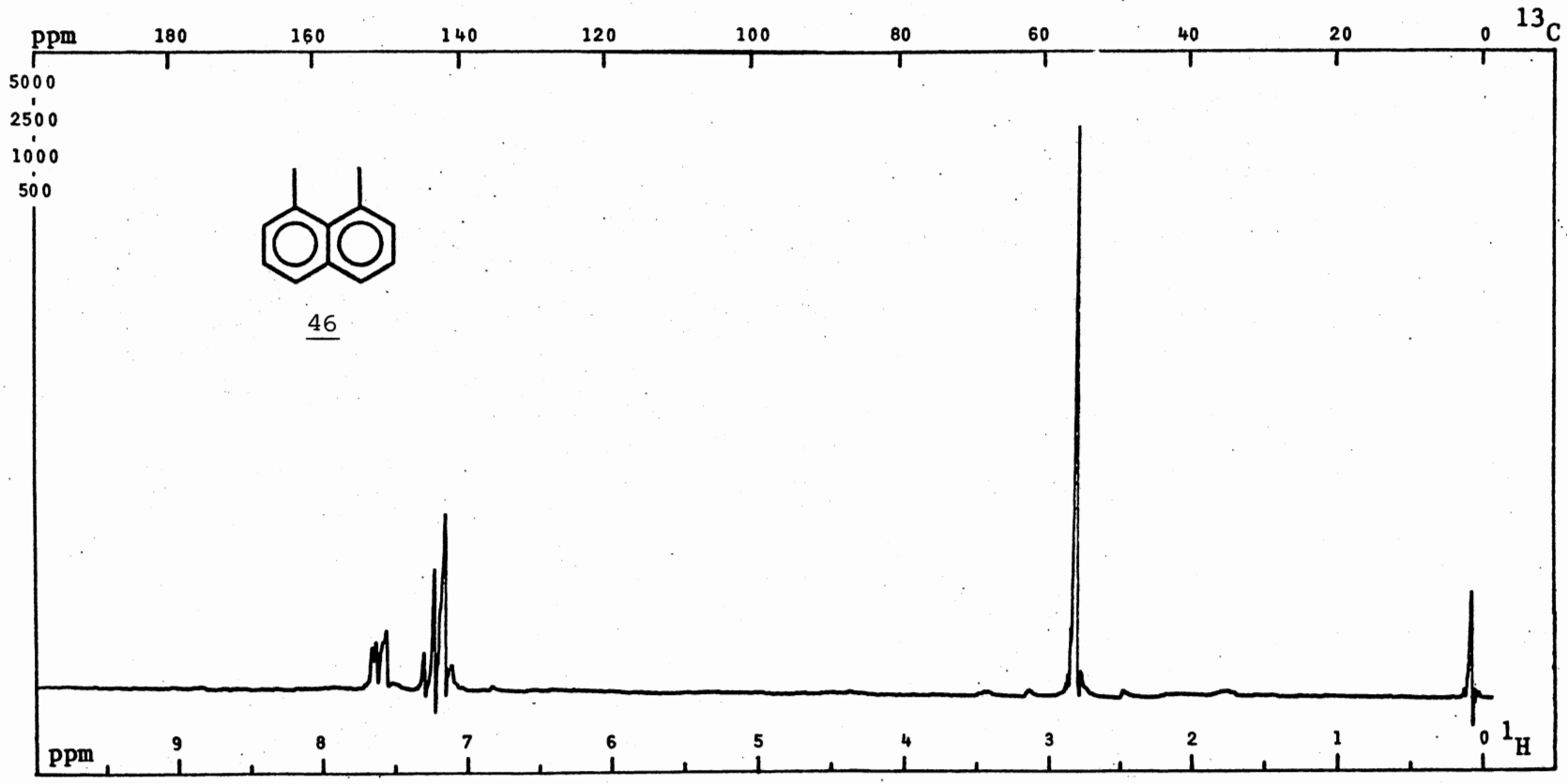
Spectrum 12. ^{1}H NMR of 1-Ethyl-8-methyl-1,2,3,4-tetrahydronaphthalene (43)



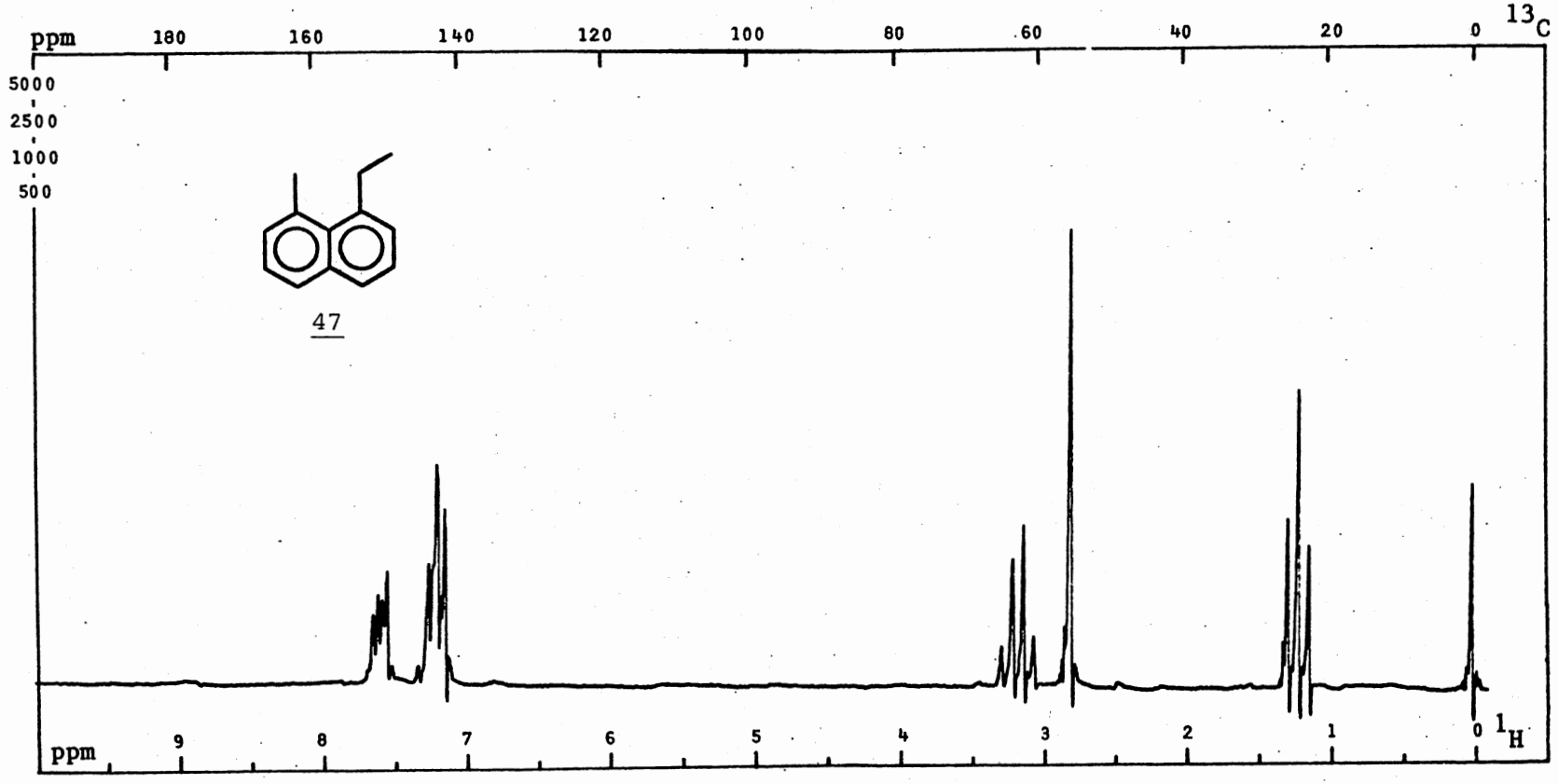
Spectrum 13. ^{1}H NMR of 1-Isopropyl-8-methyl-1,2,3,4-tetrahydronaphthalene (44)



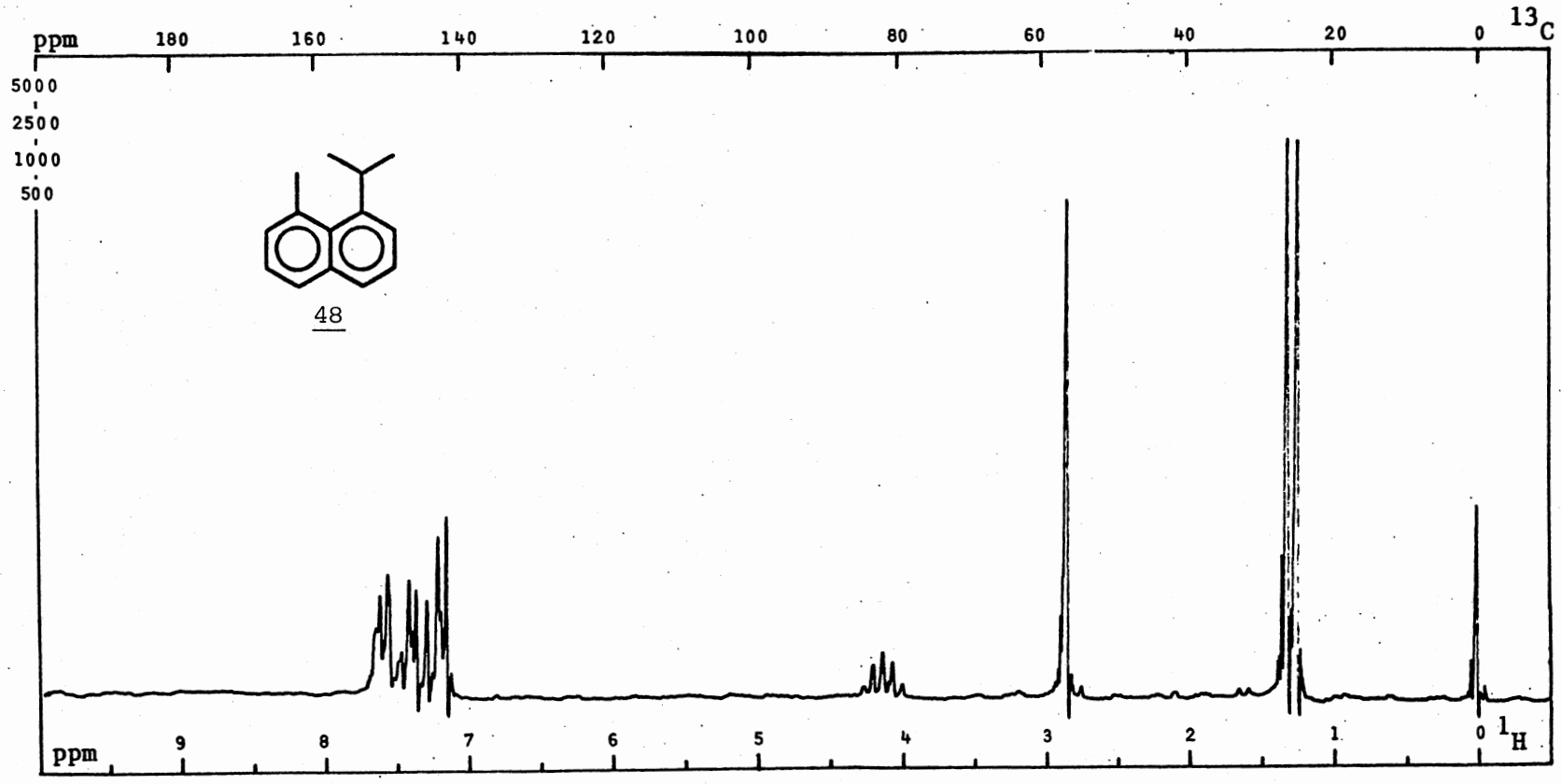
Spectrum 14. ^{1}H NMR of 1-Methylnaphthalene (45)



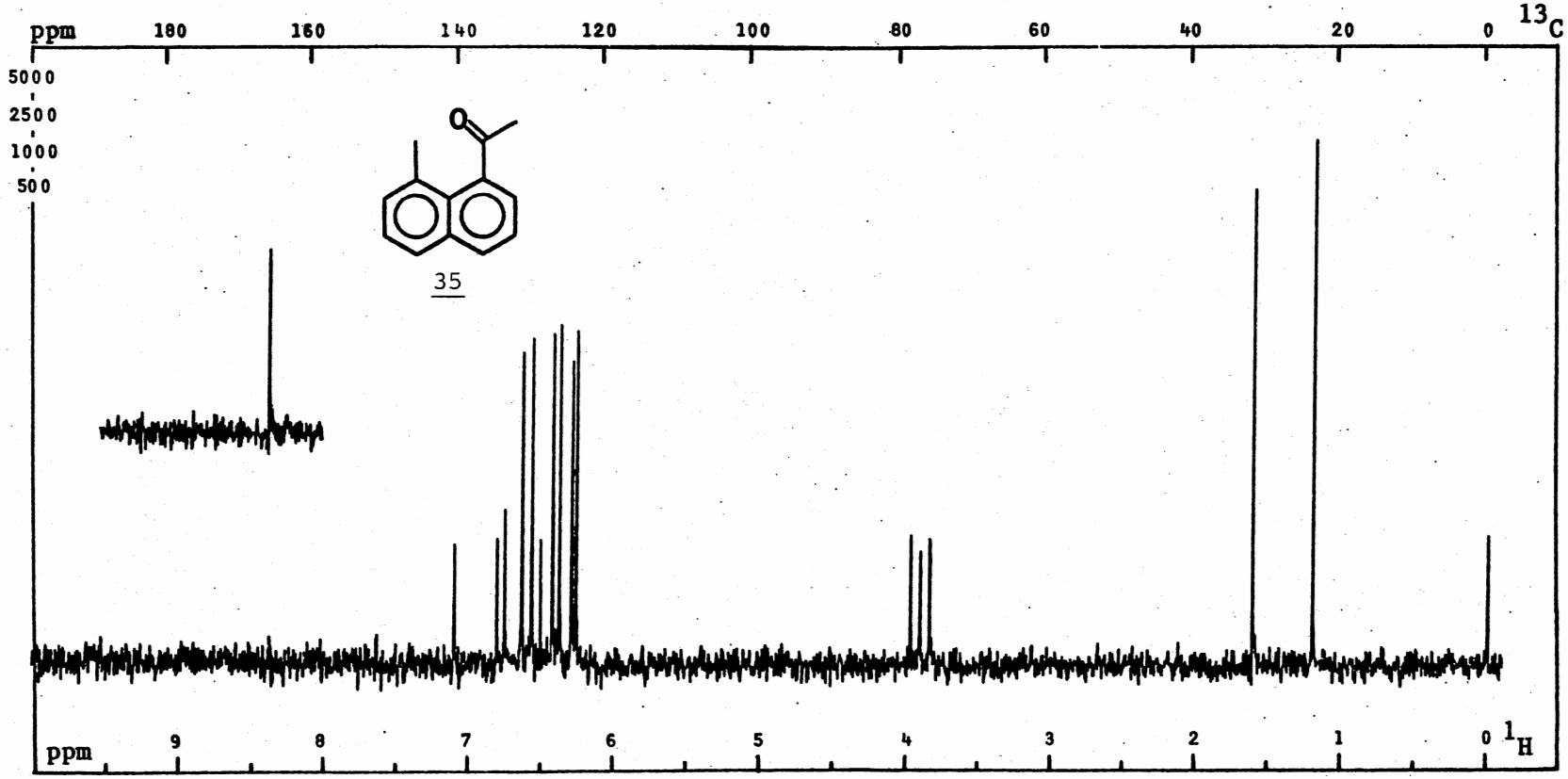
Spectrum 15. ^{1}H NMR of 1,8-Dimethylnaphthalene (46)



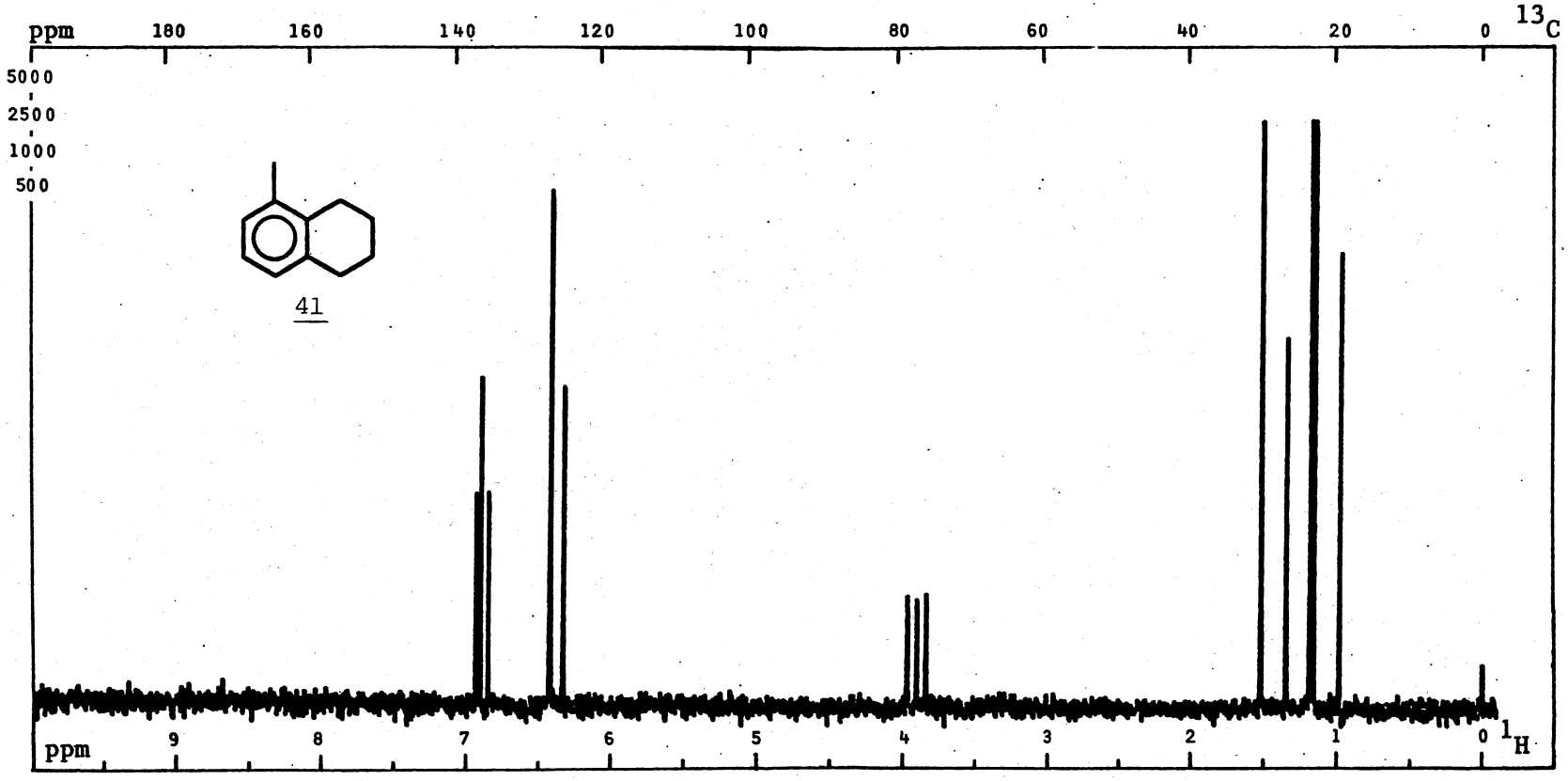
Spectrum 16. ^{1}H NMR of 1-Ethyl-8-methylnaphthalene (47)



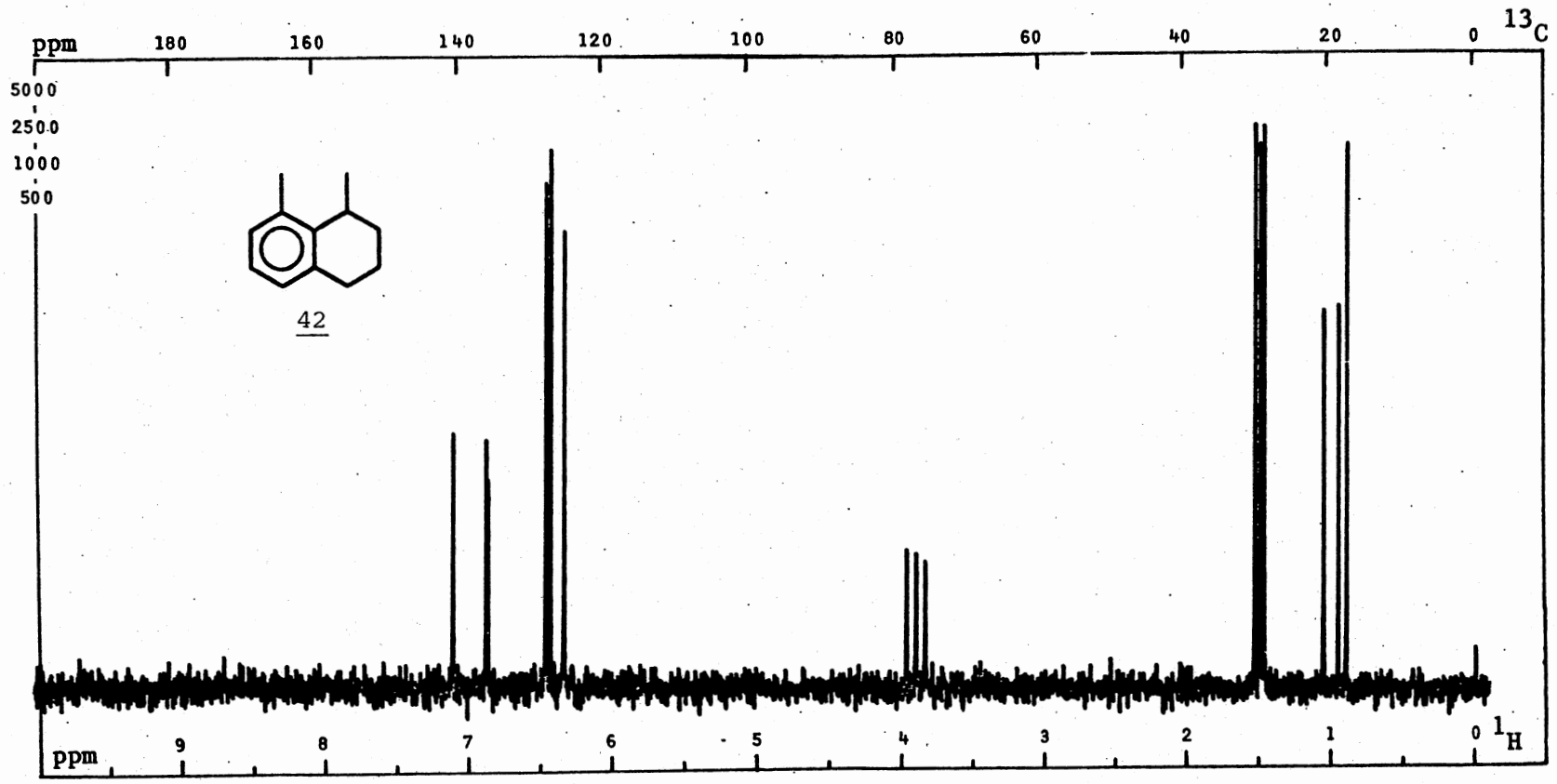
Spectrum 17. ^{1}H NMR of 1-Isopropyl-8-methylnaphthalene (48)



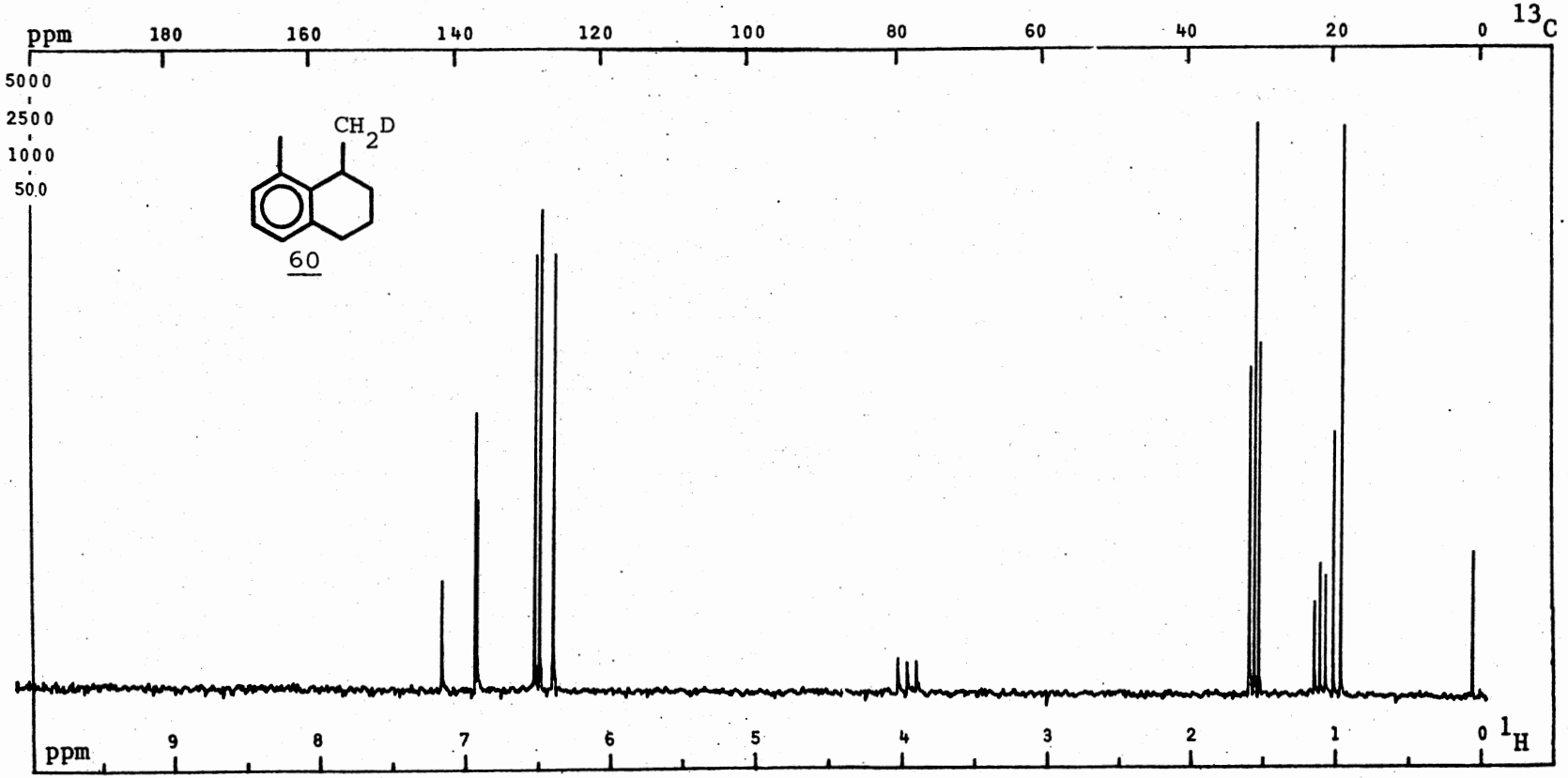
Spectrum 18. ^{13}C NMR of 8'-Methyl-1'-acetonaphthone (35)



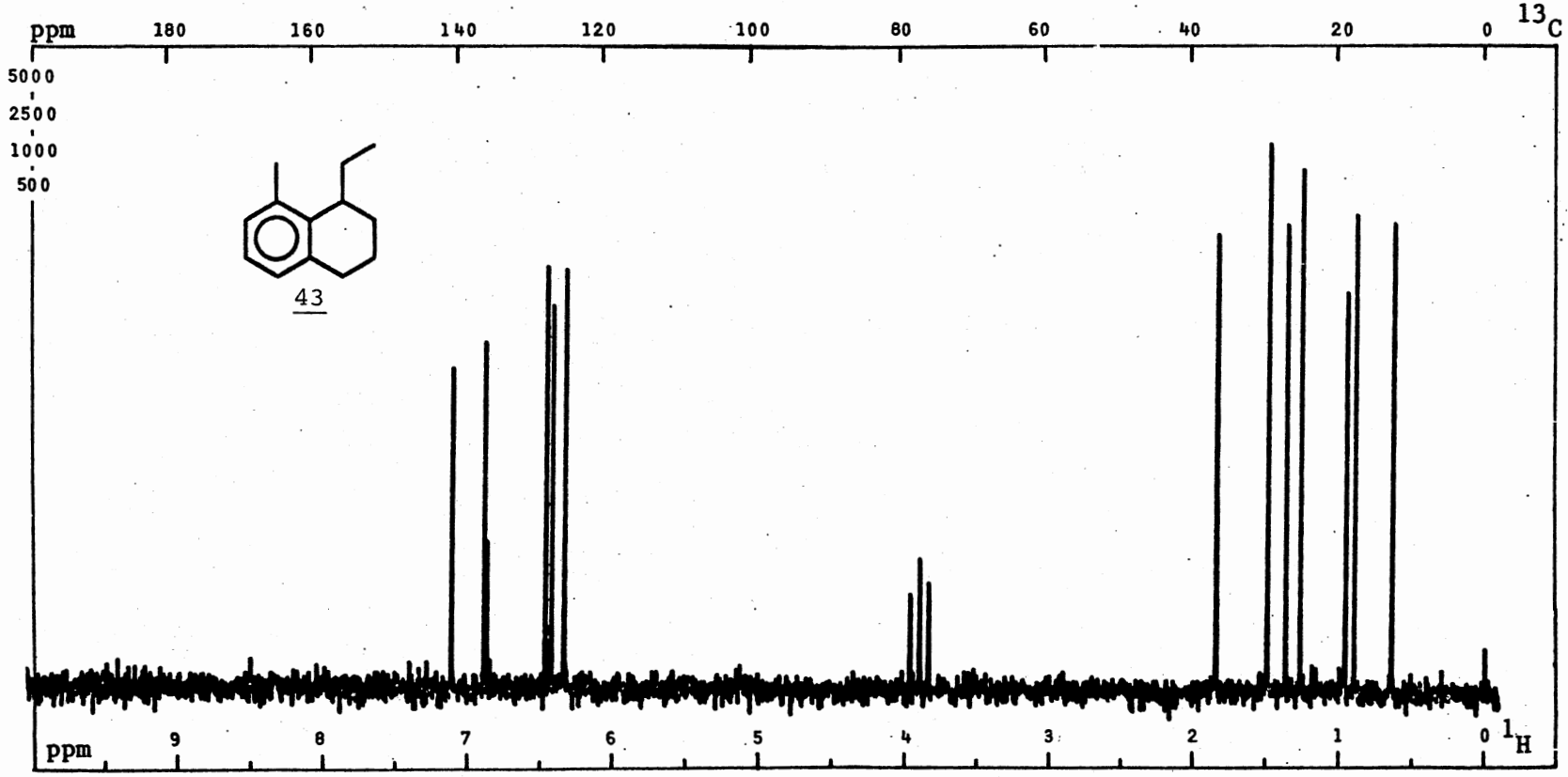
Spectrum 19. ^{13}C NMR of 5-Methyl-1,2,3,4-tetrahydronaphthalene (41)



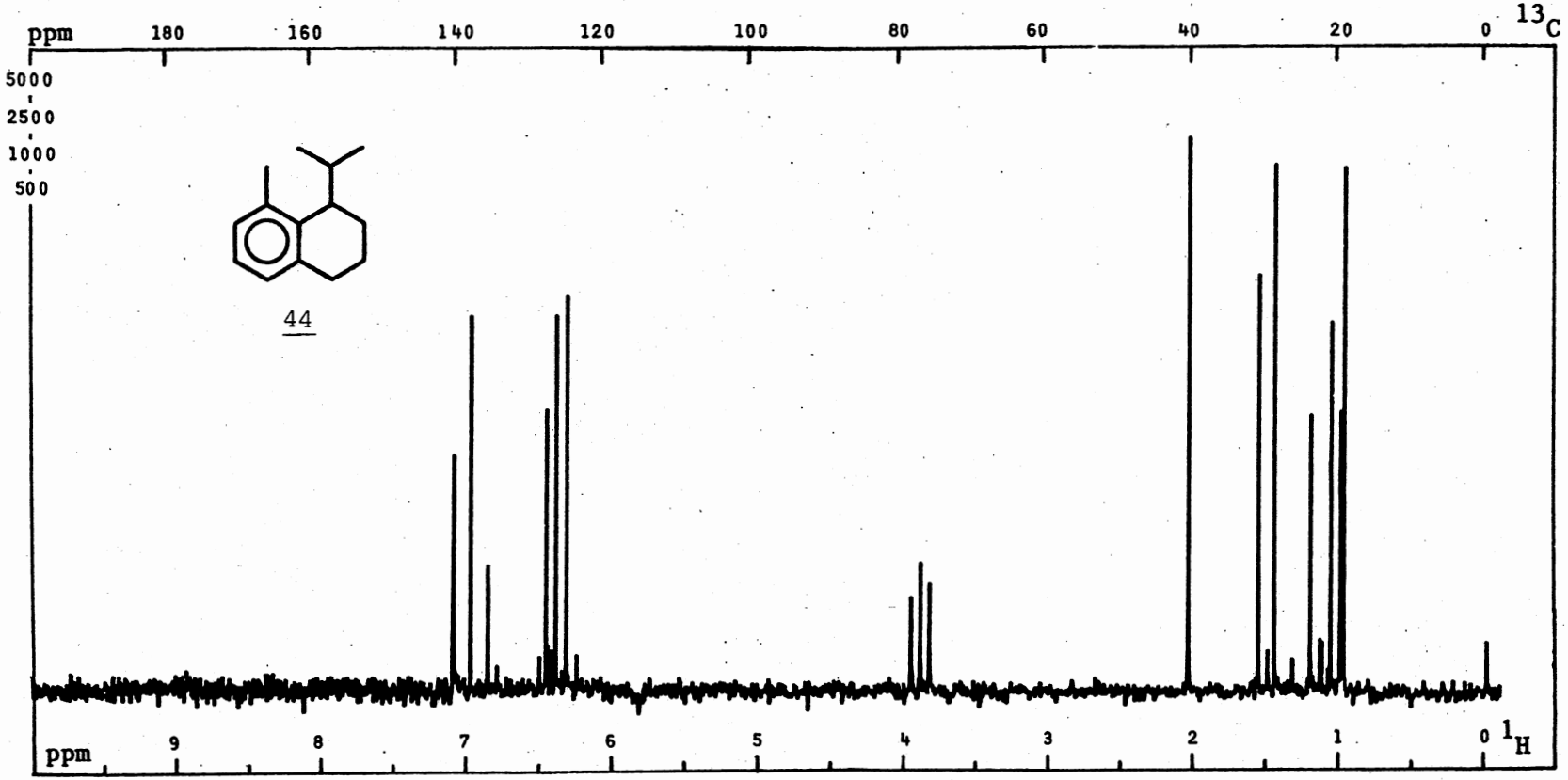
Spectrum 20. ^{13}C NMR of 1,8-Dimethyl-1,2,3,4-tetrahydronaphthalene (42)



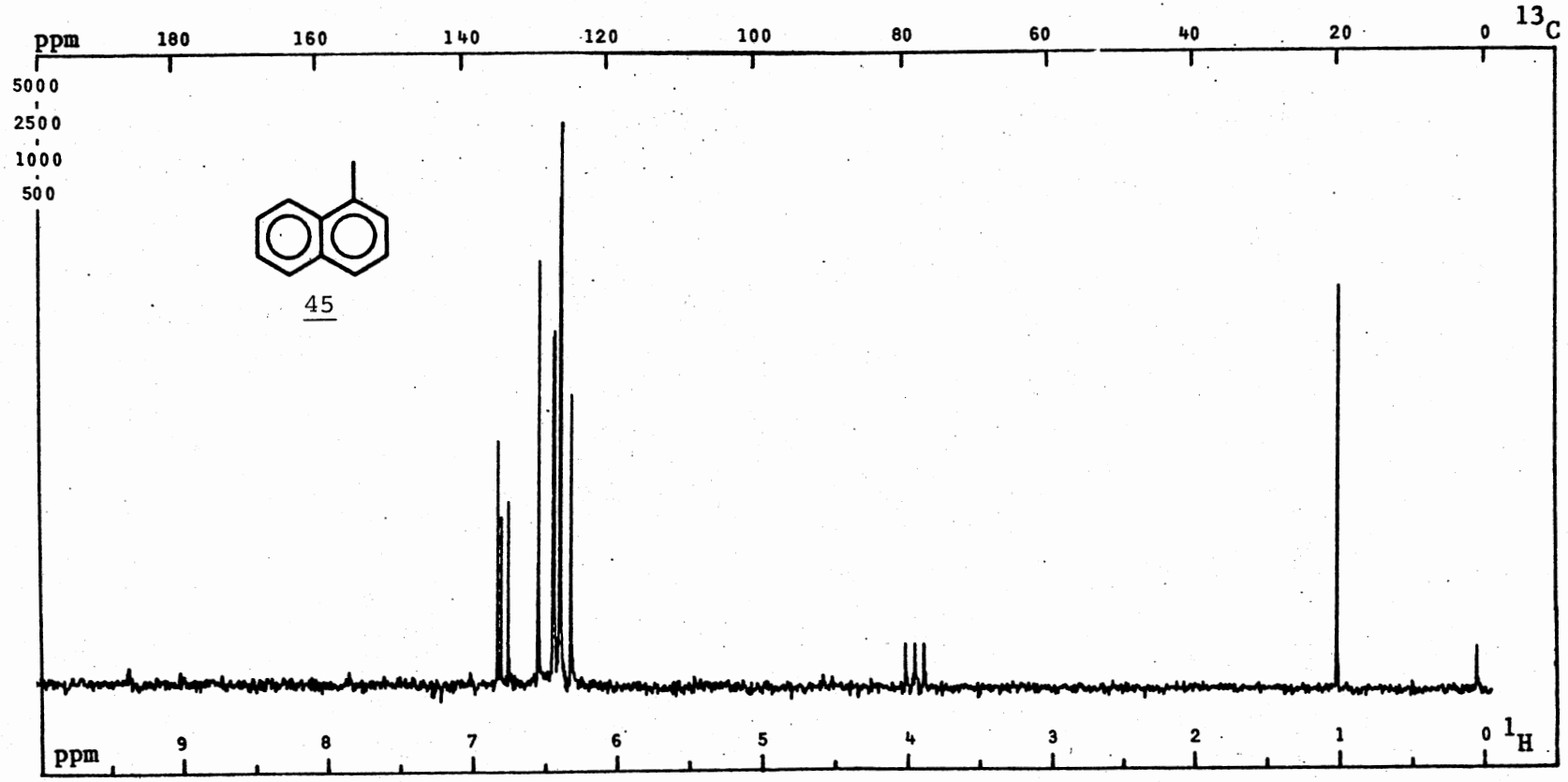
Spectrum 21. ^{13}C NMR of 1-Deuteromethyl-8-methylnaphthalene (60)



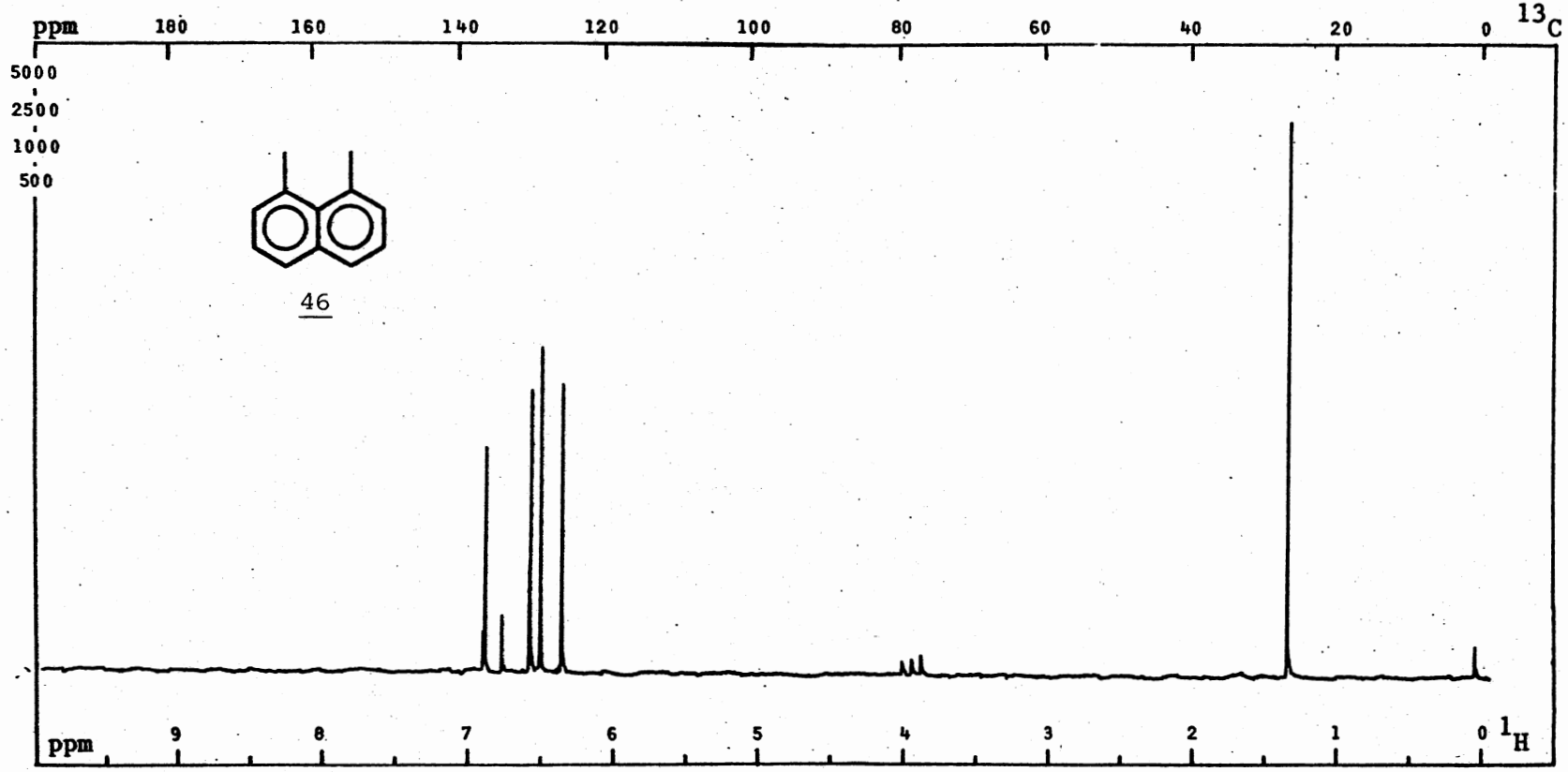
Spectrum 22. ^{13}C NMR of 1-Ethyl-8-methyl-1,2,3,4-tetrahydronaphthalene (43)



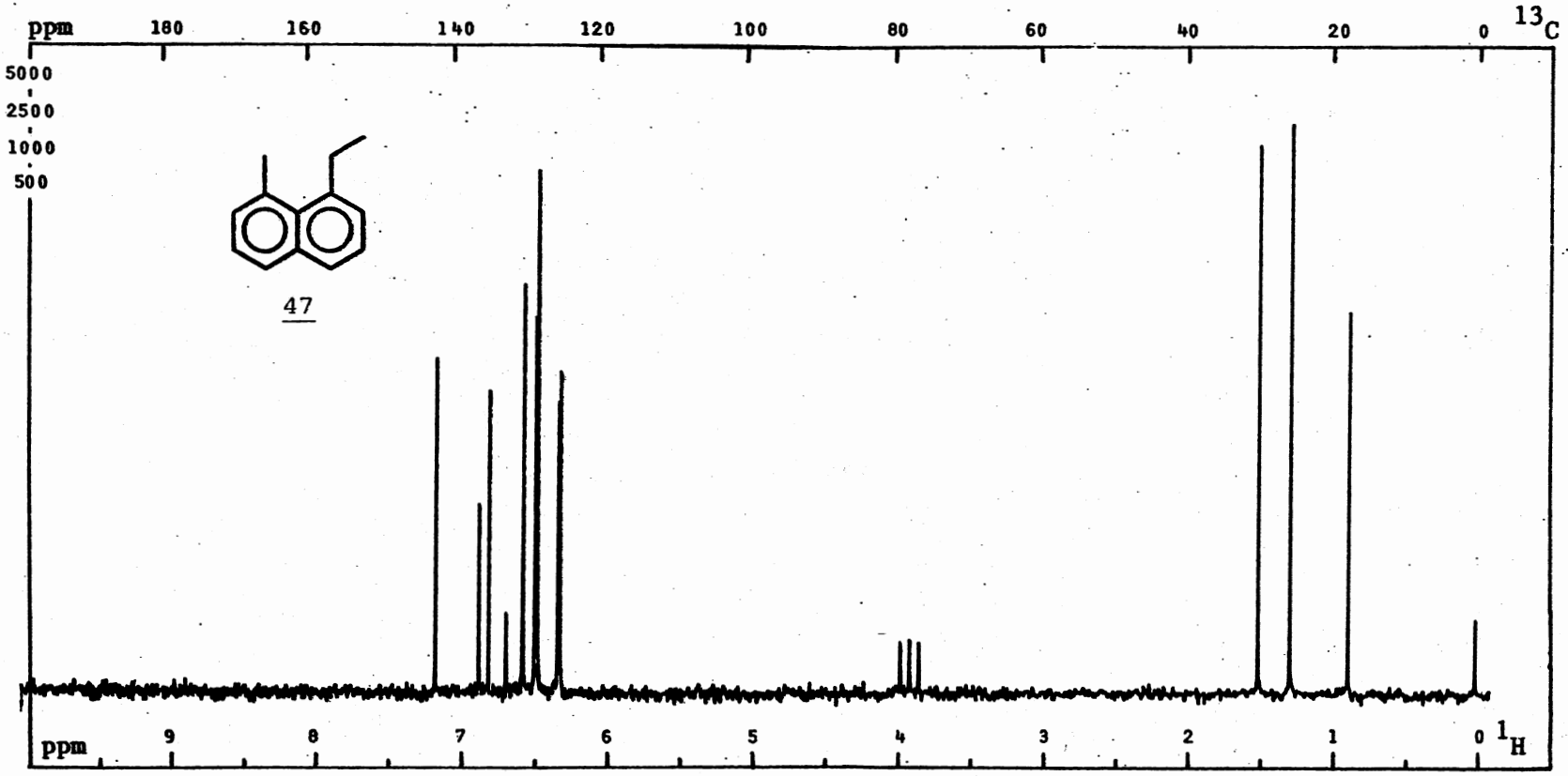
Spectrum 23. ^{13}C NMR of 1-Isopropyl-8-methyl-1,2,3,4-tetrahydronaphthalene (44)



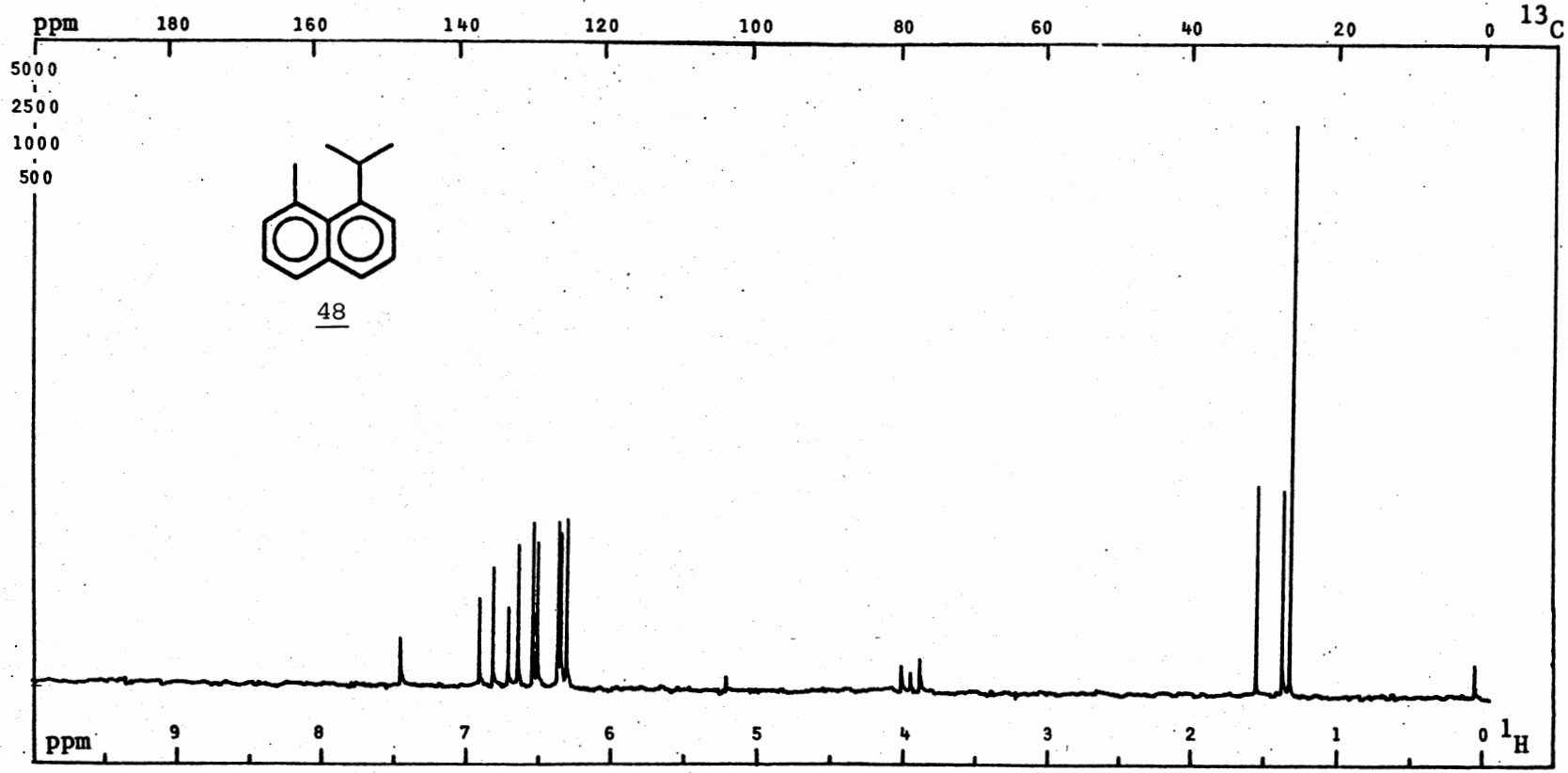
Spectrum 24. ^{13}C NMR of 1-Methylnaphthalene (45)



Spectrum 25. ^{13}C NMR of 1,8-Dimethylnaphthalene (46)



Spectrum 26. ^{13}C NMR of 1-Ethyl-8-methylnaphthalene (47)



Spectrum 27. ^{13}C NMR of 1-Isopropyl-8-methylnaphthalene (48)

VITA[2]

NASER POURAHMADY

Candidate for the Degree of

Doctor of Philosophy

Thesis: I. as-OCTAHYDROANTHRACENES: SYNTHESIS AND STEREOCHEMICAL STUDIES

II. SYNTHESIS OF 1,8-DISUBSTITUTED NAPHTHALENES AND 1,2,3,4-TETRAHYDRONAPHTHALENES: STUDY OF PERI-INTERACTION USING ^{1}H AND ^{13}C NMR

Major Field: Chemistry

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