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I. Generation of dibromocarbene under neutral conditions. II. Generation and reactions of 11-carbena[4.4.1]propella-3,8-diene. III. The oxidation of cyclopropylidenes

Gurumurthy, Ramaswamy, Ph.D.

Iowa State University, 1989

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I. Generation of dibromocarbene under neutral conditions
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III. The oxidation of cyclopropylidenes

by

Ramaswamy Gurumurthy

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DOCTOR OF PHILOSOPHY

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1989

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DEDICATION

To my spiritual teacher Swami Tanmayananda, my beloved parents Ramaswamy and Meenakshi, and Shanti.

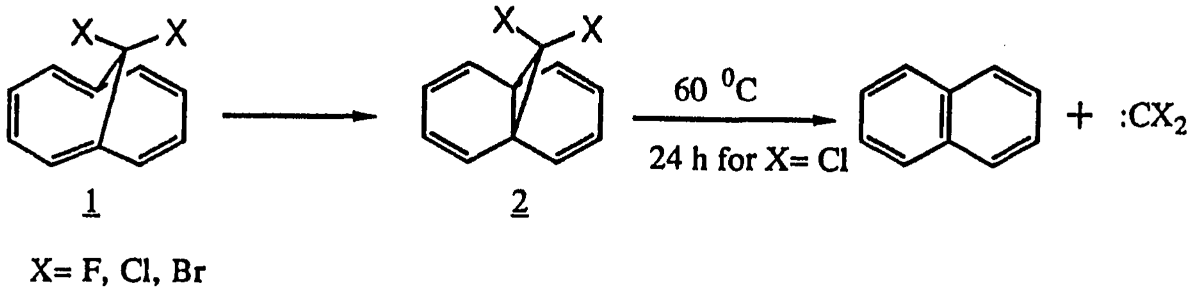
CHAPTER I. GENERATION OF DIBROMOCARBENE UNDER NEUTRAL CONDITIONS

Introduction

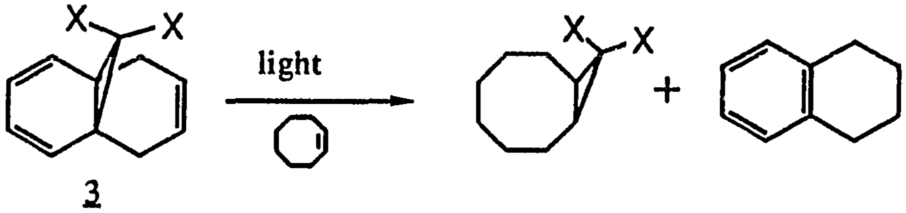
Dihalocarbenes, $:CX_2$, are very simple but useful intermediates in organic chemistry. Interest in the preparation and reactions of gem-dibromocyclopropanes has been significant since the initial report of the synthesis of this class of compounds by Doering and Hoffmann[1] in 1954, by dibromocarbene addition to olefins. Their method and some of its modifications leading to dibromocarbene are based on the treatment of a tribromomethide ion, CBr_3^-, with a strong base in the presence of an olefinic substrate. These methods work very well for the preparation of many dibromocyclopropanes, but in some cases the yields are very low. If the olefin contains base sensitive functional groups like -OAc, these methods cannot be employed. Thermal decarboxylation of alkali metal tribromoacetates,[2] another method to generate dibromocarbene, avoids basic reaction conditions, but with weakly nucleophilic olefins, a side reaction occurs between the carbene and the trihaloacetate ion, thus giving low yields of the desired product. Both the methods described above have another disadvantage in common - the trihalomethide ion intermediate is intercepted in part by some substrates before it has a chance to decompose to dihalocarbene.

Seyferth et al.'s method[3] makes use of phenyltrihalomethylmercury compounds as dihalocarbene sources. The decomposition of organomercurials proceeds under mild conditions to give singlet carbenes. Although this method neither involves trihalomethide ion nor requires basic reaction conditions, it has certain problems. The Seyferth reagent has dual reactivity with electron-deficient alkenes.[4] For example, trans-1,2-dichloroethane reacts both with the free carbene to give cyclopropane stereospecifically, and with a complex between the carbene and a second molecule of Seyferth reagent to give a rearranged propene. Addition of good pi donors such as p-xylene decreases the pathway to rearranged propene via the complexed carbene. The presence of insoluble materials such as zinc chloride, on the other hand, serves to decrease the pathway that leads to the cyclopropane through the free carbene. The free carbene may react with the surface of the additive and be removed as a reactive species.

Attempts to derive dihalocarbenes from the halogenation of diazomethane with t-butyl hypohalite led to dihalodiazomethanes which were too unstable to be characterized.[5] The thermal extrusion of dihalocarbenes from 1, was reported by Rauten Strauch et al.,[6] but for X = Cl or Br the preparative yields of 1 were very low.



Recently, Hartwig et al.[7a] reported the photochemical extrusion of $:CX_2$ (X = Cl, Br) from 3. The selectivity index for dibromocarbene from 3 was lower, for unknown



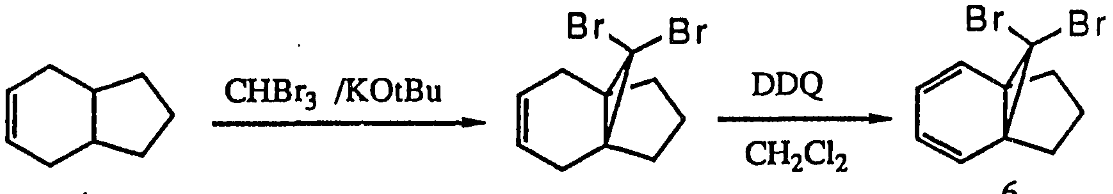
reasons, than that from bromoform in the presence of 18-Crown-6. Compounds 1 and 3 were prepared via dehydrogenation of the corresponding 11,11-dihalo[4.4.1]-propella-3,8-dienes. These and Vogel's compounds are the only ones available currently that can be used to generate dibromocarbene under neutral conditions. So there is a real need to search for easily accessible sources of dibromocarbene.

This thesis includes an additional source of dibromocarbene. Both thermal and photochemical methods of generation under neutral conditions will be discussed.

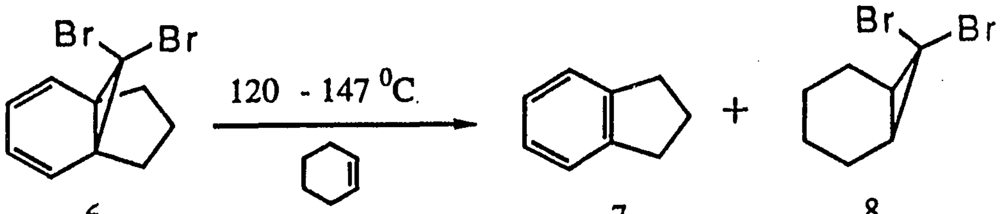
Results and Discussion

Warner and Lu, in the course of their studies of solvolysis of dihalocyclopropanes, heated 10,10-dibromotricyclo[4.3.1]deca-2,4-diene (6) at 100°C in HOAc/NaOAc. They observed the formation of indan (7) in this reaction. This interesting observation led us to investigate in detail the possible thermal extrusion of $:CBr_2$ from 6 under nuetral conditions.[7b]

Compound 6 was prepared by DDQ dehydrogenation of 10,10-dibromotricyclo[4.3.1.0]deca-3-ene (5).[8] Thermolysis of 6 was carried out in cyclohexene solution at various temperatures. The minimum temperature at which extrusion of $:CBr_2$ was observed to occur, as evidenced by the formation of 7,7-dibromonorcarane (8),[9] was 120°C. At this temperature 7 was formed in 9% yield and 8 in 10% yield.



4 5 6



6 7 8

The starting material was recovered to the extent of [illegible]. The product yields were determined by capillary GC using a known amount of mesitylene as internal standard. The response factors (R_f) for all compounds with respect to mesitylene were determined using FT-NMR and GC (see experimental section for the general procedure). Table 1 gives the product yields at various temperatures. The products were identified by comparing their GC retention times and their mass spectra with those of a commercial (Aldrich) sample of 7 and a synthetic sample of 8. At 147°C, although 91% of the starting material had decomposed, the yields of 7 and 8 were only 64% and 56%, respectively. However, neither 7 nor 8 decomposed in a control experiment.

It is clear from the above results that 6 transfers $:CBr_2$ under neutral conditions. It should be noted that in reference 6, it is reported that the dichloro analog of 6 can transfer dichlorocarbene to olefins at temperatures >150°C. In our hands, when trans-stilbene (10 equivalents) was used to capture $:CBr_2$, no dibromocyclopropane could be observed even on heating the reaction mixture to 147°C for 12 h. But indan was formed in 42% yield. This was not

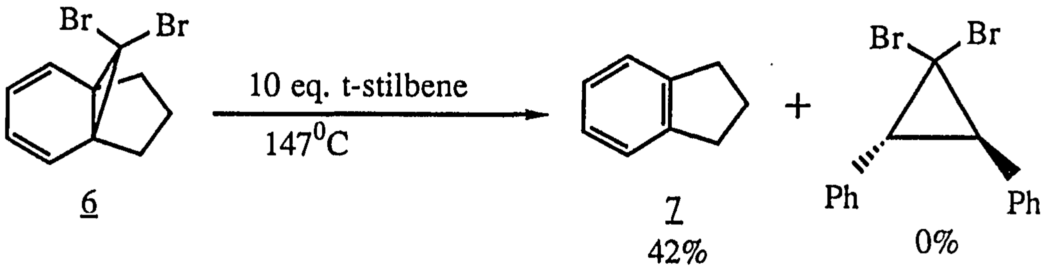
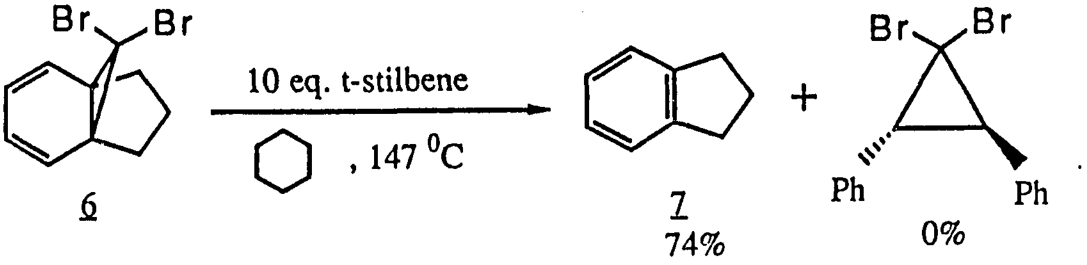


Table 1. Yields of thermal $:CBr_2$ transfer to cyclohexene

Temperature (°C)	Reaction time (h)	% Yields 7	8	Recovered 6 (%)
120	6	9	10	>90
120	19	18	20	74
135	6	23	27	70
147	6	56	53	21
147	12	64	56	9

surprising because trans-stilbene does not react with $:CBr_2$ generated from $CHBr_3$ and KOtBu.

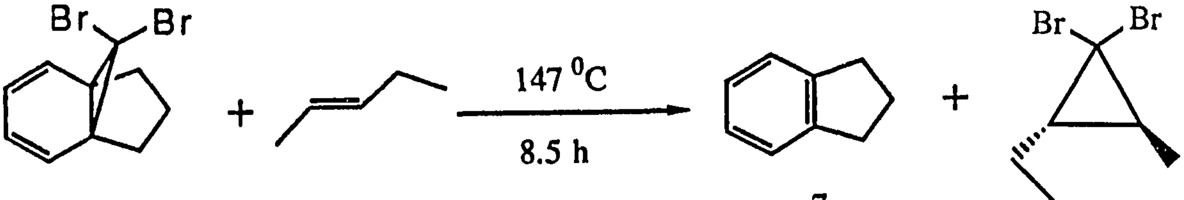
The thermolysis of 6 was subject to solvent effects. On heating 6 with 10 equivalents of trans-stilbene in cyclohexane as solvent at 147°C for 10 h, a 74% yield of



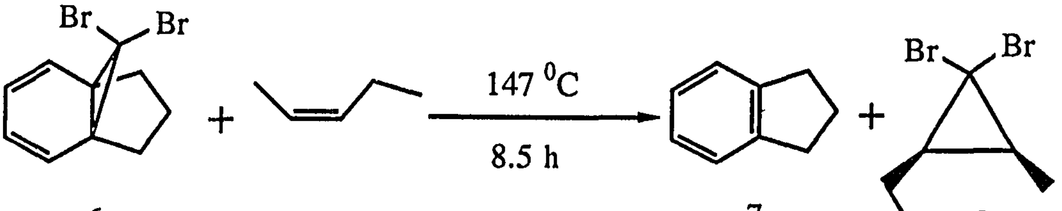
indan was obtained. Again no dibromocyclopropane was observed.

It was of interest to find out the kinetic order of this extrusion reaction. The formation of indan without any $:CBr_2$ adduct with stilbene suggested that the reaction was unimolecular. That is, $:CBr_2$ was extruded without kinetic interference from the alkene present. The kinetics were determined by following the loss of 6 under psuedo-first order conditions in cyclohexene or cyclohexene/cyclohexane solution. The derived psuedo-first order rate constants (Table 2) are unchanged over an eight-fold change in [cyclohexene]. This confirms the unimolecular nature of the thermal $:CBr_2$ extrusion from 6.

The stereochemistry of the $:CBr_2$ addition was examined by using cis- and trans-2-pentenes as the olefinic acceptors. The reaction was carried out by heating a mixture of 6 and a large excess of the alkene at 147°C for 8.5 h. Table 3 shows the products and their yields.



6 7 9b



6 7 9a

Authentic samples of 9a and 9b were prepared by reacting the corresponding alkenes with $CHBr_3$/KOtBu. The GC retention

Table 2. Kinetics of thermal decomposition of 6[a]

[cyclohexene], M	$k \times 10^5$ (s^{-1})
9.6[b]	2.8 ± 0.1
4.8[c]	3.0 ± 0.1
1.2[d]	2.9 ± 0.2

[a] In each case $[6]_o$ = 0.16 M, T = 134° ± 1°C.

[b] Pure cyclohexene.

[c] Fifty percent cyclohexene/50% cyclohexane.

[d] Twelve and one-half percent cyclohexene/87.5% cyclohexane.

Table 3. Products and percent yields from thermal extrusion of $:CBr_2$ in 2-pentenes

Starting materials[a]	Products[b]			Recovered 5
	7	9a	9b	
6 + cis-2-pentene	65	40	0	20
6 + trans-2-pentene	87	0	55	24

[a] In each case the molar ratio of 6 to the alkene was 1:161.

[b] The yields of products are based on unrecovered 6.

times of 9a and 9b (9a, 4.46 m; 9b, 4.16 m) differed by 0.3 m under the program conditions (80°/2 min, 80-250 °C @ 20 °/min) used. They showed different NMR patterns (see the expanded spectra attached to Figures 3 and 5). The yields reported are GC yields with respect to mesitylene as internal standard. The addition is clearly stereospecific.

The room temperature photochemical extrusion of $:CBr_2$ was also examined by using a 254 nm light source for 18.5 h. The results are shown in Table 4.

The yield of dibromocyclopropane product was comparable to that reported from 3.[7a] Again the photochemical reaction is stereospecific. The small amount of 9b formed from cis-2-pentene might raise some concern about this conclusion, but it should be pointed out that 1-2% of 9b was also formed from cis-2-pentene and $CHBr_3$/KOtBu. Also, photolysis of 4.5 mg of 6 in 0.2 mL cis-2-pentene/1 mL pentane for 9 h led to a 75% yield of indan, a 63% yield of 9a but no trans isomer 9b. A control experiment was performed to test the plausible photoisomerization of 9a by photolyzing a solution of 9a in cis-2-pentene. No more than 0.5% isomerization was observed after 18.5 h.

In conclusion, it should be emphasized that 6 is a readily available source of $:CBr_2$; it is made in just three steps from the commercially available indan. This method of

Table 4. Products and percent yields of photochemical extrusion of $:CBr_2$ in 2-pentenes

Starting materials[a]	Products[b]			Recovered 6
	7	9a	9b	
6 + cis-2-pentene	90	90	2.7[c]	51
6 + trans-2-pentene	75	0	75	52

[a] In each case the molar ratio of 6 to the alkene was 1:161.

[b] The GC yields are based on unrecovered 6.

[c] Average of three GC analyses of the same sample.

generation of $:CBr_2$ should set a precedent to explore the generation of other carbenes.

Experimental

General

Infrared spectra were recorded on an IBM FT-IR 98 spectrometer. All bands are reported in reciprocal centimeters (cm^{-1}). The proton and carbon magnetic resonance spectra were recorded on a Nicolet 300 MHz FT-NMR and a Bruker model WM-300 FT-NMR spectrometers. All chemical shifts are reported as parts per million (δ scale) using deuterochloroform, tetrahydrofuran-d_8 and benzene-d_6 as solvents. GC-IR spectra were recorded on an IBM FT-IR 98 spectrometer coupled with a HP 5880 capillary GC. GC anayses were performed on a HP 5890 gas chromotograph, which was fitted with a 30 meter DB-1 capillary column and a flame ionization detector. Melting points were taken on a Thomas-Hoover melting point apparatus and were not corrected. GC-MS data were obtained at 70 eV unless otherwise stated, on a Finnegan 4000 quadrupole mass spectrometer coupled with a HP 5880 capillary GC. Exact mass data were recorded on a high resolution MS-50 mass spectrometer. All GC yields were calculated from predetermined correction factors. A medium pressure Hanovia lamp was used for photolysis experiments.

General procedure for obtaining response factors of compounds with respect to mesitylene

An NMR sample containing a mixture of the compound A, for which the response factor is required, and mesitylene was prepared. The mole ratio of the two was determined by integration obtained from a 300 MHz NMR instrument (corrected to the number of protons). The NMR sample was then analyzed by capillary GC to obtain the area ratio of the two compounds (average of 4-5 determinations) and the response factor calculated using the following equation.

$$\text{Response factor of A} = \frac{\text{GC area of } \underline{\text{A}} \text{ x moles of mesitylene (NMR)}}{\text{GC area of mesitylene x moles of } \underline{\text{A}} \text{ (NMR)}}$$

Syntheses and reactions

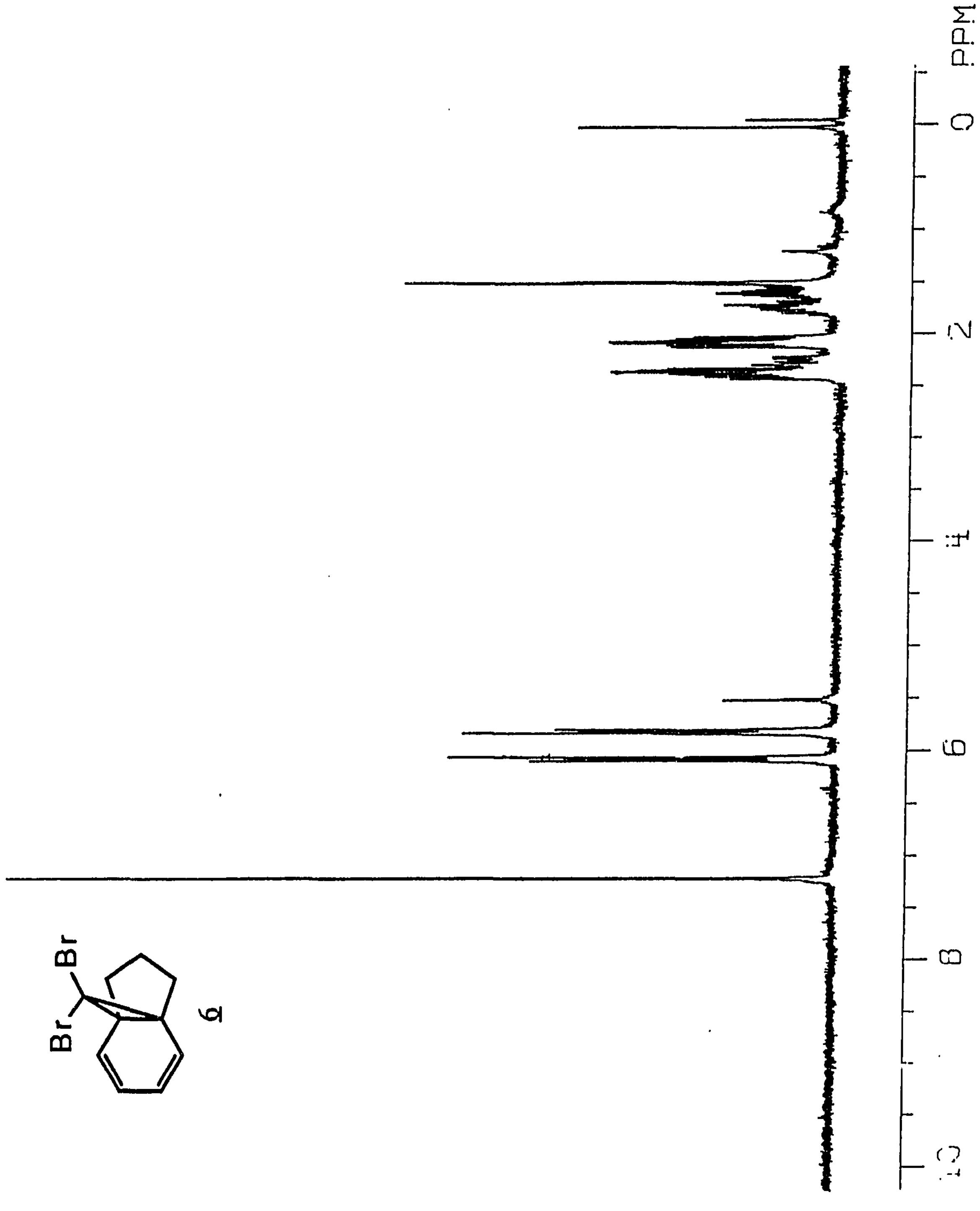
Preparation of 10,10-dibromotricyclo[4.3.1.0]deca-2,4-diene (6) (Figures 1, 2) A solution of 2.4 g (8.3 mmol) of 5[8] and 4.2 g (18 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 10 mL methylenechloride was heated in a sealed tube at 75°C for two days. The cooled tube was opened, and the filtered greenish solid washed with hexane. Subsequent chromatography on alumina gave 0.8 g (35%) of 6 as colorless crystals: mp 72-73°C.

IR (KBr):	3034 (w), 2968 (m), 2932 (m), 2862 (w), 1549 (m), 1443 (s), 1040 (m), 812 (s), 723 (s), 633 (s).
^{1}H NMR ($CDCl_3$):	5.7-6.2 (m, 4 H), 1.5-2.6 (m, 6 H).
^{13}C NMR ($CDCl_3$):	125.6, 123.4, 49.2, 48.0, 37.8, 25.5.

UV and exact mass have been reported.[9]

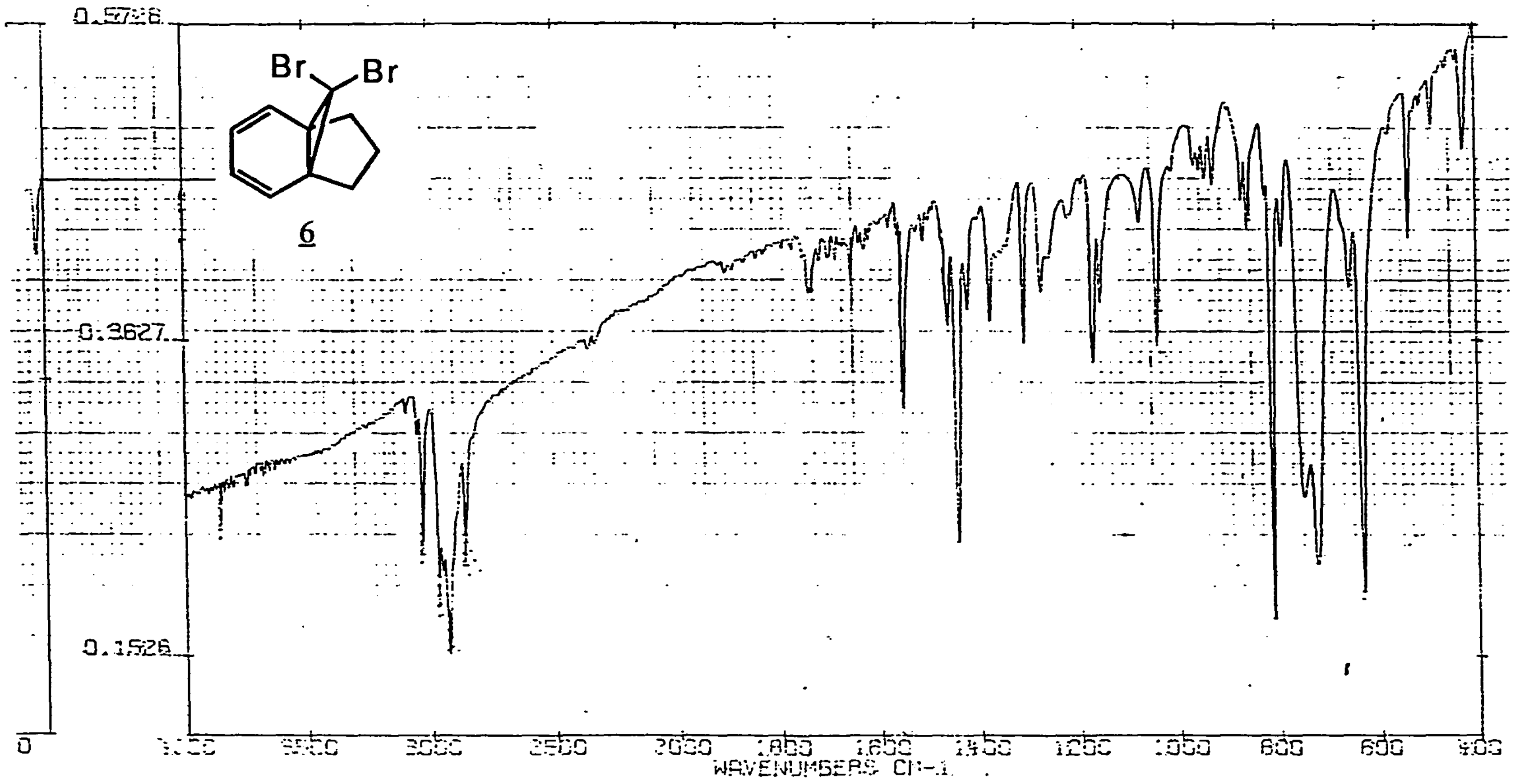
Synthesis of (Z)-1,1-dibromo-2-ethyl-3-methylcyclopropane (9a) (Figures 3, 4) Addition of 15.2 g (60 mmol) of bromoform to a mixture of 3.5 g (50 mmol) of cis-2-pentene (Aldrich) and 7.8 g (70 mmol) of KOtBu in 20 mL pentane at -20°C was effected dropwise. The resulting solution was stirred for another 30 min at this temperature and then slowly warmed to 25°C. Addition of 10 mL water was followed by extraction with ether (3 x 25 mL). The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The

Figure 1. ^{1}H NMR ($CDCl_3$) of 6



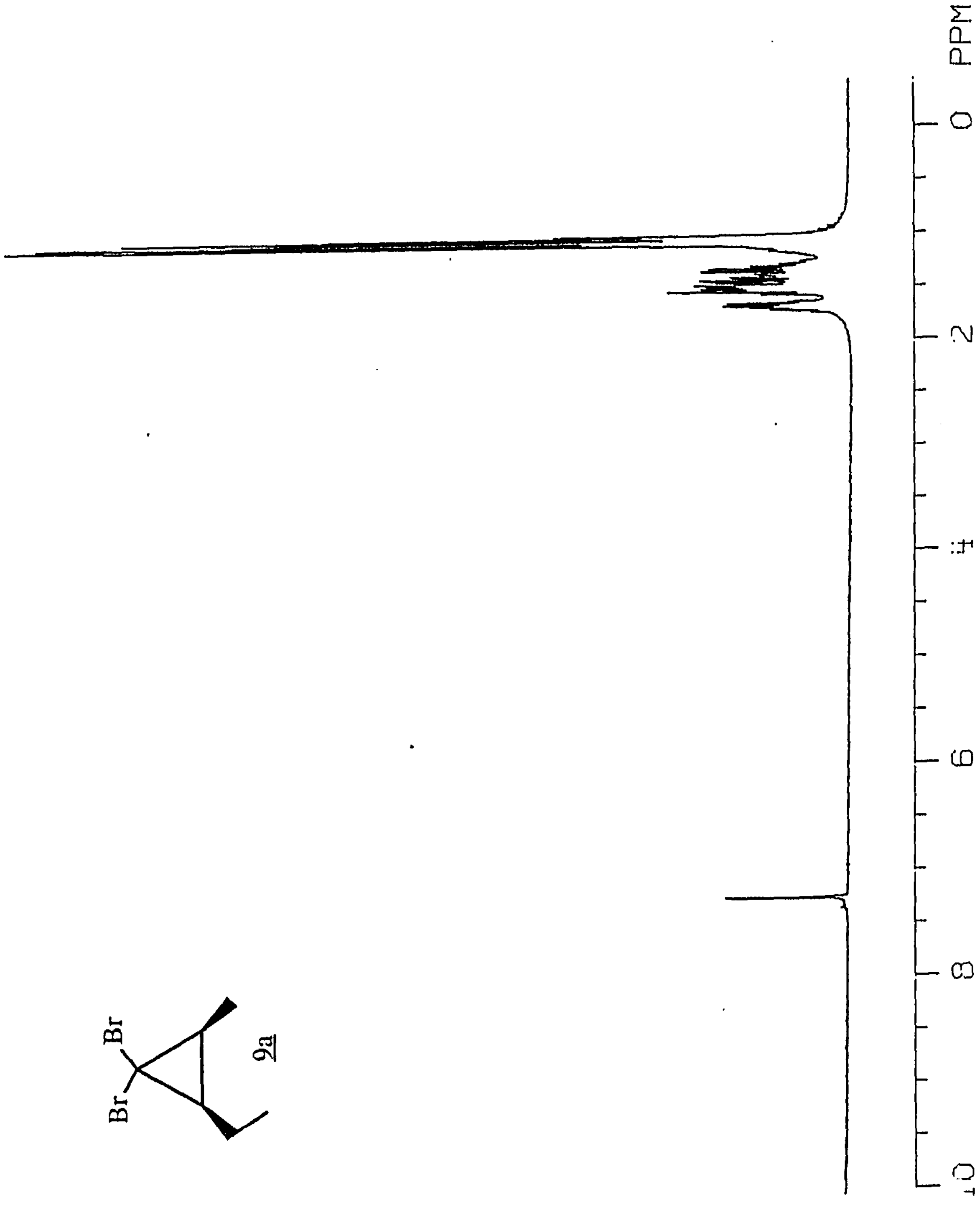
6

Figure 2. IR (KBr) of 6


Br
Br
0.5728
0.3627
0.1526
0
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1

6

Figure 3. ^{1}H NMR ($CDCl_3$) of 9a



9a

Expansion of 0.2-2.0 ppm region of Figure 3

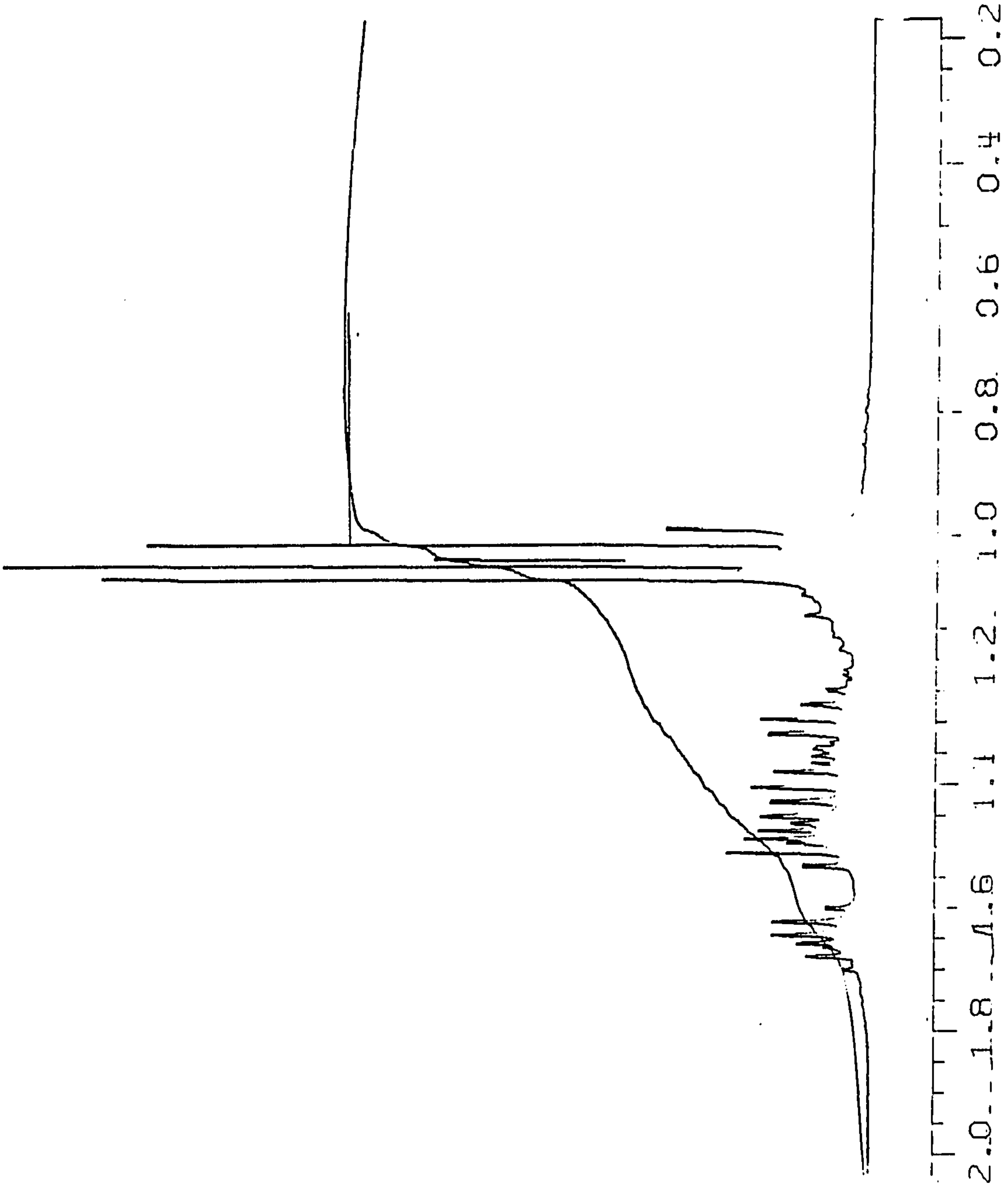
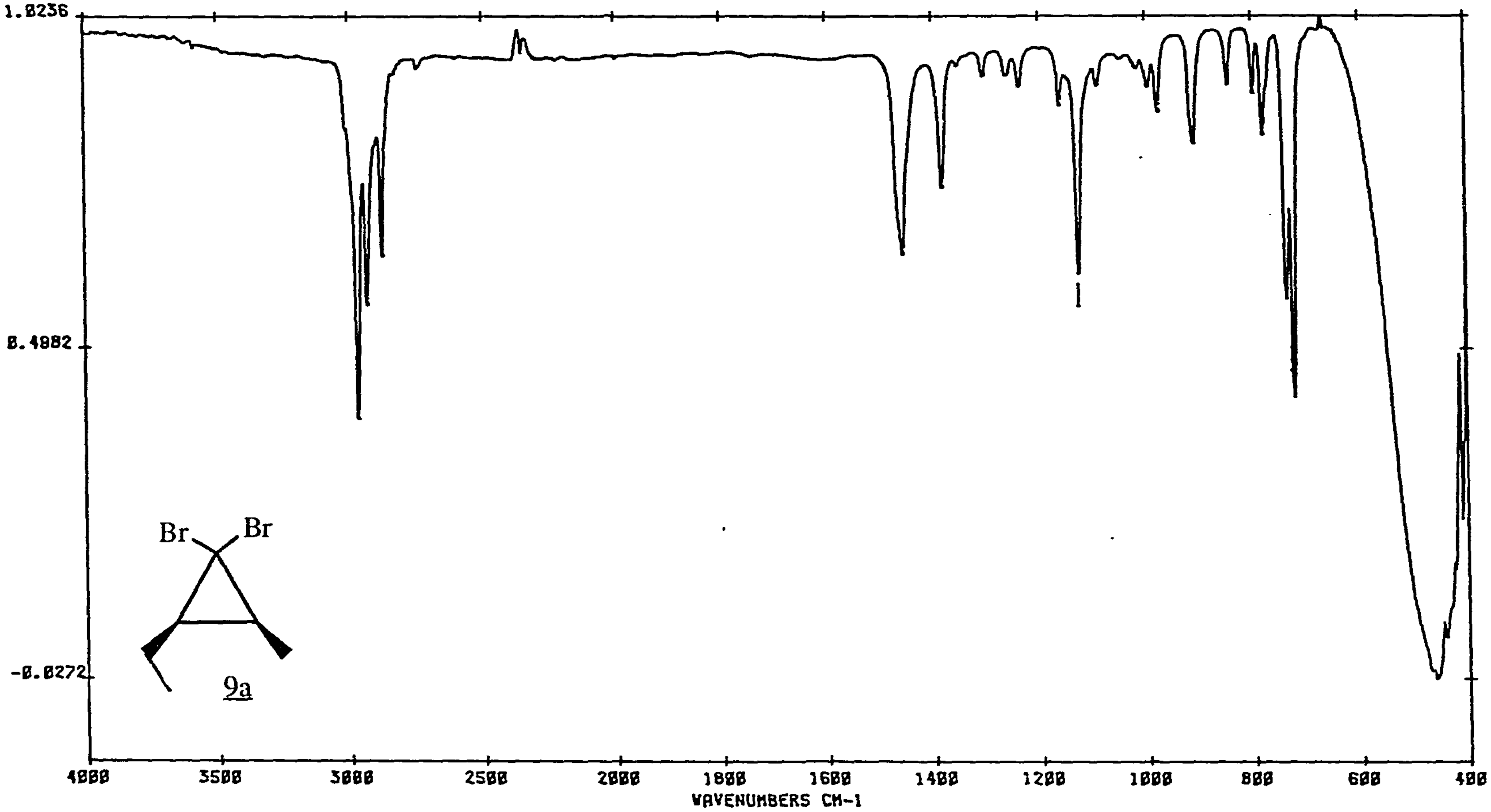

0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0

Figure 4. IR (neat) of 9a


1.0236
0.4982
-0.0272
Br
Br
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1

9a

resulting crude liquid was distilled to yield 10 g (83%) of 9a as a colorless liquid: bp 25-26°C/0.05 torr.

HRMS: Calculated for $C_6H_{10}Br_2$ m/e 241.9129; measured m/e 241.9132.

IR (neat): 2966 (s), 2932 (m), 2876 (w), 1456 (m), 1126 (m), 737 (s).

^{1}H NMR ($CDCl_3$): 1.3-1.7 (m, 4 H), 1.08 (d, 3 H), 1.03 (t, 3 H).

^{13}C NMR ($CDCl_3$): 38.6, 35.0, 28.1, 20.2, 12.6, 11.1.

Synthesis of (E)-1,1-dibromo-2-ethyl-3-methylcyclopropane (9b) (Figures 5, 6) trans-2-Pentene (Aldrich) was used to prepare 9b by exactly the same procedure used for 9a. Compound 9b was obtained (80%) as a colorless liquid: bp 25-26°C/0.05 torr.

HRMS: Calculated for $C_6H_{10}Br_2{}^{79}$ m/e 239.9149; measured m/e 239.9153.

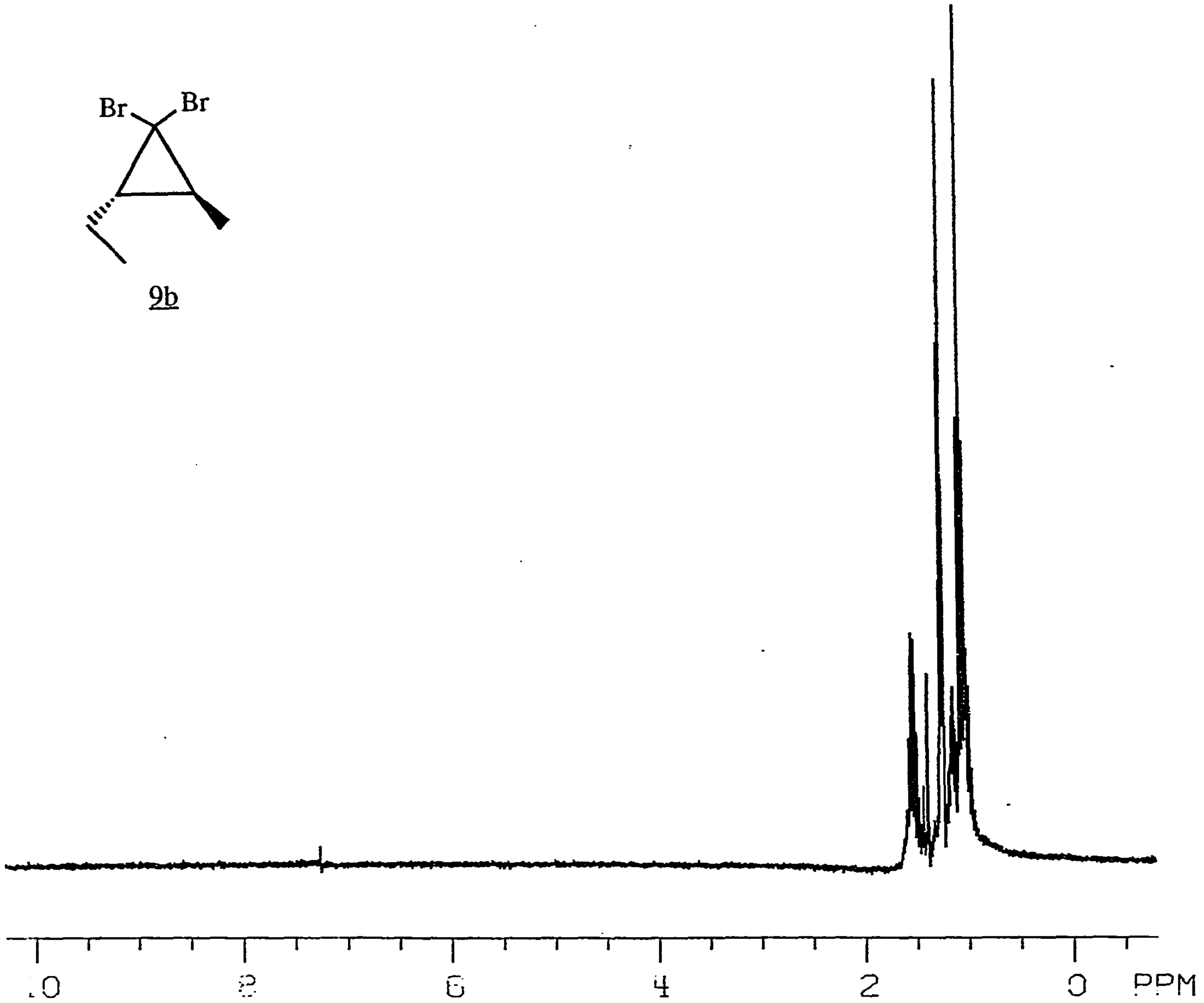
IR (neat): 2964 (s), 2932 (m), 2876 (m), 1458 (s), 1381 (m), 1138 (m), 825 (m), 756 (w), 737 (s).

^{1}H NMR ($CDCl_3$): 0.9-1.2 (m, 2 H), 1.04 (t, 3 H), 1.4 (d, 3 H), 1.5-1.6 (m, 2 H).

^{13}C NMR ($CDCl_3$): 39.9, 39.3, 31.4, 26.1, 17.4, 12.6.

Under our GC conditions, 9b has a retention time between that of indan and 6.

Figure 5. ^{1}H NMR ($CDCl_3$) of 9b



9b

Expansion of 0.5-1.8 ppm region of Figure 5

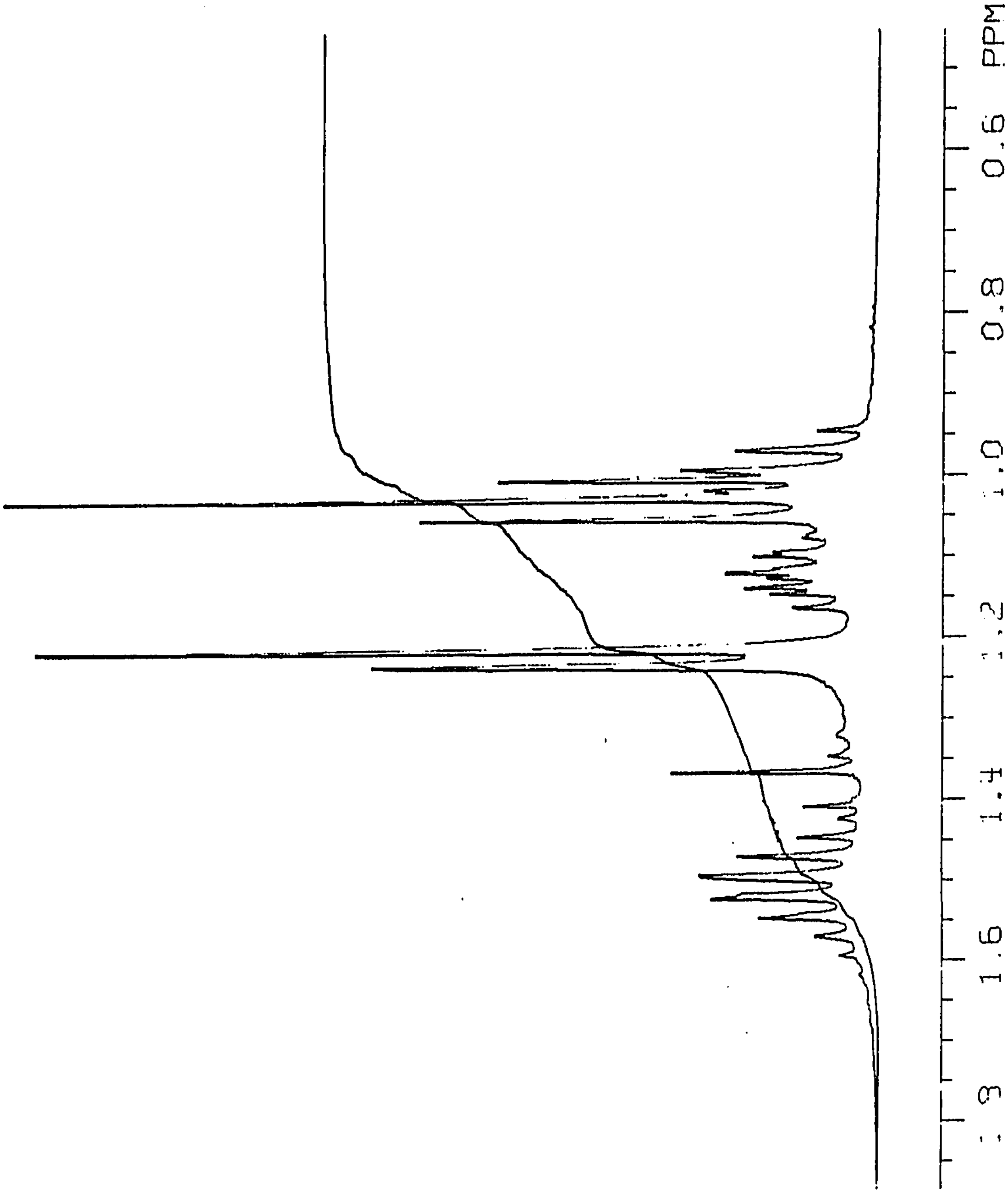
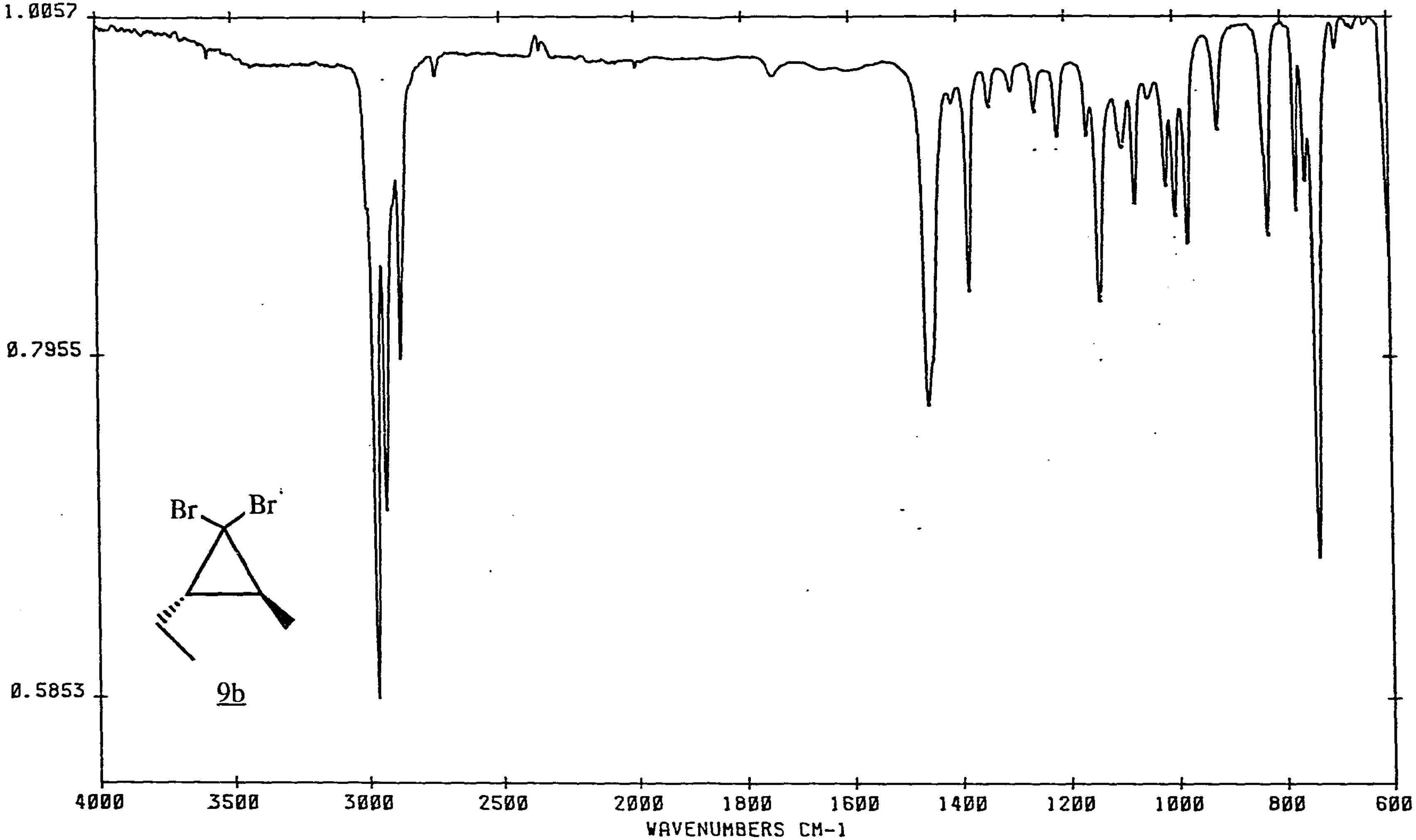

PPM
0.6
0.8
1.0
1.2
1.4
1.6
1.8

Figure 6. IR (neat) of 9b


1.0057
0.7955
0.5853
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
WAVENUMBERS CM-1
Br
Br
9b

Thermolysis of 6 in cyclohexene Solutions of 0.15 g (0.5 mmol) of 6 in 0.4 g (5 mmol) of cyclohexene were sealed in tubes and immersed in an oil bath at the temperature and for the times indicated in Table 1. The cooled tubes were then opened, and contents diluted with chloroform to appropriate analytical GC concentrations. After 15 μL mesitylene had been added, GC analyses were performed. Response factors were obtained using commercial samples of indan and independently prepared 7,7-dibromonorcarane.[10] The results are given in Table 1. For the kinetic runs (Table 2), five sealed pyrex tubes with identical contents were immersed simultaneously in an oil bath held at 134 ± 1°C. One tube each was withdrawn after 3, 6, 12, 24 and 48 h, and the cooled solutions analyzed by GC with the internal standard mesitylene. The rate constants were calculated by the standard method for first order reactions.

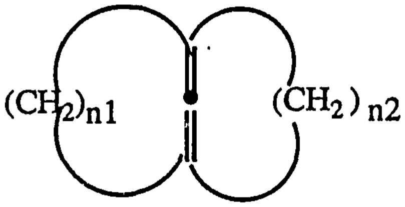
Thermolysis of 6 in 2-pentenes A solution of 9 mg (0.03 mmol) of 6 in 0.35 g (5 mmol) of Z- or E-2-pentene was sealed in a pyrex tube and immersed in an oil bath at 147°C for 8.5 h. The cooled tube was opened, the contents diluted with ether, mesitylene added, and the mixture analyzed by capillary GC. The results are given in Table 3.

Photolysis of 6 in 2-pentenes Exactly the same sealed solutions as described above were irradiated with 254 nm light in a Rayonet reactor for 18.5 h.

CHAPTER II. GENERATION AND REACTIONS OF 11-CARBENA[4.4.1]PROPELLA-3,8-DIENE

Introduction

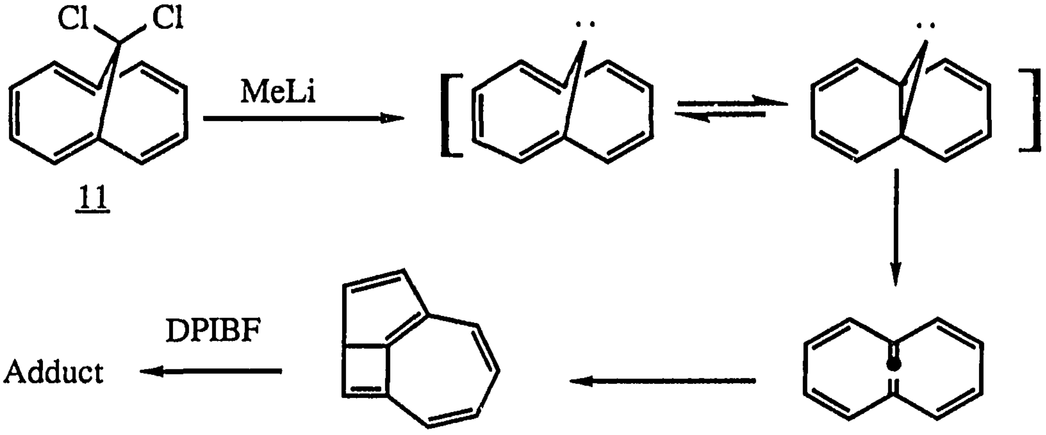
Molecules in which an allene unit is incorporated in a cyclic structure have fascinated chemists. There are many monocyclic allenes reported in the literature. But the reports of doubly bridged allene structures of the type shown below are few.[11] Nakazaki et al. synthesized[11] the



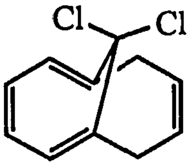
10

first doubly bridged allene (±)-bicyclo[10.8.1]heneicosa-1(21),12(21)-diene (10, m = 8, n = 10). Due to the strain involved in incorporating an allene unit in the cyclic structure, it is generally stable only in a relatively large bicyclic framework. Construction of models suggests [5][5] doubly bridged allene 10 (m = 5, n = 5) is the smallest member of this class of compounds which can be constructed without severe strain. The key step in the synthetic route of Nakazaki involved the well-precedented ring-opening reaction[12] of an alkyllithium and a gem-dibromocyclopropane.

Some time ago, Charlton and Levin[13a] and Charlton et al.[13b] reported that the carbenoid(s) derived from 11 gave rise to products which could have arisen from the corresponding bicyclic allene or the cyclized isomer

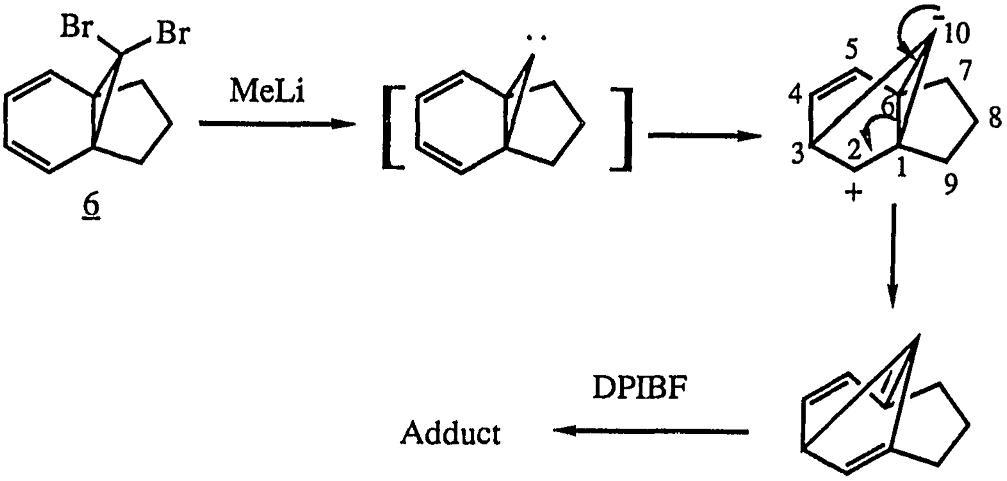


bicycloheptatriene. This conclusion was deduced after the characterization of the Diels-Alder adducts with diphenylisobenzofuran (DPIBF). They also studied the analogous reaction of 12. They proposed a mechanism in

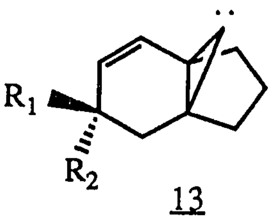


12

which the carbene or carbenoid opened to the allene. The allene was envisioned to either internally cyclize and then externally cycloadd to DPIBF, or possibly react in the reverse fashion. Later, Warner et al.,[9] studying the carbenoid derived from 6, reported that such a pathway was unlikely, and that bonding between C-3 and C-10 probably preceeded ring-opening. In other words, they proposed a zwitterionic mechanism to explain the Diels-Alder adducts with DPIBF. The evidence was based on the finding that



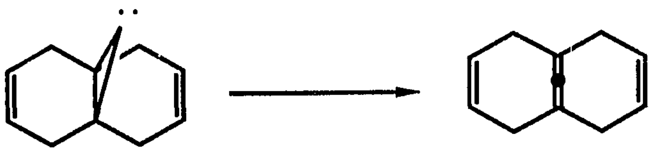
stereoisomeric carbenes 13a and 13b, derived from the corresponding α-bromotrimethyltin derivatives, gave stereoisomeric Diels-Alder products with DPIBF without cross over.



13

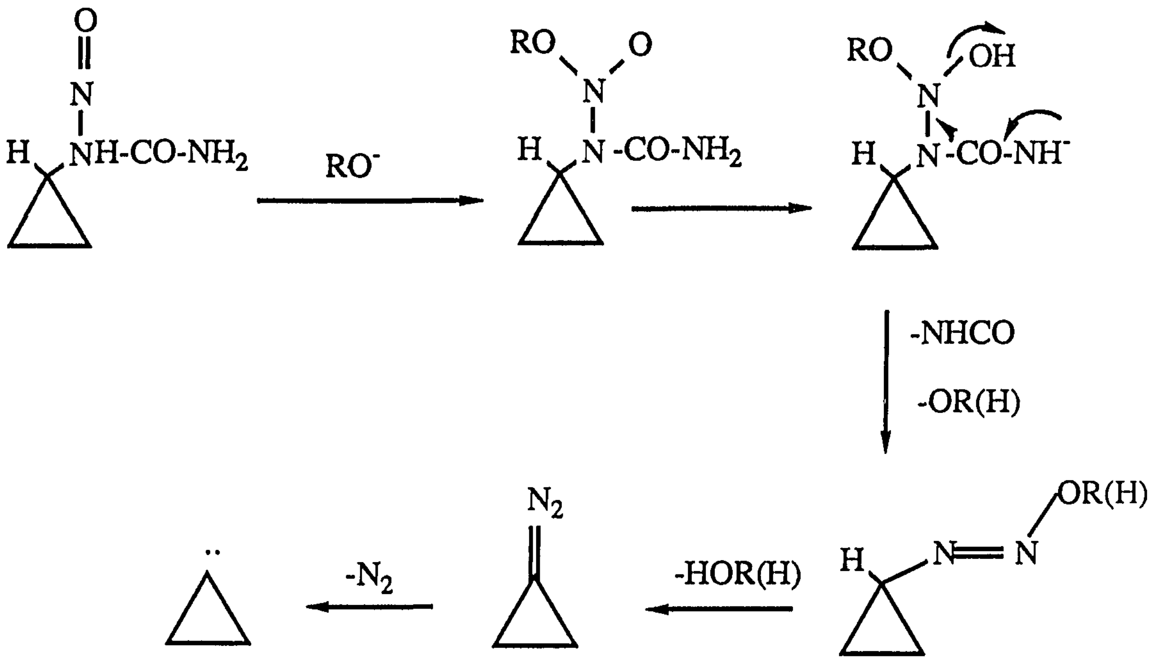
a. R_1=OMe, R_2=H
b. R_1=H, R_2=OMe

It should be noted that in all these reactions there is the question of the involvement of free carbenes vs α-bromo anions. We wanted to generate a free carbene in a system analogous to the above examples to find out whether it would give any allene-derived products. The carbene chosen was



14 25

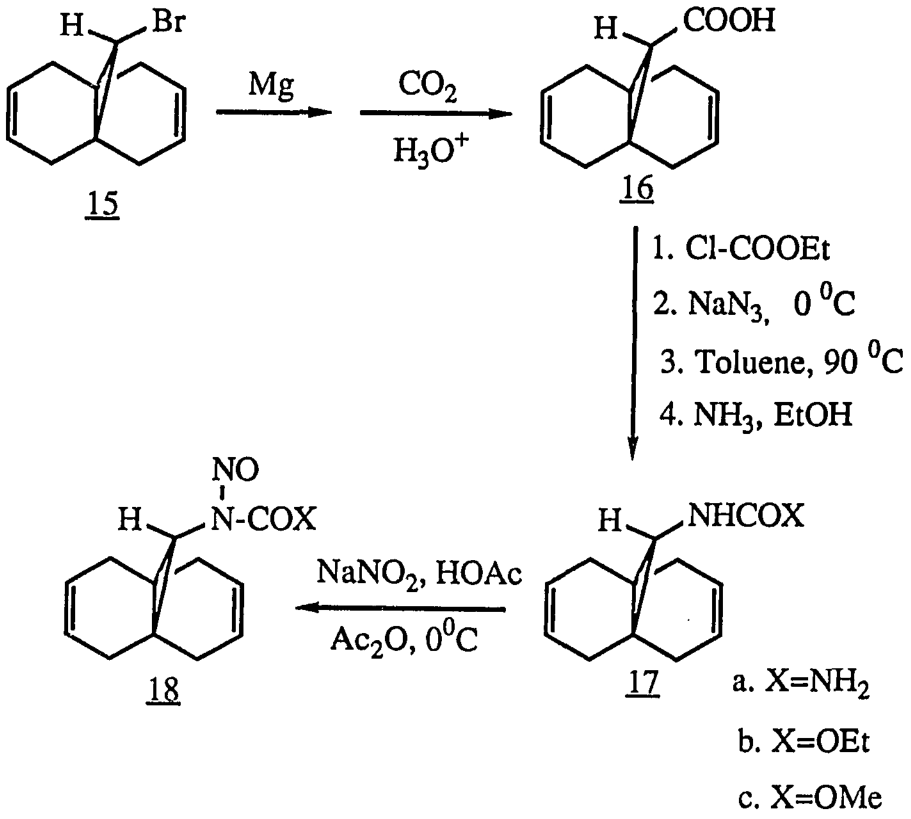
14. The standard method[14] for generation of "free" cyclopropylidenes is via diazocyclopropane intermediates. The precursor for a diazo compound is the corresponding N-nitroso urea. Jones et al.[15] elucidated the following general mechanism for the base catalyzed decomposition of an N-nitroso urea. The base adds in a nucleophilic manner to the N=O bond, whose basic oxygen then deprotonates the amide nitrogen. The resulting intermediate then loses a molecule of isocyanic acid, followed by the loss of either hydroxide or alkoxide to give the diazotate. Finally, loss of water


O
N
H
NH-CO-NH2
RO-
RO
O
N
H
N-CO-NH2
RO
OH
N
H
N-CO-NH-
-NHCO
-OR(H)
OR(H)
H
N=N
-HOR(H)
N2
-N2

or alcohol gives diazocyclopropane which rapidly loses nitrogen to give cyclopropylidene. Since this method is known to give free carbenes, we chose this method to generate 14. This chapter will describe its preparation, reactions, and address the question whether it ring opens to allene 25.

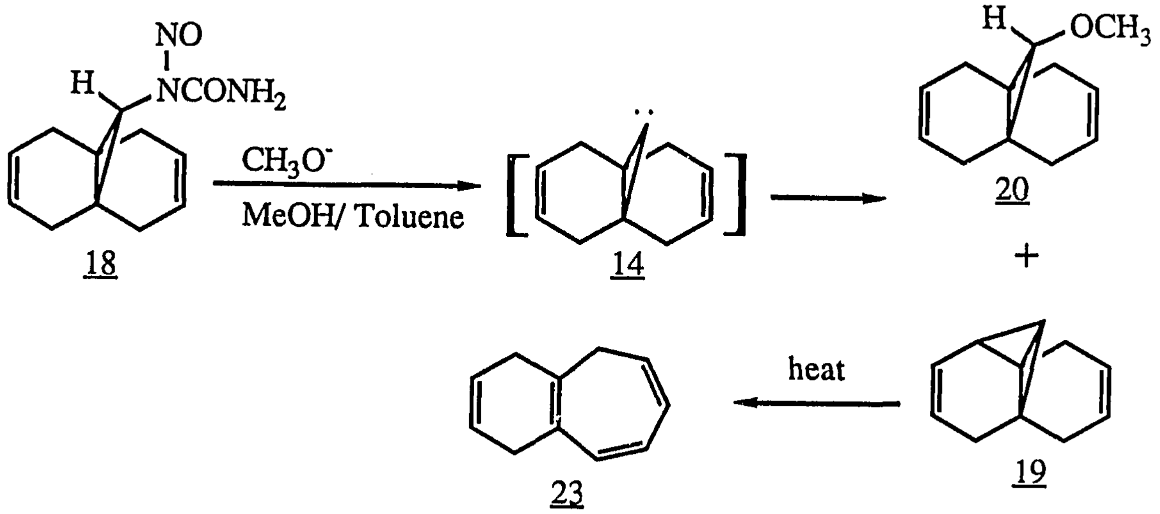
Results and Discussion

The following synthetic route was chosen to synthesize the N-nitrosourea 18. The known carboxylic acid 16[16] was used to prepare 17 by a standard procedure.[14] Nitrosation

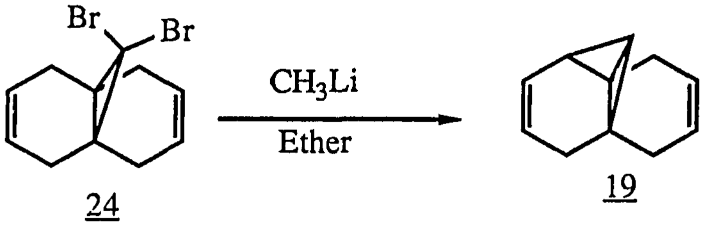

H
Br
15
Mg
CO_2
H_3O^+
H
COOH
16
1. Cl-COOEt
2. NaN_3, 0 °C
3. Toluene, 90 °C
4. NH_3, EtOH
H
NHCOX
17
a. X=NH_2
b. X=OEt
c. X=OMe
$NaNO_2$, HOAc
Ac_2O, 0°C
NO
H
N-COX
18

of 17 was effected with either $NaNO_2$/HOAc or N_2O_4 to give 18.

Treatment of 18 with 15 equivalents of $LiOCH_3$ (fully dissolved) or $NaOCH_3$ in various amounts of CH_3OH/toluene led to a mixture of the intramolecular insertion product 19,[17] the intermolecular methanol insertion product 20, and two other products which were isomers of 20.

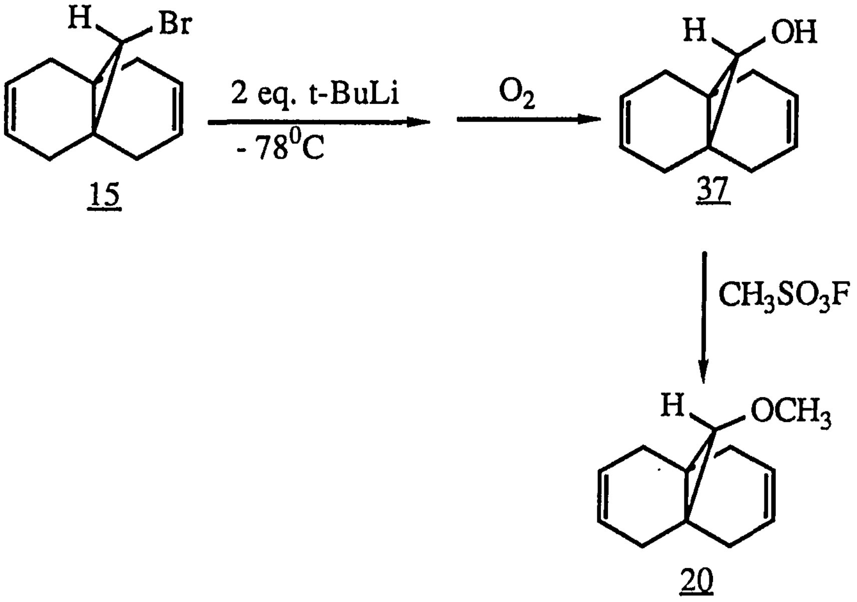


Compound 23 is not a primary product in the base-catalyzed decomposition of 18 at room temperature. However GC and GC-MS analysis of the product mixture showed varying amounts of 19 and 23. Reaction product mixtures kept over time showed 23 as the major isomer and sometimes as the only isomer by GC-MS analysis. Attempted synthesis of 19[17] by the reaction of 24 with methyllithium at room temperature followed by purification of the crude product by preparative



GC led to 23 with a small amount of 19. Diene 19 was reported to be very sensitive to acids.[18] Its rearrangement to 23 by Ag^+ was reported by Paquette et al.[17] When the product mixture obtained from the base treatment of 18 was refluxed in benzene for 1 h, 19 was completely converted to 23, but the ratio of the three ether products remained unchanged. Also neither 19 nor 23 gave rise to 20-22 in methanol under the reaction conditions. The retention times of 19 and 23 differed by 0.72 min under the chromatographic conditions.

The identification of 20 was accomplished by comparison to an independently synthesized sample produced from 11-bromo[4.4.1]propella-3,8-diene 15.[19] The synthetic sample of 20 was not pure, but it was contaminated with an aldehyde. As this aldehyde was not one of the products from



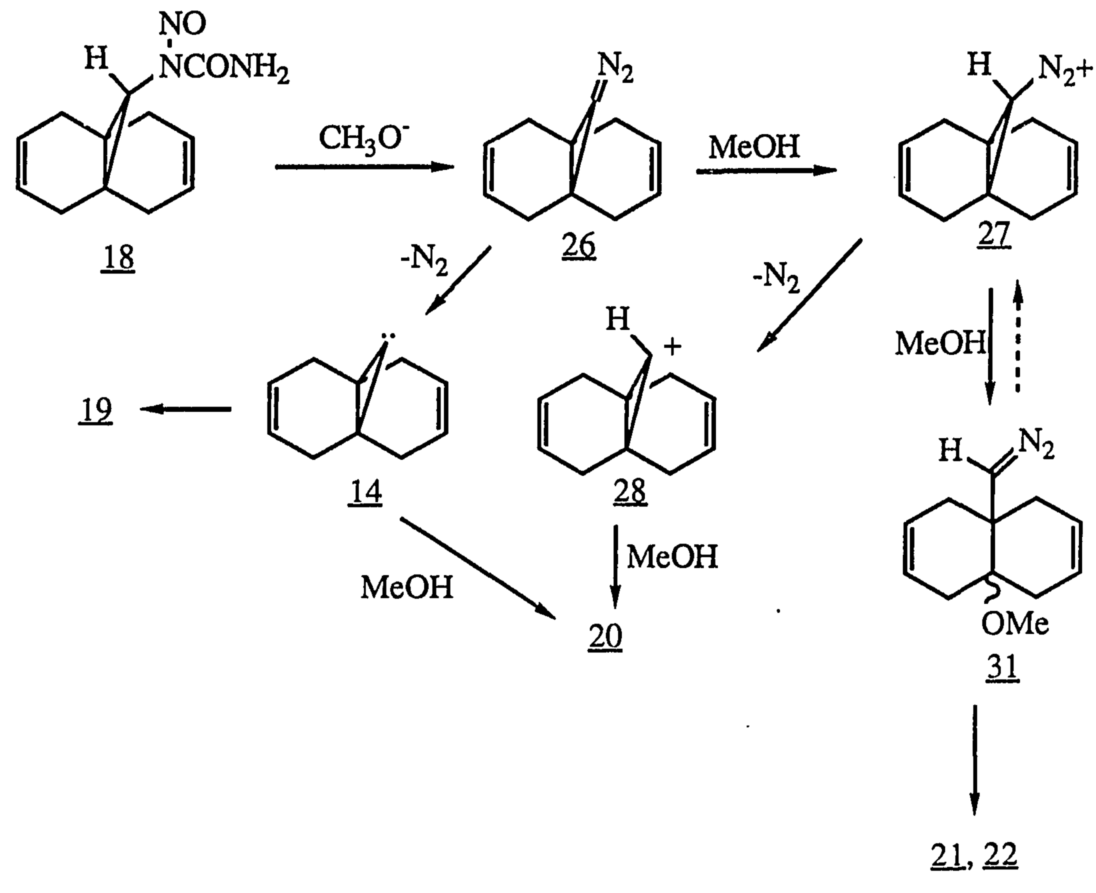
the carbene 14, purification of the synthetic sample was deemed unnecessary. The major ether product from 14 had the same retention time and mass spectral pattern as the above-prepared 20.

The three ether products had different retention times. The retention times of 20, 21, 22 were 6.93 min, 6.81 min, and 7.92 min, respectively. The structures of 21 and 22 are unknown. The response factors of compounds 20 and 23 with respect to mesitylene were 0.75 and 0.78, respectively. The response factors of 21 and 22 were assumed to be the same as that of 20 in calculating the percent yields of the products. Also the response factor of 19 was assumed to be the same as that of 23. The overall yield (GC) of products, assuming the solid 18 was pure, was 50-75% at reaction temperatures between 10° and 60°C. The ratio of intramoleclar insertion product(s) 19 and 23 to 20 varied with methanol concentration. The ratio of 20:21:22 was in the range of 5:1.5:1. No higher molecular weight oligomers of 14 or 25, or bis-methanol adducts of 25 were observed.

Also, when 18 was treated with LiOMe/80% MeOD/20% toluene (base prepared from Li/MeOD) 19 (analyzed as 23) showed no D incorporation, while 20-22 showed a high degree of a single D (20:93%, 21:100%, 22:98% - all determined by GC-MS).

In the decomposition of nitrosoureas one must consider the intermediacy of both diazo compounds (i.e., 26) and diazonium ions (i.e, 27). At the high base concentration used here, one would expect to virtually eliminate chemistry from 27.[20] However, sometimes diazonium ion chemistry persists even at high base concentration.[21] Based on the above results, the mechanism of base catalyzed decomposition of 18 is shown in Scheme 1. The following experiments and comments justify the above mechanism. To explain the origin of minor products 21 and 22, we carried out two key

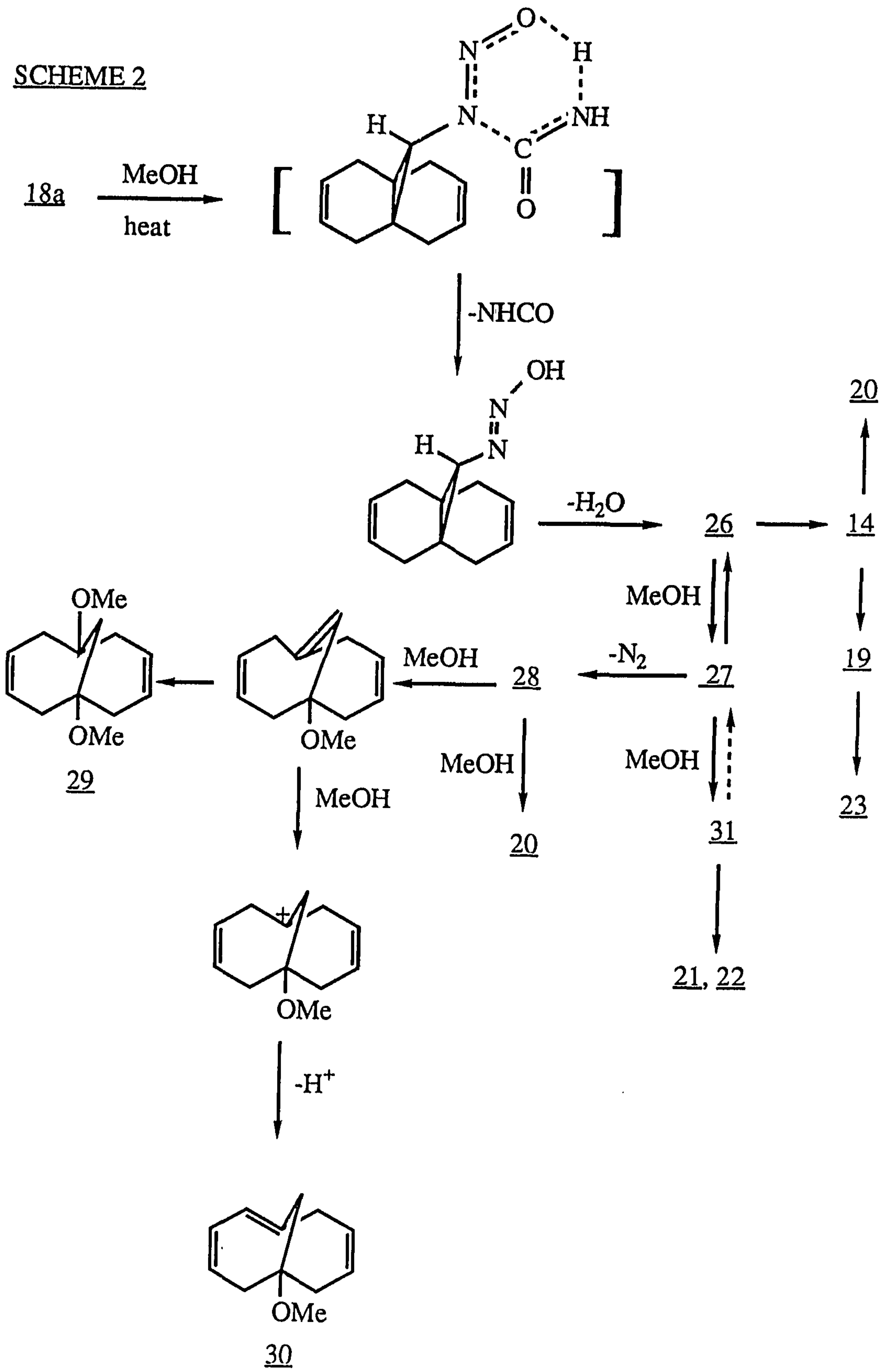
SCHEME 1


NO
H
NCONH2
18
CH3O-
N2
26
MeOH
H
N2+
27
-N2
-N2
19
14
H
+
28
MeOH
MeOH
20
MeOH
H
N2
OMe
31
21, 22

experiments using 18b. In one experiment, methanolic solution of 18b was added to a large excess of 2 M LiOMe/MeOH, while in the other experiment, the same base was added to 18b dissolved in MeOH (both at room temperature). The former case favors the diazo compound (rather than the diazonium ion), and hence carbene chemistry, while the latter conditions allow for diazonium ion chemistry. The former experiment gave a ca. 7:2:1 ratio of 20:21:22, while the latter gave 5:1.5:1 ratio of these compounds. In addition, the rato of 19 to 20 decreased by ca. 20-25% on going from the former to the latter experiment. These results indicate that (a) some 20 is formed from diazonium ion 27, and (b) 21 and 22 are likely formed via 27, too. Since the structures of 21 and 22 remain unknown, not much can be said. We, however, postulate that they may arise via ring-opening of 27 to 31. Although this process is unknown, it is analogous to cyclopropanol ring-opening.

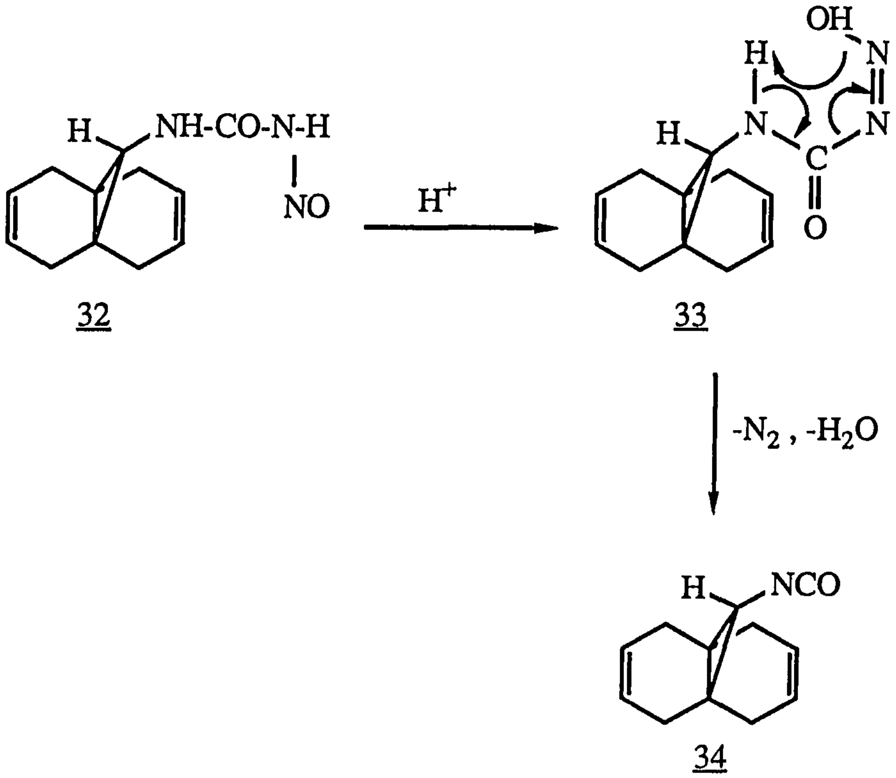
We also carried out the thermal decomposition of 18a. Simple thermolysis of 18a in methanol (reflux 5-10 min, no base) gave a bis-methanol adduct 29, an additional ether product 30, and 19-23. The ratio of 30:20:21:22 was in the range of 6:2.5:1:1.5. The ratio of 19 + 23:20 was 6:1. A plausible mechanism to explain the thermolysis products is shown in Scheme 2.

SCHEME 2


18a
MeOH
heat
-NHCO
-H2O
26
14
20
19
23
MeOH
27
-N2
28
MeOH
MeOH
20
MeOH
31
21, 22
MeOH
29
MeOH
-H+
OMe
30

Due to the presence of many compounds in the product mixture, and the difficulty in making 18, no attempt was made to separate the products. The structural assignments for products 29 and 30 are not rigorous, and are based only on the GC-MS data. Based on the known[22,23] chemistry of 28 and related systems, it is highly probable that 29 and 30 are formed as shown. When MeOD was used, all the products except 19, 23 showed a high degree of D incorporation. Importantly 29 and 30 showed two D atoms per molecule, which is consistent with the diazonium ion chemistry shown. The thermolysis results are consistent with some of the conclusions drawn in the base-catalyzed decomposition of 18.

In addition to the chemistry of 14, we discovered an aspect of urea chemistry which, to our knowledge, has not been previously reported. Because the yield of solid nitrosourea 18a from 17a was very poor, we began to generate 14 directly from the oily mixture obtained from nitrosation of 17a. To our surprise, urethane 17c became the major product. This was also true when 18a was prepared via treatment of 17a with N_2O_4 (via the procedure described by Kirmse et al.[24]). But 17c was not formed when either solid 18a, or nitrosourethane 18b was the starting material. Further IR examination of the crude nitrosourea 18a revealed that it contained a large amount of 34[25] (ν-2285 cm^{-1}); 34 was the previously isolated precursor to 17. The 17a used to make 18a contained no 34. We propose that 34, which reacted with MeOH to give 17c, was formed via nitrosation at the terminal nitrogen of the urea group in 17a. The "wrong-way" nitroso compound 32 should be highly unstable.

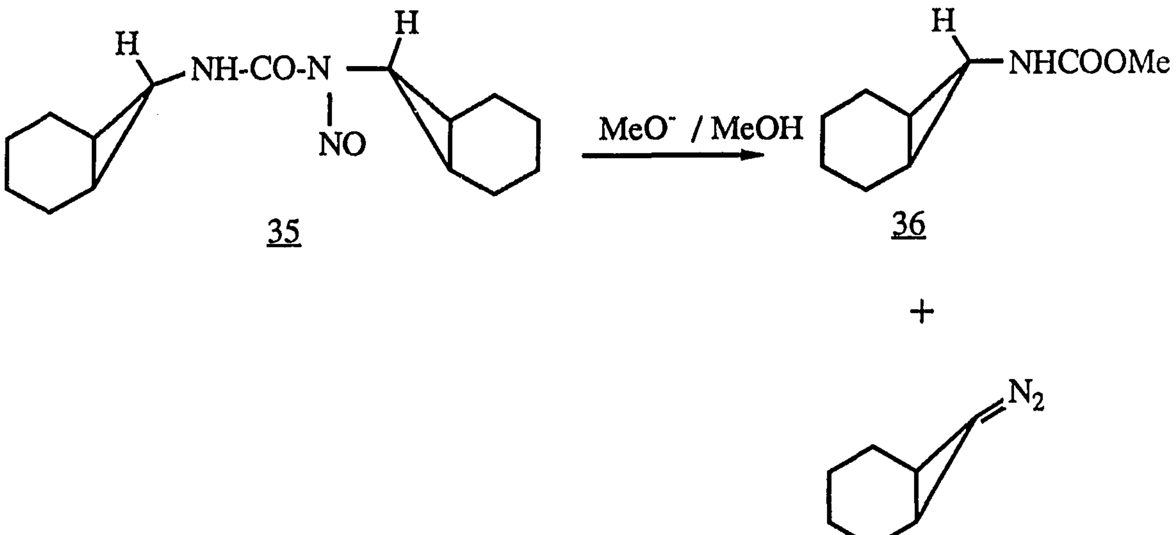


32

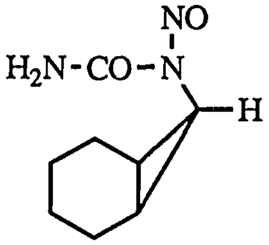
33

34

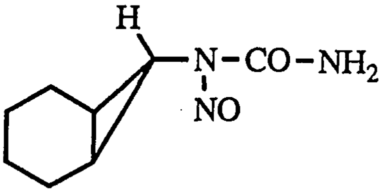
Consistent with this idea is the observation that 35 also produced urethane 36 under basic conditions.[26,27] The "wrong-way" nitrosation is presumably due to steric factors,


H
NH-CO-N
NO
H
MeO⁻ / MeOH
H
NHCOOMe
35
36
+
N₂

and previously[20] manifested itself in the low yield of endo-38 (13%) vs the high yield of exo-39 (86%) from the corresponding ureas.



38



39

In conclusion, the free tricyclic carbene 14 has been generated in solution. It does not open to allene 25. The diazonium ion 27 undergoes some interesting chemistry that was previously unknown. The "wrong-way" nitrosation observed may be of importance in the pharmacology of nitrosation.

Experimental

Synthesis of 11-bromo[4.4.1]propella-3,8-diene (15) (Figures 7, 8)

Compound 15 was prepared by the method of Thompson et al.[16] Thus, to a stirred solution of 9.1 g (30.0 mmol) of 11,11-dibromo[4.4.1]propella-3,8-diene in 30 mL anhydrous benzene, was added 10.4 g (36.0 mmol) of tri-n-butyltin hydride over 10 min at 25-30°C and the solution was stirred at 35-40°C for 2.5 h. The solvent was evaporated, the residue was distilled through a 6-in Vigreux column, and the distillate (bp 55-75°C/0.1 torr) was chromotographed on alumina (neutral); 15 eluted with hexane to provide 3.4 g (51%) as white crystals: mp 47-50°C (lit.[16] mp 48-51°C).

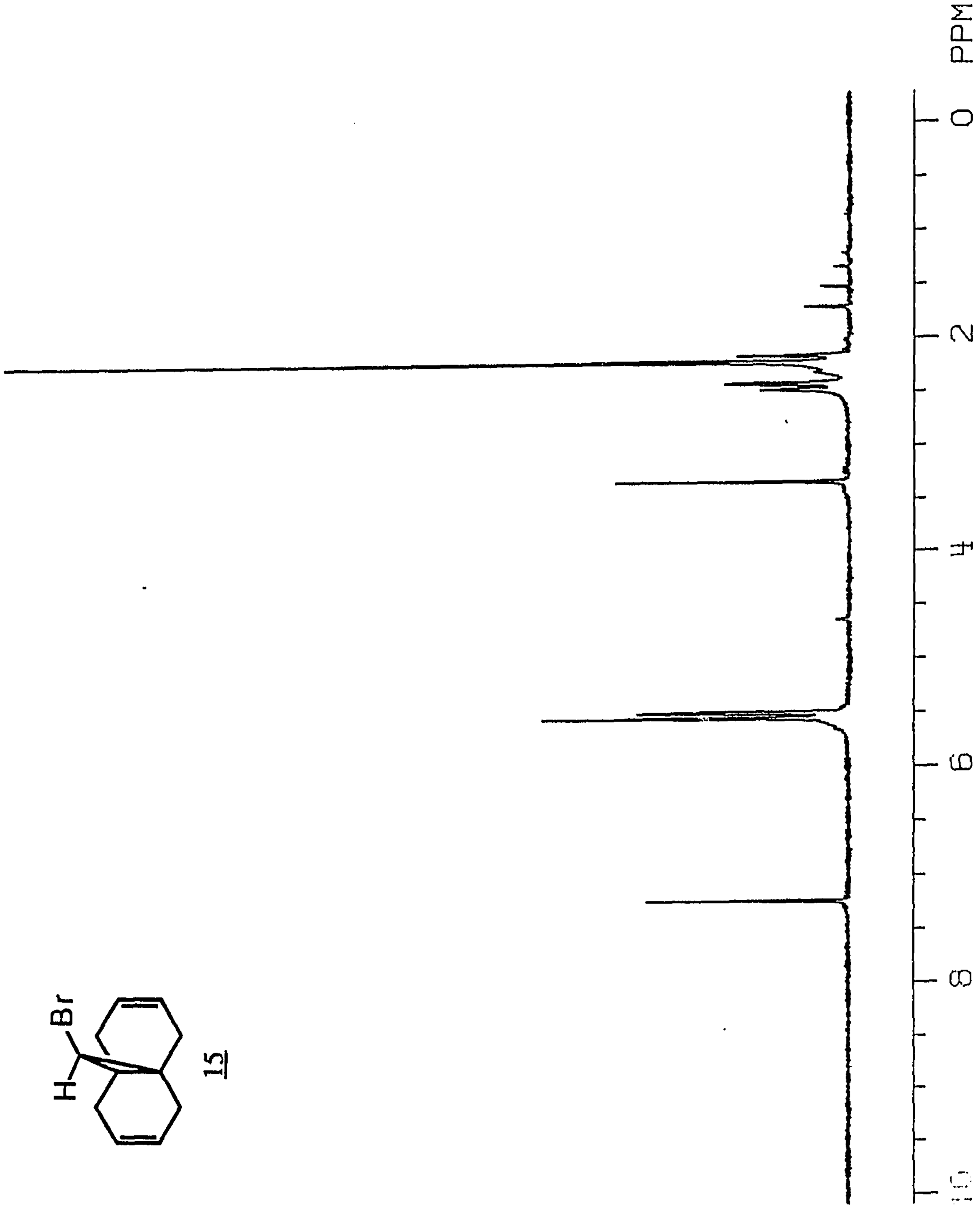
GC-MS: 225 (1.7), 223 (1.7), 145 (82.0), 128 (7.6), 117 (49.7), 105 (13.2), 91 (100.0), 79 (32.5), 67 (67.4), 51 (15.4), 39 (26.9).

IR (KBr): 3028 (m), 2957 (w), 2891 (m), 2820 (w), 1429 (s), 1240 (s), 1015 (s), 1009 (s), 726 (s), 679 (s), 667 (s).

^{1}H NMR (CDCl$_3$): 5.5 (m, 4 H), 3.3 (s, 1 H), 2.1-2.5 (m, 8 H).

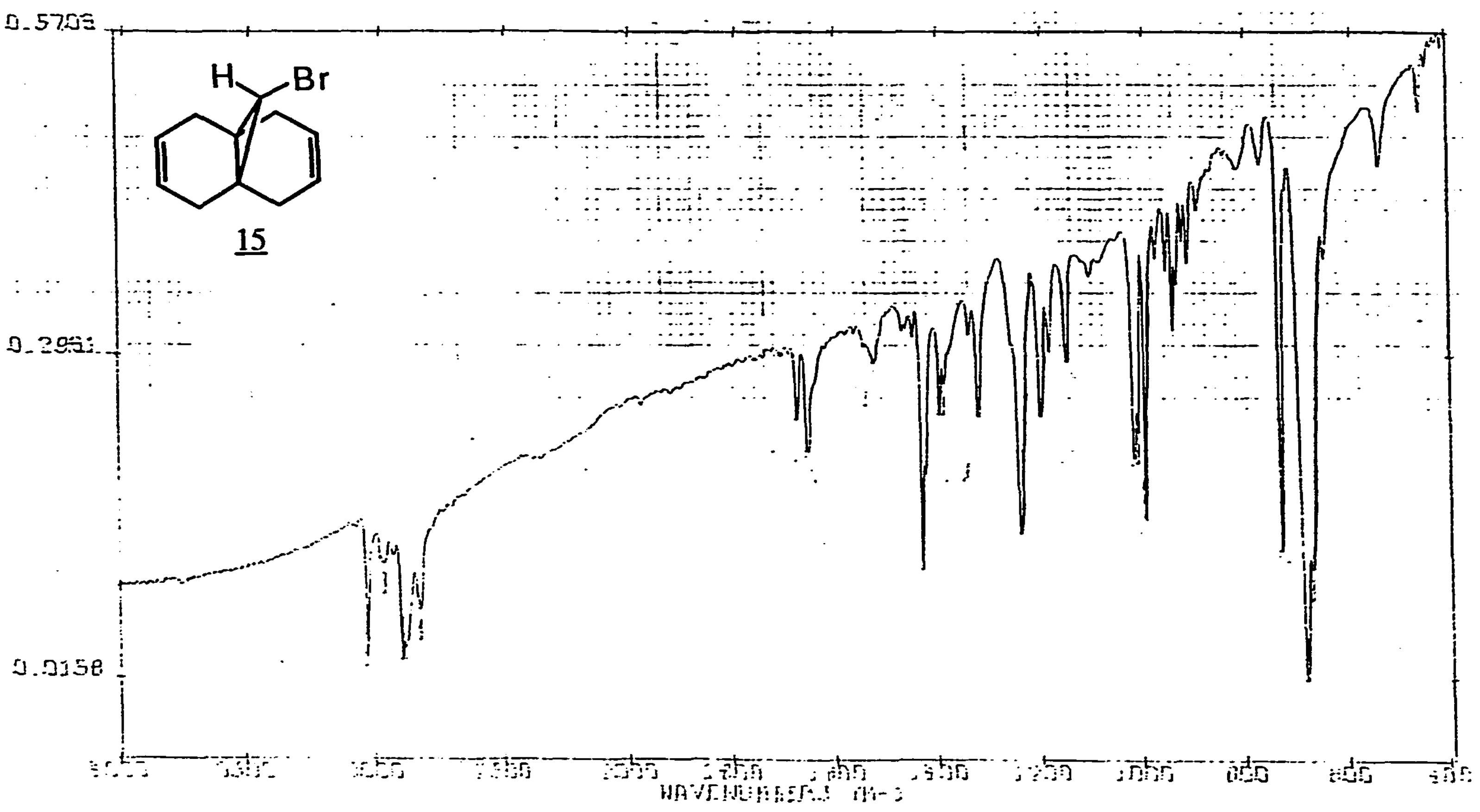
^{13}C NMR (CDCl$_3$): 124.4, 124.0, 36.5, 32.0, 30.1, 21.4.

Figure 7. ^{1}H NMR ($CDCl_3$) of 15



15

Figure 8. IR (KBr) of 15



15

Synthesis of [4.4.1]propella-3,8-diene-11-carboxylic acid (16) (Figures 9, 10)

Compound 16 was prepared by the method of Thompson et al.[16] Thus, a stirred mixture of 10.2 g (45.4 mmol) of 15 and 4.4 g (0.18 g-atom) of magnesum powder in 110 mL of anhydrous tetrahydrofuran under dry argon was brought to reflux, 0.4 mL of ethylene bromide was added dropwise, and the mixture was stirred at reflux for 10 h. After cooling to room temperature, the supernatant solution was decanted under argon from the excess magnesium onto a large excess of crushed dry ice, and the slurry was stirred under argon until the temperature had risen to 20°C. The mixture was acidified with 10% HCl (50 mL), saturated with solid NaCl, and extracted with ether (2 x 50 mL). The combined ether layers were extracted with 10% sodium hydroxide (3 x 50 mL), and the alkaline phase was washed with ether (100 mL), acidified with concentrated HCl, and treated as above. After drying ($MgSO_4$) and concentration, there remained 3.6 g (42%) of 16, mp 133-135°C.

IR (KBr):	3028 (s), 2878 (s), 2829 (s), 1695 (s), 1454 (s), 1433 (s), 1344 (m), 1290 (s), 1244 (s), 935 (s), 683 (s).
^{1}H NMR ($CDCl_3$):	11.5 (s, 1 H), 5.5 (m, 4 H), 1.9-2.6 (m, 9 H).

Figure 9. ^{1}H NMR ($CDCl_3$) of 16

16

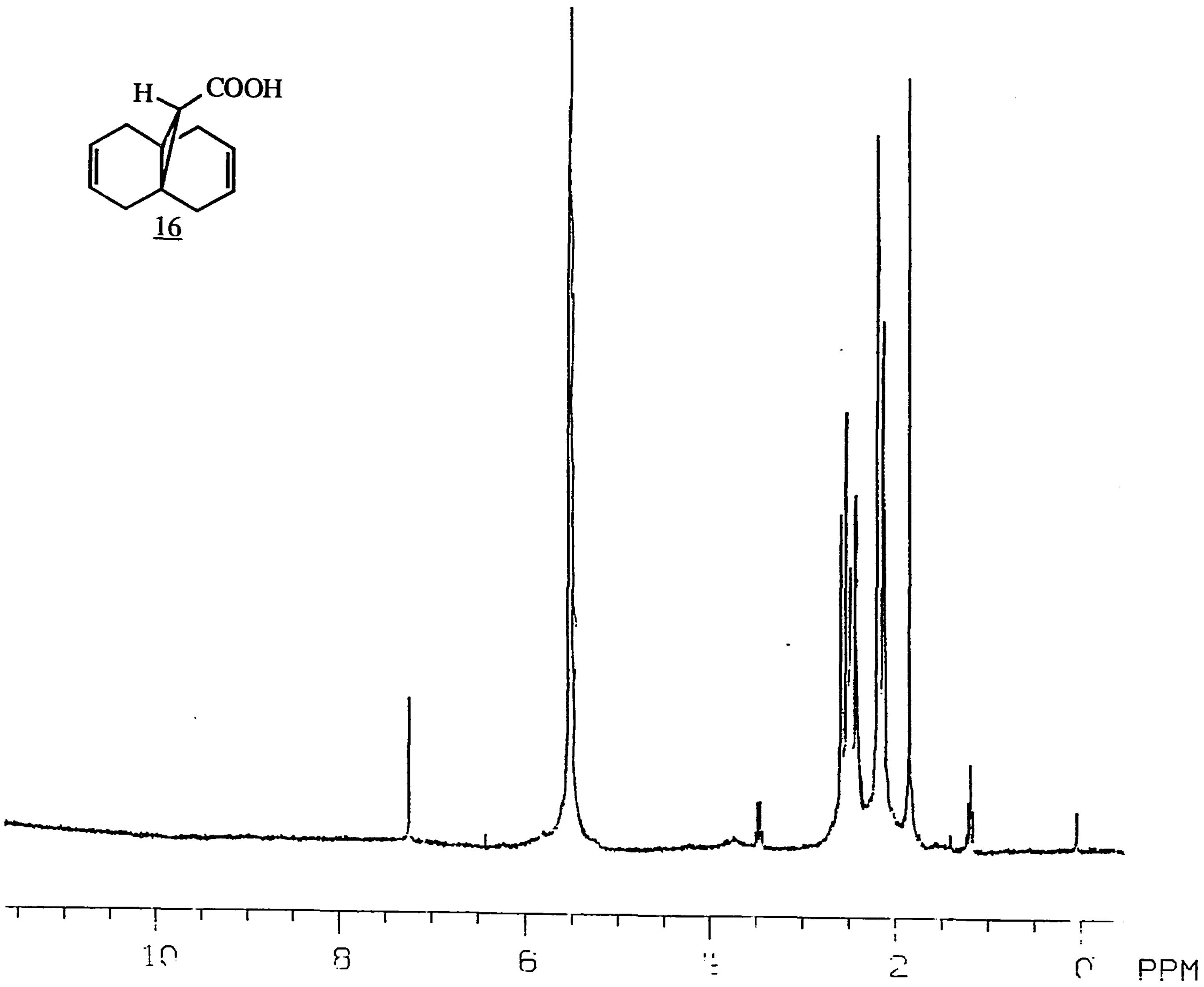
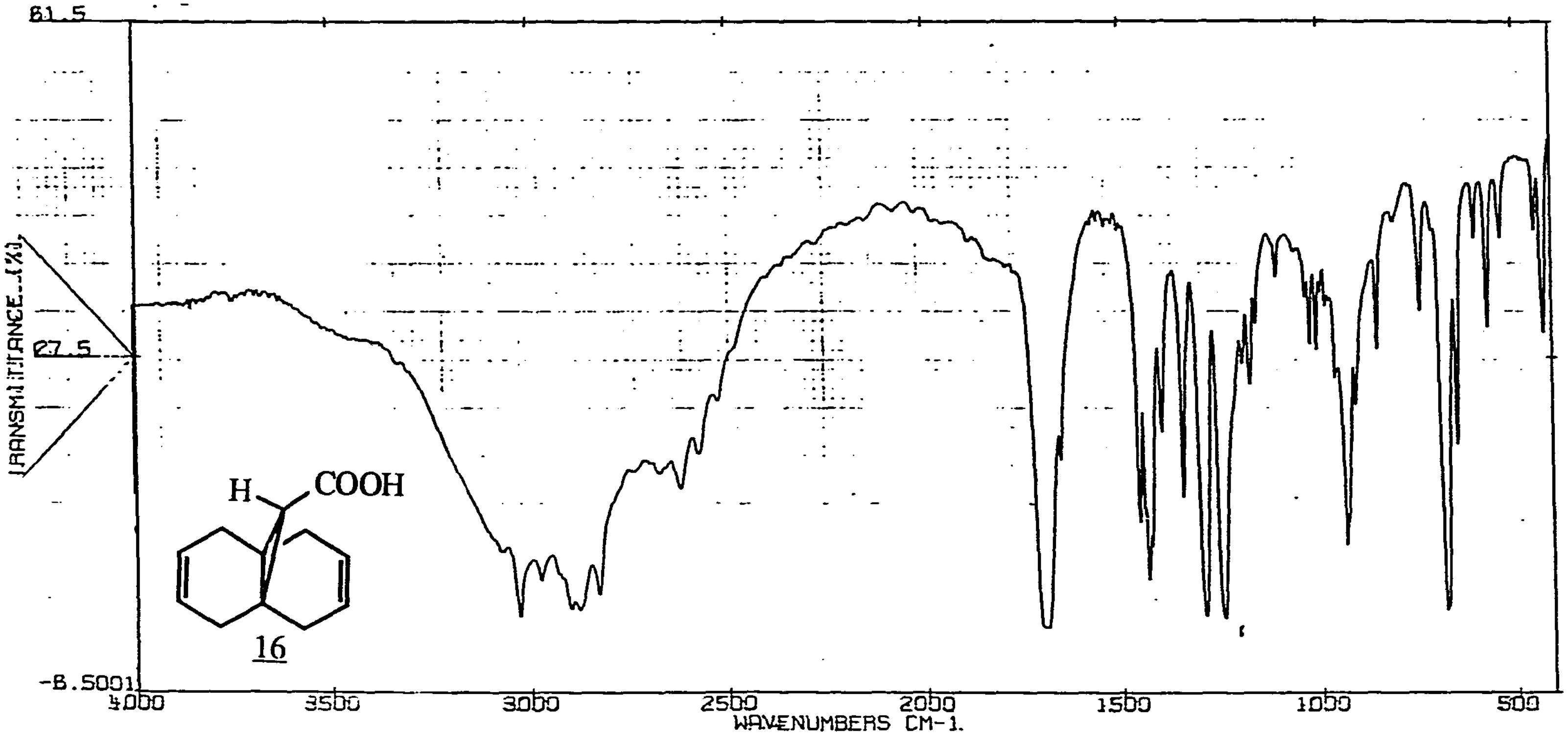


Figure 10. IR (KBr) of 16


81.5
27.5
-8.5001
TRANSMITTANCE (%)
4000
3500
3000
2500
2000
1500
1000
500
WAVENUMBERS CM-1.
H
COOH
16

^{13}C NMR ($CDCl_3$): 177.9, 124.9, 124.3, 32.1, 29.1, 25.7, 25.1.

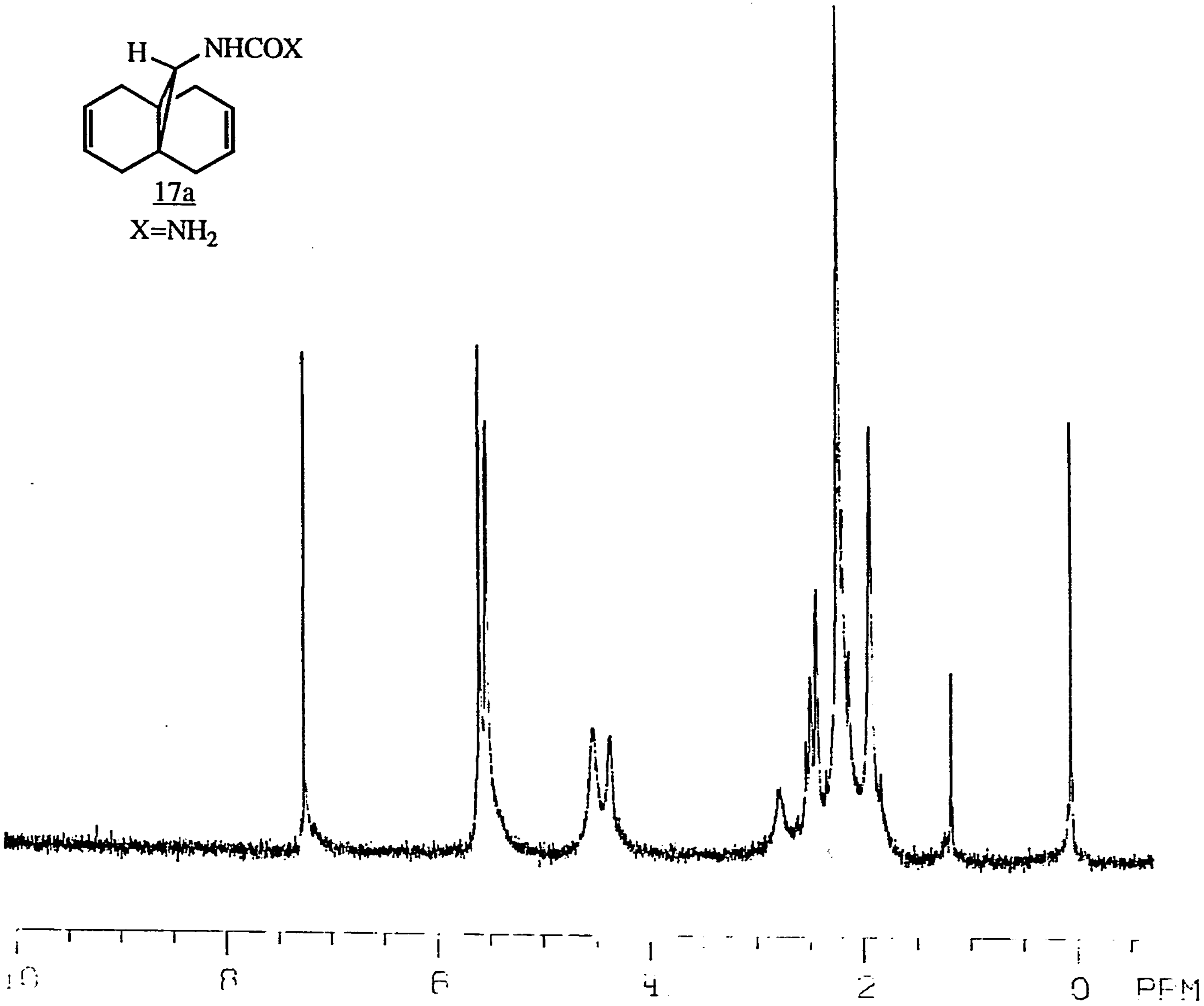
Synthesis of N-[4.4.1]propella-3,8-dienyl-11-urea (17a) (Figures 11, 12)

To a solution of 380 mg (2.0 mmol) of [4.4.1]propella-3,8-diene-11-carboxylic acid (16) in acetone (20 mL), was added triethylamine (0.3 mL), and the reaction mixture was stirred at room temperature for 5 min. It was then cooled to -5°C, and a solution of 240 mg (2.2 mmol) of ethyl chloroformate in acetone (5 mL) was added dropwise. After stirring at this temperature for 45 min, toluene (20 mL) was added and the organic material extracted. The toluene layer was dried ($MgSO_4$ and molecular sieves). The IR spectrum of this solution of 34 showed an intense peak for the NCO group at 2284 cm^{-1}. The dried toluene solution was refluxed at 90-100°C for 45 min. The solution was cooled to 25°C and gaseous ammonia was bubbled in at 0°C. Filtration of the precipitated solid gave 110 mg (27%) of 17a, mp 176-177°C.

HRMS: Calculated for $C_{12}H_{16}O_2$ m/e 204.1263; measured m/e 204.1184.

IR (KBr): 3485 (s), 3354 (s), 3277 (m), 3169 (m), 3022 (m), 2901 (m), 2826 (m), 1647 (s), 1618 (s), 1593 (s), 1435 (s), 1209 (m), 689 (s), 648 (m), 600 (m).

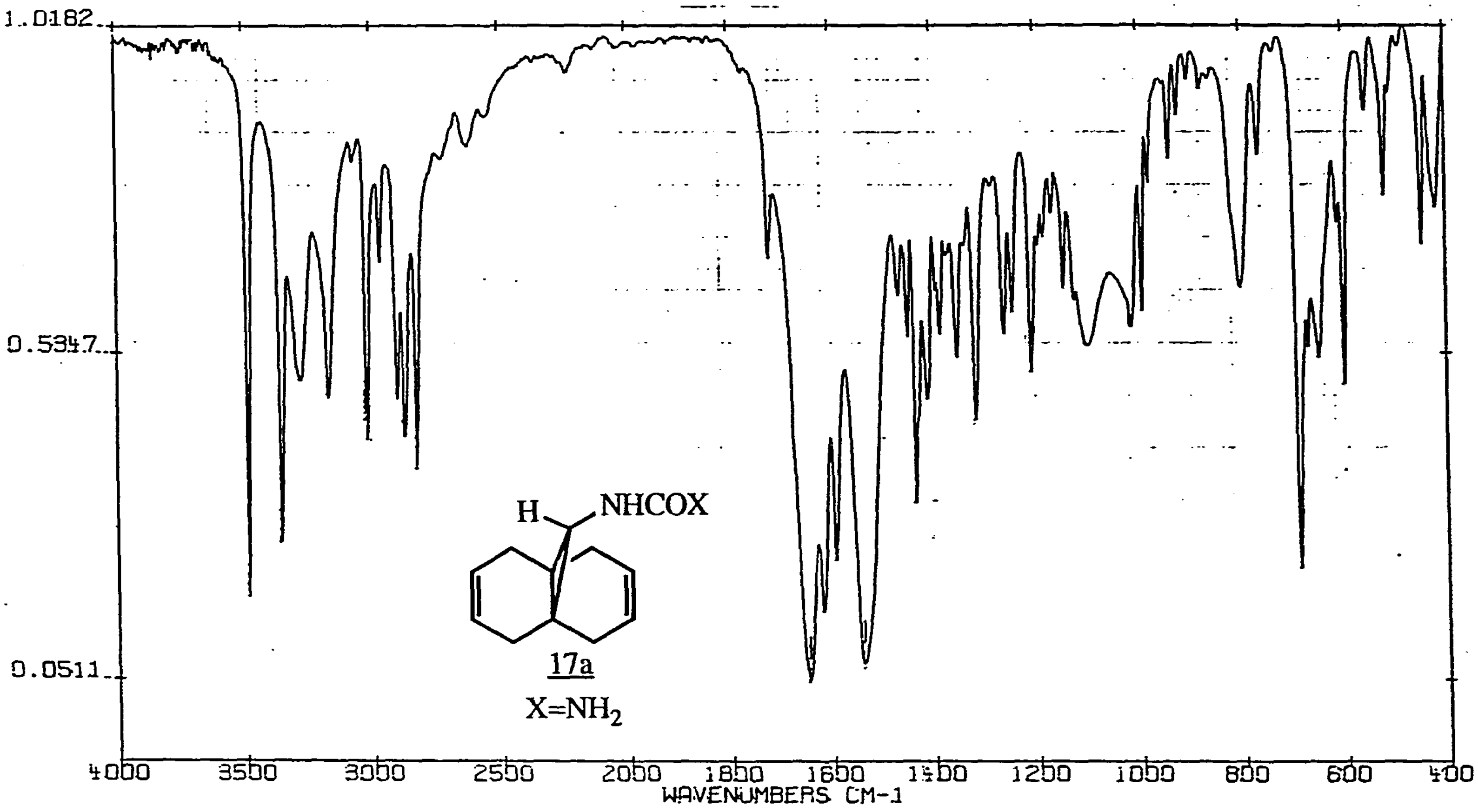
Figure 11. ^{1}H NMR ($CDCl_3$) of 17a



17a

X=NH$_2$

Figure 12. IR (KBr) of 17a


1.0182
0.5347
0.0511
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1
H
NHCOX

17a

X=NH$_2$

^{1}H NMR ($CDCl_3$): 5.5-5.6 (m, 4 H), 4.3-4.5 (m, 3 H), 1.9-2.4 (m, 9 H).

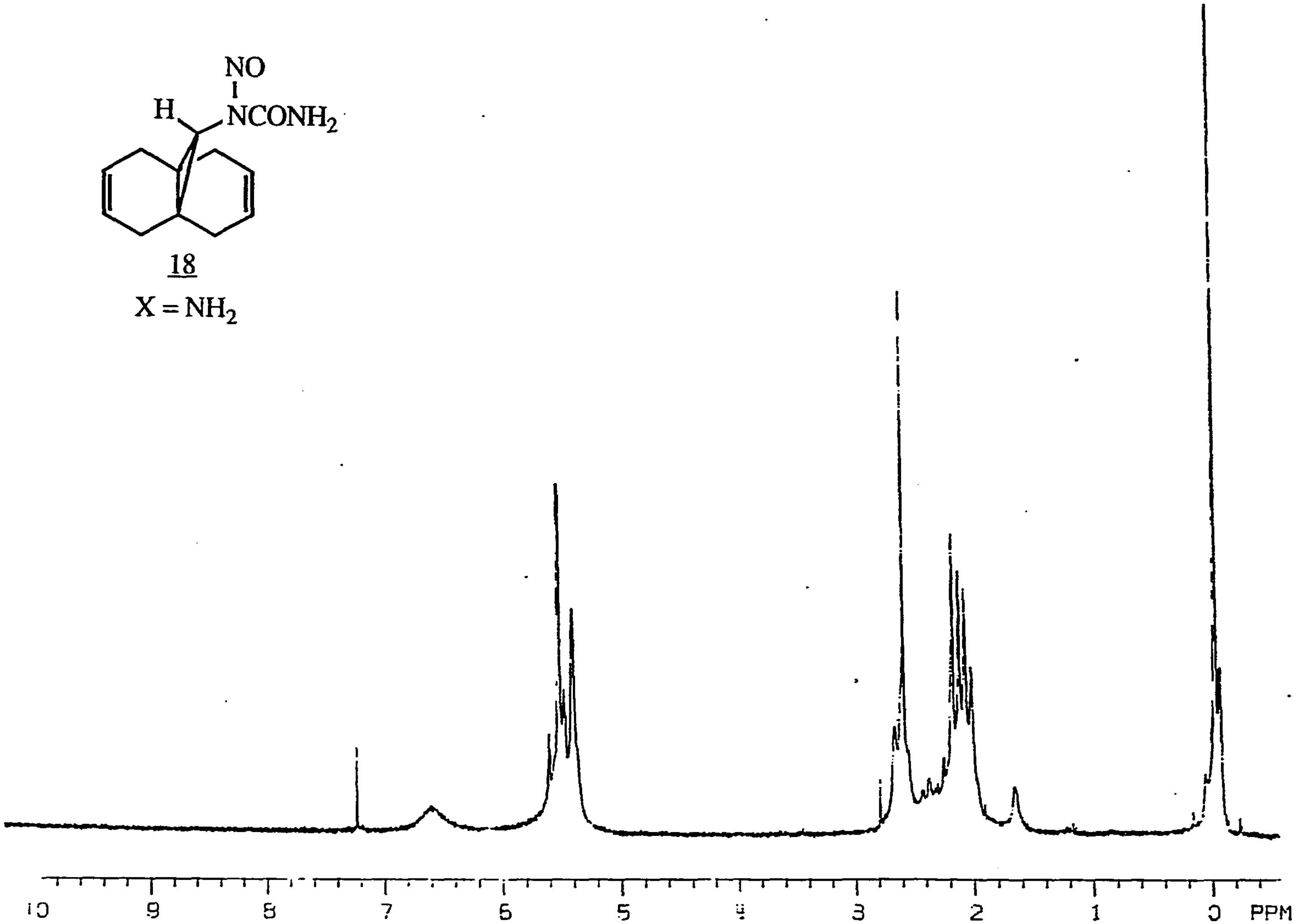
^{13}C NMR ($CDCl_3$): 159.9, 124.8, 124.4, 35.4, 31.8, 27.8, 21.6.

Synthesis of N-nitroso-N-[4.4.1]propella-3,8-dienyl-11-urea (18a) (Figure 13)

$NaNO_2$/HOAc method: To a solution of 204 mg (1 mmol) of N-[4.4.1]propella-3,8-dienyl urea 17a in glacial acetic acid (1 mL) and acetic anhydride (5 mL) at 0°C, was added 210 mg (3 mmol) of sodium nitrite in several small portions. The mixture was stirred for another 45 min, and poured into 200 mL of ice water. A yellow oil separated at the bottom. Ether (25 mL) was added, followed by separation of the layers. The aqueous layer was extracted with ether (2 x 10 mL) and the combined organic phases was dried ($MgSO_4$) and concentrated in vacuo. The crude yellow oil was kept in the freezer overnight. The desired 18a was deposited as a yellow solid on the sides of the flask. This was separated from the oil (IR; 2284 cm^{-1}) by washing with cold pentane. The maximum amount of 18a obtained was 70 mg (30%), mp 86-89°C. Due to the instability of the compound, analysis was not performed.

^{1}H NMR ($CDCl_3$): 6.6 (br s, 2 H), 5.4-5.6 (m, 4 H), 2.0-2.6 (m, 9 H).

Figure 13. ^{1}H NMR (CDCl$_3$) of 18a



18

$X = NH_2$

^{13}C NMR ($CDCl_3$): 155.5 (s), 124.8 (d, J = 157 Hz), 124.2 (d, J = 157 Hz), 37.4 (dd, J = 165, 5.2 Hz), 31.1 (t, J = 127.5 Hz), 29.1 (t, J = 127.5 Hz), 25.6 (s).

N_2O_4 method: To a suspension of 85.2 mg (4.2 mmol) of N-[4.4.1]propella-3,8-dienyl-11-urea (17a) and 0.5 g of anhydrous NaOAc in anhydrous ether (20 mL), a solution of 0.65 g (7 mmol) of freshly distilled N_2O_4 was added dropwise at -35°C. After stirring for 20 min at this temperature the mixture was allowed to warm to 20°C, and filtered. The solid was washed with ether (15 mL). The combined ether layers was washed with 5% $NaHCO_3$ solution (20 mL) followed by washing with cold water (20 mL). The ether layer was dried ($MgSO_4$) and concentrated in vacuo to yield a crude oil (IR = 2284 cm^{-1}), which on trituration with cold pentane yielded a maximum of 300 mg (31%) of 18a as a yellow solid: mp 69-70°C.

Reaction of solid 18a with base

A solution of 5-7 mg of nitrosourea 18a in toluene/methanol solution (0.5 mL) (concentrations of 20-100% methanol were used) was added to a large excess of freshly prepared $LiOCH_3$ or $NaOCH_3$ in MeOH at various temperatures (10-60°C). Evolution of nitrogen began immediately and stopped within 30-40 seconds. The mixture was stirred for 3 min to insure complete reaction. The mixture was treated with a 50% aqueous ammonium chloride solution (1 mL) and extracted with ether (1 mL). The products 19-23 were analyzed by a capillary GC and mass spectroscopy. The response factors of 23 and 20 with respect to mesitylene were 0.75 and 0.78, respectively. The overall yield of the products, assuming the solid 18a was pure, was 50-75% at reaction temperatures between 10 and 60°C. The typical yields, at T = 40°C and [MeOH] = 9 M, of 19 + 23, 20, 21 + 22 were 34%, 11% and 7%, respectively. The ratio of intramolecular insertion products 19 (+23) to 20 varied with methanol concentration. The ratio of 20:21:22 was in the range of 5:1.5:1.

GC-MS of 19: 144 (16.8), 143 (14.9), 130 (11.1), 129 (100.0), 128 (78.7), 127 (20.6), 117 (10.0), 116 (16.2), 115 (33.1), 91 (123.6), 77 (10.2), 63 (11.4), 51 (12.7), 39 (18.5).

GC-MS of 23: 144 (46.0), 143 (17.7), 130 (10.7), 129 (100.0), 128 (69.9), 127 (17.0), 117 (4.5), 116 (15.3), 115 (32.8), 91 (10.3), 77 (8.3), 63 (10.7), 51 (9.9), 39 (13.8).

GC-MS of 20: 176 (8.1), 161 (3.8), 144 (59.8), 129 (100.0), 121 (97.5), 109 (5.0), 105 (18.4), 91 (84.5), 77 (35.9), 65 (17.6), 39 (25.1).

GC-MS of 21: 176 (12.5), 161 (16.8), 14.4 (27.9), 135 (35.5), 129 (77.6), 121 (66.4), 109 (70.0), 105 (50.8), 91 (100.0), 77 (59.9), 65 (36.5), 39 (56.4).

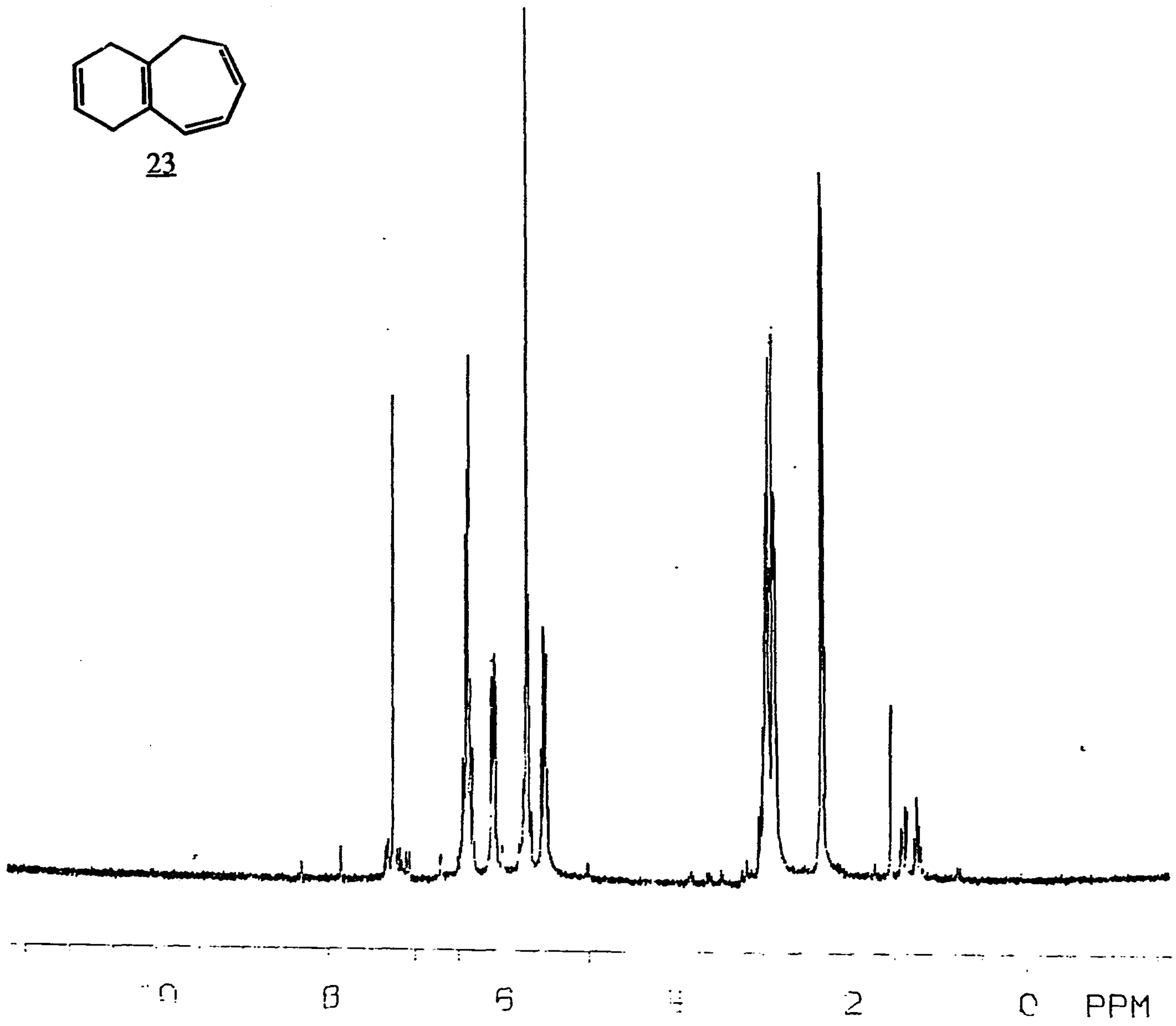
GC-MS of 22: 176 (31.7), 161 (6.7), 144 (39.1), 129 (100.0), 121 (12.5), 117 (34.5), 105 (16.4), 91 (88.2), 77 (24.5), 65 (16.9), 39 (24.7).

Synthesis of tetracyclo[4.4.1.0.$0^{2,11}$]undeca-3,8-diene (19) (Figure 14)

Diene 19 was prepared by the method of Paquette et al.[17] Thus, a solution of 3.0 g (10 mmol) of 11,11-dibromo[4.4.1]-propella-3,8-diene (24) in 50 mL anhydrous ether was stirred under nitrogen at 0°C while 7.1 mL of 1.4 M methyllithium (10 mmol) in ether was added. The resulting solution was allowed to warm with stirring for 2 h, washed with water and brine, dried ($MgSO_4$) and concentrated in vacuo. The GC of the crude product showed 19 and 23 in the ratio of 3:1 (temperature program: 80°C/2 min, 80-250°C @20°C/min). Attempted purification of 100 mg of the crude product by preparative GC resulted in the complete conversion of 19 to 23 (20 mg).

GC-MS of 19: 144 (20.9), 143 (16.1), 130 (9.6), 129 (100.0), 128 (28.7), 127 (6.7),

Figure 14. ^{1}H NMR ($CDCl_3$) of 23



23

117 (5.3), 116 (11.1), 115 (6.0), 91 (3.0), 66 (5.7).

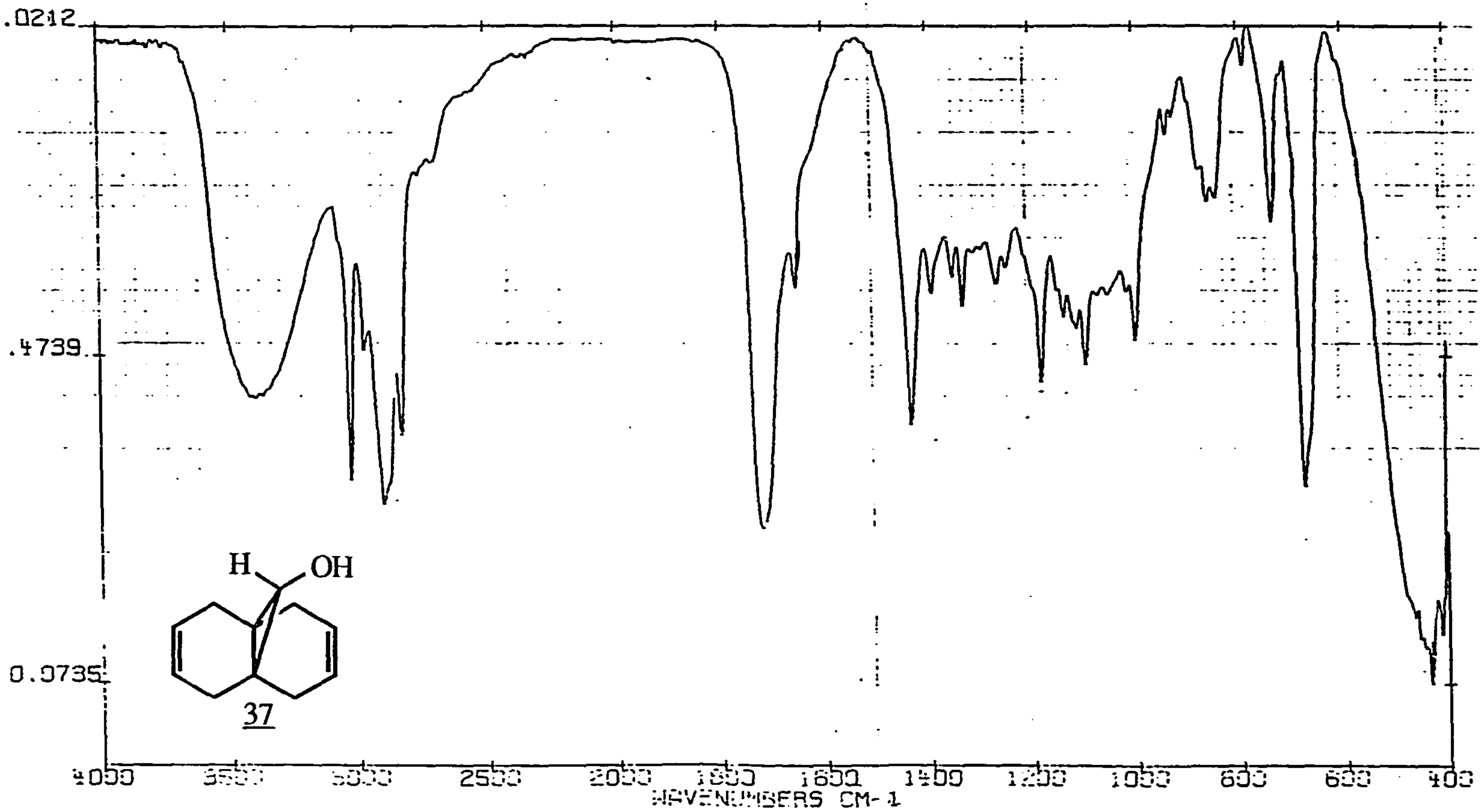
GC-MS of 23: 144 (72.4), 143 (16.2), 130 (11.1), 129 (100.0), 128 (25.4), 127 (4.9), 117 (2.7), 116 (11.9), 115 (4.6), 91 (1.6), 66 (3.7).

^{1}H NMR of 23 ($CDCl_3$): 5.4-6.4 (m, 4 H), 2.8-2.9 (m, 4 H), 2.3 (d, J = 7.2 Hz, 2 H).

Synthesis of 11-hydroxy[4.4.1]propella-3,8-diene (37) (Figures 15a and 15b)

To a solution of 225 mg (1 mmol) of bromide 15 in 5 mL dry THF at -78°C, was added dropwise a solution of 1.3 mL of t-butyllithium (1.7 M) under a nitrogen atmosphere. The solution was then stirred for another 1 h at this temperature, following which dry oxygen was bubbled through the solution for 20 min at -78°C. The solution was quenched with 0.5 mL of glacial acetic acid and allowed to warm to room temperature. The organic material was extracted with ether (20 mL), and the ether layer dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified over a column of neutral alumina. Elution with 50% ether-50% hexane gave 90 mg of 37 as a colorless solid (deliquescent). This solid was not GC-pure. The IR of this crude product showed the presence of an aldehyde in addition to the OH stretching.

Figure 15a. IR ($CHCl_3$) of 37



.0212
.4739
0.0735
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1
H
OH

37

GC-HRMS: Calculated for $C_{11}H_{14}O$ m/e 162.1045; measured m/e 162.1043.

IR ($CHCl_3$): 3396 (br, s), 3026 (s), 2899 (s), 2831 (m), 1722 (s), 1437 (m), 1182 (m), 677 (s).

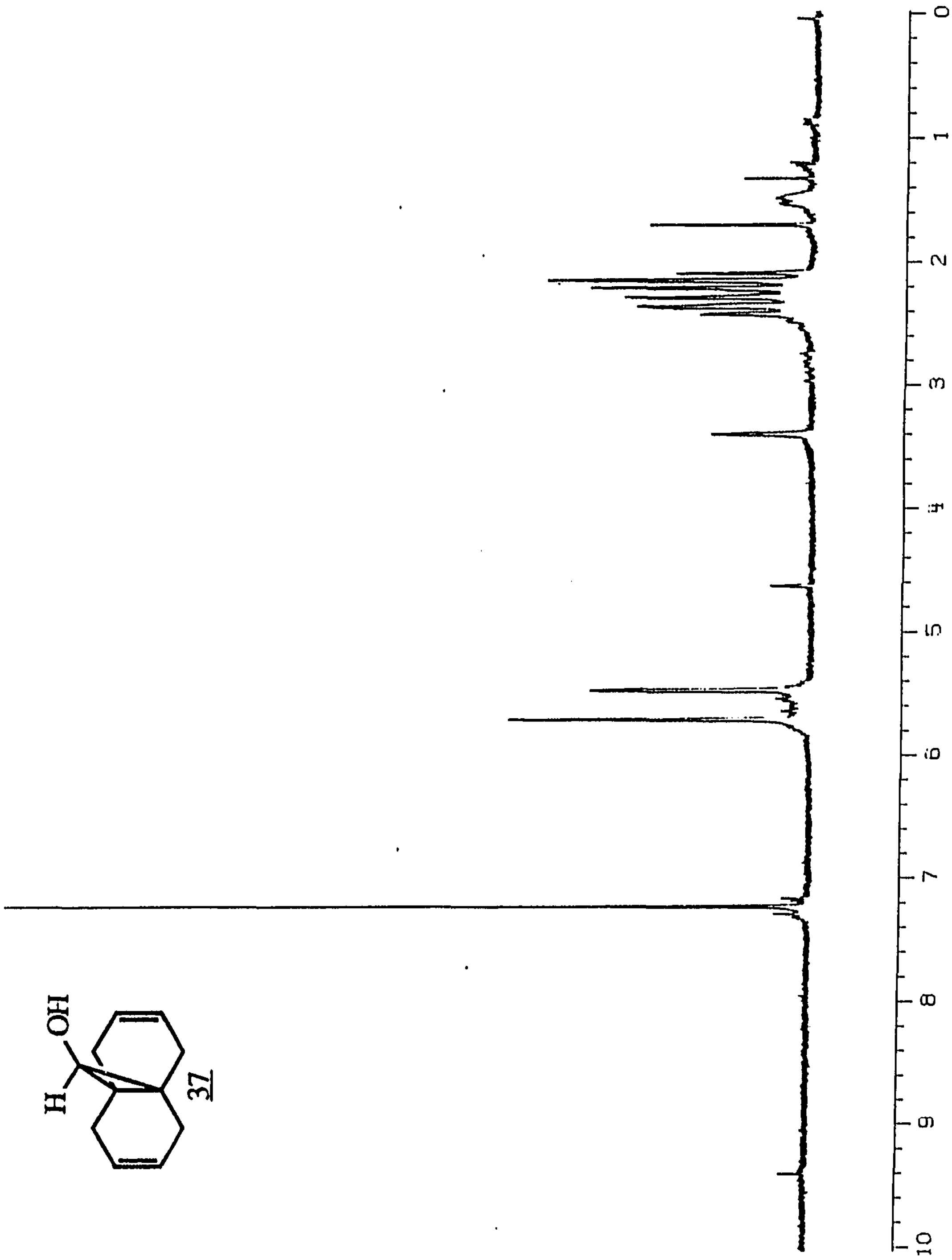
^1H NMR ($CDCl_3$): 9.4 (s), 5.4-5.7 (m), 4.6 (s), 3.4 (s), 2.0-2.4 (m).

Synthesis of 11-methoxy[4.4.1]propella-3,8-diene (20)

To a solution of 324 mg (2.0 mmol) of 37 in 10 mL dichloromethane at -78°C containing 48 mg (2 mmol) of sodium hydride, was added a five-fold excess of methyl fluorosulfonate. The solution was stirred for 1 h at this temperature. The solvent and excess methyl fluorosulfonate were distilled off at reduced pressure. Then ether (25 mL) was added to the residue; the ether layer was washed with 10% $NaHCO_3$ (2 x 20 mL), saturated NaCl, dried ($MgSO_4$) and concentrated in vacuo to give 50 mg of crude methyl ether 20 (20 was contaminated with the aldehyde impurity, which had a retention time close to 20). The retention time of 20 was 5.1 min and that of the aldehyde was 4.8 min at a column temperature of 140°C.

GC-MS: 176 (11.8), 161 (5.0), 144 (69.9), 129 (100.0), 121 (96.0), 109 (6.1), 105 (16.1), 91 (77.9), 77 (30.0), 65 (16.6), 39 (23.5).

Figure 15b. ^{1}H NMR ($CDCl_3$) of impure 37



37

^1H NMR ($CDCl_3$): 5.5-5.6 (m), 3.3 (s), 1.6-2.5 (m).

^{13}C NMR ($CDCl_3$): 124.8, 124.3, 65.7, 59.1, 32.1, 27.5, 20.8.

Reaction of solid 18a with LiOMe/MeOD

A solution of 10 mg of 18a in 1 mL of 80% MeOD/20% toluene was treated with a large excess of LiOMe (prepared from Li/MeOD). After the evolution of nitrogen stopped, the solution was stirred for 3 min, treated with 0.5 mL 50% ammonium chloride solution, and extracted with 1.0 mL ether. The ether layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was analyzed by GC-MS. Bicyclobutane 19 (analyzed as 23) showed no D incorporation, while 20-22 showed a high degree of D incorporation (20, 93% d_1, 21, 100% d_1, 22, 98% d_1 - all determined by GC-MS at 11 eV).

Thermolysis of solid 18a in MeOH or MeOD

A solution of 5 mg of 18a in 2 mL of MeOH or MeOD was refluxed for 5-10 min. The solvent was distilled off at reduced pressure and the residue was analyzed by GC-MS. The major products (from uncorrected GC areas) were 19 (+23), 29 and 30. Also 20-22 were formed as minor products. The ratio of 19 (+23):20 was in the range of 6:1. Of the products from MeOD reaction, 19 (analyzed as 23) showed approximately 19% d_1 incorporation. Also 30 showed a small degree of incorporation of two D atoms; 29 was not analyzed for D content.

GC-MS of 29: 208 (4.9), 193 (4.5), 177 (18.0), 176 (48.5), 161 (24.8), 153 (34.4), 135 (45.2), 122 (90.4), 121 (66.4), 109 (31.6), 97 (100.0), 91 (55.4), 79 (67.8), 67 (40.7), 59 (49.5), 45 (73.4).

GC-MS of 30: 176 (74.0), 161 (44.7), 145 (16.5), 144 (10.4), 135 (65.7), 129 (62.0), 121 (82.7), 105 (32.2), 91 (100.0), 77 (55.4), 65 (31.0), 51 (28.2).

GC-MS (11 eV) of 23-H: 143 (12.0), 144 (100.0), 145 (12.0), 146 (0.7).

GC-MS (11 eV) of 23-D: 143 (1.3), 144 (100.0), 145 (36.4), 146 (3.7).

The deuterium incorporation (% D incorporation) was determined from the relative intensities of (P-1), P, P+1, . . . peaks by iterative calculation.

Preparation of ethyl-N([4.4.4]propella-3.8-diene-11-yl)-carbamate (17b) (Figures 16, 17)

A solution of 34 in toluene (20 mL) derived from 2.3 g (12.0 mmol) of 16 as described for the preparation of 17a, was mixed with absolute ethanol (40 mL) and refluxed for 12 h. The solvents were distilled off at reduced pressure and the residue was placed on a silica gel column. Elution with

Figure 16. IR (KBr) of 17b

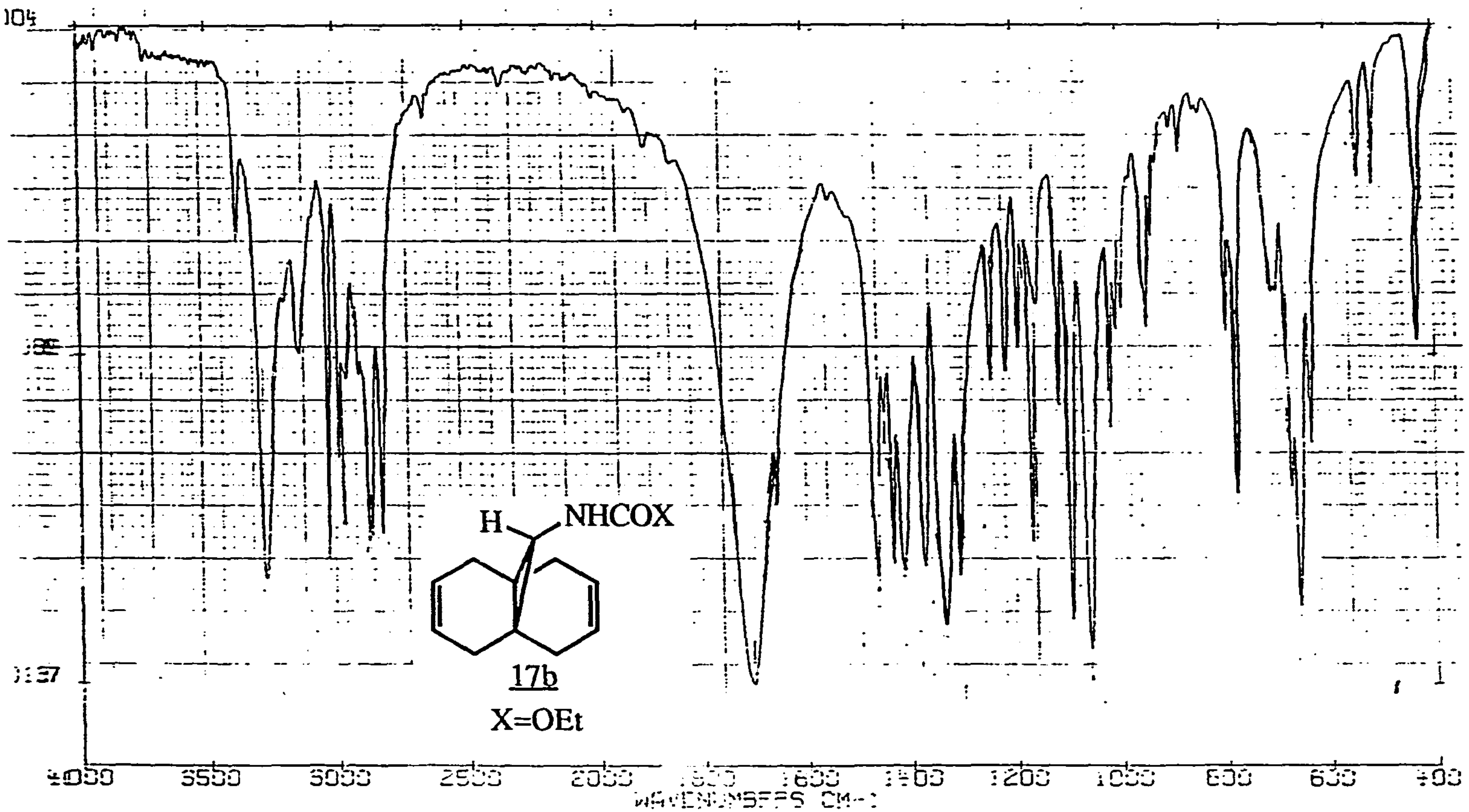
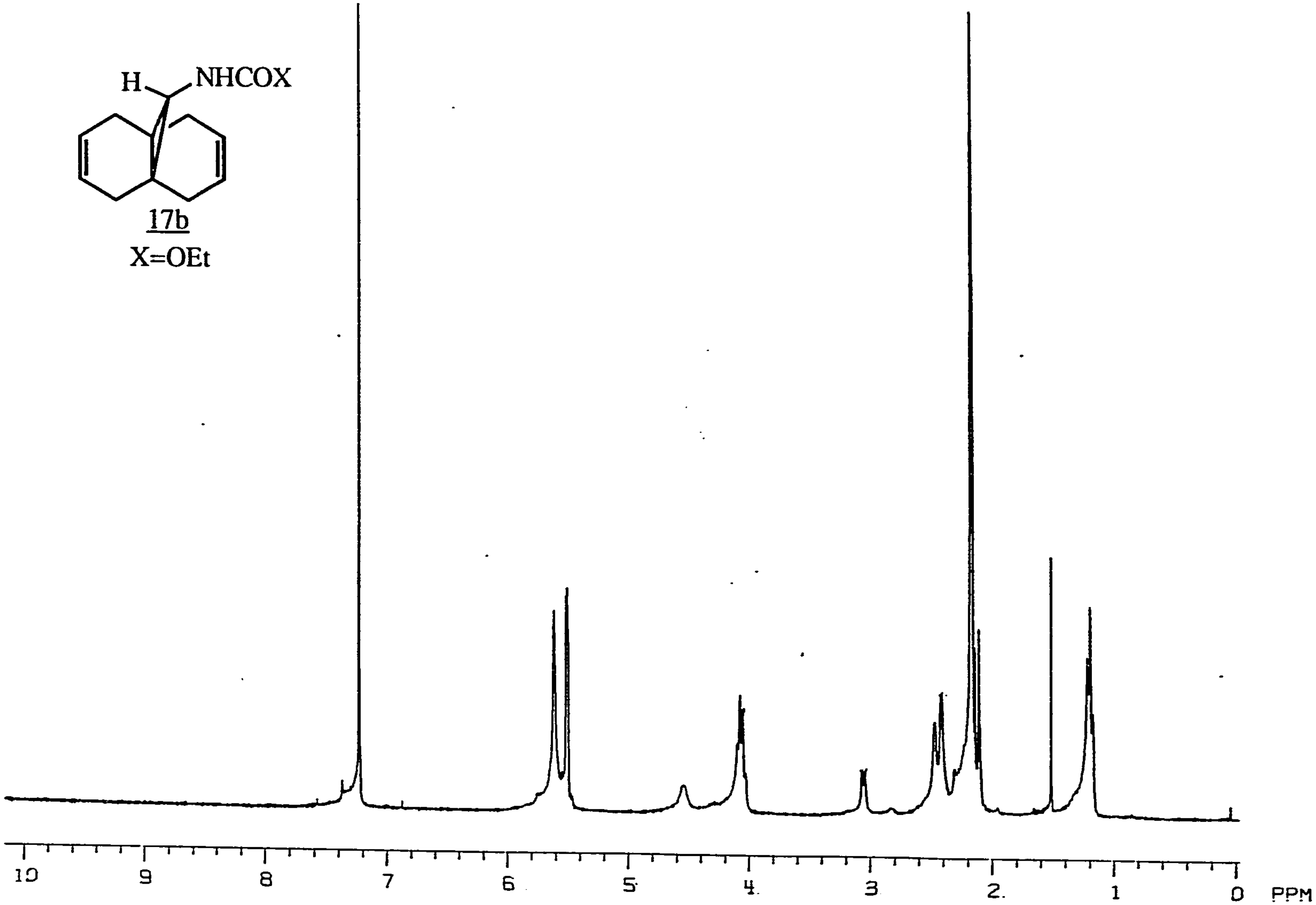

H
NHCOX
17b
X=OEt
104
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1

Figure 17. ^1H NMR ($CDCl_3$) of 17b


H
NHCOX
17b
X=OEt
10
9
8
7
6
5
4
3
2
1
0
PPM

a 40% ether-60% hexane mixture afforded 1.4 g (50%) of 17b as a colorless solid: mp 58-59°C.

HRMS: Calculated for $C_{14}H_{19}NO$ m/e 233.1416; measured m/e 233.1420.

IR (KBr): 3275 (s), 3032 (s), 2993 (m), 2878 (s), 2866 (s), 1705 (s), 1659 (m), 1464 (s), 1335 (s), 1169 (s), 1096 (s), 1061 (s), 777 (m), 660 (s).

^{1}H NMR ($CDCl_3$): 5.5-5.6 (m, 4 H), 4.5 (bs, 1 H), 4.0 (q, 2 H, J = 7.8 Hz)), 3.1 (d, 1 H, J = 7.8 Hz), 2.1-2.5 (m, 8 H), 1.1-1.2 (t, 3 H, J = 7.8 Hz).

^{13}C NMR ($CDCl_3$): 157.3, 125.2, 124.3, 60.6, 35.9, 31.5, 27.7, 20.3, 14.6.

Nitrosation of 17b

Compound 17b was nitrosated using N_2O_4 by the method described for 18b. The crude oily product was not characterized, but immediately used for further reaction.

Reaction of 18b with base

A. To a solution of 10 mg of 18b in methanol (1 mL) was added a large excess of 2 M $LiOCH_3$/MeOH at room temperature. The solution was stirred for 3 min and quenched with 50% ammonium chloride solution (0.5 mL) and extracted with ether (3 mL). The ether layer was dried ($MgSO_4$) and analyzed by

GC-MS. The GC showed a 20:21:22 ratio of ca. 5:1.5:1. The ratio of 19 (analyzed as 23) to 20 was 1.5:1.

B. In this method the mode of addition was reversed. A solution of 10 mg of 18b in methanol (1 mL) was added to a large excess of the same base as in method A. Work-up as described above and analysis by GC showed a 20:21:22 ratio of ca. 7:2:1. The ratio of 19 (analyzed as 23) to 20 was 2:1.

Reaction of crude (oil) 18a with base

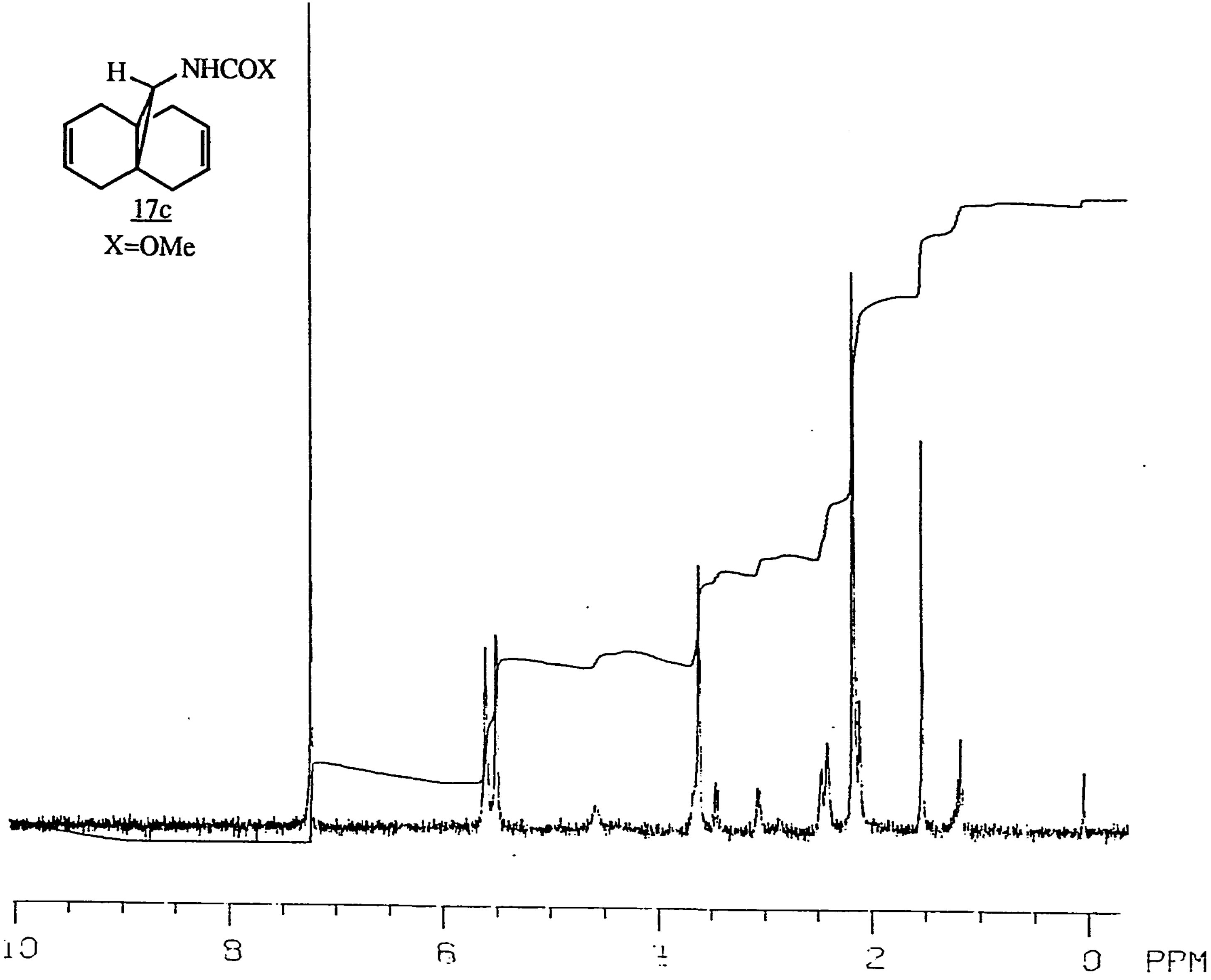
To a solution of 10 mg of crude 18a in methanol (0.5 mL) was added a large exces of 2 M $LiOCH_3/MeOH$ at room temperature. The solution was stirred for 3 min, quenched with 50% ammonium chloride solution (0.5 mL) and extracted with ether. GC-MS analysis of the product mixture revealed 17c as the major product in addition to 20-23 as minor products.

Synthesis of methyl-N([4.4.1]propella-3,8-dien-11-yl)-carbamate (17c) (Figures 18, 19)

Carbamate 17c was prepared in 45% yield, by refluxing a toluene solution of 34 with methanol, mp 39-40°C.

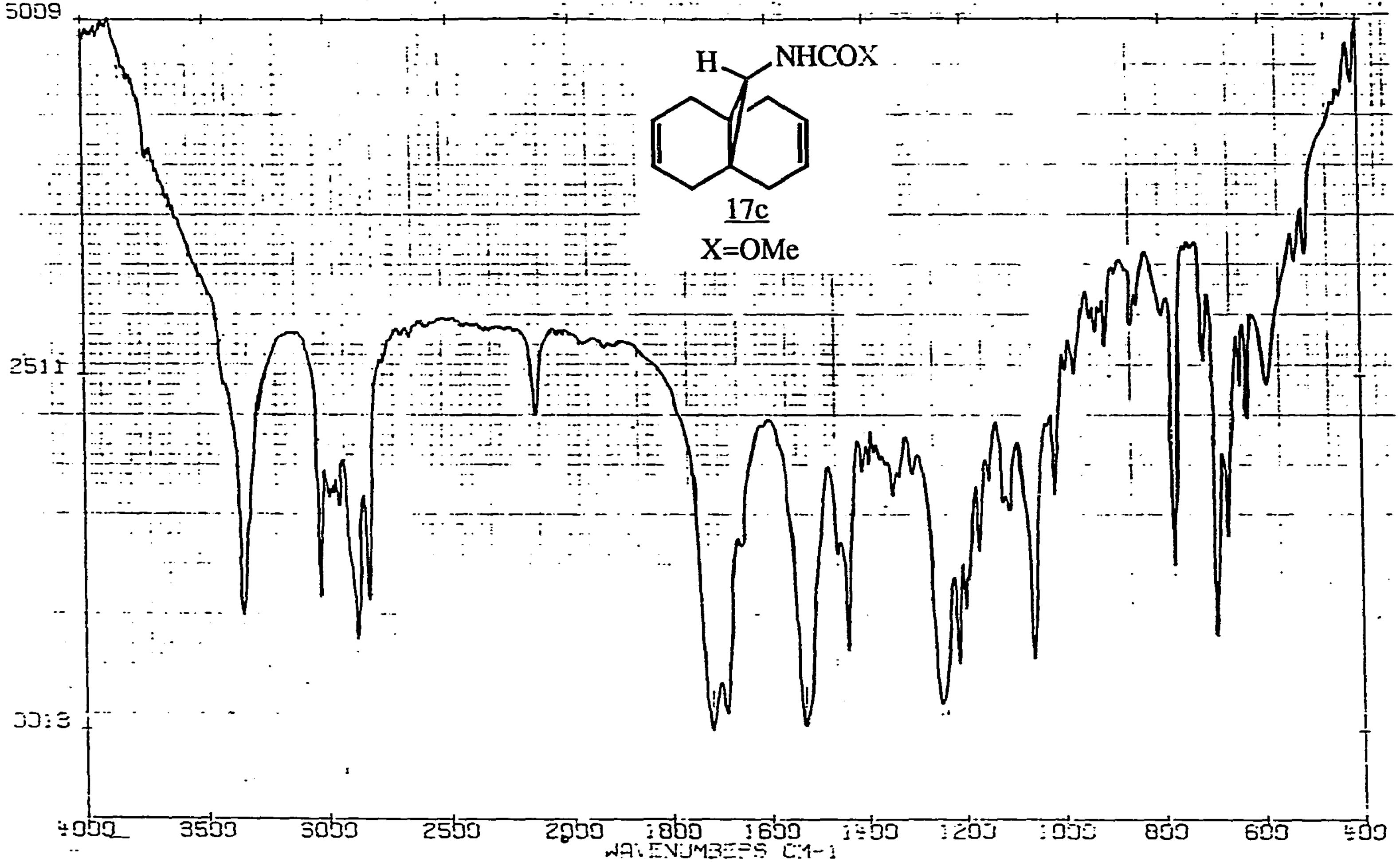
GC-MS:	219 (10.4), 204 (2.4), 164 (94.0), 144 (54.1), 129 (100.0), 118 (28.2), 91 (32.8), 76 (62.1), 55 (15.0).

Figure 18. ^{1}H NMR ($CDCl_3$) of 17c



17c
X=OMe

Figure 19. IR (KBr) of 17c


H
NHCOX
5009
2511
00:3
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
WAVENUMBERS CM-1

17c

X=OMe

IR (KBr): 3342 (s), 3026 (s), 2878 (s), 2829 (s), 1718 (s), 1690 (s), 1659 (m), 1529 (s), 1441 (m), 1250 (s), 1063 (s), 779 (s), 694 (s), 673 (s).

^{1}H NMR ($CDCl_3$): 5.5-5.6 (m, 4 H), 4.6 (bs, 1 H), 3.6 (s, 3 H), 2.1-2.5 (m, 9 H).

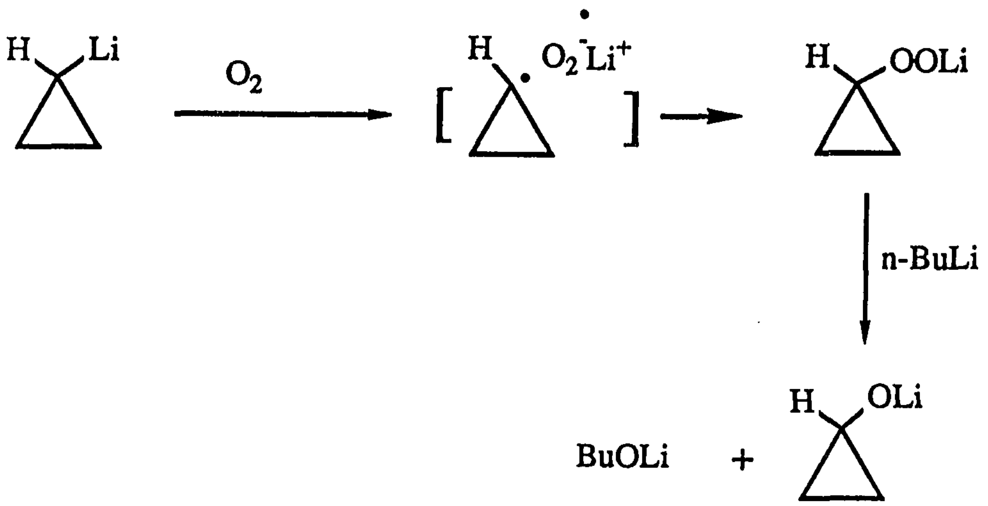
Reaction of a mixture of 19 and 23 with $LiOCH_3$/MeOH

A solution containing 10 mg of 19 and 23 and a five fold excess of 2 M $LiOCH_3/CH_3OH$ in methanol (4 mL) was refluxed for 5 min. The solution was treated with 50% ammonium chloride solution (1 mL), extracted with ether (3 mL) and the ether layer was dried ($MgSO_4$). GC analysis of the ether layer showed a small amount of 23 along with some unidentifiable compounds. More importantly, none of compounds 20-22 was detected.

CHAPTER III. THE OXIDATION OF CYCLOPROPYLIDENES

Introduction

Molecular oxygen is seldom useful for selective oxidation of organic compounds due to its triplet ground state. But the reaction of molecular oxygen with reactive species like radicals takes place at almost the diffusion-controlled rate.[28] Oxidations of carbanions with oxygen are known. For example, triphenylmethide reacts with oxygen at a rate approaching the diffusion-controlled rate.[29] Triphenylmethide is actually more reactive toward oxygen than triphenylmethyl radical. Oxidation of organometallics like RMgX and RLi occur via an electron transfer mechanism. The oxygenation of cyclopropyllithium,[30,31] for example, is a useful reaction for the synthesis of cyclopropanols. The reaction proceeds via an electron transfer mechanism. The

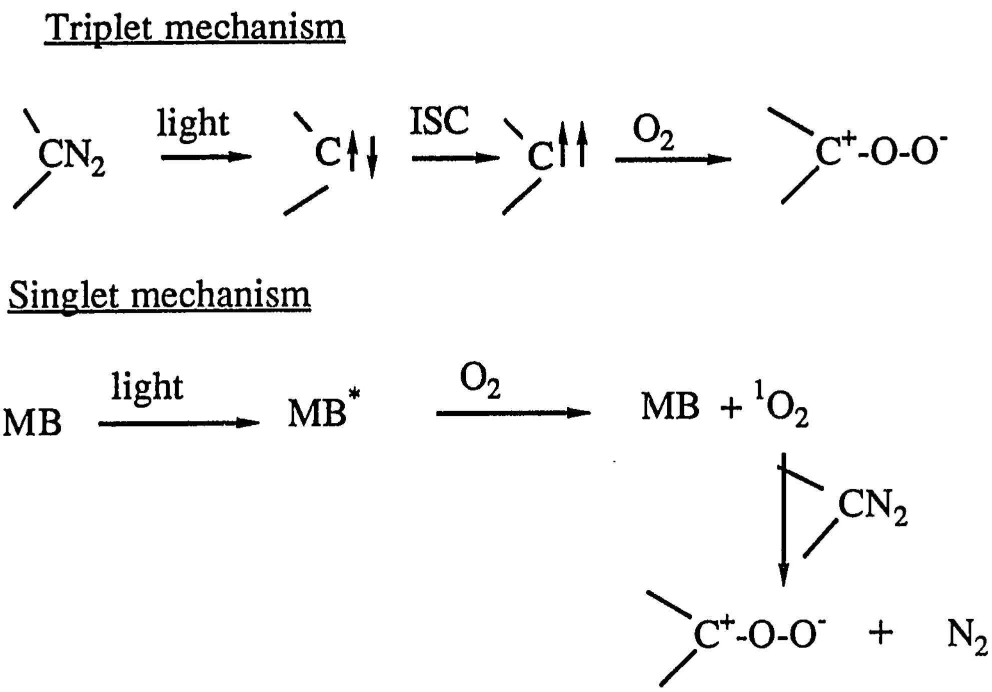


initial step in this reaction is the formation of cyclopropyl radical-lithium superoxide ion pair which subsequently leads to the hydroperoxide salt, probably by a chain mechanism. As a large excess of n-BuLi is used to generate cyclopropyllithium from the corresponding bromo compound, further reaction of the hydroperoxide salt with n-BuLi produces alkoxides of n-butanol and cyclopropanol.

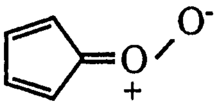
Like radicals and carbanions, triplet carbenes also react with oxygen.[32-35] For example, diphenylcarbene reacts with oxygen with a rate constant of 5 x 10^9 $M^{-1}s^{-1}$ in acetonitrile at 300 K.[36] The interest on the oxidation of carbenes was mainly to characterize the intermediate carbonyl oxides and dioxiranes, which were originally postulated as intermediates in the ozonolysis of alkenes[37-40] and the Baeyer-Villiger oxidation of ketones.[41] Carbonyl oxides and dioxiranes have also attracted attention as models for monooxygenase enzymes.[42]

Carbonyl oxides can be generated either by the reaction of triplet oxygen with triplet carbenes, or by the reaction of singlet oxygen with diazo compounds. The mechanisms[43] for these reactions are shown in Scheme 3. Methylene blue (MB) is a singlet oxygen sensitizer. A number of carbonyl oxides have been studied in low temperature matrices as well as in solutions at ambient temperatures. Techniques such as conventional flash photolysis and laser flash photolysis have been used to generate these intermediates. Some

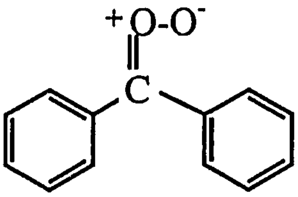
Scheme 3


Triplet mechanism
CN2
light
C
ISC
C
O2
C+-O-O-
Singlet mechanism
MB
light
MB*
O2
MB + 1O2
CN2
C+-O-O-
+
N2

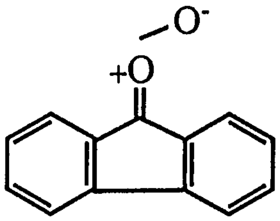
representative examples of carbonyl oxides are shown below, spectroscopic data for these species are given in Table 5.



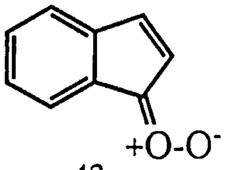
40



41



42



43

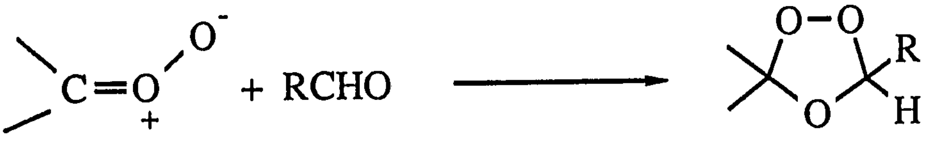
Unless otherwise stated, all the spectroscopic data in Table 5 were obtained in low temperature matrices.

Carbonyl oxides are quite reactive species. The half-life ($t_{1/2}$) of fluorenone oxide (42), for example, in Freon-113 is 370 microseconds[44] at 27°C. The second-order

Table 5. Spectroscopic data of carbonyl oxides

Carbonyl oxide	UV (nm)	IR (cm^{-1})
40	420	1395 (s), 1385 (vs), 1184 (m), 1179 (w), 1142 (m), 1023 (w), 983 (w), 895 (vs), 741 (s), Chapman, et al.[45]) 1478 (w), 1397 (w), 1320 (m), 1221 (w), 1075 (w), 1063 (w), 1018 (m), 1007 (w), 949 (m), 888 (m), 754 (m), 693 (w), 603 (w) (Dunkin, et al.[46])
41	422	1377 (m), 1185 (w), 1158 (w), 983 (m), 897 (s) (Sander[36])
	410	(laser flash[37])
42	460[48]	
43	445[48]	

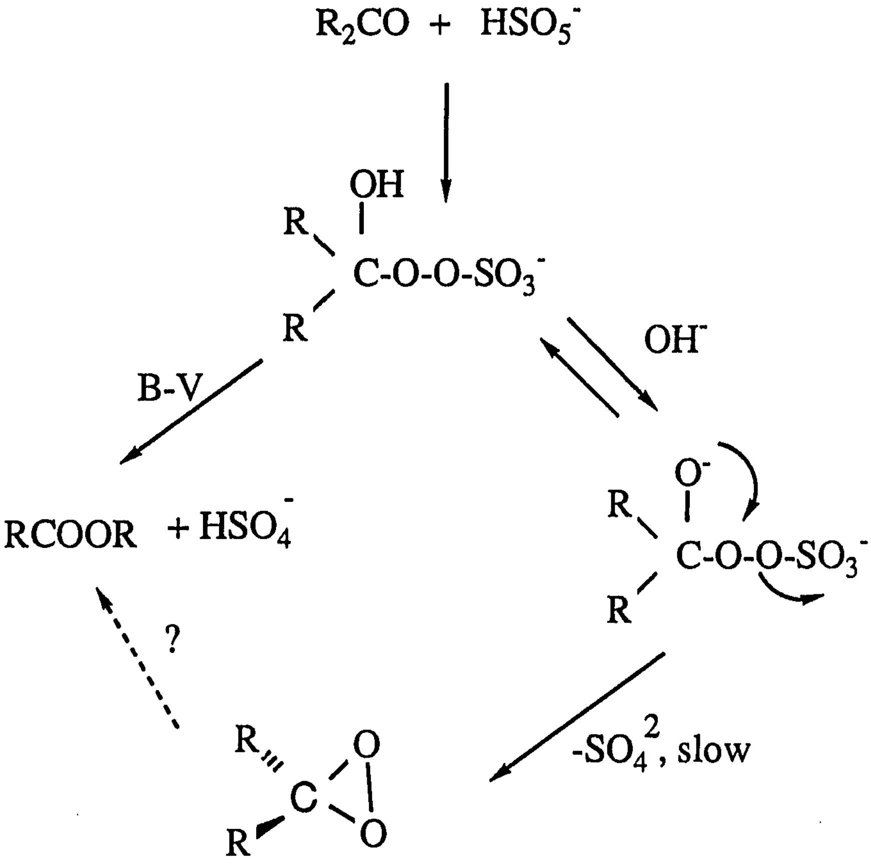
decay of a carbonyl oxide[49] leads to the formation of the corresponding ketone and oxygen. For example, benzophenone oxide decays by self reaction with a rate constant of 1.33 x 10^7 $M^{-1}s^{-1}$ at 20°C in acetonitrile.[43] Carbonyl oxides also react with aldehydes to form 2° ozonides at diffusion-controlled rates. For example, fluorenone oxide (42) reacts



with acetaldehyde with a rate constant, k_1 = 1.21 x 10^9 $M^{-1}s^{-1}$ at 27°C.[44] Reactions with alkenes[50] give epoxides in low yield and in a nonstereospecific manner. Reactions with cyclohexanone in benzene give the corresponding alcohols in low yields.[50] Carbonyl oxides can transfer oxygen atoms to sulfur compounds. Sulfoxides are more reactive than sulfides. For example, Ph_2S is oxidized to Ph_2SO in 3% yield, while Ph_2SO is oxidized to Ph_2SO_2 in 43% yield by fluorenone oxide.[50] The oxidations by carbonyl oxides are believed to be nucleophilic oxygen reactions.

Dioxiranes are isomeric with carbonyl oxides and are formed by irradiation of the latter with visible light.[46,47,51] Curci et al.[52,53] developed a method of synthesis of dioxiranes by a modified Baeyer-Villiger oxidation of ketones using peroxymonosulfate (Scheme 4). Using this method, Murray and Jeyaraman have synthesized

Scheme 4

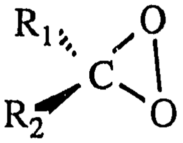

R_2CO + HSO_5^-
OH
R
C-O-O-SO_3^-
R
B-V
OH⁻
RCOOR + HSO_4^-
O⁻
R
C-O-O-SO_3^-
R
?
R
O
C
R
O
-SO_4^{2}, slow

Factors such as the pH and the migratory aptitude of the R groups on the ketone influence the course of the reaction.

various dioxiranes.[54] The spectroscopic data for some representataive dioxiranes are shown in Table 6.

In contrast to carbonyl oxides, dioxiranes are stable in solution. For example, the half-life ($t_{1/2}$) of dimethyldioxirane is (48 ± 1) h at 25°C.[54] Dioxiranes react with olefins to give epoxides in high yield and in a

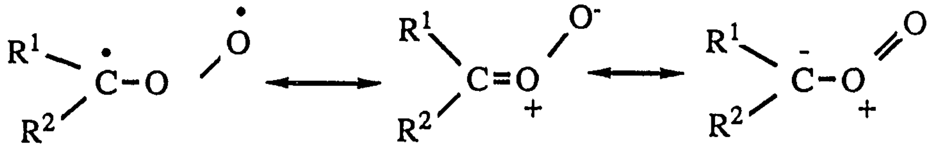
Table 6. Spectroscopic data of dioxiranes



R_1	R_2	^{13}C NMR (ppm)	^{1}H NMR (ppm)	UV (nm)	IR (cm^{-1})
Me	Me	22.6 102.0[55]	1.65[54]	335[54]	3012, 3005, 1209, 1094, 894, 784 (acetone solution[55])
Me	CF_3	14.5, 97.3, 122.2[56]	1.97[54]		
CF_3	CF_3			306[54]	
Me	Et			333[54]	

stereospecific manner. For example, dimethyldioxirane oxidizes ethyl trans-cinnamate, cis-stilbene and trans-stilbene to the corresponding epoxides in 75-95% yield.[54] Carbonyl oxides react with some nucleophiles, e.g., pyridine, to give largely polymeric products, while dioxiranes give the N-oxides via an apparently simple O atom transfer reaction.[54] Carbonyl oxides react with aldehydes to give 2° ozonides, while dioxiranes give the corresponding carboxylic acids.

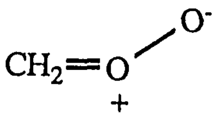
Ab initio calculations[57] on simple carbonyl oxides predict that the ground state of these species should be singlets, and generally favor the zwitterionic or dipolar



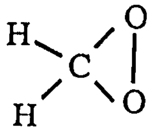
44a 44b 44c

description of bonding [cf. (44b) and (44c)]. For the least substituted examples [e.g., 44, R^1, R^2 = H], however, the calculations prefer a biradical description [cf. 44a].

Spectroscopic investigations have provided evidence that dioxiranes can be formed by thermal or photochemical isomerization of carbonyl oxides, e.g., in the ozonolysis[58,59] or the oxidation of carbenes.[45-47,51] Simple dioxirane 46 is 31.3 kcal mole^{-1} more stable than the corresponding carbonyl oxide 45, according to an MP4



45



46

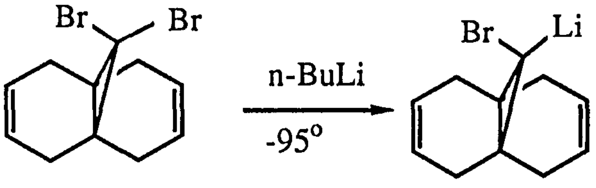
(SDQ)/6-31 G* calculation.[60] According to ab initio calculations,[60] the activation energy for the isomerization of 45 to 46 in the gas phase is 22.8 kcal mole^{-1}.

These intermediates have been of interest not only to theoretical chemists, but also to synthetic organic and biochemists for the last 10 years. Also, since the parent dioxirane has been identified as a product of gas-phase ozonolysis of ethylene, it seems likely that dioxiranes could be involved in air pollution chemistry.[61]

In the light of the results on the oxidation of cyclopropyllithiums and the oxidation of carbenes, we undertook a study of the oxidation of cyclopropylidenes. As opposed to free carbenes, we studied the oxidation of lithium halocarbenoids. Organolithium derivatives containing group VII heterosubstituents (F, Cl, Br, I) at the metallated carbon are called carbenoids.[62] Carbenoids undergo reactions similar to free carbenes.

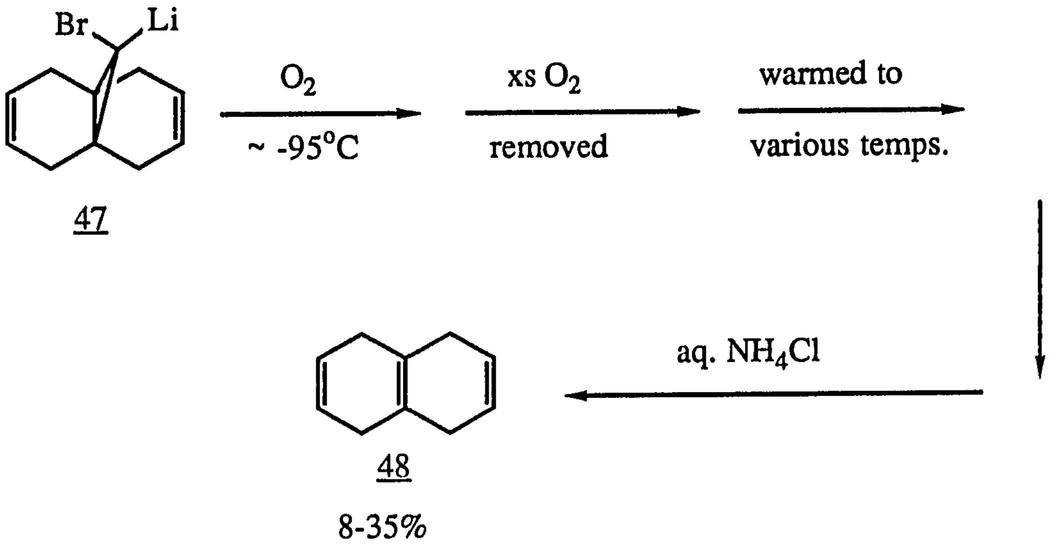
Results and Discussion

The carbenoids studied were generated by the reaction of the corresponding dibromocyclopropanes with 1 eq. of n-BuLi.



24 47

The first carbenoid we studied was 47. After generation in THF, 47 was reacted with oxygen (precooled at -78°C) at -95°C to -90°C for 30 min., excess oxygen removed by three vacuum thaw cycles, the solution allowed to warm to various

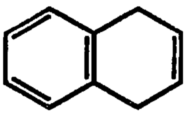


47

48

8-35%

temperatures (-85° to 25°C), and quenched by the addition of methanol. After aqueous work-up, the reaction mixture on analysis by GC showed isotetralin (48). The yields of 48 at various temperatures are shown in Table 7. The yield of 48 was found to increase with an increase in temperature of the oxygenated solution before quenching. The other products in these reactions were monobromide 15 and dihydronaphthalene



70

Table 7. Yield of 48 obtained at various temperatures

T°C[a]	Percent yield of 48[b]	Number of experiments done
-85[c]	4	1
-60[c]	5, 7	2
-15	9, 10	2
20	17, 19, 21, 22	4
25	18, 25, 30	3

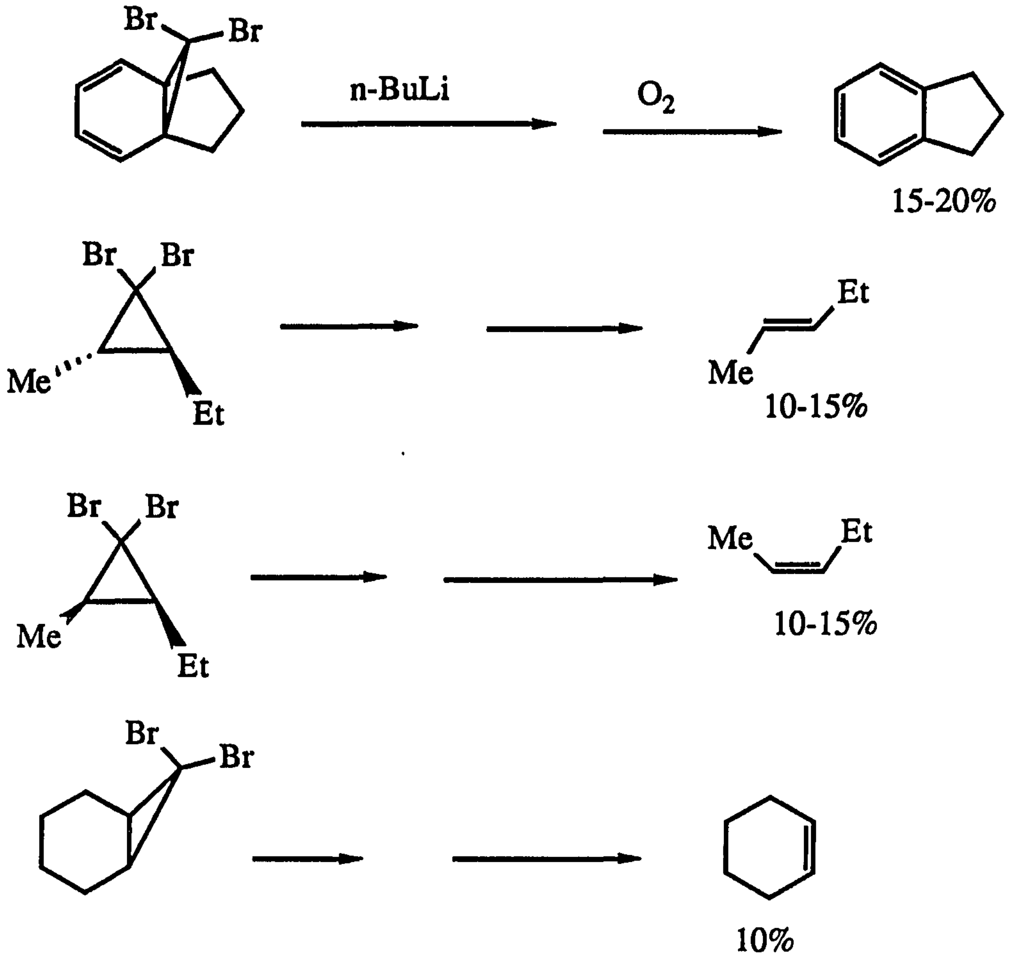
[a] T refers to the temperature to which the oxygenated solution was warmed, after removing excess oxygen.

[b] Includes the yield of 70.

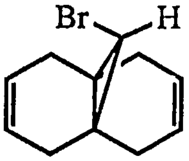
[c] In these experiments a small amount of esters 59 and 60 were formed.

(70). The yield of 15 was in the range 7-30% and showed neither correlation with the yield of 48 nor dependence on temperature. This suggests that 15 was formed during the oxygenation step (see later for more details). The GC area ratio of 70 to 48 in most cases was in the range 1:2-1:3. Aromatized 70 was found to arise from 48. Thus a control experiment where 48 was treated with a solution of n-BuLi in THF at -78°C, warmed to room temperature, and quenched with NH_4Cl, revealed the formation of 70 to the extent of 50%. So the yield of 48, wherever metioned, includes 70. The response factors of 48 and 70 with respect to mesitylene were the same (0.9). The higher the temperature to which the solution was warmed before quenching, the higher was the yield of isotetralin.

Intrigued by this net carbon loss, we wanted to determine the generality of this reaction. Similar oxidation was carried out with other cyclopropylidenoids.


Br
Br
n-BuLi
O_2
15-20%
Br
Br
Me
Et
Et
Me
10-15%
Br
Br
Me
Et
Me
Et
10-15%
Br
Br
10%

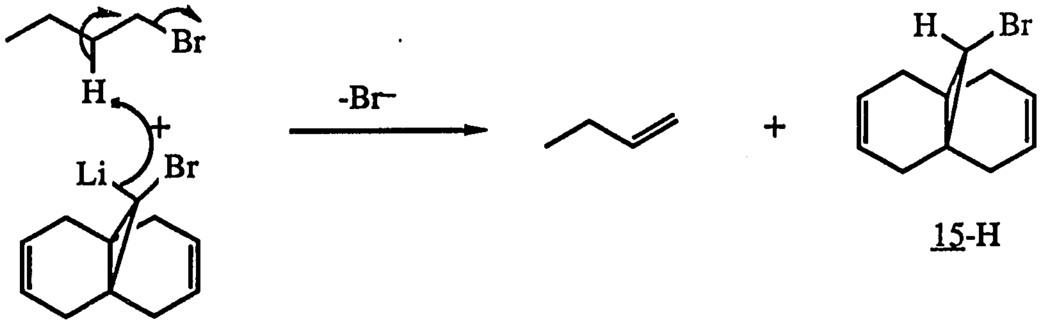
The reaction thus seems to be quite general for various substituted cyclopropylidenes, and also the olefin formation is stereospecific. In all these cases, the corresponding reduced monobromides were formed and particularly in the case of 47, the monobromide 15 was formed in 18-35% yield.



15

When MeOD, instead of MeOH, was used to quench the reaction after oxygenation of 47, the monobromide 15 formed did not contain deuterium. A control reaction was performed, where the carbenoid 47 was quenched at -90°C with MeOD instead of reacting with oxygen. This reaction yielded mainly 15-d$_1$ (the mass spectral ratio of 15-H: 15-d$_1$ was 1:2.5). Thus the 15 was apparently present prior to methanol quenching (vide supra).

The absence of deuterium coupled with a relatively high yield of 15 prompted us to investigate the source of H in 15. To find whether the n-BuBr generated in the reaction of dibromide 24 with n-BuLi is the source of H, quantitation of

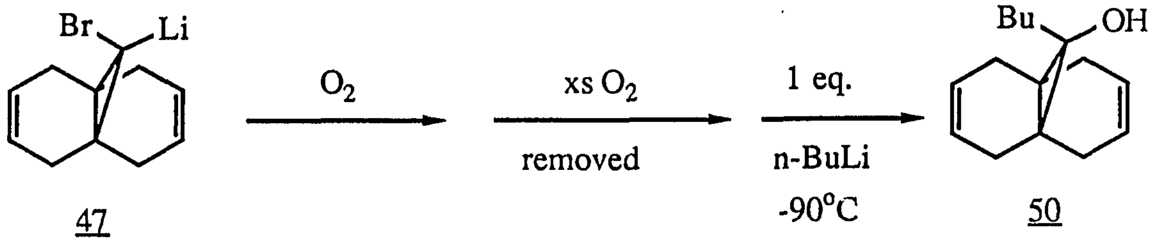


15-H

47

the n-BuBr formed was performed. The yield of n-BuBr, determined with a premeasured response factor, was found 96 ± 2%. The yield of isotetralin (48) in this case was 34% and the yield of 15 was 16%. This clearly showed that n-BuBr was not the source of H. We think it may be moisture in the oxygen that is responsible for the reduction of the carbenoid. If one takes into account this unproductive reduction reaction, the yield of 48 from oxygenated carbenoid was really greater than what was observed.

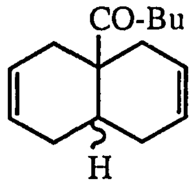
Most of the other aspects of this general reaction were studied with the carbenoid 47. The first objective was to find a suitable trap for the intermediate which leads to olefin formation. n-BuLi was initially chosen as the trap. When one equivalent of n-BuLi was added to the oxygenated solution at -90°C (after sweeping the solution with argon at -95°C to remove excess O_2), no isotetralin was observed.



47

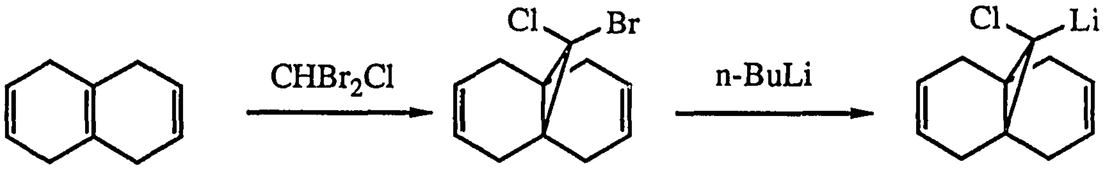
50

The major product was the alcohol 50. Alcohol 50 always gave some ring-opened isomeric butyl ketone 49 in the GC-MS.



49

After finding a trap, the second objective was to determine the temperature at which the intermediate gave isotetralin (48). After adding n-BuLi at the various temperatures to which the oxygenated solution was warmed, the formation of isotetralin (48) was followed by GC (Table 8). In this way the minimum temperature at which 48 was formed was found to be near -60°C. The third question we wanted to address was whether the yield of 48 depended on the nature of the halogen on the carbenoid. To determine this, compound 51 was synthesized and its carbenoid 52 oxidized. The oxidation of 52 and 47 were run side by side (parallel experiments). The yield of 48 was only 1-4% higher from 47 than from 52 (Table 8). This indicates that the yield of 48 is virtually independent of the nature of the halogen in the carbenoid.



48 51 52

In these experiments 1-1.1 equivalents of n-BuLi were used to generate the carbenoids. If more than one equivalent of n-BuLi was used, one could possibly expect that the pathway shown in Scheme 5 would be operative and

Table 8. Results of the n-BuLi quenching experiments[a]

T°C[c]	Percent yield[b] of 48		Percent yield[b] of 50	
	47	52	47	52
-90	0	0	>80	>80
-80	0	0	>80	>80
-70	trace	trace	>80	>80
-60	7	6	80	80
-55	7	11	75	80
-50	8	6	54	56
-45	9	6	52	46
-40	11	9	41	40
-35	16	13	18	20
20[d]	17	not done	0	-
20[d]	not done	22	-	3
20[e]	25	24	-	-

[a] In these experiments the yield of the reduced monohalides varied from 6 to 22% with no observable correlation to the yields of 48 and 50.

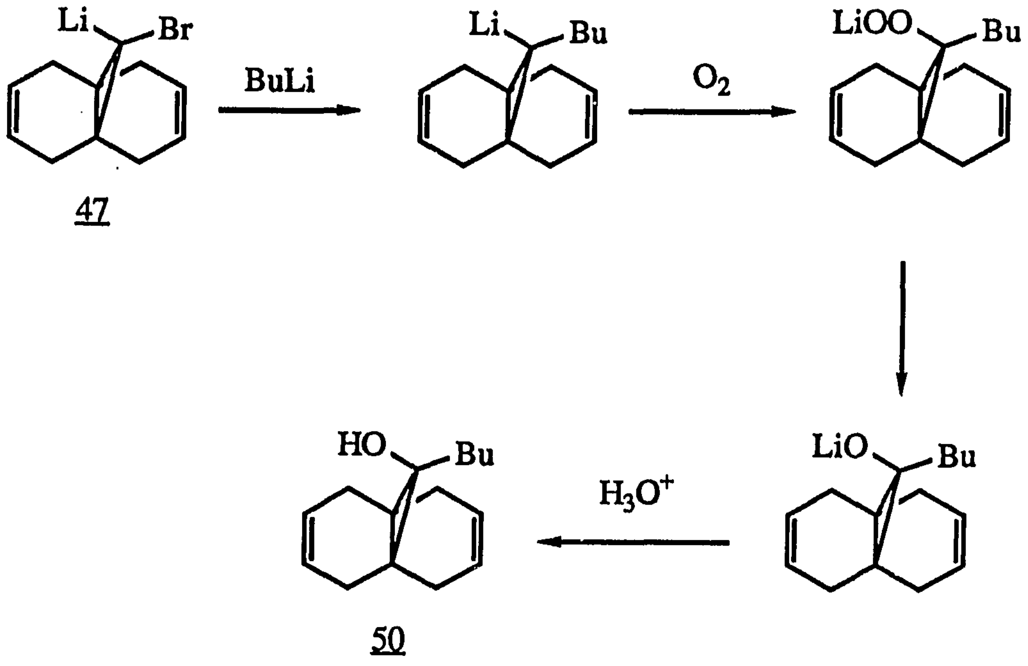
[b] The error in these values is ± 2-3%

[c] T refers to the temperature to which the oxygenated solution (after sweeping with argon at -95°C) was warmed before quenching with n-BuLi at -90°C.

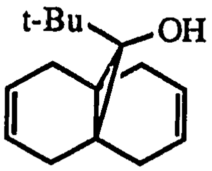
[d] In these experiments small amounts of n-butyl ketone were formed.

[e] No n-BuLi quench (quenched with aqueous NH_4Cl).

Scheme 5

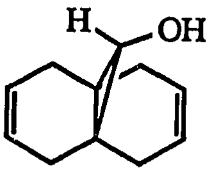


lead to the formation of 50. But the data from Table 8 indicated a common intermediate, which upon warming gave 48, and which upon quenching with n-BuLi gave 50. The formation of 48 cannot occur from any of the intermediates shown in Scheme 5, which is, therefore, eliminated. We also generated 47 by the reaction of 24 with 2 equivalents of t-BuLi and carried out its oxygenation in the same manner. After sweeping with argon, the solution was warmed to -60°C, recooled to -90°C, and quenched with 1 equivalent of n-BuLi. Again alcohol 50 was observed as the major product. The other products were monobromide 15 and 48 (7%). The ratio 15 to 50 was 1:1.6. No t-butyl-substituted alcohol product 71 was observed. A small amount of 71 was obtained in a

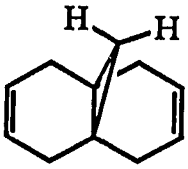


71

reaction similar to the one described above, except that 2 equivalents of t-BuLi were used to quench the oxygenated solution. In this experiment the major product was the alcohol 37. A small amount of hydrocarbon 72 and isotetralin (48) (7%) were also formed. A possible

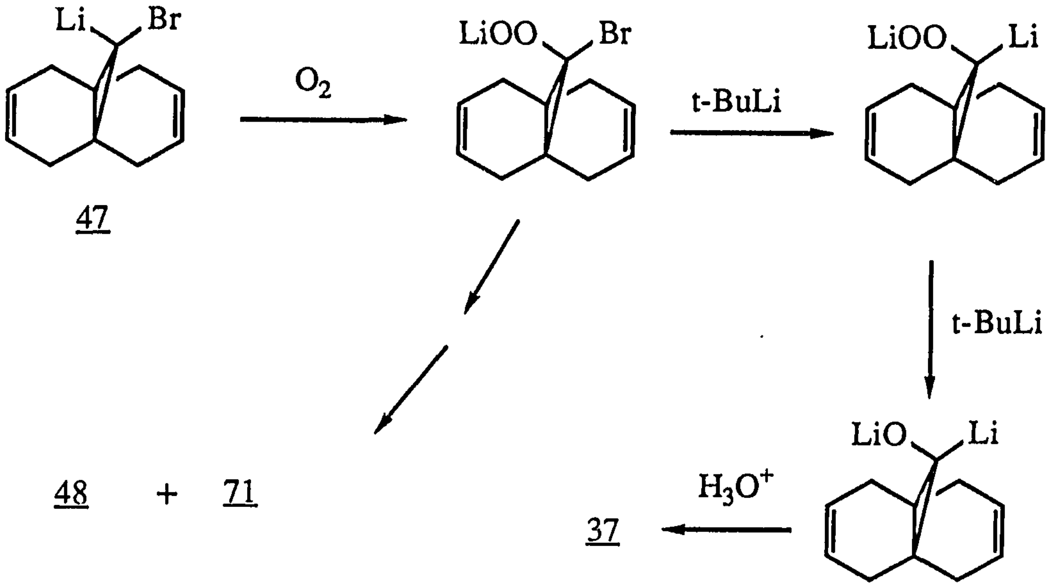


37



72

Scheme 6


Li
Br
47
O$_2$
LiOO
Br
t-BuLi
LiOO
Li
t-BuLi
LiO
Li
H$_3$O$^+$
37
48
+
71

mechanism to explain the products is shown in Scheme 6. The distinction between 50 and 71 was based on their mass spectral fragmentation patterns. Quenching the oxygenated solution at temperatures between 10° and 25°C with n-BuLi produced a small amount of di-n-butyl ketone. The formation of di-n-butyl ketone indicated possible formation of either CO or CO_2. Reactions of CO[63] and CO_2[64] with n-BuLi to give di-n-butyl ketone are documented in the literature. We also repeated these reactions and observed the formation of di-n-butyl ketone and tributylcarbinol.

Analysis of the gaseous product of the reaction by high resolution mass spectroscopy and high resolution gas-phase IR (Figure 20) revealed mainly CO formation. Some CO_2 was also observed. The relative amounts are unknown, since we do not know the necessary correction factors. The formation

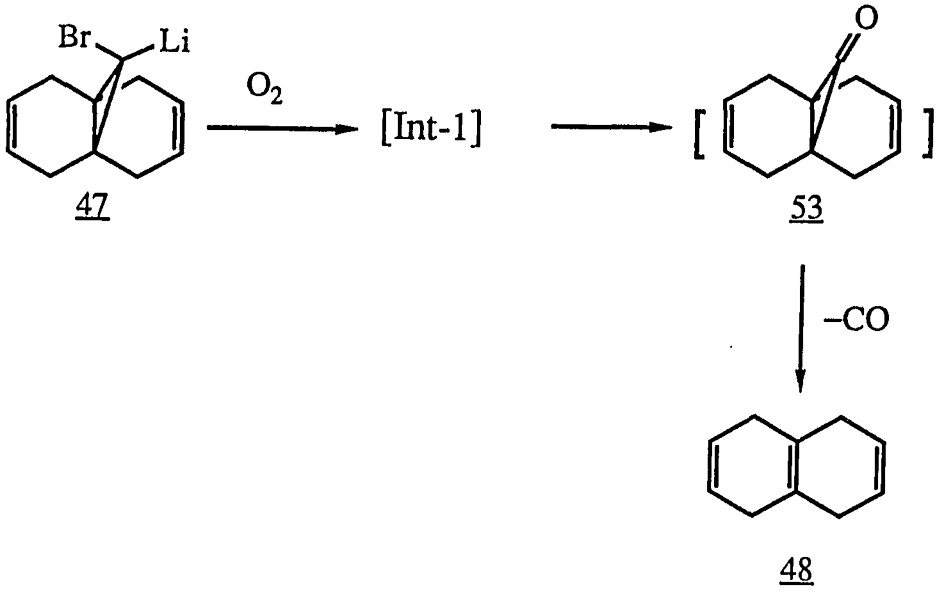
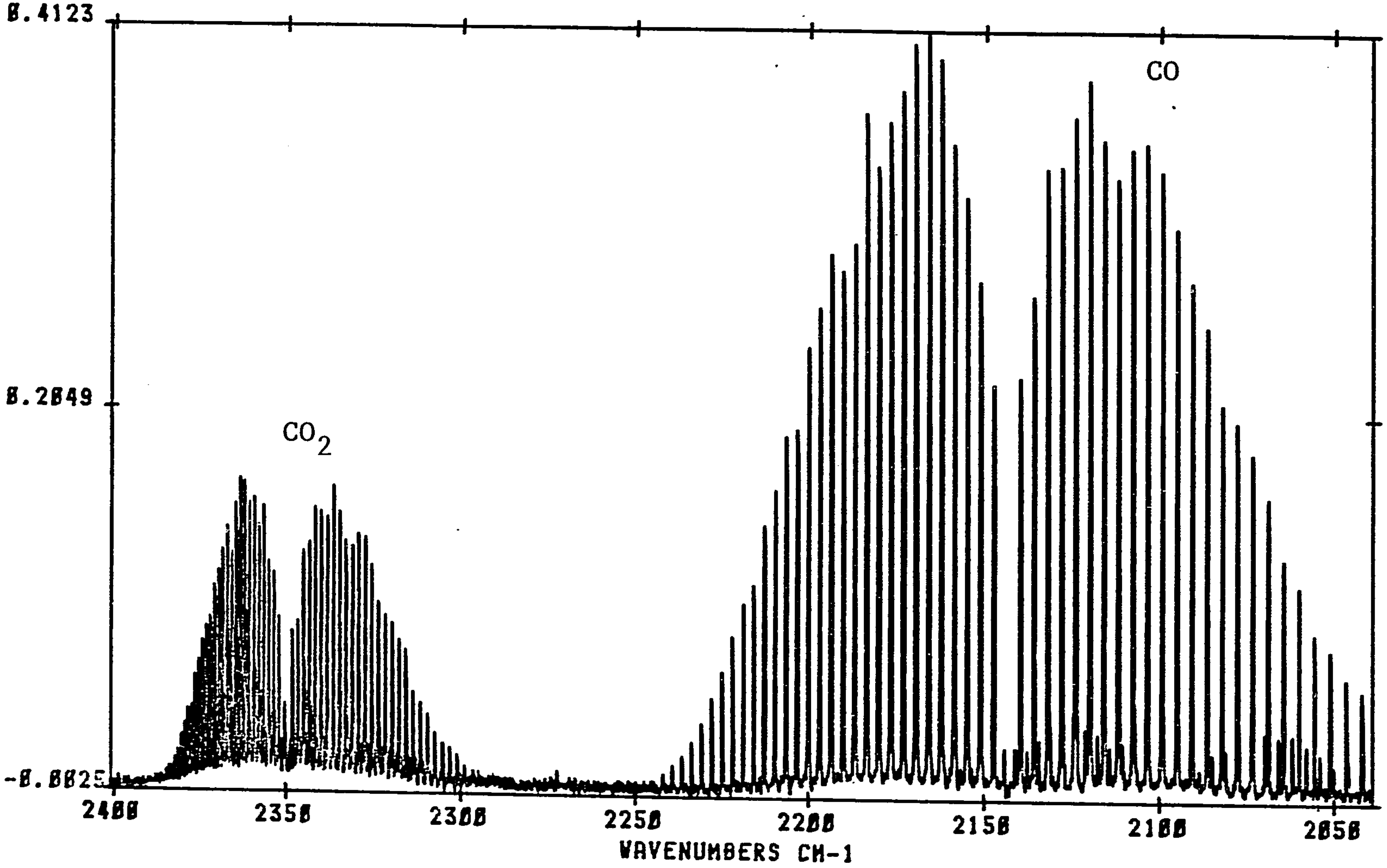
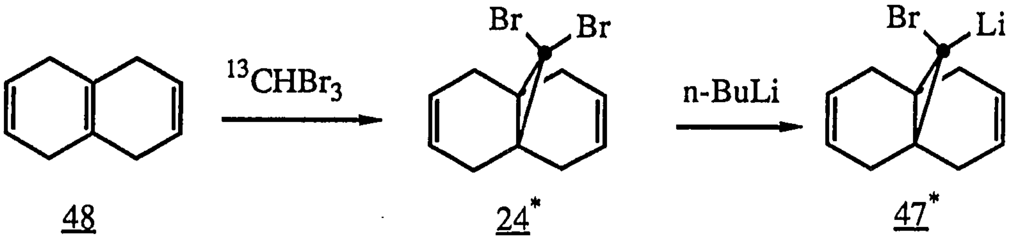


Figure 20. IR (gas phase) of gaseous products involved in the oxygenation of 47


0.4123
0.2049
-0.0025
CO$_2$
CO
2400
2350
2300
2250
2200
2150
2100
2050
WAVENUMBERS CM-1

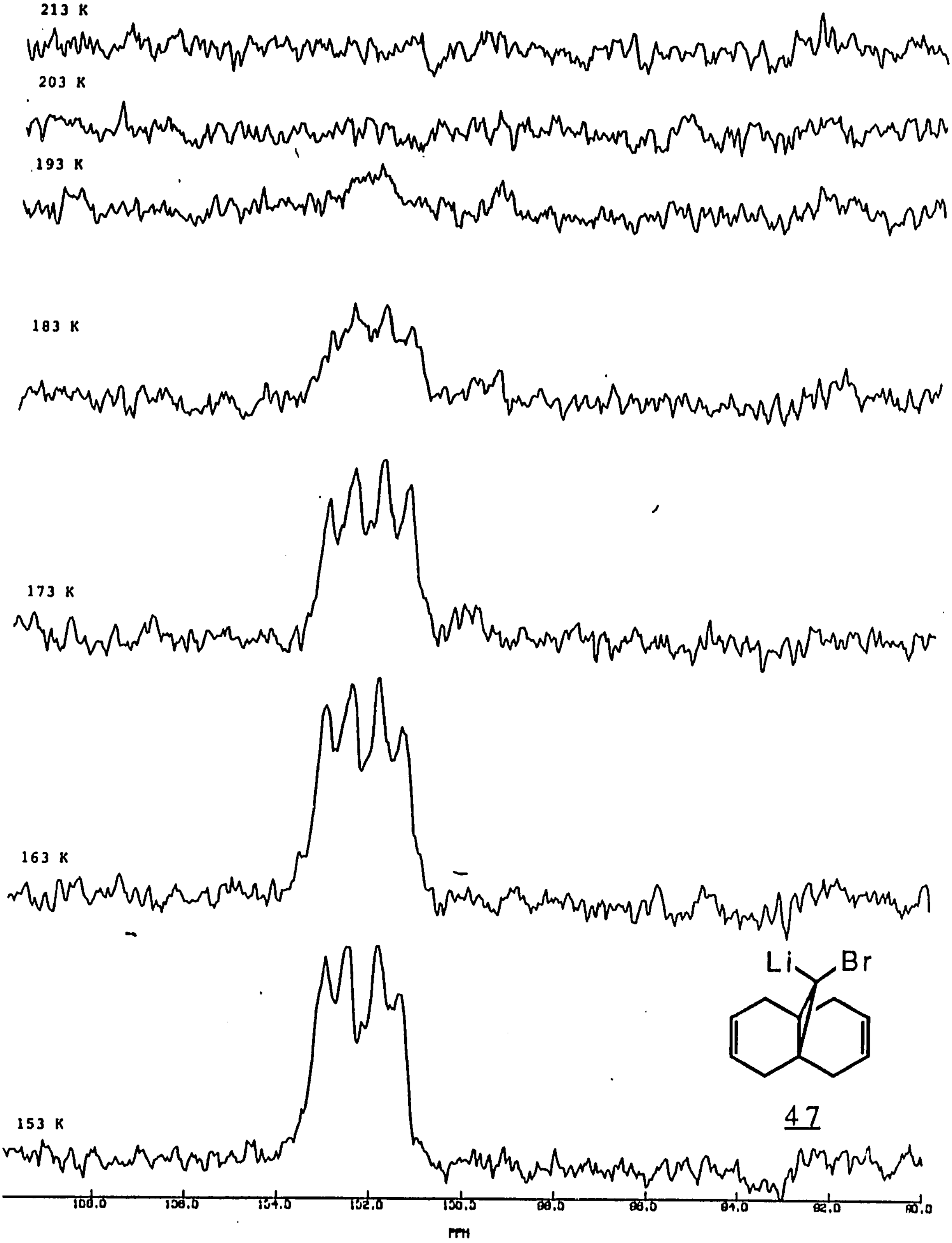
of CO suggested the probable involvement of the cyclopropanone intermediate 53. In order to probe the structures of the intermediates, the C-13 labeled dibromide 24* was synthesized and the oxidation of the derived carbenoid 47* was followed by ^{13}C NMR. Thus, 0.13-0.16 mmol



*= ^{13}C

of labeled dibromide 24* in 2 mL d$_8$-THF was converted to the carbenoid 47* at -95°C with one equivalent of n-BuLi in an NMR tube. The carbenoid was oxygenated and excess oxygen was removed by freeze vacuum thaw cycles. The ^{13}C NMR was recorded at various temperatures between -110° and 20°C. Some representative spectra are shown in Figures 22-24. The spectrum of the starting carbenoid is shown in Figure 21. In Figures 22-24, we assign the peak at δ 224.5 ppm to the carbonyl oxide 56. There are two peaks at δ 99 and δ 104 ppm, one of which we assign to the dioxirane 55 and the other either to bromoperoxylithium compound 54 (Scheme 7) or a diperoxide intermediate (vide supra). These peaks persist until -60° to -50°C, which is consistent with the results of the trapping experiments with n-BuLi. The relaxation time (T$_1$) (measured by the spin inversion recovery technique) of

Figure 21. ^{13}C NMR (d_8-THF) of carbenoid 47*


213 K
203 K
193 K
183 K
173 K
163 K
153 K
Li
Br
108.0
106.0
104.0
102.0
100.0
98.0
96.0
94.0
92.0
90.0
PPM

47

Figure 22. ^{13}C NMR (d_8-THF) of the intermediates involved in the oxygenaton of 47*

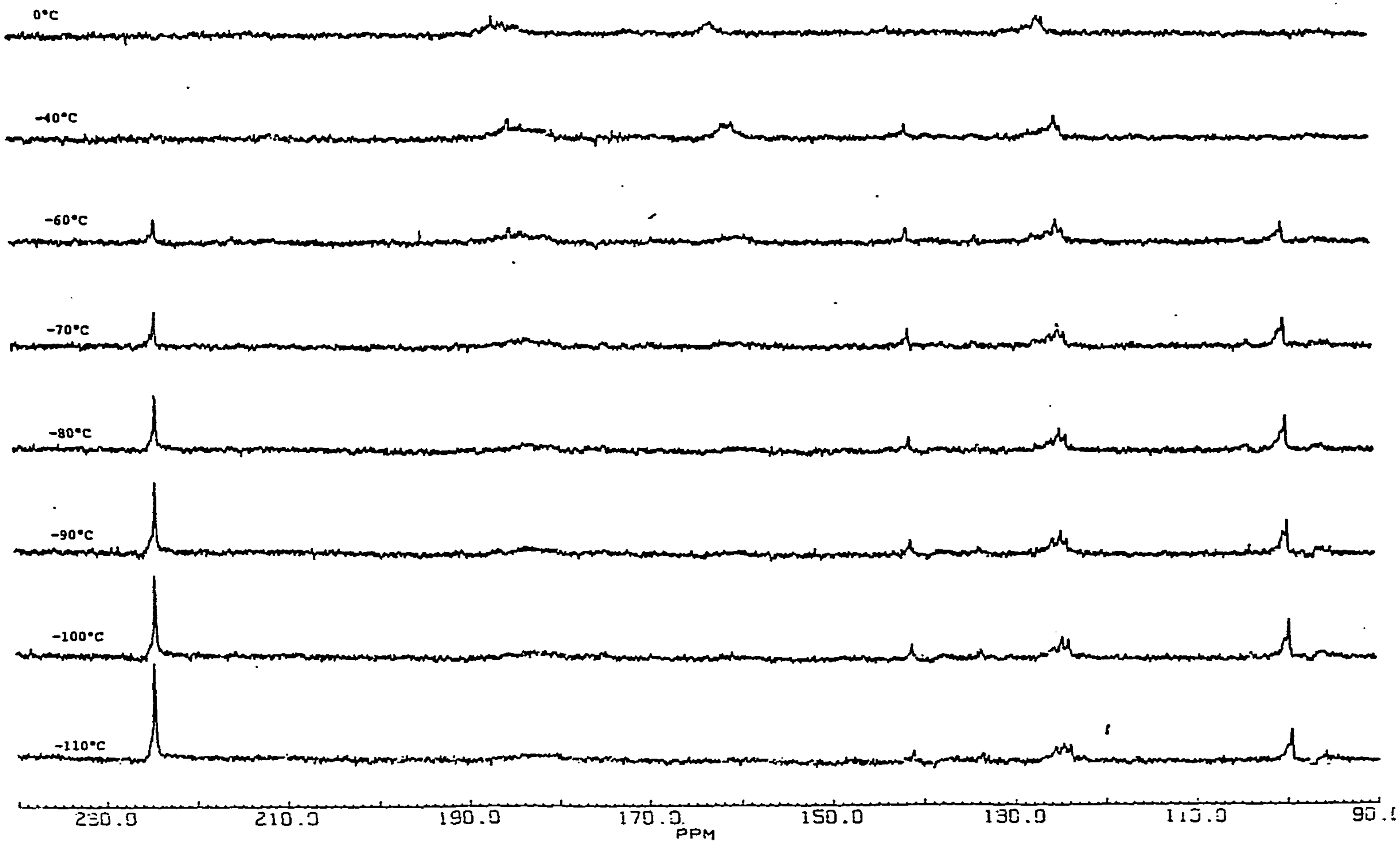

0°C
-40°C
-60°C
-70°C
-80°C
-90°C
-100°C
-110°C
230.0
210.0
190.0
170.0
150.0
130.0
110.0
90.0
PPM

Figure 23. ^{13}C NMR (d_8-THF) of the intermediates involved in the oxygenation of carbenoid 47*

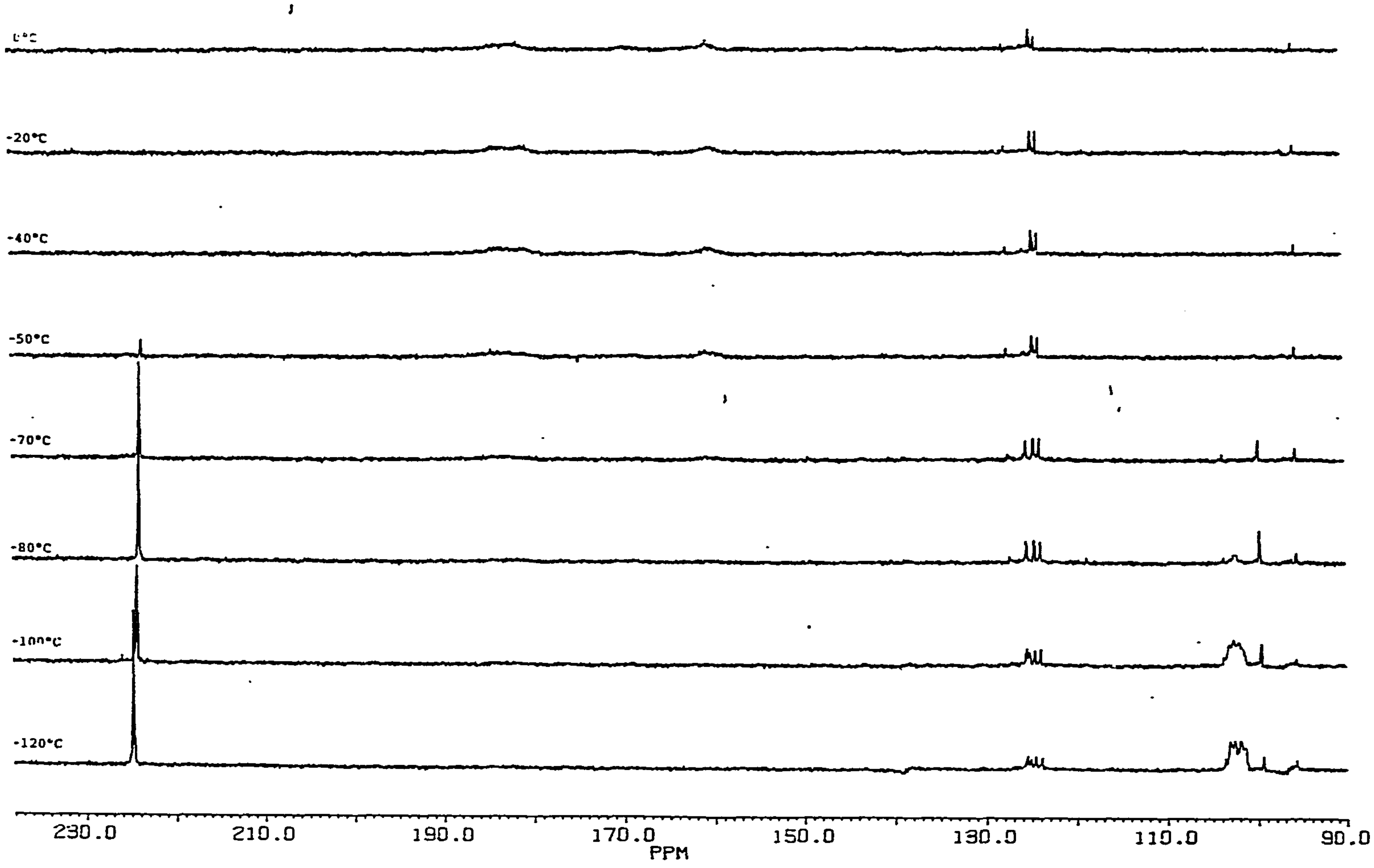
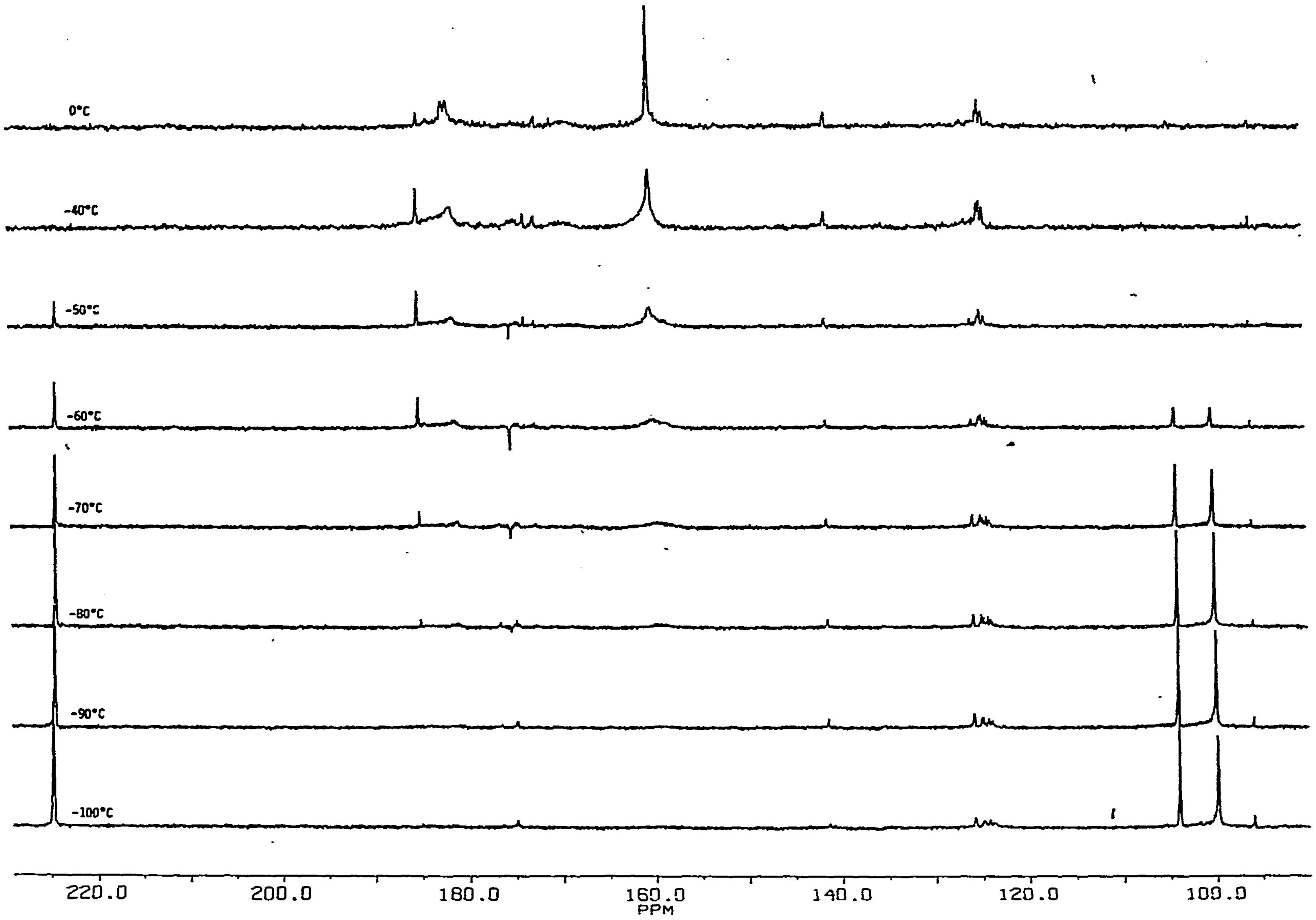
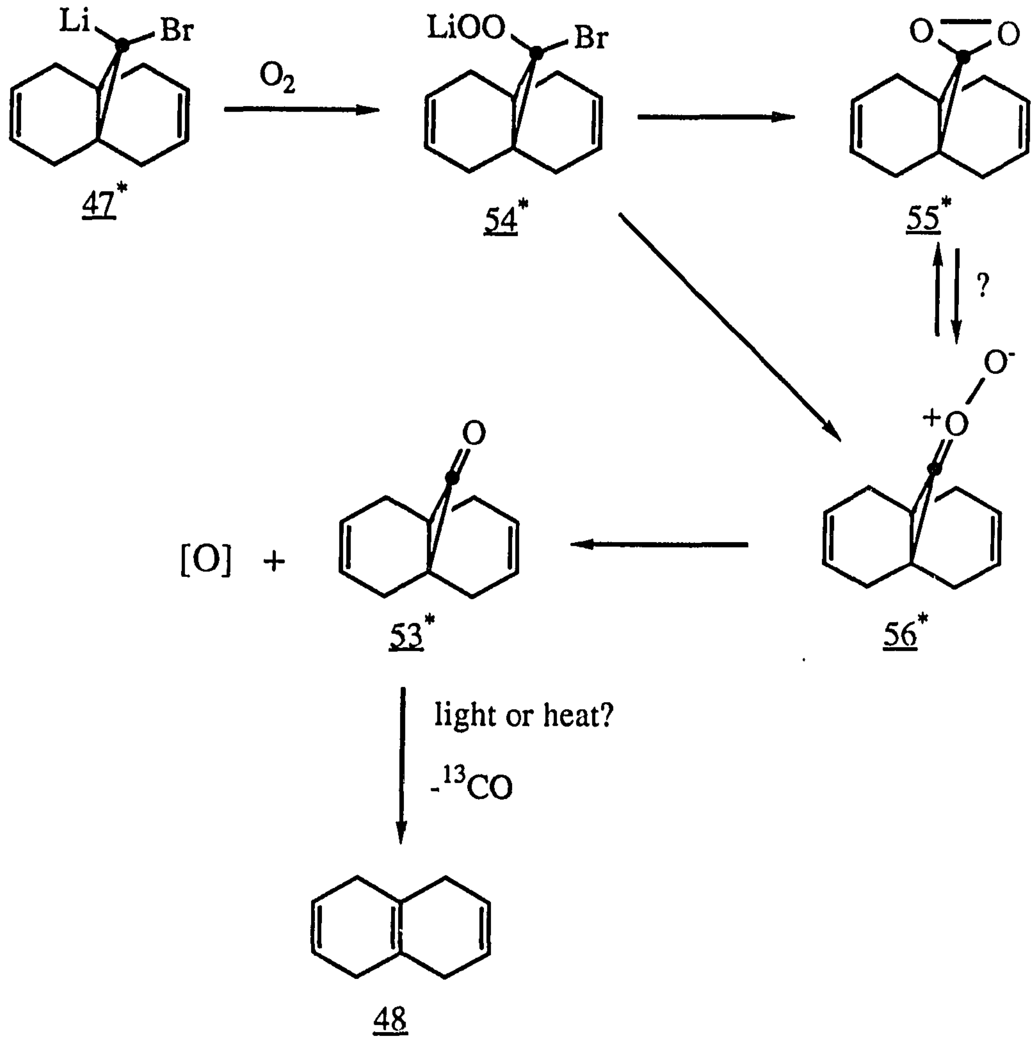

0°C
-20°C
-40°C
-50°C
-70°C
-80°C
-100°C
-120°C
230.0
210.0
190.0
170.0
PPM
150.0
130.0
110.0
90.0

Figure 24. ^{13}C NMR (d_8-THF) of intermediates involved in the oxygenation of 47*

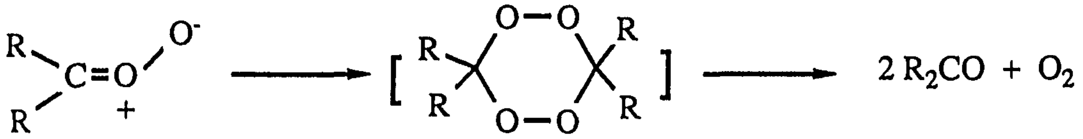

0°C
-40°C
-50°C
-60°C
-70°C
-80°C
-90°C
-100°C
220.0
200.0
180.0
160.0
PPM
140.0
120.0
100.0

the peak at δ 224.5 ppm is 1.3 s, and those of the peaks at δ 99 and δ 104 ppm are 2.0 and 2.5 s, respectively.

Scheme 7


Li
Br
47*
O2
LiOO
Br
54*
O
O
55*
?
O-
+O
56*
[O] +
O
53*
light or heat?
-13CO
48

Both 55 and 56 are probably formed through the same intermediate 54 in a parallel pathway, although one cannot rule out a possible conversion of 56 to 55 by light under the conditions of the NMR experiment. In the latter case, an equilibrium between 55 and 56 is what one has to assume from the ^{13}C NMR results. The decomposition of carbonyl oxides to the corresponding carbonyl compounds and oxygen is known in the literature.[49] In some cases (e.g., R = Ph) the



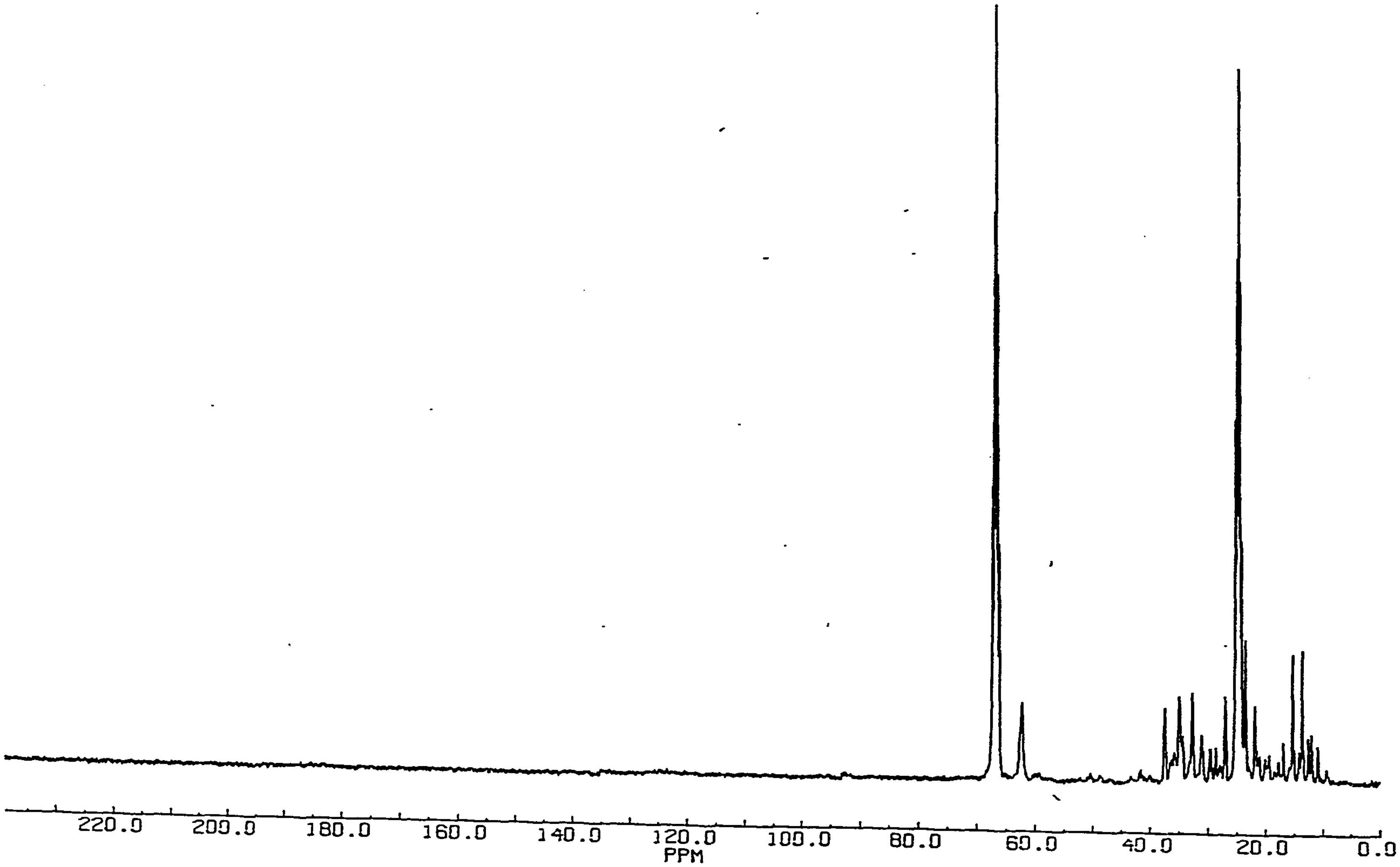
diperoxide intermediates are stable, and in such cases the conversion of carbonyl oxides to the corresponding carbonyl compounds do not proceed through these intermediates. Murray and Jeyaraman[54] have suggested the same dimerization leading to diperoxides for dioxiranes, too. So in our study, one could anticipate such a reaction leading to the cyclopropanone 53. The dioxygenated carbon of cyclic acetals and ketals absorbs in the range of ~ δ 88-112 ppm. In our case, it is possible that one of the peaks in the δ 99-104 ppm region is due to a diperoxide intermediate. We did not observe any peak for 53 in our NMR study, the probable reason for which will be discussed later. In Figure 24, one wants to know the assignment for the peak at δ 160 ppm that builds up from -70°C onwards. In this particular experiment, the solution was allowed to rise in temperature rather rapidly compared to the other experiments. This peak could not be reproduced in subsequent experiments. One would expect a more deshielded chemical shift for 53, and hence it is difficult to assign this peak to 53.

Another problem to be addressed is the decarbonylation of 53. Generally, decarbonylation of cyclopropanones requires a relatively high temperature, although decarbonylation under photolytic conditions takes place easily.[65] A control experiment, carried out in the absence of light, still showed the formation of isotetralin. Perhaps the cyclopropanone 53 is formed in a "hot" state with excess energy that is responsible for spontaneous decarbonylation. We attempted to obtain ^{13}C NMR evidence for the production of CO (recall that CO was observed by IR and MS). The reported chemical shift of CO is 181.3.[66] We attempted to find the chemical shift of CO in THF, but failed.

We also thought about a possible CO_2 extrusion from 55 (recall that some CO_2 was observed by IR), but none of it was observed from these reactions by ^{13}C NMR. The reported[66] chemical shift of carbon dioxide is δ 132 ppm, which we also observed after dissolving some dry ice in d_8-THF. The chemical shift we found was δ 125.9 ppm. The absence of CO_2 in the ^{13}C NMR is consistent with the high resolution mass spectral data which showed only a trace of CO_2. Perhaps some air had leaked into the IR cell, which was responsible for the larger CO_2 peak.

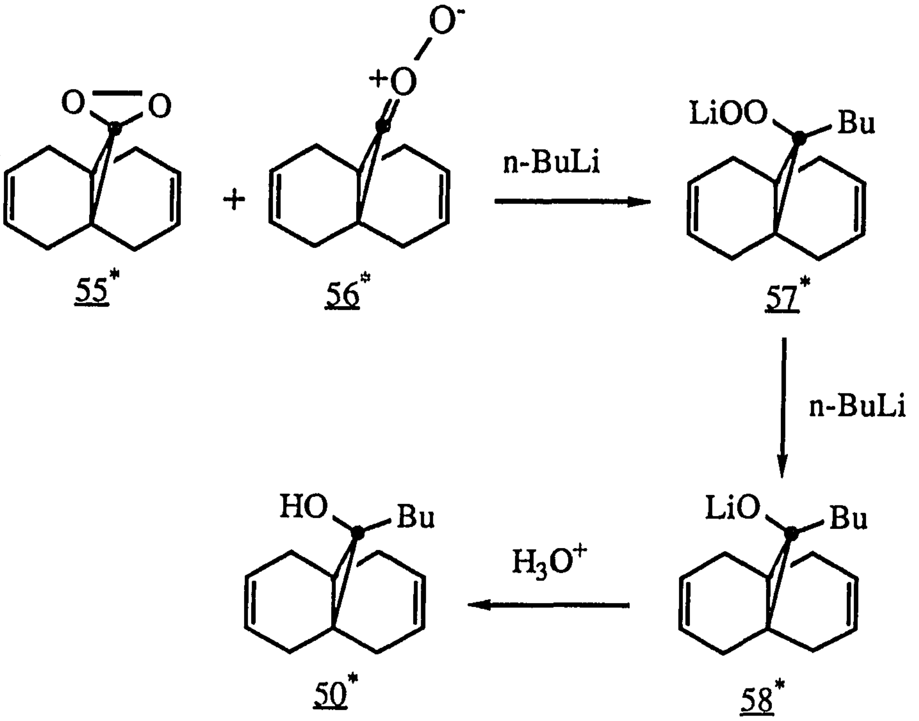
Quenching of the oxygenated solution of 47* at 10°C with n-BuLi gave rise to a small amount of di-n-butyl ketone with

Figure 25. ^{13}C NMR (d_8-THF) of n-BuLi quenched product of the intermediates


220.0
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
PPM

the C-13 label on the carbonyl carbon (mass spectrum). On quenching the oxygenated solution at -95°C with n-BuLi, the peaks due to carbonyl oxide and dioxirane disappeared in the ^{13}C NMR (Figure 25). The peaks due to 57 and 58 were

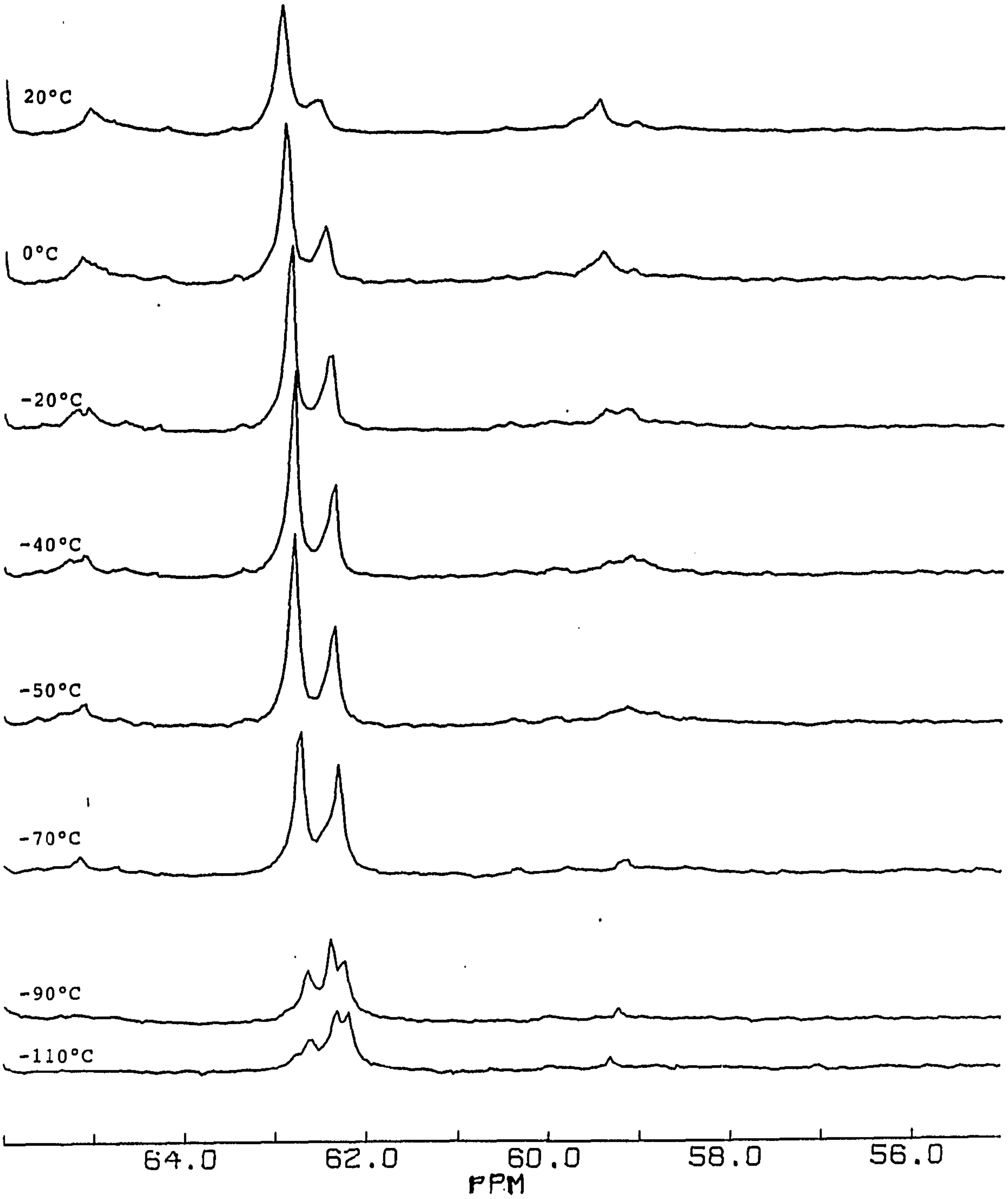
Scheme 8



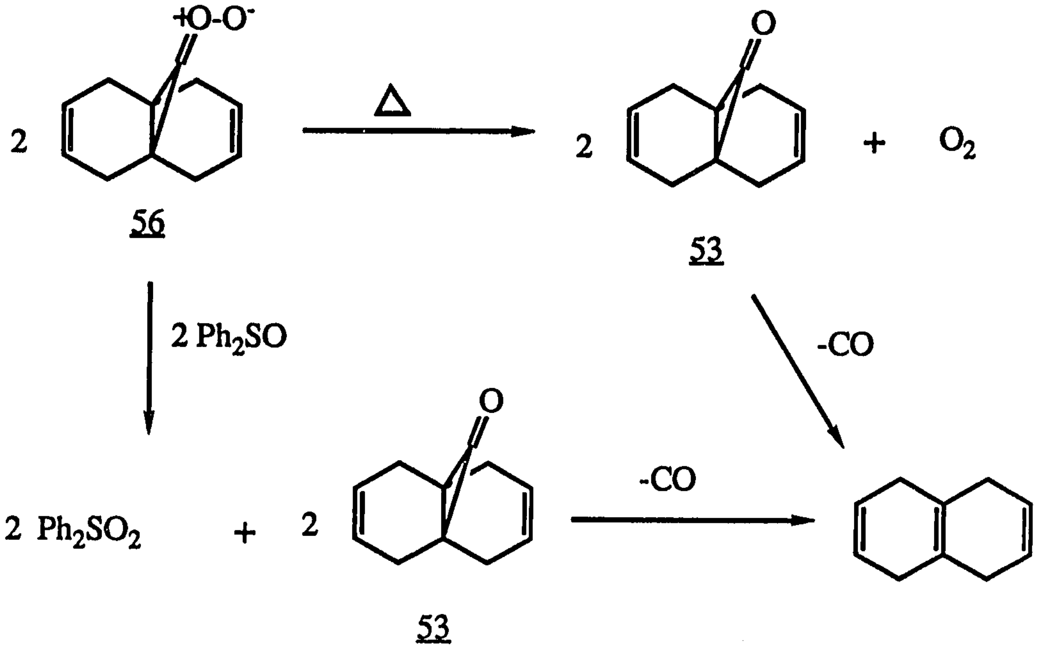
observed at δ 62.3 and δ 62.7, respectively (Figure 26). Aqueous work-up of the reaction mixture gave rise to the labeled alcohol 50* (mass spectrum). These products are rationalized in Scheme 8.

So far all the evidence supports the carbonyl oxide 56 and the dioxirane 55 as intermediates. Based on the known reactions of carbonyl oxides and dioxiranes, some oxidation reactions were attempted. Oxidation of olefins like t-stilbene, and 2-pentene failed to give any epoxides.

Figure 26. ^{13}C NMR (d_8-THF) of n-BuLi quenched product of the intermediates

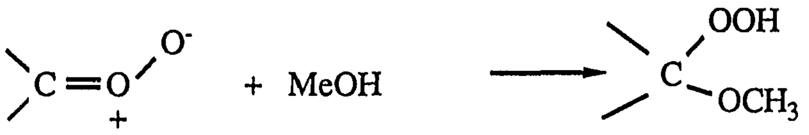

20°C
0°C
-20°C
-40°C
-50°C
-70°C
-90°C
-110°C
64.0
62.0
60.0
58.0
56.0
PPM

Oxidation of Ph_2SO gave 3-7% yield of Ph_2SO_2. We carried out control experiments to make sure that the oxidation was effected only by the reaction intermediates of interest, and not by O_2 or BuOOLi (see Experimental). When two experiments were run in parallel, one with added sulfoxide (after oxygenation of the carbenoid and excess oxygen removal), and the other without any added sulfoxide, the yield of 48 formed in both experiments was 11%. The yield of sulfone formed in the former was 7%. This supports the mechanism of bimolecular decomposition of carbonyl oxide 56

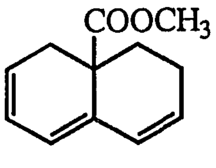


to the corresponding cyclopropanone 53, which subsequently undergoes decarbonylation. The added sulfoxide is oxidized to sulfone with 53 as the other product.

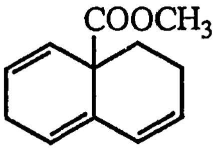
Reaction with CH_3CHO did not seem to indicate any ozonide formation. The probable reasons for the poor oxidation or failure of these reactions are the low yield of the intermediate, and the low temperature at which these intermediates exist. Reaction of carbonyl oxide with MeOH is known to give hydroperoxides.[50]



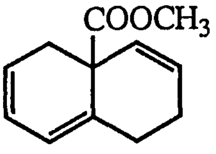
In this case, when MeOH was added to the oxygenated solution at -90°C, two methyl esters 59 and 60 were formed in an approximately 2:1 ratio. The structures of 59 and 60 are based on the GC-IR and GC-MS of the (capillary GC) separated esters and the ^{13}C NMR, ^{1}H NMR and UV spectra of the mixture of esters. The UV spectrum was particularly helpful in assigning the structure for 59. The λ_{max} of 270 nm is indicative of a homoannular diene with three ring residues and one exocyclic double bond. The other possible structures are the isomers 73-76.



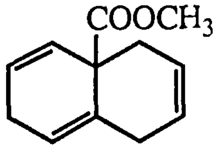
73



74

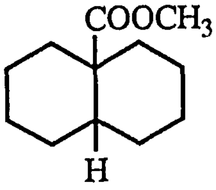


75



76

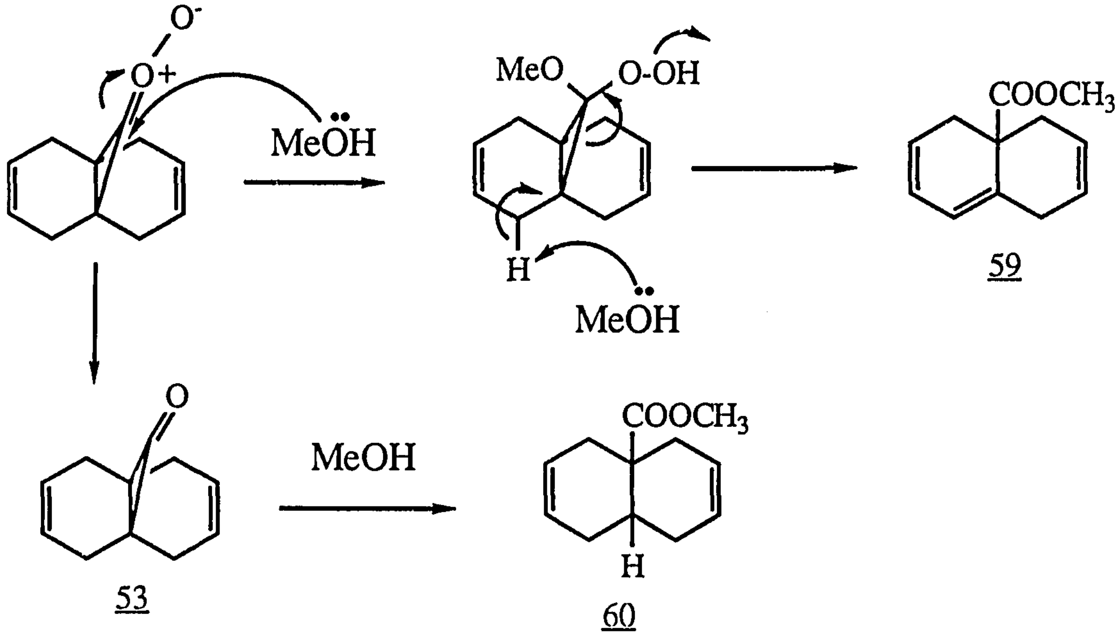
Triene 73 would be expected to have an absorption at 303 nm. Trienes 74 (a heteroannular diene, λ_{max} (expected) 234 nm) and 76 (a non-conjugated diene, λ_{max} (expected) < 200 nm) are expected to absorb at much lower wavelengths. Structure 75 is less probable because the double bond isomerization from 59 to 75 does not lead to any extra stabilization. Catalytic hydrogenation of the mixture of esters 59 and 60 led to the saturated ester 78, the stereochemistry[67] of which was found to be cis. The



78

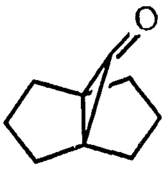
probable mechanism leading to the formation of these esters is shown in Scheme 9.

Scheme 9


O-
O+
MeOH
MeO
O-OH
H
MeOH
COOCH3
59
O
53
MeOH
COOCH3
H
60

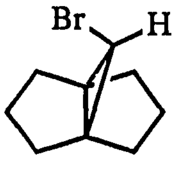
We also carried out concentration dependence studies to test whether the bimolecular self reaction of carbonyl oxide 56 or dioxirane 55 leads to isotetraline (48) via the diperoxide and cyclopropanone intermediates. Thus, when solutions of two different concentrations, 0.08 M and 0.016 M, of the carbenoid 47 were oxygenated under identical conditions, the yields of 48 formed were 24% and 15%, respectively. Thus, the high concentration solution led to a higher yield of 48 compared to the low concentration solution. The increase in yield is much lower than what one would expect for a five-fold increase in concentration of the carbenoid. But there is no way to know whether there was a five-fold increase in concentration of carbonyl oxide formed.

We also wanted to study the oxygenation of a carbenoid which might lead to a stable cyclopropanone. Warner and Lu[68] isolated the cyclopropanone 61 in their studies of the silver assisted hydrolysis of the corresponding



61

dihalocyclopropane. They reported the ^{13}C chemical shifts (carbonyl carbon: δ 174 ppm) and the IR spectrum of this compound. We prepared the dibromide 62 as per the literature procedure[69] in seven steps starting with 1,5 cyclooctadiene. We generated its carbenoid 63 and carried out the oxidation. Again the corresponding olefin, 67, was observed in addition to the monobromide 77 and some unidentified products. We also synthesized the ^{13}C labeled dibromide 62^* and performed the oxidation of its carbenoid 63^*. The ^{13}C NMR spectrum of 63^* is shown in Figure 27. The ^{13}C NMR was recorded at various temperatures between -110°C and -40°C and is shown in Figure 28. We observed



77

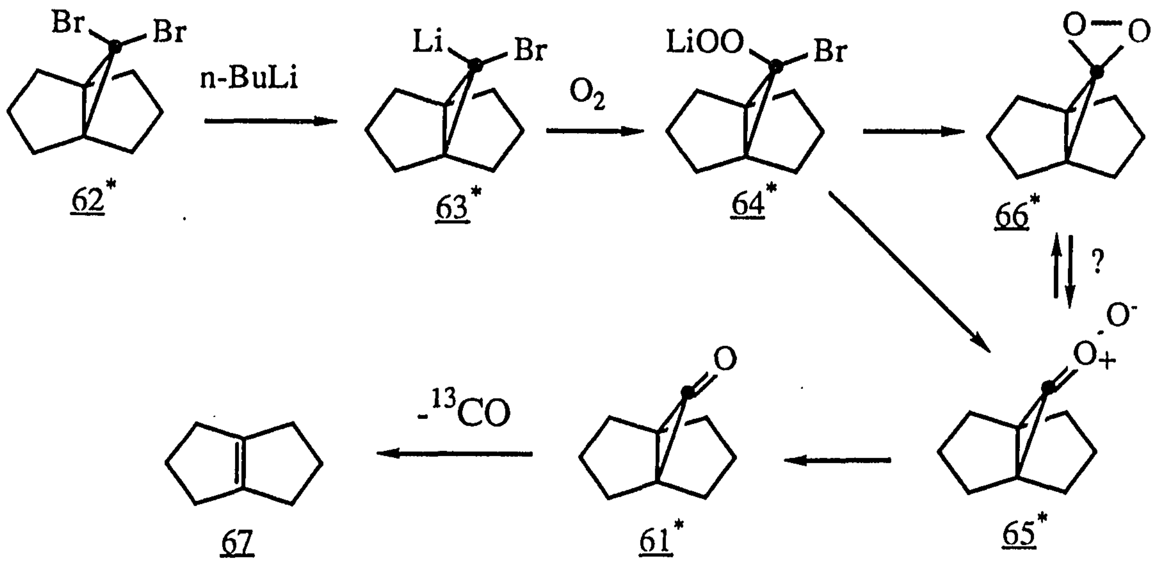
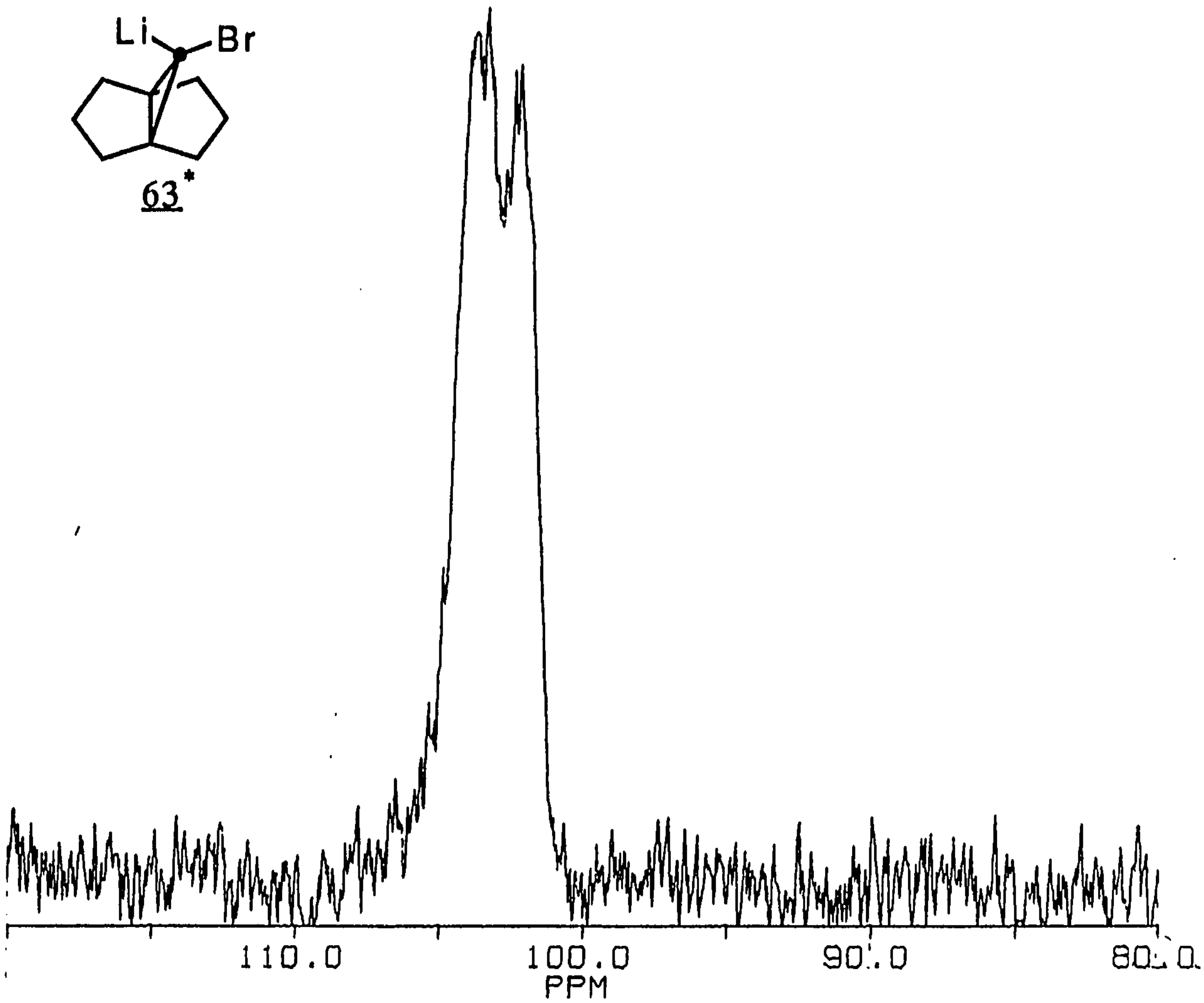
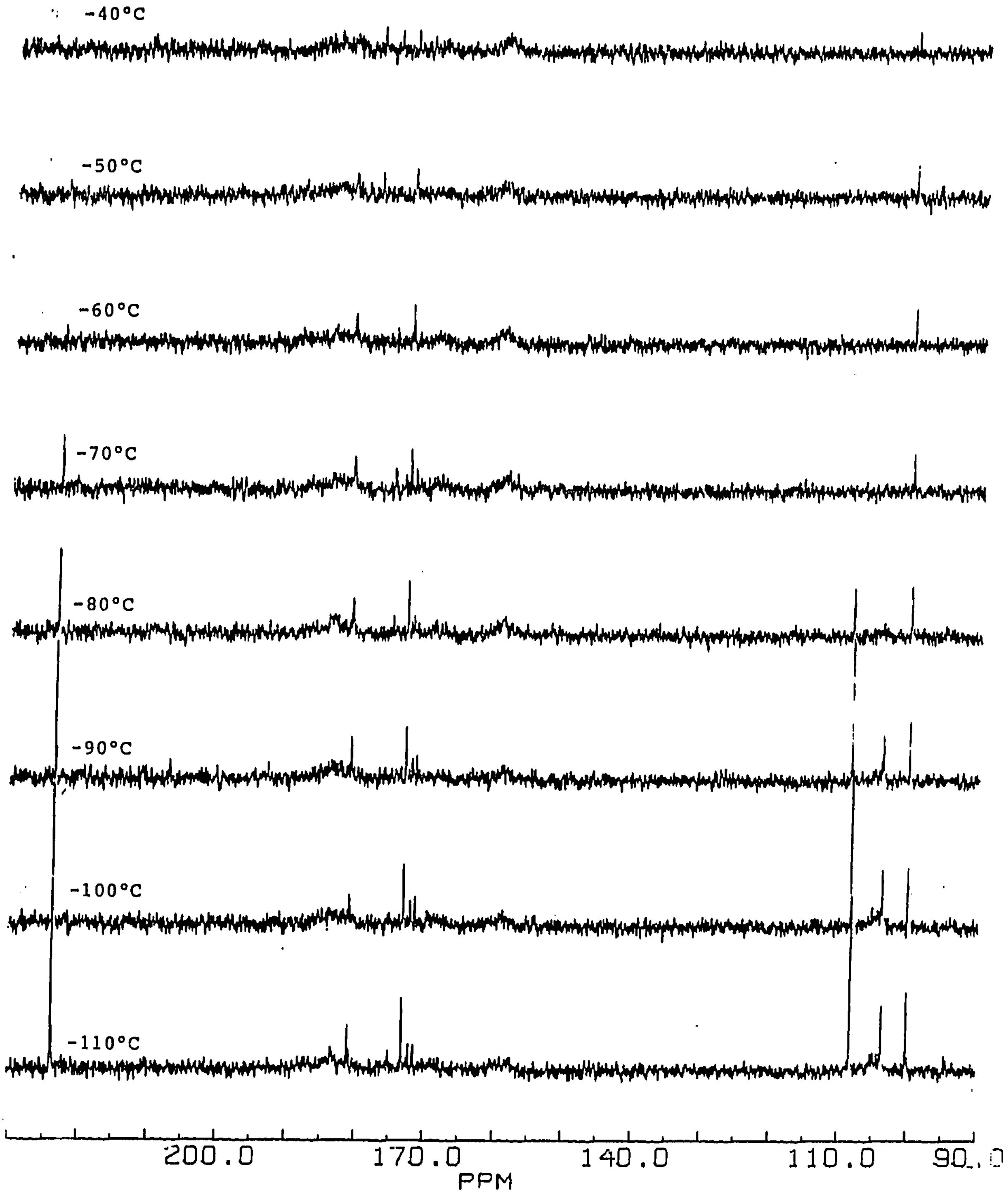

Br
Br
62*
n-BuLi
Li
Br
63*
O2
LiOO
Br
64*
O
O
66*
?
O-
O+
65*
O
61*
-13CO
67

Figure 27. ^{13}C NMR (d_8-THF) of carbenoid 63

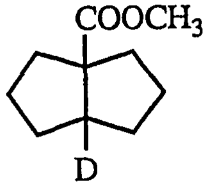


$\underline{63}^*$

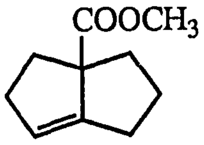
Figure 28. ^{13}C NMR (d_8-THF) of the intermediates involved in the oxygenation of 63


-40°C
-50°C
-60°C
-70°C
-80°C
-90°C
-100°C
-110°C
200.0
170.0
140.0
110.0
90.0
PPM

peaks due to 65 at δ 224.5 ppm and peaks for 64 and 66 in the δ 100-109 ppm region. Importantly we also observed a peak for the cyclopropanone 61 at δ 173 ppm. The IR of the crude product showed a carbonyl stretching at 1820 cm^{-1}. This strongly supports a cyclopropanone intermediate in these reactions. The GC-MS of the product mixture showed a small amount of 67. Trapping of the intermediates in the oxidation of unlabeled carbenoid 63 with MeOD at -90°C gave rise to two methyl esters, 68 and 69, in the ratio (GC) of 1:1.5. The structures for these esters are supported by the IR, ^{1}H NMR and GC-MS spectra of the mixture.



68



69

In conclusion, we have observed, for the first time, the ^{13}C chemical shifts of carbonyl oxides, and ours is the first report of the coexistence of both carbonyl oxides and dioxiranes in solution.

Experimental

Preparation of 11,11-dibromo[4.4.1]propella-3,8-diene (24) (Figures 29, 30)

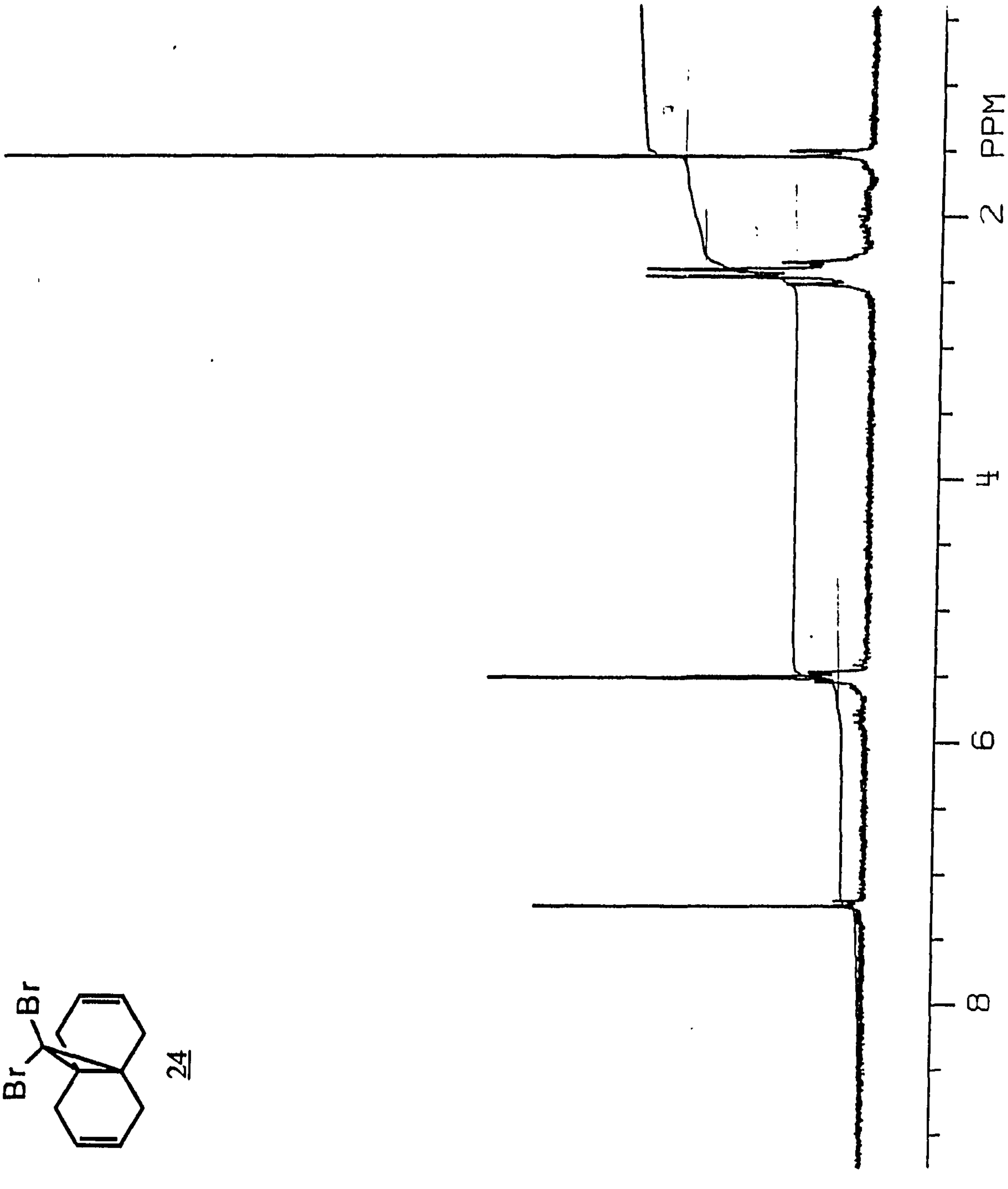
Compound 24 was prepared by the method of Thompson et al.[16] Thus, a solution of 15.4 g (60.5 mmol) of bromoform in 60 mL of pentane was added dropwise to a mechanically stirred slurry of 8.0 g (60.5 mmol) of isotetralin (48) and 10.2 g (91.0 mmol) of KOtBu in 100 mL pentane cooled to -40°C under nitrogen. After the addition was complete, the stirred mixture was allowed to slowly warm to room temperature over 4 h. The supernatant solution was decanted, washed with cold water, and concentrated. The wash water was added to the reaction sludge with an additional 100 mL of water, the aqueous mixture was extracted with methylene chloride (4 x 50 mL), and the combined organic layer was washed with saturated sodium chloride (100 mL), dried, and concentrated. The semisolid residue was heated until molten, diluted with 8 mL of hot ethyl acetate, and triturated with 8 mL of methanol. The filtered solid was sublimed (110°-120°C, 1-2 torr) to give 7 g (38%) of 24 as white crystals, mp. 108-112°C (lit. mp[16] 104-120°C).

IR (KBr): 3030 (m), 2934 (m), 2826 (w), 1443 (s), 1433 (s), 1182 (m), 1130 (m), 1111 (s), 1016 (s), 988 (m), 933 (m), 783 (s), 721 (s), 667 (s), 644 (s), 619 (m).

^{1}H NMR (CDCl$_3$): 5.5 (m, 4 H), 2.4 (m, 8 H).

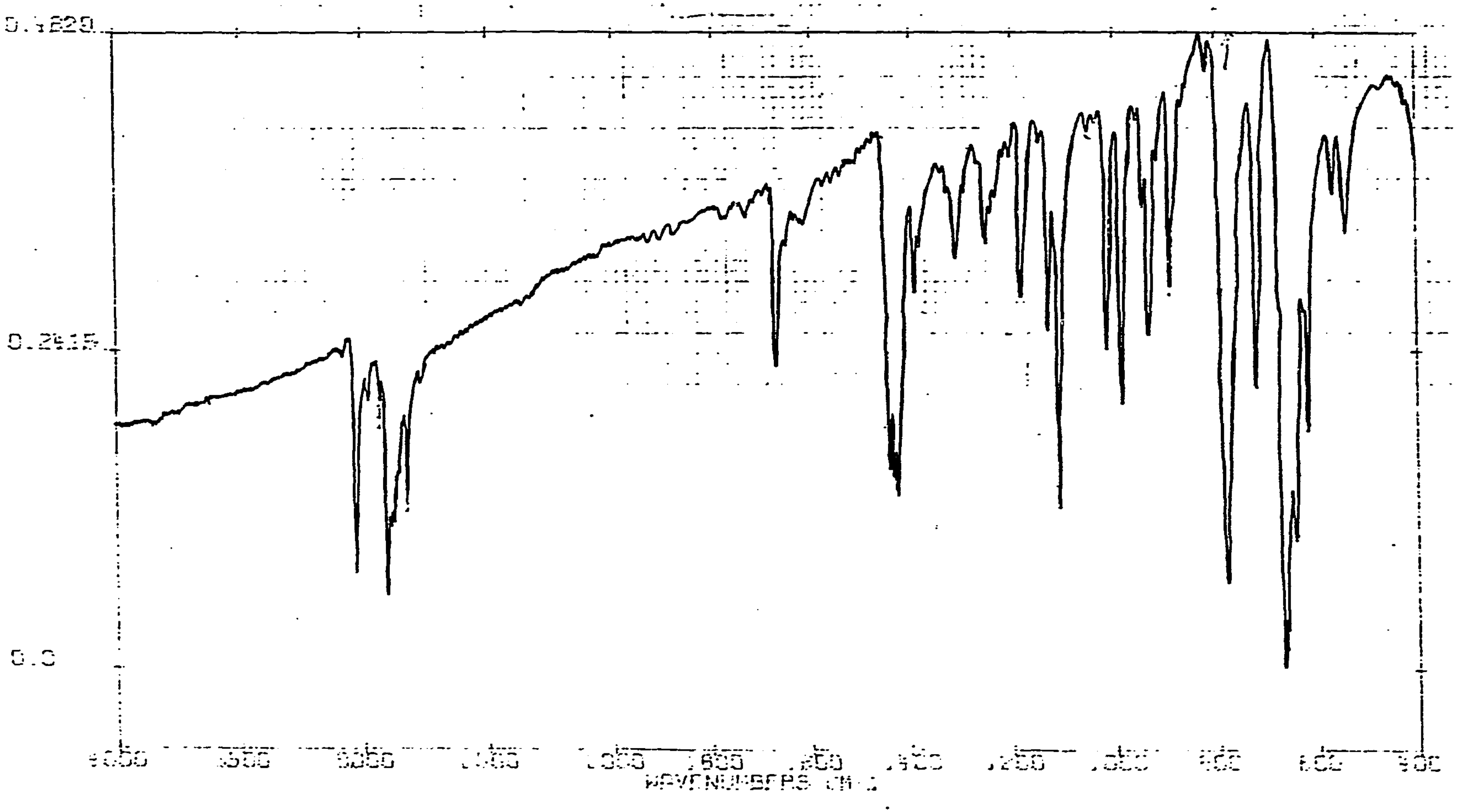
^{13}C NMR (CDCl$_3$): 123.5, 54.3, 32.7, 25.1.

Figure 29. ^{1}H NMR ($CDCl_3$) of 24



24

Figure 30. IR (KBr) of 24


0.4829
0.2415
0.0
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
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Procedure for the oxygenation of carbenoid 47

To a solution of ∼0.25 mmol of dibromide 24 in 4 mL THF at -90°C to -95°C was syringed slowly under argon, 0.25 mmol of 2 M n-BuLi in hexane. After stirring for 2-3 min at this temperature, dry oxygen (precooled by passing through a spiral glass tube of ID = 8 mm immersed in a -78°C bath) was bubbled very slowly for 20-30 min at -90°C to -95°C. Excess oxygen was removed by three freeze vacuum thaw cycles. [In some experiments, excess O_2 was removed by sweeping with (bubbling) Ar through the solutions for 20-25 min at -95°C.] The solution was allowed to warm to various temperatures and treated with 50% aqueous NH_4Cl solution (2 mL). The organic material was extracted with ether (5 mL) and the ether layer was analyzed by GC-MS. The yields of isotetralin (48) and monobromide 15 were determined with the use of predetermined response factors with mesitylene as internal standard (R_f: 48, 0.9, 15, 1.4).

GC-MS of 48: 132 (100.0), 131 (25.3), 128 (20.6), 117 (74.1), 116 (18.4), 115 (33.4), 104 (27.2), 91 (92.1), 78 (87.4), 65 (24.6), 54 (63.0), 51 (23.7).

GC-MS of 71: 130 (100.0), 129 (49.5), 127 (22.2), 115 (43.4), 102 (5.7), 77 (7.9), 64 (23.8), 51 (16.2).

GC-MS of 15: 226 (4.0), 224 (4.2), 145 (100.0), 129 (13.4), 128 (13.1), 117 (36.2), 115 (17.9), 105 (11.0), 91 (74.1), 79 (27.4), 77 (15.0), 67 (52.3), 51 (13.3).

Preparation of labeled carbenoid 47^*

Labeled dibromide 24^* was prepared by the reaction of isotetralin (48) with $^{13}CHBr_3$/KOtBu as per the procedure described by Seebach, et al.[69] and was lithiated with 1 equivalent of nBuLi at -90°C in THF.

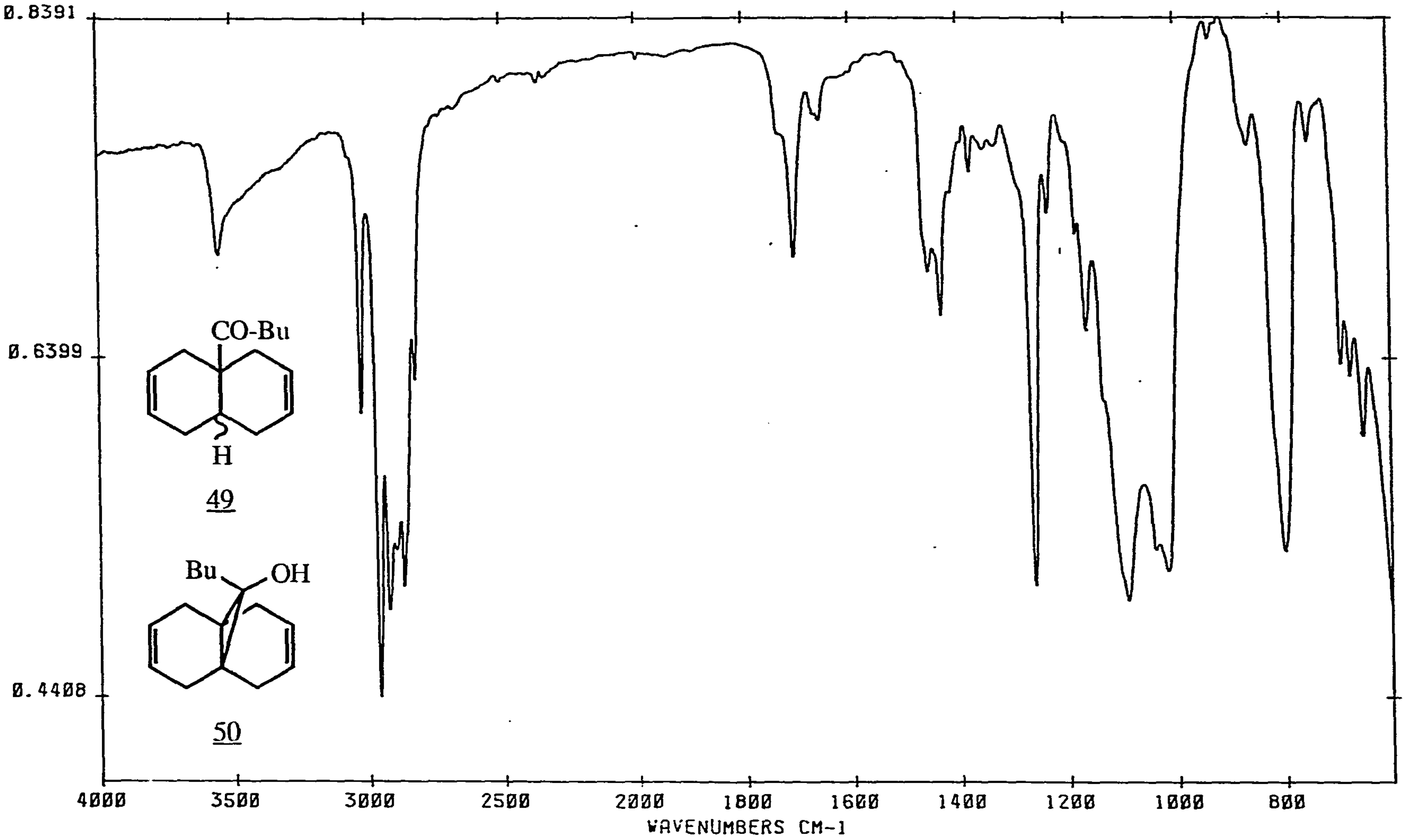
General procedure for the oxygenation of labeled carbenoids 47^* for ^{13}C NMR experiments

The experimental procedure was the same as described above for the oxidation of unlabeled carbenoid, except for the fact that the reactions were done on 0.12-0.16 mmol scale in 2.0 mL d_8-THF in a 10 mm NMR tube. GC-MS analysis of the products after aqueous work up showed 48, and 15^* ($M^+ = 225/227$).

Trapping of the intermediates with n-BuLi (Figures 31, 32, 33)

A solution of 0.32 mmol of carbenoid 47 in 5.0 mL THF was oxygenated at -95°C as described above. After removing the excess oxygen, 0.32 mmol of 2 M n-BuLi was added at -90°C. The solution was allowed to warm slowly to room temperature. Addition of 2.0 mL of 50% NH_4Cl solution was

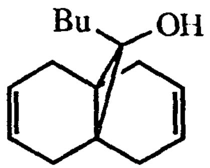
Figure 31. IR (neat) of a mixture of 50 and its ring opened ketone isomer 49


0.8391
0.6399
0.4408
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBERS CM-1
CO-Bu
H
Bu
OH

49

50

Figure 32. ^{1}H NMR ($CDCl_3$) of 50



50

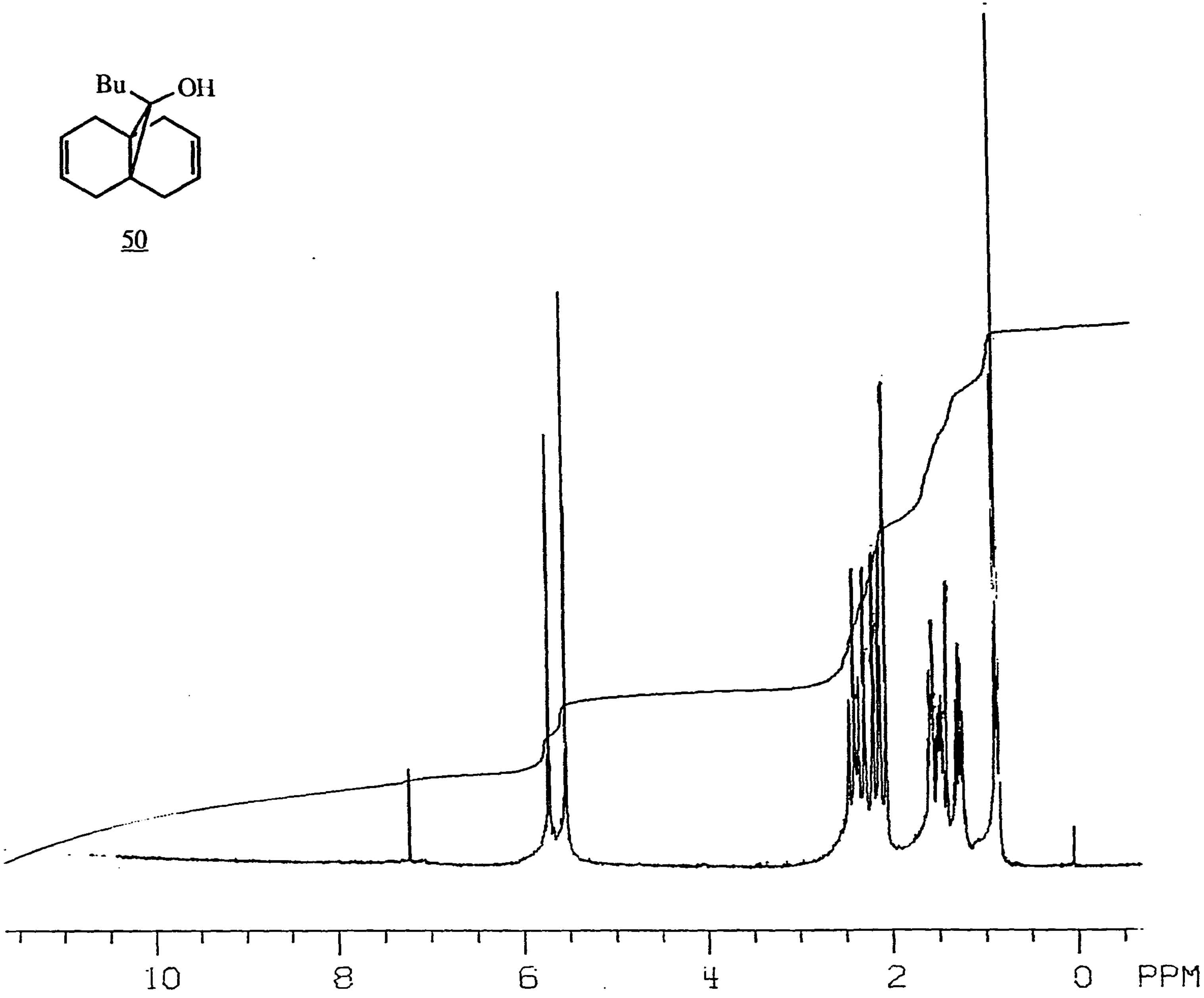
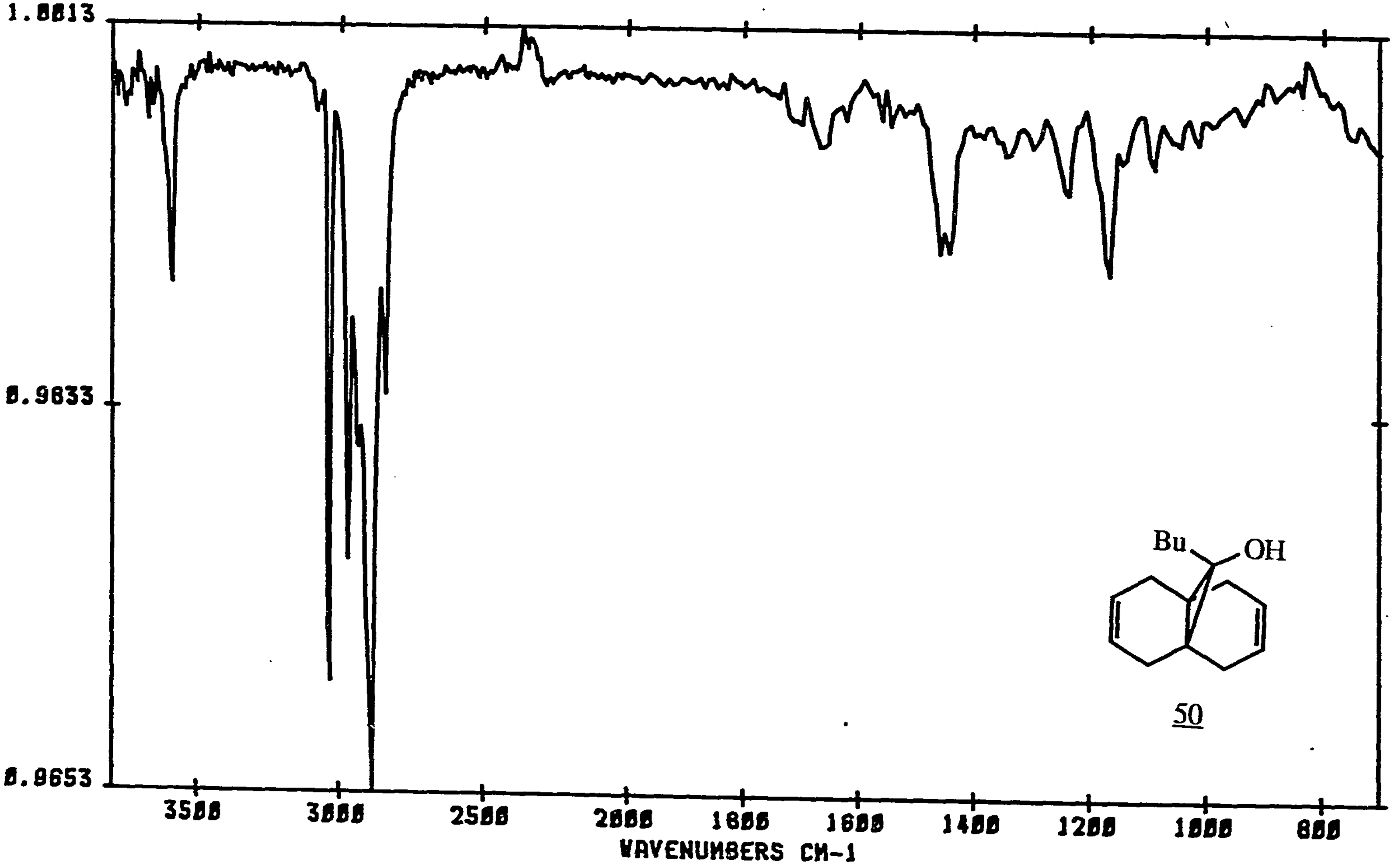


Figure 33. GC-IR of 50


1.0013
0.9833
0.9653
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBERS CM-1
Bu
OH
50

followed by extraction with ether (5 mL). The ether layer was dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by passing through a column of silica gel. Elution with a 50% hexane-50% ether mixture gave 20 mg (30%) of 50 as a light brown viscous oil. GC of this product showed 50 and its ring-opened ketone isomer 49 in the ratio of 3.4:1.

GC-HRMS: Calculated for $C_{15}H_{22}O$ m/e 218.16707; measured m/e 218.16730.
For the ketone isomer 49: measured m/e 218.16715.

GC-MS of 50: 218 (8.7), 200 (0.8), 189 (2.5), 176 (1.6), 163 (12.8), 162 (3.0), 161 (23.5), 143 (7.2), 133 (50.2), 132 (23.6), 131 (11.5), 117 (21.0), 105 (24.4), 91 (100.0), 85 (43.5), 79 (43.3), 67 (37.7), 57 (67.8), 55 (30.4), 41 (43.3).

IR (neat): 3553 (br, m), 3024 (m), 2961 (s), 2926 (s), 2827 (m), 1707 (m), 1433 (m), 1261 (s), 1092 (s), 1018 (s), 800 (s).

GC-IR of 50: 3587 (m), 3031 (s), 2920 (s), 2885 (s), 1458 (m), 1442 (m), 1164 (m).

^1H NMR ($CDCl_3$): 5.5-5.7 (m, 4 H), 1.3-2.4 (m, 15 H), 0.8 (t, 3 H, J = 7.2 Hz).

^{13}C NMR ($CDCl_3$): 126.9, 124.9, 63.8, 29.7, 29.1, 28.9, 28.1, 23.3, 19.7, 14.1.

The corresponding reaction with 47* gave 50* with a ^{13}C label.

GC-HRMS of 50*: Calculated for $C_{14}C^{13}{}_1H_{22}O$ m/e 219.17042; measured m/e 219.17028.

Adding n-BuLi at temperatures between 10°-25°C to the oxygenated solution gave a small amount of di-n-butyl ketone which was identified by comparing its GC retention time and mass spectrum with those of a synthetic sample obtained by the reaction of n-BuLi and CO_2.

GC-MS: 142 (9.3), 113 (3.3), 100 (6.8), 85 (69.7), 58 (72.7), 57 (100.0), 41 (47.4).

The corresponding reaction with 47* gave ^{13}C labeled di-n-butyl ketone.

GC-MS: 143 (15.0), 114 (4.3), 101 (6.5), 86 (77.5), 59 (78.0), 58 (16.4), 57 (100.0), 41 (41.2).

Trapping of the intermediates by t-BuLi

A solution of 0.25 mmol of carbenoid 47 in 5.0 mL of THF, prepared by the reaction of 0.25 mmol of 24 and 0.5 mmol of 1.3 M t-BuLi, was oxygenated as described above. After removing the excess oxygen, the solution was warmed to -60°C and recooled to -90°C. To this solution 0.5 mmol of t-BuLi was added, and the solution was allowed to warm gradually to room temperature. After aqueous work up the product mixture was analyzed by GC-MS. The products were 37 (major), a small amount of 71, and a trace of 72. No monobromide 15 was formed.

GC-MS of 71: 218 (3.6), 203 (2.9), 179 (31.7), 161 (23.0), 148 (14.4), 143 (40.3), 133 (59.0), 132 (59.0), 131 (74.1), 117 (44.6), 107 (25.9), 105 (24.5), 91 (100.0), 87 (28.8), 79 (49.6), 67 (41.7), 57 (46.0), 55 (34.5), 41 (71.2).

GC-MS of 72: 146 (28.3), 131 (23.2), 117 (35.6), 104 (26.2), 92 (53.4), 91 (100.0), 79 (26.2), 77 (19.8), 65 (17.9), 51 (15.3) (identical with GC-MS of a synthetic sample obtained by Bu_3SnH reduction of 24).

GC-MS of 37: 162 (14.6), 144 (21.9), 133 (35.0), 129 (57.4), 115 (20.3), 107 (54.2), 91 (100.0), 79 (72.2), 77 (47.2), 65 (20.0) (for analysis see chapter II experimental).

Attempted oxidation of olefins by the reaction intermediates

The oxidation of carbenoid 47 on 0.5 mmol scale was performed in the manner described earlier. After removing excess oxygen by freeze vacuum thaw cycles, a solution of

0.5 mmol of olefins (such as 2-pentene, 2,3-dimethyl-2-butene, trans-stilbene and p-trifluoromethyl t-stilbene) in 1 ml of dry THF was added at -90°C, and the solution was stirred for 30 min between -90°C and -70°C, and allowed to warm to 20°C. After aqueous work up, the products were analyzed by GC-MS. The products were 48 (14-18%), 15, and unreacted olefins. No epoxides were detected.

Oxidation of Ph_2SO by the reaction intermediates

A solution of 150 mg (0.5 mmol) of 24 in 10 mL of THF was treated with a solution of 2 M n-BuLi (0.5 mmol) at -95°C, and the carbenoid formed was reacted with O_2 in the manner described above. After removing the excess oxygen by freeze vacuum thaw cycles, a solution of Ph_2SO (0.5 mmol, 1 equivalent) in 2 mL argon flushed dry THF was added at -95°C. The solution was stirred for 15 min at -95°C, slowly warmed to room temperature and quenched with water (4 mL) and extracted with ether. The ether layer was dried ($MgSO_4$), filtered, and concentrated. The products were analyzed by GC-MS: Ph_2SO_2 (7%) (calculated with the predetermined response factor of 0.9), 48 (11%).

A parallel experiment was also carried out under the same conditions as above, but without any added sulfoxide. The yield of 48 in this case was also 11%. When the reaction was repeated with 0.5 mmol of dibromide 24, 0.44 mmol of n-BuLi, and 0.3 mmol of sulfoxide, the yield of sulfone based on sulfoxide was 3%. The yield of isotetralin was 12%.

Control reaction to test the possible oxidation of sulfoxide by oxygen

A slow stream of dry oxygen was bubbled for 30 min through a solution of 5 mL THF at -90°C. As in the oxygenation experiments, excess molecular oxygen was removed by freeze vacuum thaw cycles. After removal of the O_2 (save for the possibility that some O_2 remained even after the freeze vacuum thaw cycles), a solution 15 mg of Ph_2SO in 2 mL of THF was added at -95°C. The solution was stirred for 15 min between -95° and -98°C and slowly warmed to room temperature. The organic products were analyzed by GC. As expected, no sulfone was detected. In experiments where the oxygen was not removed, and the solution containing the Ph_2SO warmed to 0°C and worked up, no sulfone was detected either. In experiments where the oxygen was not removed, but the solution was warmed to 20°C, a trace of sulfone was detected after work up.

Control reaction to test the possible oxidation of sulfoxide by BuOOLi

A slow stream of oxygen was bubbled into a solution of 0.06 mmol of 2 M n-BuLi in 8 mL of dry THF over a period of 15-20 min at -90°C. Excess oxygen was removed by freeze vacuum thaw cycles. To this solution, 0.25 mmol of Ph_2SO in 0.5 mL THF was added at -90°C, and the solution stirred until the temperature rose to 20°C. After aqueous work up, the products were analyzed by GC-MS. No sulfone was detected.

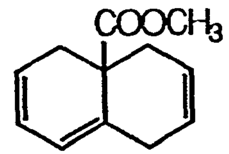
Reaction of CO with n-BuLi

A slow stream of dry CO was bubbled through a solution of 0.2 mL of 2.1 M n-BuLi in 8.0 mL of dry THF for 10 min at -78°C. The solution was stirred for 5 min between -78° and -65°C and quenched with a few drops of saturated NaCl solution and the organic products analyzed by GC-MS. Dibutyl ketone, tributyl carbinol and some other unidentified products were formed. The uncorrected GC area ratio of di-n-butyl ketone to tributylcarbinol was 4:1. The mass spectra of these compounds were identical with the literature spectra from the Finnegan library.

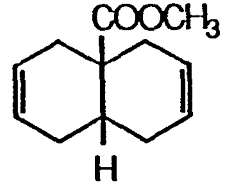
Reaction of CO_2 with n-BuLi

To a solution of 5 mL dry THF at -70°C, a slow stream of dry CO_2 was bubbled for 5 min. To this solution, 0.4 mL of 1.8 M n-BuLi in hexane was added slowly, and the solution stirred until the temperature rose to 10°C. The solution was then quenched with a few drops of saturated NH_4Cl and the organic products analyzed by GC-MS. GC indicated a 1:2 ratio of di-n-butyl ketone to tributylcarbinol. The mass

Figure 34. ^{1}H NMR ($CDCl_3$) of a mixture of 59 and 60



59



60

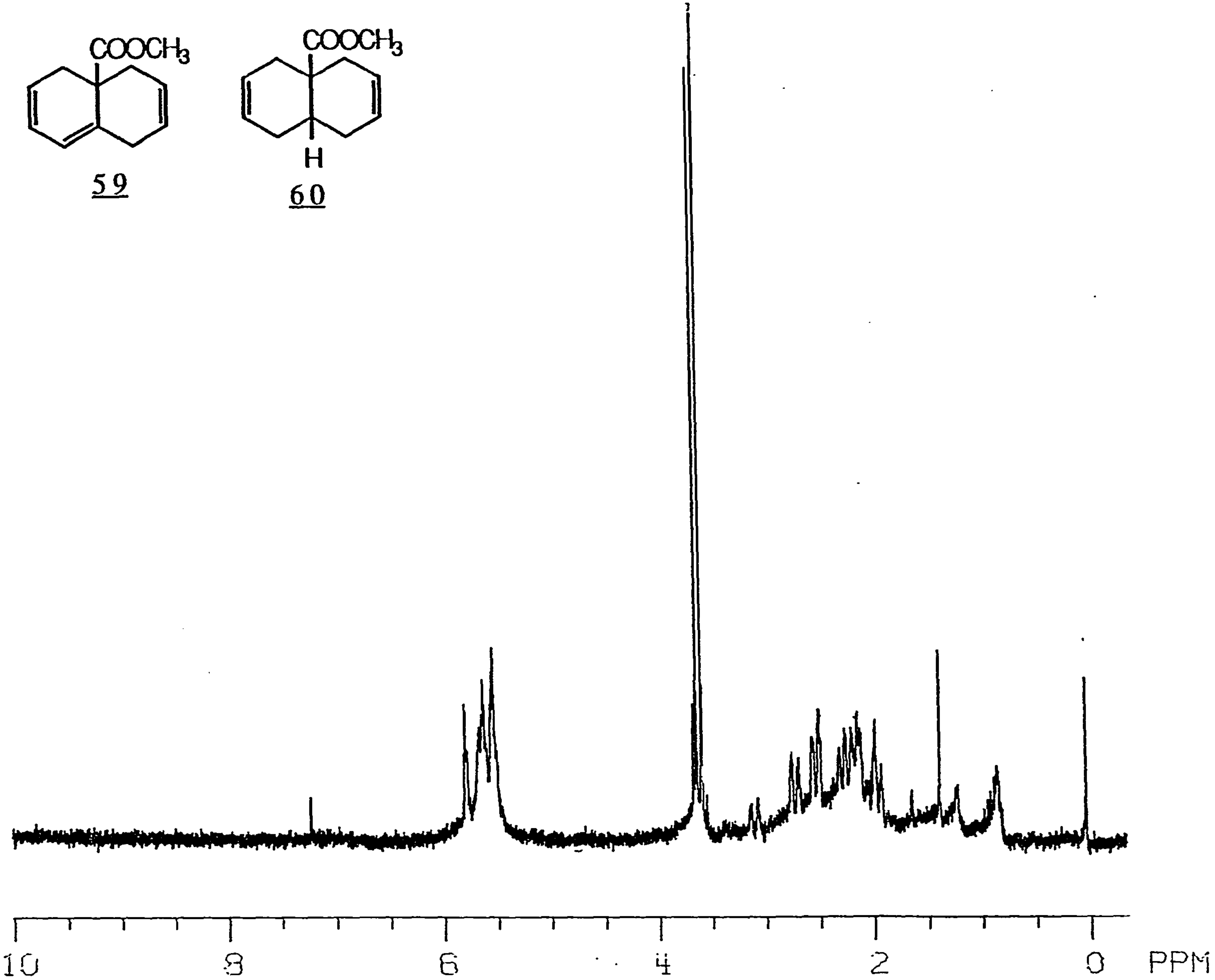
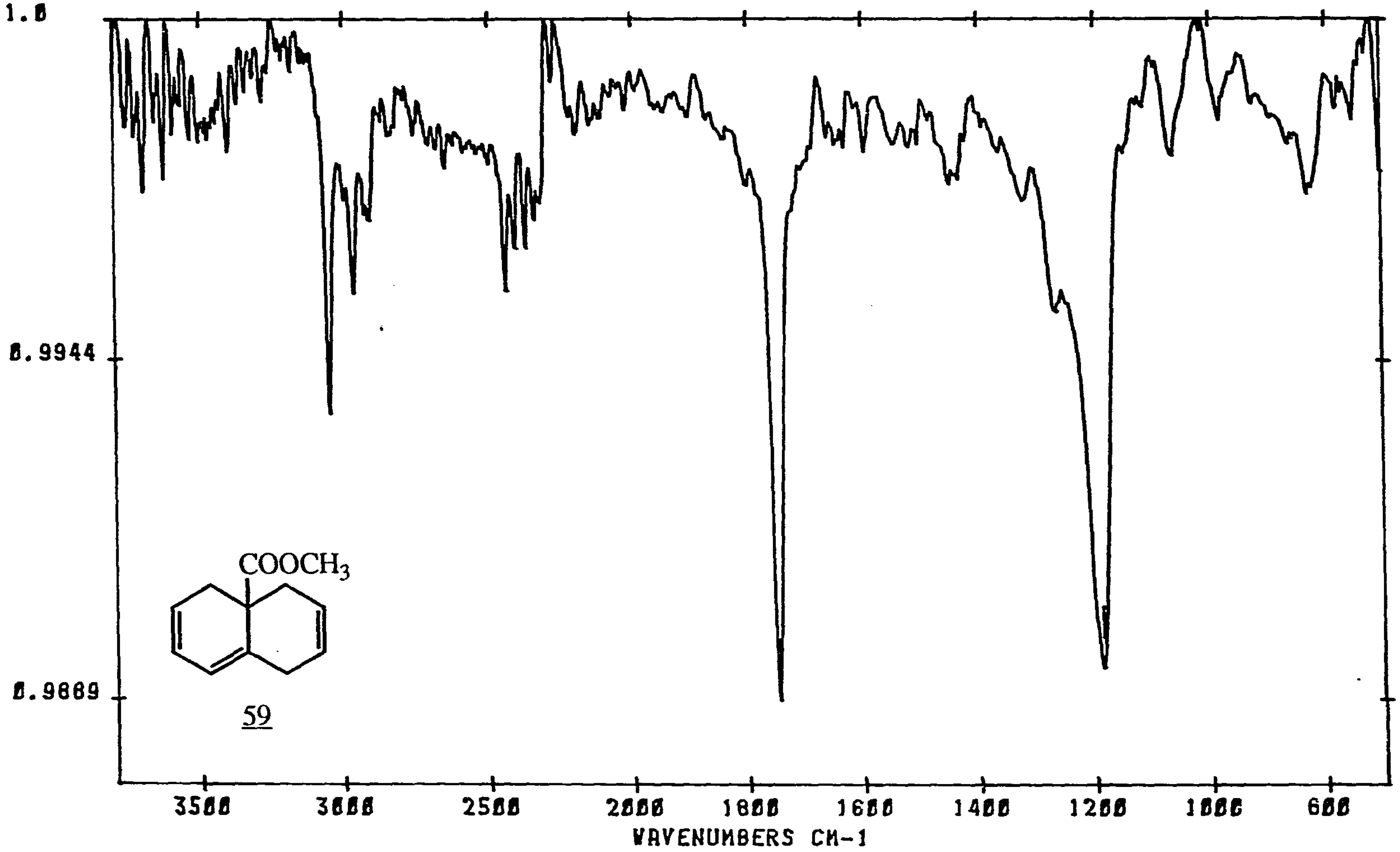
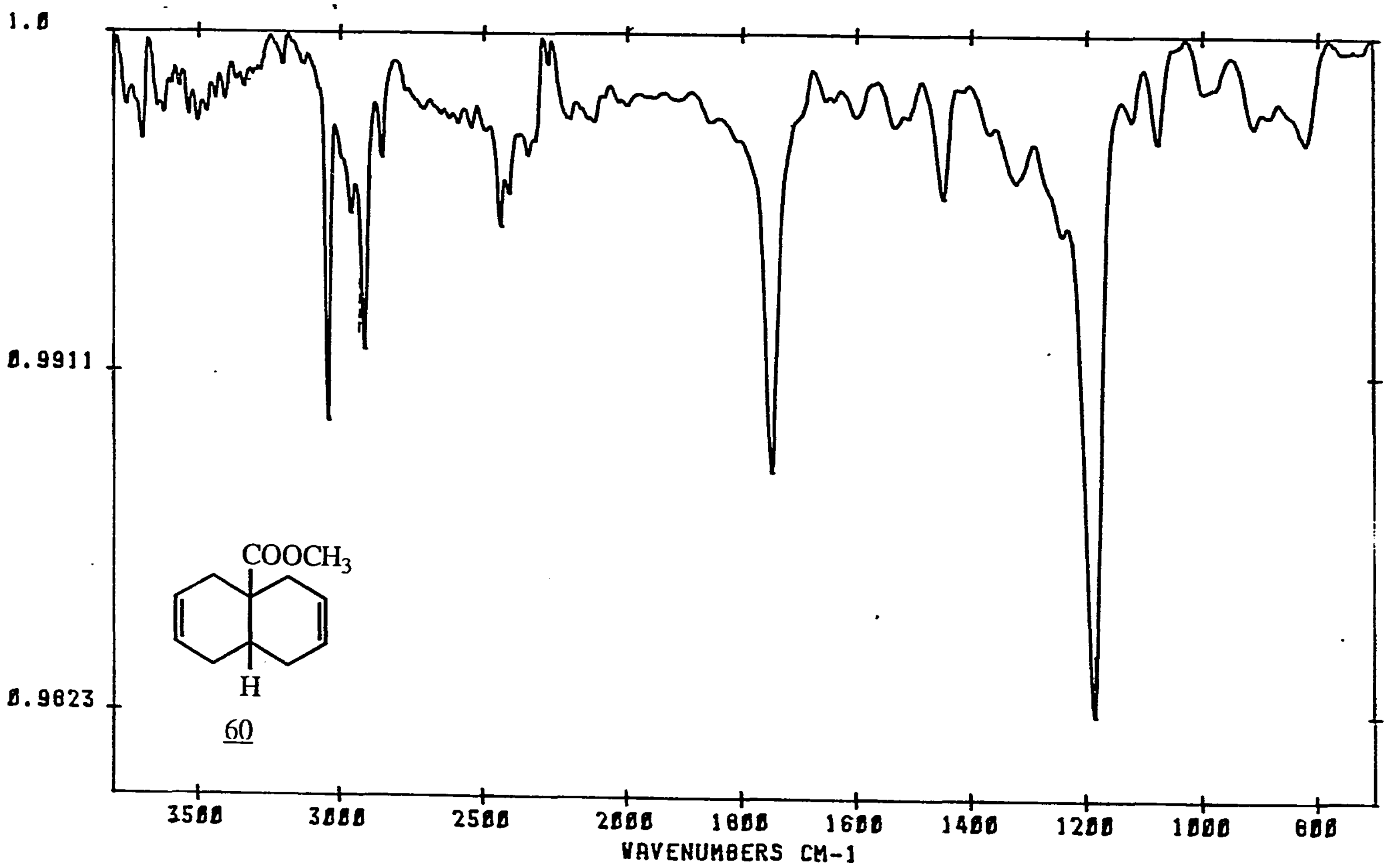


Figure 35. GC-IR of 59


1.0
0.9944
0.9889
COOCH$_3$
3500
3000
2500
2000
1800
1600
1400
1200
1000
600
WAVENUMBERS CM-1

59

Figure 36. GC-IR of 60


1.0
0.9911
0.9823
COOCH3
H
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBERS CM-1

60

spectra were identical with the literature spectra from the Finnegan library.

Trapping of the intermediates with MeOH (Figures 34, 35, 36)

A solution of 3.3 mmol of carbenoid 47 in 25 mL of THF was oxygenated at -95°C as described above. After removing the excess oxygen, 5 mL of MeOH was slowly syringed into the reaction mixture at -90°C to -95°C. The resulting solution was allowed gradually to warm to room temperature. The organic material was extracted with ether (20 mL), the ether layer dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromotography over silica gel. Elution with a 20% ether-80% hexane mixture gave 30 mg of a mixture of two esters 59 and 60 in the ratio 2:1.

GC-HRMS of 59: Calculatd for $C_{12}H_{14}O_2$ m/e 190.09938; measured m/e 190.09872.

GC-HRMS of 60: Calculated for $C_{12}H_{16}O_2$ m/e 192.11503; measured m/e 192.11428.

GC-IR of 59: 3044 (m), 2959 (w), 1747 (s), 1188 (s).

GC-IR of 60: 3036 (m), 2959 (w), 2912 (m), 1747 (s), 1447 (w), 1184 (s).

UV (MeOH): 265, 270 nm (ε = 15,000).

^1H NMR ($CDCl_3$: 5.5-5.8 (m), 3.63 (s), 3.58 (s), 1.8-2.8 (m).

^{13}C NMR ($CDCl_3$): 176.6 (s), 175.6 (s), 135.9 (s), 127.4 (d), 126.8 (d), 124.8 (d), 123.8 (d), 123.1 (d), 121.5 (d), 119.7 (d), 52.2 (s), 51.3 (s), 37.2 (t), 36.6 (t), 34.8 (t), 32.2 (t), 30.6 (t).

Reaction with labeled carbenoid 47* gave the corresponding ^{13}C incorporated ester 59*.

GC-MS of 59*: 191 (7.9), 159 (1.3), 131 (100.0), 130 (24.3), 129 (20.9), 128 (10.8), 127 (5.2), 116 (11.9), 115 (12.4), 91 (37.5), 77 (7.5), 65 (4.1).

Hydrogenation of the mixture of esters 59 and 60

The mixture of esters 59 and 60 was dissolved in EtOH and hydrogenated at 40 psi H_2 pressure and 5% Pd on charcoal as catalyst for 5 h. The GC of the crude product showed a single peak with a tiny impurity.

GC-HRMS of 79: Calculated for $C_{12}H_{20}O_2$ m/e 196.14633; measured m/e 196.14472.

IR of crude product 79 (CH_2Cl_2)^{67}: 3050 (s), 2980 (s), 2910 (s), 1720. (s), 1420 (s), 1250 (s), 1200 (w), 1140 (w), 890 (s).

Mass spectral and IR analysis of the gaseous products in the oxygenation experiments

The oxygenations of carbenoid 47 were done on a 4 mmol scale. After removing excess oxygen by freeze pump thaw cycles, the complete removal of oxygen was tested by analyzing the gaseous product pumped at -90°C. The gaseous products were contained in a bulb which was connected to the high resolution mass spectrometer probe through a needle valve. The composition of nitrogen, oxygen, carbon dioxide and carbon monoxide (Chart 2) were the same as the background spectrum obtained with an evacuated empty bulb (Chart 1). The reaction solution was warmed slowly to 25°C and recooled to -95°C. The gaseous products were pumped again and analyzed (Chart 3) in the same manner. For high resolution IR analysis, the gaseous products were pumped into an IR gas cell. The mass spectrum and IR (Figure 20) revealed the presence of CO (possibly the major product) and CO_2. For reference, the mass spectrum of air obtained under these conditions is also shown (Chart 4). The literature spectra (Finnegan library) of CO and CO_2 are shown in Charts 5 and 6 respectively. All mass spectra shown in Charts 1-6 were recorded at 70 eV. Chart 3 clearly shows CO as the major component. CO_2 fragments to CO (at 70 eV) and the intensity of the latter is about 11.5% of the parent ion. considering the presence of the small amount of CO_2 (see Chart 3) its contribution to CO is negligible.

In Charts 1-4 the masses correspond as follows:

18.01	H_2O
27.99	CO
28.01	N_2
31.99	O_2
39.96	Ar
43.99	CO_2

The retention times shown on Charts 1-4 simply represent the time interval during which scans were collected, and are not to be confused with the conventional GC retention times.

```
Run: MS2370
Title: DUMMY REACTION WITH NEEDLE VALVE
 102802 channels: (        1 to  102802)
      6 scans summed
Retention times:  3:17 to  4: 8
Intensities         27 to     120944
TIC =     149509

             Mass      Intensity   % Base

          13.9986        4314.00     1.03
          15.9932        2152.00      .51
          17.0019       15326.00     3.66
          18.0106       83888.00    20.04
          27.9948        1212.00      .29
          28.0061      418599.00   100.00
          29.0031        2926.00      .70
          31.9898       94740.00    22.63
          39.9624        7615.00     1.82
          43.9899        3970.00      .95
```

Chart 1. Composition of background air in the instrument

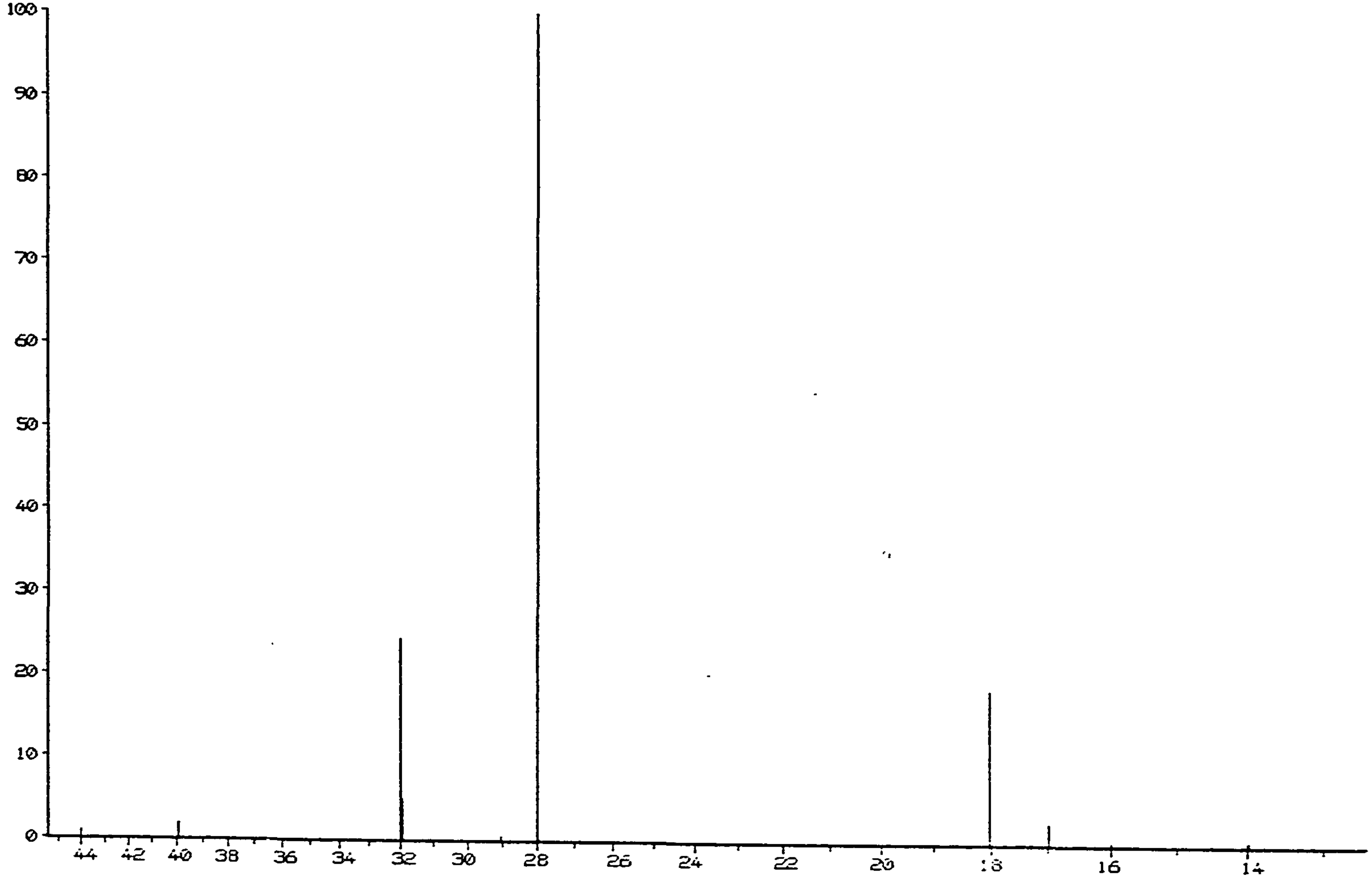


Chart 1. Composition of background air in the instrument

```
Run: MS2378
Title: INTERMEDIATE  P=6E-7 TORR
  65001 channels: (  35000 to  100000)
       6 scans summed
Retention times:  6:44 to  7:36
Intensities         28 to     153040
TIC =     127264

                Mass      Intensity   % Base

             13.9967        4822.00      .98
             14.6150        7099.00     1.44
             15.9929        1560.00      .32
             17.0019        8191.00     1.67
             18.0107       46929.00     9.55
             27.0239        1552.00      .32
             27.9950        1303.00      .27
             28.0063      491319.00   100.00
             29.0031        4050.00      .82
             29.0394         477.00      .10
             31.9898      105549.00    21.48
             39.0231        1018.00      .21
             39.9623        9231.00     1.88
             40.0310         530.00      .11
             41.0388        4376.00      .89
             42.0467        8011.00     1.63
             43.0540        2096.00      .43
             43.9890        2475.00      .50
```

Chart 2. Composition of gaseous products at the intermediate stage (after oxygenation but before warming) in the oxygenation experiment

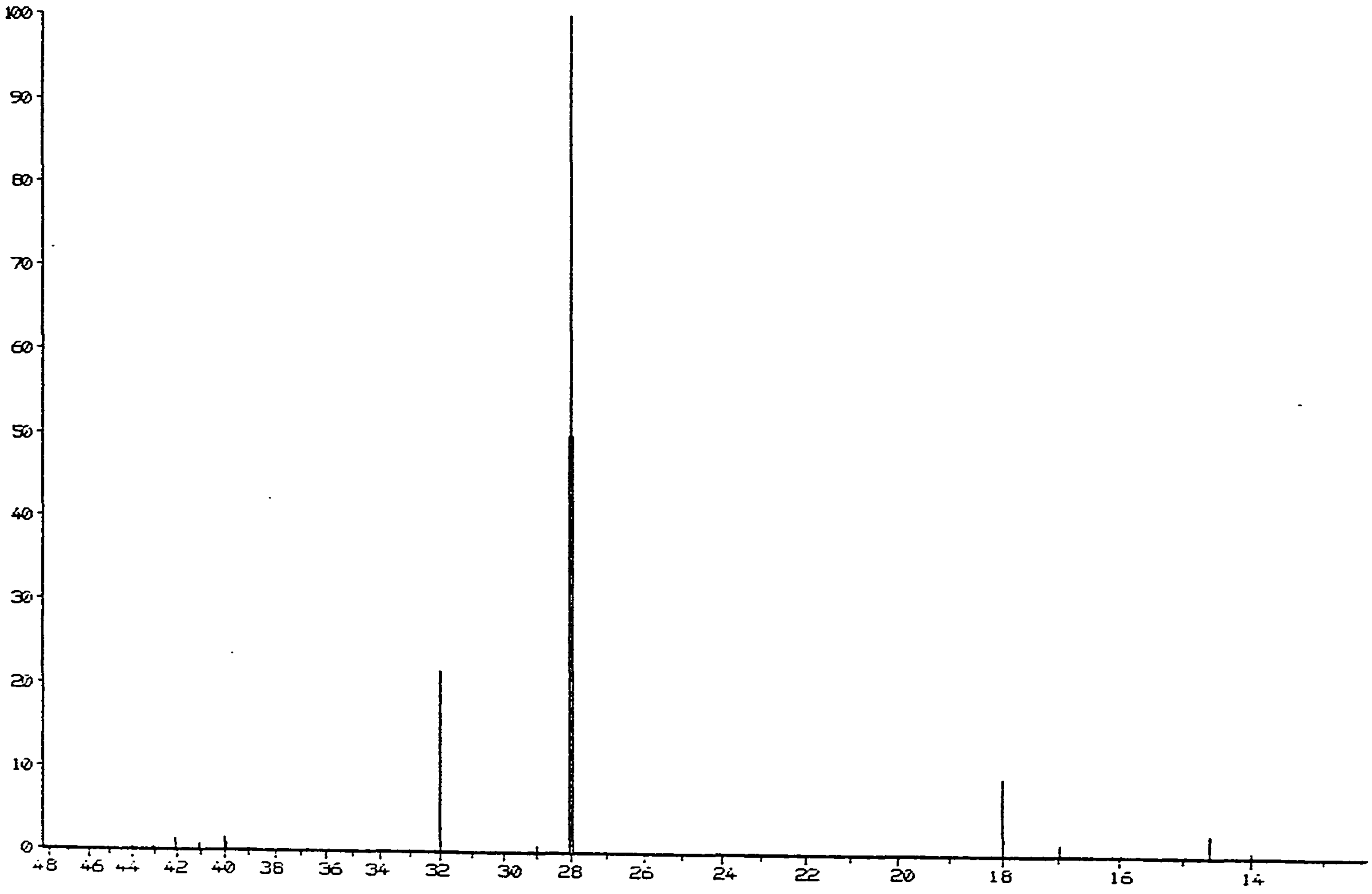


Chart 2. Composition of gaseous products at the intermediate stage (after oxygenation but before warming) in the oxygenation experiment

```
Run: MS2379
Title: SAMPLE  P=5E-7 TORR
 100000 channels: (      1 to  100000)
      6 scans summed
Retention times:  5:31 to  6:23
Intensities        28 to     131344
TIC =     133882

          Mass       Intensity   % Base

       13.9974       2694.00        .61
       15.9935        776.00        .18
       17.0026        778.00        .18
       18.0115       5118.00       1.16
       27.0246        640.00        .14
       27.9925        526.00        .12
       27.9962     442466.00     100.00
       28.0074     239155.00      54.05
       29.0000       4939.00       1.12
       29.0048       2101.00        .47
       30.0001        773.00        .17
       31.9911      47294.00      10.69
       39.9632      21629.00       4.89
       41.0399       1989.00        .45
       42.0477       5089.00       1.15
       43.0561       1538.00        .35
       43.9909       1229.00        .28
       70.9805        984.00        .22
       71.9819       1280.00        .29
```

Chart 3. Composition of gaseous products (after warming) in the oxygenation experiment

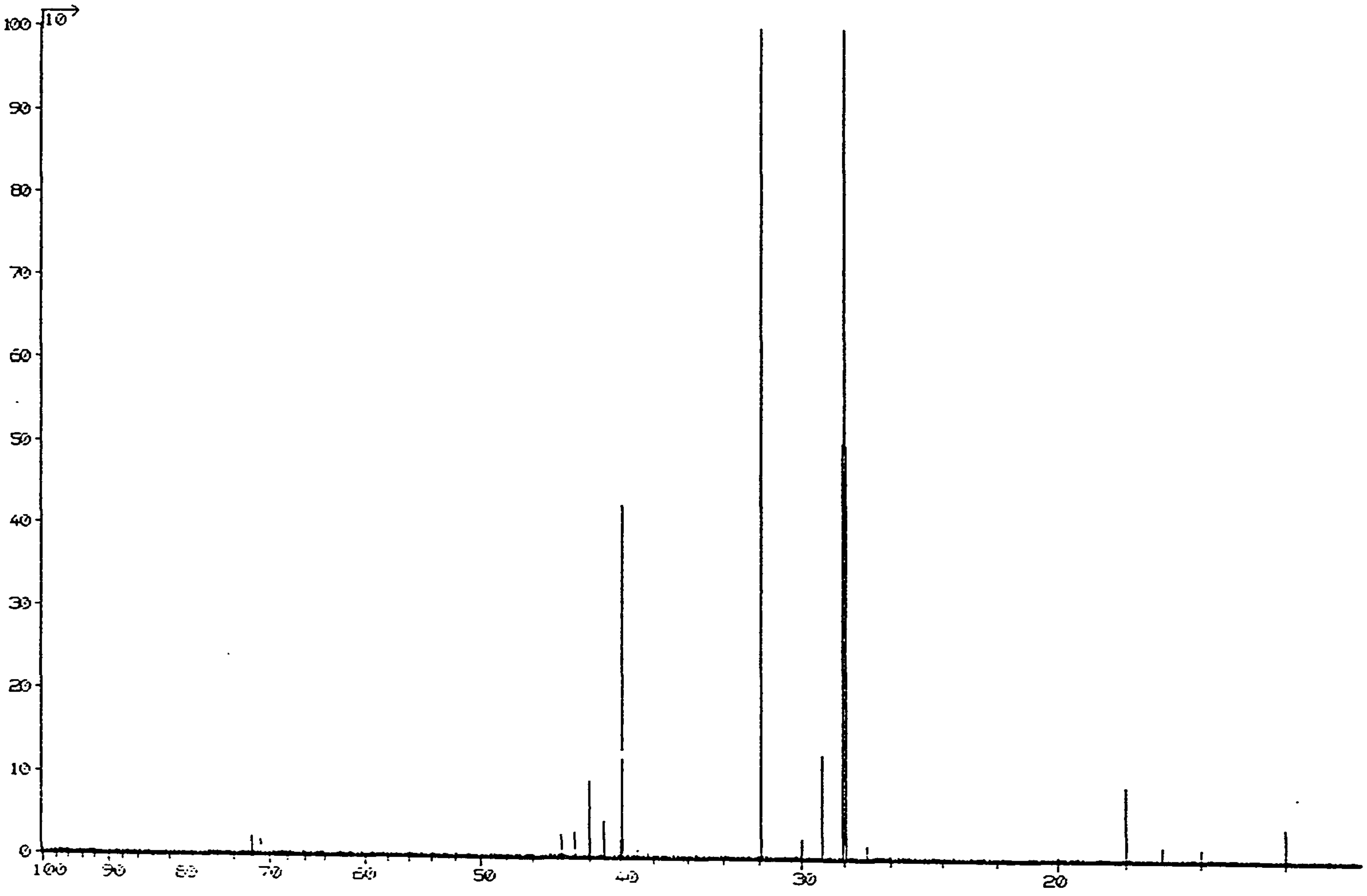


Chart 3. Composition of gaseous products (after warming) in the oxygenation experiment

```
Run: MS2367
Title: EMPTY BULB; BLEEDING AIR IN THRU A SYRINGE
 102333 channels: (       1 to  102333)
      3 scans summed
Retention times:  5:21 to  5:41
Intensities        23 to      61776
TIC =     79171

              Mass      Intensity   % Base

           14.0111        3720.00     1.58
           15.9978        1095.00      .47
           18.0104         890.00      .38
           28.0062      235279.00   100.00
           29.0033        1482.00      .63
           31.9896       59781.00    25.41
           39.9624        4722.00     2.01
           43.9901         869.00      .37
```

Chart 4. Composition of air

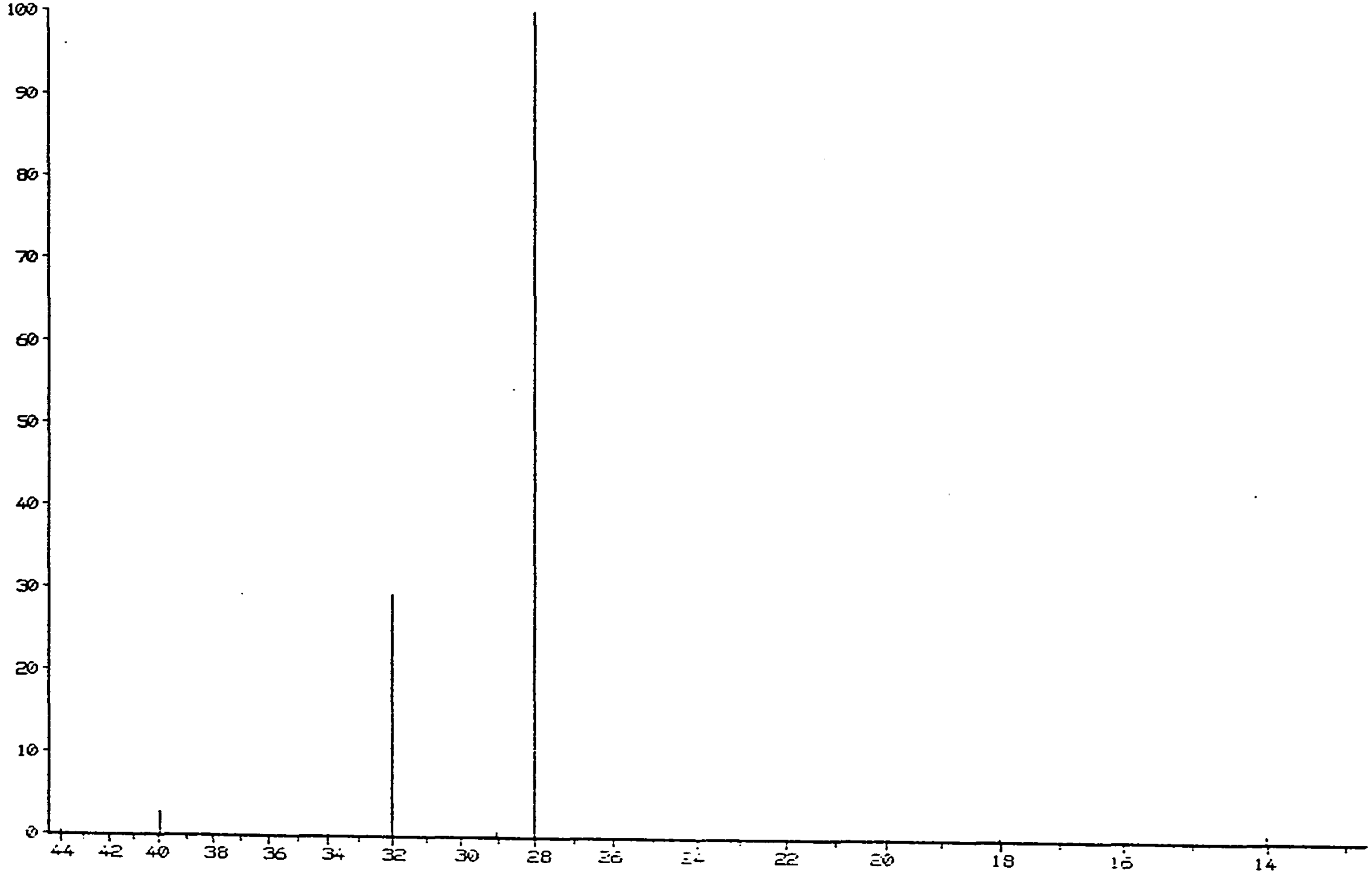
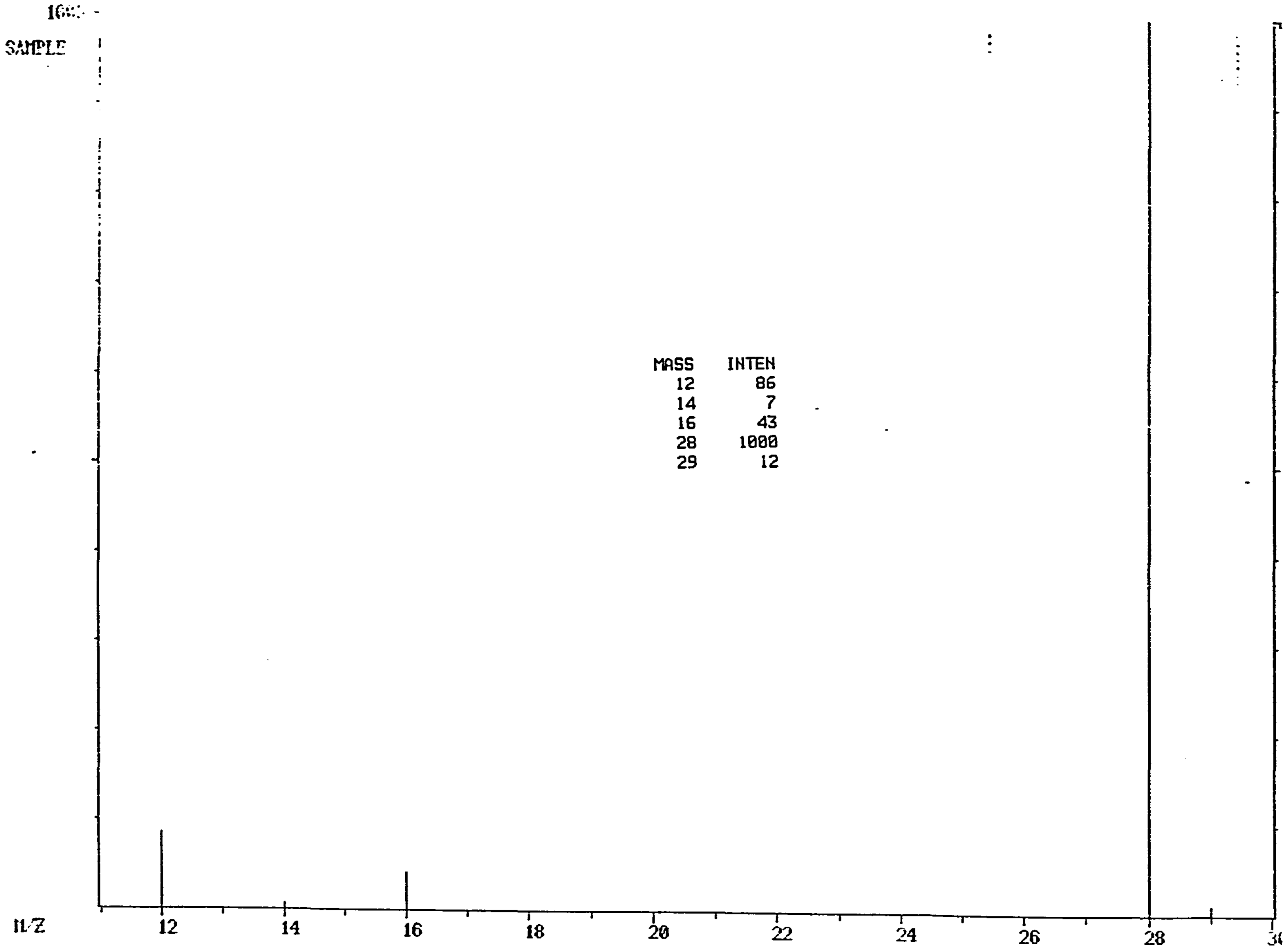
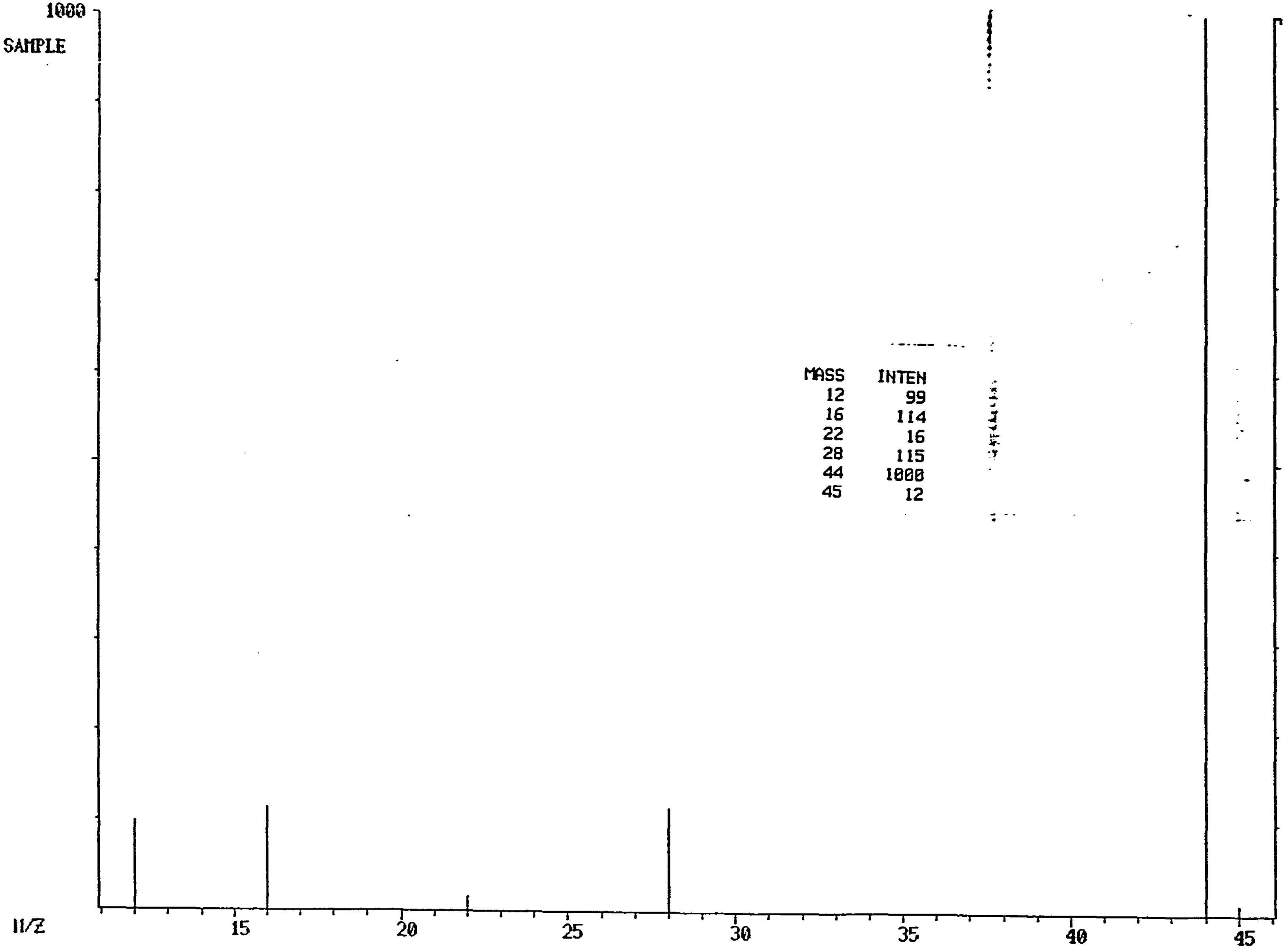


Chart 4. Composition of air



```
MASS   INTEN
  12      86
  14       7
  16      43
  28    1000
  29      12
```

Chart 5. Mass spectrum of CO



MASS	INTEN
12	99
16	114
22	16
28	115
44	1000
45	12

hart 6. Mass spectrum of CO_2

Synthesis of 11-bromo-11-choloro[4.4.1]propella-3,8-diene (51) (Figures 37, 38)

To a vigorously stirred solution of 10.0 g (75.8 mmol) of isotetralin (48) and 11.0 g (98.2 mmol) of KOtBu in 90 mL

HRMS: Calculated for $C_{11}H_{12}BrCl$ m/e 257.98109; measured m/e 257.98117.

IR (KBr): 3032 (m), 2906 (s), 2895 (m), 1445 (m), 1435 (m), 1115 (m), 816 (s), 669 (s), 648 (m).

^1H NMR ($CDCl_3$): 5.5 (m, 4 H), 2.2-2.5 (m, 8 H).

^{13}C NMR ($CDCl_3$): 123.4, 65.3, 32.6, 30.5, 25.1.

Synthesis of 9,9-dibromo[3.3.1]propellane (62)

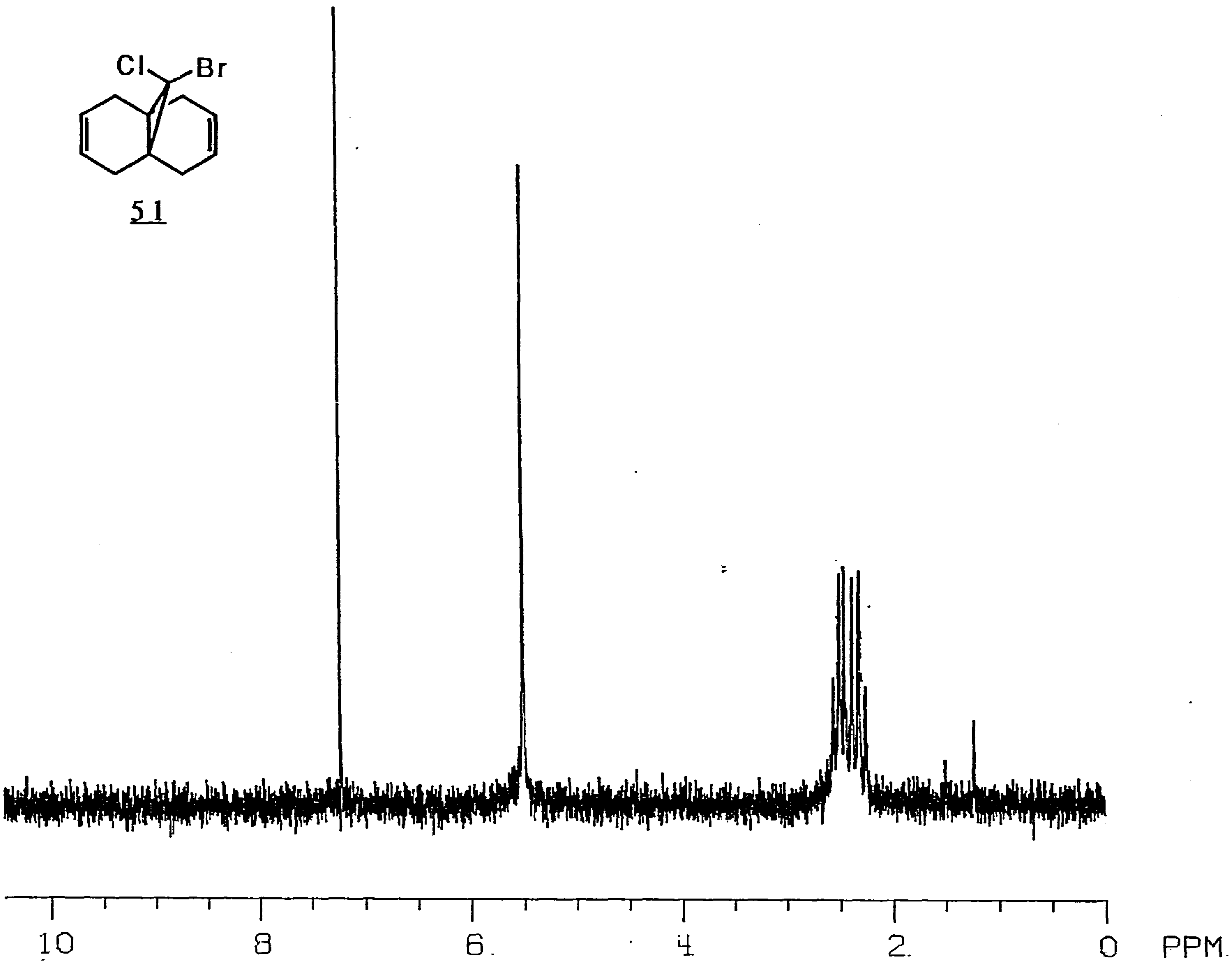
Compound 62 was synthesized as per the procedure by Warner, et al.[69]: mp 67-68°C (literature[69] mp 68-69°C). Analysis, IR, and ^1H NMR are reported.[69] ^{13}C NMR ($CDCl_3$): 57.4, 55.1, 35.6, 33.8.

Oxidation of carbenoid 63 (Figure 39)

The carbenoid 63 was generated from the dibromide 62 and oxidized in the same manner as described for 47. The GC-MS of the products, after aqueous work up of the oxygenated solution, showed the formation of the olefin 67,[69] monobromide 77, and some unidentified products.

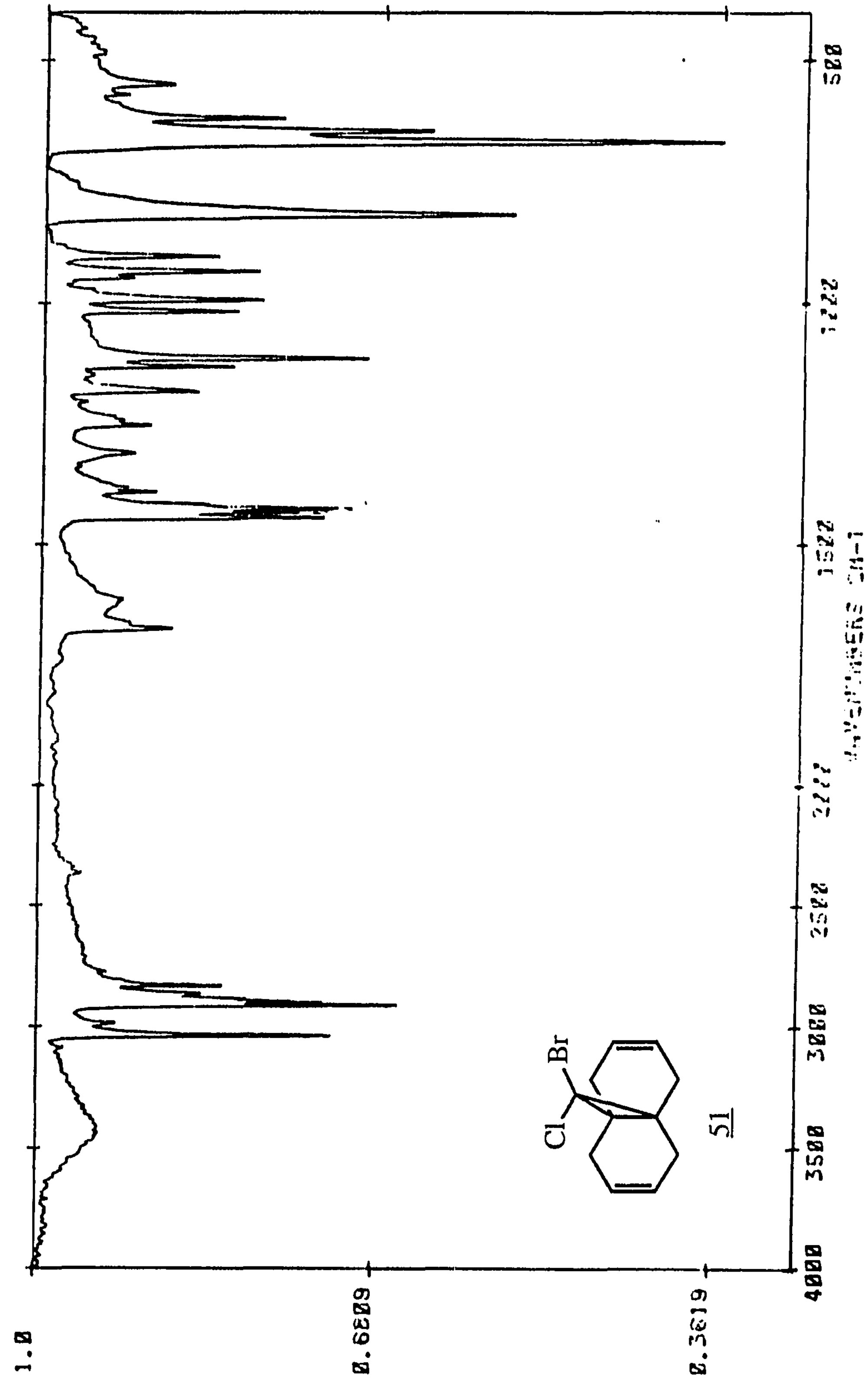
GC-MS of 67: 108 (41.3), 93 (39.4), 91 (20.2), 80 (100.0), 79 (85.9), 77 (24.4), 67 (21.2), 51 (14.4), 39 (29.8).

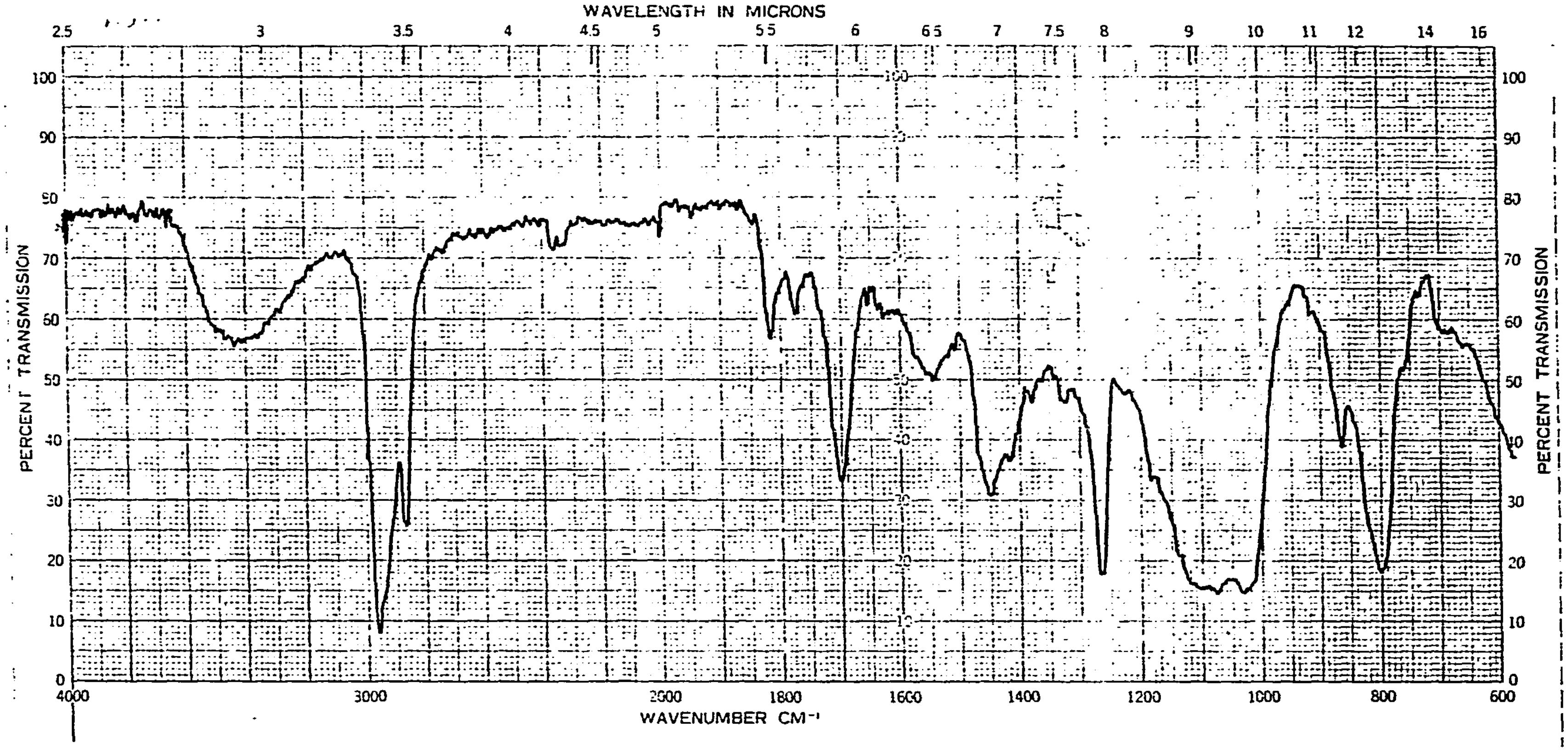
Figure 37. ^1H NMR ($CDCl_3$) of 51



51

Figure 38. IR (KBr) of 51


1.0
0.6809
0.3619
4000
3500
3000
2500
2000
1500
1000
500
WAVENUMBERS CM-1
Cl
Br
51


WAVELENGTH IN MICRONS
2.5
3
3.5
4
4.5
5
5.5
6
6.5
7
7.5
8
9
10
11
12
14
16
PERCENT TRANSMISSION
0
10
20
30
40
50
60
70
80
90
100
4000
3000
2000
1800
1600
1400
1200
1000
800
600
WAVENUMBER CM⁻¹

GC-MS of 78: 202 (28.3), 200 (29.0), 174 (85.8), 172 (89.3), 122 (35.6), 121 (100.0), 105 (9.6), 93 (95.0), 91 (75.3), 79 (99.1), 77 (75.3), 67 (31.9), 51 (34.6), 39 (79.5).

IR of crude product (neat): 3400 (br, m), 2960 (s), 2870 (s), 1820 (w), 1700 (m), 1450 (s), 1270 (s), 1020-1140 (br, s), 800 (s).

Preparation of labeled carbenoic 63*

Carbenoic 63* was prepared analogously to the procedure described for 47*.

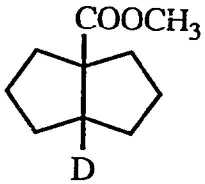
Oxidation of carbenoid 63*

The oxidation of 63* was performed in a 10 mm NMR tube as described for 47*, and the ^{13}C NMR was recorded at various temperatures between -110° and -40°C (Figure 28). The GC-MS analysis of the products, after aqueous work up of the oxygenated solution, showed 67 and 77* (M^+, 201/203) in addition to some unidentified products.

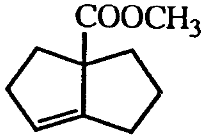
Trapping of intermediates with MeOD (Figures 40, 41)

This experiment was done in the same manner as described for the MeOH trapping reaction in the oxygenation of 47. The GC-MS of the product mixture showed the presence of two esters 68 and 69, in the ratio of 1:1.5 (GC) in addition to a small amount of 67 and unreacted dibromide 62.

Figure 40. NMR ($CDCl_3$) of the mixture of 68 and 69 (crude products)



68



69

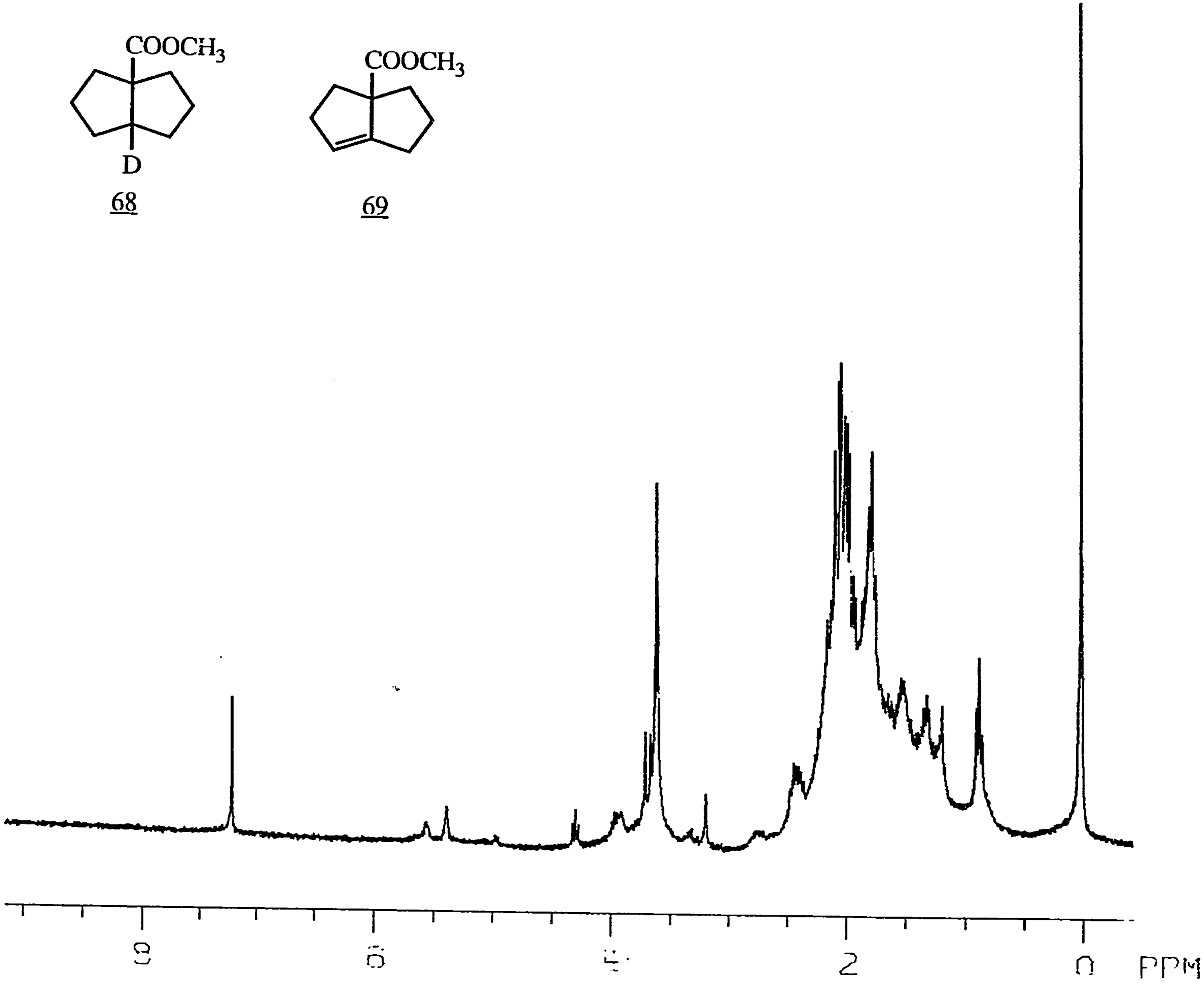
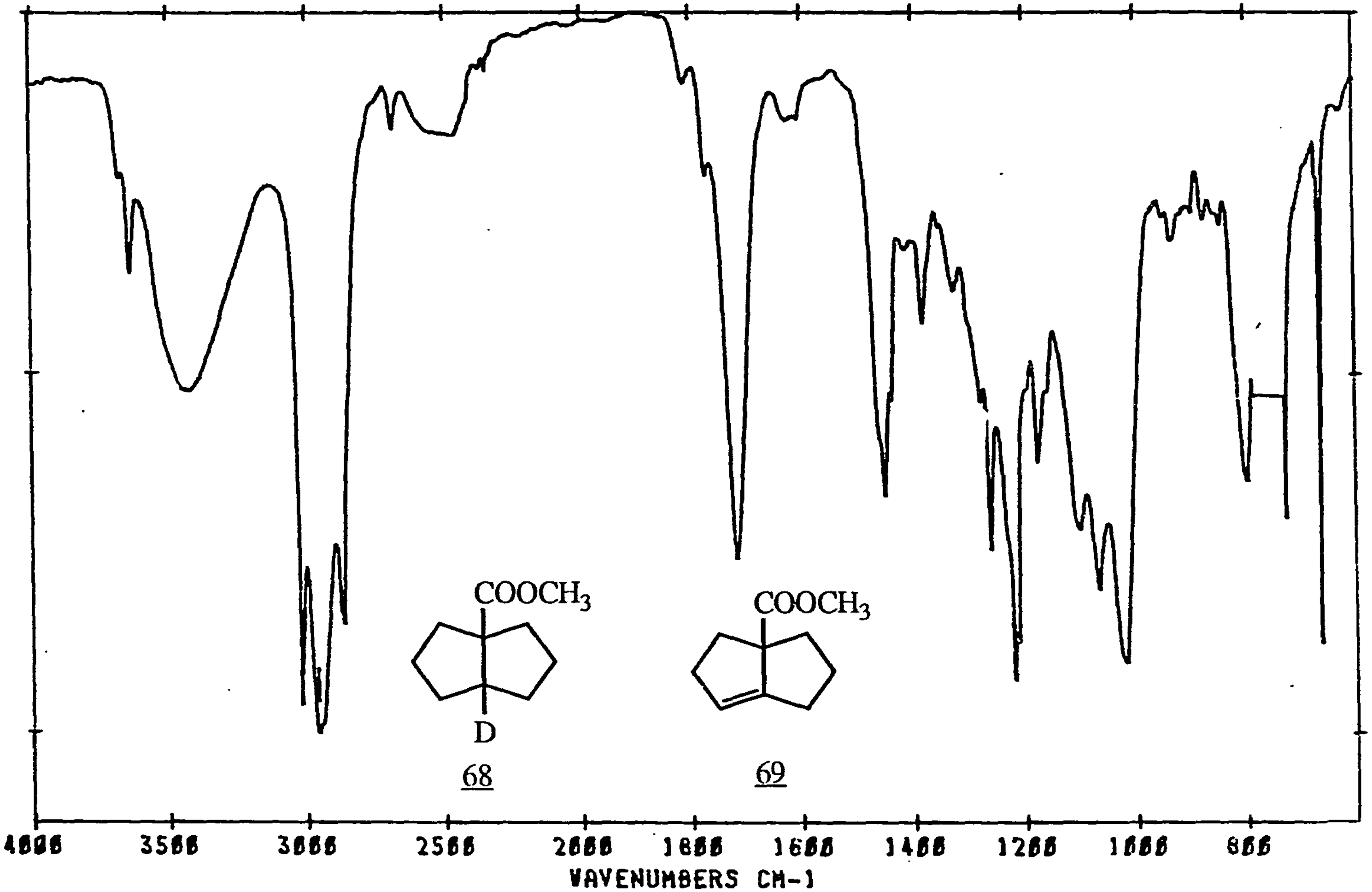


Figure 41. IR (neat) of the mixtures of 68 and 69 (crude products)


COOCH$_3$
D
68
COOCH$_3$
69
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
WAVENUMBERS CM-1

GC-MS of 68:	169 (18.8), 154 (1.3), 141 (31.2), 128 (100.0), 110 (66.8), 82 (24.6), 68 (40.8), 67 (47.9).
GC-MS of 69:	166 (15.4), 151 (1.4), 134 (2.1), 107 (100.0), 91 (18.1), 79 (69.2), 65 (4.5).
IR of the crude product mixture (neat):	3180 (br, m), 3018 (s), 2959 (s), 2866 (s), 1718 (s), 1450 (s), 1261 (m), 1221 (s), 1018 (s), 798 (m), 665 (s).
^{1}H NMR the product mixture ($CDCl_3$):	3.65 (s), 3.6 (s), 1.5-2.2 (m).

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