THE CYCLOHEPTATRIENE-NORCARADIENE EQUILIBRIUM

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By

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ABSTRACT

The effect of a C-7 substituent on the position of the cyclo-heptatriene/norcaradiene equilibrium has been investigated. For this purpose a series of monosubstituted cycloheptatrienes was prepared in which the C-7 substituent was a carbonium ion grouping. From the spectral properties of these systems, it has been concluded that proportion of the norcaradiene valence tautomer present increases as the electron withdrawing ability of the carbonium ion substituent is enhanced.

From a comparison of the pmr spectra of 7-norcaradienylmethyl cations with suitable model systems it is suggested that these norcara-dienes are aromatic and that they support an induced diamagnetic ring current when in a magnetic field. It would appear that this type of cyclic delocalization is enhanced by the presence of an electron defficient substituent at C-7 of a norcaradiene and possible reasons for this are discussed.

The 7-norcaradienylmethyl cations underwent a thermal isomeriza-tion to give benzenoid materials at relatively low temperatures. A mechanism for this rearrangement has been proposed and the implication of these results to the general pathways involved in the rearrangements of the $C_8H_9^+$ family of cations discussed.

Several synthetic routes to 9-substituted-3,4-homotropylidenes were investigated. A number of new compounds were isolated and a new synthetic approach to this class of compounds is suggested.

Diamagnetic susceptibility exaltations of a series of substituted cycloheptatrienes were determined and used as a criterion of aromaticity. It was concluded that cycloheptatrienes are best regarded as homoaromatic molecules. Moreover it would appear that the substantial diamagnetic susceptibility exaltations observed with these compounds are related to the bulk of a C-7 substituent. One neutral norcaradiene was examined by this technique and was found to be nonaromatic.

A Mme et M. Paul André

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CHAPTER I

INTRODUCTION

Cycloheptatriene is perhaps the most intensively studied member of the odd-numbered cyclic polyenes. Yet despite this, the structure of cycloheptatriene which was variously reported as $\underline{1}$ or $\underline{2}$, was not definitely established until fairly recently.[1]
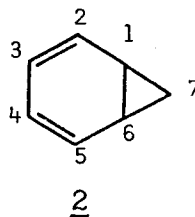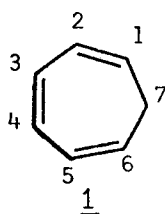
In 1885 Büchner and Curtius reported that the thermal decomposition of methyl diazoacetate in benzene led to a series of isomeric esters, consequently to become known as the "Büchner esters". They concluded that the mixture consisted of the methoxycarbonylcycloheptatrienes $\underline{3}$, $\underline{4}$, $\underline{5}$, and 7-methoxycarbonylbicyclo [4.1.0] hepta-2,4-diene, $\underline{6}$.[2]
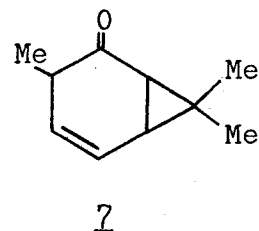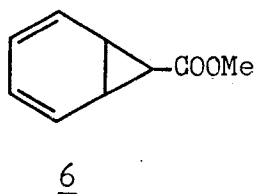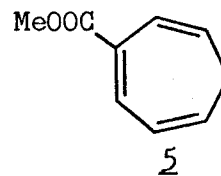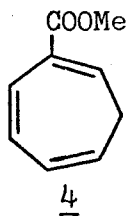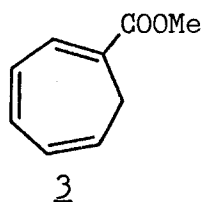
While the evidence presented by Büchner and Curtius was not unambiguous, for a long time the structure of 6 was generally accepted. Indeed compounds of this type were called norcaradienes on the basis of the similarity of the basic ring system to that of the natural product carone, 7.

In 1957 Meerwein claimed to have prepared norcaradiene itself by the photolysis of diazomethane in benzene.[3] In contradiction to this report, Doering insisted that apart from a small amount of toluene, cycloheptatriene was the only product formed in this reaction.[4] On repeating Büchner's original experiments, Doering also suggested that the Büchner esters were all positionally isomeric cycloheptatrienes and that in particular, 6 was not a norcaradiene derivative but had the structure 8.[5]
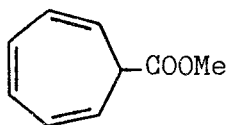
8

Chemical evidence was of little help in distinguishing between structures such as 1 and 2. For example, while oxidation of the carboxylic acid derived from 8 with potassium permanganate gave a cyclopropane-1,2,3-tricarboxylic acid,[2] 8 was readily converted on heating to the three isomeric cycloheptatriene esters, 3, 4 and 5.[2] Similarly, while the addition of a dienophile to cycloheptatriene usually gives products derived from norcaradiene,[6] eq.1, cycloheptatriene can be hydrogenated to give cycloheptane, eq. 2. Under conditions where

hydrogenolysis of the cyclopropane ring should be minimized (Rh catalyst), cycloheptatriene has been shown to give less than 0.005% of norcarane.[7]

$$\text{(1)}$$

$$\xrightarrow{\text{H}_2/\text{Rh}} \qquad \text{(2)}$$
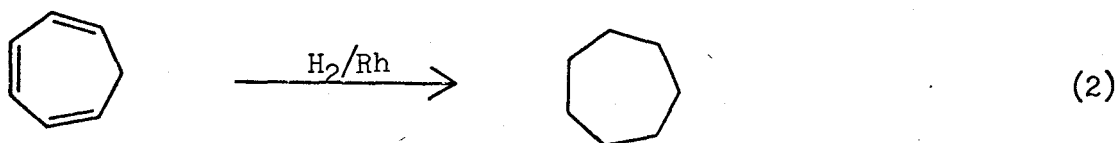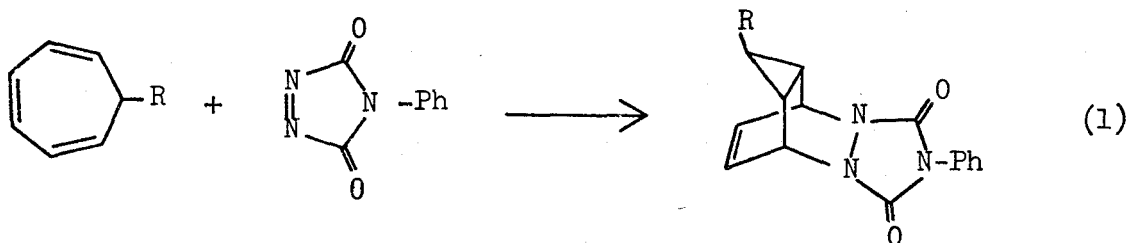
This duality of the chemical reactions of these systems has been rationalized by two hypotheses:

a. Cycloheptatriene can be regarded as a pseudo-aromatic compound[5] in which the C-1, C-6 σ bond is fully uncoupled but with overlap of the C-1 and C-6 π-orbitals.

In this view the structures 1 and 2 represent just two resonance forms of the resonance hybrid 9 and the molecule can be regarded as "homobenzene".[8]

9
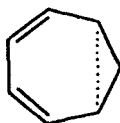
b. Norcaradiene and cycloheptatriene (NCD and CHT) are rapidly equilibrating valence tautomers.

In suggesting the homoaromatic structure of cycloheptatriene,

Doering assumed that the molecule had a planar structure, it being thought that this was a necessary condition for effective cyclic delocalization.[5]

The Geometry of the Cycloheptatriene Molecule

While the room temperature proton magnetic resonance (pmr) spectrum of cycloheptatriene is consistent with a planar structure in that only a single resonance is observed for the two C-7 hydrogens, at very low temperatures two signals are found for these protons. This would imply that the seven-membered ring of 1 is not planar and is consistent with a boat conformation as illustrated in 1a.

The two C-7 protons in a conformation such as 1a are non-equivalent and at low temperatures when ring inversion is slow, two separate resonances would be expected for these protons in the pmr spectra.[9,10] As the temperature of the sample is raised, ring inversion would become more rapid and these signals would be expected to coalesce and average. The barrier to inversion of the two boat conformations was found to be 6 kcal/mol.[9]

1a   1b
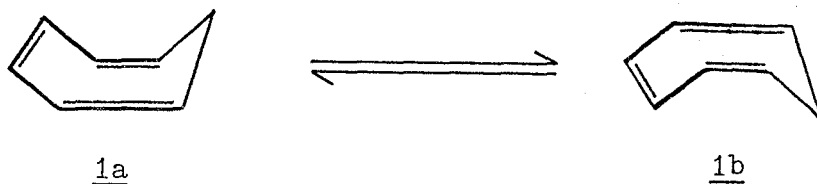
The structure of cycloheptatriene has also been examined by microwave spectroscopy[11] and electron diffraction measurements[12] and the boat shape has been confirmed. Such a conformation is also consistent with the ease of the transannular 1,5-hydride shifts that cyclo-

heptatriene and many of its derivatives undergo.[13] In the solid phase, the structure of 7,7-dimethylcycloheptatriene-3-carboxylic acid has been determined by X-ray crystallography and again a boat shape was found for the seven-membered ring.[14]

While the structural analyses performed by either of the aforementioned methods invariably indicated that cycloheptatriene exists in a boat conformation as shown in Figure 1, the detailed shape of the ring seems to be dependent upon the presence and nature of any substituents as well as the experimental method used.

Figure 1: The geometry of cycloheptatriene and some of its derivatives.
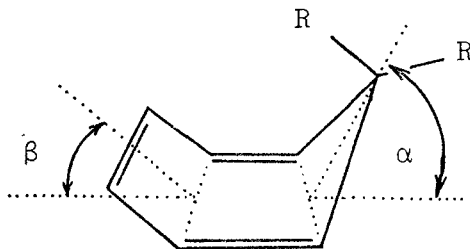
			ref.
$R = H$	$\beta = 40.5 \pm 2°$	$\alpha = 36.5 \pm 2°$	12
$R = H$	$\beta = 29.5 \pm 4°$	$\alpha = 50 \pm 5°$	15
$R = CH_3$	$\beta = 24.4°$	$\alpha = 47.9$	14
$R = CF_3$	$\beta = 25°$		11,16

From the position of pmr absorption of the C-7 protons and the coupling constants between protons at C-1 and C-7 in monosubstituted cycloheptatrienes, Müller[17] and Günther[18] have concluded that a substituent preferentially adopts the pseudo equatorial position.

Seemingly, after the establishment of the non-planar structure

of 1, the Doering homoaromatic model of cycloheptatriene has largely

fallen into disfavour. However, although the C-1, C-6 separation in 7,

7-dimethylcycloheptatriene-3-carboxylic acid, as determined by X-ray

crystallography,[13] is much greater than that expected for a bicyclic

structure, it does not exclude the possibility of some overlap of the

C-1, C-6 π-electrons.

The Cycloheptatriene - Norcaradiene Equilibrium

It is currently accepted that the cycloheptatriene and nor-

caradiene are valence tautomers and that they are in rapid equilibrium,[19]

eq. 3. This equilibrium is similar to that known for some time for

bicyclo 4.2.0 octa-2,4-diene/cyclooctatriene,[20] eq. 4.

$$\text{(3)}$$

$$\text{(4)}$$
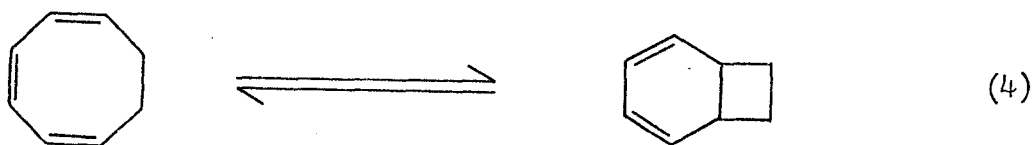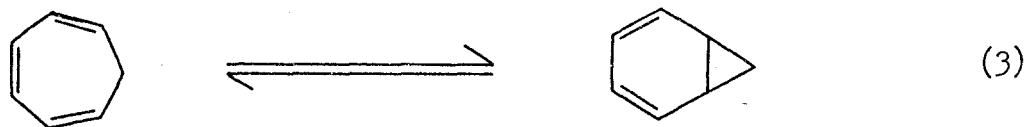
The existence of such a tautomerism was definitely established

only with the advent of nuclear magnetic resonance spectroscopy.[1] Where-

as the chemical evidence is ambiguous, nmr spectroscopy can clearly

distinguish between the two tautomers. For example, the protons on

carbons C-1 and C-6 of cycloheptatriene resonate in a typical olefinic region (above δ 5.0), while the corresponding cyclopropyl-proton signals of a norcaradiene appear around δ 3.5. In rapidly equilibrating mixtures of certain substituted cycloheptatrienes and norcaradienes, these proton resonances often occur in some intermediate position between these two values, the exact position being dependent on the equilibrium concentration of the respective isomers.[19] Examples of systems have been found in which the cycloheptatriene form predominates, the norcaradiene form predominates, and in which both isomers are present in about equal amounts.

The existence of unsubstituted norcaradiene remains as yet to be demonstrated. Both kinetic[21] and spectroscopic[22] methods have failed to detect 2 in cycloheptatriene and only an upper limit to the concentration of norcaradiene can be set.

The magnitude of the energy difference between the isomers 1 and 2 remains obscure. The value of 11±4 kcal/mole suggested[23] on the basis of bond energy calculations[24], is frequently cited in the literature.[1a,21,25] This number would correspond to an equilibrium norcaradiene concentration of some 8.3×10^{-4} to 1.3×10^{-9} % at room temperature. Kinetic norcaradiene trapping experiments could be taken to suggest a much smaller energy difference, 4.0-4.5 kcal/mole, and a norcaradiene equilibrium concentration of 0.1%. However this latter value is open to criticism.[21]

With some substituted cycloheptatrienes, when both valence tautomers are present in more or less equal amounts, low temperature nmr can be used to obtain the equilibrium ratio directly.[26] Other spectroscopic techniques have been of limited (Raman[26]) or little use (ir, uv[27])

in determining the ratio of the two forms present.

Just as with the parent compound, the majority of simply sub-
stituted cycloheptatrienes also exist very largely in the monocyclic
form. It is worth noting at this point however that the position of
the equilibrium between the cycloheptatriene and norcaradiene forms of
these substituted systems could be considerably different from that
encountered with the parent compound and yet still be beyond the range
of detection by nmr (usually 5-10%).

To state the obvious, two general methods can be employed to
make the norcaradiene form predominate in these equilibria. These are –

a) to stabilize the norcaradiene form in some way

b) to destabilize the cycloheptatriene form

Either or both of these two methods have been used to prepare stable
norcaradienes.

Stable Norcaradienes

One method of stabilizing the bicyclic form is to incorporate
one or both double bonds of a norcaradiene into an aromatic system. For
example the rearrangement of benzonorcaradiene 10, into its seven-
membered ring valence tautomer 11, eq.5 would involve the loss
of considerable resonance energy. It is thus not unexpected that 10 is
the predominant valence tautomer present.[26]

10   11   (5)
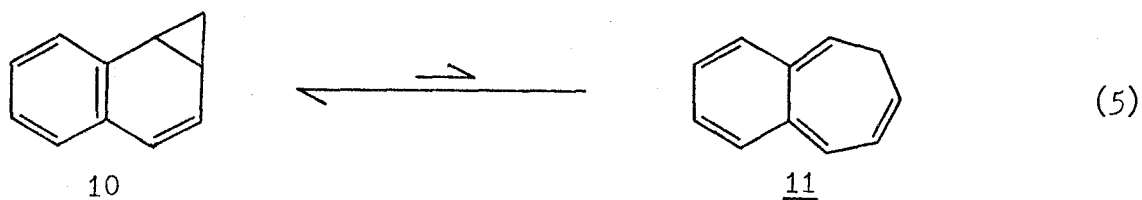
The norcaradiene structure can also be stabilized by placing a

three carbon bridge between the C-1 and C-6 of these systems. An example

of this type of compound is 12.[28] The cycloheptatriene derivative

derived from this compound would have two bridgehead double bonds and

therefore would not be expected to be stable. In fact, 12 is the only

isomer observed. The extension of the C-1, C-6 bridge by a fourth

methylene group eliminates some of the strain in the cycloheptatriene

form and this later valence tautomer, 13, now predominates.[28c]

12

13
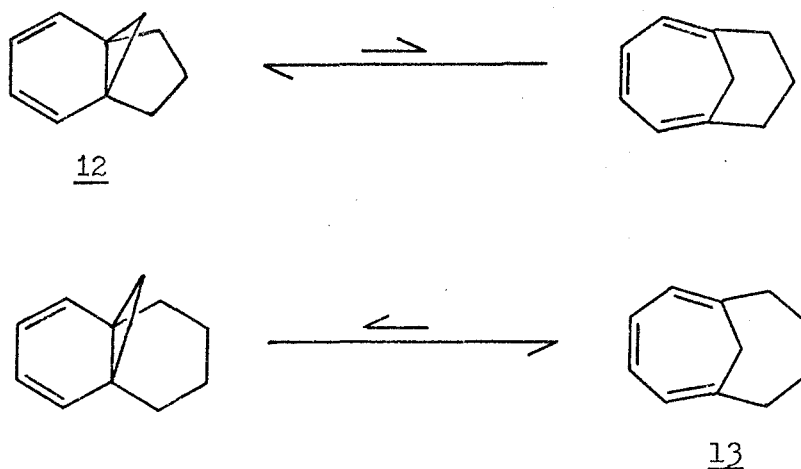
Compound 14 presents another type of "sterically stabilized"

norcaradiene. The cycloheptatriene isomer derived from this compound

would be expected to experience a severe steric interaction between the

methyl groups and the benzene rings. The bicyclic form 14 has been found

to predominate.[29]
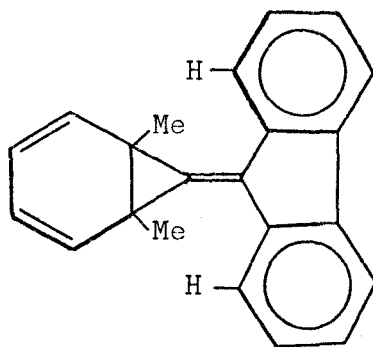
14

The hydrocarbon **15** had also been found to exist very largely in the norcaradiene form. It has been suggested that the wide external angle at C-7, necessitated by the attached five-membered ring, causes the C-1, C-7, C-6 angle to be small and to thus stabilize the bicyclic form of this compound.[30] If this is indeed so, then an opposite effect may be expected in **16** and indeed this compound was found to exist almost completely in the monocyclic form.[31]
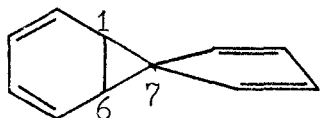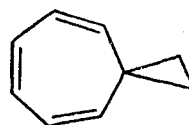
15   **16**

The norcaradiene structure also can be stabilized by the incorporation of heteroatoms into the ring system, e.g. **17**, **18** and **19**, **20**. It can be readily calculated from tables of average bond energies, that 3,4-diazanorcaradiene, **17**, is expected to be thermodynamically more stable than the monocyclic isomer **18**. Experimentally **17** was found to be

the more stable tautomer.[32]

17   18
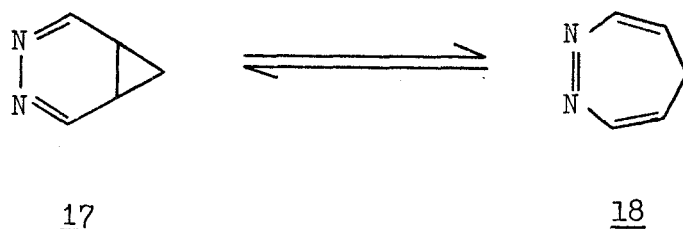
The reasons for the increased stability of the bicyclic form of oxepine are much less obvious, however the bicyclic compound 19 was found to exist in a 1/10 ratio with 20.[33]

19   20
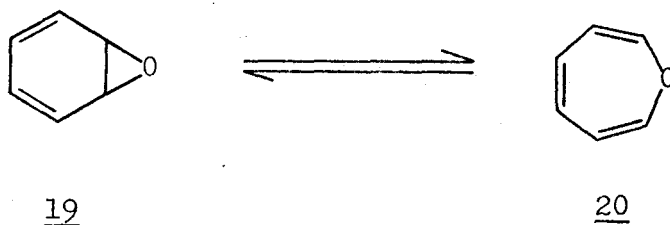
Compounds 14 and 15 are examples of norcaradiene systems stabilized by substitution at carbon 7. The preference for the bicyclic form in these compounds is very likely due to steric reasons. Of greater interest is a series of C-7 substituted CHT/NCD systems in which the bicyclic form seems to be stabilized by an electronic rather than a steric effect.

7-Substituted Cycloheptatriene/norcaradiene Systems

Cycloheptatrienes substituted at C-7 can be prepared by the addition of a suitably substituted carbene to benzene.[2,3,5,34-37] Therefore when Ciganek[26b] attempted the photolytic decomposition of dicyanodiazomethane in benzene, he had every reason to believe that the product of the reaction would be 7,7-dicyanocycloheptatriene. The uv and pmr spectra of the major product, 21, however did not resemble the spectra of 7-cyanocycloheptatriene[4] but rather those of a norcaradiene such as 12.[28] Comparison of the spectral data of this new compound with those of 22, confirmed the norcaradiene structure of 21.
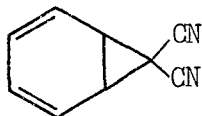
21
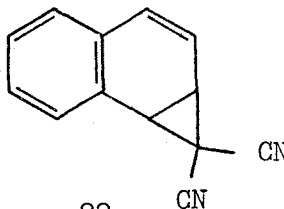
22

A series of related disubstituted cycloheptatrienes was consequently prepared and many of these systems were shown to exist as rapidly equilibrating mixtures of 23 and 24. At the start of this work however, 21 was the only known compound of this type which had the equilibrium position located almost completely on the norcaradiene side. Thermodynamic data for several systems of this type, 23 ⇌ 24, are compiled in Table 1.

23   24
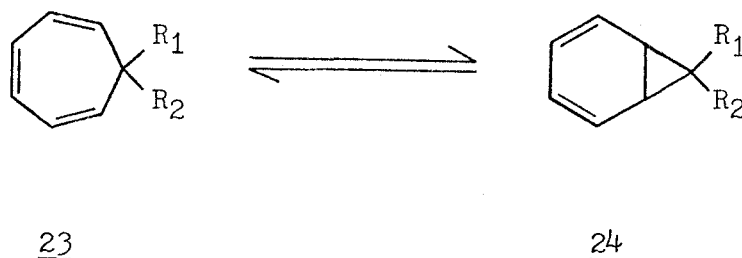
Table 1: Ground state enthalpy and entropy differences,
H^o (24) $-$ H^o (23) and S^o (24) $-$ S^o (23).

R_1	R_2	ΔH^o Kcal/mole	ΔS^o eu	ref.
CN	CN	6[a]		38
CN	COOMe	4[a]		26
CN	Ph	3-5[a]		26
COOMe	Ph	5.4	16.8	19
COOMe	p-MeOPh	2.3	7.4	19
COOMe	p-O_2NPh	3.5	11.0	19
CN	CF_3	0.4	5	26
COOMe	COOMe	0.2	3	39
CF_3	CF_3	b		40
CN	H	b		41
H	H	b		42

a. estimated values

b. only the tautomer 23 is observed

Examination of these results indicate that π-electron deficient

substituents are essential for norcaradiene stabilization. As all

electroneutral monosubstituted cycloheptatrienes, with the possible

exception of 7-cycloheptatrienyl carboxylic acid,[43] are reported to exist

in the monocyclic form,[1,4,5,40] it would seem that two substituents are normally necessary to measurably shift the position of equilibrium between 23/24 towards the norcaradiene side.

Recent reports seem to indicate that the carboxyl group (-COOH) has a greater NCD stabilizing ability than the cyano group.[43,44] However no data about 24, $R_1=R_2=$COOH are available, even though the corresponding diester is known.[39]

Although these NCD stabilizing substituents can be classified as electronwithdrawing, there appears to be no simple correlation between ΔH° and any parameter that measures the electronwithdrawing ability of these substituents. For example, although the cyano and the trifluoro-methyl group have similar σ constants (+0.66 and +0.54),[45] compound 21 is a stable norcaradiene while 7,7-bis(trifluoromethyl)cyclohepta-triene exists almost exclusively in the triene form.[40]

Origin of the C-7 Substituent Effect

Several explanations have been put forward to account for the effect of a C-7 substituent on the position of the CHT/NCD equilibrium. Ciganek[26] suggested that a dipole-dipole interaction between two cyano substituents could possibly increase the bond angle between the two groups and consequently decrease the internal bond angle at C-7 so as to favour the norcaradiene structure. This proposal is in accord with the X-ray structures of 7,7-dicyano-2,5-dimethyl/norcaradiene[34] and malononitrile,[46] for both of these molecules the NC-C-CN angle (115° and 114° respectively) is distorted form the normal sp^3 value of 109°. The stability of norcaradiene 15, with a wide external angle at

C-7, as opposed to the stability of cycloheptatriene 16, also seems
to support Ciganek's argument.

A second explanation that has been suggested[47] is based on the
difference in σ bond energies between carbon atoms of different
hybridization. The C-7 carbon of norcaradiene, which as a cyclopropyl
carbon is approximately sp^2 hybridized, should form stronger bond with a
sp or sp^2 hybridized substituent than would the sp^3 hybridized carbon of
cycloheptatriene. This difference in bond energies would favour the
bicyclic isomer when unsaturated substituents are bound to C-7.

Other factors mentioned in this connection include a possible
intramolecular charge transfer complex of the norcaradiene double bonds
with one of the C-7 groups[26] or the attenuation of the homoaromaticity
of cycloheptatriene by the C-7 substituents.[19] However these rationaliza-
tions are difficult to accommodate with the experimental evidence.[26,19]

A widely accepted explanation of the effect of a C-7 substituent
on the CHT/NCD equilibrium was advanced independently by Hoffmann[48] and
Gunther.[49] They both suggested that there is a donor acceptor inter-
action between the π-molecular orbitals of a C-7 substituent and the
Walsh orbitals[50] of the cyclopropyl ring of a norcaradiene (Figure 1).
When the ligand π-system possesses low lying electron deficient molecu-
lar orbitals, then the electrons of the antisymmetric Walsh orbital, W_3,
of the cyclopropane will delocalize over the adjacent π-system. As a
consequence of this net electron transfer from cyclopropane to the sub-
stituent, the antibonding contribution to the C-1, C-6 bond is weakened.
The net result of this would be to strengthen the C-1, C-6 bond.

Figure 2: Donor acceptor interaction in a substituted norcaradiene.
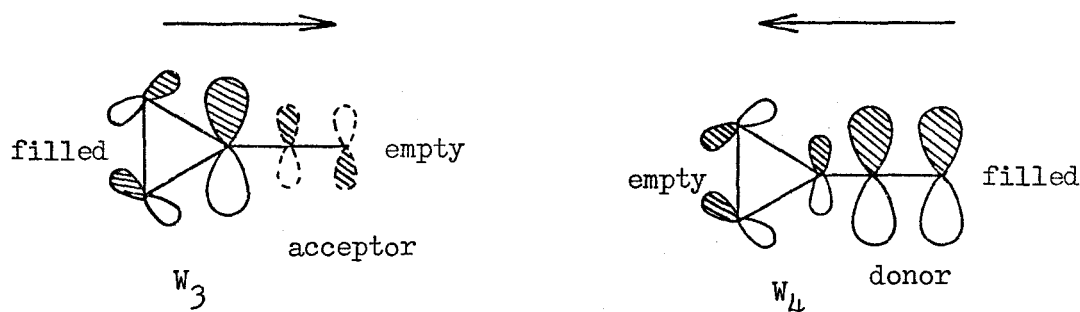
If on the other hand, the C-7 substituent possesses an occupied, high energy molecular orbital of suitable symmetry, this could interact with the unoccupied antibonding orbital, W_4, of the cyclopropane ring. This additional antibonding interaction will weaken the C-1, C-6 bond. Thus, according to this suggestion, electrondonating substituents on C-7 should cause the CHT form to be preferred.

It is interesting to note that, according to this suggestion the thermodynamic stability of the cycloheptatriene tautomer is little affected by substitution at C-7 but rather it is the energy of the norcaradiene form that is dependent on the nature of the C-7 substituent.

This explanation of the effect of a C-7 substituent is consistent with the results of an X-ray determination of the structure of 2,5-di-methyl-7,7-dicyanonorcaradiene. The C-1, C-6 bond was found to be considerably shorter (1.501 Å) than the remaining two cyclopropyl bonds (1.554 and 1.559 Å).[51] It should be pointed out however, that this pattern of bond distortion is not found in all norcaradienes. For

example all three cyclopropane bonds of 7-dimethoxyphosphoryl-7-phenyl-norcaradiene were found to be equal.[52]

On the basis of these considerations, a carbonium ion, which of course is a strongly electronwithdrawing π-substituent, was suggested to be perhaps the most effective norcaradiene stabilizing substituent.[49] Some confirmation of this prediction was derived from the results of solvolytic studies of some 7-cycloheptatrienylcarbinyl esters. Sargent[53] and other workers[54,55] have suggested on the basis of rate and product studies that norcaradienylcarbinyl cations are involved in these reactions, eq.6.

$$\text{(6)}$$
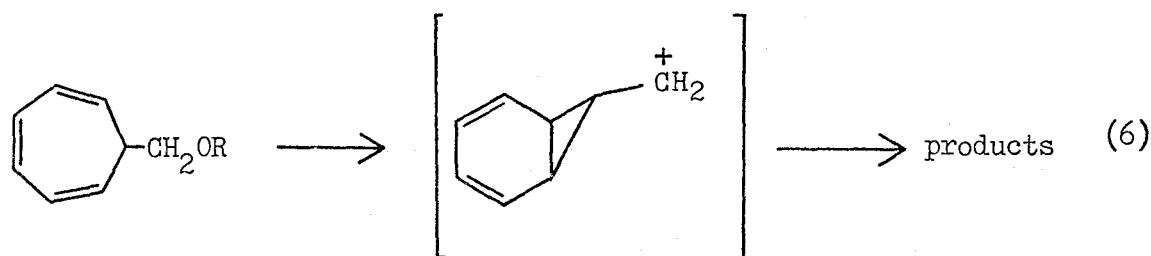
Some recent studies of 7-cyclohepta-1,3,5-trienylcarbinyl cations[56,57] will be discussed in the next chapter.

Theoretical Calculations of Substituent Effects on Related Systems

Semibulvalene, 25 R=H, is one of several compounds with a π-molecular orbital system analogous to that of 2. The energy barrier to the interconversion of 25a and 25b and the effect of a substituent R on the position of this equilibrium have been calculated using MINDO/2[58] and extended Hückel treatments.[44] Both of these approximate methods led

to predictions which were qualitatively the same. Some conclusions

from the calculations of Hoffmann and Stöhrer[44] are presented in Table 2.
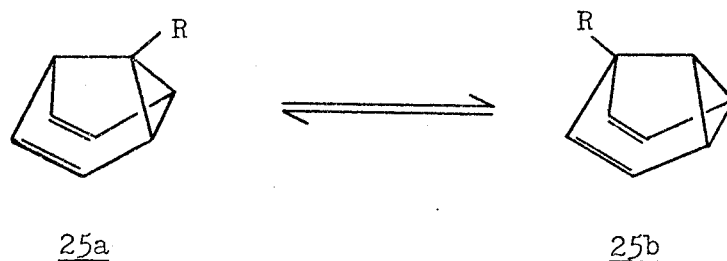
$\underline{25}a$ $\rightleftharpoons$ $\underline{25}b$

Table 2: Calculated effect of some substituents on the equilibrium $\underline{25}a \rightleftharpoons \underline{25}b$.[a]

R	Δn	ΔE Kcal/mole
$-\overset{+}{C}<$	0.058	16.6
CHO	0.030	10.0
COOH	0.024	9.2
CN	0.020	8.5
OH	-0.016	-11.5
F	-0.016	-11.5
NR_2	-0.021	- 2.8

a - results of extended Hückel calculations reported by Hoffmann and Stöhrer[44]

Δn - C-2, C-8 bond order change compared to $\underline{25}a$ R=H

ΔE - difference in energy between $\underline{25}a$ and $\underline{25}b$.

A positive number indicates that $\underline{25}a$ is more stable than $\underline{25}b$.

Two limitations should be kept in mind in considering the data in

Table 2. Firstly, the energies resulting from the extended Hückel

calculations should be regarded as indicators of relative trends and not as

a quantitative guide to stability. Secondly, these calculations can not

account for the effect of a σ electron accepting group, such as CF_3.

From the results in Table 2, the authors have concluded that

π-electrondonors shift the equilibrium between 25a and 25b markedly to-

wards 25b, while π-electron accepting groups shift the equilibrium in

the opposite direction. Recently the equilibrium position between 25a

and 25b has been studied experimentally. Although only a limited range

of substituents R was examined, the results were consistent with the

trends indicated in Table 2.[59]

Criticism of Prevailing Ideas on the Origin of the C-7
Substituent Effect

While the donor acceptor molecular orbital arguments presented

by Hoffmann and Günther have received wide acceptance, there appears to be

an increasing number of systems found that contradict their model. For

example, the observed decrease in ΔH^o caused by both p-nitro and p-methoxy

substituents on the phenyl ring of 7-methoxycarbonyl-7phenylcyclohepta-

triene/norcaradiene (Table 1) cannot be accounted for on this basis.

Moreover, the intriguing recent report by Klärner that the replacement

of the methine hydrogen in 7-methoxycarbonylcycloheptatriene by a methyl

group, an ostensibly electron donating substituent, destabilizes the CHT

form and shifts the equilibrium towards the NCD side, would also seem to

contradict this approach.[60]

The following order of magnitude of NCD stabilizing substituent

effect was recently observed on a 7-substituted-7-methylcycloheptatriene/

norcaradiene: CN > COOMe > COOH.[60] This sequence does not correspond to

the order of energies calculated by MINDO/2 method (Table 2) nor to the

order of their size (COOMe > COOH > CN). Therefore this observation can

not be explained by Hoffmann's concept of a donor acceptor interaction

nor by the Ciganek's suggestion concerned with C-7 bond angles.[26]
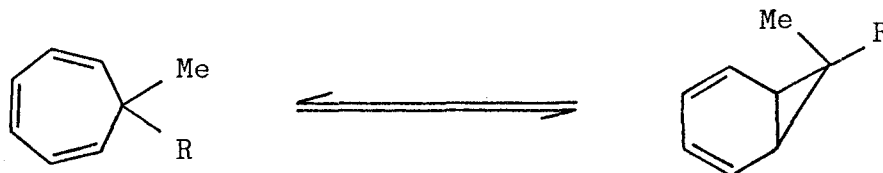
It is obvious from these examples that the effect of substituents on the

position of the cycloheptatriene - norcaradiene equilibrium is by no

means fully understood.

Objective of this Work

As has been pointed out, the equilibrium positions of the CHT/NCD

system do not seem to follow any simple trend. One possible reason for

this could be that two substituent effects are operative. Not only

perhaps is the electronwithdrawing ability of each individual substituent

important but the mutual interaction of these could also be a contribut-

ing factor.

In order to overcome this problem it would be of value to prepare

some mono-C-7 substituted systems in which there was sufficient norcara-

diene form present to enable the equilibrium positions to be determined.

As it has been suggested that a carbonium ion attached to C-7 should be

one of the most powerful norcaradiene stabilizing substituents, attempts

have been made to prepare and study such systems. Chapter II discusses
the results that have been obtained in this area.

A further factor impeding the investigation of the CHT/NCD
valence tautomerism is the great difference in thermodynamic stability
of the parent monocyclic, 1, and bicyclic, 2, forms. As a result, only
the effect of a limited number of electronwithdrawing substituents can be
studied.

To overcome the problems associated with this large energy gap
between 1 and 2, the preparation of some substituted 3,4-homotropilidenes,
28/29, has been attempted. This system can also undergo a facile taut-
omeric rearrangement, however an important feature of this degenerate Cope
rearrangement[20] is that the basic carbon skeleton is regenerated in the
reaction. The tautomers 28 and 29 differ only in the position of the
substituent and thus there is no difference in energy of the two forms
attributable to a change in the basic carbon framework. The synthesis

28   29
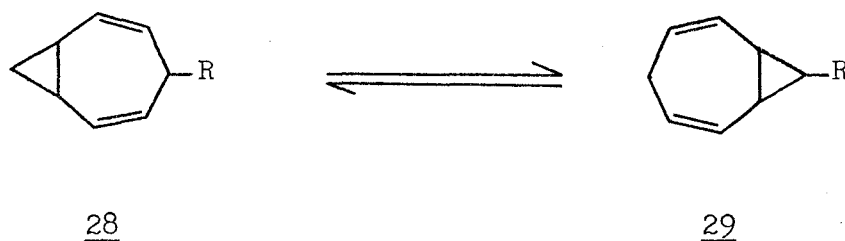
of such systems should enable a much more systematic study of the
substituent effects to be made. The results of this study are presented
in Chapter III.

CHAPTER II

PREPARATION OF SOME 7-NORCARADIENYLCARBINYL CATIONS

As has been discussed earlier in this thesis, it has been suggested that a carbonium ion substituent attached to C-7 of a cycloheptatriene should be one of the most effective groups with which to stabilize the norcaradiene valence tautomer.[44,48] However, in addition to this valence tautomerism, a 7-cycloheptatrienylcarbinyl cation could undergo several other types of reaction. As are depicted below, these include ring expansion to a homotropilium cation,[49] elimination of a carbene to give the tropilium cation[57] or loss of a proton and formation of a heptafulvene.[57]

Scheme 1

22
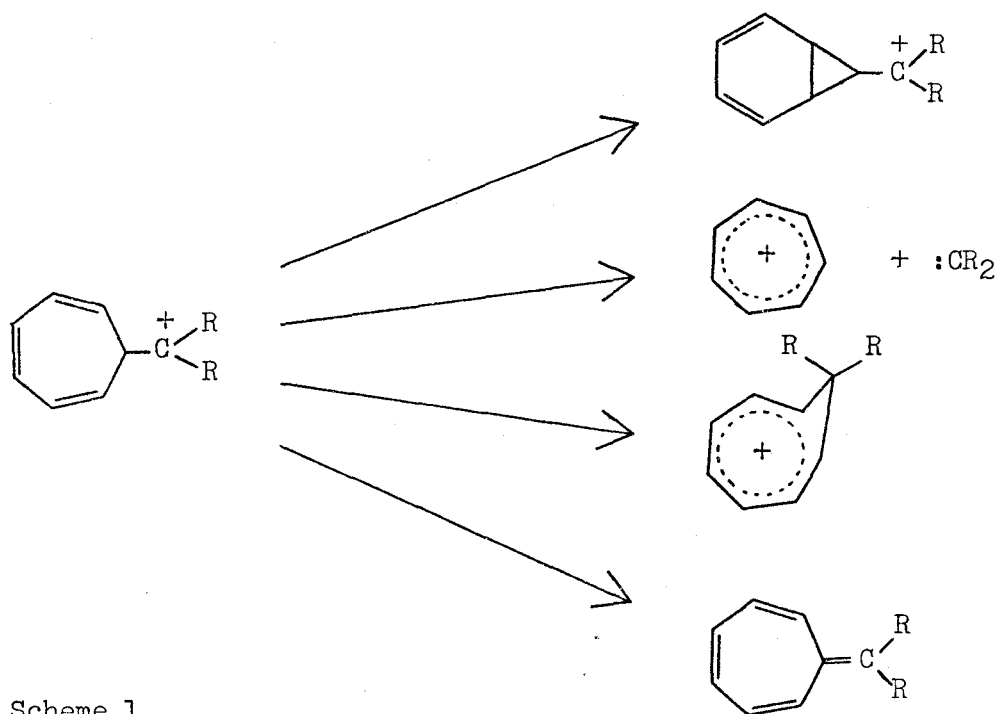
To examine these possibilities and to evaluate the effect of the electronwithdrawing ability of a C-7 substituent on the position of the CHT/NCD equilibrium, the preparation of some carbonium ion substituted cycloheptatrienes was attempted.

The 7-cycloheptatrienyl methyl cation was first invoked by Cope as a possible intermediate in the oxidation of cyclooctatetraene to phenylacetaldehyde, eq.8. Although this report appeared before the existence of the CHT/NCD tautomerism was recognized, the possibility of a norcaradiene intermediate in this reaction was considered.[61]

$$\text{(diagram: cyclooctatetraene} \xrightarrow[\text{Hg(O Ac)}_2]{\text{H}^+} \left[\text{cycloheptatriene–}HC^+\text{–OCH}_3 \right] \longrightarrow \text{phenyl–CH}_2\text{CHO} \quad (8)$$
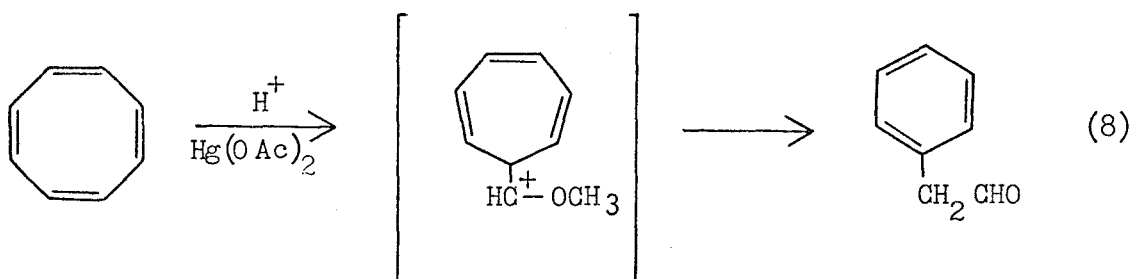
A similar intermediate was postulated by Pettit in the acid catalyzed rearrangement of 7,8-epoxy-1,3,5-cyclooctatriene, eq.9.[62]

$$\text{(diagram: epoxide} \xrightarrow{\text{H}^+} \left[\text{cycloheptatriene–}HC^+OH \right] \longrightarrow \text{phenyl–CH}_2\text{CHO} \quad (9)$$
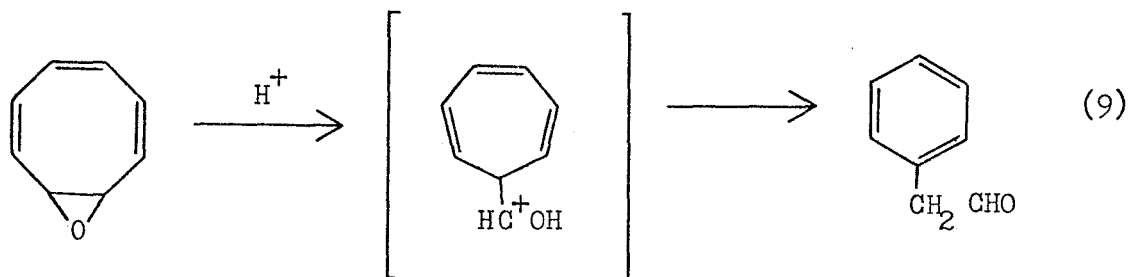
This reaction has been reinvestigated by Huisgen and co-workers, who reported that reaction of cyclooctatetraene epoxide with $HFSO_3$ gave

the 8-hydroxyhomotropilium cation.[63] However they proposed that there was some contribution from a 7-cycloheptatrienyl cation to the overall structure, eq.10.[63]

(10)
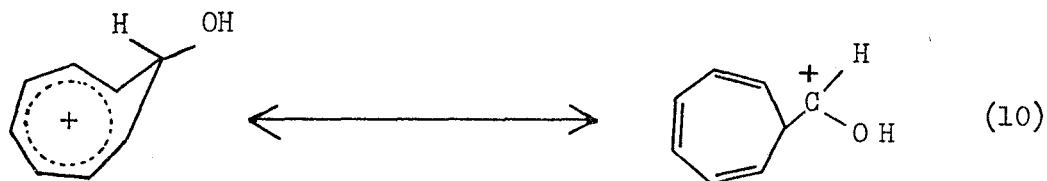
Diazotation of 2(7-cycloheptatrienyl)2-aminodiethylmalonate has been reported to give a substituted heptafulvene as the major product, eq.11.[57] It seems very likely that a cycloheptatrienylmethyl cation is involved in this reaction, however in this case no ring contraction was observed.[57]

(11)
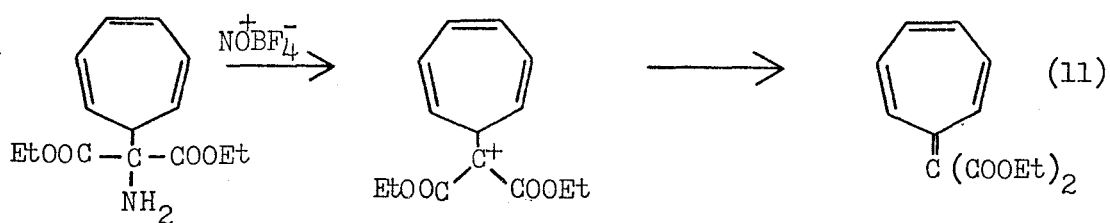
As was mentioned earlier the 7-norcaradienylcarbinyl cation has been suggested to be an intermediate in the sovolysis and rearrangement of several cycloheptatrienylcarbinyl esters.[53,54,55]

Although cycloheptatrienyl- and/or norcaradienylmethyl cations have been invoked as reactive intermediates, no stable carbonium ion of this type had been reported at the start of this project. Simultaneously

with our work, several such systems were investigated by Betz and Daub[56] and their reported results are in some respects similar to those found in this work.

A direct route for the production of stable 7-cycloheptatrienyl-methyl cations appeared to be the elimination of a leaving group X from the compound 30. However previously attempted preparations of 31 or 32 using the reactions indicated in eq.12, were unsuccessful. Polymerization was reported to occur when R=H and aromatic rearrangement products were observed with R=Ph or p-MeOC$_6$H$_4$.[64] Thus the stabilization of the positive charge by two anisyl groups did not prevent a rapid collapse of the seven-membered ring, eq.12.
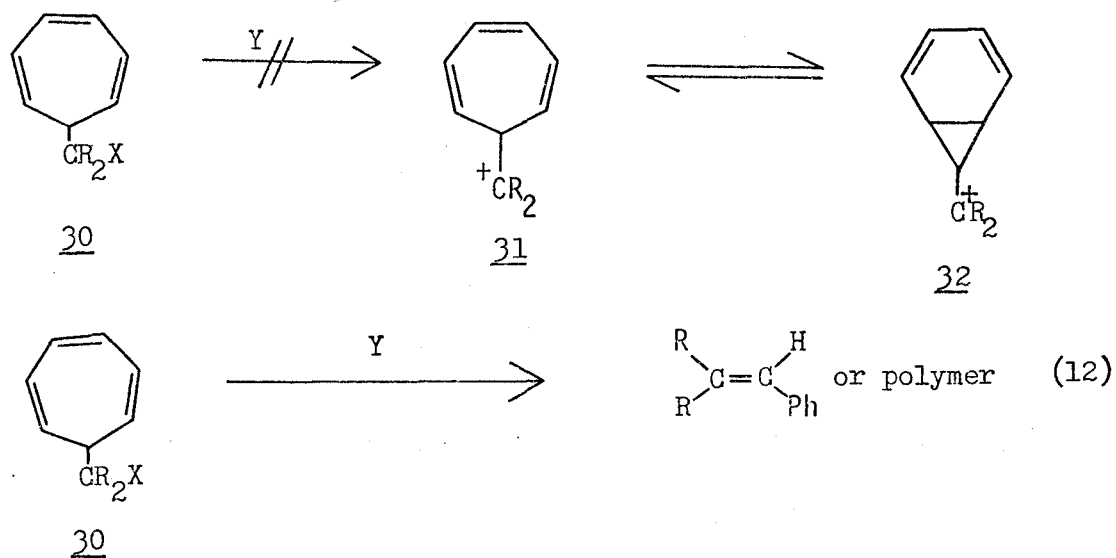
a)	R = H	X = Cl	Y = SbCl$_5$, SbF$_5$, AgBF$_4$
b)	R = H	X = OH	Y = HFSO$_3$
	R = Ph		
	R = pMeO-Ph		

Further stabilization of the positive charge in <u>31/32</u> could possibly be achieved by employing heteroatom groups as the substituents R. For example the oxygen substituted carbonium ion system <u>33/34</u> would be expected to be more stable than <u>31/32</u>.
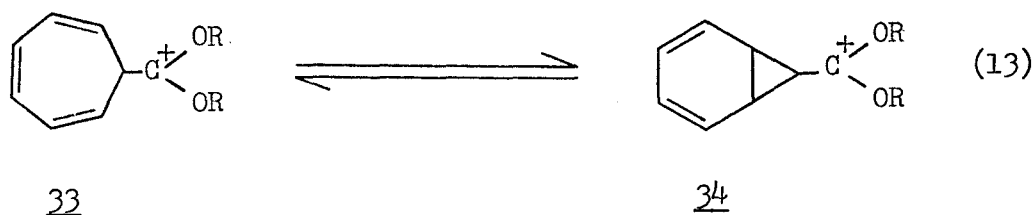
One possible approach to this system appeared to be the protonation of the ester <u>35</u> with a strong acid, eq.14. The attempts to protonate <u>35</u> with HFSO$_3$ led only to the formation of black polymeric material.[64]
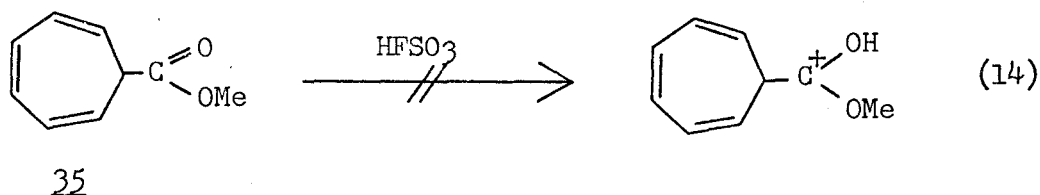
A similar protonation reaction of a 5-acetylcyclopentadiene has been studied and it was found that a strong Brönsted acid protonated not only the oxygen of the carbonyl group but also the carbon of the diene system to give a dication, eq.15.[65] Lewis acids, on the other hand, were found to react only with carbonyl oxygen and no electrophilic attack on the diene moiety was observed.[65] It is known that strong Lewis acids, (L.A.) form stable complexes with a carbonyl group eq.16,[66] and the

$$\text{(15)}$$
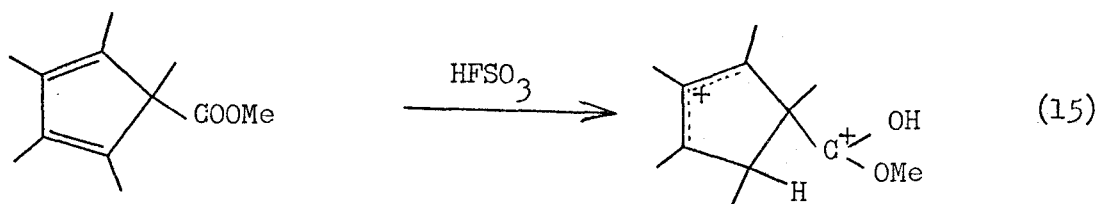
extension of this technique to the preparation of cycloheptatrienyl and norcaradienyl carbonium ions has been attempted.

$$\text{(16)}$$
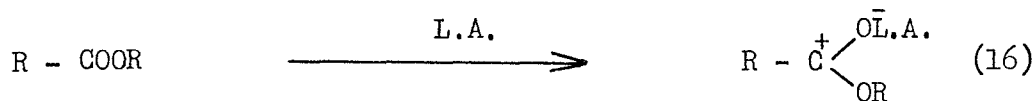
Lewis Acid Complexes of Methyl Cycloheptatrienyl-7-carboxylate

The addition of a slight excess of BCl_3 at -78° to a solution of 35 in CD_2Cl_2, resulted in formation of a 1:1 complex between the ester and the Lewis acid. The low temperature pmr spectrum of this complex was found to be independent of the ratio of the Lewis acid to the ester used provided there was at least one equivalent of the acid present. The complex was stable at -78° and could be reacted with dimethylamine to regenerate 35 in high yield, eq.17.

The pmr spectrum of the complex (Figure 3) was fully consistent with the formation of a zwitterion in which the Lewis acid was complexed to the carbonyl oxygen of the ester. For example, the resonance of the methyl group is deshielded by 0.44 ppm on reaction with BCl_3. Formation
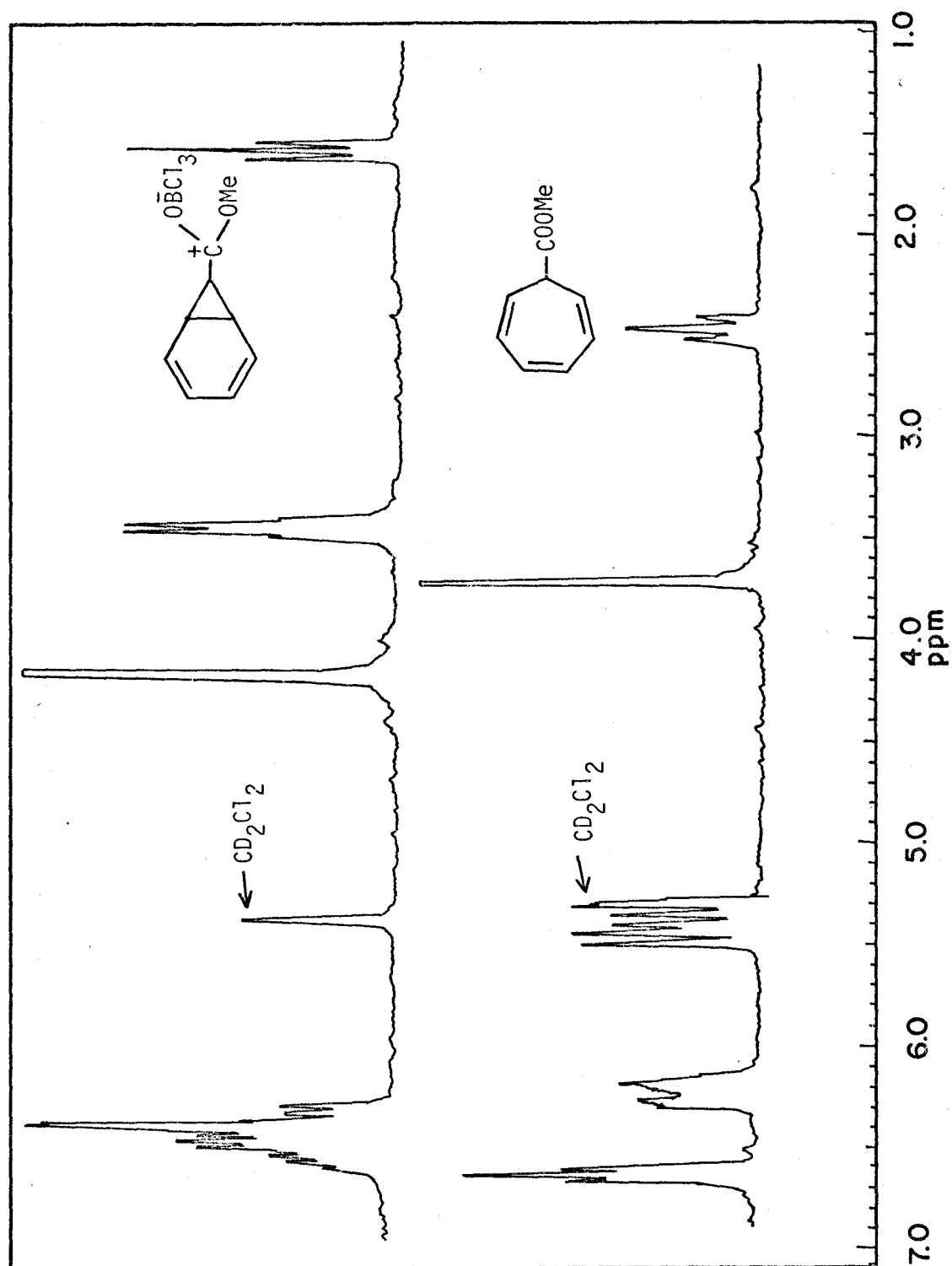
Figure 3: Pmr spectrum of 35 and 37.

$$35 \xrightleftharpoons[\text{Me}_2\text{NH}]{\text{BCl}_3} 36 \qquad (17)$$
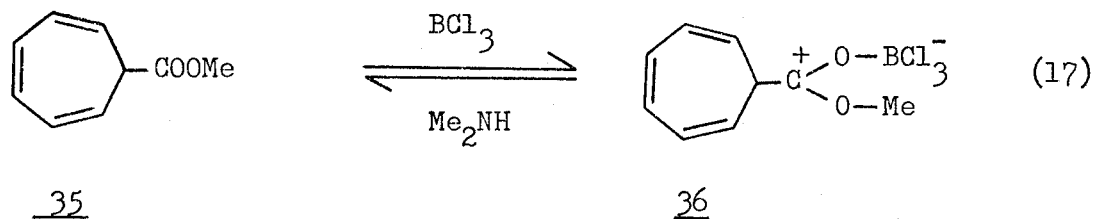
of a similar complex from methylacetate is reported to cause a downfield shift of the methoxy resonance.[67] Moreover, only one pmr signal was observed for the C-1 and C-6 protons, indicating that the complexed molecule at least retained its plane of symmetry on a time averaged basis. The recovery of ester 35 in the reaction of the complex with a stronger Lewis base showed that no extensive and irreversible reorganization of the carbon framework had occurred.

The resonance positions of the ring protons however, had drastically changed on complexation. Thus the signals of the olefinic hydrogens on C-2, C-3, C-4 and C-5 appeared as multiplet centred at δ 6.39. The absorption of the C-7 hydrogen, which in 36 is in a geminal position to the strongly electron withdrawing trivalent carbon substituent, might well have been expected to resonate downfield from the corresponding hydrogen in 35. In fact the resonance of this hydrogen is shifted 0.88 ppm upfield on complexation! An even greater upfield shift, 1.93 ppm, was observed for the C-1, C-6 resonances on complexation of 35. These protons, which in a structure such as 36 are vicinal to

to the carbonium ion group, might also be expected to resonate at a lower field than the related protons of $\underline{35}$.[66] Clearly, structure $\underline{36}$ is not compatible with the pmr spectrum of the complex.

The pmr data however, are compatible with the formation of the norcaradiene complex $\underline{37}$. The upfield shift of C-1, C-6 resonances is then understandable as these protons are attached to cyclopropyl carbons in $\underline{37}$, rather than to olefinic carbons. The resonance of the C-7 hydrogen however seemed to appear at somewhat too high a field even for a structure such as $\underline{37}$ and this factor will be discussed in more detail later. It would appear therefore that the position of the CHT/NCD equilibrium between $\underline{36}$ and $\underline{37}$ must reside very largely on the norcaradiene side, eq.18. Daub and Betz[56] have also prepared a dimethoxycarbonium

$$\underline{36} \qquad\qquad \underline{37} \qquad (18)$$
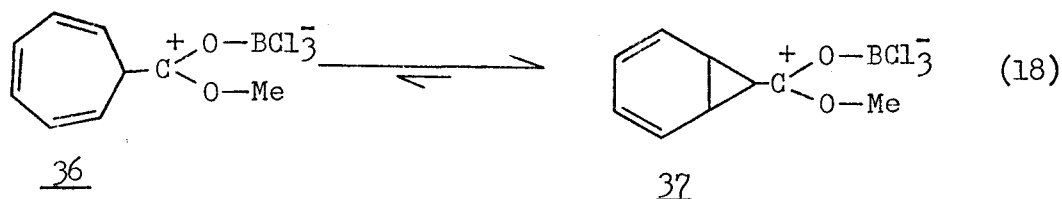
substituted norcaradiene (see p. 44) and from the pmr evidence have concluded, that this compound existed fully in the bicyclic form.

Some additional information about the structure of the complex was derived from its uv spectrum. A methylene chloride solution of the complex at $-50°$ exhibited an absorption band with a $\lambda_{max} = 284$ nm ($\log \varepsilon = 4.3$). This absorption cannot simply be due to the complex of the ester group, as the BCl_3 complex of methylacetate, prepared under the same conditions, had no absorption with an extinction coefficient greater than 100 above 235 nm. Since the uv spectra of cycloheptatrienes

typically exhibit maxima between 257 and 268 nm[1], the longer wavelength

absorption of the complex would seem to indicate that its structure is

different from 36. Stable norcaradienes have been reported to have the

absorption maxima in the region of 268-279 nm.[67,38]

In order to determine how much monocyclic isomer was present in

equilibrium with 37, the low temperature pmr spectrum of the complex was

examined. It has been reported that the CHT-NCD rearrangement is

sufficiently slow at -112° that signals attributable to the separate

isomers can be observed.[35] No additional signals were found in the pmr

spectrum of a $CHClF_2$ solution of 37 recorded at -135°. Although the

resolution of this low temperature was not that good, it is estimated

that 5-10% at 36 could have been observed if it were present.

Formally two different stereoisomers of 37 are possible in which

the C-7 substituent can be either in the exo or endo position, 37a and

37b respectively.
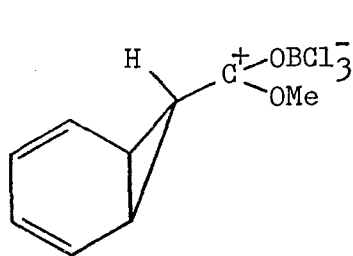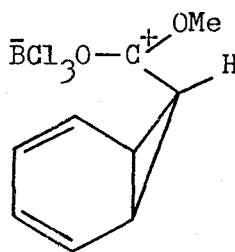
37a   37b

From the nmr spectrum obtained, it is clear that only one of

these isomers is present. Comparison of the magnitude of the coupling

constant between the proton at C-7 and protons at C-1 and C-6 (3.1 Hz)

with that reported for other cyclopropanes, would indicate that the

isomer formed is 37a. Typical values for cyclopropyl coupling constants are J_{trans} = 3.0-6.5 Hz and J_{cis} = 6.0-9.5 Hz.[68] A similar preference for the formation of the exo isomer was reported by Betz and Daub.[56] This behaviour has been attributed to unfavourable secondary orbital interactions in the endo isomer.[69,56]

It is concluded therefore that C-7 substitution of cyclohepta-triene with a carbonium ion resulted in reversal of the normal position of the CHT/NCD equilibrium and converted at least 90% of 36/37 into the bicyclic form. In accord with Hoffmann's[48] and Günther's[49] model and from semiempirical calculations[44], it can be expected that by modification of the electron deficiency of the C-7 carbonium ion substituent, it would be possible to regulate the amount of the bicyclic tautomer in the CHT/NCD mixture.

Modification of the Electronwithdrawing ability of C-7 Substituent

The electronwithdrawing ability of the substituent 38 can be amended by an exchange of one or both groups attached to the trivalent carbon. Three types of such group alterations were examined:

a) exchange of the Lewis acid

b) exchange of one or both oxygen groups for another heteroatom group

c) exchange of one or both oxygen groups for hydrogen atoms or carbon groups.

The results of these experiments are described in the next three sections.

$$- \overset{+}{\underset{}{C}} \overset{O - \bar{L}.A.}{\underset{O - Me}{<}}$$
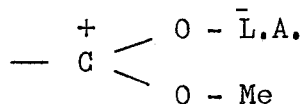
$$\underline{38}$$

Complexation of 35 with Different Lewis Acids

The reaction of a CD_2Cl_2 solution of $\underline{35}$ with BBr_3, eq.19.

resulted in the formation of complex $\underline{39}$. This complex was stable at

$-78°$ and could be reacted with dimethylamine to give back $\underline{35}$. The pmr

spectrum of zwitterion $\underline{39}$ was almost identical with that of $\underline{37}$, Table 3,

suggesting that both these complexes exist predominantly in the norcara-

diene form.

$$\underline{35} \qquad\qquad\qquad \underline{39}$$

(19)
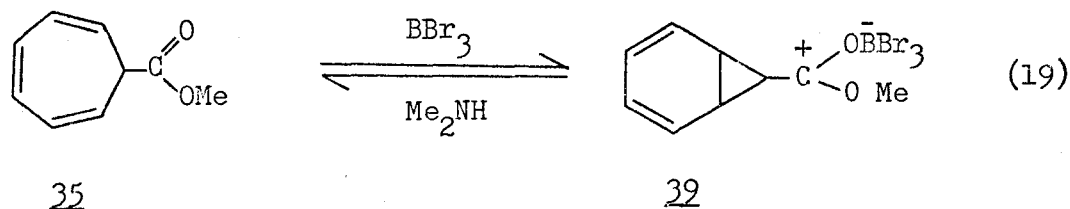
Borontribromide is reported to be the strongest of the common

Lewis acids.[70] Complexation of the oxygen atom of a carbonyl group with

BBr_3 results in the accumulation of a larger fraction of a positive

charge on the carbon atom of the group than is found with similar BCl_3

complexes.[65,66,71] Hoffmann and Stöhrer have suggested that the amount

of the norcaradiene tautomer in a CHT/NCD equilibrium mixture should

increase as the electronwithdrawing power of C-7 substituent is increas-

ed.[44,48] If this were so then the BBr_3 complex of $\underline{35}$ would be expected

to contain a greater percentage of the bicyclic tautomer than the corresponding BCl_3 complex. As the equilibrium composition of the BCl_3 and BBr_3 complexes of 35 would appear to be the same this could either mean that both complexes exist almost completely in the NCD form or that the position of the CHT/NCD equilibrium is independent of the electron-withdrawing power of a C-7 substituent. As it will be shown later the first possibility is correct.

Table 3: Proton chemical shifts of 35 and its complexes

Lewis acid	Lewis acid to ester ratio	Temp °C	Proton chemical shifts, δ [a]		
			H-7	H-1/H-6	methyl
none[b]	0.0	-40	2.48	5.34	3.72
BCl_3[b]	1.3	-40	1.60	3.41	4.14
BBr_3[b]	1.2	-40	1.65	3.48	4.14
$AlCl_3$[b]	1.3	37	2.26	4.90	3.91
$AlCl_3$	10.0	37	1.92	4.16	4.07
$SnCl_4$[c]	1.2	37	2.53	5.32	3.82
$SnCl_4$[c]	1.2	-20	2.21	4.60	4.00
$SnCl_4$[d]	1.3	-75	1.71	3.56	3.95

[a] $CHCl_3$ used as internal standard (δ 7.3)

[b] CD_2Cl_2 used as the solvent

[c] $CDCl_3$ used as the solvent

[d] $CHClF_2$ used as the solvent

The reaction of 35 with other Lewis acids was also examined however, the low solubility of the so formed complexes generally hindered their study. The products formed on reaction of 35 with $SbCl_5$, SbF_5, $TiCl_4$ and BF_3 were insufficiently soluble in such solvents as $CDCl_3$, CD_2Cl_2 and SO_2, or mixtures of these solvents, to obtain satisfactory pmr spectra. The results obtained with 35 and Al_2Cl_6 were not very reproducible and seemed to depend on an L.A./ester ratio. This again probably stems from the very low solubility of Al_2Cl_6 in the solvents listed above and resulting incomplete reaction with the ester.

The complex of 35 with $SnCl_4$, 40, had a low temperature pmr spectrum which was very similar to that of 37. However, at room temperature the spectrum resembled that of 35, Table 3. It would appear that dissociation of a complex such as 40 is occurring at higher temperatures.[72]
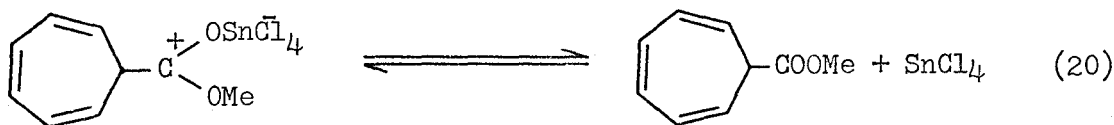
40

Replacement of the Methoxy Group with a Nitrogen Function

N,N-Dimethyl(7-cycloheptatrienyl)carboxamide, 41, was reacted with BCl_3 in CD_2Cl_2 solution. The pmr spectrum of the product was consistent with complexation of the carbonyl oxygen with the Lewis acid,[70] Figure 4.
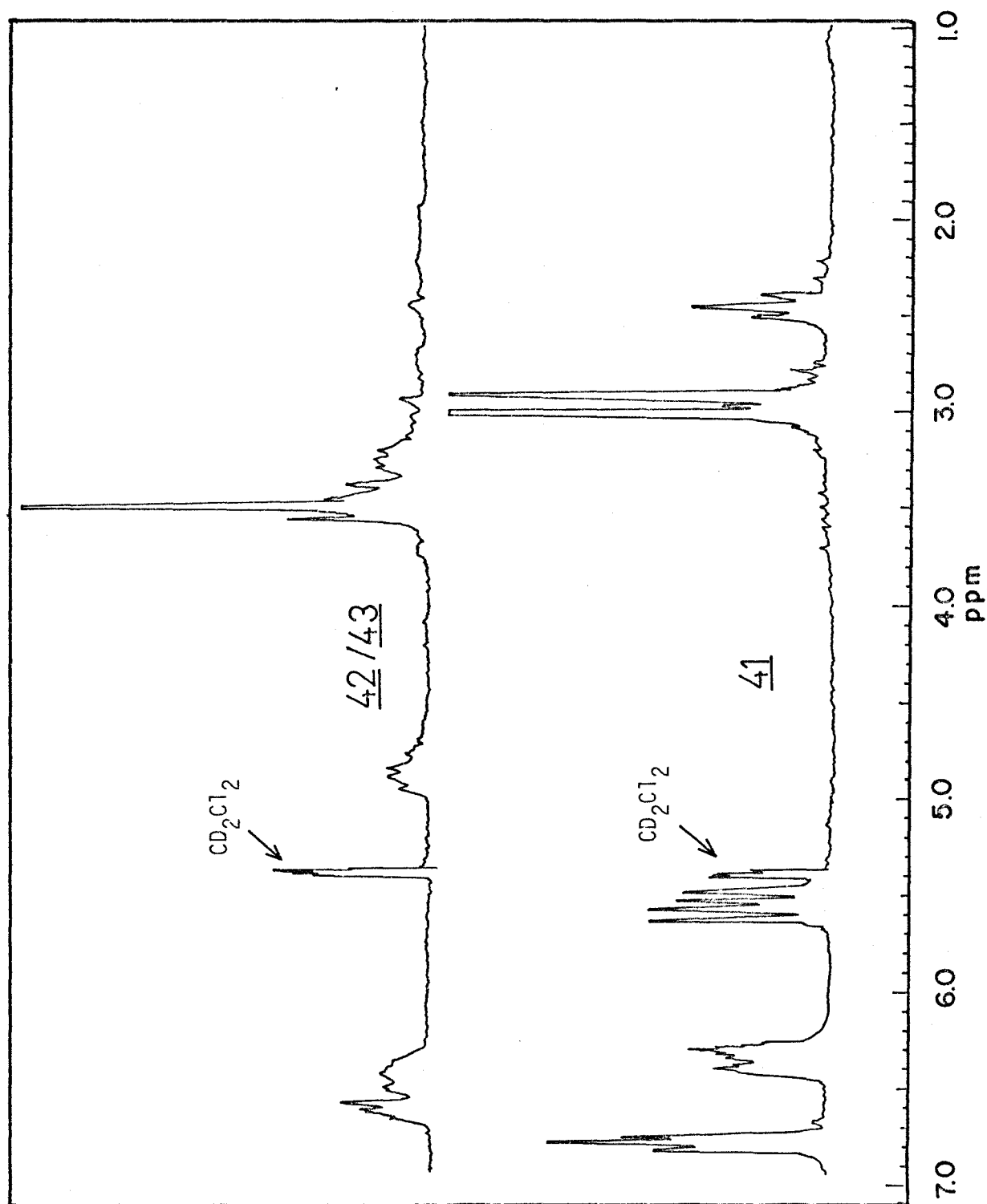
Figure 4: Pmr spectrum of 41 and 42/43.

However, the positions of the ring proton resonances were now inter-
mediate between those observed for 35 and complexes 37 and 39. Thus it
appeared that this product was a mixture containing a considerable
amount of both 42 and 43, interconverting sufficiently rapidly at $-40°$
for their pmr spectra to be averaged. Reaction of the complex with
dimethylamine or water regenerated 41 in high yield, eq.21.

(21)
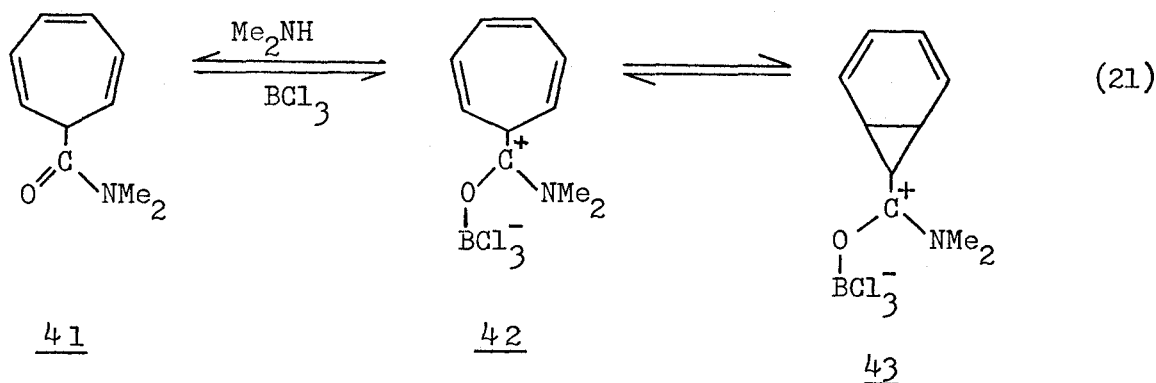
As the dimethylamino group is known to be more effective at
stabilizing a positive charge than is a methoxy group,[73] it appears that
the position of the CHT/NCD equilibrium of these zwitterion is dependent
on the electrondeficiency of the C-7 substituent. The more electron-
withdrawing is the substituent, the greater is the amount of norcaradiene
in the mixture of tautomers. The observation that the BCl_3 complex 37
and its BBr_3 analogue 39 have the same tautomeric composition despite
the   different withdrawing powers of their respective C-7 substituents
implies that they both exist almost entirely in the norcaradiene form.

In order to evaluate the position of a CHT/NCD equilibrium such as
42/43 it is necessary to know the resonance positions of some of the

protons in the pmr spectra of the individual isomers. One way this can
be achieved is to record the pmr spectra at a sufficiently low tempera-
ture where the interconversion becomes slow in the pmr time scale.[38]
In the case at hand, the poor solubility of the BCl_3 complex of 41, pre-
vented measurement of pmr data at sufficiently low temperatures to stop
interconversion of 42 and 43. It was therefore necessary to estimate
the expected chemical shifts of various protons in 42 and 43 using suit-
able model compounds.

The BCl_3 complex of 3-methoxycarbonyl-1,4-cycloheptadiene, 45,
was chosen as a model for 42. As the synthesis of the neutral precursor
of this complex, 44, has not been reported previously, a new procedure
for preparation of 3-substituted-1,4-cycloheptadienes was developed and
is described at the end of this chapter.

$$\text{(22)}$$
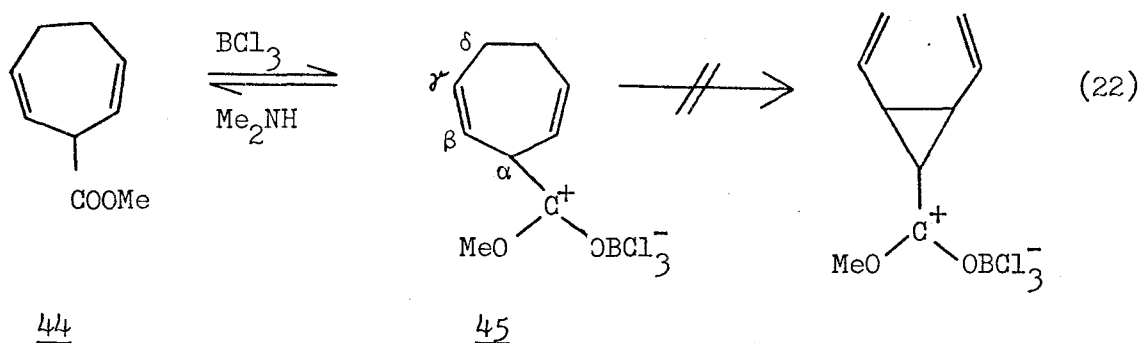
The complex 45 was prepared by reaction of 44 with a slight excess
of BCl_3, eq.22, in a CD_2Cl_2 solution. The complex was stable at -78°

and its pmr parameters, recorded at this temperature, are presented in Table 4. From the pmr data it is clear that $\underline{45}$ has the structure indicated. For example, the low field absorptions of the α and β protons are an unambiguous evidence that the rearrangement of $\underline{45}$ to 1,2-divinyl-cyclopropane, which would parallel the isomerization of $\underline{36}$ to $\underline{37}$, did not occur.[73] The reaction of $\underline{45}$ with dimethylamine at low temperature produced a high yield of 2-methoxycarbonyl-1,3-cycloheptadiene, rather than the starting ester, $\underline{44}$. However, as $\underline{44}$ was found to undergo a facile rearrangement to give the conjugated diene, this result is not surprising and does not cast any doubt on the structure of $\underline{45}$. Heated to 0°, $\underline{45}$ rearranged to an unidentified product.

Table 4:   Proton chemical shifts of some BCl$_3$ complexes and their

neutral precursors.[a]

Compound	Proton chemical shifts[b,c] (δ)				
	H$_\alpha$	H$_\beta$	H$_\gamma$	H$_\delta$	CH$_3$
<u>35</u>	2.48	5.34	6.24	6.63	3.72
<u>37</u>	1.60	3.45	6.14-6.54		4.14
<u>41</u>	2.40	5.46	6.25	6.68	2.85,2.95
<u>42+43</u>	3.20	4.81	6.35	6.52	3.43
<u>44</u>	4.23	5.78	5.78	2.25	3.69
<u>45</u>	5.31	5.58	6.13	2.38	4.28

a)   in CD$_2$Cl$_2$ at -40°C

b)   the subscript indicates the position of the proton

with regard to the ester group

c)   CHCl$_3$ (δ7.30) used as an internal standard

A striking feature of the pmr spectrum of <u>35</u> is the unexpectedly high field position of the C-7 proton (H$_\alpha$) resonance. This resonance appears at δ 2.48, while that of H$_\alpha$ of the model compound <u>44</u> occurs at δ 4.23 (Table 4). The reasons for this behaviour will be discussed in more detail in Chapter IV. At this point however, it can be concluded that since <u>44</u> does not appear to be a good model for <u>35</u>, probably the complex <u>45</u> cannot be considered to be a good model for the cycloheptatriene complexes.

It was therefore necessary to estimate what the proton resonance positions of the fully cycloheptatriene complex 42 and norcaradiene complex 43 would be. To this end it was assumed that the deshielding of the C-1, C-6 and C-7 proton resonances, accompanying the transformation of 41 to 42, would be the same as those observed for the corresponding protons of 44 as it was transformed into 45. This of course assumes that the deshielding expected in the amide and ester cases would be much the same, and based on the similarity of the downfield shifts of the appropriate methyl resonances of protonated methylacetate and N,N-dimethylacetamide this would appear to be a reasonable assumption.[75,76] As a model for the chemical shifts of the norcaradiene complex, 43, the chemical shifts of 37 were used and it was again assumed that the cyclopropyl protons of 43 would resonate at nearly the same position as those of 37.

The amount of the norcaradiene form present can then be calculated using the following formula:[19]

$$P_N = (\delta_C - \delta) / (\delta_C - \delta_N) \times 100\%$$

where δ is the observed chemical shift of a proton, δ_N and δ_C are the chemical shifts of the same proton in the individual cycloheptatriene and norcaradiene isomers. As the β-proton resonances appear at considerably different positions in cycloheptatriene and norcaradiene, these resonances appear to be especially suitable for this type of calculation. Using H_β : $P_N = (5.26 - 4.81) / (5.26 - 3.45) \times 100 = 25\%$. That is, the equilibrium concentration of norcaradiene tautomer 43 is 25%.

Replacement of One Oxygen Group with a Hydrogen Atom

Huisgen[77] has reported that cyclooctatetraene epoxide, 46, can

be protonated with FSO_3H to give the 8-hydroxyhomotropylium cation. The

epoxide, 46, was reacted with various Lewis acids, in order to see if a

comparable homotropylium cation or a 7-norcaradienylmethyl cation, 47,

could be prepared.
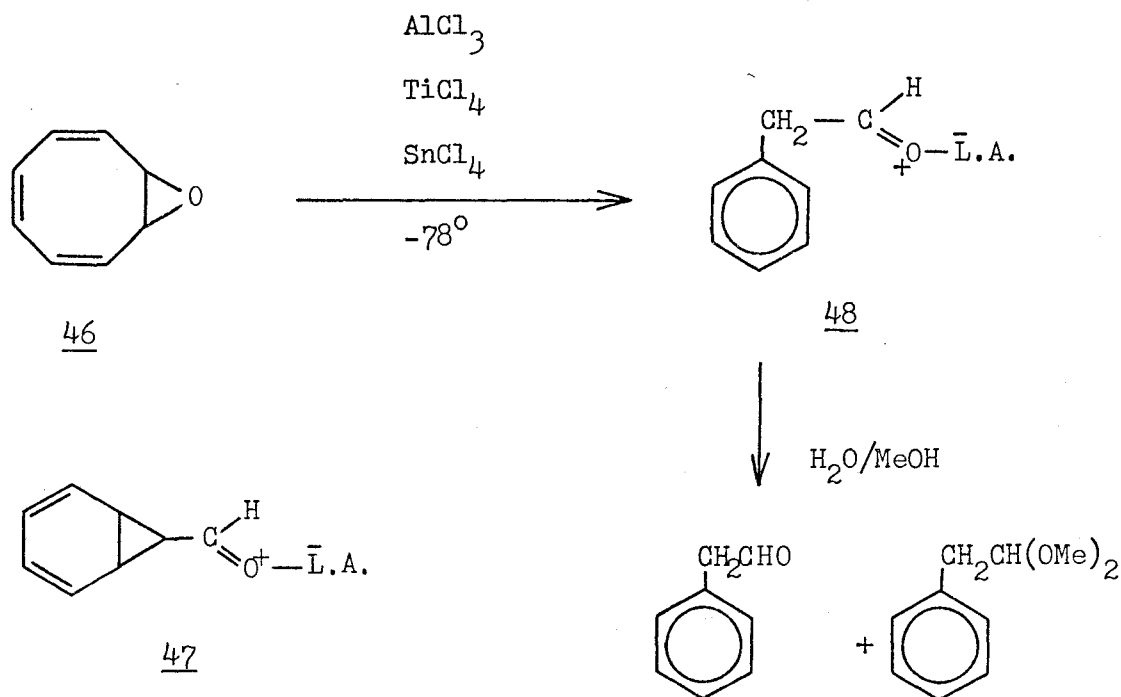
Treatment of $CDCl_3$ solution of 46 at -78° with a series of Lewis

acids gave in each case only benzenoid products. No indication of the

presence of a homotropylium cation, norcaradiene 47, or its cyclohepta-

triene tautomer was found when the pmr spectra were recorded at -75°,

shortly after mixing 46 with the Lewis acids. The spectra obtained under

these conditions resembled the spectrum of the complex 48 prepared by

reacting the Lewis acids with phenylacetaldehyde.

Reaction of an Al_2Cl_6 complex of 46 with a mixture of water, methanol and sodium bicarbonate, resulted in recovery of phenylacetaldehyde, the dimethylacetal of this aldehyde and some apparently polymeric material. The latter material was involatile and exhibited a broad resonance in the aromatic region of its pmr spectrum. The volatile products were separated and identified by comparing their pmr and ir spectra and gc retention times with those of authentic materials.[78] The reasons for the difference in behaviour of 46 on protonation and on complexation with Lewis acids are not clear at this time.

7-Formylcycloheptatriene, 49, became available in 1971 when Grigg[79] reported that it could be prepared by a rhodium catalyzed rearrangement of 46. All attempts to prepare 47 by reaction of 49 with a series of Lewis acids were unsuccessful. Once again, the Lewis acid complex of phenylacetaldehyde was the only product detected by pmr, even when the aldehyde and the Lewis acid were reacted and the pmr spectrum recorded at $-100°$.
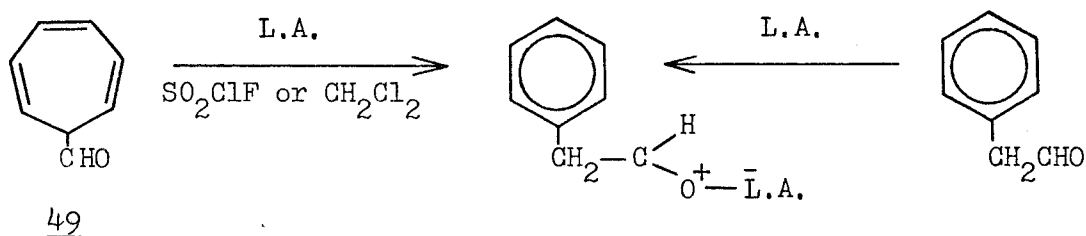
L.A. = BCl_3, $TiCl_4$, $SnCl_4$

Conclusions from the Experiments in which the Electronwithdrawing

Power of the C-7 Substituent was Modified

In this work it has been shown that the position of the CHT/NCD

equilibrium in 7-cycloheptatrienylmethylcations which have two C-8 oxygen

substituents, resides almost entirely on the NCD side. Another compound

of this type, 50, was reported by Betz and Daub.[56] Based on the pmr

spectrum of this system, which incidentally is very similar to that of

37 and 39, the authors have also concluded that this cation exists com-

pletely in the norcaradiene form.
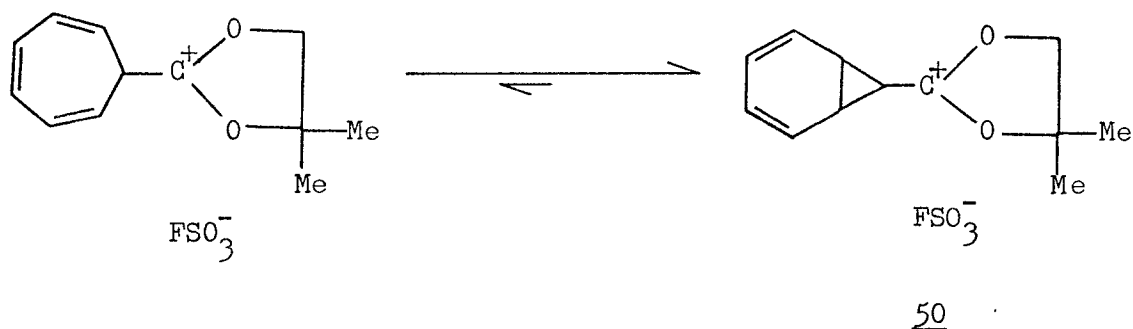
Zwitterions 37, 39 and the cation 50 are the first examples of

monosubstituted norcaradienes and their existence demonstrates that

norcaradiene can be made stable by attachment of a single substituent at

C-7.

When the positive centre at C-7 of these systems is stabilized

with both an oxygen and a nitrogen substituent, both tautomers, cyclo-

heptatriene and norcaradiene, are present in substantial amounts. Thus

in this work 42 and 43 were shown to exist in a ratio 3:1. A series of

similar cations has been prepared by Betz and Daub[56] and with all these systems the tautomeric composition was found to be close to that of 42/43. The same authors have also reported the prepartion of one 7-cycloheptatrienylcarbonium ion, which had two nitrogen containing substituents at C-8, 51. From the pmr data of this cation they concluded that it existed completely in the monocyclic form 51.
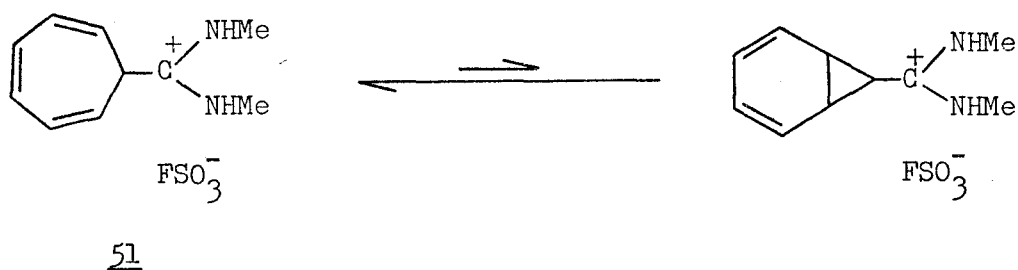
The electronwithdrawing ability of these cationic substituents would be expected to diminish in the following order:
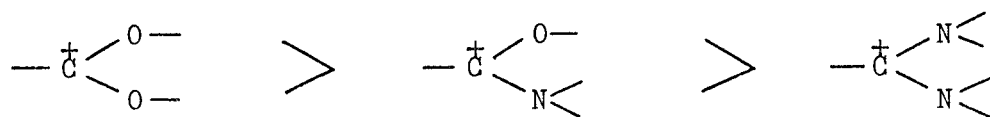
This same order was observed for the norcaradiene stabilizing ability of these substituents. It would thus seem that the amount of norcaradiene tautomer present in   equilibrium with the norcaradiene   increases with the rising electronwithdrawing ability of the C-8 carbon.

7-formylcycloheptatriene/norcaradiene

Although the attempted complexation of 49 with Lewis acids resulted only in formation of benzenoid materials, the neutral aldehyde itself, was found to be of interest. In the original paper[79], this compound was assumed to have the monocyclic structure. However the pmr spectrum of 46, Fig. 3, would seem to indicate that it exists as a rapidly equilibrating mixture containing a detectable amount of the bicyclic tautomer. For example, the overlap of the pmr resonances of the C-2/C-5 and C-3/C-4 protons is a common feature of norcaradienes or tautomeric mixtures of norcaradienes and cycloheptatrienes.[19] The higher field position of the resonance of the C-1/C-6 protons of 49, as compared with that of corresponding 7-methoxycarbonylcycloheptatriene protons, also indicates the presence of some of the norcaradiene tautomer. Taking the C-1/C-6 proton chemical shifts of 35 as a model for those of 49, and if the corresponding resonances of 52[43] are used as model for those of 7-formylnorcaradiene, the amount of the NCD isomer in the equilibrating mixture could be estimated to be 7%.

$$P_N = (5.43 - 5.25) / (5.43 - 2.63) \times 100 = 7\%$$

According to the calculations of Stöhrer[44] (Table 2) the formyl group should be the best uncharged norcaradiene stabilizing substituent and a carboxylic acid function the next best norcaradiene stabilizing group. It is interesting that, as has been shown very recently, some 3% of the norcaradiene form, 52, exists in an equilibrium with 7-cycloheptatrienylcarboxylic acid.[43]
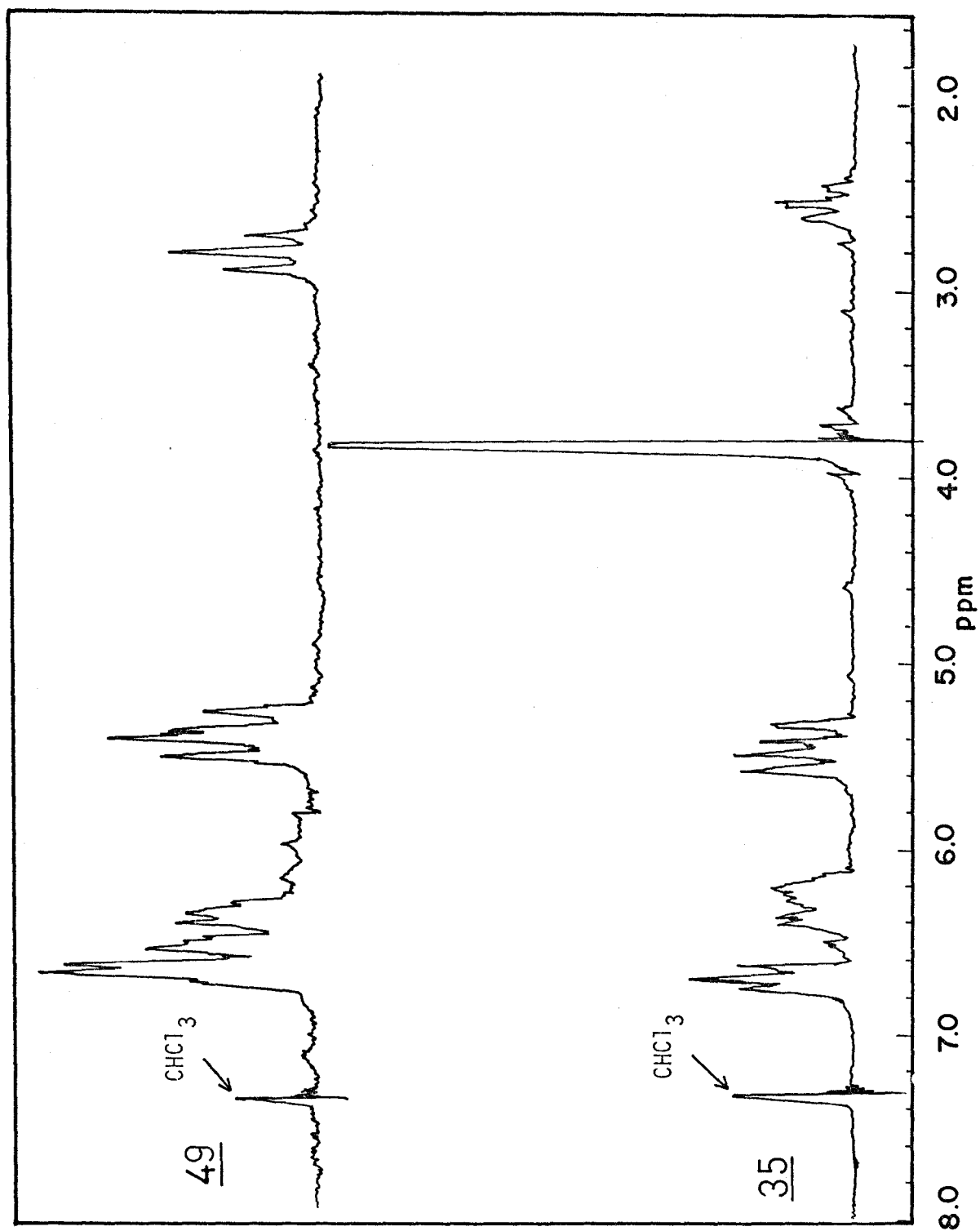
Figure 5 : Pms spectrum of 35 and 49.

δ 6.2-6.7

δ 5.25

δ 6.2

49

δ 6.6

δ 5.43

35

δ 2.63

52
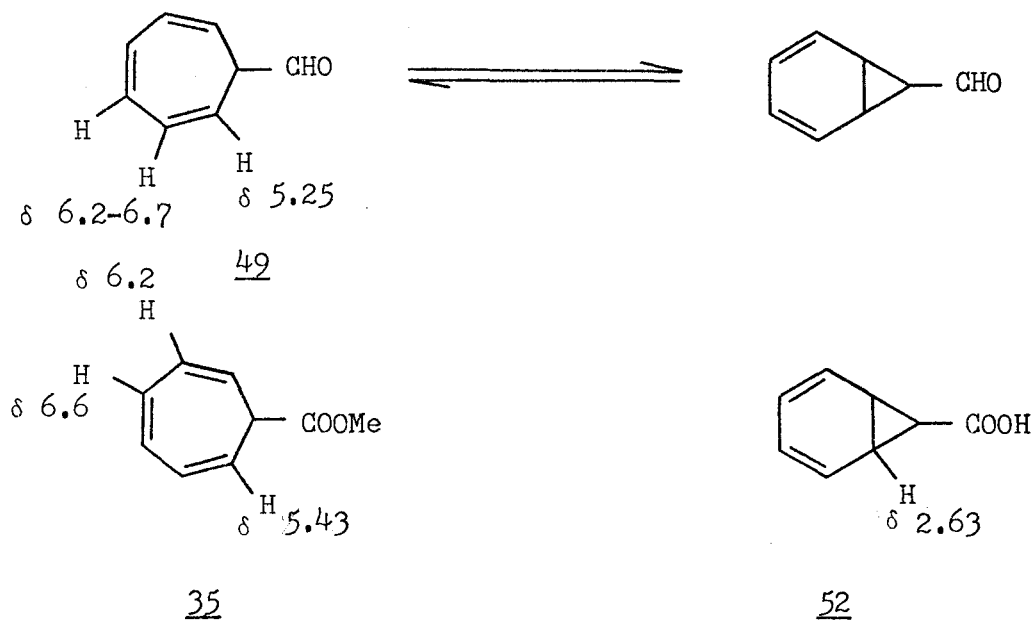
The Structure of Norcaradienes 37 and 39

Examination of the pmr spectra of the complexes 37 and 39 revealed that the positions of the resonances attributable to the three cyclopropyl protons were seemingly anomalous. For example, the C-7 proton signal of both 37 and 39 occurred at about δ 1.6. This resonance is found at much higher field than would be expected for the resonance of an α proton of a cyclopropylcarbinyl cation (typically δ 2.8 – 3.8).[80,81] Moreover resonances of β protons of cyclopropylmethyl cations either occur at higher field than that of the α proton (δ 1.8 – 3.0),[80,81] or the resonances of both the α and β protons overlap and appear as one multiplet. In the norcaradiene complexes 37 and 39 however, this order is reversed and the α proton signals appear as much as 1.8 ppm upfield from those of β protons.

δ 1.8-3.0

δ 2.8-3.8

δ 1.6

δ 3.4
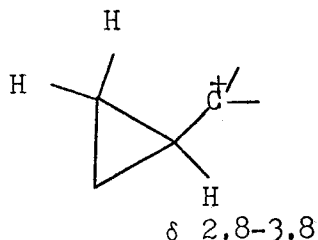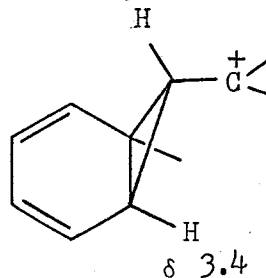
<u>37</u> or <u>39</u>

The unusual chemical shifts found in the complexes <u>37</u> and <u>39</u> could either be due to the norcaradiene structure of these compounds or be a common feature of cyclopropylcarbinyl cations substituted with -OMe and -O$\bar{B}$X$_3$ groups. In order to distinguish between these two possibilities, the pmr spectra of some BCl$_3$ complexes of some cyclopropylcarboxylic esters were investigated.

The model cyclopropyl zwitterions were prepared from methyl cyclopropylcarboxylate, <u>53</u>, and 9-methoxycarbonylbicyclo[6.10]nona-triene, <u>54</u>. Ester <u>53</u> was prepared from the commercially available acid and the bicyclic compound <u>54</u> was obtained by transesterification of the known corresponding ethyl ester.[82]

Reaction of the cyclopropyl compound <u>53</u> in CD$_2$Cl$_2$ with BCl$_3$ resulted in the formation of the zwitterion <u>55</u>, eq. 23. The pmr spectrum of <u>55</u> (Table 5) consisted of a singlet at δ 4.10, multiplet at δ 1.65 and a further multiplet at δ 2.76 in a ratio 3 : 4 : 1. This

COOMe

_53_

COOMe
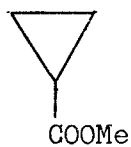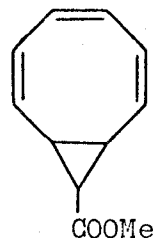
_54_

spectrum is comparable to that of similar cations in which the positive

charge was induced by protonation of the carbonyl oxygen.[81]

$$\underset{\text{COOMe}}{\overset{\text{H}}{\triangleright\!\!\!<}} \quad \underset{\text{Me}_2\text{NH}}{\overset{\text{BCl}_3}{\rightleftharpoons}} \quad \underset{\overset{|}{\text{O}}\,-\,\bar{\text{BCl}}_3}{\overset{\text{H}}{\underset{\overset{+}{\text{C}}-\,\text{OMe}}{\triangleright\!\!\!<}}} \qquad (23)$$

_53_   _55_
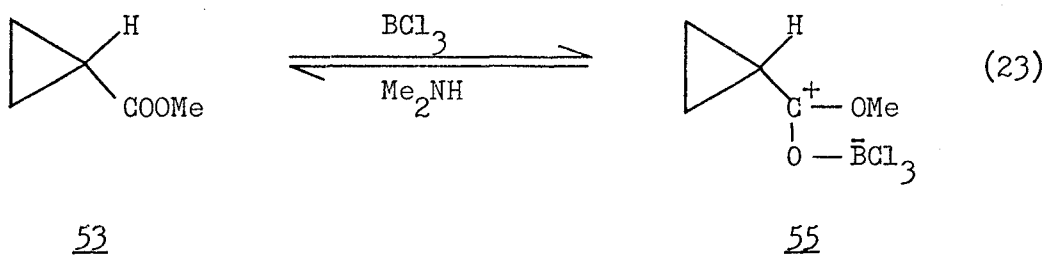
While the chemical shifts of cyclopropyl protons of _55_ are quite

different from those of _37_, it could be argued that _55_ is not a good

model for one of these norcaradiene complexes. For example the cyclo-

propyl ring in _55_ does not have any vinyl substituents and these would be

expected to deshield the β protons. However the cyclopropyl group of
the zwitterion 56 bears two such vinyl substituents and this complex
could therefore be considered to be a fairly good model for the norcara-
dienes 37 and 39. Complex 56 was prepared by reaction of 54 in
CD_2Cl_2 with BCl_3 at low temperatures eq.24. The complex was found to be
stable below 0°, and could be reacted with dimethylamine to recover 54 in
a high yield.
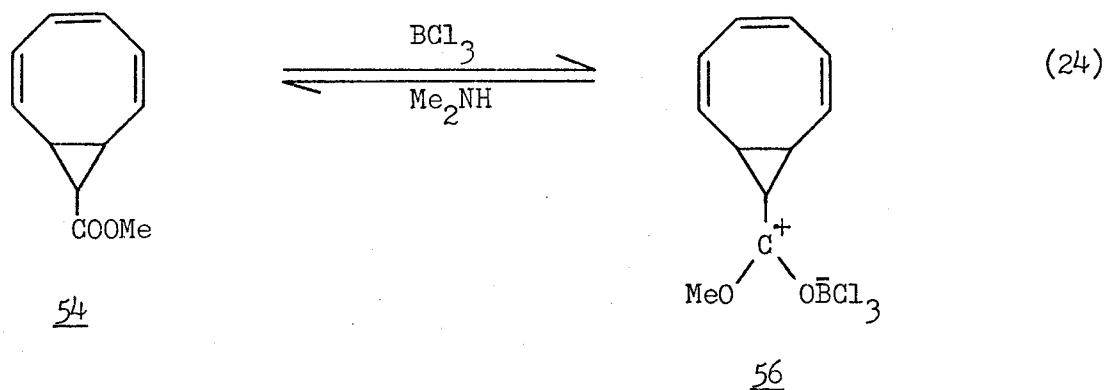
In the pmr spectra of 56, recorded at −40° (Table 5), the reson-
ances of the cyclopropyl protons appeared as one overlapping multiplet
between δ 2.56 and 2.83 and the individual α and β proton resonances
could not be assigned. Although it is apparent that the resonances of the
β protons of 56 are deshielded as compared to that of 55, they are still
within the range of values expected for a cyclopropylcarbinyl cation.[81]

Thus in both model compounds 55 and 56, the chemical shifts of
the cyclopropyl protons do not seem to be different from that which would
be expected if the positive charge had been induced by protonation. In

other words, the seemingly anomalous resonance position of the cyclo-propyl protons of 37 and 39 must be a function of the norcaradiene structure itself and not of the Lewis acid moiety.

Table 5: Proton chemical shifts of cyclopropyl zwitterions

Compound	Proton chemical shift (δ)[a]			
	H_α	H_β	Vinyl Hydrogens	CH_3
37	1.60	3.41	6.14-6.54	4.14
55	2.76	1.65		4.10
56	2.56	- 2.83	5.84-6.08	4.12

a. in $CDCl_3$ at $-40°C$, $CHCl_3$ used as internal standard

It could be suggested, that the unexpected resonance positions of the cyclopropyl protons of 37 could be accounted for on the basis of the diamagnetic anistropy of the double bonds in the six-membered ring. Since the norcaradiene ring system is rigid and its geometry is fairly well established,[51,52] the magnitude of such an effect can be calculated. However the shielding effect of the double bonds of norcaradienes on the cyclopropyl protons, estimated using the tabulated results of Pople,[83] was found to be very small. Thus the endo C-7 proton would be expected to experience a shielding of 0.1 ppm while the C-1 and C-6 protons were predicted to be deshielded by the same amount, Table 6. Tillieu[84] has reported a different calculation of the diamagnetic anisotropy of a double bond and using his results the effect on the cyclopropyl atoms was again found to be very small.

An alternative possibility is that norcaradienes _37_ and _39_ are aromatic. If this were the case then in a magnetic field, a ring current would be induced in the six-membered ring. This situation would result in a shielding of the protons above and below the centre of the ring and deshielding of the protons residing in the periphery of the ring, Figure 6.

Figure 6: Ring current in norcaradiene
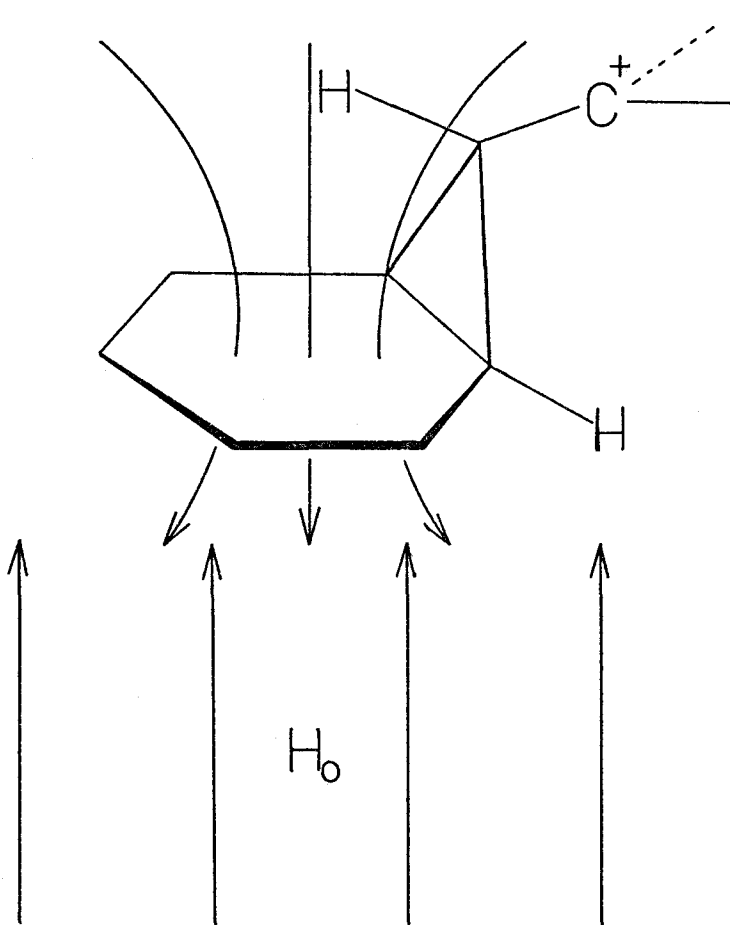
The effect of the induced diamagnetic ring current of a benzene on protons located in its vicinity has been estimated using theoretical[85] and semiempirical[86] calculations. The latter methods appear to give

better results for the protons located in close proximity to a benzene ring[86] and the tabulated results obtained by this method have been used in this work. Table 6 presents the experimentally measured shielding of the cyclopropyl protons of 37 obtained using 56 as a model, the shielding calculated for the structure 37 with localized double bonds and the shielding calculated for norcaradiene in which the six-membered ring is assumed to have the same degree of aromaticity as benzene.

Table 6: Shielding of norcaradiene cyclopropyl protons[a]

Protons	H_α	H_β
Measured shielding[b]	1.0	-0.6
Calculated for localized double bonds[c]	0.1	-0.05
Calculated for aromatic norcaradiene[d]	1.0	-0.4

a) in ppm, the negative values refer to deshielding;

b) obtained as a difference in chemical shifts of the corresponding protons in 37 and 56;

c) obtained using data in ref. 83;

d) obtained using data in ref. 85b.

The results in Table 6 seem to indicate that a model for norcaradiene with an aromatic structure fits the experimental data better than a structure with isolated double bonds.

Molecular orbital methods[87] have been frequently used to describe the interaction of the cyclopropyl ring with the diene moiety in norcaradiene[54b,56c,69] and analogous molecules.[44,88-90] According to this

view point the highest occupied molecular orbitals (HOMO) of norcaradiene

arise from a mixing of the two cyclopropyl Walsh orbitals W_{2a} and W_{1s}[50] with

the butadiene molecular orbitals (MO) ψ_{2a} and ψ_{1s}. The symmetry element

used for qualification of the MO's of norcaradiene is the plane inter-

secting C-7 and the centre of C-1, C-6 and C-3, C-4 bonds. The subscript

"a" denotes antisymmetric and "s" symmetric with regard to this symmetry

element, Figure 7.[56c]

Figure 7: Highest occupied molecular orbitals of norcaradiene
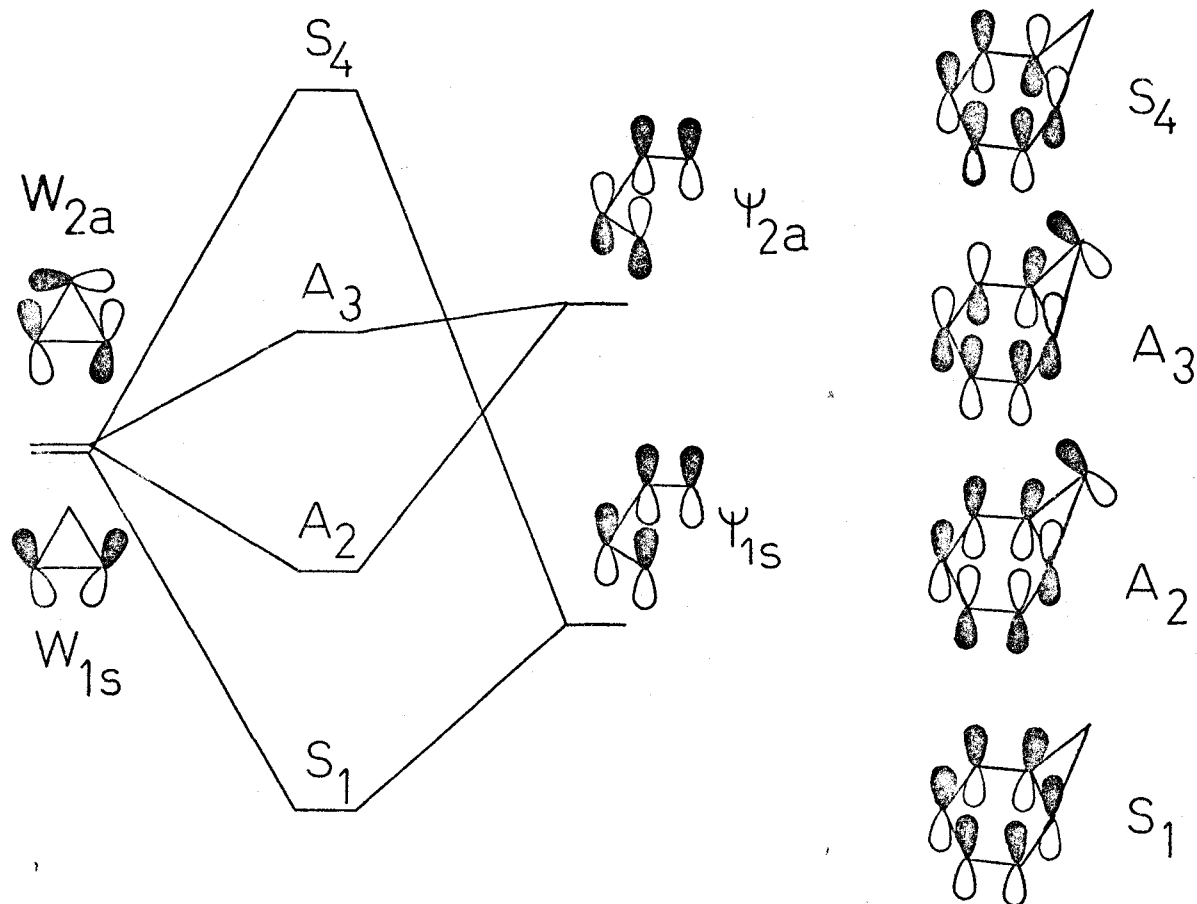
While this method can account for the effect of a C-7 substituent on the stability of a norcaradiene, it reveals little about the possible aromatic character of such a system. In Winstein's original formulation of the concept of homoaromaticity, it was suggested that when a suitable geometrical arrangement is maintained, an interruption of a cyclic polyene array (for example by a CH_2 group) does not completely prevent the cyclic delocalization. In this sense homoaromaticity is an extension of Hückel aromaticity to cyclic systems with an interrupted polyene chain.

Previously, the concept of homoaromaticity has been applied mainly to the charged species, cations and anions. Perhaps the best known representative of such compounds is the homotropylium cation. It is interesting to note that this system is isoelectronic with norcaradiene.

An insight into the mechanism of homoconjugation can be derived from consideration of the interaction between cyclopropane and the residual π-system. One factor which affects such an interaction is the difference between the energies of the donor and the acceptor orbitals. Haddon[89] has considered the union of a butadiene with a cyclopropane to form a homobenzene. He assumes that there is some homoconjugative interaction in the norcaradiene molecule. Nevertheless he has concluded that the large energy gap between the molecular orbitals involved $(\psi_{3s} + W_{1s}$ and $\psi_{2a} + W_{3a})$ and the lack of drive for a charge delocalization in this neutral system reduces the interaction and the homoaromaticity.[89]

This situation may well be changed when an electron withdrawing substituent is placed on C-7. Withdrawal of the electron density from W_{2a}

Energy
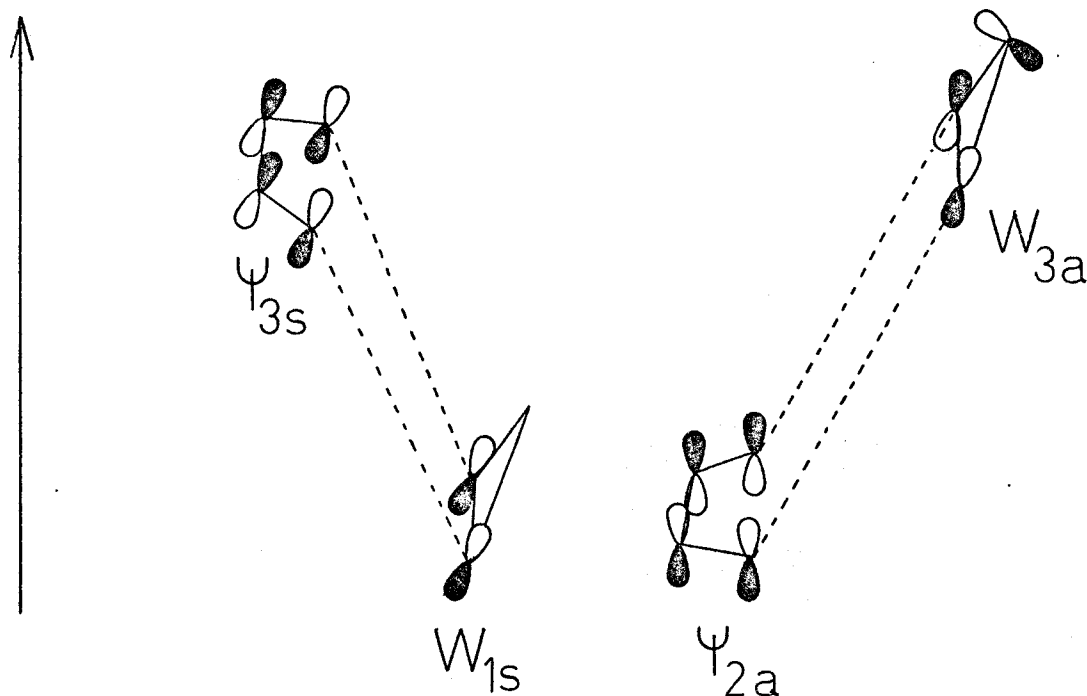
to the substituent would induce donation from Ψ_{2a} of the diene

to the electron deficient W_{2a}. [44,69] In this situation the back

donation from W_{1s} into Ψ_{3s} may be of increased importance. The

net result of such an interaction should be a stabilization of the

norcaradienylcarbinyl cation. Thus an electron defficient C-7 sub-

stituent could facilitate the homoconjugative overlap of the formally

neutral ring system and enhance the homoaromaticity of norcaradiene
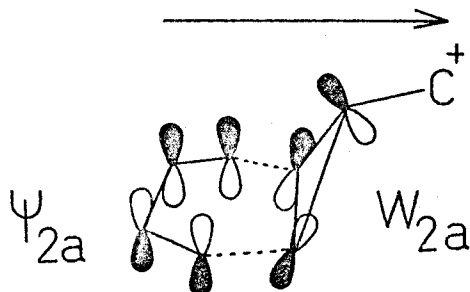
A slightly different formulation of homoaromaticity was put forward by W. J. Hehre.[90] He visualized homoaromatic compounds as derivatives of aromatic polyenes formed by replacement of one double bond by a cyclopropyl ring. The logic behind such a move is suggested by the resemblance of the symmetric Walsh orbital to the π orbital of the double bond. According to this view the two electrons occupying

$$W_{1s}$$

double bond
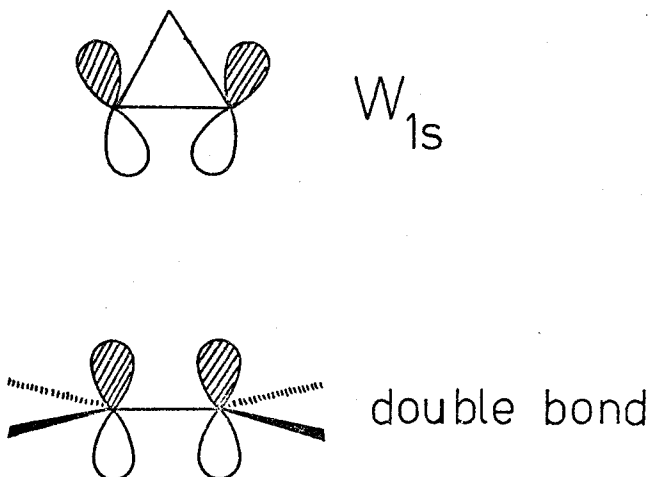
W_{1s} should be able to delocalize over the ring. The resulting homoaromatic polyene would have a similar structure as the aromatic parent compound and would contain an identical number of electrons in cyclic conjugation.[90]

In this view, 6- electrons of norcaradiene would delocalize over the six carbons in a Hückel ring. The relationship between norcaradiene and benzene would be analogous to that of the tropylium and homotropylium cation.
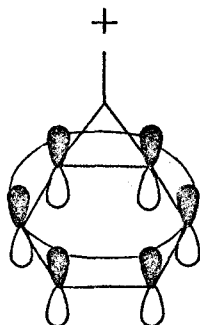
6 π electrons

Hückel aromatic

One consequence of this would be that in the presence of an external magnetic field a ring current should be induced in the six membered ring.[91] Shielding of the C-7 proton and deshielding of the C-1, C-6 protons, compatible with the presence of a ring current was in fact observed in both 37 and 39. It can be concluded that the 7-norcaradienylcarbinyl cations are homoaromatic compounds. In this connection it is interesting to note that when Sargent initially considered the 7-norcaradienylmethyl cation he remarked that formulation of the cyclopropylmethyl cation in a conventional way imparts some benzenoid character to norcaradiene.[53]

A controversy has developed recently about the length of the homoconjugated linkage (a-b) in systems such as the homotropylium cation. Using a perturbational approach based on frontier orbitals, Haddon[89a,c] has arrived at the conclusion that homotropylium has an "open" cyclopropane unit, and using a MINDO/3 method he has calculated the length of a-b bond to be 1.621 Å.[89b] On the other hand, based on ab initio

calculations at the STO-3G level, Hehre[90] has formulated homotropylium

as the bicyclo[5.1.0]octadienyl cation, with an a-b bond length of

1.512 $\overset{o}{A}$. No experimental data are presently available to corroborate

either of these calculations.
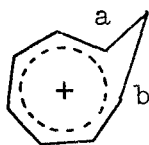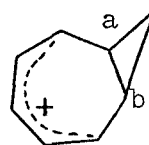
Haddon   Hehre

This work presents some evidence that homoaromatic compounds 37

and 39 are norcaradienes rather than compounds with an "open" cyclopropyl

ring (cycloheptatrienes). An experimentally determined value of the

C-1, C-6 distance in these compounds would be of a great interest.

Thermal Rearrangement of Zwitterions

The norcaradiene complexes were found to be stable when kept at

low temperatures however, on heating they underwent a ring contraction

to give benzenoid products. Thus at temperatures above 0°, 37 rearranged

to give three products, one of which was identified as the BCl_3 complex

of methyl phenylacetate. The pmr spectrum of this product (resonances

δ 4.19, 4.62 and 7.4) was consistent with the structure 57. Methyl

phenylacetate, 58, was recovered when the solution containing the re-

arranged product was reacted with dimethylamine. The reaction of 58 with

BCl_3 in a CD_2Cl_2 solution gave the complex 57, which had an identical pmr spectrum to that described above.

In addition to the signals attributable to 57, the pmr spectrum of the rearrangement products of 37 contained some other resonances. In particular, signals at 3.87, 4.16 and part of signal at 7.4 δ remained to be accounted for, Table 7.

Table 7: Proton chemical shifts of rearranged products of 37 and 39

Product	Proton chemical shift[a], δ		
	ArH	CH_2	CH_3
57	7.2 - 7.6	4.71	4.30
62	7.2 - 7.6	4.75	4.48
60 + 61	7.2 - 7.6	4.16	3.87
60 + 63	7.2 - 7.6	4.27	3.96
64	7.1 - 7.5	4.55	3.20

a) $CHCl_3$ (δ 7.30) used as an internal standard

When the solution of the rearrangement products of 37 was reacted with ethanol, two compounds were formed. These products were isolated and identified as 58 and 59. A similar reaction of 57, prepared from phenylacetaldehyde and BCl_3, gave 58 as the sole product. On this basis and by comparison with the results obtained with rearrangement of 39 (vide infra) it would seem that the additional products formed on thermal rearrangement of 37 were the acylium cation 60, $\bar{B}Cl_4$, and 61, Scheme 2. Some evidence for the presence of 61 has been obtained from the pmr

study of the reaction product of BCl_3 and MeOH. This reaction has been

reported to give methoxyboronhalides such as $\underline{61}$ in the following manner:[94]

$$BCl_3 + MeOH \xrightarrow{-80^\circ} (MeO)_n BX_{3-n} + nX^-$$
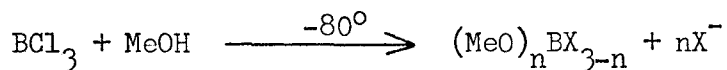
The methyl resonance ascribed here to $\underline{61}$ occured in the same region of

the pmr spectrum as that of an equimolar solution of BCl_3 and methanol

in $CDCl_3$.
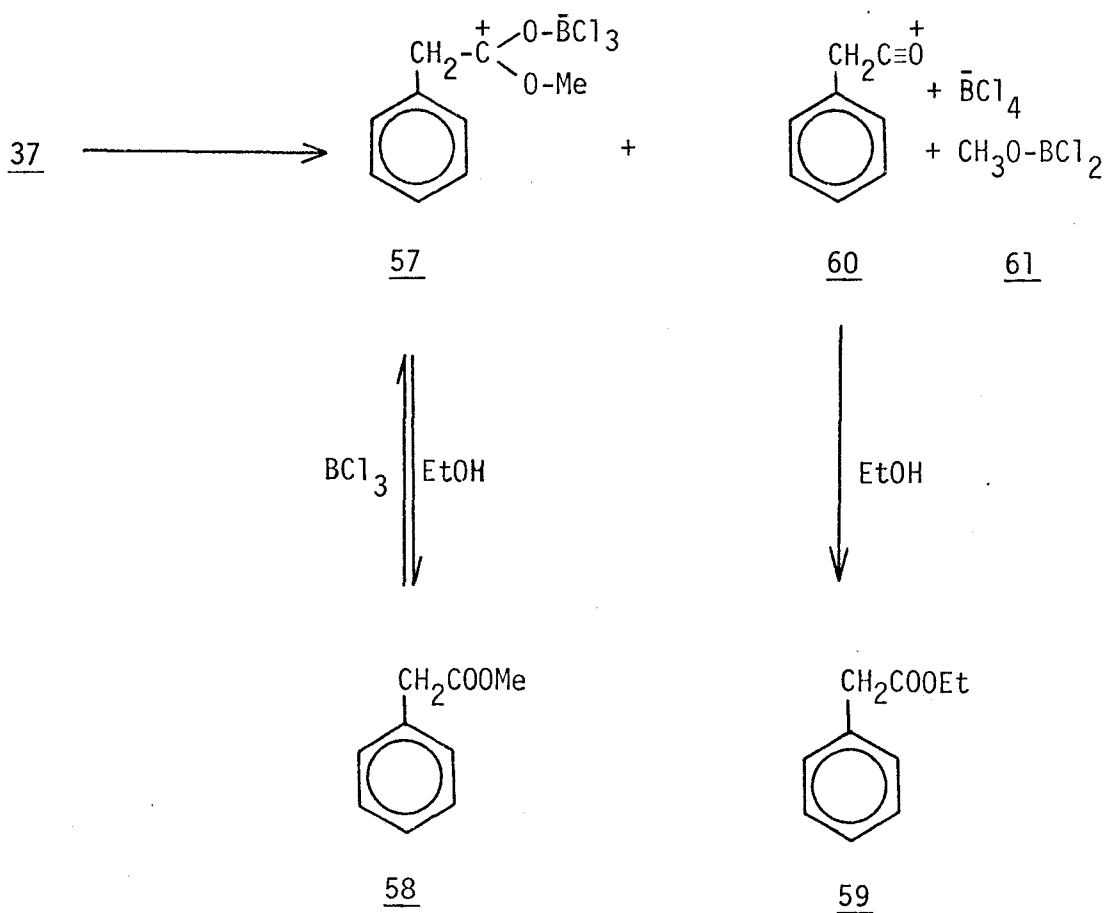
Scheme 2: Thermal rearrangement of $\underline{37}$

The BBr$_3$ complex $\underline{39}$ rearranged in a comparable manner to that of $\underline{37}$, to give the BBr$_3$ complex of methyl phenylacetate, $\underline{62}$, the acylium cation $\underline{60}$, the counterion $\overline{BBr}_4$, and $\underline{63}$, Table 7. The rearrangement of $\underline{39}$ however, occurred at much lower temperatures than those required for $\underline{37}$. Thus with a two-fold excess of BBr$_3$, $\underline{39}$ rearranged at -43° with a half life of 40 min, Table 8.

Table 8: Rate constants for rearrangement of norcaradiene complexes[a]

Complex	ester to Lewis acid ratio	k_{obs} (sec^{-1})	temp °C
$\underline{37}$	1 : 1.1	4.6 x 10^{-5}	0
$\underline{37}$	1 : 10	2.8 x 10^{-4}	0
$\underline{39}$	1 : 2	2.7 x 10^{-4}	-43
$\underline{42}$ + $\underline{43}$	1 : 1.1	5.2 x 10^{-6}	0

a) obtained by following the reaction by pmr.

The complex $\underline{62}$, formed on thermal rearrangement of $\underline{39}$ or by reacting $\underline{58}$ with BBr$_3$, was at -43° slowly converted to $\underline{60}$ and $\underline{63}$. The ir spectrum of the rearranged product was obtained and this exhibited an absorption at 2270 cm^{-1}. This would confirm that an acylium cation had been formed, as typically cations of this type exhibit the carbonyl absorptions in this region. For example the phenylmethylacylium cation, with a SbF$_6^-$ counter ion, has been reported to absorb at 2279 cm^{-1}.[95]

$$39 \quad \xrightarrow[-40^\circ C]{\triangle} \quad \underset{62}{\begin{array}{c} CH_2-\overset{+}{\overline{C}}\overset{O\overline{B}Br_3}{\underset{OMe}{<}} \\ \bigcirc \end{array}} + \underset{60}{\begin{array}{c} CH_2-C\equiv\overset{+}{O} \\ \bigcirc \end{array}} + MeOBBr_2 + \underset{63}{B\overline{B}r_4} \qquad (25)$$

$$62 \quad \xrightarrow[(slow)]{-40^\circ C} \quad \underset{60}{\begin{array}{c} CH_2-C\equiv\overset{+}{O} \\ \bigcirc \end{array}} + MeOBBr_2 + \underset{63}{\overline{B}Br_4} \qquad (26)$$
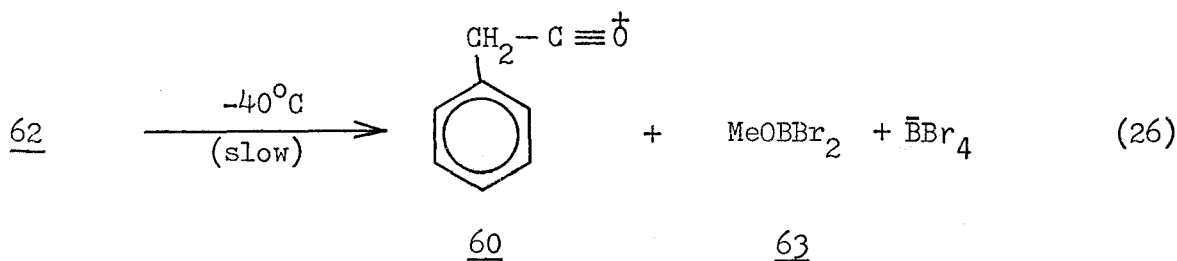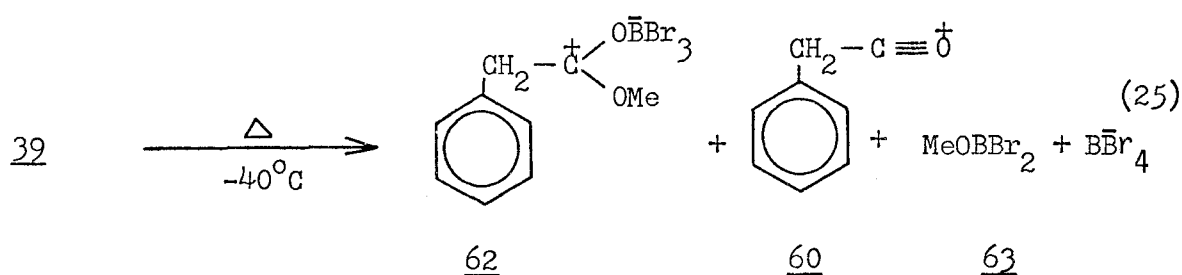
The BCl_3 complex of N,N-dimethyl-7-cycloheptatrienylcarboxamide,
42 / 43, rearranged at 0° very slowly to give the BCl_3 complex of N,N-di-
methylphenylacetate, 64. No formation of the acylium cation 60
was observed in this reaction. A complex with a pmr spectrum identical
to that of the rearrangement product of 42 / 43, could be prepared by
reacting N,N-dimethylphenylacetaldehyde, 65, with BCl_3 in a CD_2Cl_2
solution. A 94% yield of the amide 65 was obtained on reaction of the
solution of rearrangement product of 42 + 43 with water or dimethyl-
amine, Table 9.

$$\underline{42} + \underline{43} \longrightarrow \underset{\underline{64}}{\overset{\displaystyle CH_2-\overset{+}{C}\begin{smallmatrix}O\bar{B}Cl_3\\\\NMe_2\end{smallmatrix}}{\bigcirc}} \underset{HNMe_2,\ H_2O}{\overset{BCl_3}{\rightleftharpoons}} \underset{\underline{65}}{\overset{\displaystyle CH_2-CONMe_2}{\bigcirc}}$$
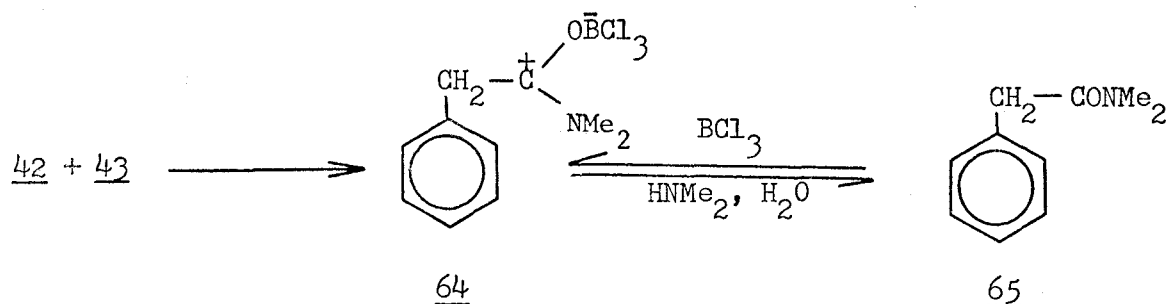
Table 9: Products obtained on quenching complexes and thermally

rearranged materials.

Material	Quenching agent	Product [a]
$\underline{37}$	Me_2NH	$\underline{35}$ (100%)
$\underline{39}$	Me_2NH	$\underline{35}$ (100%)
$\underline{42}$ + $\underline{43}$	water or Me_2NH	$\underline{41}$ [b]
$\underline{57}$ (58%) + $\underline{60}$ (42%)	Me_2NH	$\underline{58}$ (70%)
$\underline{57}$ (60%) + $\underline{60}$ (40%)	EtOH	$\underline{58}$ (58%) + $\underline{59}$ (42%)
$\underline{60}$ + $\underline{63}$	EtOH	$\underline{58}$ (13%) + $\underline{59}$ (87%)
$\underline{64}$	water or Me_2NH	$\underline{65}$ (94%)

a) yield determined by comparison with internal hexamethylbenzene

b) no other product detected by pmr.

Both the distribution of the rearrangement products and the rate of rearrangement of $\underline{37}$ were found to be dependent on the ratio of the ester to Lewis acid used. Thus as is shown in Table 8, when the ratio of BCl_3 to $\underline{35}$ was increased the rate of the rearrangement of $\underline{57}$ was enhanced and also the relative amount of the acylium cation $\underline{60}$ produced was increased, Table 10.

Table 10: Products of thermal rearrangement of $\underline{37}$

ester to Lewis acid ratio	temp $^{\circ}C$	Products	
		$\underline{57}$	$\underline{60}$
1:0.9	20	93	7
1:2	20	77	23
1:8	20	42	58

a) the ratio of the products was determined by integration of the

pmr spectra

It is important to note however, that the enhanced rate can not be accounted for simply by the increase in the amount of the acylium cation produced, but that the rate of formation of $\underline{37}$ was also increased by the addition of BCl_3.

While the formation of acylium cations from protonated carboxylic acid derivatives is well known,[95] in this case $\underline{60}$ was not formed from $\underline{57}$. Thus when a solution of $\underline{57}$ prepared by reaction of $\underline{58}$ with BCl_3, or by thermal rearrangement of $\underline{37}$, was heated for 1 hour to 50° no formation of $\underline{60}$ was detected by pmr. The acylium cation $\underline{60}$ must therefore be a primary rearrangement product of $\underline{37}$.

A reaction sequence which can account for these experimental observations is outlined in the Scheme 3. The starting norcaradiene can be considered to be in an equilibrium with the cyclobutyl zwitterion $\underline{66}$[96]
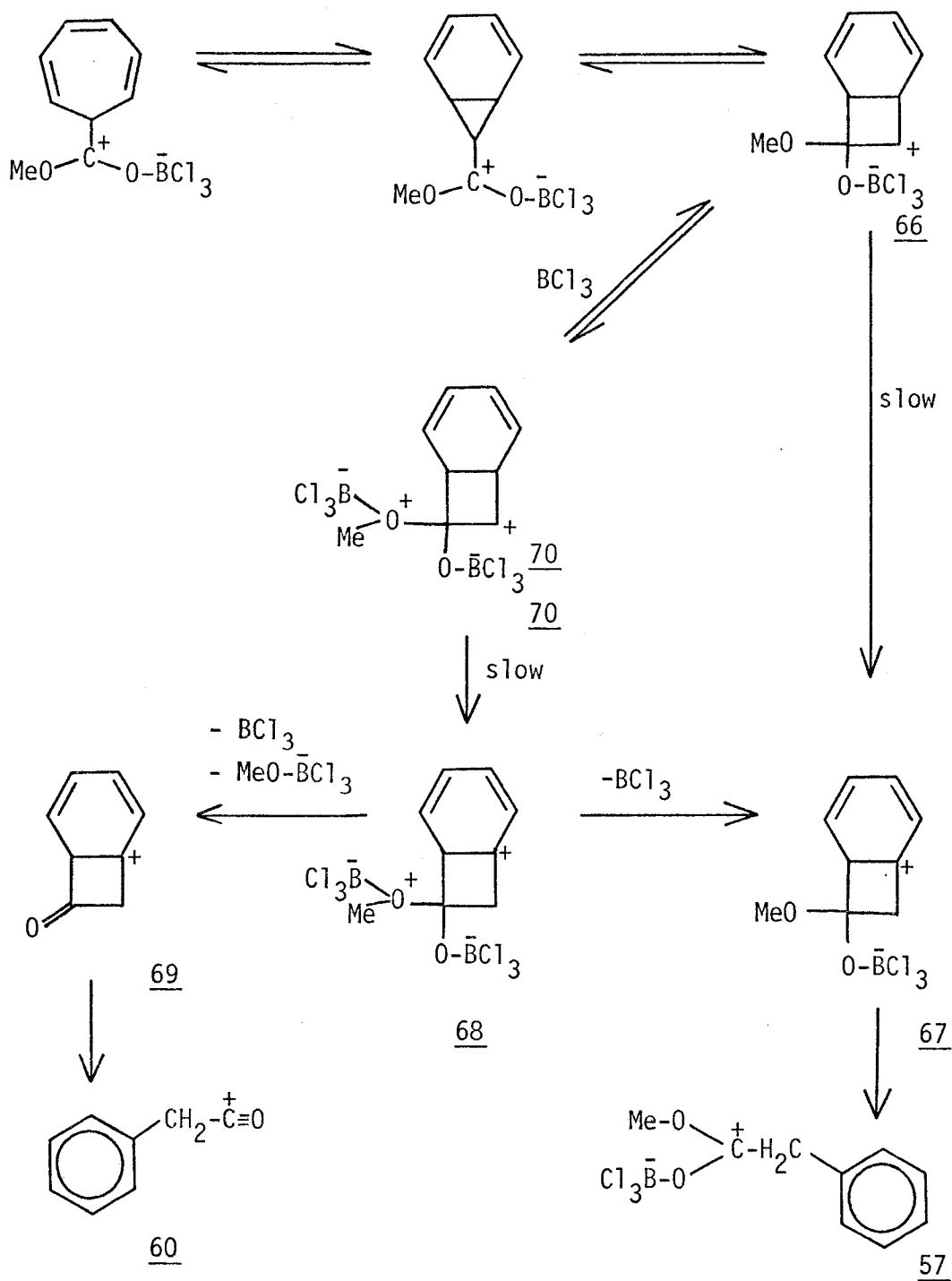
Scheme 3: Thermal rearrangement of 37

and this could undergo a 1,2 hydride shift to give 67. Comparable

cyclobutyl cations have been suggested as intermediates in the ring

contraction reactions of certain homotropylium cations.[97] The energy

difference between 66 and 67 might not be all that great as the cyclo-

hexadienyl cation in 67 is forced to be twisted by the fused cyclo-

butane ring and some homodienylic stabilization of the positive charge

in 66 is possible. Rigidity of the system would make it difficult for

the appropriate geometry for this hydride shift to be attained. For

these reasons the transformation of 66 to 67 might well be the slow

step in such a rearrangement.

The rate of isomerization of 37 and the product distribution were

found to be dependent on the ratio of the Lewis acid to the ester used.

As the ester is almost completely complexed under the reaction conditions,

this would suggest that a further isomerization pathway is available which

involves a second molecule of BCl_3. In the suggested intermediate 66, the

positive charge is removed from the ester oxygen and this could interact

with a further molecule of Lewis acid to give 70. The rate of the

hydride shift which leads from 70 to 68 could well be expected to be

faster than the comparable shift linking 66 to 67 as a result of the

additional positive charge in the complex 70.

There are two possible reaction pathways open for 68. Elimina-

tion of one Lewis acid molecule would lead to 67 which would probably

rapidly aromatize to 57. Competing with this reaction could be the

fragmentation of 68 into 69, $\bar{B}Cl_4$ and methyldichloroborinate, followed by

rearrangement of 69 into the acylium cation 60. A comparable ring open-

ing of cyclobutanone cations similar to 69 have been reported.[99]

The suggested mechanistic scheme can account for the product

distribution and the kinetics of isomerization of 37 under different conditions, Tables 8 and 10. Scheme 3 is also consistent with the observed rates of isomerization of 39 and 42/43. The overall rate of isomerization of these complexes would not only be a function of the rates of the slow hydride shifts, but would also be dependent on the several pre-equilibrium steps involved. In the amide case, the amount of the norcaradiene form present in equilibrium with the cycloheptatriene is substantially smaller than with 37, and this factor might be at least partially responsible for the slower rate of isomerization encountered with the amide complexes 42/43. It is interesting to note that no acylium cation was produced on isomerization of these complexes. The absence of 60 in the rearrangement products of 42/43 might be due to the fact that the elimination of $(Me)_2N-\bar{B}Cl_3$ from an intermediate similar to 68, is relatively slow so that rearrangement to a nitrogen analogue of 67 prevails. This explanation is consistent with the poor leaving ability of the NR_3^+ group in E_1 elimination reactions.[100]

The borontribromide complex 39 was observed to rearrange much more rapidly than the BCl_3 analogue, 37. This increase in the rate of isomerization could be attributed to a different position of equilibrium between the norcaradiene and bicyclooctadiene cation when BBr_3 is used as a Lewis acid. Furthermore, the higher Lewis acidity of BBr_3 would alter the equilibrium between species comparable to 66 and 70 in favour of the latter.

It would seem that both the proportion of the norcaradiene form present in the tautomeric mixtures of these cationic systems and also the ease of their rearrangement to benzenoid compounds are directly

related to the ability of the C-7 substituents to stabilize the positive charge. This being the case it is not surprising that it has proved to be impossible to detect any unsubstituted, diarylsubstituted or mono-oxysubstituted 7-norcaradienyl carbonium ions in this or earlier work,[64,53] as it would be expected that cations of this type would aromatize very rapidly even at low temperatures. No evidence was found for the formation of heptafulvene, tropylium or homotropylium cations (Scheme 1) in the thermal rearrangement of the norcaradiene complexes.

The 7-cycloheptatrienylcarbinyl and the 7-norcaradienylcarbinyl cations are just two of a family of cations with the molecular formula $C_8H_9^+$. A common entry into this or related substituted series of cations is the addition of an electrophile to cyclooctatetraene, and very frequently the end products of such addition reactions have been reported to be substituted benzenes.[61-63,101-103] Ganelin and Pettit[61] have found some evidence for the intermediacy of seven-membered ring compounds in these rearrangements and they suggested that the initial cation produced is the homotropylium cation, 71, Scheme 4. The homotropylium cation which in certain reactions can be trapped to give cyclooctatriene products, was thought to rearrange to the cycloheptatrienyl cation, 72, which again under certain conditions can be trapped. The results described in this present thesis would seem to indicate that yet another cation, the 7-norcardienyl methyl cation, is also involved in this rearrangement sequence and that it can lead, possibly via a bicyclo [4.1.0] octadie cation, to benzenoid materials. It should be pointed out that there are other possible rearrangements pathways from homotropylium cations.[61]
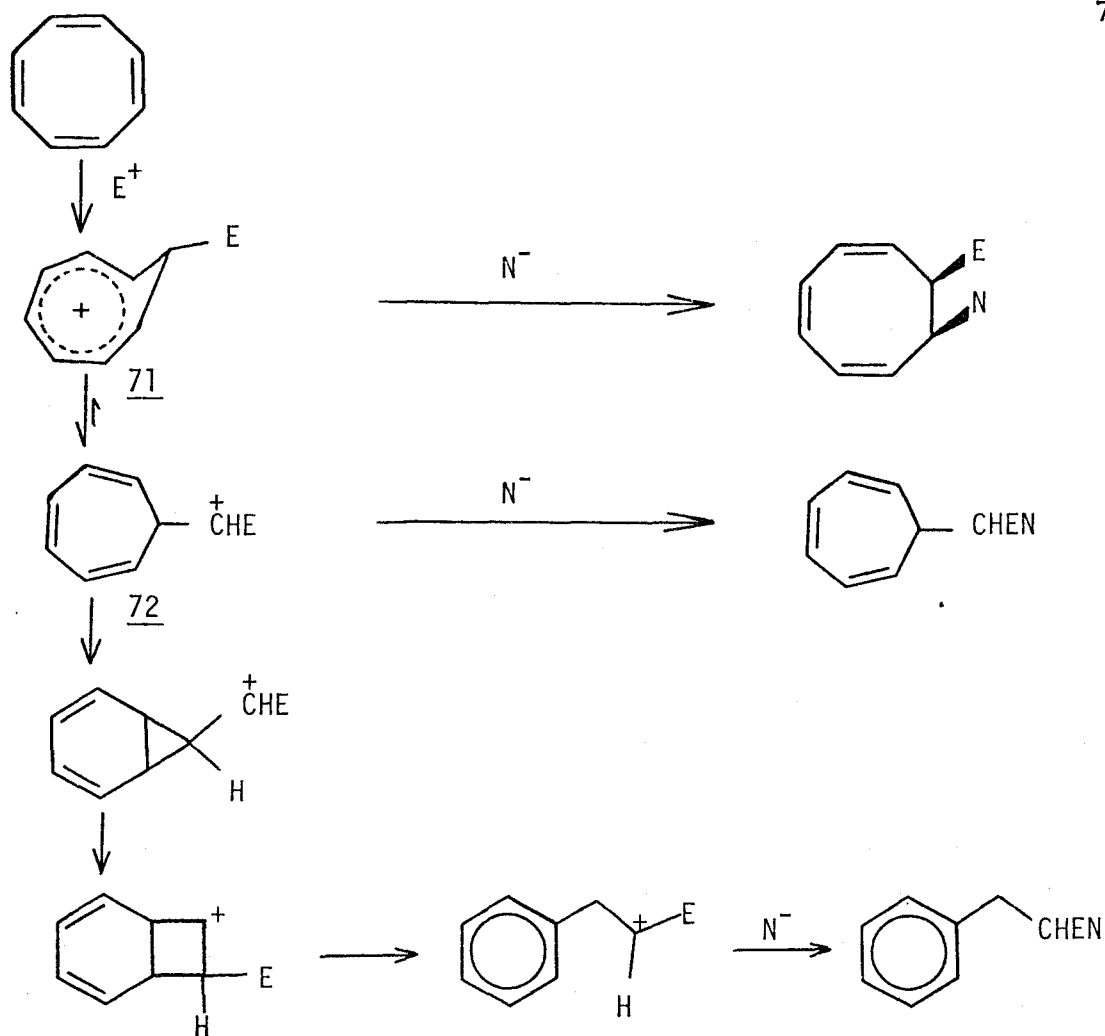
Scheme 5: Rearrangements of cations $C_8H_9^+$

Synthesis of 3-substituted-1,4-cycloheptadienes

As was discussed earlier, 3-methoxycarbonyl-1,4-cycloheptadiene, _44_, was required as a precursor of the zwitterion _45_. Since no report of the preparation of this ester was found in the literature, a new synthetic route to _44_ had to be designed. Surprisingly, the synthesis of _44_ was not as straightforward as one might have expected for such an ostensibly simple, low molecular weight compound.

The first attempted approach to 44 involved the preparation of the cycloheptadiene anion, 73, and the reaction of this anion with a potential source of a carboxy group, Scheme 5.
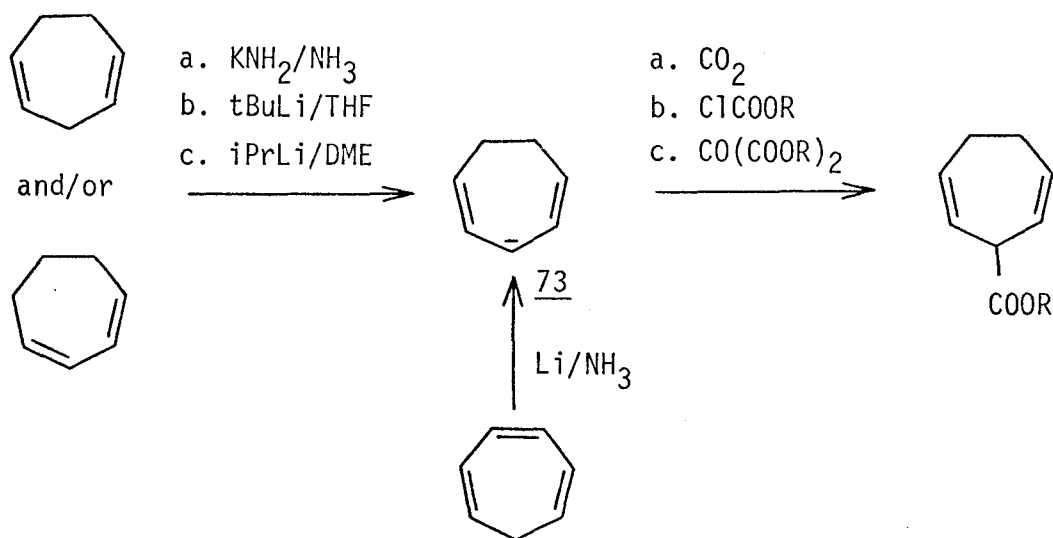
Scheme 5: Attempted synthesis of 44

The cycloheptadiene anion 73 has been described before[104-106] and has been used to obtain 5-substituted 1,3-cycloheptadienes.[104,106a] Dark red solutions of 73 were prepared by abstraction of a proton from 1,3- or 1,4-cycloheptadiene, 74, with strong bases such as KNH_2, tBuLi, or iPrLi, or directly from cycloheptatriene by reacting it with two equivalents of lithium dissolved in liquid ammonia.

Several different trapping reactions were attempted in attempts to obtain 44. Reaction of 73 with an excess of solid carbon dioxide gave two isomeric cycloheptadienes and a mixture of carboxylic acids. The carboxylic acids were reacted with CH_2N_2 and the mixture of esters so formed was separated by vpc into 7 fractions. Although not all of these

fractions were identified, in no case were the spectral data compatible with 44. Ter Borg has reported somewhat similar results.[105]

73   in NH_3 CO_2 COOH   +   +

25%   30%   8%
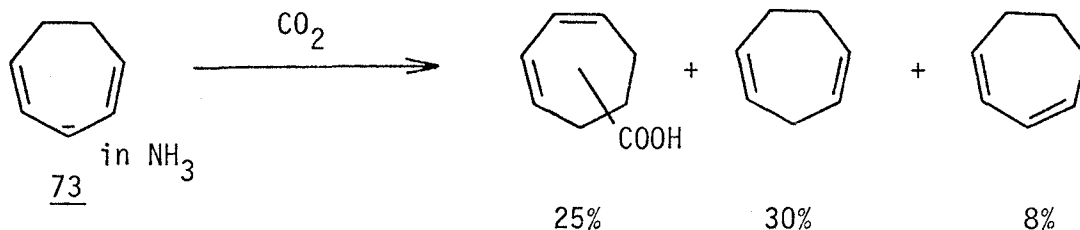
Reaction of 73 with ethylchloroformate led to a similar mixture of esters.

As cycloheptatriene can be reduced with lithium in liquid ammonia, a similar reduction[107] of cycloheptatriene-7-carboxylic acid was attempted, eq. 27, however once more a complex mixture of esters was obtained upon treatment of the product with diazomethane.

$$\text{COOH} \xrightarrow{\text{Li}/NH_3} \text{COOH} \qquad (27)$$
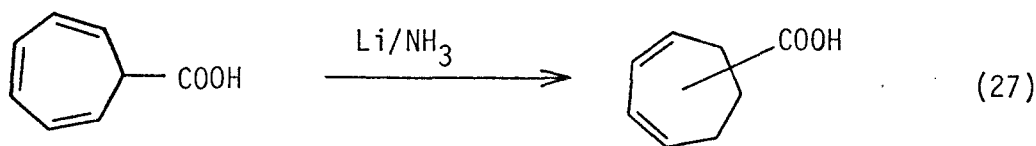
In view of the complexity of these reactions involving anionic species a milder, more specific route was sought. Allred and Hinshaw have reported that the azocompound 75 decomposes thermally at 25° to give 1,4-cycloheptadiene and nitrogen, eq. 28.[108]

$$\xrightarrow{25°} \qquad (28)$$

75
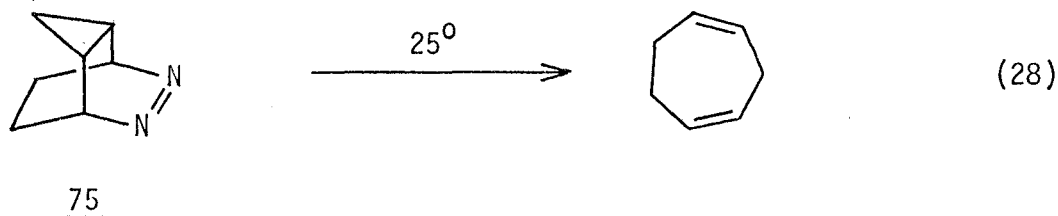
It appeared likely, that a similar reaction of 76 would produce the
desired ester 44 in a pure form and under very mild conditions.

COOMe

?
⟶

COOMe

76   44
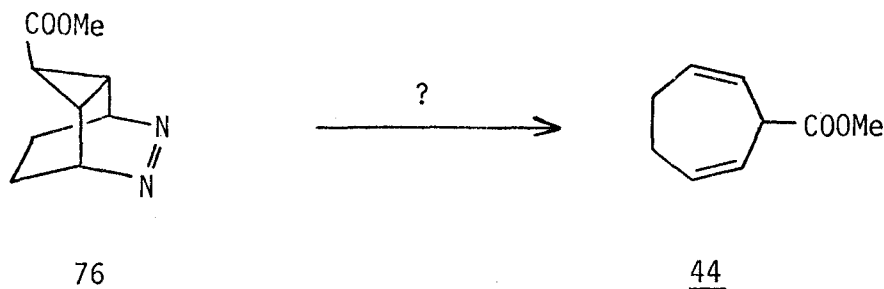
Since 75 was prepared by hydrogenation of the Diels-Alder
adduct of cycloheptatriene and 4-phenyl-1,2,4-triazoline-3,5-dione,
77,[6d,109] a similar route was employed for preparation of 76 (Scheme 6
and 7).

The addition of 77, prepared "in situ" by oxidation of 79 with
leadtetraacetate, to 7-substituted cycloheptatrienes proceeded rapidly
at low temperatures to give a high yield of the tetracyclic compound
78. The structure of 78 was established from its spectral data, ele-
mentary analysis, and the subsequent chemical reactions. The stereo-
chemistry at the carbon bearing the substituent R was determined from the
magnitude of the coupling constant between the bridgehead cyclopropyl
hydrogens, and the proton adjacent to the ester group, J = 3.0 Hz. A
coupling of this magnitude is clearly indicative of the proposed geometry,
78.[68]

The cycloheptatrienes entered the Diels-Alder reaction only in
the norcaradiene form. No adduct such as 81, derived from the cyclo-
heptatriene form, was detected.

The adduct 78 was hydrogenated at atmospheric pressure using a
Pd/C catalyst to give 80 in a high yield. The resonance of the

a) R = COOMe

b) R = CH(OMe)₂

c) R = COOEt
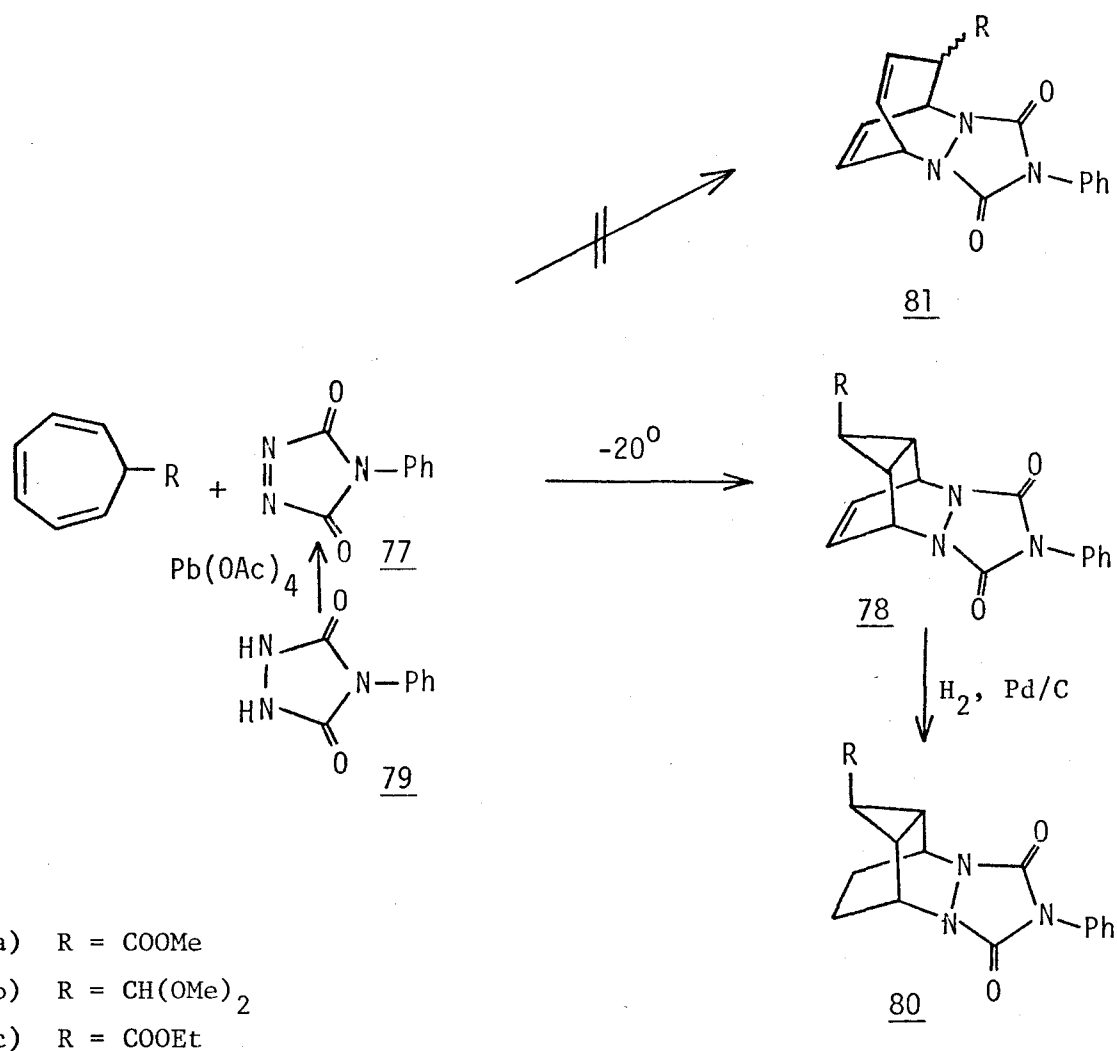
Scheme 6: Synthesis of 80

bridgehead cyclopropyl protons of 78 and 80, R=COOMe, appear at almost

the same position (2.19 and 2.11 δ respectively) in their pmr spectra,

however the proton geminal to the ester group resonated at 1.41 δ in 78

and at 1.87 δ in 80. The shift of the resonance of this proton by 0.45

ppm on saturation of the double bond indicates that the proton was locat-

ed in the shielding region of the double bond and further confirms the

assignment of the stereochemistry of the cyclopropyl ring.

Hydrolysis of 80 with alcoholic potasium hydroxide yielded the
hydrazo compound 83 and aniline. Shorter reaction times led to the re-
covery of partially hydrolyzed product, compound 82.

80 $\xrightarrow[\text{-CO}_2]{\text{KOH/MeOH, 4 hr}}$

82

80 $\xrightarrow[\text{-2 CO}_2]{\text{KOH/MeOH, 24 hr}}$ + PhNH$_2$

83

83 $\xrightarrow{\text{1. HCl} \quad \text{2. CuCl}_2}$

76

84

a) R$_1$ = COO$^-$ R$_2$ = COOH
b) R$_2$ = CH(OMe)$_2$ R$_2$ = CHO
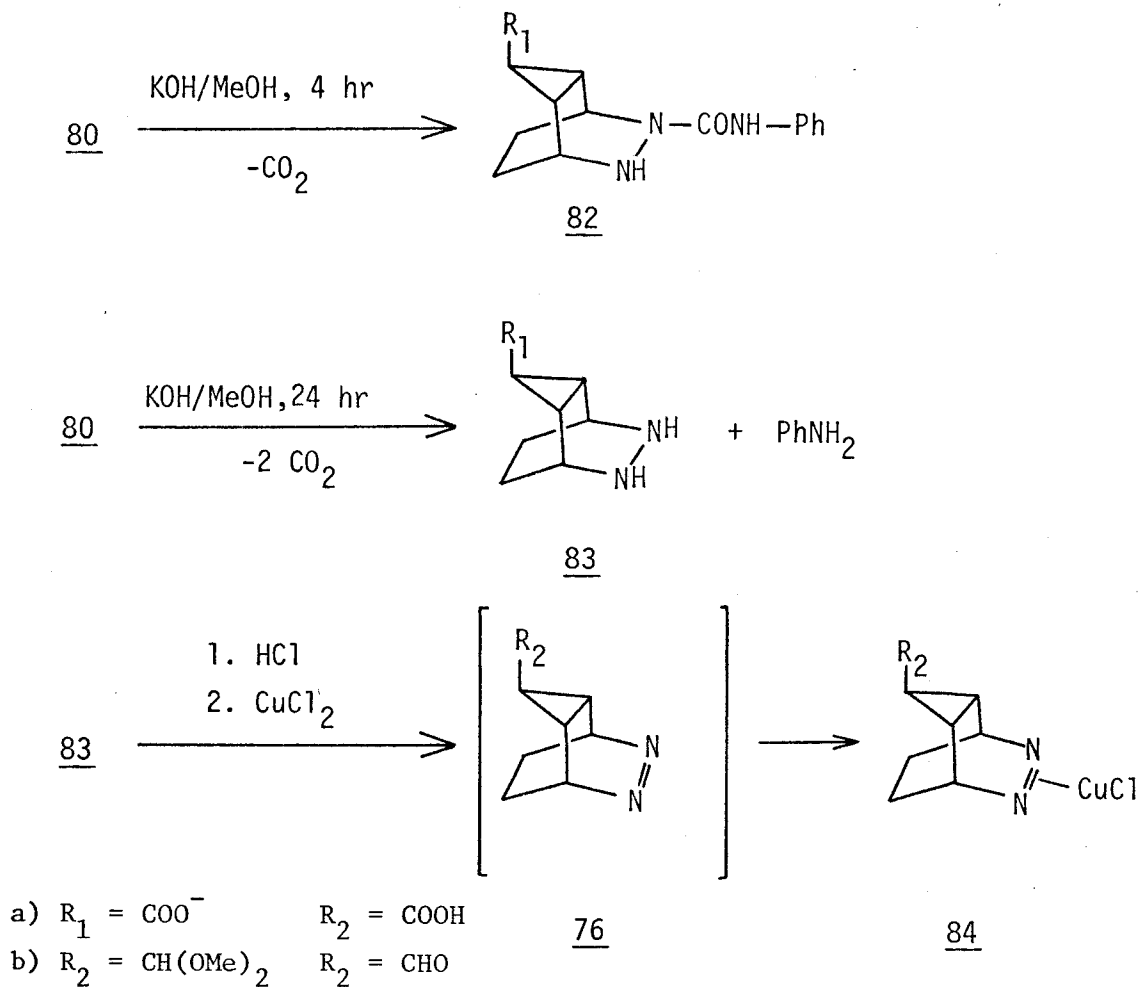
Scheme 7: Synthesis of 84

Compound 83 was found to be sensitive towards oxygen and when
exposed to air, it was rapidly converted into a dark gluey polymeric
material. Thus in a typical reaction, 83 was not isolated but the reac-
tion mixture was dissolved in nitrogen saturated water, acidified to
pH 4 and treated with 2 equivalents of CuCl$_2$. The role of cupric

chloride was two-fold; it oxidized 83 into 76, and subsequently reacted
with this azocompound to form the stable 84. The copper complexes such
as 84 could be prepared in reasonable quantities and stored as stable
precursors of 1,4-cycloheptadienes, such as 44.

Treatment of 84 with aqueous base liberated 76. The azo compound
76 was thermally unstable and when heated to 35° eliminated nitrogen and
gave substituted cycloheptadienes, Scheme 8. The structure of the pro-
duct was found to depend on the base used. Thus if the copper complex
84a was decomposed with a 0.1 N KOH solution, only the conjugated acid
85 was eventually isolated, however, 86 was the sole product of the
reaction when 1 equivalent of potassium carbonate was used as a base.
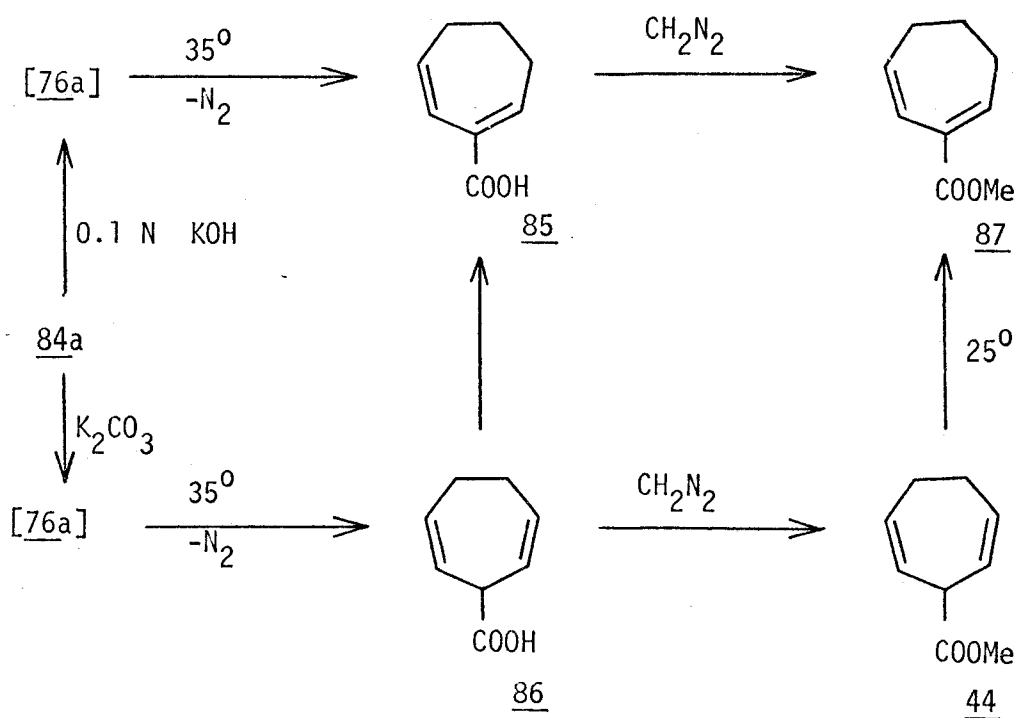
Scheme 8: Synthesis and rearrangement of 44

The synthesis was then completed by acidification of the solution to pH 2.5, extraction of the organic acid with ether and subsequent esterification with diazomethane to give 44. The ester 44 was found to be rather unstable, and at room temperature it rearranged to the conjugated ester 87, with the half life of about 12 hours.

A similar reaction sequence was used to prepare 3-dimethoxymethyl-1,4-cycloheptadiene, 88. However, since the acetal group of 88 is acid sensitive the last step of the synthetic procedure had to be modified. Instead of preparing the copper complex, the solution of 83b obtained from hydrolysis was directly oxidized with air to 76b. The thermolysis of this azocompound at 35° afforded 88, eq. 29.

$$\underline{83b} \xrightarrow{\text{O}_2 \text{ (air)}} \left[\begin{array}{c} \text{CH(OMe)}_2 \\ \vdots \end{array} \right] \xrightarrow[\text{-N}_2]{35°} \text{CH(OMe)}_2 \qquad (29)$$

$$\underline{76b} \qquad\qquad\qquad \underline{88}$$
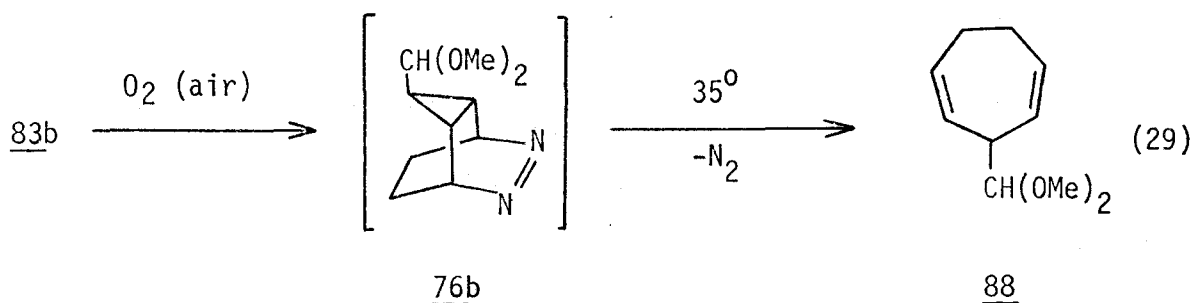
Scope and Evaluation of Synthesis Scheme 5-7

The reaction sequence outlined in Schemes 5-7, may appear to be a cumbersome synthesis of such simple compounds as 44. However, in spite of the number of steps and intermediates involved, it is a reasonably fast and efficient procedure. For example the yield of the Diels-Alder adducts is in vicinity of 80%, and both the hydrogenation and esterification steps proceed fairly rapidly with almost 100% efficiency. The hydrolysis, decarboxylation, nitrogen cleavage and esterification,

$\underline{80} \rightarrow \underline{44}$ (Schemes 6 and 7), gave typically a combined yield of 35%, thus making the overall yield of $\underline{44}$ from cycloheptatriene $\underline{35}$ about 29%.

Variously substituted cycloheptadienes can be prepared by the appropriate choice of starting cycloheptatriene, or by modification of the cyclopropyl substituent of $\underline{80}$. For example treatment of $\underline{80}$b, prepared from 7-dimethoxymethylcycloheptatriene[61], with aqueous acid, eq. 30, converted the acetal quantitatively into the aldehyde $\underline{89}$. The difficult preparation of the unstable 7-formylcycloheptatriene $\underline{46}$[79] was thus avoided.

$$(30)$$
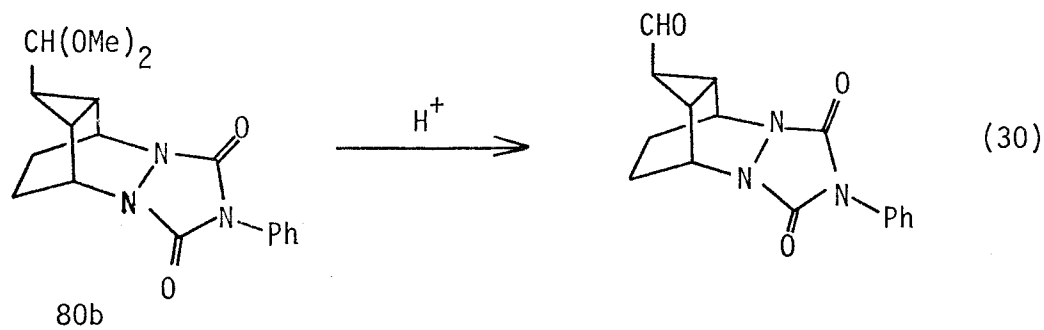
Similarly, $\underline{90}$ could be prepared by reacting $\underline{80}$ with MeLi and subsequent hydrolysis and oxidation reactions, Scheme 6 and 7.
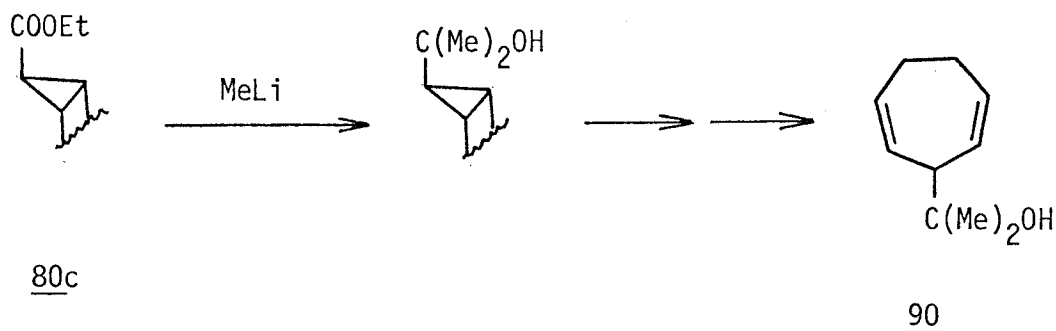
The 1,4-cycloheptadienes were found to be thermally unstable and to rearrange readily into the corresponding 1,3-isomers, eq. 31. The rate of this rearrangement appeared to depend on the electron-withdrawing power of the substituent. For example the following order of stabilities of 3-substituted-1,4-cycloheptadienes was qualitatively

observed: H $\simeq$ C(Me$_2$)OH $\simeq$ CH(OMe$_2$) > COO$^-$ > COOMe > COOH > CHO. Thus for

example while 88 can be heated to 60° without a noticeable rearrangement

ester 44 rearranged rapidly above 40° and the corresponding acid was

even more thermally labile. The attempted synthesis of 3-formyl-1,4-

cycloheptadiene from 89 resulted in isolation of the conjugated isomer,

even when the synthesis was carried out in a cold room at +4°. The rate

of rearrangement,eq.,31 increased drastically in the presence of strong

acids or bases. The advantage of the synthesis outlined in Schemes 5 to

7 is that the 1,4 dienes are prepared at low temperatures.

(31)
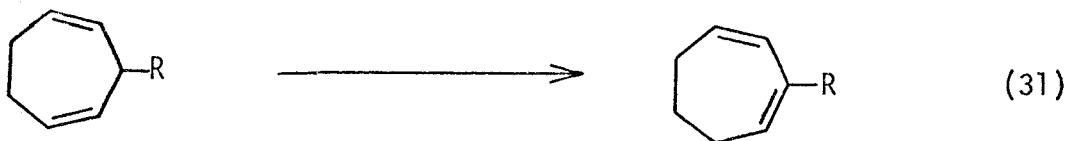
CHAPTER III

PREPARATION OF SUBSTITUTED HOMOTROPYLIDENES

A major difficulty in investigation of the effect of a substitu-
ent on a position of the CHT/NCD equilibrium is the large thermodynamic
preference for one of the isomers. The doubly degenerate homotropyli-
dene system does not possess this inherent structural disadvantage and
for this reason it was decided to study the effect of a substituent on
the equilibrium between 28 and 29. The electronic structure of 3,4-homo-
tropylidene is very similar to that of cycloheptatriene and nor-
caradiene[44,58] and consequently it was felt that the homotropylidene
system would serve as a good model for the CHT/NCD equilibrium.

28   29
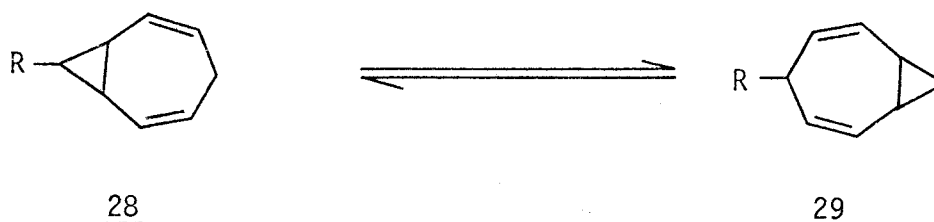
3,4-Homotropylidene (28, R=H) is just one member of a series of
related fluxional systems which can undergo degenerate Cope transforma-
tions. Also included in this series are bullvalene, 91, bullvalone, 92,
barbaralane, 93, barbaralone, 94, semibullvalene, 95, and several com-
pounds derived from azabullvalene, 96.

91 - 96, 28   (X is indicated on the next page)

81
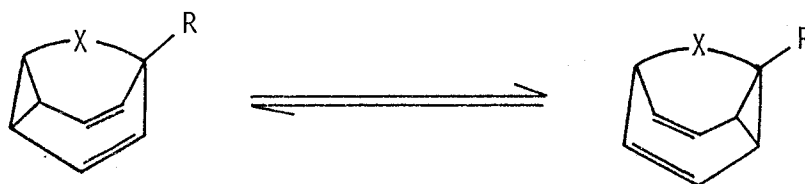
			ref.
91	X = CH═CH		110
92	X = CH₂—CO		111
93	X = CH₂		111, 112
94	X = CO		111, 113, 114
95	X = direct link		115, 116
96	X = N═CR		117
28	X is absent		118, 119

Not all of these systems are equally suited for use as models for the CHT/NCD equilibrium. For example, substituted bullvalenes can undergo a 1209600 fold degenerate rearrangement and the substituent can be scrambled around the entire molecule.[118]
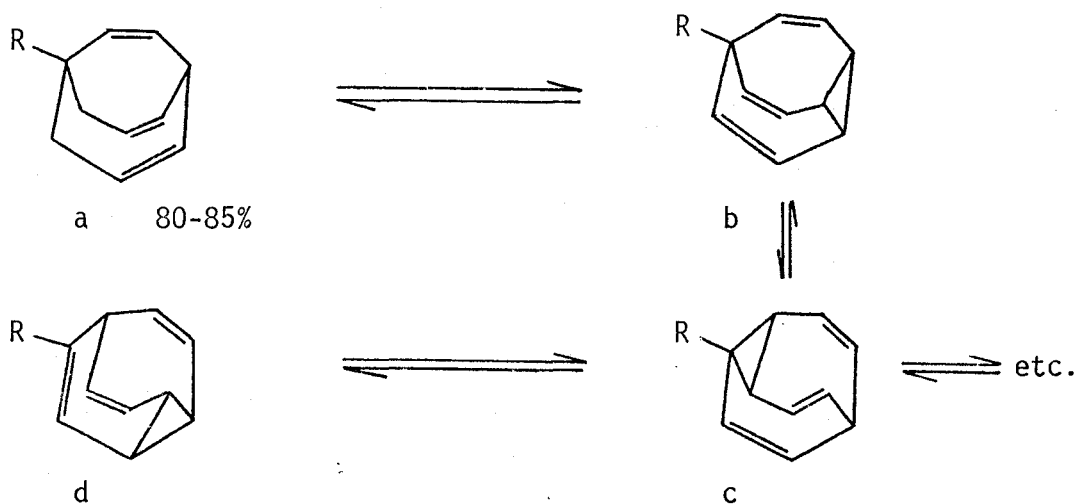
Fluorobullvalene 91 R=F was found to exist predominantly as the isomer "a" just as might be expected on the basis of the theoretical calculations of the related semibulvallene system.[44,58] However, determination of the composition of the equilibrium mixture in 91 R=F was

hampered by the availability of additional sites for the fluorine. More-over, all bridged homotropylidenes are only capable of monosubstitution on C-4 or C-8 and thus steric effects resulting from disubstitution can not be readily studied. Therefore the preparation of substituted 3,4-homotropylidenes which do not possess these disadvantages was attempted.

While the synthesis of 1,4-homotropylidenes was being attempted, several studies of the effect of a substituent on bridged homotropyl-idenes have been reported. The deuterium and methyl substituted bar-balones were investigated by Schleyer and co-workers.[114] They showed that deuterium was preferentially located on the sp^3 rather than on the cyclopropyl carbon. The reverse situation was found with the methyl substituted system in which the methyl group was largely located on the cyclopropyl carbon. It should be pointed out however, that the bridging carbonyl group could be attenuating or modifying the effects of these substituents.

| R = Me | 77% | 23% |
| R = D | 46% | 54% |
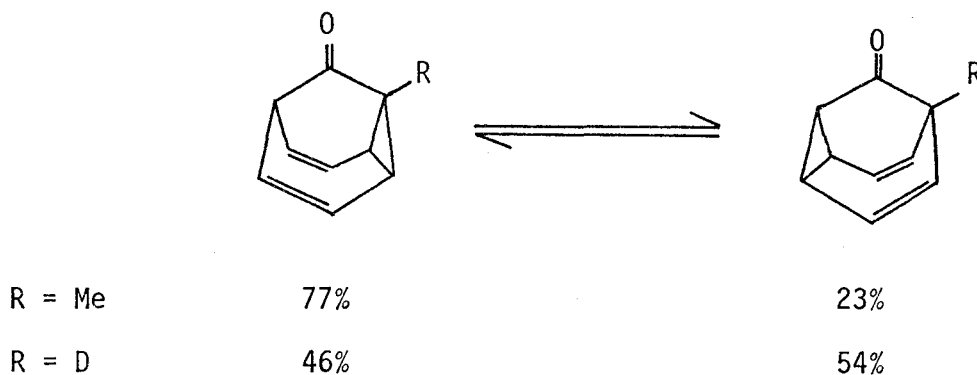
Another doubly degenerate system of this type, semibullvalene 95, has been extensively studied by Paquette and co-workers.[116] All the substituted compounds they were able to prepare existed predominantly as 95a.
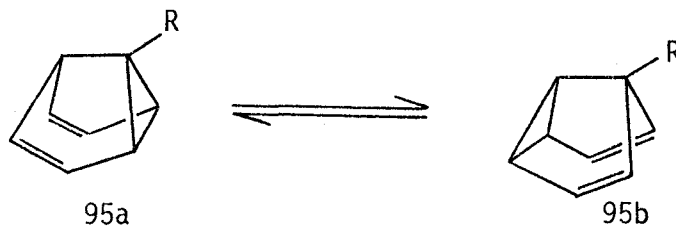
		95a		95b
R = Me		75%		23%
R = CH$_2$OMe		86%		14%
R = CH$_2$OH		54%		46%
R = Ph		95%		5%
R = CN		99%		1%

While the equilibrium position for the systems bearing electron-withdrawing substituents, such as Ph or CN, is that expected on the basis of Hoffmann's[44] and Dewar's[58] calculations the interpretation of the effect of alkyl substituents is much less simple. In its interaction with semibulvallene the methyl group would be expected to be a net electron donor[120] and to have a bond strengthening effect on the fused cyclopropane bond. For example, it has been observed that a methyl group bonded to a cyclopropane ring causes a shortening of the β and lengthening of the α cyclopropyl C-C bonds.[121] The results obtained with 95 do not seem to follow this pattern.

Semibulvallene is the only bridged homotropylidene which has been used for a systematic investigation of substituent effects. However the range of substituents studied so far is rather narrow and for example, it does not include any strongly electrondonating substituents. Furthermore, due to the considerable strain intrinsic to a semibulvalene molecule, 95 might not be the ideal model for a CHT/NCD system. Thus the synthesis of the substituted homotropylidenes still appears to be desirable.

Attempted Synthesis of Substituted 3,4-homotropylidenes

Three routes to substituted homotropylidenes have been investigated:

a) Addition of a carbene to cycloheptatriene.

b) Elimination of nitrogen from 9,10-diazatetracyclo [3.3.2.0^{2,4}.0^{6,8}]dec-9-ene.
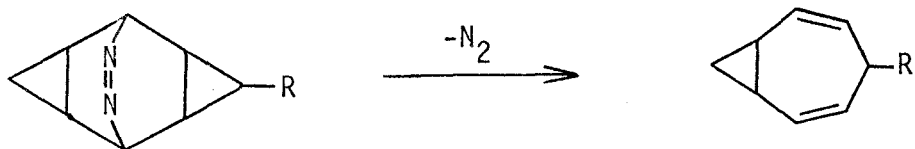
c) Introduction of a second double bond into substituted bicyclo[5.1.0]oct-2-ene.
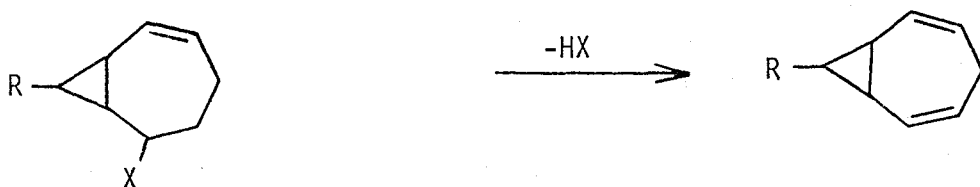
Work on each of these routes is discussed in separate sections.

ADDITION OF A CARBENE TO CYCLOHEPTATRIENE

The first reported synthesis of unsubstituted 3,4-homotropylidene involved the addition of :CH$_2$ to cycloheptatriene.[118] The reported yield of the desired product was low and this method involves a rather difficult separation of 3,4-homotropylidene from its 1,2- isomer.

The adoption of this method for the preparation of substituted

homotropylidenes could be achieved by the use of either a substituted
cycloheptatriene or a substituted carbene (or carbenoid). Some pre-
liminary experiments on both these routes were carried out.
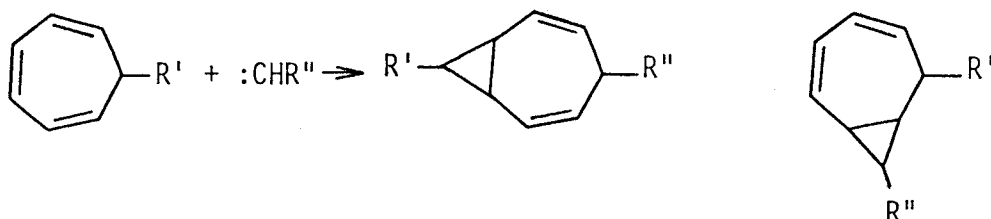
a.   R' = COOEt,   R" = H
b.   R' = H,   R" = COOEt

Simmons-Smith Reaction on 7-ethoxycarbonylcycloheptatriene

One useful method of converting an olefin into a cyclopropane
is the Simmons-Smith reaction.[122] This reaction is particularly suitable
for   alkenes which are flanked by a group which can function as a
Lewis base and coordinate with the attacking carbenoid species.[123]
However when this reaction was attempted with 7-ethoxycarbonylcyclohepta-
triene a whole range of products was obtained. The products were
separated by preparative vpc and tentatively identified on the basis of
their spectroscopic properties, Scheme 9. It is possible that a small
amount of the desired 3,4-homotropylidene was present in one of the
fractions, however it could not be successfully isolated.

It will be noted that the bis adduct 97 has been formulated as
arising from a norcaradiene precursor. Similar adducts have been re-
ported as products from the catalysed decomposition of ethyldiazoacetate
in benzene.[124] In view of the results described previously with the

Scheme 9:   Simmons-Smith reaction with 7-ethoxycarbonylcycloheptatriene

Lewis acid complexes of 35, it is possible that   similar copper or

zinc complexes are formed during these carbenoid reactions.

Addition of   :CHCOOEt to Cycloheptatriene

The copper catalysed reaction of ethyldiazocetate in cyclohepta-

triene, eq. 32 has been previously reported to give only one monoadduct,

namely 98.[125] This reaction was reinvestigated however, even though

monoadduct species were detected, it was not possible to isolate

them in a pure state and characterize them.

This seemingly simple approach to substituted 3,4-homotropyl-idenes was not further investigated.

ELIMINATION OF NITROGEN FROM 9,10-DIAZATETRACYCLO [3.3.2.0^{2,4}.0^{6,8}] DEC-10-ENE

The ready synthesis of compounds such as 78a, discussed in the previous chapter of this thesis, suggested that they might serve as a convenient precursor for substituted 3,4-homotropylidenes. Thus as is shown in Scheme 10, the addition of a further cyclopropane to 78a, foll-owed by hydrolysis, decarboxylation, oxidation and nitrogen elimination would be expected to yield 28. Several closely related synthesis of multi-cyclic systems have been reported.[108,116,126]
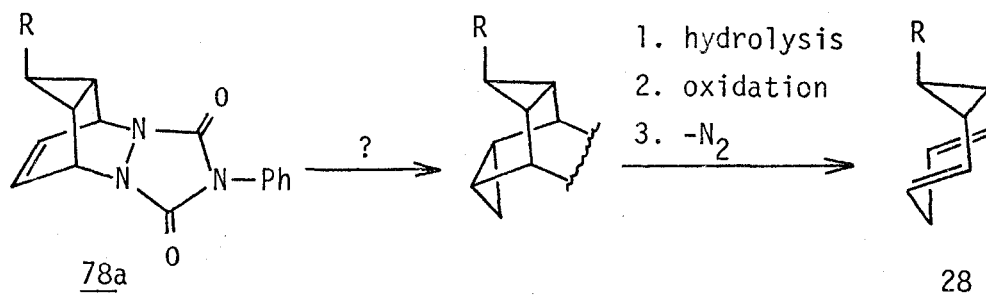
Scheme 10: Possible synthesis of 28

In spite of seemingly good literature precedence for such a synthetic route to 28, it did not prove possible to achieve the first stage of this sequence, namely the cyclopropylation of the double bond of 78a. Attempts to add a methylene using a Simmons-Smith procedure,[122]

to add :CHCOOEt by using ethyldiazoacetate,[127] and to add :CCl$_2$ using

Seyferth's Ph-Hg-CCl$_3$ reagent,[128] all failed. Similarly it was not

possible to induce diazomethane to undergo a 1,3-dipolar addition to

the double bond of 78a.[129]

One difficulty in working with 78a, was its very low solubility

which caused these attempted cyclopropylation reactions to be carried

out either in very dilute solutions or as heterogenous mixtures. In

order to circumvent this inconvenience, the preparation of the diester

99 was attempted, eq. 33.

(33)

R = COOEt
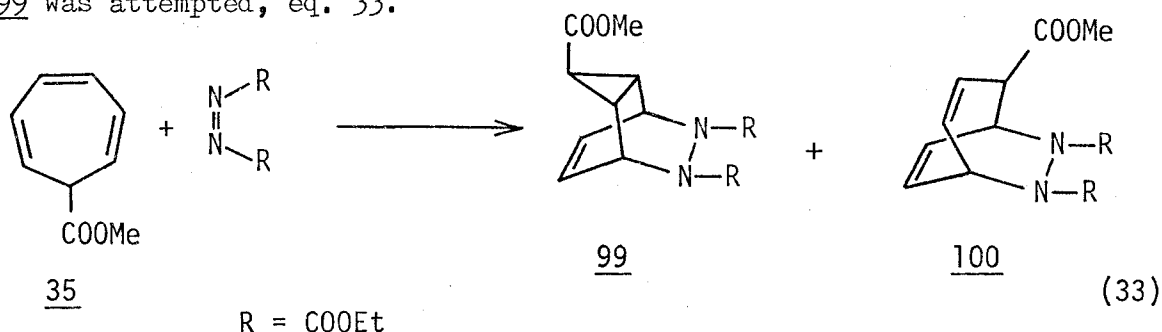
The reaction of 35 with diethylazodicarboxylate gave two com-

pounds, the adduct 99, derived from the norcaradiene form and the cyclo-

heptatriene adduct, 100. The ratio of the two products formed was found

to be dependent on the temperature at which the Diels-Alder reaction was

carried out. For example when the reaction was performed at 50° the ratio

of 99 to 100 was 1.7 : 1 however this ratio increased to 5.7:1 when the

reaction was allowed to proceed slowly at -5°. The products of this

reaction were separated by column chromatography. The tricyclic compound

99 was isolated in a pure form, however 100 appeared to be a mixture of

different stereoisomers, probably involving the ester group on the three

carbon bridge.

MeOOC H   H COOMe

N—COOEt   N—COOEt
N—COOEt   N—COOEt
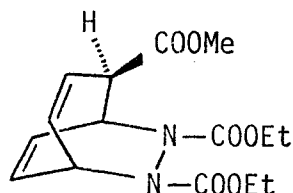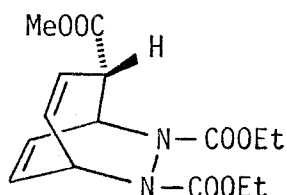
Temperature Dependence of the pmr Spectra of 99

When the pmr spectrum of 99 was recorded at +90° the absorptions
of all the protons, except those at C-1 and C-5, appeared as sharp
signals with a well-defined fine structure. Only one set of signals
was recorded for the two ethyl group under these conditions. In the pmr
spectrum obtained at +35° all the resonances except those of the methoxy
group, appeared to be broadened. Despite the limited solubility of 99 at
low temperatures, at -50° it would seem that two sets of signals corres-
ponding to two ethyl groups were present, Figure 8. This temperature
dependence of the pmr spectrum of 99 is similar to that observed for the
related 2,3-diazabicyclo[2.2.2]octanes, such as 101[130] and can reason-
ably be accounted for on the basis of the pyramidal inversion of the
ester group about the nitrogen atoms.

N-Me
N-Me
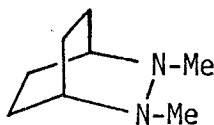
101

Reaction of 99 with Diazomethane

The 1,3-dipolar addition of diazomethane to 99 was attempted,
however, this compound again was found to be very resistant to this type
of reaction. Thus when 99 dissolved in ether was treated with a 10 fold
excess of diazomethane at -5° for one month, although the pmr spectrum
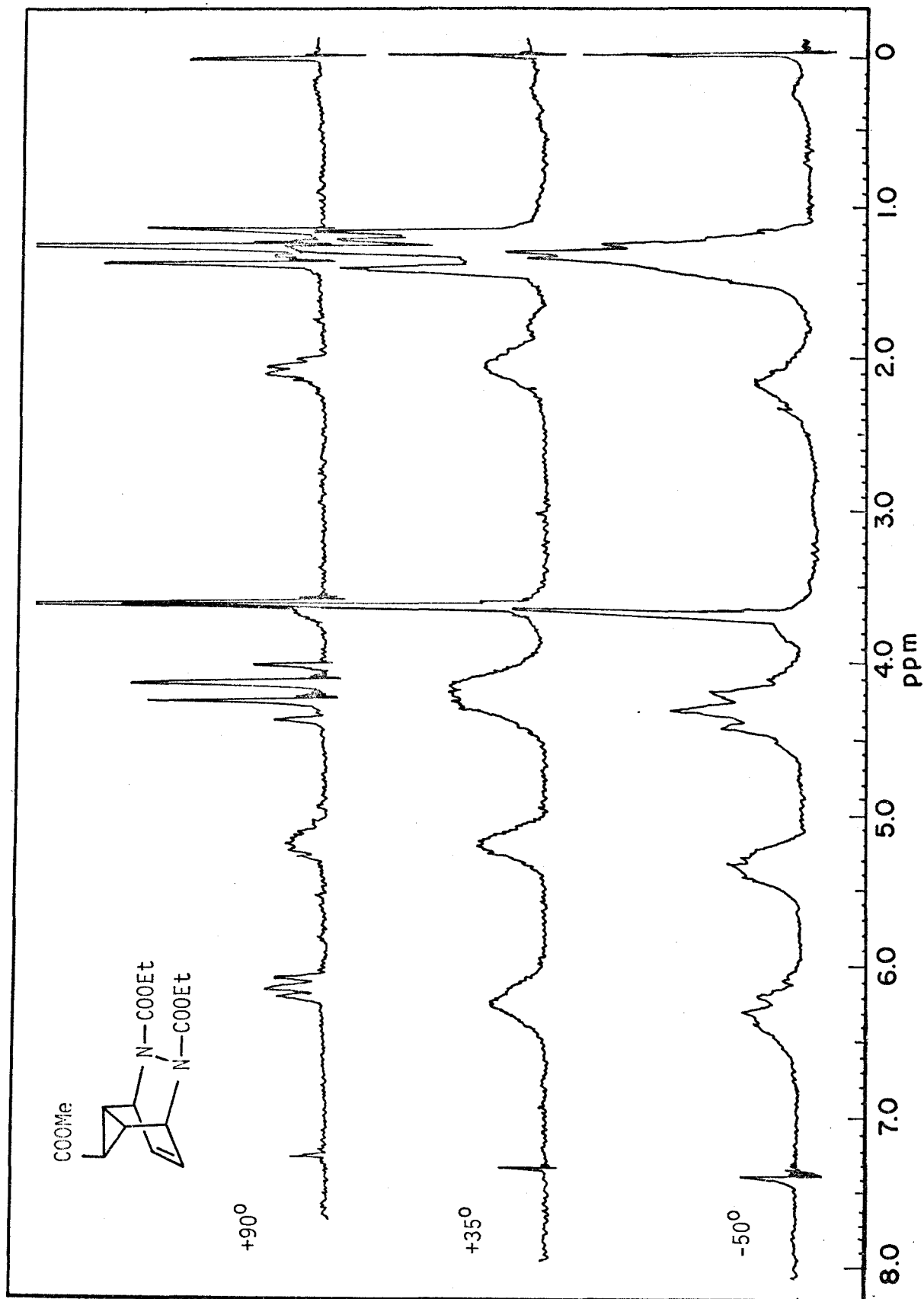
Figure 8:   Pmr spectrum of 99

indicated that the double bond of 99 had reacted, no adduct could be isolated. No significant amount of N_2 was developed when the intractable, honey-like product of this reaction was either heated[131,116] or irradiated.[126,108]

(34)

(35)
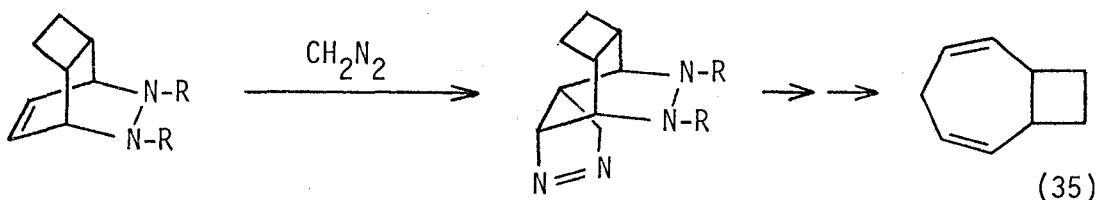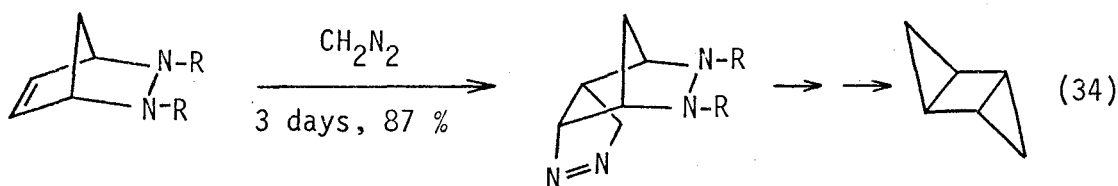
It is not clear why 78 and 99 seem to be so resistant to the addition of diazomethane, considering that the reactions of similar compounds, eq. 34[108] and eq. 35[126] have been reported to take place readily.

INTRODUCTION OF A SECOND DOUBLE BOND INTO SUBSTITUTED BICYCLO[5.1.0] OCT-2-ENES

Cyclohepta-2,4-dienones can be prepared by a variety of methods. The parent compound itself can be obtained from cycloheptatriene although the overall yields reported thus far are not very high.[132] 2,6,6-Trimethylcyclohepta-2,4-dienone 102, eucarvone, can be readily prepared from carvone[133] and this more readily available cycloheptadienone was used as a model compound in many of the subsequent reactions.

As shown in the Scheme 11, the conversion of a cyclohepta-2,4-diene into a 3,4-homotropylidene species formally requires but two steps. These are the conversion of the 2,3-double bond into a cyclopropane and

93
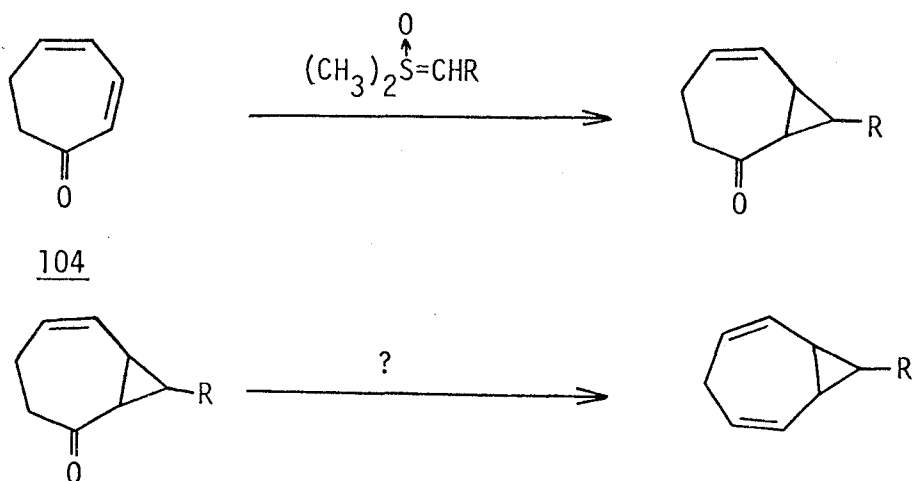
Scheme 11: Conversion of <u>86</u> into 3,4-homotropylidene

the subsequent replacement of the ketone function by a double bond.

Corey[134] has in fact shown that eucarvone, <u>102</u>, when treated with

$(CH_3)_2SOCH_2$ gives <u>103</u> eq. 36 and there would seem no reason why this

reaction could not be applied to other cycloheptadienones. Substituted

ylid reagents are available and it was thought that it should also be

possible to form a functionalized cyclopropane by a comparable reaction.

(36)

<u>102</u>   <u>103</u>
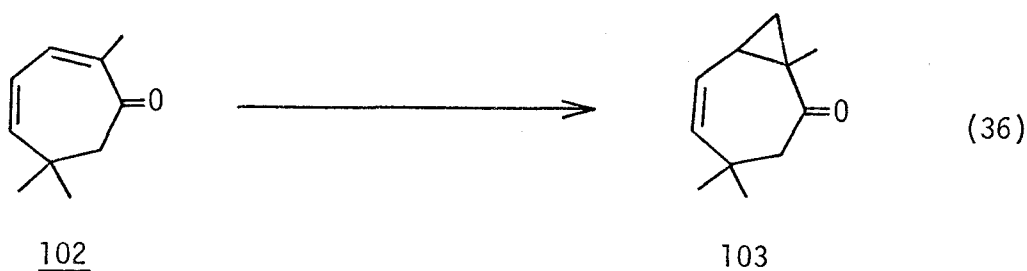
The Synthesis of 2,4-cycloheptadienone, <u>104</u>

The seemingly easiest route to this material is that shown in

Scheme 12. However, as was mentioned earlier, the overall yield of <u>104</u>

from cycloheptatriene, 3%, is not that good. It has been found that

minor changes in the reaction procedures can increase the overall yield

to some 11% and permit batches of several grams of cycloheptadienone

<u>104</u>   to   be   prepared at a time. The changes made are indicated

in Scheme 12 and in the experimental section.

a.	SeO_2, Radlick[135], 25%
b.	SeO_2, this work, 49%
a.	$LiAlH_4$, Schuster[136], 30%
b.	$Li(BuO)_3AlH$, Hine[132] 15%
c.	$LiAlH_4$, this work 44%
a.	$NaHCO_3$/MeOH, Hine[132] 80%
b.	NaOH, H_2O, EtOH
	this work 50%

<u>104</u>
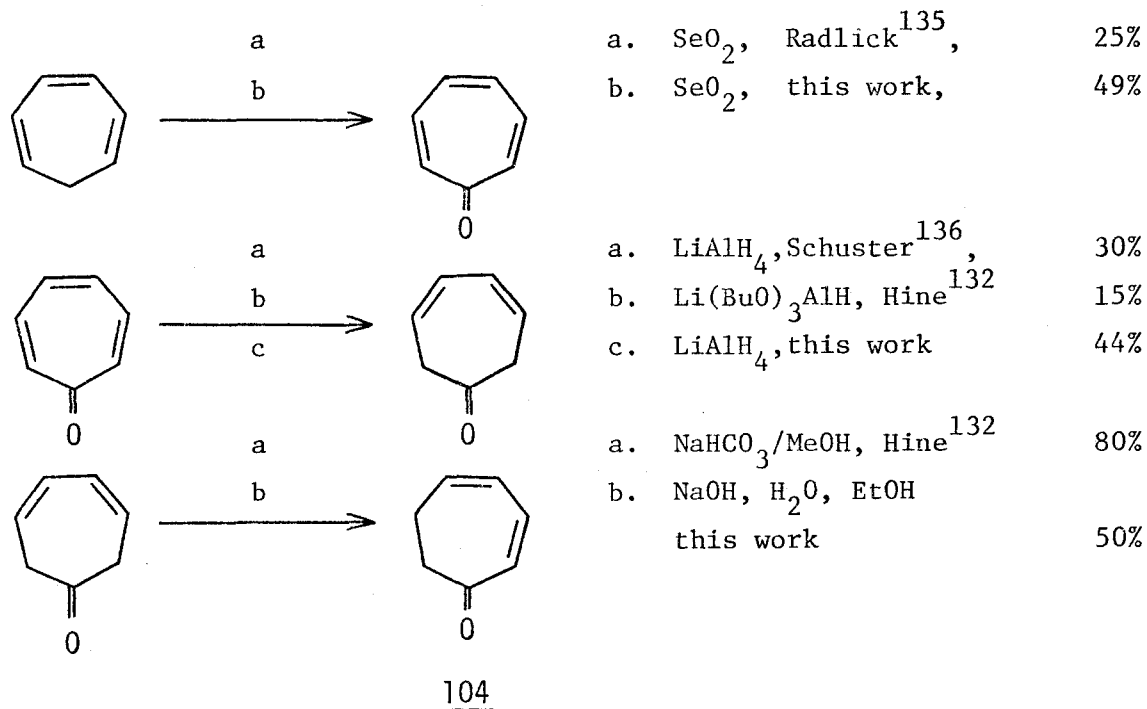
Scheme 12: Synthesis of 2,4-cycloheptadienone, <u>104</u>

Cyclopropylation of cycloheptadienones

The bicyclic ketone <u>103</u> was prepared from eucarvone using the

procedure described by Corey[134], eq. 36. A comparable reaction with the

parent compound <u>104</u> also resulted in the formation of a bicyclic ketone,

however <u>105</u> was in this case only a minor product, eq. 37.

$$(CH_3)_2\overset{O}{\overset{\uparrow}{S}}=CH_2$$

+ a dimer of <u>104</u>

(37)

<u>104</u>   <u>105</u>
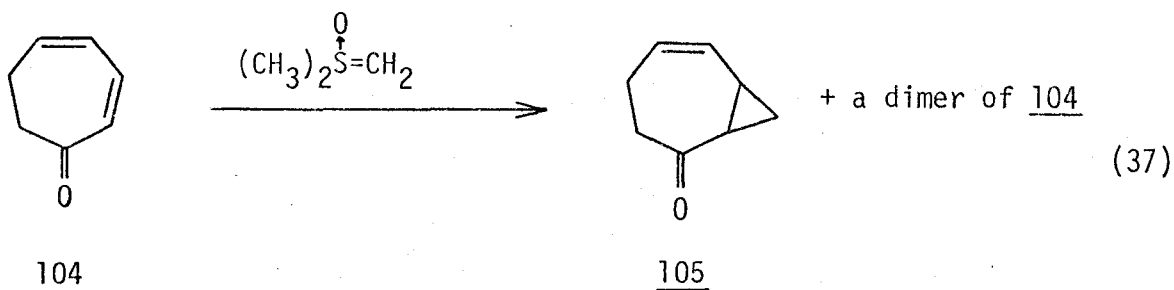
The main product of reaction eq. 37 was a colourless material with a molecular weight (m/e = 216.115) corresponding to a dimer of 104. The ratio of aliphatic to olefinic resonances in the pmr spectrum of this compound was found to be 3:1, and only one carbonyl absorption at 1709 cm^{-1} was observed in its ir spectrum. One structure compatible with these data is 106. The tricyclic dione 106 could be formed by two consecutive Michael additions[137] of 104 catalyzed by the strongly basic ylid, Scheme 13. The structure of this product was not rigorously established.
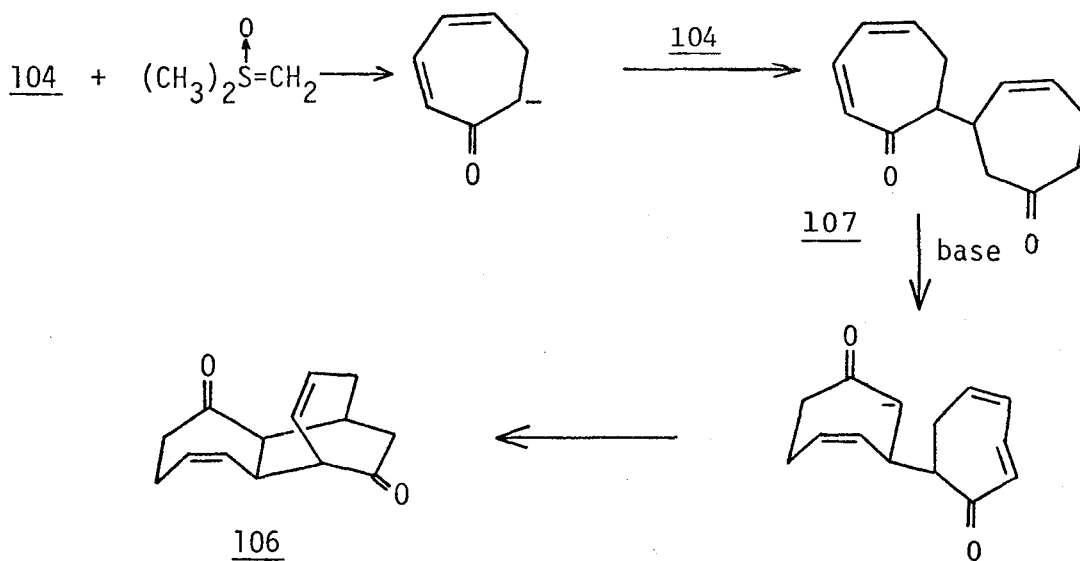
Scheme 13: Dimerization of 2,4-cycloheptadiene

A room temperature reaction of 104 with the resonance stabilized ylid 108[138] gave a 37% yield of two products, eq. 38 in ratio of 1:2.3. The two compounds were separated on an alumina column and further puri-fied by vpc.

$$\text{104} \quad + \quad (CH_3)_2\overset{\overset{O}{\uparrow}}{S}{=}CHCOOEt \quad \longrightarrow \quad 2 \;\; \text{monoadducts} \qquad (38)$$

104
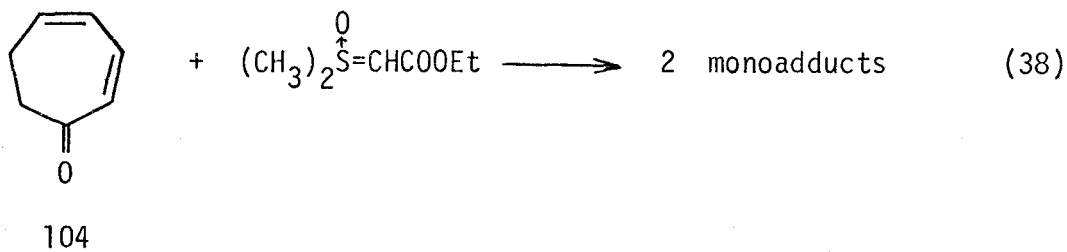
Although the addition of a $:CR_2$ element in the reaction of ylids with dienones is known to proceed preferably in the α,β position,[134] the formation of a bis adducts under more strenuous conditions[138] indicates that the γ,δ double bond is not completely inert. Thus the reaction of 104 with the ylid could possibly give four products; 109, 110, and two stereoisomers of 111.

109   110   111
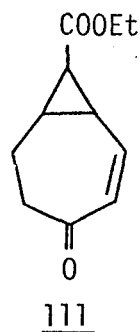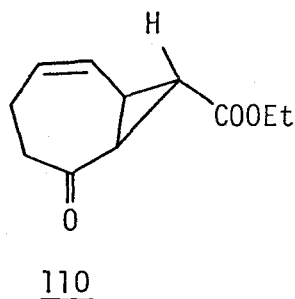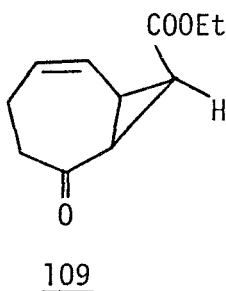
The solid compound with a shorter retention time was identified as a 2,3-addition product on the basis of its spectral properties. The uv spectrum of this compound, $\lambda_{max}^{MeOH}= 202$ nm, is not compatible with the structure 111 as α,β unsaturated ketones absorb typically around 230 nm.[139] The uv absorption maxima of α-cyclopropyl ketones has been found to depend on the geometry of the molecule. The reported values vary between 197 and 220 nm for the saturated systems,[140] while the introduction of a double bond substituent on the cyclopropane ring can cause a bathochromic effect of some 3-15 nm.[140,141]

The pmr spectrum of this product contained olefinic and aliphatic proton resonances in a relative amount of 2:7 in addition to the signals attributable to the ethoxy group. While the resonances of the β hydrogens of α,β unsaturated cyclic ketones typically occur at a considerably lower field than those of the α hydrogens[142], this addition product displayed only one narrow band in the olefinic region of the pmr spectrum.

The other product obtained was a liquid, the elementary analysis and the spectral data of which were consistent with both structures, 110 and 111.
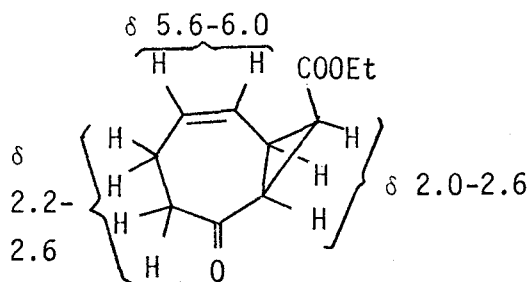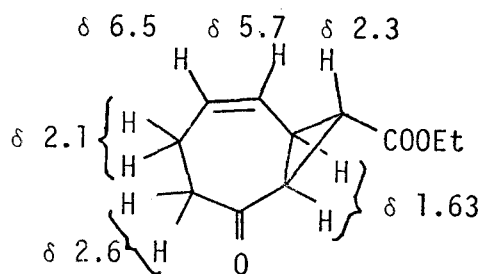
$J_{4,5}=2.8$ Hz

$J_{5,6}=12.0$ Hz

109   110

While it seems certain that the products of reaction eq. 38 are 109 and 110, determination of the stereochemistry at C-8 proved to be difficult. It is tentatively assumed that the larger fraction with the longer retention time, has the less crowded exo structure, 110.

Formally one would expect that two different isomers of 28 could be formed from 109 and 110. However the stereochemical identity of the two carbons residing in the plane of symmetry of the rapidly rearranging

system 28/29 would be lost, if the Cope rearrangement occured via both chair-like and boat-like transition states,[143,144] Scheme 14.
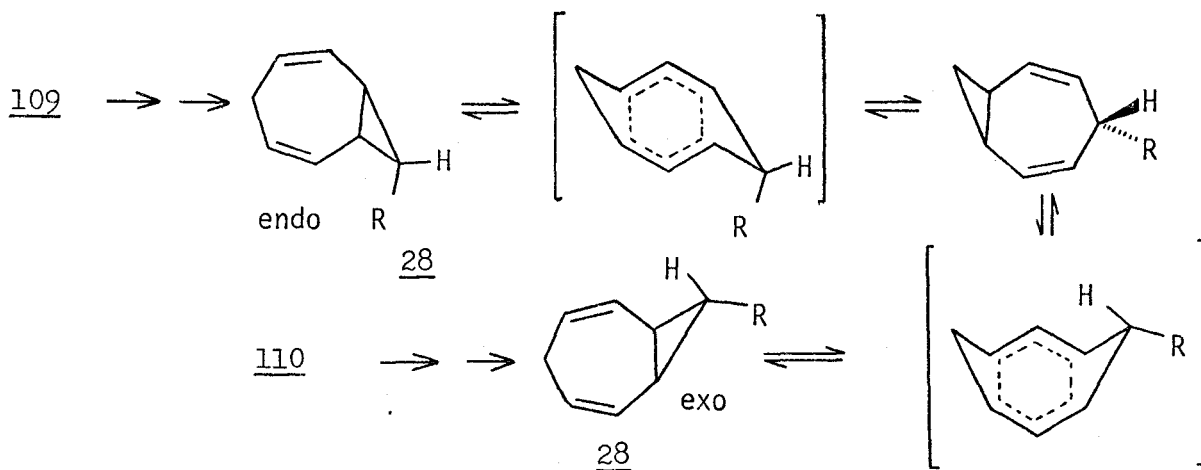
Scheme 14: Synthesis of 28 from 109 and 110

It was therefore expected that the mixture of both of the isomers, 109 and 110 could be used for preparation of 28.

Transformation of Carbonyl Function to a Double Bond

The number of different procedures described in the chemical literature for the introduction of a double bond into a molecule is immense and this perhaps testifies to the difficulties that can be encountered with this type of reaction. Basically, starting with a ketone function, there are some four different general types of reaction sequences that have been employed. These are:

a) Reduction to alcohol and an ionic type elimination of water or some other molecule after suitable derivatization of the alcohol.

b) Reduction to alcohol, formation of an ester or a related derivative, and a thermal, concerted elimination.

c) Reaction of the ketone with a hydrazine; its subsequent conversion to a diazo compound, elimination of nitrogen followed by a hydrogen shift to give the olefin.

d) Formation of an enol ester derivative from the ketone and appropriate cleavage of the enol ester group.

Each of the above mentioned routes has been investigated and the results of these studies are given in the subsequent sections of this chapter

Reduction to Alcohol, Ionic Elimination

1. Reduction

The carbonyl group of <u>103</u> has been previously reduced using lithium aluminium hydride.[150] Since this reagent would also reduce the ester group in compounds such as <u>109</u> and <u>110</u>, the reduction of the carbonyl group of these bicyclo[5.1.0]oct-5-en-2-ones was attempted with sodium borohydride. However, instead of formation of the alcohol in high yield as would be expected,[145] esters of boric acid were obtained as the principal products. Thus <u>103</u> on treatment with $NaBH_4$, gave a high yield of <u>113</u> Similarly the esters <u>109</u> and <u>110</u> were largely converted to boric esters on reaction with $NaBH_4$.

The formation of the esters of boric acid during the borohydride reduction of hindered ketones has been previously noted[117-119] and their hydrolysis has sometimes proved to be difficult.[116] It was found that the alcohol <u>112</u> could be liberated from the corresponding boric ester <u>113</u> by treating it with $MeOH/H^+$,[146] H_2O/H_3O^+,[147] or NH_4OH.[148] The last mode of reaction was found to be most convenient.

Alternatively <u>103</u> could be reduced with Li $(BuO)_3AlH$,[149] eq. 39.
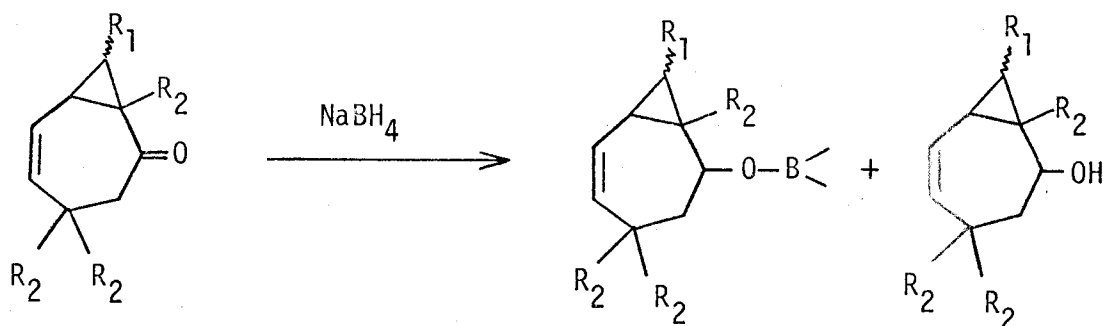
103		R$_1$ = H,	R$_2$ = Me	113	112
105		R$_1$ = H,	R$_2$ = H	114	116
109, 110		R$_1$ = COOEt,	R$_2$ = H	115	117

Since this reagent is normally unreactive towards ester groups under the conditions used, this procedure would also be expected to be suitable also for reduction of 109 and 110.

$$ \text{(39)} $$
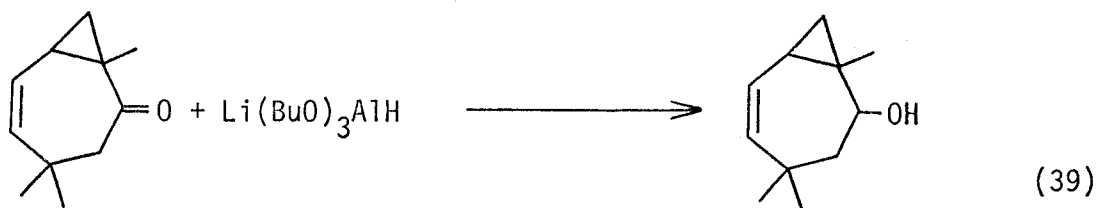
ii. Elimination

Bellamy and co-workers have recently reported that they were unable to dehydrate 112 by either direct or indirect methods.[150] For example treatment of 112 with P$_2$O$_5$ in benzene or with polyphosphoric acid or the pyrolysis of the corresponding acetate, were all reported to result in complete destruction of the bicyclic structure and formation of a number of products.[150] As the conditions of these reactions were rather strenuous, some milder reactions were attempted in this work.

The direct dehydration of 112 was attempted by injection of the alcohol on a gas chromatographic column filled with neutral alumina

under a variety of conditions (temperature, length of column, flow rate). The product of the reaction was invariably a mixture of benzenoid compounds which was not further analyzed.

In an attempt to introduce a better leaving group, 112 was reacted with methane sulfonylchloride (MsCl) in 2,6-lutidine using similar conditions to those used with other alcohols.[151] The product of this reaction was decomposed with sodium ethoxide, or with lutidine at 70°. A major reorganization of the compound ocurred in both cases, leading to at least 16 products none of which constituted more than 25% of the mixture. A similar result would seem to have been obtained by Bellamy upon reacting 112 with POCl$_3$ in pyridine.[150]
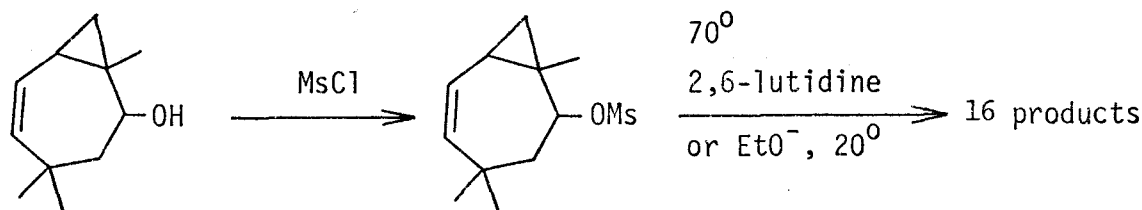
A very efficient dehydrating agent, bis(hexafluoro-2-phenyl-2-propyloxy) diphenylsulfurane, 118, was recently developed by Martin.[152] Sulfurane 118 was reported to dehydrate secondary alcohols in seconds at room temperature. Moreover it was reported that while the acid catalyzed dehydration of 119 led only to ring opened products,[153] 31% of 120 was formed on reacting 119 with the sulfurane 118, eq. 40.[152]

The addition of 118 to a chloroform solution of 112 caused an immediate reaction as was shown by the drastic change in the pmr spectrum of the solution. However the vpc analysis of the products obtained once more indicated that many products were formed. Five major fractions were

$$119 \qquad + \qquad \underset{\substack{|\\CF_3}}{\overset{\substack{CF_3\\|}}{Ph-C}} - O - \underset{\substack{|\\Ph}}{\overset{\substack{Ph\\|}}{S}} - O - \underset{\substack{|\\CF_3}}{\overset{\substack{CF_3\\|}}{C}} - Ph \quad \longrightarrow \quad 120 \qquad (40)$$

<u>119</u>   <u>118</u>   <u>120</u>
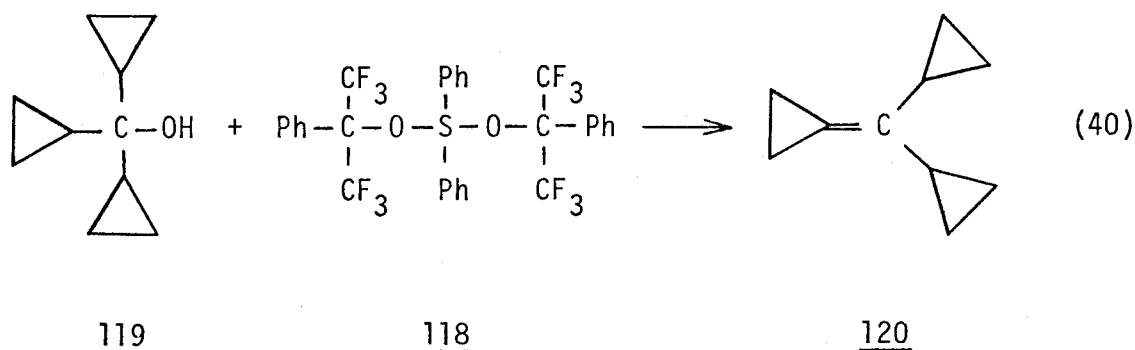
collected and were shown to be hexafluoro-2-phenyl-2-propanol, <u>121</u>, di-phenylsulfoxide, <u>122</u>, and three different hydrocarbons. The mass spectra of these hydrocarbons indicated that they were isomers with a molecular formula corresponding to $C_{11}H_{18}$. The pmr spectra of these compounds were incompatible with the structure of trimethyl-3,4-homotropylidene, <u>123</u>, and the materials were not further identified.

$$\text{—OH} \quad + \quad \underline{118} \quad \longrightarrow \quad \underset{\substack{|\\CF_3}}{\overset{\substack{CF_3\\|}}{Ph-C}}-OH \quad + \quad \underset{\substack{|\\Ph}}{\overset{\substack{Ph\\|}}{S}}=O \quad +$$

3 isomers $C_{11}H_{16}$ +

11 other products
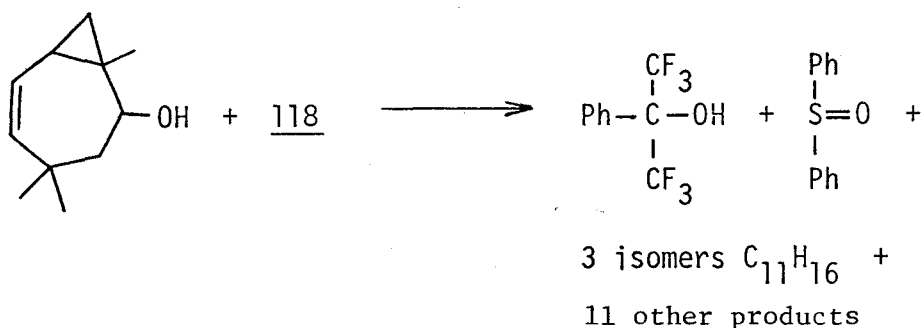
Dehydration of <u>112</u> was also attempted by treating it with SO_2Cl_2 in pyridine,[154] with tosylchloride in pyridine[155] and by heating it with iodine.[156] None of these reactions led to isolation of <u>123</u>.

Pyrolysis of Esters of 112

In an attempt to avoid the formation of the seemingly rearrange-
ment prone cationic intermediates, the dehydration of 112 was attempted
by the pyrolysis of some of its ester derivatives. Eliminations of this
type are generally considered to occur in a concerted fashion and
structural changes in the rest of molecule are less likely to be en-
countered.[157]

The pyrolysis of the acetate of 112 has been recently attempted
by Bellamy.[150] Neither this reaction, not the pyrolysis of corresponding
boric ester[158] investigated in this work, led to the formation of 123.
The temperature required for pyrolysis of esters depends on the nature
of the ester group. For example while the acetate of 112 was pyrolysed
at 460°,[150] the pyrolysis of xanthates (Chugayev reaction) typically
occurs at 100-200°.[157] As it was expected that 123 would survive this
temperature, the Chugayev reaction was attempted with 112.

124
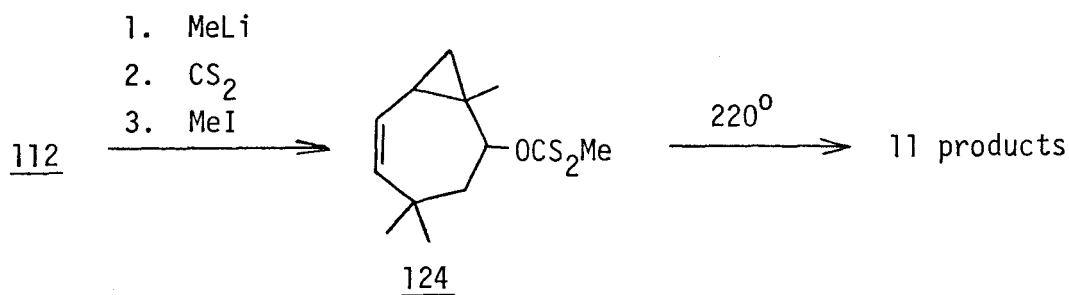
Xanthate 124 was prepared from 112 and purified by distillation
at reduced pressure. The thermal decomposition of 124 did not take place
until it was heated to 220° and then a mixture of some 11 products was
obtained. Three major constituents of the reaction mixture were isolated
but neither of these had pmr spectrum compatible with the structure 123.

Scheme 15 summarizes all the types of dehydration attempted.

Ionic eliminations:

1. Al_2O_3 150-250°

2. SO_2Cl_2/pyridine

3. TsCl/pyridine

4. MsCl/pyridine

5. Sulfurane 118 reaction

6. I_2,

7. polyphosphoric acid

8. P_2O_5/benzene

9. $POCl_3$/pyridine

Concerted eliminations:

10. xanthate pyrolysis

11. boric ester pyrolysis

12. acetate pyrolysis

112   reactions 1-6,10 and 11, this work   123
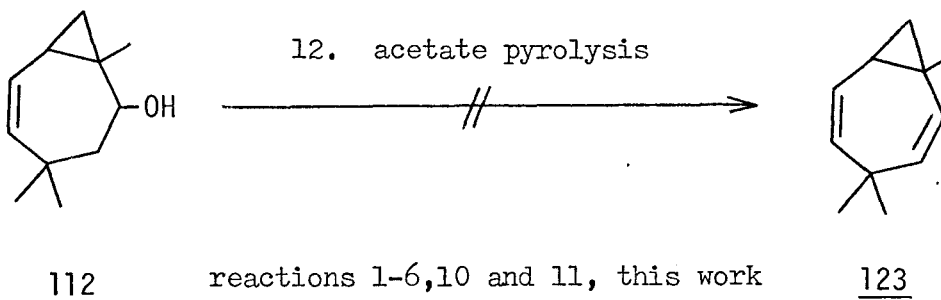
reactions 7-9 and 12 Bellamy [150]

Scheme 15: Attempted dehydration of 112.

Fragmentation of 6-diazo-4,4,7-trimethylbicyclo[5.1.0]oct-2-ene

The difficulties encountered with the dehydration of 112 stimulated

the investigation of alternative routes for transformation of a ketone

function in a double bond. In one such alternative procedure, the

ketone is first converted into a tosylhydrazone and the sodium salt of

the latter is then thermally decomposed to yield, after liberation of

nitrogen, the desired olefin.[159-161] This reaction probably involves

the intermediacy of a carbene[159] or a carbanion[160,161] rather than a

rearrangement prone carbonium ion and it seems to be suitable for cyclo-

propyl ketones. For example, vinylcyclopropane was prepared in a good

yield from the methyl vinyl ketone using this procedure,[160] eq. 41

$$\text{(image: cyclopropyl methyl ketone)} \quad \longrightarrow \quad \text{(image: vinylcyclopropane)} \qquad (41)$$
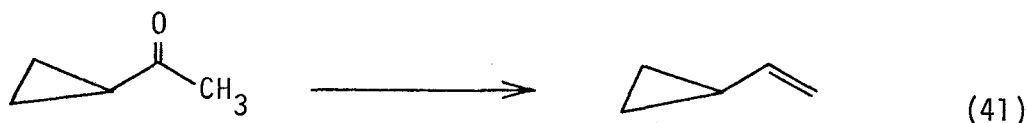
Tosylhydrazone 125 was prepared by reaction of 102 with a 10% excess of

p-toluenesulfonylhydrazide. This hydrazone, 125, was reacted with NaH

in refluxing benzene to give a single product which was shown to be the

acetylene 126. The structure of this new product was assigned on the

basis of its spectral data (ir, uv, high resolution mass spec., single

and double irradiation pmr and cmr experiments) which are given in full

in the experimental section.
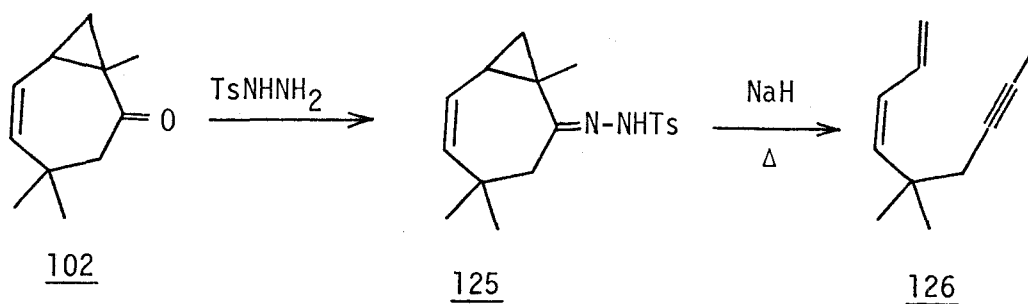
In a parallel reaction, the tosylhydrazone 127 prepared from

104 was heated at reduced pressure with NaH in refluxing parafin and the

single volatile product was condensed in a cold trap. Again an acetylene

(128) was the only product. The identity of 128 was established from its

spectroscopic data and by its hydrogenation to give a product whose ir

spectrum and vpc retention times on two different columns were identical

with those of n-octane.

104   127   128
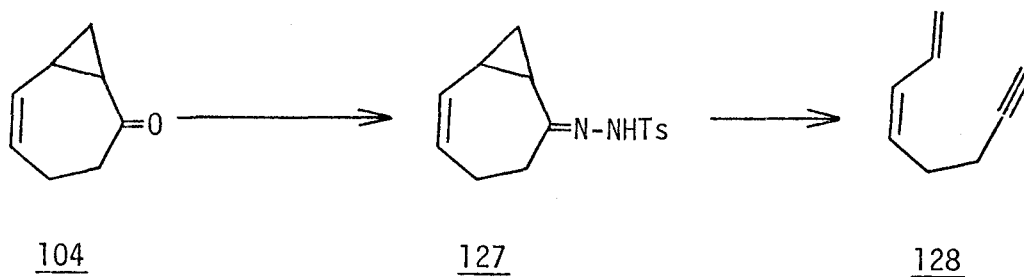
Cleavage of the Enol Ester Group

A simple two step procedure for preparation of olefins from

ketones was developed by Ireland.[162] In this method the ketone is first

converted to an enol ester of tetramethylphosphorodiamic acid (TMPD) and

the ester group is then removed by a reduction with dissolving metal in

liquid amine or ammonia, to give a high yield of the olefin.[162]

In the analogy with Ireland's[162] method, the enolate 129 was pre-

pared by reacting 102 with $(iPr)_2NLi$ and immediately reacted with tetra-

methyldiamidophosphorochloridate, 130. The product of this reaction was

a white solid, the pmr spectrum of which was consistent with the struc-

ture 131. The crude material was dried and without further purification

treated with an excess of Li in liquid ammonia.

102 $\xrightarrow{(iPr)_2NLi}$ $\xrightarrow[130]{ClPO[N(Me)_2]_2}$

129   131
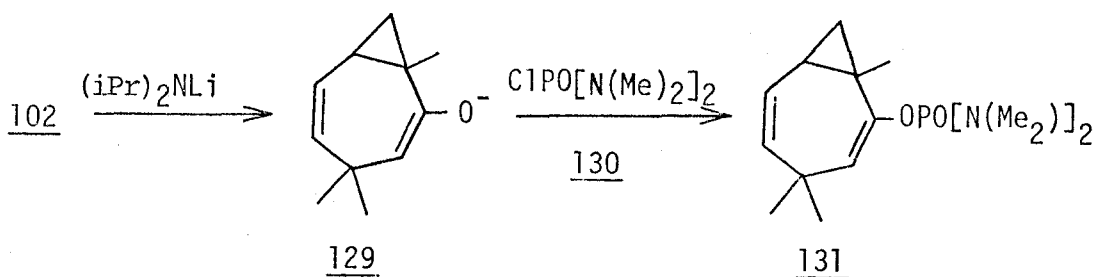
The vpc analysis of the reduction product revealed that it was composed mainly (95%) of two components with a similar retention time. These major constituents were separated by preparative vpc and investigated by spectroscopic methods. The pmr spectrum of each one of these compounds contained a complex resonance between δ 0.9 and 2.2 and a signal of smaller area between δ 5.0 and 6.0. Integration of the pmr spectra revealed that the ratio of aliphatic to olefinic resonances was approximately 15:1 and 8.6:1 respectively. A molecular ion m/e = 150.1408, corresponding to a molecular formula of $C_{11}H_{18}$ was found in the high resolution mass spectrum of both of these compounds.
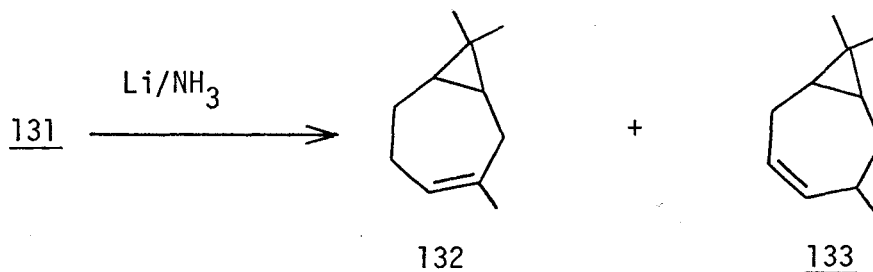
While the identity of the last two compounds has not been definitely established, structures such as 132 or 133 are possible. It is clear that the Birch reduction not only removed the HMPD group, but also saturated one of the double bonds of 123, which possibly occured as an intermediate. As isolated double bonds are not normally reduced under these reaction conditions[107] it is possible that base catalysed isomerization of the double bonds is occurring to give a conjugated diene.
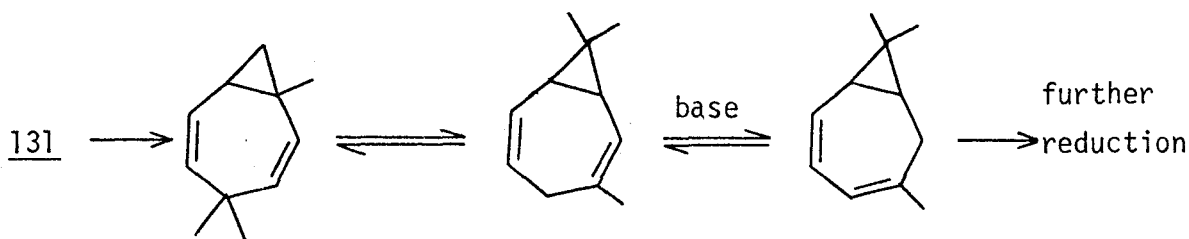
Conclusion

The plethora of products encountered in these attempted deyhdrations that involved cationic intermediates, probably results from the adjacent vinylcyclopropyl system. Opening of the cyclopropane would not only relieve the strain energy inherent in this three-membered ring[164] but would also lead to a relatively stable allyl cation, 134.

134
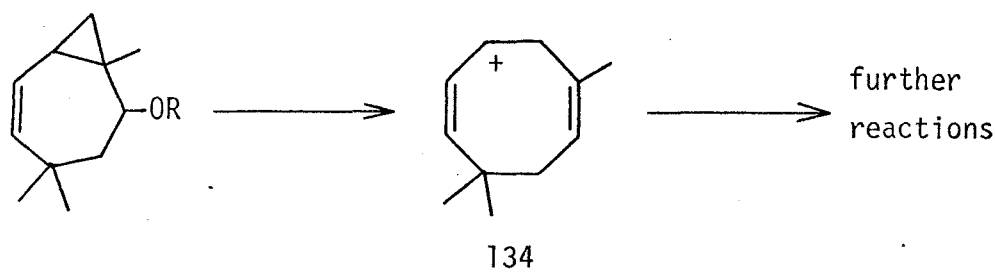
The structural features of the derivatives of 112 mentioned above possibly cause the ester pyrolysis reaction to proceed by a polar mechanism. For example, even though the pyrolysis of xanthates is usually assumed to be a concerted process with a six-membered transition state, 135 being involved, eq. 42, a polar mechanism, eq. 43, is also conceivable. This might be especially favoured, if it is enhanced by release of the strain energy of the cyclopropyl ring and by the stability of the carbonium ion formed in the process.

135
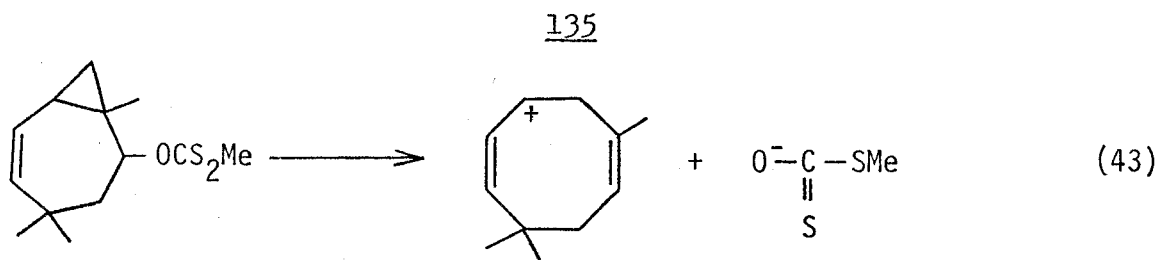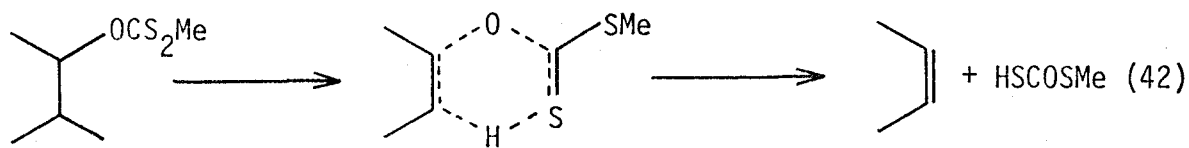
The thermal decomposition of tosylhydrazone salts usually gives olefins as the major products,[160,161] however formation of acetylenes has been reported in the case of α-oxiranyl and certain α-cyclopropyl-tosylhydrazones.[163] For example, the hydrazone 136 decomposes to a mixture of the olefin 137 and acetylene 138.[159]

COOEt

136 ⟶ COOEt

137 + 138
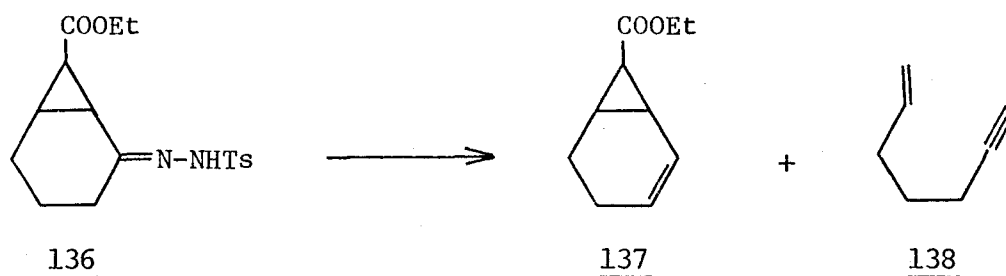
The difference in behaviour of 136 and the hydrazones 125 and 127 could be caused by the stabilizing effect of the vinyl group on the anionic intermediate formed on opening of the cyclopropane ring of the latter compounds.

127 $\xrightarrow[{- \text{Ts}^-}]{\text{base}}$ N=N ⟷ N≡N

138 $\xleftarrow{- N_2}$ N≡N
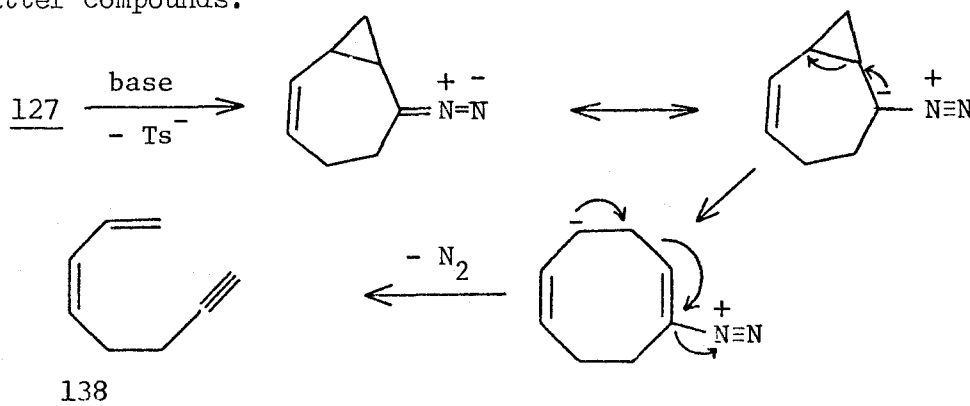
It is interesting to note that a 3,4-homotropylidene was actually prepared by the last route attempted, the enol ester cleavage reaction. The enol ester 131 is in fact 3,4-homotropylidene and should be capable of undergoing a valence tautomerism, eq. 44.

OHMPD   OHMPD

(equation structures)   (44)
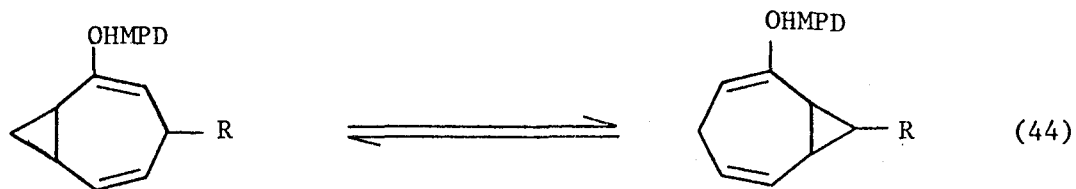
Although the resonances attributable to the ester function cover

a large part of the pmr spectra of 131 and render this particular type

of ester unsuitable for variable temperature pmr studies, it should be

possible to form some simpler ester derivatives. As a substituent on the

central carbon of a homotropylidene should not affect the position of the

equilibrium between the two possible valence tautomers, perhaps further

work in this area might be directed towards the preparation of such

derivatives as the enolacetates or enol ethers of 129.

CHAPTER IV

DIAMAGNETIC SUSCEPTIBILITY MEASUREMENTS OF SOME

CYCLOHEPTATRIENES AND A NORCARADIENE

As was mentioned in Chapter 1 of this thesis, Doering originally

suggested that cycloheptatriene and norcaradiene were but two resonance

forms of a single homoaromatic molecule.[5] Although such a structural

representation was subsequently rejected in the light of evidence which

demonstrated that these two molecules were valence tautomers, it is still

possible that each individual tautomer could possess some homoaromatic

delocalization.

Before discussing the existing evidence regarding the possible

aromaticity of these systems, it is advisable to review carefully what

is meant by this term. While there is no common agreement about the

definitions of the terms aromatic or aromaticity, it is generally recog-

nized that this property is somehow related to the thermodynamic stability

of a molecule and its ability to sustain an induced diamagnetic ring cur-

rent. This latter phenomenon has been used by several authors as a basis

for a definition of aromaticity. For example Garratt[165] would define an

aromatic molecule as being -

"a cyclic system which exhibits a diamagnetic ring

current and in which all the ring atoms are in-

volved in a single conjugated system."

Inextricably linked to the problem of the definition of aromatic

character, is also the problem of establishment of criteria for both its

111

presence and also its importance in a molecule. Suggested criteria include reactivity, thermodynamic stability, various spectroscopic properties, bond lengths, and the presence of an induced diamagnetic ring current when the molecule in question is placed in a magnetic field.[166] As most of these criteria are dependent upon a comparison of the properties of the molecule with a "wisely chosen non-aromatic molecule"[167], frequently the pronouncement of a compound as being aromatic is a highly subjective thing. One reason that a definition based on an induced magnetic ring current would seem to be gaining increased favour among organic chemists is that it provides a physical property which can be experimentally determined. Indeed Jackman[167] has gone one stage further in the definition of aromaticity in suggesting that the magnitude of the induced diamagnetic ring current is a measure of the degree of aromaticity of a molecule.

It has been suggested that the presence and magnitude of an induced diamagnetic ring current can be evaluated from proton magnetic resonance experiments by an analysis of the chemical shifts of the resonances of various, appropriately placed nuclei.[167] This is difficult to do however, as once more model compounds are required. Such a procedure for example, is used in the Chapter 2 of this thesis and the success of an argument of this type is only good as the model compounds chosen. In this present chapter the question of the aromaticity of cycloheptatriene and norcaradiene is reexamined using a technique which enables the diamagnetic susceptibilities of these compounds to be measured directly.

Earlier in this thesis it was proposed that the zwitterions _37_ and _39_ were aromatic molecules and that they were capable of sustaining

an induced diamagnetic ring current. It was suggested that the aromatic

character of these zwitterions, which derives from a mixing of the

molecular orbitals of the diene and cyclopropyl moieties, was enhanced by

the presence of a π electron accepting C-7 susbtituent. It is interesting

to examine the possible aromaticity of some neutral norcaradienes which do

not have strongly electron withdrawing substituents on C-7.

In 1963 Vogel and Günther reported the synthesis of norcaradiene 12

the bicyclic form of which is stabilized by the three carbon bridge be-

tween C-1 and C-6.[28a] On the basis of an analysis of its pmr spectrum,

these authors concluded that 12 is not an aromatic molecule. They pro-

posed however that the $Co(CO)_3$ complex of 12, 139,was aromatic.[168] The

upfield positions of the resonances of the bridge protons, and the down-

field position of the resonances of olefinic protons in 139 were assumed

to be at least partially caused by a ring current induced in the six

membered ring. This rationalization contains one obvious discrepancy.

The resonances of both of the two methylene bridge protons of 12 moved

upfield on complexation of 12 to give 139 by about the same amount

(1.6 ppm). As was pointed out earlier (Table 6)   semiempirical cal-

culations indicate that the endo proton is expected to be shielded by the

ring current of such a six membered ring, however the same type of

calculations[86] reveal that the exo-proton should be little affected.

The equal difference in the chemical shifts of the two bridge protons of

12 ($\delta_{ex} - \delta_{en}$ = 1.66 ppm) and 139 ($\delta_{ex} - \delta_{en}$ = 1.61 ppm) seems to

indicate that no change in the degree of aromaticity has in fact

occured upon complexation of 12. The upfield shift of the resonances of

both of the methylene protons of 139 as compared to 12 may well be caused

by the different distribution of the electron density in the chromium complex 139 and in the free ligand 12. The question of the aromaticity of these compounds can not be considered to be resolved.

The geometry of the cycloheptatriene molecule was discussed earlier and it was concluded that the compound exists in a boat form. Despite its nonplanar conformation, some evidence for the homoaromaticity of this compound has been obtained. For example the resonance energy of 1, determined by comparison of the heats of hydrogenation of 1 and 1,3-cycloheptadiene, is 7 Kcal/mol., about 20% of that of benzene.[169] The diamagnetic susceptibility of 1[170] and more recently the effect of 1 as a solvent on the chemical shift of a solute,[171] also seem to indicate the presence of an induced diamagnetic ring current in a molecule of

As mentioned in Chapter 2, there is a striking difference in the chemical shifts of the C-7 proton of 35 and the C-3 proton of 44. Examination of these chemical shifts reveals, that the "normal" value is that found for 44, while the resonance of the C-7 proton of 35 appears to be at an unexpectedly high field. For example, the value of the chemical shift of the proton attached to a tertiary carbon substituted with two vinyl groups and one ester function can be calculated from Schoolery's equation[172] as δ 4.4.

H   δ 2.48
COOMe

35

H   δ 4.23
COOMe
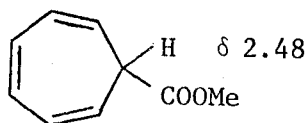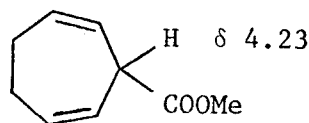
44

It could be argued that the high field position of C-7 proton resonance of 35 is caused by the magnetic anisotropy of the C-3, C-4 double bond in the boat conformation 35a . However using the results of calculation of Tillieu[83] and Pople[84] for the long range shielding of a double bond, the resulting shielding effect on the C-7 proton of 35 is found to be less than 0.2 ppm.

Alternatively the position of the C-7 proton resonance of 35 could be explained in terms of a deshielding caused by an induced ring current in 35.

35a

35b
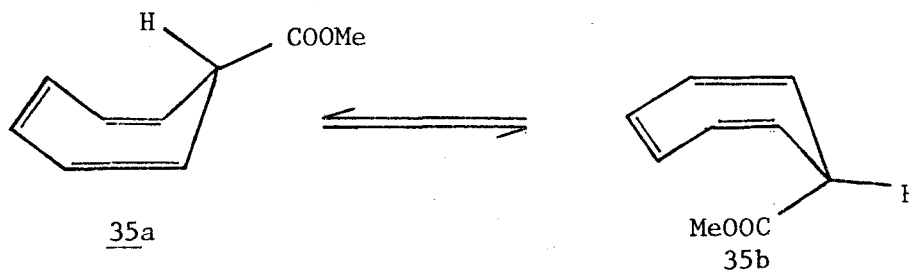
Measurement of Diamagnetic Susceptibility Exaltation

The diamagnetic susceptibility of a compound may be readily determined using a two-compartment nmr tube and a high resolution nmr spectrometer.[173, 174]   In order to determine whether the susceptibility includes a contribution from the induced ring current, it is necessary to evaluate the expected susceptibility in the absence of any ring current. Following the early work of Pascal,[175] it has been shown that the molar magnetic susceptibilities of organic compounds are approximately additive functions of their constituent groups and several systems have been deviced for estimation of susceptibilities based on this fact. While the molar susceptibilities, $\chi_{M'}$, so estimated are usually very close to the

measured susceptibility, χ_M , for non-aromatic compounds, benzenoid and other aromatic compounds exhibit somewhat larger susceptibilities than those predicted using an incremental system. The difference in the calculated and measured susceptibilities has been defined as the diamagnetic susceptibility exaltation Λ .[176] The presence of a diamagnetic susceptibility exaltation can be taken as a criterion of aromaticity and the magnitude of the exaltation can be related to the degree of the delocalization within the molecule.[170]

$$\Lambda = \chi_M - \chi_M{}'$$

A series of cycloheptatrienes and related compounds were prepared and their volume magnetic susceptibilities κ were determined using the Douglass and Fratiello method.[173] The densities of the investigated compounds were determined at the same temperature as that measured in the probe of the nmr instrument (36°). From the experimentally measured separations, densities and from molecular weights of the compounds, the diamagnetic susceptibilities per gram, χ , and molar diamagnetic susceptibilities, $\chi_M{}'$ were calculated. This procedure is illustrated for example with cycloheptatriene: The calibration of the reference assembly with eight standard solvents (see the Experimental Section for details) gave a calibration equation for volume magnetic susceptibility, κ , and reference peak separation, n (Hz): $10^6 . \kappa = 0.008655 . n + 0.2314$

Measured separation (Fig. 8), n = 39.35 Hz

Measured density (35°), $\rho = 0.8743$ g/cm^3

$\kappa = (0.008655 \times 39.35 + 0.2314) . 10^{-6} = 0.572 . 10^{-6}$

$$\chi = \kappa/\rho = 0.572/0.8743 = 0.6540 \times 10^{-6} \text{ cm}^3/\text{g}$$

$$\chi_M = \chi \cdot M = 0.6540 \times 92.14 = 60.2 \times 10^{-6} \text{ cm}^3/\text{mol}.$$

The pertinent data for all the other compounds are compiled in Table 11.

The calculated diamagnetic susceptibilities were obtained using the semiempirical increment system of Haberditzl.[177] A typical calculation for cycloheptatriene is shown in Table 12.

Table 12: Calculation of χ_M of cycloheptatriene:

element	No. of elements	increment	sum
C	7	0.15	1.05
$C_2^* - H$	6	3.2	19.2
$C^* - C^*$	5	2.4	12.0
$C^* - C$	2	2.6	5.2
$C_2 \, \pi \, C_2$	3	2.2	6.6
$C_2 - H$	2	3.8	<u>7.6</u>
	χ_M (cycloheptatriene)		$= 51.7 \text{ cm}^3/\text{mol}.$

*indicates sp^2 hybridization; subscript represents the number of atoms (other than H) attached directly to the carbon atom; π indicate a π bond; the increments have units of cm^3/mol.

Some difficulties were encountered in calculation of χ_M, for 7-cyanocycloheptatriene, since the increment for the $C \equiv N$ bond has not been reported. Using the reported diamagnetic susceptibilities of

Table 11: Separations, densities, mol. weights, and experimentally determined diamagnetic susceptibilities

Compound		n (Hz)	ρ (g/cm^3)	mol. weight (g/mol.)	$\kappa \cdot 10^{-6}$	$\chi \cdot 10^{-6}$ (cm^3/g)	$\chi_M \cdot 10^{-6}$ (cm^3/mol.)
Cycloheptatriene[a]	1	39.35	0.8743	92.14	0.572	0.654	60.3
7-methoxycarbonylcycloheptatriene[c]	35	10.90	1.0419	150.12	0.606	0.581	87.3
7-methylcycloheptatriene[b]	140	102.93	0.8432	106.17	0.597	0.709	75.2
7-methoxycycloheptatriene[b]	141	102.37	0.9131	122.17	0.592	0.648	79.2
7-cyanocycloheptatriene[b]	142	106.44	1.0026	117.15	0.628	0.626	73.4
7-dimethoxymethylcycloheptatriene[c]	143	107.80	0.9958	166.17	0.640	0.634	106.8
7-t-butylcycloheptatriene[c]	144	109.38	0.8484	148.24	0.654	0.771	114.3
2-methoxycarbonyl-1,3-cycloheptadiene[a]	87	45.82	1.0731	152.12	0.628	0.585	99.0
2-methoxycarbonyl-1,3-cycloheptadiene[b]	87	45.78	1.0731	152.12	0.627	0.584	88.9
bicyclo 4.1.0 deca-2,4-diene[c]	12	114.37	0.9495	134.21	0.698	0.735	98.7
bicyclo 4.1.0 dec-3-ene[c]	145	116.48	0.9169	136.23	0.717	0.782	106.5

a. the calibration equation: $\kappa = 0.008655 \times n + 0.2314$, reference toluene, CH_3 resonance

b. the calibration equation: $\kappa = 0.008616 \times n + 0.2325$, reference toluene, CH_3 resonance

c. the calibration equation: $\kappa = 0.008830 \times n - 0.3119$, reference nitromethane

several nitriles[178] it was possible to estimate the value of the $C \equiv N$

bond increment as the difference between the measured values of χ_M and

the sum of all other increments involved.

Table 13: Calculation of the increment of $C \equiv N$ bond

Compound	χ_M [a]	Calculated susceptibility in absence of $C \equiv N$ increment	$C \equiv N$ increment
butyronitrile	49.4	40.6	8.8
propionitrile	38.5	29.6	8.9
benzonitrile[b]	65.2	56.6	8.6

a) ref. 178; the increments have units of 10^{-6}. cm^3/mol.

b) increment of 51.6^{177} was used for the phenyl group.

A value of 8.8 was used as the increment of a $C \equiv N$ bond in the

calculation of χ_M, of <u>142</u>. The measured and calculated molar diamagnetic

susceptibilities, and the exaltations Λ are compiled in Table 14.

<u>Discussion of Diamagnetic Susceptibility Exaltations</u>

As the data in Table 14 show, the reproducibility of this nmr

instrument technique of measuring diamagnetic susceptibilities would ap-

pear to be fairly good. Thus the value of χ_M for cycloheptatriene deter-

mined in this work (60.2×10^{-6}) and that reported by Dauben[170] ($59.8 \times$

10^{-6}) are close and well within the error limits of this type of measure-

ment ($\pm 0.5 \times 10^{-6}$, the values are given in units of cm^3/mol.).

While the calculation of χ_M, has been shown by Dauben[170] and

others[183] to be reliable for hydrocarbons and alcohols, the incremental

values associated with other functional groups are less well defined.

Table 14: Diamagnetic exaltation data

compound	reference to synthesis	$\chi_M \pm 0.5$ 10^{-6}cm^3/mol.	$\chi_M{}'$ 10^{-6}cm^3/mol.	Λ 10^{-6} cm^3/mol.	(lit.)[170]
<u>1</u>		60.2	51.7	8.5	8.1
<u>35</u>	this work	87.3	77.8	9.5	
<u>140</u>	179	75.2	63.8	11.4	
<u>141</u>	179	79.1	67.3	11.8	
<u>142</u>	180	73.4	61.5	11.9	
<u>143</u>	61	106.8	94.0	12.8	
<u>144</u>	181	114.3	99.5	14.8	
<u>87</u>	this work	88.9	87.3	1.6	
<u>12</u>	182	98.7	90.1	8.1	
<u>145</u>	168	106.5	101.2	5.3	
cycloheptene					- 0.4
1,3-cycloheptadiene					0.3
1,3-cyclohexadiene					- 0.7
benzene					13.7

However, as is shown in the Table 14, the difference in χ_M and $\chi_M{}'$ for the cycloheptadiene <u>87</u> is only $1.6 \cdot 10^{-6}$ and this does not greatly differ from zero as would be obtained ideally for a non-aromatic molecule. (All values of Λ are given in units of cm^3/mol.)

It is interesting to note that all the substituted cyclohepta-trienes exhibit a greater Λ than the parent compound <u>1</u>. There seems to be no correlation between the electronic requirements of the substituent

and the Λ value of the cycloheptatriene. Thus the exaltations of cyclo-
heptatrienes 140 and 141, with electron donating C-7 substituents, are
the same as that of 142 which bears at C-7 a powerful electron with-
drawing substituent. There appears to be some indication that Λ could
depend on the size of the C-7 substituent. For example cycloheptatrienes
susbtituted at C-7 with a bulky substituent, 143 and 144, have the values
of Λ greater than 140 or 141, which in turn have Λ greater than 1. How-
ever it should be pointed out that compounds such as 142 and 35 do not
seem to fit in with this general trend.

One possible explanation for this apparent variation in Λ with
substituent size could be that the C-7 substituent, which preferentially
occupies the pseudoequatorial position, is changing the conformation of
the cycloheptatriene and so affecting the amount of delocalization. Perhaps
the most important feature of these results is however the general magni-
tude of Λ found in these systems. Thus the magnitudes of the exaltations
determined for cycloheptatrienes are comparable to that measured for
benzene and substituted benzenes. This clearly indicates that cyclohepta-
triene and its substituted derivatives can be regarded as aromatic
molecules.

Dauben and co-workers have determined that the Λ of cyclopropane
ring is 5.1.[170] If a correction of this value is applied to the Λ found
for the norcarene 145, the corrected exaltation (Λ corr.(145) = 5.3 -
5.1 = 0.2) is then very close to zero, just as expected for a non-
aromatic compound. If a similar correction is applied to the exaltation
of the norcaradiene 12, the corrected value of Λ (Λ corr.(12) = 8.1 -
5.1 = 3.0) is again small and would suggest that there is little induced

ring current set up when $\underline{12}$ is placed in a magnetic field. It would seem that this norcaradiene can not be considered to be an aromatic molecule but predominantly exist as noninteracting diene and cyclopropane moieties.

In Chapter II some chemical shift evidence was presented for the aromaticity of norcaradienes $\underline{37}$ and $\underline{39}$. Unfortunately, the solubility of these zwitterions in common solvents prevented determination of their Λ values, and thus the aromaticity of these systems can not be evaluated by this method. In future work in this area it would be interesting to determine the susceptibility of some norcaradienes such as 7,7-dicyanonorcaradiene which do possess electronwithdrawing substituents on C-7, to test the suggestion made in Chapter II concerning the role of the substituent in enhancing the interaction of the cyclopropane and diene molecular orbitals in these systems.

CHAPTER V

EXPERIMENTAL SECTION

INSTRUMENTAL

The proton magnetic spectra of all new compounds were recorded using a frequency sweep mode with a Varian HA 100 spectrometer. The chemical shifts were determined using a Varian V4 315 frequency counter and are reported in ppm downfield from tetramethylsilane. A Hewlett-Packard 201C audiogenerator was employed for the double irradiation experiments. Varian A60 and T60 spectrometers were used for routine recording of pmr spectra. The cmr spectra were recorded on a Brucker BNC-12 instrument.

The variable temperature pmr spectra were measured with Varian HR 100 or A60 spectrometers equipped with variable temperature probes, controlled by Varian V6040 temperature regulators. Probe temperature was measured using a copper-constantan thermocouple inserted in a nonrotating nmr tube and connected to a Leeds-Northrup 8692 potentiometer.

TMS was used as an internal standard and locking signal in all carbon tetrachloride solutions. In the solutions containing strong Lewis acids, chloroform, taken as δ 7.30 served as the internal standard. The chemical shifts are reported in units of δ, followed by the multiplicity, relative area of the signals, and in some cases also coupling constants and assignment in brackets.

The infrared spectra were recorded on Perkin-Elmer 521 and 337

123

spectrometers calibrated with a polystyrene film and are reported in units of cm^{-1}. The ultraviolet spectra were recorded on a Cary 14 spectrometer.

Vapour phase chromatography was performed on a Varian Aerograph A90-P3 (preparative) and Aerograph 204 (analytical) instruments using helium as the carrier gas at 150 ml/min for the preparative and 50 ml/min for the analytical experiments. The term "SE-30 column" refers to a 10' x $\frac{1}{4}$" copper column containing 15% SE-30, the expression "carbowax column" to a 10' x $\frac{1}{4}$" copper column filled with 15% carbowax, and the term "analytical carbowax column" is used for a 10' x1/8" copper column made with 5% carbowax. Chromosorb W,60-80 mesh was used in all cases as the solid phase.

High resolution mass spectra were obtained on a Consolidated Electrodynamic Inc. Model 21-110b mass spectrometer. All melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Elementary analyses were performed by Galbraith Laboratories in Knoxville, Tennessee.

MATERIALS

Deuterated methylene chloride,chloroform, boron trichloride and boron tribromide,used for preparation of the complexes, were purified by distillation onto phosphorous pentoxide and were subsequently distilled again immediately before use. Chloroform was washed with water, sulfuric acid, 0.1 N sodium bicarbonate, water, dried over P_2O_5 and distilled twice. CF_2ClH and SO_2 were doubly distilled before use. Aluminum trichloride was sublimed twice at reduced pressure and stored in a dry box. $SbCl_5$ $TiCl_4$ and $SnCl_4$ were distilled before use. Fluorosulfuric

acid was distilled from a small amount of NaF at atmospheric pressure and subsequently redistilled. The purified acid was stored in sealed glass ampules. SbF_5 was distilled at 15 mm Hg and also stored in sealed ampules. All liquid chromatography was performed on columns filled with Basic or Neutral Alumina Activity I, supplied by Fisher Scientific Company. Pentane used in the protonation experiments was purified by a treatment with concentrated H_2SO_4, followed by washing with water, drying over $MgSO_4$ and two distillations.

TECHNIQUES

Protonation

Protonations were carried out in a similar manner to that previously described.[132]

Preparation of Borontrihalide Complexes

All manipulations were carried out under high vacuum conditions. The starting organic compound (ca. 30 mg) was weighed into a small reaction vessel which contained a magnetic stirrer, was fitted with a sealed on nmr tube, and could be attached to a vacuum line through a suitable high vacuum stopcock. The reactor, Figure 9, was cooled and CD_2Cl_2 (1 ml) was transferred from a reservoir where it had been stored over P_2O_5. The organic material was dissolved and then a weighed amount of the appropriate Lewis acid was slowly distilled in while the solution was being stirred and maintained at $-78°$. On completion of the addition, the reactor was separated from the vacuum line and the appropriate amount of the solution transferred to the nmr tube which was then sealed. During this transfer the apparatus was kept at $-78°$.

to vacuum

organic
material

nmr
tube

Lewis acids
solvents
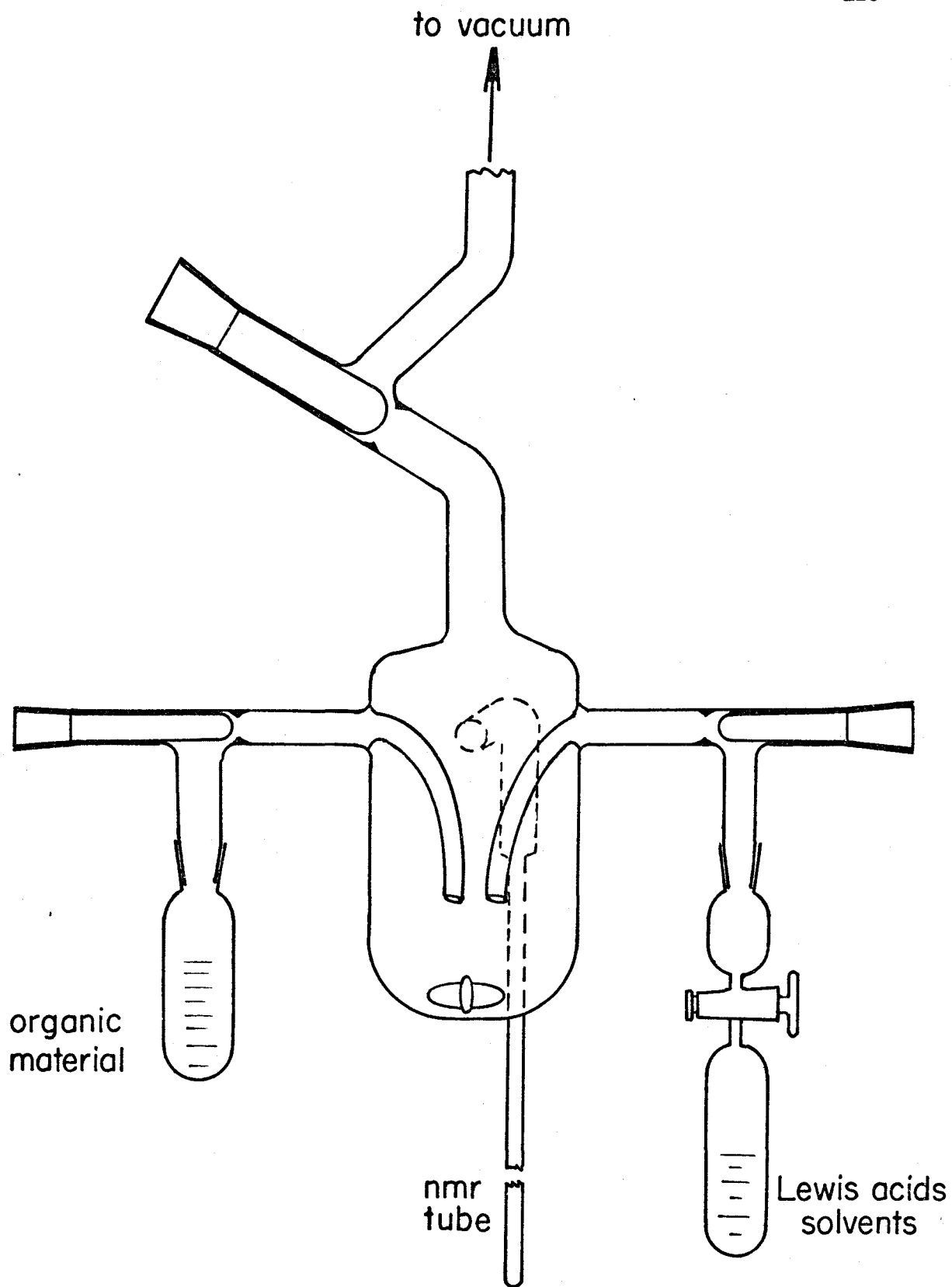
Figure 9:   Reactor used for preparation of BX_3 complexes

For the uv determinations, a similar technique was used except that a larger reaction vessel with an attached 0.2 cm uv cell was employed.

Preparation of Other Complexes

The following procedure was applied for preparation of all complexes except those using BCl_3 or BBr_3 as Lewis acids. Approximately 10% excess of the Lewis acid was placed in a thin wall nmr tube and cooled in a dry-ice/acetone bath. The material to be complexed (15 mg) was dissolved in 0.5 ml of $CDCl_3$ or other solvent, and using a small pipet this solution was in a nitrogen atmosphere slowly poured down the cooled wall of the nmr tube containing the acid. After waiting several minutes for the temperatures to equilibrate the contents of the nmr tube were mixed by vigorous shaking.

Ir Spectrum of Benzylcarboxonium ion, 60

The BBr_3 complex 39 was prepared in usual fashion and the thermal rearrangement was allowed to occur in the probe of an nmr spectrometer. When the acylium cation was fully developed, the solution was transferred into a wider tube in a dry box and the volatile components were removed under a high vacuum at room temperature. The residue in the tube was mixed with nujol, placed between two nujol covered KBr plates and its ir spectrum recorded. A reasonably intense absorption was observed at 2270 cm^{-1}. The KBr cell was opened and the material was exposed to the atmosphere for 8 minutes. In the ir spectrum recorded after this time, there was no absorption at 2270 cm^{-1} and a new signal was found at 1700 cm^{-1}.

Thermal Rearrangement of Complexes

A sealed nmr tube containing a solution of one of the complexes was inserted into a precooled probe of the pmr spectrometer and the spectrum was recorded. The temperature of the probe was then gradually increased while the pmr spectrum was scanned periodically until a rearrangment was observed by the appearance and disappearance of certain resonances. The rate of the rearrangement was measured at such temperatures that the half life of the complex was approximately 30 minutes. The spectrum was obtained at known time intervals and the relative amounts of the starting complex and rearrangement products determined by comparison of the peak heights of the various methoxy resonances. Pseudo first order kinetics were observed in all cases.

Neutralization of Complexes

An excess of gaseous $(CH_3)_2NH$ was passed into the CD_2Cl_2 solution of the zwitterions at $-78°$. The resulting mixture was treated with water and the organic material was extracted three times with ether. The combined ether extracts were dried over $MgSO_4$ and the solvent removed in vacuo prior to analysis by vpc and pmr. Hexamethylbenzene was used as an internal standard in some of the reactions in order to quantitatively measure the recovery of the starting compounds.

Measurement of Diamagnetic Susceptibility

Volumetric diamagnetic susceptibilities were determined by method of Douglass and Fratiello.[173] This method requires the use of precision bored concentric sample tubes, which were obtained from Wilmad Glass Company. The sample of unknown susceptibility was placed

in the central tube, and the reference compound in the surrounding annular region. The pmr spectrum of the non spinning assembly was recorded and the resonance signal of the reference sample was found to be split into two peaks, Figure 10. The separation of the two peaks is proportional to the diamagnetic susceptibility of the sample.

A Varian HR 100 spectrometer operated in a no-lock mode was used for these measurements. Since it is not possible to completely eliminate any drift of the magnetic field under these conditions, the error caused by the drift was reduced by scanning the signal 12 to 18 times alternately in the forward and backward direction, and calculating the average separation.

As this method of determination of the diamagnetic susceptibility is not an absolute one, the sample cell and the spectrometer were calibrated with a series of compounds of known susceptibility. The compounds used for this calibration were: methylene iodide, bromoform, methylene chloride, water, toluene, acetonitrile, ethanol and nitromethane. It was found to be necessary to tune up the spectrometer to a very high degree of field homogenity and to calibrate the spectrometer and measure the unknown diamagnetic susceptibilities of the samples in one sitting. To check that no change in the calibration had occurred during the course of the measurements, the susceptibilities of several standards were redetermined at the end of the series of measurements.

A plot of the known susceptibilities of these compounds versus the separation of the CH_3 resonance of nitromethane or toluene (used in the outer part of the sample cell) gave a straight line. Least
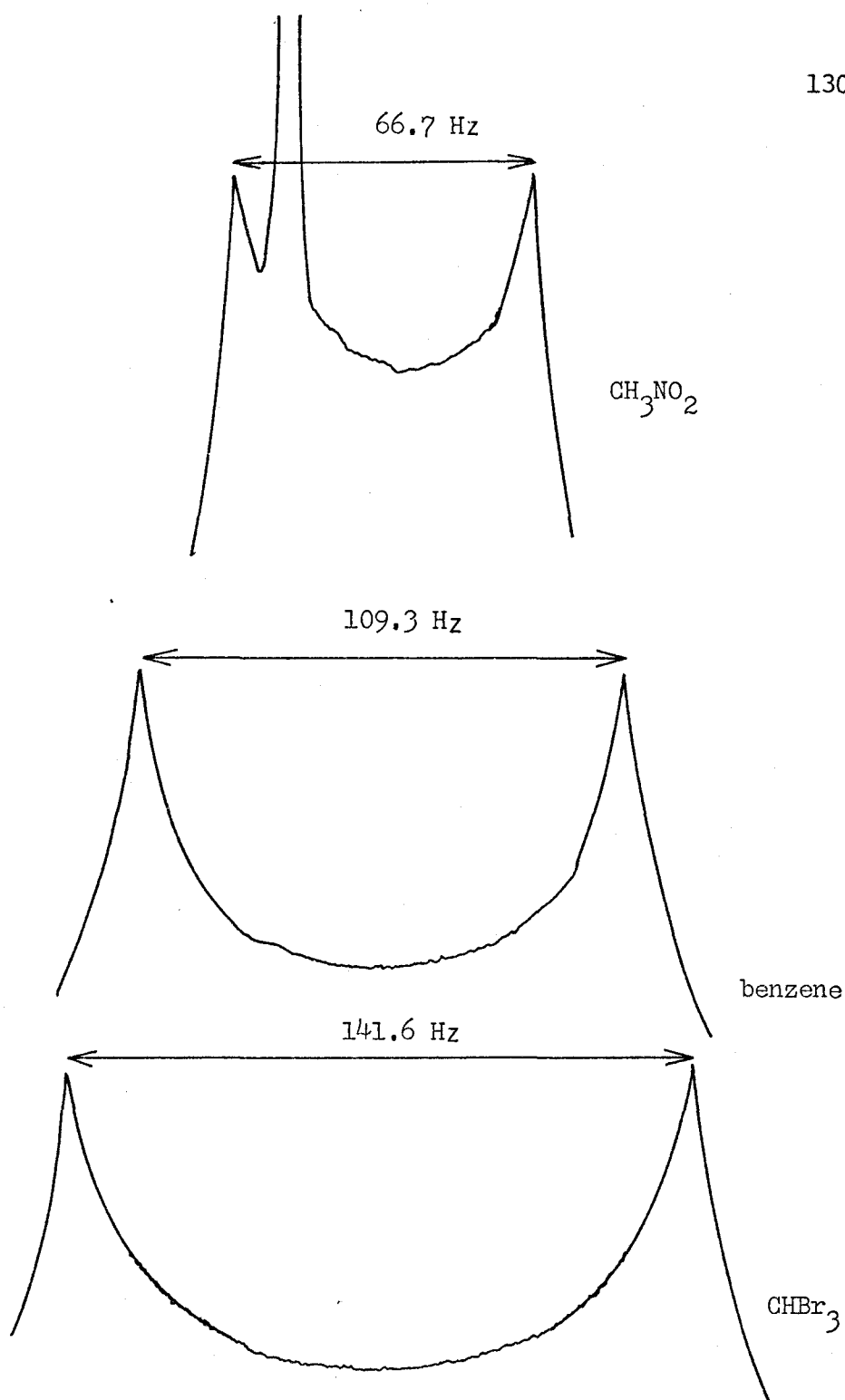
Figure 10: Separation of the CH_3 resonance of toluene, observed for three of the standards

square analysis of the data gave the following three equations for three different sets of measurements:

$$\kappa = 0.008655 \cdot n + 0.2314$$

$$\kappa = 0.008616 \cdot n + 0.2325$$

$$\kappa = 0.008830 \cdot n - 0.3119$$

Toluene was used as the reference in case 1 and 2, and nitromethane was the standard in the third series of measurements. The change of the standard was necessary because the resonances of the measured compounds in some cases coincided with those of the standard. The correlation coefficient was in each case at least 0.999 and the standard deviation in κ less than 0.004.

The magnetic susceptibility per gram, χ , is given by

$$\chi = \kappa/\rho$$

where ρ is density of material in g/cm^3.

The molar susceptibility is given by

$$\chi_M = M \cdot \chi$$

where M is the molecular weight of the substance. The units of χ_M are $10^{-6} cm^{-3}/mole$, κ is in units of 10^{-6}.

A Lipkin bicapillary pycnometer (0.25 ml, Ace Glass Company), calibrated with water, was used to measure the density of the liquids. The solvents used for calibration of the spectrometer were carefully purified by established methods[184] and finally distilled through a 20" column filled with glass helices under a constant flow of helium. The purified standards were stored in the dark under helium.

REACTIONS AND SYNTHESES

7-Methoxycarbonylcycloheptatriene (35)

7-cyanocycloheptatriene (10 g) was refluxed under N_2 in MeOH

(150 ml) containing concentrated H_2SO_4 (30g) for 30 h. The bulk of the

solvent was removed in vacuo and the residue poured into H_2O (400 ml).

The solution was extracted with petroleum ether $(30-60^{\circ})$ (3 x 100 ml),

the extract dried over $MgSO_4$, and the solvent removed in vacuo to give

the crude ester. Distillation gave 9.0 g (80%) of 35 (b.p. $60^{\circ}/0.5$ Torr)

containing a small amount of methyl phenylacetate (2%). Pure material

was obtained by preparative vpc at a temperature below 130°.

N,N-Dimethyl-1,3,5-cycloheptatriene-7-carboxamide (41)

An excess of gaseous dimethylamine was added to a 10% solution

of 7-chlorocarbonylcycloheptatriene in anhydrous ether. The dimethyl-

amine hydrochloride formed was filtered off and the filtrate concentra-

ted in vacuo to give a brown oil. This was chromatographed on neutral

alumina eluting with ether to give a colorless solid. Recrystalliza-

tion from pentane gave 41 as colorless crystals (m.p. 64.5°) which

slowly became colored on standing. Nuclear magnetic resonance spectral

data are given in Table 4.

9-Methoxycarbonylbicyclo[6.1.0]nona-2,4,6-triene (54)

Compound 54, prepared by ester exchange of the corresponding

ethyl ester, had properties identical to those previously reported.[82]

Reaction of the Rearrangement Products of 37 with EtOH

Ethanol (2ml) was slowly added to a CD_2Cl_2 solution of the

rearrangement products of $\underline{37}$ at -78°. Water (10 ml) was added, the mixture extracted with ether (3 x 5 ml), and the extract dried over $MgSO_4$. Evaporation of the ether gave an oil which was analyzed by both pmr and also analytical vpc using authentic samples of $\underline{58}$ and $\underline{59}$ for comparison purposes. The two esters, $\underline{58}$ and $\underline{59}$ in the quenched material were separated by preparative vpc and the pmr spectra of the isolated compounds were identical in all respects to that of the authentic samples.

Reaction of 7,8-Epoxy-1,3,5-cyclooctatriene with Lewis acids

Powdered Al_2Cl_6 (8.9 mg, 0.07 mmol.) was mixed with 0.15 ml CD_2Cl_2 and cooled in a dry-ice/acetone bath. A solution of the epoxide (8 mg, 0.07 mmol.) in CD_2Cl_2 (0.2 ml) was added slowly and the suspension mixed by vigorous shaking. The pmr spectrum of the mixture, recorded at -75°, consisted of absorptions at δ 7.3 (large relative area) and δ 3.11, 3.90, and 4.90.

A solution prepared in a comparable manner from the epoxide (210 mg) and Al_2Cl_6 (245 mg) in CH_2Cl_2 (10 ml) was poured into a cooled (-20°) and stirred mixture of water (5 ml), methanol (5 ml), and Na_2CO_3 (0.5 g). The mixture was then allowed to warm up to room temperature, diluted with water (10 ml) and extracted with ether (3 x 10 ml). The ether layer was washed with water dried over $MgSO_4$ and the ether was removed in vacuo to give 47 mg of a colourless oil. This product was identified by comparison of its pmr and ir spectra with the spectra of authentic compounds as the phenylacetaldehyde and dimethylacetal of phenylacetaldehyde[61] in a ratio of 2 to 1. Attempted separation by vpc, carbowax, 130°, gave the same two compounds and also 2-styryl methyl ether. This

latter compound was shown to be a decomposition product of the di-
methylacetal of phenylacetaldehyde by injection of a sample of
authentic acetal into a vpc column under comparable conditions.

Reaction of Phenylacetaldehyde with Al_2Cl_6 and Subsequent

Neutralization of the Complex

Phenylacetaldehyde (45 mg, 0.42 mmol.) was reacted with Al_2Cl_6
(53 mg, 0.42 mmol.) in $CDCl_3$ (2 ml) in a directly comparable manner to
that outlined above. The pmr spectrum of the solution had absorptions
at 7.3 (large relative area) δ 3.90 and 3.11.

The $CDCl_3$ solution of this complex was reacted with a $MeOH/H_2O/$
Na_2CO_3 mixture as described above to yield after extraction, drying
and evaporation of the solvent, phenylacetaldehyde and the dimethylacetal
of phenylacetaldehyde in a ratio of 2 to 1.

Preparation and Trapping of the 1,4-Cycloheptadiene anion, 73

a) Cycloheptatriene (10 g, 0.1 mol.) was dissolved in liquid
ammonia (150 ml) and lithium (1.4 g, 0.20 mol.) was added in small
pieces to the vigorously stirred solution. The liquid was dark blue
at first but after several minutes it turned dark red as the anion 73
was formed. The reaction mixture was stirred for 2 hours at $-40°$ and
then poured onto a large excess of crushed dry-ice. The dry-ice was
allowed to evaporate and the volatile portion of the residue removed
in vacuo at room temperature. This distillate (3.8 g) was separated by
vpc (SE-30 column, $50°$) into two fractions which were shown to be the
1,3- and 1,4-cycloheptadiene (in ratio of 1 to 3.7) by comparison of
their pmr spectra with those of the authentic materials. The

involatile residue was dissolved in water (20 ml), acidified with HCl,
and extracted with ether (3 x 10 ml). The combined ether extracts were
washed with water (3 x 10 ml), dried over $MgSO_4$, and treated with diazo-
methane (made from N-methyl-N-nitrosourea[185]). The ether was removed
and the residual product distilled under reduced pressure to give 2.7 g
of a mixture of esters. This oil was separated by preparative vpc
(carbowax column, 160°) into seven fractions. These fractions were
further purified by reinjection on the same column. The spectral pro-
perties of the isolated esters are given in the Table 15.

Table 15: Spectral properties of the esters obtained from 73

fr. No.	ret. time (min)	relative amt. (%) by vpc	λ max (nm)	chemical shifts in δ (and integration)		
1	4.2	6	230	1.5-2.6, (10);	3.7, (3);	5.6-5.9, (2.8);
2	4.4	6	230	1.5-2.6, (11);	3.7, (3);	5.6-5.9, (3.2);
3	5.9	4	243	1.4-2.8, (6);	3.7, (3);	5.7, (3.5);
4	6.4	8	247	1.5-2.8, (7);	3.7, (3);	5.6-5.9, (4);
5	7.1	8	275	1.3-2.8, (10);	3.7 3.75 (3);	5.3-6.1, (4);
6	9.3	34	278	2.0, (2); 2.5, (4);	3.75, (3);	6.6, m, (2); 6.9, d, (1);
7	11.0	34	270	2.0, m, (2); 2.4, m, (4);	3.75, (3);	6.0, m, (1); 6.4, d, (1); 7.1, t, (1);

   b) 1,3-cycloheptadiene (0.2 g, 1.9 mmol.) was mixed in a nmr
tube at -78° with hexane solution of tBuLi (0.9 ml, 2.2 N) and dry

tetrahydrofuran (THF, 0.5 ml) was added. The two solvents were miscible at first but after standing 15 minutes at that temperature two layers separated. The dark red lower layer contained the anion 73 in THF as was shown by its pmr spectrum.[103-105] The upper hexane layer was removed and the THF layer was poured into cold stirred methylchloroformate (1 ml). Water (7 ml) was added and the mixture was extracted with ether (3 x 3 ml). The extract was washed with water (2 x 5 ml), dried over $MgSO_4$, the ether was removed in vacuo, and the residue distilled. The pmr spectrum of the oil so obtained contained a sharp singlet δ 1.0 and broad multiplets at δ 1.4-2.6 and 5.5-6.0. The resonances of the ethyl group at δ 1.4 and 4.2 were split into several different sets of signals of unequal size. There were no sharp absorptions at δ 2.3 and 5.9 which are characteristic of 44. Injected onto a vpc column (carbowax, 140°), the material separated into four peaks which were not further identified.

Reduction of 7-Cycloheptatrienecarboxylic Acid

A solution of 7-cycloheptatrienecarboxylic acid (0.9 g, 6 mmol.) in ether (2 ml) was mixed with liquid ammonia (60 ml), and sodium (0.4 g) was added in small pieces to the stirred solution maintained at -75°. After 15 minutes ammonium chloride (2 g) was added and the ammonia was allowed to evaporate at room temperature. The residue was dissolved in 15 ml of water, acidified with HCl, and extracted with concentrated HCl (3 x 5 ml). The extract was washed with water (2 x 10 ml), dried over $MgSO_4$ and treated with CH_2N_2. The solvent was then removed in vacuo and the residue was distilled at reduced pressure.

The distillate (0.4 g) was separated by vpc (carbowax column, 150°)
into 5 fractions. The pmr and the ir spectra of the major fraction
(66% of the product by vpc, ret. time 6.5 min.) were found to be
identical with those of 85. The minor fractions were not identified.

Synthesis of 4-Phenyl-9-methoxycarbonyl-2,4,6-triaza-tetracyclo [5.3.2.0^{4,6}.0^{8,10}] dodec-12-en-3,5-dione, 78a

A mixture of 4-phenyl-1,2,4-triazoline-3,5-dione, 79, (4.25 g,
24.7 mmol.) and 35 (4.0 g, 24.4 mmol.) in CH_2Cl_2 (120 ml) was cooled in
a dry-ice/acetone bath to -60°. A solution of lead tetraacetate
(14.5 g, 33.7 mmol.) in methylene chloride (120 ml) was added at once
to the rapidly stirred solution. The temperature of the mixture was
allowed to rise to +20° and the stirring continued for four additional
hours. The solvent removed in vacuo and the residue was washed with
0.1 N HNO$_3$ (100 ml), 0.1 N NaOH (100 ml) and water (100 ml). The remain-
ing brown material was dissolved in boiling methanol (400 ml), treated
with charcoal, and the volume was reduced to 300 ml. On cooling this
solution to room temperature 6.07 g of 78a crystallized and was filtered
out. An additional 0.7 g of material was obtained as a second crop,
bringing the total yield of 78a to 82%. The product was recrystalized
from methanol to give pure 78a, m.p. 187°. Pmr (CDCl$_3$): 1.41 (t, 1,
J = 3.0 Hz, H-9); 2.19 (m, 2, H-8, 10); 3.67 (s, 3, OMe); 5.23 (m, 2,
bridgehead protons); 6.15 (t, 2, J = 3.7 Hz, olefinic protons); 7.40
(s, 5, Ph). Ir (KBr): 1770, 1730, 1417, 1323, 1240. Anal, calcd for
$C_{17}H_{15}N_3O_4$: C, 62.77; H, 4.62; found: C, 62.76; H, 4.72.

Synthesis of 9-Methoxycarbonyl-4-phenyl-2,4,6-triaza-tetracyclo [5.3.2.0^{4,6}.0^{8,10}] dodeca-3,4-dione, 80a

The olefin 78a (3 g) was mixed with dioxane (100 ml) and partially dissolved. Palladium catalyst (5% Pd/C, 185 mg) was added and the mixture was vigorously stirred in a hydrogen atmosphere at 760 Torr. One equivalent of H_2 was consumed in 10 min to give 80a. (All the solid material dissolved during this reaction). Recrystallized from MeOH 80a melted at 156°. Pmr ($CDCl_3$): 1.55-2.22 (m, 7, cyclopropyl and methylene protons); 3.66 (s, 3, OMe); 4.7 (broad s, 2, bridgehead protons); 7.47 (m, 5, Ph). Ir (KBr): 1775, 1720, 1500, 1440, 1410, 1250. Anal., calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; found: C, 62.53; H, 5.26.

Synthesis of 4-Phenyl-9-dimethoxymethyl-2,4,6-triaza-tetracyclo [5.3.2.0^{4,6}.0^{8,10}] dodec-12-ene-3,5-dione, 78b

The compound 78b was prepared from dimethoxymethylcyclohepta-triene using the same procedure as that described above for the preparation of 78a. Yield: 73%. M.P.: 158°. Pmr ($CDCl_3$): 0.97 (d of t's, 1, H-9); 1.76 (m, 2, H-8, 10); 3.33 (s, 6, OMe); 4.26 (d, 1, C-9 substituent); 5.22 (m, 2, H-1,7); 6.17 (t, 2, olefinic protons); 7.42 (s, 5, Ph). Ir (KBr): 1773, 1755, 1605, 1500, 1398. Anal, calcd for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.63; found: C, 63.12; H, 5.70.

Synthesis of 4-Phenyl-9-dimethoxymethyl-2,4,6-triaza-tetracyclo [5.3.2.0^{4,6}.0^{8,10}] dodeca-3,5-dione, 80b

Olefin 78b was reduced in a directly comparable manner to that described above for reduction of 78a, to give a 100% yield of 80b: Pmr (CDCl$_3$): 1.41 (t, 1, H-9); 1.60-2.20 (m, 6, H-8,10,11,12); 3.34 (s, 6, OMe); 4.22 (broad s, 2, bridgehead H's); 7.3-7.7 (m, 5, Ph). Ir (KBr): 1750, 1696, 1500, 1430, 1410. Anal, calcd for C$_{18}$H$_{21}$N$_3$O$_4$: C, 62,93; H, 6.18; found: C, 62.85; H, 6.18. M.p.: 121°.

Synthesis of 9-Ethoxycarbonyl-4-phenyl-2,4,6-triaza-tetracyclo [5.3.2.0^{4,6}.0^{8,10}] dodeca-12-en-3,5-dione, 78c

7-Ethoxycarbonylcycloheptatriene was used as the starting material and the procedure used was the same as that described for the preparation of 78a. Yield: 73%. M.p.: 172.5°. Pmr (CDCl$_3$): 1.26 (t, 3, Me); 1.45 (t, 1, H-9); 2.23 (d of d's, 2, H-8,10); 4.14 (q, 2, CH$_2$); 5.25 (m, 2, bridgehead H's); 6.18 (t, 2, olefinic H's); 7.42 (s, 5, Ph). Ir (KBr): 1770, 1719, 1500, 1415, 1241. Anal, calcd, for C$_{18}$H$_{17}$N$_3$O$_4$: C, 63.71; H, 5.05; found: C, 63.81; H, 5.13.

Synthesis of 9-Ethoxycarbonyl-4-phenyl-2,4,6-triaza-tetracyclo [5.3.2.0^{2,6}.0^{8,10}] dodeca-3,5-dione, 80c

Starting with 78c the procedure used was the same as that described above for the preparation of 80a. Yield: 95%. M.p.: 156°. Pmr (CDCl$_3$): 1.27 (t, 3, Me); 1.60-2.20 (m, 7, H-8-12); 4.15 (q; 2, CH$_2$); 4.73 (broad s, 2, bridgehead H's); 7.32-7.62 (m, 5, Ph).

Ir (KBr): 1770, 1720, 1502, 1409, 1320, 1255. Anal, calcud for

$C_{18}H_{19}N_3O_4$: C, 63.34; H, 5.61; found: C, 63.23; H, 5.52.

Synthesis of 6,7-Diaza-3-dimethoxymethyltricyclo[3.2.2.0^{2,4}] nonanyl-6-phenylcarboxamide, 82b

The acetal 80b (0.42 g) was refluxed for 4 hr in methanol (10

ml) containing KOH (0.5 g). The solvent was evaporated at reduced

pressure the residue was extracted with CH_2Cl_2 (3 x 10 ml) and the

extract was dried over $MgSO_4$. On removal of the solvent in vacuo 0.16 g

of 79a was obtained. This material was three times recrystalized from

ether/CH_2Cl_2 to give a pure product, m.p. 157-5°(N_2 sealed capillary).

Yield of crude product: 35%. Pmr ($CDCl_3$): 1.00-1.95 (m, 7, H-2,3,

4,8,9); 3.37 (s, 6, OMe); 3.50 (m, 2, H-1,5) 4.10 (d, J=5 Hz, 1, C-3

substituent); 4.67 (broad s, 0.7, NH); 7.0-7.8 (m, 5, Ph); 8.86 (broad

s, 0.7, NH). Ir (KBr): 3305, 3220, 1670, 1605, 1520, 1450. Anal,

calcd for $C_{17}H_{23}N_3O_4$: C, 64.95; H, 7.39; found: C, 64.70; H, 7.25.

Synthesis of the Copper Complex of 6,7-Diazatricyclo[3.2.2.0^{2,4}]nona-ne-3-carboxylic acid 84a

A solution of 80a (2.85 g, 8.81 mmol.) in methanol (15 ml) con-

taining KOH (3 g, 65 mmol.) was refluxed for 24 hr in a nitrogen

atmosphere. The reaction mixture was cooled and dissolved in water

(500 ml). The solution was titrated with 10% HCl to pH 4 and $CuCl_2$

(3 g, 22.3 mmol.) was dissolved in the mixture. After 30 min the green

solution started turning red and during the following 15 hr crystals

of ochre-red 84a accumulated on the bottom of the vessel. The complex

was filtered out and thoroughly washed with acetone and ether. Compound 84a was found to be insoluble in common solvents but to readily decompose in presence of bases. Yield: 1.5 g (64%). M.p.: 147°(decomposition). Ir (KBr): 1697, 1470, 1340, 1280.

Synthesis of 3-Methoxycarbonyl-1,4-cycloheptadiene, 44

Copper complex 84a (0.9 g, 3.22 mmol.) was mixed with water (20 ml) containing K_2CO_3 (0.089 g, 6.44 mmol.). The red solid immediately turned brown and a slow development of gas was observed. After 1 hr of stirring bulky precipitate was filtered off and the filtrate was heated to 35°, until the production of nitrogen was completed (12 hr). The solution of 86 so obtained was cooled to 2° acidified with HCl to pH 3 and extracted with ether (3 x 15 ml). The ether extract was dried with $MgSO_4$ and immediately esterified with a slight excess of diazomethane. The solvent was removed in vacuo and the residue was distilled to give 44, 0.29 g (55%). B.p., 30°/0.1 Torr. Pmr (CDCl$_3$): 2.25 (m, 4, H-6,7); 3.68 (s, 3, CH$_3$); 4.2 (m, 1, H-3); 5.79 (m, 4, H-1,2,4,5). Ir (neat): 1725, 1465, 1415, 1295. Kept at room temperature 44 slowly rearranged to 87 (followed by pmr). Attempts to separate 44 from 87 on a short alumina column caused a complete rearrangement of 44 to give 87, pmr (CDCl$_3$): 1.85 (m, 2); 2.35 (m, 4); 3.54 (s, 3); 5.80 (d of t's, 1); 6.19 (broad d, 1); 6.91 (t, 1).

Rearrangement of 1,4-Cycloheptadiene-3-carboxylic acid, 86,
to 1,3-Cycloheptadiene-2-carboxylic acid, 85

An ether solution of 86 was prepared from 84a as described above. The solution was dried over $MgSO_4$ and the solvent was removed in vacuo,

to give $\underline{86}$ as a colourless oil. Pmr ($CDCl_3$): 2.24 (broad s, 4, H-4,5); 4.16 (m, 1, H-1); 5.78 (broad s, 4, H-2,3,6,7); 11.2 (s, 1, acidic OH). Ir (neat): 2500-3500, 1715, 1421, 1289.

Pure $\underline{86}$ was heated for 1 hr at $45°$ to give $\underline{85}$ as a yellow oil. Pmr ($CDCl_3$): 1.85 (m, 2, H-4,5); 2.38 (m, 4, H-3); 5.91 (d of t's, 1, H-6); 6.35 (d of d's, 1, H-7); 7.26 (t, 1, H-2); 11.2 (s, 1, OH). On irradiation at 2.38 the signal at 7.26 collapsed to a singlet, that at 5.91 to a doublet and the absorption at 1.85 collapsed to a broad singlet. $J_{2,3}$=5.3 Hz, $J_{6,7}$= 11.5 Hz; $J_{5,6}$= 4.5 Hz; $J_{5,7}$= 1.0 Hz.

Synthesis of 3-Dimethoxymethyl-1,4-cycloheptadiene, 88

A solution of acetal $\underline{80}$b (2.0 g, 5.8 mmol.) in methanol (15 ml) containing KOH (1.5 g, 27 mmol.) was refluxed under N_2 for 48 hr. De-oxygenated water (30 ml) was added and the mixture extracted with methylene chloride (3 x 15 ml). The combined extract was dried with $MgSO_4$ and the solvent was removed in vacuo, to give an oil, pmr ($CDCl_3$): 1.05-2.02 (m, 7); 3.35 (s, 6); 4.20 (m, 4); 3.55 (s, 2); 6.9 (m, 5). This product was dissolved in CH_2Cl_2 and the solution was exposed to air for 8 hr. Development of gas was observed during this time. The solvent was removed in vacuo, and the mixture of $\underline{88}$ and aniline so obtained was separated on a short column of basic alumina eluting with ether. Yield of $\underline{88}$, 0.47 g (48%). Pmr ($CDCl_3$): 1.80-2.50 (m, 4, H-6,7); 3.25 (s, 6, OMe); 3.39 (m, 1, H-3); 4.17 (d, 1, H-8); 4.36-4.80 (m, 4, H-1,2,4,5). Anal, calcd for $C_{10}H_{16}O_2$: C, 72,26; H, 9.70; found: C, 71.97; H, 9.77.

4-Phenyl-2,4,6-triazatetracyclo[5.3.2.0^{4,6}.0^{8,10}]dodeca-3,5-dione-9-carbaldehyde, 89

Acetal 80b (0.8 g) was dissolved in acetone (30 ml), aqueous 37% HCl (0.5 ml) was added and the solution was kept for 30 min. at room temperature. At the end of this time NaHCO$_3$ (0.5 g) was slowly added and the solvent was removed in vacuo. The white residue was triturated with methanol, the inorganic salt removed by filtration and the solvent evaporated in vacuo to yield the crude 89 (0.65 g, 95%). Three recrystallizations from CCl$_4$/acetone mixtures gave pure 89, M.p.: 204°. Pmr (CDCl$_3$): 1.50-2.30 (m, 7, H-8-12); 4.72 (broad s, 2, H-1,7); 7.28-7.62 (m, 5, Ph); 9.72 (d, 1, H-8). Ir (KBr): 1770, 1710, 1600, 1500, 1411, 1259. Anal. calcd for C$_{16}$H$_{15}$N$_3$O$_3$: C, 64.63; H, 5.08; found: C, 64.60; H, 5.00.

9(2-Hydroxy-2-propyl)4-phenyl-2,4,6-triazatetracyclo [5.3.2.0^{4,6}.0^{8,10}]dodeca-3,5-dione, 80 R = C(Me)$_2$OH

Methyllithium (4 ml, 1.3 N in hexane) was added to a vigorously stirred solution of 80c (1.4 g, 4.10 mmol.) in dry 1,4-dioxane (100 ml). After 15 min, water (15 ml) was added and the volume of the solution was reduced to 30 ml in vacuo. Additional water (20 ml) was added, the mixture neutralized with 10% HCl and extracted with CH$_2$Cl$_2$ (3 x 20 ml). The organic layer was dried over MgSO$_4$ and reduced to 10 ml. Addition of CCl$_4$ (10 ml) caused precipitation of 0.2 g of white product. This material was recrystallized from CH$_2$Cl$_2$/CCl$_4$ mixtures.

Attempted Preparation of 3-Formyl-1,4-Cycloheptadiene

a) Acetal 80b (1 g) was hydrolyzed and treated with CuCl$_2$ in the same manner as described above for the preparation of 84a, to give 84b (0.3 g, 33%). M.p.: 120-122° (decomposition). Ir (KBr): 1695, 1619, 1401. Complex 84b (0.2 g) was added to a 5% solution of K$_2$CO$_3$ (10 ml) the mixture was stirred for 3 hr at +4°, and extracted with three 5 ml portions of methylene chloride. The combined extract was dried with MgSO$_4$ and the solvent was removed in vacuo to give 76b (0.15 g). Pmr (CDCl$_3$, -20°): 1.2 (m); 1.9 (broad s); 5.6 (broad s); 9.3 (d), and absorptions of much smaller area at δ 1.7-2.9; 6.0-6.6 and 6.8. The CDCl$_3$ solution of 76b in an nmr tube was kept at 35° for 5 hr. Development of gas was observed during this time and 76b was converted into 2-formyl-1,4-cycloheptadiene. Pmr (CDCl$_3$): 1.65-2.20 (m, 2, H-6); 2.2-2.9 (m, 4, H-5,7); 6.05-6.60 (m, 2, H-3,4); 6.78 (t, 1, H-1; 9.37 (s, 1, -CHO).

b) Compound 89 was reacted in a similar manner as described above for 80b. The product obtained from this reaction had a pmr spectrum identical with that of 2-formyl-1,4-cycloheptadiene, described above.

c) Acetal 88 (20 mg) was dissolved in ether (4 ml) and stirred for 30 min at -5° with 3 drops of 37% aqueous HCl. The ether solution was then washed with 5% NaHCO$_3$ solution (5 ml) and water, dried with MgSO$_4$ and the solvent was removed in vacuo. All these operations were performed below +4°. The pmr spectrum of the product so obtained was again identical with that of 2-formyl-1,3-cycloheptadiene.

Synthesis of 3(2-Hydroxy-2-propyl)1,4-cycloheptadiene, 90

The title compound was prepared from 80, R=C(Me)$_2$OH using a similar procedure to that used for the synthesis of 44. The products were separated on a short alumina column eluting with ether and the final fraction was distilled, (60°/0.5 Torr) to yield 90 (30%). Pmr (CCl$_4$): 1.18 (s, 6, Me); 1.54 (s, 1, OH); 2.21 (m, 4, H-6,7); 3.15 (m, 1, H-3); 5.66 (m, 4, H-1,2,4,5). Ir (neat): 3400, 1170, 1370, 1450. Anal, calcd for C$_{10}$H$_{16}$O: C, 78.90; H, 10.59; found: C, 78.70; H, 10.71.

Simmons-Smith Reaction with 7-Ethoxycarbonylcycloheptatriene

Zinc copper couple[122] (0.6 g), anhydrous ether (10 ml), CH$_2$I$_2$ (2.2 g, 42 mmol.), and the title ester (0.3 g, 21 mmol.) were heated under nitrogen for 48 hr. (The progress of the reaction was followed by periodic analysis of samples by vpc). The reaction mixture was filtered and the solid residue washed with ether. The combined ether solutions were washed with saturated aqueous ammonium chloride solution (twice), 10% sodium bicarbonate solution, and water, dried with MgSO$_4$ and the solvent was removed in vacuo. The colourless oil so obtained was distilled and separated by vpc (carbowax column, 180°) into nine components. The first four constituents of the mixture were identified as methylene iodide ethylbenzoate, 3-, and 7-ethoxy-carbonyl-cycloheptatriene by comparison of their respective pmr spectra and vpc retention times with those of authentic materials.[186] Fraction 5, was purified by two subsequent vpc separations. Mass spectrum, m/e = 192 (calc for C$_{11}$H$_{14}$O$_2$ = 192); pmr(CCl): 0.15-0.40 (m,2); 0.75-1.16

(m, 2); 1.16-1.70 (m, 8); 4.25 (q, 2); 5.63 (s, 2). Fraction 6 was also purified by further vpc separation. Pmr (CCl$_4$): 0.3 (m, 1); 0.9-1.8 (m, 10); 4.4 (d of q, 2); 5.8 (m, 2). Fraction 7: Pmr (CCl$_4$): 0.25 (m, 2); 0.4-1.5 (m, 11.6); 4.25 (q, 2); no olefinic signals. Fraction 8: Pmr (CCl$_4$): 0.25 (m, 2); 0.4-1.5 (m, 12); 2.30 (m, 1); 4.25 (q, 2). Insufficient material was present in the fraction 9 for it to be analyzed.

Decomposition of N$_2$CHCOOEt in Cycloheptatriene

Ethyldiazoacetate[187] (10 g, 88 mmol.) and cycloheptatriene (16 g, 176 mmol.) in CH$_2$Cl$_2$ were irradiated in a Srinivasan-Griffin photochemical reactor, fitted with 3500 Å lamps for three days, during which time 900 ml of N$_2$ were released. Anhydrous CuCl$_2$ (0.1 g) was added to the solution and further 600 ml of N$_2$ was rapidly evolved. The solvent was removed in vacuo and the residue was distilled under reduced pressure to give two fractions. The first fraction, b.p. 72°/0.2 Torr, was by vpc (carbowax column, 150°) separated into two components the pmr and ir spectra of which were identical with those reported for ethyl fumarate[188a] and ethyl maleate.[188b] The second fraction, b.p. 72-78°/0.2 Torr (2.5 g, was chromatographed on a 25 cm basic alumina column eluting with petroleum ether to give a small amount of ethyl fumarate and maleate and an oil (1.5 g), uv, λ_{max}^{MeOH} = 262 nm; pmr (CCl$_4$): 1.35 (t, 3); 1.5-2.9 (m, 5); 4.13 (q, 2); 5.5-6.4 (m, 4). Analysis of this oil by vpc on an analytical carbowax column showed it to consist of two materials, the first, retention time 32 min, 13%, and the second, retention time 35 min, 87%.

Synthesis of 6,7-Diaza-6,7-diethoxycarbonyl-3-methoxy-

carbonyltricyclo[3.2.2.0^{2,4}]non-6-ene, 99

The ester 35 (3.0 g, 20 mmol.) and diethylazodicarboxylate

(2.5 g, 20 mmol.) were dissolved in ether (5 ml) and heated for 12 hr

at 50°. The ester was then removed in vacuo and the product mixture

separated on a 20 cm basic alumina column eluting with 10% ether in

pentane. The first fraction contained a small amount of 35.

The second fraction consisted of 99, a viscous, honey-like

material. Pmr (CDCl$_3$+CS$_2$) 35°: 1.12-1.42 (m, 7); 1.75-2.23 (broad s,

2); 3.59 (s, 3); 4.05 (broad, 4); 5.12, (broad s, 2); 6.18 (broad s, 2).

+90°: 1.27 (d of t's,7); 2.08 (q, 2, J=2.7 Hz); 3.62 (s,3); 4.20 (d of

q's, 4, J=7.0 Hz); 5.20 (m, 2); 6.18 (t, 2, J=4.0 Hz). Ir (neat):

1750, 1730, 1515, 1460, 1325. Anal, calc for C$_{15}$H$_{20}$N$_2$O$_6$: C, 55.52;

H, 6.21; found: C, 55.70; H, 6.26. The third fraction to be eluted

consisted of a mixture of 99 and 100. This was further separated on

an alumina column, eluting with 10% ether in petroleum ether to give

100 containing some 8% 99 (estimated by pmr). Pmr (CDCl$_3$): 1.27

(d of t's, 7); 3.62 (s, 0.8); 3.78 (s, 0.78); 3.81 (s, 0.1); 4.0-4.5

(m, 4); 5.5-7.3 (m, 4). There were two methoxy resonances in this

spectrum (in addition to that of 99). This pmr spectrum was not

temperature dependent in the range of 0° to 60°. The ratio of 99 to

100, estimated from   integration of the pmr resonances of respec-

tive CH$_3$ groups, was found to be 1.7:1.0. A similar reaction was

carried out at 0°, with the reaction time of 48 hr. The ratio of 99

to 100 was estimated to be 5.7:1.0.

Synthesis of 2,4,6-Cycloheptatrienone (tropone)

A solution of potasium dihydrogen phosphate (61 g, 0.45 mol.) in water (100 ml) and a solution of cycloheptatriene (83 ml, 0.9 mol., 91% J.T. Baker Chemical Co. product containing 7% toluene) in dioxane (750 ml) were placed in a 2 l flask equipped with a mechanical stirrer and a reflux condenser. Selenium dioxide (100 g, 0.9 mol., J.T. Baker Chemical Co.) was added at once and the mixture was stirred under N_2 and heated to 92° using an oil bath for 15 hr. The mixture was cooled, filtered and the solid material was washed with CH_2Cl_2, the combined filtrate and washings were treated with water (200 ml) and extracted with CH_2Cl_2 (4 x 300 ml), the extract was dried ($MgSO_4$) and the solvent was removed in vacuo to yield a dark brown product. Distillation through a short Vigreux column gave tropone (47 g, 49%), b.p. 75°/1 Torr with identical spectral properties to those previously reported.[135]

Synthesis of 3,5-cycloheptadienone

A solution of tropone (40 g, 0.3 mol.) in dry ether (500 ml) was slowly added to a well stirred mixture of lithium aluminium hydride (LAH) (10 g, 1.14 equivalent) and ether (0.5 l) in a 3 l flask equipped with a mechanical stirrer and cooled in an ice bath. When all tropone solution had been added the mixture was stirred, 30 min, and the excess of LAH destroyed by the slow addition of ethyl formate (50 ml) dissolved in ether (200 ml). Water (15 ml) and 10% KOH solution (11 ml) were added dropwise and the reaction mixture was stirred until a granulated precipitate was formed (20 min.). The reaction mixture was filtered, the precipitate was washed with ether, and the solvent was

removed at a reduced pressure. Distillation yielded 19.7 g (49%) of colourless 3,5-cycloheptadienone, b.p., 45°/5 Torr. The spectral properties of the ketone were identical with those reported previously.[189]

Synthesis of 2,4-Cycloheptadienone, 104

3,5-Cycloheptadienone (8 g) was dissolved in $HFSO_3$ (90 ml) and the solution was kept at room temperature until rearrangement was complete.[132] Water (500 ml) and petroleum ether (200 ml) were mechanically stirred in a 2 l beaker cooled with a salt ice bath while a solution of 10% NaOH (150 ml) and the $HFSO_3$ solution were slowly added simultaneously in such a manner that the mixture was basic at all times. The thick mixture formed in this process was filtered and the two layers of filtrate separated. The water solution was extracted with ether (4 x 125 ml) and the combined ether solution dried over $MgSO_4$. The solvent was removed at atmospheric pressure through a 25 cm Vigreux column and the residue was distilled. B.p. 40°/0.2 Torr. Yield: 3.4 g (43%). The physical and spectroscopic properties of the product were identical with those reported for 104.[132]

Synthesis of Bicyclo[5.1.0]oct-5-en-2-one, 105

A solution of 104 (1.5 g, 12.3 mmol.) in dimethylsulfoxide (4 ml) was slowly added to a solution of dimethylsulfoxonium methylide, prepared from trimethylsulfoxonium iodide (2.7 g, 12.3 mmol.) and NaH (0.38 g of 50% dispersion in oil) in dimethylsulfoxide (15 ml), kept at +5°. After completion of the addition (2 hr), the reaction mixture was allowed to warm up to room temperature and stirred at

this temperature for 2 hrs. The reaction mixture was poured into water (80 ml) and extracted with ether (5 x 50 ml). The combined extract was washed with water (2 x 50 ml), dried over $MgSO_4$, and the solvent removed in vacuo. A colourless solid material crystallized from the residual oil (0.23 g, 60%). Recrystallized from methanol this material melted at 170°. Mass spectrum, m/e: 216.1150; calcd for $C_{14}H_{16}O_2$: 216.1150; uv, λ_{max}^{MeOH} = 255 (ϵ = 654), local maximum at λ = 245 (ϵ = 616) and λ = 268 (ϵ = 390). Ir (KBr): 3030, 1709, 1118, 1045. Pmr ($CDCl_3$): 1.55-1.78 (m, 3); 2.10-2.93 (m, 9); 5.64-6.19 (m, 4).

Distillation of the remaining liquid gave 0.6 g (16%) of colourless distillate, b.p., $70^\circ/0.5$ Torr. Injected on a preparative column, the material gave rise to a single peak with retention time of 10 min (150°, carbowax column). Ir (neat): 1700, 1445, 1360. Pmr (CCl_4): 1.00-2.74 (m, 8); 5.70 (m, 1); 5.96 (d of d's, 1). Double irradiation experiment:

Irradiated at δ	signal at δ	changed from	into
2.18	5.70	m	d
2.18	5.96	broad d of d	sharp d of d
1.73	5.96	d of d	d

Synthesis of 8-Ethoxycarbonylbicyclo[5.1.0]oct-5-en-2-ones, 109 and 110

Ethoxycarbonylmethylenedimethylsulfurane,[190] $(CH_3)_2S=CHCOOEt$, (3.2 g, 21.3 mmol.) was added to a solution of 104 (2.5 g,

21.3 mmol.) in tetrahydrofuran (6 ml) and the solution was kept at room temperature for 24 hrs. (The progress of the reaction was followed by monitoring changes in the pmr spectra of small, periodically withdrawn samples). After 24 hrs, the solvent was removed in vacuo and the product distilled. The first fraction (0.94 g, 35%, b.p., $25°/0.4$ Torr) contained some 85% of 104 and 15% of monoadduct (estimated by pmr). The second fraction (1.6 g, 37%, b.p., $104°/0.2$ Torr) was essentially pure monoadduct. This fraction was separated by vpc (carbowax column, $155°$) into component "A", ret. time 8 min 40 sec, and component "B", ret. time 9 min 20 sec. The ratio of A:B was 1:2.3. The two components were also separated on an alumina column eluting with a petroleum ether/ether mixture.

The first fraction was recrystalized three times from a pentane / ether mixture (50:1) at $-20°$ and purified by vpc (carbowax column). The white solid obtained in this manner had the following properties: M.p., $52°$. Ir (KBr): 1725, 1678, 1425, 1360, 1305 and 1185. Pmr (CCl_4): 1.25 (t, 3, J=7 Hz); 2.02-2.62 (m, 7); 4.10 (q, 2, J=7 Hz); 5.60-6.00 (m, 2). Uv, $\lambda \frac{MeOH}{max} = 202$. Anal, calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26; found: C, 68.17; H, 7.25.

The second fraction from the liquid chromatography was purified by vpc and had the following properties: Ir (neat): 1725, 1668, 1425, 1307, and 1175. Pmr (CCl_4): 1.25 (t, 3, J=7 Hz); 1.63 (t, 2, J=4.5 Hz); 1.94-2.22 (m, 2); 2.22-2.72 (m, 3); 4.12 (q, 2, J=7 Hz); 5.37 (d, 1, J=12 Hz); 6.49 (d of d's of d's, 1, J=12,2.8 and 2.8 Hz). Irradiation at δ 2.1 reduces the signal at δ 2.60 into a singlet, and

the resonance at δ 6.49 into a doublet. Anal, calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26; found: C, 68.28; H, 7.32.

Synthesis of 1,4,4-Trimethylbicyclo[5.1.0]oct-5-en-2-ol, 112

a) NaBH$_4$ reduction of 103:

Sodium borohydride (4.5 g, 128 mmol.) was added to the solution of 103 (3.0 g, 18.4 mmol.) in EtOH (10 ml) containing 30% aqueous KOH (0.5 ml). The mixture was stirred and refluxed under nitrogen for 30 min., cooled to 25°, and poured into 30 ml of water. The water solution was extracted with ether (3 x 15 ml) the combined ether extracts dried over MgSO$_4$, and the solvent was removed in vacuo. Only a small amount (0.2 g) of the volatile alcohol 112 could be distilled out of the extract (80°, 0.2 Torr). Alcohol 112, recrystalized from CCl$_4$, had a m.p. of 48-60°. M.p. of twice sublimed material was 49-62°. Pmr (CCl$_4$): 0.36 (d of d's, 1, J=5.5 and 3.5 Hz); 0.67 (d of d's, 1, J=3.5 and 9.3 Hz); 0.97 (m, 1); 1.05 (s, 3); 1.10 (s, 6); 1.43 (d of t's, 1, J=13.5 and 1.5 Hz); 1.71 (broad s, 1, disappeared if shaken with D$_2$O); 2.16 (d of d's, 1, J=10 and 1.5 Hz); 3.33 (d of d, 1, J=10 and 1.5 Hz); 4.97 (d of m's, 1, J=11.7 Hz); 5.43 (d of d's, 1, J=11.7 and 2.8 Hz). Ir (KBr): 3310, 1459, 1448, 1340, 1142. Anal, calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91; found: C, 79.21; H, 10.66.

The involatile portion of the reaction product, 113, was a colourless viscose material which readily solidified at room temperature. The pmr spectrum of this material resembled that of 112 except that the resonance at δ 3.33 was shifted downfield by 0.6 ppm, to δ 3.93. Ir (neat): 3390, 1650, 1300-1500, 1035. Two procedures for liberation of 112 from this material are described below.

The solid boric esters (the nonvolatile portion of the reaction products, (0.5 g) was dissolved in MeOH (150 ml) the solution was acidified with 37% HCl (0.5 ml) and refluxed 5 min. The bulk of solvent was removed in vacuo, fresh alcohol and HCl were added and the procedure repeated three times. The distillation of the product of this reaction yielded 112 (0.2 g).

The second portion of the boric ester (0.5 g) was dissolved in methanol (15 ml) and treated with 35% NH_4OH (8 ml). After standing at room temperature for 1 hr the bulk of solvent was removed in vacuo, 50 ml of water was added and the mixture was extracted with ether (3 x 15 ml). The combined ether extracts were dried over $MgSO_4$, the ether removed in vacuo, and the residue distilled to give 112 (0.3 g).

b) LiAl(OBu)$_3$H Reduction of 103

A solution of 103 (1.3 g, 7.9 mmol.) in ether (5 ml) was slowly added to a stirred mixture of LiAl(OBu)$_3$H (2.5 g, 10 mmol.) and ether (20 ml) cooled to 0°. The reaction mixture was refluxed under nitrogen until all ketone was reduced. (Progress of reaction was followed by examining the carbonyl absorption in the ir spectra of small samples removed from the reaction mixture). After 22 hr virtually all ketone was reduced, heating was discontinued, water (0.3 ml) added and the mixture was agitated for 30 min. The white precipitate was filtered off, washed with ether, the ether solutions combined and the solvent removed in vacuo. The residue was distilled at reduced pressure to give 112 (0.29 g, 97%).

Synthesis of Bicyclo[5.1.0]oct-5-en-2-ols, 116

Sodium borohydride (0.8 g, 20 meq.) was added to a solution of 105 (0.36 g, 3 mmol.) in 3 ml of 50% EtOH and the mixture was refluxed under N_2 for 90 min. The solution was poured into water (10 ml) acidified with HCl to pH 2, and extracted with ether (3 x 15 ml). The combined organic extracts were washed with water, dried over $MgSO_4$ and the solvent was removed in vacuo. Vacuum distillation of the residue gave 0.15 g (42%) of colourless 116. Pmr ($CDCl_3$): 0.7-2.7 (m, 12); 3.7-4.3 (d of m's, 1); 5.3-5.9 (m, 2). Ir (neat): 3320, 3009, 2710, 1420, and 1370. Injected on a SE-30 column (110°) this material gave rise to two peaks in ratio 3.6:1 with retention times 10 min 35 sec and 11 min 45 sec respectively. Anal, of the mixture, calcd for $C_8H_{12}O$: 77.38; H, 9.74; found: C, 77.12 H, 9.90.

Attempted Dehydration of 1,4,4-Trimethylbicyclo[5.1.0]oct-5-en-2-ol, 112

a) On alumina:

Alcohol 112 was injected in 0.01 ml portions onto a 1/8" x 1' preparative gc column filled with a neutral alumina (activity I). The temperature was varied from 150 to 250° and flow rate of helium between 300 and 1500 ml/min. At lower temperatures and flow rates the bulk of material remained on the column. At higher temperatures the retention times were of order of 60 sec and only the benzenoid products (pmr) were collected. These products were not further analyzed.

b) Reaction of 112 with SO_2Cl_2 in pyridine:

The procedure described in ref.[154] was followed directly. The alcohol was recovered.

c) <u>Reaction of 112 with Methanesulfonylchloride in 2,6-Lutidine:</u>

A solution of <u>112</u> (0.28 g, 0.17 mmol.) in 2,6-lutidine (5 ml) was cooled to 0° and the solution of mesylchloride (0.3 ml, 0.27 mmol.) in 2,6-lutidine (2 ml) was added. The mixture was stirred at 50° for 30 min, then poured into water (50 ml) and the organic material extracted with ether (3 x 20 ml). The combined ether extracts were washed with dilute HCl and water, dried over $MgSO_4$ and the solvent removed in vacuo. The residue was divided into two equal portions. One of them was heated for 60 min at 70° in 2,6-lutidine (3 ml), and the other was treated for 5 min with an ethanol solution of EtONa (5 ml, 10%) at room temperature. Both reaction mixtures were worked up with water and ether, the products were distilled and injected on analytical gc column (carbowax, 130°). The distillate obtained by either route gave rise to at least 15 peaks which had almost identical retention times and relative amounts in the two cases. None of the peaks represented more than 20% of the mixture. The retention time of the last fraction was identical with that of <u>112</u> (18.5 min).

d) <u>Reaction of 112 with bis(2- henylhexafluoro-2-propyloxy)-</u>
<u>dimethylsulfurane, 118:</u>

The solid sulfurane <u>118</u>[152] (3.9 g, 5.98 mmol.) was added to the solution of <u>112</u> (0.87 g, 5.27 mmol.) in dry, ethanol free chloroform (10 ml). The pmr spectrum of the mixture recorded shortly after dissolution of <u>118</u>, was totally different from that of the starting <u>112</u>. Some of the chloroform was evaporated in vacuo and the mixture was analysed by vpc (SE-30 column, programmed temperature increased from 95 to 150°C). Some 16 different peaks were observed and the major ones

of these were collected. The first and last of these fractions were identified as 2-phenylhexafluoro-2-propanol and diphenylsulfoxide by comparing their gc retention times, ir and pmr data with those of authentic materials. Fractions 2, 3 and 4 with retention times at 95° of 7.5, 11 and 13 min, each displayed in their mass spectrum, molecular peaks (m/e=148) corresponding to formula $C_{11}H_{16}$, and had the following spectral properties: Fraction 2: Pmr ($CDCl_3$): 1.07 (s, 6); 2.07 (s, 3); 5.20 (d of d's, 2); 5.93-6.40 (m, 3). Ir (neat): 1450, 1375, 1357. Fraction 3: Pmr ($CDCl_3$): 0.98 (s, 3); 1.08 (s, 3); 1.65 (d of d's, 3); 2.1-3.5 (m, 4); 4.82 (m, 2); 5.68 (s, 2). Ir (neat): 1670, 1463, 1450, 1358. Fraction 4: Pmr ($CDCl_3$): 1.06 (s, 6); 1.22 (s, 1); 1.95 (s, 1); 1.98 (s, 3); 2.30 (s, 2); 4.73-5.00 (m, 5). Ir (neat): 1600, 1460, 1352, and 1293.

e) Reaction of 112 with p-Toluensulfonylchloride in Pyridine

Tosylchloride (0.46 g, 2 mmol.) was added to the solution of 112 (0.2 g, 1.2 mmol.) in dry pyridine (5 ml) and the mixture was stirred at room temperature for 3 hr. The solution was cooled below $+5^o$ and the remaining tosylchloride was decomposed by adding 0.1, 0.2 and 0.4 ml of water in 5 min intervals. Water (20 ml) was added and the mixture was extracted with ether (3 x 5 ml). The combined extract was washed with 10% HCl (5 ml), water (2 x 10 ml), dried over $MgSO_4$ and the solvent was removed in vacuo to give the starting alcohol (0.3 g, 70%).

f) Heating of 112 with I_2

No change in the pmr spectrum of 112 was observed when this compound was treated with I_2 at temperatures up to 110°.

Pyrolysis of Esters of 112

The xanthate of 112 was prepared from 112 (1.6 g, 10 mmol.) MeLi (10 ml of 1.5 N solution), carbon disulfide (1.5 g, 20 mmol.) and MeI (2.1 g, 15 mmol.) using a procedure previously described for a different alcohol.[157] The distilled xanthate (b.p., 100°/0.1 Torr) had the following pmr data: Pmr (CDCl$_3$): 0.6-1.0 (m, 3) 1.18 (s, 3); 1.21 (s, 6); 2.6 (s, 3); 5.4 (m, 2) and a broad resonance between δ 1 and 2. This material was heated under nitrogen at 250° for 60 min in a flask equipped with a cold trap. The pressure was then reduced to 15 Torr and the volatile products were collected in the cold trap. Analysed by vpc (preparative carbowax column, 120°) this distillate produced 11 peaks with retention time between 3.5 and 16 min. Three largest of these comprised about 20% of the mixture each.

The boric ester obtained by a NaBH$_4$ reduction of 102 vide supra was heated to 180° at 0.2 Torr. No distillate was collected in the cold trap.

Synthesis of Oct-7-yn-1,3-diene, 128

Tosylhydrazine (0.47 g, 2.5 mmol.) was added to a solution of 104 (0.25 g, 2.0 mmol.) in MeOH (1 ml), and the mixture refluxed under nitrogen for 30 min. (Ir spectra of a sample removed after 30 min revealed that the carbonyl absorption at 1708 cm^{-1} was replaced completely by a C = N stretch at 1595 cm^{-1}). The solution was dried over MgSO$_4$ and the solvent was removed in vacuo. The solid residue was mixed with melted parafin (20 ml) containing sodium hydride (0.2 g, 4.2 mmol. of 50% mixture with parafin) in a flask

equipped with stirrer, and a reflux condenser. A water pump was joined to the top of the condenser through a cold trap and the pressure was maintained at 15 Torr. The temperature of the flask was increased to the boiling point of the parafin (190°), and maintained at this level for 1 hr. During this time 15 mg (7%) of <u>128</u> was collected in the cold trap. The product gave only one peak (ret time, 3 min, 20 sec) when injected on a SE-30 column at 90°. Pmr (CCl_4): 1.78 (t, 1, H-8); 2.00-2.54 (m, 4, H-5,6); 4.98-5.28 (m, 2, H-1,1'); 5.38-5.60 (m, 1, H-4); 5.98 (t, 1, H-3); 6.55 (d of t's, 1, H-2); $J_{1,2}$=10.5; $J_{1',2}$=16.8; $J_{2,3}$=10.5; $J_{3,4}$=10.5; $J_{6,8}$=2.5 Hz. Ir (neat): 3310, 3097, 2120, 1420. Uv, λ_{max}^{MeOH} = 227 nm, log ε = 4.37

$$C = C - C = C - C - C - C \equiv C$$
$$1 \quad 2 \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8$$
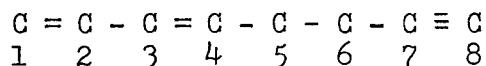
Reduction of oct-7-en-1,3-diene, <u>128</u> (7 mg) with hydrogen at 30 psi, in MeOH (1 ml) using a Pd/C catalyst gave a product which had and identical ir spectrum and retention times on both, the carbowax and SE-30 column with that of authentic n-octane.

Synthesis of 5,5-Dimethylnon-7-yn-1,3-diene, 126

Tosylhydrazine (1.9 g, mmol.) was added to the solution of <u>102</u> (1.6 g, 10 mmol.) in MeOH (15 ml), and the mixture refluxed for 30 hr. (Ir spectra of small samples were examined periodically). The solution was then dried over $MgSO_4$ and the solvent was removed in vacuo, to give tosylhydrazone <u>125</u> (3.2 g, 88%).

Crude <u>125</u> (0.9 g, 3 mmol.) was dissolved in benzene (50 ml) and a 7 fold excess of sodium hydride (1.5 g, of a 53% dispersion in oil) added. The solution was refluxed for 6 hr, and during this time

the initially clear solution developed a white precipitate. The mixture was washed with water (50 ml), dried over $MgSO_4$, and the solvent was removed through a 1' column filled with glass helices at atmospheric pressure. Distillation of the residue gave 0.31 g (70%) of pure 126. This material gave only one peak when analysed by vpc (SE-30 column, 95°) with retention time 11.6 min. Uv, λ_{max}^{MeOH} = 229 nm, log ϵ = 4.58. Pmr ($CDCl_3$): 1.28 (s, 6, H-7); 1.83 (t, 3, H-6); 2.25 (q, 2, H-5); 5.07-5.28 (m, 2, H-1,1'); 5.46 (d, 1, H-4); 5.95 (t, 1, H-3); 6.86 (d of t's, 1, H-2).

$$C = C - C = C - C(Me)_2 - C - C \equiv C - C$$
$$1 \quad 2 \quad 3 \quad 4 \quad 5 \: 10 \qquad 6 \quad 7 \quad 8 \quad 9$$
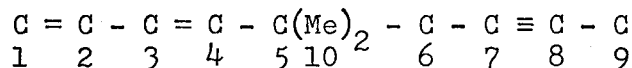
$J_{1,2}$ = 12; $J_{1',2}$ = 16; $J_{2,3}$ = 11; $J_{3,4}$ = 12; $J_{5,6}$ = 12 Hz. Cmr ($CDCl_3$, in ppm downfield from TMS): C-1, 118.14 C-2,3,4, 129.06, 133.48, 140.02, the specific assignment of th se bands was not determined; C-5, 37.25; C-6, 34.43; C-7,8, 3.57; C-9, 0.13; C-10, 28.67. Ir (neat): 3090, 3000, 2980, 2917 and 1460. Mass spec., m/e: 148.1252; calcd for $C_{11}H_{16}$, 148.1252.

Reduction of 1,4,4-Trimethylbicyclo[5.1.0]oct-2,5-dienyl-2-tetramethylphosphorodiamidate, 131

The enol ester 131 was prepared from 102 using the procedure used previously for preparation of similar enol esters.[162] Unpurified, dry 131 (1.2 g, 4.2 mmol.) was added to a solution of lithium (0.29 g, 40 gatoms) in a mixture of liquid ammonia (120 ml) and tetrahydrofuran (12 ml), kept at -78°. The mixture was stirred and the temperature was maintained at -40° for 60 min. The blue solution was

then discoloured by addition of sodium benzoate (1.2 g) and ammonium

chloride (0.8 g). After evaporation of the ammonia, the residue

was dissolved in water (20 ml) and the water solution was extracted

with CH_2Cl_2 (3 x 5 ml). The organic solution was washed with 10%

NH_4Cl and water and dried over $MgSO_4$. The solvent was removed through

a short column at atmospheric pressure and the residue was distilled

to give 0.39 g, 65% of colourless liquid. Injected on an SE-30 column

(90°) this material separated into five components. The two major

components were collected.

Component "A" with a ret. time of 18 min, 58% of the mixture

(determined by gc) had the following properties: m/e, 150.1408;

calculated for $C_{11}H_{18}$: 150.1408. Ir (neat): 3022, 2960, 2925, 2870,

1360. Pmr (CDCl$_3$): 0.9-2.2 (m, 15); 5.2-5.8 (m, 1).

Component "B": ret. time 21.5 min, represented 37% of the

mixture: m/e, 150.1408. Ir (neat): 2960, 2918, 1440, 1361; Pmr

(CDCl$_3$): 0.91 (s, 6); 1.22-1.55 (m, 4); 1.72 (s, 3); 2.08 (m, 4);

5.23 (t, 1).

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