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    I. ON THE MECHANISM OF IRON CARBONYL-PROMOTED
COUPLING OF STRAINED OLEFINS TO CARBON
MONOXIDE. II. ON THE MECHANISM OF
CARBETHOXYCARBENE-INDUCED BETA ELIMINATION
OF HX FROM ALKYL HALIDES.

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First name also appears as Bobby.

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THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

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II. ON THE MECHANISM OF CARBETHOXYCARBENE-INDUCED BETA

ELIMINATION OF HX FROM ALKYL HALIDES

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the
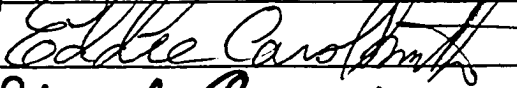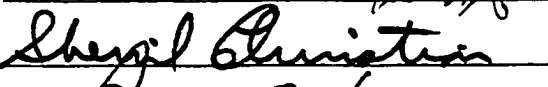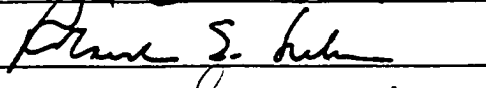
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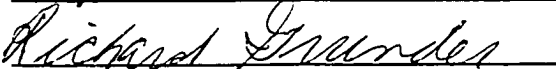
BOB R. HAYES

Norman, Oklahoma

1975

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APPROVED BY

DISSERTATION COMMITTEE

To the memories of

R.J.H. and G.T.H.

ACKNOWLEDGEMENTS

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I. ON THE MECHANISM OF IRON CARBONYL-PROMOTED

COUPLING OF STRAINED OLEFINS TO CARBON MONOXIDE

CHAPTER 1

INTRODUCTION

Since Mond's[1] discovery of the transition metal
carbonyl complexes, the art and science of organometallic
chemistry has burgeoned into a complex and varied field.
In more recent years, considerable attention has been
given to transition metal assisted reactions. These reactions
include oligomerization,[2] olefin metathesis,[3,4] and cyclo-
dimerization.[4,5] Of more immediate interest to synthetic
organic chemists are the extensively studied OXO process[6]
and the reactions of alkyl halides with tetracarbonyl-
ferrate.[7] Included among these reactions is the iron
carbonyl-induced formation of cyclopentanones from olefins,
the subject of this thesis.

The coupling of strained olefins with concomitant
insertion of carbon monoxide to form cyclic ketones has
its origins in studies by Reppe and Vetter.[8] They reported
the isolation of hydroquinone from the reaction between

iron pentacarbonyl and acetylene. In addition, numerous organo-iron complexes, some of whose infrared spectra displayed carbonyl absorptions, were isolated in this reaction.[8]

Since that singularly impressive beginning, a number of organic functionalities, such as allylic halides,[9] vinyl cyclopropanes,[10] and vinyl cyclobutanes,[11] have been shown to undergo carbonyl insertion upon reaction with iron carbonyls. In addition to undergoing carbonylation, acetylenic compounds are intermolecularly coupled by iron carbonyls to afford cyclic ketones. Examples of these transformations are shown in Table 1.

Compared to the reactions of iron carbonyls with acetylenic compounds, the cycloaddition-carbonylation of carbon-carbon double bonds by metal carbonyls has received relatively little attention.[15] The first reported instance of a ketonic product isolated from the reaction of an olefin with an iron carbonyl was due to Pettit[16] in 1959. The ketone, derived from the thermal reaction of norbornadiene with iron pentacarbonyl, was first assigned (by Bird[17]) the structure shown as Ia. That this structure had been misassigned was first indicated as a result of an early application of the Karplus relationship (NMR).[18] Cookson[19] later synthesized all of the trans isomers of the ketone and thereby unequivocally established the exo-trans-exo stereochemistry as shown for ketone Ib. In addition to ketone (Ib), the reaction sequence gave four other ketonic

OMe

Cl

$\xrightarrow{Fe(CO)_5}$ ref. 9a

OMe

Fe(CO)$_3$

CO

Me

Me

Me

$\xrightarrow{Fe_3(CO)_{12}}$ ref. 9b

Me

Me

Me

Fe(CO)$_3$

CO

HC≡CH

$\xrightarrow{Fe(CO)_5}$ ref. 8

OH

OH

$CH_3C≡CCH_3$

$\xrightarrow{Fe(CO)_5}$ ref. 12

Me

Me

Me

Me

O

O

PhC≡CPh

$\xrightarrow{Fe(CO)_5}$ ref. 13

Ph

Ph

Ph

Ph

O

HC≡CH

$\xrightarrow{Fe_2(CO)_9}$ ref. 14

Fe(CO)$_3$

O

Table 1 continued

Ia   Ib
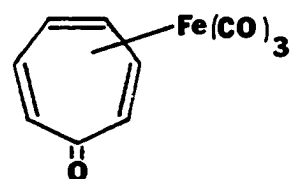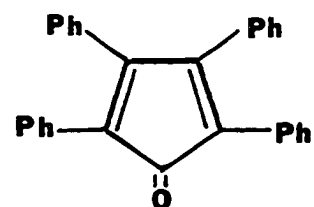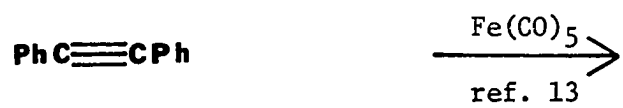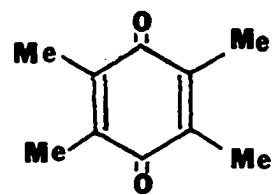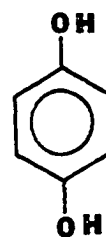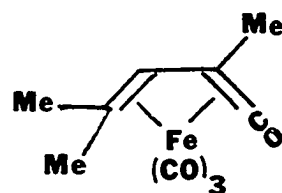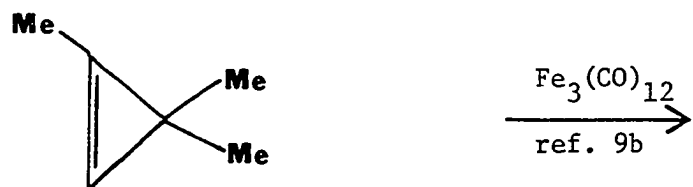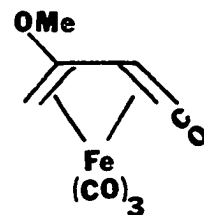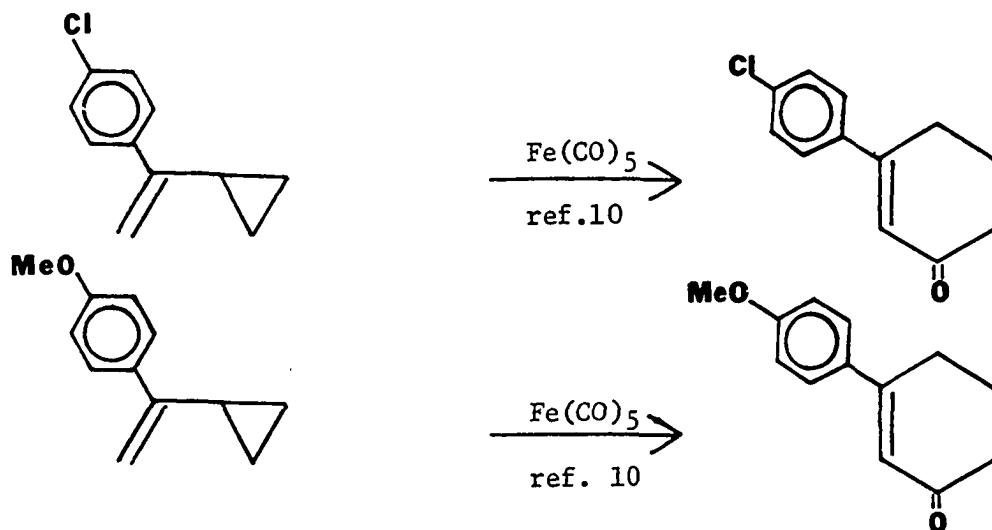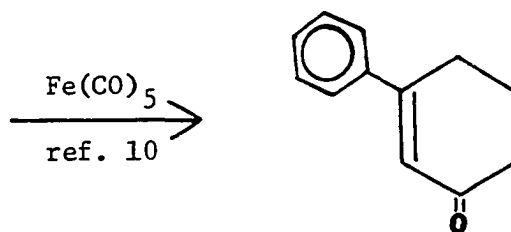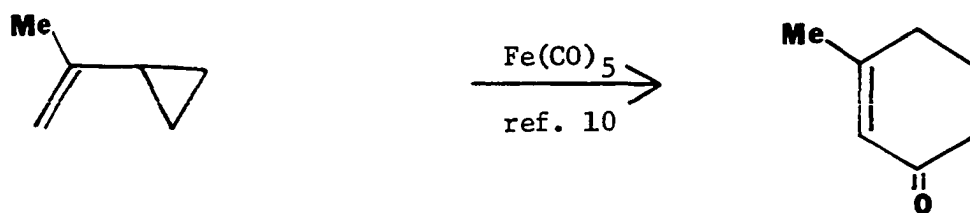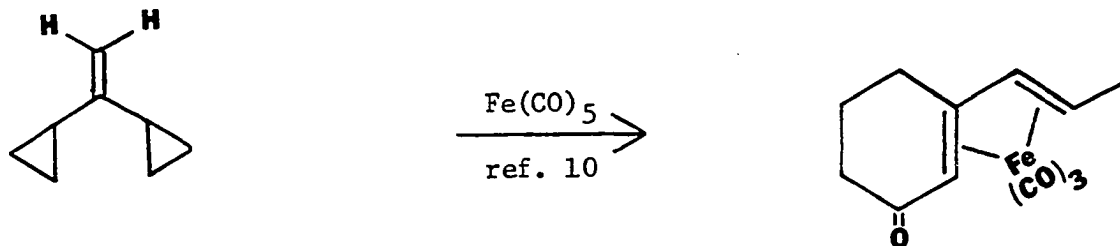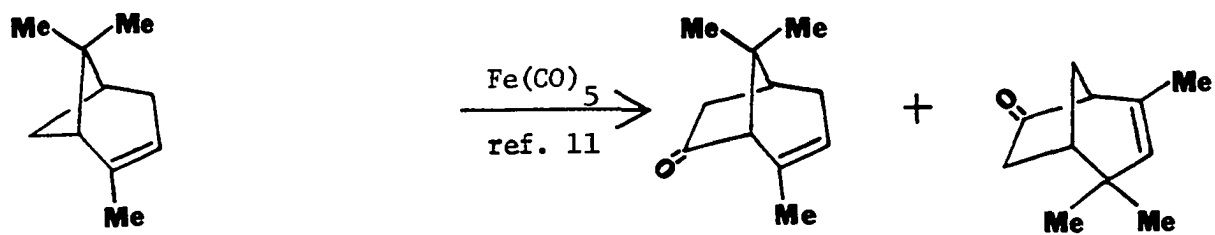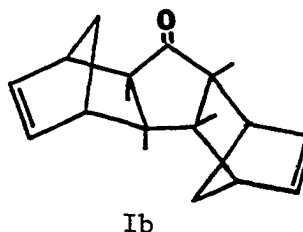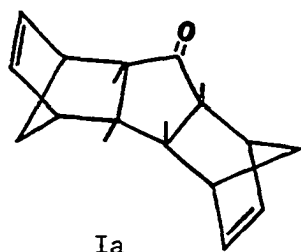
products and four dimeric hydrocarbons; of these, only
ketone Ib has been fully characterized.

In the period 1960-1972 very little work was reported
on the iron carbonyl-induced coupling reaction. However, the
year 1972 saw a resurgence of interest in this reaction
and, with it, a better understanding of its mechanism.
The studies of Mantzaris and Weissberger[22a-c] provided a
firm basis for many details of the reaction mechanism.
The isolation and characterization by von Gustorf[23] of
a number of the proposed intermediates (vide infra) further
substantiated the suggested mechanism.[22c] In Table 2 are
listed a few of the cyclopentanone derivatives afforded
by this unique reaction.

When considering these cyclopentanones and the
mechanism of their formation, we will make use of the de-
signations as outlined in Figure 1. The four hydrogen
atoms about the cyclopentanone ring consists of two sets

6
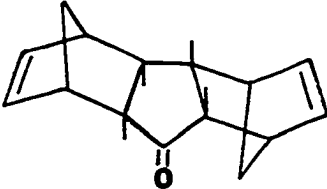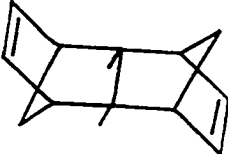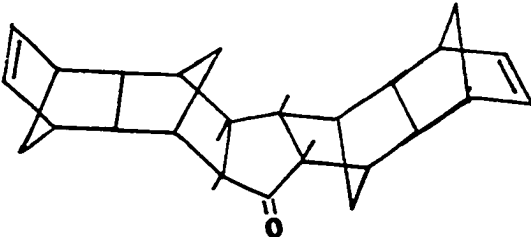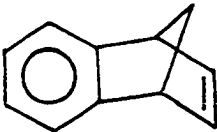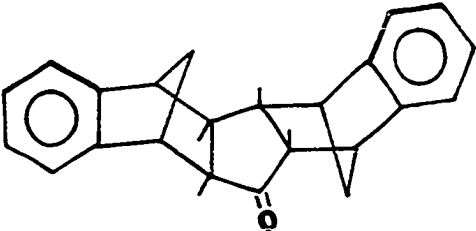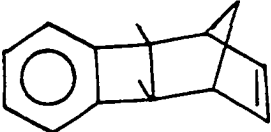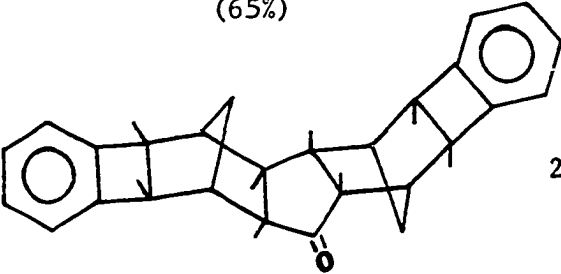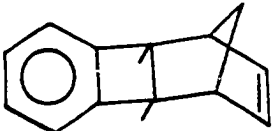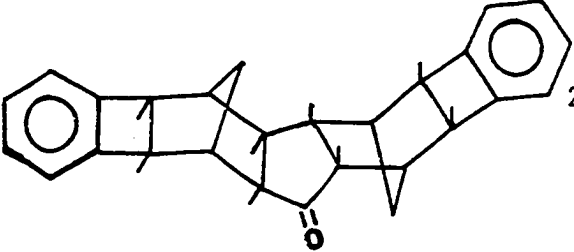
Table 2

Substrate	Reaction	Product (yield)	Reference
	I	Ib (16%)	17
	II	II (70%)	22b
	III	III (65%)	22b, 25
	IV	IV (10%)	22b
	V	V (12%)	22b

Table 2 continued
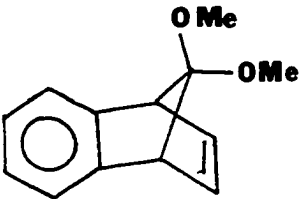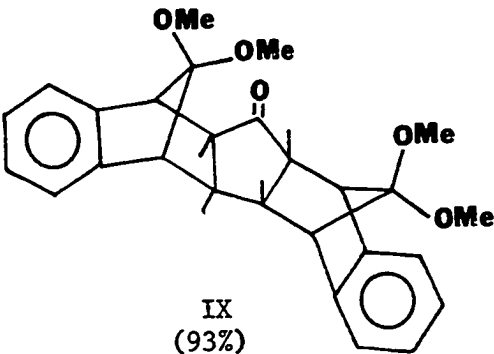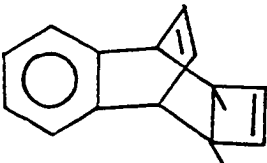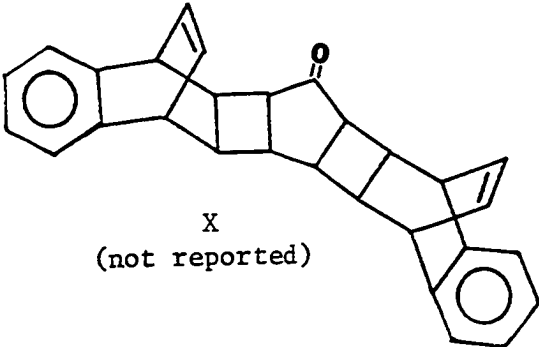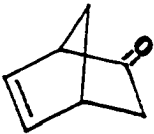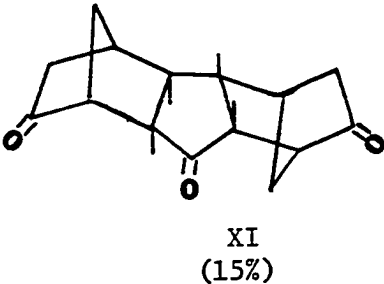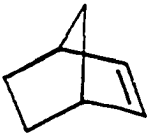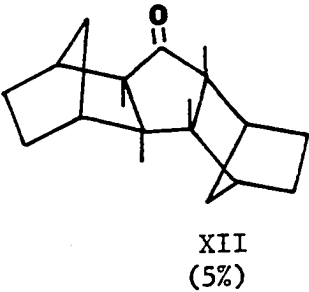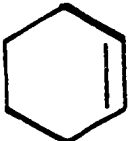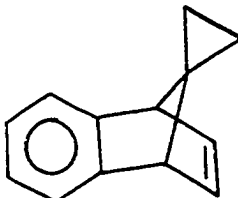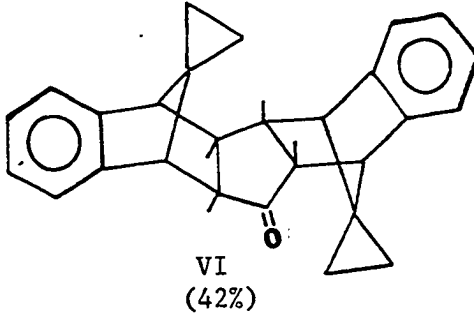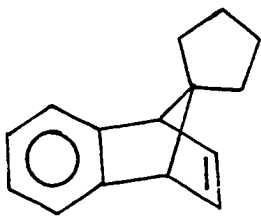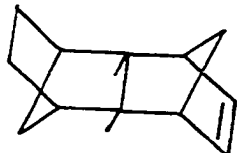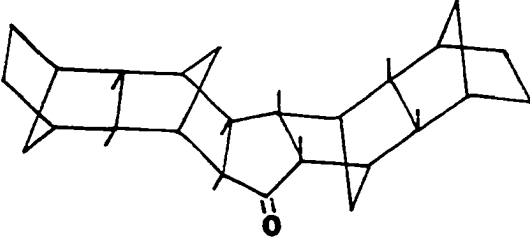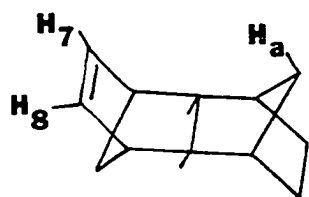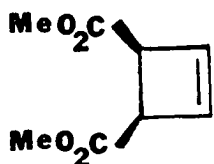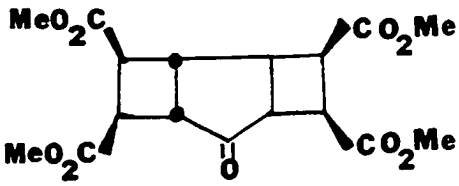
Substrate	Reaction	Product (yield)	Reference
	XI	IX (93%)	25
	XII	X (not reported)	26
	XIII	XI (15%)	27
	XIV	XII (5%)	22b
	XV	none isolated, see text	22b

Table 2 continued

Substrate	Reaction	Product (yield)	Reference
	VI	VI (42%)	22b
	VII	(0%)	22b
	VIII	VII (62%)	22b
	IX	(0%)	22b
	X	VIII (not reported)	24

(α, β and α', β') which have been derived from two separate olefinic species. The members of each set (α, β and α', β') are, by necessity, mutually cis, while the sets (β and β') may be either cis (C) or trans (T), as shown. The cyclopentanone ring itself may be either exo (X) or endo (N) relative to the norbornyl system. Substituents on the methylene bridge (C_7) may be directed toward the central cyclopentanone ring, and are designated as syn (S), or away from it, designated as anti (A). In a like manner substituents at C_1, C_4, C_5 and C_6 will be coded as either syn (S) or anti (A) relative to the carbonyl function, while their relationship to the norbornyl ring will be either exo (x) or endo (n). Thus, the ketone (Ib) would be described as having an exo-trans-exo (XTX) configuration, while IX (Table 2) would be exo-trans-endo (XTN) and XI (Table 2) would be designated as syn-exo-trans-exo-syn (SXTXS).

Considering the generalized reaction of 7-substituted norbornadienes with Fe(CO)$_5$, shown in Eq. 1, the

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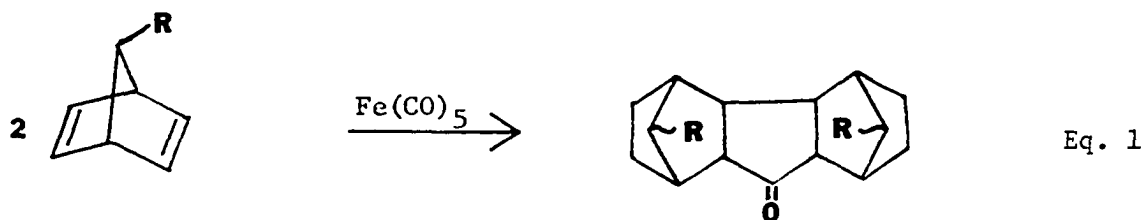
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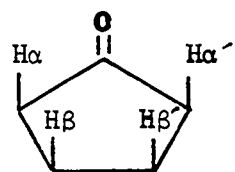
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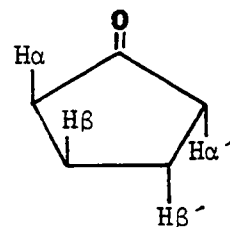
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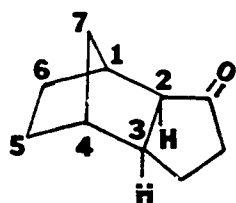
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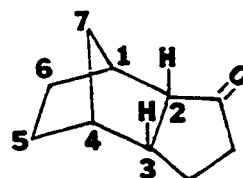
endo (N)
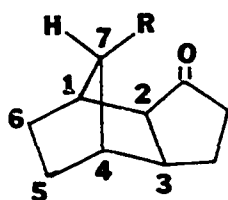
syn (S)
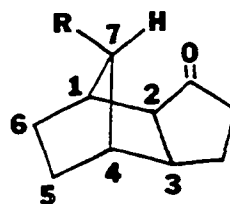
anti (A)
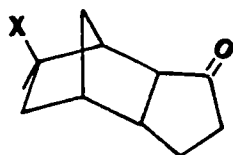
syn (s)
exo (x)
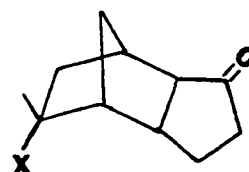
anti (a)
endo (n)

dimeric ketone produced can be bonded exo or endo to either of the norbornyl systems, with either a cis or trans configuration at the β, β' positions on the cyclopentanone ring. Finally, it can have either R group syn or anti to the cyclopentanone ring. These choices allow a possible 36 stereoisomers (16 enantiomeric pairs and 4 meso isomers) that can be produced. The truly remarkable feature of the coupling-carbonylation reaction is that of the many possible stereoisomers (ranging from 8 for ketone Ib to 36 for ketone XI) one and only one dimer ketone stereoisomer has been isolated from the reactions reported so far. Although the stereospecificity of the reaction would be enough to distinguish it among organic reactions, there is yet another and perhaps more valuable aspect of this reaction: e.g., that there is enantiomeric discrimination on the level of the first organometallic intermediate. When Laszlo, et al.[27] reacted (R,S)2-norbornenone with iron pentacarbonyl (Eq. 2)

$$ \xrightarrow{\text{Fe(CO)}_5} \qquad\qquad \text{Eq. 2} $$

(R,S)
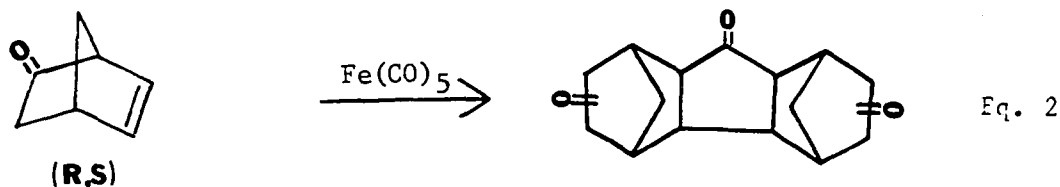
only one compound, other than starting material and polymer,

could be found. On the basis of symmetry arguments, PMR

XI
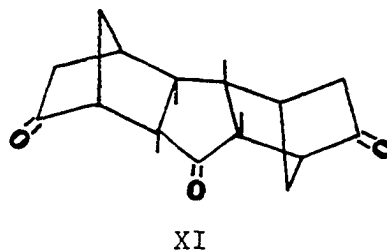
and CMR analysis, and dipole moment studies they suggested

structure XI for this ketone. The fact that no other isomer

could be found indicated that only those organometallic

species which contained norbornenones of the same configura-

tion (i.e., R, R or S, S) would continue to product. Since

no isomeric ketones were found and since the syn-syn con-

figuration was proven for the reaction product, enantiomeric

recognition did indeed take place.

Another feature of the coupling-insertion process

is the apparent trend that is developing in product stereo-

chemistry and substrate reactivity (see Table 2). Whenever

there are alkyl substituents on the bicyclic structure, the

olefin either does not react (compare reactions II, VIII,

and IX, Table 2) or gives without exception a dimeric

ketone of the exo-trans-exo (XTX) geometry. In reaction

IX (Table 2) the lack of substrate reactivity is attributed[22a]

to the $\Delta^{7,8}$ double bond being directly opposed to the H_a

bridge hydrogen, while that in reaction VII (Table 2) is

due to steric hindrance of the bulky C_7 substituent, pre-

cluding exo-attack by a metal species.[22c] The lower relative

yields of ketones IV, V and XII (Table 2) were due to de-

creased olefin ring strain resulting in diminished metal-

olefin complexation.[28,29,22c] Although cyclohexene (reaction

XV, Table 2) yielded no isolated dimer ketone, the presence

of a dimer ketone in the reaction mixture was suggested by

an infrared absorption at 1720 cm^{-1}. This prompted Mantzaris

and Weissberger to consider the reaction general for cyclic

olefins, but they suggested that high yields are obtained

only in the case of strained olefins.[22b] The exo-trans-exo

configuration is obtained even when there is an oxygen

substituent present as in ketone XI (Table 2). However,

when there are groups present which are capable of competing

with the olefin as ligand for the metal center there is a

dramatic switch in stereospecificity. When Marchand, et al.,[25]

heated 7,7-dimethoxybenzonorbornadiene with $Fe(CO)_5$ ketone

IX (reaction XI, Table 2) was the only product isolated

from the reaction. The geometry of IX (exo-trans-endo)

was proven by pmr analysis and via computer simulation of

its pmr spectrum. Ketone IX was the first confirmed case[17,22b]

of a non-exo-trans-exo dimer ketone arising from the reaction

of a norbornadiene with iron carbonyls. The formation of

ketone IX and the unreactivity of the substrate in reaction
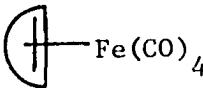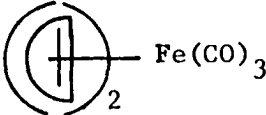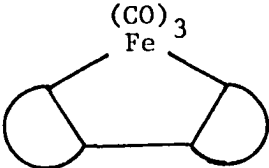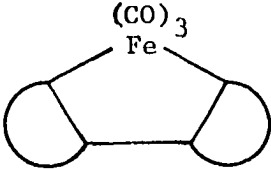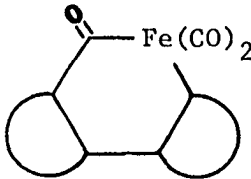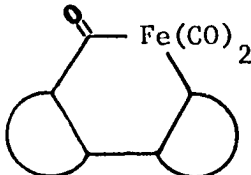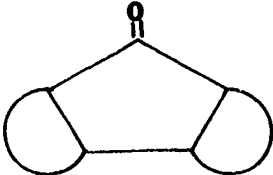
VII (Table 2) led Weissberger to conclude that ".... the methoxy groups are participating directly in the reaction and that the dimethoxy compound couples by a significantly modified mechanism."[22c] We take exception to the latter part of this statement. In the next Chapter we will propose a mechanism which explores the possibility of intramolecular participation of suitably located donor atoms. Our proposed mechanism differs only slightly from Weissberger's, which we discuss next.

Mantzaris and Weissberger's mechanism is shown in Scheme I; here, the symbol " " represents a generalized cyclic olefin. In the following and subsequent discussions, the 16-18 electron rule for organometallic reactions is imposed.[30] This rule implies the stability of 18-electron systems (coordinatively saturated) and the kinetic reactivity of coordinatively unsaturated systems (i.e., 16-electron systems). The rule also restricts Lewis base ligand dissociation, reductive elimination, insertion, and oxidative coupling processes to occur only when the metal has an effective atomic number of the next higher inert gas, i.e., 18-electron complexes. The microscopic reverses of these processes, i.e., Lewis base ligand association, oxidative addition, deinsertion, and reductive coupling occur only in 16-electron systems (refer to Table 3).

The first step of the mechanism, eq. 3, is the formation of the coordinatively unsaturated and highly

Table 3

Elementary Organometallic Reactions[30]

Reaction	Example			Reverse Reaction

Lewis Base Ligand Disassociation $\quad$ $Fe(CO)_5$ $\rightleftarrows$ $Fe(CO)_4 + CO$ $\quad$ Lewis Base Ligand Association

Lewis Base Ligand Disassociation $\quad$ Fe(CO)$_4$ $\rightleftarrows$ Fe(CO)$_4$ + $\quad$ Lewis Base Ligand Association

Oxidative Coupling $\quad$ Fe(CO)$_3$ $\rightleftarrows$ $\overset{(CO)_3}{Fe}$ $\quad$ Reductive Coupling

Insertion $\quad$ $\overset{(CO)_3}{Fe}$ $\rightleftarrows$ Fe(CO)$_2$ $\quad$ Deinsertion

Reductive Elimination $\quad$ Fe(CO)$_2$ $\rightleftarrows$ $\quad$ Oxidative Addition

Scheme 1

$$Fe(CO)_5 \xrightarrow{h\nu} Fe(CO)_4 + CO \xrightarrow[Eq.\ 4']{Fe(CO)_5} Fe_2(CO)_9$$

Eq. 4

 $-Fe(CO)_4 \xrightleftharpoons[+CO]{-CO}$ $-Fe(CO)_3$ Eq. 5

 $-Fe(CO)_3$ + $\rightleftharpoons$ $-Fe(CO)_3$ Eq. 6

 $-Fe(CO)_3 \longrightarrow$ Eq. 7

 $\longrightarrow$ Eq. 8

 $\xrightarrow{- (Fe(CO)_2}$ Eq. 9
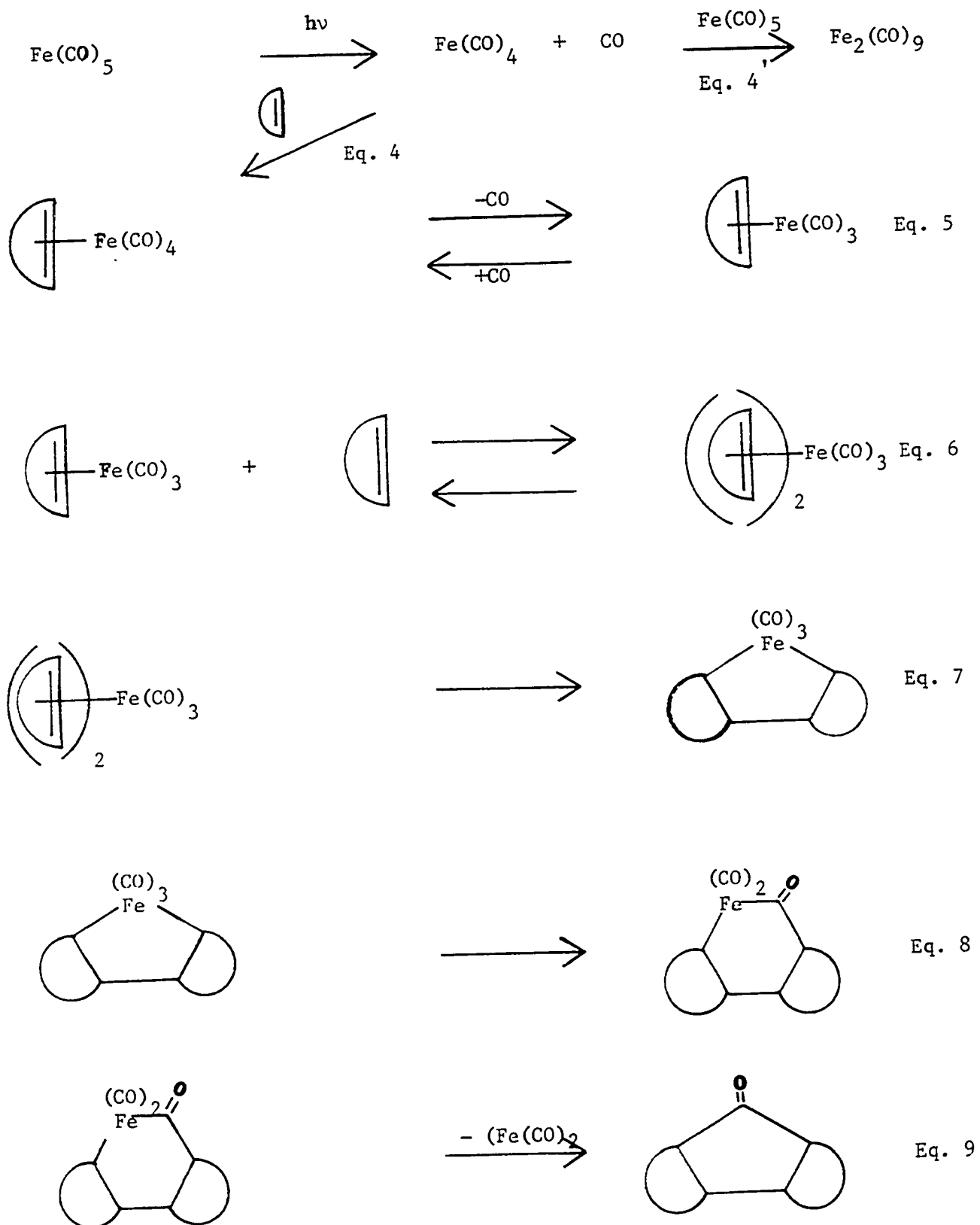
reactive species, $Fe(CO)_4$. Although the mechanism as shown is initiated photochemically, Weissberger[22c] assumed that, in the absence of conflicting data, the thermal and photochemical mechanisms are similar (although their initiation steps differ). The iron tetracarbonyl thereby produced is either trapped (eq. 4) by an olefinic species or, in the absence of olefin, it reacts with $Fe(CO)_5$ to produce the insoluble diiron enneacarbonyl (eq. 4'). The trapping of $Fe(CO)_4$ is an efficient process since the presence of even unreactive olefins (such as cyclohexene) allow little or no $Fe_2(CO)_9$ formation.

The reversible loss of carbon monoxide in eq. 5 was suggested by the three-fold reduction in rate of ketone formation when the reaction was conducted under an atmosphere of carbon monoxide (relative to the rate of ketone formation when the reaction system was purged with nitrogen). The reversibility of this step was further indicated by observing ketone formation in reactions where no product was formed until the system was purged of CO. Since the reversal of eq. 3 is a relatively inefficient process, these experiments point to the operation of a reversible, carbon monoxide-inhibited step consistent with that shown in eq. 5.

That eq. 6 is an equilibrium step in which ligand exchange can occur was shown by trapping experiments. When an olefin was reacted with iron pentacarbonyl in a solution saturated with carbon monoxide for a standard

period of time no ketone was formed. The addition, then,
of a second olefin followed by purging of the system with
nitrogen produced the three possible dimeric ketones (e.g.,
AA, AB, BB). When this experiment was performed in inverse
order the final ratio of dimeric ketones was the same as
for the initial experiment. These results indicate the
equilibrium nature of this step and the occurrence of ligand
exchange. The experiments also gave an estimation of the
relative binding constants for the olefins used.[22c]

The oxidative coupling postulated in eq. 7 requires
that the two olefinic ligands be located in the basal plane
($<$LFeL' = 120°) of a trigonal bipyramid. Carbon-carbon
bond formation would be prohibited if the olefins were in the
apical positions ($<$LFeL' = 180°) as would be the situation
were one ligand equatorial and one axial. A similar argu-
ment can be made to support an intermediate in a square
pyrimidal conformation (below). The isolation by von
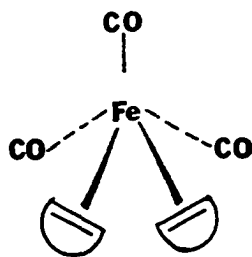
Gustorf, et al.[23] of the iron metallocycle (complex XIV)

shown in Scheme 2 lends further support for the postulated

metallocycle shown in eq. 7 (Scheme 1). Another ferracyclo-

pentane has been isolated by von Gustorf[24] which, upon

reaction with CO or PPh$_3$, afforded ketone VIII (Table 2).

The last two steps of the mechanism, migratory

insertion (eq. 8) followed by reductive elimination (eq.

9) are both depicted as involving coordinatively unsaturated

iron species. As such, they are required by the 16-18

electron rule[30] to have an activating ligand to effect the

transformation. The role of the activating ligand could

be assumed by unpurged (residual) carbon monoxide or by

the presence of another iron species in solution. At this

point, it is unclear as to the nature of the activating

ligand, or, indeed, if one is required.[22c] In the conver-

sion of XIV to XV (Scheme 2) von Gustorf[23] found that

forcing conditions were required for activation by CO (40

atm., 60°C) whereas relatively mild conditions (60°C) were

needed for PPh$_3$ assistance. It would therefore seem that

residual carbon monoxide is not serving in this capacity.

The results of our work on the iron pentacarbonyl-

induced coupling of 7-tert -butoxynorbornadiene, syn-7-

tert-butoxynorbornene, and anti-7-tert-butoxynorbornene

are presented in this dissertation. We will also present

a mechanism which accounts for the influence of Lewis base

substitutents in the syn-7-position of norbornenes and

Scheme 2
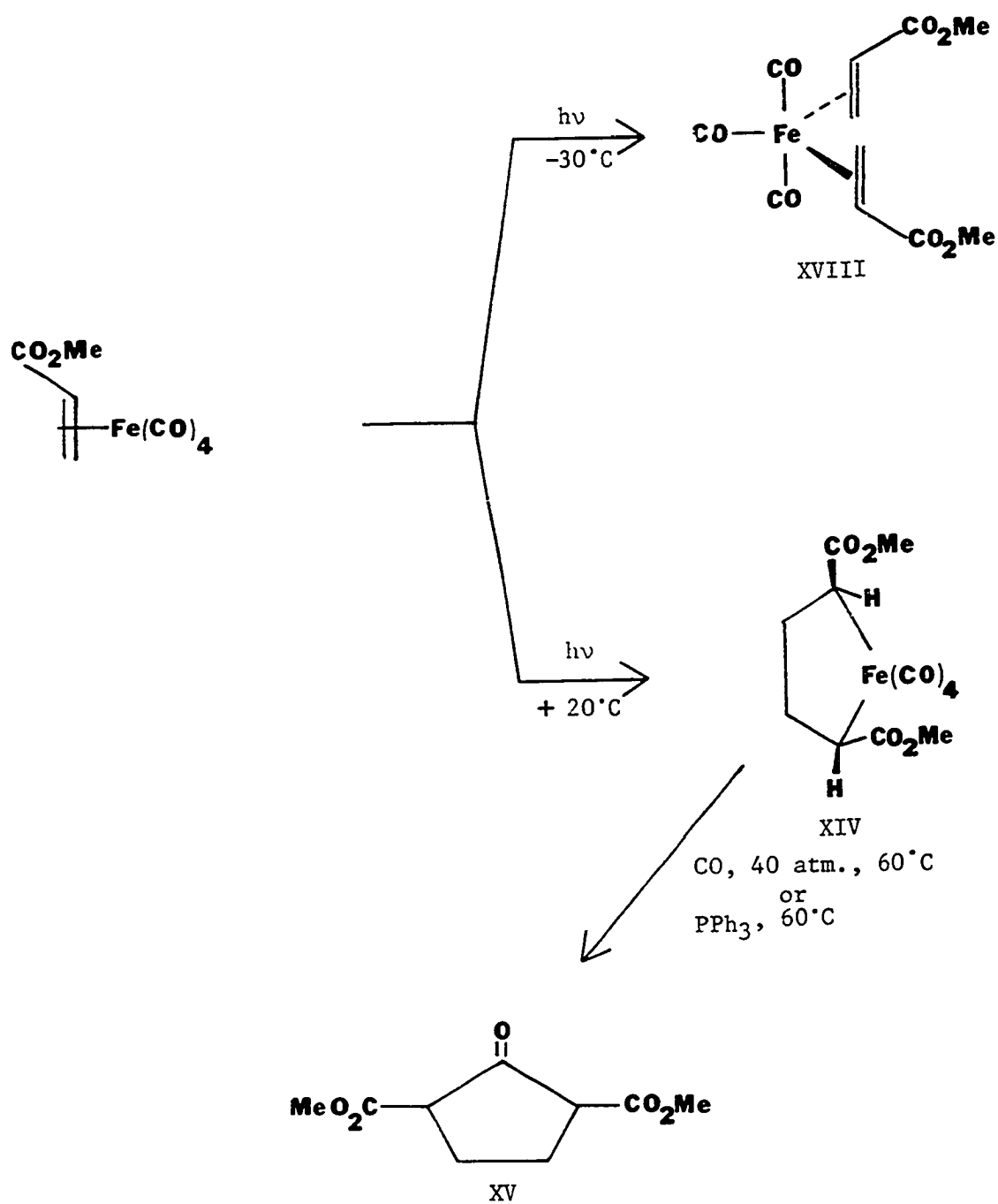
Norbornadienes, upon the stereochemistry of the product

dimer ketone.

CHAPTER 2

RESULTS AND DISCUSSION

The objective of this work was to gather informa-
tion pertaining to the mechanism of the iron carbonyl in-
duced coupling of olefins to carbon monoxide. To this
end, we chose 7-t-butoxynorbornadiene (1) as the olefin to
be coupled, for a number of reasons. First, this molecule

$$OC(CH_3)_3$$

1
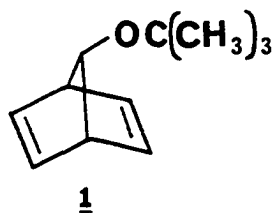
possesses the ring strain required for ketone formation
to be achieved in convenient quantities. Secondly, it
possesses two distinct olefinic linkages, both of which
are capable of undergoing coupling. Thus, competition
between two reactive sites is offered, one syn to the t-
butoxy group and one anti. The double bond syn to the 7-
t-butoxy group is of course the more sterically hindered
of the two. However, if the oxygen atom of this group is
an active participant in the mechanism, the sterically
hindered syn double bond could prove to be the more reactive

22

olefinic linkage toward Fe(CO)$_5$ despite the steric hinderance.
Therefore, 7-$\underline{t}$-butoxynorbornadiene ($\underline{1}$) provides a clear
choice between the latent stabilizing electronic inter-
action of the $\underline{syn}$-7-$\underline{t}$-butoxy group and the destabilizing
steric effect of this large substituent. This steric effect
is amply demonstrated when one compares reactions VII and
XI, Table 2, Introduction.

Reaction of 7-t-Butoxynorbornadiene ($\underline{1}$) with Fe(CO)$_5$

The thermal reaction of iron pentacarbonyl with $\underline{1}$,
under dry nitrogen for 24 hours, affords a dark black hetero-
geneous mixture. Filtration of this mixture through a bed
of celite leaves an iron-rich deposit which is mildly
pyrophoric.[31] In all cases, upon completion of the reaction,
the reaction mixture was oxidized with an acetone solution
of ferric chloride for 24 hours.[32] This procedure destroyed
any organometallic species formed in the reaction, leaving
only the metal-free organic compounds as products. The
separation of the complex product mixture (see Scheme 3)
provided by this reaction was achieved by careful column
chromatography. The small differences in the R$_f$ values of
the products of this reaction necessitated the use of TLC
grade silica gel as the chromatography support. Although
either silica gel G or H (Brinkmann Instruments, Inc.,
catalog numbers 7731 and 7736, respectively) could be used,
optimum results were obtained by using silica gel PF-254 +

Scheme 3

Fe(CO)$_5$

Di-n-butyl ether
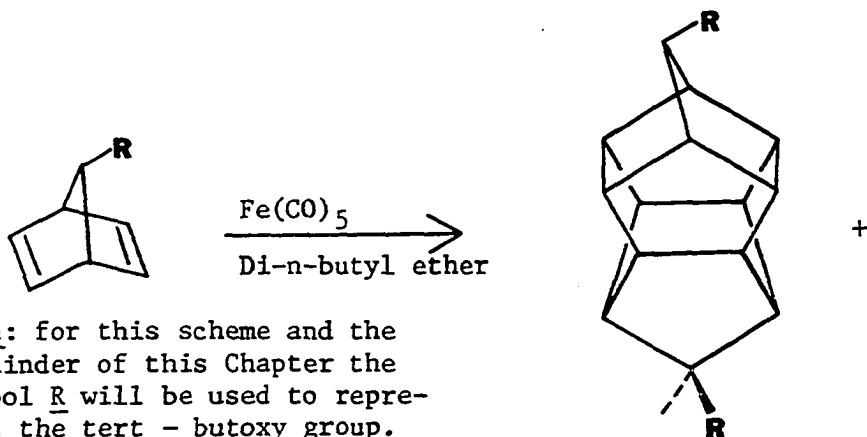
(note: for this scheme and the
remainder of this Chapter the
symbol R will be used to repre-
sent the tert – butoxy group.

R= OC(CH$_3$)$_3$

2

+

3

+

4

+

5

+

Polymer
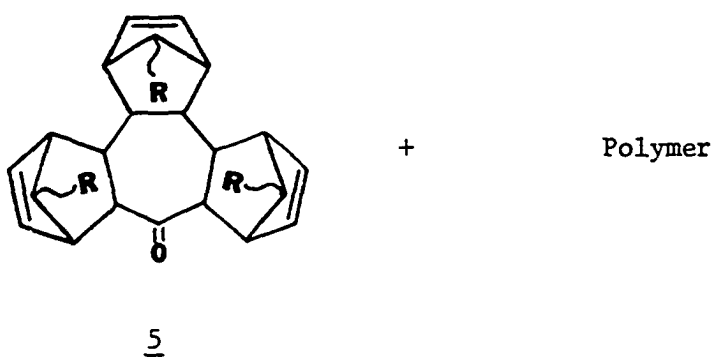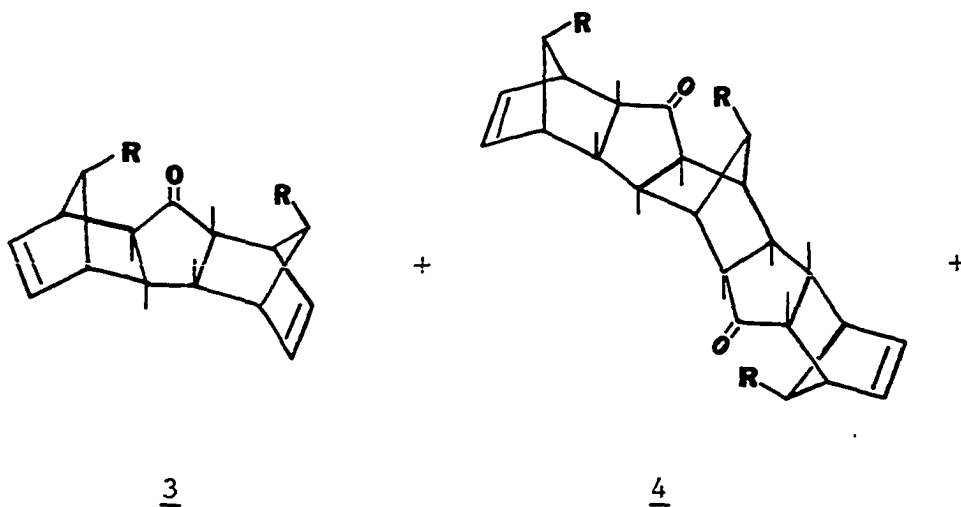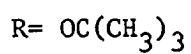
366 (Brinkmann Instruments, Inc., catalog number 7748).

The optimum solvent system for elution was found to be

1:9 ethyl acetate-hexane.

The first product eluted off the column was a dimeric

hydrocarbon as evidenced by its mass spectrum (Figure 2C)

which shows the molecular ion at m/e 328. The formation

of dimeric species in these and similar reactions is well

known.[15,17,33] The dimerization of 7-t-butoxynorbornadiene

(1) by the action of $Fe(CO)_2(NO)_2$ has also been reported.[34]

However, no physical data or structural information has

been reported for this dimer.

In 1961 Bird[20] and Lemal[21] simultaneously reported

the isolation of an interesting hydrocarbon dimer of norborna-

diene. That the dimer was a saturated compound was evi-

denced by its chemical inertness, by its lack of infrared

absorption in the carbon-carbon double bond region, and

by the absence of pmr absorption below δ 2.45. Both Lemal[21]

and Bird[20] suggested either of the following two (7a or 7b)

7a

7b
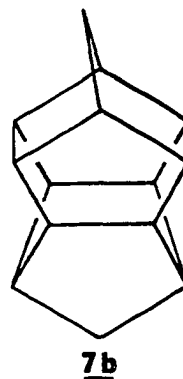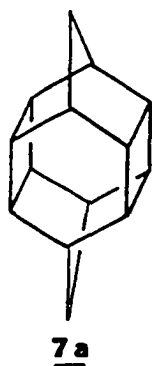
structures for the dimer product. While favoring structure

7b, their data did not permit a distinction to be made.

Indirect evidence supporting 7b as the structure for the

hydrocarbon dimer has been reported by Katz, et al.[35]

Dimerization of norbornadiene by a rhodium catalyst afforded

a number of dimeric and trimeric hydrocarbons. Included

among these products was the dimer reported by Lemal[21]

and Bird.[20] Treatment of 6 (another dimer isolated by

Katz) with hydroiodic acid (Equation 8) gave, among other

products, the hydrocarbon dimer (7) in question. Katz

suggested, on the basis of these results, that the dimer
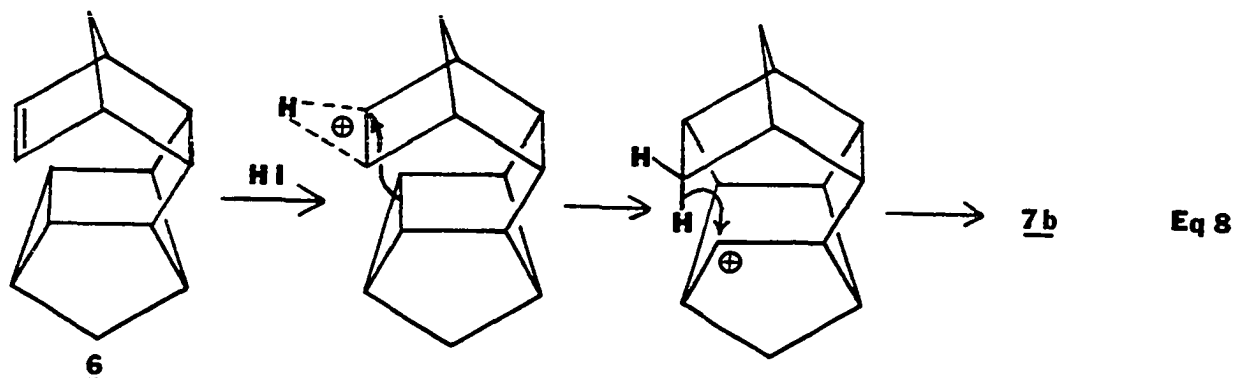
had the structure 7b since the isomeric structure (7a)

could not be related simply to the starting material 6.[35]

The first clue as to the structure of our hydro-

carbon dimer (2) came from its pmr spectrum (Figure 2a).

The pmr spectrum shows no absorption below δ 4.3. Also,

the infrared spectrum of 2 (Figure 2b) displayed no ab-

sorption in the region between 2800 and 1500 cm^{-1}. These
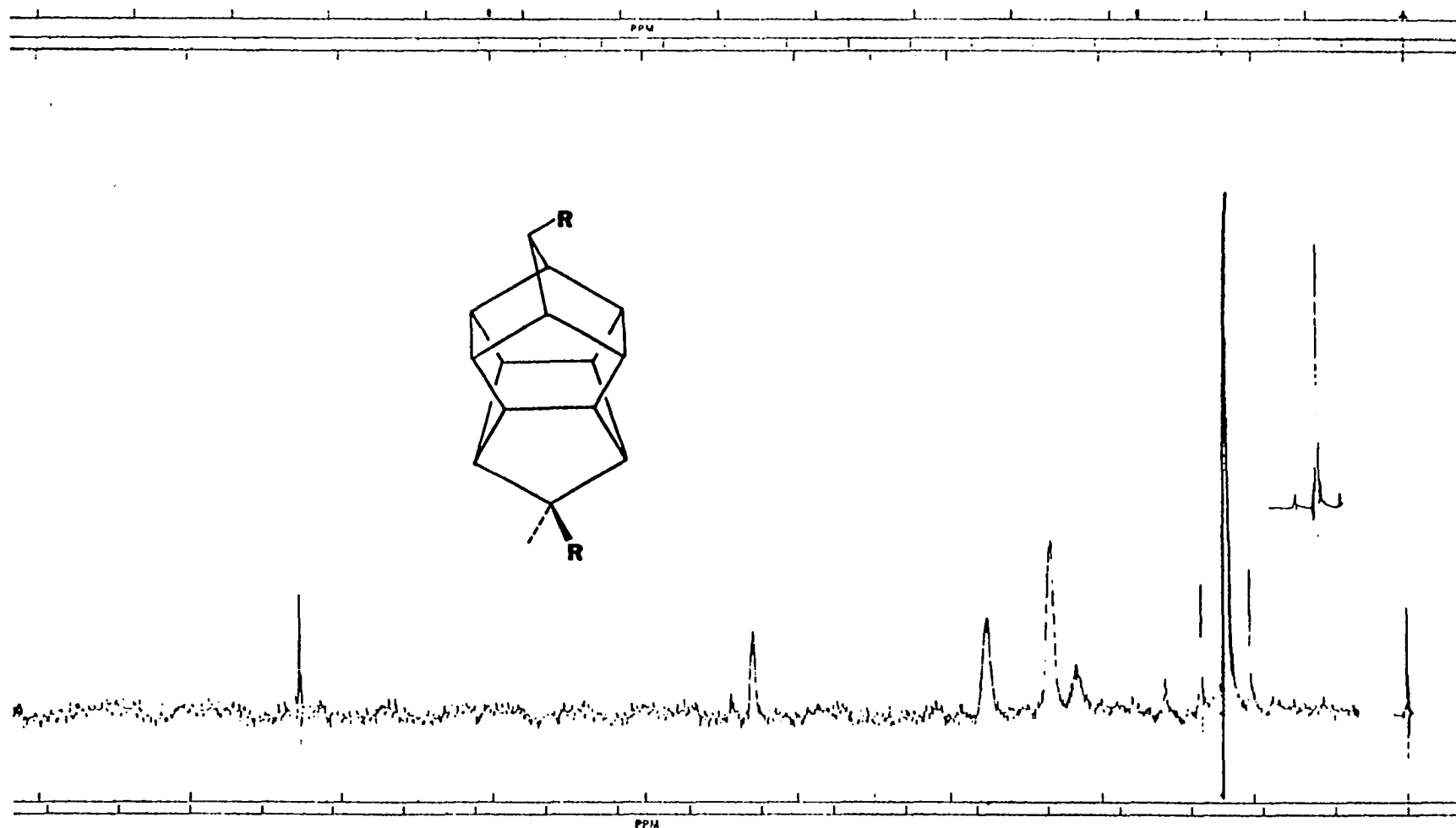
Figure 2a. Proton nmr spectrum (100 MHz, CDCl$_3$/TMS) of 2.
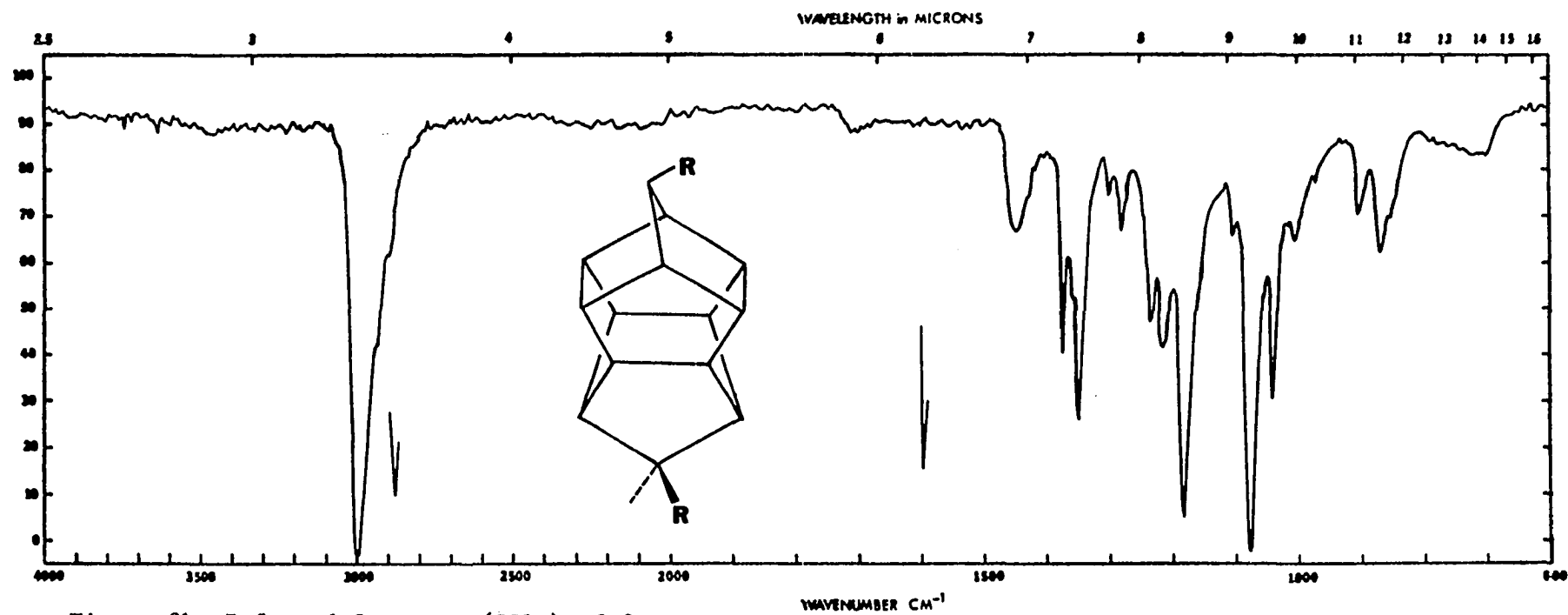
Figure 2b. Infrared Spectrum (CCl_4) of 2.
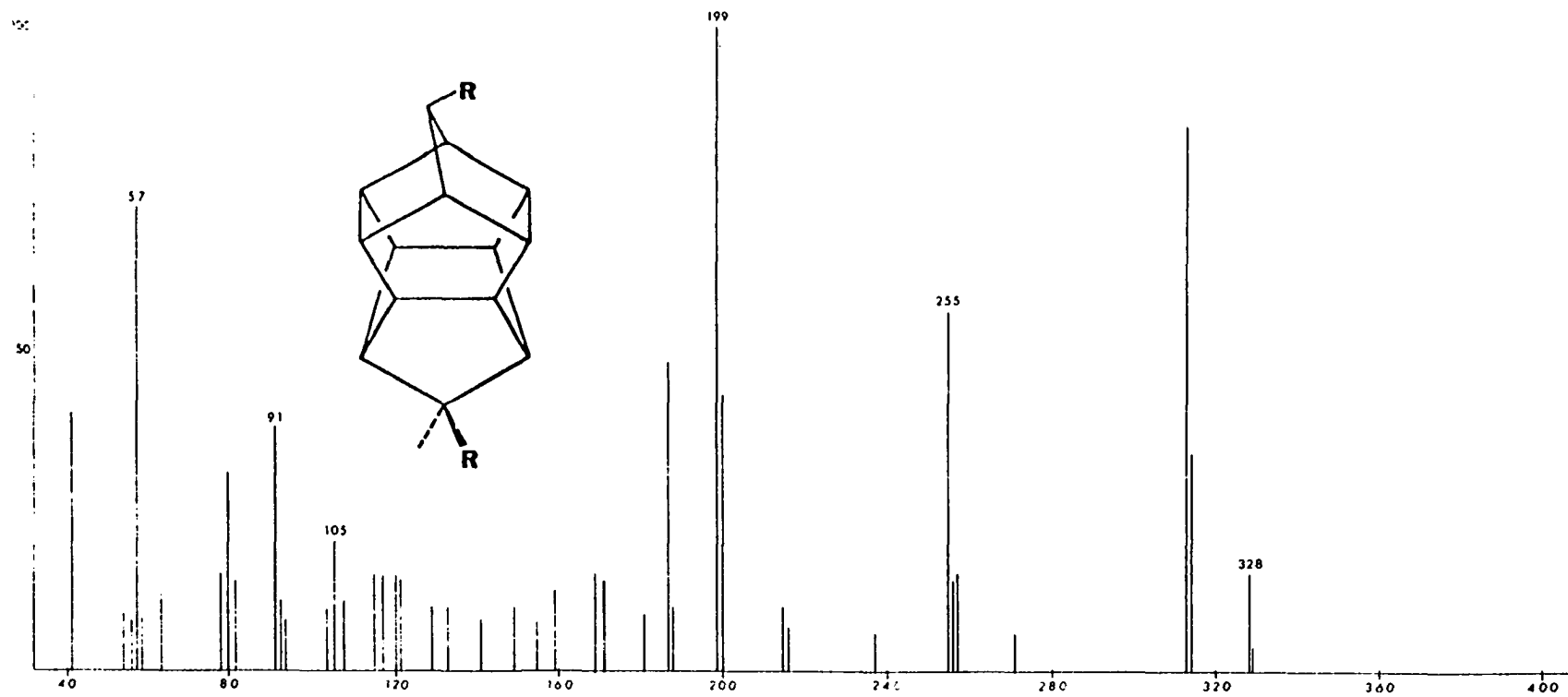
Figure 2c. Mass spectrum of 2.
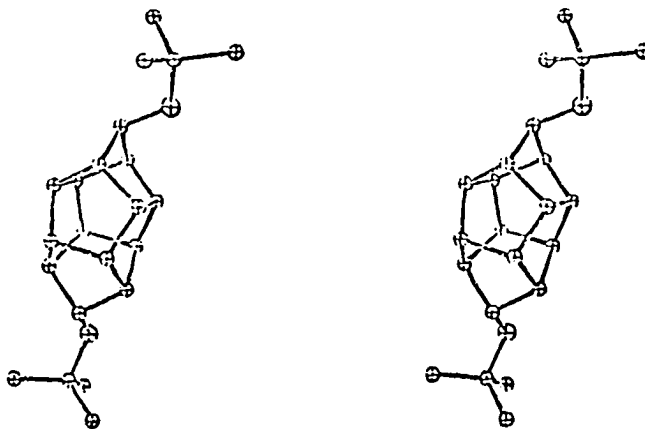
Figure 2d. Computer drawn stereoview of 2.

two observations indicate the lack of carbon-carbon un-
saturation and are consistent with either structure <u>2a</u>,
<u>2b</u>, or <u>2c</u> (below), analogous to those described above.
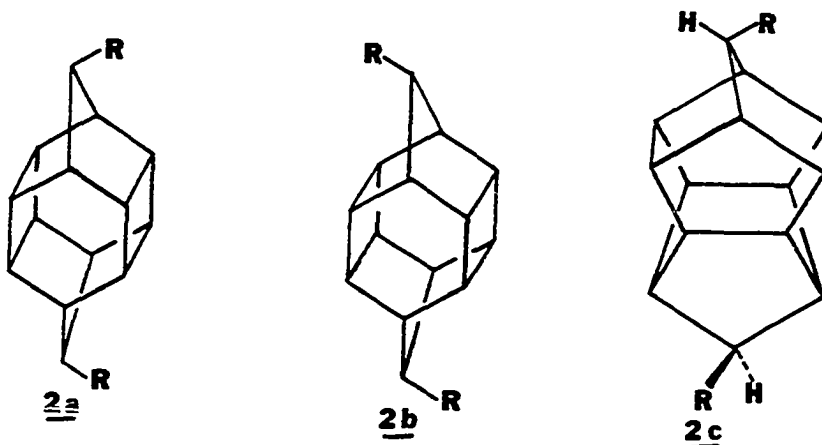
The symmetry elements present in these structures (Point
groups C_{2v}, C_{2h} and C_2 for <u>2a</u>, <u>2b</u> and <u>2c</u>, respectively)
precluded a choice by either pmr, ^{13}CNMR, or ir analysis.
The compound was therefore subjected to single crystal
x-ray analysis. Crystals for analysis were obtained by
cooling (0°C) a solution of <u>2</u> in pentane, which afforded <u>2</u>
as small needles (triclinic, space group P $\bar{1}$). The density
of <u>2</u> was determined by the flotation method; using Na_2SO_4-
H_2O as the flotation medium, a value of $\rho^{31°}$=1.174 was obtained.
(calculated ρ = 1.155). The cell dimensions are a = 6.282(1),
b = 11.159 (2), c = 14.219 (3) Å, α = 106.49 (2)°, β =
92.66 (2)° and γ = 97.17 (2)°. The structure was deter-
mined by direct methods and refined with least-squares
calculations using 3220 data. The final R-value is 0.081.
The computer generated stereoview of the dimer is shown in

Figure 2d, <u>i.e.</u>, structure <u>2c</u> (above).[36]

The mass (Figure <u>3c</u>) and infrared (Figure 3b) spectra of the next component to be eluted from the column suggested that it was a dimeric ketone. The mass spectrum displayed a molecular ion at <u>m/e</u> 356. The carbonyl stretching frequency observed at 1727 cm^{-1} for this compound is consistent with that reported for strained cyclopentanone rings.[22,38] The coupling-insertion of 7-t-butoxy-norbornadiene (1) can conceivably provide a total of 36 stereoisomers. These stereoisomers are shown below in matrix form. The designations used are discussed in the Introduction and shown in Figure 1 (Introduction).
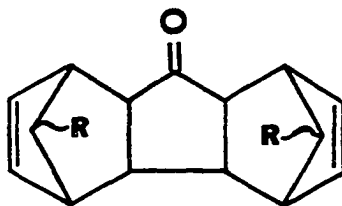
SNCNS	SNCNA	SNCXS	SNCXA
ANCNS	ANCNA	ANCXS	ANCXA
SXCNS	SXCNA	SXCXS	SXCXA
AXCNS	AXCNA	AXCXS	AXCXA

<u>cis</u> series: contains four <u>meso</u> isomers
                 and six enantiomeric pairs.

SNTNS	SNTNA	SNTXS	SNTXA
ANTNS	ANTNA	ANTXS	ANTXA
SXTNS	SXTNA	SXTXS	SXTXA
AXTNS	AXTNA	AXTXS	AXTXA

<u>trans</u> series: contains ten enantiomeric
                   pairs, four of which have
                   a C_2 axis.
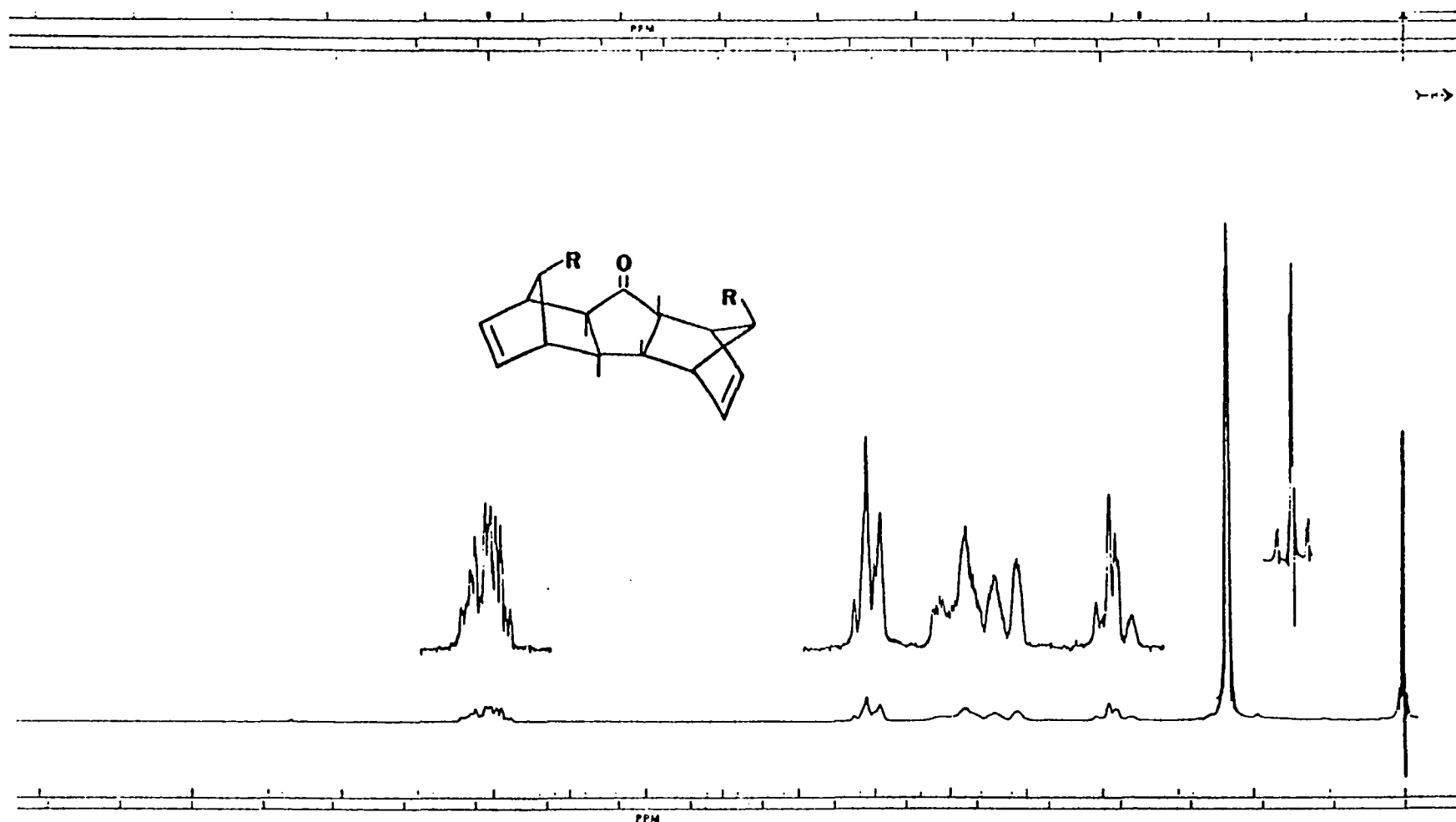
Figure 3a. Proton nmr spectrum (100MHz, CDCl$_3$/TMS) of 3.
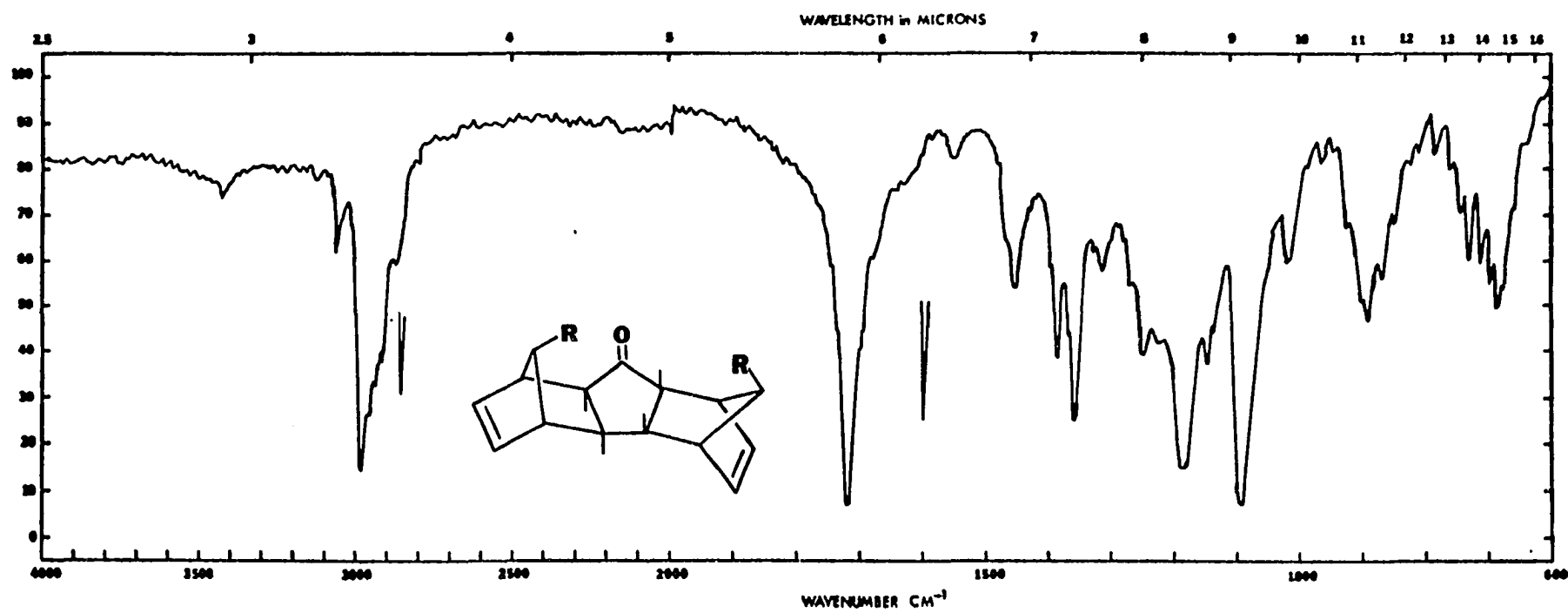
Figure 3b. Infrared Spectrum (CCl$_4$) of 3.
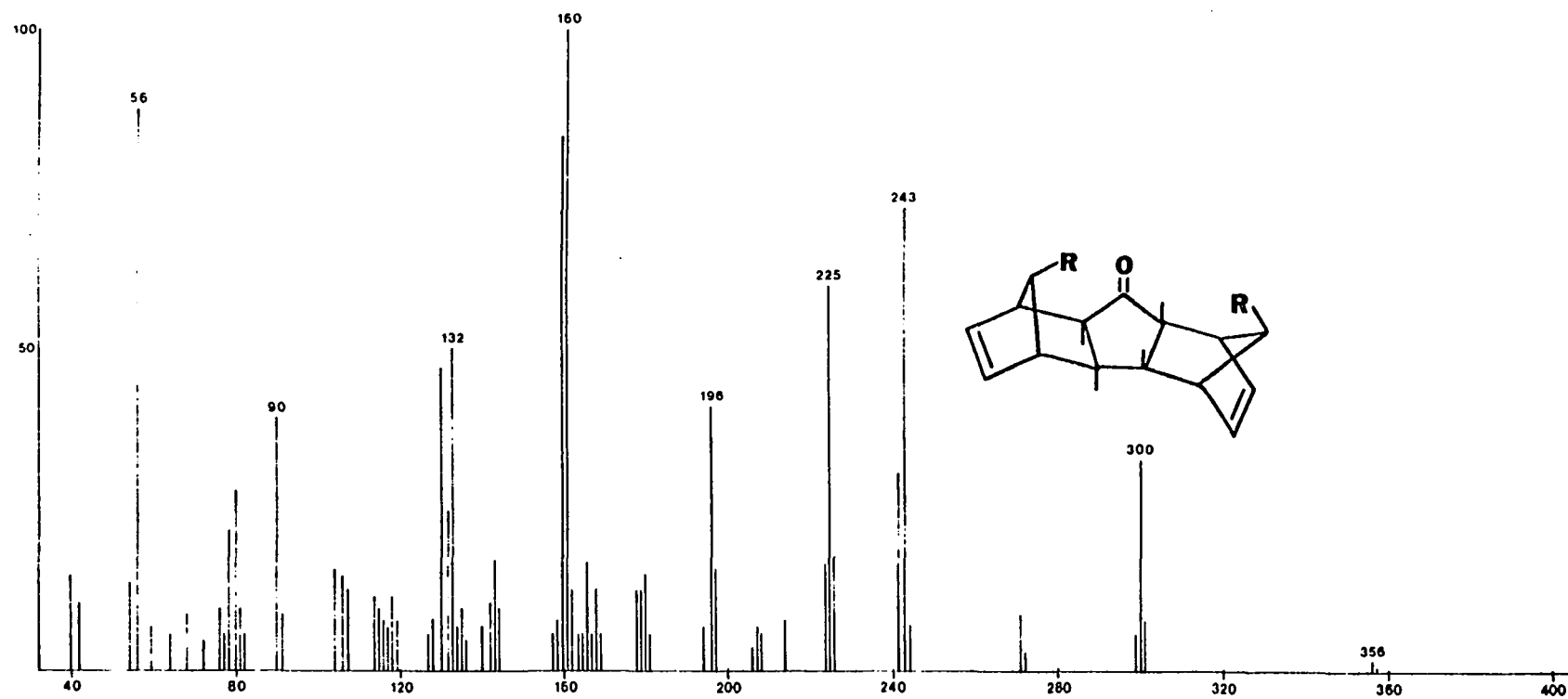
Figure 3c. Mass spectrum of **3**.
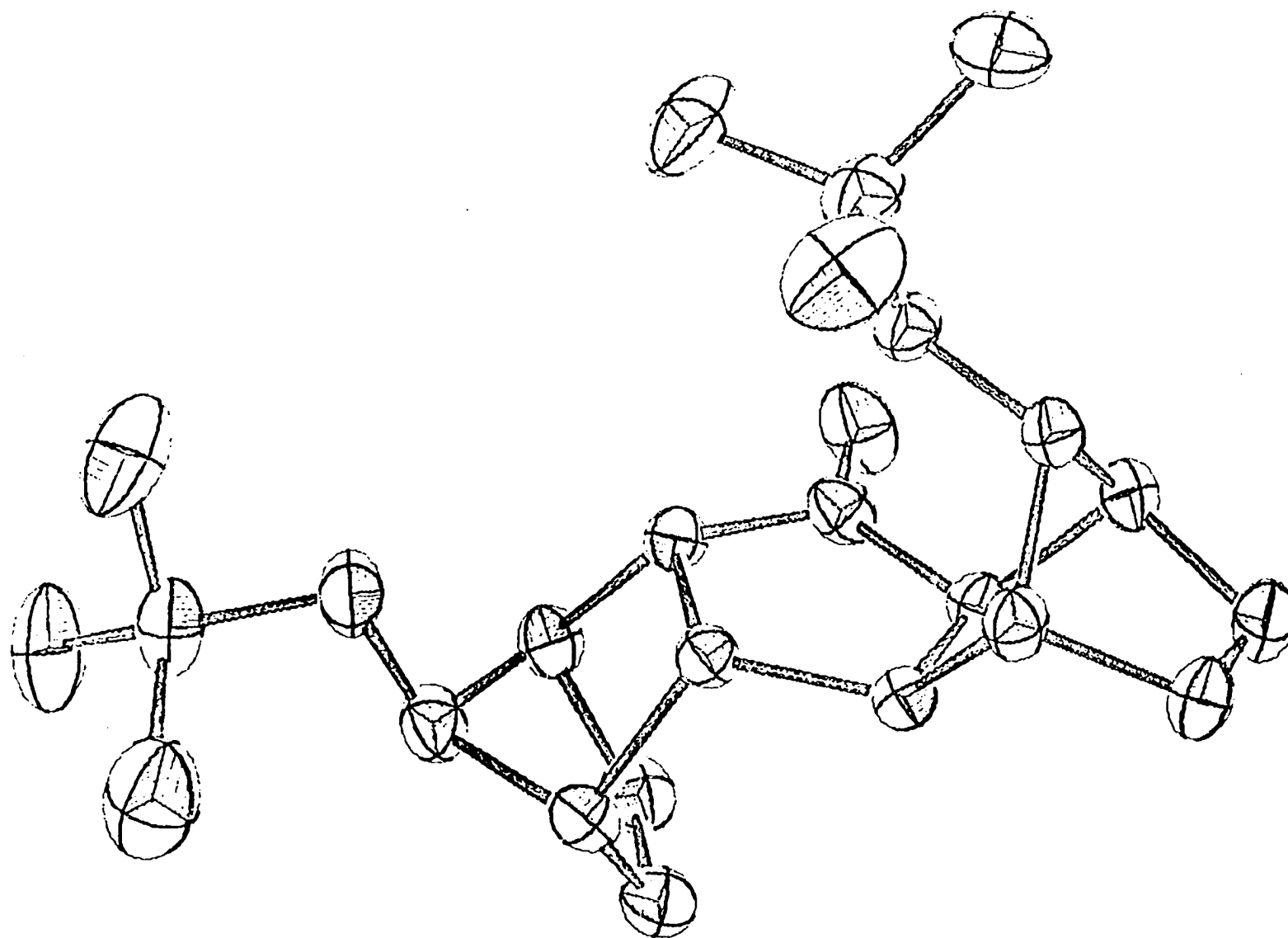
Figure 3d. Computer drawing of 3.

The 100 MHz pmr spectrum (Figure 3a) of the dimer ketone 3 provided us with our first clue to the structure of this product. The observance of two t-butyl resonances in the spectrum immediately allowed us to eliminate those structures with either a C_2 axis or a plane of symmetry (i.e., the diagonal elements of the above matrices). Further elucidation of the structure was achieved by proton magnetic double resonance (pmdr) experiments. When either of the absorptions at δ 3.43 or δ 3.47 (hydrogens geminal to the t-butoxy groups) were irradiated, there was no change in the multiplet centered at δ 6.0 (olefinic hydrogens). The coupling between an anti-7-hydrogen and the olefinic hydrogens of norbornenyl systems, although small (≤ 1 Hz), has been observed.[39]

The lack of coupling between the C_7 hydrogen and the olefinic hydrogens suggest that the C_7 hydrogen is syn to the carbon-carbon double bond and consequently the t-butoxy groups are syn to the cyclopentanone ring. This single observation allowed us to then eliminate all of the matrix elements containing an anti designation. The two remaining stereoisomers (SXTNS and SXCNS) both contain the exo-endo geometry. This result is in line with the trend mentioned in the Introduction in which olefins with an appropriately oriented Lewis base substituent (e.g., the syn-C_7-position of norbornenes) yield coupling products (cyclopentanones) with an exo-endo configuration. The

ketone 3 is only the second dimer ketone formed in the reaction of a norbornadiene with Fe(CO)$_5$ which has been found to possess a non-exo-trans-exo configuration.[25]

Additional evidence indicating the exo-endo configuration was obtained from the ultraviolet spectrum of ketone 3. In 1966 Cookson[19] synthesized all three trans isomers (i.e., XTX, XTN, NTN) of the ketone derived from the reaction of norbornadiene with iron pentacarbonyl.
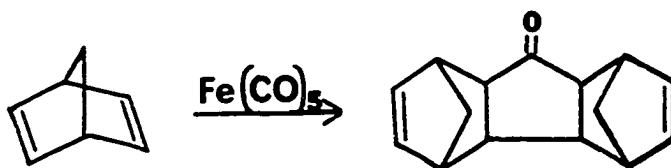
While characterizing these ketone isomers, he noted that only those containing an exo bound cyclopentanone ring gave an additional UV absorption with a maximum at about 223 nm (ε_{max} = ca. 1300). The additional absorption maximum at 223 nm was attributed to a new type of chromophore.[40] In a 1,5-diene (below) which is held in a conformation
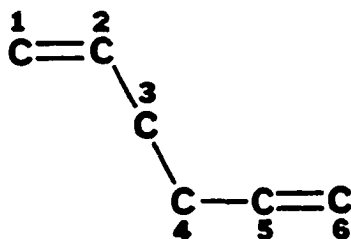
where the central C_3-C_4 bond is in a plane at right angles to both double bonds there is a coupling of the two π-systems through the central C_3-C_4 σ bond. This coupling leads to a new π→π* transition which is very sensitive

to the geometry of the system. A terminal carbon of the 1,5-diene may be replaced by a heteroatom (e.g., oxygen). The norbornenyl ketones, with which we are dealing, are structurally related to 1,5-diene systems of this type (i.e., a γ,δ-unsaturated ketone). The central C_3-C_4 bond of the unsaturated exo-ketone is held in a conformation such that its plane is nearly normal to the planes of the
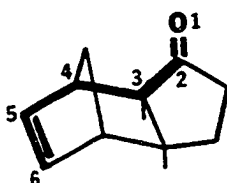
carbon-oxygen and carbon-carbon double bonds. To illustrate the contribution of this chromophore, λ_{max} and ε_{max} values of the three isomeric dimer ketones (XTX, XTN, NTN) are shown below:

isomer	λ_{max}, nm (EtOH)	ε_{max}
XTX	225	2540
	309	137
XTN	221	1410
	308	83
NTN	–	–
	302	33.5
ketone 3	220	1060
	290	56.2

The observed maxima and, more importantly, their extinction coefficients for ketone 3 are in fair agreement with those reported for the XTN isomer.

At this point, we were reasonably confident of

the syn-exo-endo-syn stereochemistry of ketone 3. However,

the cis or trans nature of the cyclopentanone backbone

still remained in question. To determine the cis or trans

configuration, ketone 3 was subjected to single crystal

X-ray analysis. Suitable crystals for analysis were ob-

tained from a cold (-78°C) pentane solution of 3 which

yielded crystals of 3 as square platelets (space group

Pb_{CN} (No. 60). The calculated density of ketone 3 is

ρ = 1.137. The cell dimensions are a = 29.248 (1), b =

12.2059 (5), c = 11.6621 (6) Å. The structure was deter-

mined by direct methods and refined with least-squares cal-

culations using 3538 data. The final unweighted R-value

for all data is 0.057. The computer generated stereo-

view of the dimer ketone is shown in Figure 2d, i.e.,

the SXTNS isomer.[41]

The next compound from the column chromatography

was a trimer ketone. The mass spectrum (Figure 4c) of this

component displayed its parent ion at m/e 548. The in-

frared spectrum (Figure 4b) of this compound displays a

strong absorption at 1722 cm^{-1} (>C=0 stretching frequency).

The pmr spectrum (Figure 4a) has two distinct resonances

for the olefinic hydrogens and three separate absorptions

attributed to the t-butyl groups. These observations sug-

gest a trimeric ketone such as 4a or 4b (on the next page).

The compound was submitted for single crystal X-ray analysis.

The data crystal was obtained from an acetone solution by
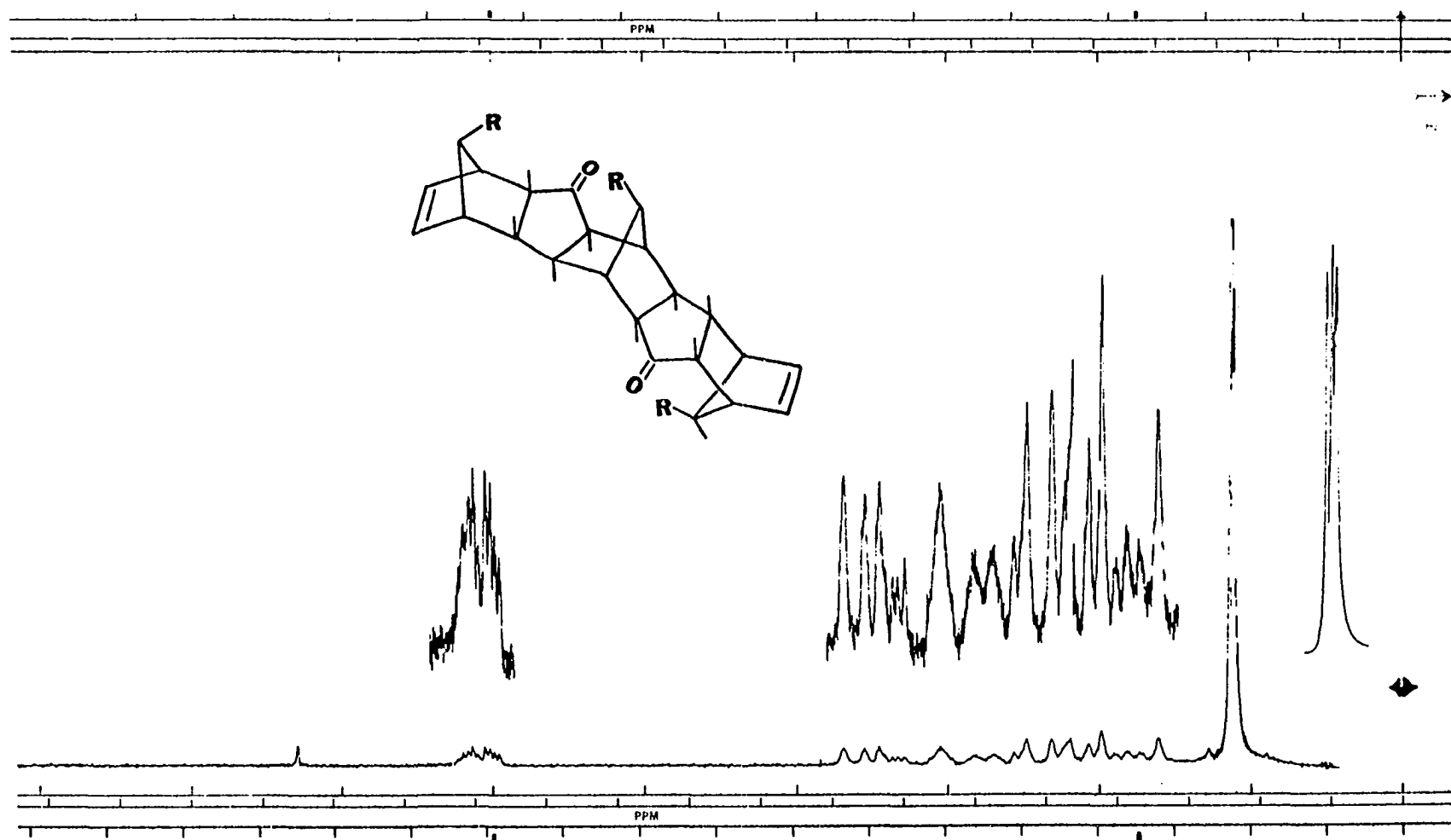
Figure 4a. Proton nmr spectrum (100 MHz, CDCl$_3$/TMS) of 4.
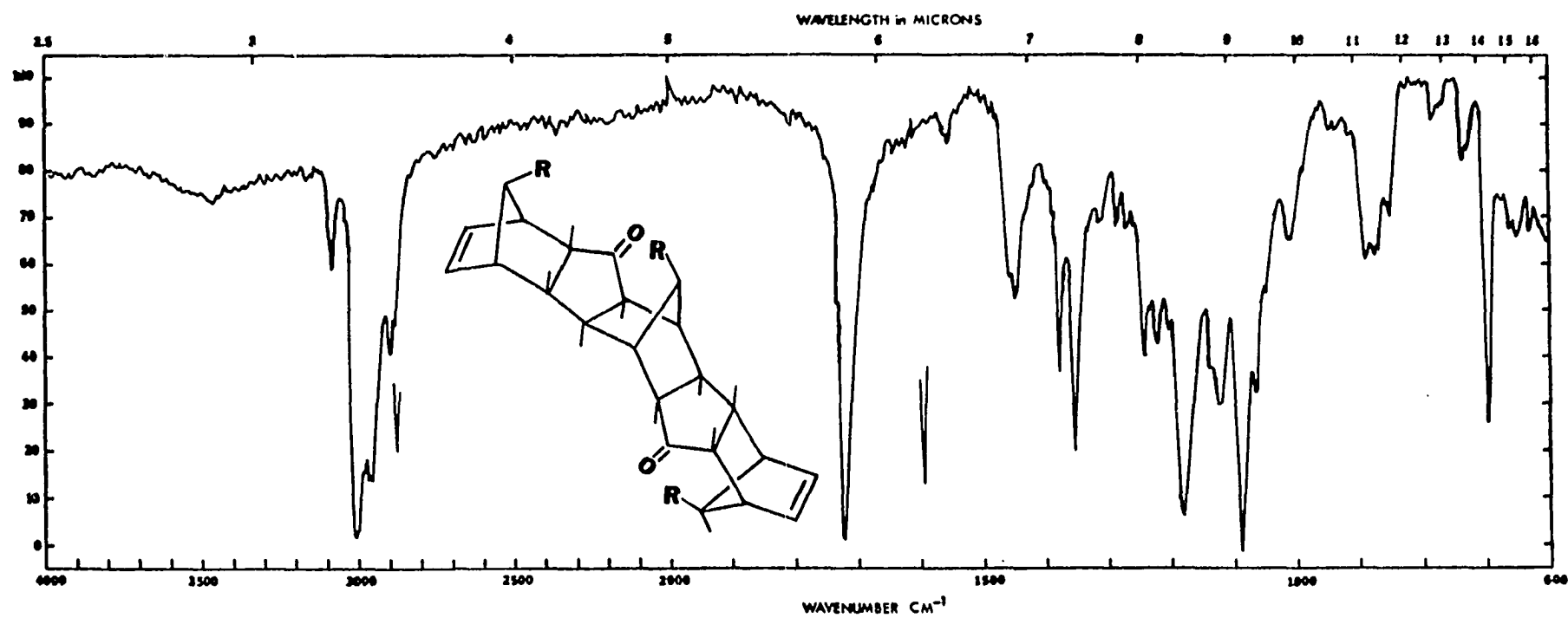
Figure 4b. Infrared Spectrum (CCl$_4$) of 4.
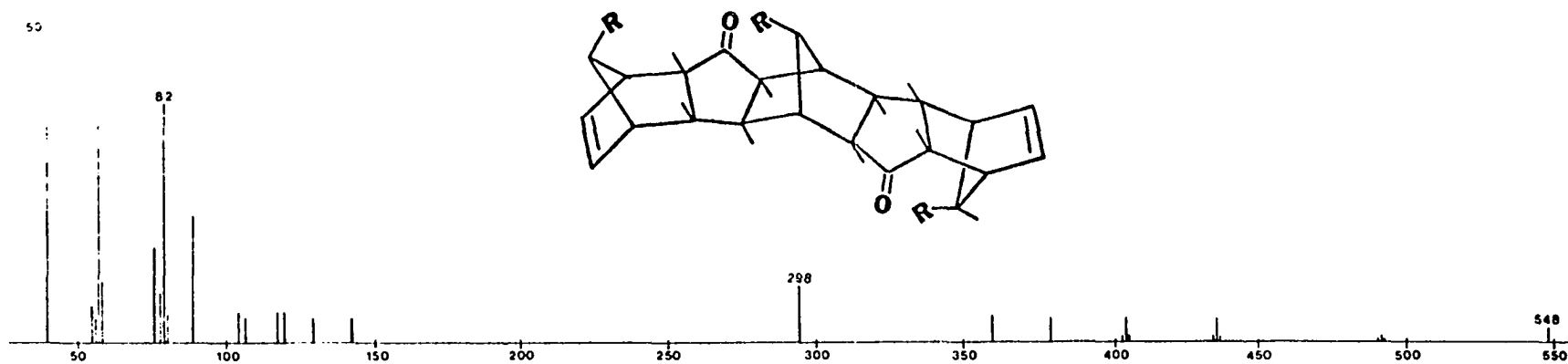
Figure 4c. Mass spectrum of 4.
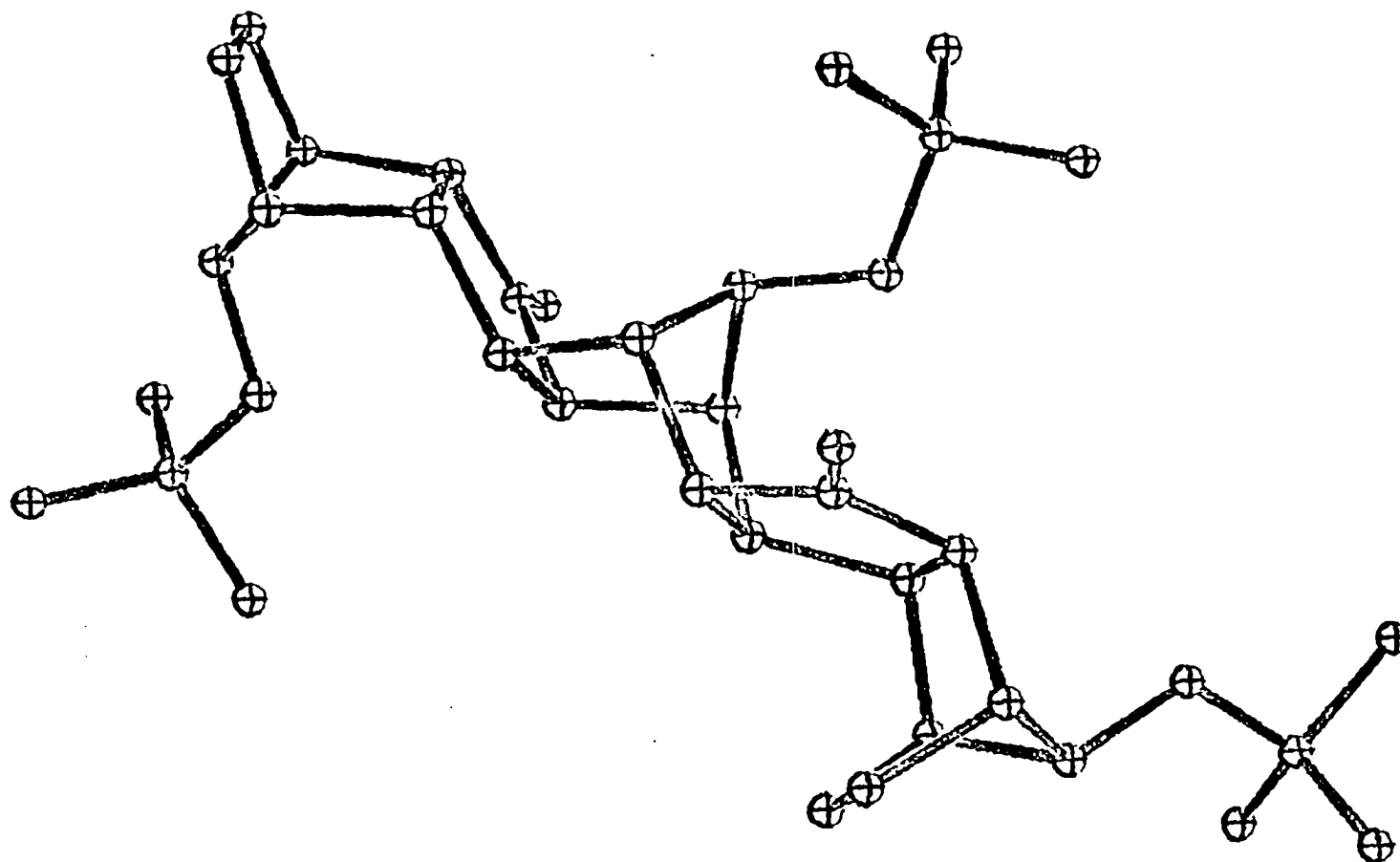
Figure 4d. Computer drawing of 4.
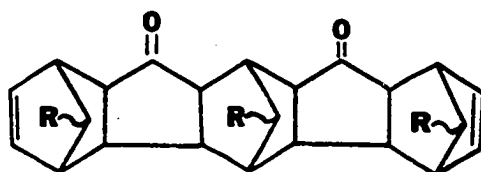
4a
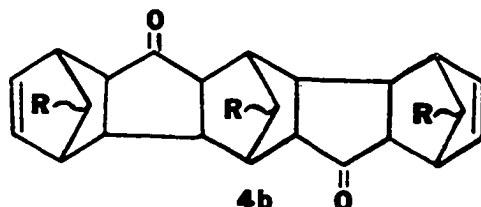
4b

the slow evaporation of the solvent (space group $P2_{1/c}$).
The dimensions of the cell are a = 10.5378 (8), b =
27.084 (3), c = 12.7897 (6) Å, β = 120.928 (5)°. The
structure was determined by direct methods and refined
using 6520 data. The present R-value is 0.068. The cal-
culated density for $\underline{4}$ is ρ = 1.164. The computer generated
drawing of the structure of $\underline{4}$ is shown in Figure 4d and
drawn below.
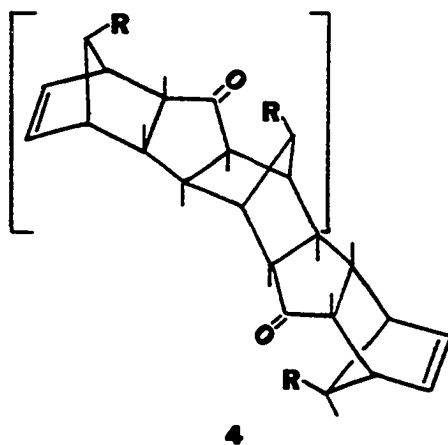
4

Several features of this structure are very inter-
esting: First, a portion of the structure (in brackets,
above) is identical to the structure of ketone $\underline{2}$ (*i.e.*,

SNTXS); Second, all of the t-butoxy substituents are
oriented toward a cyclopentanone ring; and Third, the
ketonic functions are directed away from each other (we
suggest the designations periplanar and antiperiplanar to
describe the configurations of the carbonyl groups in 4a
and 4b, respectively).

These facts suggest a possible mechanism of forma-
tion of diketone 4. Although a binuclear iron species
was proposed as a possible intermediate in the formation
of the trimer diketone obtained from the reaction of norbor-
nadiene and $Fe(CO)_5$,[17] such a species may not necessarily
be involved in the formation of diketone 4. We instead
suggest the sequence shown in Equation 9 to account for the
formation of 4. Attack of the complex 15 (vide infra, Scheme
4, pg 82) occurs on the least hindered side of the double

$$2 \quad + \quad 15 \quad \longrightarrow \quad 4 \qquad Eq.\,9$$
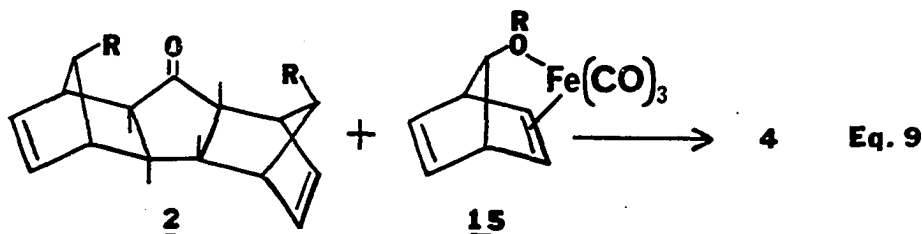
bond of the exo norbornyl system of ketone 2. Models in-
dicate that if a like attack occurred on the endo norbornyl
ring, rehybridization of the sp^2 carbon to an sp^3 configura-
tion would cause considerable non-bonded interaction between
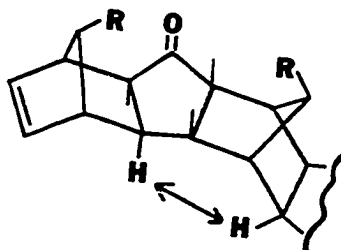
the adjacent hydrogen atoms as shown above.

The remarkable stereospecificity of this reaction is again demonstrated when one considers that out of 2,304 stereoisomers for diketone 4 (36 stereoisomers for ketone 2, two double bonds on ketone 2, exo or endo on these two double bonds, cis or trans and periplanar or anti-peri-planar for the cyclopentanone rings, exo or endo on the third norbornyl ring, and syn or anti for the third t-butoxy group 36 x 2^6 = 2,304) only one stereoisomer, as far as could be detected, was formed.

The infrared spectrum (Figure 5a, 1722 cm^{-1}) of the next component from the column indicated it to be another ketone. The compound was isolated as a viscous, colorless oil which would not solidify even after standing for an extended period under vacuum heating. Purification of the oil was attempted by means of recrystallization, sublima-
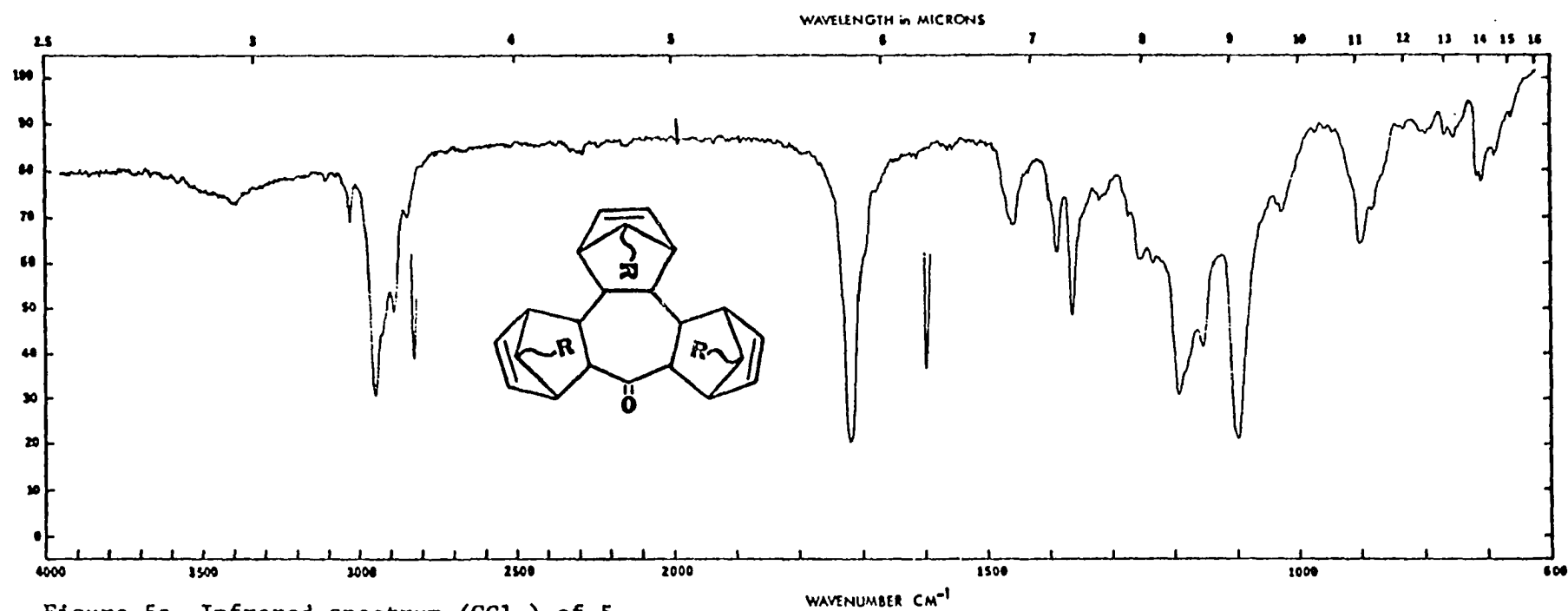
Figure 5a. Infrared spectrum (CCl$_4$) of 5.

48

tion, and various chromatographic techniques, all to no
avail. Attempts at sublimation were accompanied by de-
composition of the sample (as evidenced by its discolora-
tion) at ca. 170°. Attempts at purification by vapor phase
chromatography were unsuccessful as the compound could not
be made to elute from the various columns used. This
situation was encountered even under conditions designed
to facilitate elution (e.g., oven temperatures <300°,
short columns, etc.) and after extended waiting periods.
Repeated elutions on preparative layer chromatography plates
yielded the original oil as did elution on a column packed
with TLC grade silica gel. High pressure liquid chroma-
tography attempts met with the same success on either an
absorption column (Porasil A) or on a reverse phase parti-
tion column (Chromosep RVP).

The mass spectrum of this oil exhibited a peak at
m/e 492 as its highest detectable ion (at either 70 or
10 eV ionizing voltage). The compound is thought to be
the cyclic trimer monoketone (5), by analogy with the
cyclic trimer ketone obtained from the reaction of norborna-

5
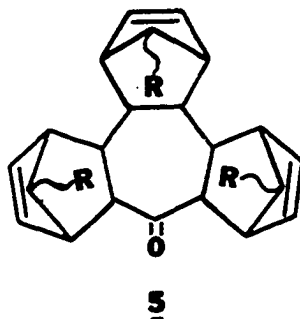
diene and Fe(CO)$_5$.[17] The molecular weight of $\underline{5}$ is 520 g-mole^{-1}, and loss of carbon monoxide[37] (28 g-mole^{-1}) in the mass spectrum of $\underline{5}$ would result in an ion at m/e 492, as observed. However, since the loss of either two carbon monoxide moieties or an isobutylene group (=<) from a linear trimer diketone (e.g., $\underline{4}$, MW = 548) would also result in the appearance of an ion at m/e 492. Hence, the mass spectrum of $\underline{5}$ was not uniquely indicative of the suggested structure. A further complication was that the observed small difference in the R_f values between $\underline{4}$ and $\underline{5}$ (0.18 and 0.12, respectively, 1:9 ethyl acetate-hexane) suggested the possibility that $\underline{5}$ might be isomeric with $\underline{4}$.

Due to our lack of success in purifying $\underline{5}$ and since its mass spectrum did not permit a distinction to be made between a linear (e.g., $\underline{4}$) and a cyclic (e.g., 5) trimer, we were forced to an alternative method to obtain the required information. The LiAlH$_4$ reduction of the oil resulted in the formation of an alcohol (as suggested by its infrared spectrum, OH stretch, 3500 cm^{-1} (br) and the absence of absorption in the region 2800-1500 cm^{-1}). The mass spectrum of the alcohol had a parent ion at m/e 522 (two units higher than the molecular weight of $\underline{5}$, as expected from the reduction of the ketone to an alcohol) which suggest that ketone $\underline{5}$ has the indicated cyclic trimer configuration.

The last component from the column was a very polar material which required elution with undiluted ethyl acetate

in large volumes (relative to the elution volumes needed
for the other components) to effect passage from the column.
The eluted material was a very viscous, heavy oil. The
mass spectrum of this oil showed the highest detectable
ion at m/e 588. Commencing with this ion, six clusters of
ions each differing by a value of m/e 28 units were ob-
served. This observation suggests that the material con-
tains at least six ketonic groups.

As far as could be detected by chromatographic and
spectral methods, this material was homogeneous. Since
the prior components were eluted in the approximate order
of increasing molecular weights, and this material required
a much more polar eluant for elution, and the mass spectral
information suggests the presence of at least six carbonyl
functions, we conclude that the last component is polymeric
in nature. The formation of a polymeric material was also
observed in the reaction of norbornadiene and $Fe(CO)_5$.[17]

The Reactions of Syn- and Anti-7-t-Butoxynorborandiene with $Fe(CO)_5$

As stated earlier, 7-t-butoxynorbornadiene (1) was
used as a substrate in this study because it offered a clear
choice between a stabilizing electronic and a destabilizing
steric effect. Our observation that both t-butoxy groups
are syn to the cyclopentanone ring in the dimer ketone ob-
tained from the reaction of 7-t-butoxynorbornadiene (1) and

Fe(CO)$_5$ is of considerable mechanistic importance. It was nec-
essary, therefore, to determine whether the t-butoxy groups
were stereochemically stable to the reaction conditions. E.g.,
was an AXTNA intermediate involved (See Equation 10) which
subsequently epimerized to the observed syn-syn product?

1   **A X T N A**   **3**   **Eq 10**
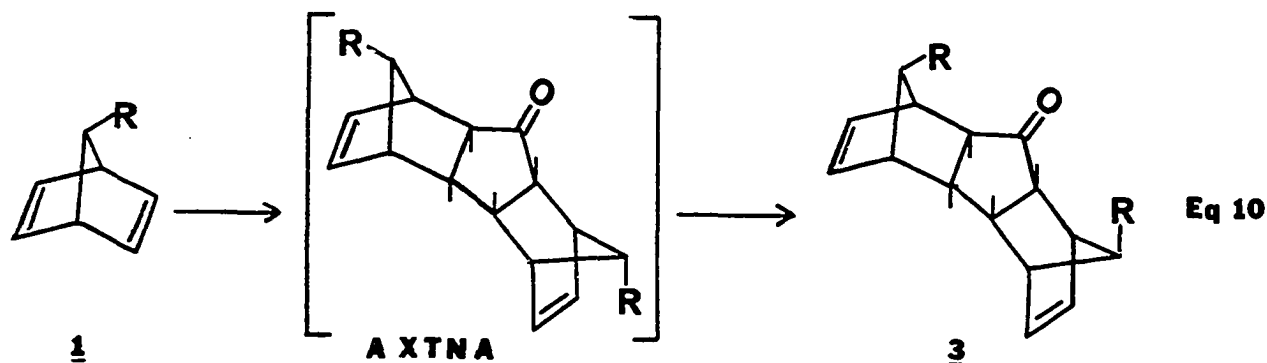
The models chosen for the control experiment were syn-(**8**)

8   **9**
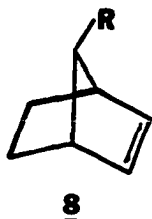
and anti-7-t-butoxynorbornene (**9**).

Syn-7-t-butoxynorbornene (**8**) was synthesized via
the method of Kochi, et al.,[42] (Equation 11). Partial
hydrogenation of 7-t-butoxynorbornadiene (1) was achieved
at atmospheric pressure and at ambient temperature. The
use of ethyl acetate as solvent afforded better yields of
8 than did the reported solvent, ethanol. The use of pre-
reduced 5% Pd/C was necessitated by the fact that a more
active catalyst (e.g., pre-reduced 10% Pd/C) gave complete

reduction as did experiments performed using pre-reduced

Eq 11
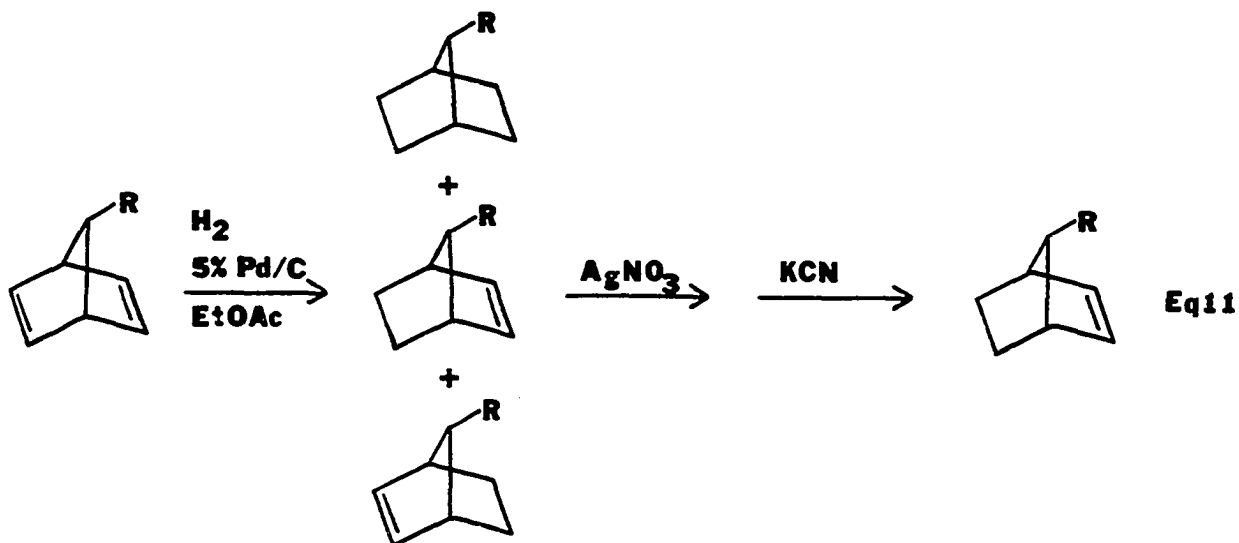
5% Pd/C at higher pressures (e.g., 3 atmospheres, Parr Shaker). After one equivalent of hydrogen had been taken up by the reaction mixture, the product was obtained via extraction with aqueous $AgNO_3$. This silver complex was then destroyed by addition of KCN; and after extraction and distillation, pure 8 could be obtained in an average isolated yield of 20%.

The anti isomer 9 was obtained as a mixture of 9 and 7-t-butoxynorbornane in a 1:3 ratio, respectively. The synthesis of 9, shown in Equation 12, was achieved by the diimide reduction of 7-t-butoxynorbornadiene.[43]

Eq 12

3 : 1
    9
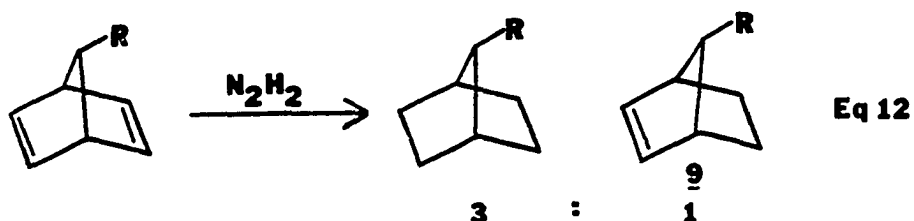
Diimide was generated in situ by the acid catalyzed decomposition of potassium azodicarboxylate. This mixture was deemed suitable for reaction with $Fe(CO)_5$ since the saturated compound is inert to this reagent.

Analytical separation of the isomers 8 and 9 was achieved by vpc using a 100 ft. x 0.02" support coated open tubular (S.C.O.T.) capillary column coated with FFAP (Stationary phase, operating at 90°C, He flow rate 24 ml/min). The starting material and the three reduction products are shown below with their respective retention times, as measured from hexane. The syn isomer 8 was unaccompanied by any detectable trace of the anti isomer

	1	8		9
min	7.5	6.5	3.85	3.55
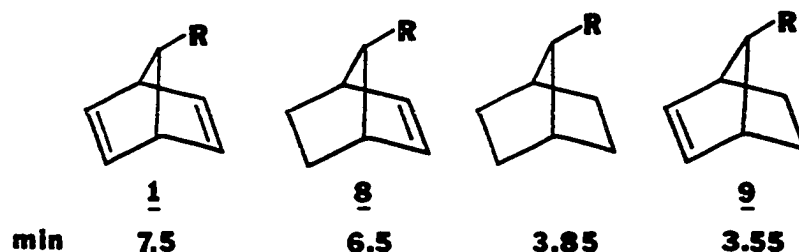
9 or starting diene (1). The mixture of 9 and 7-t-butoxy-norbornane (1:3 respectively) had a trace (<1%) of the syn isomer 8 present but no starting diene.

The mixture of 7-t-butoxynorbornane and 9 was re-fluxed with $Fe(CO)_5$ and di-n-butyl ether for 20 hours. After filtration and oxidative workup (vide supra), vpc analysis of the reaction mixture showed no trace of the presence of the syn isomer 8. The vpc tracings displayed only the presence of 7-t-butoxynorbornane and 9 in the original 3:1 ratio.

Furthermore, the reaction mixture was concentrated, and
evidence for the presence of a ketonic product was sought.
Infrared analysis of this concentrate showed no absorption
in the region 2500-1600 cm^{-1}. Analysis of the concentrate
by TLC, PMR and VPC (several columns under various con-
ditions of column temperature and He flow rate) provided
no evidence for a ketonic product. Indeed no reaction pro-
duct at all could be found. These observations indicate
that the <u>anti</u> isomer <u>9</u> is completely inert to the Fe(CO)$_5$
reagent (<u>i.e.</u>, no isomerization of <u>9</u> → <u>8</u> took place nor did
<u>9</u> couple under the influence of Fe(CO)$_5$).

However, when the <u>syn</u> isomer <u>8</u> was subjected to the
same conditions a number of products resulted as indicated
in Equation 13. A similar reaction of norbornene with an
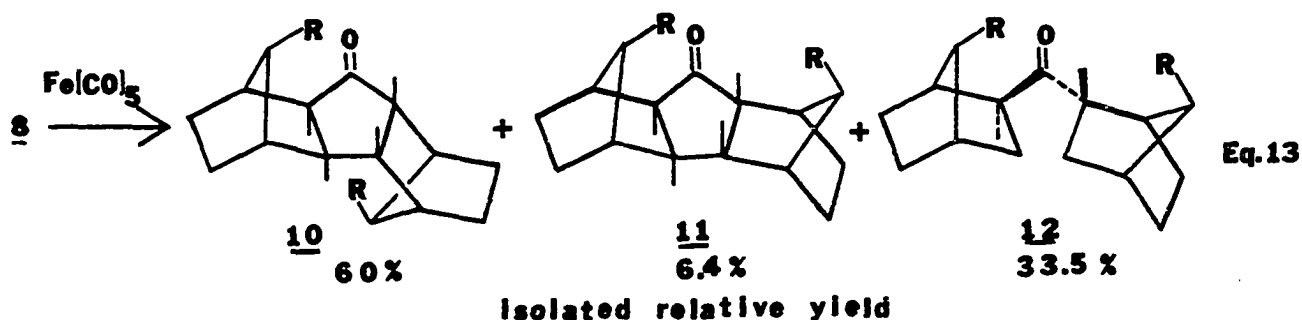
iron carbonyl (Reaction XIV, Table <u>2</u>, Introduction) yielded
only one product in low yield (5%).[22b] Comparison of these
two reaction sequences points out the considerable in-

fluence an appropriately substituted (e.g., the syn-7-t-butoxy group) Lewis base substituent can have on product distribution and especially on product yield. Also, comparison of the sequence shown in Equation 13 and that shown in Scheme 3 (reaction of 7-t-butoxynorbornadiene (1) with Fe(CO)$_5$) points to the possible influence the second double bond (the anti double bond in 1) has on the specificity of dimer ketone formation.

VPC analysis (3% SE-30 on Varaport 100/120, 5 ft. x 1/4 in., column temperature 210°C, He flow rate 150 ml/ min.) of the reaction products of Equation 13 indicated the presence of three major components. In addition there were at least ten other products whose combined vpc areas represented ca. 6% relative yield. Identification of these minor products was not attempted. Separation of the major products was achieved by column chromatography. The reaction products were placed on a column of TLC grade silica gel (Brinkmann Instruments, Inc., Silica Gel G, Cat. 7731) and eluted with 5% ethyl acetate-hexane.

The first product to be eluted was a dimeric ketone as indicated by its mass spectrum (Figure 6c) which shows a parent ion at m/e 362 and by its infrared spectrum (Figure 6b, C=O absorption at 1702 cm^{-1}). These observations indicate not only that this first component was a dimeric ketone, but an unusual one for these reaction conditions. The molecular weight of 362 is two units higher
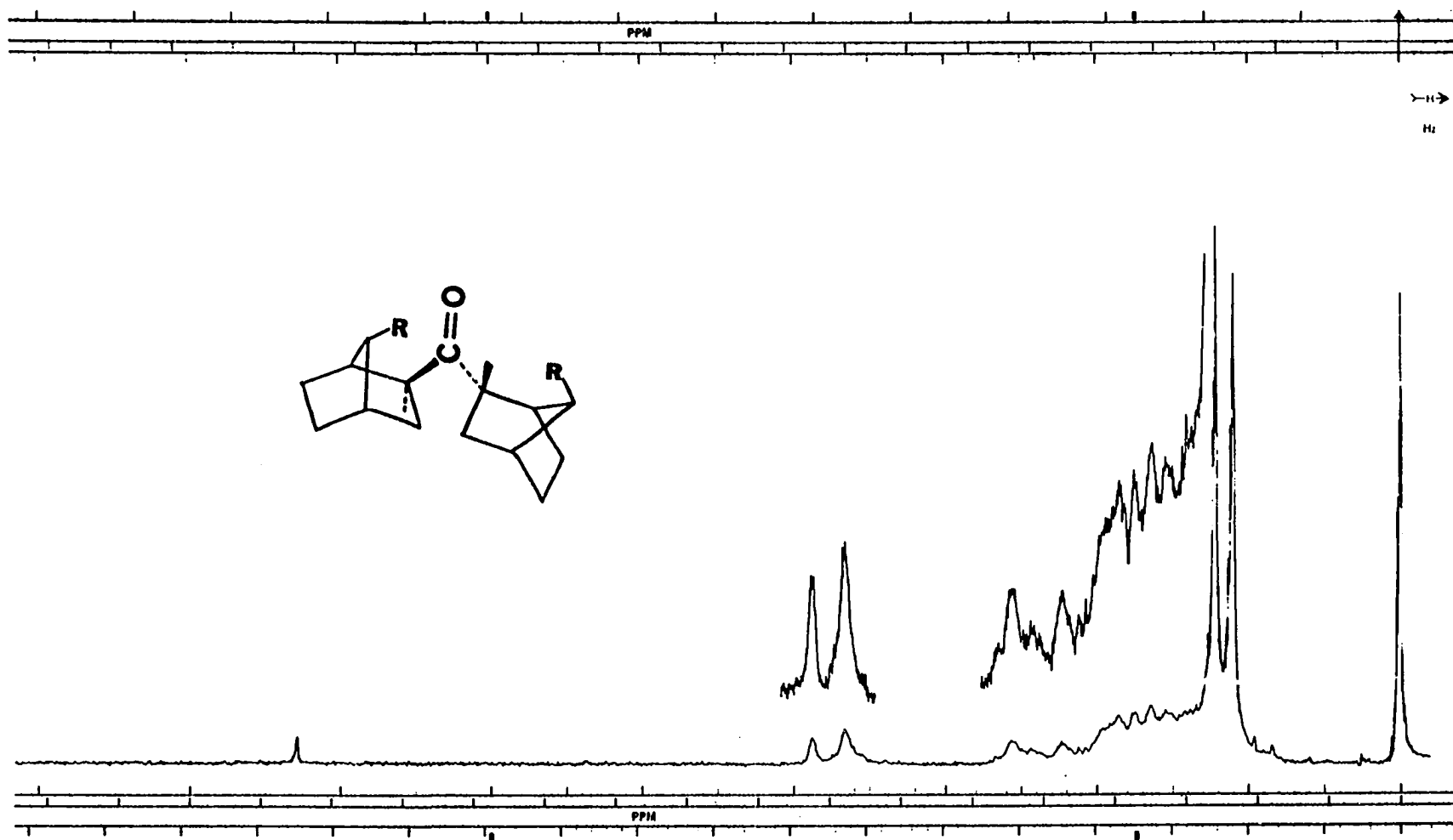
Figure 6a. Proton nmr spectrum (100 MHz, CDCl$_3$/TMS) of 12.
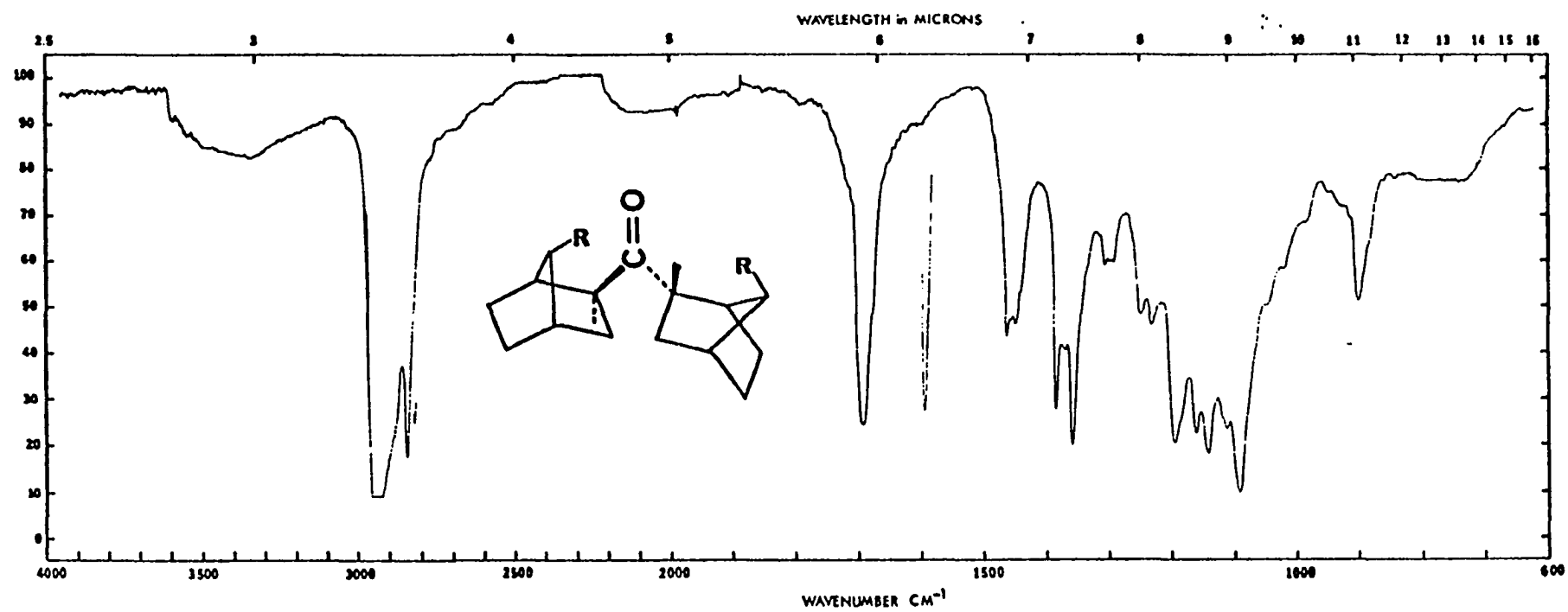
Figure 6b. Infrared spectrum (film) of 12.
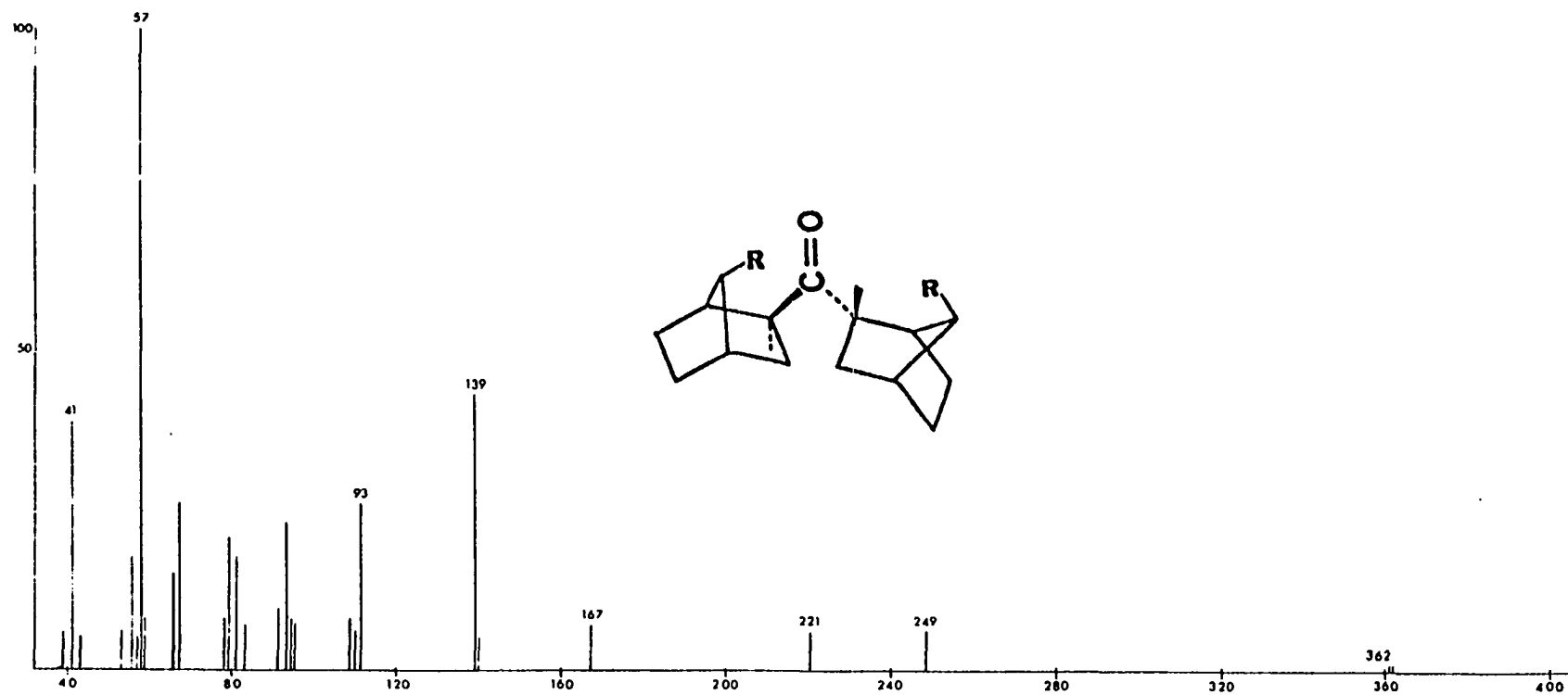
Figure 6c. Mass spectrum of 12.

than that of the expected dimer ketone product indicating
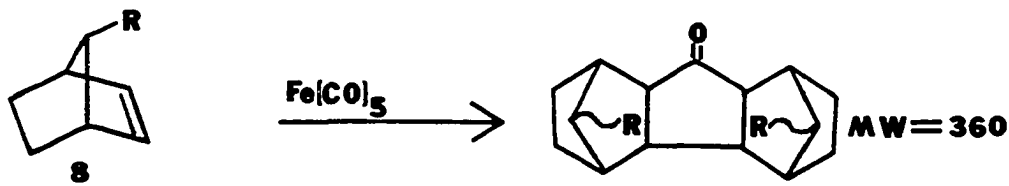
that reduction of a carbon-carbon bond has occurred. Also

the carbonyl absorption is ca. 20 cm^{-1} lower than what is

normally observed for these strained cyclopentanones (ca.

1722 cm^{-1}).[35,22] This lowered carbonyl absorption is indica-

tive of an acyclic ketone.[44a,b] These observations point

to a structure such as shown below. Bis-norbornyl ketones

of this type have been isolated previously from the Ni(CO)$_4$

promoted coupling of norbornadiene, Equation 14.[33,22] The
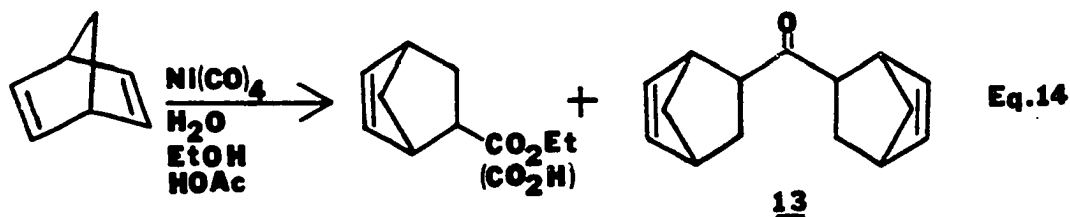
infrared spectrum of ketone 13 displays a carbonyl absorption

at 1700 cm^{-1} [33] as does our ketone (12) (1702 cm^{-1}).

The fact that the pmr spectrum (Figure 6a) of 12

displays two t-butoxy resonances in addition to the fact

that the 7-t-butoxy group is configurationally stable under

the reaction conditions requires that 12 have the syn-exo-endo-syn configuration:

12
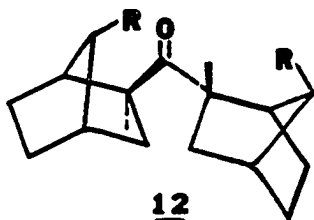
Any other configuration would have a symmetry element (e.g., a mirror plane) present and as such would necessitate the magnetic equivalence of the t-butoxy groups.
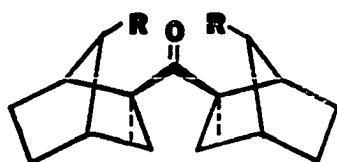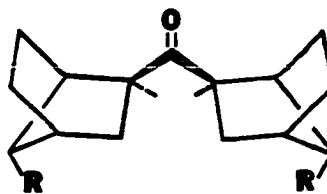
SX XS   or   **SNNS**

To the best of our knowledge this is the first example of an iron carbonyl-induced coupling of a norbornene to carbon monoxide resulting in the formation of a bis-norbornyl ketone. The formation of 12 was thought to be due to the presence of water in the reaction system, even though the system and solvent (di-n-butyl ether stirred and distilled from over CaH_2 just prior to use) were scrupulously dried. When the reaction was repeated in the presence of added water the formation of ketone 12 could not be reproduced.

The mass (Figure 7c) and infrared spectra (Figure 7b) of the next component from the column chromatography suggested the presence of another dimeric ketone. A molecular ion at $\underline{m/e}$ 360 and a carbonyl absorption at 1723 cm^{-1} was observed for this product. The structure of this component, ketone $\underline{10}$, was elucidated by chemical and spectroscopic methods.

The pmr spectrum of $\underline{10}$ (Figure 7a) displays a two hydrogen singlet at δ 3.64 due to the hydrogens geminal to the $\underline{t}$-butoxy groups ($H_{7,7'}$) and a two hydrogen doublet centered at δ 2.57 assigned to the α,α' hydrogens on the cyclopentanone ring ($H_{2,2'}$). A doublet (area 4H) centered
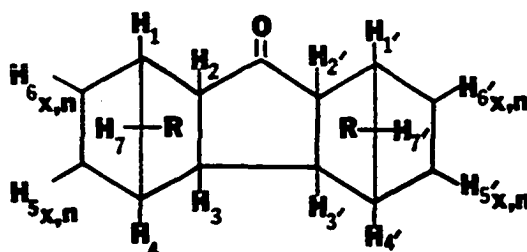
at δ 2.24 is attributed to the β,β' hydrogens ($H_{3,3'}$). The downfield portion of this doublet (δ 2.24) is broadened by the coincident absorption of the bridgehead hydrogens $\underline{syn}$ to the carbonyl carbon ($H_{1,1'}$). The broad singlet at δ 1.92 (area 2H) is due to the bridgehead hydrogens $\underline{anti}$ to the ketone function ($H_{4,4'}$). The remaining hydrogens ($H_{5X,N5'X,N}$, $H_{5X,N6'X,N}$, area 8H) comprise the complex multiplet centered at δ 1.54, with the eighteen hydrogens of the $\underline{t}$-butoxy groups affording a single sharp
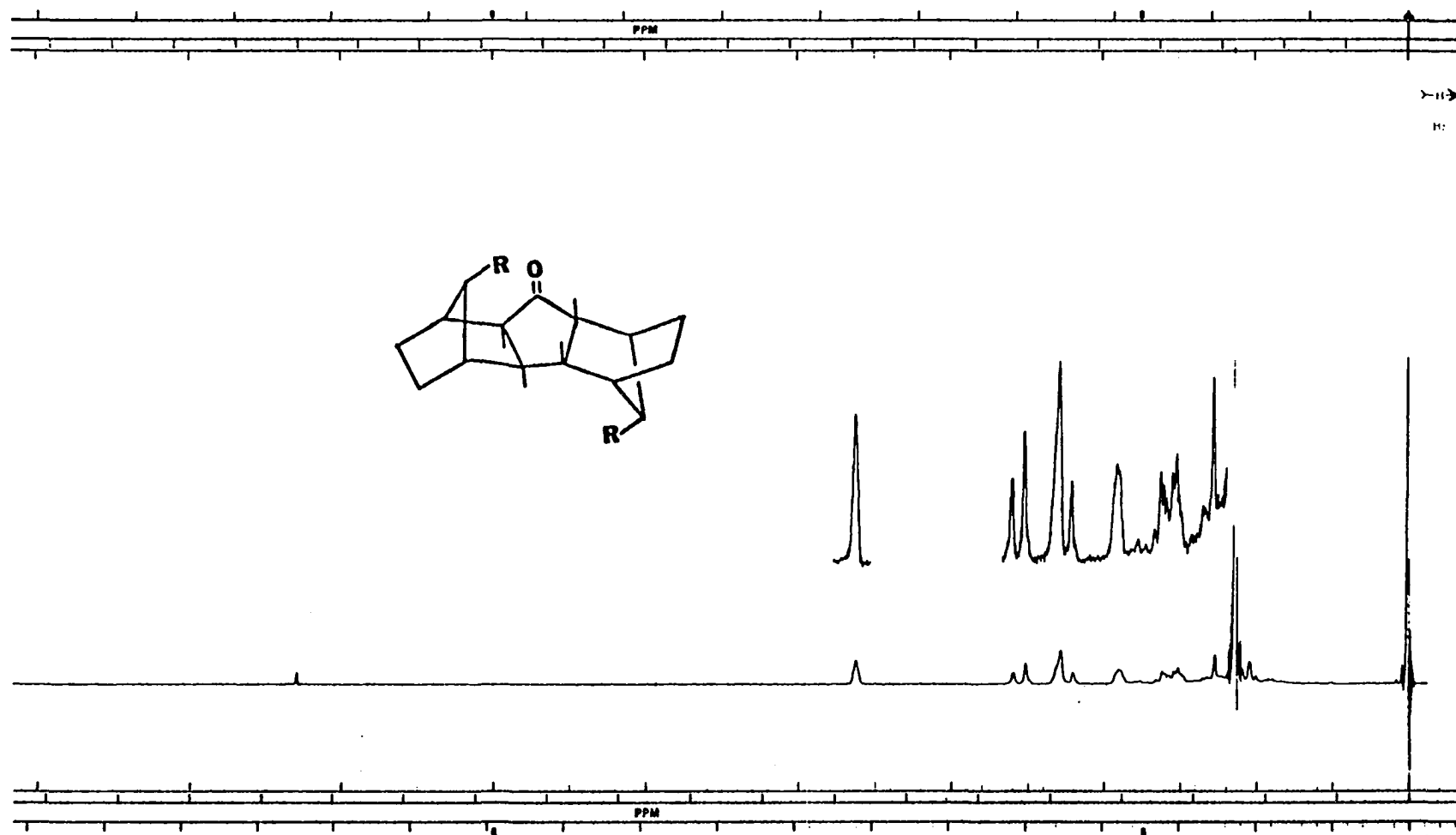
Figure 7a. Proton nmr spectrum (100 MHz, CDCl$_3$/TMS) of 10.
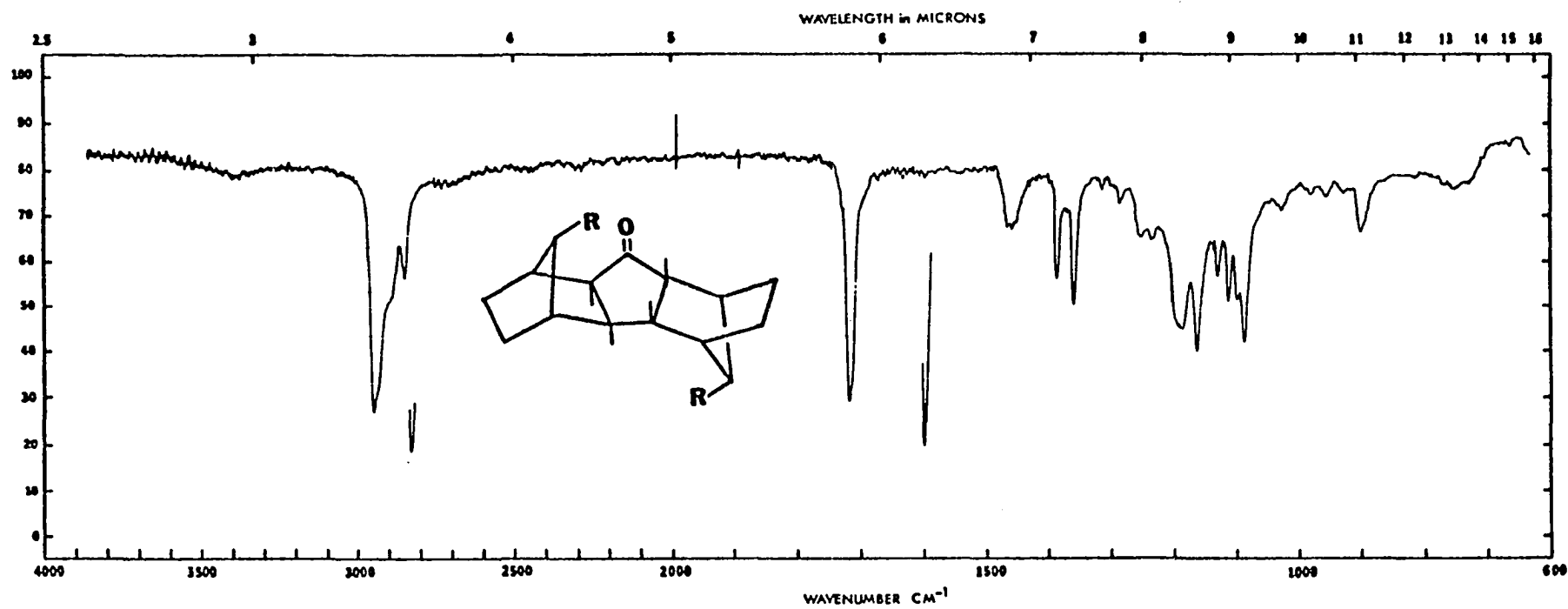
Figure 7b. Infrared spectrum (CCl$_4$) of 10.
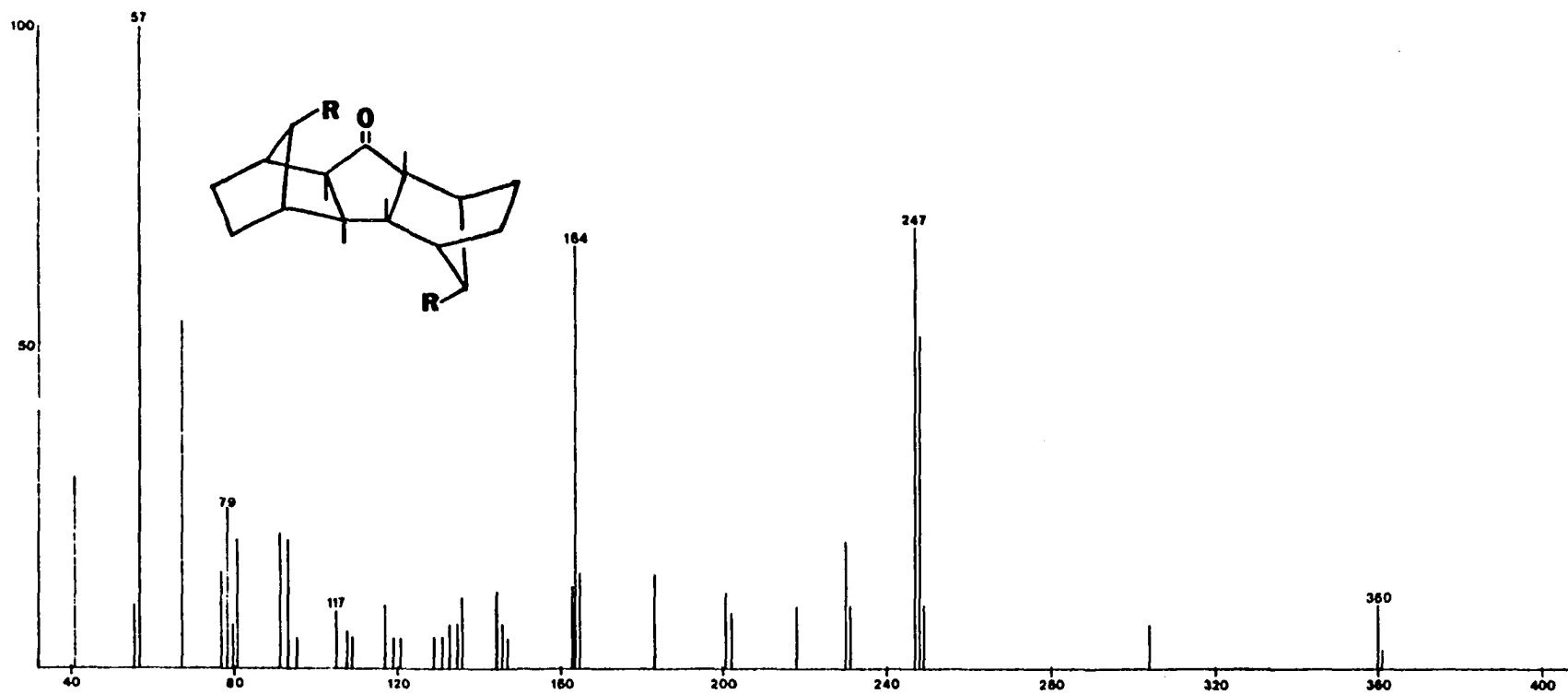
Figure 7c. Mass spectrum of 10.

normal

decoupled
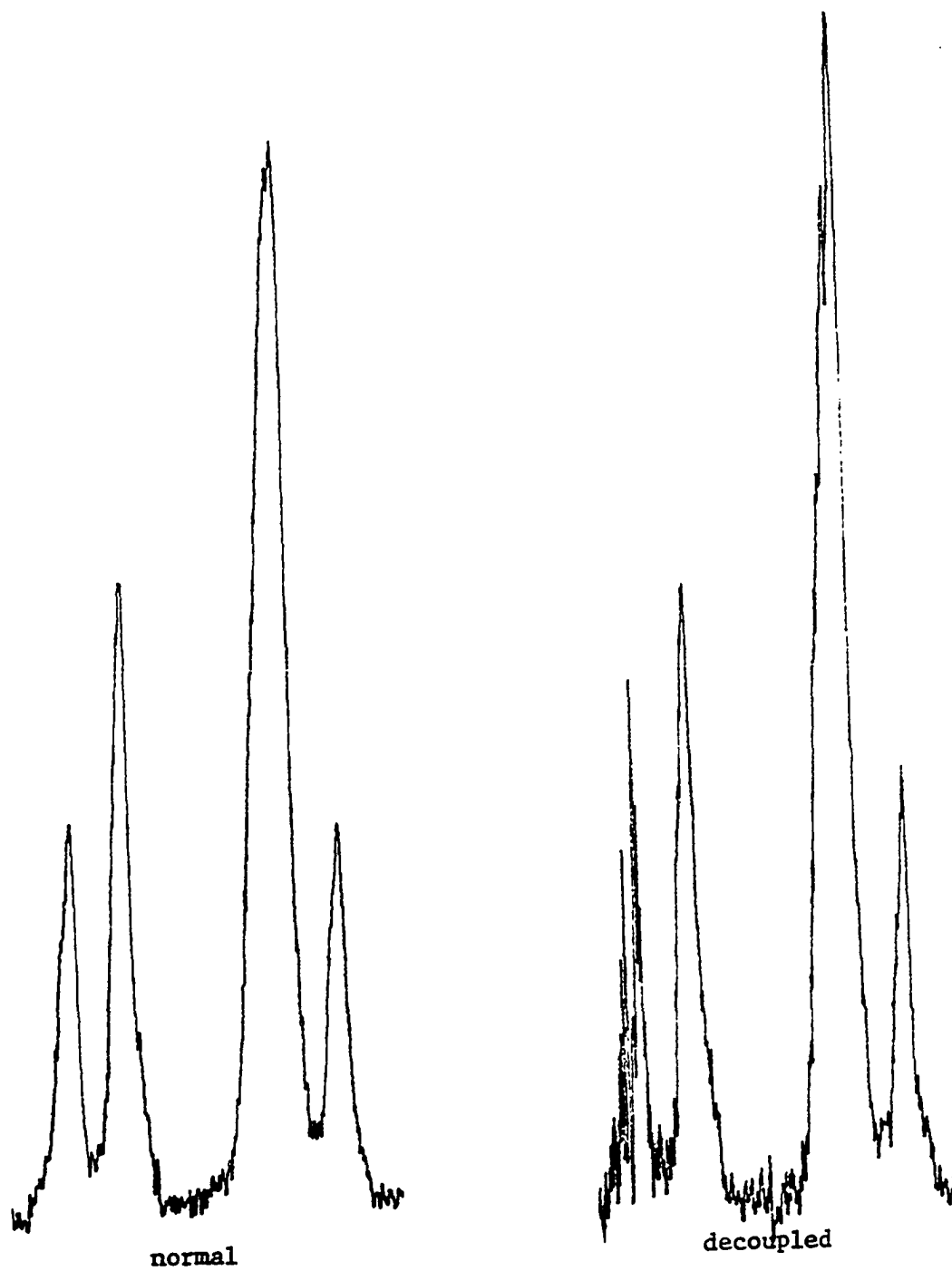
Figure 7d. $H_{2,2'}$ hydrogens of ketone 10.

normal   decoupled
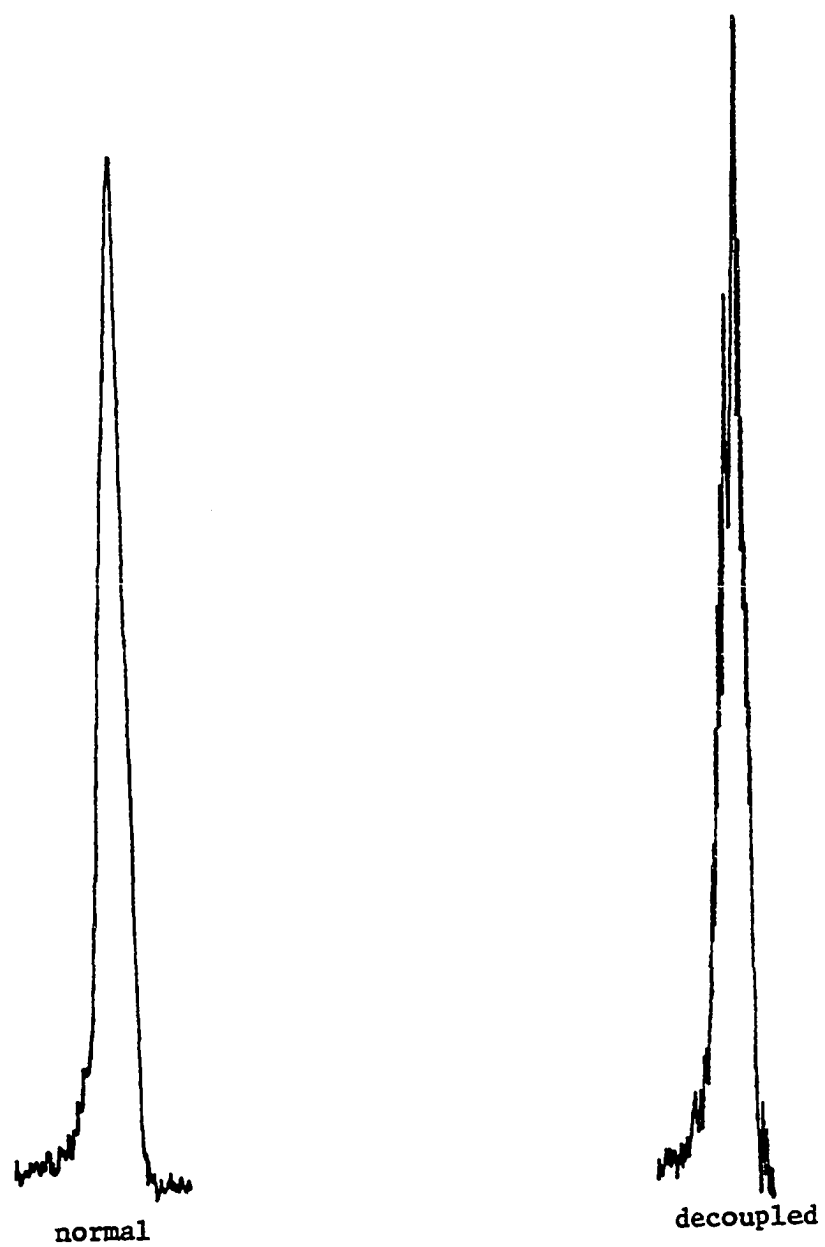
Figure 7d. $H_{7,7'}$ hydrogens of ketone 10.

resonance signal at δ 1.12. These assignments are consistent with those made by Mantzaris and Weissberger on analogous compounds.[22b,c,45]

The following table compares ketones 10 and 11 (prepared by the hydrogenation of ketone 3), and clearly indicates that 10 and 11 are isomeric. Recalling that 10

ketone	infrared spectrum	mass spectrum	pmr spectrum	melting point
10	1723 cm^{-1}	360 (M$^+$) 57 (base peak)	one signal for the t-OBu groups	179-180°C
11	1723 cm^{-1}	360 (M$^+$) 57 (base peak)	two signals for the t-OBu groups	115-116°C

has only one pmr absorption for the t-butoxy groups, ketone 10 must possess one of the following four configurations:

SXTXS

SXCXS

SNTNS

SNCNS
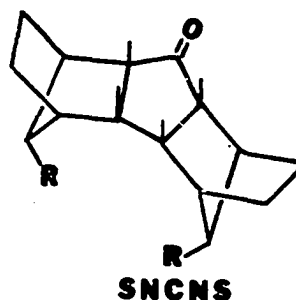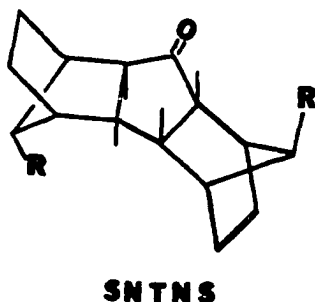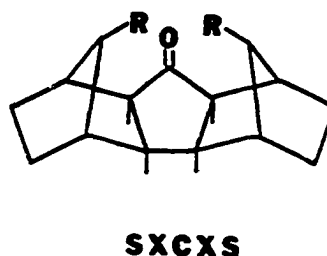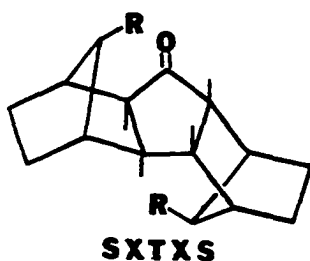
To decide between the SXXC and SNNS isomers we per-
formed a series of double irradiation pmr experiments. The
decisive coupling would involve the $H_{7,7'}$ hydrogens and the
α, α' and β, β' hydrogens. This long range W-letter coupling
(heavy outline, below) has been observed in a number of

SXXS   **SNNS**
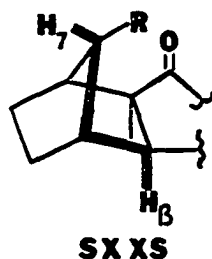
norbornyl systems.[46,47] This coupling is stereospecific;[48]
only hydrogens in the <u>endo</u> configuration on the 2,3-carbons
of the norbornyl structure (<u>e.g.</u>, H_α and H_β in the SXXS
isomer) will couple with the <u>anti</u> H_7 hydrogen. When the
singlet at δ 3.64 ($H_{7,7'}$, see Figure 7d) was irradiated,
the doublet at δ 2.57 (α,α' hydrogens) was transformed
into a complex multiplet. When the inverse experiment was
performed (<u>i.e.</u>, irradiation of the doublet at δ 2.57 and
observation of the singlet at δ 3.64) the $H_{7,7'}$ singlet
(δ 3.64) was observed to collapse into a multiplet (Figure
7d). This experiment showed that the $H_{7,7'}$ and the
$H_{\alpha,\alpha'}, H_{\beta,\beta'}$ hydrogens were indeed coupled and established
the SXXS configuration for ketone 10. This also allowed
us to narrow the choices for the structure of ketone 10
to either SXTXS or SXCXS.

The next experiment established the _trans_ relation-
ship of ketone 10. The reduction of 10 with $LiAlH_4$ in
refluxing THF (Equation 15) yielded a white crystalline

Eq.15
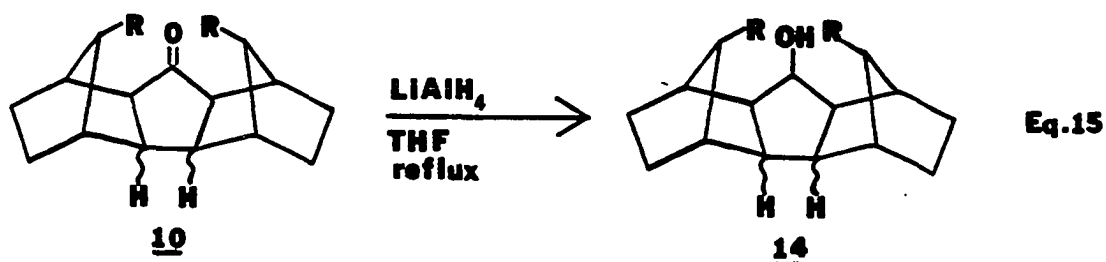
product in essentially quantitative yield (99%). This mate-
rial was identified as the alcohol on the basis of its mass
(parent ion at m/e 362, Figure 8c) and infrared spectra (no ab-
sorbtion in the region 2500-1500 cm^{-1}, Figure 8b). The
relatively small absorption in the infrared region norm-
ally associated with the hydroxyl stretch of alcohols
(3200-3700 cm^{-1}) is attributed to intramolecular hydrogen
bonding[44a,b,49] of the alcohol with a proximate (less
than 1 Å distant, as estimated from models) _t_-butoxy
group. The melting point of this crude product was 160-
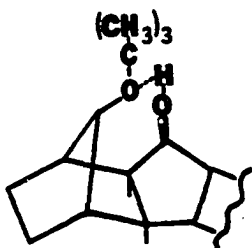
162°C (uncorrected). The pmr spectrum (Figure 8a) displays
two resonances of equal area for the _t_-butoxy groups.

Since the SXTXS isomer possesses a C_2 symmetry axis,
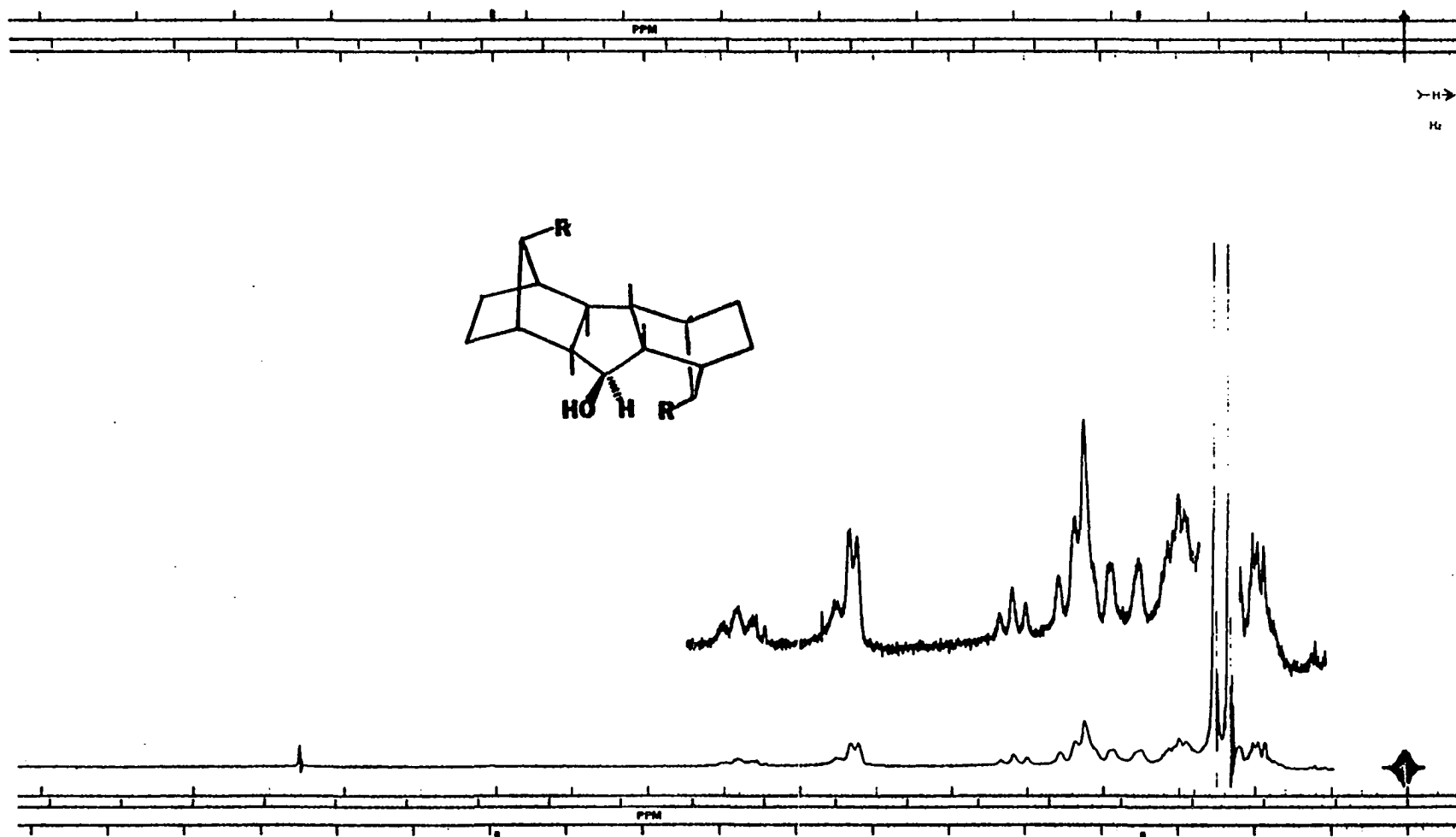
Figure 8a. Proton nmr spectrum (100 MHz, $CDCl_3$/TMS) of 14.
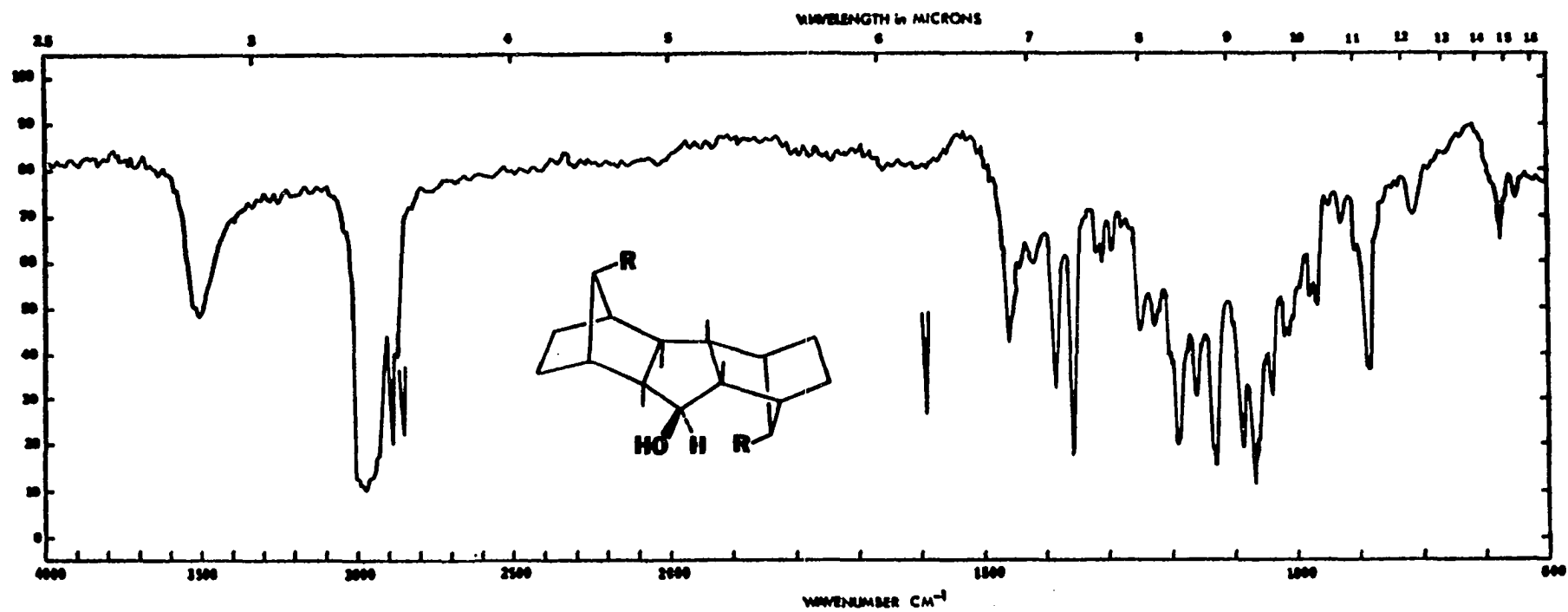
Figure 8b. Infrared Spectrum (CCl$_4$) of 14.
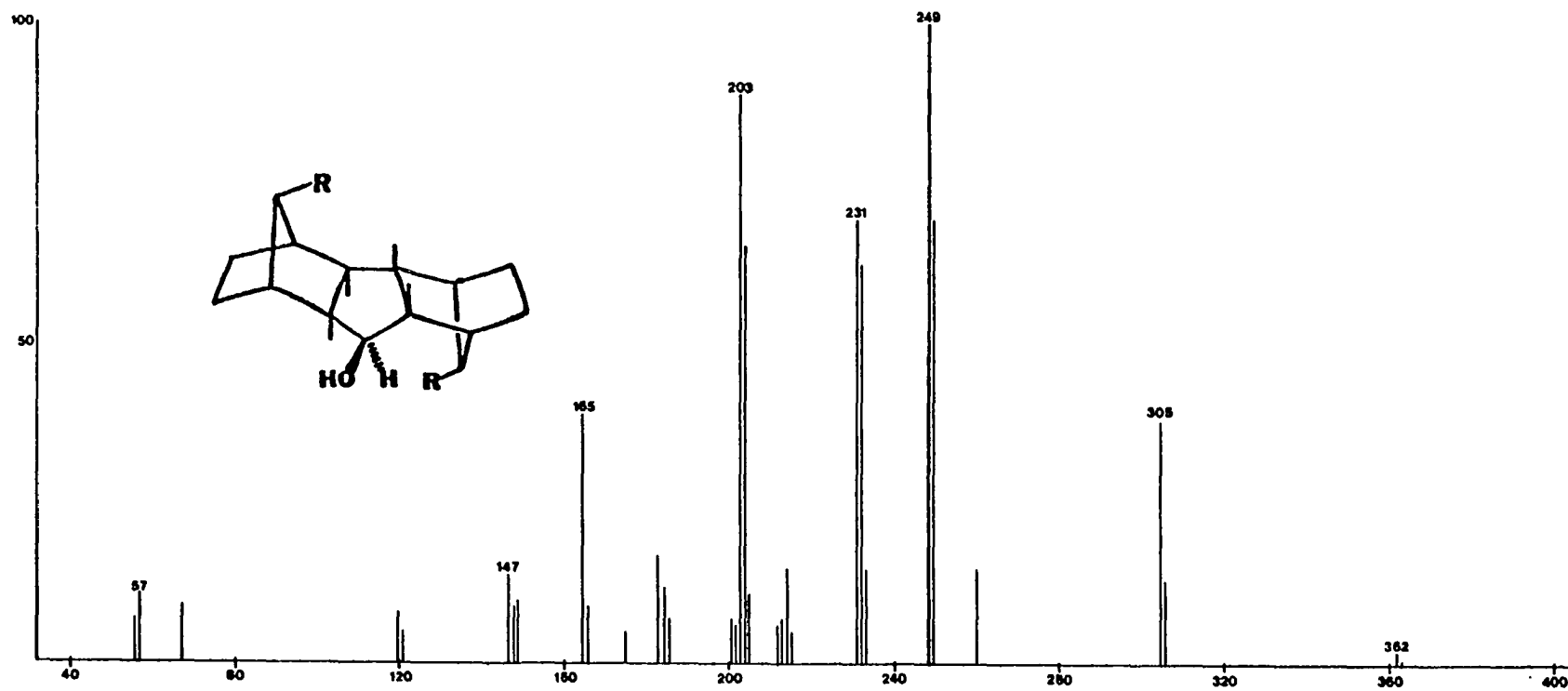
Figure 8c. Mass spectrum of 14.

reduction would afford only one stereoisomer in which the
t-butoxy groups are non-equivalent and would, accordingly,
display two resonances of equal area in the pmr spectrum.
Reduction of the SXCXS isomer (which has a mirror plane
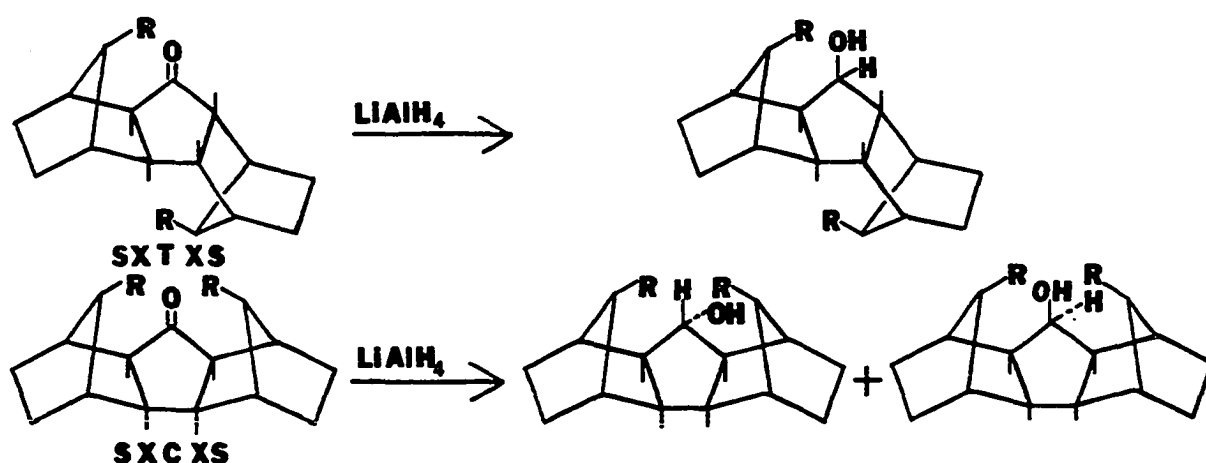
of symmetry) would yield two diastereomers. The t-butoxy
groups of each of the diastereomers would be equivalent,
but as a mixture would display two resonances in the pmr
spectrum for these groups, and must fortuitously occur in
a 1:1 ratio for these resonances to be of equal area.
The isolated product must then be either the lone stereo-
isomer from the SXTXS isomer or a 1:1 mixture of diaster-
eomers from the SXCXS isomer.

The alcoholic product was subjected to TLC (three
different eluant systems) and VPC (a number of columns, under

various conditions of column temperature and He flow rates)
analysis which indicated it to be a single component. The
narrow melting point range (160-162°C) of the crude pro-
duct also argues against it being a mixture unless a 1:1
eutectic mixture was fortuitously obtained. These facts
establish the structure of alcohol 14 and ketone 10 as
being SXTXS.

The final product from the chromatography column
was yet another dimer ketone (mass spectrum, Figure 9c,
m/e 360 = M^+; infrared spectrum, Figure 9b, carbonyl ab-
sorption at 1723 cm^{-1}). The pmr spectrum (Figure 9a),
which shows two resonances for the t-butoxy groups, was
our first indication as to the structure of this ketone.
The homogeneity of this product was established by TLC
and vpc analysis. The pmr, mass, and infrared spectra
pointed to a SXNS configuration. The structure was es-
tablished by comparison with ketone 11 (hydrogenation
product of ketone 3). The infrared, mass, and pmr spectra
of this product were identical to those of ketone 11.
The melting point of the product (113-115°C, uncorrected)
was very close to that of 11 (115-116°C, uncorrected) and
a mixed melting point of the two (mmp 113-115°C, uncorrected)
confirmed the identity of these two compounds.

A Suggested Mechanism

To explain our proposed mechanism the salient points
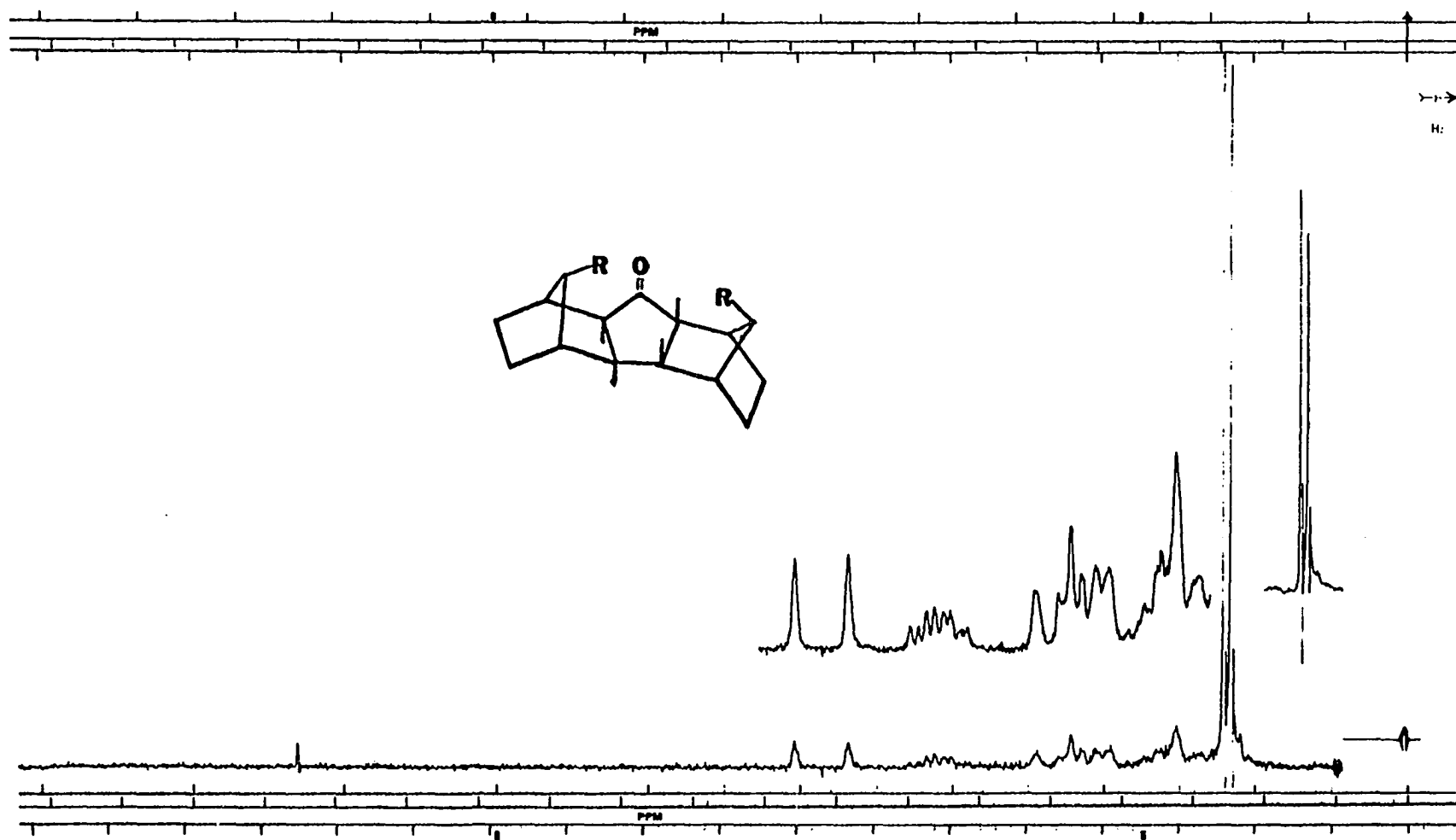
Figure 9a. Proton nmr spectrum (100 MHz, CDCl$_3$/TMS) of 11.
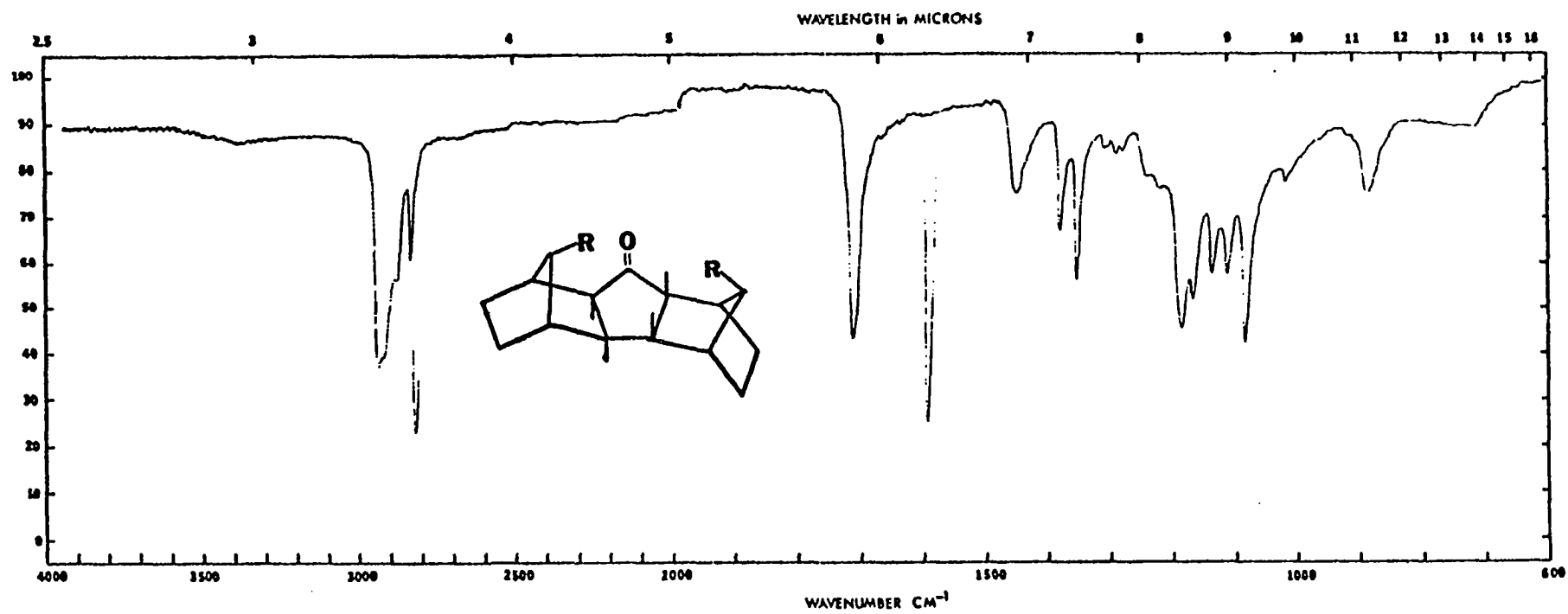
Figure 9b. Infrared spectrum (CCl$_4$) of 11.
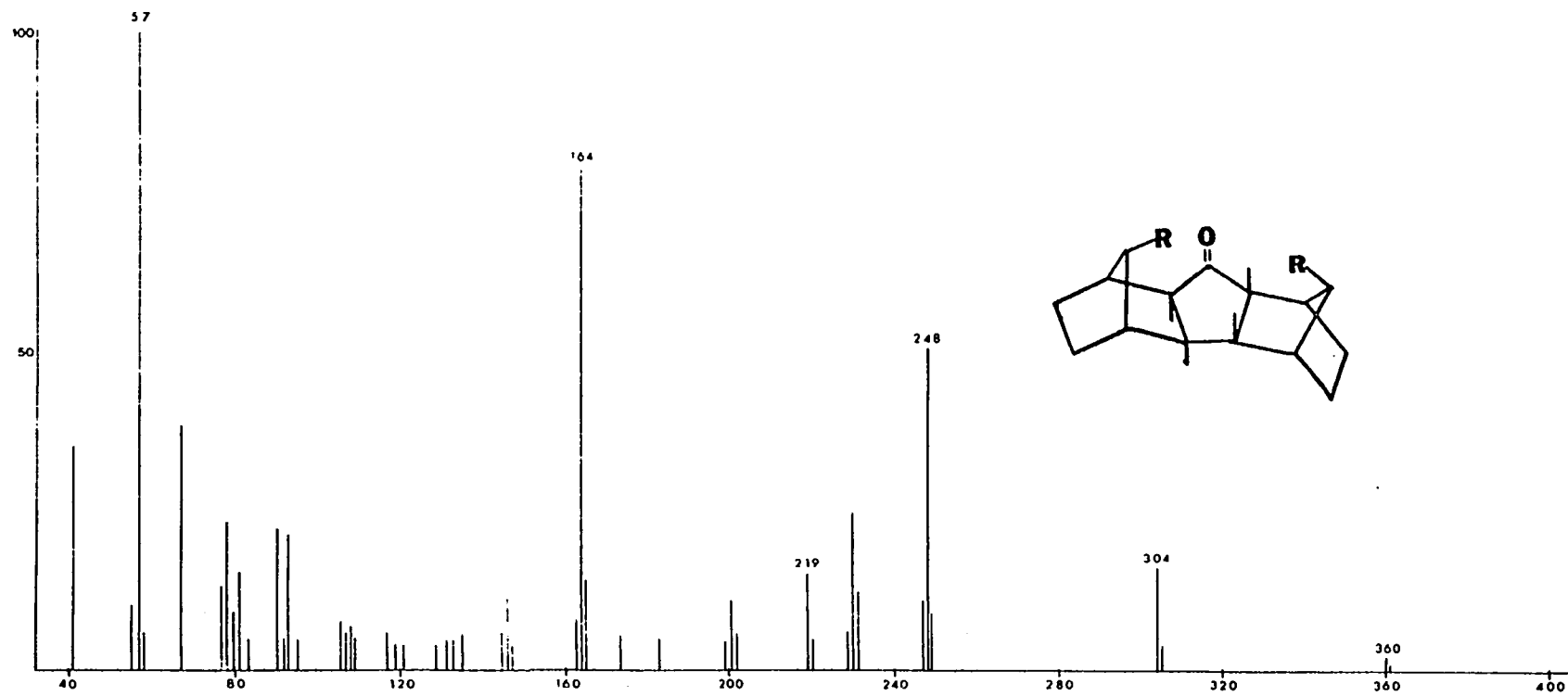
Figure 9c. Mass spectrum of 11.

provided in the previous two sections are summarized below:

1) the dimer ketone (3), obtained from the reaction of 7-t-butoxynorbornadiene (1) and Fe(CO)$_5$, has both t-butoxy groups syn to the central cyclopentanone ring;

2) anti-7-t-butoxynorbornene (9) failed to react, in any manner (i.e., no epimerization of the t-butoxy groups, or coupling), with Fe(CO)$_5$ under the standard reaction conditions;

3) syn-7-t-butoxynorbornene (8) reacted with Fe(CO)$_5$, under standard conditions, and yielded three dimer ketonic products.

The first two results convincingly demonstrate that the initial iron intermediate reacts exclusively with the olefinic linkage syn to the bulky t-butoxy group. This occurs despite the fact that this double bond is sterically hindered relative to the anti double bond. The steric bulk of the t-butoxy group would presumably preclude (c.f., reaction VII, Table 2, Introduction) attack by an iron species at this site. We conclude from this that the stabilizing electronic interaction of the Lewis base substituent (i.e.-o-tBu) at the syn-7 position overides any destabilizing steric effect of the t-butoxy group.

The stereospecific nature of the coupling of 7-t-butoxynorbornadiene (1) with Fe(CO)$_5$ and the non-stereo-specific coupling of syn-7-t-butoxynorbornene (8) with Fe(CO)$_5$ strongly suggests that the second double bond in

7-<u>t</u>-butoxynorbornadiene (<u>i.e.</u>, the one <u>anti</u> to the 7-<u>t</u>-butoxy

group) plays a definite role in the reaction of 7-<u>t</u>-butoxy-

norbornadiene with Fe(CO)$_5$. The exact nature of the function

of the second double bond is a matter of some dispute.

When Cookson[17] erroneously assigned the NTN (Ia) configura-

tion to the ketone obtained from norbornadiene and Fe(CO)$_5$,
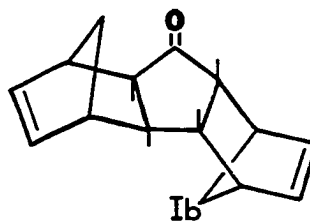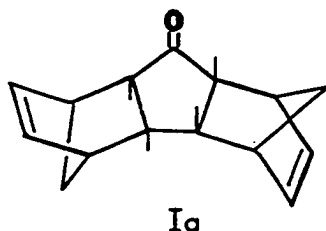
it was suggested that the unreacted olefinic linkage was

stabilizing an iron intermediate in some fashion. However,

when the correct structure (Ib, XTX) was proven[19] this sug-

gestion was retracted and no alternative given. Stone,

<u>et al.</u>, have suggested: "....although only one <u>pi</u>-bond

from each norbornadiene molecule is formally involved,

the specificity observed suggests that the second <u>pi</u>-bond

of the organic ligand also contributes in the transition

state."[34] Mantzaris and Weissberger[22b] maintain that the

function of the second double bond in norbornadiene is

simply to add strain to the bicyclic system, thereby in-

creasing the reactivity of the remaining endocyclic double

bond toward Fe(CO)$_5$. We agree with Stone, <u>et al.</u>, (<u>vide</u>

<u>supra</u>) that, indeed, the noncomplexed double bond is con-

tributing to the stability of the transition state. The
mechanism proposed in Scheme 4 accommodates the above ob-
servations.

The first step in the mechanism involves forma-
tion of the complex 15 (Equation 16), in which 7-$\underline{t}$-butoxy-
norbornadiene reacts as a bidentate ligand. Complexes such
as 15 in which iron is the metal atom, have not been re-
ported. However, Laszlo and Stockis have isolated the
complex 19 in work as yet unpublished.[50] Also, Wege and
Wilkinson[51] have isolated analogous complexes ($\underline{e.g.}$, 20
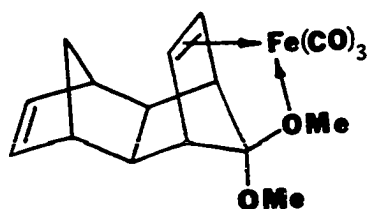
19

and 21) in which chromium was the metal atom.

20

21

Scheme 4

Eq. 16

Eq. 17

Eq. 18

Eq. 19

Eq. 20
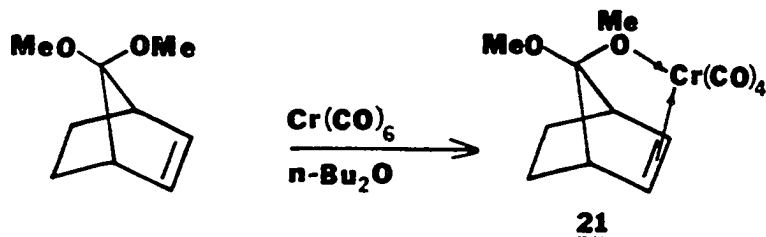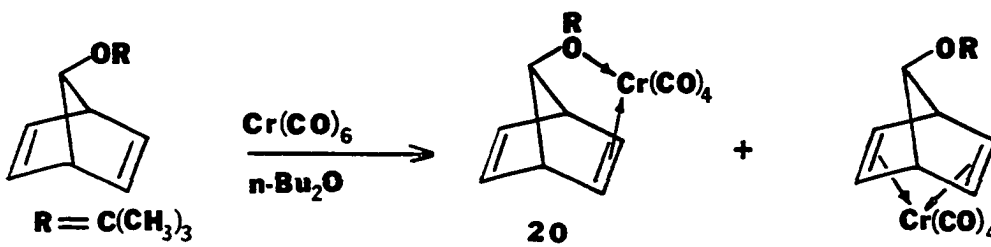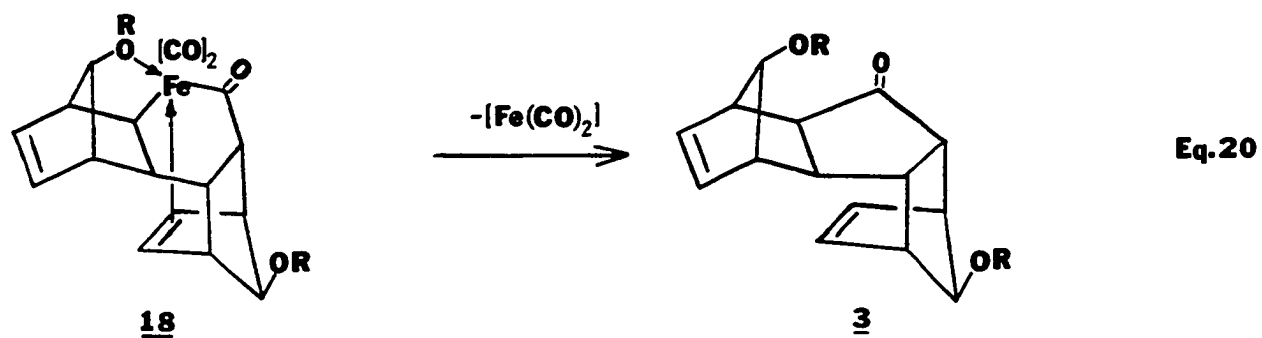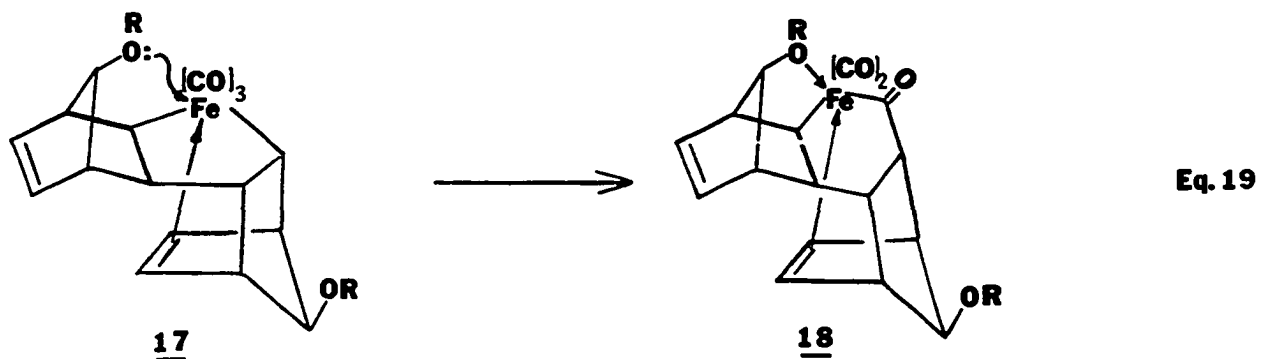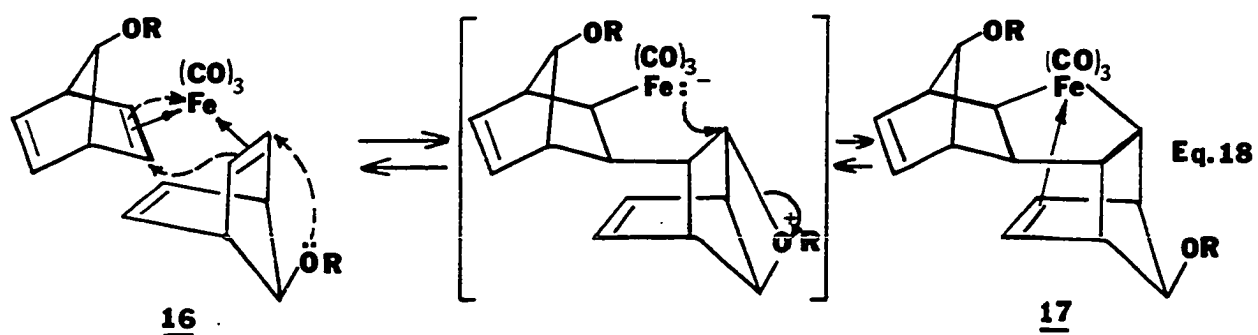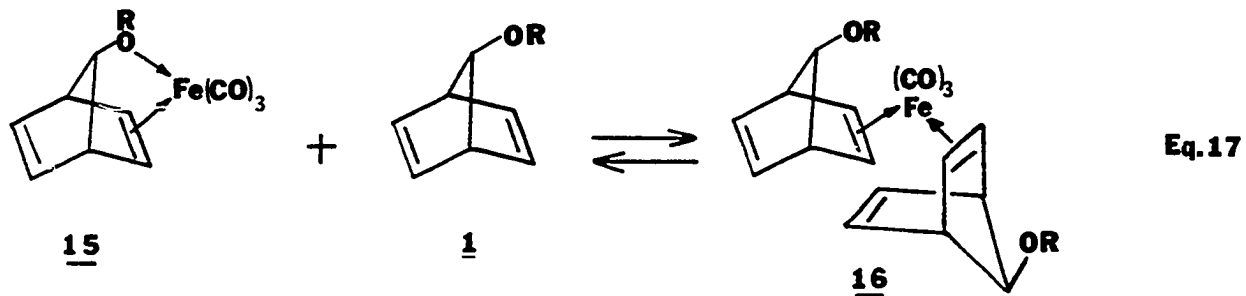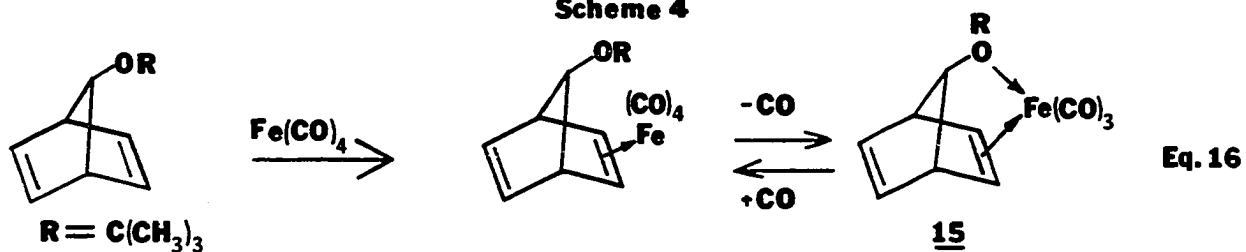
Complex 15 then undergoes a simple ligand exchange reaction with a molecule of the diene 1 to form the bis-olefin complex 16. In addition to the syn-exo-endo-syn configuration shown for 16 there are three other possible configurations for the combination of complex 15 with 1 (22, 23, and 24, below). The two anti complexes (i.e.,

22   23   24
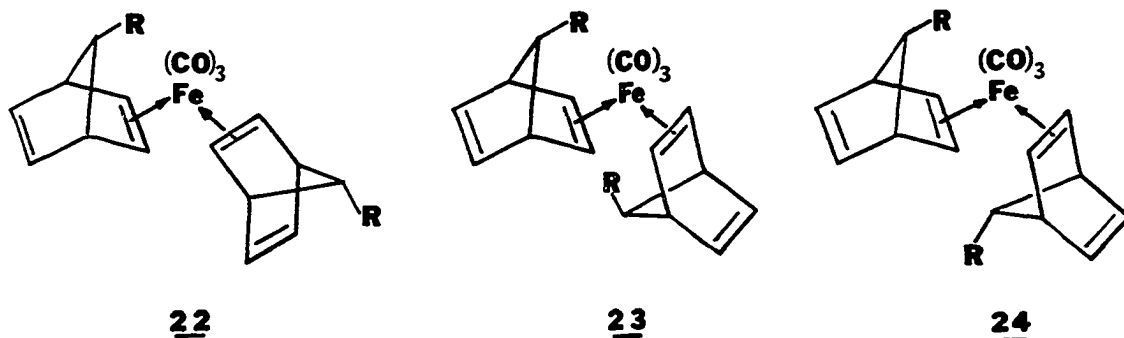
22 and 24, SXNA and SXXA, respectively) are thought not to be stable under the reaction conditions (refluxing nBu_2O, 148°C), for the following reasons. The ligands most effective in stabilizing the low valent states of metals are those in which retro-dative bonding can occur.[52] Bonding in organometallic species is considered to be by electron donation from the ligand (e.g., a carbon-carbon double bond) to the metal via a bonding molecular orbital of the ligand to an empty metal d-orbital of appropriate symmetry. The metal reinforces this bond by back donating electrons to the ligand via a filled d-orbital to the anti -bonding ligand molecular orbital. The closer the filled metal d-orbital and the ligand anti-bonding orbital are in energy, the stronger the metal-ligand bond and the more stable the

complex.[53,54]

The syn-double bond of 7-t-butoxynorbornadiene (1)
is a better ligand, by the above criteria, than the anti-
double bond. Since, in addition to the normal retrodative
bonding of the olefinic ligand, the syn ether oxygen
stabilizes complex formation at the syn double bond by
interaction of an oxygen lone pair with a metal d-orbital
of the appropriate symmetry. This preference for complexa-
tion at the syn double bond is seen also in the formation
of complexes 19 and 20 (vide supra). In the anti complexes
(22 and 24) the added stabilization of the ether oxygen
interaction is absent. Therefore the anti complexes, if
formed, would be less stable under the reaction conditions
and would probably revert back to reactants in this
equilibrium step (Equation 17, Scheme 4).

The absence of products from the SXXS complex (23)
is probably kinetic in origin. The anchimerically assisted
formation of the metallocycle (complex 17, Equation 18,
Scheme 4) from complex 16 should be much faster than the
unassisted formation of an analogous metallocycle from
complex 23. The equilibrium involving the SXXS complex 23
(Equation 21) would then be shifted to the left by the con-
sumption of 15 and 1, affording complex 16 which then
goes rapidly to product.

Furthermore, the metallocycle (25) obtained from
the bis-olefin complex 23, should be less stable than the

Eq.21
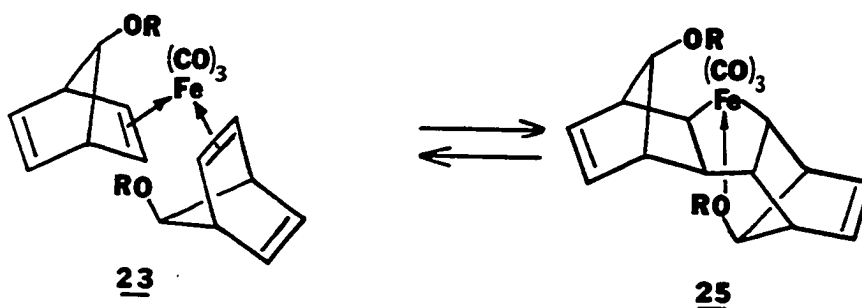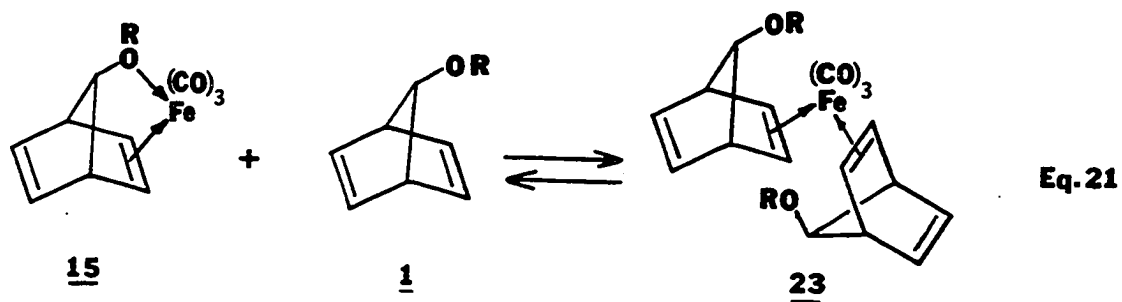
metallocycle 17. The anti double bond of the endo bound

norbornyl system of 17 is a more effective stabilizing

ligand than the oxygen lone pair in the SXXS metallocycle

25 (vide supra). This situation is suggested by the fact

that more than one dimer ketone is formed in the reaction

of syn-7-t-butoxynorbornene (8) and Fe(CO)$_5$ (i.e., the

anti double bond is absent in this reactant). When the
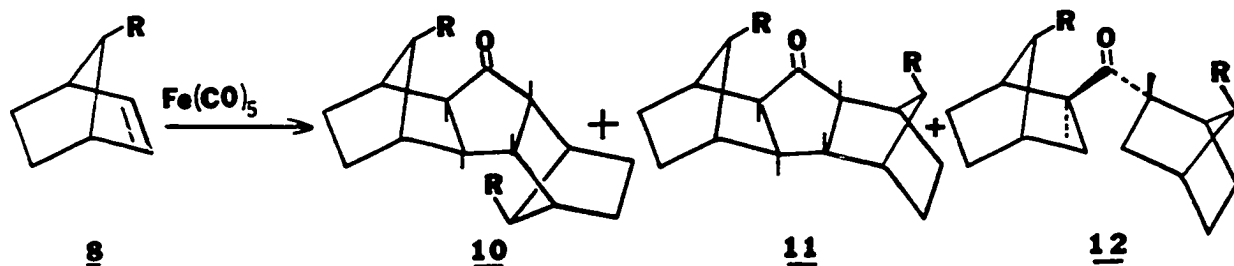
stabilizing effect of the _anti_ double bond is absent, as in 27,

below, the stabilization of the metallocycle 28 by the
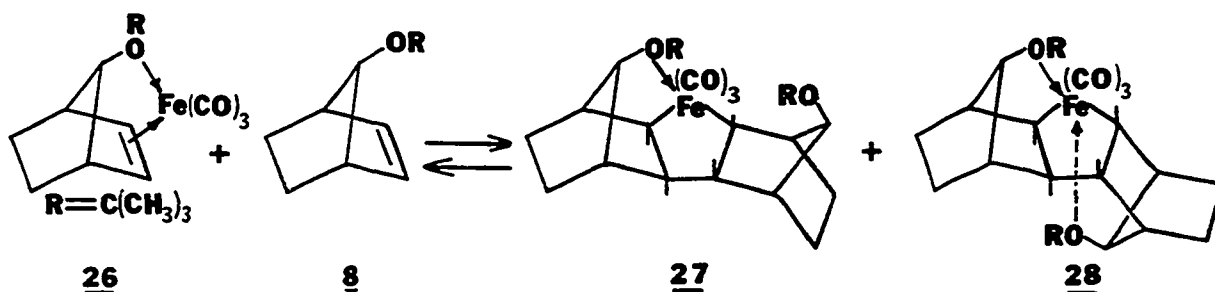
extra oxygen lone pair allows the formation of 28 to com-

pete effectively with the more rapid anchimerically assisted

formation of complex 27.

In Equation 19 (Scheme 4) the formation of the

metal acyl (complex 18) is assisted by the neighboring

syn alkoxy group of the _exo_ bound norbornyl system. The

current view[55,56,57] of alkyl migration-insertion reactions

to give metal acyls is that an attacking ligand (_e.g._,

PPh$_3$, CO, etc.) enters the coordination sphere of the metal

causing a concerted migration of the ligand and insertion

into a precoordinated carbon monoxide. However, there is

some doubt as to whether an activating ligand is necessary[22c]

or if free carbon monoxide (or an iron species in solution)

is effecting the migratory insertion in these reactions

(See Introduction and ref. 23).

The extrusion of the elements of Fe(CO)$_2$ (Equation

20, Scheme 4) to yield the dimer ketone 3 completes the

mechanism. There are no reports in the literature or

evidence that indicates the nature of this step. It is felt that an intervening iron species, perhaps a diiron species forming an Fe-Fe bond, is assisting this extrusion.

Summary

In this chapter, the reaction products of 7-$\underline{t}$-butoxynorbornadiene (1) and Fe(CO)$_5$ have been reported and discussed. Among the products is a single dimer ketone which has been shown to possess a SXTNS configuration. To the best of our knowledge this is only the second dimer ketone obtained from this general reaction sequence which has a non-XTX configuration.

Control experiments involving the reactions of syn-(8) and anti-7-$\underline{t}$-butoxynorbornene (9) have been described. The anti isomer (9) has been shown to be inert to Fe(CO)$_5$ under standard reaction conditions, while the syn isomer (8) proved to be quite reactive under the standard conditions yielding three dimeric ketones compared to the formation of a single ketone from (1), above.

The mechanistic implications of the control experiments and the stereochemistry of the reaction products have been discussed and incorporated into a suggested mechanism.

CHAPTER 3

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover Capillary melting point apparatus and are uncorrected. Infrared (ir) spectra were recorded on a Perkin-Elmer IR-8 infrared spectrophotometer and were calibrated against the 1601 cm^{-1} and 2850 cm^{-1} bands of polystyrene film. Strong, medium and weak intensities are denoted by (s), (m) and (w), respectively. Spectra were generally determined as dispersions in potassium bromide or as solutions in carbon tetrachloride. Mass spectra were recorded on a Hitachi Perkin-Elmer Model RMU-6E mass spectrometer operating at 70 eV. Proton nuclear magnetic resonance (pmr) spectra were recorded either at 60 MHz with a Varian Model T-60 spectrometer or at 100 MHz with a Varian XL-100-15 spectrometer utilizing tetramethylsilane (TMS) as an internal standard. Peak positions are reported in parts per million (δ) downfield from TMS. The center of gravity of a broad singlet (br s) or a multiplet (mult) absorption is given as the peak position. Complex multiplets are, however, reported as a range between the highfield and lowfield ends of the multiplet. Elemental microanalyses were

performed by Chemalytics, Inc., Tempe, Arizona.

Unless otherwise noted, all reagents and solvents were reagent grade and used without additional purification. Reagent grade acetone was refluxed with and distilled from potassium permanganate. Carbon tetrachloride was refluxed with potassium hydroxide for several days, distilled and stored over Linde 3A Molecular sieves. Anhydrous diethyl ether was distilled from lithium alluminum hydride immediately before use, as was tetrahydrofuran. Di-n-butylether was stirred for twenty-four hours with lithium aluminum hydride and then distilled at reduced pressure from the same. The distillate was then stored over Linde 3A Molecular sieves.

Reaction of iron pentacarbonyl with 7-(1,1-dimethylethoxy) norbornadiene (1)

A mixture of 7-tert-butoxynorbornadiene (11.08 g, 0.0675 mole), Fe(CO)$_5$ (25 g, 0.1275 mole), and di-n-butyl-ether (75 ml) was refluxed for 20 hr. Dry nitrogen was bubbled through the reaction mixture during the course of the reflux, and the exit gases were vented into the hood. At the end of 20 hr the reaction mixture was filtered hot through a bed of Celite. The black, pyrophoric residue[31] was rinsed twice with di-n-butyl ether. The combined filtrates were filtered through a fresh bed of Celite until clear and then concentrated to give a dark brown mass.

This residue was then dissolved in a solution of acetone (150 ml) and $FeCl_3 \cdot 6H_2O$ (35 g)[32] and stirred for 24 hrs. The solution was added to 500 ml of water and the organic layer separated. The aqueous layer was extracted with diethyl ether (100 ml x 3) and the organic layers combined. The combined extracts were washed with water (5 x 50 ml), dried (Na_2SO_4), filtered and concentrated yielding a very viscous brown oil (4.40 g). Chromatography of the concentrate on silica gel PF-254 + 366 (125 g, TLC grade, Brinkman Instruments, Inc., Cat. 7748), using ethyl acetate-hexane (1:9) as eluant with a flow rate of 30 ml/hr, afforded the following fractions:

Fraction	Component	Weight (g)	rel. %
1-5	eluant	0.00	
6-9	cage dimer (2)	0.60	14.35
10	eluant	0.00	
11-14	dimer ketone (3)	1.05	25.12
15-16	dimer ketone- linear trimer (3,4)	<0.01	
17-26	linear trimer (4)	0.81	19.38
27-31	linear trimer- cyclic trimer	0.02	
32-37 +1 ℓ ethyl acetate	cyclic trimer	0.53	12.77
	polymeric material	1.19	28.47
	Total	4.21	

Recrystallization from pentane (-78°C) gave pure 13,14-di-(1,1-dimethylethoxy) hepta cyclo-$[5.5.1.1^{4,10}0^{2,6}0^{3,11}0^{5,9}0^{8,12}]$-tetradecane (cage dimer, 2) as a white crystalline solid, mp 131-132°. Suitable crystals for X-ray analysis were afforded by recrystallization from pentane at 0°C yielding the cage dimer as needles. Density

measurements were made by the flotation method (Na_2SO_4-H_2O) providing a value of ρ^{31} = 1.173603 g/cc.

IR spectrum (KBr, figure 2b): 2970(s), 1455(w), 1385(m), 1360(m), 1292(w), 1245(m), 1225(m), 1195(s), 1085(s), 1055(m), 920(w), 887 cm^{-1} (w);

PMR spectrum (CDCl$_3$, figure 2a): δ 4.28 (mult., 2H CH-OtBu), δ 2.76 (mult., 4H, norbornyl ring bridgehead protons), δ 2.33 (mult., 8H, methine C-H), δ 1.18 (s, 18H, OC(CH$_3$);

Mass spectrum (figure 2c) m/e (% of base peak): 328 (parent ion, 16%), 314(34), 313(84), 255(66), 200(44), 199(100), 187(49), 91(39), 79(31), 57(73), 41(42).

Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.50; H, 9.75.

Found: C, 80.37; H, 9.91.

Repeated crystallizations from pentane (-78°C) afforded pure anti, anti-10,11-di(1,1-dimethylethoxy)-1,4:5,8-dimethano-1,4,4aα,4bβ,5,8,8aβ,9aα-octahydrofluoren-9-one (dimer ketone, 3) as a white crystalline solid, mp 95-96°C (uncorrected).

IR spectrum (CCl$_4$, figure 3b): 3060(m), 2980(s), 2940(s), 2870(m), 1727(s), 1460(m), 1389(m), 1362(m), 1233(m), 1192(s), 1132(m), 1100(s), 1025(w), 905(w), 715 cm^{-1}(m);

PMR spectrum (CDCl$_3$, figure 3a): δ 6.04 (mult., 4H, olefinic hydrogens), δ 3.50 (mult., 2H, CH-O-tBu), δ 3.06 (mult., 2H, bridgehead hydrogens), δ 2.90 (mult., 2H, bridgehead hydrogens), δ 2.70 (mult., 1H, endo-α hydrogen), δ 2.56 (mult., 1H, exo-α hydrogen), δ 1.94 (mult., 2H, β hydrogens), δ 1.18 (s, 9H, O-tBu), δ 1.16 (s, 9H, O-C(CH)$_3$)$_3$);

Mass spectrum (figure 3c), m/e (% of base peak): 356 (parent ion, 2%), 300(33), 243(72), 242(31), 225(60), 196(42), 161(100), 160(83), 132(50), 131(25), 130(47), 90(39), 80(28), 56(87).

Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.55; H, 8.98.

Found: C, 77.55; H, 9.22.

Recrystallization from pentane (-78°C) afforded pure

anti,anti,anti-13,14,15-tri(1,1-dimethylethoxy)-
1,4:6,12:7,10-trimethano-1,4,4aα,5aβ,6,6aβ,6bα,
7,10,10aα,11aβ,12,12aβ,12bα-tetradecahydroindeno-
[1,2-b]fluoren-5,11-dione (linear trimer diketone,
4) as a white crystalline solid, mp 226-227°C
(uncorrected).

IR spectrum (KBr, figure 4b): 3060(w), 2980(s), 1722(s),
1458(m), 1390(m), 1362(m), 1253(m), 1190(2), 1023(w),
900(m), 692 cm^{-1} (m);

NMR spectrum (CDCl$_3$, figure 4a): δ 6.1 (mult, 4H,
definic hydrogens), δ 3.70, 3.56, 3.46 (mults., 1H ea.,
 CHO-tBu), δ 2.70, 2.82, 3.04 (mults., 4H, α hydrogens),
δ 2.07, 2.18, 2.31, 2.48 (mults., 6H, bridgehead
hydrogens), δ 1.98 (mult., 2H, β hydrogens), δ 1.61
(mult., 2H, β hydrogens), δ 1.12, 1.11, 1.10 (s,
9H ea., O-C(CH$_3$)$_3$);

Mass spectrum (figure 4c), m/e (% of base peak):
548 (parent ion, 10 eV only), 91(20), 82(37), 57(100),
41(19).

Anal. Calcd for C$_{35}$H$_{48}$O$_5$: C, 76.66; H, 8.75.

   Found: C, 76.56; H, 9.07.

The cyclic trimer monoketone (5) was obtained as

an oil which resisted all attempts at purification (see

Results and Discussion section). The structure of 5 was

suggested by the results of the following experiment.

The oil (0.11 g) was dissolved in dry THF (1 ml)

and added dropwise to a stirred slurry of LiAlH$_4$ (0.60 g)

in 2 ml of dry THF. The mixture was heated at reflux for

36 hours. After cooling, the mixture was treated success-

ively with 0.5 ml of water, 0.5 ml of 15% (w/w) aqueous

NaOH, and finally with 1.5 ml of water. The suspension

was filtered and the filtrate extracted with diethyl ether

(3 x 10 ml). The organic extracts were combined, washed

with water (3 x 10 ml), separated, dried (Na_2SO_4), and

concentrated. The oily concentrate (0.010 g) was subjected

to infrared and mass spectral analysis.

IR spectrum (film): 3500 (hydroxyl stretch),
1072 cm^{-1} (C-O);

Mass spectrum: m/e 522 (M^+, parent ion), m/e
216 (base peak, $C_{15}H_{20}O^+$), m/e 78 ($C_6H_6^+$).

Preparation of syn-7-(1,1-dimethylethoxy)norbornene (8).

This is a procedure adapted from Kochi, et al.[42]

A solution of 7-tert-butoxynorbornadiene (10 g, 0.061 mole)

in ethylacetate (37 ml) was hydrogenated under one atmos-

phere of hydrogen in the presence of pre-reduced Pd/C

(5%, 0.40 g). After one equivalent of H_2 had been taken

up the reaction mixture was filtered through a bed of celite

and then concentrated. The concentrate was dissolved in

hexane (200 ml) and extracted with a 5 M solution of $AgNO_3$

(3 x 20 ml). The aqueous extracts are cooled to 5°C and

a previously cooled (5°C) solution of 4 N KCN (250 ml)

is added slowly. The aqueous mixture is then extracted

with pentane (4 x 75 ml). The organic extracts were com-

bined, washed with water (2 x 50 ml), separated, dried

(Na_2SO_4), filtered and concentrated to yield 2.21 g (21.79%)

of syn-7-tert-butoxynorbornene, bp 47-48°, 2 mm (lit.[1]

37°, 1.5 mm). PMR and VPC (column - 100' x 0.02" FFAP

S.C.O.T; Column Temp. - 90°C; Flow rate - 5 ml/min; Hewlett-

Packard 5750 Research Chromatograph, flame ionization

detector) analysis revealed the absence of 7-tert-butoxy-

norbornane, anti-7-tert-butoxynorbornene and 7-tert-

butoxynorbornadiene.

Preparation of anti-7-(1,1-dimethylethoxy)norbornene (9).

This is essentially the procedure of Baird, et al.[43]

A stirred suspension of potassium azodicarboxylate (11.83

g, 0.061 mole), 7-tert-butoxynorbornadiene (5.0 g, 0.0305

mole), and methanol (60 ml) was treated dropwise with a

solution of glacial acetic acid (8.04 g, 0.134 mole) and

methanol (40 ml). After the addition was complete the

mixture was added to water (200 ml) and the organic material

separated by extraction with pentane (3 X 50 ml). The

extracts were combined, washed with water (t X 50 ml),

dried (Na_2SO_4), and concentrated to yield 4.1 g of a color-

less oil. PMR and VPC analysis (see preceding experiment)

indicated the presence of anti-7-tert-butoxynorbornene

and 7-tert-butoxynorbornane in a ratio of 1:3, respectively.

Reaction of anti-7-(1,1-dimethylethoxy)norbornene (9) with

iron pentacarbonyl.

The mixture, prepared above (4.0 g, 1.0 g,

0.006 mole of the anti isomer present), was refluxed with

$Fe(CO)_5$ (2.5 g, 0.01275 mole) and di-n-butylether (7 ml)

for 20 hrs. During the reflux dry nitrogen was continuously

bubbled through the reaction mixture. The exit gases

were vented into the hood. At the end of the reflux period
the reaction mixture was filtered hot through a bed of
celite. The black, pyrophoric residue[31] was rinsed with
di-n-butyl ether (2 X 10 ml) and the combined filtrates
were concentrated. Infrared analysis on the concentrate
revealed no absorptions in the 2800-1600 cm^{-1} region.
Vpc analysis (100' X 0.02" FFAP, S.C.O.T. column, 90°C,
5 ml/min.) showed the absence of syn-7-tert-butoxynorbornene
and the presence only of starting material in the
original ratio, i.e., 7-tert-butoxynorbornane and anti-
7-tert-butoxynorbornene in a ratio of 3:1 respectively.

Hydrogenation of dimer ketone 3.

A suspension of ketone 3 (2.60 g, 0.0073 mole)
and Pd/C (10%, 0.5 g) in dry diethyl ether (150 ml) was
shaken on a Parr hydrogenater for 48 hrs under 3 atm of
hydrogen. The solution took up 1.25 psig (requires 1.28
psig) of hydrogen. The mixture was filtered through celite
to remove the catalyst. Concentration of the filtrate
yielded 2.80 g of an off-white solid. Sublimation of
this solid (90°C, 2.0 mm) afforded dimer ketone (11) as
a white solid (2.52 g, 96.5%). Recrystallization of this
solid from pentane (-78°C) gave pure dimer ketone 11,
mp 115-116°C (uncorrected).

> IR spectrum (CCl$_4$, figure 9b): 2980(s), 2880(m),
> 1725(s), 1460(w), 1387(m), 1360(m), 1190(m), 1160(m),
> 1127(w), 1110(w), 1083(m), 895 cm^{-1}(w);

NMR spectrum (CDCl$_3$, figure 9a): δ 4.02, 3.68
(mults, 1H ea., CH-OtBu), δ 3.12 (mult., 2H, β
hydrogens), δ 2.91 (mult, 2H, bridgehead hydrogens),
δ 2.44 (mult, 2H, bridgehead hydrogens), δ 2.20
(mult, 2H, β hydrogens), δ 2.00 (mult, 4H, exo
norbornyl ring hydrogens), δ 1.52 (mult., 4H, endo
norbornyl ring hydrogens), δ 1.18, 1.14 (s, 9H ha.,
OC(CH$_3$)$_3$);

Mass spectrum (figure 9c), m/e (% of base peak):
360 (parent ion, 2%), 248(51), 230(25), 164(79),
93)21), 91(22), 79(23), 67(38), 57(100), 41(35).

Anal. Calcd for C$_{23}$H$_{35}$O$_3$: C, 76.69; H, 9.99.

Found: C, 76.35; H, 10.03.

Reaction of iron pentacarbonyl with syn-7-(1,1-dimethyl-ethoxy)norbornene (8).

Syn-7-tert-butoxynorbornene (8) (5.0 g, 0.30 mole),
Fe(CO)$_5$ (12.5 g, 0.064 mole), and di-n-butylether (35 ml)
were heated at reflux for 34 hrs. Dry nitrogen was bubbled
through the reaction mixture during the period of reflux.
The exit gases were vented into the hood. After reflux
the reaction mixture was filtered hot through a bed of
celite. The black, pyrophoric residue[31] was rinsed with
di-n-butylether (3 X 25 ml) and the filtrates were com-
bined and concentrated. The dark brown viscous concentrate
(1.95 g) contained three components by vpc analysis (1.5%
JXR on Gas Chrom Q, 8' X 3/8", 235°C, 160 ml/min). The
concentrate was dissolved into a solution of FeCl$_3$·6H$_2$O
(25 g) in acetone (65 ml).[32] The mixture was allowed to
stir for 8 hrs and then added to water (400 ml). The
organic material was extracted by diethyl ether (3 X 100

ml) and the combined extracts were washed with water (3 X

200 ml), separated, dried (Na$_2$SO$_4$) and concentrated to

yield 1.84 g of a clear, light brown, viscous liquid.

Chromatography of this liquid on silica gel G (100 g,

TLC grade, Brinkman Instruments #7731), using ethyl acetate-

hexane (1:19) as eluant with a flow rate of 30 ml/hr,

afforded the following fractions:

Fraction	Component	Weight (g)	rel. %
1-13	eluant	-	-
14-36	dimer ketone 12	0.58	31.7
37-38	eluant	-	-
39-59	dimer ketone 10	1.10	62.3
60-65	dimer ketones		
	10 and 11	0.08	
66-76	dimer ketone 11	0.07	6.0
		1.83 g	

Preparative vpc (1.5% JXR on Gas Chrom Q, 8' X 3/8",
210°C, 160 ml/min) gave syn,syn-7,7'-di(1,1-dimethyl-
ethoxy)-2,5"2',5"-dimethano-1α,2α,3,4,5α,6,1'β,2'β,
3',4',5'β,6'-dodecahydrohenzophenone (dimer ketone
12) as a very viscous liquid, bp (micro) 293°C.

Ir spectrum (film, figure 6b): 2990(s), 2880(s),
1702(s), 1465(m), 1385(s), 1360(s), 1300(w), 1250(w),
1230(w), 1195(s), 1160(s), 1140(s), 1090(s), 898
cm^{-1} (m);

NMR spectrum (CDCl$_3$, figure 6a): δ 3.88 (mult., 1H,
CH-O-tBu), δ 1.30-2.70 (mult., 18H), δ 1.21 (s, 9H,
OC(CH$_3$)$_3$), δ 1.09 (s, 9H, OC(CH$_3$)$_3$);

Mass spectrum (figure 6c), m/e (% of base peak):
362 (parent ion, 1%), 139(43), 111(26), 93(23),
79(21), 67(26), 57(100), 41(39).

Anal. Calcd for C$_{23}$H$_{38}$O$_3$: C, 76.27; H, 10.49.

Found: C, 75.68; H, 10.33.

Repeated recrystallization (pentane, -78°C) and

sublimation (50°, 0.8 mm) gave pure

syn, syn-10,11-di(1,1-dimethylethoxy)-1,4:5,8-
1α,2,3,4α,4aα,4bβ,5β,6,7,8β,8aβ,9aα-dodecahydro-
fluoren-9-one (dimer ketone 10) as a white
crystalline solid, mp 179-180° (uncorrected).

Ir spectrum (CCl$_4$, figure 7b): 2970(s), 2870(m),
1723(s), 1460(w), 1388(m), 1360(m), 1190(s), 1172(m),
1143(m), 1117(m), 1087(s), 893 cm^{-1} (w);

NMR spectrum (CDCl$_3$, figure 7a): δ 3.62 (mult.,
2H, CH-OtBu), δ 2.57 (d, 2H, α hydrogens), δ 2.25
(broad d, 4H, β hydrogens and bridgehead hydrogens),
δ 1.92 (mult., 2H, bridgehead hydrogens), δ 1.58
(mult., 8H, exo and endo norbornyl ring hydrogens),
δ 1.12 (s, 18H, OC(CH$_3$)$_3$);

Mass spectra (figure 9c), m/e (% of base peak):
360 (parention, 10%), 248(52), 247(69), 230(20),
164(66), 93(20), 91(21), 81(20), 79(25), 67(54),
57(100), 41(30).

Anal. Calcd for C$_{23}$H$_{36}$O$_3$: C, 76.69; H, 9.99.

Found: C, 76.92; H, 10.09.

Two recrystallizations from pentane at -78°C gave

ketone 11 as a white crystalline solid, mp 113-115°C

(uncorrected). An intimate mixture of this ketone and

authentic ketone 11 (preparation described earlier in this

section, mp 115-116°C), was prepared and the observed mmp

was 113-115°C.

Reduction of dimer ketone 10.

In a flame dried, N$_2$ purged flask fitted with a

reflux condenser, addition funnel, and magnet placed 10

ml of dry tetrahydrofuran (THF) and 0.20 g (5.25 mmole)

of LiAlH$_4$. To this suspension was added dropwise ketone

10 (0.17 g, 0.47 mmole) in 5 ml of dry THF. After the

addition was complete the mixture was refluxed for 53 hrs.

The reaction mixture was then cooled and added successively

1 ml H_2O, 1 ml 15% aq. NaOH, and 3 ml. H_2O. The two phase

system was transferred to a separatory funnel and the

organic layer was separated. The aqueous layer was ex-

tracted with diethyl ether (3 X 20 ml). The organic ex-

tracts were combined, washed with H_2O (3 X 20 cc), separated,

dried (Na_2SO_4) and concentrated. Concentration yielded

0.18 g of a white solid. This solid was recrystallized

once from hexane and yielded 0.169 g of a white solid,

mp 160-162°C (uncorrected). Repeated recrystallization

from hexane (-78°C) gave pure

syn,syn-10,11-di(1,1-dimethylethoxy)-1,4:5,8-
1α,2,3,4α,4aβ,4bβ,5β,6,7,8β,8aβ,9aα-dodecahydro-
fluoren-9-ol (dimer alcohol 14), mp 163-164°
(uncorrected).

Ir spectrum (CCl_4, figure 8b): 3500(m), 2970(s),
2890(s), 1475(m), 1469(w), 1422(w), 1389(s), 1361(s),
1325(w), 1315(w), 1305(w), 1255(m), 1235(m), 1198(s),
1168(m), 1139(s), 1135(s), 1095(s), 1075(s), 1050(m),
1028(w), 1020(w), 988(w), 978(w), 939(w), 898(m),
825(w), 695(w), 665 cm^{-1} (w).

NMR spectrum ($CDCl_3$, figure 8a): δ 4.38 (t, 1H,
CH-OH), δ 3.75 (mult, 1H, C-OH), δ 3.66 (mult, 1H,
CHOtBu), δ 3.61 (mult, 1H, CHOtBu), δ 2.58 (t,
1H, syn CH-CHOH), δ 2.28 (mult, 1H, anti CH-CHOH),
δ 2.15 (mult, 4H, bridgehead hydrogens), δ 1.94
(mult, 1H, syn β hydrogen), δ 1.75 (mult, 1H, anti
β hydrogen), δ 1.58 (mult, 4H, exo norbornyl ring
hydrogens), δ 1.24 (s, 9H, OC(CH_3)$_3$), δ 1.14 (s, 9H,
OC(CH_3)$_3$), δ 1.00 (mult, 4H, endo norbornyl ring
hydrogens);

Mass spectrum (figure 8c), m/e (% of base peak):
362 (parent ion, 2%), 305(38), 250(70), 249(100),
232(63), 231(70), 204(66), 203(89), 165(39).

<u>Anal</u>. Calcd for $C_{23}H_{38}O_3$: C, 76.26; H, 10.49.

Found: C, 76.03; H, 10.77.

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II. ON THE MECHANISM OF CARBETHOXYCARBENE-

INDUCED BETA ELIMINATION OF HX FROM ALKYL HALIDES

CHAPTER 1

INTRODUCTION

The alkyl diazoacetates (N_2CHCO_2R) are widely used
as precursors for carbalkoxycarbenes ($:CHCO_2R$).[1] The
carbalkoxycarbenes generated (e.g., photochemically,
thermally or catalytically) from the diazoesters undergo
a variety of reactions.[1] These reactions include the
usual carbene addition (e.g., to a carbon-carbon double
bond yielding cyclopropane derivatives)[1a] and insertion
(e.g., into the C-H bond)[1b] processes, and certain mis-
cellaneous reactions such as 1,3-dipolar cycloadditions[1c]
and Wolff rearrangements (e.g., $:CHCO_2Et \rightarrow Et-O-C=C=O \rightarrow$
products).[1d] In addition to these noted reactions carbal-
koxycarbenes are also known to take part in a somewhat
unusual reaction for carbenes, i.e., the carbalkoxy-
carbene induced elimination of HX from alkyl halides.

In 1970 Marchand and Brockway[2,3] reported their
studies on the mechanism of HX elimination from alkyl
halides induced by photochemically generated carbethoxy-

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carbene ($:CHCO_2Et$). After studying the reaction of $:CHCO_2Et$ and a number of alkyl halides they found that in nearly all cases the reaction yielded only traces of the expected carbon-halogen bond insertion products. Instead the alkyl halides gave olefinic products in yields ranging from 30-41%.[3]

Ethyl bromide was chosen as their model substrate (Equation 1), and the mechanistic information which they obtained from this reaction is summarized below:[2,3]

$$N_2CHCO_2Et + CH_3CH_2Br \xrightarrow{h\nu} CH_2 = CH_2 + BrCH_2CO_2Et + N_2 \qquad Eq. \ 1$$
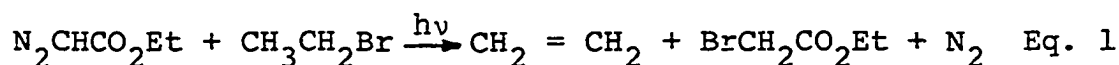
1) the rates of nitrogen and ethylene formation were identical within experimental error ($k_1 = 4 \times 10^{-3} \ min^{-1}$ at $10 \pm 1°C$). This suggested that the rate determining step was the photochemical generation of $:CHCO_2Et$ from the diazoester with concomitant loss of N_2.

2) ethylene formation was indicated not to arise from an electronically excited ethyl bromide (e.g., Equations 2 and 3). Also, product formation from an initially formed insertion product via a Norrish Type II photoelimination (e.g.,

$$(CH_3CH_2Br)^* \rightarrow CH_2 = CH_2 + HBr \qquad Eq. \ 2$$

$$N_2CHCO_2Et + HBr \rightarrow BrCH_2CO_2Et + N_2 \qquad Eq. \ 3$$
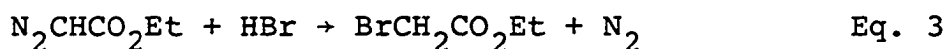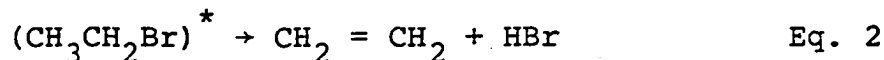
Equation 4) was shown not to be occurring, i.e., ethyl α-bromobutyrate (1) was shown to be stable to the reaction

$$CH_3CH_2Br + N_2CHCO_2Et \xrightarrow{h\nu} \mathbf{1} \longrightarrow products \qquad Eq. 4$$

conditions.

3) olefin formation occurred *via* a β-elimination mechanism rather than by an α-elimination process (Equation 5). Mass spectral analysis showed the products to be $BrCHDCO_2Et$ (d_1, no d_0 observed) and $D_2C = CH_2$ (d_2, no d_3 observed).

$$D_3CCH_2Br + :CHCO_2Et$$

α-elimination
$$\longrightarrow BrCH_2CO_2Et + D_3C\ddot{C}H \xrightarrow{\overset{D}{}} D_2C=CHD$$
$$d_0 \qquad\qquad\qquad d_3$$

$$Eq. 5$$

β-elimination
$$\longrightarrow BrCHDCO_2Et + D_2C=CH_2$$
$$d_1 \qquad\qquad d_2$$

4) the stereochemistry of the elimination process was determined using 3-deuterio-2-bromobicyclo-[2.2.2] octane (**2**, Equation 6). Mass spectral analysis of the reaction products revealed a stereoselective cis-β-elimination. However,

$$\xrightarrow{DBr} \quad \begin{array}{c} 80\% \underline{cis} \\ 20\% \underline{trans} \end{array} \xrightarrow{:CHCO_2Et} \quad + BrCHCO_2Et \qquad Eq. 6$$

there was also a rearranged olefinic material observed in the products (see footnote 10 in ref. 2, *vide infra*).

The mechanism suggested[2,3] (Equation 7) involved

the formation of an intermediate bromonium ylide. The

$$CH_3CH_2\ddot{B}r \ + \ :CHCO_2Et \ \longrightarrow \ \ \longrightarrow \ + \qquad \text{Eq. 7}$$
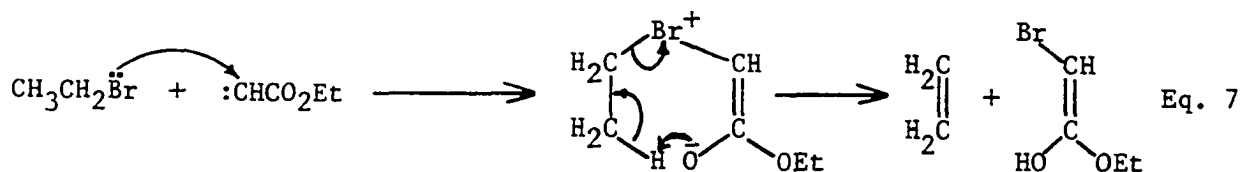
ylide collapses to either a diradical or a tight ion-pair

intermediate which can then break down rapidly to give

predominantly the <u>cis</u>-elimination product. However, in

the vpc analysis of the olefinic product in Equation 6

the presence of a rearranged product (<u>i.e.</u>, bicyclo-[3.2.1]-

2-octane, <u>3</u>) was observed. The source of this olefin was

<u>3</u>
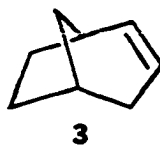
not known. There are two possible sources of the rearranged

olefin; it might result during the formation of <u>2</u> (Equation

6), or during the reaction of <u>2</u> with carbethoxycarbene

(Equation 6). If the rearranged olefin arose in the

carbethoxycarbene elimination process, a third possibility

for the ylide collapse in Equation 6 is suggested, <u>i.e.</u>,

the formation of a free carbonium ion (Equation 8).

$$\longrightarrow \ \xrightarrow{-H^+} \ + \ \textbf{BrCH}_2\textbf{CO}_2\textbf{Et} \qquad \textbf{Eq.8}$$

In this chapter we describe the preparation of a

deuterated 2-bromobicyclo-[2.2.2]octane which is essentially

free of any rearranged isomeric products. The bromide thus prepared is then subjected to reaction with photochemically generated carbethoxycarbene. The reaction products are analysed for their deuterium content and for the presence of rearrangement products.

CHAPTER 2

RESULTS AND DISCUSSION

The aim of this study was to further delineate

the mechanism of HX elimination from alkyl halides by the

action of carbethoxycarbene ($:CHCO_2Et$). The model chosen

for this study was the bicyclo-[2.2.2]octyl system. This

system has two distinct advantages for the study of the

elimination mechanism: the monosubstituted derivatives

(e.g., 1), unlike the norbornyl systems, appear to be

1
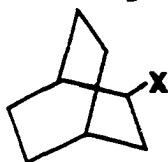
free of any steric factors that might prejudice it in

favor of one particular stereochemical mode of elimina-

tion; also, this system (1) is quite prone to rearrange

(vide infra).[4a-e,5] Thus, the facile ability of the

[2.2.2]octyl system (e.g., 1 or 2) to rearrange to the

isomeric [3.2.1] octyl system (e.g., 3) is a sensitive

probe for carbonium ion participation in the elimination

mechanism involving carbethoxycarbene.

The bicyclo-[2.2.2]octyl derivative selected

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for study was 2-bromobicyclo-[2.2.2]octane (2). For the

mechanistic investigation at hand 2 was required to be

2   **3**
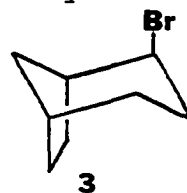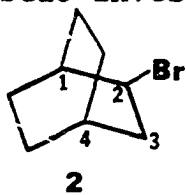
singly deuterated at the β-position (C_3), with the cis-

trans relationship of the deuterium and bromine atoms known.

Also, ideally, 2 was to be synthesized by a procedure

which yielded none of the isomeric rearranged halide (2-

bromobicyclo-[3.2.1]octane, 3]. Alternatively, an analytical

procedure must be devised which is capable of determining

the amount of 3, if present as a mixture of 2 and 3.

There are no reports in the literature dealing

with the separation of the isomeric halides 2 and 3. We

were thus faced with the task of finding a technique

which would allow us to separate the isomers analytically

and/or preparatively. Our attention was centered on

separation by vapor phase chromatography (vpc), and,

after an extensive search for stationary phases and supports,

conditions were found which afforded analytical separation.

The only stationary phase and column available to us

which would separate the isomers was a 100 ft x 0.02 in

support coated open tubular (S.C.O.T.) capillary column

(FFAP stationary phase).

The problem of analysis was compounded by the fact

that neither 2 nor 3 could be prepared isomerically pure.

Thus, we could not assign with certainty the individual

peaks in the vpc tracings of halides 2 and 3. We were

forced to then identify these peaks by an alternative

means. The two isomeric olefins, bicyclo-[2.2.2]-2-octane

(4) and bicyclo-[3.2.1]-2-octene (5), can be obtained

isomerically pure. Olefin 4 is available commercially

and 5 is prepared as shown in Equation 9. A mixture of

4

ref. 34,35, Eq. 9
36a-c
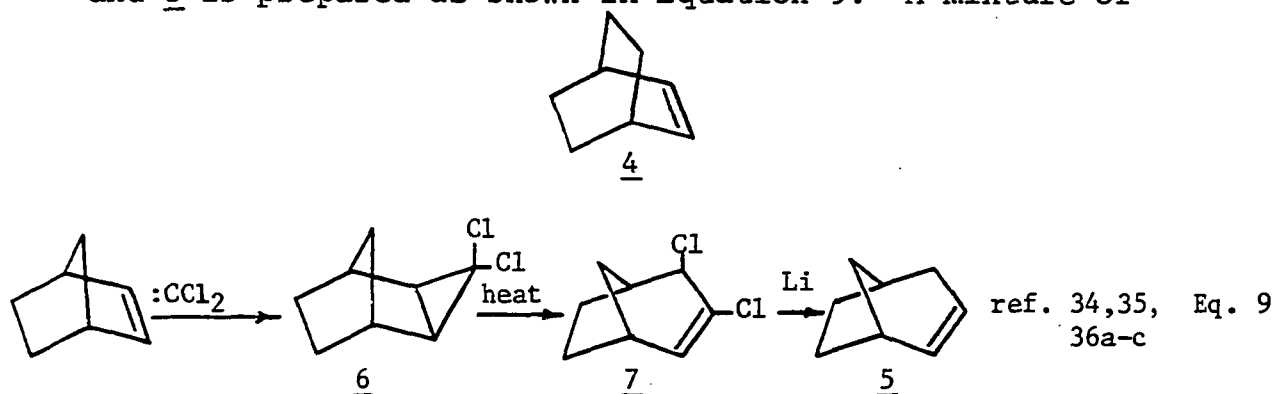
these two olefins can be separated analytically by the use

of a 150 ft x 0.02 in S.C.O.T. column (FFAP). This column

was calibrated by injecting known weight ratios of 4 and

5. This gave a correction factor of one (i.e., the weight

ratios of 4:5 = area ratios of 4:5).
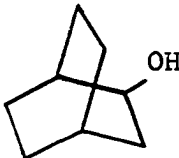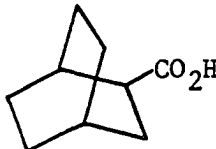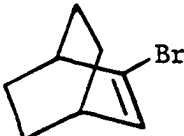
The elimination reaction shown in Equation 10 was

then performed on mixtures of halides 2 and 3 which con-

tained various ratios of the halides 2 and 3. Since

olefins 4 and 5 were available isomerically pure, we were

able to assign with certainty the peaks in the vpc tracings

of the products from Equation 10. The ratio of products

4 and 5 were, in each case and within experimental error,

$$\text{Eq. 10}$$
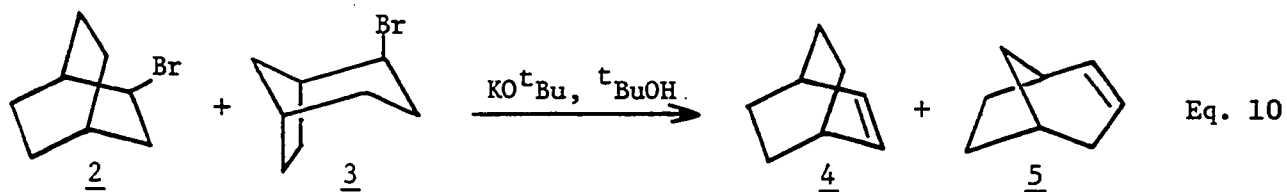
identical to the known ratios of 2 and 3, respectively.
Thus, by correlation of these known ratios (i.e., 2:3
and 4:5 respectively) we were able to assign the peaks
in the vpc tracings of the halides to either 2 or 3.
This analytical procedure is based on the assumption that
rearrangement does not occur under the elimination con-
ditions. This assumption is supported by the known[45]
low nucleophilicity of either t-butyl alcohol or potassium
t-butoxide, and by the fact that rearrangements of carbanions
occur almost exclusively in situations where the negative
charge is stabilized in some manner (e.g., by delocalization
via conjugation with an unsaturated substituent).[46] Since
the carbanion generated in Equation 10 (most likely an
Elcb elimination mechanism)[45] is not so stabilized, re-
arrangement via the carbanion is unlikely in this situation.

A number of synthetic attempts were made to prepare
2 free of its isomer, 3. These various attempts are
shown in Table 1. Each experiment was attempted at least
twice with the results indicated. The ratios shown for
either the halides, 2 and 3, or the olefins, 4 and 5, are
an average of three vpc injections (vide supra) and are
reliable within ca. ±10%.

Table 1

Reaction		Results	Ref.
(bicyclo[2.2.2]oct-2-ene)	DBr	$\underline{2}:\underline{3}$ = 80:20	3
"	1. BH_3 2. NaOMe, Br_2	No Reaction	6,7,8
(2-hydroxybicyclo[2.2.2]octane, OH)	PPh_3, Br_2 CH_3CN	No Reaction	9
"	PPh_3, Br_2 CH_3CN, Pyridine	"	10
"	PPh_3, Br_2 CH_3CN, Pyridine, LiBr	"	
"	PPh_3, Br_2 CH_3CN, LiBr	$\underline{4}:\underline{5}$ = 1:1	
"	PPh_3, Br_2 Triglyme	$\underline{2}:\underline{3}$ = 75:25	11
"	PPh_3, Br_2 DMF	No Reaction	
"	PPh_3, CBr_4 Et_2O	$\underline{2}:\underline{3}$ = 80:20	12, 13
"	PPh_3, CCl_4	No Reaction	12, 13
"	HBr (48%)	$\underline{2}:\underline{3}$ = 70:30	
(bicyclo[2.2.2]octane-CO_2H)	Br_2, HgO CCl_4	No Reaction	14
(2-bromobicyclo[2.2.2]oct-2-ene, Br)	1. BH_3 2. AcOH	No Reaction	15, 16, 17, 18.

The preparation of a suitably deuterated 2-bromo-bicyclo-[2.2.2]octane was achieved via the route shown in Scheme 1. The pivotal compound, 2-bromobicyclo-[2.2.2]-2-octene (14), can be prepared by either of the methods shown. Although the route via the olefin 4 appears to be shorter, it is accompanied by a tedious and time consuming separation step.[24] Thus, the route starting with cyclohexadiene was chosen.

Cyclohexadiene (8)[19] was refluxed with an excess of acrylonitrile to give 9 in an average yield of 48%. This procedure is more convenient than the reported method and gives comparable yields.[20] The preparation of compounds 10, 11, and 12 was achieved by the reported methods.[21,22]

The dibromide 13 was obtained in a manner analogous to that used to prepare 2,2-dichlorobicyclo-[2.2.1]-heptane.[23] Phosphorous pentabromide was generated in situ by the reaction of Br_2 and PBr_3. It was found necessary to have a base present during the reaction to prevent the occurrence of rearrangement products. The base best suited for the reaction proved to be 2,6-lutidine as other, less hindered amines resulted in spurious results.

The structure of dibromide 13 follows from an analysis of its pmr, infrared, and mass spectra (figure 1a-c, respectively), and from the results of the reaction shown in Equation 11. The pmr spectrum shows no absorption below δ 3.2. This suggests the absence of the CHBr

Scheme 1
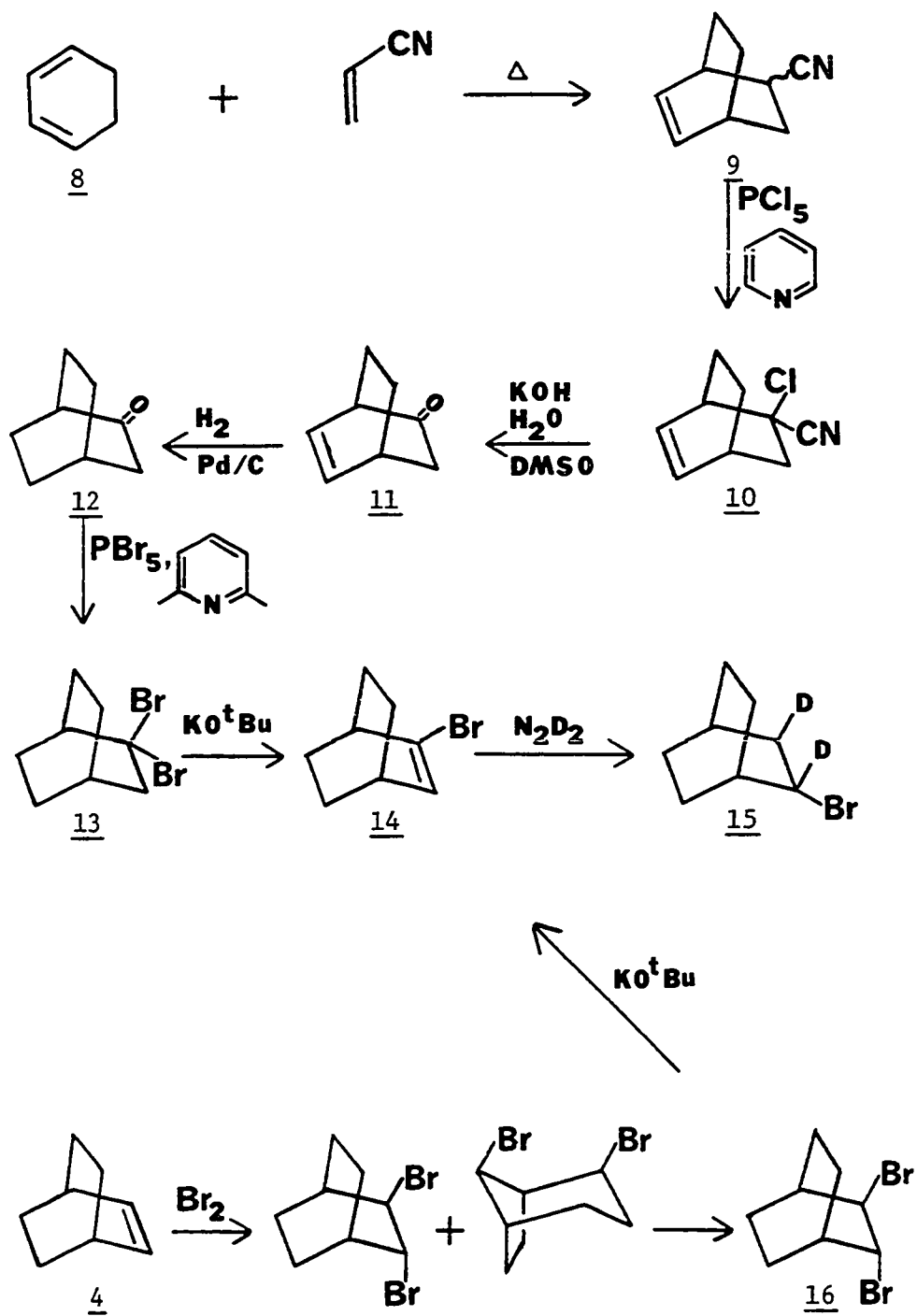
moiety since hydrogens geminal to bromine in these systems

absorb at ca. δ 4.5.[24] The mass spectrum displays the

parent ions at m/e 266, 268, 270 in the ratio of 1:2:1

(respectively) as required for compounds containing two

bromine atoms.[25] The infrared spectrum shows no absorption

in the region 2800-1500 cm^{-1} indicating the absence of

both a carbonyl and a carbon-carbon double bond function

in the molecule.

The basic hydrolysis (e.g., Equation 11) of gem-

dihalo compounds has been used preparatively[26] and as a

test for this functionality.[27,28] The base hydrolysis of

13    $\xrightarrow{\text{KOH, H}_2\text{O}}$ +   Eq. 11
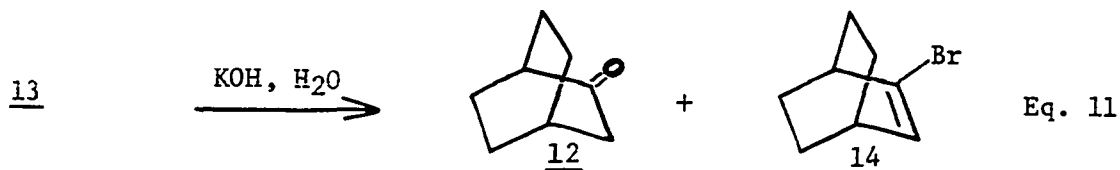
compound 13 yielded ketone 12 and the vinyl bromide 14,

in a ratio of 17:83, respectively. These two compounds

accounted for more than 95% of the expected yield and were

the only two products found. The reaction products were

identified by comparison of their pmr and infrared spectra

with those of authentic 12 and 14. The identity of the

ketonic product was further established by mixed melting

point with authentic 12 (which showed no depression).

Authentic 14, prepared by the method reported by LeBel[24]

(Scheme 1), was identical to the olefinic product in

Equation 11. These observations suggest that the structure

of the dibromide is that of the gem-dibromide 13.
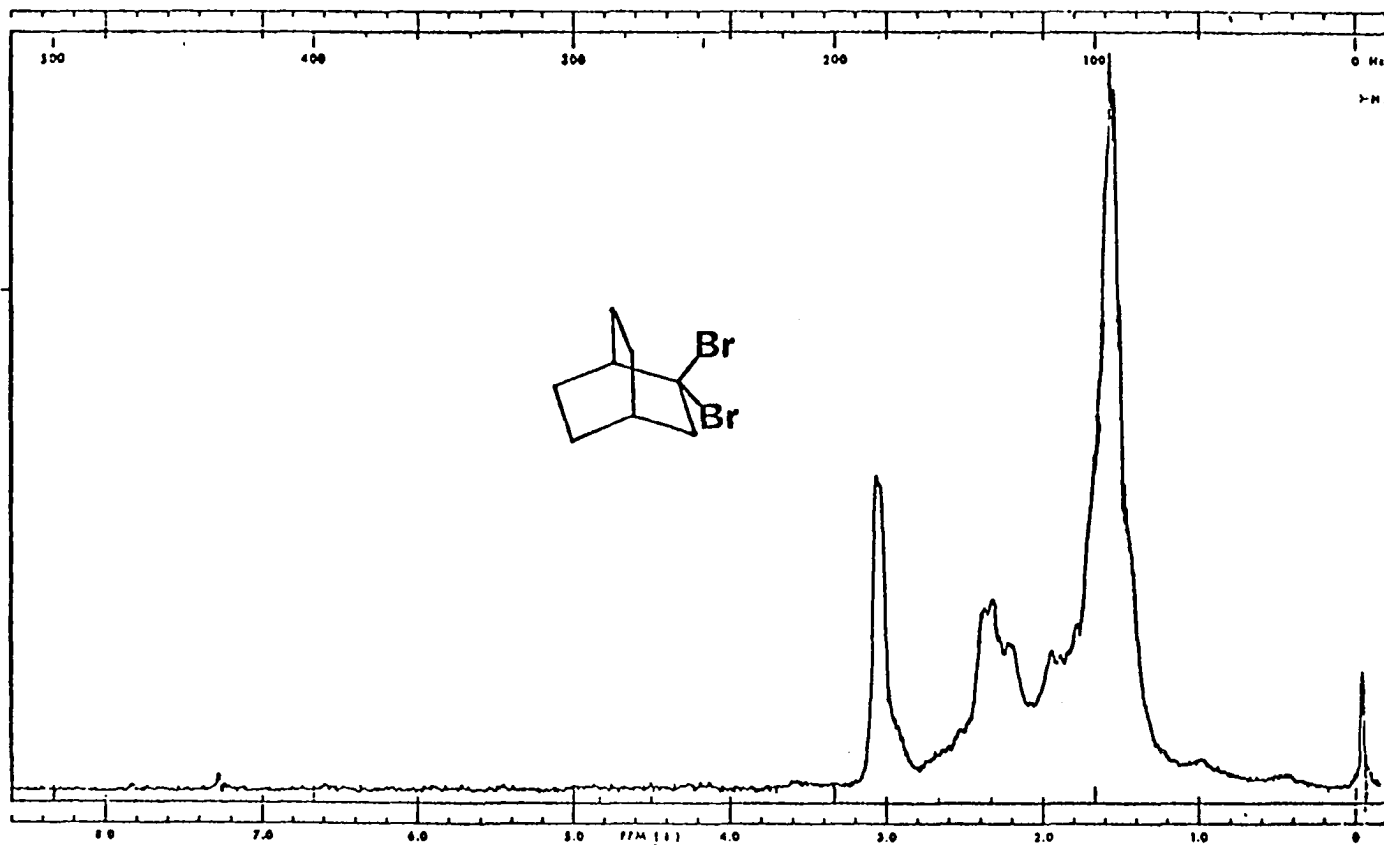
Figure 1. Proton nmr spectrum (60 MHz, CDCl$_3$/TMS) of 13.
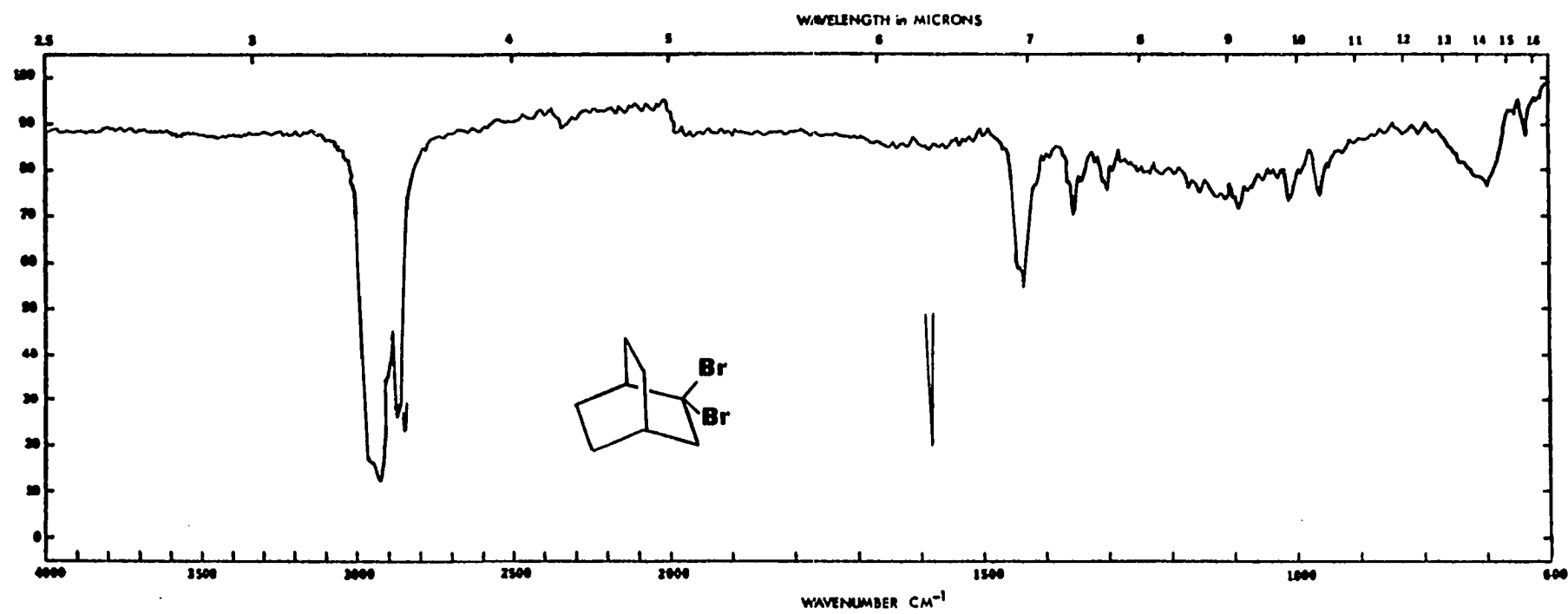
Figure 1b. Infrared Spectrum (CCl$_4$) of 13.
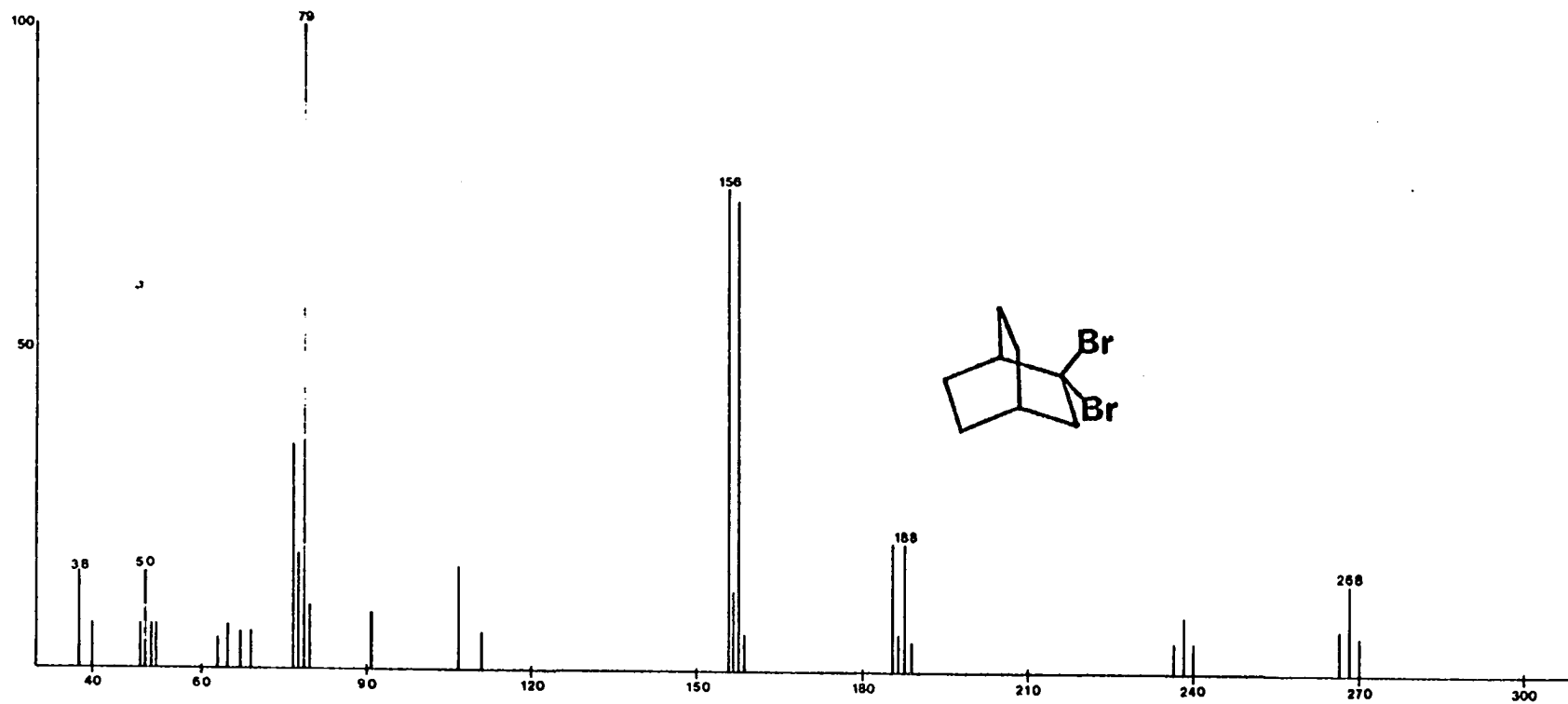
Figure 1c. Mass spectrum of 13.

Our use of the method of hydrogenation of the vinyl bromide 14 with diimide was suggested by several reports of reduction of analogous compounds with this reagent.[29-32] The common methods of reducing carbon-carbon double bonds (i.e., H_2 and a catalyst) usually cause hydrogenolysis of the carbon-halogen bond, especially in the case of vinyl bromides.[33] This was also the result when 14 was reacted with hydrogen and Rh/C as catalyst, or with Pt/C and cyclohexene (used as a source of hydrogen by disproportionation).[33]

Although the recommended procedure[31] for using potassium azodicarboxylate as a precursor of diimide involves anhydrous conditions, water was found beneficial, and indeed, necessary for the reduction of 14. There are no reports in the literature in which water is stipulated as a necessary reagent. However, the reduction of 7-t-butoxynorbornadiene (17) with diimide (Equation 12)[37] yields only two products; the completely reduced compound
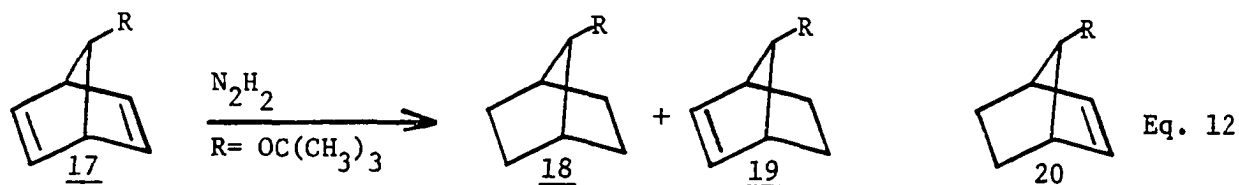
18, and anti-7-t-butoxynorbornene (19). The isomer of 19 (i.e., syn-7-t-butoxynorbornene, 20) was not observed as a product. This observation has prompted House to state that perhaps..."the transition state for transfer

of hydrogen atoms from diimide to the double bond can be stabilized by electrostatic interaction....".[38] Our ob- servation on the necessity of water for the diimide re- duction of 14 supports this statement. However, cur experiments with analogous vinyl halides showed that water was not generally needed in these diimide reductions.

The reduction of 14 yielded cis-2,3-dideuterio-2- bromobicyclo-[2.2.2]octane (15). The cis addition of hydrogen to a carbon-carbon double bond by the action of diimide is well documented[38] and is presumed to be the mode of addition in our case. Vpc analysis (vide supra) revealed the presence of a rearranged product (3.96 ± 0.12%), analogous to the [3.2.1] bromide (3). The starting vinyl bromide (14) was also present to the extent of 36%. This 64:36 ratio of 15:14 was reached after a ten-fold excess of the diimide precursor had been added and remained constant even after a thirty-fold excess had been used.

Separation of 15 from 14 was attempted by sublima- tion, but the mixture simply co-distilled onto the sublimator cold finger. The same results were obtained even when the mixture was cooled during sublimation. Attempted column chromatography of this mixture on silica gel G (Brimkmann Instruments, Inc., Cat. no. 7731) resulted in essentially quantitative rearrangement of 15 to the isomeric [3.2.1] bromide (3). A 1:1 rearrangement mixture was obtained when aluminum oxide (Merck and Co., Inc.,

Cat. no. 71695) was used as support as was the case when

Florisil (Floridin Co., Cat. no. A-1064-69) was used.

Crystallization from various solvents was attempted as a

means of separation but to no avail. Separation was

also attempted by vpc on several different columns but,

as with the other chromatographic techniques, rearrangement

was observed in all attempts. The 64:36 mixture was

therefore used as is in the subsequent reactions with

carbethoxycarbene.

Reaction of Cis-2,3-dideuterio-2-bromobicyclo-[2.2.2]octane

with Carbethoxycarbene.

Brockway[3] reacted 2-bromo-3-deuteriobicyclo-[2.2.2]

octane with ethyl diazoacetate using hexafluorobenzene

as solvent. Irradiation was provided by two 275 watt

General Electric Sunlamps and performed in a Pyrex vessel.

Photolysis was continued, with ethyl diazoacetate being

added as necessary (as indicated by the absence of its

characteristic infrared absorption at 2100 cm^{-1}), until

the starting alkyl halide had been consumed (ca. 120 hours).

The reaction mixture was cooled during this period with

tap water maintaining the reaction temperature at 25 ±

2°C. This method was adopted as our standard procedure

for the photolysis reactions to be performed.

Since the bromooctane 15 could not be separated

from the vinyl bromide 14 without suffering the loss

of the isomeric purity of 15, the following control experi-
ments were performed:

1) the vinyl bromide 14 was irradiated in the
presence of ethyl diazoacetate using the standard procedure
outlined above. After 184 hours of continuous irradiation
the reaction mixture was analyzed by vpc (15% Dibutyl
Tetrachloropthalate on chromosorb W 60/80, 135°C, 136
ml/min (He), Varian Aerograph, Model 90-P, thermal conduc-
tivity detector). This column and instrument were calibrated
for analysis of 14 by injecting known weight ratios of 14
and syn-7-bromonorbornene, and calculating the area ratio
correction factor. Analysis of the above reaction mixture
showed that the vinyl bromide 14 had not been consumed
and, furthermore, no trace of bicyclo-[2.2.2]-2-octene
nor ethyl bromoacetate (i.e., the reaction products ex-
pected from the reaction of 15 with carbethoxycarbene)
could be found. Thus the presence of 14 in the photolysis
reaction mixture would not give rise to the expected reaction
products;

2) next the vinyl bromide (14), ethyl bromoacetate,
and ethyl diazoacetate were irradiated for 110 hours under
the standard conditions. The reaction mixture was analysed
on the above column and instrument. The column and in-
strument were calibrated for the analysis of ethyl bromo-
acetate by injecting known weight ratios of ethyl bromo-
acetate and ethyl α-bromobutyrate and calculating the area

ratio correction factor. Analysis of this reaction mixture

revealed that ethyl bromoacetate was neither being con-

sumed nor produced when irradiated in the presence of 14;

3) finally, 15 and 14 were irradiated for the

standard time in the absence of ethyl diazoacetate. The

reaction mixture was analysed on a 100 ft X 0.02 in S.C.O.T.

capillary column (vide supra, Hewlett-Packard 5750 Research

Chromatograph with a flame ionization detector). Analysis

revealed that the initial amount of rearrangement product

(3.96%) had not been increased. In addition the reaction

mixture was heated with KOtBu (refluxing t-butyl alcohol,

36 hours) and the olefinic product, bicyclo-[2.2.2]-2-

octene (4), was collected by preparative vpc (15% Silicone

704 on chromosorb W 60/80, 8 ft X 3/8 in, 130°C, 120 ml/

min, Varian Aerograph, Model 90-P). Subsequent mass

spectrometric analysis revealed that this olefin contained

76.17 ± 0.84% d_2 and 23.83 ± 0.84% d_1. The deuterium

findings are in agreement with the elimination studies

reported later in this chapter.

The reactions of cis-2,3-dideuterio-2-bromobicyclo-

[2.2.2]octane (15) with carbethoxycarbene were performed

as follows: standard solutions of the mixture of 14 and

15 in hexafluorobenzene were prepared and photolyzed in

the presence of ethyl diazoacetate. The progress of the

reaction was monitored by observing the disappearance of

15 via vpc analysis (8% SF-96 on Fluoropak, 10 ft X 1/4 in,

160°C, 120 ml/min, Varian Aerograph, Model 90-P). Periodic

additions of ethyl diazoacetate were made as the diazoester

was consumed. When the reaction was complete the reaction

products were isolated by preparative vpc (15% Silicone

704 on Chromosorb W 60/80, 8 ft X 3/8 in, 130°C, 120 ml/

min).

The reaction products were first analyzed for

olefinic rearrangement products. Vpc analysis on the

S.C.O.T. columns (vide supra) revealed the following:

Run	% 4	% 5
1	95.27±0.13	4.73±0.13
2	95.11±0.33	4.89±0.33
3	95.56±0.19	4.44±0.19
	95.3±0.33	4.7±0.33

Recalling that the original percentage of rearranged halide

present with 15 was 3.96 ± 0.12%, these results suggest

that little, if any, rearrangement was occurring during

the reaction of 15 with carbethoxycarbene.

The reaction products, bicyclo-[2.2.2]-2-octene

(4) and ethyl bromoacetate were submitted for mass spectral

analysis. To obtain reproducible results it was found

necessary to reduce all heating in the mass spectrometer

to maintain a temperature of ca. 50°C. At this tempera-

ture the thermal fragmentation of the compounds, especially

15, was essentially nonexistent. In this and subsequent

mass spectrometric analyses, the conditions for analysis

were established by reducing the ionizing voltage until

no (M$^+$-1) peak was apparent in the spectrum of the un-
deuterated sample of each reaction product. Once these
conditions were established for each component, the in-
dividual components were introduced and their deuterium
contents were determined. The following results were
obtained on the reaction products.
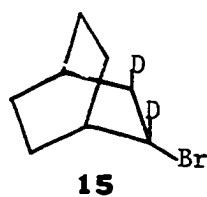
d_2-97.00±0.89%

d_1-0.00

d_0-3.00±0.89%
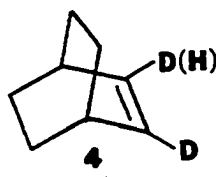
Run	% d_2	% d_1
1	77.84±1.53	22.16±1.53
2	78.29±0.63	21.71±0.63
3	78.93±0.36	21.07±0.36
	78.35±1.53	21.65±1.53

$BrCHCO_2Et$
H
(D)
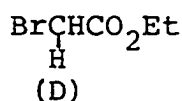
Run	% d_1	% d_0
1	20.29±0.54	79.71±0.54
2	20.26±0.97	79.74±0.97
3	19.83±0.67	80.17±0.67
	20.13±0.97	79.87±0.97

These results are indicative of a stereoselective cis
(ca. 4:1, cis:trans) elimination process in the reaction
of carbethoxycarbene with 15. Also, they are in good
agreement with those reported by Marchand and Brockway

for this reaction sequence (i.e., ca. 80% cis stereo-selectivity).[2]

The bromooctane (15) was next subjected to typical E2 conditions (concentrated potassium t-butoxide in refluxing t-butyl alcohol). The reaction products were collected via preparative vpc and submitted for mass spectrometric analysis. The deuterium analysis of the olefinic product (4) is shown below. These results indicate that under typical E2 conditions this system (15) undergoes a stereo-
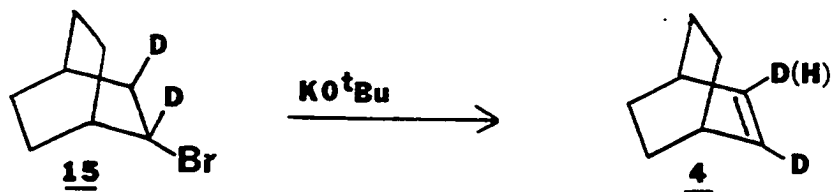
Run	% d_2	% d_1
1	75.07±0.63	24.93±0.63
2	76.35±1.21	23.65±1.21
3	76.17±0.84	23.83±0.84
	75.86±1.21	24.14±1.21

selective cis elimination. Cis E2 elimination is not un-common in rigid systems such as the bicyclooctane (e.g., 15) and norbornyl rings.[39,40] The usual driving force for trans E2 elimination of HX (anti coplanar arrangement of H and X)[41] in these systems is absent since the dihedral angle for cis elimination is ca. 0°, while for trans the angle is ca. 120°.[42]

The above results would, at first glance, appear to be opposite of those obtained by Brockway[3] in the same reaction (Equation 14). The results obtained from Equation 14 indicated that there was 76% <u>trans</u> elimination and
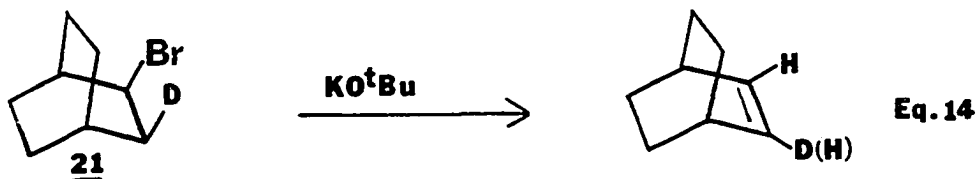
2.4% <u>cis</u> elimination (<u>vis-a-vis</u> our 76% <u>cis</u> and 24% <u>trans</u> elimination). However, the presence of β-deuteriums in the two substrates (<u>15</u> and <u>21</u>) suggests that a primary kinetic deuterium isotope effect might possibly be the source of the inconsistent results. The mechanism of the elimination reaction (either E2 or Elcb) is expected to exhibit a substantial primary kinetic deuterium isotope effect.[45]

The primary kinetic isotope effect for the elimination reactions (Equations 13 and 14) is obtained by the following derivation. The product rate ratios are given by

$$\frac{k'_c}{k'_t} = \frac{76}{24} = 3.17 \qquad \text{(for Equation 13)}$$

and

$$\frac{k'_c}{k'_t} = \frac{24}{76} = \frac{1}{3.17} = 0.32 \qquad \text{(for Equation 14)}$$

where k'_c and k'_t are the <u>observed</u> product rate constants for the <u>cis</u> and <u>trans</u> (respectively) elimination of HX from

the substrates 15 and 21. The true rate constants for the

cis and trans (k_c and k_t, respectively) eliminations are

related to the observed rate constants in the following

manner. In the halide 15 the β-deuterium is trans to

the bromide, while the β-hydrogen is cis. Thus, the ob-

served trans rate constant (k'_t) is slower than the true

trans rate constant (k_t) by a value f (which is the primary

kinetic isotope effect), while the observed constant (k'_c)

is equal to the true constant (k_c):

$$k'_t = k_t/f \qquad\qquad \text{Eq. 15}$$

and

$$k'_c = k_c \qquad\qquad \text{Eq. 16}$$

and

$$\frac{k'_c}{k'_t} = 3.17 \qquad\qquad \text{Eq. 17}$$

substituting for k'_c and k'_t

$$\frac{fk_c}{k_t} = 3.17 \qquad\qquad \text{Eq. 18}$$

and

$$\frac{k_c}{k_t} = 3.17/f \qquad\qquad \text{Eq. 19}$$

However, in the other substrate (21) the observed k'_c is

slower, by the same factor f, than the true constant k_c

and the observed trans rate constant k'_t is equal to the

true <u>trans</u> constant giving:

$$k'_c = k_c/f \qquad\qquad \text{Eq. 20}$$

and

$$k'_t = k_t \qquad\qquad \text{Eq. 21}$$

and

$$\frac{k'_c}{k'_t} = 0.32 \qquad\qquad \text{Eq. 22}$$

substituting for k'_c and k'_t

$$\frac{k_c}{fk_t} = 0.32 \qquad\qquad \text{Eq. 23}$$

and

$$\frac{k_c}{k_t} = 0.32\ f \qquad\qquad \text{Eq. 24}$$

The primary kinetic isotope effect is found by equating Equations 19 and 24 and solving for f:

$$0.32f = k_c/k_t = 3.17/f \qquad\qquad \text{Eq. 25}$$
$$f^2 = 3.17/0.32 \qquad\qquad \text{Eq. 26}$$
$$f = \pm\ 3.15 \qquad\qquad \text{Eq. 27}$$

The derived value of the primary kinetic isotope effect for the bicyclo-[2.2.2]octyl halides (<u>15</u> and <u>21</u>) is in good agreement with reported values obtained for analogous systems and conditions:[45,48]

$$\frac{k_H}{k_D} = \quad 3.6^* \qquad\qquad 3.4^* \qquad\qquad 3.15 \qquad\qquad 3.15$$
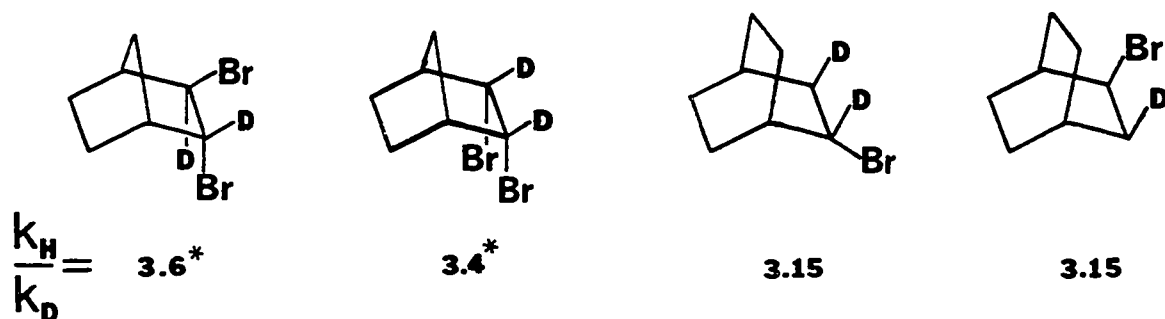
*determined in sodium t-amyloxide/t-amylalcohol

By substituting the derived value of f (=3.15) into Equation 19 or 24 we arrive at a value for the cis to trans elimination rate ratio of:

$$k_c/k_t = 3.17/f = 3.17/3.15 = 1.01$$

and

$$k_c/k_t = 0.32f = 3.17(0.32) = 1.01$$

This derivation implies that the bicyclo-[2.2.2]octyl system, rather than being prejudiced toward either cis or trans elimination, has essentially no preference as to the stereochemical mode of elimination.

In summary, our results indicate that, in a system (e.g., 15) that is not inherently biased toward either cis or trans elimination, carbethoxycarbene induces a stereoselective (ca. 80%) cis elimination of HX. The mechanism of carbethoxycarbene elimination also proceeds by a process which does not involve a free, classical carbonium ion since no rearrangement products were observed.

Incorporating our results with those reported by Marchand and Brockway[2,3] allows us to suggest the mechanism shown in Scheme 2. The photolytic generation of carbethoxy-carbene is the overall rate determining step. The carbene thus formed reacts with the halide substrate yielding the bromonium ylide 22. If the ylide is formed irreversibly no primary kinetic isotope effect is expected to be seen. There was no primary kinetic isotope effect observed by Marchand and Brockway[2,3] when they reacted CH_3CH_2Br and CD_3CH_2Br competitively with carbethoxycarbene. The ylide then collapses rapidly, with stereoselective cis elimination, to yield the olefinic products.

The breakdown of the ylide (22) is thought to occur by an initial significant stretching of the C-X bond in the transition state. The elongation of the C-X bond should lessen the geometrical constraints on the system. This increased flexibility thus allows the bromoenolate moiety easier access to the trans hydrogen to effect its removal. The postulation of significant C-X bond lengthening derives support from the Variable Transition State Theory.[45,49,50]

The theory suggests that one or more of the bond breaking or bond forming processes in an elimination re-action may be farther advanced than the others in the transition state. Once past the energy peak of the transi-tion state the slower processes then "catch up" on the down-hill slope of the reaction coordinate. The variations in

Scheme 2
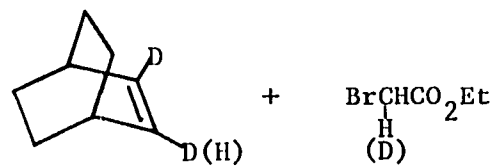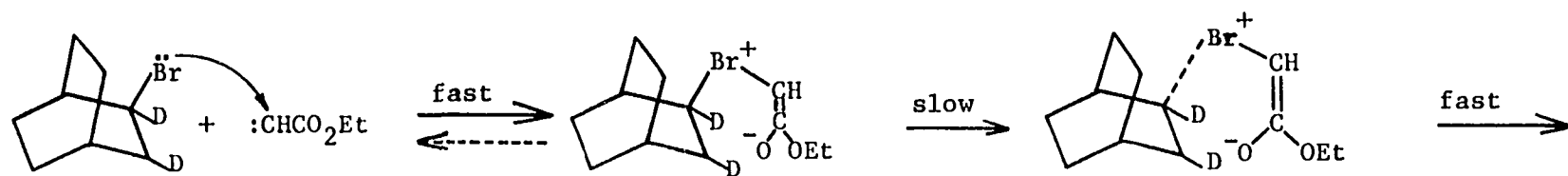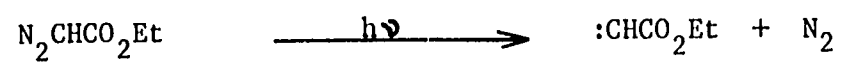
the transition states for the elimination reaction con-

stitute a spectrum ranging from "E1-like" (24) through

a synchronous transition state (25) to the "E1cb-like"

state (26). The two extremes of the spectrum (24 and 26)

$$>C—C< \qquad >C=\!\!=\!\!=C< \qquad >C—C<$$

24   **25**   **26**
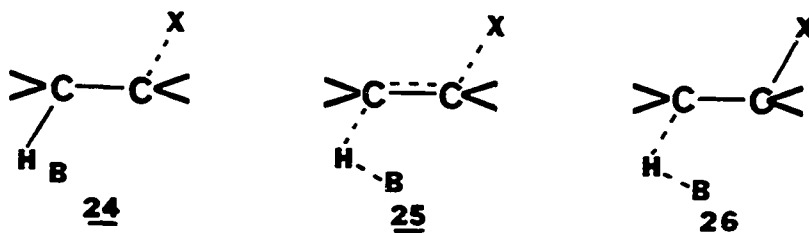
do not represent the two step E1 and E1cb mechanisms (re-

spectively) but concerted mechanisms whose transition states

resemble that of the E1 and E1cb.

The E1 extreme (24) is suggested as the most likely

situation encountered in the eliminations induced by

carbethoxycarbene. In the "E1-like" model there is con-

siderable stretching of the C-X bond and very little, if

any, of the β-CH bond. The slower C-H cleavage then "catches

up" on the downhill slope of the transition state. This

implies that little, if any, primary kinetic isotope effect

should be seen, as was the observed case.[2,3] Also, the

results obtained from the reactions of 15 and 21 (Equations

13 and 14, respectively) with carbethoxycarbene support

the contention that little C-H stretching is occurring in

the transition state. Both reactions (Equations 13 and 14)

gave essentially the same results (i.e., ca. 80% stereo-

selective cis elimination). This occurs despite the fact

that in one substrate (21) the weaker C-H bond is trans

to the halide. The occurrence of ca. 20% trans elimination is consistent with an elongation of the C-X bond. The increased flexibility of the system that the C-X bond stretching suggests should then allow the negatively charged atom in 23 (Scheme 2) easier access to the trans β-hydrogen. The breakdown of the ylide is thus thought to occur via an intramolecular cyclic elimination, with significant C-X bond stretching, to give stereoselective, but not stereospecific, cis elimination.

A loss of stereospecificity has also been observed in reactions which are considered[45] to be prototypes of the cyclic intramolecular cis elimination mechanism (E_i). The loss of the trans deuterium in 27 was suggested to occur
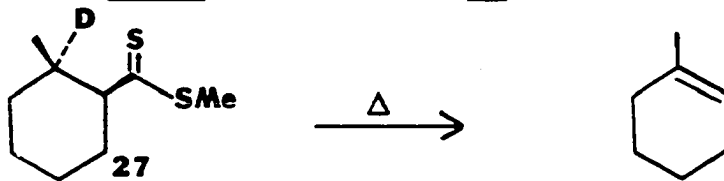
via an ion-pair mechanism during the pyrolysis. However, the observed small primary kinetic isotope effect (1.6) was suggestive of an E_i mechanism.[51] The pyrolysis of the sulfoxide 28 yields both cis and trans stilbenes.[52] The
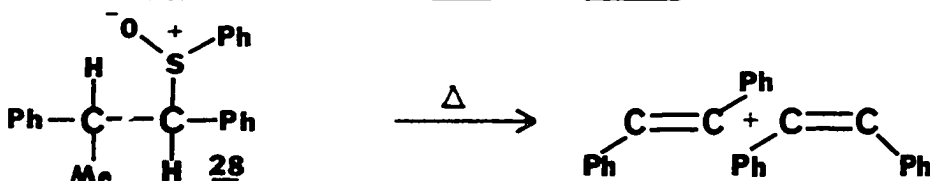
occurrence of an anti elimination product was attributed to a radical-pair mechanism,[52] but calculations indicate that significant C-S bond stretching in the transition state may contribute to the loss of stereospecificity.[45]

Thus even in systems predisposed toward <u>cis</u> intramolecular eliminations the loss of stereospecificity can occur suggesting that such a case is not unlikely in the carbene induced eliminations.

Appendix

The deuterium contents of the products from the reactions reported in this chapter were determined in the following manner. The reactant halide $\underline{15}$ contained
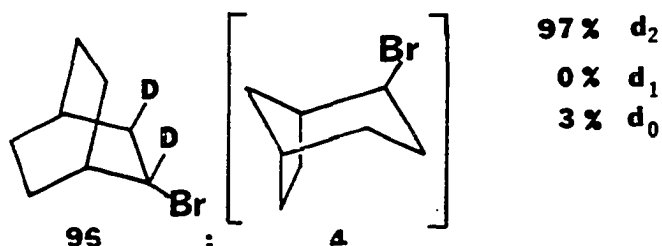
97% d_2
0% d_1
3% d_0

4% of the rearranged halide, and the sample contained 97% d_2, 0% d_1, and 3% d_2. Assuming that the contaminating [3.2.1] halide to have the configuration shown below, its presence would contribute to the d_2 analysis of the olefin

$+ \ BrCH_2CO_2CH_2CH_3$
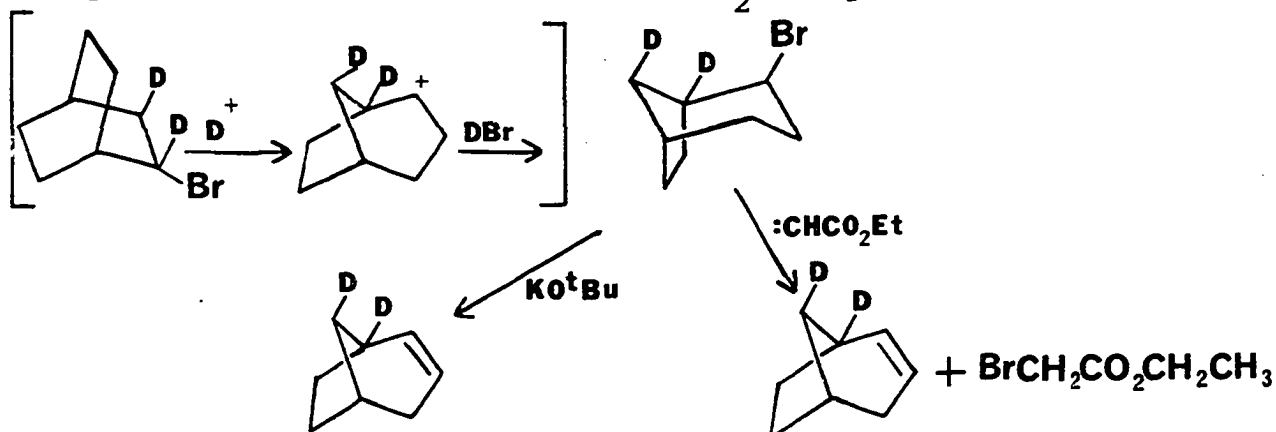
and to the d_0 analysis of the bromoester. The 3% d_0 in the original mixture of halides would also contribute to the d_0 analysis of the bromoester. Therefore the d_2 peak

140

in the mass spectrum of the olefin was multiplied by a factor of 0.96 (1.00-0.04 = 0.96) to correct for the amount of rearranged product present. This was done on the analysis of the olefin from both the carbene and base eliminations.[*] The d_0 peak in the mass spectrum of the bromoester was multiplied by a factor of 0.93 (1.00-0.04-0.03 = 0.93) to correct for the amount of rearranged product present and for the amount of d_0 present in the starting material. The peaks were also corrected for ^{13}C contribution from the next lowest mass unit (the olefin $\underline{m/e}$ 110 peak (d_2) was corrected for the ^{13}C contribution from the $\underline{m/e}$ 109 peak (d_1), and the bromoester $\underline{m/e}$ 170 peak (d_1) was corrected for the ^{13}C contribution from the $\underline{m/e}$ 169 peak (d_0).

For example:
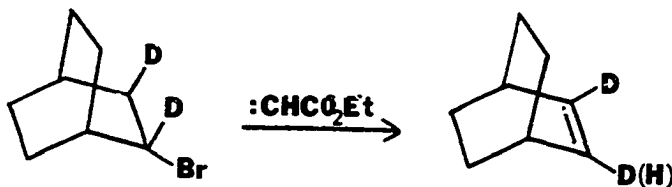
area $\underline{m/e}$ 109	area $\underline{m/e}$ 110	area $\underline{m/e}$ 110X0.96	% $\underline{m/e}$ 109 (d_1)	% $\underline{m/e}$ 110 (d_2)
40.5	154.05	147.89	21.50	78.50
37.5	146.59	140.73	21.04	78.96
35.25	134.61	129.23	21.43	78.57
38.25	142.08	136.40	21.90	78.10
37.5	133.09	127.77	22.69	77.31
			21.71±0.63%	78.29±0.63%

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[*] Both the carbene and base eliminations were allowed to proceed to completion thus negating any rate differences between the [2.2.2] and [3.2.1] halides.
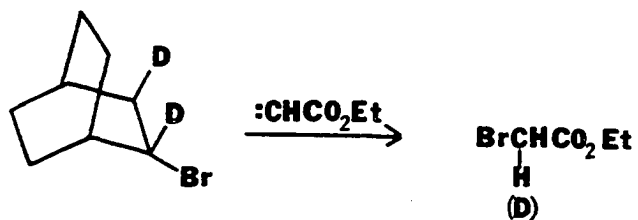
area m/e 168	area m/e 189	area m/e 168X0.93	% m/e 168 (d_0)	% m/e 169 (d_1)
63	16.5	58.59	78.03	21.97
69	16.5	64.17	79.55	20.45
79.5	19.5	73.95	79.13	20.87
88.5	19.5	82.31	80.85	19.15
55.5	12.0	51.62	81.14	18.86
			79.74±0.97%	20.26±0.97%

Summary

The synthesis of cis-2,3-dideuterio-2-bromobicyclo-[2.2.2]octane (15) is described. The diimide (N_2D_2) reduction of 2-bromobicyclo[2.2.2]-2-octene provided 15 essentially free of its (<4%) rearranged isomer 2-bromobicyclo-[3.2.1] octane. This preparation was the only one found which did not provide substantial amounts of rearrangement products.

The bromooctane (15) was then subjected to reaction with carbethoxycarbene and the elimination products were analyzed for deuterium content and for rearrangement products. The analysis suggested that the carbene induces stereoselective cis (ca. 80%) β-hydrogen elimination. Incorporating these results with earlier[2,3] data a mechanism is suggested. In addition the [2.2.2]-bromide (15) was subjected to typical E2 conditions (KO^{t}Bu, refluxing ^{t}BuOH). The preliminary results suggested a stereoselective cis (ca. 75%) elimination. However, by combining these results with prior elimination studies[2,3] a 1° deuterium isotope effect was calculated (k_H/k_D = 3.15). Inclusion of the calculated isotope effect into the observed product rate ratio (k'_c/k'_t) indicated that the bicyclo-[2.2.2]octyl system has essentially no preference as to the stereochemical mode of elimination.

CHAPTER 3

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover
Capillary melting point apparatus and are uncorrected.
Infrared (ir) spectra were recorded on a Perkin-Elmer IR-8
infrared spectrophotometer and were calibrated against the
1601 cm^{-1} and 2850 cm^{-1} bands of polystyrene film. Strong,
medium and weak intensities are denoted by (s), (m) and (w),
respectively. Spectra were generally determined as dis-
persions in potassium bromide or as solutions in carbon
tetrachloride. Mass spectra were recorded on a Hitachi
Perkin-Elmer Model RMU-6E mass spectrometer operating at
70 eV. Proton nuclear magnetic resonance (pmr) spectra
were recorded either at 60 MHz with a Varian Model T-60
spectrometer or at 100 MHz with a Varian XL-100-15 spectro-
meter, utilizing tetramethylsilane (TMS) as an internal
standard. Peak positions are reported in parts per million
(δ) downfield from TMS. The center of gravity of a broad
singlet (br s) or a multiplet (mult) absorption is given
as the peak position. Complex multiplets are, however,
reported as a range between the highfield and lowfield

ends of the multiplet. Elemental microanalyses were per-
formed by Chemalytics, Inc., Tempe, Arizona.

Unless otherwise noted, all reagents and solvents
were reagent grade and used without additional purifica-
tion. Reagent grade acetone was refluxed with and distilled
from potassium permanganate. Carbon Tetrachloride was re-
fluxed with potassium hydroxide for several days, distilled
and stored over Linde 3A Molecular sieves. Anhydrous
diethyl ether and tetrahydrofuran were prepared by dis-
tilling from lithium aluminum hydride just prior to use.

Preparation of Tricyclo-$[3.2.1.0^{2,4}]$-3,3-dichlorooctane ($\underline{6}$).

The following procedure, adapted from Makosza and
Wawrzyniewicz,[34] doubled the yield of $\underline{6}$ reported by Combs
and DeSelms,[36b] who used the traditional method of pre-
paring dichlorocarbene, $:Cd_2$ (i.e., potassium t-butoxide
and chloroform). This procedure is as convenient and, as
noted, provides higher yields than the potassium t-butoxide
method of preparing $:CCl_2$.

Norbornene (Aldrich Chem. Co., Cat. N3240-7, 10.0
g, 0.105 mole), $CHCl_3$ (12.5 g, 0.105 mole), 21.0 ml of 50%
aqueous NaOH (w/w), and 0.05 g (0.00022 mole) of triethyl
benzyl ammonium chloride were mixed together in a round
bottom flask fitted with a reflux condenser. The reaction
mixture was allowed to stir for 24 hrs at ambient tempera-
tures, and then diluted with water (150 ml). The two phase

system was transferred to a separatory funnel and the organic
layer separated. The aqueous layer was extracted with
pentane (4 X 50 ml). The organic layers were combined
and washed with cool water (2 X 100 ml). The organic layer
was separated, dried (Na_2SO_4) and concentrated on a flash
evaporator while allowing cool water to run over the dis-
tilling flask. The yellow-green liquid concentrate was
then distilled under vacuum to yield 10.17 g (54.7%) of
pure 6 (bp $_{0.1}$ 25°-26°, lit.[36b] $bp_{0.7}$ 44.0-45.5°C).

Preparation of 2,3-dichlorobicyclo-[3.2.1]-2-octene (7).
_____

    Purified 6 or more commonly the crude work up
product (above) was placed in acetone (50 ml) and refluxed
for 24 hrs. The mixture was concentrated on a flash
evaporator. The concentrate was then distilled to give
essentially a quantitative yield of 7, $bp_{0.9}$ 59-60°, lit.[36a]
$bp_{0.3}$ 50-51°.

Preparation of bicyclo-[3.2.1]-2-octene 5.
_____

    A 250 ml (24/40), three neck flask, fitted with a
nitrogen inlet, reflux condenser and mercury bubbler,
was flame dried and purged with dry nitrogen. While
maintaining a nitrogen atmosphere at all times, the di-
chloride 7 (10.0 g, 0.0565 mole), dry THF (100 ml), and
t-butyl alcohol (16.07 g) were added to the flask. To
this mixture was then added Li wire (2.36 g, 0.399 g atom)
which had been cut into small sections (ca. 0.5 cm in

length) and washed with hexane. The suspension was then stirred and heated slowly to reflux. An ice-bath was kept at hand since the reaction can suddenly and exothermally occur. Once the reaction has commenced, as evidenced by the suspension becoming cloudy and then purple in color, the heat evolved will maintain reflux for about 90 min. At the end of this period considerable Li metal still remains and the suspension is brought to reflux and maintained at that temperature for 36 hours. At the end of this time the mixture (all or nearly all of the Li has been consumed) is cooled and added to 200 g of ice. If Li wire is still present, the mixture is filtered through a wire gauze to remove the metal. The metal is disposed of by stirring with t-butyl alcohol. Once the ice has melted the mixture is extracted with pentane (5 X 100 ml). The pentane extracts are combined and washed with water (10 X 50 ml) to remove THF and t-butyl alcohol. The organic layer is separated, dried (Na_2SO_4) and concentrated on a flash evaporator while the distilling flask is cooled with running cold water. The concentrate, a <u>volatile</u>, clear, waxy solid was then sublimed (room temperature, <u>ca</u>. 25 mm Hg). This yielded pure <u>5</u> as a waxy solid, mp 39-40° (ST), lit.[26b] mp 37.5-38° (ST), lit.[44] 42-44° (ST).

Preparation of 2-cyanobicyclo-[2.2.2]-5-octene 9.

The following procedure offers a convenient alternative to the reported method[20] and gives comparable yields.

Cyclohexadiene[19] (33.43 g, 0.418 mole), acrylonitrile (62.0 g, 1.17 mole), and hydroquinone (0.10 g) were placed in a 250 ml (24/40) flask fitted with a reflux condenser and drying tube. The mixture was refluxed for 189 hours and then cooled. Hexane (150 ml) was then added to the reaction mixture and an immediate white suspension formed. The suspension within minutes adheres to the sides of the flask and separation was easily accomplished. The transferred hexane solution was washed with water (2 X 50 ml), separated, dried (Na_2SO_4) and concentrated. The concentrate, a white, waxy solid, was sublimed (70°, 1.0 mm) and 26.54 g (48%) of 9 was recovered, mp 55-57°, lit.[20] mp 58°.

Preparation of 2-cyano-2-chlorobicyclo-[2.2.2]-5-octene (10).

(10) was prepared by the reaction of 9 with phosphorous pentachloride following the procedure of Freeman, et al.[21] For best results reagent grade chloroform was washed successively with concentrated sulfuric acid, then with 10% aqueous NaOH (until the aqueous wash was basic to pH paper) and finally with water. The chloroform was then stored over anhydrous Na_2SO_4 for four days and distilled from the same, directly into the reaction flask.

Preparation of bicyclo-[2.2.2]-5-octen-2-one (11).

(11) was prepared by the reaction of (10) with aqueous potassium hydroxide in dimethylsulfoxide following the procedure of Freeman, et al.[21]

Preparation of bicyclo-[2.2.2]-octa-2-one 12.

A suspension of 11 (22.0 g, 0.1805 mole), Pd/C (10%, 0.25 g), and ethyl acetate (200 ml) was shaken on a Parr shaker for 30 hrs under 45 psig of hydrogen. After 15.5 psig (theoretical, 15.9 psig) had been taken up, the reaction mixture was filtered through a bed of celite and the filtrate concentrated. The concentrate, a white, waxy solid, was sublimed (50°, 1.0 mm) to give pure 12, 18.55 g (80.5%), mp 173-175° (ST), lit.[22] mp 175.5-177.5.

Preparation of 2,2-dibromobicyclo-[2.2.2]octane 13.

A 100 ml (24/40) three neck flask fitted with a nitrogen inlet, addition funnel and a gas outlet (leading to a mercury bubbler) was flame dried and flushed with dry nitrogen. An atmosphere of dry nitrogen was maintained at all times. To the cooled and dry flask was added PBr_3 (9.88 g, 0.0364 mole) and dry CCl_4 (25 ml). Dropwise addition of Br_2 (2.58 g, 0.0162 mole) in CCl_4 (10 ml) to the ice-cooled (o°-5°C) and stirred mixture was accomplished over a period of 1 hr. Yellow, insoluble PBr_5 formed immediately upon addition of the Br_2. While the yellow suspension was maintained at 0°-5°C by the ice bath,

2,6-lutidine (8.5 cc) was added. A solution of ketone $\underline{12}$

(1.0 g, 0.00806 mole) in 10 ml of CH_2Cl_2 was then added

to the yellow suspension during a 30 min period. The

reaction was monitored by observing the disappearance of

the infrared carbonyl absorption of the ketone. At the

end of 36 hours the reaction was judged complete and the

reaction mixture was added to a suspension of ice (200 g)

in 5% (w/w) aqueous NaOH (100 ml). The organic layer was

separated and the aqueous layer extracted with pentane

(3 X 100 ml). The organic extracts were combined and

washed with cold water (30 X 100 ml) to remove the amine

(2,6-lutidine is less soluble in warm water than in cold).

The organic layer was separated, dried (Na_2SO_4) and con-

centrated. The concentrate, a white, waxy solid, was then

sublimed (50°, 1.0 mm) to yield 1.37 g (63.45%) of $\underline{13}$.

Preparation of 2-bromobicyclo-[2.2.2]-2-octene, $\underline{14}$.

The vinyl bromide ($\underline{14}$) may be prepared by the

method of LeBel, et al.[24] or by the following procedure.

Gem-dibromide $\underline{13}$ (14.20 g, 0.053 mole), potassium

t-butoxide (12.0 g) and t-butanol (350 ml) were heated at

reflux for 41 hours in a 500 ml (24/40) flask fitted with

a reflux condenser and a drying tube. The cooled reaction

mixture was then added to a mixture of ice (500 g) and

water (1.2 l). Once the ice had melted the mixture was

extracted four times with pentane (300 ml each). The

pentane extracts were combined and washed with water (20

X 100 ml) to remove t-butyl alcohol. The organic layer

was separated, dried (Na_2SO_4) and concentrated. The

slightly brown liquid concentrate was distilled to give

12.89 g (57.5%) of pure 14, bp_{24} 96-98°, lit.[24] bp_6 64-65°.

Preparation of cis-2,3-dideuterio-2-bromobicyclo-[2.2.2]

octane 15.

a 1 ℓ (24/40) three neck flask fitted with a

nitrogen inlet, addition funnel, and a reflux condenser

equipped for nitrogen outlet was flame dried and purged

with dry nitrogen. The gas inlets and outlets were pro-

tected from moisture by drying tubes partially filled with

phosphorous pentoxide. All other equipment (graduated

cylinders, funnels, etc.) were oven dried just prior to use.

A dry nitrogen atmosphere was maintained in the flask at

all times. The double distilled vinyl bromide 14 (5.0 g,

0.02675 mole), methanol-d_1 (200 ml, 99.44%-OD as deter-

mined by the ^{13}C satellite method[47]), and potassium

azodicarboxylate (PADC, 52.0 g, 0.268 mole, freshly pre-

pared and vacuum dried over P_2O_5 for 24 hours) were added

to the reaction flask. In the addition funnel was placed

acetic acid-d_1 (34.25 ml, 35.75 g, 0.585 mole, 98.17%-OD

as determined by the ^{13}C satellite method[47]), D_2O (2.6 ml,

99.8% d_2, freshly opened bottle from Stohler Isotope

Chemicals, Cat. D320, Lot No. 0718), and methanol-d_1 (30

ml, as above). The acetic acid-d_1 solution was added, dropwise, to the yellow suspension during a one hour period. The reaction was monitored by vpc by observing the disappearance of the vinyl bromide 14. After 4 1/2 hours of stirring the reaction mixture was a white suspension (the azo precursor had been consumed) and the ratio of 15:14 was 64:36. Fresh PADC (20 g, 0.103 mole), acetic acid-d_1 (13 ml, 0.234 mole), and D_2O (1.0 ml) were added to the reaction mixture. After 17 hours of stirring, the mixture was again a white suspension but the ratio of 15:14 was still 64:36. This ratio remained the same through the addition of 60 additional grams of PADC and the proportional amounts of acetic acid-d_1 and D_2O. After 104 hours of stirring, the reaction mixture was added to 1 ℓ of water. The aqueous mixture was extracted with pentane (5 X 150 ml). The pentane extracts were combined and washed with water (2 X 50 ml), separated and dried (Na_2SO_4). Concentration of the pentane extracts yielded 5.18 g of a solid-liquid mixture. VPC analysis (8% SF-96 on Fluoropak, 160°, 120 ml/min, Varian Aerograph Model 90-P, thermal conductivity detector) revealed the product to be a 63.77:36.23 ratio of 15:14. This material resisted the usual separation methods (see the Results and Discussion section) and was used as is in the subsequent reactions.

Ethyl Diazoacetate

Ethyl diazoacetate was prepared by the method reported by N. M. Brockway.[3]

Standard Procedure

A solution of the substrate (0.5 g) in 1 ml of hexafluorobenzene and 1 ml of ethyl diazoacetate was prepared. This solution was placed in a cylindrical pyrex vessel provided with a water jacket. The solution was protected from atmospheric moisture by means of a drying tube. The reaction temperature was maintained at 25 ± 2°C by means of tap water circulating through the water jacket. The solution was photolyzed by means of four 275 watt Sylvania sunlamps. Photolysis was continued until vpc analysis indicated the absence of substrate (usually ca. 120 hours). This necessitated the periodic addition of additional ethyl diazoacetate. These additions were made in 1 ml incrementsuntil the reaction was judged complete. The reaction products were collected via preparative vpc (15% Silicone 704 on Chromosorb W 60/80, 8 ft X 3/8 in, 130°C column temperature, 120 ml/min He flow rate) by direct injection of the reaction mixture.

Photolysis of Ethyl Diazoacetate in a Hexafluorobenzene solution Containing 2-Bromobicyclo-[2.2.2]-2-octene 14.

The standard photolysis procedure was used. Photolysis was continued for 184 hours and vpc analysis

at this time indicated no loss of 14. In addition neither bicyclo-[2.2.2]octene (4) nor ethyl bromoacetate were formed.

Vpc analysis was performed on a Varian Aerograph Model 90-P gas chromatograph using a 11 ft X 3/8 in glass column packed with 15% dibutyl tetrachloropthalate (DBTCP) on chromosorb W 60/80, operating at 135°, helium flow rate 136 ml/min. The internal standard used for the analysis of 14 was syn-7-bromonorbornene (7BN). The following correlation between area and weight ratios was found employing a standard solution.

$$\frac{\text{area } 14}{\text{area } 7BN} = \frac{\text{weight } 14}{\text{weight } 7BN}$$

Photolysis of Ethyl Diazcacetate in a Hexafluorobenzene Solution Containing 14 and Ethyl Bromoacetate

The standard photolysis procedure was used except that 0.3 g of 14 and 0.3 g of ethyl bromoacetate was used. Photolysis was continued for 110.5 hours and vpc analysis at this time showed no change in the amount of ethyl bromoacetate present.

Vpc analysis was performed on a Varian Aerograph Model 90-P gas chromatograph using a 10 ft X 1/2 in glass column packed with 1.5% JXR on Gas Chrom Q 60/80, operating at 103°, helium flow rate 125 ml/min. The internal standard used for the analysis of ethyl bromoacetate was ethyl α-bromobutyrate. The following correlation between

area and weight ratios was found employing a standard

solution.

$$\frac{\text{area ethyl bromoacetate}}{\text{area ethyl } \alpha\text{-bromobutyrate}} = 1.06 \frac{\text{weight ethyl bromoacetate}}{\text{weight ethyl } \alpha\text{-bromobutyrate}}$$

Photolysis of a Hexafluorobenzene Solution of 14 and Cis-

2,3-dideuterio-2-bromobicyclo-[2.2.2]octane 15.

The standard photolysis procedure was used except

ethyl diazoacetate was not present. The photolysis was

continued for 120 hours and vpc analysis showed no change

in the amount of 15 present. Also there was no bicyclo-

[2.2.2]-octene (4) present.

The above mixture was then concentrated. The con-

centrate (14 and 15) was then mixed with potassium t-butoxide

and t-butyl alcohol. The mixture was then heated at reflux

for 36 hours. The mixture cooled and washed with water,

and extracted with pentane. The pentane extracts were

dried (Na_2SO_4), and concentrated on a steam bath. The

bicyclo-[2.2.2]octene product was collected via vpc. Sub-

sequent mass spectral analysis revealed that the olefin

contained 76.35 ± 1.21% d_2 and 23.65 ± 1.21% d_1.

Photolysis of Ethyl Diazoacetate in a Hexafluorobenzene

Solution Containing 14 and 15.

The standard photolysis procedure was used. The

photolysis was continued for 159 hours at which time vpc

analysis showed the absence of 15. The ethyl bromoacetate

and bicyclo-[2.2.2]octene products were collected <u>via</u>

vpc. Subsequent mass spectrophotometric analysis revealed

that ethyl bromoacetate product contained $20.13 \pm 0.97\%$ d_1

and $79.87 \pm 0.97\%$ d_0; whereas the other elimination pro-

duct, bicyclo-[2.2.2]octene, contained $78.35 \pm 1.53\%$ d_2

and $21.65 \pm 1.53\%$ d_1. These figures reflect the results

from three independent runs.

Potassium t-Butoxide Reaction with <u>Cis</u>-2,3-dideuterio-2-

bromobicyclo-[2.2.2]octane

A solution containing 0.5 g of the 64:36 mixture of

<u>15</u>:<u>14</u>, 2 g (0.017 mole) of potassium <u>t-butoxide</u>, and 10 ml

of <u>t</u>-butyl alcohol was refluxed for 36 hours. The solution

was added to 150 ml óf ice water and extracted three times

with 40 ml portions of pentane. The combined pentane

extracts were washed 10 times with 100 ml portions of

water to remove <u>t</u>-butyl alcohol. After drying over anhy-

drous sodium sulfate the pentane solution was filtered and

most of the pentane removed by distillation on a steam bath.

The bicyclo-[2.2.2]octene was obtained from the concentrate

by preparative vpc. Subsequent mass spectral analysis re-

vealed that the product contained $75.86 \pm 1.21\%$ d_2 and

$24.14 \pm 1.21\%$ d_1. These results reflect the results from

three independent runs.

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