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CATALYSED REARRANGEMENT OF BICYCLOBUTANES

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CONCERNING THE 1,5-BISDEHYDRO[10]ANNULENE SYSTEM
and
SOME ASPECTS OF TRANSITION METAL-CATALYSED REARRANGEMENT OF BICYCLOBUTANES

by

Nicholas Darby

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF DOCTOR OF PHILOSOPHY

Department of Chemistry

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Fall, 1972

THE UNIVERSITY OF ALBERTA

FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled

CONCERNING THE 1,5-BISDEHYDRO[10]ANNULENE SYSTEM

and

SOME ASPECTS OF TRANSITION METAL-CATALYSED
REARRANGEMENT OF BICYCLOBUTANES

submitted by Nicholas Darby in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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ABSTRACT

Part I

To date, no example of a planar, homonuclear, monocyclic 10 π-electron system is known, which is somewhat surprising in view of the fact that Huckel's "4n+2" rule predicts that this type of system should show aromatic properties. 1,5-Bisdehydro[10]annulene (**32**) represents this type of system, and would be expected to be aromatic. Synthesis of **32** would then constitute a valuable contribution to aromatic chemistry.

Attempts were made to synthesize both 3,4-benz-1,5-bisdehydro[10]annulene (**35**) and 3,4-tetramethylene-1,5-bisdehydro[10]annulene (**37**). In both cases, the target molecule was found to be too reactive to allow isolation. The 3,4-benz-derivative (**35**) reacted to form anthracene (**60**); the 3,4-tetramethylene derivative (**37**) gave 1,2,3,4-tetrahydroanthracene (**93**) and 3,4-benzcyclodec-3-ene-1,5-diyne (**94**). It was concluded that **60** and **93** were formed from diradical intermediates, and that **94** was the result of a "Cope-like" rearrangement of the in-plane electrons of compound **37**. These results were indicative of the behaviour of the (hypothetical) parent molecule (**32**) and to some extent the chemistry of this system is now understood. The results obtained also suggested

that a trimethylene derivative of **32** may be isolable. Preliminary work towards this goal is presented. The 1,5-bisdehydro[10]annulene system is also discussed with reference to other 10 π-electron aromatic systems.

The 1,5-bisdehydro[11]annulenyl cation (**33**) is also a potentially planar, 10 π-electron aromatic system, in analogy with compound **32**. Hydride abstraction from 3,4-benzcycloundeca-3,7,10-triene-1,5-diyne (**36**) and 3,4-tetramethylenecycloundeca-3,7,10-triene-1,5-diyne (**38**) failed to yield the corresponding dehydro[11]annulenyl cation derivatives. A discussion of these results in terms of the molecular geometry and in reference to a known bridged [11]annulenyl cation is presented.

Part II

Recently there have been reported numerous examples of transition metal-catalysed rearrangements of highly strained hydrocarbons. These reactions promise to yield valuable information concerning strained molecules, transition metals, and their interaction. Some of these rearrangements are discussed. Particular emphasis is placed on the Ag(I)-, Pd(II)- and Rh(I)- catalysed conversion of substituted bicyclobutanes into butadienes. The dependence of the course of the reaction on the metal, the metal ligands and the substitution pattern of the bicyclobutane is

emphasized. Mechanistic possibilities for these rearrangements are presented.

At the start of this work, no intermediates in the conversion of bicyclobutanes into butadienes had been detected. It was found that $PdCl_2(C_6H_5CN)_2$ (**66**) rearranges tricyclo[4.1.0.0^{2,7}]heptane (**43**) into 3-methylenecyclohexene (**45**). Monitoring this reaction by cold temperature nmr spectroscopy showed that two intermediates (**67** and **68**) are involved in this reaction. Intermediate **68** was shown to be a carbene-metal complex which had been proposed earlier as an intermediate. Complex **68** represents the first detection and characterization of an intermediate in the transition metal-catalysed rearrangement of bicyclobutanes. Details of the conversion of **43** into **45** by catalytic amounts of **66** are presented.

ACKNOWLEDGEMENTS

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PART I

CONCERNING THE 1,5-BISDEHYDRO[10]ANNULENE SYSTEM

"And if a thing is unknown, how is it possible for anyone to endeavour to produce it or to destroy it?"

Avicenna
De Mineralibus
circa 1020 AD

CHAPTER 1

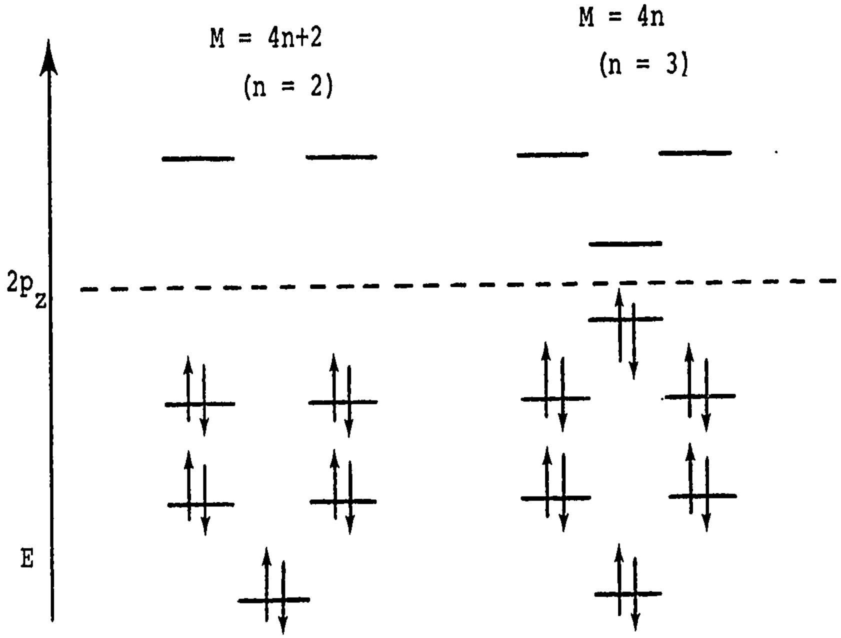
INTRODUCTION

A. Cyclic π-Electron Systems

In 1931, Erich Hückel reported the first application of Molecular Orbital (MO) Theory to organic chemistry.[1] His representation of the structure of benzene thus placed earlier, more empirical descriptions[2] on a firmer theoretical basis, and allowed extending the concept of aromaticity to other π-electron systems, thereby providing impetus for a vast amount of theoretical and synthetic organic chemistry.

Hückel's theory for conjugated monocyclic polyenes has had remarkable success, considering the rather generous assumptions inherent to it.[3] The planar σ-bond framework is considered to be completely separable from the π-system, which is made up of $2p_z$ carbon orbitals perpendicular to the plane of the molecule. The interaction of the non-adjacent p_z orbitals is assumed to be nonexistent. The molecule is also assumed to consist of equivalent CH units with equal carbon-carbon bond distances around the periphery.

Linear combination of atomic orbitals (LCAO) then leads to a set of molecular orbitals. Some of these molecular orbitals have energies lower than the constituent p_z orbitals (bonding MO's) and some are of higher energy (anti-bonding MO's). The lowest lying MO is always single, and therefore accommodates two electrons of opposite spin. Higher bonding levels occur in degenerate pairs, each pair requiring 4 electrons to fill them. Each group of bonding MO's can be thought of as a shell, and so it is that 4n+2 electrons (n is an integer) are required to yield a filled-shell configuration. These features are illustrated below.



π-Type Molecular Orbitals for Cyclic Polyenes, C_MH_M

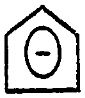
In some 4n-electron cases, absence of alternation in bond lengths results in degenerate MO's containing 1 electron each. The system will distort in order to remove the degeneracy and pair the electrons in a highest bonding MO, leaving a lowest non-bonding MO vacant. This is illustrated above for a 12-electron system.

Hückel's theory leads to a rule, which has become known as the "4n+2" rule; it may be stated as follows:[3]

> "those monocyclic coplanar systems of trigonally hybridized atoms which contain 4n+2 electrons will possess relative electronic stability."

Thus, benzene (1) (n=1) is a particularly inactive compound. Cyclopentadienyl anion[4] (2) and cycloheptatrienyl cation[5] (3) are far more stable than might be expected for classical organic ions. The next extension

1



2

3

of Hückel's rule is that the particular electronic stability associated with a filled-shell configuration is reflected in the classical concept of aromaticity. In this way, aromatic character might be expected of any planar, cyclic array of 4n+2 π-electrons.

Originally, the concept of aromaticity was associated with low chemical reactivity. This however, is a reflection of the transition state energy, which is not easily calculated, nor particularly convenient. That tropylium cation (3) is stable is irrefutable, but it is also highly reactive.

A far more useful description of aromaticity would be one based on ground-state properties, which would be a better reflection of electronic structure, and therefore more in keeping with Hückel's theory. Some measurable property of 4n+2 π-electron systems is thus needed as a basis for a new definition of aromatic character.

The attempt to reconcile the classical concept of aromaticity with the more modern idea of low ground-state enthalpy has resulted in recent years in a plethora of new terms and classifications of polyenic molecules:

1) pseudo-aromaticity[6]
2) quasi-aromaticity[7]
3) anti-aromaticity[8]
4) non-aromaticity[9]
5) homo-aromaticity[10]
6) pseudo-anti-aromaticity[11]

The suggestion has even been made that the term "aromaticity" be discarded altogether.[12]

This host of terms is a reflection of the fact that no single physical criterion has emerged as a definitive means of establishing whether or not a compound is aromatic. This omission is not due to a lack of suggestions.[13] For instance, low enthalpy of formation is thought to be indicative of aromatic character. However, the "lowness" of this enthalpy of formation must be judged relative to a hypothetical molecule, whose enthalpy of formation is dependent on some rather arbitrary assumptions about the geometry and electronic structure of this (fictitious) molecule.[14] Thus this criterion is hardly rigorous. The designations of "alternant" and "non-alternant" hydrocarbons, and Craig's symmetry rules also fail to provide a rigorous definition of aromaticity.[13]

Benzenoid aromatic compounds show diamagnetic susceptibility effects. In order to explain this phenomenon, Pauling[15a] and London[15b] proposed the existence of an interatomic ring current induced in the cyclic, conjugated π-electron system when a magnetic field is applied perpendicular to the plane of the ring. Aromatic hydrocarbons also exhibit characteristic chemical shifts in the nmr spectra of protons attached to the aromatic ring. These shifts are generally downfield from the "normal olefinic" positions. The ring current model was invoked[16,17] to explain these shifts, the effect of a diamagnetic ring current being to cause considerable downfield shifts (deshielding) in the molecular plane outside the ring and even larger upfield shifts (shielding) inside.

In 1966, Pople and Untch[18] pointed out that

London's theory of ring currents[15b] did not restrict them to diamagnetic effects. Indeed, by mixing in of non-bonding MO's, the theory predicts a negative contribution to the magnetic susceptibility (diamagnetic ring current) for 4n+2 π-electron systems and a positive contribution (paramagnetic ring current) for 4n systems.

A few interesting facts emerge from this description:[18]

1) For all sizes of rings, the magnitude of the ring current is partially quenched by bond alternation. This quenching gets larger in larger rings.

2) For 4n systems, infinite paramagnetism is predicted in the absence of bond alternation. This, however, is not likely to occur because the molecule will distort to remove the degeneracy of the highest occupied and lowest unoccupied orbitals.

3) For 4n+2 systems, $n<7$, the theory predicts an increase in diamagnetic ring current with ring size. In the event that rings are buckled, the magnitude of the ring currents will decrease with the decrease in the effective overlap of the $2p_\pi$ atomic orbitals.

4) In the nmr spectrum of these molecules, protons on the outside of a diamagnetic (4n+2) ring current will be deshielded; those inside will be shielded. For paramagnetic systems (4n) these effects are precisely reversed.

By this theory, some measure of ring planarity, type of π-conjugation, and degree of conjugation is indicated by nmr spectroscopy. These factors are precisely those dealt with by the Hückel theory. Accordingly, chemical shifts of protons bonded to cyclic polyenic systems may reflect the aromaticity of the system. Indeed, such effects were proposed as a new, qualitative measure of aromatic character.[17,19]

However, such a description is apparently not accurate enough as a quantitative measure of aromaticity.[13] Musher[20] has attacked the ring current model, arguing that the chemical shifts displayed by aromatic hydrocarbons can be explained by the sum of contributions from localized electrons of both σ- and π-character. In turn, this theory was criticized[21] in that it failed to predict shielding of protons inside the aromatic ring.

It is the view of the present author that the ring current model gives a qualitative account of chemical shifts, and therefore may be used as a test of aromatic character, but it is not indicative of the degree of aromaticity. Discussion of degree of aromaticity appears futile; any such discussion presupposes an exact definition of aromaticity, none of which has been generally accepted (see for instance, ref. 14). The MO description of aromaticity is a good, qualitative means of understanding the phenomenon, and any attempts at quantitative measure have been based on measurement of physical properties which can be accounted for on the basis of a delocalized π-electron system.

In all branches of chemistry (indeed, in all branches of knowledge) there exists a tendency to classify or group facts according to certain patterns. The periodic table is a prime example of this. Once grouped, a common criterion is sought or proposed, to place on an objective plane the reasons for the grouping of the facts--the source of their common characteristics. This process is exceedingly valuable for garnering deeper understanding of the physical realities in question.

Benzene is an aromatic compound. Its curious properties, as related to polyolefinic compounds, then led to the development of the class of compounds called aromatic. Those molecules with features in common with benzene (low chemical reactivity, delocalized electron systems, diamagnetic susceptibility, etc.) have thus been included in this class. Hückel's theory, and extensions of it, allowed prediction of unknown structures that should exhibit similar properties.

Measurement of physical properties that may arise from factors delineated by Hückel's theory as quantitative measures of the <u>concept</u> of aromaticity will lead to situations in which compounds intuitively considered aromatic are then excluded from the class, which in turn, is bound to cause disagreement among those working in the field.

Discussion of aromaticity as a class of compounds has to some extent been confused with discussion of aromaticity as a physical phenomenon, this latter description being, at the very least, a controversial means of proceeding (see for instance, ref. 12-14). However, aromaticity as a class of compounds necessarily involves subjective and/or intuitive judgement when the question arises as to whether or not a particular compound is aromatic; any comparison, for instance, of a non-benzenoid hydrocarbon with benzene obviously must discount differences between the two as being unimportant relative to the similarities that may exist. This discounting thus involves subjectivity, insofar as quantitative assessment of the relative importance of physico-chemical facts is not possible.

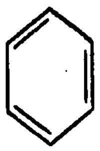
Finally, the following statement may be pertinent: "In these cases in which a given theoretical notion is made to correspond to two or more experimental ideas, it would be absurd to maintain that the theoretical concept is explicity defined by each of the two experimental ones in turn."[22]

For the purposes of this Thesis, the term "aromatic" or "possessing aromatic character" will be used to mean that the compound under consideration is a member of the class of aromatic compounds; that is, the compound possesses certain properties, in common with benzene in kind, if not degree, that are at least explicable in terms of Hückel's molecular orbital theory. These properties will include, for instance, planarity of the molecule, lack of bond alternation, evidence for extensive electron delocalization (with reference to uv spectroscopy) and particularly diamagnetic anisotropy effects. This preceding discussion is not intended as a definition of aromatic character, but rather a working description of particular molecules that allow their classification as aromatic compounds. The description is used with recognition of the limitations inherent in applying these physical phenomena, but also with recognition of the utility of dealing with compounds as groups, rather than individuals. Labelling a compound in no way affects the reasons why that compound is interesting.

The prediction of aromaticity for cyclic, planar fully conjugated $4n+2$ π-electron systems was mentioned at the outset. Perhaps in no other endeavour in chemistry has the coupling of theory and experiment been so fruitful in gaining understanding of the electronic structure of molecules. This section has briefly discussed some theoretical aspects of aromatic chemistry; the next section will present some representative experimental work which supports the "4n+2" rule.

B. Some 4n and 4n+2 π-Electron Systems

The annulenes are monocyclic, fully conjugated polyenes, with the ring size being indicated by a number in brackets. Conjugated polyene-polyynes are called dehydroannulenes, with *bis*, *tris*, *tetra*, etc , being used as prefixes to indicate the number of acetylenic bonds in the ring. Thus, benzene (**1**) is [6]annulene, cyclooctatetraene (**4**) is [8]annulene, and compound **5** is 1,3,7,9-tetradehydro-[12]annulene. This system of nomenclature was suggested by Sondheimer[23] in order to simplify the names of macrocyclic polyenic compounds, and it will be used throughout the remainder of this Thesis.



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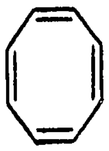

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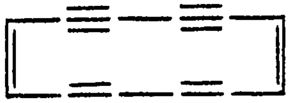
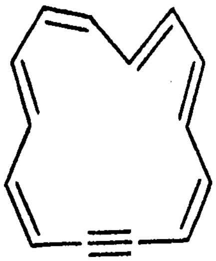


5

Sondheimer has done much of the synthetic work in the higher annulene series.[24,25] This followed from his discovery[26] that oxidative coupling of α,ω-diacetylenes led to the formation of cyclic polyacetylenic compounds. Rearrangement of these compounds in strong base gave rise to fully conjugated dehydroannulenes, which on partial catalytic hydrogenation produced the desired annulenes.

Both annulenes and their dehydro-analogues are useful compounds for investigating the limits of Hückel's theory. Dehydroannulenes are particularly interesting because the acetylenic bonds induce planarity and some degree of rigidity into the annulene ring, which still possesses the correct number of out-of-plane π-electrons.

Monodehydro[14]annulene (6, or an isomer) was formed by coupling of trans, trans-4,10-tetradecadiene-1,7,-13-triyne, followed by treatment with potassium t-butoxide. Hydrogenation of 6 over Lindlar catalyst gave [14]annulene



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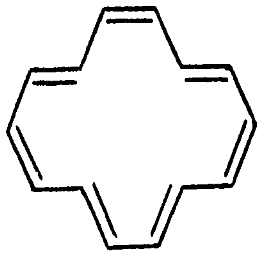
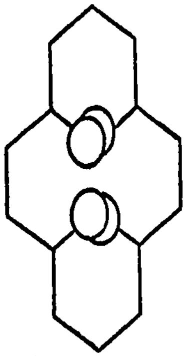


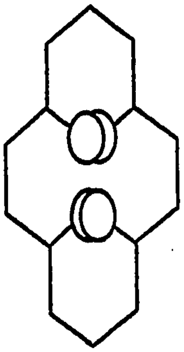
7

(7), a (4n+2) π-electron system (n=3).[27] [14]Annulene is not very stable, but exhibits a uv spectrum characteristic of a conjugated system (λ_{max} 321 and 378 nm; ε = 69,000 and

5,700). [14]Annulene exists in two forms, thought to be **7A** and **7B**, which result from the crowding of the internal protons. This crowding probably accounts for the instability of this compound.[28]

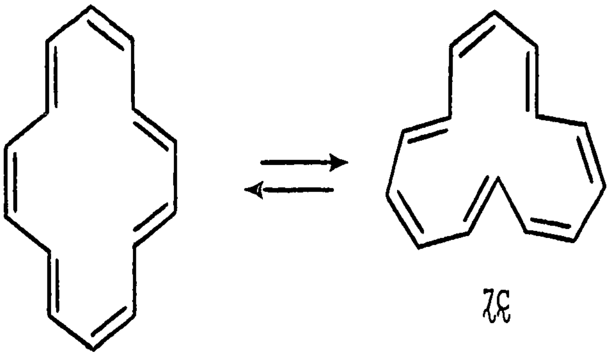


7A



7B

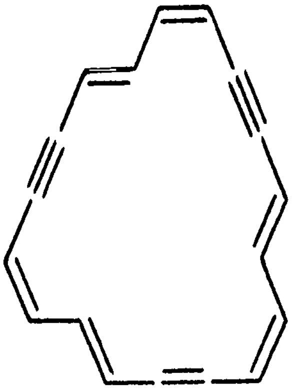
The nmr spectrum of isomer **7A** at -126° shows peaks at τ 2.12 (10H) and τ 10.61 (4H), assigned to the outer and inner protons respectively.[29] The presence of a diamagnetic ring current is indicated. Recently, Oth has shown[29b] that the temperature dependence of the nmr spectrum of [14]-annulene (**7**) is due to a fast isodynamic transformation between the two conformers, **7A** and **7C**. X-ray analysis[30] shows that **7A** is the crystalline form of [14]annulene. The molecule is not quite planar, but the near centrosymmetric structure, and C-C bond lengths (1.350 - 1.407 Å), indicate that there is no chemically significant alternation in bonds. [14]Annulene (**7**) is in accord with



7 **7a**

Hückel's rule, and is aromatic. Several dehydro-derivatives show similar properties,[17] and are also aromatic.

The first higher annulenes that Sondheimer reported were those containing the 18 π-electron system.[31-37] 1,7,13-Tridehydro[18]annulene (**8**)[31] is a stable aromatic



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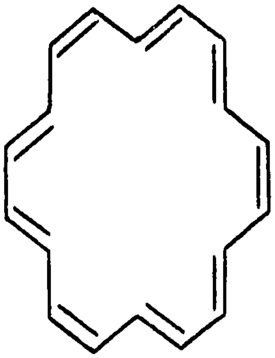
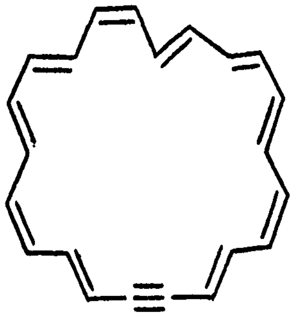


9

compound; its nmr spectrum shows absorptions for the outer ring protons at τ 1.7-3.1 and for the inner protons at τ 8.26.[17] Partial hydrogenation of **8** led to [18]annulene (**9**).[32] The uv spectrum of **9** shows maxima (benzene) at 378, 415, and 456 nm (ε = 297,000, 8,700 and 28,400). A stabilization energy of 100±6 kcal/mole was determined by combustion analysis.[33] The size of the 18-membered ring permits conformational mobility, and thus the nmr spectrum of [18]annulene is temperature-dependent, a phenomenon which is observed in other large annulenes.[17] At -60°, **9** shows peaks in the nmr at τ 0.72 (12H, outer protons) and τ 12.99 (6H, inner protons).[29,35] Compound **9** also undergoes electrophilic substitution.[37] [18]Annulene is an aromatic compound. Several dehydro[18]annulenes have been prepared,[34,36] and they show properties consistent with them being aromatic.

Dewar had calculated[38] that annulenes containing 4n+2 π-electrons and a reasonably planar carbon skeleton would be aromatic up to and including [22]annulene, but that [26]annulene would no longer be aromatic. Similar considerations apply to the dehydro analogues. Thus Sondheimer's synthesis of monodehydro[22]annulene (**10**) was of considerable interest.[39]

Compound **10** shows uv absorption (ether) at 280 nm (ε = 28,800), 372 (132,000), 438 (11,900), 452 (12,200) and 495 (3,600). The nmr spectrum of **10** showed multiplets



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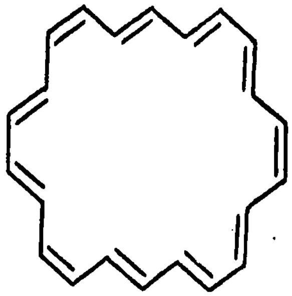
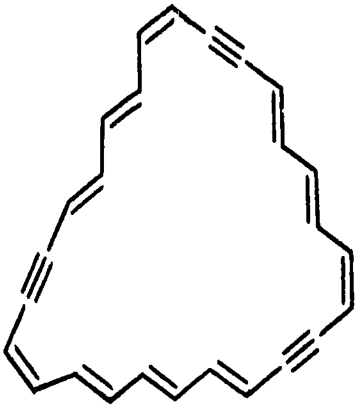


11

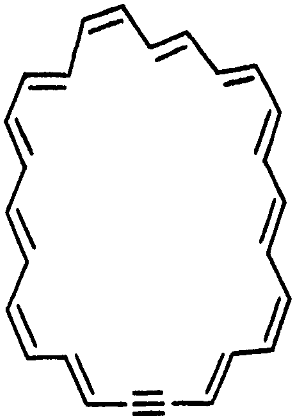
at τ 1.55-3.75 (13H, outer protons) and τ 6.55-9.30 (7H, inner protons). The exact structure of this compound (10) is unknown, and 10 represents one of several possibilities. The compound is aromatic.

Partial hydrogenation of 10 gave [22]annulene (11).[40] The nmr spectrum of 11 was found to be temperature-dependent. At -90°, it consisted of multiplets at τ 0.35-0.7 and τ 0.9-1.5 as well as a high-field multiplet at τ 10.4-11.2. At 65°, the spectrum is a broad singlet at τ 4.35. [22]Annulene is aromatic, by virtue of the diamagnetic shifts in its low-temperature nmr spectrum.

A tridehydro[26]annulene (for instance, 12) has been synthesized by Sondheimer's group.[41] The nmr spectrum of 12 showed only a very broad multiplet at τ 2.0-4.5. Cooling did not significantly alter the spectrum. Thus there is no evidence that this compound (12) can sustain a diamagnetic ring current; it is not aromatic.



12

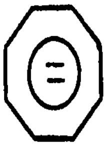


13

However, a monodehydro[26]annulene (13) has recently been reported.[42] At -90°, this compound has absorptions in the nmr spectrum at τ 2.1-3.8 and τ 5.8-6.0. This difference in the chemical shifts for the inner and outer protons indicates that 13 is capable of sustaining some diamagnetic ring current, and is therefore aromatic. The limit, then, of aromaticity with ring size[38] appears to be the 26-membered ring. Compound 13 is the largest monocyclic compound for which a diamagnetic ring current has been detected.

All of the above compounds contain 4n+2 π-electron systems. Hückel's theory allows the prediction[3] that systems of 4n+3 π-electrons should be capable of giving up an electron to form a cation with 4n+2 π-electrons; systems of 4n+1 π-electrons should similarly add an electron to form a closed-shell 4n+2 π-electron anionic system. [4n]-Annulenes may also add 2 electrons to form 4n+2 π-electron annulenyl dianions.

Examples of each of these systems are known. [5]Annulenyl anion (2)[4] and [7]annulenyl cation (3)[5,45] have already been mentioned. Non-aromatic [8]annulene (4) is converted into [8]annulenyl dianion (14) by reduction of 4 with alkali metals.[46] 9-Chlorobicyclo[6.1.0]nona-2,4,6-triene gives the anion 15.[47] That these compounds even exist should justify their inclusion into the aromatic class of compounds. The nmr spectrum of 15 is a sharp singlet at τ 2.96, a low field absorption in spite of the shielding effect of the negative charge. Thus 15 sustains a diamagnetic ring current.



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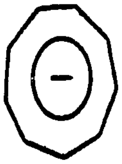

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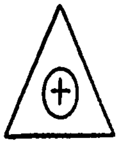
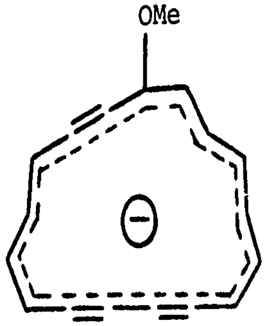
The simplest of all aromatic systems is the



16

cyclopropenyl cation (16) (n = 0), which has been prepared in substituted and unsubstituted form.[48]

Sondheimer has begun extending his annulene chemistry to ionic systems.[25,49] One example of this work is the [17]annulenyl anion (17).[49d] This compound shows

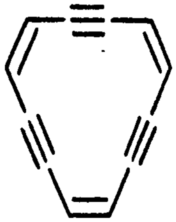


17

nmr absorptions at τ -0.47-2.16 for the outer protons, and τ 18.54, 18.85, and 19.01 for the inner protons. These unusually large differences in chemical shifts are demonstrative of a ring current for this 4n+2 π-electron system.

The simplest of [4n]annulenes is cyclobutadiene (n = 1). It is unknown, and still presents a considerable challenge to synthetic organic chemistry; some derivatives of [4]annulene have reportedly been isolated in the lattice at liquid nitrogen temperatures.[50] [8]Annulene (4) was synthesized in 1911;[51] it is not at all like benzene, a fact that provided further impetus in looking for an explanation of aromaticity.

Dehydro-analogues of [12]annulene have been synthesized (compounds 18 and 19).[52] The two protons on the



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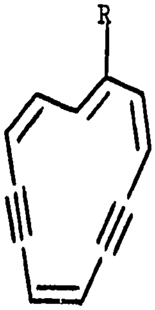
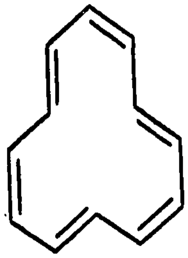


19 a) R = H
b) R = Br

trans- double bond of 19a resonate in the nmr spectrum at τ -0.9; it was suggested that this is the result of an averaging process caused by interconversion of two planar conformers, and that the ring is sustaining a paramagnetic ring current.[18] This conformational change is not possible in compound 19b because of the size of the bromine atom. The synthesis of compound 19b was achieved by Untch and Wysocki.[53a] The single, inner proton appeared at τ -6.4. 19b is therefore planar, or nearly planar, and supports an induced paramagnetic ring current, which is elegantly in agreement with the theory briefly discussed earlier.[18] [12]Annulene (20) has been prepared, but not isolated.[53b] Compound 20 is thermally unstable above -40°.



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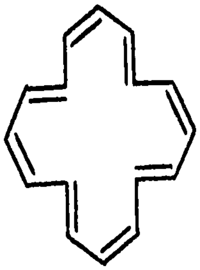
[16]Annulene (**21**) has been prepared, and is a very unstable compound.[54] Evidence has been presented to show that dehydro-analogues of **21** sustain an induced paramagnetic ring current.[18]



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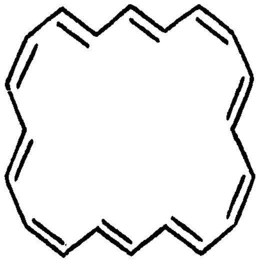


22

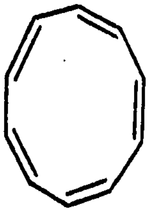
[20]Annulene (**22**) has also been reported.[55] Both **21** and **22** are definitely not aromatic. [24]Annulene is also known,[56] and it has paramagnetic properties.[57]

Experimental work in annulene chemistry appears to be in complete agreement with theory. The ring current model seems also to have been vindicated, at least as a means of explaining otherwise anomolous chemical shift data.

In all of the above work, there is one notable blank space. No mention has been made of the 10 π-electron system, [10]annulene (n = 2), or its dehydro-analogues.[58] They merit a separate discussion on their own.

C. The 10 π-Electron System

[10]Annulene is the next highest 4n+2 homologue of benzene, and thus might intuitively be assumed to be aromatic. Three configurations of the molecule are possible (23, 24, 25).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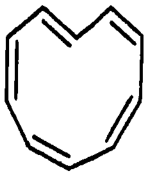
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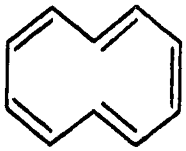
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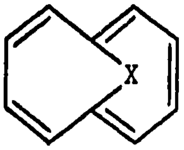
Isomer 25 is free of angle strain, but the transannular interaction of the internal hydrogens appears to be so great that the carbon skeleton is not expected to be planar. Isomer 23 has no such interactions, but the bond angles for a planar structure (144°) are considerably distorted from the normal angle (120°) for sp^2 hybridized carbons. Structure 24 can be considered a compromise between **23** and **25**, and it too would involve considerable angle strain and geometric distortion.

Isomer **25**, however, does suggest a means of constructing a 10-membered annulene with only minor distortion from planarity. This involves replacing the internal hydrogen atoms with a one atom bridge. Such an approach has been successfully employed by Vogel[59] who synthesized compounds **26a-c**.

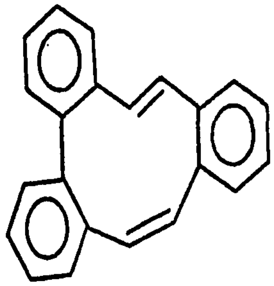


26 **a**) X = CH_2
b) X = O
c) X = NH

These compounds do indeed exhibit aromatic character. Further discussion of them is deferred to Chapter 5.

Whichever of the isomers of [10]annulene (**23**, **24** or **25**) are considered, a lack of planarity and a tendency for transannular reaction would be expected.[60] This lack of electronic stabilization coupled with the expected high reactivity were evidently responsible for the failure of synthetic attempts to make this molecule.

Sondheimer has reported the synthesis of the tribenz[10]annulene (**27**).[58] He concluded that the 10-



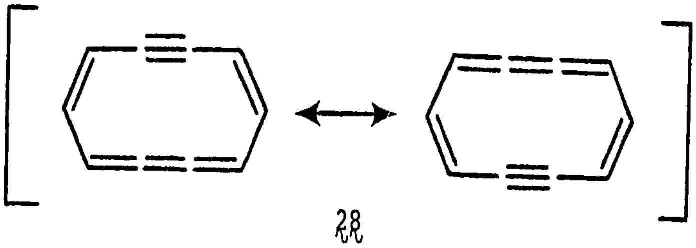
27

membered ring in 27 is not planar, and no evidence for a delocalized electron system around this ring existed. This indicated that any stability achieved by such delocalization was outweighed by the steric and strain effects involved in a planar structure, as expected.

In 1967, van Tamelen and Burkoth reported the apparent trapping of an intermediate [10]annulene generated by the photolysis of trans-9,10-dihydronaphthalene;[61] the first synthesis, isolation and characterization of [10]annulenes was finally accomplished in 1971 by Masamune and co-workers, by low temperature photolysis of cis-9,10-dihydronaphthalene, followed by low temperature workup.[60,62]

The two isomers, $(cis)^5$-[10]annulene (23) and trans,$(cis)^4$-[10]annulene (24) were indeed very reactive, stable only up to -10° and -50° respectively. The nmr spectra showed only olefinic absorptions; both ^1H and ^{13}C nmr spectra of 24 were temperature dependent, indicating that this isomer was not planar. Neither compound (23 or 24) can be called aromatic. It should be pointed out that these two compounds are not exceptions to Hückel's rule; they simply fail to meet its requirements.

In 1948, Sworski briefly discussed incorporating acetylenic and/or cumulenic bonds into 4n+2 π-electron systems;[63] the triple bonds in some instances induce the molecule to assume a planar configuration. Sondheimer has used this approach with particular success in [12]- and higher annulenes, as outlined previously. Sworski made particular reference to 1,6-bisdehydro[10]annulene (28), for which the Kekulé structures are shown. The molecule should be planar, with only moderate apparent strain.



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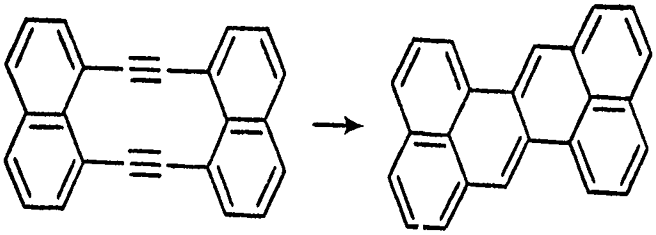
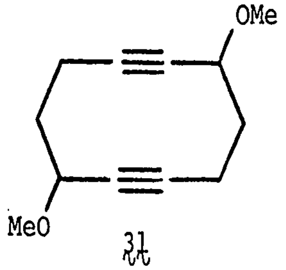
Sondheimer has reported an attempted synthesis of a molecule (29) which formally incorporates the bisdehydro[10]annulene (28).[58] The only isolable product from



29 30

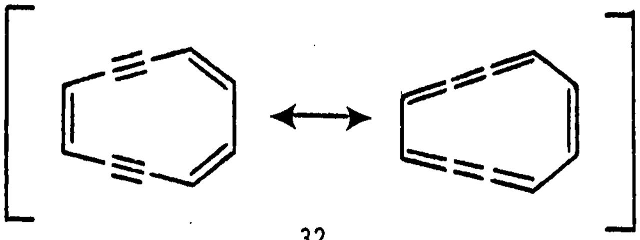
this attempt was zethrene (30). The formation of 30 indicated that 29 was very unstable (assumedly this compound was an intermediate) and readily undergoes transannular reactions.

This instability is probably a reflection of the interaction of the in-plane π-electrons of the acetylenic bonds. The centre of the molecule might well be expected to be crowded for this reason, and transannular reaction would relieve repulsive interactions. Little is known about 10-membered ring cyclic acetylenes. Recently, Reese reported the synthesis of compound 31[64] (along with the unwarranted claim that this was the first example of a 10-membered ring containing two acetylenes[65]). 31 is apparently a stable compound, indicating that the interaction of the in-plane π-electrons, in this case, is not severe. 31 also is an intermediate in a possible synthetic pathway to 1,6-bisdehydro[10]annulene (28), although how promising this route is awaits further work.



31

It is apparent, however, that 28 will probably suffer severe interaction of the acetylenic π-electron clouds. There is an alternate bisdehydro[10]annulene: 1,5-bisdehydro[10]annulene (32)[65] (for which, Kekulé structures are shown). This molecule should be planar, and, as indicated by Dreiding models, should not be unduly strained --certainly it should be less strained than a planar (*cis*)^5-[10]annulene (23). It also contains a 10 π-electron system, and thus should be ideally suited for studying the properties of planar 10 π-electron systems, making 32 a desirable synthetic objective.



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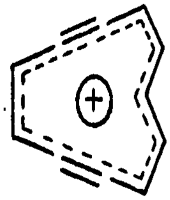
The structure of 32 suggests another interesting, potentially planar 10 π-electron system, and that is the 1,5-bisdehydro[11]annulenyl cation, 33.



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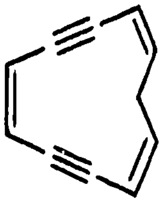

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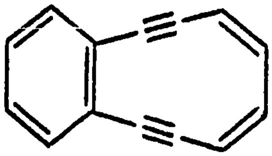
Assumedly, the cation 33 could be generated by hydride abstraction from cycloundeca-1,5-diyne-3,7,10-

triene (34). The attractive aspect of this latter molecule is that models suggest that it is virtually strain-free, and it therefore should be a stable compound, which augured well for the ultimate preparation of cation 33.

Our synthetic objectives were then to build molecules 32 and 34, or compounds which formally contained these systems. In practice, the first synthetic targets were compounds 35 and 36, the 3,4-benz-fused analogues of 32 and 34, respectively.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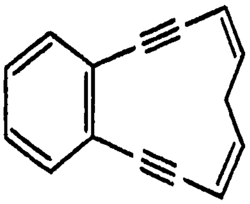
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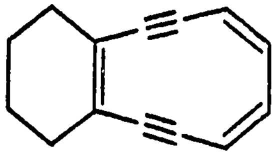
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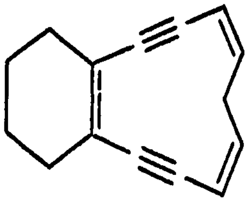
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This choice was made for two reasons: 1) the starting materials necessary for the projected synthetic schemes were readily available; 2) it was hoped that the presence of the benzene ring in the synthetic intermediates would help stabilize them, thus facilitating the synthesis of both 35 and 36. This body of work is the subject of Chapter 2.

For reasons that will be delineated later, we also pursued the synthesis of compounds **37** and **38**, which are the 3,4-tetramethylene- derivatives of the 10 π-electron systems **32** and **34**. Some intriguing chemistry arose from these studies, which are presented in Chapter 3.

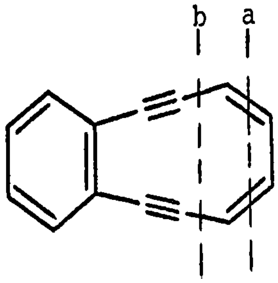
Chapter 4 deals briefly with other synthetic approaches to the 1,5-bisdehydro[10]annulene system. Chapter 5 is a summary and assessment of this body of work as it relates to other 4n+2 π-electron systems.

CHAPTER 2

SYNTHETIC APPROACHES TO A BENZ-FUSED 1,5-BISDEHYDRO-[10]ANNULENE

A. The 10-Membered Ring

The first synthetic objectives in our study of bisdehydro[10]annulenes were the benz-fused systems 35 and 36, as was mentioned previously.



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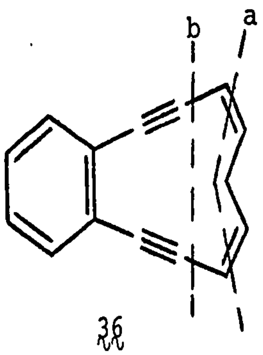
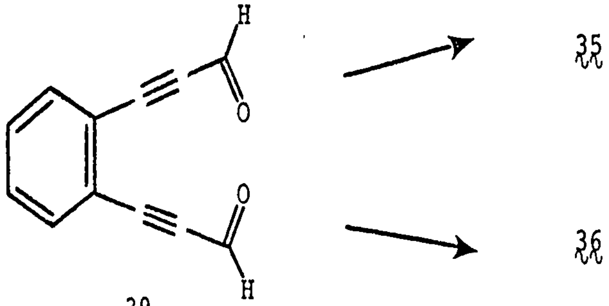


36

It would obviously be of great advantage if the respective syntheses of these two molecules were similar in concept, or even if they involved some of the same synthetic intermediates. Consider first the "dissection" of the molecules into possible "building blocks". The only difference between 35 and 36 is the methylene carbon at position 9 in 36, and therefore, in order to utilize common synthetic intermediates, the breaking up of the molecules must occur at points to the "left" of this carbon atom. Two lines of dissection can then be considered, as indicated by the broken lines (*a* and *b*) in the figure above.

The first line (line *a*) implies a synthetic route in which, at some stage, a benz-fused, 8-carbon unit is condensed with a 2- or 3-carbon unit to form the 10- and 11-membered rings of **35** and **36** respectively. Inclusion of acetylenic bonds in the 8-carbon unit offered the advantage of approximately correct geometry for the ring formation. The Wittig reaction converts carbonyl functions into double bonds, with concommitant introduction of carbon atoms. There was some precedence for using a bis-ylid in ring forming reactions,[58,66] and thus formation of at least the (strain-free) 11-membered ring by this route seemed quite favourable. These considerations dictated that the desired structure of the 8-carbon unit was the dialdehyde **39**.



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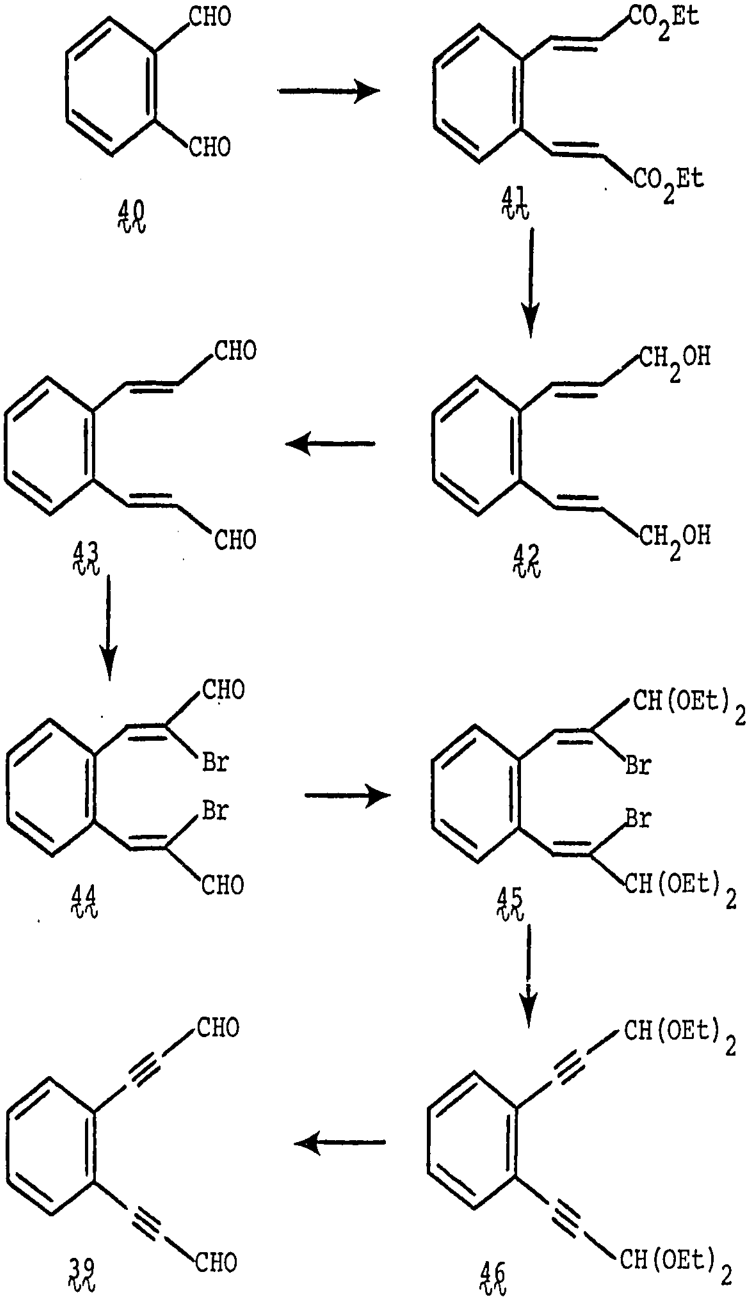
A readily available starting material was *o*-phthalicdicarboxaldehyde (**40**). The synthesis of **39** consisted of adding 2-carbon moities to each of the aldehyde groups in 40, followed by functional group modification leading ultimately to 39. The synthesis is outlined below,



as first performed by S. Sarkar of our laboratory.

Condensation of phthalicdicarboxaldehyde (40) with 2 mole equivalents of carboethoxymethylenetriphenylphosphorane gave without complication, the bis-vinylic ester 41, as colourless crystals (mp 77.5-78°). The ir spectrum of 41 showed absorption for the α,β-unsaturated ester carbonyl at 1710 cm^{-1}.

In order to avoid possible 1,4-addition to the α,β-unsaturated ester groups in a metal hydride reduction of 41, di-isobutyl aluminum hydride in benzene was chosen as the reducing agent. This reagent has proven to be more satisfactory than lithium aluminum hydride for these types of reduction.[67] Reduction of 41 by this method gave the allylic diol 42, as colourless crystals (mp 91-91.5°). Presence of OH absorption (3600 cm^{-1}) in the ir spectrum of 42 confirmed that the reduction had occurred; a complex multiplet at τ 2.4-4.0 in the nmr spectrum showed that the double bonds were still intact after the reduction.

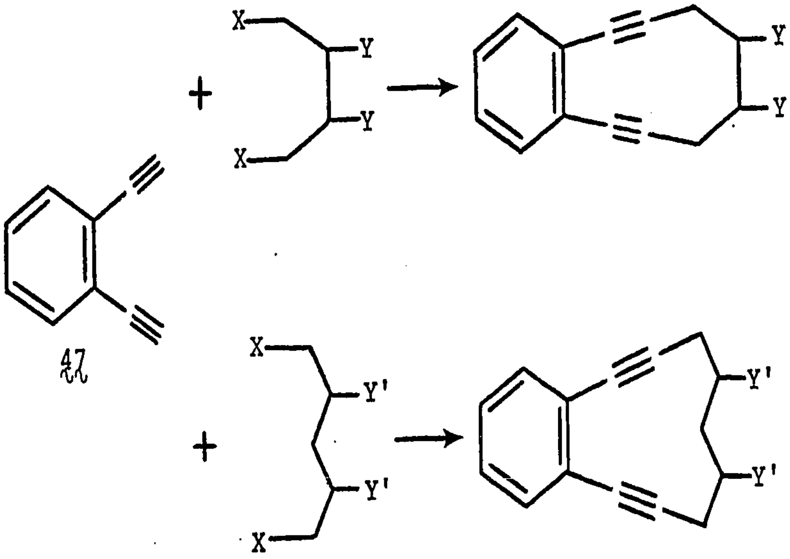
Oxidation of the diol 42 to the dialdehyde 43 was achieved in good yield by reaction with MnO_2 in methylene chloride.[68] The ir spectrum of 43 (2700 cm^{-1} and 1680 cm^{-1}) confirmed the presence of the aldehyde residues. Treatment of 43 with bromine in acetic acid, followed by anhydr. K_2CO_3, gave the vinylic dibromide 44 (aldehyde proton at τ 0.5 in the nmr spectrum of 44), which, on treatment with ethyl orthoformate and a trace of acid gave the bis-diethyl acetal 45. This compound was bis-dehydrobrominated by the action of potassium hydroxide in ethanol to give the acetylenic diethyl acetal 46, which gave the desired bis-acetylenic aldehyde 39 upon mild acid hydrolysis.

Unfortunately, the overall yield of 39 was not very good (37%), and the procedure was somewhat lengthy, and not particularly amenable to the production of large quantities of 39, which we expected would be necessary. Several attempted conversions of 39 into an 11-membered ring compound failed, as did attempts at chain extension reactions, in order to ultimately construct the 10-membered ring. At the time that the synthesis of 39 was complete, a second approach to the synthesis of 35 and 36 was offering promising results, and so the route through dialdehyde 39 was abandoned.

This second synthetic approach is indicated by the dotted lines marked *b* in the figure on page 30. Condensation of a benz-fused 6-carbon unit with an appropriate 4- or 5-carbon unit would lead to a molecule containing the required 10- and 11-membered rings, respectively. Further modification of these latter compounds would then lead to 35 and 36.

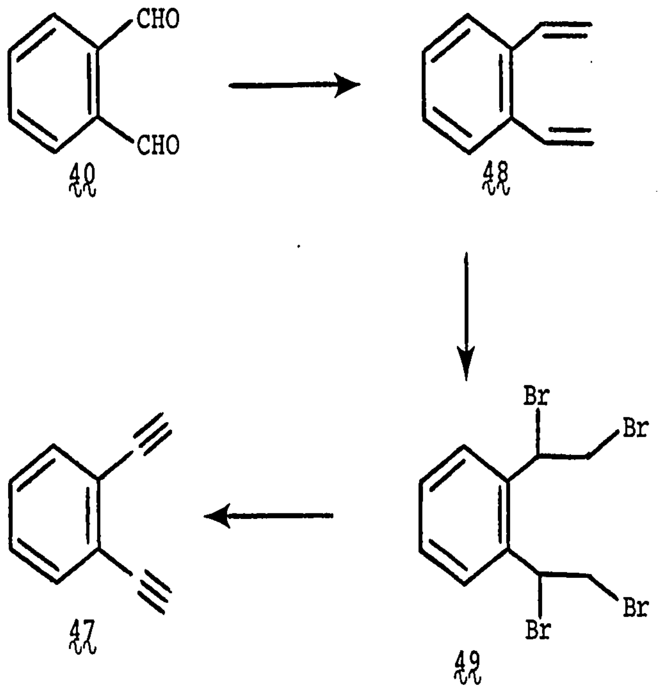
The choice of the 6-carbon unit was obvious.

o-Diethynylbenzene (47) contained the required acetylenic



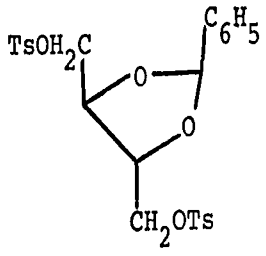
bonds, and suggested that the ring formation could be achieved by nucleophilic displacement by the bis-acetylenic anion. *o*-Diethynylbenzene was a known compound, and our synthesis of 47 was modelled on that reported.[69]

Once again, *o*-phthalicdicarboxaldehyde (40) was the chosen starting material. Reaction of 40 with 2 mole equivalents of methylenetriphenylphosphorane gave *o*-divinylbenzene (48) without complication. Reaction of 48 with bromine in carbon tetrachloride quantitatively gave the tetrabromide (49) as colourless prisms (mp 74-75°). Treatment of 49 with 4 moles of potassium *t*-butoxide in *t*-butanol gave the desired *o*-diethynylbenzene (47) in *ca*



65% yield as a colourless liquid (bp 59° at 3.5 mm Hg), which turned red-brown on exposure to air. 47 exhibited a sharp singlet at τ 6.65 (2H) in its nmr spectrum, attributable to the acetylenic protons. Bands at 3230 and 2110 cm^{-1} in the ir spectrum confirmed this assignment.

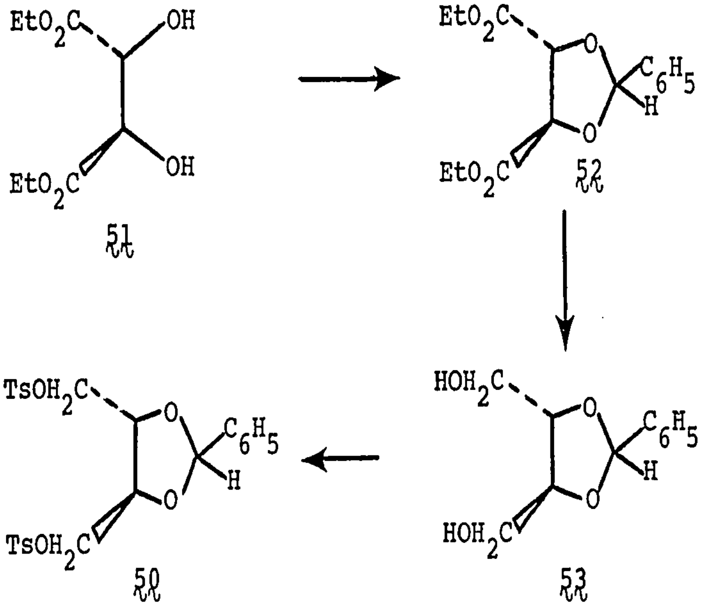
In order to form the 10-membered ring, the 4-carbon unit chosen was 2-phenyl-4,5-trans-ditosyloxymethyl-dioxolane (50). The actual cyclization reaction was envisaged as a nucleophilic displacement of the tosylate groups by the bis-acetylenic anion formed from o-diethynylbenzene (47). This condensation involves the formation of a somewhat strained ring system. Therefore the most favourable arrangement of the tosyloxymethyl groups was that in which



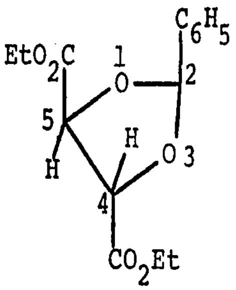
50

the distance between them most closely matched the distance between the ends of the acetylenic groups. Molecular models indicated that this arrangement was best achieved by the trans stereochemistry on the dioxolane ring, implying a molecule with a dl-configuration (50).

Attempted reaction of dilithio diethynylbenzene with 1,4-dibromobutane failed to yield any of the 10-membered ring compound. This indicated that some rigidity in the 4-carbon unit was desirable to facilitate the cyclization reaction. The dioxolane ring system of 50 was suitable from this point of view. In addition, after the cyclization, hydrolysis of the dioxolane ring would result in the formation of a 10-membered ring substituted by two hydroxyl groups, which could be converted into functionality suitable for β-elimination to the desired bisdehydro-[10]annulene (35). The synthesis of 50, which was achieved in collaboration with Dr. J. Salaün of this laboratory, is outlined below.



The desired *dl*-stereochemistry of **50** dictated the choice of starting materials to be diethyl *dl*-tartarate (**51**). The dioxolane ring was formed by acid-catalysed reaction of **51** with benzaldehyde, under benzene reflux, with azeotropic removal of water formed. The dioxolane diester (**52**) was formed in excellent yields. That the stereochemistry of this compound was as desired was evident from the nmr spectrum. The protons on the ethyl groups resonated at τ 8.72 as a triplet of doublets (6H) and at τ 5.70 as a quartet of doublets (4H), indicating that two different ethyl groups were present, as is necessary in a structure such as **52**, with the phenyl group on one side of the ring. The protons at positions 4 and 5 on the ring showed

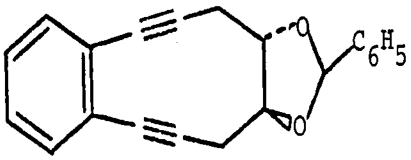


52

as an AB quartet centred at τ 5.08 ($J_{A,B}$ = 4), thus confirming the stereochemical assignment.

Compound 52 was reduced by lithium aluminum hydride in excellent yields to give diol 53 as colourless crystals; 53 was not further purified, but reacted directly with p-toluenesulfonyl chloride in pyridine to give the desired ditosylate (50) as colourless crystals (mp 131.5-132.5°). Besides aromatic absorptions (τ 2.42, m, 13H) and the tosylate methyl absorptions (τ 7.60, s, 6H), the nmr spectrum of 50 showed a sharp singlet (τ 4.20, 1H) for the benzylidene proton, and a broad singlet (apparent) (τ 5.80, 6H) for the methylene protons and the protons on the dioxolane ring.

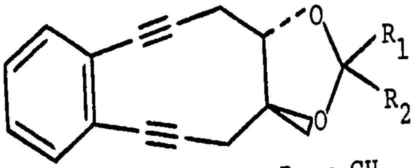
The condensation of o-diethynylbenzene (47) with the ditosylate (50) was attempted under many different conditions. Generally, the dilithio salt of 47 was generated by reaction with n-butyllithium. In refluxing ether, THF, and liquid NH_3, no reaction with 50 occurred, and 47 could be recovered. The use of THF-DMF as a solvent system resulted in the destruction of the dilithio o-diethynylbenzene. The only solvent in which reaction occurred as desired was dioxane. Thus, reaction of 47 in dioxane with 2 mole equivalents of n-butyllithium in hexane resulted in the precipitation of a fine white solid. After adding 1 mole equivalent of the ditosylate (50), and refluxing the mixture for ca 100 hr, chromatographic separation on alumina with hexane/benzene (1:1) eluent gave the desired compound (54) in 10-15% yield.



54

Compound 54 was a colourless, crystalline compound (mp 143.1-144.3°). Mass spectroscopy showed a molecular ion at m/e = 300. The ir spectrum of 54 showed a sharp absorption at 2220 cm^{-1}, indicating that the acetylenic bonds were intact. The nmr spectrum showed peaks at τ 2.66 (m, 9H) for the aromatic protons, and at τ 4.20 (s, 1H) for the benzylidene proton. Peaks centred on τ 5.61 (m, 2H) and τ 7.08 (m, 4H) were assigned to the remaining dioxolane and propargylic protons, respectively.

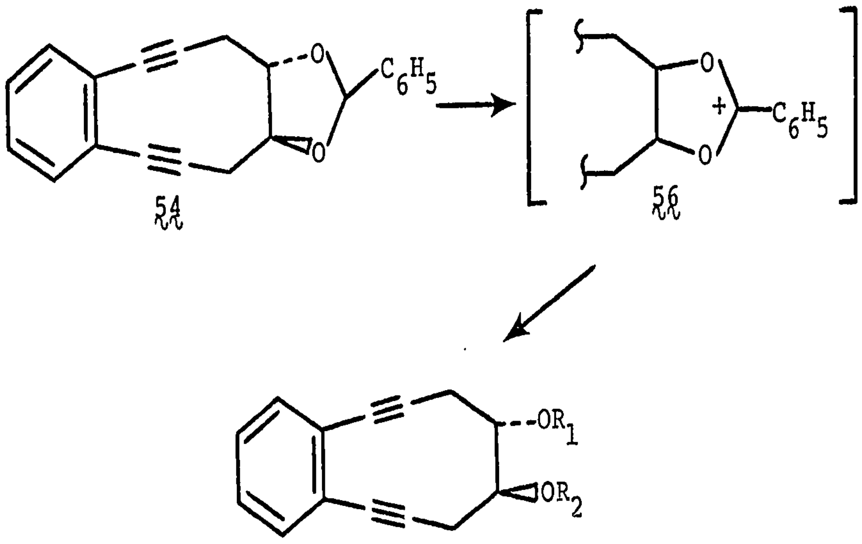
The dioxolane ring of compound **54** proved remarkably resistant to acid hydrolysis.[70] Under those conditions (6N HCl in refluxing dioxane/water) under which some dioxolane hydrolysis was detected (presence of benzaldehyde), it was evident that attack on the acetylenic bond had occurred, which is probably a reflection of the strained nature of these bonds. Compound **55a** (formed in a manner identical to that of **54**) proved no more amenable to hydrolysis. Compound **55b**, which might have been expected to be quite acid-sensitive, could not be made. Clearly some rather different approach to the hydrolysis of the dioxolane ring was necessary.



55 a) $R_1 = R_2 = CH_3$
b) $R_1 = OEt$; $R_2 = H$

In 1960, Meerwein had published work concerning the abstraction of a hydride ion from the 2-position of dioxolane rings.[71] He reported isolating several fluoroborate salts of these systems, the most stable of which was the 2-phenyl case, in which the positive charge is delocalized through the aromatic ring as well as over the two adjacent oxygen atoms. Hydrolysis of these salts gives an α-hydroxybenzoate, which in turn is readily hydrolysed by alkali to the parent diol.

This seemed to be the ideal solution to our problem--the desired destruction of the dioxolane ring in 54 could be achieved under neutral conditions. Thus, treatment of 54 as a solution in CH_3CN with trityl fluoroborate[45b] gave a bright yellow crystalline compound (which was not characterized, but presumably was the salt, 56). Hydrolysis of 56 with aqueous NaH_2PO_4 (1M; pH 7 buffer), followed by chromatography on silicic acid (to remove the triphenylmethyl species) gave excellent yields (>80%) of the hydroxybenzoate 57. The ir spectrum of 57 showed



54

56

57 R_1 = H; R_2 = Bz

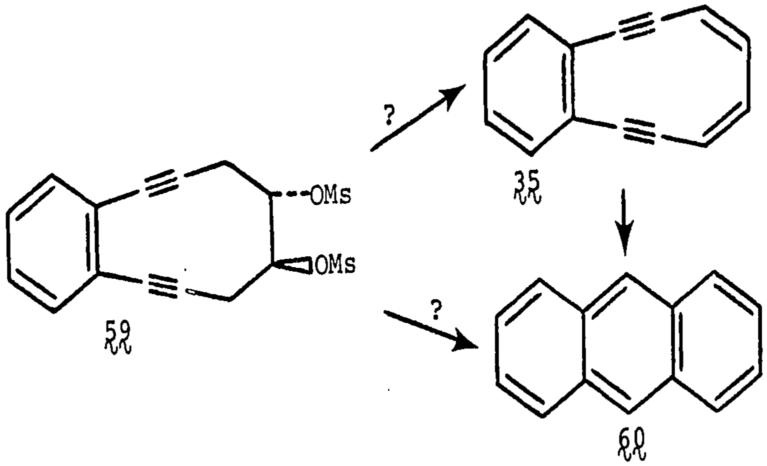
58 R_1 = R_2 = H

59 R_1 = R_2 = Ms

absorptions at 1725 cm^{-1} (carbonyl) and 3400 cm^{-1} (hydroxyl), indicating that the reaction had occurred as indicated above.

Transesterification of **57** with methanol, sodium methoxide catalyst, gave diol **58** quantitatively (ir: 3340 cm^{-1}, broad), which was a colourless highly crystalline compound. Reaction of **58** with methanesulfonyl chloride in THF in the presence of triethylamine gave the dimesylate derivative **59**, as yellow-brown crystals (mp 113°). The nmr spectrum of **59** showed absorptions at τ 2.76 (broad s, 4H; aromatic protons), τ 5.00 (m, 2H; methine protons), τ 6.92 (s, 6H; methylsulfonate protons) and τ 7.04 (m, 4H; propargylic protons).

Dimesylate **59** was the penultimate compound in this synthetic scheme leading to 3,4-benz-1,5-bisdehydro[10]annulene (**35**). The next reaction was envisaged as a base-induced elimination of the mesylate groups to introduce the necessary double bonds. Several different bases were employed in this reaction. Representative of these are: potassium t-butoxide, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), lithio hexamethyldisilazane ($LiN[Si(CH_3)_3]_2$), n-butyllithium, and sodium methoxide. In each case, in various solvent systems (protic and aprotic) the result was always the same. The only detectable product formed was anthracene (**60**) (<10% yield), along with large amounts of intractable tarry materials.



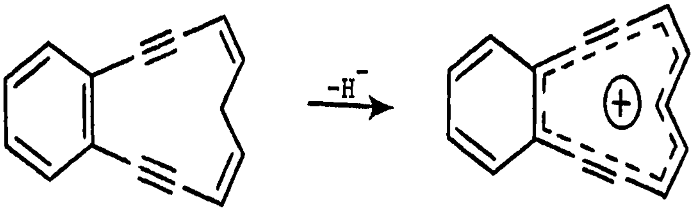
Lowering the temperature of the reaction to -30° did not change its course. (Much of the work on the elimination reaction was done in collaboration with Dr. S. Takada, of this laboratory).

Anthracene (60) ($C_{14}H_{10}$) is not isomeric to benzbisdehydro[10]annulene (35) ($C_{14}H_8$), but contains two more hydrogen atoms. When the dimesylate elimination was carried out in THF-d_8, with DBN as the base, there was about 50% incorporation of deuterium into the 9,10-positions of the product anthracene. The use of benzene as solvent gave trace amounts of a product whose mass spectrum (m/e = 256) suggested that it was a phenylanthracene (62). These results are readily accounted for, as depicted in the following scheme.

The assumption implicit in this scheme (that the

B. The 11-Membered Ring

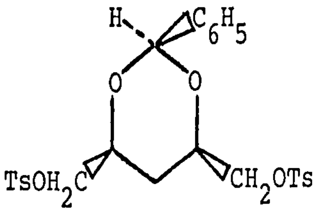
Concurrent to the work on the 10-membered ring, a synthesis of 3,4-benzcycloundeca-1,5-diyne-3,7,10-triene (36) was undertaken. As discussed earlier, loss of a



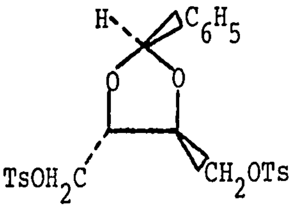
36 63

hydride ion from 36 would give the potentially aromatic 3,4-benz-1,5-bisdehydro[11]annulenyl cation (63). The synthesis was analogous to that of the 10-membered ring compound (see the previous section) and was based on the addition of a 5-carbon unit to o-diethynylbenzene (47).

The 5-carbon unit chosen was cis-4,6-ditosyloxymethyl-2-phenyl-1,3-dioxane (64). Again, the cyclization



64



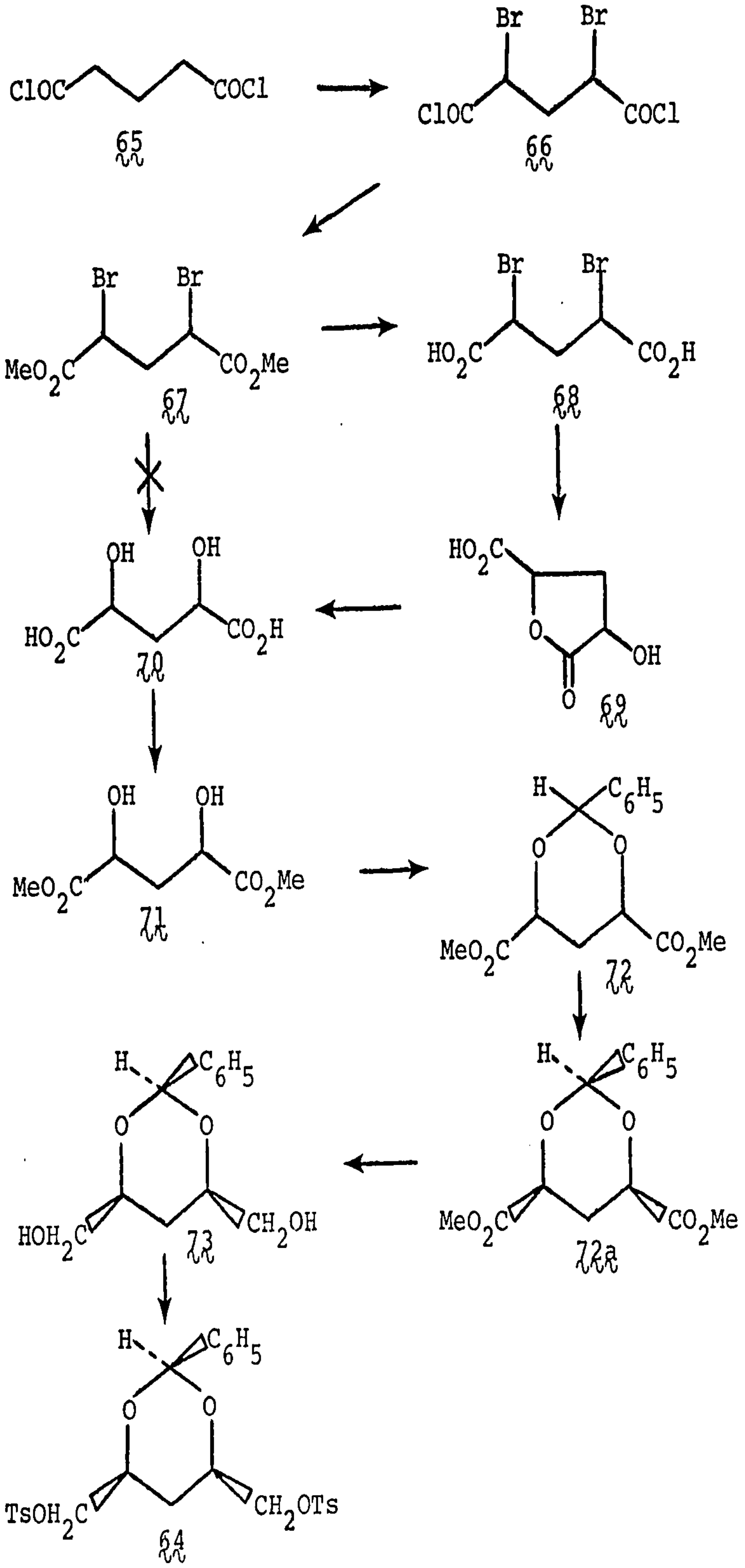
50

reaction was to involve displacement of the tosylate groups of 64 by the acetylenic dianion derived from 47, thus forming the 11-membered ring. Hydrolysis of the benzylidene blocking group leads to a diol, which, on appropriate modification, would permit the introduction of the requisite double bonds in 36.

The stereochemical considerations for 64 are defined by the same analysis applied to ditosylate 50. In the case of 64, however, the meso- configuration (as illustrated) is best suited for the cyclization reaction to occur.

The synthesis of ditosylate 64 was quite different from that of 50; the extra carbon atom had a rather profound effect, as is seen below. This synthesis was originally performed in collaboration with Dr. K. W. Shelton, of this laboratory.

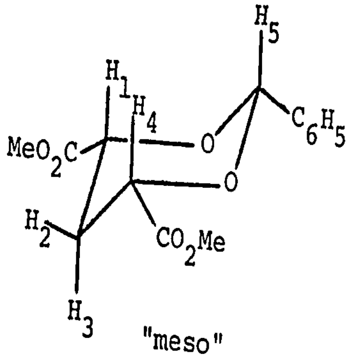
Neat glutaryl dichloride (65) was brominated directly in the presence of a tungsten filament lamp, giving the dibromide 66. Methanolysis of 66 gave, in good yield, dimethyl 2,4-dibromoglutarate (67). Unfortunately, the two bromine atoms could not be hydrolysed to give the desired dihydroxyglutaric ester. This behaviour had been reported previously.[72] Hydrolysis of 67 would give 2,4-dibromoglutaric acid (68), and hydrolysis of the two bromine atoms (by NaOH in aqueous methanol) led to the lactone

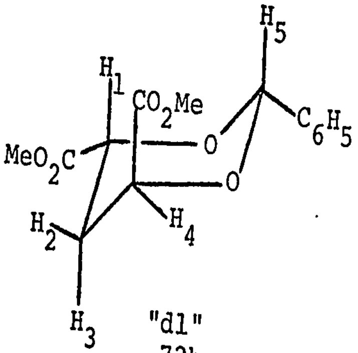

ClOC
COCl
65
Br
Br
ClOC
COCl
66
Br
Br
MeO2C
CO2Me
67
Br
Br
HO2C
CO2H
68
OH
OH
HO2C
CO2H
70
HO2C
O
OH
O
69
OH
OH
MeO2C
CO2Me
71
H
C6H5
O
O
MeO2C
CO2Me
72
H
C6H5
O
O
HOH2C
CH2OH
73
H
C6H5
O
O
MeO2C
CO2Me
72a
H
C6H5
O
O
TsOH2C
CH2OTs
64

69.[72] From our point of view, this lactone formation was an unfavourable circumstance. The difficulty arose in trying to convert **69** into the desired 2,4-dihydroxyglutaric acid (**70**); the reverse reaction was by far the favoured process, and was catalysed by acid or base. Thus diacid **70** had to be handled under conditions as mild and as nearly neutral as possible.

This difficulty was overcome in the following manner: lactone **69** was titrated with aqueous NaOH; two mole equivalents of the base were absorbed, and thus, presumably, the disodium salt of diacid **70** was formed. Passage of this solution over an acidic cation exchange resin (Dowex 50WX8) gave a nearly neutral solution of the diacid (**70**), which was freeze-dried as rapidly as possible. Without further purification, the residual crystalline diacid was esterified with diazomethane in methanol, to give the dimethyl 2,4-dihydroxyglutarate (**71**) in <u>ca</u>. 80% overall yield from the dibromide **67**. Reaction of **71** with benzaldehyde in the presence of anhydrous, fused, $ZnCl_2$ gave the 1,3-dioxane diester (**72**) as a mixture of isomers (**72a** and **72b**).

It is reasonable to assume that the bulky phenyl group on compound **72** would assume an 'equatorial' configuration, as shown, in order to avoid non-bonded interactions. For the same reason, the carbomethoxy groups would also


"meso"
72a


"dl"
72b

prefer an 'equatorial' position. In the "dl" form of 72 (72b), one carbomethoxy group suffers non-bonded interaction with protons H_1 and H_5. This analysis would then predict that the "meso" isomer, 72a, is the more stable form.

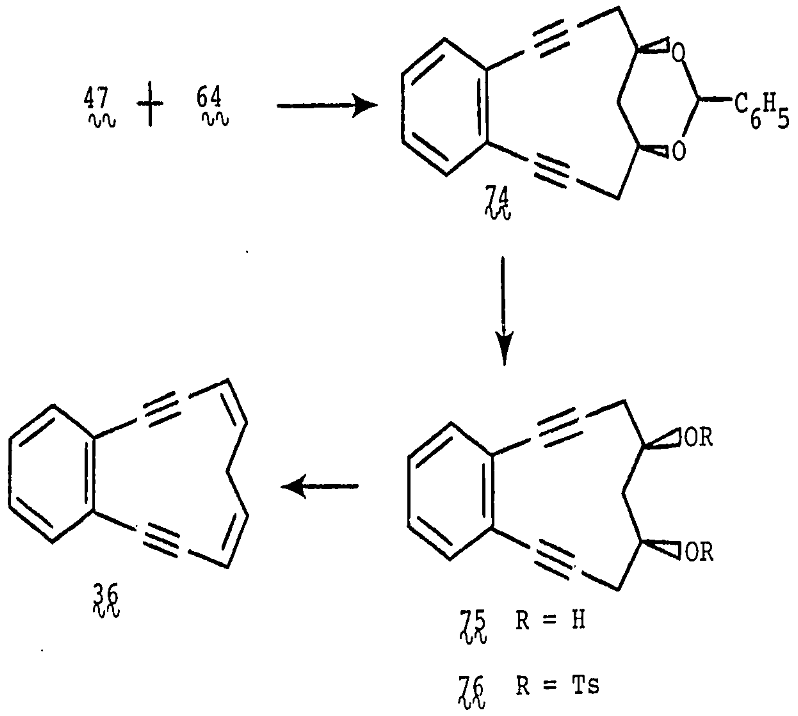
The mixture of isomers of 72 was subjected to equilibration by NaOMe in methanol. As expected, the "meso" isomer (72a) predominated, and could be obtained free of 72b by fractional recrystallization from methanol. Repetition of the equilibration-recrystallization procedure converted virtually all of the isomeric mixture into the desired 72a.

The distinction between the two isomers was made in the following way. In both isomers, protons H_2 and H_3 are in different environments, and therefore are expected to resonate at different frequencies in the nmr spectrum of 72. However, in the "meso" isomer, protons H_1 and H_4

should be identical as far as the nmr is concerned. The protons H_1 (H_4) and H_2, H_3 are in sufficiently different environments to allow a crude first-order analysis (that is, the chemical shift differences between H_1 and H_2, H_3 are much larger than the coupling constants $J_{1,2}$ and $J_{1,3}$). Thus the "meso" isomer (72a) would be expected to exhibit a quartet (doublet of doublets) for the protons H_1 and H_4. In fact, the nmr spectrum of the more stable isomer of 72 shows a clear doublet of doublets centred on τ 5.49 (2H) for the protons H_1 and H_4. Coupling constants are assigned as: $J_{1,2} = 4$ and $J_{1,3} = 10$, on the assumption that the Karplus relationship generally holds true in this system.[73] 72a also exhibits a multiplet (τ 7.7-8.1, 2H) for protons H_2 and H_3, and a sharp singlet (τ 4.46, 1H) for the benzilidene proton.

The "dl" isomer was never obtained in a pure state, but the complexity of the nmr absorptions for protons H_1 and H_4 (τ 5.1-5.7, m, 2H) and H_2 and H_3 (τ 7.4-8.0, m, 2H) allowed the distinction between 72a and 72b. The position of the proton H_5 of 72b (τ 4.07) compared to that of 72a (τ 4.46) also reflects the differences in the conformations and stereochemistry of these two isomers.

The diester 72a was reduced by lithium aluminum hydride to the diol 73, which was then converted into the desired "meso" ditosylate 64, a colourless, crystalline compound (mp 135-137°). The ir spectrum of 64 showed peaks at 1600 cm^{-1} (phenyl ring) and 1350 cm^{-1} (sulfonate esters). The nmr spectrum of 64 consisted of a quartet centred on τ 2.50 (8H, tosylate aromatic protons); a broad singlet at τ 2.70 (5H, phenyl protons); a singlet at τ 4.60 (1H, benzylidene proton); an unresolved doublet centred on τ 5.95 (6H, tosyloxymethyl protons and the protons adjacent to the O atoms); a singlet at τ 7.62 (6H, tosylate methyl groups); and a complex multiplet at τ 8.25-8.80 (2H, methylene protons).



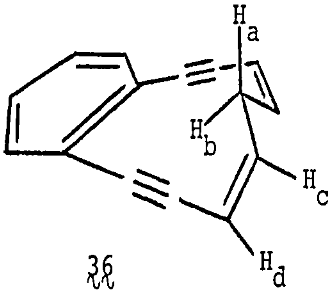
The cyclization reaction of diethynylbenzene (47) with the ditosylate (64) was performed under the same conditions as those used to form the 10-membered ring. Thus, the dilithio salt of **47** was refluxed in dioxane with ditosylate **64** for about 100 hr. Chromatography on alumina with benzene eluent, gave the desired product (**74**) in 5-8% yield, as colourless crystals (mp 253-254°). The ir spectrum of **74** showed absorption at 2240 cm^{-1} for the acetylene bonds and 1130 and 1025 cm^{-1} for the dioxane ring (C-O). The nmr spectrum of **74** exhibited lines at τ 2.4-3.0 (m, 9H) for the aromatic protons; a singlet at τ 4.50 (1H) for the benzylidene proton; a multiplet at τ 5.40-5.9 (2H) for the methine protons; and a multiplet at τ 6.9-7.6 (6H) for the methylene protons. Compound **74** was exceedingly stable, remaining unchanged in air at room temperature for over three years.

The yields for this formation of the 11-membered ring were consistently lower than those for the formation of the 10-membered ring, which is somewhat surprising in view of the fact that virtually no strain is involved in the product molecule (**74**). However, no intensive attempts were made at improving the result; the reactants could be made in quantity, so that the disappointing yield was not too great a hindrance to further pursuit of the synthetic scheme.

The hydrolysis of 1,3-dioxanes generally proceeds faster than hydrolysis of 1,3-dioxolane rings.[70]

Thus, the 1,3-dioxane ring in 74 proved amenable to hydrlysis (compare this to compound 54), which gave diol 75 as colourless crystals (mp 193-194°). This diol was then converted into the ditosylate 76 (mp 176-177.5°) by the action of toluenesulfonyl chloride in pyridine. Elimination of the ditosylate moities by potassium t-butoxide gave, in 83% yield, hydrocarbon 36, the desired product.

Compound 36 was a stable, colourless crystalline compound, (mp 78.5-79.5°), being unchanged in air at room temperature for at least two months. The uv spectrum showed maxima (cyclohexane) at 252 nm (ε = 36,000), 256.5 (34,900), 264.5 (60,900). The mass spectrum (parent ion, m/e = 190.0761 (measured); calculated mass for $C_{15}H_{10}$ = 190.0771) was particularly heartening for us, because the base peak occurred at m/e = 95, which was probably due to the doubly charged parent ion, indicating the willingness of the system to accept positive charge.

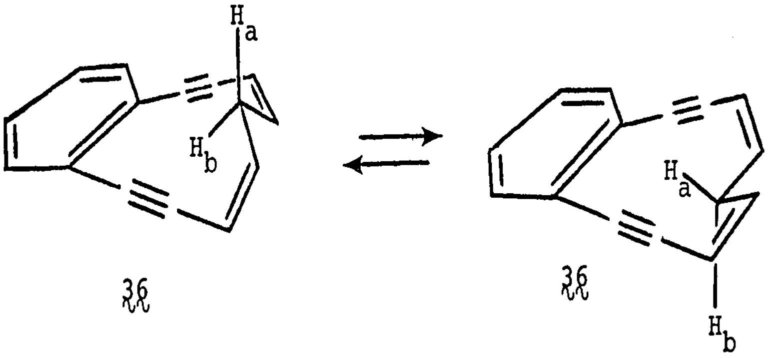


36

The nmr spectrum of 36 in $CDCl_3$ proved quite interesting (see figure 1). The aromatic protons showed as an AA'BB' multiplet (4H) centred on τ 2.50. The vinylic protons showed as an apparent triplet of doublets (2H) centred on τ 3.68 and a doublet of doublets (2H) centred on τ 4.05. The methylene protons (H_a and H_b), at -15°, appeared as two groups of multiplets (2H) in the τ 6.4-7.5 region. From the model, it is apparent that H_b lies within the deshielding region of the acetylenic bonds, and therefore might be expected to resonate at a lower field than H_a.

Double irradiation experiments provided further information. Irradiation at τ 3.68 (at -15°) collapsed the methylene multiplet to an apparent AB quartet. The coupling constant ($J_{a,b}$ = 12) and chemical shifts (τ_a 7.30; τ_b 6.63) were then available for the protons H_a and H_b. Irradiation at τ 4.05 collapsed the methylene multiplet into two sets of multiplets, each appearing as a doublet of triplets. This pattern then allowed assignment of coupling constants ($J_{a,c}$ = 5.5; $J_{b,c}$ = 9.5; $J_{c,d}$ = 10) and chemical shifts (τ_c 3.68; τ_d 4.05) to the remaining protons, H_c and H_d. Some long-range coupling between protons H_d and H_a could be seen, but not measured accurately ($J_{a,d}$ = ca 1). A computer-simulated spectrum of hydrocarbon **36** was calculated on the basis of the above parameters. The calculated spectrum reproduced the essential features of the olefinic and methylene absorptions of the experimentally determined (in $CDCl_3$) spectrum of 36.

The H_a, H_b coupling constant ($J_{a,b} = 12$) indicates that the methylene carbon of 36 is not distorted from a normal tetrahedral geometry,[73] which is a reflection of the unstrained nature of the molecule. More convincing evidence of this fact was obtained from temperature-dependent nmr studies on compound 36.



36 36

H_a and H_b of 36 are in different magnetic environments. Models indicate that the methylene carbon (C_9) is capable of conformational 'flipping' through the ring, as illustrated, so that the environments of H_a and H_b are interchanged. Thus, if the energy barrier for this flipping is low enough, heating the sample should collapse the signals due to the H_a, H_b quartet to a singlet.[74] This would then imply a flexibility in the ring incompatible with a strained structure.

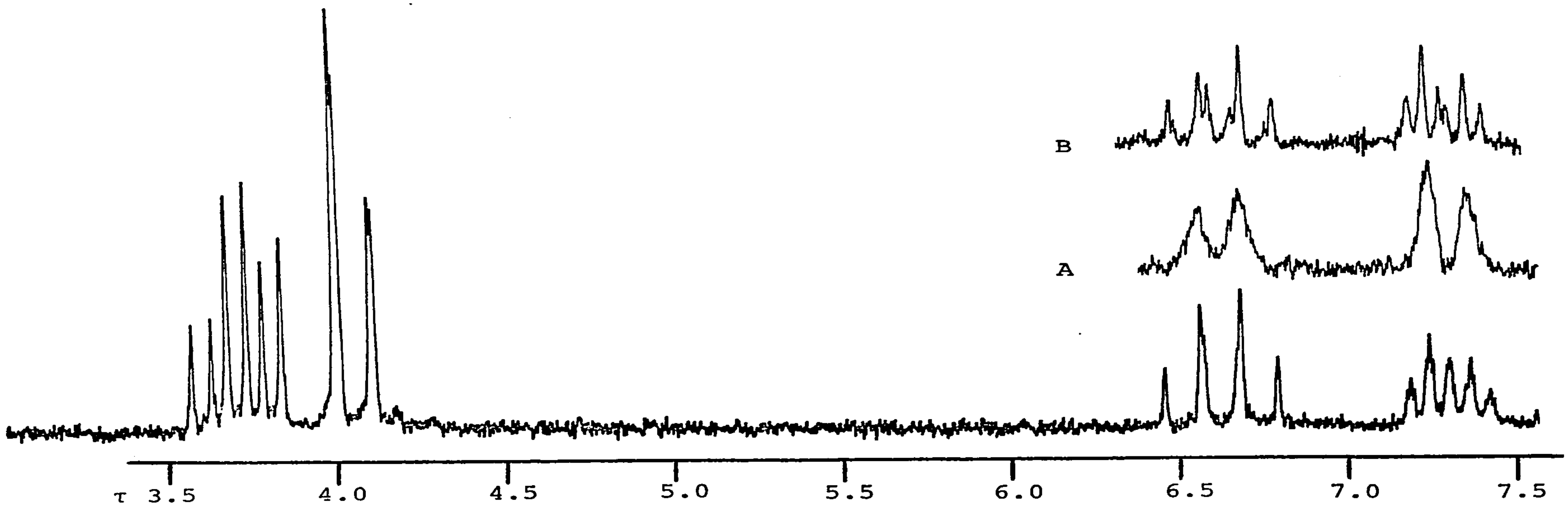


Fig. 1: nmr spectrum of hydrocarbon **36**, olefinic and methylene protons at −15°. Double irradiation: A) at τ 3.68 B) at τ 4.05.

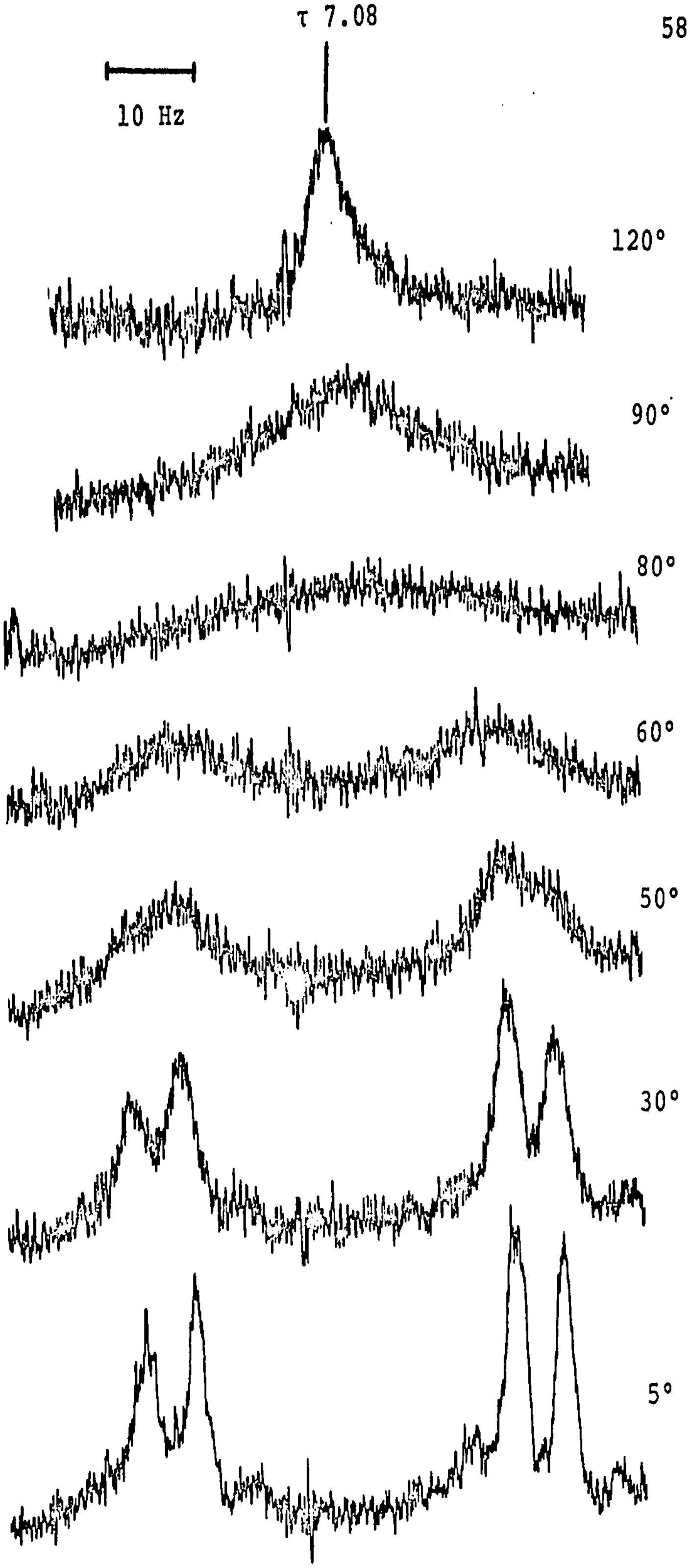


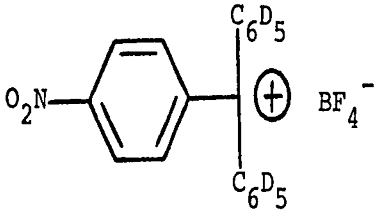
Fig. 2: Temperature-dependent nmr spectrum of the C-9 protons of hydrocarbon 36; double irradiation 608 Hz.

In methylcyclohexane-d_{14}, with hexamethyldisilane (HMDS) as internal standard, the nmr spectrum of hydrocarbon **36**, at 5°, exhibited absorptions for the aromatic protons as an AA'BB' multiplet (τ 2.5-3.0, 4H); for the olefinic protons as a complex multiplet (τ 3.8-6.4, 4H); the methylene protons as a pair of multiplets (τ 6.4-7.4, 2H). Irradiation at 608 Hz from HMDS collapsed the methylene multiplets to a virtual AB system (see figure 2) ($\tau_b = 6.63$, $\tau_a = 7.53$, $J_{a,b} = 12$). Heating the sample to 50° caused the AB quartet to coalesce to two broad singlets. This temperature and frequency separation (12 Hz) corresponds to a rate of 'flipping' at 50°: $k \simeq 26.6\ \text{sec}^{-1}$ ($\Delta G^{\ddagger} \simeq 16.9$ kcal/mole). Further heating to 75° caused the doublet to coalesce to a broad singlet, corresponding to a rate: $k \simeq 200\ \text{sec}^{-1}$ ($\Delta G^{\ddagger} \simeq 16.8$ kcal/mole). Heating further to 120° gave rise to a broad singlet centred on τ 7.08. The spectra were too complex to obtain accurate rate constants easily; however, the fact that coalescence of the AB multiplet was achieved demonstrates the strain-free nature of hydrocarbon **36**.

It should be emphasized that protons H_a and H_b are actually passing through the ring, if the geometry of the molecular model (Dreiding) is a true reflection of the actual molecule. The relevance of this point will be further discussed in Chapter 5.

Hydrocarbon 36 could not be induced to surrender a hydride ion to yield a stable cation (63). Treatment of 36 with trityl fluoroborate gave only intractable tarry material, although the formation of small amounts of triphenylmethane was evident in the nmr spectrum of the reaction mixture (CD_3CN solvent).

The mononitro-triaryl methyl fluoroborate 77 was synthesized in a routine manner. The nitro-group should destabilize the trityl cation, making this compound a better hydride abstractor, and the deuterated phenyl rings considerably simplified the nmr spectrum of a reaction mixture containing 36 and 77. No peaks attributable to the desired product cation 63 could be detected in the nmr spectrum of such a mixture in the range τ -10 to τ +20.



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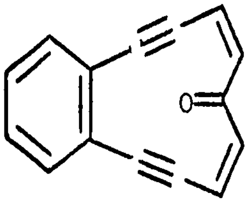
In hopes of generating compound 78, a tropone analogue of 36, hydrocarbon 36 was treated with SeO_2 under various conditions.[75] Those conditions strong enough to effect any reaction at all resulted in total destruction



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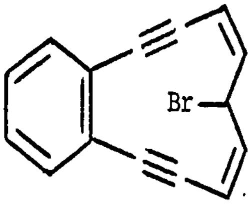

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of the starting material (36) giving only tarry material as product. Nor could the hydrocarbon 36 be induced to react with N-bromosuccinimide, to give the bromide 79.

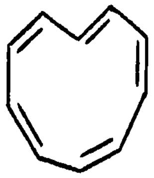
A discussion of all these results is presented in Chapter 5.

CHAPTER 3

SYNTHETIC APPROACHES TO A TETRAMETHYLENEBISDEHYDRO-[10]ANNULENE

A. The 10-Membered Ring

Substitution of one double bond in a polyenic system by incorporating it in a fused benzene ring often stabilizes that system by lowering its reactivity. One example of this phenomenon is the difference in stability between *trans*,(*cis*)^{4}-[10]annulene (**24**)[62] (stable only below -40°) and its tribenz-derivative (**27**), (stable up to 100°).[58] Compound **24** isomerizes thermally[77] to *trans*-9,10-dihydronaphthalene.[62] In order for **27** to undergo such a rearrangement, the aromatic configuration of a benzene ring must be destroyed, thus increasing the energy barrier for the reaction.



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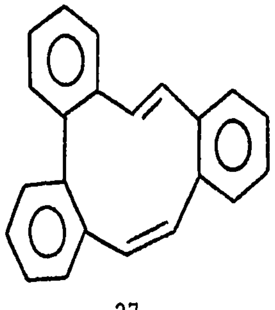
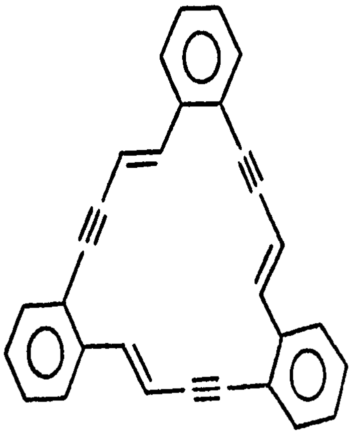


27

On the other hand, fusing a benzene ring to an aromatic annulene system can dramatically change the aromatic properties of the annulene, and in some cases, destabilize considerably the aromatic nucleus. Sondheimer has synthesized compound **80**, a tribenz-derivative of tridehydro[18]annulene (**8**). The 18-membered ring of **80** does not show evidence of a diamagnetic ring current, although the parent compound does.[24] Compound **81** is a benz-fused derivative of 1,6-methano[10]annulene (**26a**), which is a stable, 10 π-electron aromatic system. Hydrocarbon **81** is an unknown compound, in spite of attempts at synthesis by E. Vogel and others.[78]



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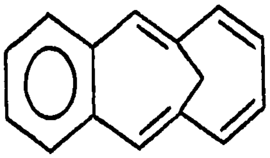
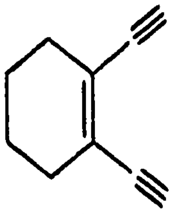


81

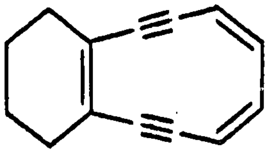
These considerations suggested that the fused benzene ring of 3,4-benz-1,5-bisdehydro[10]annulene (**35**) may disrupt the 10 π-electron system to such a degree that the isolation of **35** was not possible. Thus the parent compound, or a suitable derivative, might yield to synthesis.

Sondheimer had reported in a preliminary communication the synthesis of 1,2-diethynylcyclohexene (82).[79]



82

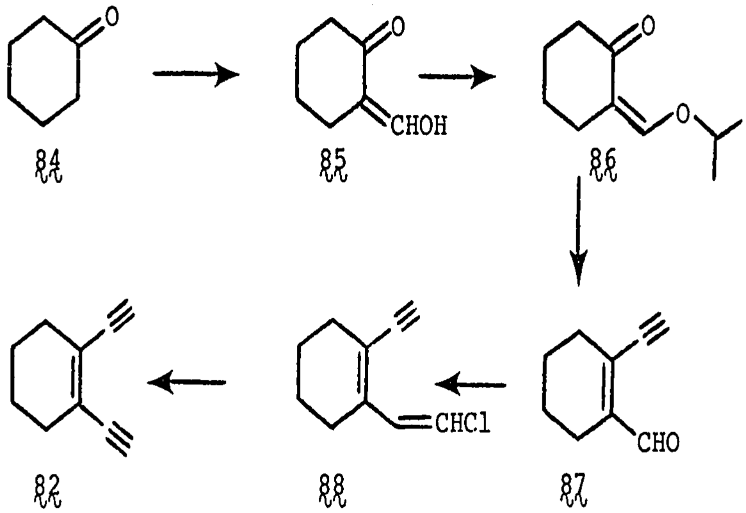
83



37

This compound (82) offers two advantages in a synthesis of a bisdehydro[10]annulene over the 1,2-diethynylethylene (83) necessary for construction of the parent compound (32). In the first place, the 6-membered ring of 82 ensures that the two acetylenic groups are held in a cis-configuration and yet the 4-carbon bridge should not significantly affect the delocalization of the double bond into a 10-electron system. Secondly, the synthesis of 82 appeared less tedious than that of 83. (This latter synthesis necessitates separation of double-bond isomers.[80a] A stereospecific synthesis of 83 was later reported,[80b] but it did not appear amenable to large-scale manipulation.) We thus embarked on a synthesis of 3,4-tetramethylenebisdehydro[10]annulene (37). The synthetic route was modelled on the approach described for the 3,4-benz-fused molecule (35).

Our synthesis of 1,2-diethynylcyclohexene (**82**) followed the reported brief outline.[79] After experimental procedures had been worked out, Sondheimer published full details of his synthesis,[81] which differed from ours mostly in reaction workup procedures. There were no major differences.



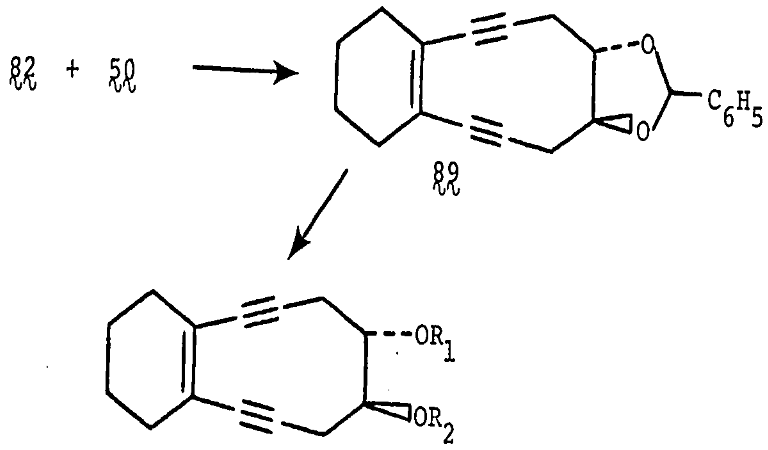
Condensation of cyclohexanone (**84**) with ethyl formate in the presence of sodium methoxide gave the hydroxymethylene derivative (**85**), the hydroxyl group of which was blocked by reaction with 2-iodopropane in the presence of K_2CO_3 to yield the 2-isopropyloxymethylenecyclohexanone (**86**). Reaction of **86** with lithium acetylide ethylenediamine complex,[82] followed by mild acid hydrolysis, gave, on sublimation and recrystallization, the 1-ethynylcyclohexene-2-carboxaldehyde (**87**) (mp 47-49°) in *ca* 50% yield. This compound showed ir absorptions at 3230 cm^{-1} (acetylenic hydrogen), 2080 cm^{-1} (acetylene bond) and 1672 cm^{-1} (conjugated carbonyl); the nmr spectrum exhibited peaks (among others) at τ 6.58 (s, 1H; acetylenic proton) and τ -0.02 (s, 1H; aldehydic proton). The presence of the aldehyde and acetylene functional groups was thus assured.

Reaction of 87 with chloromethylenetriphenylphosphorane Wittig reagent[83] gave, in *ca* 65% yield, the chlorovinyl compound 88, as a mixture of *cis*- and *trans*-isomers (*ca* 1:3). The vinylic region of the nmr spectrum of 88 showed an AB quartet centred on τ 3.25 ($J_{A,B}$ = 14) for the *trans*- isomer; another AB quartet centred on τ 3.55 ($J_{A,B}$ = 8) was assigned to the *cis*-isomer. The mixture of compound 88 isomers was isolated by vacuum distillation (bp 46-47° at 0.05 mm Hg); it was a colourless to pale yellow liquid, which showed some tendency to polymerize, but was not overly difficult to handle. Sondheimer's group isolated 88 by chromatography on silicic acid;[81] it appeared as though 88 isolated in this manner was far less stable than that isolated by distillation, possibly because of the presence of trace amounts of acid picked up on the column.

The chlorovinyl compound (88) was dehydrochlorinated by the action of sodium amide in liquid ammonia, to give the desired 1,2-diethynylcyclohexene (**82**) in *ca* 65% yield after distillation (bp 27° at 0.1 mm Hg) as a colourless liquid. Pure **82** froze at *ca* 10°. Exposure to air turned **82** a red-brown colour. **82** absorbed in the ir at 3360 cm^{-1} (acetylenic hydrogen) and 2130 cm^{-1} (mono-substituted acetylenic bond). The nmr spectrum of **82** was very clean, with absorptions at τ 8.35 (m, 4H; homoallylic methylene protons); τ 7.78 (m, 4H; allylic methylene protons); and τ 6.88 (sharp s, 2H; acetylenic protons).

From this point on, the approach to tetramethylenebisdehydro[10]annulene (**37**) was exactly analogous to the approach to the benz-fused system (**35**). Thus, reaction of the dilithio salt of **82** with the ditosylate (**50**) in refluxing dioxane for *ca* 100 hr gave the desired 10-membered ring benzylidene derivative, **89**, in *ca* 10% yield as colourless crystals (mp 154.5-155.5°).

The nmr spectrum of **89** showed absorptions at τ 8.42 (m, 4H), τ 7.88 (m, 4H), and τ 7.27 (m, 4H) for the three kinds of methylene protons present; τ 5.76 (m, 2H) for the protons on the 10-membered ring adjacent to the oxygen atoms; τ 4.19 (s, 1H) for the benzylidene proton and τ 2.64 (m, 5H) for the aromatic protons. In the mass spectrum, **89** had a molecular ion at m/e = 304 (calculated mass for $C_{21}H_{20}O_2$: 304.1463; measured, m/e = 304.1467).



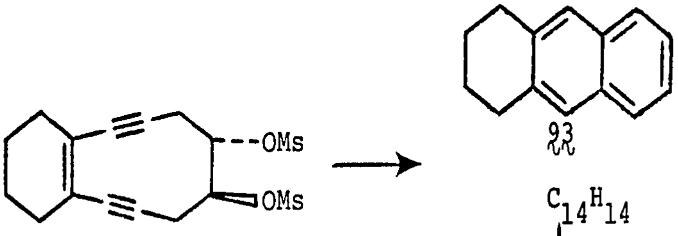
90 R_1 = OH; R_2 = Bz

91 R_1 = R_2 = H

92 R_1 = R_2 = Ms

Reaction of 89 with trityl fluoroborate[45b] as a suspension in CH_3CN gave a dark red-brown solution, which, on hydrolysis with pH 7 buffer solution, followed by chromatography on silicic acid gave as pale yellow crystals (mp 145°, dec.) the hydroxy-benzoate 90. Compound 90 showed ir absorptions at 3520, 2195 and 1720 cm^{-1} for the hydroxyl, acetylenic and ester functional groups, respectively. Methanolysis of 90 with sodium methoxide in methanol gave the diol 91 as colourless platelets (chars at 100°) (ir 3380 cm^{-1}, hydroxyl groups; 2198 cm^{-1}, disubstituted acetylene). No carbonyl absorption was seen in the ir spectrum of 91. Reaction of this diol with methanesulfonyl chloride and triethylamine in THF gave the dimesylate

92 as a colourless glass, which was unstable at room temperature in air. After two weeks at -30°, 92 was partially crystalline, but no melting point was obtainable. The ir spectrum of 92 showed strong absorption at 1340 and 1169 cm^{-1} for the sulfonate esters, and a singlet at τ 6.92 (6H) in the nmr spectrum for the sulfonyl methyl protons.



92

93

$C_{14}H_{14}$

+

94

$C_{14}H_{12}$

Elimination of the dimesylate functions of 92 by strong base (KO<u>t</u>-Bu, $LiN[Si(CH_3)_3]_2$, DBN) in aprotic media (e.g., THF) gave small amounts (<u>ca</u> 1-5% yield) of 1,2,3,4-tetrahydroanthracene (93), and large amounts of intractable tars. This situation was reminiscent of the elimination reaction of dimesylate 59 in the benz-fused series of compounds, which yielded anthracene (see Chapter 2).

However, treatment of 92 with 2 mole equivalents of sodium methoxide in a methanol-THF mixture gave, in 30-40% yield, a new hydrocarbon (94) as colourless crystals (mp 73.0-74.5°); calculated mass for $C_{14}H_{12}$, 180.0939;

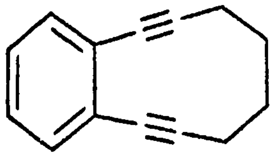
found, m/e = 180.0937 (base peak in the mass spectrum). Tetrahydroanthracene (93, $C_{14}H_{14}$) was also formed in this reaction (20-30% yield).

Catalytic hydrogenation of 94 over Rh at -80°[84] and then over PtO_2 in acetic acid afforded in 85% yield a bicyclic compound, $C_{14}H_{26}$, which was identical with bicyclo[8.4.0]tetradecane, prepared in an unambiguous manner (see below). The proton signals in the low-field nmr spectrum of 94 constituted an AA'BB' system (τ 2.80 and 2.89; $J_{A,B}$ 7.5, $J_{A,B'}$ 1.4, $J_{B,B'}$ 8.8, $J_{A',B'}$ 0.0) and additional signals appeared at τ 7.82 (m, 4H) and τ 8.04 (m, 4H). The uv spectrum of 94 showed absorption maxima: λ_{max} (cyclohexane) 223 nm ($\log\varepsilon$ 4.61), 234 (4.85), 262 (3.98), 267 (3.93), 276 (3.89), 290 (2.56) and 323 (2.12).

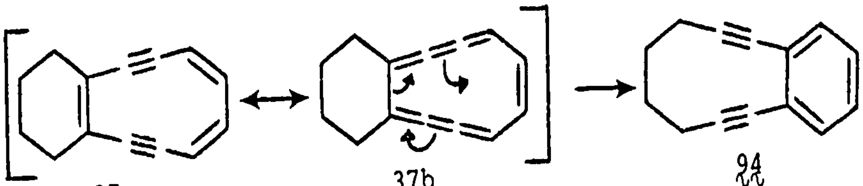
This information and the synthetic scheme were compatible with assigning the desired structure--3,4-tetramethylene-1,5-bisdehydro[10]annulene (37)--to the hydrocarbon 94. However, some doubt was cast upon this assignment in comparing these data with those obtained in our previous work.

We had obtained, from the benz-fused series of compounds, molecules containing the o-diethynylbenzene moiety incorporated into a 10-membered ring (see Chapter 2). All of these intermediates containing the o-diethynylbenzene system had uv spectra similar to that of 94. This opened up the possibility that 94 was not the desired structure, 37, but rather 3,4-benzcyclodec-3-ene-1,5-diyne, an isomer of 37. Because chemical and spectral data could not differentiate rigorously between these two possibilities (the results of catalytic hydrogenation under various conditions were inconclusive) and because 3,4-benzcyclodec-3-ene-1,5-diyne could not be synthesized directly from *o*-diethynylbenzene and 1,4-dibromobutane, an x-ray analysis of 94 was undertaken by Professor M. J. Bennett and Mr. R. Smith of this department. Some problem of disorder was presented, but the main features were those of the undesired isomer, and not the desired tetramethylenebisdehydro[10]annulene (37).

94 ≡



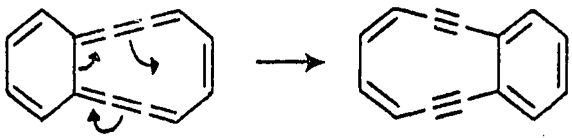
The formation of 94 can most readily, if not uniquely, be explained by considering the resonance forms of the bisdehydro[10]annulene (37a and 37b). A "Cope-like" rearrangement of the in-plane π- and σ-electrons, as depicted (37b), would lead directly to 94. The distance (or interaction) between the in-plane π-electrons of structure 37a (or 37b) is little different from that in 94, and molecular models indicate that not a large difference in the strain of the two 10-membered rings exists. Thus, if the



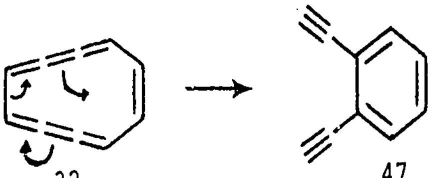
37a 37b 34

rearrangement does occur as shown, then one can conclude that any stability associated with the 10 π-electron system of 37 is at most comparable with that associated with benzene.

Considering again the benz-fused bisdehydro[10]-annulene (35), a "Cope-like" rearrangement would lead to degenerate isomerization, as depicted below.



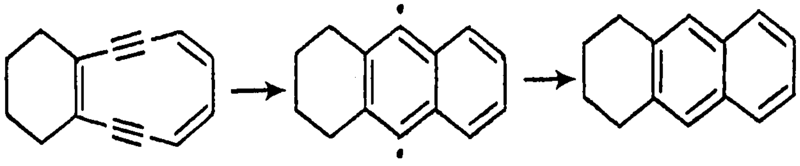
35 35



32 47

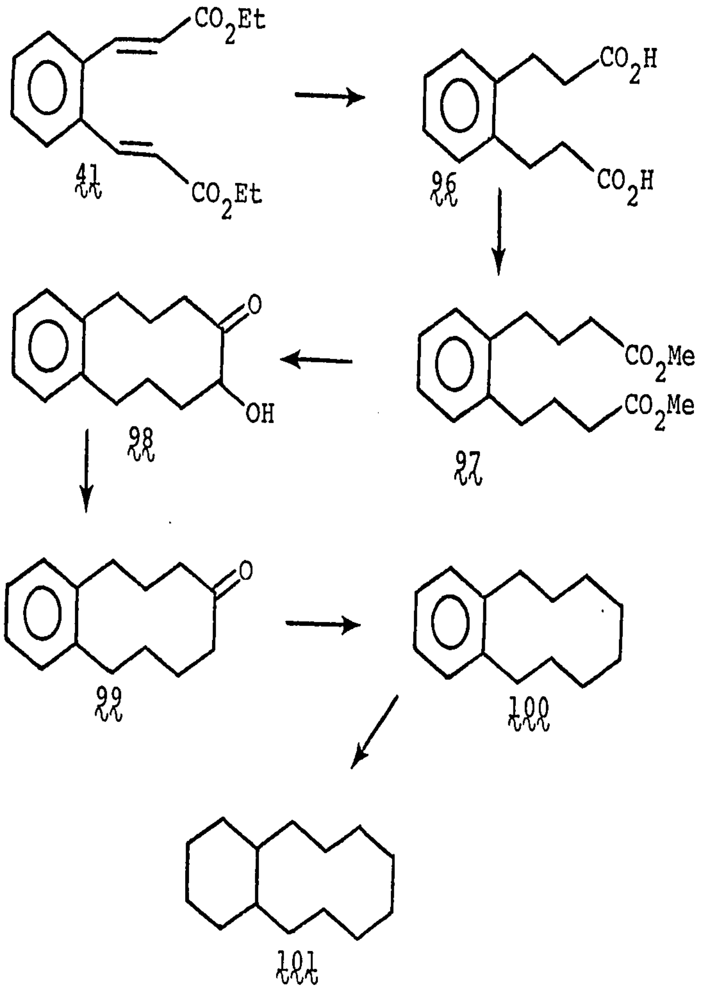
Likewise, a similar synthetic approach to the parent hydrocarbon (32) might be expected to give o-diethynylbenzene (47), ironically enough, the starting point in our studies of the 1,5-bisdehydro[10]annulene system.

The origin of the 1,2,3,4-tetrahydroanthracene (93) from the dimesylate 92, is as pointed out earlier, comparable to the formation of anthracene (60) from dimesylate 59. Thus, it is postulated that transitory formation of 37 can lead to diradical 95, which abstracts two protons to form 93. A discussion of this, and the formation of 94 is presented more fully in Chapter 5.



A very brief description of the synthesis of bicyclo[8.4.0]tetradecane, mentioned previously, is presented below (see the Experimental section for details). The route chosen was somewhat lengthy, but yields were good at each step, and no difficulties were encountered.

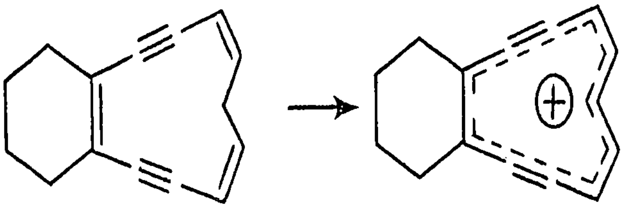
Hydrogenation of diester 41 (previously described) followed by hydrolysis of the ester groups gave the diacid (96) as colourless needles (mp 171.0-171.8°). An Arndt-



Eistert bishomologation[85] gave the diester 97 (bp 80-85° at 0.1 mm Hg) (calculated mass for $C_{16}H_{22}O_4$, 278.1519, found m/e = 278.1518). Diester 97 was converted into the acyloin 98 (mp 93-94°) (ir; 3520 and 1705 cm^{-1}) by the action of sodium in refluxing xylene. The acyloin 98 was acetylated by acetic anhydride in pyridine, and the acetyl group was then removed by reaction with calcium in liquid ammonia,[86] to give the 10-membered ring ketone 99 as a colourless liquid (bp *ca* 70° at 0.08 mm Hg), which showed carbonyl absorption in the ir spectrum at 1702 cm^{-1}. Wolff-Kishner reduction[88] of ketone 99 gave the hydrocarbon 100 as a colourless liquid (bp *ca* 50° at 0.1 mm Hg). Compound 100 showed no carbonyl absorption in its ir spectrum, and was homogeneous to glpc on various columns (UC-W98, Reoplex, Carbowax). Hydrogenation of 100 over PtO_2 in acetic acid gave a *cis-*,*trans-* mixture (*ca* 5:1) of bicyclo[8.4.0]tetradecane (101) (mass spectrum: m/e = 194).

B. The 11-Membered Ring

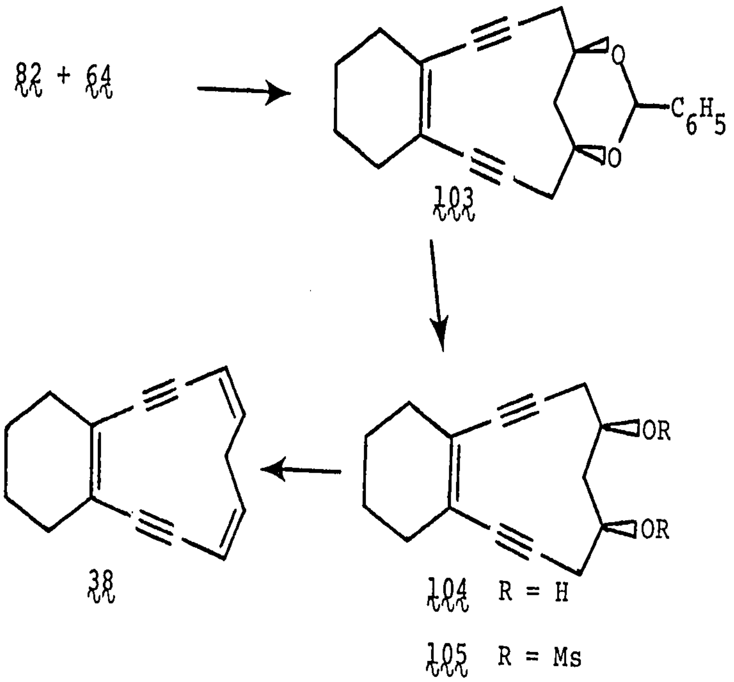
For the same reasons that the synthesis of 3,4-tetramethylene-1,5-bisdehydro[10]annulene (37) was undertaken, it seemed wise to synthesize 3,4-tetramethylene-cycloundeca-1,5-diyne-3,7,10-triene (38) in hopes that it would easily surrender a hydride ion to form the cation 102.



38

102

Because the synthesis of the benz-fused analogue of 38 had been successful, the synthesis of 38 itself was in exact analogy to it. The stereochemical considerations for the "5-carbon unit" to be added to 1,2-diethynylcyclohexene (82) were identical in each synthetic scheme, and thus ditosylate 64 was again employed (see Chapter 2). The synthesis of hydrocarbon 38 was done in collaboration with Dr. C. U. Kim of our laboratory.

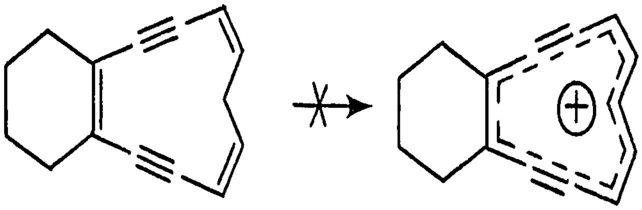


Condensation of the dilithio salt of 1,2-diethynylcyclohexene (82) with the ditosylate (64) in refluxing dioxane (ca 100 hr) gave, in ca 5% yield, the desired 11-membered ring benzilidene derivative (103) as a colourless crystalline compound (mp 215-217°, dec). Compound 103 showed absorptions in its nmr spectrum at τ 8.0-9.0 (m, 4H) and τ 7.6-8.0 (m, 4H) for the 6-membered ring methylene protons, and τ 7.0-7.5 (m, 6H) for the remaining methylene protons. The 11-membered ring protons adjacent to the oxygen atoms absorbed at τ 5.8-6.3 (m, 2H). The benzylidene proton appeared as a singlet at τ 4.60 (1H) and the aromatic protons as a multiplet (5H) at τ 2.5-3.0.

Hydrolysis of compound **103** by mild acid led directly to the diol **104** (mp 184-185°), which was converted into its dimesylate derivative (**105**) in the usual way. Dimesylate **105** was a colourless glass which could not be induced to crystallize. The methylsulfonate protons resonated at τ 6.90 as a sharp singlet (6H) in the nmr spectrum of **105**.

Elimination (by DBN) of the mesylate groups of **105** gave, in 70% yield, the desired hydrocarbon (**38**) as colourless platelets (mp 46-48°). Calculated mass for $C_{15}H_{14}$, 194.1096; found, m/e = 194.1090. The nmr spectrum showed peaks at τ 8.0-8.5 (m, 4H) for the homoallylic methylene protons; τ 7.0-7.7 (m, 6H) for the allylic methylene and the C-9 methylene protons; τ 3.7-4.3 (m, 4H) for the olefinic protons.

The similarities between the syntheses of **38** and its benz-analogue (**36**) are obvious. Unhappily, the similarities extended one step further. Treatment of **38** with trityl fluoroborate^{45b} in CH_3CN gave no detectable products, and large amounts of intractable tars. No starting material (**38**) could be recovered from such reaction mixtures.



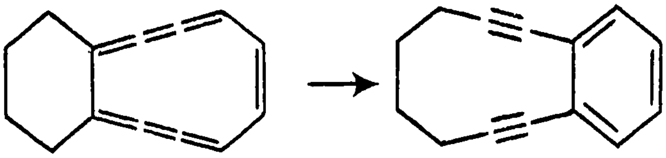
38 **102**

A discussion of this result is given in Chapter 5.

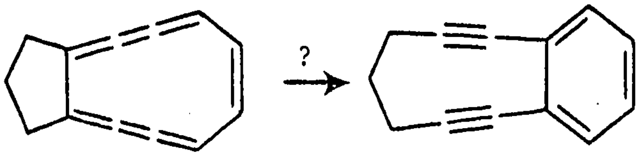
CHAPTER 4

A THIRD GENERAL APPROACH

If, as was briefly discussed in Chapter 3, a "Cope-like" rearrangement is responsible for the formation of compound 94 from 37, then a means of preventing this type of reaction can be visualized.



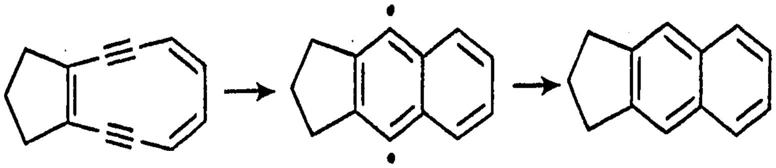
37 94



106 107

Consider the effect of replacing the tetramethylene-bridge in hydrocarbon 37 with a 3-carbon bridge (106). Rearrangement of compound 106 would lead to the hydrocarbon 107, which contains two acetylenic bonds and (formally) a double bond in a 9-membered ring. Molecular models indicate that such an array would be impossibly strained (indeed, the Dreiding model of 107 cannot be built using "normal" bond lengths and angles). This introduction of so much strain would then raise the energy barrier of a "Cope-like" rearrangement to a level that would possibly prevent the reaction from occurring at all.

There is, of course, an alternate mode of decomposition open to a (hypothetical) compound 106. Formation of diradical 108 (in the same manner as was postulated for



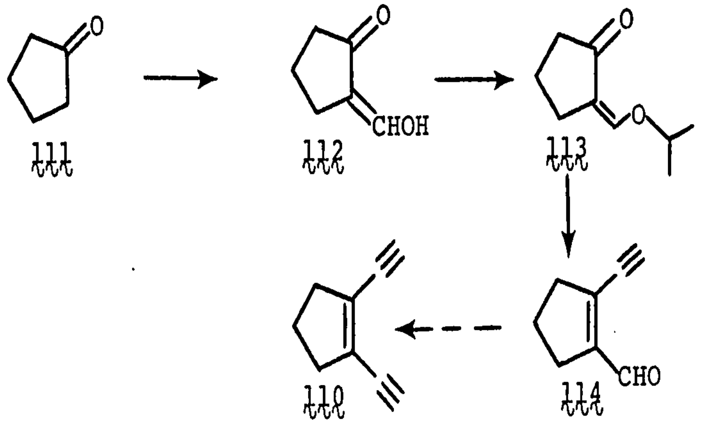
106 108 109

the formation of tetrahydroanthracene (93) from 37) would lead, via abstraction of convenient species, to trimethylene-bridged naphthalene derivatives (e.g. 109). However, molecular models of compound 106 indicate that inclusion of the cyclopentenyl double bond (in 106) results in the spreading of the distance between the carbons C-1 and C-6, which would lower the in-plane interaction of the π-electron clouds, thus lowering the tendency of this molecule to form diradical 108. Such an analysis, by its hypothetical nature, is somewhat oversimple, but at least incorporation of a cyclopentenyl double bond into the 10-membered ring is indicated to be a favourable circumstance.

Again, the synthetic plan of previous approaches was adopted in this third attempt at making a bisdehydro-

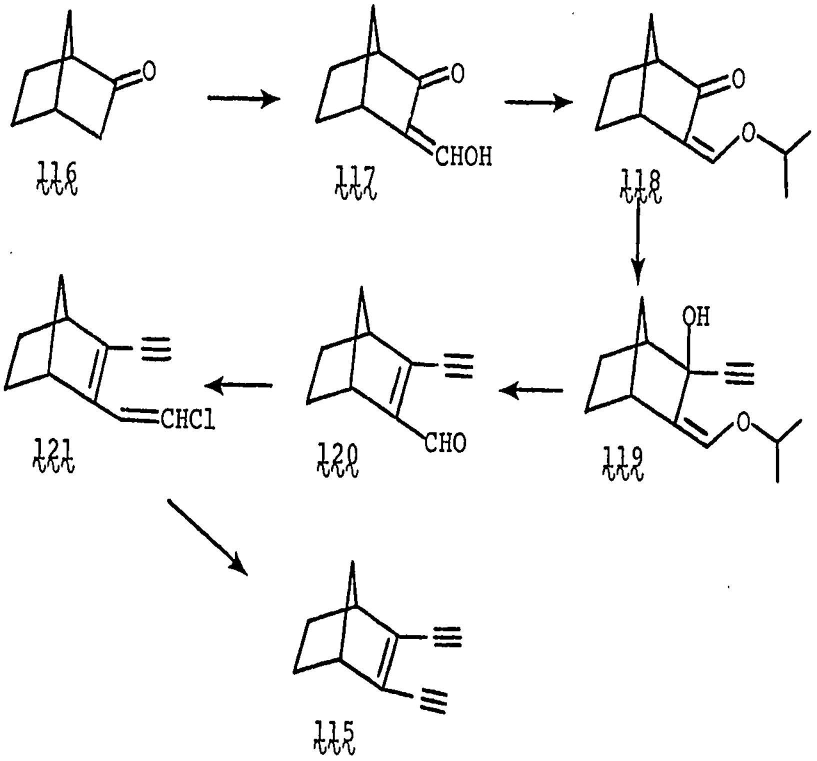
[10]annulene derivative. Therefore a synthesis of 1,2-diethynylcyclopentene (110) was undertaken, based on the method of synthesizing 1,2-diethynylcyclohexene (82).

Condensation of cyclopentanone (111) with ethyl formate proceeded in only fair yields (35-40%) to give 2-hydroxymethylenecyclopentanone (112), the hydroxyl group of which was blocked by reaction with 2-iodopropane to give in good yields, compound 113. Reaction of 113 with lithium acetylide ethylenediamine complex, followed by mild acid hydrolysis gave only poor yields (8-10%) of the desired acetylenic aldehyde (114). The lithium acetylide ethylenediamine reaction with cyclopentanone itself reportedly goes in good yields.[82] The reason for the failure of this reaction on compound 113 is not immediately apparent. It may be due to self-condensation of 113 (with the lithium acetylide acting as base).



At this point, the proposed synthesis of 1,2-diethynylcyclopentene (110) included two poor steps, making the synthesis of a bisdehydro[10]annulene derivative a dim prospect, especially in consideration of the low expected yield of the cyclization reaction. However, if indeed the failure of the lithium acetylide reaction was due to the acidity of the protons α- to the cyclopentanone carbonyl in compound 113, then lowering the acidity of these protons might well improve the situation. Enolization of a norbornanone derivative would involve a double bond at the bridgehead of a small ring-containing bicyclic compound, thus violating Bredt's rule. The target molecule was therefore changed to 2,3-diethynylnorbornene (115), which satisfied all of the requirements for this third approach to a bisdehydro[10]annulene derivative.

The synthesis of 115 paralleled that of 1,2-diethynylcyclohexene (82), but differed significantly in one aspect. 2-Norbornanone (116) was converted via its hydroxymethylene derivative (117) to the 3-isopropyloxymethylenenorbornanone (118). This compound did not react cleanly with lithium acetylide ethylenediamine complex, resulting in poor yields of the desired acetylenic aldehyde (120). The reason for this is obscure; the most obvious explanation is that steric hindrance between the methylene bridge and the approaching nucleophile was re-



sponsible for the low yield.

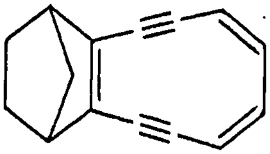
However, reaction of **118** with sodium acetylide in liquid ammonia gave good yields of the acetylenic alcohol (**119**), which, on acid hydrolysis, was smoothly converted into the desired acetylenic aldehyde (**120**). (This reaction sequence was originally performed by Dr. K. Abé of this laboratory). Compound **120** was an unstable, yellow crystalline compound (mp ca 25°) which showed ir absorption for the aldehyde carbonyl at 1725 cm^{-1}. The nmr spectrum of **120** showed sharp singlets at τ 0.08 and τ 6.18 for the aldehydic and acetylenic protons, respectively.

Reaction of **120** with the chloromethylenephosphorane[83] gave reasonable yields (ca 50%) of the chlorovinyl compound **121**, as a mixture of isomers. **121** was an unstable liquid. The acetylenic proton absorption in the nmr spectrum of **121** showed as an unsymmetrical doublet (1H) centred on τ 6.54, reflecting a difference of magnetic environments for the acetylenic protons of the *cis*- and *trans*-double bond isomers of **121**. The vinylic protons absorbed at τ 3.0-4.1 (m, 4H).

Dehydrochlorination of **121** by the action of sodium amide in liquid ammonia gave, in 75% yield, 2,3-diethynylnorbornene (**115**) as a colourless liquid, isolated by vacuum distillation (25° at 0.1 mm Hg) onto a dry-ice cooled cold-finger. Compound **115** was unstable in air, turning red-brown, with a marked increase in viscosity. The ir spectrum of **115** showed absorptions at 3300 and 2100 cm^{-1}, indicating the presence of the acetylene groups. The nmr spectrum of **115** showed peaks at τ 8.0-9.0 (m, 6H) for the methylene protons; τ 6.92 (m, 2H) for the bridgehead protons; τ 6.45 (s, 2H) for the acetylenic protons.

Reaction of both *o*-diethynylbenzene (**47**) and 1,2-diethynylcyclohexene (**82**) with *n*-butyllithium in dioxane produced white precipitates, which presumably were the respective dilithio salts of **47** and **82**. However, diethynylnorbornene (**115**) produced no such precipitate, even after the solution was heated at 60°. That the dilithio salt had formed was evident from the evolution of a gas (presumably butane) on admixture of the hydrocarbon and n-butyllithium. Apparently dilithio diethynylnorbornene is soluble in dioxane.

The cyclization reaction between 115 and the ditosylate 50 failed completely, with no identifiable products being produced. Many different solvents, reaction times and reaction temperatures were tried, with no success. Refluxing the dilithio salt of 115 in dioxane for 24 hr completely destroyed the acetylenic compound. It was apparent, therefore, that the prolonged heating that is necessary to effect cyclization may destroy the starting material at a rate which is too fast for the cyclization reaction to be competitive. Models of 115 indicate that the separation between the two acetylenic groups (4.7 Å) is greater than in, say, diethynylcyclohexene (82) (4.1 Å). Thus, compound 115 may surpass the geometric limits needed for this type of cyclization to occur. In any case,



122

a synthetic approach to hydrocarbon 122 must somehow circumvent any step like that just described.

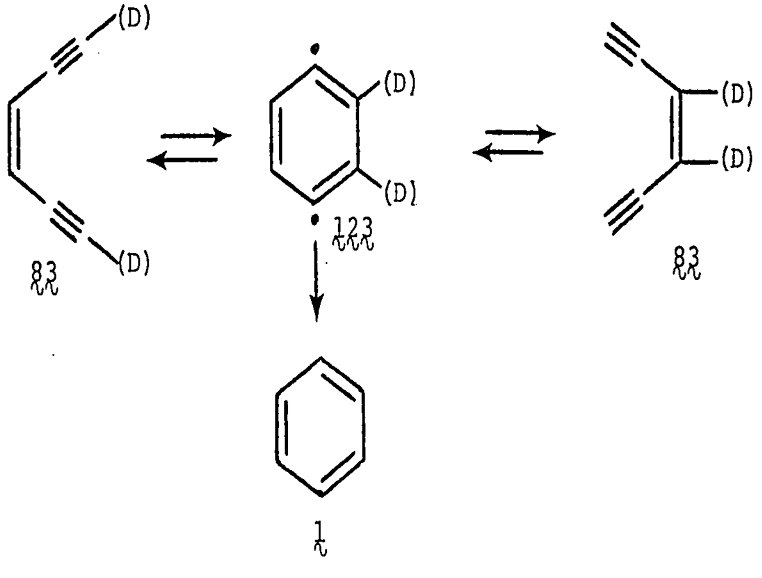
CHAPTER 5

AN ASSESSMENT

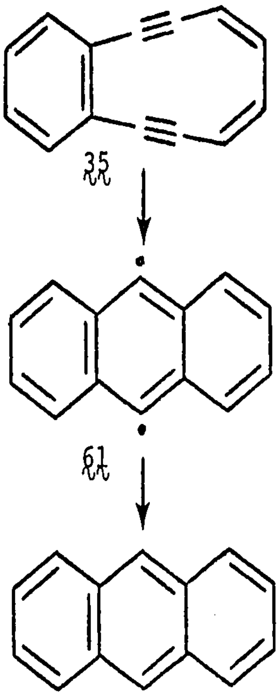
A. The 10-Membered Ring

A synthesis of a bisdehydro[10]annulene system has been a challenge for some years now, and considerable effort has been expended to solve this problem.[58,63,65] The impediments offered by the interaction of the in-plane π-electrons are severe; however, to some extent the chemistry resulting from this interaction is now understood.

There was recently published[88] a study of the thermolysis of 1,2-diethynylethylene (83). This study was centred around elucidating the properties of the 1,4-benzenediyl radical (123). Heating 83-1,6-d_2 to 200° resulted in scrambling of the label to give 83-3,4-d_2, with

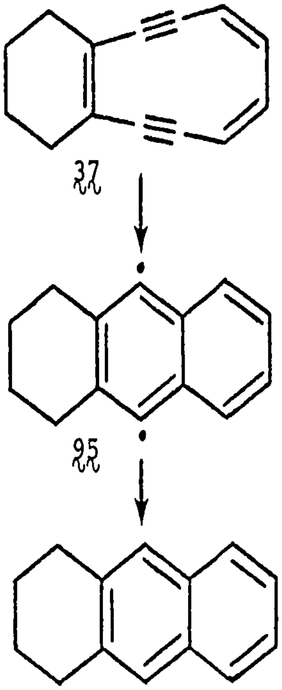


no evidence of any unsymmetrically substituted isomers. Pyrolysis of 83 in hydrocarbon solvent produced benzene (1) at the expense of 83. In toluene, diphenylmethane is produced. Using CCl_4 as solvent gives 1,4-dichlorobenzene. Thus the transitory existence of the diradical seems secure. The activation enthalpy for the reaction was estimated: $\Delta H \approx 32$ kcal/mole.


35

61

60


37

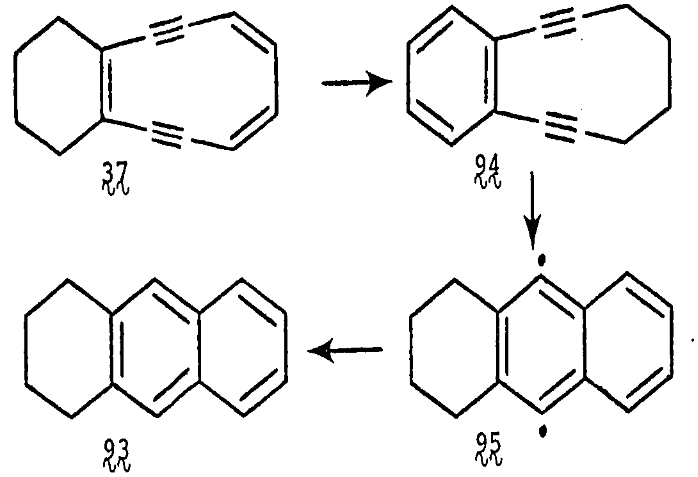
95

93

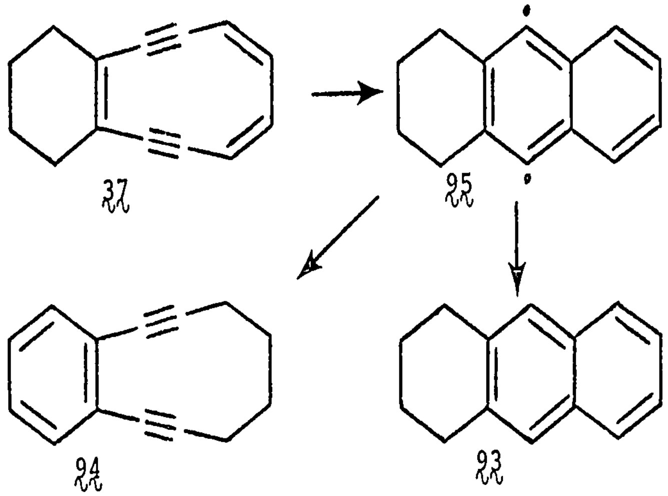
Both compounds 35 and 37 formally incorporate the diethynylethylene molecule, although this system would be considerably strained, and probably distorted to some extent because of its incorporation into the 10-membered ring. This strain is such that reaction to form the respective diradicals (61 and 95) should be facilitated, relative to the reaction not involving the ring system.

Consider first 3,4-benz-1,5-bisdehydro[10]annulene (35). The diradical that is presumably formed is a dibenz-derivative of the 1,4-benzenediyl radical, and thus, is expected to behave in a similar fashion. In deuterated solvents at -30°, some 9,10-dideuteroanthracene (60) was formed, as mentioned previously. In benzene, there is some evidence (mass spectrum, m/e = 256) that a phenylanthracene is also formed. Thus, it is apparent that the in-plane π-interaction is severe enough that the energy barrier to produce 61 is overcome with facility, and anthracene or its derivatives are the only detectable products. A "Cope-like" rearrangement in this system is degenerate, and therefore the formation of anthracene is again favoured, in that an alternate route of decomposition of 35 is not available.

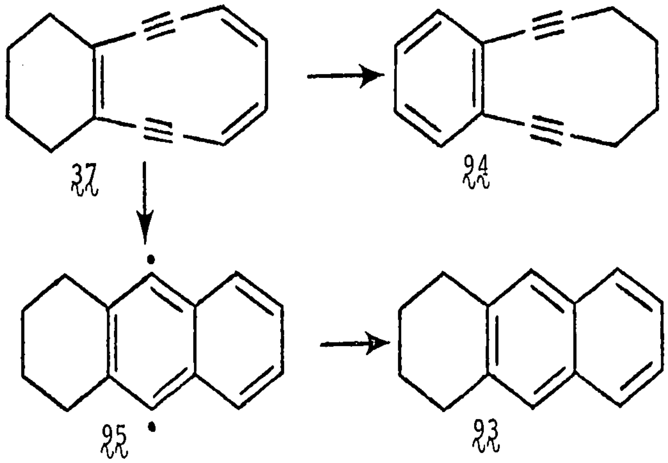
The 3,4-tetramethylene-1,5-bisdehydro[10]annulene (37) case is more complex, and therefore more interesting, but is completely analogous to the benz-substituted compound. The yield of identifiable products (93 and 94) is considerably greater, however, and as such, processes in some ways different from the benz-fused case may be involved. Three routes of decomposition of 37 may be con-



ROUTE 1



ROUTE 2



ROUTE 3

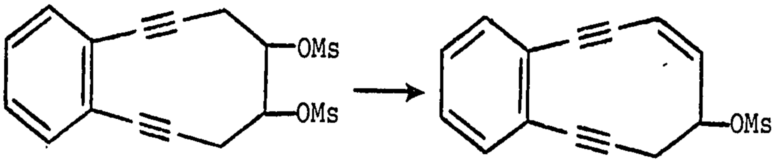
sidered, as depicted on the preceeding page.

Route 1 involves the isomerization of the tetramethylene[10]annulene (37) to hydrocarbon 94, followed by collapse to the diradical (95), and then proton abstraction to form the anthracene derivative 93. This route can be excluded as a possible mechanism. Hydrocarbon 94 forms the anthracene derivative (93) only at higher temperatures, and has a half-life of ca 2 hr at 140° (methylcyclohexane; sealed tube). Comparing these conditions to those under which 93 is formed in the elimination reaction suggests that 94 cannot be the precursor to 93.

The second route offers somewhat more promise; the bisdehydro[10]annulene derivative (37) collapses to form the diradical (95) which then either forms 93 or 94. However, these two products are formed in comparable amounts, and thus the energy barrier for their formation from the diradical should be about the same in each case. Bond reorganization to form hydrocarbon 94 (from diradical 95) involves the introduction of strain, whereas, formation of the anthracene derivative (93) involves no strain at all. Moreover, product 94 has less resonance energy than 93. Indeed, the only barrier to form the anthracene derivative (93) is in the abstraction of protons from whatever source is available. Both THF and MeOH, co-solvents for the elimination reaction of dimesylate 92 are ready hydrogen sources, and thus, this energy barrier is low. Route 2, therefore, is tenuous at best. There is little reason to suppose it is operational, when compared to route 3.

This latter pathway gives the tetramethylenebisdehydro[10]annulene (37) two destructive alternatives. One is the "Cope-like" rearrangement to form hydrocarbon 94 directly; the other is direct formation of the diradical 95, followed by hydrogen abstraction. Such a route would suggest that the two rearrangements are of comparable energy. The first ("Cope-like") might be expected to have relatively low energy, because of the proximity and relative positions of the relevant orbitals (all are in-plane), which are ideally disposed for this sort of bond reorganization. Relief of ground-state strain is also a favourable factor. The ease with which hydrocarbon 94 is formed (<0°) suggests that a low energy process is indeed involved. The same types of conditions are also favourable for the diradical (95) formation, even though the result is a high energy species. That the 3,4-benz-1,5-bisdehydro[10]annulene (35) showed no tendency to survive supports the fact that decomposition through the diradical species is not energetically unfavourable. Thus it seems that of the three alternatives for the destruction of 37, the last route (#3) is the most likely to be occurring.

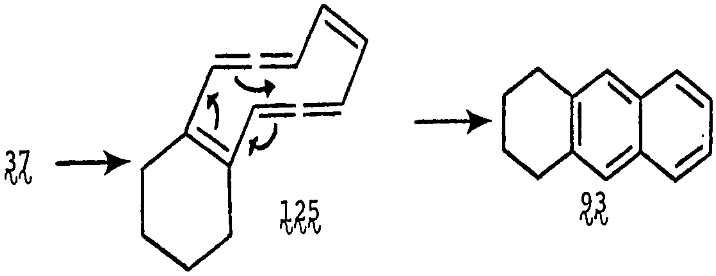
In the foregoing discussion, several assumptions have been made. One is that the dehydro[10]annulene system has been formed at all, even as a transient species. Only indirect evidence supports this claim. The monomesylate 124, the product of elimination of one mesylate moiety from compound 59, has been isolated, and it showed reasonable



59 124

stability. Basic elimination of 124 again gave only anthracene as the product. This suggests that 2 mole equivalents of base are required for hydrocarbon formation. Secondly, presence of the diene unit in the 10-membered ring would promote the rearrangements (for instance, to form hydrocarbon 94 or the diradical 95) by providing an aromatic system in the products, thus facilitating the reaction. Again the ease with which these products are apparently formed supports the fact that the bisdehydro[10]annulenes have at least transient existence.

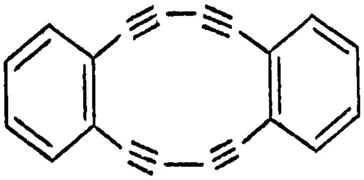
Another assumption is that, in the tetramethylene-bridged case (37), a diradical intermediate is involved in the rearrangement of 37 to the anthracene derivative (93). There is an alternate explanation. The bisdehydro[10]annulene system may abstract two hydrogens in a concerted fashion, to give the intermediate diallenic compound 125, which,



ROUTE 4

as has been predicted,[77] would be very susceptible to thermal isomerization to the anthracene derivative (93). Such a postulate is aesthetically pleasing, but there is no evidence to suggest that it is valid. Indeed, intervention of a diradical species in the benz-fused case (35) is strongly indicated, thereby disfavouring this process. As far as the tetramethylene-bridged system is concerned, however, this process cannot be rigorously excluded.

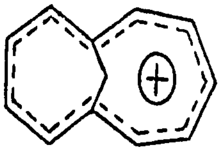
Compound 126 has been synthesized, and shows reasonable stability.[89] It is certainly more strained than



126

cationic species 63 and 102 failed. The hydrocarbons intended as the precursors to these species were stable and apparently strain-free, as demonstrated earlier.

It is apparent from the behaviour of the 10-membered ring compounds that the centres of these ring systems are somewhat crowded, due to the in-plane π-electrons. An explanation of the failure of the cation synthesis could lie here. In order to achieve sp^2 hybridization at the carbon atom forfeiting the hydride ion, the remaining proton on the methylene carbon is forced further into the centre of the ring than it is during the thermally induced "flipping" of this carbon. It is conceivable then that the resultant crowding forces the proton out of the plane of the π-system, and thus the cation is destabilized by the reduction in the amount of overlap between the filled and empty p-orbitals. The degree of the resulting non-planarity is then too great to allow any sort of stability.

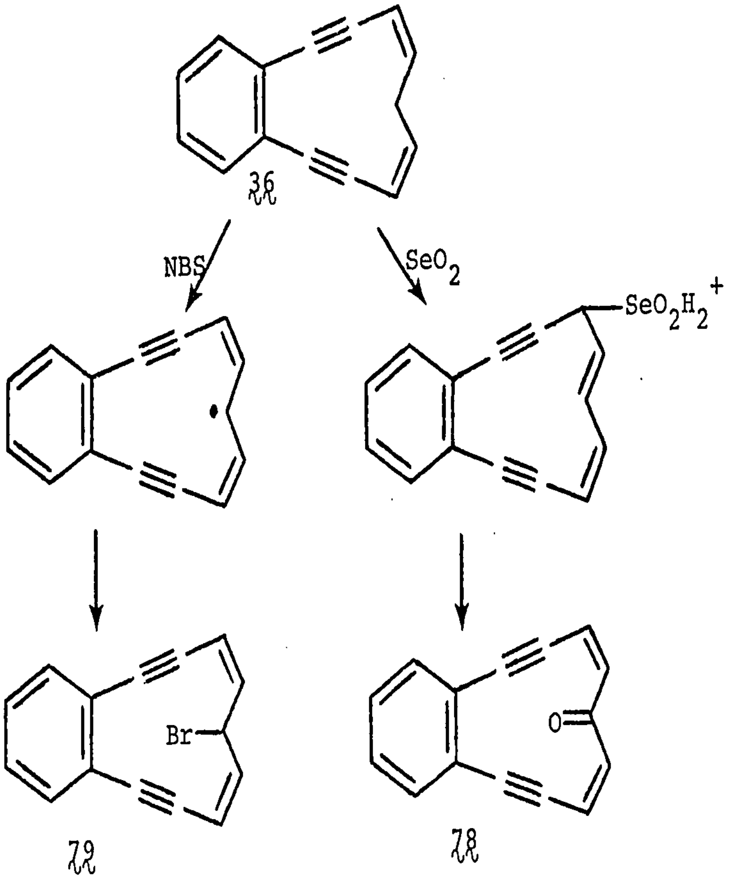


129

This distortion, however, must be more severe than is indicated by models. The bicyclic system 129 has been synthesized, and is stable.[66] In fact, its stability is quite remarkable. Assumedly the peripheral carbon atoms do not all lie in a plane, as is the case in its parent hydrocarbon.[91] Thus some distortion from planarity of the ring carbons can be tolerated. The analogy between the compound **129** and **63** or **102** is somewhat tenuous (see the next section). However, it is apparent that the cationic systems **63** and **102** would be far less stable than any other aromatic cations such as **129**, tropylium cation (**3**) or cyclopropenium cation (**16**). Whether this instability is due to the geometry of **63** (or **102**), or to some peculiarity of the 10 π-electron system is an open question. Only indications to a solution can be given at this time.

The reluctance of this 11-membered ring system (in **36** or **38**) to achieve planarity may be reflected in some attempted reactions of the methylene carbon. Treatment of **36** with SeO_2 in aqueous ethanol at reflux, or acetic acid at room temperature, did not effect any oxidation. In refluxing acetic acid, the hydrocarbon was destroyed, and no products were detectable. Nor was attempted allylic bromination with NBS successful. The hydrocarbon **36** was inert to this reagent under several conditions.

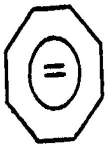
It was hoped that the expected products of the SeO_2 reaction (**78** or the corresponding intermediate alcohol) on protonation in strongly acidic media would yield the 11-membered ring cation in solution, so that it could



be studied spectrometrically. Likewise, compound 79 might also have provided information about the ion. It is noteworthy, however, that for both reactions, the mechanisms that would presumably be operating demand trigonal carbon at C-9;[75,76] this ring system is apparently reluctant to incorporate such an array. However, the synthesis of, say, 38, substituted in an appropriate manner at C-9 probably offers the best opportunity for studying the 11-membered ring cationic system.

C. The 10 π-Electron Aromatic System

Few monocyclic, non-benzenoid 10 π-electron aromatic compounds are known. Cyclooctatetraenide dianion[46] (**14**) and cyclononatetraenide anion[47] (**15**) are considered to be aromatic, and are 10 π-systems. Cycl[3.2.2]azine (**130**), is a bridged [10]annulene in which a nitrogen atom acts as a link to three carbon atoms. The nmr spectrum of **130** shows absorptions (τ 2.14-2.80) characteristic of aromatic systems.[6]



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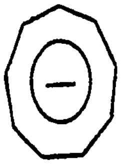

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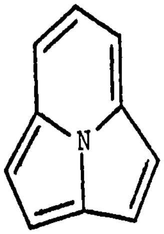
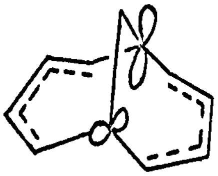


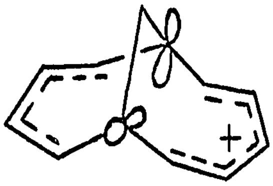
130

Each of these compounds have features peculiar to them, other than the 10 π-system, that account for their stability relative to the parent [10]annulenes. The ionic species have the advantage that any distortion from planarity (so as to relieve the strain associated with this geometry) would result in localization of the negative charge(s), clearly an unfavourable circumstance. The cyclazine (**130**), on the other hand, is a rigid system prevented from transannular reaction and held nearly planar by the nitrogen atom.

Some 10 π-electron systems that show particular stability are the 1,6-bridged [10]annulenes (**26**) and the 1,6-methano[11]annulenyl cation (**129**). These species are all very stable, and little doubt exists that they are in fact aromatic.[59] But these compounds too have a peculiarity that may, in fact, be responsible for this (extraordinary) stability.

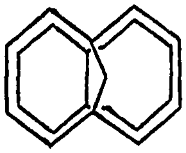


26a



129

As mentioned previously, the periphery of **26** (and by inference, **129**) is not planar; the distortion from coplanarity is *ca* 20°.[91] Models of **26** show that the carbon $2p_z$ orbitals at positions 1 and 6 are considerably distorted from being parallel to the other $2p_z$ orbitals on the ring, and in fact, these orbitals (at C-1 and C-6) are directed *toward each other* across the 10-membered ring. This particular geometry could then result in homoconjugation, which would stabilize these systems, as illustrated. In such a case, these compounds might best be described as substituted naphthalenes.



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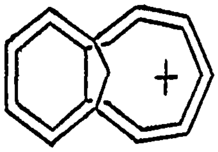
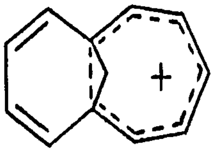


129

Some evidence for this type of homoconjugation exists. Heilbronner has calculated the uv spectra of 26 and 129,[92] and invokes homoconjugation across the ring in order to explain the experimentally determined spectra. Similarly, the explanation of the esr spectrum of the radical-anion of 26 involves homoconjugation between the C-1 and C-6 positions.[93] Recently a natural abundance ^{13}C nmr spectrum of 129 was obtained in this department.[94] The spectrum indicated that the positive charge is not evenly distributed over the peripheral carbon atoms. Cation 129 might better be represented as shown below. This diagram implies that 129 is a "benz-fused homotropylium ion" if any name at all is required.



129

These considerations in no way detract from the interest and fascination of these compounds (26 and 129); if anything, the homoconjugation increases their importance.

It is becoming increasingly evident, however, that these systems are not true reflections of mono-cyclic, planar, 10 π-electron systems.[65]

Thus it is that no planar, monocyclic, homonuclear, neutral, aromatic 10 π-electron systems are known at the present time. A gap in our knowledge of aromatic systems therefore exists; a synthesis of a bisdehydro[10]-annulene could go a long way to filling this gap.

CHAPTER 6

EXPERIMENTAL

All melting points and boiling points are uncorrected.

The ir spectra were obtained on Perkin-Elmer model 21 or model 257 infrared spectrometers, $CHCl_3$ solvent, unless otherwise specified. In reporting ir spectral data, the following abbreviations are used:

s	strong absorption
m	medium absorption
w	weak absorption
b	broad absorption

The nmr spectra were measured with Varian Associates A-60 or HA-100 spectrometers; $CDCl_3$ was used as solvent unless otherwise stated, and tetramethylsilane was used as internal standard, unless otherwise stated. All coupling constants are reported in Hz. In reporting nmr spectral data, the following abbreviations are used:

m	multiplet
s	singlet
d	doublet
t	triplet

q	quartet

The mass spectra were measured on A.E.I. MS-2, MS-9 and MS-12 mass spectrometers. The uv spectra were measured on a Cary model 14M recording spectrometer.

Analytical glpc was performed on a F & M model 5750 research chromatograph employing 6 ft. x 3/16 in. columns (packing indicated in the text), with a flame ionization detector.

Alumina column chromatography employed Woelm Neutral Alumina, Activity Grade II, as the column packing. Silicic acid columns were prepared from Mallinckrodt Silic AR-CC-4, 100 mesh silicic acid, unless otherwise specified.

The following abbreviations are used for chemical names:

THF	tetrahydrofuran
MeOH	methanol
NaOMe	sodium methoxide
$HC(OEt)_3$	ethyl orthoformate
_t_-BuOH	tertiary butanol
KO_t_-Bu	potassium tertiary butoxide
DBN	1,5-diazabicyclo[4.3.0]non-5-ene

All experiments were conducted under a dry nitrogen atmosphere, unless otherwise specified.

Diethyl *o*-phenylenediacrylate (**41**)

Carboethoxymethylenetriphenylphosphorane (5.6 g; 14.8 mM) was dissolved in CH_2Cl_2 (50 ml). To this solution was added dropwise, with stirring, a solution of *o*-phthalicdicarboxaldehyde (1 g; 7.4 mM) in CH_2Cl_2 (20 ml). The solution was refluxed 18 hr. Acetone (7 ml) was then added and refluxing continued a further 1 hr. Solvents were then removed *in vacuo*, and the semi-crystalline residue was extracted with pentane (5 x 10 ml). The pentane was removed *in vacuo* and the residue recrystallized from MeOH, giving 1.66 g (82%) of **41** (mp 77.5-78°).

nmr: τ 1.7-3.9 (m, 8H); 5.5-6.0 (q, 4H); 8.5-8.9 (t, 6H).

ir: 1710 cm^{-1} (s); 1640 (s); 975 (m).

o-Phenylenedi-1-hydroxyprop-2-ene (**42**)

To a stirred solution in benzene (50 ml) of **41** (1.6 g; 5.82 mM) was added a 25% solution of di-isobutylaluminum hydride in benzene (30 ml) under N_2 atmosphere. The temperature of the mixture was not allowed to rise above 45°. The mixture was then stirred at 40° for 12 hr. The excess hydride was then destroyed by the addition of methanol. The resulting mixture was filtered over Celite, and the solvents then evaporated to give a crystalline residue. Recrystallization from benzene gave 1.1 g (98%)

of diol 42 (mp 91-91.5°).

nmr: τ 2.5-4.1 (m, 8H); 5.5-5.8 (dd, 4H); 8.3 (s, 2H).

ir: 3330 cm^{-1} (broad); 965 (s).

o-Phenylenediacrolein (43)

The diol 42 (291 mg; 1.53 mM) was dissolved in CH_2Cl_2 (30 ml) and to it was added active MnO_2 (3 g) and the mixture was shaken at room temperature for 6 hr. The MnO_2 was then filtered off, and the filtrate evaporated to give pale yellow crystals of the dialdehyde 43 (mp 115-116°). Yield 233 mg (82%).

nmr: τ 1.8-3.6 (m, 8H); 0.0-0.3 (d, 2H).

ir: 1680 cm^{-1} (s); 1125 (m); 970 (m).

o-Phenylenedi-2-bromoacrolein (44)

The dialdehyde 43 (1.0 g; 5.38 mM) was dissolved in glacial acetic acid (15 ml) and to this solution was added dropwise a solution of Br_2 (1.72 g; 10.7 mM) in acetic acid (4.5 ml), at which point no more bromine colour was discharged. The solution was stirred for another 15 min and then anhydr. K_2CO_3 (1 g) was added. After 5 min, evolution of gas had ceased. The solution was heated at 80° for 30 min, and then cooled. The acetic acid was evaporated by co-distillation with xylene, and the residue was treated with water (5 ml) and extracted with $CHCl_3$. The organic layer was washed with 1M NaH_2PO_4 solution (10 ml) and dried (anhydr. Na_2SO_4). Evaporation of solvents gave a crystalline residue that was recrystallized from MeOH to give colourless crystals (1.4 g; 76%) (mp 122.5-123°, dec).

nmr: τ 1.6-2.8 (m, 6H); 0.5 (s, 2H)

ir: 1700 cm^{-1} (s); 1610 (s); 1110 (s).

o-Phenylenedi-2-bromoacrolein, bisdiethylacetal (45)

The dibromo-dialdehyde (44) (1 g; 2.91 mM) was treated with $HC(OEt)_3$ and abs. ethanol (3 ml) and NH_4Cl (50 mg). This mixture was refluxed 9.5 hr. The reaction mixture was poured into ice-cold $NaHCO_3$ solution (5%) and extracted with $CHCl_3$ (3 x 5 ml). The organic phase was washed with brine (5 ml), dried (anhydr. Na_2SO_4) and evaporated. The residue was chromatographed on alumina, pentane eluent, to give the bisdiethylacetal 45 as a colourless solid.

Yield: 1.23 g (86%).

o-Phenylenedipropargylcarboxaldehyde, bisdiethyl acetal (46)

The dibromo-bis-diethylacetal (45) (9.1 g; 18.5 mM) was dissolved in abs. ethanol (10 ml) and to it was added KOH (50 ml) in abs. ethanol (1.1 N), and the mixture was stirred 10 hr. The mixture was heated at 50° for 30 min, and then poured into a pH 7 buffer solution (Na_2HPO_4-NaH_2PO_4; 50 ml) and the resulting mixture was extracted with CH_2Cl_2 (4 x 100 ml); the combined organic layers were washed with brine (25 ml), dried (anhydr. Na_2SO_4) and evaporated to give 6.15 g of a semi-crystalline residue, which was not purified further, but used as is in the next reaction.

o-Phenylenedipropargylcarboxaldehyde (39)

The bisdiethyl acetal (46) (6.1 g; 18.5 mM) was dissolved in THF (125 ml) and to it was added p-toluenesulfonic acid monohydrate (4.2 g) and water (74 ml). Thus the whole solution was 0.11N in the sulfonic acid. The solution was heated at 60° under N_2 for 7 hr. After this time, Na_2CO_3 (1.48 g; 14 mM) was added keeping the solution at 0°. The THF was evaporated, and the residue extracted with CH_2Cl_2 (3 x 50 ml). The combined organic layers were washed with brine (25 ml), dried (anhydr. Na_2SO_4) and evaporated. The crude crystalline residue was sublimed at 65°, 0.025 mm Hg, which gave 2.4 g (72%) of colourless crystals of the dialdehyde 39 (mp 64-66°).

o-Divinylbenzene (48)

Sodium (13.7 g; 0.596 M) was dissolved in liquid NH_3 (1.5 l.) in the presence of $Fe(NO_3)_3.6H_2O$, giving a grey suspension. To this was added triphenylmethylphosphonium bromide (218 g; 0.596 M), and the NH_3 was allowed to evaporate overnight under a stream of N_2. Ether (1.0 l.) was distilled into the reaction mixture, and the resulting suspension was refluxed 30 min. To this suspension was added dropwise with stirring a solution of the phthalicdicarboxaldehyde (40 g; 0.298 M) in THF (220 ml), at a rate sufficient to reach and maintain reflux. Reflux was continued for 1 hr. The solvents were then evaporated, and the residue extracted with ether (5 x 200 ml). Evaporation of the ether, and filtration of the precipitated triphenylphosphine oxide at stages gave a brown oily residue. Distillation of this crude product gave 25g (65%) of 48.

bp 53° at 3 mm Hg (lit.[69] bp 80-82° at 16 mm Hg).

ir: 1625 cm^{-1} (s); 1483 (s); 1450 (m); 1410 (broad, m); 985 (s); 910 (broad, s).

o-(α,α',β,β'-Tetrabromo)diethylbenzene (49)

The divinylbenzene (48) (28.0 g; 0.215 M), dissolved in CCl_4 (60 ml) and cooled to 0°, was treated with Br_2 (68.8 g; 0.431 M) in CCl_4 (100 ml), at a rate sufficiently slow so as to allow disappearance of the Br_2 colour. The mixture was stirred overnight at room temperature. Evaporation of the solvent left pale brown crystals. Recrystallization from ether/pentane gave colourless prisms of 49 mp 73-74° (lit.[69] mp 72-74°)

Yield: 91.0 g (94%).

nmr: τ 2.4-2.7 (m, 4H); 4.3-4.7 (t, 2H); 5.9-6.1 (s, 4H).

o-Diethynylbenzene (47)

Potassium metal (52.6 g; 0.834 M) was dissolved in dry *t*-BuOH (1400 ml). The tetrabromide (49) (91.0 g; 0.202 M) was dissolved in benzene (250 ml) and this solution was added dropwise to the *t*-BuOH solution over 90 min at gentle reflux. The resulting mixture was refluxed a further 2.5 hr. Most of the solvents were distilled off at 50°, 30 mm Hg. To the residue was added aqueous HCl (0.9M; 1.0 l.) and the aqueous phase was extracted with ether (3 x 200 ml). The ether extracts were washed with H_2O (100 ml) and brine (100 ml), dried (anhydr. Na_2SO_4), and evaporated. The residual oil was distilled to give a colourless oil. bp 56-57° at 2.5 mm Hg. (lit.[69] 80-82° at 14 mm)

Yield: 16.15 g (64%).

nmr: τ 2.4-2.9 (m, 4H); 6.65 (s, 2H).

ir: 3250 cm^{-1} (s); 2090 (w); 1470 (s); 1440 (m); 950 (m).

2-Phenyl-4,5-biscarboethoxy-1,3-dioxolane (**52**)

Diethyl *dl*-tartarate (**51**) (154 g; 0.75 M) was dissolved in dry benzene (500 ml). To this solution was added freshly distilled benzaldehyde (82.7 g; 0.78 M). After the addition of *p*-toluenesulfonic acid monohydrate (650 mg) the solution was refluxed under a Dean-Stark apparatus for 88 hr, after which time the theoretical amount of H_2O had been collected. The benzene solution was washed with 5% Na_2CO_3 solution (150 ml), H_2O (150 ml), brine (100 ml), then dried (anhydr. Na_2SO_4). Removal of the solvents and excess benzaldehyde gave pale yellow crystals. Recrystallization from MeOH (-20°) gave colourless prisms (mp 44.5-45.5°).

Yield: 165 g (75%).

nmr: τ 2.2-2.7 (m, 5H); 3.80 (s, 1H); 5.0-5.25 (q, 2H); 5.4-6.0 (qd, 4H); 8.5-8.9 (td, 6H).

dl-2-Phenyl-4,5-bis(hydroxymethyl)-1,3-dioxolane (**53**)

$LiAlH_4$ (28.5 g; 0.75 M) was dissolved in dry THF (1500 ml). To this solution was added dropwise, with stirring, a solution of the diester **52** (147 g; 0.5 M) in THF (400 ml) at a rate sufficient to reach and maintain reflux. The mixture was refluxed a further 2 hr following the addition. H_2O (28.5 g), then 15% NaOH solution (28.5

g) then more H_2O (85.5 g) were added slowly in sequence, leaving a colourless solution and a white precipitate. After filtering, the solvents were evaporated, leaving a semi-crystalline solid. Azeotropic drying with benzene gave colourless prisms, which were used without further purification in the subsequent reaction.

Yield: 86.1 g (82%).

dl-2-Phenyl-4,5-bis(tosyloxymethyl)-1,3-dioxolane (**50**)

The diol **53** (86 g; 0.41 M) was dissolved in dry pyridine (680 ml) and cooled to 0°. To this solution was added *p*-toluenesulfonyl chloride (234 g; 1.23 M) and the mixture was stirred at 0° until all of the solids had dissolved. This solution was stood at 0° for 18 hr. The resulting mixture was poured onto crushed ice (500 g) and a white solid crystallized out, which was filtered off, then washed successively with H_2O (2 x 400 ml), MeOH (2 x 100 ml), then cyclohexane (2 x 200 ml). The resulting solid was recrystallized from ethyl acetate to give colourless crystals of **50** (mp 131.5-132.5°).

Yield: 174 g (83%).

nmr: τ 2.1-2.8 (m, 13H); 4.25 (s, 1H); 5.83 (bs, 6H);
7.60 (s, 6H).

ir: 1600 cm^{-1} (ss); 1380 (bs); 1170 (s); 970 (bs).

3,4-Benz-8,9-dihydroxycyclodeca-1,5-diyne-3-ene-O,O'-benzylidene (54)

Diethynylbenzene (47) (9.50 g; 75.4 mM) was dissolved in dioxane (400 ml), then reacted with *n*-butyllithium in hexane (155 mM), giving a white suspension. The ditosylate (50) (39.0 g; 75.4 mM) was dissolved in dry dioxane (300 ml) and added to the dilithio salt at room temperature. This mixture was then refluxed for 96 hr, giving a very dark mixture. CO_2 was bubbled into the cooled reaction mixture, followed by addition of H_2O (10 ml). The solvents were evaporated *in vacuo*, and the resultant dark semi-solid residue was extracted with 1M NaH_2PO_4 solution (100 ml) and ether (4 x 300 ml). The combined ether extracts were washed with brine (100 ml) and dried (anhydr. Na_2SO_4), then evaporated. The dark residue was chromatographed on alumina (600 g, Woelm, neutral, activity II), hexane/benzene (1:1) eluent, which gave as the second fraction, light brown crystals. Recrystallization from CH_3CN gave colourless needles (mp 145.0-145.5°).

nmr: τ 7.08 (m, 4H); 5.61 (m, 2H); 4.20 (s, 1H); 2.66 (m,9H)
ir: 2220 cm^{-1} (s); 1062 (s); 970 (s).
Mass spectrum: Calc. for $C_{21}H_{16}O_2$: 300.1150
Meas. for " : 300.1145

3,4-Benz-8-hydroxycyclodeca-1,5-diyne-3-ene-9-yl benzoate (57)

The benzylidene derivative 54 (400 mg; 1.33 mM) was dissolved in CH_3CN (11 ml). To this solution was added trityl fluoroborate (485 mg; 1.47 mM) in CH_3CN (5 ml). The resultant dark solution was stirred overnight at room temperature, producing a yellow crystalline precipitate. This mixture was poured into 1.5M NaH_2PO_4 solution (30 ml) and the resultant mixture was extracted with CH_2Cl_2 (3 x 25 ml); the combined organic phases were dried (anhydr. Na_2SO_4) and evaporated, leaving a pale yellow crystalline residue. Chromatography on silicic acid (20 g) gave the hydroxybenzoate (57) as pale yellow platelets (mp 133-135°dec.).

Yield: 400 mg (95%).

nmr: τ 1.7-2.9 (m, 9H); 4.63 (m, 1H); 5.70 (m, 1H); 7.00 (m, 5H).

ir: 1725 cm^{-1} (s).

3,4-Benz-8,9-dihydroxycyclodeca-1,5-diyne-3-ene (58)

The hydroxybenzoate 57 (400 mg; 1.27 mM) was dissolved in MeOH (25 ml) and THF (7 ml). NaOMe (ca 40 mg) was added, and the mixture was stirred at room temperature for 1 hr. CO_2 was then bubbled in, and the flask contents were then poured into 1M NaH_2PO_4 solution (75 ml). This mixture was extracted with CH_2Cl_2 (3 x 50 ml), and the organic phase was washed with brine (30 ml) and dried (anhydr. Na_2SO_4). Evaporation of the solvents left a yellow oil. Chromatography on silicic acid, 2% MeOH in $CHCl_3$

eluent, gave the diol **58** (mp 110-112° dec.).

Yield: 240 mg (90%).

nmr: τ 7.30 (m, 4H); 6.64 (m, 2H); 5.92 (m, 2H); 2.76 (bs, 4H).

ir: 3340 cm^{-1} (broad, m); 1045 (s); 978 (s).

3,4-Benzcyclodeca-1,5-diyne-3-ene-8,9-diyl dimesylate (**59**)

The diol **58** (530 mg; 2.5 mM) was dissolved in benzene (20 ml) and THF (1.5 ml), and methanesulfonyl chloride (855 mg; 7.5 mM) was added. This solution was cooled to 0° and to it was added triethylamine (760 mg; 7.5 mM) in benzene (3 ml). After stirring 1 hr, at 0°, the mixture was poured into NaH_2PO_4 solution (50 ml) and then extracted with ether (3 x 30 ml). The ether extracts were washed with brine (20 ml), dried (anhydr. Na_2SO_4), and evaporated, leaving a yellow syrup. Chromatography on silicic acid (8 g) followed by recrystallization from benzene gave the dimesylate **59** as light brown crystals (mp 113°).

Yield: 782 mg (82%).

nmr: τ 7.04 (m, 4H); 6.92 (s, 6H); 5.00 (m, 2H); 2.76 (s, 4H).

Dimethyl 2,4-dibromoglutarate (**67**)

Thionyl chloride (300 g; 2.5 M) was added dropwise to glutaric acid (132 g; 1.0 M) and this mixture was refluxed 14 hr. The excess thionyl chloride was distilled off, and the residual liquid was pumped out under high vacuum. The residual acid chloride was then heated to 100° with stirring, and bromine (384 g; 2.5 M) was added dropwise under reflux. The mixture was stirred overnight at 100° with simultaneous irradiation from a 400 W tungsten lamp. The crude dibromide was then slowly poured into ice-cold methanol (200 ml). Ether (600 ml) was added, and the organic layer was washed with 5% $NaHCO_3$ solution (200 ml) and dried (anhydr. Na_2SO_4). Evaporation of the solvents, followed by distillation (bp 125° at 2.5 mm Hg) gave **67** as a colourless liquid.[72]

Yield: 267 g (84%).

nmr: τ 5.4-5.8 (q, 2H); 6.20 (s, 6H); 7.2-7.5 (t, 2H).

Dimethyl 2,4-dihydroxyglutarate (**71**)

A solution of the dibromoester **67** (265 g; 0.835 M) in MeOH (200 ml) and 5.0N NaOH (800 ml) was refluxed for 90 min. The cooled solution was then acidified with conc. HCl to pH 1, and stirred overnight at room temperature. After removal of the H_2O (*in vacuo*), the residue was extracted with hot acetone. The hot acetone solution was filtered, and evaporated, leaving a dark oil. This dark oil was dissolved in H_2O (800 ml) and washed with ether (5 x 100 ml) to remove the dark impurities. The resulting

Water solution was titrated with 5N NaOH (phenolphthalein indicator), then passed over an acid-form ion-exchange column (Dowex 50WX8; 500 g). The eluent was freeze-dried overnight, leaving crude dihydroxyglutaric acid (70). This crude acid was immediately dissolved in methanol (100 ml) and esterified with diazomethane (ca 5M). The solvents were removed in vacuo, giving an oily pale yellow residue (71), which was used in the next step without further purification.

2-Phenyl-4,6-biscarbomethoxy-1,3-dioxane (72)

The diester 71 (150 g; 0.78 M) was dissolved in benzaldehyde (350 ml) and cooled to 0°. $ZnCl_2$ (fused and powdered; 120 g) was added, and the resulting mixture was stirred 24 hr at room temperature. Ice-water (500 ml) was added, and the mixture was extracted with $CHCl_3$ (3 x 100 ml). The solvent and excess benzaldehyde were removed in vacuo. The residue was then dissolved in MeOH (400 ml) containing NaOMe (21.6 g; 0.4 M) and refluxed 60 min. The MeOH was then removed in vacuo, and the residue extracted with $CHCl_3$ (3 x 100 ml). The $CHCl_3$ solution was then filtered, and the solvents evaporated. The residue was recrystallized from MeOH to give the pure meso- dioxane diester (72). (mp 127-129°).

Yield: 158 g (73%).

See text for spectroscopic details of compound **72**.

meso-2-Phenyl-4,6-bis(hydroxymethyl)-1,3-dioxane (**73**)

A solution of the diester **72** (26 g; 92 mM) in THF (100 ml) was added dropwise to a suspension of $LiAlH_4$ (7.2 g; 190 mM) in THF (200 ml) at reflux. The mixture was refluxed 11 hr, then cooled to 0°. H_2O (20 ml) in THF (100 ml) was added slowly, followed by Celite (50 g). After filtering, the THF was evaporated *in vacuo* and the residue was a colourless oil, which was not further purified.

Yield: 20.6 g (100%).

ir: 3330 cm^{-1} (broad, s).

meso-2-Phenyl-4,6-bis(tosyloxymethyl)-1,3-dioxane (**64**)

p-Toluenesulfonyl chloride (52 g; 260 mM) was added to the diol **73** (24 g; 100 mM) in pyridine (100 ml) at 0°. This mixture was stirred at 0° for 10 hr, then poured into crushed ice (500 g). The white solid was filtered off, and washed with H_2O (100 ml), MeOH (100 ml), then hexane (100 ml). The solid was then dissolved in $CHCl_3$ (300 ml), and this solution was then washed with 1N HCl until the aqueous layer remained acidic. The $CHCl_3$ layer was then washed with H_2O (100 ml), brine (50 ml) and dried (anhydr. Na_2SO_4). Removal of the $CHCl_3$ and recrystallization from ethyl acetate gave colourless needles (mp 135-137°).

Yield: 45 g (84%).

nmr: τ 2.1-2.9 (m, 13H); 4.61 (s, 1H); 5.8-6.1 (m, 6H);
7.52 (s, 6H); 8.3-8.8 (m, 2H).

ir: 1600 cm^{-1} (s); 1350 (s); 1160 (s).

3,4-Benz-8,10-dihydroxycycloundeca-1,5-diyne-3-ene-O,O'-benzylidene (74)

Diethynylbenzene 47 (5.82 g; 46.2 mM) dissolved in dry dioxane (500 ml) was treated with a solution of n-butyllithium in hexane (92.4 mM). After stirring 30 min at room temperature, the ditosylate (64) (23.1 g; 46.2 mM) in dioxane (500 ml) was added. The mixture was refluxed for 110 hr. The resulting dark brown mixture was filtered, and bubbled with CO_2 while adding H_2O (10 ml). The solvents were removed in vacuo and the residue thoroughly extracted with $CHCl_3$ (5 x 25 ml). The $CHCl_3$ extracts were washed with H_2O (25 ml) and brine (25 ml) then dried (anhydr. Na_2SO_4) and evaporated. The dark brown residue was dissolved in a minimum amount of benzene and chromatographed on alumina (500 g; benzene eluent). The second band was crystalline, and recrystallization from $CHCl_3$/hexane gave the desired compound 74, as colourless crystals (mp

253-254°).

Yield: 740 mg (5.1%).

nmr: τ 2.4-3.0 (m, 9H); 4.50 (s, 1H); 5.4-5.9 (m, 2H); 6.9-7.6 (m, 6H).

3,4-Benz-8,10-dihydroxycycloundeca-1,5-diyne-3-ene (75)

The benzylidene derivative 74 (630 mg; 2.01 mM) was suspended in distilled dioxane (50 ml) and stirred at room temperature. *p*-Toluenesulfonic acid in H_2O (840 mg in 4.6 ml) was added all at once, and the mixture stirred vigorously for 24 hr. The resulting clear solution was treated with H_2O (35 ml) and then extracted with $CHCl_3$ (3 x 50 ml). The combined organic extracts were then washed with 5% Na_2CO_3 solution (25 ml), and dried (anhydr. Na_2SO_4). Removal of the solvents *in vacuo* gave a solid residue that was recrystallized from $CHCl_3$ to give the desired diol 75 as colourless crystals (mp 193-194°).

Yield: 407 mg (90%).

3,4-Benzcycloundeca-1,5-diyne-3-ene-8,10-diyl ditosylate (76)

The diol 75 (340 mg; 1.50 mM) was dissolved in dry pyridine (2.0 ml) and cooled to 0°. *p*-Toluenesulfonyl chloride (600 mg; 3.15 mM) was added all at once, and the resultant solution was stood at 0° for 18 hr. The solution was then poured onto crushed ice (50 g) and this mixture was stirred until the sticky precipitate had crystallized. The solid was then filtered off and washed with H_2O. Recrystallization from CH_2Cl_2/hexane gave colourless crystals of the ditosylate **76** (mp 176-177.5°).

Yield: 596 mg (77%).

nmr: τ 2.1-2.8 (m, 12H); 5.2-5.6 (m, 2H); 7.2-7.4 (d, 4H);
7.55 (m, 6H); 7.9-8.5 (m, 1H); 6.7-7.1 (m, 1H).

ir: 1600 cm^{-1} (m); 1350 (broad, s); 1150 (s); 1090 (s);
960 (s).

3,4-Benzcycloundeca-1,5-diyne-3,7,10-triene (**36**)

The ditosylate **76** (490 mg; 0.918 mM) was dissolved in dry THF (50 ml) and stirred at 0° under N_2 while KO*t*-Bu (285 mg; 2.55 mM) was added in 100 mg portions. A blue colour appeared, which faded in *ca* 1 min. After 10 min, the solution was quenched by pouring it into 1M NaH_2PO_4 solution (125 ml). This mixture was then extracted with CH_2Cl_2 (3 x 50 ml), and the combined organic extracts were washed with H_2O (25 ml) and brine (25 ml), then dried (anhydr. Na_2SO_4) and evaporated, leaving a solid residue. Sublimation at 50°, 0.02 mm Hg, followed by recrystallization from MeOH gave hydrocarbon **36** as colourless crystals (mp 78.5-79.5°).

Yield: 145 mg (83%).

nmr: See text for details.

ir: 2190 cm^{-1} (w); 1470, 1450, 1430 (m); 1100 (m); 945 (s); 895 (s).

uv: 252 nm (ε = 36,000); 256.5 (34,900); 264.5 (60,900).

mass spectrum: calc. for $C_{15}H_{10}$: m/e = 190.0771
meas. for $C_{15}H_{10}$: m/e = 190.0761
base peak: m/e = 95.

2-Isopropyloxymethylenecyclohexanone (86)

K_2CO_3 (207 g; 1.5 M) was suspended in dry acetone (1600 ml). To it was added 2-hydroxymethylenecyclohexanone (125 g; 1.0 M), followed by freshly distilled 2-iodopropane (212 g; 1.25 M). This mixture was refluxed for 72 hr, after which time the reaction mixture did not give a positive test with $FeCl_3$. The acetone and excess isopropyliodide were evaporated and H_2O (1.0 l.) was added to the residue. This mixture was extracted with ether (3 x 300 ml), and the combined ether extracts were washed with 5% NaOH (200 ml), H_2O (200 ml), brine (200 ml) and then dried (anhydr. Na_2SO_4). The ether was evaporated, and the residue was fractionally distilled. The fraction boiling at 72-77° at 0.05 mm Hg was collected to give compound 86 as a colourless liquid.[81]

Yield: 151 g (90%).

nmr: τ 2.55-2.7 (m, 1H); 5.4-6.1 (sept., 1H); 7.4-8.0 (m, 4H); 8.0-8.5 (m, 4H); 8.7 (d, 6H).

1-Ethynylcyclohexene-2-carboxaldehyde (87)

Lithium acetylide ethylenediamine complex (49 g; 0.533 M) was suspended in dry THF (350 ml) in a 3 litre flask. To this suspension, at 0°, was added dropwise compound 86 (60 g; 0.358 M) in THF (100 ml). This mixture was stirred 15 min at 0°, then 21 hr at room temperature. Ice (150 g) was added at 0°, and this mixture was stirred 30 min. H_2SO_4 (2.12N, 1360 ml; 1.44 M) was then added, and the mixture was then stirred vigorously for 1.5 hr. The resulting mixture was extracted with ether (3 x 200 ml) and the combined ether extracts were then washed with saturated $NaHCO_3$ solution (100 ml), brine (50 ml) and then dried (anhydr. Na_2SO_4) and evaporated, leaving a dark oil. This oil was sublimed at 50°, 1.0 mm Hg, onto a cold finger at 0°. The sublimed product was then recrystallized from hexane to give yellow prisms of the desired acetylenic aldehyde mp 47-49° (lit.[81] mp 49.5-50°).

Yield: 24.0 g (50%).

nmr: τ 8.37 (m, 4H); 7.68 (m, 4H); 6.85 (s, 1H); -0.02 (s, 1H).

ir: 3230 cm^{-1} (s); 2080 (w); 1672 (s).

1-Ethynyl-2-(β-chlorovinyl)cyclohexene (88)

Triphenylchloromethylphosphonium chloride (22.9 g; 66 mM) was suspended in dry THF (100 ml), and treated with *n*-butyllithium in hexane (64 mM) at -78°. This mixture was stirred 15 min at -78°, giving a red-orange mixture, which was then allowed to warm to room temperature. The resulting yellow-orange mixture was then stirred 15 min at room temperature, and then the aldehyde 87 (8.05 g; 60 mM) in THF (25 ml) was added dropwise. The resulting dark green suspension was then stirred overnight at room temperature. H_2O (12 ml) was then added, and the solvents were removed *in vacuo*. The dark semi-crystalline residue was then thoroughly extracted with pentane (6 x 75 ml), and the pentane extracts were dried (anhydr. Na_2SO_4) and evaporated. Distillation of the residue gave the chlorovinyl compound 88 as a pale yellow liquid (bp 46-48° at 0.05 mm Hg).[81]

Yield: 7.0 g (70%).

nmr: τ 8.38 (m, 4H); 7.76 (m), 7.38 (m); 6.74 (s, 1H);
3.25 (q, $J_{A,B}$ = 14); 3.55 (q; $J_{A,B}$ = 8).

ir: 3290 cm^{-1}(s); 2080 (w); 1572 (m).

1,2-Diethynylcyclohexene (82)

$NaNH_2$ was prepared in liquid NH_3 (700 ml) from

Na metal (8.55 g; 372 mM) using $Fe(NO_3)_3.6H_2O$ (150 mg) as a catalyst. To the grey suspension of $NaNH_2$ was added the chlorovinyl compound 88 (19.4 g; 116 mM) in dry ether (200 ml), with vigorous stirring. The red-brown mixture was then stirred 2 hr at NH_3 reflux, and then NH_4Cl (28 g; 520 mM) was added in portions, followed by more ether (450 ml). The NH_3 was evaporated and H_2O (150 ml) was added. The layers were separated, and the H_2O layer washed with ether (50 ml). The combined ether extracts were washed with H_2O (50 ml), brine (50 ml) and then dried (anhydr. Na_2SO_4). After evaporation of the solvents, the residual brown oil was distilled to give as a colourless oil, diethynylcyclohexene (82) (bp 27-28° at 0.1 mm Hg; lit[81] 52-53° at 18 mm). Yield: 9.50 g (63%).

nmr: τ 8.35 (m, 4H); 7.78 (m, 4H); 6.88 (s, 2H).

ir: 3360 cm^{-1} (s); 2130 (w); 1452 (m).

3,4-Tetramethylene-8,9-dihydroxycyclodeca-1,5-diyne-3-ene-O,O'-benzylidene (89)

Diethynylcyclohexene (12.6 g; 97 mM) was dissolved in dry dioxane (500 ml). To this solution was added n-butyllithium in hexane (194 mM) at room temperature. After stirring 1 hr at room temperature, a white precipitate had formed. To this suspension was added a solution of the ditosylate (50) (50.3 g; 97 mM) in dry dioxane (300 ml).

This mixture was refluxed for 90.5 hr. After cooling, CO_2 was bubbled into the mixture for 5 min, followed by the addition of H_2O (10 ml). The solvents were evaporated under reduced pressure, and the dark residue was then hydrolysed with 1M NaH_2PO_4 solution (200 ml). The resulting mixture was extracted with ether (4 x 200 ml). Any insoluble solids were then filtered off, and the combined ether extracts washed with brine (100 ml) and dried (anhydr. Na_2SO_4). Evaporation of the ether left a dark brown semi-crystalline residue which was chromatographed on alumina (600 g) giving as the second band, light brown crystals. Recrystallization from hexane/benzene (4:1) gave compound **89** as colourless crystals (mp 154.5-155.5°).

Yield: 2.95 g (10%).

nmr: τ 8.42 (m, 4H); 7.88 (m, 4H); 7.27 (m, 4H); 5.76 (m, 2H); 4.19 (s, 1H); 2.64 (m, 5H).

ir: 1383 cm^{-1} (m); 1074 (m).

mass spectrum: calc. for $C_{21}H_{20}O_2$: 304.1463
found for $C_{21}H_{20}O_2$: 304.1467.

3,4-Tetramethylene-8-hydroxycyclodeca-1,5-diyne-3-ene-9-yl benzoate (**90**)

The benzylidene derivative (**89**) (300 mg; 1 mM) was suspended in dry CH_3CN (7 ml), and to it was added trityl fluoroborate (420 mg; 1.25 mM) in CH_3CN (4 ml). The yellow suspension was stirred at room temperature for 9 hr, after which time, all of the precipitate had dissolved. This solution was hydrolysed with 1M NaH_2PO_4 solution (45 ml) and the resulting suspension was extracted with CH_2Cl_2 (3 x 25 ml). The combined organic layers were washed with brine (25 ml) and then dried (anhydr. Na_2SO_4) and evaporated, leaving a brown semi-crystalline mass. Chromatography on silicic acid (25 g) gave as a yellow solid a mixture of the hydroxybenzoate (90) and triphenylmethyl species, which was not usually further purified, but used directly in the subsequent step. On one run, the hydroxybenzoate was chromatographed four times on silicic acid to remove the impurities, which gave the hydroxybenzoate as colourless crystals (mp 145° dec.).

Yield: 288 mg (90%).

nmr: τ 8.38 (m, 4H); 7.86 (m, 4H); 7.26 (m, 4H); 5.78 (m, 1H); 4.68 (m, 1H); -1.80-2.83 (m, 5H).

ir: 3520 cm^{-1} (broad, m); 2195 (w); 1720 (s).

3,4-Tetramethylene-8,9-dihydroxycyclodeca-1,5-diyne-3-ene (91)

The mixture of the hydroxybenzoate 90 and the triphenylmethyl species (*ca* 650 mg) was dissolved in dry MeOH (20 ml) and dry benzene (5 ml). To this solution, at 0° was added NaOMe (32 mg). This solution was stirred at 0° for 75 min, then hydrolysed with 1M NaH_2PO_4 solution (150 ml). This mixture was then extracted with CH_2Cl_2 (3 x 30 ml), and the combined organic layers were washed with brine (50 ml) and then dried (anhydr. Na_2SO_4). Evaporation of the solvents left a light brown oil which was chromatographed on silicic acid (15 g) to give as the third band the diol **91**, as colourless crystals (mp 100°, dec.).

Yield: 80% overall from the benzilidene derivative **89**.

nmr: τ 8.38 (m, 4H); 7.88 (m, 4H); 7.46 (m, 4H); 6.13 (m, 4H).

ir: 3380 cm^{-1} (broad, m); 2198 (w).

3,4-Tetramethylenecyclodeca-1,5-diyne-3-ene-8,9-diyl dimesylate (**92**)

The diol **91** (216 mg; 1 mM) was dissolved in THF (6 ml). Methanesulfonyl chloride (345 mg; 3 mM) in THF (1 ml) was added, followed by the addition of triethylamine (335 mg; 3.3 mM) in THF (2 ml) at 0°. A white precipitate formed immediately. This mixture was stirred for 15 min at 0°, and then evaporated. The residue was dissolved in $CHCl_3$ (25 ml), washed briefly with brine (25 ml) and then dried (anhydr. Na_2SO_4) and evaporated, leaving a pale yellow glass. Chromatography on silicic acid (7 g) gave the dimesylate **92** as a colourless glass that rapidly turned green-brown in air.

Yield: 370 mg (100%).

nmr: τ 8.38 (m, 4H); 7.90 (m, 4H); 7.30 (m, 4H); 6.92 (s, 6H); 5.18 (m, 2H).

ir: 2190 cm^{-1} (w); 1340 (s); 1169 (s).

3,4-Benzcyclodeca-3-ene-1,5-diyne (**94**)

The dimesylate **92** (150 mg; 0.404 mM) was dissolved in THF (2.5 ml) and MeOH (1.3 ml) at 0°. NaOMe (49 mg; 0.910 mM) was added in MeOH (3 ml). This solution was stirred overnight at room temperature, resulting in a light brown solution containing a small amount of silky precipitate. The mixture was hydrolysed with 1M NaH_2PO_4 solution (50 ml), and this mixture was then extracted with pentane (5 x 25 ml). The combined pentane extracts were washed with brine (25 ml) and dried (anhydr. Na_2SO_4) and evaporated, leaving greenish crystals, which were a mixture of hydrocarbons **92** and **94**. This crude residue was dissolved in a minimum amount of MeOH. Cooling this solution to -78° crystallized out the tetrahydroanthracene (**93**). Evaporation of the mother liquors gave a pale yellow solid residue. Recrystallization from hexane at -30° gave **94** as colourless crystals (mp 73-74.5°) (<u>ca</u> 95% pure).

Yield: 22 mg (30%) of **94**; 18 mg (25%) of **93**.

See Chapter 3 for spectroscopic data of compound **94**.

Diethyl *o*-phenylenedipropionate

The diene diester **41** (20.7 g; 75.5 mM) was dissolved in THF (150 ml), and 5% Pd/C (1.40 g) was added. This mixture was shaken under H_2 pressure (40 psi) for 50 min, after which time no more H_2 was absorbed. The catalyst was filtered off, and the THF evaporated, leaving a yellow oil, which showed no trace of starting material in its nmr spectrum. This saturated ester was used without further purification in subsequent reactions.

Yield: 20.6 g (98%).

o-Phenylenedipropionic acid (**96**)

The diethyl ester (see above) (20.5 g; 74.0 mM) was dissolved in ethanol (200 ml). To this solution was added 2.1N KOH solution (98 ml), and the resulting yellow solution was refluxed 2.5 hr, then stirred overnight at room temperature. The solvents were removed *in vacuo* and H_2O (100 ml) was added to the residue. The H_2O solution was acidified with conc. HCl to pH 2, which produced a white precipitate. Recrystallization from hot H_2O gave colourless needles of the diacid **96** (mp 171.0-171.8°).

Yield: 13.2 g (80%).

nmr: τ 7.20 (m, 8H); 2.72 (s, 4H).

Dimethyl o-phenylenedibutyrate (97)

The diacid 96 (10.0 g; 45 mM) was suspended in benzene (200 ml), and to it was added oxalyl chloride (27 g; 210 mM), with stirring at room temperature. This mixture was stirred at 45° for 19 hr, at which point the solution was clear. Solvents were removed in vacuo and the residual diacid chloride was dissolved in benzene (200 ml) and then added dropwise, with stirring, to a solution of CH_2N_2 (270 mM) in ether at 0°. This solution was stirred 17 hr at 0°. Evaporation of the solvents left a yellow, semi-crystalline residue. This was dissolved in dry MeOH (300 ml) and to it, with stirring, was added dry $AgOCOC_6H_5$ (7.5 g) in triethylamine (50 ml), in portions, until no more N_2 evolution occurred. The resulting brown mixture was stirred 17 hr at room temperature. Activated charcoal (2 g) was then added to the mixture, and the mixture was then refluxed 30 min. After filtration and evaporation, the residual brown oil was dissolved in CH_2Cl_2 (50 ml) and washed with 5% HCl (25 ml), H_2O (25 ml), saturated $NaHCO_3$ (25 ml) and brine (25 ml), and then dried (anhydr. Na_2SO_4). Evaporation of the solvent left a dark brown oil. Distillation (bp 120° at 0.05 mm Hg) gave the diester 97 as a pale yellow oil.

Yield: 7.5 g (60%).

nmr: τ 6.9-7.7 (m, 12H); 6.34 (s, 6H); 2.86 (s, 4H).

mass spectrum: calc. mass for $C_{16}H_{22}O_4$: 278.1519

meas. m/e = 278.1518.

6,7-Benz-2-hydroxycyclodeca-6-ene-1-one (98)

Sodium metal (2.30 g; 100 mM) was suspended in refluxing xylene (160 ml). With vigorous stirring, a solution of the diester 97 (6.0 g; 21.6 mM) in xylene (60 ml) was added dropwise, at reflux. The resulting mixture was refluxed for 22 hr. Acetic acid (10 ml) in xylene (50 ml) was added dropwise to the cooled (0°) mixture, followed by H_2O (100 ml). The resulting mixture was stirred at 0° for 15 min, after which time the organic phase was a pale yellow colour. After filtering with glass wool, the organic layer was washed with brine (25 ml) and then evaporated, leaving a yellow, semi-crystalline mass. Sublimation (70° at 0.05 mm Hg) gave the acyloin 98 as colourless crystals (mp 93-94°).

Yield: 3.1 g (65%).

nmr: τ 2.6-3.0 (m, 4H); 5.7-6.0 (m, 1H); 6.1-6.4 (bs, 1H); 6.9-9.0 (m, 12H).

ir: 3520 cm^{-1} (broad, m); 1705 (s); 1100 (m).

5,6-Benzcyclodeca-5-ene-1-one (99)

The acyloin 98 (1.67 g; 7.65 mM) was dissolved in acetic anhydride (4 ml) and pyridine (6 ml) and this solution was then heated at 50° for 3 hr. Xylene (5 ml) was added, and the solvents were removed *in vacuo*. The residue was dissolved in CH_2Cl_2, and washed with H_2O (10 ml) and brine (10 ml), then dried (anhydr. Na_2SO_4) and evaporated, leaving a yellow syrup. Chromatography on silicic acid gave pale yellow crystals, which were sublimed (100° at 0.08 mm Hg) to give colourless crystals (mp 104-105°) of the 6,7-benzcyclodeca-6-ene-1-one-2-yl acetate (95% yield). (ir: 1725 cm^{-1} (s), 1745 (s))

Calcium (1.05 g; 26.2 mM) was freshly cleaned with emery cloth and then dissolved in a mixture of liquid NH_3 (120 ml) and dry THF (40 ml) at -78°. The keto-acetate (490 mg; 1.88 mM) was dissolved in THF (40 ml) and this solution was added dropwise to the dark blue Ca/NH_3 solution, with vigorous stirring. After 10 min at -78°, the mixture was poured onto crushed ice (300 g), and this mixture was then extracted with CH_2Cl_2 (3 x 25 ml). The combined organic phases were washed with 10% HCl (25 ml), saturated $NaHCO_3$ (25 ml) and brine (25 ml). After drying (anhydr. Na_2SO_4) the solvents were evaporated, leaving a pale yellow oil. Distillation (oil bath temperature 70°; 0.08 mm Hg) onto a cold finger (at 0°) gave **99** as a colourless oil.

Yield: 270 mg (71%).

ir: 1702 cm^{-1} (s).

Benzcyclodecene (**100**)

Powdered KOH (600 mg) was dissolved in ethylene glycol (6 ml) and this solution was bubbled with argon to remove oxygen. Hydrazine hydrate (85%; 0.6 ml) was then added, followed by the ketone **99** (240 mg; 1.19 mM). This solution was heated at reflux for 90 min, and then volatile components were allowed to slowly distil off until distillation ceased. The residual solution was then refluxed 19 hr, then poured into H_2O (50 ml); this mixture was extracted with CH_2Cl_2 (3 x 10 ml), and the combined organic layers were washed with H_2O (10 ml) and brine (10 ml), then dried (anhydr. Na_2SO_4) and evaporated. Distillation of the residue (oil bath 50°; 0.1 mm Hg) onto a cold finger (0°) gave the hydrocarbon **100** as a colourless oil.

Yield: 150 mg (67%).

ir: 3010 cm^{-1} (s); 2950 (m); 2870 (m).

Bicyclo[8.4.0]tetradecane (**101**)

The benzcyclodecene (86 mg; 0.458) was dissolved in acetic acid (3 ml) and PtO_2 (40 mg) was added; this mixture was stirred under H_2 (1 atm) for 22 hr. The mixture was filtered, and the filtrate was diluted with pentane (15 ml). The pentane solution was washed with H_2O

(3 x 5 ml), saturated $NaHCO_3$ (5 ml), and brine (5 ml). After drying (anhydr. Na_2SO_4), the pentane was evaporated, leaving a colourless oil. Glpc analysis of this oil on UC-W98, Reoplex, and Carbowax showed 2 peaks in the ratio 5:1 whose mass spectra (glpc-MS12) were virtually identical (P^+: m/e = 194). The peaks were assigned the *cis*- and *trans*-bicyclo[8.4.0]tetradecane structures for the small and large components, respectively. Hydrogenation of hydrocarbon **94** gave identical results.

3,4-Tetramethylene-8,10-dihydroxycycloundeca-1,5-diyne-3-ene-O,O'-benzylidene (103)

Diethynylcyclohexene **82** (1.00 g; 7.69 mM) was dissolved in dry dioxane (60 ml), and this solution was then treated with *n*-butyllithium in hexane (15.38 mM). After 1 hr at room temperature, a white precipitate had formed. To this mixture was added the ditosylate **64** (4.09 g; 7.69 mM) in THF (30 ml). This mixture was refluxed 94 hr. The reaction mixture was cooled to 25°, and CO_2 was bubbled in for 10 min, followed by the addition of H_2O (2 ml). The solvents were removed *in vacuo*, leaving a dark brown residue. This residue was triturated with 2M NaH_2PO_4 solution (25 ml), and this mixture was extracted with ether (4 x 50 ml). The combined ether extracts were washed with brine (25 ml) and dried (anhydr. Na_2SO_4). Evaporation of the solvents left a dark brown residue, which was chromatographed on alumina (200 g; benzene eluent) to give as the second band, the benzylidene derivative **103** as pale yellow crystals. Recrystallization from hexane/benzene (1:4) gave **103** as colourless needles (mp 215-217° dec.).

Yield: 110 mg (4.5%).

nmr: τ 8.0-9.0 (m, 4H); 7.6-8.0 (m, 4H); 7.0-7.5 (m, 6H); 5.8-6.3 (m, 2H); 4.6 (s, 1H); 2.5-3.0 (m, 5H).

3,4-Tetramethylene-8,10-dihydroxycycloundeca-1,5-diyne-3-ene (**104**)

The benzylidene derivative **103** (102 mg; 0.32 mM) was dissolved in $CHCl_3$ (4 ml) and MeOH (4 ml). To this solution, p-toluenesulfonic acid monohydrate (60 mg; 0.31 mM) in H_2O (0.5 ml) was added. The solution was stirred at 25° for 7 hr. The solvents were removed in vacuo and the residue was dissolved in $CHCl_3$ (30 ml) and washed with 5% $NaHCO_3$ solution (20 ml), H_2O (20 ml) and brine (20 ml); after drying (Na_2SO_4), the solvents were removed to give **104** as yellow crystals. Recrystallization from hot $CHCl_3$ gave the diol **104** as colourless needles (mp 184-185°).

Yield: 55 mg (75%).

Mass spectrum: Calc. for $C_{15}H_{18}O_2$: 230.1307; found 230.1311 nmr: τ 8.1-8.8 (m, 6H); 7.7-8.1 (m, 4H); 7.0-7.7 (m, 4H); 6.0-6.5 (m, 2H).

3,4-Tetramethylenecycloundeca-1,5-diyne-3-ene-8,10-diyl dimesylate (105)

Methanesulfonyl chloride (80 mg; 0.46 mM) in THF (0.5 ml) was added to a solution of the diol 104 (53 mg; 0.23 mM) in THF (2 ml) at 0°. To this solution was added triethylamine (70 mg; 0.69 mM) in THF (1 ml) at 0°. After 5 min, the colourless mixture was evaporated, and the residue was dissolved in $CHCl_3$ (10 ml) which was washed with H_2O (2 x 3 ml). After drying (anhydr. Na_2SO_4) and removal of the $CHCl_3$, a pale yellow glass remained, which was the desired dimesylate 105.

Yield: 177 mg (100%).

nmr: τ 8.2-8.6 (m, 4H); 7.6-8.0 (m, 6H); 6.8-7.2 (m, 4H); 6.9 (s, 6H); 4.9-5.4 (m, 2H).

3,4-Tetramethylenecycloundeca-1,5-diyne-3,7,10-triene (38)

To a solution of the dimesylate 105 (92 mg; 0.238 mM) in THF (3 ml) at 0° was added a solution of DBN (350 mg; 2.81 mM) in THF (0.5 ml). The solution was stirred 4 hr at room temperature, turning a deep orange colour. Ether (100 ml) was then added, and the resulting solution was washed with saturated boric acid solution until the aqueous phase was acidic. The organic phase was then washed with brine (25 ml) and dried (Na_2SO_4). Removal of the solvents gave a slightly yellow oil. Sublimation at 60°, 0.05 mm Hg gave hydrocarbon **38** as colourless crystals (mp 46-48°).

Yield: 32 mg (70%).

nmr: τ 8.0-8.5 (m, 4H); 7.0-7.7 (m, 6H); 3.7-4.3 (m, 4H).

mass spectrum: calc. mass for $C_{15}H_{14}$: 194.1096

Meas: m/e = 194.1090.

3-Isopropyloxymethylenenorbornan-2-one (**118**)

To a solution of 3-hydroxymethylenenorbornan-2-one (7.0 g; 51 mM) in dry acetone (120 ml) was added anhydr. K_2CO_3 (10.5 g; 75 mM) and 2-iodopropane (10.8 g; 64 mM). This mixture was refluxed 66 hr. After filtration, the solvents were removed *in vacuo*, and the residue was distilled to give the desired **118** as a colourless liquid (bp 68° at 0.05 mm Hg).

Yield: 7.85 g (84%).

nmr: τ 2.9 (s, 1H); 5.6-6.1 (sept., 1H); 6.7 (bs, 1H); 7.4 (bs, 1H); 8.0-8.6 (m, 6H); 8.7 (d, 6H).

ir: 1725 cm^{-1} (s); 1210 (m).

2-Ethynyl-2-hydroxy-3-isopropyloxymethylenenorbornane (119)

$NaNH_2$ was generated in liquid NH_3 (50 ml) from Na (460 mg; 20 mM). Dry acetylene was then bubbled into this mixture, at -78°, for 15 min. Compound 118 (2.76 g; 20 mM) in dry ether (3 ml) was added dropwise at -78°. The reaction mixture was stirred for 48 hr at -78° under an atmosphere of acetylene, after which time NH_4Cl (1.5 g; 28 mM) was added. The NH_3 was evaporated, and the residue was dissolved in H_2O (10 ml). This mixture was extracted with ether (3 x 30 ml), and the combined ethereal extracts were washed with brine (25 ml) and dried (anhydr. Na_2SO_4). After removing the solvents, the residue was recrystallized twice from pentane, to give the acetylenic alcohol 119 as a yellow solid (mp 40-41°). (*ca* 90% pure)
Yield: 2.12 g (51%).

2-Ethynylnorborn-2-ene-3-carboxaldehyde (120)

To a stirred solution of compound 119 (5.25 g; 25.4 mM) in THF (50 ml) was added 1.87N H_2SO_4 (59 ml). After stirring 2 hr, NaCl (5 g) was added. The resulting mixture was extracted with ether (3 x 100 ml) and the combined ethereal extracts were washed with H_2O (3 x 75 ml), and brine (2 x 35 ml), then dried (anhydr. Na_2SO_4). After evaporation of the solvents, the residue was chromatographed on silicic acid which gave the acetylenic aldehyde as an unstable, yellow semi-crystalline solid.

Yield: 4.0 g (75%).

nmr: τ 0.1 (s, 1H); 6.2 (s, 1H); 6.4-6.7 (m, 1H); 6.8-7.0 (m, 1H); 8.0-9.0 (m, 6H).

ir: 1725 cm^{-1} (s); 1640 (m).

2-Ethynyl-3-(β-chlorovinyl)norborn-2-ene (121)

Chloromethyltriphenylphosphonium chloride (16 g; 46 mM) was suspended in dry THF (75 ml) at -78°. *n*-Butyllithium in hexane (40 mM) was added at this temperature, and the resulting dark red mixture was stirred 45 min. The aldehyde 120 (5.0 g; 35 mM) in dry THF (20 ml) was added dropwise at -78°, and the resulting dark brown mixture stirred for 2 hr at this temperature. This mixture was warmed to room temperature and stirred for 3 hr. H_2O (30 ml), NaCl (5 g) and ether (30 ml) were then added, and the organic phase was separated and washed with brine (25 ml) and dried (anhydr. Na_2SO_4). After evaporation of the solvents, the dark semi-solid residue was extracted thoroughly with pentane (6 x 25 ml). After evaporation of the solvents, the residue was chromatographed on silicic acid/supercel (3:1; 75 g), pentane eluent, to give the vinylchloride 121 as a pale yellow oil.

Yield: 3.61 g (56%).

nmr: τ 3.1-4.1 (m, 2H); 4.1 (bs, <1H); 6.55 (d, 1H); 6.6 (bs, <1H); 7.0 (bs, 1H); 8.0-9.2 (m, 6H).

2,3-Diethynylnorborn-2-ene (115)

$NaNH_2$ was generated from Na (3.3 g; 143 mM) in liquid NH_3 (300 ml) using $Fe(NO_3)_3.6H_2O$ (50 mg) as catalyst. To this suspension was added the vinylchloride 121 (5.60 g; 31.3 mM) in dry THF (30 ml) at -78°. This mixture was stirred for 2.5 hr at -78°, after which the mixture was warmed to NH_3 reflux, and stood 2 hr. NH_4Cl (7.70 g; 144 mM) was added, and the NH_3 was evaporated. The residue was treated with ether (150 ml) and H_2O (30 ml). The ether layer was washed with brine (30 ml) and dried (anhydr. Na_2SO_4). Evaporation of the solvent left a dark oil which, after distillation at room temperature (0.05 mm Hg) gave the diethynylnorbornene as a colourless liquid.

Yield: 3.33 g (75%).

nmr: τ 6.45 (s, 2H); 6.8-7.0 (bs, 2H); 8.0-9.0 (m, 6H).

ir: 3300 cm^{-1} (s); 2100 (w).

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PART II

SOME ASPECTS OF
TRANSITION METAL-CATALYSED REARRANGEMENT OF BICYCLOBUTANES

"Those properties that are perceived by the senses are probably not the differences which distinguish one metallic species from another, but rather accidents or consequences, the essential specific differences being unknown."

Avicenna
De Mineralibus
circa 1020 AD

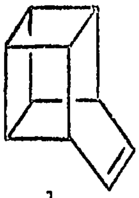
CHAPTER 1

THE TRANSITION METAL-CATALYSED REARRANGEMENT OF STRAINED SYSTEMS

Strained carbon frameworks have long fascinated organic chemists as probes to study the degree to which the normally tetrahedral carbon atom can be distorted. These molecules have made up an intriguing chapter of the science, from which has come ingenious solutions to both theoretical and synthetic problems. The strained systems have, in some instances, shown what first appeared to be anomalous properties, which have in turn been the key to closer understanding of the chemical bond and the laws that govern its existence and behaviour.

By this time, the concept of the conservation of orbital symmetry, as presented by Woodward and Hoffmann,[1a] has gained wide acceptance and utility. Strained systems have provided a unique means of testing the extent of orbital symmetry control by providing geometry in which otherwise improbable bond reorganization is more likely to occur.

One molecule which proved extremely interesting from this point of view was pentacyclo[$4.4.0.0^{2,5}.0^{3,8}.0^{4,7}$]dec-9-ene (basketene, 1), which was synthesized several years ago nearly simultaneously by two independent groups.[2,3] Later, this compound (1) was inter-related with other $(CH)_{10}$



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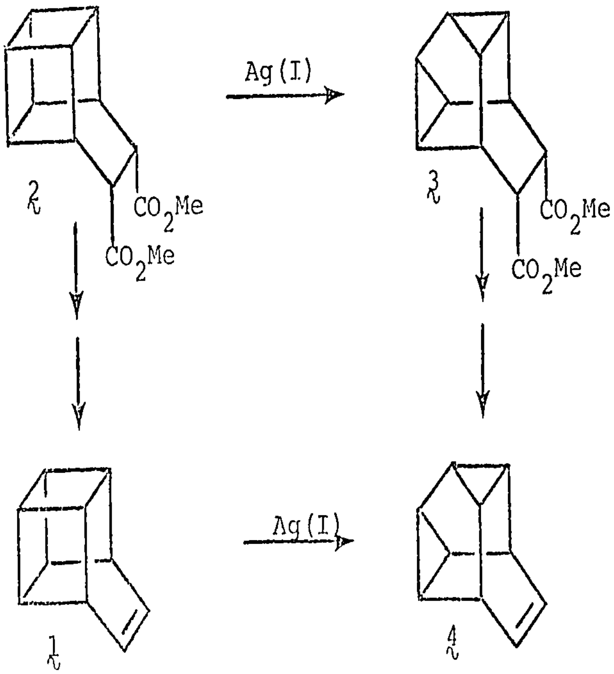
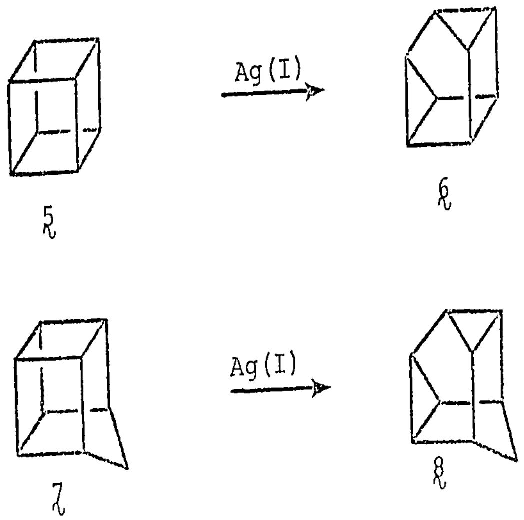
isomers, a group of molecules whose transformations elegantly demonstrated the power of the conservation of orbital symmetry.[4]

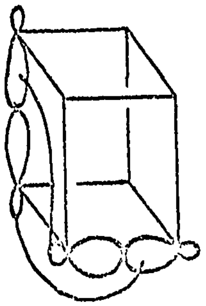
A third group[5] was also pursuing a study of the basketane ring system, along lines closely parallel to those followed by the other two groups. There were, however, large discrepancies in physical and spectral properties of some key intermediates obtained by the French and North American teams. Closer examination of the French



work revealed that the intermediate diester **2** had been purified by chromatography on a silicic acid column impregnated with silver nitrate. Under these conditions, rapid conversion of **2** into compound **3** occurred; subsequent hydrolysis and oxidative bisdecarboxylation gave rise to pentacyclo$[3.3.2.0^{2,4}.0^{3,7}.0^{6,8}]$dec-9-ene (**4**). It was soon shown that addition of catalytic amounts of silver fluoroborate to dilute solutions of **2** in chloroform rapidly converted **2** into **3** (<3 min).[5] Basketene (**1**) can also be converted into **4** under the same conditions, but at a slower rate.

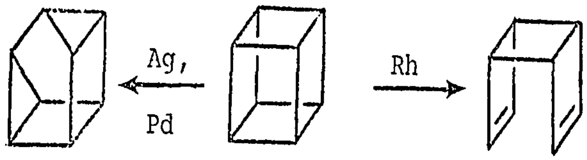
This rearrangement of the cubyl skeleton is now known to be a general reaction type. Cubane (**5**) rearranges to cuneane (**6**) and homocubane (**7**) to homocuneane (**8**).[6] If these rearrangements are concerted, then the overall transformation is a $[_{\sigma}2_{a}+{}_{\sigma}2_{a}]$ reaction, which is thermally forbidden.[1] In order to maintain the protons on the carbon





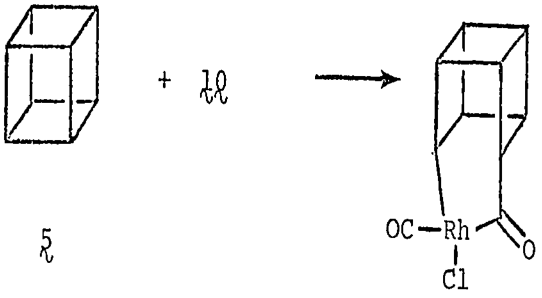
atoms on the outside of the molecular framework, then two of the carbons participating must undergo inversion of configuration. Several questions immediately arise: if the silver-catalysed reaction is concerted, how does the metal atom interact with the hydrocarbon framework in order to maintain orbital symmetry control? If the reaction is not concerted, then what is the mechanism of the rearrangement? Is silver the only transition metal to effect these changes, and if not, are there any differences with other metals, and what is the origin of such differences?

Answers to some of these questions were soon forthcoming. Both Rh(I) and Pd(II) rearrange cubane (**5**), but in a dramatically different manner. Pd(II), in this instance, behaved much like Ag(I), rearranging **5** to compound **6**. Treatment of **5** with Rh(I), however, produced syn-tricyclo[4.2.0.0^{2,5}]octa-3,7-diene (**9**).[7] Thus, not only do other transition metals catalyse rearrangements of the cubyl system, but they do not all act in the same manner. Studies on the Rh(I)-catalysed reaction indicated that



6 5 9

the mechanism was not concerted;[7] isolation of an intermediate has been reported.[8] Treatment of cubane (5) with $[Rh(CO)_2Cl]_2$ (10) gives, via an oxidative addition to a carbon-carbon bond, an acyl-rhodium adduct (11). Thus, at least the Rh(I)-catalysed rearrangement of cubane is



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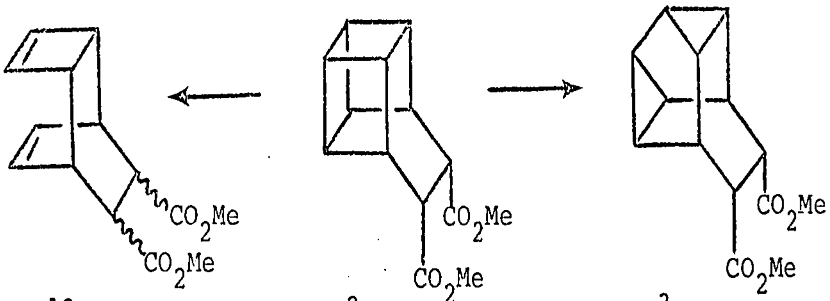
a multi-step process.

Dauben recently reported a study of the effects of the metal ligands on the course of the cubyl rearrangement.[9] With the basketane diester (2) as the organic substrate, various complexes of Rh(I) and Pd(II) were employed as catalysts. Either diester 3 or 12, or varying combinations of the two were the products, as expected. Transition metal complexes with ligands that were weak σ-donors

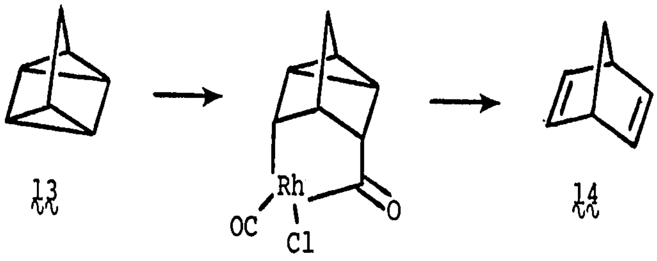


12 2 3

and π-acceptors, (e.g., $PdCl_2(C_6H_5CN)_2$), acted in the same manner as the uncomplexed metal ion, and gave rise exclusively to the dicyclopropyl derivative (3). This rearrangement was viewed as the transition metal interacting, edge-on, with a strained carbon-carbon σ-bond, the metal acting as a strong σ-acceptor, to yield an intermediate with an electron deficient centre (i.e., carbonium ion-like intermediate) which collapses to the product.

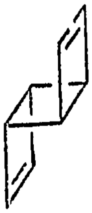
The production of the dienes (12) from Rh(I) complexes, (e.g., $Rh((C_6H_5P)_3Cl)$, and some Pd(II) complexes, (e.g., $PdI_2[(C_6H_5)_3As]_2$), is in agreement with the suggestion that the rearrangement proceeds *via* a bidentate interaction of the strained carbon system with the transition metal complex. This sort of interaction is equivalent to an oxidative addition of the metal to the strained organic substrate; there existed a good correlation between those ligands which enhance the oxidative addition of a transition metal, and those ligands on Pd(II) which favour the formation of the dienes (**12**). Dauben's study indicated systematically for the first time the manner in which the product distribution from a transition metal-catalysed rearrangement of a strained system is variant with the nature of the ligands on the metal.

The cubyl system is not the only strained carbon framework which undergoes rearrangement catalysed by transition metals. Another such molecule is quadricyclene (**13**),



13 **15** **14**

which is converted on treatment with Ag(I),[10] Pd(II),[11] and Rh(I)[12] to norbornadiene (**14**). In analogy with the Rh(I)-catalysed reaction of cubane (**5**), Halpern reported isolation of an acyl-rhodium intermediate (**15**) from the quadricyclene isomerization; thus this reaction also appears to proceed in a step-wise fashion. Caution should be exercised in this instance, however. In our laboratory, attempts at reproducing Halpern's results, as reported in the brief communication,[12] were completely unsuccessful. Following the reaction by nmr spectroscopy (in methylcyclohexane-d_{14}) did not give any evidence that an intermediate such as that reported was in fact involved. The source of this discrepancy may lie in differences in experimental detail; resolution of this problem awaits publication of full procedures.



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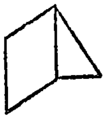

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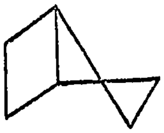

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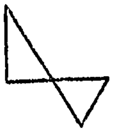

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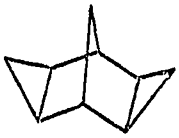


20

Strain is apparently not the only factor which determines whether or not a hydrocarbon will rearrange under the influence of transition metals. The *anti*-tricyclooctadiene (16) is stable to Ag(I), although the *syn*-isomer (9) is not.[13] The strained systems 17 and 18 and 19 are likewise inert;[14] nor does hydrocarbon 20 rearrange in the presence of Ag(I).[10] These results may be interpreted as the result of unfavourable steric interactions, or unsuitable geometry, although at this time, such proposals are speculative.

Many metals have been found to promote rearrangement of strained systems; Zn(II), Hg(II), Ir(I), Cu(I), Ru(I), Pt(II), and Sn(II) are some examples. The following discussion will, however, be limited to Ag(I), Rh(I) and Pd(II), because these metals have been used most frequently in studying the mechanisms of these rearrangements.

CHAPTER 2

THE REARRANGEMENT OF BICYCLO[1.1.0]BUTANES-- Ag(I) AND Rh(I)

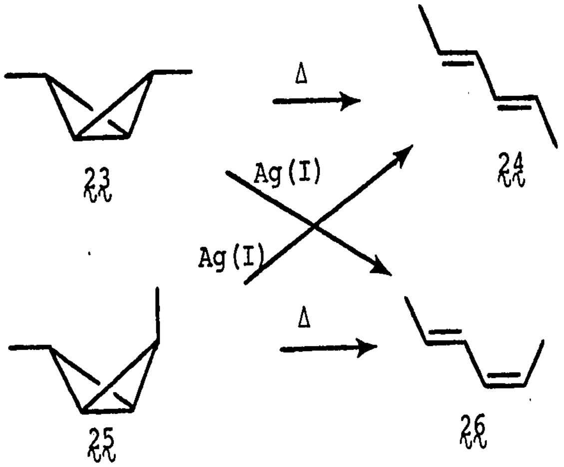
Bicyclo[1.1.0]butane (21) is a highly strained (63-68 kcal/mole)[15] hydrocarbon. In spite of this high strain energy, thermal isomerization of bicyclobutanes to butadienes (e.g., 21→22) requires a high activation energy (41-43 kcal/mole).[16] If such isomerizations are concerted, they must involve a $[{}_{\sigma}2_{s} + {}_{\sigma}2_{a}]$ process, which is thermally allowed.[1]

21

22

The bicyclobutane skeleton is particularly amenable for the study of these types of processes because it can be specifically labelled, with, for instance, methyl groups or deuterium, so that the stereochemical course of a reaction can be deduced from the product structure.

Evidence that the thermal isomerization of bicyclobutanes to butadienes is concerted was provided by Closs and Pfeffer in 1968.[17] *exo*,*exo*-2,4-Dimethylbicyclo[1.1.0]-butane (23) on thermolysis yields predominantly the *cis*, *trans*-hexa-2,4-diene (24); the *endo*,*exo*-isomer (25) gives mostly the *trans*,*trans*-hexa-2,4-diene (**26**). These results are in accord with the operation of a [$_{\sigma}2_{s} + {}_{\sigma}2_{a}$] concerted mechanism.[1]



Catalytic amounts of transition metals such as Ag(I), Rh(I) and Pd(II) also, in general, convert bicyclobutanes to butadienes. Before 1971, a few scattered examples of these reactions were known, and all could be formulated as [$2_{s} + 2_{s}$] or [$2_{a} + 2_{a}$] type reactions, as was the case in the cubyl rearrangements (see above). The proposal was therefore made that these rearrangements of bicyclobutanes were concerted. However, the organic substrates studied were so constituted that only one mode of reaction was possible to explain the observed geometry of the product and alternate stereochemical pathways were structurally prohibited.

As in the thermal isomerization, compounds **23** and **25** allowed a probe of the stereochemical consequences of

Ag(I)-catalysed rearrangements of bicyclobutanes, by providing more than one possible reaction pathway.[18] Treatment of **23** with catalytic amounts of $AgClO_4$ in benzene, at room temperature or 5°, gives predominantly the hexadiene **26**, and under the same conditions, **25** gives **24**[18] (see above diagram). The Ag(I)-promoted isomerizations are not completely stereospecific (see Table I), but it appears as though the stereochemistry of the bicyclobutane-Ag(I) reaction may be governed at some stage by the orbital symmetry of the whole system undergoing skeletal rearrangement.

Table I

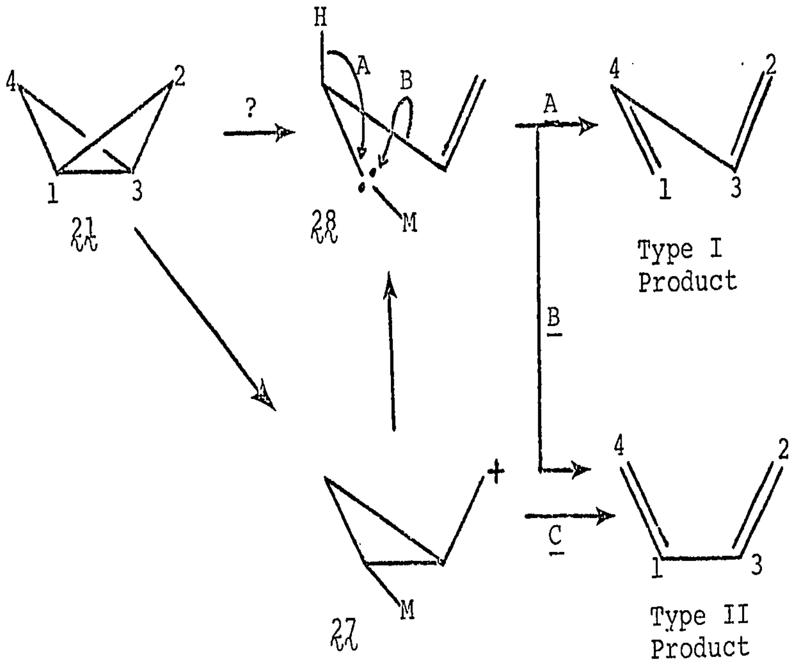
% Yield

Product Distribution of Ag(I)-Catalysed

Reaction of 2,4-Dimethylbicyclobutanes

Compound	**24**	**26**	Total Yield
23	22	78	89
25	95	5	99

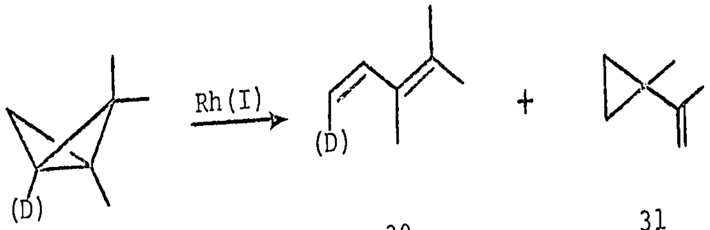
These changes (**23**→**26** and **25**→**24**) represent $[_{\sigma}2_{s} + {}_{\sigma}2_{s}]$ (or possibly for **25**, $[_{\sigma}2_{a} + {}_{\sigma}2_{a}]$) reactions, in the orbital symmetry sense. However, rapid accumulation of data concerning the structural relationship between starting materials and products soon demonstrated that the mechanism is not concerted, but in fact proceeds in a step-wise manner. Three possibilities are presented for the mechanism of the metal-catalysed rearrangement of bicyclobutanes.[19]



In the conversion of bicyclobutanes into butadienes, two bonds of the starting material must be broken. Cleavage of the C-1,2 bond (to give a species like **27**) followed by C-1,3 bond breakage, gives rise to a (formal) carbene-metal complex (**28**). Two modes of decomposition are open to such an intermediate. Hydrogen migration to the carbenoid centre (*mechanism A*), followed by loss of the metal atom, produces a butadiene (**22**) of a sort that will be called the *Type I Product*. An analogous *vinyl* migration (*mechanism* *B*) leads to a butadiene which will be called the *Type* *II* *Product*. (See diagram above.) As will be seen below, specific labelling allows distinction between these two types of products.

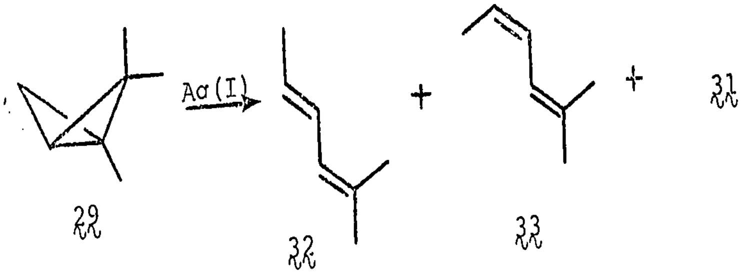
Alternately, cleavage of the C-3,4 bond in **27**, with concomitant loss of the metal (*mechanism* *C*) also leads to the *Type* *II* *Product*. It is important at this point to emphasize that a Type II product is the result of *either* mechanism *B* or mechanism *C*. The Type I product can only arise from mechanism *A*.

Since the recognition that the metal-catalysed rearrangement of bicyclobutanes is probably a step-wise process, a considerable number of specifically labelled bicyclobutanes have been prepared, in attempts to elucidate the mechanism of this reaction. One particularly interesting example was published by Gassman.[20] Reaction of the trimethylbicyclobutane **29** with catalytic amounts of $[Rh(CO)_2Cl]_2$ gives the diene **30** and the cyclopropyl compound **31** as products. Compound **31** is a strong



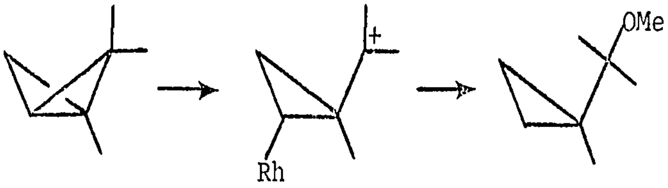
29 **30** **31**

indication of a step-wise mechanism, through an intermediate like 27. Diene 30 is either a Type I or a Type II product. However, deuterium labelling at C-3 of 29, as shown above, established that 30 must be a Type I product, and is therefore formed by mechanism A (hydrogen migration to a carbenoid centre). Later, Paquette studied bicyclobutane 29 on treatment with Ag(I).[14] The products



are the dienes 32 and 33, and compound 31 (71:19:8). Again the presence of 31 suggested a step-wise mechanism. Both dienes 32 and 33 are Type I products, and therefore arise via mechanism A.

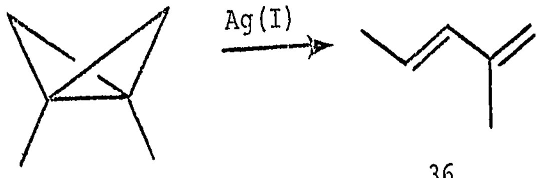
Gassman has performed a further series of experiments concerning compound 29.[20] In MeOH, with $[Rh(CO)_2Cl]_2$ (10) as catalyst, 29 gives the methyl ether 34 (see reference 29 for a refutation of this type of experiment), which supports the fact that a carbonium ion intermediate is involved and is trapped by the solvent. This result is subject to the proviso that the production of 34 by acid-catalysed reaction must be excluded. In our laboratories,



29 34

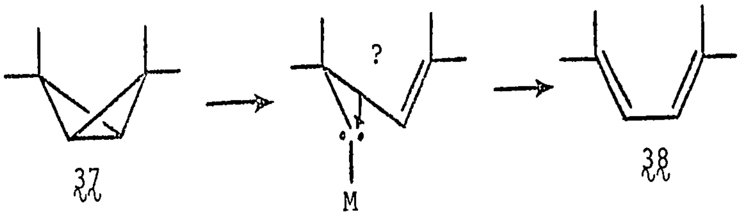
a trace of p-toluenesulfonic acid in MeOH converts 29 into 34 quantitatively within 2 min at room temperature. Dicarbonylrhodium acetoacetonate [Rh(CO)$_2$acac] in CHCl$_3$ converts 29 into 30 and 31; in MeOH, in the presence of base (BaCO$_3$), mostly 34 is produced, but at a rate only 5 times faster than the reaction of 29 with MeOH alone. Gassman claims that these results prove that Rh(I) produces a carbonium ion intermediate like 27. However, both the instability of these Rh(I) complexes in MeOH,[29] and the fact that the metal-catalysed reaction is not exceptionally faster than that not involving the metal, mitigate against any definitive claims of mechanistic proof.

The dimethylbicyclobutane 35, on treatment with Ag(I), gives rise exclusively to the diene 36, which is again a Type I product.[14,19] Again a carbene-metal complex appears to be an intermediate in this reaction; it would decompose via a hydrogen shift to the diene 36.



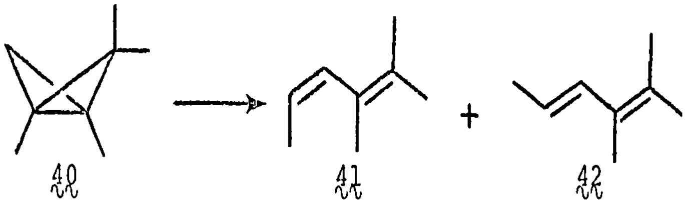
35 36

The tetramethylbicyclobutane 37 is particularly interesting, because if a carbene-metal intermediate (39) is involved, no hydrogen migration is possible. Treatment of 37 with Ag(I) or Rh(I) gives diene 38, which is a Type II product, and therefore may arise from either mechanism B or C. However, both Paquette and Gassman chose to invoke mechanism B.[21,22] Such a mechanism demands a vinyl migration to the carbenoid centre.



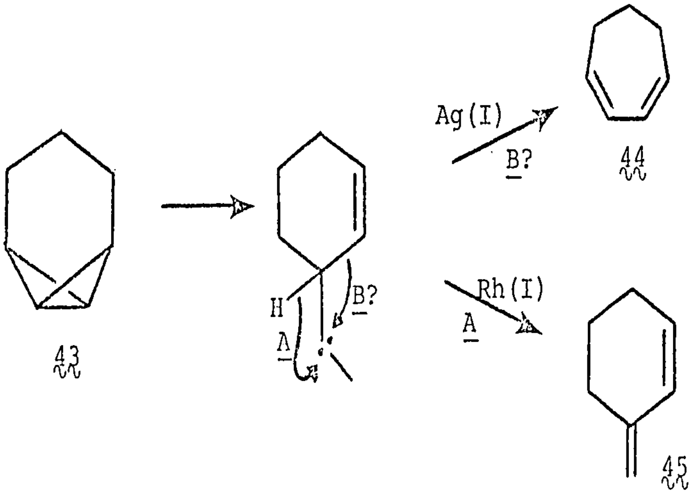
37 38 39

Compound 40 is another tetramethylbicyclobutane isomer. Again the effect of varying alkyl substitution on the strained system is evident in the rearrangement of this molecule. Thus 40, on treatment with $[Rh(CO)_2Cl]_2$ gives 41 and 42 in about equal amounts. Both these dienes



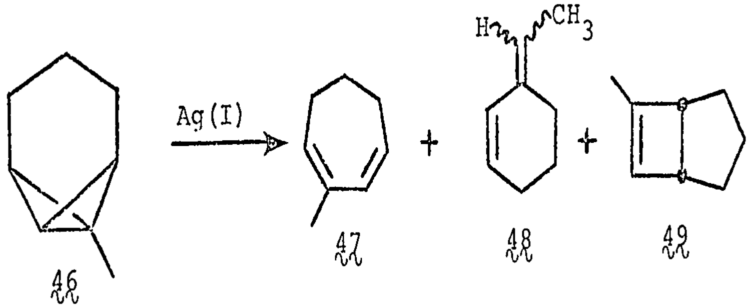
are Type I products, and their formation has been interpreted in terms of a carbene-metal complex intermediate,[22] and mechanism *A*.

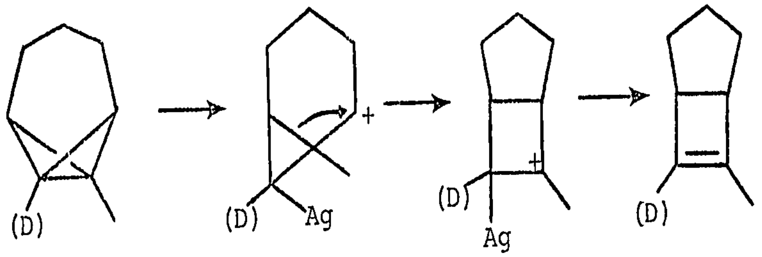
Tricyclo[4.1.0.$0^{2,7}$]heptane (43), on treatment with catalytic amounts of Ag(I) gives 1,3-cycloheptatriene (44), which is a Type II product. Once again, Paquette has chosen to interpret this result in terms of mechanism *B*, in which a vinyl migration, *instead of a possible hydrogen migration*, is responsible for the product formation.[14] Reaction of 43 with [Rh(CO)$_2$Cl]$_2$ gives an entirely different product, the methylenecyclohexene 45, which is a Type I product, and is therefore formed by migration of hydrogen to a carbenoid centre (mechanism *A*).



Hydrocarbon 43 provides a particularly clear-cut example of how different metals provide different results in this type of catalytic action.

Methyl substitution on 43 again results in some changes in the course of the reaction.[14,21] Thus, treatment of the 1-methyl-derivative (46) with Ag(I) produces dienes 47 (Type II product) and 48 (Type I product) and the bicyclic compound 49. Again these results were interpreted as arising solely from mechanism A (for 48) and mechanism B (for 47); the formation of 49 was described as the result of "deep-seated skeletal rearrangement" of the intermediate carbene-metal complex.[21] However, if the initial step in the reaction is breakage of a side-bicyclobutane bond (to form 50), then it is easy to see that formation of 49 could arise simply from bond reorganization to give a tertiary carbonium ion (51) which then collapses directly to 49.[22,23] If the first step in this sequence is rate determining, then the reported $k_H/k_D = 1.74$ may be explained by this mechanism, and there would be no demand to invoke the rather complex proposal

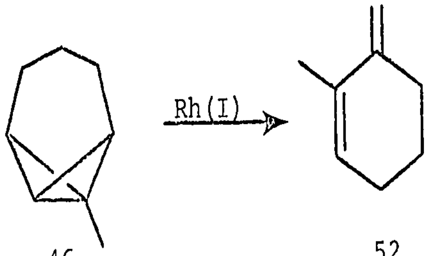




46 50 51 49

offered.[21b] No reason was given for excluding such a carbonium ion mechanism; nor was explained the rejection of mechanism C as a possibility to explain the formation of 47.

Rh(I) rearranges 46 into the diene 52,[22,23] which is again a Type I product; the reaction was interpreted as



46 52

an example of mechanism A by Gassman. Again, the different catalytic actions of Rh(I) and Ag(I) are obvious in this case.

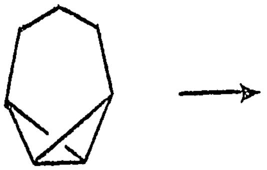
The foregoing instances of transition metal-catalysed rearrangement of bicyclobutanes are not exhaustive, but are intended to be exemplary. Several pertinent facts have arisen, which must be considered in discussing proposals for mechanisms of these reactions:

1) There are significant differences in the actions of different metals. Thus, if a rigorous proof of the action of one metal is forthcoming, it cannot be generalized to other metals. Indeed, it has been shown[9] that changes in the ligands on one metal can significantly alter its catalytic action, so that discussion of the reactions of one metal must include a consideration of its ligands.

2) It has been shown that variation in the substitution pattern of the bicyclobutanes has a profound effect on the course of the reaction. Therefore discussing the isomerization of one or two bicyclobutanes to provide a general mechanism explaining all such isomerizations is, at best, a risky means of proceeding.

3) In most of the cases of Type II product formation, both mechanisms B and C can explain the products that are formed. In few instances is it possible to rigorously distinguish between the two alternate routes, nor is it possible to say that only one, rather than both, mechanisms are operating in any particular instance. To say that a product is a Type II product is merely a formalism. Thus it is curious that at least one author[14] has specifically proposed mechanism B (involving a carbene-metal complex as an intermediate) for nearly all Ag(I)--catalysed rearrangements of bicyclobutanes, to give Type II products.

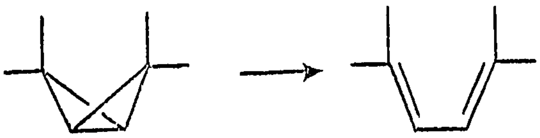
Two papers concerning the Ag(I)-catalysed reaction appeared recently[19] which at least cast doubt upon the interpretation of these reactions as involving mechanism B. As discussed previously, Ag(I) catalyses the following rearrangements.



43 **44**

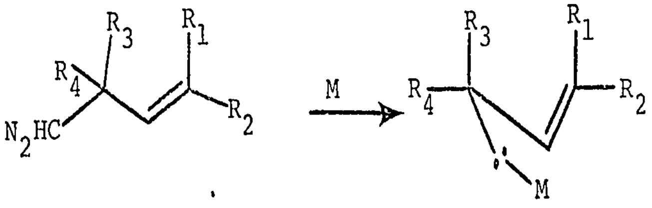
23 **26**

25 **24**



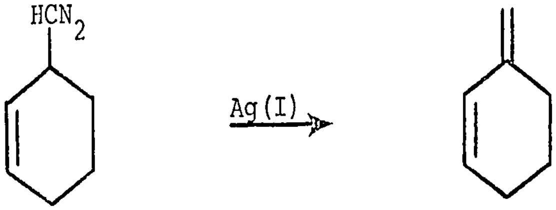
37 **38**

Recent studies have indicated that reactions of diazoalkanes with transition metals (including Ag(I)) lead to the formation of complexes consisting of the metal and the carbene species formally derived from the diazoalkane.[24] Therefore, reaction of a diazoalkene of general structure

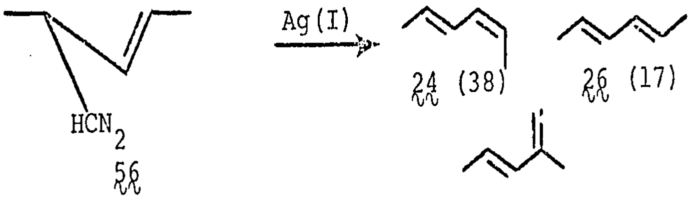


53 54

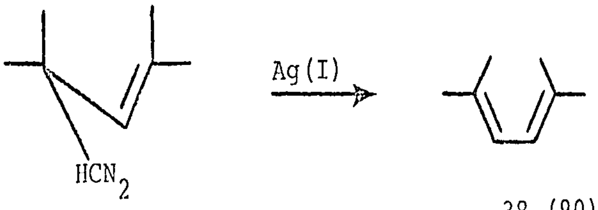
53 with Ag(I) will provide useful information as to whether carbene-metal intermediates are involved in the Ag(I)-catalysed rearrangements of bicyclobutanes to give Type II products. The following reactions were carried out.



55 45 (95%)



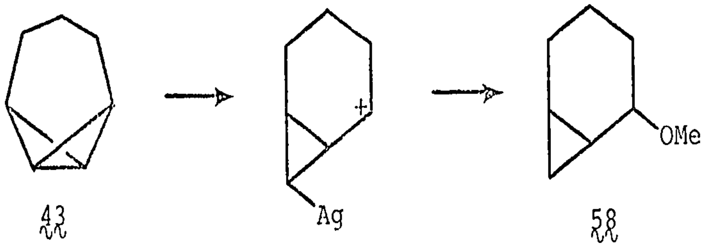
56 24 (38) 26 (17) 36 (45)



57 38 (90)

Thus, *if* the proposal by Kirmse[24a] for the mechanism of diazoalkane-metal reactions is applicable to the present case, then the intermediacy of the carbene-metal complex is excluded in one case (**43**→**44**) and is not mainly responsible for product formation in at least two others (**23**→**26** and **25**→**24**). A mechanistic alternative is necessary for these cases.

Treatment of **43** with Ag(I) in methanol gives a nearly quantitative yield of the methoxynorcarane (**58**) as a mixture of isomers. (Care was taken to eliminate the possibility that this reaction is the result of acid catalysis). This result strongly indicates that the

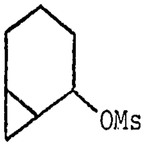
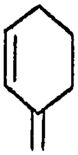
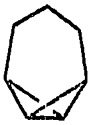
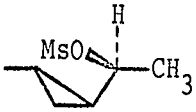
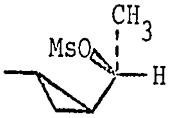
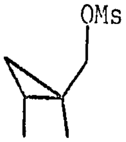
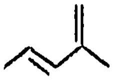


43 **59** **58**

initial intermediate in the Ag(I)-bicyclobutane reaction in an aprotic solvent such as benzene would possess the structure shown as **59** (resulting from the initial cleavage

TABLE II

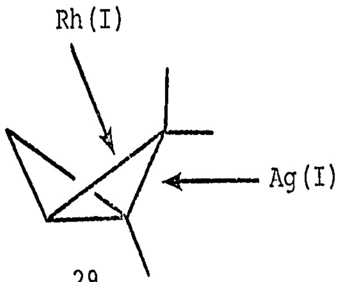
Comparison of cyclopropylcarbinyl and Ag(I)-catalysed rearrangements

Compound	Reagent	Products (%)		
 63	pyr; DBN	 44 (95)	 45 (0)	
 43	Ag(I)	44 (97)	45 (0)	
 64a	pyr; DBN	 26 (75)	 24 (20)	 36 (0)
 43	Ag(I)	26 (78)	24 (22)	36 (0)
 64b	pyr; DBN	26 (8)	24 (86)	36 (0)
 25	Ag(I)	26 (5)	24 (95)	36 (0)
 65	DBN	 36 (95)		
 35	Ag(I)	36 (95)		

The similarities between the Ag(I)-bicyclobutane and cyclopropylcarbinyl mesylate reactions are striking. It is therefore reasonable to propose that bond cleavage in **60** proceeds in such a fashion as to produce the more substituted carbonium ion, which in turn ejects Ag(I) (or H^+) to complete the reaction.

It is now apparent that there is insufficient evidence to invoke the intermediacy of an Ag(I)-carbene complex in the catalytic rearrangement of some bicyclobutanes. All the experimental evidence so far presented tends to suggest that the initial one-bond cleavage intermediate **60** is the dividing point leading to various types of products for the bicyclobutanes thus far examined.[19] However, in the absence of detailed knowledge concerning C-Ag and C:-Ag bonds, additional work is required before the exact mechanism of the Ag(I)-catalysed reaction can be defined.

Some trends are evident at this point. In the case of an unsymmetrically substituted bicyclobutane, Ag(I) generally attacks at the most substituted bicyclobutane bond, whereas Rh(I) (and Pd(II), for which see Chapter 3) attacks the least substituted side. An example of this is the trimethylbicyclobutane **29**.



29

Rh(I) (and Pd(II)) generally prefers a mechanism (A or B) involving a carbene-metal intermediate. Ag(I)-catalysed reactions, however, may involve each of the three possible mechanisms (A, B, or C). Which pathway is preferred (through intermediates like 61 and 62) appears to depend very much on the substitution pattern at the C-1 and C-3 positions.

Pd(II)-catalysed rearrangements of bicyclobutanes differ in many instances from both the Ag(I) and Rh(I) reactions. Some of these differences, and the first detailed description of a Pd(II)-catalysed reaction, with confirming experimental data, are presented in Chapter 3.

CHAPTER 3

THE REARRANGEMENT OF BICYCLO[1.1.0]BUTANES--Pd(II)

As mentioned previously, Pd(II) catalyses the isomerization of bicyclobutanes to butadienes. The catalyst most commonly employed is palladium(II) chloride-benzonitrile [($PdCl_2(C_6H_5CN)_2$; **66**)]. This compound offers several advantages over other Pd(II) complexes:

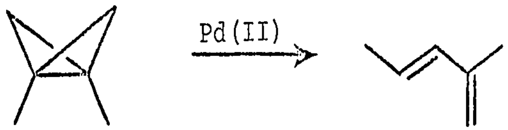
1) the preparation of **66** is straightforward[25] ($PdCl_2$ in benzonitrile at 100° for 0.5 hr);

2) **66** is a stable crystalline compound;

3) it is soluble in most organic solvents;

4) it is a convenient starting material for making other Pd(II) complexes, because of the lability of the nitrile ligands.[26]

Treatment of 1,3-dimethylbicyclobutane (**35**) with **66** gives the diene **36**, as does Ag(I)-catalysis. However, treatment of the isomeric dimethylbicyclobutanes **23** and **25** with Pd(II) gives different results from that with Ag(I), as summarized in Table III.[27]



35 **36**

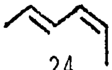
TABLE III

Comparison of Ag(I) and Pd(II) catalysis

Bicyclobutane	Metal	Products (%)		
		24	26	36
23	Pd(II)	16	37	47
23	Ag(I)	22	78	0
25	Pd(II)	24	51	24
25	Ag(I)	95	3	0

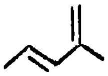
23

25



24

26



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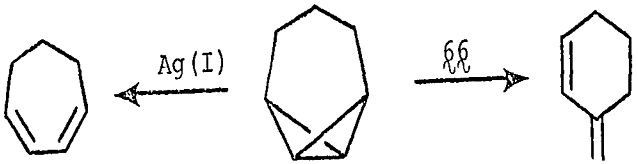
Compounds 24 and 26 are interconverted by Pd(II), and therefore the values in the table represent equilibrium mixtures.

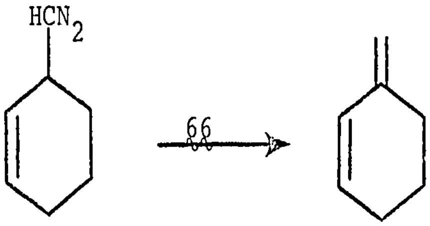
As mentioned previously, the Ag(I)-catalysed reaction is stereoselective. The Pd(II) reaction clearly is not; the types and distribution of the products are dissimilar from those obtained by a cyclopropylcarbinyl carbonium ion type of reaction. These results then clearly indicate mechanistic differences between the two metals.

The Pd(II) complex (66) also catalyses the rearrangement of 43 into 45, and not 44.



44 43 45

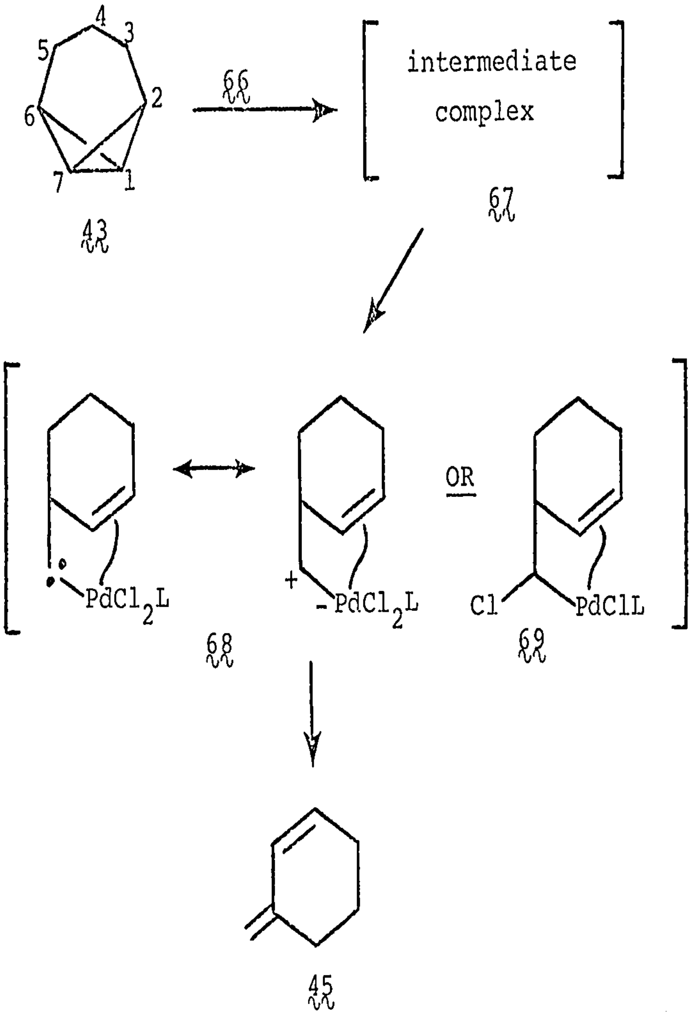
The treatment of diazo compound 54 with $PdCl_2(C_6H_5CN)_2$ gives exclusively the diene 45. These data were consis-



54 45

tent with a palladium-carbene complex being involved in *some* rearrangements of bicyclobutanes. A mechanistic scheme can be constructed, as follows (for the tricycloheptane 43).[27]

The initial intermediate or complex (67), of as yet unspecified structure, is not necessary, but is included for generality. The second intermediate is the proposed Pd-carbene complex (68), or the complex (69) resulting from Cl^- transfer to the carbenoid centre. Both 68 and 69 result from a cleavage of the C-1,7 and C-2,7 bicyclobutane bonds in 43. Hydrogen migration and expulsion of the metal from 68 then results in the forma-



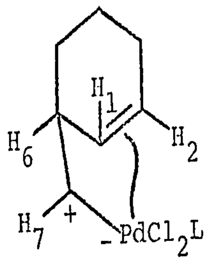
tion of the diene 45.

Such a proposal lacked rigorous definition. If intermediates in the reaction could be detected spectrometrically, then little doubt would remain as to the mechanism of the rearrangement. Up to this point, all of these isomerizations of bicyclobutanes involved the use of catalytic amounts (up to *ca* 10 mole %) of the transition metals.

Obviously the best conditions for detecting intermediates in these reactions would involve *ca* 1:1 mole ratios of metal and organic substrate. Just as obvious is the necessity of working at low temperatures in order to slow the reaction sufficiently to allow characterization of any intermediates.

With these factors in mind, we proceeded to examine the reaction of **43** with $PdCl_2(C_6H_5CN)_2$ (**66**) in methylene chloride-d_2 by means of low temperature nmr spectroscopy (100 MHz).[28] Thus, **45** dissolved in CD_2Cl_2 was added slowly with vigorous mixing to a solution of 1.2 mole equivalent of **66** in CD_2Cl_2 at -50°. In the nmr spectrum of the resulting canary yellow solution, no signals due to starting material (**43**) were present after 15 min at -50°. There appeared new signals indicating the formation of a new complex or complexes (**67**) at τ 5.39 and 5.72 (m, total integration 1H) and τ 6.8-8.6 (complex m, total integration 9H). These signals remained unchanged for at least one hr at -50°, but on warming to -30°, gradually disappeared to give an orange solution, exhibiting a new set of signals for a new complex (**68**): τ 4.42 (broad d, 1H; J = 6.5); τ 4.73 (m, 1H); τ 6.21 (s, 1H) and τ 7.7-8.5 (m, 7H).

This spectrum is consistent with a structure for **68** as the carbene-metal intermediate. The first two sig-



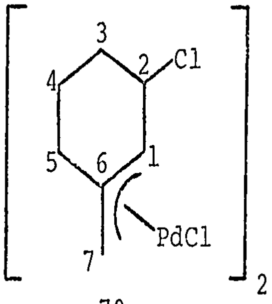
68

nals (τ 4.42 and 4.73) are assigned to H_1 and H_2. The third signal, a sharp singlet at τ 6.21 is assigned to H_7. This proton is attached to a formal carbene-metal centre and the chemical shift is lacking in appropriate precedence, but the assignment is at least reasonable. 69 also satisfies the spectral data, and cannot be excluded at this time.

The structure of 68 implies that the double bond is also coordinated to the metal. Models of 68[29] indicate that it is less strained than norbornadienylpalladium complexes, and also show that the hydrogen at C-7 is orthogonal to that at C-6, which accounts for the singlet at τ 6.21. This data represents the first detection of a carbene-metal intermediate (68) in the transition metal catalysed rearrangements of strained systems, and thus constitutes an important key to understanding these reactions.

At almost the same time as our work was reported, Dauben and Kielbania also published data on 68, apparently scanning the nmr spectrum very rapidly immediately after 43 and 66 are mixed in $CDCl_3$ at room temperature;[29] both reports were essentially identical in the interpretation of the spectral data.

Further warming of solutions of 68 to 0° for 2 hr or 30° for 20 min, effected another transformation of 68, as expected, giving a red-orange solution of a new complex (70) which exhibited absorptions in the nmr spectrum at τ 5.61 (broad s, 1H); τ 5.88 (broad s, 1H); τ 6.21 (broad s, 1H); τ 7.14 (broad s, 1H); τ 7.36 (m, 2H); and τ 7.6-8.5 (m, 4H). A 1:1 mixture of the diene 45 and $PdCl_2(C_6H_5CN)_2$ (66) in CD_2Cl_2 reproduced this spectrum. Dauben isolated this last complex (70)[29] (mp 60-65°) and agreed with our assignment of the structure of 70 as the π-allyl complex.



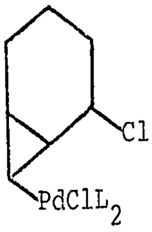
70

The dimeric nature of 70 is a possibility suggested by analogy to the known structures of other π-allyl

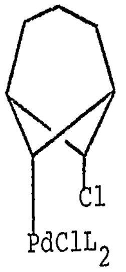
Pd(II) complexes.[26]

Addition of diene 45 to 66 at -50° gave an nmr spectrum totally unlike that of complex 67. Warming this solution did not give 68. At -30°, the mixture of 45 and 66 slowly forms the π-allyl complex 70. The adduct of diene 45 and complex 66 at -50° may be that in which one double bond of 45 is coordinated to the metal,[30] but this has not been rigorously defined.

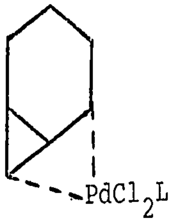
We propose that the initial Pd-hydrocarbon adduct (67) (which Dauben did not detect)[29] is a mixture of complexes 67 and 67', which result from "Pd-Cl addition" across the C-2,7 and C-1,7 bonds of 43, respectively.



67



67'



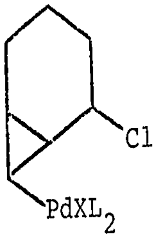
71

These structures are analogous, for instance, to that of the dihydrobullvalene-$PdCl_2(C_6H_5CN)_2$ adduct isolated by Vedejs.[31] Structures such as 71[8] cannot at this time be rigorously excluded, but spectral data, and MeOH quenching experiments (see below) make them less likely than those proposed.

The quenching experiments were performed as follows. If solutions of **43** with **66** in CH_2Cl_2 are treated (at -50°) in the presence of K_2CO_3 with MeOH, the only product detectable is diene **45**. Complexes **68** (at -30°) and **70** (at room temperature) also give only the diene **45** on reaction with MeOH. Reaction of **43** with **66** in MeOH at room temperature in the presence of K_2CO_3 also only gives diene **45**. All these results indicate that a cyclopropylcarbinyl cation species, if involved in this reaction, cannot be trapped, which is completely unlike the analogous reaction (**43**→**44**) catalysed by Ag(I).

Each of the intermediates (**67**, **68** and **70**) possesses catalytic action, and effects the destruction of **43** at approximately equal rates at -50°. Thus, addition of 1 equivalent of the tricycloheptane **43** to the **67**-**67**' mixture at -50° afforded, after *ca* 0.5 hr, a mixture of diene **45** and **67**-**67**'. Addition of **43** to **68** at -50° gave the *same mixture*. Warming both these solutions to -20° led to a mixture of **68** and diene **45**; at 0°, a solution of π-allyl complex **70** and diene **45** was formed. Thus it is apparent that a second molecule of hydrocarbon **43** attacks the intermediates **67**, **67**' or **68**, ejecting the "hydrocarbon ligand" as the diene **45**, with the second molecule of **43** concomitantly reforming this ligand. Repetition of this process suggests the mechanism for the catalytic action of $PdCl_2(C_6H_5CN)_2$ (**66**) at low temperatures.

In contrast to 67, 67' and 68, the π-allyl complex 70, when mixed with 43 at -50°, showed an nmr spectrum with absorptions characteristic of 70 and 67-67' (no diene 45 was present). Warming to -20° gave a species with peaks characteristic of 70 and 68. We formulate these species



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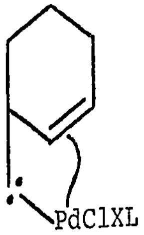
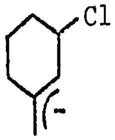


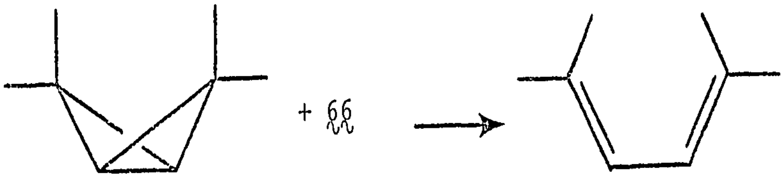
68

a) X = Cl

b) X = 

respectively as 67b-67'b and 68b, in which one Cl atom on the metal has been replaced by the π-allyl fragment, as shown above. At room temperature, 68b formed 70 and 45. These results strongly indicate that the catalytic species at room temperature in the conversion of 43 to 45 is the π-allyl complex, 70. Attack on 70 by a molecule of 43 results in the formation of the new intermediates 67b and 67'b, then 68b is formed, which is in turn transformed into 70 and diene 45. Thus is the catalyst (70) regenerated, and a molecule of product (45) formed. Repetition of the process leads to the total catalytic destruction of the tricyclic hydrocarbon (43). The formation of 70 from 68a may proceed by expulsion of diene 45 from 68a, with subsequent formation of the π-allyl group of 70, but distinguishing this from a direct route has not been accomplished. Indeed, both these processes may be operating.

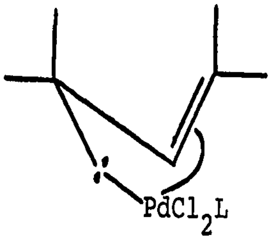
We had hoped to extend this type of work to other bicyclobutanes in which the cleavage mechanism might be defined. Reaction of hydrocarbon 37 with $PdCl_2(C_6H_5CN)_2$ (66) at low temperatures was particularly interesting. At -70°, 1:1.2 mixtures of 37 and 66 showed absorptions in



37

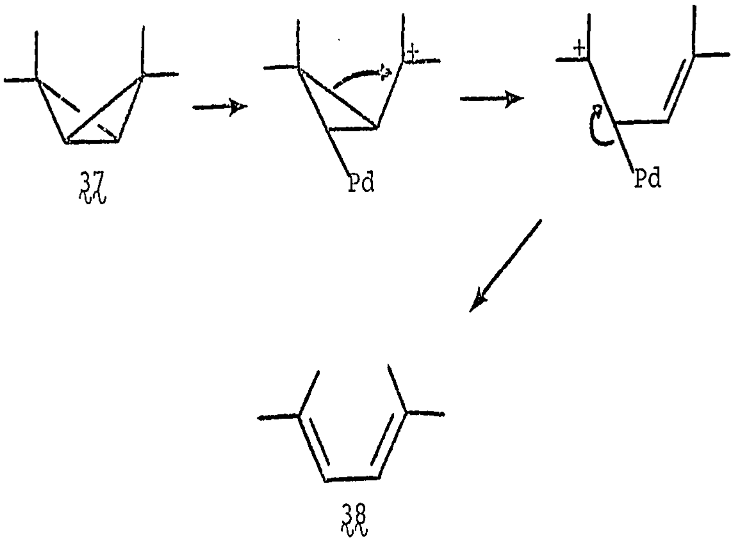
38

the nmr spectrum characteristic of 37 and 38. No peaks attributable to intermediate species were detectable. At this temperature (-70°), 37 was fairly rapidly converted into 38. Thus the mechanism of this conversion is still an open question. However, both Paquette and Gassman have used the rationale that hydrogen migration to a carbenoid centre is favoured over vinyl migration. Methyl groups are even less likely to migrate. Consider the structure of a carbene-Pd complex (72) that might arise from bicyclo-



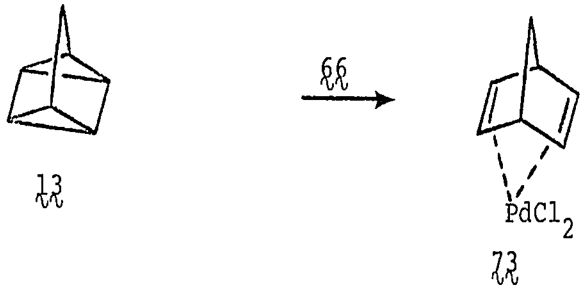
72

butane 37. No hydrogen is available for migration. Thus the vinyl group must migrate to form the product. The structures of 68a and 72 are analogous; therefore, applying the rationale of the relative migratory aptitudes of hydrogen vinyl and methyl, it might be expected that 72 would be a fairly stable intermediate, at least as stable as 68a. No 72 could be detected. Thus, by this rather negative reasoning, it may be that the isomerization of 37 to 38 involves mechanism C, as shown below. This proposal is of course highly speculative. It depends on the relative migratory aptitudes of vinyl groups, which both Paquette and Gassman had reported to them by means of a private communication. It may also be worthwhile to point out that Paquette's original explanation for the Ag(I)-catalysed reaction of 43 to 44 necessitates invoking vinyl migration in preference to hydrogen migration.



The reaction of the dimethylbicyclobutane 35 with the Pd-complex 66 at cold temperatures also has not, as yet, yielded positive evidence of detectable intermediates. The nmr spectra of reaction mixtures were quite complex, but at low temperatures consisted mainly of products. However some small peaks not attributable to these species were evident, although the information obtainable is at this time too sparse to allow any conclusions.

Quadricyclene, (13) is converted by Pd(II)-catalysis to norbornadiene (14). This reaction, at -70°, is quenched. Warming the solution ($CDCl_3$) of 13 and 66 (1:1) to temperatures high enough to effect reaction (*ca* -20°) results in the precipitation of the norbornadienyl-palladium chloride complex (73). No intermediates could be detected in such reaction mixtures.

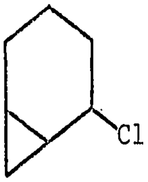

13
66
PdCl$_2$
73

CHAPTER 4

AN ASSESSMENT OF TRANSITION METAL-CATALYSED REARRANGEMENTS OF STRAINED SYSTEMS

The isomerization of tricyclo[4.1.0.0^{2,7}]heptane (43) to 3-methylenecyclohexene (45) on treatment with $PdCl_2(C_6H_5CN)_2$ (66) is the only transition metal-catalysed rearrangement of bicyclobutanes for which intermediates have been identified. The mechanism of this particular reaction is the best understood of all such isomerizations. It is not possible, however, to generalize from this reaction to any others. As pointed out previously, changes in hydrocarbon substrate, metal, or ligands on the metal can all dramatically alter the course of these reactions.

Some details of the mechanism of the 43 to 45 conversion are still obscure. The major problem is the exact structure of the first intermediate (67-67'). One report has appeared on the reduction of organo-palladium σ-bonds.[32] Our attempts at effecting such a reduction of 67 met with limited success. Treatment of CH_2Cl_2 solutions of 67 at -50° with $NaBH_4$, followed by dry MeOH resulted in immediate precipitation of the Pd as the elemental metal. The major, organic product was methoxynorcarane (58). A small (<2%) amount of two other products was present. Glpc-mass spectral analysis showed m/e = 130 and 132 ($C_7H_{11}Cl$) for both these compounds; this molecular composition could represent structure **74** and **75**, but isomers containing double bonds (e.g., **76**) have not been eliminated. Obviously more work is necessary to de-



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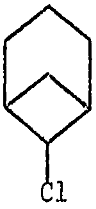

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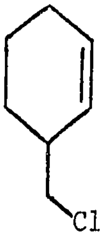


76

fine further the structure of intermediate(s) **67** (**67**'). A specific reduction of the Pd-C bond would be the most desireable means of such an identification, because it would allow introduction of deuterium at a specific site as a marker for the position of the carbon-metal bond.

The mechanisms of other metal-catalysed rearrangements of other strained systems also need more extensive study. The most desireable objective of such work is the characterization of intermediates. In rearrangements catalysed by Ag(I), usually ClO_4^- and BF_4^- have been used as counter ions; both are poor nucleophiles. Replacing them with more nucleophilic species (such as tosylate anion) may stabilize intermediate species in aprotic solvent, and allow their identification.

The transition-metal catalysed rearrangements of strained systems still presents many unanswered questions, although relationships among the mode of reaction, the substitution pattern and the trend toward oxidative addition of the metal as described earlier are beginning to emerge. Future investigation of these reactions holds promise of closer understanding of the chemistry of transition metals, strained bonds, and their interaction.

CHAPTER 5

EXPERIMENTAL

All melting points and boiling points are uncorrected.

All nmr spectra were run on a Varian Associates HA-100 100 MHz spectrometer (12 inch and 15 inch magnets) in CCl_4 solvent, with TMS as internal standard, unless otherwise specified.

Analytical glpc was performed on a F & M model 5750 research chromatograph, employing 6' x 1/16" columns (packing indicated in the text), with a flame ionization detector. Preparative glpc was performed on a F & M model 700 preparative chromatograph, employing 6' x 3/16" columns (packing indicated in text) with a thermal conductivity detector.

Preparation of Quadricyclene (13)

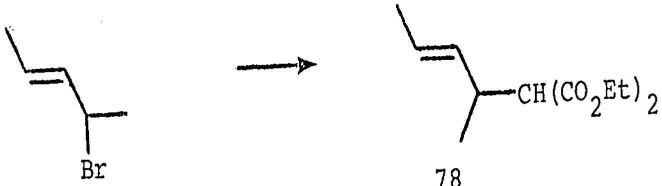
The synthesis of 13 was performed as per reference 34.

Norbornadiene (25 g; 0.27 M) was dissolved in pentane (1300 ml) and to this solution was added acetophenone (50 ml). This solution was irradiated (Hanovia 450 watt high pressure lamp) through a pyrex filter, with external cooling. Irradiation time was 5 hr. The pentane was distilled off through a spinning band column. The distillation residue was then fractionally distilled through a short Vigreux column and the fraction boiling at 103-104° was collected as a colourless liquid. Yield: 12.3 g (49.2%).

nmr: τ 7.98 (t, 2H); τ 8.4-8.7 (m, 6H).

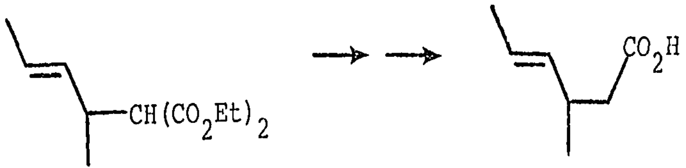
Preparation of exo,exo-2,4-Dimethylbicyclo[1.1.0]butane (23) and endo,exo-2,4-Dimethylbicyclo[1.1.0]butane (25)

The bicyclobutanes 23 and 25 were prepared according to the outline given in reference 17. Prof. Closs kindly provided us with experimental details. This synthesis was performed by Dr. M. Sakai.



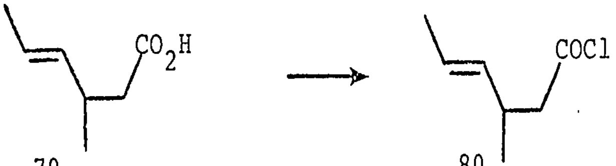
77 78

Diethyl malonate (120 g, 0.75 M) was dissolved in dry ethanol (350 ml) containing Na (17.5 g, 0.75 M). The bromide 77 (111 g, 0.75 M) was added, and the mixture was heated to reflux for 19 hr. After the ethanol had been distilled off, the product was washed with H_2O (50 ml). Distillation gave the diester 78 as a colourless liquid (bp 100-105° at 5 mm of Hg). Yield: 160 g (93%).



78 79

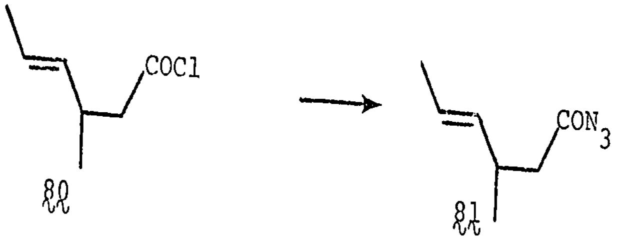
The diester 78 (160 g, 0.704 M) was suspended in aqueous KOH solution (80 g KOH in 100 ml H_2O) and heated at 100° for 15 hr. The reaction mixture was acidified to <u>ca</u> pH 1, and then extracted with ether (3 x 150 ml). The combined ether extracts were washed with H_2O (2 x 75 ml), dried (anhydr. Na_2SO_4), and evaporated, leaving the dicarboxylic acid. Heating the diacid at 135° for 15 hr, followed by distillation gave the 3-methylhex-4-enoic acid 79 (bp 110-115° at 10 mm Hg). Yield: 90 g (96%).
nmr: τ 4.1-4.4 (m, 2H); τ 6.9-7.5 (m, 2H); τ 7.9-8.1 (d, 3H); τ 8.5-8.7 (d, 3H).



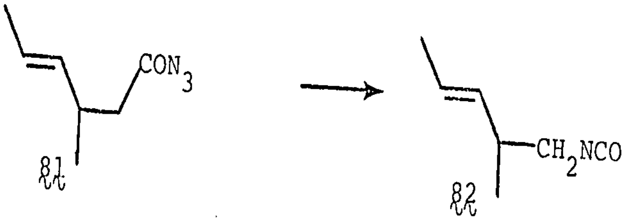
79 80

The acid 79 (90 g, 0.68 M) was suspended in benzene (200 ml) and to it was added $SOCl_2$ (180 g, 1.5 M). After refluxing 0.5 hr, the benzene and excess $SOCl_2$ were distilled off. Distillation gave 3-methylhex-4-enoyl chloride (80) (bp 90-93° at 20 mm Hg) as a colourless liquid. Yield: 95 g (93%).

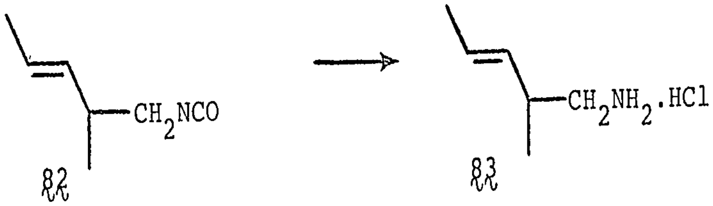
nmr: τ 4.5-4.9 (m, 2H); τ 7.1-8.0 (m, 3H); τ 8.4-8.6 (d, 3H); τ 8.9-9.1 (d, 3H).



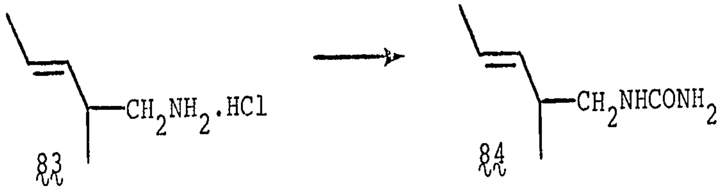
NaN_3 (50 g, 0.77 M) was dissolved in water (150 ml) and cooled in an ice-bath. The acid chloride 80 (95 g, 0.63 M) in acetone (150 ml) was then added dropwise at such a rate that the reaction temperature never exceeded 15°. After stirring at 0° for 1 hr, the water layer was carefully separated, and the upper layer was added carefully to toluene (500 ml). The acid azide (81) was used without further purification.



The toluene solution of the acid azide 81 was warmed to 60°. A rapid evolution of gas ensued, and the mixture was kept at 80-90° until no more N_2 evolved (ca 2 hr). The crude isocyanate 82 was distilled with the toluene, and not further purified.

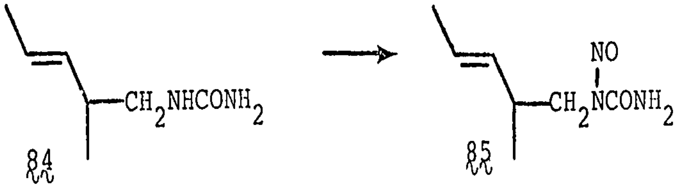


The toluene/isocyanate (82) distillate was heated to reflux with conc. HCl (250 ml) and water (300 ml) for 3 hr with vigorous stirring. Separation of the phases and evaporation of the aqueous phase yielded the amine hydrochloride 83 (ca 45 g) which was used without further purification.



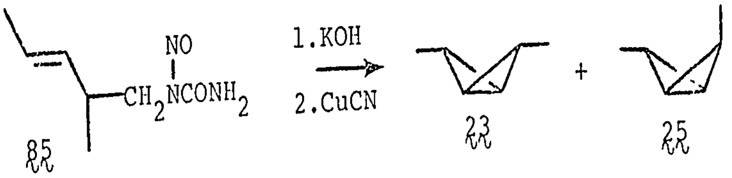
The crude amine hydrochloride 83 (45 g) was heated at reflux in a solution of KCNO (50 g, 0.62 M) in H_2O (200 ml) for 1.5 hr. Extraction of this mixture with ether (3 x 150 ml), followed by evaporation of the ether, and recrystallization of the residue from benzene-heptane gave the N-(2-methylpent-3-enyl)urea (84) as colourless crystals (mp 80-82°). Yield: 40 g (44.6% from the acid chloride 80).

nmr: τ 4.3-4.8 (m, 1H); τ 4.9-5.3 (m, 1H); τ 6.8-7.1 (m, 2H); τ 7.5-7.9 (m, 1H); τ 8.2-8.4 (d, 3H); τ 8.9-9.1 (d, 3H).



To the urea 84 (40 g, 0.28 M) in acetic acid-acetic anhydride (7:3; 300 ml) was added $NaNO_3$ (23 g, 0.30 M) in H_2O (100 ml) over a period of 1 hr. This mixture was stirred an additional 30 min, then H_2O (1000 ml) was added and the mixture cooled to 0°. N-(2-methylpent-3-enyl)-N-nitrosourea (85) precipitated, and was filtered off and dried _in vacuo_, to give pale yellow crystals (mp 55-57°). Yield: 25 g (52%).

nmr: τ 3.0-4.2 (m, 1H); τ 4.6-5.0 (m, 1H); τ 6.2-6.5 (m, 1H); τ 7.3-8.2 (m, 2H); τ 8.4-8.6 (d, 3H); τ 9.0-9.2 (d, 3H).



To a mixture of ether (100 ml) and 50% KOH solution (10 ml) was added, with shaking, the nitrosourea **85** (2.0 g, 11.7 mM) as a fine powder in small portions over 2 min. The bright yellow ether phase was decanted, and dried over KOH pellets. This ether solution of the 1-diazo-2-methylpent-3-ene was then added to CuCN (2 g, 22.2 mM) in ether (25 ml) with stirring. N_2 evolution was instantaneous. After filtration, the ether was removed by distillation through a spinning band column; the products were then separated from the distillation residue by preparative glpc (dimethylsulfolane, 40°). The *exo*,-*exo*-2,4-dimethylbicyclobutane (**23**) was the first C_6 peak, and was collected as a colourless liquid. Yield: 118 mg (12.3%).

nmr of **23** (benzene-d_6): τ 8.0-8.2 (m).

The *endo*,*exo*-isomer (**25**) was the second C_6 peak on the glpc and was collected as a colourless liquid. Yield: 200 mg (21.2%).

nmr of **25** (benzene-d_6): τ 6.7-7.4 (complex m, 2H; C-2 and C-4 protons); τ 7.8-8.2 (m, 8H; bridgehead and methyl protons).

Rearrangement of *exo*,*exo*-2,4-Dimethylbicyclobutane (**23**) by $PdCl_2(C_6H_5CN)_2$ (**66**)

In a typical experiment, to the *exo*,*exo*-dimethylbicyclobutane (**23**) (30 mg, 0.37 mM) in $CHCl_3$ (1.5 ml), was added **66** (1.0 mg, 0.026 mM). This mixture was stood for 14 hr at room temperature. The solution was washed with dilute NH_4OH solution, then dried over anhydr. Na_2SO_4. The products were separated by preparative glpc (dimethylsulfolane, 40°) and identified by comparing them with authentic samples (nmr spectra and glpc retention times). The products were the substituted butadienes **24**, **26** and **36**. (See Table III for product distribution).

In a similar fashion, the *endo*,*exo*-isomer (**25**) was rearranged to **24**, **26** and **36** by the action of the palladium complex **66**. (See Table III for product distribution).

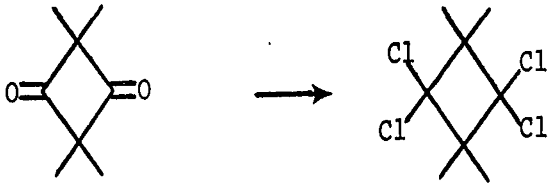
nmr of *cis*,*trans*-hexa-2,4-diene (**24**): τ 3.6-5.2 (complex m, 4H); τ 8.3-8.6 (m, 6H).

nmr of *trans*,*trans*-hexa-2,4-diene (**26**): τ 4.0-5.0 (complex m, 4H); τ 8.4-8.7 (d, 6H; J = 5.5).

Preparation of 2,2,4,4-Tetramethylbicyclo[1.1.0]butane (**37**)

The synthesis of **37** was performed as in reference 35 according to the following scheme.

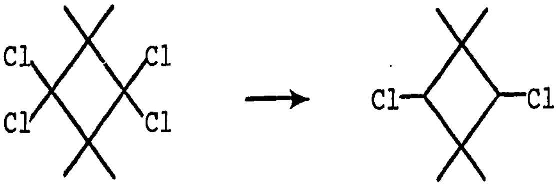
Dimethylketene dimer (**86**) (100 g, 0.715 M) and phosphorous pentachloride (500 g, 2.4 M) were dissolved in CCl_4 (1 l.) and refluxed 3 hr. The reaction mixture was cooled in ice, and excess PCl_5 was filtered off. The filtrate was poured into ice (500 g) and the CCl_4 layer was



86 87

washed with H_2O (3 x 200 ml), saturated $NaHCO_3$ solution (200 ml), brine (200 ml) and then dried (anhydr. Na_2SO_4). Evaporation of the CCl_4 gave a crystalline residue which was recrystallized to give 1,1,3,3-tetrachloro-2,2,4,4-tetramethylcyclobutane (87) as colourless crystals. Yield: 84 g (47%).

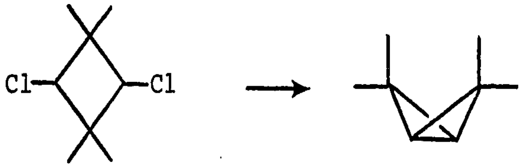
nmr: τ 8.5 (s) (lit.[37] τ 8.47 (s)).



87 88

The tetrachloride (87) (11.7 g, 47 mM) was dissolved in dry benzene (80 ml), and to this solution was added 2,2'-azobis(2-methylpropionitrile) (50 mg). Tri-*n*-butyltin hydride (30.1 g, 103 mM) dissolved in dry benzene (50 ml) was added dropwise at reflux over 1 hr. Another portion of the azonitrile (50 mg) was then added and refluxing was continued 3 hr. A third portion of the

azonitrile was added (50 mg) and the mixture was refluxed a further 19 hr. After this time, the reaction mixture was steam-distilled. The aqueous layer of the distillate was washed with benzene (2 x 25 ml). The combined benzene layers were washed with brine (50 ml), dried (anhydr. Na_2SO_4) and evaporated, leaving a colourless oil. Distillation gave 88 as a colourless solid, bp 70° at 20 mm Hg. (lit.[37] bp 85-85.5° at 32 mm Hg). Yield: 4.75 g (56%).
nmr: τ 6.13 (s) and 6.30 (s, total integration, 2H); τ 8.8-9.0 (d, total integration, 12H).



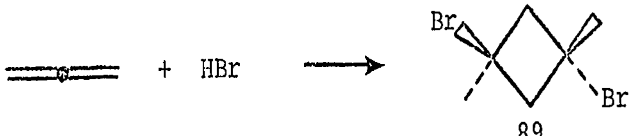
88 37

Sodium metal (1.19 g, 51.8 mM) was suspended in dry triglyme (30 ml), at 125° and under 80 mm Hg pressure. To this suspension, with vigorous stirring, was added dropwise a solution of the dichloride (88) (2.5 g, 13.8 mM) in triglyme (10 ml). The resulting mixture was heated for 3 hr at 125°, 80 mm Hg. The product was distilled on forming into a dry-ice cooled trap. This crude product was distilled to give 37 as a colourless liquid, bp 94-98° (lit.[37] bp 104°) Yield: 1.04 g (68%).
nmr (CD_2Cl_2): τ 8.75 (s, 6H; exo-methyl protons); τ 8.94

(s, 6H; endo-methyl protons); τ 9.04 (s, 2H; bridgehead protons).

Preparation of 1,3-Dimethylbicyclo[1.1.0]butane (35)

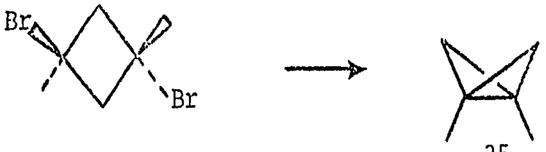
Compound 35 was prepared as per reference 36, according to the following scheme.



89

Allene (28 g, 0.7 M) and HBr (57 g, 0.7 M) were condensed into a Carius tube at -78°. The tube was sealed and stood at -78°, with occasional shaking, for 6 days, after which time it was gradually warmed to room temperature over 24 hr. The tube was then opened, and the gaseous components removed by bubbling the reaction mixture with argon. The residue was a pale yellow liquid, which was distilled until the fraction boiling at 65°, 90 mm Hg, had all been removed. The distillation residue was treated with pentane (6 ml) and cooled to -30°, whereupon crystals formed. These crystals were collected and washed briefly with cold pentane to give the dibromodimethylcyclobutane 89 as colourless prisms. Yield: 9.6 g (10%).

nmr: τ 6.82 (s, 4H); τ 7.88 (s, 6H).



89 **35**

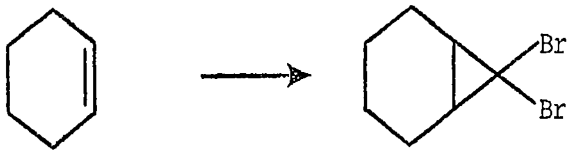
The dibromide **89** (3.0 g, 12.4 mM) was added to lithium amalgam (0.5%; 100 g) in dry dioxane (50 ml). This mixture was stirred vigorously at room temperature for 46 hr. The organic layer was decanted from the remaining amalgam, then filtered. The dioxane solution was then distilled at atmospheric pressure, stopping when the boiling point reached 94°. The distillate consisted of dioxane and the desired bicyclobutane. The bicyclobutane (**35**) was obtained pure by preparative glpc (UC-W98, 70°) as a colourless liquid. Yield: 824 mg (81%).

nmr (CD_2Cl_2): τ 8.63 (s, 6H; methyl protons); τ 8.93 (s, 2H; *exo*-methylene protons); τ 9.46 (s, 2H; *endo*-methylene protons).

Preparation of Tricyclo[4.1.0.$0^{2,7}$]heptane (**43**)

The preparation of **43** followed that given in reference 37.

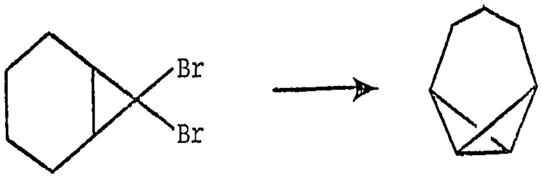
KO*t*-Bu was prepared freshly from potassium metal (9.0 g, 0.231 M) and *t*-BuOH. To the dry, powdered KO*t*-Bu was added cyclohexene (16.4 g, 0.20 M) in dry olefin-free



90

pentane (100 ml). This mixture was cooled to 0°, and to it was added dropwise, with vigorous stirring, bromoform (51.8 g, 0.205 M). The mixture was then stirred at room temperature overnight. Water (70 ml) was added to dissolve the solids, and the aqueous layer was extracted with pentane (25 ml). The combined organic phases were washed with brine (30 ml), dried (anhydr. Na_2SO_4) and evaporated, leaving a yellow oil. Distillation gave the 7,7-dibromonorcarane 90 as a colourless oil (bp 58° at 0.8 mm Hg). Yield: 35.2 g (70%).

nmr: τ 7.6-9.1 (2 overlapping multiplets centred on τ 8.1 and 8.65).



90 43

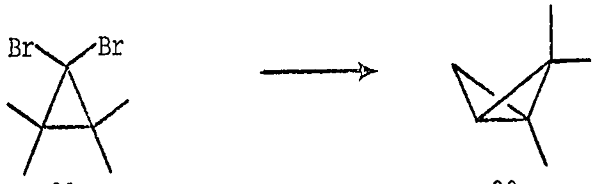
The dibromide 90 (10 g, 39.4 mM) was dissolved in dry pentane (150 ml) and cooled to -45°. To it, slowly over 1 hr, was added a solution of methyllithium in ether

(47 mM) at -45°. This mixture was stirred for 1 hr at -40°, then warmed to 0° for 1 hr. After recooling to -40°, wet ether was added to the mixture until excess methyllithium had been destroyed. After warming to 0°, NaH_2PO_4 solution (1M; 100 ml) was added and the organic layer was separated and dried, at 0° (anhydr. Na_2SO_4 and K_2CO_3 mixture). The solvents were then evaporated at 0°, 145-155 mm Hg, then the residue was distilled at room temperature, 10 mm Hg onto a dry-ice cooled cold finger. Preparative glpc (UC-W98, 80°) gave the tricycloheptane (43) as a colourless liquid. Yield: 444 mg (12%).

nmr (CCl_4): τ 7.54-7.76 (m, 2H; C-2, C-6 protons); τ 8.38-8.56 (t, 2H; C-1, C-7 protons); τ 8.60-8.76 (m, 6H; methylene protons).

Preparation of 1,2,2-Trimethylbicyclo[1.1.0]butane (29)

The preparation of 29 followed that given in reference 38.



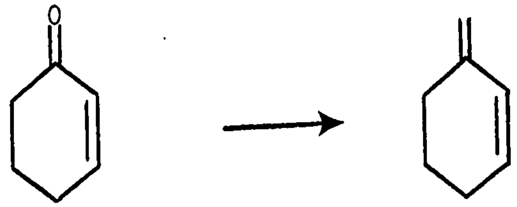
91 29

The dibromide 91 was prepared from tetramethylethylene and dibromocarbene in the same manner as 7,7-dibromonorcarane (90) was prepared.

The dibromide **91** (10 g, 39 mM) was dissolved in dry ether (30 ml) and cooled to 0°. To this solution was added dropwise an ether solution of methyllithium (40 mM). The resulting mixture was stirred 1 hr at 0°, then hydrolysed with H_2O (25 ml). The organic phase was washed with brine (25 ml) and dried (anhydr. K_2CO_3). Evaporation of the solvents gave a yellow oil which was distilled to give the trimethylbicyclobutane (**29**) as a colourless liquid, bp 84-85° (lit.[38] bp 84°). Yield: 1.69 g (45%).

nmr: τ 8.54 (s, 3H; C-1 methyl protons); τ 8.94 (s, 3H; C-2 <u>exo</u>-methyl protons); τ 9.22 (s, 3H; C-2 <u>endo</u>-methyl protons); τ 8.2-9.1 (m, 3H; bicyclobutane ring protons).

Preparation of 3-Methylenecyclohexene (**45**)



45

Methyltriphenylphosphonium bromide (31 g, 87 mM) was suspended in dry ether (400 ml) and reacted with *n*-butyllithium in hexane (85 mM). This mixture was stirred 30 min at room temperature. Cyclohexenone (7.0 g, 73 mM) was dissolved in ether (25 ml) and added to the methylenetriphenylphosphorane solution at room temperature at a rate sufficient to maintain reflux. The resulting mixture was refluxed 2 hr. H_2O (20 ml) was added, and the ether was distilled off at atmospheric pressure. The residue was thoroughly extracted with pentane (6 x 30 ml) and the combined pentane extracts were dried (Na_2SO_4) and evaporated. The residual oil was distilled onto a dry-ice cooled cold-finger (at room temperature, 10 mm Hg). The 3-methylenecyclohexene (45) was obtained pure by preparative glpc (UC-W98, 80°) as a colourless liquid. Yield: 1.25 g (18%).

nmr: τ 3.7-4.3 (m, 2H); τ 5.2-5.4 (m, 2H); τ 7.5-8.1 (m, 4H); τ 8.1-8.4 (m, 2H).

Preparation of Palladium(II) Chloride-Benzonitrile (66)

Palladium dichloride (510 mg, 2.88 mM) was added to dry benzonitrile (10 ml) and heated at 100° for 25 min under an N_2 atmosphere. The resulting mixture was filtered hot and cooled. The precipitated crystals were filtered off and washed with hexane (3 x 25 ml), to give the palladium(II) chloride-benzonitrile as yellow-orange crystals (mp 128-129°).[25] Yield: 780 mg (70%).

Detection of Intermediates 67, 68 and 70

In a typical experiment, $PdCl_2(C_6H_5CN)_2$ (66) (14.0 mg, 0.037 mM) was dissolved in CD_2Cl_2 (0.25 ml) containing *ca* 4% TMS (by weight). This solution was placed in an nmr tube (which had been previously been washed with dilute NH_4OH solution and dried at 110° for 24 hr, then cooled under a stream of argon). Into the nmr tube was inserted a narrow (1 mm diameter) glass rod, flattened at the end. The nmr tube containing the solution of the palladium complex (66) was then cooled to -50°, under a stream of argon, by inserting most of its length into an acetone/dry-ice bath at this temperature. After 15 min, a solution of the tricyclo[4.1.0.0^{2,7}]heptane (43) (3.3 mg, 0.035 mM) in CD_2Cl_2 (0.1 ml) was added dropwise (<u>ca</u> 30 drops) to the cold metal complex solution under argon, by means of a very fine capillary pipette. During the addition of 43, a constant and vigorous agitation of the reaction mixture was maintained by means of the glass rod inserted in the nmr tube. Care was taken not to splash any of the reaction mixture onto those sections of the walls of the nmr tube which might have been at temperatures above -50°. After the addition of 43, a canary yellow solution resulted. The nmr tube was tightly capped and inserted into the nmr spectrometer probe at -50°. This solution (of complex 67 and 67') showed nmr signals at τ 5.39 and 5.72 (m, total integration 1H) and τ 6.8-8.6 (complex m, total integration 9H). No peaks due to starting material (43) were detectable after 15 min at -50° (see text).

Warming the solution of 67 and 67' to -20°, gave the carbene-Pd complex **68**, as an orange solution at -20° The nmr spectrum of **68** showed peaks at τ 4.42 (broad d, 1H; J = 6.5); τ 4.73 (m, 1H); τ 6.21 (s, 1H); and τ 7.7-8.5 (m, 7H). (See text for interpretation of this spectrum).

Warming the solution of **68** to room temperature gave a dark red-orange solution of the π-allyl complex **70** after *ca* 20 min. The nmr spectrum showed peaks at τ 5.61 (broad s, 1H; C-2 protons); τ 5.88 (broad s, 1H; C-1 proton); τ 6.21 (broad s, 1H; C-7 *endo*-proton); τ 7.14 (broad s, 1H; C-7 *exo*-proton); τ 7.36 (m, 2H; C-5 methylene protons); and τ 7.6-8.5 (m, 4H; C-3 and C-4 methylene protons).

All of the above spectra also showed absorptions due to the benzonitrile protons (τ 2.2-2.7, m).

Reaction of **70** with excess NH_3, pyridine or triphenylphosphine generated the diene **45** as the sole organic product.

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APPENDIX TO PART I

At the request of the examiners, the analytic data for the following compounds is now included.

Compound **50**. Calcd for $C_{25}H_{26}O_8S_2$: C, 57.90; H, 5.05.
Found: C, 58.26; H, 5.18.

Compound **52**. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.17.
Found: C, 61.28; H, 6.24.
Calcd m/e = 294.1103.
Meas m/e = 294.1111.

Compound **54**. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37.
Found: C, 83.96; H, 5.37.

Compound **64**: Calcd for $C_{26}H_{28}O_8S_2$: C, 58.63; H, 5.30.
Found: C, 58.92; H, 5.39.

Compound **74**. Calcd for $C_{22}H_{18}O_2$: m/e = 314.1307.
Meas m/e = 314.1314.

Compound **96**. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35.
Found: C, 64.90; H, 6.45.
Calcd m/e = 222.0892
Found: m/e = 222.0897

Compound **98** - acetate. Calcd for $C_{16}H_{20}O_3$: C, 73.82;
H, 7.74.

Found: C, 73.74; H, 8.19.

Calcd m/e = 260.1413.

Meas m/e = 260.1422.

Compound 100. Calcd m/e for $C_{14}H_{20}$ = 188.1565.

Found: m/e = 188.1570.

The following experiments are also included at the request of the examiners.

Attempted Preparation of 3,4-Benz-1,5-bisdehydro[10]annulene (35)

The dimesylate 59 (105 mg; 0.287 mM) was dissolved in a mixture of methanol (1 ml) and THF (1.8 ml) at 0°. To this solution was added sodium methoxide (32.9 mg; 0.575 mM) in methanol (1.8 ml). This solution was stirred at 0° for 0.5 hr, then at room temperature for 6 hr. A silky precipitate formed. The mixture was hydrolyzed with 1M NaH_2PO_4 solution (50 ml) and extracted with benzene (50 + 2 x 25 ml). The organic players were dried (anhydr. Na_2SO_4) and evaporated, leaving a brown semi-crystalline residue. Nmr analysis of this residue showed it to contain anthracene. Sublimation of the residue (90°, 0.05 mm Hg) gave nearly pure anthracene (*ca* 10% yield).

Repetition of this experiment in anhydrous THF, using DBN, KO*t*-Bu and $LiN[Si(CH_3)_3]_2$ gave similar results.

Attempted Preparation of 3,4-Benz-1,5-bisdehydro[11]-annulenyl cation (**63**)

The hydrocarbon **36** (22.5 mg; 0.116 mM) was dissolved in dry CD_3CN (0.1 ml) and placed in an nmr tube. To it was added a solution of trityl fluoroborate (38.3 mg; 0.116 mM) in CD_3CN (0.25 ml). The mixture turned black instantly. After standing 19 hr, all of the starting material had disappeared. Monitoring the reaction by nmr spectroscopy gave no indication that **63** had formed. Only tarry material could be obtained by workup of the reaction mixture.

In an attempt at forming cation **102**, 3,4-tetramethylenecycloundeca-1,5-diyne-3,7,10-triene (**38**) was treated with trityl fluoroborate in the above manner. The results were qualitatively the same, and again no evidence of product formation could be obtained.