Progress Toward the Synthesis and Characterization of 1, 4-Dehydroaromatic Systems: I. 1, 4-Dehydrobenzene (para-Benzyne or Butalene); II. 1, 4-Dehydrotropyl Cation, Anion and the Bicyclo[3.2.0]heptatrien-3-one

A Thesis by

Richard R. Jones

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'Down the Rabbit-Hole'

From Lewis Carroll,
"Alice's Adventures in
Wonderland,"
illustrated by John Tenniel

Dedication

To my parents, Ted and Louise, whose love, encouragement, and continued support made the completion of this manuscript possible.

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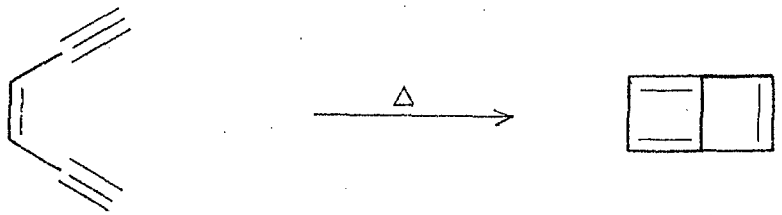
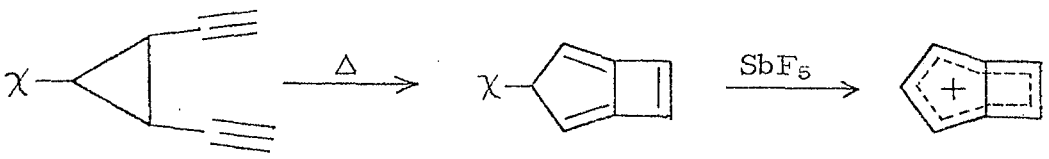
Foremost, I wish to thank Professor Robert G. Bergman for suggesting this project and for always staying one step ahead of what must have been for him a very difficult student. I only wish I had been more competent to carry out his ideas. The encouragement and support by Professor Franz Sondheimer during the author's leave of absence from this work at The University College London is gratefully acknowledged. This work also owes much to Dr. Michael B. D'Amore on whose shoulders I stood. The technical assistance of Dr. Timothy J. Henry when four hands and two feet were required to get data from a temperamental mass spectrometer is deeply appreciated. To all those in the Chemistry Store Room, Purchasing Department, Shops and to those experts in the building across the street whose patience I tried goes my sincerest appreciation, for without their cheerful assistance, this work would have been even more difficult than it was. Lastly, the patience and skill of Sharon Vedrode in typing and organizing this manuscript is gratefully acknowledged. This work was supported by the California Institute of Technology through grants to R. G. Bergman and in part directly by the National Science Foundation.

Abstract

This thesis concerns the attempted synthesis of two strained nonbenzenoid, conjugated bicyclic systems, 1, 4-dehydrobenzene (butalene or para-benzyne, 28) and the 1, 4-dehydrotropylium ion (30c). Both 28a and 30c contain a fused cyclobutadiene ring with



cis-60 28a

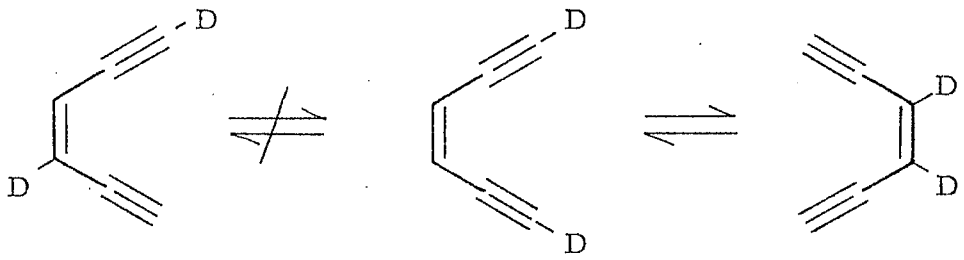


61 30c

its accompanying antiaromaticity but overall possess $4n+2$ π electrons. The concept of nonbenzenoid aromaticity as it applies to compounds such as these is reviewed. The synthetic approach to 28 and 30 systems is based on the pyrolytic cyclization of a 1, 5-hexadiyne moiety to form a dimethylenecyclobutene, thereby introducing the strain and unsaturation of the fused four-membered ring in one step.

In Part I, the synthesis and pyrolysis of cis-1, 6-dideutero-1, 5-hexadiyn-3-ene (cis-60a) is described. By a combination of nmr and ms techniques, it is demonstrated that cis-60a undergoes

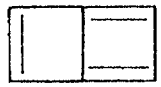
a degenerate rearrangement at 200°C in the gas phase at atmospheric pressure, interconverting cis-60a with its 3, 4-dideutero isomer cis-60b with an equilibration half-life of 30 sec. None of the single exchange isomer cis-60c or any trans-60 was formed in this pyrolysis. These data require a transition state or intermediate between cis-60a and cis-60b with C_{2v} symmetry, i.e.,



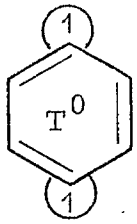
cis-60c cis-60a cis-60b

1, 4-dehydrobenzene. Similarly prepared trans-60a did not undergo isomerization or rearrangement at these temperatures.

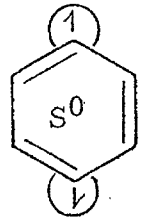
Pyrolysis of cis- and trans-60 in solution provided a high yield of benzene in the presence of hydrogen donors at the expense of cis-60. In carbon tetrachloride, para-dichlorobenzene was the major product. In methanol, a 10% yield of benzyl alcohol but no anisole was formed. Since these are typical products of radical abstraction, it is suggested that the symmetrical species implicated in the deuterium scrambling is a true intermediate and of 1, 4-benzenediyl structure 28d or e (instead of 28a).



28a



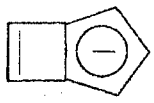
28d



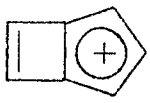
28e

While traces of benzene were seen in the atmospheric and vacuum pyrolysis of cis- and trans-60, no satisfactory gas phase trapping experiment has been performed. Neither have substantial levels of deuterium scrambling been demonstrated in liquid phase pyrolysis. These points together with some indication of the stereospecificity of the benzene forming reaction in solution remain to be answered. The added complication of a possible triplet ground state for the 1, 4-benzenediyl (28d) must also be resolved before a truly consistent story can be told. A possible direct route to a triplet 28d, photosensitized irradiation of cis-60a, failed to produce scrambling in competition with a demonstrated approach to the photostationary state. No transfer of acetylenic label was observed also under direct (254 nm) irradiation of cis-60a.

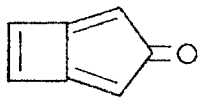
In Part II, toward formation of the 1, 4-dehydrotropylium ion (30c) as well as the 1, 4-dehydrotropyl anion (30a) and the bicyclo-[3.2.0]heptatrien-3-one (52), the synthesis of



30a

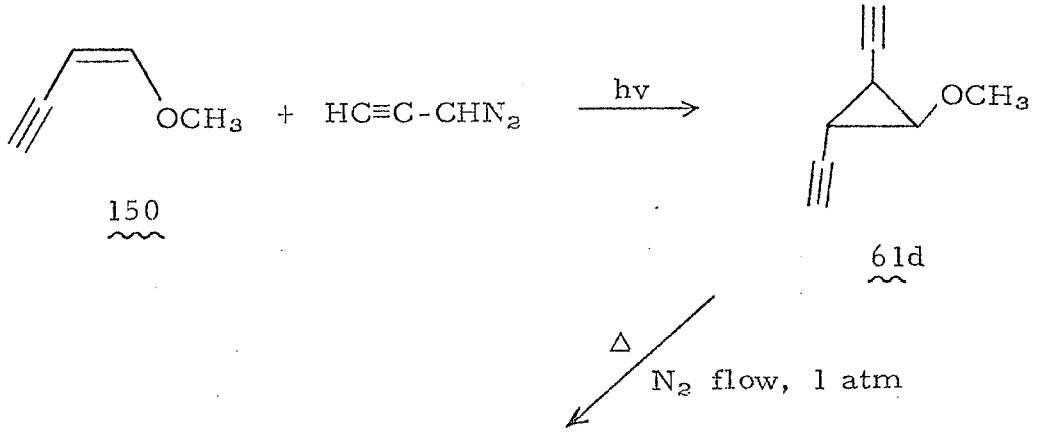


30c



52

bicyclo[3.2.0]hepta-1, 4, 6-trienes substituted in the 3-position is discussed. The required 3-substituted 1, 2-diethynylcyclopropanes were approached via carbene addition to hexadiynenes, eneynes, and via γ-elimination routes. Of these, only the addition of propargyl carbene to methoxybuten-3-yne (150) provided any cyclopropane product. The 3-methoxy-1, 2-diethynylcyclopropane (61d)



150

61d

62d

prepared in < 1% isolated yield by this method readily isomerized to the air sensitive 3-methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d)

upon pyrolysis under atmospheric pressure flow conditions at 305°C (contact time 10 sec). Attempted formation of 30a by ether cleavage reduction of 62d with potassium led only to polymer without any evidence for formation of an anion. However, treatment of 62d with SbF_5 containing a catalytic amount of $HOSO_2F$ in a soft matrix at -180°C gave evidence in the nmr of formation of 30c although at such low concentrations that a clear spectrum was not obtained. This interesting result is currently under reinvestigation.

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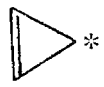
GENERAL INTRODUCTION

Aromaticity and Strained, Cyclic Conjugated Hydrocarbons

A Brief History

The chemical and physical properties of cyclic, fully conjugated olefinic molecules ([m]-annulenes,[1] where m = the number of p-π electron centers, Figure I) have attracted the attention of organic chemists since the publication of A. Kekulé's classical treatment of the structure of carbon compounds in the years following 1865. In these papers[2] Kekulé proposed the now familiar resonating cyclohexatriene structure for benzene (4b, Figure II). This six-carbon compound,[3] containing four units of unsaturation,[4] was known to be the simplest member of a class of compounds each of which, possessing the benzene ring in its molecular structure, was characterized to various degrees by ease of formation (especially in pyrolytic reactions), relative thermodynamic stability, symmetrical structure (e.g., only one ortho di-substituted isomer), tendency to undergo electrophilic substitution rather than addition reactions, and general unreactivity under conditions prone to attack such heavily unsaturated molecules.[6] Since many of the natural oils such as oil of wintergreen, aniseed, sassafras, cinnamon and vanilla contained benzenoid compounds as their principal components, these compounds were classified as aromatic[2] and their properties referred to as aromatic properties.

Attempts to rationalize the unusual behavior of benzenoid aromatics by a reasonable physical structure for benzene led to many alternative representations[7] (4a-h, Figure II). Of these, the most successful structural explanation for the chemical properties



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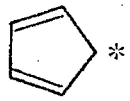
1b, * = .
1c, * = +

2a = --
2c = ++

2



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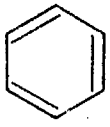

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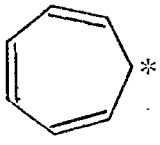

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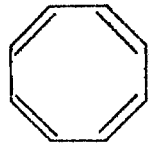

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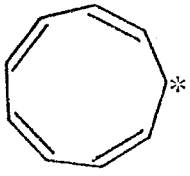
6c = ++

6



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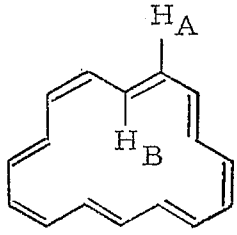

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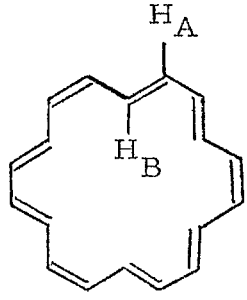
8

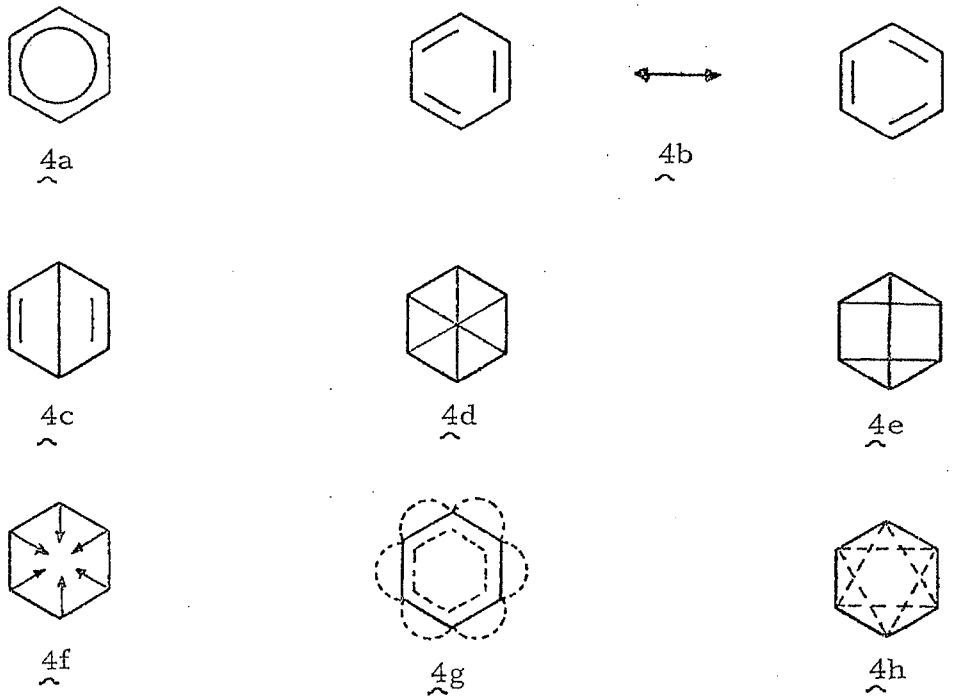


9a = --
9c = ++

9

Figure I

[m]-Annulenes



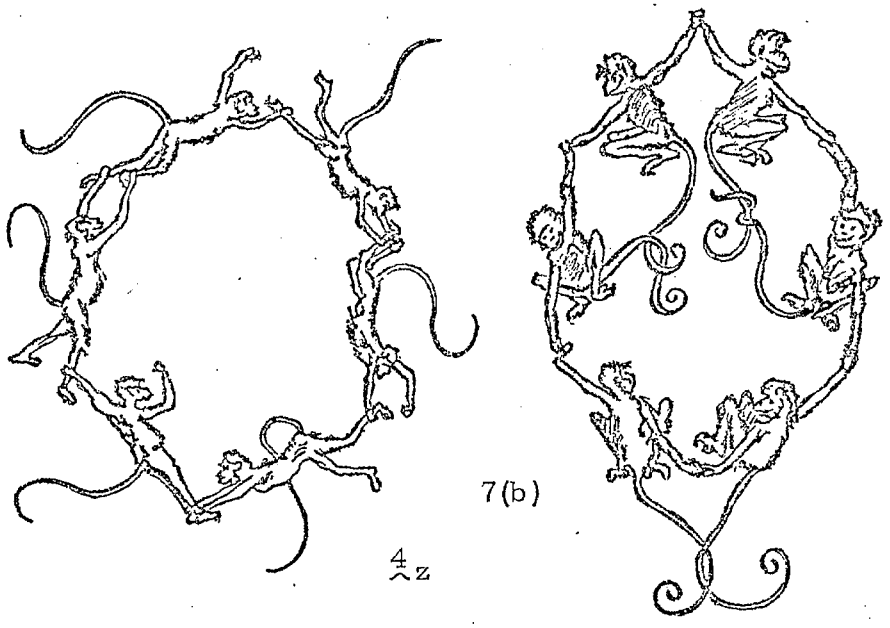
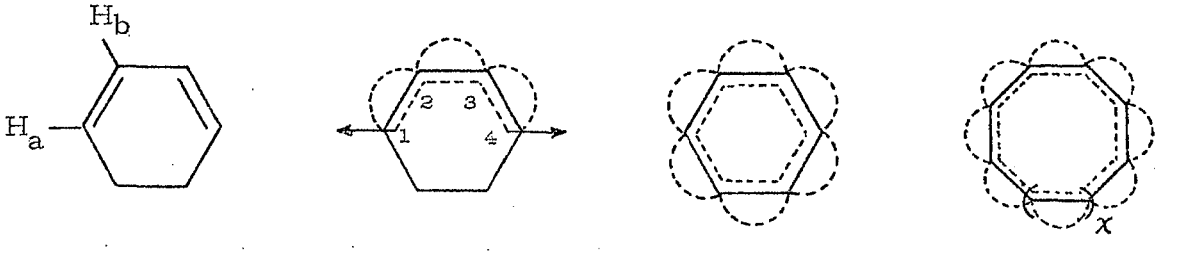


Figure II

Proposed Structures for Benzene[7(a)]

of the aromatic nucleus prior to the discovery of the electron was made by J. Thiele[8(a)] in 1899 (4g, Figure II). His theory of partial valence for olefins when applied to benzene predicts a closed configuration with no free carbon valence[8(b)] in contrast to that given to carbons C-1 and C-4 in 1,3-cyclohexadiene (10) by this method.



10 '10' 4g [x+6]-annulene

Figure III

Thiele's[8] Partial Valence Representation

(unsatisfied or free valence →)

Thus the expectation is that 10 will undergo predominant 1,4-electrophilic addition while 4 and in fact all fully conjugated cyclic molecules (Figure I) will possess completely satisfied olefinic valences and be relatively inert.

The first test of this hypothesis was provided by R. Willstätter when in 1905 he attempted preparation of cyclobutadiene[9] ([4]-annulene, 2) and when in 1911 he succeeded in preparing cycloöctatetraene[10] ([8]-annulene, 6). However, the

quite ordinary polyolefinic chemical nature of cycloöctatetraene[10,11] (vide infra) and the apparent instability (reactivity?) of cyclobutadiene[9, 12] compared to that of the structurally similar benzene proved that alternating double and single bonds in a cyclic hydrocarbon was not a sufficient condition for aromaticity. Nevertheless, the discovery of the benzene-like properties of the nonbenzenoid furan (11), pyrrole (12) and thiophen (13) rings[13] demonstrated that the cyclic six-carbon triene 4 was not unique and forced a definition of aromaticity which could be applied to completely conjugated cyclic or polycyclic molecules in addition to those containing only benzenoid nuclei.

After the discovery of the electron and the formulation mainly by Lewis[14] of the electronic theory of valence, explanations for the unusual nature of benzene and its derivatives centered on the importance of an "aromatic sextet" of electrons. That the nonaromatic cycloöctatetraene (6) possessed eight π electrons and the apparently highly reactive cyclobutadiene (2) four lent support to the idea that six π electrons in a cycle were essential for aromatic properties. This rule, stated by Armit and Robinson[15] and expressed for benzene by formula 4a (Figure II), correctly predicted that the cyclopentadienyl anion[16] (3a) and the cycloheptatrienyl cation[17] (5c) should be stabilized by an aromatic π electron interaction. However, it required the application of quantum mechanics to actually provide some theoretical justification for the importance of six π electrons versus four or eight.

Erich Hüchel[18] applied the variation principle to the π electrons of a fully conjugated cyclic system in the years 1931-1937. Hückel used linear combinations of atomic orbitals to generate a set of molecular orbitals possessing the essential symmetry of the molecule, making the assumption that aromaticity is a property of the π orbitals alone which could be treated separately from the orthogonal σ orbitals. The molecular orbital levels thus generated were either bonding (stabilized compared to an electron in an atomic 2p orbital of carbon), nonbonding, or antibonding (destabilized compared to a carbon 2p electron). For symmetrical noncyclic conjugated systems such as cyclobutadiene, benzene, and cyclooctatetraene ([m]-annulenes, Figure I), the molecular orbital pattern consists of one lowest energy orbital and "n" pairs of other bonding or nonbonding orbitals. An [m]-annulene will thus have all its bonding and nonbonding orbitals fully occupied and possess a closed shell similar to the completely filled shells of atomic orbitals in the inert gas (Group Zero) atoms if it contains $4n+2$ π electrons. On the other hand, an annulene with $4n$ π electrons will possess partially occupied bonding or nonbonding orbitals and a type of "valence," tending to gain or lose electrons to achieve a closed shell. Thus the "aromatic sextet" of Robinson becomes the special case of $n = 1$ in the $4n+2$ rule.

Considering the simplicity of this approach, the success of the Hückel $4n+2$ rule for predicting systems which might be stabilized by an aromatic interaction has been phenomenal. Besides the cyclopentadienyl anion (3a) and the cycloheptatrienyl cation (5c)

already mentioned, the cyclopropenyl cation[19] (1c, n = 0), cyclooctatetraenyl dianion[20] (6a, n = 2), cyclononatetraenyl anion[21] (7a, n = 2), and [18]-annulene[22] (9, n = 4) are examples of 4n+2 π systems which have been synthesized and found to be relatively stable, perhaps due to aromaticity (vide infra). Similarly, nonaromaticity or even aromatic destabilization[23] have been proposed for the 4n π systems of cyclobutadiene[12] (2, n = 1), [16]-annulene[26] (8, n = 4) and even the nonplanar cyclooctatetraene[11, 24, 25] (6, n = 2) for instance. However, there are 4n+2 systems which appear to be highly reactive or destabilized, for example from Figure I the cyclooctatetraenyl dication[27, 28] (6c, n = 1) and the cyclobutadienyl dication[29] (2c, n = 0) or dianion[30] (2a, n = 1), since they have resisted all efforts at synthesis so far. The first two, 6c and 2c, are open shell systems (even though the unfilled levels are nonbonding) which may make them unusually reactive, but the latter, 2a, possesses a completely filled valence shell. But the presence of two negative charges on a four-membered ring may make 2a unstable due to electron-electron repulsion, a factor not taken into account by simple Hückel theory.

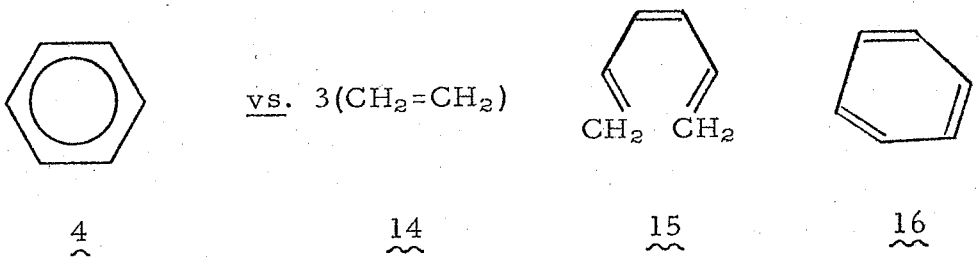
The nature of aromaticity and its theoretical basis is a subject of intense current interest and debate,[31] challenging both the synthetic and theoretical abilities of the organic chemist. Since the introduction of the concept by Kekulé, several hundred publications have appeared in this area, and many excellent reviews are available.[32] It is therefore certainly not my intention to review this field in its entirety in the context of this thesis, but in the

following sections I have attempted to define aromaticity in terms of its measurement and to introduce an area of active current research where many interesting problems arise.

An Empirical Definition of Aromaticity

The historical definition of aromaticity was based primarily upon the chemical properties of a substance. Reaction type and reactivity are, however, more functions of the relative favorability of various transition states leading to products than fundamental properties of a molecule itself. In the case of benzene and its derivatives, which remain the aromatic compounds 'par excellence,' their tendency to 'retain the type'[6] in reactions is a reflection of the fact that transition states which retain or regenerate the aromaticity of the benzene ring are energetically favored over those that do not. Thus aromaticity is a state property which contributes to the stabilization of the state relative to some standard.[23] While it is not a sufficient condition for aromatic stabilization, the aromaticity of benzene most certainly arises from its cyclic conjugation (vide supra). The ideal standard state for benzene then would be one which isolates the cyclic delocalization separate from all other factors such as the hybridization of the carbons, symmetry and strain which affect the total energy.

The two standard states most often employed for potentially aromatic cyclically conjugated molecules are (1) a system of paired atomic orbitals with isolated two-electron π interactions and (2) a linear polyolefin containing the same number of atomic centers with normal alternating π interactions. An example of standard state '(1)' for benzene would be three ethylenes (14, Figure IV) whereas standard state '(2)' would be the cis-1, 3, 5-hexatriene



4 14 15 16

Figure IV

Benzene and Its Standard States

(15, Figure IV). Of the two, 15 perhaps isolates the cyclic delocalization more precisely since normal polyolefinic "2, 3" interactions are allowed as well as the 1, 2 π bonding. But clearly while hexatriene 15 is an attainable standard state from a synthesis point of view, it possesses only two such "2, 3"-type interactions instead of the three in localized benzene, thus overestimating the effect of aromatic delocalization. But even the hypothetical cyclohexatriene (16, Figure IV) would require a symmetry change including σ bond compression and σ, π bond stretching with their attendent rehybridization (sp^2 olefinic $\rightarrow$ sp^2 aromatic) to form benzene. Seen in this light, aromaticity is a theoretically defined quantity and not a physically observable one. However, this lack of appropriate, accessible standard states does not mean that the aromatic delocalization does not exist as a factor over and above ordinary π conjugation, just that it can never be measured without reference to a calculated standard.

Methods for calculation of the standard heat of formation of such imaginary compounds as 16 are available based on the additivity of group equivalent values determined by computer fitting of a large volume of experimental data on linear and cyclic olefins.[36] The aromatic delocalization energies (Table Ia, column five) obtained from these numbers and measured heats of formation (combustion analysis or hydrogenation to compounds of known ΔH_f°) are often quoted in the literature as experimentally derived. In reality they include an estimation of the ring strain and the internal nonbonded interactions obtained by analogy to reference compounds of arbitrarily assigned zero strain. Thus, the significance of such values as +0.8 kcal/mole for the aromatic delocalization energy of potentially homoaromatic cycloheptatriene or the -1.1 kcal/mole for the potentially antiaromatic although nonplanar cyclooctatetraene[37] are subject to question as they represent the limit of detection, errors on the order of ±0.5 kcal/mole being not uncommon in such a procedure. The numbers ($\Delta\Delta H_f^\circ$) in column four of Table Ia have been referred to as interaction energies[36] since they include both strain and aromaticity. Such numbers may or may not reflect the true aromaticity of a given π system but are at least reliably obtained from experimental data. The 24 kcal/mole value for the aromatic resonance energy of benzene calculated from the values in Table Ia is probably more accurate than the other numbers in this table since this molecule is relatively strain free. In general, however, this method of measuring aromaticity is difficult to apply since many of the most

Table Ia

Heats of Formation[a] and Interaction Energies[36] for Cyclic Olefins

Compound		ΔH_f° obs.[b]	ΔH_f° calc.[c]	Strain[e]	$\Delta\Delta H_f^\circ$[g]	D.E.[h]
cyclopentene	(19)	8.2	2.7	5.9	+5.5	-0.4
cyclopentadiene	(3)	31.9	26.5	6.0	+5.4	-0.6
cyclohexene		-1.1	-2.2	1.4	+1.1	-0.3
1, 3-cyclohexadiene	(10)	25.4	21.2	4.8	+4.2	-0.6
benzene	(4)	19.8	40.7[d]	3.0[f]	-20.9	-23.9
cycloheptene		-2.2	-7.2	5.4	+5.0	-0.4
1, 3-cycloheptadiene		22.6	16.3	6.6	+6.3	-0.3
cycloheptatriene	(5)	43.9	40.0	4.7	+3.9	-0.8
cycloöctene		-6.4	-12.1	6.0	+5.7	-0.3
cycloöctatetraene	(6)	71.1	52.9	17.1	+18.2	+1.1

Table 1a (Continued)

---

[a]All data are in kcal/g.f.w. for an ideal gas standard state at 1 atm, 298°K unless otherwise noted. The average error in all columns is ~±0.2 kcal/mole.

[b]Where more than one determination is reported, the value preferred by Cox and Pilcher[35] is reported.

[c]Calculated from the tables in Benson[36] for nonbenzenoid olefins.

[d]Calculated for hypothetical cyclohexatriene 16.

[e]Includes ring strain and an estimate of the nonbonded "cis" interaction, ~1 kcal/mole per cis.

[f]Ring strain assumed to be zero, 3 kcal = 3X value for cis nonbonded interaction.

[g]Interaction energy.[36]

[h]Empirical delocalization energy: $DE = \Delta\Delta H_f^\circ$ - strain.

Table Ib

pk_{R+}[a] and Aromaticity[b] in Cations

Compound	pK_{R+}	Strain[d]	$\Delta\Delta H_f$[e]	DE[f]	Ref.
cyclopropenyl (1c)	-7.4	54.0	-3.8	-57.8	19
allyl	-20.0	0	0	0	
cycloheptatrienyl (5c)	+4.8	4.7	-10.5	-15.2	
heptatrienyl	-18.0[c]	1.0	0	0	c

[a] pk_{R+} defined for $R^+ + H_2O \rightleftharpoons ROH + H^+$

[b] Note that this table, in contrast to Table Ia, uses the acyclic ion as the standard state.

[c] Based on a measured value of -20 for allyl and 1.0 for each additional π bond

[d] See Table Ia, note c.

[e] $\Delta\Delta H_f = \Delta H^\circ$ (cyclic) - ΔH° (acyclic) + $\Delta\Delta H_f^\circ$ (alcohols, cyclic - acyclic), a thermodynamic cycle.

[f] Empirical delocalization energy: DE = $\Delta\Delta H_f^\circ$ - strain.

Table Ic

pK_a[a] and Aromaticity[b] in Anions

Compound	pK_a	Strain[d]	$\Delta\Delta H_f°$[c]	DE[f]	Ref.
cyclopentadienyl (3a)	15	6.0	-4.1	-10.1	81
pentadienyl	35[c]	0	0	0	c
cycloheptatrienyl (5a)	36	4.7	15.7	11.0	81
heptatrienyl	34.5[c]	1.0	0	0	c

---

[a] pK_a defined for $RH + H_2O \rightleftharpoons R^- + H_3O^+$

[b] Note that this table, in contrast to Table Ia, uses the acyclic ion as the standard state.

[c] Based on a measured value of 35.5 for allyl - 0.5 for each additional π bond.

[d] See Table Ia, note c.

[e] $\Delta\Delta H_f° = \Delta H°$ (cyclic) - $DH°$ (acyclic) + $\Delta\Delta H_f°$ (hydrocarbons, cyclic - acyclic)

[f] Empirical delocalization energy: DE = $\Delta\Delta H_f°$ - strain.

interesting potential aromatics cannot be prepared in sufficient quantity for accurate analysis (approximately one gram for heats of combustion) and present other experimental difficulties even when available since they rarely burn cleanly. Use of the more easily determined heats of hydrogenation[38] to compounds for which accurate heats of combustion are known is one way around this latter difficulty for neutral systems. For cations the pK_{R+}[86] and for anions the pK_a on the MSAD scale[80] (Tables Ib and Ic) can be used to give a rough estimate of the heat of formation of these species based on appropriate standards. At present, however, the direct calculation of ΔH_f° for a standard state charged species is not possible due to an absence of the volume of data such as was available for the neutral hydrocarbons.

Since aromaticity is a function of cyclic conjugation of π electrons, perhaps some measure of electronic properties will provide a suitable empirical definition of aromaticity. In this direction considerable use has been made of the fact that benzene is strongly diamagnetic[40] in the presence of an applied magnetic field while nonplanar cyclooctatetraene is not.[41] In general, all monocyclic π systems are predicted by Hückel theory to possess relatively high energy excited states, especially if significantly stabilized as is benzene, and be diamagnetic.[42] On the other hand, a 4n π system contains two partially occupied degenerate nonbonding orbitals in the simple Hückel treatment (vide spura). Jahn and Teller[45] have shown that such systems should distort geometrically to remove this degeneracy, thereby

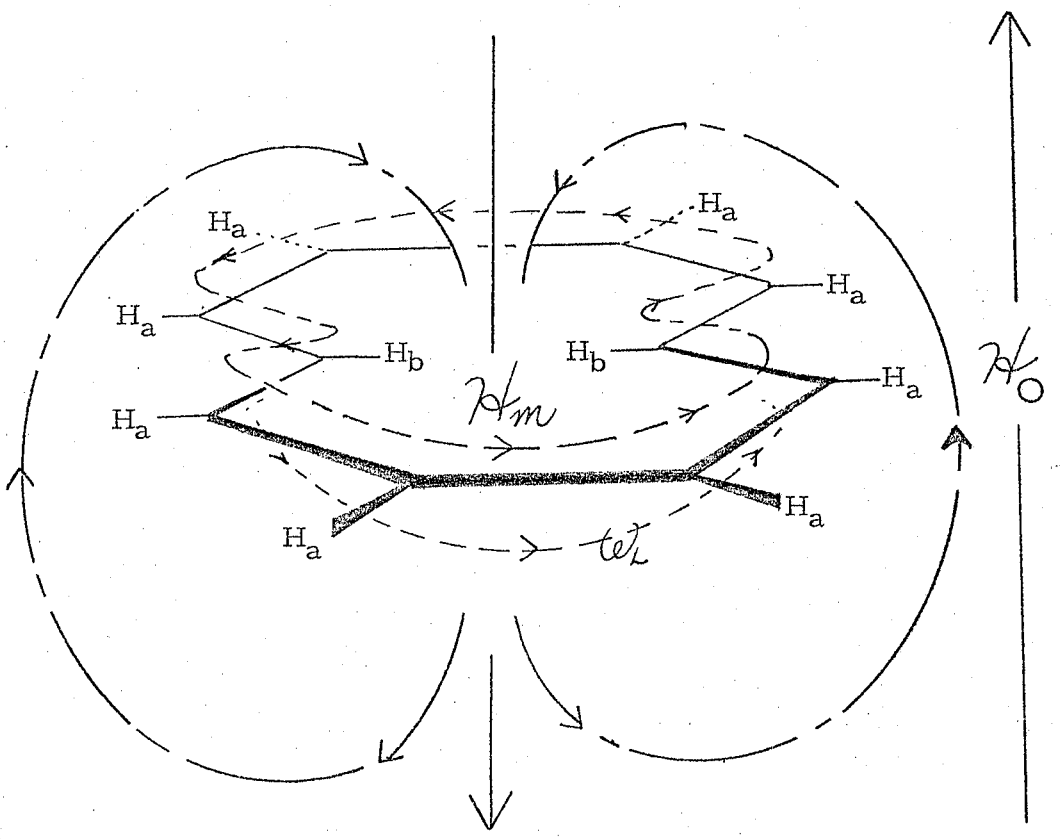


Figure V

Induced Diamagnetism

(--➤-- Larmor flow of electrons, ω_L; H_o the applied magnetic field, H_m the induced molecular field, —·➤· the magnetic lines of force.)

lowering the total π energy (neglecting pairing energy). Thus, in this first order treatment, 4n π electron systems are predicted to have unpaired electrons or low energy electronic transitions accessible through magnetic dipole interaction and be appreciably paramagnetic in an applied magnetic field.[43] H. J. Dauben[46] has used the empirical magnetic susceptibility exaltation defined as the difference between the measured susceptibility and that calculated for the appropriate localized cyclopolyene standard state by the bond equivalent method of Haberditzl[47] very successfully as an experimental indication of the extent and type of aromatic character. (Selected examples of measured and calculated magnetic susceptibilities for neutral monocyclic conjugated systems are presented in Table II.) These measurements confirm that 4n π electron cyclic systems do indeed have appreciable paramagnetic character. When corrected for the area of the cyclic system, such measurements give a quantative as well as a qualitative indication of the extent of aromatic delocalization.

Pople[48] recognized that such induced molecular magnetic fields would have a great effect on the chemical shifts of protons in the nmr spectrum. The diamagnetic ring current should shield the protons inside the ring (H_b in Figure V) causing them to resonate at much higher field strength than an ordinary olefinic proton and to a lesser extent deshield the outer protons since the field density will be less outside the ring than inside. Predominant paramagnetism, on the other hand, should cause outer protons to resonate at high field and inner protons at very low field.

Table II

Magnetic Susceptibility Exaltation Data[46]

(in units of -10^{-6} cm^3 mol^{-1})

Compound	χ_M[46]	$\chi_{M'}$[47]	Λ[a]
benzene (4)	54.8	41.1	13.7
cyclohexadiene (10)	48.6	49.3	-0.7
cyclopentadiene (3)	44.5	38.0	6.5
cycloheptatriene (5)	59.8	51.7	8.1
cycloöctatetraene (6)	53.9	54.8	-0.9
[16]-annulene (8)	105	110	-5
pentafulvene (22)	43	41.9	1.1
heptafulvalene (24)	94	92	2
furan (11)	43.1	34.2	8.9
pyrrole (12)	47.6	37.4	10.2
thiophen (13)	57.4	44.4	13.0

[a]Exaltation, $\Lambda = \chi_M - \chi_{M'}$, experimental corrected for a calculated standard. A large positive difference implies enhanced diamagnetism and thus aromaticity.

(Selected examples of measured chemical shifts for neutral and charged conjugated systems together with some appropriate reference compounds are presented in Table III.) The consistency of the chemical shifts of the inner and outer protons of the 4n and 4n+2 π-electron systems with the expectations of the ring current theory discussed above is remarkable. Although the theory has been subjected to some serious questioning,[50] it remains the only explanation which fits all the data collected thus far.[51]

Calculation of the expected nmr chemical shift of an appropriate localized standard state is far more difficult than similar estimations for the standard states in the other criteria of aromaticity proposed. The chemical shift is not only a function of charge distribution but also is quite sensitive to steric effects as well. It is for this reason that the magnitude of the chemical shift has not often been used as an indication of the extent of aromaticity but only of the type, i.e., aromatic (diatropic), non-aromatic (atropic) or antiaromatic (paratropic).[32(g)] Perhaps advantage could be taken of Salem's prediction[43] that introduction of exomethylene groups into cyclic systems effectively destroys the cyclic delocalization, introducing bond alternation and poly-olefinic character. In this way we would be able to synthesize standard states for nmr measurements of aromaticity. For example, 1, 4-dimethylene-2, 5-cyclohexadiene[55] (17) would be an appropriate nmr standard for the cyclic delocalization in benzene as would 1, 2-dimethylenecyclobutene[56] (18) for the elusive cyclobutadiene.

Table III

Nuclear Magnetic Resonance Data

A.

Hydrocarbons	τ[a]	Solv.	Temp. (°C)	Ref.
benzene (4)	2.66	$CDCl_3$	35°	49
cyclohexadiene (10)	4.37 (H_b)	CCl_4	35°	52
cycloöctatetraene (6)	4.32	CCl_4	35°	52
"planar COT" (21)	5.38 (H_b)	$CDCl_3$	35°	28
[16]-annulene (8)	4.60 (H_a)	CS_2/CD_2Cl_2	-120°	53
	-0.43 (H_b)			
[18]-annulene (9)	0.72 (H_a)	THF-d_8	-60°	54
	12.99 (H_b)			
dimethylene-cyclohexadiene (17)	4.90 (H_a)	THF-d_8	-80°	55
	4.57 (H_b)			
dimethylene-cyclobutene (18)	5.43, 5.32 ($H_{a,b}$)	CCl_4	35°	56
	3.30 (H_c)			
pentafulvene (22)	4.22 (H_a)	CCl_4	35°	61
	3.89 (H_b)			
	3.56 (H_c)			
linear polyene	3.87	CCl_4	35°	49

Table III (Continued)

B.

Cations	τ^a	Solv.	Temp. (°C)	Ref.
cyclopropenium (1c) $C_3H_3^+SbCl_6^-$	-1.1	CH_3CN or SO_2	-20°	21
cyclopentadienyl (3c) $C_5H_5^+SbF_6^-$	ground state triplet	SO_2ClF	-60°	62
cycloheptatrienyl (5c) $C_7H_7^+BF_4^-$	0.3	CH_3CN or SO_2	-30°	63
[16]-annulenium (8) dication $(FSO_3^-)_2$	0.5 (H_a) 14-15 (H_b)	SO_2	-80°	(32g)
cyclopentenyl (19c) $C_5H_7^+SbF_6^-$	1.53 (H_a) -0.99 (H_b) HMO avg. 0.62	SO_2ClF	-60°	64

C.

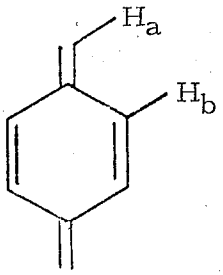
Anions	τ^a	Solv.	Temp. (°C)	Ref.
cyclopentadienyl (3a) $C_5H_5^-K^+$	4.66	THF-d_8	35°	65
cyclooctatetraenyl (6a) $C_8H_8{=}2K^+$	4.3	THF-d_8	35°	27
cyclononatetraenyl (7a) $C_9H_9^-K^+$	2.96	THF-d_8	35°	66
[16]-annulenyl (8) $C_{16}H_{16}{=}2K^+$	0-1 (H_a) 17 (H_b)	THF-d_8	35°	32(g)
[18]-annulenyl (9a) $C_{18}H_{18}{=}2K^+$	10 (H_a) -21 (H_b)	THF-d_8		32(g)

Table III (Continued)

C. Continued

Anions	τ[a]	Solv.	Temp. (°C)	Ref.
pentadienyl (20a) $C_5H_7^-K^+$	5.9 (H_a)	$THF-d_8$	35°	67
	7.0 (H_c)			
	HMO avg. 6.2			

[a] τ values referred to TMS at τ 10.0, see illustrations in text for the identity of H_a, H_b, etc.



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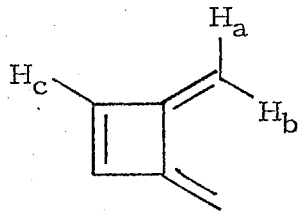

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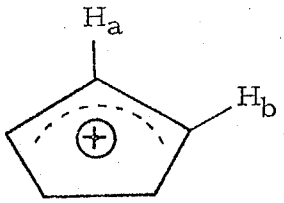
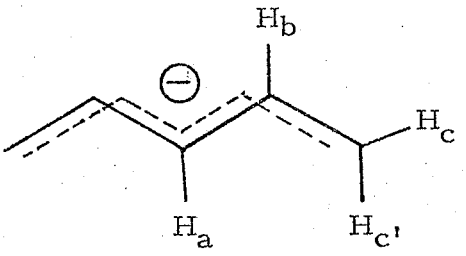
Conceivably such standard states could correct for strain in the smaller annulenes as well as the often severe effects of nonbonded interactions in the interior of the larger annulenes. However, since these molecules are usually highly reactive and difficult to synthesize, advantage has not been taken of this suggestion. The standard state which has been employed[49] is the chemical shift of the internal protons of the long chain linear polyenes (3.87τ). The reasonableness of this assumption lies in the fact that as m approaches 30 in the [m]-annulenes, all the criteria of aromaticity so far discussed approach that of the linear polyene;[32(g)] therefore nonaromaticity can be defined in the limit. This standard state cannot be used for the aromatic cations and anions due to the fact that the charge tends to localize more at the ends of the chain. Hence, the charged cyclic systems should be compared to the average chemical shift of the protons on a linear odd carbon-number ion. In Table III, due to the absence of nmr data for most acyclic cations and anions, I have used the average chemical shift (as determined by a Hückel-type weighting method[63]) of the

cyclopentenyl cation[64] (19c) and the pentadienyl anion (20a) as representative of standard localized systems.



19c



20a

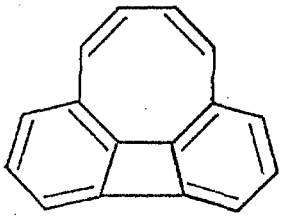
Perhaps in light of the above discussion it would be easier to first define a nonaromatic molecule as one whose collective properties could be regarded as additive functions of individual bond properties.[59] An aromatic molecule in the broadest sense then would be one whose physical properties are not additive functions of localized bonds but which exhibits anomalous stability, geometry and an ability to support closed molecular currents of electrons as a result of cyclic delocalization. This empirical definition of aromaticity (or antiaromaticity,[32(h)] vide supra) could equally well be applied to cations, anions and radicals (although the latter will always be paramagnetic). It is clear that while such systems may not possess comparable absolute stabilities or nmr chemical shifts, some property or standard state might exist which would allow comparison of such differently charged systems with each other and with neutrals. The Van Vleck paramagnetism correction for positive charge for example is small

($\sim 8 \times 10^{-6}$ cm^3 mol^{-1} or roughly 10% of the total susceptibility[46]). Thus, comparison of the exaltation criteria for the aromaticity of cations and neutrals seem to be possible with this correction term included. For this reason, the preferred measure of aromatic character for all systems together would be the diamagnetic susceptibility exaltation supplemented by nmr chemical shift data which would show the charge distribution and some thermochemical measurement ($\Delta\Delta H_f^\circ$, pK_{R+}, pK_a) of the relative stability of the species. It is unfortunate therefore that more susceptibility data have not been published, especially for charged systems, or that the additivity method of Haberditzl has not been sufficiently calibrated with nonaromatics to include charged systems and heterocycles in the calculation.

Prediction of Aromatic Stabilization

From the preceding discussion it is clear that no true empirical measure of aromaticity is possible without some theoretical estimation to isolate that part of a given property due to cyclic delocalization of electrons from that due to conjugation of the type seen in linear polyenes. In fact, to keep such a distinction from bordering on the absurd requires a clear definition of the standard cycle as one which possesses the same geometry and bond hybridization as the compound in question but with localized double bonds, in other words, one of the Kekulé resonance forms. But from the point of view of resonance theory, cyclic delocalization in all conjugated cycles should be a stabilizing factor, decreasing the potential energy of the system by allowing each electron to be in a field of effectively greater positive charge. Thus, while the above empiricism yielded many alternative and perhaps related ways of measuring aromaticity in cyclically conjugated compounds, it provided no clear understanding of why benzene is so different from cyclobutadiene or cycloöctatetraene. One might argue that if aromatic stabilization is as small as 20 kcal/mole in the most aromatic neutral molecule, then strain in a four-membered ring and in a planar eight-membered ring might well keep us from seeing any aromaticity in their thermodynamic criteria. Were these the only examples of cyclically conjugated molecules, one might well dismiss aromaticity altogether as a general phenomenon. But the work of Professor Sondheimer and others[32(g)] has amply

shown that the diamagnetic anomaly exhibited by benzene is present in 4n+2 π electron cycles as large as n = 7 ([30]-annulene) and the paramagnetism seen in Wilcox's[25] planar eight-membered ring in 21 (Table III) is seen in 4n π electron systems up to n = 6 ([24]-



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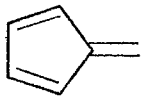
annulene). While less work has been possible on the thermodynamic properties of these higher annulenes due to their reactivity, some recent results from the Sondheimer laboratory on protonated macrocyclic ketones[68] show that aromatic stabilization in a 15-membered ring cation (4n+2, n = 3) is worth 3 kcal/mole whereas aromatic destabilization in a 13-membered cation (4n, n = 3) may be at least 1.4 kcal/mole. This near complete vindication of the Hückel 4n+2 rule together with its ability to rationalize the magnetic properties of the annulenes has led in at least one instance to a suggestion that aromaticity be defined based on the closed shell concept.[69]

The 4n+2 rule provides a qualitative determination of aromaticity. It would be nicer, if a Hückel closed shell is to be used as the theoretical definition of aromaticity, to have the theory predict

both qualitatively and quantitatively the aromaticity to be expected of a given system. One of the central assumptions of HMO theory is that the Coulomb integrals α_i are equal for all atoms of the same type and have values characteristic of the atomic orbital, independent of the molecule.[60] For alternate conjugated molecules, Coulson and Rushbrooke[70] have shown that the charge densities at all atomic centers are the same. For the nonalternate monocyclic, totally symmetric ions the same is true when occupied by $4n+2$ π electrons, as for example in the cyclopentadienyl anion, cycloheptatrienyl cation, etc. However, for all other nonalternate systems and those containing heteroatoms the unequal charge distribution may drastically change α_i from one carbon to another. The simple HMO treatment of these systems is not self-consistent, and the molecular orbital levels produced may give an erroneous full shell prediction. More elaborate iterative methods are required to achieve a stable charge distribution. These have been discussed by Dewar[33] and applied to the prediction of aromatic stabilization in conjugated molecules.[71]

The aromatic delocalization energies calculated by Dewar using a Pople-type self consistent field MO approach show an excellent correlation with the experimental criteria of aromaticity of a large variety of cyclic olefins. For example, fulvene[61, 72] (22) and heptafulvene[57, 58] (23) are both predicted by HMO theory to possess closed shells with appreciable resonance energy (1.47β and 1.99β respectively). However, neither of these molecules is aromatic by any empirical criterion.[73] Dewar's resonance energies for these



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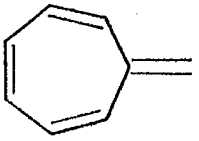


23

compounds are small and correctly predict their nonaromaticity (Table IV). Dewar can account for antiaromaticity as well. His value of 18 kcal/mole for the resonance destabilization energy of rectangular cyclobutadiene compares favorably with Breslow's estimation of this value.[74] However, as Hess and Schaad[75] have demonstrated, the failure of HMO delocalization energies to correlate with experimental criteria of aromaticity is as much a function of the standard state employed as any inherent inaccuracy of the method. When a standard state containing all the appropriate olefinic interactions of cyclic polyenes was calculated by a bond additivity technique, equally good qualitative and quantitative prediction of experimental criteria was obtained for HMO π energies as was obtained using Dewar's PPP-SCF-CI methods even in non-alternate systems. (See Table IV.). D'Amore[76] has extended Hess' method to include odd number π-center (cation, anion, or radical) systems with good experimental correlation. Quantitatively the two methods do not agree. But it should be remembered that Dewar is calculating interaction energies since he uses acyclic olefins as the

Table IV

Theoretical Predictions of Aromaticity in Monocyclic Systems

Compound	π Resonance Energy		
	Dewar[a] (kcal/mol)	Hess[b] (β)	D'Amore[b] (β)
cyclopropenyl anion (1a)	+35.9		-1.27
cyclopropenyl cation (1c)	-42.3		+0.73
cyclobutadiene (2)	+18 (+34[c])	-1.07	
cyclopentadienyl anion (3a)	-30.2		+0.66
cyclopentadienyl cation (3c)	+16.8		-0.58
benzene (4)	-20	+0.39	
cycloheptatrienyl anion (5a)	+5.7		-0.28
cycloheptatrienyl cation (5b)	-21.4		+0.64
cycloöctatetraene (6)	+2.5	-0.48	
[16]-annulene (8)	+2.8	-0.18	
[18]-annulene (9)	-3.0	+0.22	
pentafulvene (22)	-1.0	-0.01	
heptafulvene (23)	-0.5	-0.02	

[a]Ref. 33, PPP-SCF-MO, linear conjugated standard state.

[b]Ref. 75 and 76, Hückel vs. calculated localized cyclic standard state, β negative.

[c]Square singlet geometry.

standard state whereas Hess's numbers should relate directly to π-electron delocalization or aromaticity.

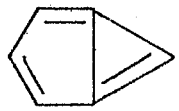
A Current Interest

I am interested in the aromaticity exhibited by certain planar bicyclic nonbenzenoid hydrocarbons (Figure VI). These compounds, formed by the fusion of two conjugated rings such that no more than two atoms are common to both rings, offer an opportunity to study several interesting questions fundamental to an understanding of the concept of aromaticity. To what extent are Hückel predictions accurate for these systems? What is the importance of a filled lone nonbonded level to the Hückel closed-shell argument? To what extent are these systems peripherally conjugated, or are they to be considered by their component rings? In other words, what is the effect of the introduction of transannular bonding (ℓ, m-dehydroaromaticity[77] where ℓ and m are not adjacent, i.e., $\ell \geq m+2$) into an aromatic $4n+2$ π electron or antiaromatic $4n$ π electron monocyclic ring? What is the relative importance of ring strain and aromaticity in these systems?

To a first approximation Platt[78] considers the perturbation caused by the dehydro ℓ, m-σ bond to be small, introducing no appreciable change in the molecule (neglecting strain) other than assuring coplanarity. Thus, a monofused (bicyclo-) system is predicted to be aromatic if it contains $4n+2$ π electrons on its perimeter. The number of systems for which this seems to be true is indeed remarkable. Thus, naphthalene[79] (35) and azulene[80] (36) are well known aromatic 10-π electron systems (vide infra and Table V). The indenyl anion[81] (34a) has also been extensively

25
(1, 3)-[4]

28
(1, 4)-[6]



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(1, 3)-[6]

26
(1, 3)-[5]

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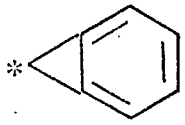
b, * = .
c, * = +



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(1, 3)-[7]

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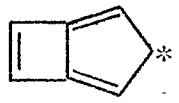

30
(1, 4)-[7]

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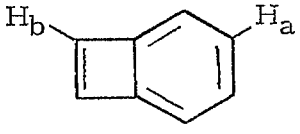
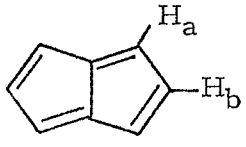
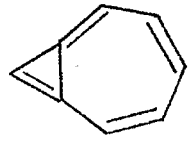
b, * = .
c, * = +



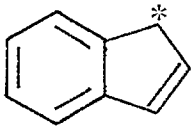
31
(1, 4)-[8]



32
(1, 5)-[8]

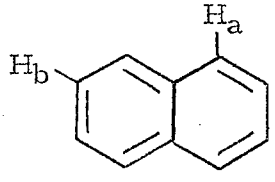


33
(1, 3)-[8]

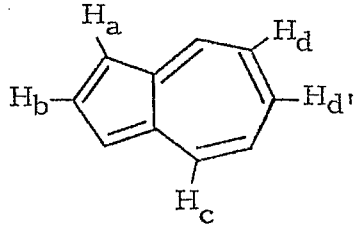


34
(1, 5)-[9]

a, * = -
b, * = .
c, * = +



35
(1, 6)-[10]

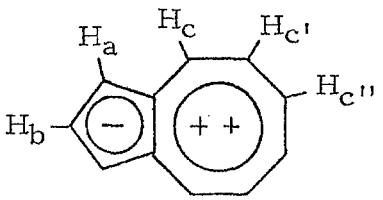


36
(1, 5)-[10]

Figure VI

(ℓ, m)-[n]-Dehydroaromatic Systems

investigated and shown to possess properties characteristic of aromaticity. A (1, 5)-dehydro[11]annulenium ion 37c, a 10-π electron system, has been prepared as a stable tetrafluoroborate salt,[82] and an argument could be made for its aromaticity based on an nmr spectrum (Table V). Often the "acid test" of whether or not



BF_4^-

37c

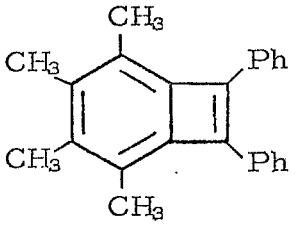
the properties assigned to a class of compounds have anything to do with aromaticity come from extending the compounds to greater numbers of π electrons. In this direction it is interesting to look at two of Professor Sondheimer's dehydroannulenes. Bicyclo[9.3.0]-tetradeca-1, 5, 7, 11, 13-pentaene-3, 9-diyne (38), a 14-π electron analogue of azulene, has been prepared as a resonably stable dark green solid whose nmr shows that the compound is aromatic in the same way as azulene. The similarity even reaches to the chemical behavior of 38 since this compound can be reversibly extracted from organic solvents with strong acid.[83] Recently Cresp and Sondheimer prepared a (1,14)-dehydro[26]annulene 39.[84(a)] While certainly more aromatic than [26]annulene,[84(b)] the compound was

Table V

^{1}H NMR[a] Criteria of Aromaticity in Unsaturated Bicyclic Hydrocarbons

I. Dehydro [8] annulenes

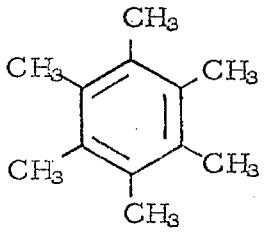
(1, 4):



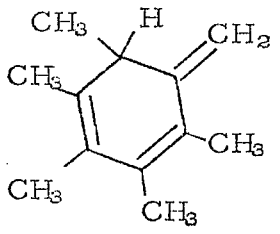
40

2, 3, 4, 5-tetramethyl-7, 8-diphenyl benzocyclobutadiene (40)

methyl τ 8.07[88(a)]



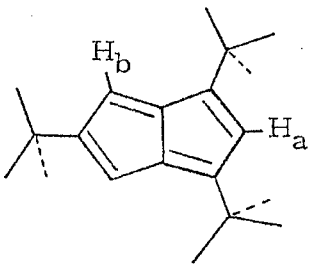
standard aromatic methyl τ 7.77[88(b)]



standard nonaromatic methyl τ 8.25[88(c)]

(1, 5):

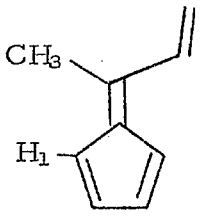
1, 3, 5-tri-t-butylpentalene (41)



41

H_a τ 4.93 H_b τ 5.28[89(b)]

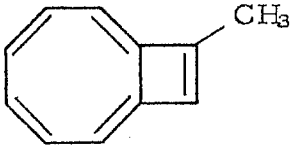
Table V (Continued)



standard nonaromatic H_1 τ 3.60[94]

II. Dyhydro [10] annulenes

(1, 4):



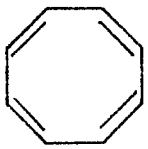
45

9-methylcyclobutadienocycloöcta-tetraene (45)

methyl τ 7.52 (d)[93]

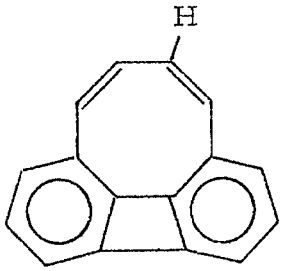
cyclobutadienyl τ 2.34 (q)

cycloöctatetraenyl τ 3.88



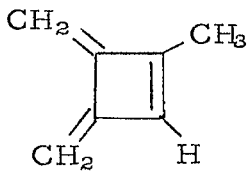
6

standard nonaromatic cycloöcta-tetraenyl τ 4.32[52]



21

standard quasi-aromatic cyclo-öctatetraenyl τ 5.38[28]



standard nonaromatic

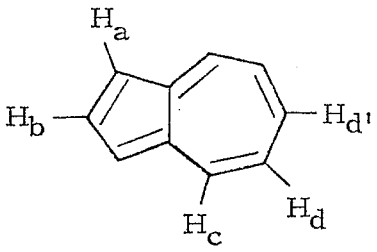
methyl τ 8.12

cyclobutadienyl τ 3.30

Table V (Continued)

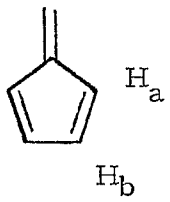
(1, 5):

Azulene (36)



36

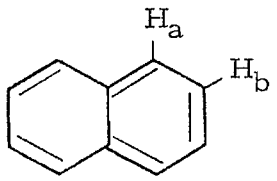
H_a τ3.8[80(c)]
H_b τ3.3
H_c τ3.0
H_d τ3.7-4.5



H_a τ3.9[61]
H_b τ3.6

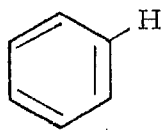
(1, 6):

Naphthalene (35)

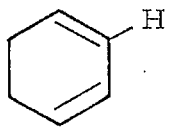


35

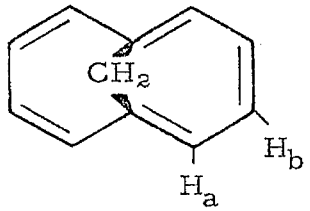
H_a τ2.23[79(b)]
H_b τ2.58



standard aromatic H τ2.66[49]

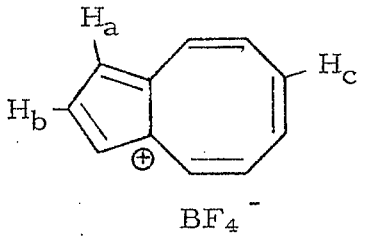
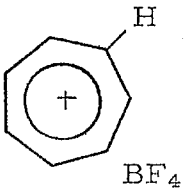
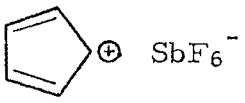
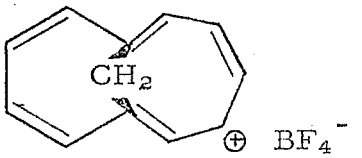


standard nonaromatic H τ4.4

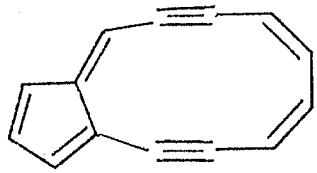


aromatic [10] annulene H_a τ, H_b τ } 2.8[85(b)]

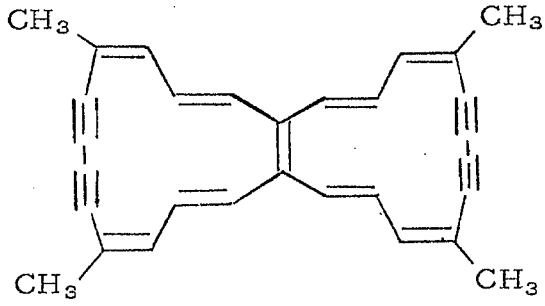
Table V (Continued)

(1, 5):	Dehydroannulenium ion (37c)
 37c	$H_{a,b}$ τ4.12[82] H_c τ2.72
	standard aromatic H τ0.3[63]
	standard antiaromatic - evidently a ground state triplet[62]
	aromatic 10-π cation ring protons τ0.4-1.7[95] methylene bridge τ11

[a]NMR reported in τ with internal standard TMS at 10.0τ.



38

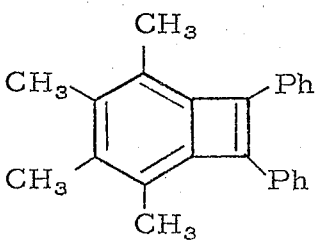


39

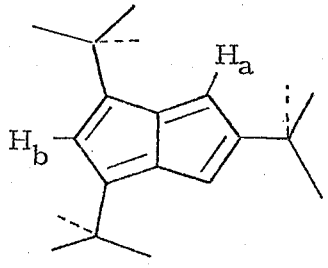
less aromatic than a [14]annulene alone. This is totally analogous to naphthalene (35) which is more aromatic than [10]-annulene but less so (per π center) than benzene by even the nmr criterion.[85]

In a similar fashion, the introduction of transannular bonding into 4n π systems leaves systems which are still nonaromatic or antiaromatic. The smallest 4n system for which bicyclic analogues have been prepared is [8]annulene. Benzocyclobutadiene (31) has been trapped in the four-membered ring as a Diels-Alder adduct

with cyclopentadiene;[86] and as in the case of cyclobutadiene, its iron tricarbonyl complex has been isolated.[87] These facts point to the existence of high lying occupied bonding orbitals and hence non-aromaticity in 31. More recently a diphenyltetramethylbenzocyclobutadiene 40 has been synthesized[88(a)] which shows an upfield shift of 0.30 τ for the aromatic methyls compared to a hexamethyl benzene standard,[88(b)] interpreted as increased paratropicity in the benzene ring due to fusion to a four membered ring. Pentalene, bicyclo[3.3.0]öctatetraene (32), has also been the subject of much attention. The first simple pentalene, 1-methylpentalene, dimerized at -140°C.[89(a)] Tri-t-butylpentalene (41) on the other hand is a stable compound.[89(b)] However, its nmr (Table V) shows what may be paratropicity compared to appropriate standards, and thus anti-aromaticity is predicted for the parent. The 10-π electron dianion of pentalene is easily isolated and apparently aromatic.[90] This is entirely analogous to the case of cycloöctatetraene (vide supra).

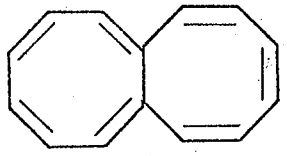


40



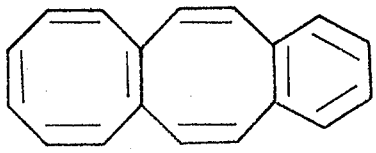
41

That this approach may be oversimplified is evident from the case of the 14-π electron bicyclic octalene 42. Although the parent bicycle in this series has not been synthesized, a benzo-annelated



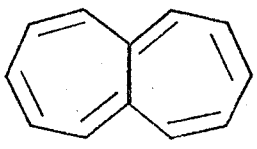
42

derivative 43 is available.[91] This molecule has terminal cyclo-öctatetraene proton signals in the same position as cycloöctatetraene



43

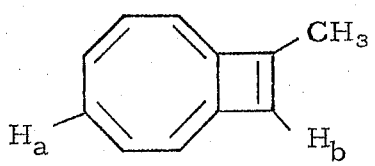
itself and a uv spectrum entirely similar to benzocycloöctatetraene. Hence, it is a polyene similar to heptalene 44, a (1, 7)-dehydro-[12]-annulene.[92] However, like cycloöctatetraene, 42 is not



44

expected to be planar, any aromaticity to be gained probably would not be sufficient to overcome strain in such a conformation.

So far, if we consider dipolar resonance forms as well as the neutral representations, we could have reached a correct prediction of aromaticity from consideration of each component ring in the bicyclic systems. As Professor Garratt points out,[32(e)] there are any number of systems, mostly benzenoid at least in part, which behave magnetically as if ring currents were localized in component rings. However, there is one example where two fused 4n systems make together an apparently stabilized, aromatic 4n+2 bicycle, that of (1, 4)-dehydro[10]annulene or cyclobutadienocyclooctatetraene. Here, a 9-methyl derivative 45 has been synthesized and shows substantial downfield shifts in its nmr[93] (Table V). Of



45

the other compounds pictured in Figure VI (25-30) little is known. Since such properties as were found for 45 should be enhanced in the smaller systems (neglecting strain) due to the fact that such molecules should find it difficult to avoid conjugation and the empirical observation that the effect we call aromaticity is larger

for the smaller systems, synthetic efforts aimed at these molecules have been initiated.

Examination of the Hückel molecular orbital diagrams for the molecules in Figure VI shows that the perturbation on an aromatic cycle brought about by transannular σ-bonding can either stabilize or destabilize the 4n+2 π electron system but that such a perturbation on an antiaromatic 4n π electron cycle invariably stabilizes the system. Dewar[96] has applied the perturbational molecular orbital (PMO) treatment to these fused systems. While only strictly applicable to alternate systems, he predicts that (1, 3), (1, 5), (1, 7), etc., π interactions will have no effect on the total π energy, whereas (1, 4), (1, 8), (1, 12), etc., will destabilize and (1, 6), (1, 10), (1, 14), etc., will stabilize the cyclic 4n+2 π system. (Illustrated in Figure VII.) This effect reaches its maximum in the (1, 4)-dehydrotropyl system 30 where the 6π electron cation 30c and the 8π

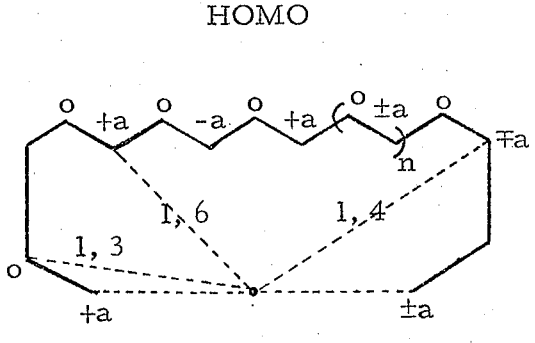


Figure VII

Interaction of Odd-Alternate Hydrocarbon Radicals[96]

electron anion 30a are predicted to be equally stabilized by aromaticity (see Table VI). Thus, although strain will probably cancel some of this, it would be interesting to compare systems such as 27 with 28, 29 with 30 and 32 with 33 to test this theoretical picture.

Table VI

Theoretical Predictions of Aromaticity
in Bicyclic Systems

Compound	Dewar[33, 96] (kcal/mole)	Hess[75] (β)	D'Amore[76] (β)
Bicyclobutadiene (25)	+16[a]	-0.40[b]	
1, 3-Dehydrobenzene (27)	+6.0	+0.34	
1, 4-Dehydrobenzene (28)	-6.4	-0.40	
1, 3-Dehydrotropyl (29)			
1, 4-Dehydrotropyl (30)			+0.11[c]
Benzocyclobutadiene (31)		-0.22	
Pentalene (32)	-6.5	+0.14	
1, 3-Dehydro COT (33)			
Naphthalene (35)	+30.5	+0.55	
Azulene (36)	+4.2	+0.23	

[a]SCF-CI, linear olefin standard state, no strain correction.

[b]Calculated from an estimated localized bicyclic standard state, no strain correction.

[c]Calculated from an estimated localized bicyclic standard state, all reasonable resonance forms given equal weight and an average taken, no correction for strain.

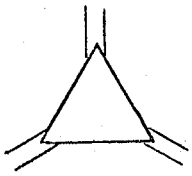
Strain and Aromaticity

The strain energy of a highly branched or cyclic compound can have meaning only by reference to some standard state which is arbitrarily assigned zero strain. Benson[36] takes the unbranched, acyclic hydrocarbons as the reference state since their measured heats of formation follow the additivity rules so well. Thus, the strain energy of a compound can be estimated as the difference in the measured heat of formation and the value calculated for it by the group additivity method. This is precisely the same definition we discussed for the thermodynamic aromatic resonance stabilization. It was pointed out at that time that these values are more properly referred to as interaction energies and that to isolate either the resonance or the strain energy from them requires an independent estimation of one or the other. Since I am most interested in calibrating the theoretically predicted aromaticity in strained systems, I would prefer a reasonable approach to strain energy estimation.

Strain in a cyclic polyolefin is composed primarily of C-C-C angle strain (deviation from sp^2 120° angles decreases σ overlap or forces rehybridization to higher energy states) which is a function solely of the σ electron framework. Thus, although resonance is sensitive to strain through distortion of the optimal π geometry, any method which separates σ from π electrons

effectively separates strain and resonance. (Distortion from planarity can often relieve strain but always at the expense of π delocalization. This is of course the major reason for nonplanarity in 4n π systems such as cycloöctatetraene where π delocalization is minimal, providing no stabilization or perhaps even destabilization. However, the bicyclic systems which are the goal of the work reported in this thesis will find it difficult to distort from planarity. As in the case of cyclobutadiene,[12] these compounds must resort to bond alternation to minimize antiaromaticity but retain virtually the same strain.) Dewar[33, 97] has developed a method which calculates the σ framework (PNDO) and gives strain energies in good agreement with experimentally determined values for this quantity in bicyclic saturated hydrocarbons where resonance is not a large factor. Ideally, this method could be applied to the σ framework of a conjugated molecule given certain geometric restrictions and, by comparison to the appropriate unstrained conjugated hydrocarbon, give strain energies separate from delocalization (interaction) energies. Alternatively, one might be able to calculate the σ framework strain directly using force field parameters such as those developed for saturated systems by Allinger[98] and employed for the strain estimation of bicycloalkanes by Boyd.[99] However, neither of these approaches, to my knowledge, has been applied to bicyclic conjugated olefins although both look promising.

This approach ignores another source of strain in cyclic conjugated olefins, that of nonbonded repulsion between the π-electrons across the ring. Such an interaction should be larger for small rings but its magnitude relative to angle strain is hard to estimate. For the larger rings the nonbonded repulsions between hydrogens forced to be in the interior of conjugated cycles is important as well. Perhaps some measure of this van der Waals strain could be obtained from the measured versus calculated heats of formation of the exo-methylene compounds discussed earlier as standard states for the magnetic properties of the annulenes together with a σ calculation of the angle strain as discussed above. Since π-type cyclic delocalization should not be important for these systems, requiring the loss of at least one π bond, such compounds provide ideal standards for separating strain from resonance in many π systems. Unfortunately, the heat of formation of molecules such as fulvene 22, heptafulvene 23, dimethylenecyclobutene 18, and 1,4-dimethylenecyclohexadiene 17 are unknown, the compounds being thermally unstable. But it is evident from Dewar's calculations that such an approach should be applied with caution in any case. Due to alteration of the σ framework Dewar shows[97] what appears to be 33 kcal/mole less strain in a calculated 3-radialene 46 compared to a calculated triafulvene 47. A similar approach to the estimation of strain in the compounds in Figure VI would require such compounds as 48, 49 and 50. Here, however, the compounds themselves are as yet unknown.



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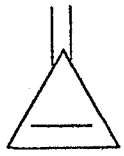

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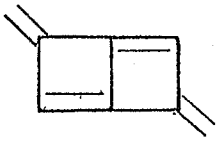

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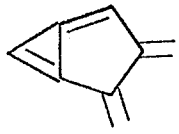

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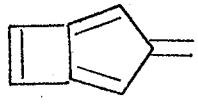
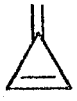
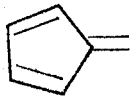


50

We are thus forced to crudely estimate strain by analogy to the well known measured (ΔH_f° exp - ΔH_f° calc.) strains of cyclic saturated hydrocarbons and cyclic monoolefins. These as well as the estimated values in parentheses are given in Table VII. Boyd[99] compared the strain energy calculated for bicyclo[m.n.0]-alkanes with those obtained by simple addition of the individual strains of the component monocyclic hydrocarbons. He found reasonably good agreement except in cases with fused three-membered rings where the strain was overestimated. If we apply the same treatment to the bicyclic olefins, a crude estimation of the strain might be obtained. Table VIII lists values obtained in this way together with measured bicyclic saturated hydrocarbon

Table VII

Measured and (Estimated) Strain Energies in Cyclic Hydrocarbons

Compound	Strain (kcal/mole)[a]	Ref.
	27.5	35
	53.8 52.6 53.3	35 33 36
	(40) 41	33 36
	(82.3)	97
	26.5	35
	30.0	35
	(50) (32)	100
	6.2	35
	5.7	35
	(2.4)	36
	(6.9)	35

[a] ΔH_f° (g) measured - ΔH_f° (g) calculated according to Benson[36].

Table VIII

Measured and (Estimated) Strain Energies in Bicyclic Hydrocarbons

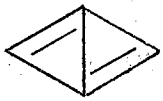
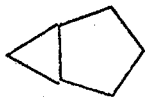
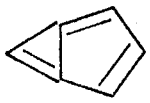
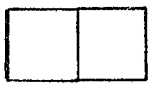
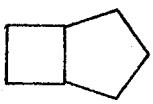
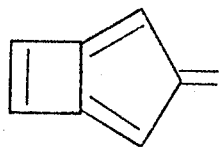
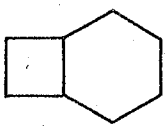
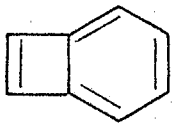
Compound	Strain (kcal/mol)	Ref.
	65.2 (55.0)[a]	35 99
	(106) (99)	97
	32.3 (33.7)	35 99
	(56)	
	(53.0)	99
	(76) (58) (62)	100 33 35
	(32.7)	99
	(58) (40)[b] (36)[c]	100 33
	26.6 (26.5)	35 99

Table VIII (Continued)

Compound	Strain (kcal/mol)	Ref.
	(50) (32)	100 33

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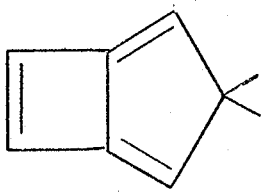
[a]Estimated by simple addition of the strain energies of the compound rings.

[b]Cyclobutadiene + fulvene.

[c]Cyclobutene + fulvene.

values. The values predicted for bicyclobutadiene 25 and bicyclohexatriene 28 are probably the most in error of the compounds written. However, if anything they appear to be too low instead of too high as in Boyd's case.[99] On the other hand, Dewar[97] has carried out SCF-MO calculations for 25 which predict, quite surprisingly, that this molecule should be stable although very reactive. His estimation of the interaction energy of 82 kcal/mole for 25 makes the strain estimate of 100 kcal/mole not too unreasonable with 18 kcal/mole π resonance energy. D'Amore[76] placed the strain energy of 48 at >51 kcal/mole based on the required exothermicity of its subsequent thermal rearrangement to ethynylcyclopentadiene. Since the introduction of one sp^2 center into a five-membered ring is a small perturbation,[33] this value is in good agreement with the first of the above estimations for 49.



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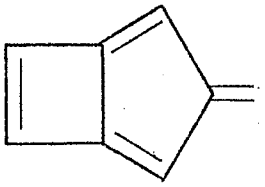
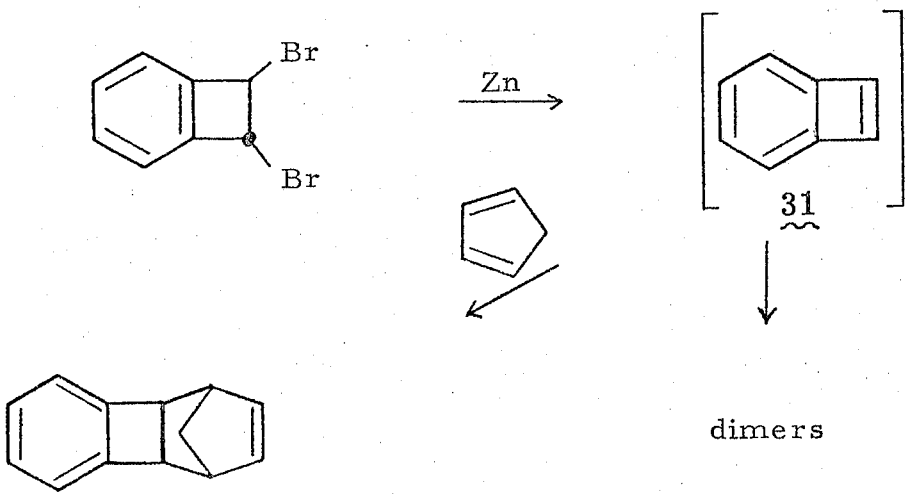


49

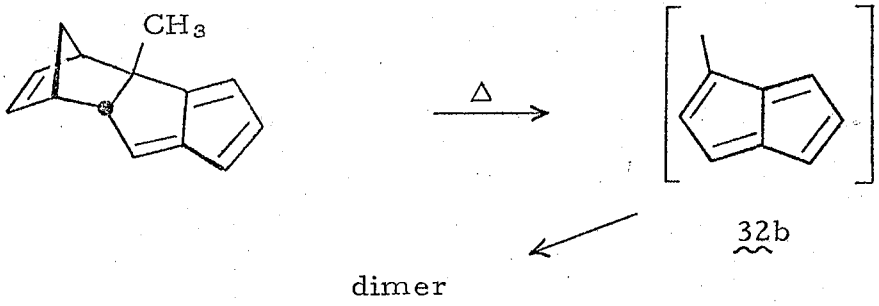
Synthesis of Potentially Aromatic Strained Systems

Many of the systems represented in Figure VI are potentially very reactive as well as thermodynamically unstable. Proposed synthetic routes must necessarily take this into account. High heats of formation of starting materials and considerable specificity

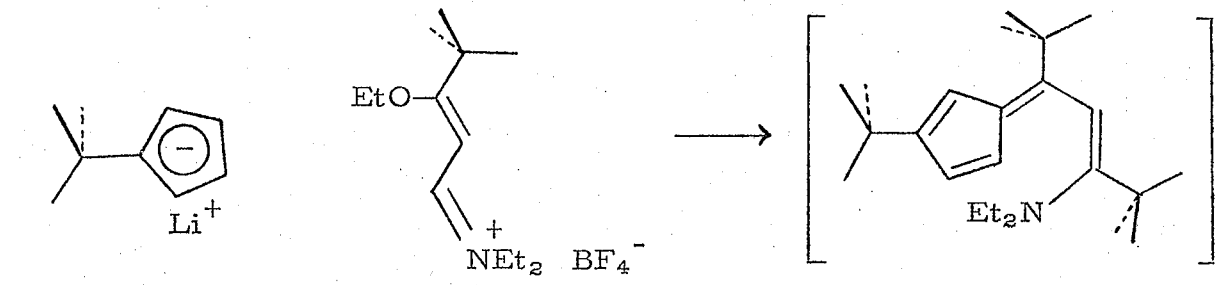
of reaction are two requirements in any synthesis of highly strained, perhaps even conjugatively destabilized molecules. The approach to benzocyclobutadiene is typical of most syntheses of such systems. After initial unsuccessful attempts at synthesis of 31 by Wilstätter and Veraguth,[101] H. F. Finkelstein[102] found benzocyclobutadiene as a reactive intermediate from the reaction of 1, 2-dibromobenzocyclobutene with zinc. Cava and Mitchell trapped this intermediate as a Diels-Alder adduct in the same reaction.[86(a)] An elimination route,

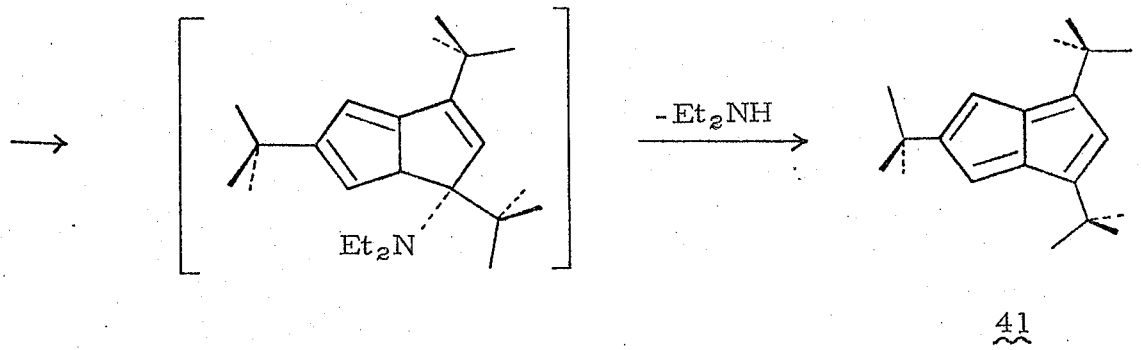


however, suffers from the disadvantage of requiring either strong base or producing Lewis acids (e.g., $ZnBr_2$) which catalyze polymerization of the products. Hence, unsubstituted pentalene was too reactive to be synthesized by such route. One successful approach to a 32 system involved a retro Diels-Alder reaction[89(a)] which has the advantage of having no strong reagents present to add back to 32. The stable 1, 3, 5-tri-t-butylpentalene, on the other hand, was formed by a cyclization-elimination route;[89(b)] but



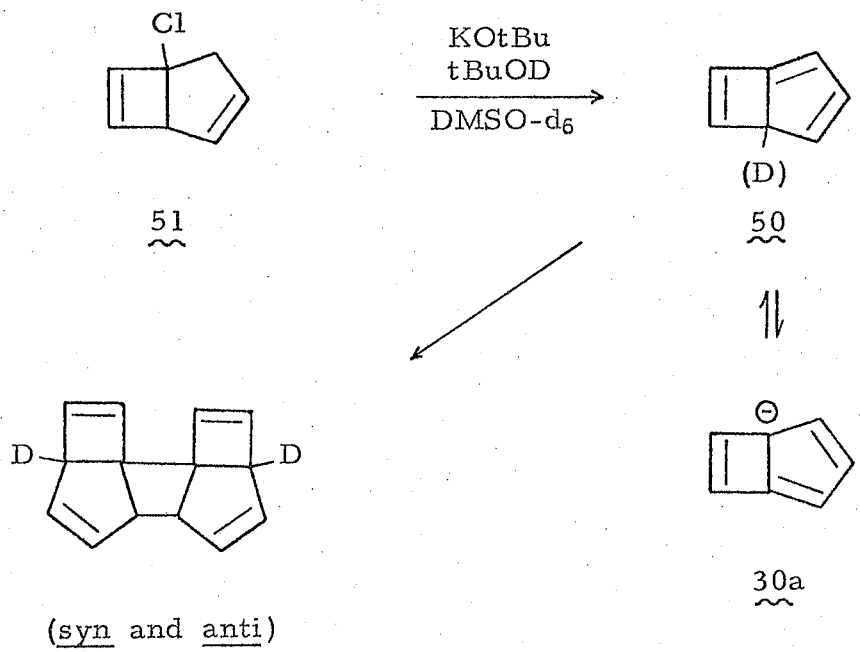
the t-butyl groups in this molecule probably impede the approach of the secondary amine for readdition as well as disfavoring the addition product which accounts for the elimination occurring in the first place.



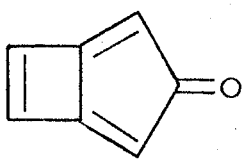


41

Breslow's group at Columbia has extensively investigated elimination routes to some of the compounds in Figure VII as well as possible hydrocarbon precursors. The hydrocarbon 50 was evidently prepared by elimination of HCl from 51 with strong base. The only products isolated were dimeric but these contained deuterium which was taken as evidence of the formation of a transient 30a.[103] More recently Breslow reported the synthesis of

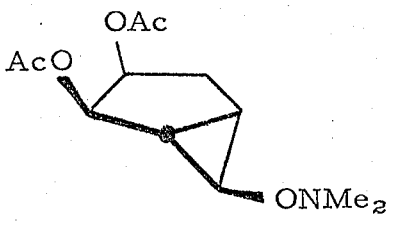


a small amount of the very reactive ketone 52 by a similar route. He was able to obtain an nmr at -48°C; but in the basic medium (Et_3N or KOtBu, tBuOH) employed, the trienone signals disappeared on warming to -10°C.[104] Routes based on hydrohalide eliminations have also been reported for the bicyclic species 27 and 28. McGriff[105] stated that pyrolysis of the dimethylamine oxide 53 led



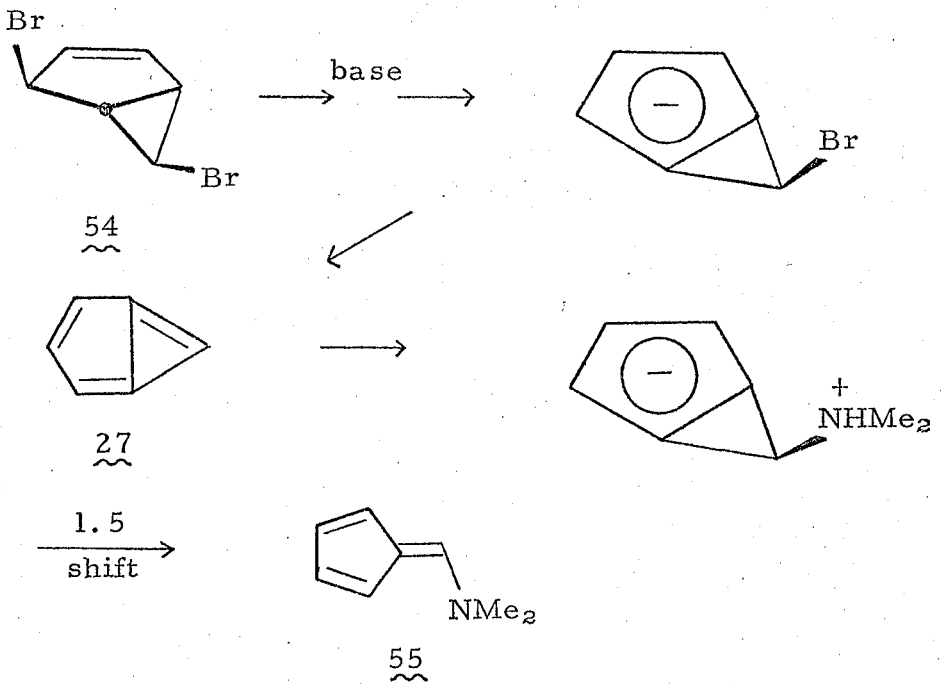
52

only to an intractable polymer and no adduct could be obtained from a monomeric C_6H_4 species. Washburn[106(a)] has reported on

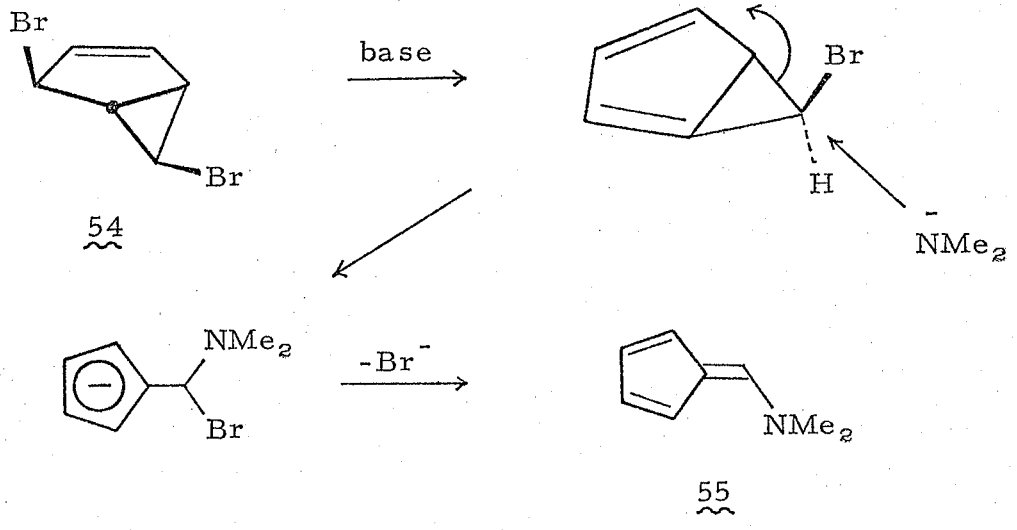


53

the base treatment of the dibromide 54 which gives 6-N, N-dimethylaminofulvene 55 in dimethylamine solution, a reaction in which it is conceivable that 27 is an intermediate (Mechanism I). However, Grohman[106(b)] has suggested that 55 could also arise from nucleophilic ring opening of the strained cyclopropane ring of the first elimination product from 54 based on an analogy to his work on bromospiro[2.4]heptadienes (Mechanism II). But since aminofulvenes are known to be the thermally stable products isolated from the thermal rearrangement of a number of isomeric

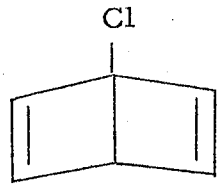


Mechanism I



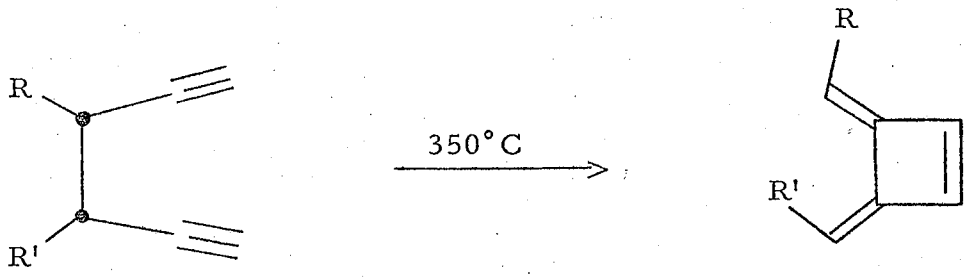
Mechanism II

nitrogen-containing cyclic olefins,[107] their presence cannot be taken as evidence of the nature of the trapped intermediate, except that it is electrophilic. Breslow has also reported a similar route to a 28 species by elimination of HCl from the chlorodewarbenzene 56.[108] Here readdition occurred to an intermediate to give a dimethylaminodewarbenzene which was trapped. (For a discussion of this reaction see page 82.)



56

Since many of the most interesting systems in Figure VI possess the dimethylene cyclobutene moiety (18), I was attracted by the high yield, stereospecific pyrolytic rearrangement of 1,5-hexadiyne (57) to dimethylenecyclobutene discovered jointly by Huntsman and Wristers[109] and by Coller, Heffernan and Jones.[110] This rearrangement possesses several advantages over most other routes to introduce unsaturation in strained ring systems. The reaction is highly stereospecific and presumably concerted. The high heat of formation of the acetylenes drives the reaction, presumably making strained rings energetically accessible. Furthermore, the reaction appears to be unimolecular and proceeds at a reasonable rate in the gas phase, introducing all the strain and



57: R = R' = H

58: R = R' = CH_3

18: R = R' = H

59: R = R' = CH_3

unsaturation in one step. The flow tube pyrolysis apparatus used by Huntsman lends itself to low temperature trapping of the products as they are swept out of the reaction zone. Hence, very reactive and unstable products can be isolated. Thus, I felt that systems designed to allow the Huntsman rearrangement would provide easy access to molecules such as the 1, 4-dehydrobenzene 28 as well as precursors to such systems as the 1, 4-dehydrotropyl 30. These are illustrated in Figure VIII. Prior to the start of my work, D'Amore and Bergman[111(a)] reported that 1-methyl-1, 2-diethynyl-cyclopropane (64) gave a clean yield of 2-methylbicyclo[3.2.0]-hepta-1, 4, 6-triene (65) upon gas phase pyrolysis. This result was particularly gratifying in light of Breslow's triene 50 which dimerized. In this connection it is also interesting to note that Sondheimer discovered a reaction in solution which is entirely similar to that proposed above. Production of the very labile

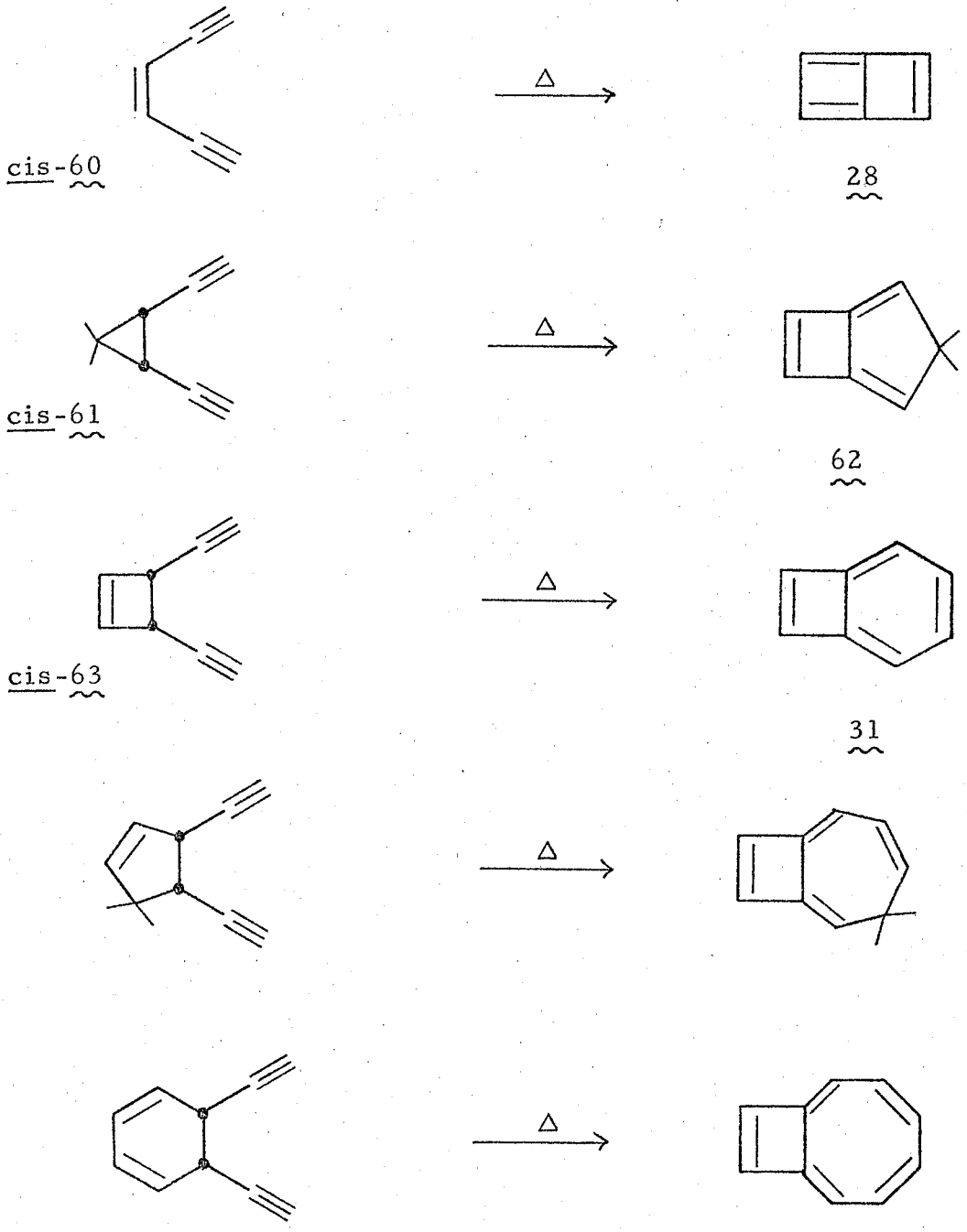
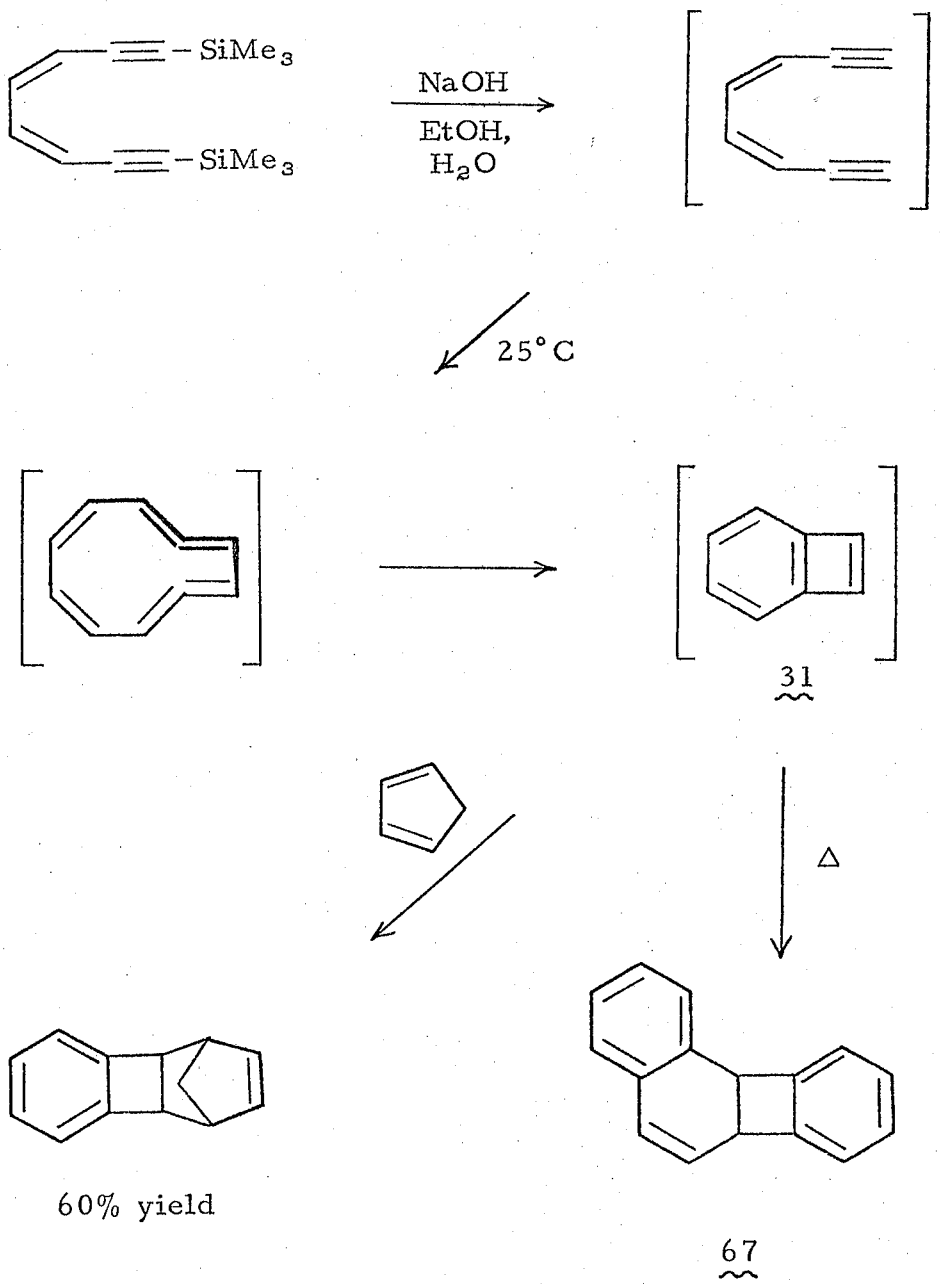


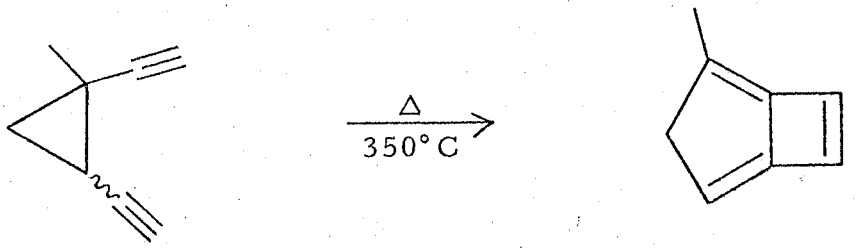
Figure VIII

Generation of Bicyclic Systems via the Coller-Huntsman Rearrangement[109, 110]



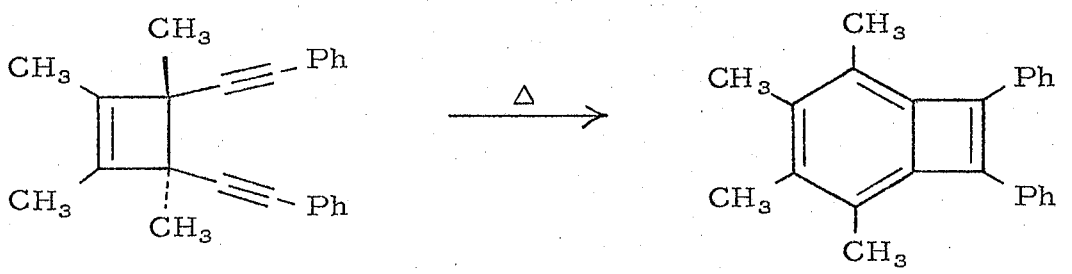
60% yield

67



64 65

1, 7-octadiyn-3, 5-diene 66 from hydrolysis of the 1, 7-bis(trimethylsilyl) derivative at room temperature gave the dimer 67. When this reaction was carried out in the presence of cyclopentadiene, a 60% isolated yield of the trapped benzocyclobutadiene was obtained.[112] However, no attempt to carry this reaction out in the gas phase was possible considering the approach. But that such a route would probably produce an nmr observable concentration of 31 at low temperature is seen from Straub's pyrolysis of the diphenyltetramethyl derivative of 63 at 110°C to give an nmr observable concentration of 40.



40

PART I

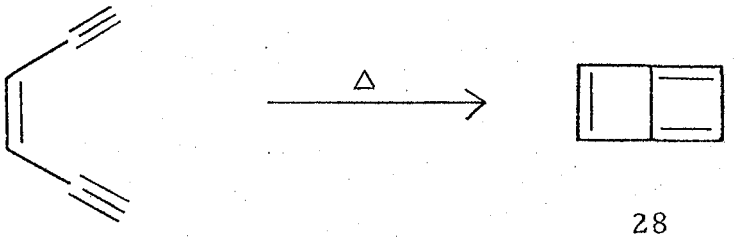
1, 4-Dehydrobenzene

(para-Benzyne or Butalene)

Introduction

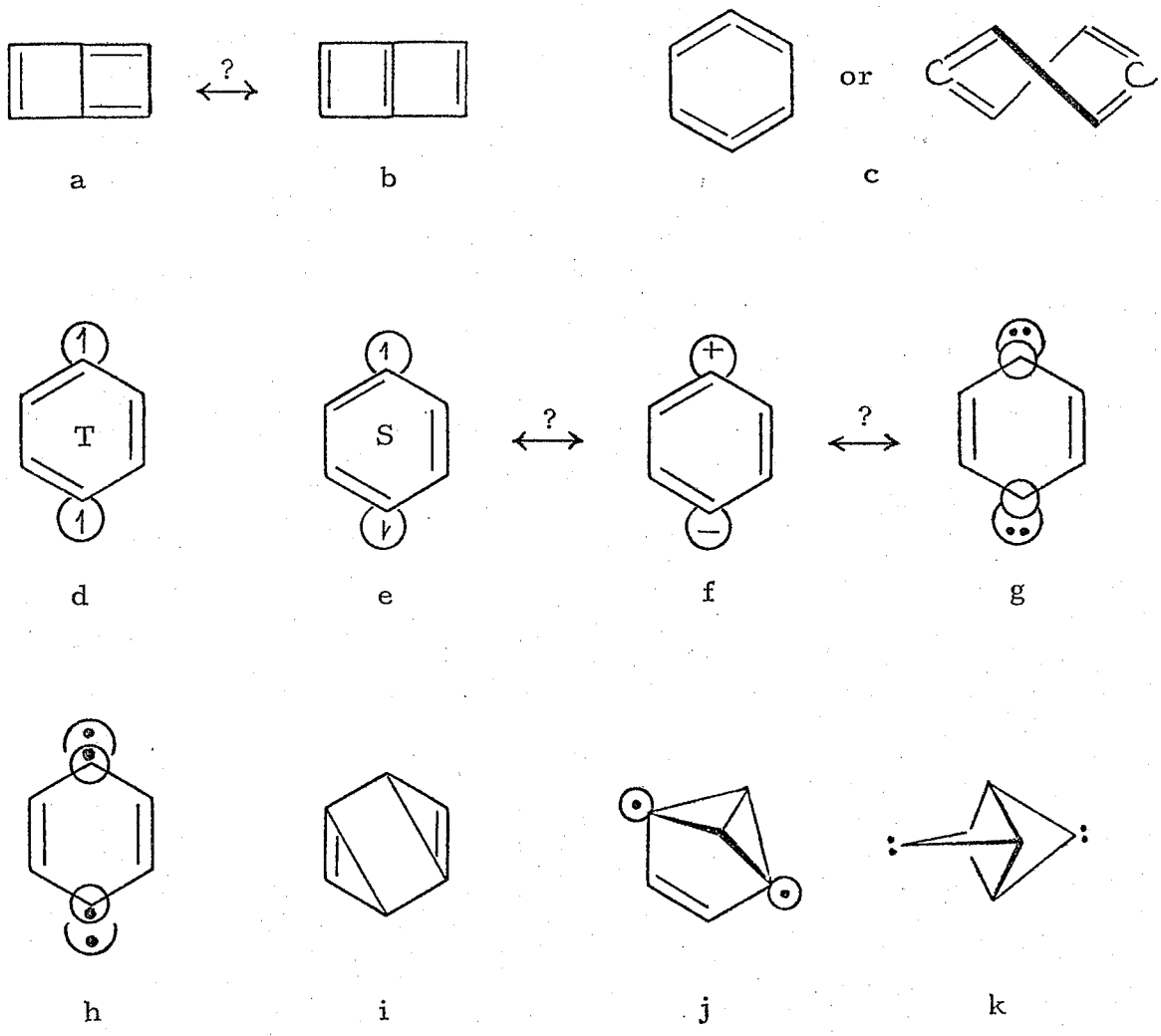
Background

If cis-1, 5-hexadiyn-3-ene (cis-60) undergoes a thermal rearrangement similar to that of the diethynylcyclopropanes[111] (64) or 1, 5-hexadiyne[109, 110] (57), one might expect formation of the theoretically interesting 1, 4-dehydrobenzene 28. This species has



cis-60 28

been indexed in Chemical Abstracts since circa 1950 under the names para-benzyne, p-didehydrobenzene, bicyclo[2.2.0]hexa-1, 3, 5-triene, butalene and 1, 4-phenylene. Several alternative structures for the product of such a rearrangement are possible. These are pictured in Figure IX; that they are not all equivalent is clear.[113] Structures 28a and 28b may be thought of as contributing resonance forms of a singlet para σ-bonded benzene or as localized, perhaps equilibrating, structures similar to those proposed for cyclobutadiene.[114] Models show that while a planar bisallenic structure is indistinguishable from a biradical 28e or a bis-carbene 28g, the nonplanar structure pictured is clearly defined. Structure 28d is a triplet benzenoid σ biradical and 28e is the corresponding singlet. Structures 28f and 28g can be resonance forms of 28e but are



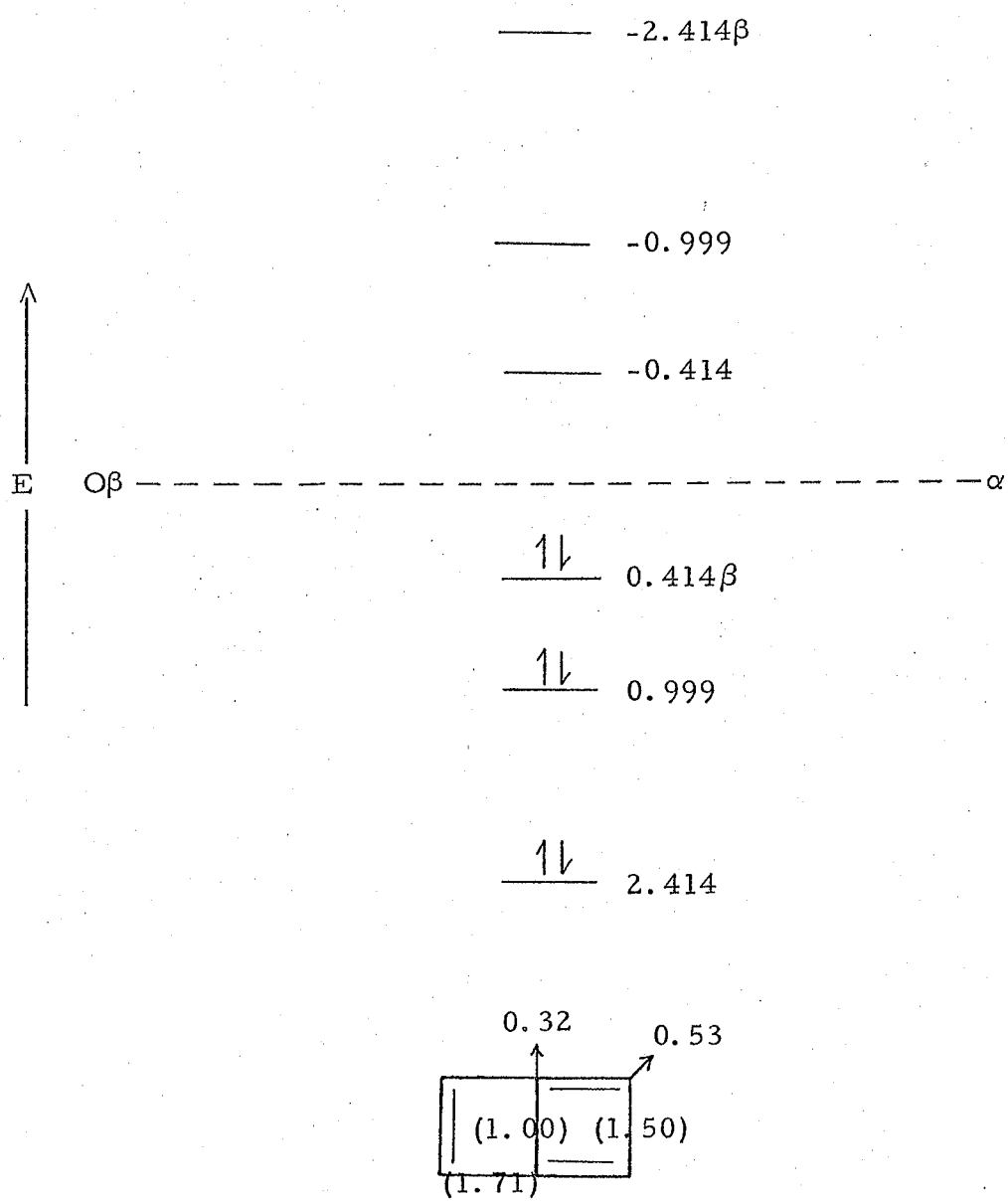
28

Figure IX

Some Possible Structures for 1, 4-Dehydrobenzene

probably of higher energy. Only if they possess different geometry due to electron pairing will they be distinct species. Structure 28g represents a bis-singlet-carbene which sacrifices benzene resonance energy, while structure 28h is a pentriplet with four unpaired spins. Structures intermediate in spin between 28f and 28g are also possible. The name butalene most clearly applies to structures 28a-c, while the term p-benzene correlates most clearly with structures 28d-h. The only feature structures 28i-k possess in common with 28a-h is that the dehydrocenters are 1, 4 disposed. In this thesis I shall use the more systematic name 1, 4-dehydrobenzene to refer to all species 28. While the generation and subsequent chemistry of 1, 2-dehydrobenzene (o-benzyne or simply benzyne) has been the subject of much recent investigation,[77, 115] very little has been reported on the other dehydrobenzenes.

The first reference to a 1, 4-dehydrobenzene system was by Roberts, et al.,[116] who calculated for the bicyclohexatriene structure 28a(b) an HMO delocalization energy of 1.66β and low free valene (Figure X). It is interesting that this first order treatment predicts a zero π-bond order between carbons 1 and 4 thus favoring 28a over 28b. The Hückel treatment also gives a closed shell and hence a prediction of aromatic stabilization for 28a. However, Hess[75] using a more realistic standard state predicted an HMO π electron (REPE) of -0.07β making 28a almost as antiaromatic as planar cycloöctatetraene (REPE -0.06β) but at the same time far more aromatic than cyclobutadiene (REPE -0.27β). Dewar's semiempirical SCF-MO methods[33] support Hess's Hückel



Total π energy 7.657β

Figure X

HMO Treatment of Butalene [28a(b)][116]

(Bond orders in parenthesis; free valency represented by →)

numbers predicting a resonance energy of -6.5 kcal/mole for 28a and -18 kcal/mole for cyclobutadiene compared to +20 kcal/mole for benzene.

Since 28a may contain approximately 25 kcal/mole less resonance energy than benzene[33] and nearly 80 kcal/mole more strain[100] (see also Tables VI and VII), 28a and 28e may be comparable in energy despite the fact that 28e contains one fewer σ-bonds. Benson's thermochemical estimations[36] allow a reasonable approximation of the heats of formation of these species. The heat of formation of cis-60 can be reliably estimated by the group equivalent technique to be +126 kcal/mole. A similar calculation for 28a using a 6.5 kcal/mole resonance destabilization and 80 kcal/mole strain predicts a heat of formation of +130 kcal/mole for butalene. For the 1, 4-benzenediyl structure 28e(d) a heat of formation may be estimated by addition of two phenyl C-H bond energies to the heat of formation of benzene after correction for the bond energy of H_2. This gives a ΔH_f° of +140 kcal/mole for 28e(d) assuming that there is no appreciable interaction of the radical centers so generated. To help answer this question, Hoffmann and Imamura[113] have carried out extended Hückel calculations on the 1, 4-benzenediyl 28e(d) and found important through-bond coupling which places the antisymmetric nonbonding combination orbital below the symmetric (Figure XI). If this picture is correct, it provides for some degree of 2, 3 σ-bond stabilization making the +140 kcal/mole an upper limit for the heat of formation of 28e(d), assuming that the benzene π system remains pretty much intact.

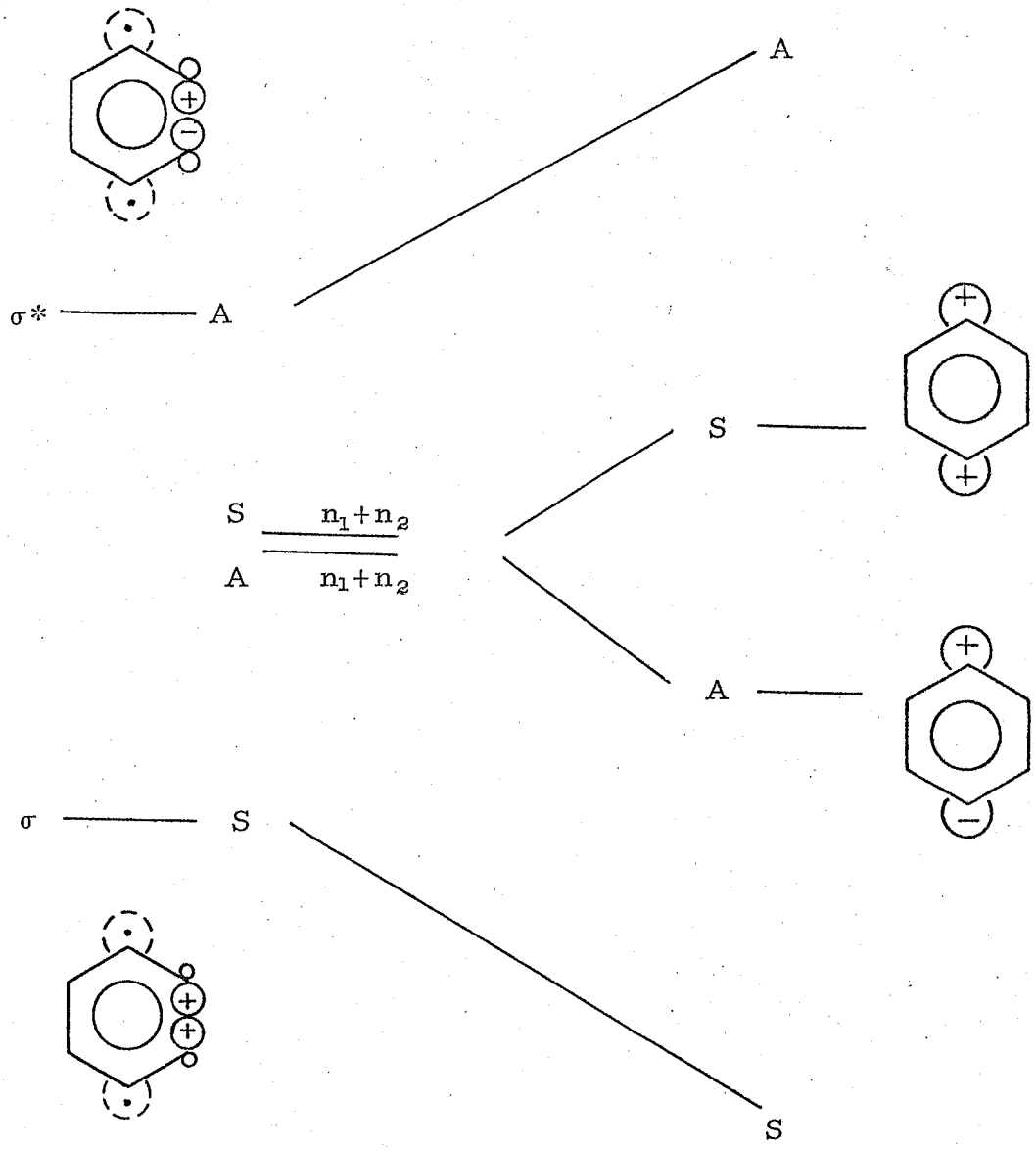


Figure XI

Interaction Diagram for the Nonbonded Orbitals in para-Benzyne, 28d, e[113]

A similar ordering (A below S) was calculated[113] for the 1,8-dehydronaphthalene diradical for which Rees and Storr[117] have found an apparently concerted, stereospecific 2+2 cycloaddition as predicted for an antisymmetric ground state. Wilhite and Whitten[118] have confirmed this predicted ordering of combination orbitals in para-benzyne with an ab initio SCF calculation which also predicts that the triplet state 28d will be more stable than the singlet. Evidently the splitting is not enough to overcome the pairing energy and hence Hund's rules are not obeyed. Wilhite and Whitten's calculations which included configuration interaction (CI, mixing of excited states into the ground state wavefunction) also predict that ionic terms such as that describing 28f are not very important to the singlet ground state description. However, all these calculations were performed essentially at the equilibrium geometry of benzene; and since the splittings between these levels are small, a slight variation in geometry might reorder the symmetric and antisymmetric combination orbitals.

Klaus Mueller[119] has kindly provided us with some initial geometry-optimized ab initio calculations (Figure XII) on 1,4-dehydrobenzene. These also show that for 28d,e the triplet state is lower in energy than the singlet and that the antisymmetric combination orbital is below the symmetric. Furthermore, he predicts a minimum ΔH_f° of 120 kcal/mole for the triplet at an internal angle of 140° at the dehydrocenters. These energies seem quite reasonable in the light of the above thermochemical estimations. Most recently Dewar[120(a)] has published full

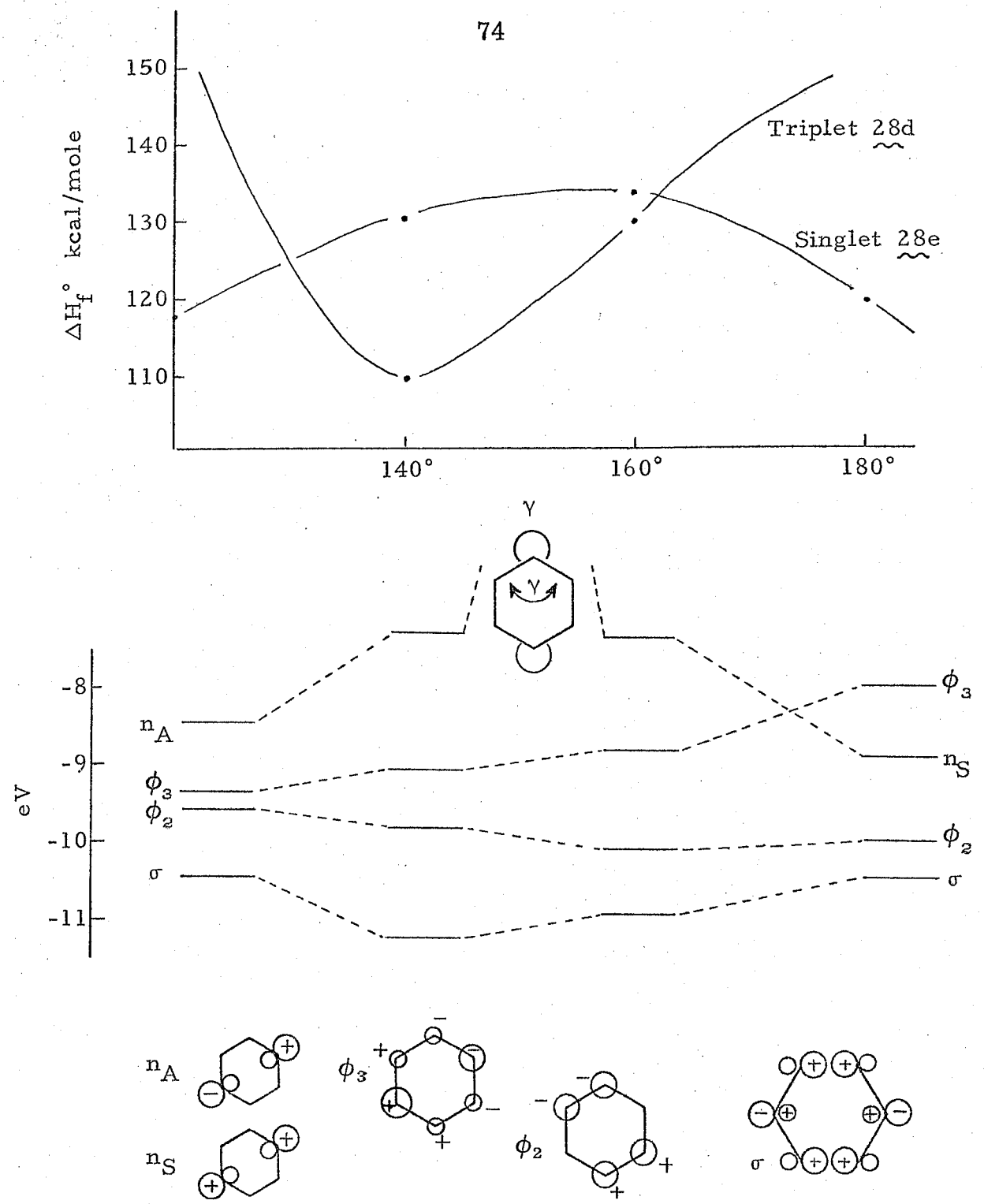


Figure XII

Geometry Optimized SCF-MO for 1, 4-Dehydrobenzene[119]

geometry optimized semiempirical PPP-SCF-MO (MINDO/3) calculations for all the benzynes. His results for 1, 4-dehydrobenzene are summarized in Figure XIII. Without configuration interaction he predicts that triplet 28d will be 11 kcal/mole more stable than the singlet 28e in agreement with the above predictions. However, when excited state configurations are included the singlet 28e is now predicted to be the more stable state by 6 kcal/mole. But since MINDO/3 is not parameterized for CI, this 6 kcal/mole really only says that as with Dewar's calculations on cyclobutadiene,[120(b)] the singlet and triplet are of comparable energy. What is perhaps most interesting about these latest estimations is that both 28a and 28e are predicted to be energy minima differing by as little as 19 kcal/mole with only a 4.6 kcal/mole activation barrier for conversion of 28a into the more stable 28e. This small a barrier is clearly at variance with Hoffmann's prediction of an antisymmetric (1, 4 σ-antibonding) ground state for 28e. Further discussion as to which if any of these predictions are correct and their interrelation is best deferred until later. But it is clear from even a brief examination of these results that some 1, 4-dehydrobenzene species should be accessible from the cis-1, 5-hexadiyn-3-ene (cis-60).

A Brief Review

The first attempt to generate a 1, 4-dehydrobenzene (28) reported in the literature seems to be that of Fischer and Lossing.[121] When these workers pyrolyzed 1, 4-diodobenzene (66)

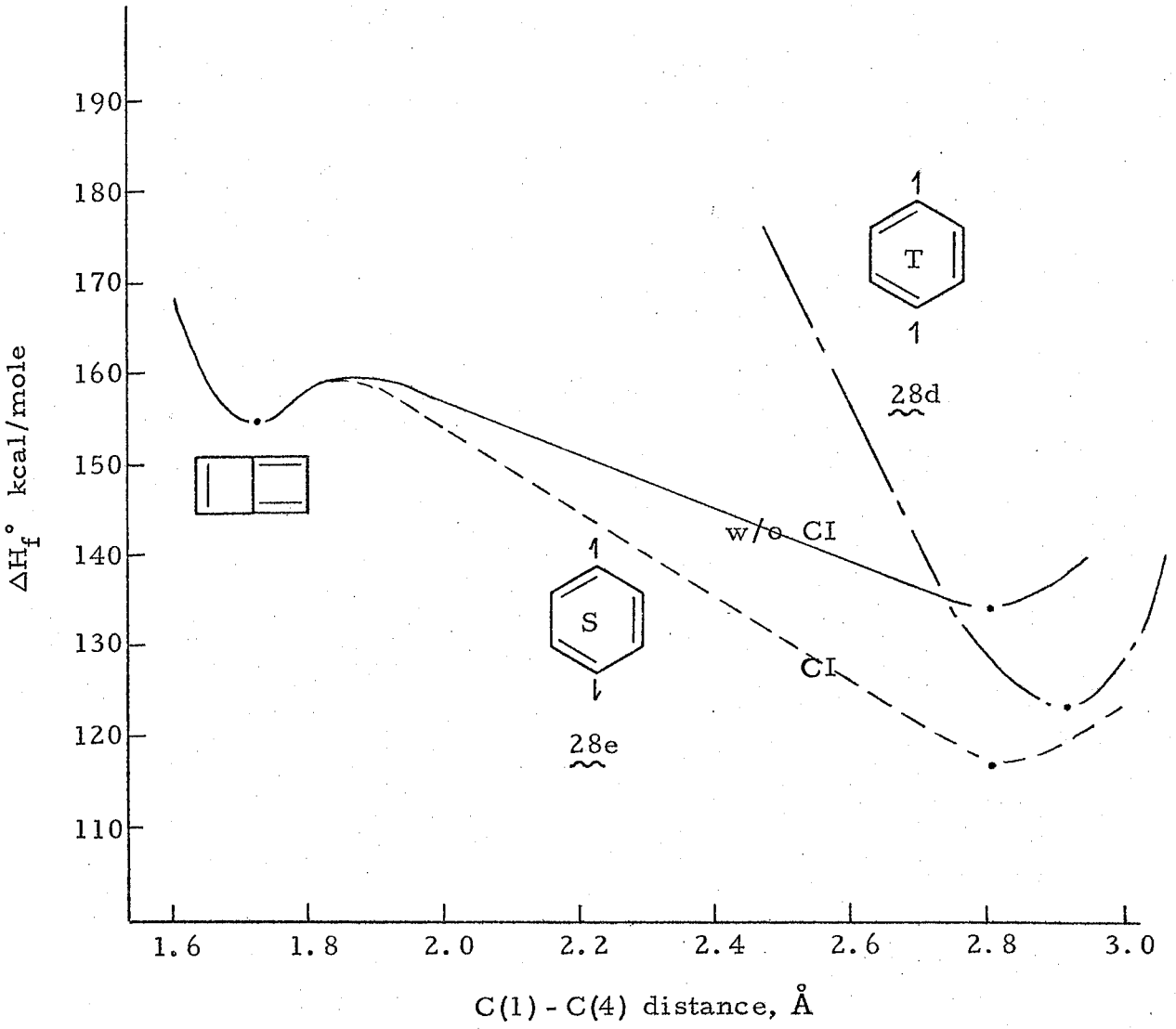
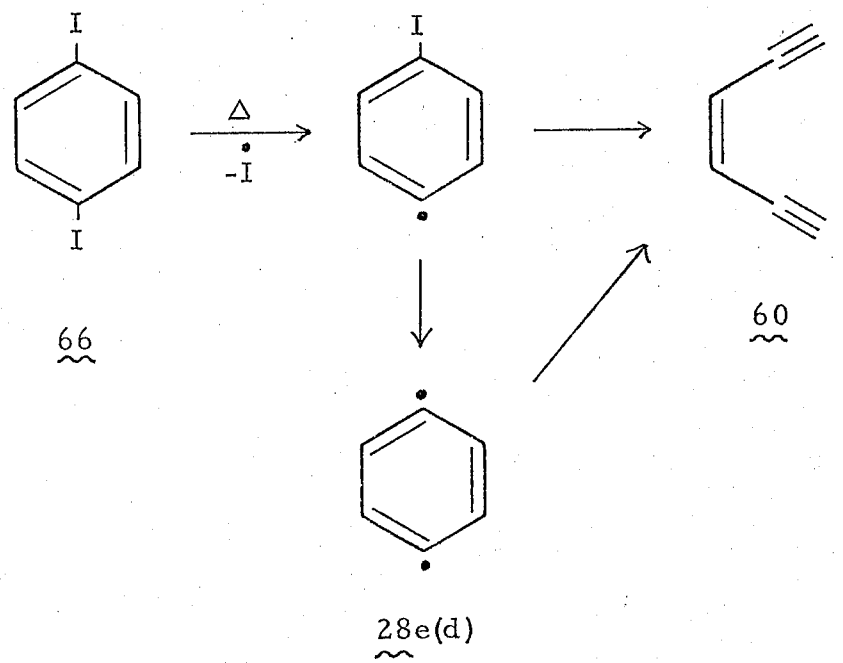


Figure XIII

MINDO/3 Predictions for 1, 4-Dehydrobenzene[120(a)]

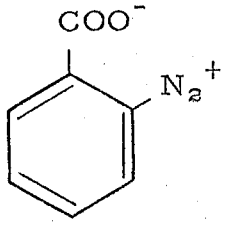
at 960°C in a reactor coupled to a mass spectrometer, a fragment of mass 76 was observed for which a vertical ionization potential of 9.46 volts could be measured. Comparison of this value with the known ionization potentials of some m/e 76 isomers suggested that the C_6H_4 fragment was 1, 5-hexadiyn-3-ene (60). The following mechanism was written:



When an identical experiment was performed with 1, 3-diiodobenzene, the same fragment (m/e 76, ionization potential 9.46 volts) appeared, requiring at least one hydrogen shift if its structure is indeed 60. With 1, 2-diiodobenzene, an m/e 152 as well as an m/e 76 was observed with an ionization potential of 9.76 volts for the latter. These fragments were assigned as parent ions of biphenylene and 1, 2-dehydrobenzene respectively in a reaction similar overall to the photolysis of 1, 2-diiodobenzene already

shown by Kampmeier[122] to proceed through 1, 2-dehydrobenzene. The photolysis of 1, 4-diiodobenzene has also been investigated and p-terphenyl found as a major product.[123]

Berry, Clardy and Schafer employed an alternative photo-initiated approach to dehydrobenzenes. Flash photolysis of benzene-diazonium-2-carboxylate (67) had previously been employed successfully by these authors to generate o-benzyne in the gas phase where its ultraviolet[124] and mass spectrum[125] were taken. When this process was repeated with benzenediazonium-4-carboxy-late[126(a)] (69) and the reaction followed by time resolved mass and ultraviolet spectroscopy, a mixture of products was produced which



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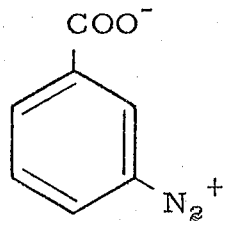

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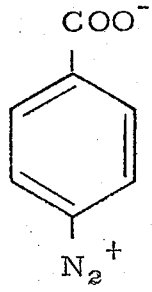
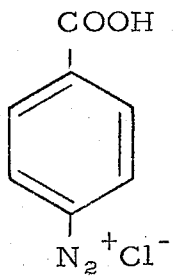


69

showed a broad absorption with a possible flat maximum at 244-246 nm similar to that seen for o-benzyne (flat maximum 242 ± 3 nm[124]). This absorption band remained for at least 0.5 seconds after flashing, while the mass spectrum contained a large m/e 76 species which was detectable up to two minutes after the initial photolysis. This contrasts sharply with the very transient m/e 76 species from 67 assigned to o-benzyne in the previous

experiment. When the m/e 76 species from 69 was allowed to fragment at higher voltages, the pattern was reported to be unlike that obtained for any known compound including the 1, 5-hexadiyn-3-ene (60). However, closer comparison of the data with that obtained for the more firmly established o-benzyne[125] and that reported for 60 and two other isomeric hexadiynenes[127] (Table IX) shows that although the absence of m/e 61 (76-CH_3) in the "para-benzyne" makes this transient unlike the other C_6H_4 species, m/e 61 is one of the smaller peaks from 60. The complete absence of information in this report about the relatively more important m/e 49 (76-C_2H_3) and m/e 73 (76-3H) peaks makes the analysis almost impossible to follow. It is interesting that in a parallel experiment with benzene diazonium-3-carboxylate[126(b)] (68) the same uv spectral pattern was found as with 69, but this time only a transient m/e 76 species was seen with a strong m/e 63-66 region, totally different from the acyclic hexadiynenes.

DeRossi, Bertorello, and Rossi have examined the behavior of the benzenediazonium carboxylates using the hydrochloride salts 70 and 71 and flash thermolysis of a solid film under vacuum.[128]



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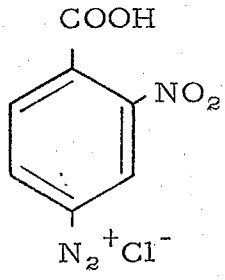

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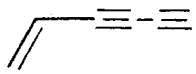
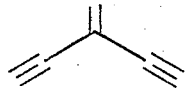
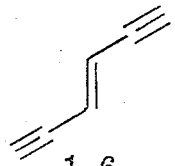
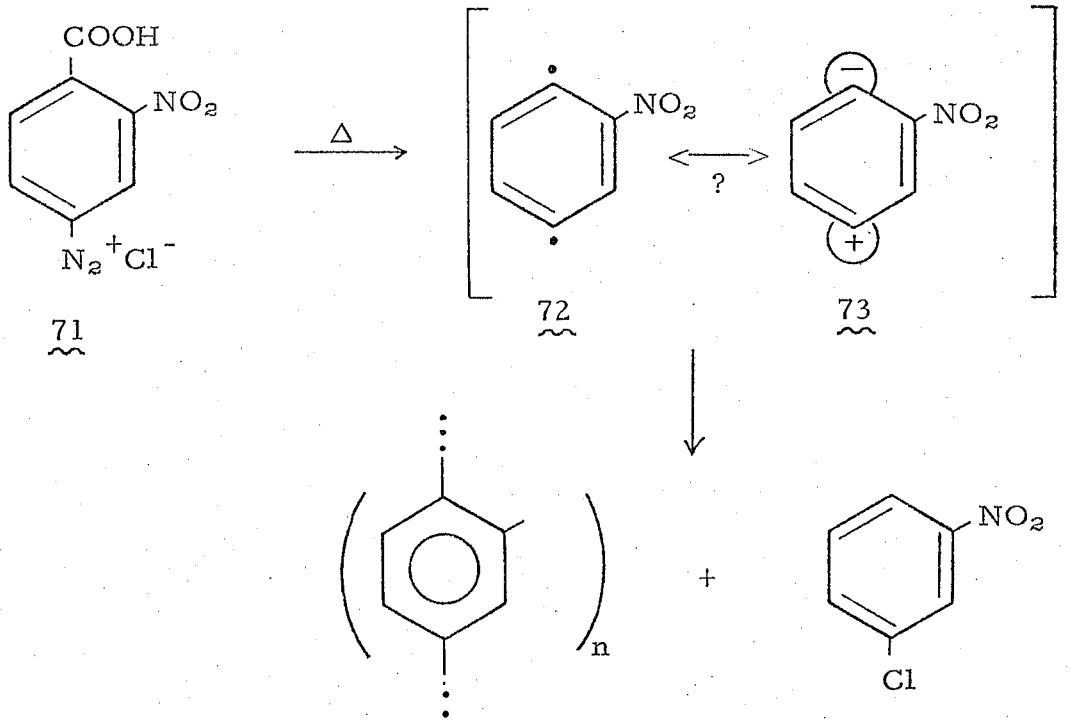
Table IX

Mass Spectra of C_6H_4 Species[125-127]

m/e				"p-benzyne"	o-benzyne
48	2.7	2.3	1.6	–	–
49	8.5	10.6	7.2	?	?
50	87.9	74.9	65.6	66	70
51	5.0	8.7	4.6	?	33
52	0.4	1.2	0.4	–	22
60	3.1	2.1	1.7	absent	?
61	6.9	4.8	3.9	absent	22
62	1.9	2.1	1.1	–	67
72	2.1	11.7	1.4	?	?
73	15.7	8.5	10.1	?	?
74	43.6	28.2	27.6	25	33
75	25.0	15.7	15.0	12.5	44
76	100.0	100.0	100.0	100	100
77	7.3	6.7	7.2	(7.0)	–

With 70 the major products were p-chlorobenzoic acid and carboxylated phenyl polymer with only a very small amount of chlorobenzene. On the other hand, when 71 was pyrolyzed, m-chloronitrobenzene was now the major product together with a large amount of a crystalline 2, 5-polymer of nitrobenzene. The authors suggest that the intermediate in this reaction could be either 72 or 73. But the total absence of products such as o-chloronitrobenzene, 2, 5-dichloronitrobenzene and nitrobenzene itself led them to postulate that the intermediate was probably 73, at least in the formation of the chloronitrobenzene. Work in solution on 70, however, implicates a radical mechanism since the product distribution is sensitive to molecular oxygen.[129]



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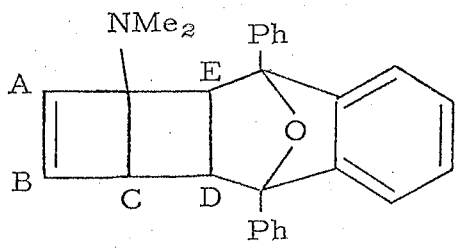
The major problem with all of the above routes to a 1,4-dehydrobenzene is that the reaction must proceed in two steps. The first radical intermediate formed is highly reactive and if it lives long enough can account for all of the products. In fact, the approximately 65 kcal/mole required to homolytically dissociate a phenyl-iodine bond in a thermal or photolytic treatment of 66 in the gas phase undoubtedly leaves the initially formed iodophenyl radical with enough excess kinetic energy to fragment directly to hexadiynene with concurrent or subsequent loss of I. Such a process, unless it can be ruled out by pressure studies, makes any conclusions drawn from acyclic products suspect. Also in Rossi's nitro-substituted salts, where the major products of thermal decomposition contain a trapped nitro-phenyl ring, a second dissociation from the first species formed (probably the m-nitro-p-carboxyphenyl-σ-carbonium ion) is not required for the specific formation of m-chloronitrobenzene since p-chloro-o-nitrobenzoic acid could also give m-chloronitrobenzene upon pyrolysis. It is possible in the case of Berry's stable "mass 76" that the stable fragment does not have mass 76 at all but forms an m/e 76 peak even at low voltage upon electron impact in the ionization chamber. Thus, a thermal rearrangement such as the one I propose possesses a substantial advantage in being only one step from a fully formed 1,4-dehydrobenzene.

An approach which could generate the covalent butalene 28a(b) first before isomerization to any other 28 species was initiated by Breslow and Napierski[108] concurrent with my own investigations.

Photolytic cyclization of 3-chloro-1, 2-dihydrophthalic anhydride (74) followed by electrolytic decarboxylation of the bicyclic diacid gave a chlorodewarbenzene 75 together with chlorobenzene (9:1). When this mixture was treated with lithium dimethylamide in deutero-dimethylamine and tetramethylenediamine at -35°, 75 was quantitatively converted to deuterodimethylanaline (76), 25% d_1, 38% d_2 and 22% d_3 with only 6.3% d_0. Since N, N-dimethylanaline did not exchange deuterium under these reaction conditions, the deuteration must be arising from an intermediate anion or olefin. Nmr with added europium contact chemical shift reagent [$Eu(fod)_3$] allowed assignment of 76%, 5% and 25% of the deuteration to the para, meta and ortho positions of 76, respectively. When this reaction was run in the presence of diphenylisobenzofuran, compound 77 was isolated >90% d_1 and >90% deuterated at position C. The mechanism favored by Breslow to account for these results begins



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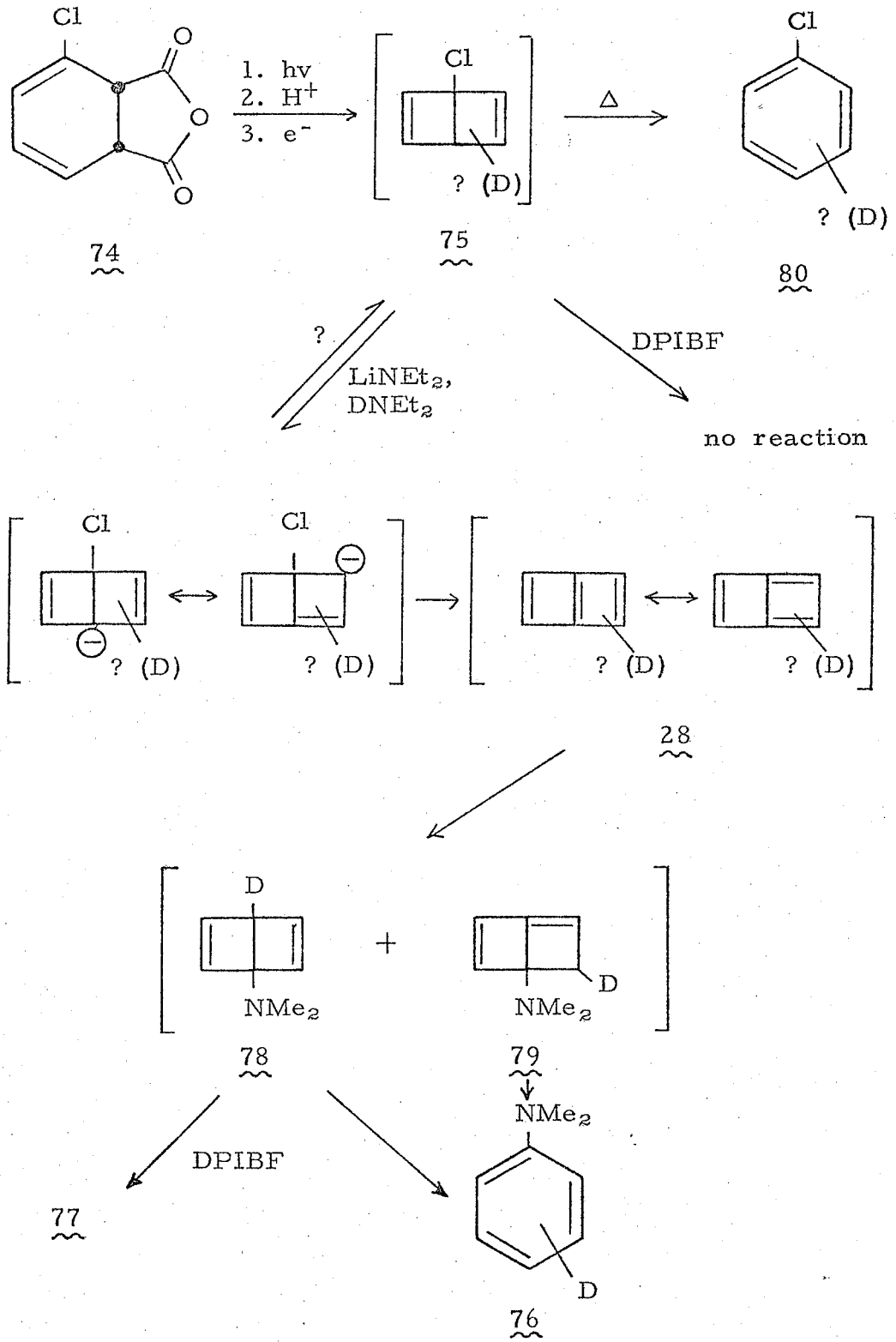

Cl
O
O
O
1. hv
2. H+
3. e-
Cl
? (D)
Δ
Cl
? (D)
74
75
80
?
LiNEt2,
DNEt2
DPIBF
no reaction
Cl
Cl
? (D)
? (D)
? (D)
? (D)
28
D
NMe2
+
D
NMe2
78
79
NMe2
DPIBF
77
D
76

with elimination of HCl from 75 to form 28a(b) followed by readdition of dimethylamine. This occurs preferentially (60%) across the 1, 4 bond to give a dimethylamino-dewar-benzene but also (40%) across the 1, 2 bond in 28a to give a dimethylaminoiso-dewar-benzene. These (78 and 79) either ring open to dimethylanaline or trap with diphenylisobenzofuran (DPIBF) in a Diels-Alder reaction. This mechanism requires that the anion first formed from 75 not live long enough to reprotonate at C-4 or C-2 (a conclusion which could be checked either by examination of 75 after partial reaction or by examination of its thermal product 80). Such exchange would be carried through to the N, N-dimethylanaline even if only nucleophilic substitution were accounting for the exchange of Cl by dimethylamine. It is also somewhat surprising that diphenylisobenzofuran does not react directly with 28a(b) or 79 if either are present in large amounts considering that both have highly strained double bonds. Only if 28 traps dimethylamine and 79 ring opens (with hydrogen shift) faster than they undergo 2+4 cycloaddition can the product mixture reported arise from this mechanism. As a further check on the presence of 79 in such a reaction, one could examine the dimethylaniline formed in competition with 77. Since 77 seems to arise only from 78, the deuterodimethylamine 76 should show greater ortho deuteration in the presence of DPIBF than in its absence.

Despite the fact that intermediacy of 28 is a most reasonable mechanism for all of the above reactions, none of the attempts to observe 1, 4-dehydrobenzene so far have provided unambiguous evidence of its existence. Of these, perhaps Fischer and Lossing's

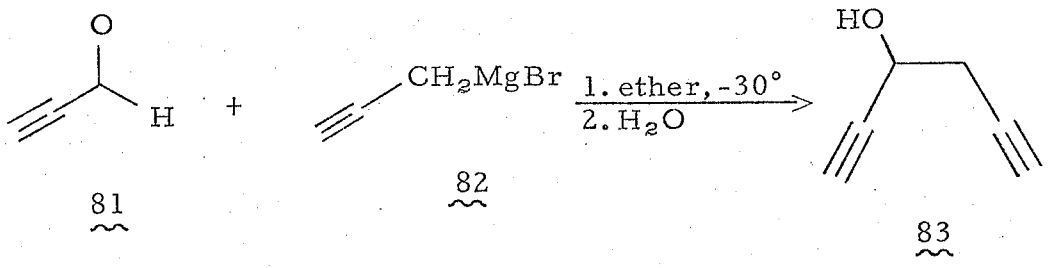
pyrolysis of para-diiodobenzene came the closest since the C_6H_4 fragment tentatively identified as 1, 5-hexadiyn-3-ene (60) is quite possibly an isomerization product of 28. The σ bond cleavage which would convert 28e into cis-1, 5-hexadiyn-3-ene trades a benzene C-C σ bond and benzene resonance energy for two developing acetylenic π bonds to a first approximation. The activation energy for such a process could conceivably be quite low. We have already seen that this reaction is predicted to be 14 kcal/mole exothermic based on estimated heats of formation.

Thus, I began my work on cis-60 in the hope that I might be able to trap 28d-g or if my estimate of the energy of 28a is correct, actually isolate a butalene species. Clearly, more direct evidence such as observation of an nmr or esr for a 28-type intermediate is necessary for conclusive proof of the existence of a 1, 4-dehydrobenzene.

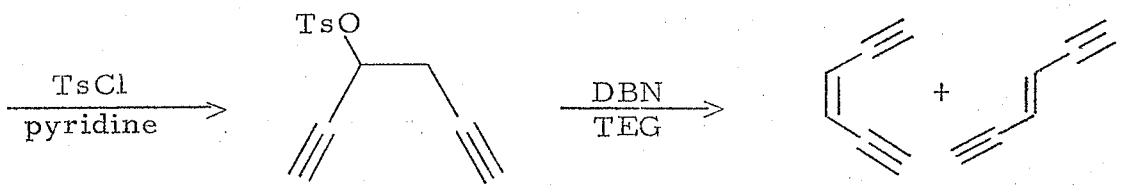
Methods and Results

Preparation of 1, 5-Hexadiyn-3-ene[130] (60)

1, 5-Hexadiyn-3-ene (60) was prepared by modification of the method of Sondheimer[131] as a 40/60 mixture of the cis and trans isomers, respectively. Propargyl aldehyde[132] (81) was coupled



81 82 83



84 60

with propargyl magnesium bromide (82) in diethylether at -30°C. Hydrolysis followed by distillation gave 1, 5-hexadiyn-3-ol (83), 83% yield based on the aldehyde, free of allenic impurities. Following an adaptation of the method of Eglington,[134] this alcohol was converted to the tosylate 84 in pyridine to give 78% of a white crystalline solid, m.p. 74.5°C. Elimination of p-toluenesulfonic acid (TsOH) from 84 in triethyleneglycol (TEG) using the hindered base 1, 5-diazabicyclo[4.3.0]non-5-ene (DBN)[135] at 23°C gave approximately 50% olefin yield after vacuum transfer with any

appropriate cosolvent as a purge. Analytical gas-liquid chromatography (glc) showed only two products which could be separated on a preparative scale and identified by their reported[130(b)] nuclear magnetic resonance (nmr), infrared (ir), and ultraviolet electronic (uv) spectra as cis- and trans-1,5-hexadiyn-3-ene (60) by all these criteria free from other impurities. In this way concentrated (< 10M) solutions of 60 could be prepared in almost any volatile, nonreactive solvent. These solutions were explosively reactive to addition of strong base and quickly darkened on exposure to air at room temperature. However, they could be stored for several weeks at 1.0M concentration under argon at -50°C.

Initial Gas Phase Pyrolysis

When 0.3 ml of a 1.0M solution of both cis- and trans-1,5-hexadiyn-3-ene (60) in hexafluorobenzene was injected into the vaporizer flask of the quartz tube apparatus pictured in Figure XIV (a complete description of this apparatus can be found in the General Experimental section of this report) and pyrolyzed by vaporization through the hot tube at 360°C oven temperature with an atmospheric pressure helium flow of 60 ml/min (STP), estimated partial pressure of 60 in the hot zone 0.01 atm, contact time 20 seconds, no new products were observed in the pyrolysate collected at -78°C either by analytical gas chromatography (80°C) or low temperature (sample kept below -10°C then analyzed at 0°C) nmr spectroscopy. Instead, nearly 80% of the initial enediynes 60 were recovered, a yield which includes losses in handling. Repetition of

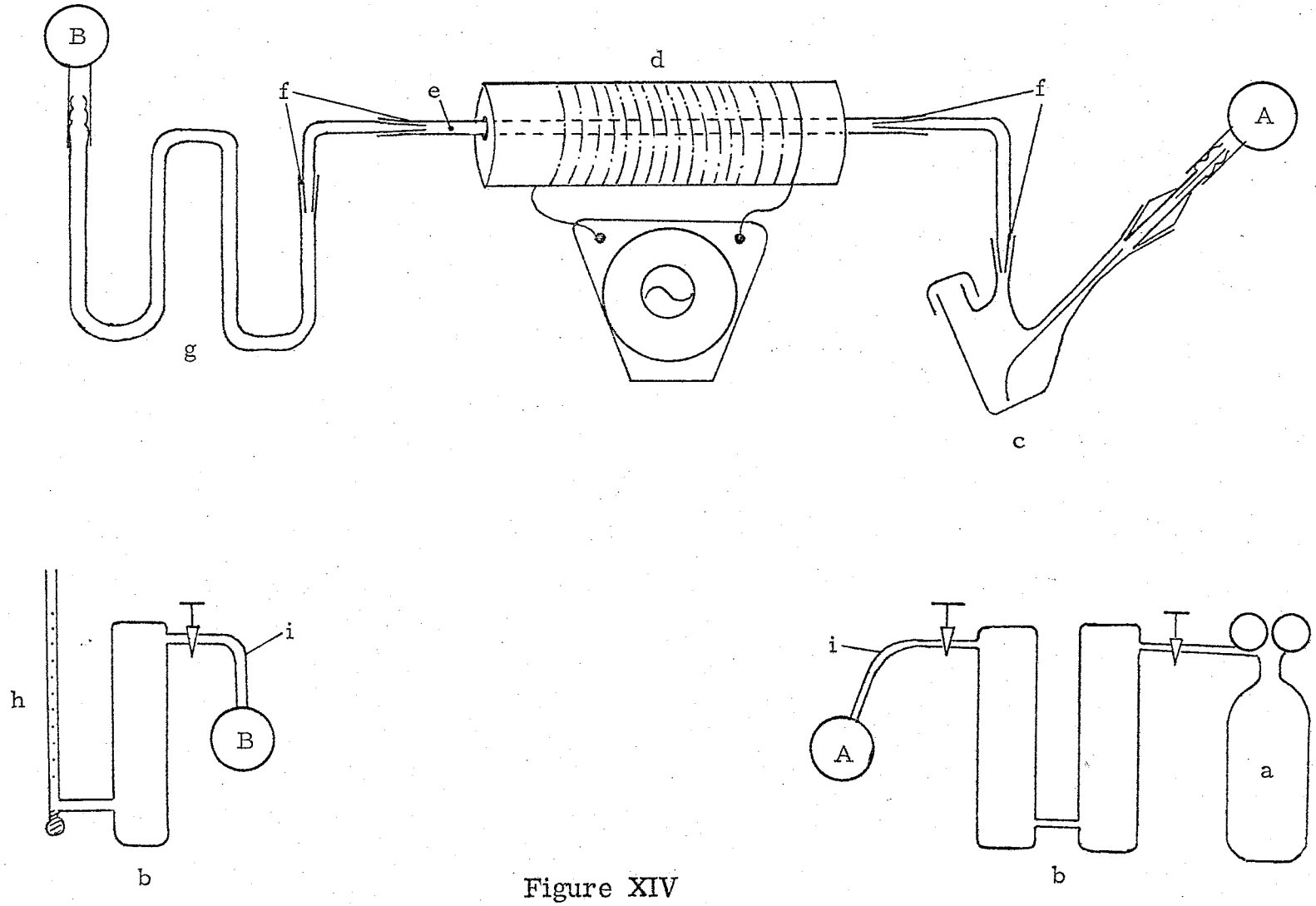


Figure XIV

Atmospheric Pressure Flow Pyrolysis Apparatus

Notes for Figure XIV

[a]Linde dry Helium (Union Carbide)

[b]3Å activated (150°C) molecular sieves drying tower

[c]Bubbler equipped with a rubber septum

[d]Tube oven, Basic Products Corp., max. temperature 2000°C

[e]Quartz tube 1.4 × 40 cm

[f]Teflon sleeves, 14/20 ground glass joints

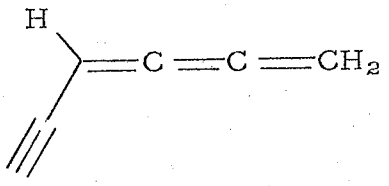
[g]U traps, LN2 or CO_2 ice cooled

[h]Soap bubbler manometer

[i]Teflon tubing, 10 mm OD

this experiment with pure (preparative glc) cis-1,5-hexadiyn-3-ene (cis-60) as a 0.5M solution (partial pressure of cis-60 in the hot zone ~0.005 atm) in hexafluorobenzene again gave nearly 80% recovery of enediyne, 100% cis-60 with no trans-60 (>1.0% detectable) by glc and nmr analysis. When the oven temperature was raised to 480°C, pyrolysis of cis-60 as before now yielded approximately 60% recovered enediyne containing 5% trans-60 as the only new volatile product. However, at 605°C, contact time 13 sec, a 20% yield of a 60/40 mixture of trans- and cis-60 was isolated after pyrolysis of 0.3 ml of a 0.5M solution of cis-60 in hexafluorobenzene. In addition, two new products were seen in this latter pyrolysate. The first, representing 20% of the recovered C_6 hydrocarbon and in 4% yield, was identified as benzene, just visible in the ^1H nmr of the pyrolyzed sample. Coinjection with an authentic sample of benzene in the glc supported this identification. The second, representing 2% of the recovered material, was not identified. It proved impossible to obtain a mass spectrum on the glc peak of this material at these concentrations but, from coinjection of various C_6 and C_7 hydrocarbons, it seems likely that it is an isomer of 60. Besides the possibilities offered by 28 structures, hydrogen shift isomers such as 85 are possible at high temperatures. Various unidentified C_2, C_3 or C_4 fragments were also present in the pyrolysate at 605°C.

In an attempt to identify such small yields of products, 5.0 ml of a 1.0M solution of cis- and trans-60 in hexafluorobenzene were pyrolyzed at 610°C as above. Here only a 1% yield of benzene



85

was discovered together with an approximately 10% recovery of cis- and trans-60. No other products were seen. The benzene was assumed to have arisen from reaction with the polymer on the walls of the pyrolysis tube. It is intriguing to speculate that its origin is hydrogen abstraction by 28d(e). Repyrolysis of cis-60, 0.5M in hexafluorobenzene, at 360°C through the now "well conditioned" quartz tube again provided greater than 80% recovery of enediyne versus an added cyclohexane internal standard, 100% cis-60 with no trans-60, benzene, or any other volatile product by glc and nmr analysis. The cis to trans isomerization of 60 has an estimated 50 kcal/mole activation energy and an Arrherius A factor of approximately $\log^{-1}$ 13 at 700°K.[36] This reaction occurred in the flow system (contact time 15 sec, partial pressure 60 approximately 0.002 atm) in the temperature range 500-600°C, being completely equilibrated above 600°C. This is entirely consistent with the above parameters for which a $t_{\frac{1}{2}}$ of 15 sec is calculated for 530°C, assuming simple first order kinetics. On the other hand, the acetylene to allene isomerization needed to produce 85 has an estimated activation energy of 100 kcal/mole (108 for a vinyl CH bond minus 8 for propargylic resonance, assuming a

radical mechanism) and an estimated log A of 13.[36] From these parameters, one would not expect to see much of the allene at 600°C ($t_{\frac{1}{2}}$ = 10 sec at 1200°C). However, such a reaction is known to be catalyzed by a carbonized surface.[136]

To the extent that the anticipated cyclization of cis-60 to 28 resembles that of the 1, 5-hexadiyne 57 to dimethylenecyclobutene 18, one might expect an E_a in the neighborhood of 32 kcal/mole and a log A of 13 since no rotational modes must be frozen in the transition state. Thus, one might have expected that the formation of 1, 4-dehydrobenzene either as an intermediate or transition state from cis-60 would be rapid even at 200°C. But if the formation of 28 is considerably endothermic, it would probably require 600°C or more to begin to see "chemistry" from this species in the gas phase. Thus, the complete absence of products and the almost quantitative recovery of starting material under conditions certainly energetic enough to cause the cyclization I · sought led one to suspect that the 1, 4-dehydrobenzene, if accessible from cis- or trans-60, was reopening in a manner similar to that proposed for Fischer and Lossing's intermediate. Indeed, if such a process is occurring, even taking the 130 kcal/mole estimate for the ΔH_f° of 28a which makes the reaction from 60 4 kcal/mole endothermic, one would only see 4% of 28a at equilibrium at 360°C. Trapping this equilibrium population, which is just on the edge of nmr detectability, at 0°C requires an activation energy of at least 19 kcal/mole for a half-life for decay back to 60 of even one minute at this temperature. Since at -50°C this half-life is on the

order of several days, a low temperature trapping was attempted.

Modification of the apparatus in Figure XIV to include an nmr tube attached to the bottom of the first trap and pyrolysis of cis-60 as a 0.5M solution in THF-d_8 at 360°C, collecting the pyrolysate at -78°C with a CO_2-ice, isopropanol bath, allowing the THF to melt at -50°C and sealing off the nmr tube under vacuum showed again >80% recovery of cis-60 but no nmr detectable products. I would expect that any 28 species formed would be quite reactive, 28a(b) to dimerization and 28d(e) to radical abstraction for instance; thus, one would not expect to see 28 directly, especially in these concentrated solutions. However, these reactions were quite clean; no polymer was formed in the nmr tube if care was taken to rigorously exclude air. The only polymer seen in a clean apparatus was where the hot flow left the tube and first struck the cold trap, indicating that at least some reactive substance was exiting from the pyrolysis zone. Thus, if a 28 species is being formed in the quartz tube and is not polymerizing there under such dilute conditions, then either the reaction is >4 kcal/mole endothermic or the back reaction has an activation energy much less than 20 kcal/mole. While trapping at even lower temperatures could conceivably allow one to see 28 if the latter is the major problem, only by pyrolysis at higher temperatures where I already know that cis-trans isomerization at least is occurring could one see spectroscopically observable quantities of 28 or its products if 140 kcal/mole is a more realistic estimation of the

heat of formation of a 1, 4-dehydrobenzene. (Calculations for hypothetical equilibria of $\Delta\Delta H_f^\circ$ 4 and 14 kcal/mole and E_a for the back reaction of 20 and 10 kcal/mole, log A = 13, $\Delta S^\circ = 0$ are tabulated in Table X below.)

That such an approach as the above is even conceivable, since it essentially asks the question of whether a product mixture at high temperature can be quenched to low temperature faster than equilibrium can be reestablished, has recently been demonstrated by Anet, et al.,[137] for the equilibrium between chair and twist boat cyclohexane, $\Delta\Delta H_f^\circ = 5.7$ kcal/mole, E_a twist $\rightarrow$ chair $\sim$ 5 kcal/mole. Here an equilibrium mixture of 30% twist boat, 70% chair at 1100°K was trapped to give approximately 25% twist boat at 20°K. The major factor upon which the success of this experiment rests is that the time between leaving a hot equilibrated zone and striking the cold trap must be on the order of one half-life for the reverse reaction. From Table X we see that for an equilibrium where the reverse activation energy is 20 kcal/mole this time is already on the order of 10^{-6} seconds at 300°C. Although every attempt was made to keep the exit tube of the apparatus near the same temperature as the oven (Figure XIV) with heating tape and insulation, it is doubtful whether such a time difference can exist in an atmospheric flow pyrolysis. Assuming a plug flow of 40 ml/min in a tube of diameter 1.5 cm, 1.3 seconds are required to move the gas 1 cm at 300°C. Even if it is assumed that the substrate molecules will accelerate from the hot to the cold layer as they freeze out of the flow, the much slower flow in the trap

Table X

Equilibrium Concentrations and $\tau_{\frac{1}{2}}$ of B in A $\rightleftharpoons$ B, $\Delta\Delta H_f^\circ$ = 4 and 14 kcal/mole, E_a for B $\rightarrow$ A = 10 and 20 kcal/mole

Temperature (°K)	%B[a] $\Delta\Delta H_f^\circ$ = 4 kcal/mole	%B[a] $\Delta\Delta H_f^\circ$ = 14	$t_{\frac{1}{2}}$ B (sec)[b] E_a = 10	$t_{\frac{1}{2}}$ B (sec)[b] E_a = 20
20	4×10^{-42}	1×10^{-150}	2.2×10^{95}	2.4×10^{203}
80	1×10^{-9}	1×10^{-36}	9.2×10^{13}	1.2×10^{41}
140	6×10^{-5}	2×10^{-20}	2.2×10^{2}	6.9×10^{17}
200	.0045	6×10^{-14}	4.9×10^{-3}	3.5×10^{8}
273	.066	6×10^{-10}	6.2×10^{-6}	5.4×10^{2}
298	.72	6×10^{-9}	1.3×10^{-6}	25
473	1.5	4×10^{-5}	2.7×10^{-9}	1×10^{-4}
573	2.9	5×10^{-4}	4.2×10^{-10}	2.6×10^{-6}
673	5.0	3×10^{-3}	1.1×10^{-10}	1.9×10^{-7}
773	8	1×10^{-2}	4.5×10^{-11}	2.8×10^{-8}
873	12	3×10^{-2}	2.1×10^{-11}	6.5×10^{-9}
973	14	7×10^{-2}	1.2×10^{-11}	2.0×10^{-9}

[a]Calculated assuming $\Delta S^\circ = 0$. [b]Calculated assuming $A = 10^{13}$.

itself will more than make up for this. Under such conditions only if the 60 to 28 equilibrium is rapid at 100°C can one reasonably expect to trap out even the 1% of 28 which may be present at such a temperature. Faster flows with higher oven temperatures might lower the half-life limit but certainly not by a factor of 10^{-6}.

Professor Anet on the other hand had to overcome a half-life of the twist boat of 10^{-11} sec at 1100°K. The trick as it turns out is to use vacuum pyrolysis. Here the increased mean free path effectively allows a low collision number or "short" path from a thermally equilibrated hot zone to the cold trap. An added advantage which further lowers the number of collisions in the cool zone is that the carrier flow (0.2 torr) can be made to freeze out as well. Ideally there is no rebound from the trap and hence no cold gas layer where equilibrium could be reestablished as there most certainly would be at higher pressures where more hot molecules have to be frozen. Thus, in Anet's apparatus the components of the equilibrium at high temperature strike the 20°K trap as a 1100°K Boltzman distribution of energies. Those with energy greater than the activation energy probably relax to the more stable isomer as effectively as to the less stable isomer, but those with energy less than this value are rapidly equilibrated to a lower Boltzman distribution with insufficient energy to rearrange at a significant rate. Again the time this process takes must be on the order of one half-life at 1100°K for the trapping to be maximally efficient. This is probably an inverse exponential function of the temperature. Thus, even ideally at below 8°K the trapping will not

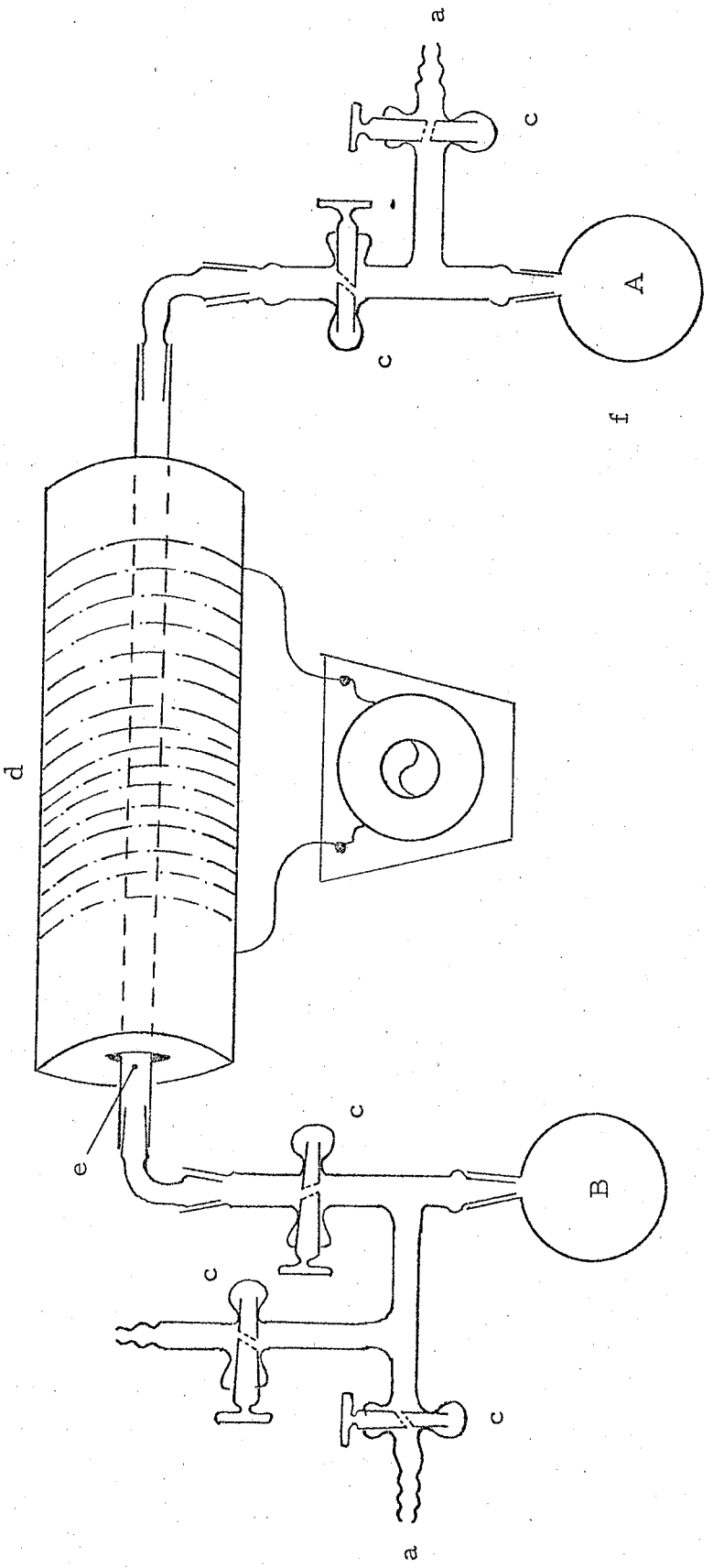


Figure XV

Vacuum Pyrolysis Apparatus

Notes for Figure XV

[a]0.001 mm Hg pressure vacuum line

[b]Hg manometer

[c]5 mm bore vacuum stopcocks

[d]Tube oven, Basic Products Corp., max. temperature 2000°C

[e]Quartz tube, 1.5 × 40 cm

[f]25 ml pear-shaped flask, Pyrex

be 100% of the high temperature distribution, but Anet predicts that a significant proportion can be trapped even with barriers to rearrangement as low as RT where T is the temperature of the hot zone.

I also did some initial experiments in a vacuum pyrolysis apparatus as pictured in Figure XV. In light of Anet's success, these now take on an added significance even though at the time no attempt was made to make the path from the oven to the cold trap very short. When 0.5 ml of a 1.0M solution of cis- and trans-60 in benzene was pyrolyzed by slowly vacuum transferring the liquid at 0.01 mm Hg pressure through a 495°C quartz tube and collecting the pyrolysate in a flask with attached nmr tube at liquid nitrogen temperature, it was noted that the pyrolysate condensed with a bluish tint. Upon warming, the blue material in the flask turned green after $\frac{1}{2}$ hour at room temperature under vacuum. A control experiment which included transferring the benzene from a DBN, triethyleneglycol solution showed that the blue color was due to pyrolysis of enediynes. A larger scale experiment with 5.0 ml of a 1.0M solution of cis- and trans-60 in benzene produced more of the blue material in the cold trap as well as a green polymer coating the walls of the exit tube. The volatiles were vacuum transferred away and examined by nmr at 0°C. A 40% yield of returned enediynes was seen but no other products. A blue oil remained in the trap which could not be vacuum transferred at 0°C. THF-d_8 was transferred in and an nmr tube prepared as before under vacuum. No nmr could be obtained even though there

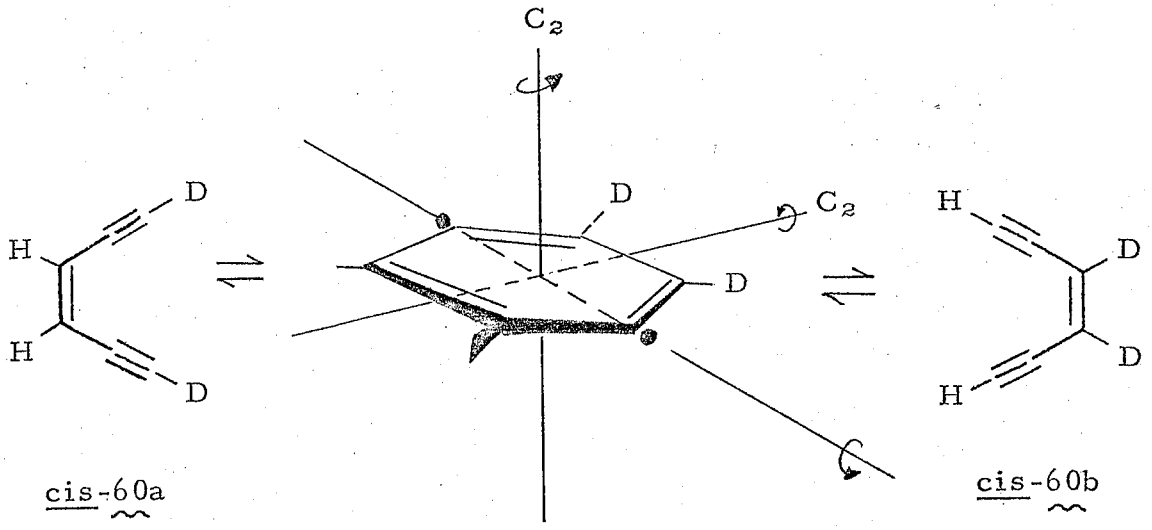
appeared to be a considerable amount of this material present. Upon exposure to air the blue color in this nmr tube changed to green and then to a brownish-yellow with precipitation of polymer. No ir or uv of this material was obtained.

A species 28 or its dimers and trimers should not have an appreciable electronic absorption in the red visible. But clearly if a reactive intermediate is condensing in a matrix which contains an appreciable concentration of enediyne, colored polymeric material might be formed even at -190°C. In this connection, when more dilute solutions of 60 in benzene were pyrolyzed at 495°C, 5.0 ml of 0.1M 60, no blue color was seen. One explanation is that here the concentration of enediynes in the frozen matrix is ten times lower and polymerization does not occur. In retrospect this latter pyrolysis should have been carried out in such a fashion as to directly condense a benzene solution into an esr tube at low temperature. Such an experiment could be sensitive to as little as a 10^{-6}M concentration of triplet 28d or a doublet 28d(e) if the two radical centers are uncoupled. That a radical is indicated was confirmed by the following experiment. When 0.5 ml of a 1.0M solution of cis- and trans-60 in cyclohexane was pyrolyzed at 475°C by vacuum transfer through the apparatus in Figure XV, no blue color was formed in the condensate in the liquid nitrogen cooled trap but instead an approximately 2% yield of benzene together with now a 60% yield of recovered enediynes was found. It is tempting to account for this by trapping of 28d(e) with the cyclohexane via radical abstraction thus leaving fewer stable

radicals to initiate polymerization of the enediyne as compared to the benzene matrix where radical abstraction of hydrogen is more difficult. Clearly 475-500°C is too low a temperature in the vacuum for appreciable fragmentation and rearrangement of the type seen at 600°C in an atmospheric flow pyrolysis to be occurring in the assumed absence of surface catalysis.

Gas-Phase Pyrolysis of a Deuterium Labeled Enediyne

Since the 1, 4-dehydrobenzenes 28a, b and 28d-h are of point group D_{2h} and 28c is D_2 compared to C_{2v} for the cis-1, 5-hexadiyn-3-ene, 28 should possess at least one new C_2 axis of symmetry at least on the average. It can therefore reopen to cis-60 in two equivalent directions creating a degenerate rearrangement which interconverts C-1 with C-3 and C-6 with C-4 (Mechanism A). To test this hypothesis and thus to provide evidence for the existence of 28 either as a reaction intermediate or transition state, I carried out the selective deuteration and pyrolysis of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a). Closure to 28 followed by reopening should "scramble" the label between the acetylenic and vinylic positions. Such a scrambling is unique in that it is intramolecular and moves both deuteria at once. Other conceivable mechanisms such as those proceeding through a cumulene intermediate 85 should not be so selective. It is conceivable that the cis-60a would scramble by Mechanism A much faster than would the trans-60a; whereas in an intermolecular or intramolecular-cumulene mechanism, both isomers should scramble at nearly



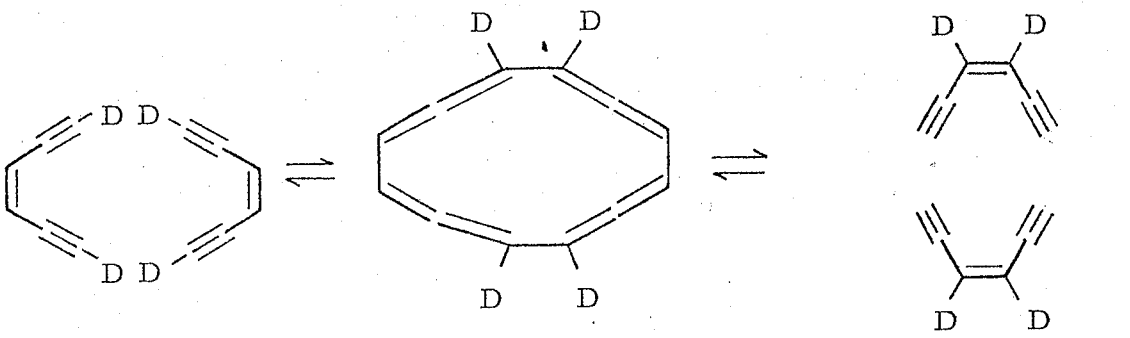
cis-60a cis-60b

28

Mechanism A

equal rates. One bimolecular process which would also interconvert only cis-60c with cis-60b as above (Mechanism B below) was suggested by Professor Martin Stiles,[138] but its occurrence in the gas phase is considered unlikely, since it would possess a large negative entropy of activation and a second order concentration dependence.

The occurrence of such a rearrangement could be detected by nmr and mass spectral techniques. The acetylenic proton signal in the nmr should increase at the expense of the vinyl proton until at equilibrium they become equal. A mass spectrum should confirm



cis-60a + cis-60a

cis-60b + cis-60b

Mechanism B

overall retention of deuterium label in this sample. Washing out the acetylenic label in the pyrolyzed product should provide a large fraction of the material with two deuteria compared to a similarly treated 60a which has not been pyrolyzed. Assuming a small amount of monodeuteration in the starting material, the pyrolyzed 60a should show 50% d_2, 50% d_0 in the mass spectrum after removal of acetylenic label if A is the only mechanism operating. To the extent that equilibrium is reached in the flow tube, Mechanism B would provide for 25% d_0, 50% d_1, 25% d_2 in the mass spectrum of the final product after washing out the acetylenic label (Figure XVI, ratio cis-60a : cis-60c : cis-60b = 1 : 2 : 1). Differentiation between Mechanisms A and B by nmr is, however, not possible since both give a vinyl : acetylenic ^1H ratio of 1 : 2 after removal of the acetylenic deuterium. There is no doubt that the preceding analysis is oversimplified since intermolecular exchange in solution after pyrolysis (if more than one pass through the

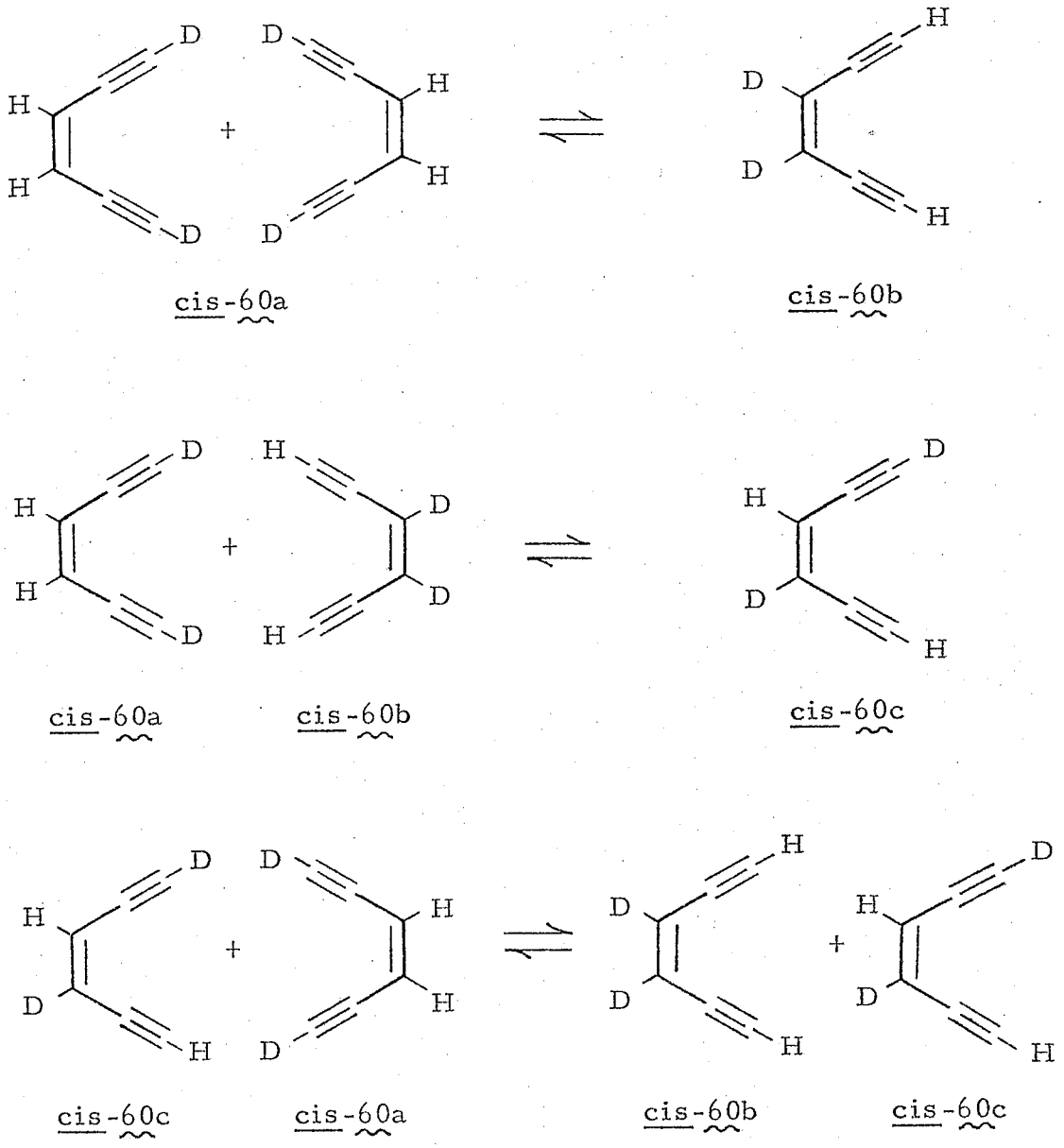


Figure XVI

Equilibration of 60a by Mechanism B

pyrolysis tube is necessary to reach equilibrium) or loss of deuterium due to exchange on the walls of the pyrolysis tube itself will introduce d_1 material. This analysis also has not included an equilibrium isotope effect which might change the 1:1 concentration ratio of 60a and 60b predicted by Mechanism A. In the event, however, this rearrangement provided to be remarkably uncomplicated.

When a mixture of cis- and trans-1, 5-hexadiyn-3-ene as a 10% solution in hexafluorobenzene was equilibrated twice with a ten-fold excess of triethyleneglycol-0, 0-d_2 (TEG-0-d_2) with a small amount of DBN as catalyst, both cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a) (greater than 94% d_2 by mass spectral analysis and greater than 95% deuterated in the acetylenic positions by nmr analysis) were produced, each free of contamination by d_0, d_3 and d_4 species (Sample 1c and 1t, Tables XI and XII). Reversing this procedure by exposing 1c and 1t (60a) to perprotiotriethyleneglycol/DBN quantitatively removed the deuterium label (Sample 2c and 2t, Tables XI and XII). Pyrolysis of 0.2 ml of a 0.2M solution of these deuterium labeled enediynes through a clean quartz tube (see Figure XIV) at 306°C, 40 ml/min helium carrier flow at STP, 30 seconds estimated contact time (0.002 atm partial pressure of 60) showed no loss of total label by mass spectral analysis (Sample 3c and 3t, Table XI). However, examination of the pyrolysate by nmr showed 100% equilibration of the label between the vinylic and acetylenic positions in the cis-60 and no such equilibration in the trans-60. Analytical gas-liquid chromatography

Table XI

Mass Spectral Data[a] for 1, 5-Hexadiyn-3-ene-d_2
In Atmospheric Flow Pyrolysis

M/C	Fragment	Relative Intensity[a]/% of Total[b]							
cis-1, 5-hexadiyn-3-ene:		Samples							
		1c		2c		3c		4c	
76	$P(d_0)$	0	0	100	100	0	0	98	49
77	$P(d_1)$, $P+1(d_0)$	5.4	5	6.6	–	7.4	7	8.0	1
78	$P(d_2)$, $P+1(d_1)$	100	95	0	0	100	93	100	50
79	$P(d_3)$, $P+1(d_2)$	6.3	–	0	0	6.8	–	7.0	–
trans-1, 5-hexadiyn-3-ene:		Samples							
		1t		2t		3t		4t	
76	$P(d_0)$	0	0	100	100	0	0	100	100
77	$P(d_1)$, $P+1(d_0)$	6.0	6	6.4	–	8.2	7	6.4	–
78	$P(d_2)$, $P+1(d_1)$	100	94	0	0	100	93	0	0
79	$P(d_3)$, $P+1(d_2)$	6.4	–	0	0	6.8	–	0	0

Sample 1: initial 1, 5-hexadiyn-3-ene, d_2 (60a)
Sample 2: after washout of acetylenic label in 1
Sample 3: after pyrolysis at 306°C, 30 sec, 0.002 atm 60a, He carrier 1 atm
Sample 4: after washout of acetylenic label in 3

[a]Mass spectra were obtained on an EAI Quad 300 mass spectrometer at 10v ionization potential, glc interface inlet - all other masses zero.
[b]Relative intensities are normalized to the base peak and are reported as average values from as many as seven data points across the glc peak.
[c]The P+1 peaks (6.5 theoretical[140]) were excluded from % calculations.

Table XII

^{1}H Nmr Data[a] for 1, 5-Hexadiyn-3-ene-d_2
In Atmospheric Flow Pyrolysis

cis-1, 5-hexadiyn-3-ene (cis-60)

τ[b]	assignment	integration[c]			
		1c	2c	3c	4c
4.46	vinyl H	65	71	26	25
7.07	acetylenic H	6	73	27	55

trans-1, 5-hexadiyn-3-ene (trans-60)

τ[b]	assignment	integration[c]			
		1t	2t	3t	4t
4.39	vinyl H	105	120	97	91
7.23	acetylenic H	8	119	7	93

Sample 1: initial 60a
Sample 2: after removal of acetylenic label in 1
Sample 3: after pyrolysis, 306°, 1 atm He flow
Sample 4: after removal of acetylenic label in 3

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[a]A60-A spectra in C_6F_6, 30°C.

[b]Resonances downfield from external standard TMS at 10.0τ.

[c]Averages of 10 integrations, 5 in each direction of scan; estimated error ± 2%.

confirmed the good yield of pyrolyzed material, the absence of other products, and the absence of cis-trans isomerization versus a cyclohexane internal standard. When the pyrolyzed enediynes were equilibrated with perprotio TEG/DBN as before to remove the acetylenic label, mass spectral analysis (Sample 4c and 4t, Table XI) showed only d_0 material in the trans-1, 5-hexadiyn-3-ene and 49% d_0, 1% d_1, and 50% d_2 material in the cis isomer, within experimental error precisely the result expected with Mechanism A predominating. This scrambling in the cis-60 was rapid even at temperatures 100° lower. An identical experiment to the above except now with the quartz pyrolysis tube at 204°C showed 43% scrambling in the cis-60a but no scrambling in the trans-60a. (The % scrambling was calculated from the nmr by use of the formula given in Preparation 9, Note E, page 282 of this report.) If 30 sec is taken as the half-life for scrambling of the acetylenic label in the cis-60 at 210°C, one can estimate that the E_a for this reaction is about 32 kcal/mole assuming an A factor of 10^{13} or a $\Delta S^{\ddagger}$ of zero. Because no free rotational modes need to be frozen out in the transition state leading from 60 to the symmetrical species, the activation entropy is undoubtedly very close to zero for this reaction.[36]

Repeated exposure of pyrolyzed cis- and trans-60a to TEG-0-d_2/DBN followed by repyrolysis yielded cis-1, 5-hexadiyn-3-ene-d_4 (cis-60d), 90% perdeuterated by mass spectral analysis (Sample 5c, Table XIII) with the trans-60a remaining dideuterated. Exposure of this sample to TEG/DBN as before resulted in the removal of a

Table XIII

Mass Spectral Data[a] for 1, 5-Hexadiyn-3-ene, Perdeuteration

M/e	Fragment	Relative Intensity/% of Total	
cis-1, 5-hexadiyn-3-ene (cis-60d)			
		Samples	
		5c	6c
76	$P(d_0)$	0 0	0 0
77	$P(d_1)$, $P+1(d_0)$	0 0	5.3 5
78	$P(d_2)$, $P+1(d_1)$	3.0 2.7	100 95
79	$P(d_3)$, $P+1(d_2)$	7.6 6.9	7.2 —
80	$P(d_4)$, $P+1(d_3)$	100 90.4	0 0
81	$P+1(d_4)$	6.3 —	0 0
trans-1, 5-hexadiyn-3-ene			
		Samples	
		5t	6t
76	$P(d_0)$	0 0	100 100
77	$P(d_1)$, $P+1(d_0)$	6.1 5.8	6.8 —
78	$P(d_2)$, $P+1(d_1)$	100 94.2	0 0
79	$P(d_3)$, $P+1(d_2)$	7.0 —	0 0
80	$P(d_4)$, $P+1(d_3)$	0 0	0 0
81	$P+1(d_4)$	0 0	0 0

Sample 5: 1, 5-hexadiyn-3-ene (60d)perdeuterated
Sample 6: after washout of acetylenic label in 5

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[a]Note a. in Table XI.

[b]Note b. in Table XI.

[c]Note c. in Table XI.

maximum of two deuteria by mass spectral analysis (Sample 6c and 6t, Table XIII). Nmr showed that the protons introduced were acetylenic and that the cis-60 remained greater than 90% deuterated in the vinyl positions even after repeated exposure to TEG/DBN in complete agreement with the assumed specific introduction and removal of deuterium label.

In an attempt to enhance reactions such as Mechanism B which would give from 1:0:1 d_0, d_1 and d_2 to 1:2:1 d_0, d_1, and d_2 after removal of acetylenic label according to how far toward the equilibrium condition the reaction has proceeded, a 50/50 mixture of 60 and 60a was pyrolyzed under the same conditions used for 60a alone. One portion of this sample was stored at -50°C warming only briefly for analysis (Sample 7, Table XIV). Another portion was allowed to stand at room temperature for three hours before analysis (Sample 8, Table XIV); while a third was immediately pyrolyzed at 300°C (Sample 9, Table XIV). Comparison of the amount of d_1 material in these samples both before and after removal of acetylenic label showed no excess d_1 species were created in the pyrolysis and that exchange of the acetylenic protons was not a very rapid process either in solution at 23°C or in the gas phase at 300°C. The extent of d_1 material that was found (the same within experimental error, vide infra, in samples 7, 8 and 9 in Table XIV) most likely has its origin on the metal glc column used to separate cis- and trans-60 for analysis or in the mass spectrometer itself, since it is not reflected in the vinyl positions as evidenced by the mass spectral analyses of Samples 10, 11 and

Table XIV

Mass Spectral Data[a] of a 50/50 Mixture of 60 and 60a in Flow Pyrolysis

m/e	Fragment	Relative Intensity[b]/% of Total[c]											
cis-1,5-hexadiyn-3-ene		Samples											
		7c		8c		9c		10c		11c		12c	
76	$P(d_0)$	100	46	97.5	44.7	99	45	100	100	100	100	100	75.8
77	$P(d_1)$, $P+1(d_0)$	22.5	7.5	26.6	9.4	27	9.3	6.8	—	5.9	—	8.1	0.8
78	$P(d_2)$, $P+1(d_1)$	100	46	100	45.8	100	45.6	0	0	0	0	31	23.5
79	$P+1(d_2)$	6.2	—	6	—	6.7	—	0	0	0	0	2.2	—
trans-1,5-hexadiyn-3-ene		Samples											
		7t		8t		9t		10t		11t		12t	
76	$P(d_0)$	98	45	100	45	100	45.5	100	100	100	100	100	100
77	$P(d_1)$, $P+1(d_0)$	24.5	9	31	11	26	9	6.5	—	6.3	—	6.3	—
78	$P(d_2)$, $P+1(d_1)$	100	46	98	44	100	45.5	0	0	0	0	0	0
79	$P+1(d_2)$	5.1	—	7	—	6.4	—	0	0	0	0	0	0

Sample 7: 50/50 60 and 60a stored at -50°C.
Sample 8: 50/50 60 and 60a, 3 hrs at 23°C.
Sample 9: 50/50 60 and 60a, pyrolyzed, 300°, atm pres.
Sample 10: washout of acetylenic label in 7.
Sample 11: washout of acetylenic label in 8.
Sample 12: washout of acetylenic label in 9.

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[a] Note a. in Table XI.

[b] Note b. in Table XI.

[c] P+1 peaks at m/e 77 and 79 excluded; $P+1(d_0)$ assumed = $P+1(d_2)$ when $P(d_0) = P(d_2)$.

12 from which the acetylenic label was removed. That such exchange is possible in the gas phase is illustrated by the following experiment. Ten microliters (1×10^{-2} ml) of a mixture of 50% cis- and trans-60 and 50% cis- and trans-60a, approximately 1.0M in hexafluorobenzene, was injected and allowed to remain in the batch analyzer of the Quad 300 mass spectrometer. The parent peaks of the various enediynes were then recorded as a function of the time spent by these materials in this one liter stainless steel container (partial pressure of 60 species $\sim 1 \times 10^{-5}$ atm) at 150°C. The data (Table XV) indicate that under these conditions intermolecular deuterium exchange proceeds at a moderately rapid rate, equilibrium being established after only 20 minutes. Using five minutes as the half-life at this temperature and assuming simple, uncatalyzed second order kinetics with an ordinary Arrhenius A factor of 10^6, one can predict that equilibrium should be established in the flow system at 300°C in approximately 1.0 seconds. Clearly this must represent a process catalyzed by a metal surface.

Further evidence against a bimolecular scrambling mechanism was provided by lowering the vapor pressure of 60a in the pyrolysis tube. When a 1M solution of 60a in hexafluorobenzene was vacuum transferred through a quartz tube apparatus (Figure XV) at 450°C and low pressure (initially 0.01 mm Hg), one pass was sufficient to cause 97% scrambling of label in the cis-hexadiynene and only 8% (±5%) in the trans isomer by nmr analysis. Although more deuterium label was lost in the vacuum pyrolysis than in the experiments at atmospheric pressure, the results of mass spectral

Table XV

Mass Spectral Data[a] of a 50/50 Mixture of 60 and 60a as a Function of Time Spent in the Batch Analyzer[c] of a Mass Spectrometer

m/e	Fragment	Relative Intensity				
	time = (min)	0.5	2.0	5.0	10.0	20.0
76	$P(d_0)$	100	100	100	67	48
77	$P(d_1)$, $P+1(d_0)$	39	86	100	100	100
78	$P(d_2)$, $P+1(d_1)$	100	100	93	59	40
79	$P+1(d_2)$	6.5	11.5	11	8	8.3

[a]Note a., Table XI.

[b]Note b., Table XI.

[c]Partial Pressure Enediynes 1×10^{-5} atm, temperature of the stainless steel container 150°C.

Table XVI

Mass Spectral Data[a] for 60a in Vacuum Flow Pyrolysis

m/e	Fragment	Relative Intensity[b]/% of Total[c]					
cis-1, 5-hexadiyn-3-ene		Sample					
		13c		14c		15c	
76	$P(d_0)$	0	0	10.1	7.3	98	47
77	$P(d_1)$, $P+1(d_0)$	5.2	5	20.7	15	10	5
78	$P(d_2)$, $P+1(d_1)$	100	95	100	72	100	48
79	$P(d_3)$, $P+1(d_2)$	6.5	—	14.4	5.7	7.0	—
trans-1, 5-hexadiyn-3-ene		Sample					
		13t		14t		15t	
76	$P(d_0)$	0	0	13.8	9.6	100	100
77	$P(d_1)$, $P+1(d_0)$	5.2	5	30.2	21	6.4	—
78	$P(d_2)$, $P+1(d_1)$	100	95	100	69.4	0	0
79	$P(d_3)$, $P+1(d_2)$	6.5	—	6.4	—	0	0

Sample 13: Deuterium labeled 60 (60a).

Sample 14: Pyrolysis of 13 at 450°C, one vacuum transfer (0.01 - 0.1 atm)

Sample 15: after removal of acetylenic label in 14.

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[a]Note a., Table XI.

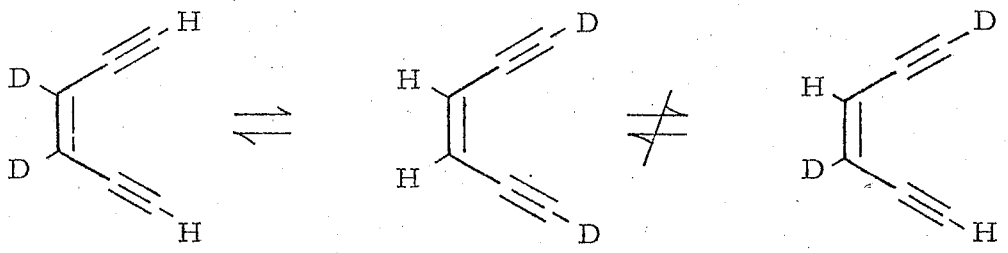
[b]Note b., Table XI.

[c]Note c., Table XI.

analysis at the various stages were practically identical to those reported in Table XI. The larger loss of deuterium and the increased scrambling in the trans-enediyne are consistent with the longer lifetime of "hot" molecules formed by collision with the wall at low pressure where collisional deactivation does not proceed as rapidly as in the atmospheric flow pyrolyses. The 150° difference in temperature required to cause complete rearrangement in the vacuum system compared to the atmospheric flow parallels nicely the 130° increase required by D'Amore[111] with the trans-1,2-diethynylcyclopropane (trans-61a, X=Y=H) shown to be unimolecular in an in-depth kinetic study. Although the actual pressure in the reaction zone was not known, monitoring the pressure at point A in the apparatus pictured in Figure XV showed a maximum of 0.1 mm Hg during the transfer. Assuming a total volume of 100 ml in the entire apparatus, an estimation of the instantaneous partial pressure of 60 in the hot zone can be made at approximately 1×10^{-6} atmosphere. I would certainly have expected a bimolecular process to have been much slower at such a low pressure.

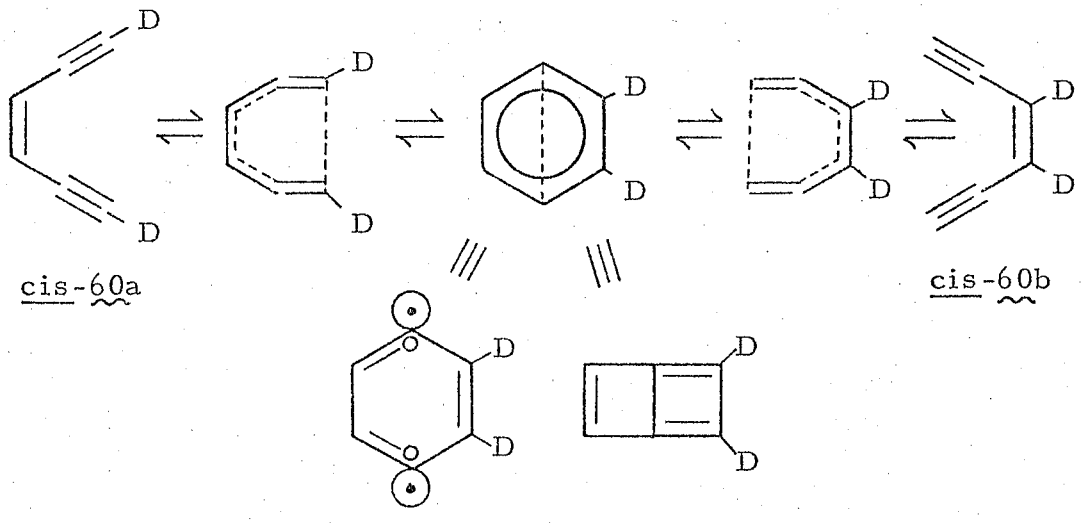
Trapping a 1,4-Dehydrobenzene Intermediate

The preceding experiments with 1,6-dideutero-1,5-hexadiyn-3-ene (60a) prove that a unimolecular, degenerate rearrangement is proceeding during the gas phase pyrolysis of cis-60 which interconverts only cis-60a and cis-60b. No single exchange products such as cis-60c are formed. This result requires that cis-60 is being transformed via an intermediate or transition state in which



cis-60b cis-60a cis-60c

C-1, C-3, C-4 and C-6 are chemically equivalent. Furthermore, since both deuteria are moved at once, C-1 and C-6 as well as C-3 and C-4 must be paired in the D_{2h} or D_2 symmetrical species. Thus, double bond character must develop between C-1 and C-6 and triple bond character between C-2 and C-3 as well as C-4 and C-5 although not necessarily at the same time. Whether any bonding occurs between C-2 and C-4 at some point between cis-60a and cis-60b is open to conjecture. Although an in depth discussion of the possible nature of this rearrangement is best left



cis-60a cis-60b

until later, the calculated heats of formation for 28 species together with the estimated 32 kcal/mole activation energy for the rearrangement of cis-60a to cis-60b strongly suggests that an intermediate of at least D_2 symmetry is involved.

One way to discriminate between a reaction passing through a transient intermediate and one which only possesses a transition state of this symmetry is via a trapping reaction. Only an intermediate can have discrete bimolecular chemistry, exhibiting selection between various paths of reaction of differing activation energy since by definition[141(b)] a transition state has zero lifetime and no barrier to further reaction along at least one internal coordinate. But since two transition states can also compete in a sense for starting material, there must be additional evidence that the two competing reactions come from a common intermediate with a definite lifetime. In my particular case, one would like to have the postulated 1, 4-dehydrobenzene intermediate select between a bimolecular trapping reaction and the degenerate (deuterium scrambling) rearrangement demonstrated in the previous section. However, since the rearrangement is unimolecular, only if the barrier to trapping is extremely low compared to ring opening of a 28 species can bimolecular trapping compete with deuterium scrambling. Since the best evidence for a free intermediate is to be found in the gas phase[142] where formation and subsequent reaction are two separate events requiring a transient species with a lifetime of at least 10^{-7} sec (diffusion rate control in the high pressure region (0.1 torr) when the trapping reaction is 100%

efficient), our initial attempts to trap a 28 species were in the gas phase.

In Breslow's presumed formation of 28a(b),[108] rapid addition of dimethylamine across the strained 1, 4-double bond was postulated to account for the diphenylisobenzofuran trapped species 77. In the absence of DPIBF, the dimethylamino-dewar-benzene ring opens to dimethylanaline. Therefore, as a first attempt to trap a 28 species, I carried out a pyrolysis of cis-60 at 300°C in the atmospheric pressure flow apparatus shown in Figure XIV, where the helium carrier gas was replaced by $HN(CH_3)_2$. Such temperatures with a 60 ml/min flow rate had previously been shown to produce complete scrambling of deuterium label in cis-60 in the manner discussed (vide supra). The appearance of significant amounts of N, N-dimethylaniline in the pyrolysate compared to appropriate controls would be strong evidence for a trapped 28a(b).

As a control, a mixture of cis- and trans-1, 5-hexadiyn-3-ene, prepared as described previously from 1.0 gm 3-tosyloxy-1, 5-hexadiyne, was vacuum transferred into 1.5 ml devolatilized pristane (2, 6, 10, 14-tetramethylpentadecane) and blown into the quartz tube apparatus at 25°C with $HNMe_2$, collecting the products in a glass helices-filled trap at -10°C. The pristane turned bright yellow immediately upon introduction of the amine and a yellow oil condensed in the traps. Glc analysis of a CCl_4 solution of the material showed several products not present in the dimethylamine itself but no returned enediynes. The major product, in approximately 10% yield, was tentatively identified as

6-(N, N-dimethylamino)fulvene 55,[143] probably formed by nucleophilic addition to one of the acetylenic bonds and subsequent cyclization.[144]

Apparently a less nucleophilic trapping agent was needed. The search for a suitable agent for gas phase pyrolysis experiments included pyrolyses with H_2O, MeOH, MeSH and H_2S. In each case, suitable controls demonstrated that the hexadiynenes were relatively inert to the reagents at 25°C, being most unreactive with H_2O and MeOH and only slightly less so with MeSH but having a disappearance half-life of one hour with concentrated hydrocarbon solutions of H_2S, yielding, however, no discernable volatile products. The only encouragement in all these experiments was found in the H_2S driven pyrolysis at 410°C (60 sec estimated contact time) where a small yield of thiophenol and a somewhat larger yield of benzene was seen. Upon attempted scale-up, however, the total yield of products could not be raised so spectral verification was impossible. Parallel control experiments with added amounts of thiophenol showed that while by my methods 1.0 mgm was easily seen in a pyrolysate, 0.1 mgm represented the limit of detection. In retrospect, all these experiments were performed at too low a temperature and with too little material if 14 kcal/mole is a more reasonable estimate for the difference in the heat of formation of a 28 species and our cis-60. Since each experiment was run at a 60 ml/min flow rate for two hours, the instantaneous concentration of cis-60 would have been 4×10^{-4}M if it is assumed that the enediyne was uniformly distributed throughout that time. This

translates into an instantaneous concentration of 2×10^{-9}M of 28d(e). The concentration of trapping agent in the gas phase at one atmosphere, 410°C is 2×10^{-2}M. Thus, it requires a bimolecular rate constant on the order of 10^2 l mol^{-1} sec^{-1} for the trapping reaction to give 1 mgm of thiophenol from a 28 species with a ΔH_f° of 140 kcal/mole in 60 sec. While this is not an impossibly high rate constant for a bimolecular reaction in the gas phase,[141(a)] it does illustrate that I am probably at the limit of detectability for anything interesting in the way of reaction of a transient 28. Increasing the concentration of 60 in the gas phase or increasing the temperature are both ways of increasing the proportion of products from 28; however, this would also increase the rate of polymerization of the enediynes. The remaining possibility is to increase the concentration of the trapping agent.

The highest concentration of trapping agent is achieved when the pyrolyses are done in solution with the trapping agent as solvent. Since the concentration of a neat liquid is on the order of 50M, one will have gained a factor of $>10^4$ in the bimolecular trapping rate by carrying out the reaction in solution. My preliminary experiments with cis- and trans-60 indicated that this molecule is very reactive to polymerization at moderate concentrations. When samples of an approximately 1.0M degassed cyclohexane solution of cis- and trans-60 were pyrolyzed at 100°C in Pyrex tubes sealed under vacuum, a half-life of two minutes was observed for the disappearance of cis-60 versus an n-octane internal standard while the half-life for disappearance of the trans

was somewhat longer. The product in all these experiments, even those in which the decomposition was only 25% complete, was a powdery brown polymer which could not be characterized. Assuming simple bimolecular, second order kinetics for the polymerization reaction and a bimolecular Arrhenius A factor of 10^6, a rate constant k_2 of 0.01 l mol^{-1} sec^{-1} can be estimated. If one makes the assumption that the liquid phase unimolecular kinetics of the degenerate rearrangement of cis-60 should approximate the atmospheric pressure kinetics where a scrambling half-life of cis-60a of 0.5 min at 210°C was measured, one can predict that at 0.01M concentration, the polymerization half-life should be more than five times longer than the scrambling half-life at this temperature.

The experiment designed to demonstrate scrambling of cis-60a in solution began with preparation of an approximately 0.01M solution of cis- and trans-1, 6-dideuterio-1, 5-hexadiyn-3-ene (60a) in olefin free pristane (2, 6, 10, 14-tetramethylpentadecane, B.P. 148-150°C at 8 mm Hg pressure) prepared as described previously by vacuum transfer from triethyleneglycol-0, 0-d_2. Previous experimentation had shown that the minimum analyzable enediyne is approximately 1.0 mgm in a 2% solution by the glc-mass spectral technique employed above. Since 0.01M solutions of 41 contain 0.7g mgm/ml total enediyne, it was seen that at least 10.0 ml of such a solution must be pyrolyzed to observe any cis-60 after two polymerization half-lives and workup by N_2 assisted transfer from the hydrocarbon. When 10.0 ml samples of this solution were

sealed in EDTA washed pyrex tubes after three freeze-thaw degassing cycles and pyrolyzed at 200°C in steel containers immersed in a thermostated oil bath, gas chromatographic analysis showed one new product being formed at the expense of the cis-60. (See Figure XVII for a plot of the relative concentration of cis- and trans-60 as a function of time at 200°C.) Combination of all samples pyrolyzed 10 minutes or longer at 200°C and preparative gas chromatographic isolation of this product showed it to be dideuterobenzene, 88% d_2 (8% d_1, 3% d_0) by mass spectral analysis. Since the starting enediynes were 90% d_2, 93% in the acetylenic positions, this represents a loss of only 3% of the label in solution. Unfortunately, the gas phase ir which would have told how much ortho, meta, and para benzene-d_2 there was in the mixture was not run. Separate pyrolyses of pure cis- and pure trans-60 in 2, 6, 10, -14-tetramethylpentadecane prepared as described earlier, each >99% free of the other isomer by glc analysis, showed that the origin of the benzene was cis-60.

The rate of disappearance of cis-60a followed reasonable first order kinetics with a half-life of approximately 2.0 minutes at 200°C. The trans-60a, on the other hand, was decomposing by a second order process with a half-life nearly three times this. The production of benzene was also first order, and the rate constant of $7\ (\pm 0.7) \times 10^{-3}$ sec^{-1} estimated compares favorably with the $6.5\ (\pm 0.7) \times 10^{-3}$ sec^{-1} calculated for the disappearance of cis-60a assuming first order kinetics. However, when this pyrolysis was carried out at 150°C in a manner identical to the above, it is

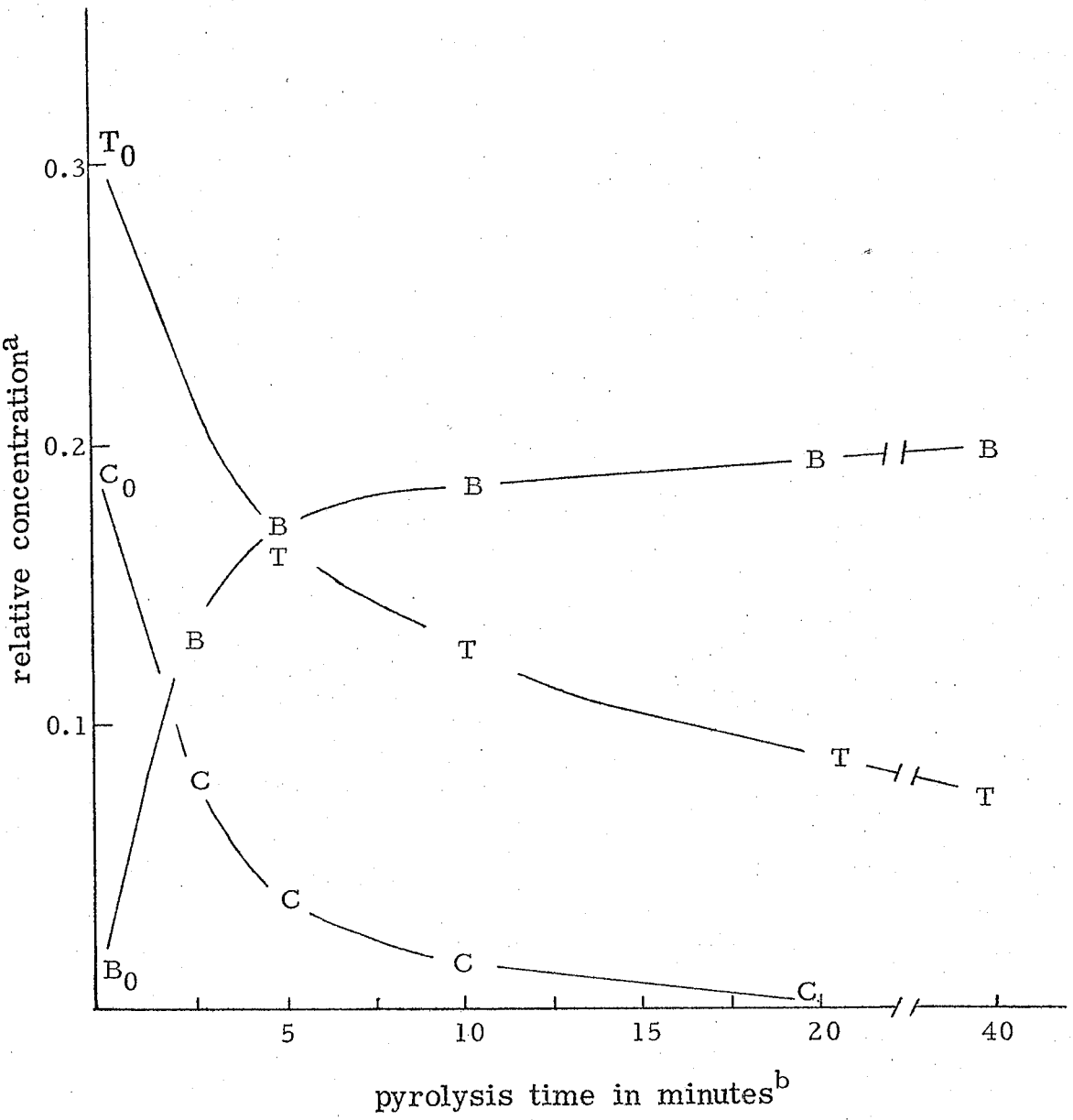


Figure XVII

Pyrolysis of 60 in Pristane,[c] 200°C

[a]Concentration relative to internal standard n-octane, T = trans-60, C = cis-60, B = benzene

[b]Real time = recorded time + 0.5 min dead time

[c]2, 6, 10, 14-tetramethylpentadecane, initial concentration 60, ~0.01M

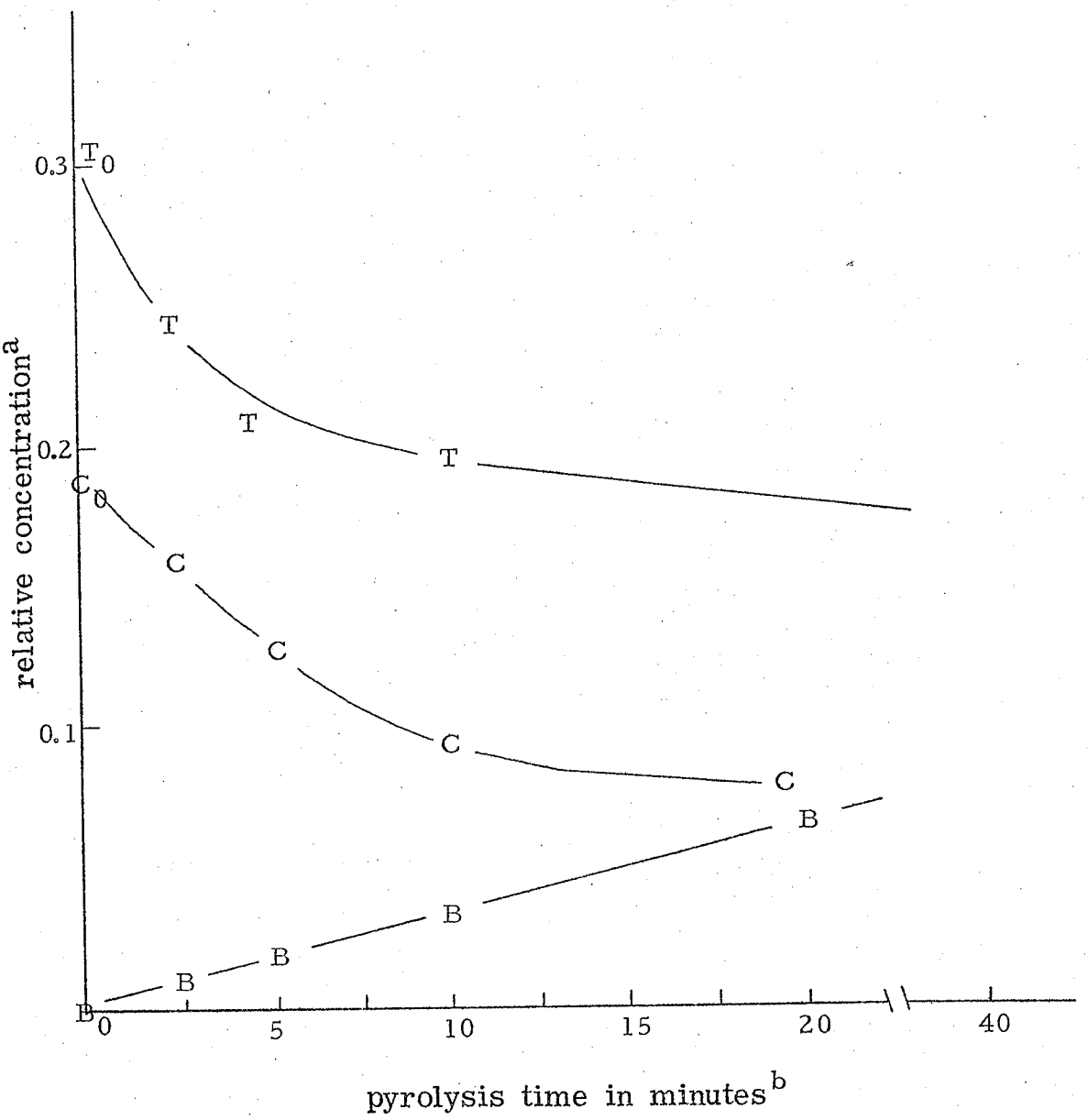


Figure XVIII

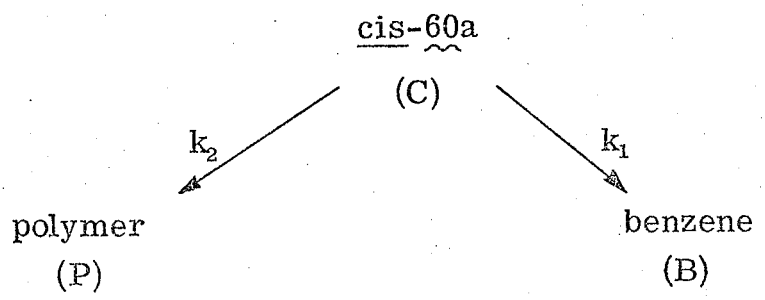
Pyrolysis of 60 in Pristane,[c] 150°C

[a]Concentration relative to internal standard n-octane, T = trans-60, c = cis-60, B = benzene

[b]Real time = recorded time + 0.5 min dead time

[c]2, 6, 10, 14-tetramethylpentadecane, initial concentration 60, ~0.01M

clear that a more complicated kinetic analysis is necessary since the disappearance of trans-60a was more rapid than expected at this temperature (Figure XVIII). Here, both cis- and trans-60a disappeared at comparable rates which fell between first and second order. The production of benzene remained first order but was now much slower than the disappearance of cis-60a. Since cis-60a gave benzene by a high yield unimolecular path at 200°C, the kinetic scheme of a competing "second order" polymerization path can be proposed. Although the differential equation for such a



$$\frac{-d[c]}{dt} = k_1[c] + k_2[c]^2$$

scheme can be solved, the integrated form is not very useful for determining k_1 and k_2. Work by Young and Andrews suggested[145] plotting $(d[c]/dt)/[c]$ versus $[c]$. This gives a k_1 of 1.3×10^{-3} sec^{-1} from the intercept, clearly too large a value based on that expected from the data at 200°C. But even a lower limit for this rate constant (obtained by plotting the actual data for the concentration of benzene over time taking the initial concentration of cis-60

as the infinity point) of $2\ (\pm 0.7) \times 10^{-4}$ sec^{-1} is too large since an activation energy of only 26 kcal/mole results upon combination with the data at 200°C in a two point Arrhenius plot.

To answer the question originally posed in this experiment, reisolation of cis- and trans-60 from a sample where roughly half of both had disappeared at 200° showed no scrambling of deuterium label under conditions where as little as 5% would have been detected, the enediynes being recovered >90% d_2 in the acetylenic positions. In the case of the trans-isomer no scrambling of label was expected but clearly in the cis-1, 5-hexadiyn-3-ene, formation of benzene must be at least 4 kcal/mole more favorable than reopening a cyclic intermediate, assuming a pseudo first order reaction with near zero activation entropy in both cases. Because free radicals are virtually the only intermediates capable of removing hydrogens from hydrocarbons, the quantitative production of benzene from the liquid phase pyrolysis of cis-60 strongly suggests that the symmetrical species implicated in the gas phase deuterium scrambling experiments is a true intermediate capable of reacting as expected of the 1, 4-benzenediyl structure 28d(e). But since almost all of the 28 species illustrated in Figure IX might be expected to give benzenoid products at these temperatures, further trapping experiments are in order.

Since the radical abstraction of chlorine atoms from chlorocarbons is as much as ten times slower than abstraction of hydrogens from secondary and tertiary carbons,[146(b)] we proposed generation of the hypothetical intermediate 28 in CCl_4 to further

test the possibility that the rate determining step in the formation of benzenoid products from cis-60 is the cyclization of 60. Furthermore, since CCl_4 is a common reference solvent for hydrogen abstraction competition rates, it is important to know the behavior of 60 in this solvent. Pyrolysis of 50 μl portions of 0.01M solutions of cis- and trans-60 in CCl_4, prepared as described above and degassed and sealed under vacuum in 0.4 cm O.D. Pyrex tubes, at 200°C in steel jackets showed one new product growing in presumably at the expense of cis-60 since no further increase was seen after all the cis-60 was exhausted while trans-60 remained. Spiking with an authentic sample suggested that the new product was 1,4-dichlorobenzene, formed in 68% yield based on cis-60. Here again, the data in Figure XIX give first order plots for the disappearance of cis-60 and the appearance of the benzenoid product with rate constants that are equal within experimental error at $6.5\ (\pm 0.7) \times 10^{-3}$ sec^{-1} and $7.5\ (\pm 0.7) \times 10^{-3}$ sec^{-1}, respectively. The virtual identity of these rate constants to those obtained at 200°C in pristane solution is consistent with cyclization of cis-60 to 28 as the rate determining step. At 150°C, pyrolysis of 0.01M cis- and trans-60 as above (Figure XX) showed again that cis-60 disappeared faster than p-dichlorobenzene was formed. The lower limit for k_1 of appearance of benzene obtained from these data was again in the neighborhood of $2\ (\pm 0.7) \times 10^{-4}$ sec^{-1} in complete agreement with the data on pyrolysis of cis- and trans-60 in pristane solution.

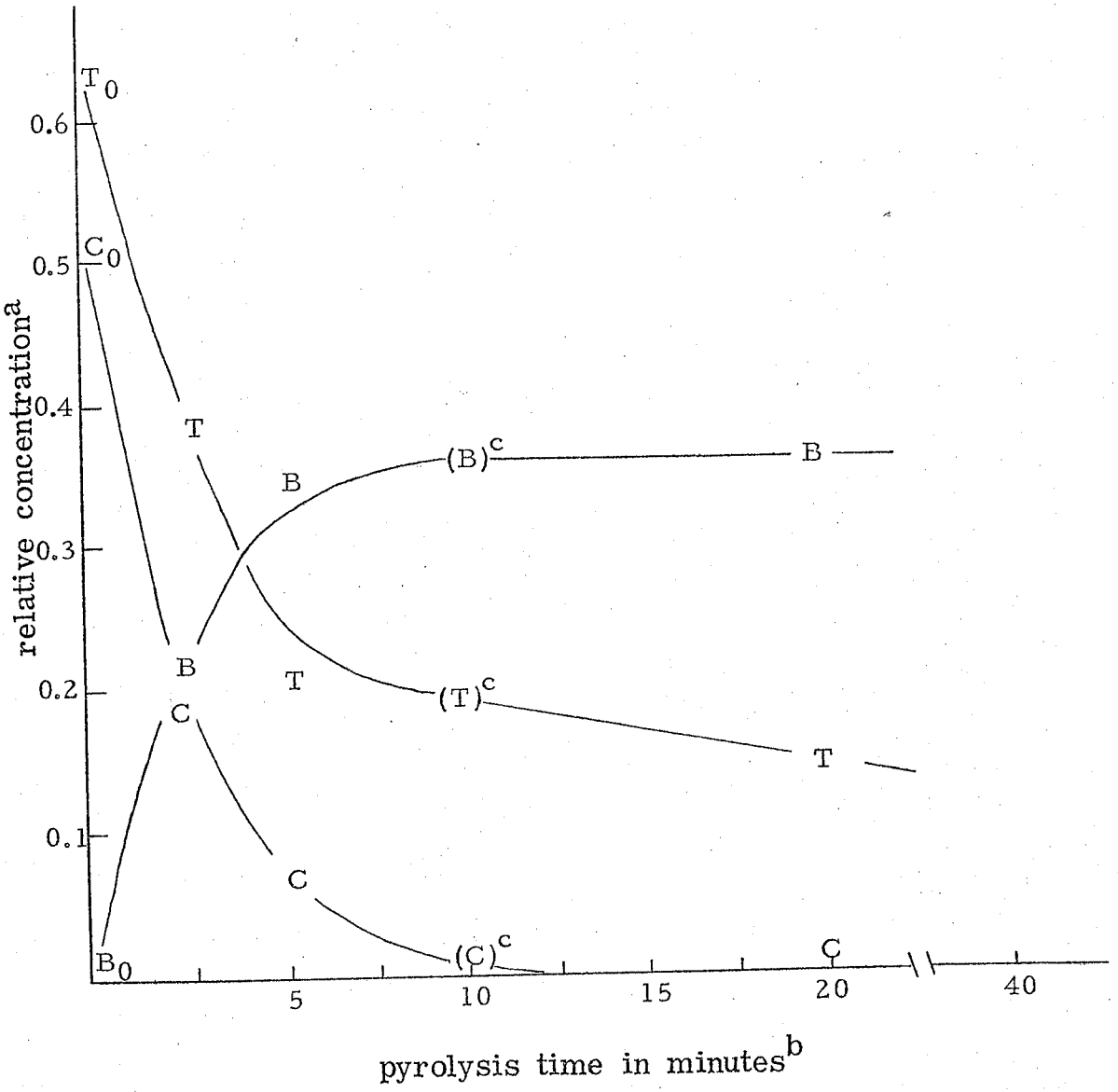


Figure XIX

Pyrolysis of 60 in CCl_4, 200°C

[a]Concentration relative to internal standard n-octane, T = trans-60, C = cis-60, B = p-dichlorobenzene

[b]Real time = recorded time + 0.5 min dead time

[c]Added 0.01M benzoquinone

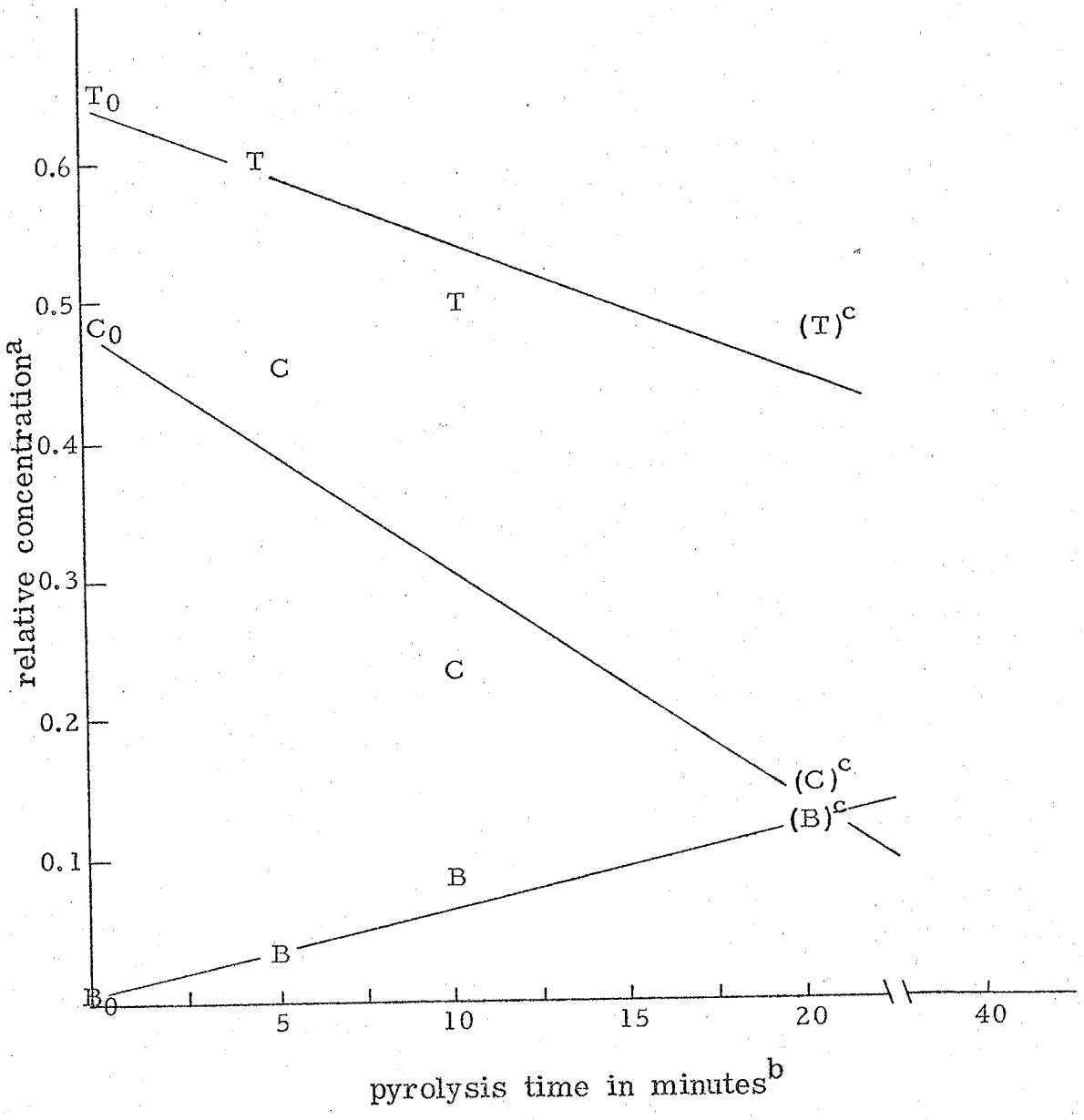


Figure XX

Pyrolysis of 60 in CCl_4, 150°C

[a]Concentration relative to internal standard n-octane, T = trans-60, C = cis-60, B = p-dichlorobenzene

[b]Real time = recorded time + 0.5 min dead time

[c]Added 0.01M benzoquinone

This reaction was run on a preparative scale by pyrolyzing 100 ml of a 0.01M solution of cis- and trans-60 in CCl_4 in a stainless steel bomb at 200°C for five minutes. Distillation of >90% of the CCl_4 followed by glc analysis as before now showed three new products in about 5% total yield as well as a 70% glc yield of the major product. This peak was isolated by preparative gas chromatography and its identity to authentic para-dichlorobenzene confirmed by nmr and ir. Of the remaining products, two were thought to be the ortho- and meta-dichlorobenzenes based on coinjection of authentic material in the glc, while the third most likely was p-chlorotrichloromethylbenzene, but this was not confirmed. The ortho- and meta-isomers were not seen in the Pyrex tube pyrolyses, although the latter should have been detectable based on its size relative to the p-dichlorobenzene. Perhaps the metal container is responsible for the formation of these products. Extensive examination of the pyrolysate using authentic samples showed no hexachloroethane, tetrachloroethylene or any other product which would provide a mass balance. It is well known[148] that chlorocarbons have a very poor response factor in a flame ionization detector. Therefore it was of interest to see how little of the various chlorocarbons could be detected by this method. A 1 μl injection of a 0.001M solution represented the minimum detectable chlorobenzene and dichlorobenzene, whereas the minimum detectable $Cl_3C\text{-}CCl_3$ or $Cl_2C{=}CCl_2$ was 1 μl of a 0.01M solution. Therefore, while one could easily see a 1% yield of the chlorobenzenes, a

minimum yield of 10% would be required for detection of the more heavily chlorinated possible products.

It was also important to rule out radical chain processes as the source of the para-dichlorobenzene. For this reason pyrolyses of 0.01M solutions of cis- and trans-60, 0.01M in p-quinone a known radical chain inhibitor,[146(a)] were carried out. One sample was pyrolyzed at 200° for 10 minutes and another at 150° for 20 minutes. Both samples showed product distributions essentially identical with the corresponding samples without p-quinone (see Figures XIX and XX). The possibility that abstraction of chlorine was now the rate determining step and that therefore one should see some scrambling of label in a pyrolysis of 60a in CCl_4 was not checked.

At least one of the possible structures for 28 in Figure IX is a dipolar species. Thus we felt that one way to characterize the intermediate was to carry out the pyrolysis of 60 in a polar solvent. Methanol was chosen since it should be able to protonate 28f and since there are numerous reports that carbenes such as 28g can insert into O-H bonds.[149] A radical intermediate, on the other hand, should abstract mainly the hydrogens on carbon, since this bond is weaker.[150] Pyrolysis of 0.01M cis- and trans-60 in Spectroquality methanol in sealed Pyrex tubes as above showed under glc analysis the rapid disappearance of cis-60, the somewhat slower disappearance of trans-60 and the appearance of benzene as the major product in high yield. (These data are summarized in Figure XXI.) Examination of a sample pyrolyzed for 20 minutes

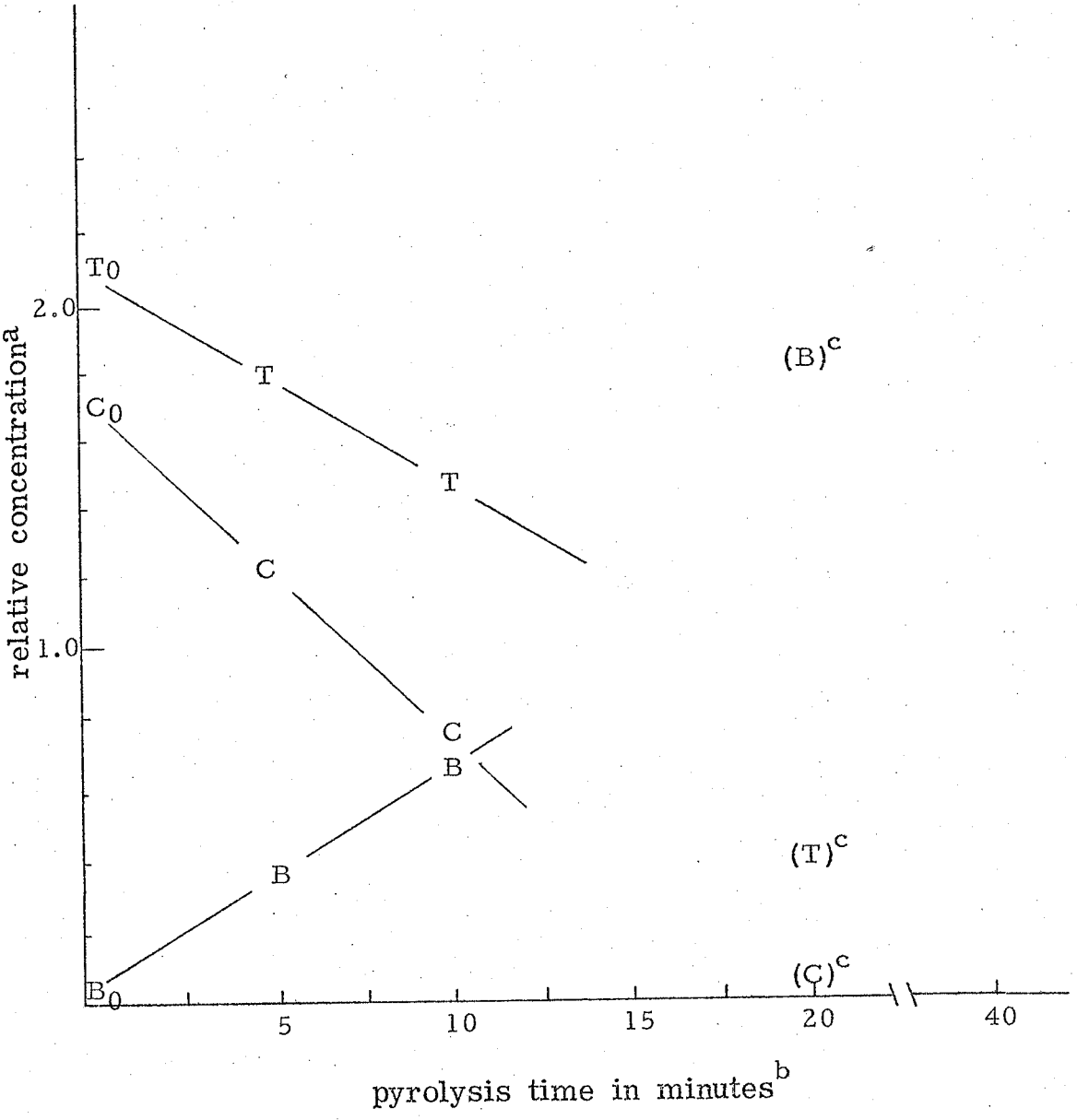


Figure XXI

Pyrolysis of 60 in MeOH, 150°C

[a]Concentration relative to internal standard n-octane, T = trans-60, C = cis-60, B = p-dichlorobenzene

[b]Real time = recorded time + 0.5 min dead time

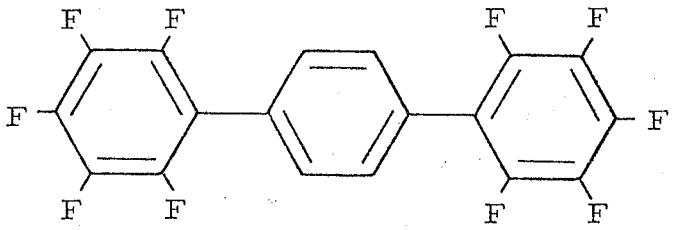
[c]20 min at 200°C

at 200°C at maximum sensitivity on the glc showed an approximately 5% yield of benzyl alcohol as the only other product. Coinjection on the glc with an authentic sample supported this identification. Anisole and 1, 4-dimethoxybenzene were expressly looked for but were not present although control experiments with added amounts of these materials showed that as little as 0.5% yield could have been detected. Thus, even when given a choice of behaving as a polar or radical species, the intermediate clearly selects the latter at least by a factor of 10.

Despite my previous reservations that bimolecular, pseudo first order trapping of a 28 species would not compete with scrambling of deuterium label in cis-60a, it is in fact too rapid. However, if a suitable solvent can be found where scrambling can occur to a significant extent, my initial goal of forcing the intermediate to select between trapping and reopening can be realized by adjusting the concentration of abstractable hydrogens or chlorines. The initial experiments were with hexafluorobenzene. Radical abstraction of fluorine is very difficult, perhaps requiring more than 30 kcal/mole activation energy.[151] Analysis of 0.01M solutions by the nmr and mass spectral methods employed in the previous section for the gas phase pyrolysis is, however, even more difficult. When large (>100 μl) samples were injected into the glc-ms equipment (see the General Experimental Section), the tailing of the hexafluorobenzene peak on the glc column and the residual C_6F_6 in the separator precluded detection of the enediynes. When the glc column temperature was lowered to increase the difference in

retention time between C_6F_6 and the cis- and trans-60a, the peaks due to the latter were evidently so broad that insufficient sample reached the mass spectrometer since no m/e 76 ions could be found. The method of choice proved to be FT-nmr. Here, by locking on a capillary sample of THF-d_8, the deuterated enediyne acetylenic residual protons could be detected after 10^5 pulses. Pyrolysis of a 0.01M solution of cis- and trans-60a (90% d_2 and 94% deuterated in the acetylenic positions by analysis before dilution) in 0.5 ml hexafluorobenzene as a degassed sample in a sealed Pyrex tube for five minutes at 200°C showed $< 30\%$ recovery of the cis-60. Fourier transform nmr analysis showed, however, only 11% scrambling of label by use of the formula given on page 282. Polymerization probably accounts for some of this loss of material, and perhaps a cyclized radical from the cis-60 is the origin of the polymerization, initiating a radical chain by addition to the cis- or trans-60a in solution. On the other hand, hexafluorobenzene is known to undergo a very facile homolytic substitution reaction with phenyl radicals.[152] Perhaps a similar process is accounting for the lack of scrambling here. No triaryl products such as 88 were seen in the glc trace, but a thorough search was not conducted. Williams reports, however, that for the phenyl radical the yield of biaryl products is considerably greater when the total reaction product is distilled. This is either due to the radical 89 being very stable or is a result of decomposition of dimeric 90.[152] In my case a stable radical such as 91 might give the interesting cyclic product 92. On the other hand if 90

type products are the rule, 91 is set up to give polymer.



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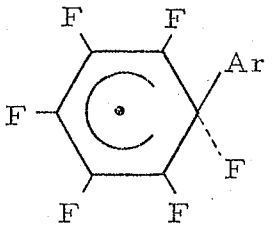

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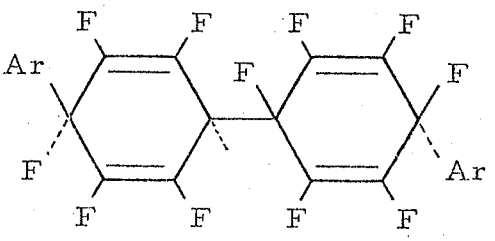

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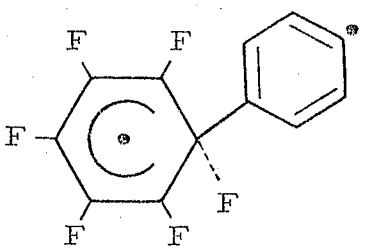

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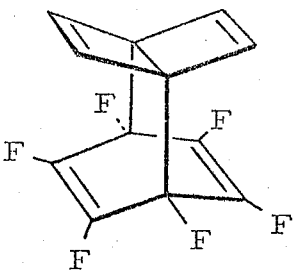
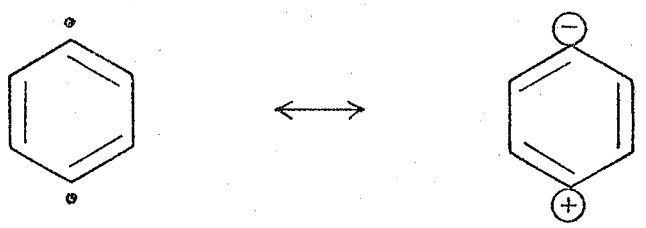


92

The homolytic substitution of an alkoxyphenyl ring is more than ten times slower than substitution of the hexafluorophenyl ring.[151] Also abstraction of hydrogen from a phenyl ring is usually a very minor component of such reactions.[153] Therefore I attempted a scrambling reaction in diphenylether, a readily available, relatively nonvolatile solvent, from which the enediynes might be recovered by transfer with nitrogen. A solution of cis- and trans-60a, 90% d_2 and 93% deuterated in the acetylenic positions, in 0.3 ml C_6F_6 was diluted to 0.01M with approximately 200 ml of devolatilized diphenylether. Pyrolysis of this sample for five minutes at 200°C showed no production of benzene or any other volatile products and a 10% recovery of the cis-60. The volatiles were recovered from the ether by passing dry nitrogen through the solution and trapping the products in consecutive U-traps at -78°C. Nmr of the recovered material (60 scans CAT, 60 MHz) showed 19% scrambling of label in the cis-60 but no scrambling in the trans-60a. This number and the 11% obtained in C_6F_6 is larger than the ±5% experimental error estimated for integration of such small signals and illustrates that the degenerate rearrangement can be made to compete with other reactions of cis-60a. However, this extent of scrambling is still too small to allow meaningful competition experiments with radical traps such as CCl_4. Perhaps pyrolysis in heavy, saturated fluorocarbons can overcome this difficulty since here the intermediate radicals cannot add or abstract.

An interesting, although incomplete experiment, which bears on our postulated 28-type radical's ability to add to a phenyl ring (as opposed to abstraction of a benzylic hydrogen) is its formation in toluene solution. Pyrolysis of 50 μl samples of 0.01M solutions of cis- and trans-60 (in glc purified toluene as above in EDTA washed Pyrex tubes at 200°C) showed benzene as the major product in 36% yield. The rate of disappearance of cis-60 is 7×10^{-3} sec^{-1}, in line with all the previous determinations of this value in solution. The rate of appearance of benzene is now much slower, but this is understandable in terms of 28d(e) selecting between abstraction and addition. What is surprising is that the proportion of side chain attack is so high. Phenyl radicals produce 12% abstraction product with toluene while the more nucleophilic p-methoxyphenyl radical produces 50%.[154] The actual ratio from a 28 species may be even higher when it is remembered that the initial abstraction produces a phenyl radical which then either abstracts (12%) or adds (88%). Thus, one is tempted to say that the 28d(e) postulated is a quite polar radical species, i.e., it may contain a large contribution from 28f. In part, however, the large



28e 28f

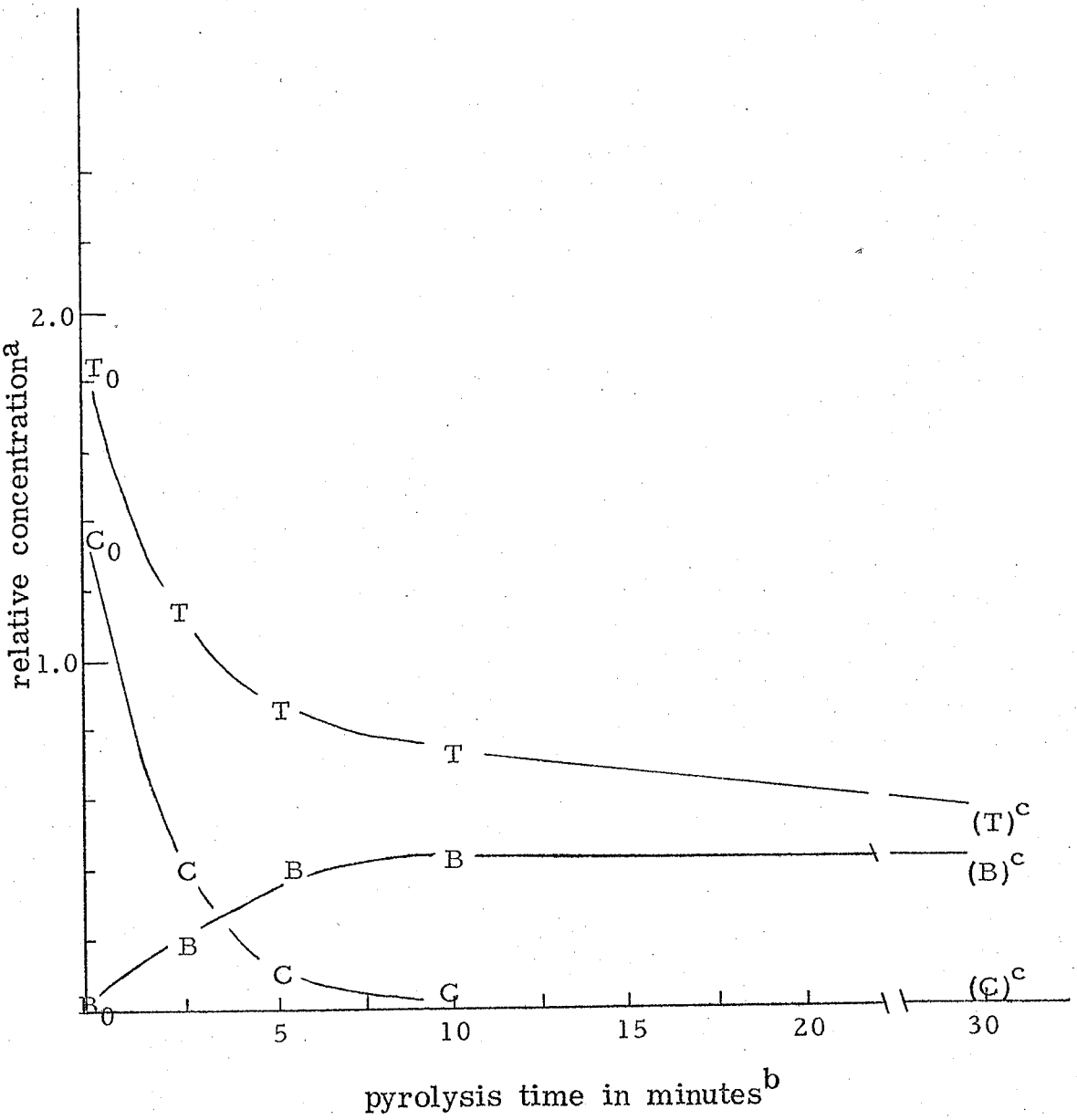


Figure XXII

Pyrolysis of 60 in Toluene, 200°C

[a]Concentration relative to internal standard n-octane, T = trans-60, C = cis-60, B = benzene

[b]Real time = recorded time + 0.5 min dead time

[c]Preparative scale pyrolysis in stainless steel bomb

abstraction yield may be due to the higher temperatures in my experiment compared to the 100°C for the data on phenyl and methoxyphenyl radicals since the addition reaction has been shown to be reversible.[155]

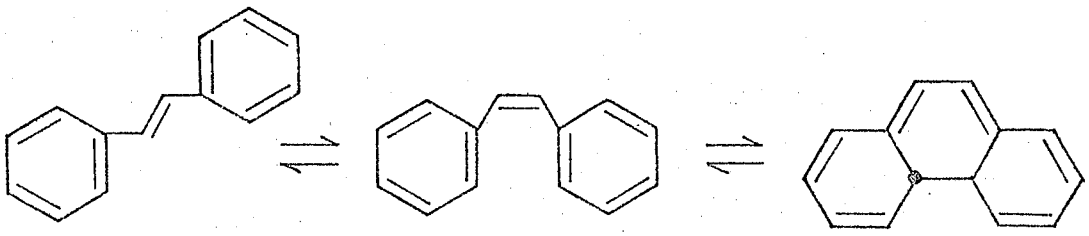
This experiment was termed incomplete since there are obviously other volatile products formed. As it turned out, all commercial sources of toluene examined were very impure. Distillation reduced this by factors of ten to a hundred. Preparative gas chromatography led to further reductions. However, when a large scale experiment was run with 80 ml toluene and the heavier products concentrated by distillation, it was obvious that there were still too many impurities which interfered with analysis of the 1% or so yields of trapped products. Diphenylmethane was definitely seen by coinjection of authentic material. Bibenzyl was definitely not present although as little as 1% yield could easily have been seen. The 2-, 3-, and 4-methylbiaryls, if present, were obscured under impurities. A trace of biphenyl was perhaps present. None of these materials was isolated although an interesting story might be told by their confirmation.

Liquid-Phase Photolysis of a Deuterium Labeled Enediyne

Spectroscopic observation of a 1,4-dihydrobenzene intermediate such as 28a is made difficult by the low concentration of 28 in thermal equilibrium with cis-60 even if all other reactions of 28 could be eliminated under the pyrolysis conditions employed above. But despite the fact that rearrangement of 28 to cis-60 may be as

much as 14 kcal/mole exothermic, this rearrangement would be expected to be slow below -50°C if 28d(e) is indeed in a substantial energy well (16 kcal/mole) with respect to 60 as is indicated by Dewar's calculations[120] (MINDO/3) and my own kinetic estimates (vide supra). Thus, a low temperature method of generating 28 is desired.

The photolytic cyclization of hexatrienes to cyclohexadienes is a well-known reaction.[163] As an example, the reversible cyclization of cis-stilbene (cis-93)[164] to 94 which sacrifices two benzene resonance energies, is a rapid process at -30°C. At this temperature, thermal ring opening is not competitive even though



trans-93 cis-93 94

more than 35 kcal/mole exothermic.[165] This system is also illustrative of the possibility which photolysis offers for selectively irradiating one component of an equilibrium, thereby favoring the build-up of the others. At 280 nm, trans-93 is absorbing more radiation than cis-93 which in turn is absorbing more than 94.

Therefore, trans-93 is converted largely to cis-93 and cis-93 to 94.

Since it may be possible to irradiate 60 in a region where 28 does not absorb appreciably, the photostationary state might well provide 28 in high enough concentration to be observed spectroscopically at temperatures where thermal decay back to cis-60 is slow. The initial photolysis experiments were designed, however, to demonstrate whether or not 28 could be in photoequilibrium with cis- or trans-60 in either the singlet or triplet manifold.

A solution of cis- and trans-60a, each greater than 90% deuterated in the acetylenic positions, was prepared in olefin free cyclohexane to a total concentration of 0.11M in enediyne. Samples of this solution, degassed and sealed in quartz tubes, were irradiated at 254 nm with an unfiltered medium pressure Hg lamp and forced air cooling. Although an external thermometer indicated that the temperature in the sealed tubes probably did not rise above 35°C under these conditions, the half-life of the total enediyne was only about 30 minutes. Glc examination clearly showed a readjustment of the cis/trans isomer ratio in favor of the cis-60, approaching 50/50 after one hour from an initial 40/60 isomer ratio. When account is taken of the fact that cis-60 usually disappears faster than trans-60 thermally, this readjustment in the cis/trans ratio becomes even more striking. Since at wavelengths in the neighborhood of 250 nm, trans-60 is absorbing more light than the cis-60 (λ_{max} cis 250 nm, $\epsilon = 15,000$; λ_{max} trans 251 nm, $\epsilon = 21,000$), this favoring of the cis-60 in the approach to the

photostationary state is exactly analogous to the case of the stilbenes discussed above.[166]

A 1% yield of dimeric materials were the only products in this direct irradiation. The remainder of the enediyne is probably accounted for in the yellow polymer remaining after vacuum transfer of the volatiles but a weight was not obtained. This hydrocarbon soluble polymer contrasts sharply with the brown, powdery, ether and pentane insoluble thermal polymer of cis- and trans-60. Repeated attempts, however, to produce the dimeric material on a scale suitable for isolation failed, although small amounts were always seen. Therefore, these materials were not characterized. But perhaps more importantly, at least regarding intermediacy of 28d(e), no benzene was seen in this reaction under conditions where as little as 1% could have been detected.

Mass spectral analysis on the Quad 300 ms-glc instrument described in the General Experimental confirmed the overall retention of label in the remaining cis- and trans-60. Nmr, however, showed that this material was unrearranged where as little as 5% scrambling in either isomer would probably have been seen. Thus, while it is clear from the readjustment of the cis/trans ratio that the S^1 excited state of 60 is being populated, cyclization to 28 is either not competitive with rotation about the 3, 4-σ bond and decay back to the ground state or leads to different chemistry from that expected based on its thermal formation from cis-60 (see Figure XXIII). While it is conceivable that the dimers arise

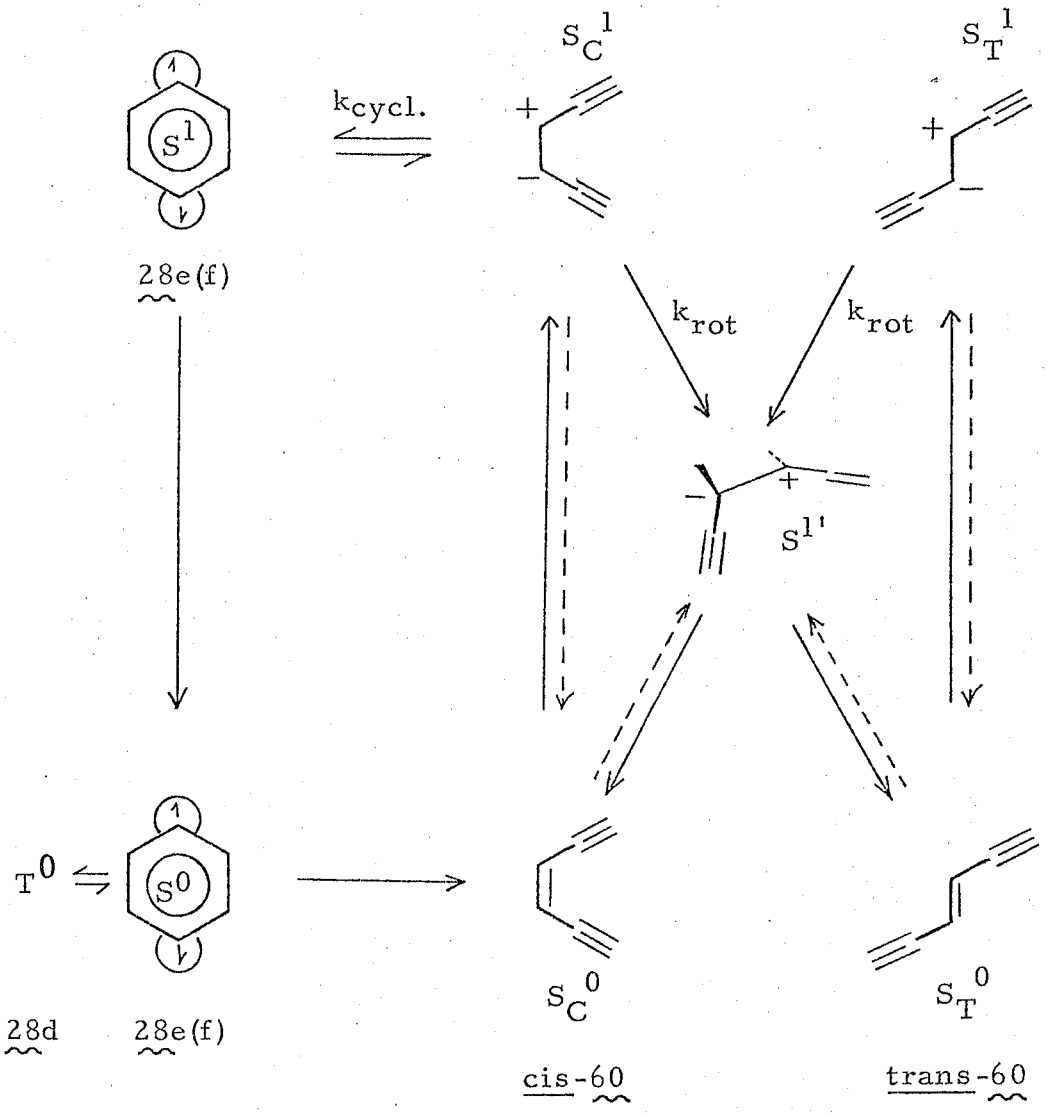


Figure XXIII

Singlet Manifold for 1, 5-Hexadiyn-3-ene

from 28a, there are several alternative pathways to dimers possible from the singlet excited states of 60.[163]

Since 28 has been predicted to be a ground state triplet diradical,[119, 120(b)] its formation may be possible from a triplet excited 60 species. Due to the fairly large energy difference between the S^1 and T^1 states of olefins, direct population of T^1 via intersystem crossing is usually not possible. Formation of the triplet excited states of 60 must therefore be brought about by the use of sensitizers. Benzophenone, a commonly used photosensitizer for conjugated olefins with T^1 energies below 69 kcal/mole above S^0,[167] was employed at 0.05M concentration in a 0.11M solution of cis- and trans-60a, 90% deuterated in the acetylenic positions, in olefin free cyclohexene. Irradiation of a degassed sample of this solution through Pyrex for three hours at 35°C yielded an approximately 50% return of total enediynes 60 but no benzene, dimers or any other volatile product. Glc confirmed an adjustment in the cis/trans ratio favoring the cis-60. Nmr again showed no rearrangement of label in either the cis- or trans-60a. An identical result (but with $t_{\frac{1}{2}}$ = one hour) was obtained with benzene as solvent, irradiating through quartz at 254 nm. Again the adjustment of the cis/trans ratio probably means that the T^1 states are being formed but that cyclization is slow compared to polymer formation and rotation/return to ground state (Figure XXIV).

Interestingly, an entirely similar situation has been observed with cis-1, 3-hexadien-5-yne (cis-95), a compound which readily gives benzene upon pyrolysis at 275°C in a flow system.[168] Direct

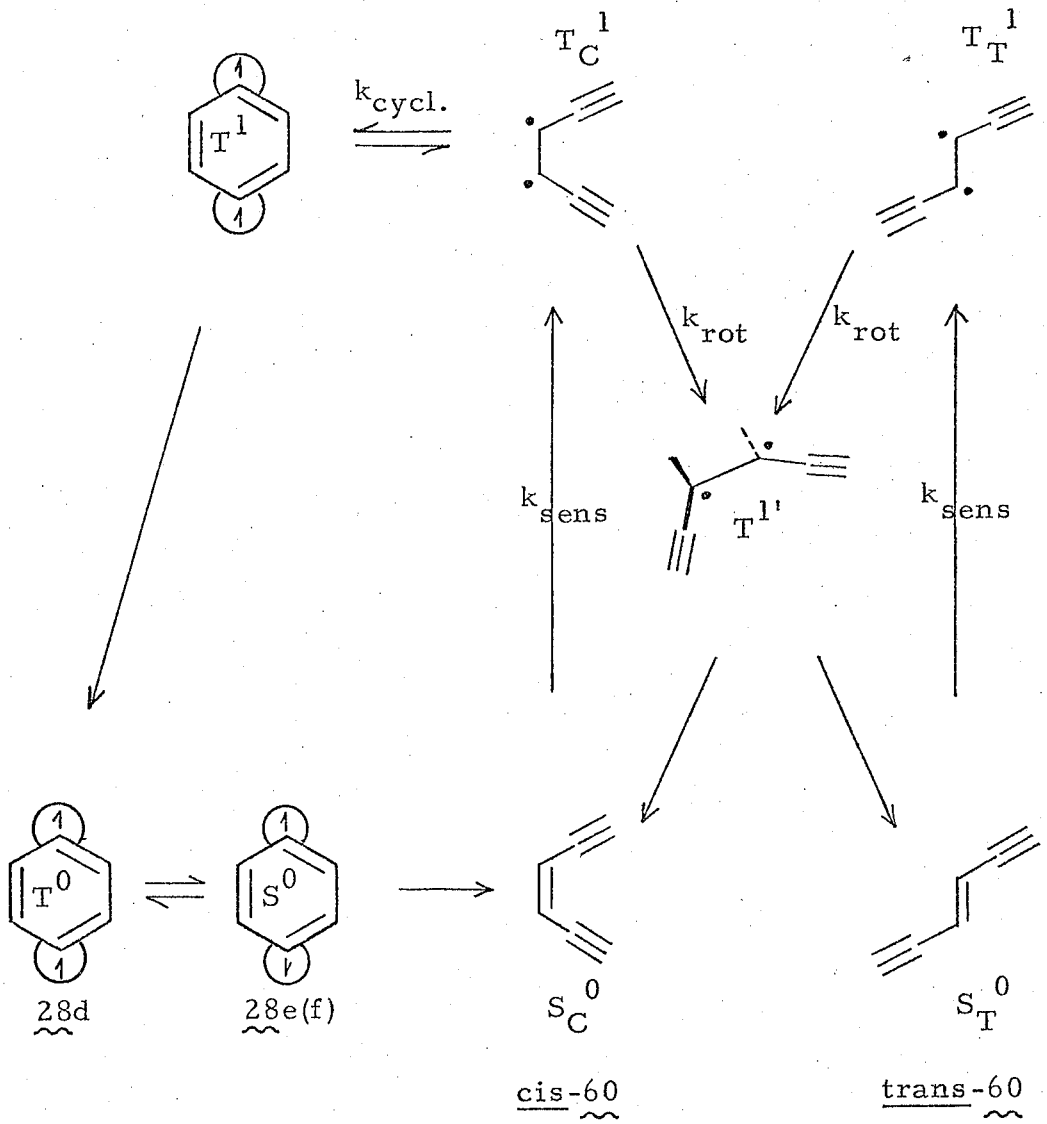
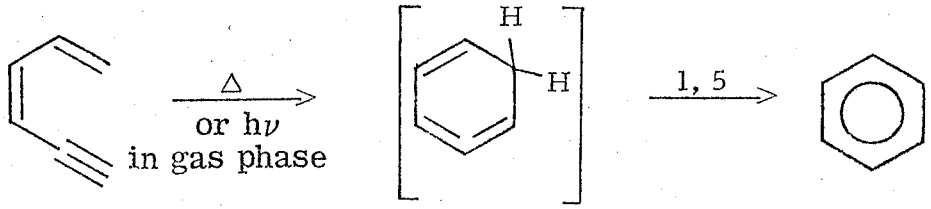


Figure XXIV

Triplet Manifold for 1, 5-Hexadiyn-3-ene



cis-95

irradiation of cis-95 in pentane solution with 254 nm light gives only polymer and cis-trans isomerization. However, when this irradiation was carried out in the gas phase at circa 0.1 torr partial pressure in one atmosphere of nitrogen, the slow formation of a 2:1 mixture of benzene and fulvene was observed together with the somewhat more rapid cis-trans isomerization observed in the liquid phase experiments.[169] Since one would not expect the lifetime of the excited species to be much longer at one atmosphere than in solution, evidently it was the high dilution achieved in the gas phase experiments which allowed the slow cyclization to benzene to compete with polymerization. The triplet sensitized photolysis of 95 has not been investigated.

In retrospect, the concentration of 60a employed above should be reduced by a factor of 10 to 100. Under such conditions, scrambling of label should compete with polymerization if cyclization of S^1 or T^1 is possible. However, since analysis is difficult at these concentrations in solution, a gas phase photolysis experiment may be more desirable as it readily allows concentration of the products for analysis.

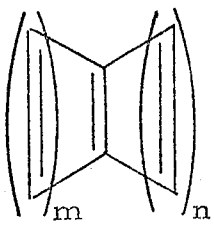
PART II

1, 4-Dehydrotropyl Cation, Anion and the Bicyclo[3.2.0]heptatrien-3-one

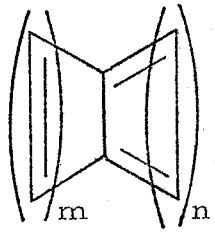
Introduction

Background: Aromaticity in Bicyclic Compounds Containing a Fused Four-Membered Ring

Despite intense current interest in the aromaticity exhibited by bicyclic conjugated systems of general formula A or B (1, 2 fused), there are but a few examples where the potentially anti-



A

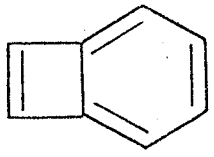


B

aromatic cyclobutadiene ring is involved. The reason for this is that such molecules may not only be resonance destabilized but also highly strained. As such they provide an interesting challenge both to the synthetic and theoretical abilities of the organic chemist. Studies of the relative importance of a 4n+2 π-electron perimeter versus the combined properties of component "localized" ring currents are particularly meaningful where such a fusion is involved. The preference in these systems for resonance forms which resemble B(m = 1) more than A and the required planarity of the dimethylenecyclobutene ring fusion make it likely that such systems will be delocalized around the perimeter to remove electron density from the four-membered ring. However, to the extent

that these molecules retain the properties of their component rings, high reactivity is expected. Proposed synthetic routes must take this into consideration.

As discussed earlier, the aromaticity of fused (4n+2) + (4n+2) π-electron systems with a (4n+2) π-electron perimeter such as napthalene is well established. Even azulene, although much less aromatic than napthalene, shows evidence for aromatic dipolar resonance forms. As a general rule for these systems, the aromaticity of the total is less per π-electron than that of either component ring alone but greater than a cycle consisting of just the perimeter. Several (4n) + (4n+2) π-electron bicyclic systems with a (4n) π-electron perimeter are now known to be characterized by instability and paratropicity as expected of antiaromatic molecules. In particular, benzocyclobutadiene (31) has recently been trapped at 8°K but dimerizes on warming to only 70°K[170] while the diphenyltetramethyl derivative 40 shows evidence of paramagnetism.[88]



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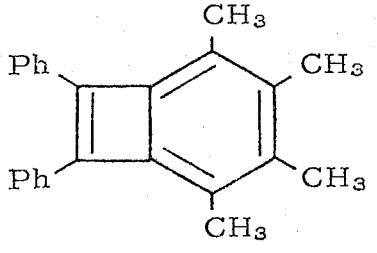
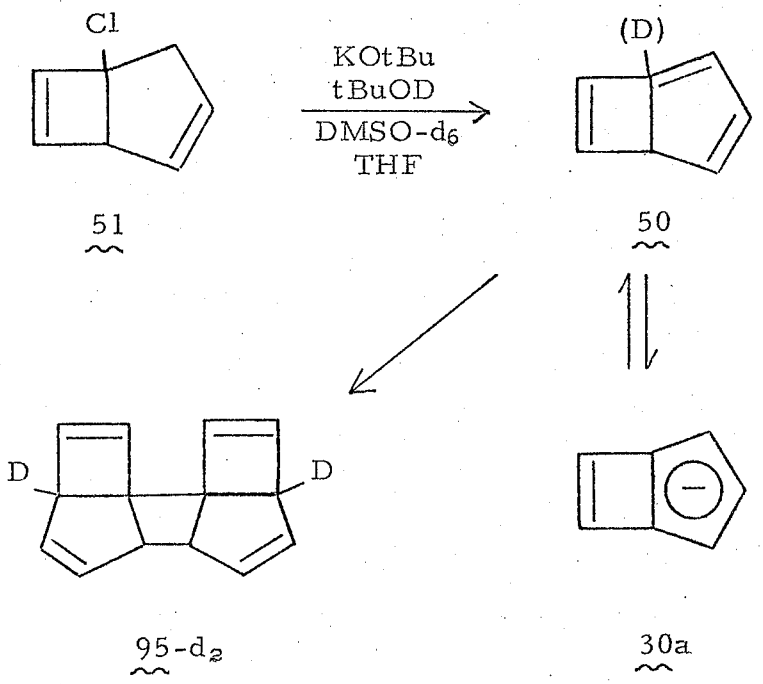


40

These 4.2.0 systems have been the subject of a review.[12] The reader is also referred to the General Introduction of this thesis for a discussion of aromaticity in such strained hydrocarbons.

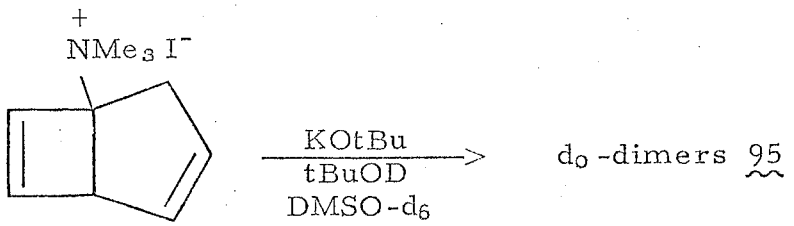
Breslow[103] and Bauld[171] have independently investigated a bicyclic hydrocarbon capable of giving an isoelectronic analogue of 31 under basic conditions. When hydrogen chloride was eliminated from 51 with potassium t-butoxide in THF, the 2+2 dimers of the strained triene 50 were isolated in over 40% yield. When the elimination was carried out in the presence of t-BuOD and DMSO-d_6, dimers 95 were isolated 100% d_2 at the 5-positions as illustrated. Since the dimers were shown not be exchange hydrogen for



51 50

95-d_2 30a

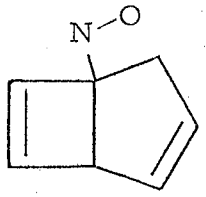
deuterium under the reaction conditions and since reisolated starting material also showed no deuterium incorporation, the reaction was interpreted as proceeding through anion 30a.[103a] By addition of various carbon acids of known pK_a to a cold solution of the anion followed by quenching with D_2O, a rough pK_a of 29 was assigned to 50 based on the partial deutaration of 95 under such conditions [100% d_2 dimers with Ph_3CH (pK_a 33) present, 50% d_1 dimers with xanthene (pK_a 29), and 0% d_1 or d_2 dimer with fluorene (pK_a 25)].[103b] In the same medium cyclopentadiene was found to have a pK_a of 18 and cycloheptatriene a pK_a of 39.[81] Thus, while the effect of the fused cyclobutadiene ring is to lower the acidity of the cyclopentadiene ring by 11 powers of ten, anion 30a is still not as destabilized as the cycloheptatrienyl anion. Bauld[171] obtained the same dimers 95 from the corresponding ammonium salt 96 but was unable to incorporate deuterium under entirely similar conditions.



96

Evidently the anion 30a is not formed here. That the dimers probably arise from the intermediate hydrocarbon 50 is seen in the pyrolysis of the N-oxide 97 where a mixture of syn- and anti-95

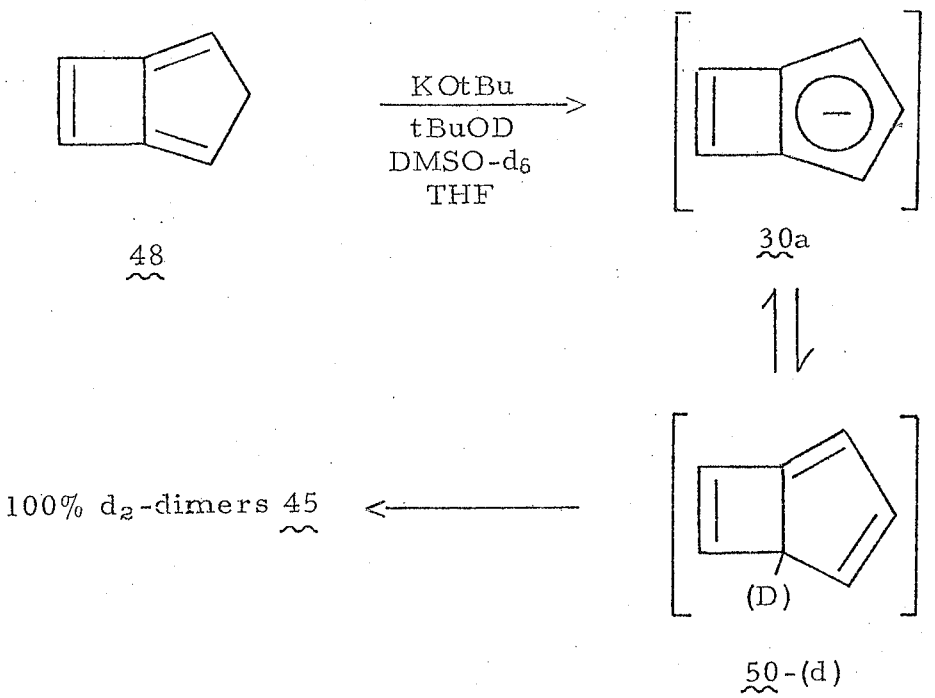
are formed, identical in all respects to the mixture obtained from the base eliminations.[171]



$\xrightarrow[120°C]{\Delta}$ dimers 95

97

D'Amore and Bergman[111] have prepared an isomeric bicycloheptatriene 48 which is considerably less reactive to dimerization and seems to be fairly stable in dilute solution (half-life in pentane, ~0.5M, is 12 hours in the absence of oxygen at 25°C) perhaps due to the smaller strain of the dimethylenecyclobutene configuration. However, reaction of 48 with potassium t-butoxide in the presence of t-BuOD as above gave a 5% yield of 100% d_2-dimers 95 . No nmr detectable concentration of anion 30a was noted. But if this reaction is interpreted as proceeding through 30a, it demonstrates the propensity of this anion to reprotonate solely at the bridgehead position (carbon 1 or 5) since no deuterium incorporation was found in reisolated 48 after 90% had been destroyed.[76] D'Amore also tried several direct routes to 30a from triene 48 in aprotic solvents but in most cases failed to produce dimers after quenching. In no case did he observe nmr concentrations of 30a or any new electronic absorptions. The major competing reaction appeared to be a rather

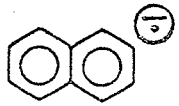


facile addition polymerization reaction of the substrate 48 in the presence of 30a and other anions. (These experiments are summarized in Table XVII.) D'Amore was able to confirm the relative ordering of ground state stability of the anion 30a with respect to the cyclopentadienyl and cycloheptatrienyl anions as determined by Breslow by studying the gas phase acidities of the hydrocarbons 48, cyclopentadiene, and cycloheptatriene by means of ion cyclotron resonance spectroscopy.[172, 76]

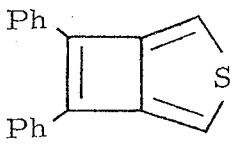
Recently Farratt and Vollhardt[173] and Vollhardt and Bergman[174, 175] have published syntheses of heteroatom analogues of 30a. Both compounds 98 and 99 seem to possess some paramagnetic character even in the five-membered ring by comparison

Table XVII

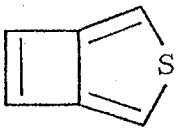
Attempted Formation of 30a from 48
(see Reference 76)

Reagents	Solvent	Temperature	Results
1.) KOtBu, tBuOD	DMSO-d_6, THF	25°C, under argon	2+2 dimers (< 5% yield)
2.) n-BuLi	THF, hexane	-78°C to 25°C, under argon	no new nmr absorptions, complete disappearance of starting material, no dimers after MeOH or H_2O quench
3.) n-BuLi	pentane	25°C, under argon	"
4.) n-BuLi	TMEDA	-40°C, under vacuum	"
5.) $\phi_3C^- Li^+$	THF	25°C, under vacuum	"
6.) Na, K mirror	THF	25°C, under vacuum	good yield of 100% d_2-dimers 95 after D_2O quench
7.) 	THF	25°C, under argon	only polymer after D_2O quench
8.) KNH_2	NH_3	25°C, under argon	no new nmr absorptions, no dimer after H_2O quench

of the $\alpha(H_1)$ protons with appropriate standards (Table XVIII). The

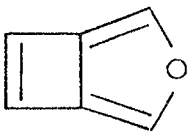


98

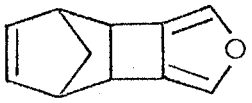


99

evidence for a paramagnetic ring current in the 3, 6-dehydrooxepin 100 is much less compelling. However, the direction of the change in chemical shift is correct for a paramagnetic contribution provided by the unsaturated four-membered ring compared to the similarly strained 101. It is also evident from Table XVIII that 100 lies



100



101

intermediate in paramagnetism between furan 11 and oxepin 102 as predicted for the corresponding anions. However, 100 is still more aromatic than the relatively unstrained vinyl ethers 103 and 104 by the nmr criterion.

All the bicyclic systems discussed above are extremely reactive. The thiophene 99 and furan 100 for instance can only be handled on a vacuum line. Exposure to air causes immediate

Table XVIII

^{1}H NMR Chemical Shifts of Heteroatom Analogues of 30a with Appropriate Standards (in τ from TMS 10.0τ)

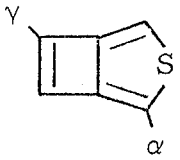
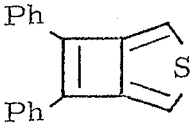
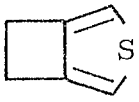
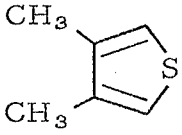
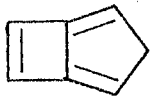
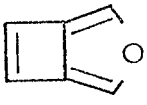
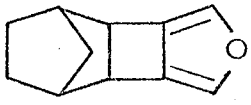
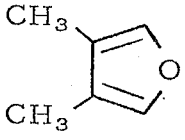
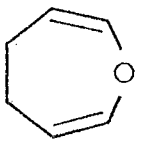
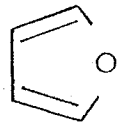
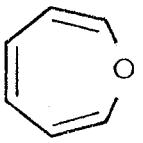
Compound		Solvent	H_α	H_γ	Reference
	99	benzene-d_6	4.50	4.00	175
		acetone-d_6	3.99	3.25	
	98	CCl_4	3.84	—	173
		CCl_4	3.24	—	176
		CCl_4	3.29	—	179
	48	CCl_4	4.92	3.27	111(b)
	100	CCl_4	3.67	3.89	174
	101	CCl_4	3.28	—	174
		CCl_4	3.00		180

Table XVIII (Continued)

Compound		Solvent	H_α	H_γ	Reference
	103	CCl_4	3.77	—	178
	104	CCl_4	3.9	—	178

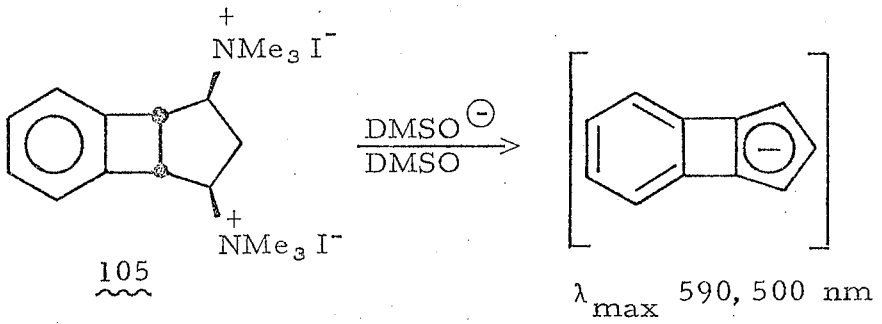


11



102

polymerization. This problem can be lessened by benzannelation. Cava has prepared what appears to be a 6,7-benzo analogue of 30a as a stable intermediate in solution at uv concentrations ($\sim 1 \times 10^{-3}$ to 1×10^{-4}M).[181] Elimination of trimethylammonium iodide from

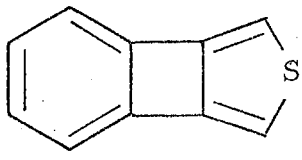


105

syn-106 (also anti)

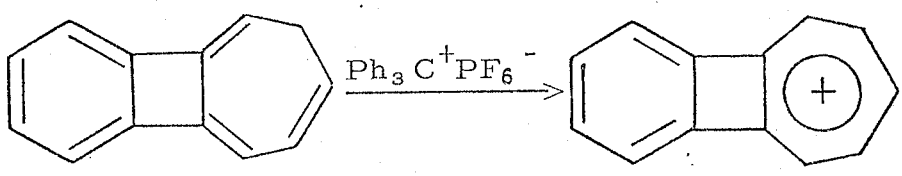
105 by treatment with excess dimsyl anion in DMSO gave a deep brown colored solution (λ_{max} 590 nm, shoulder 500 nm) which might

be attributed to the anion. Quenching with D_2O gave the benzodimers syn- and anti-106, 100% d_2 in the 5-positions at the expense of the 490 nm absorption of the anion. A control experiment with undeuterated dimer in $DMSO^-$/DMSO returned undeuterated dimer after D_2O quenching. Garratt and Vollhardt[182] have also synthesized a benzo[3, 4]cyclobuta[1, 2-c]thiophene (107) which is quite stable and slightly paratropic by virtue of a $H_\alpha(H^3)$ resonance at 3.51τ in the nmr compared to 3.24τ for a standard thiophene of approximately equal strain (see Table XVIII). Lombardo and Wege[183]



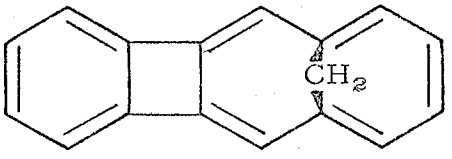
107

have prepared a 8, 9-benzo derivative of a cationic, isoelectronic analogue of benzocyclobutadiene. Treatment of the triene 108 with trityl hexafluorophosphate in acetonitrile followed by addition of ether gave a stable tropylium salt 109 as purple crystals. All the



108 109

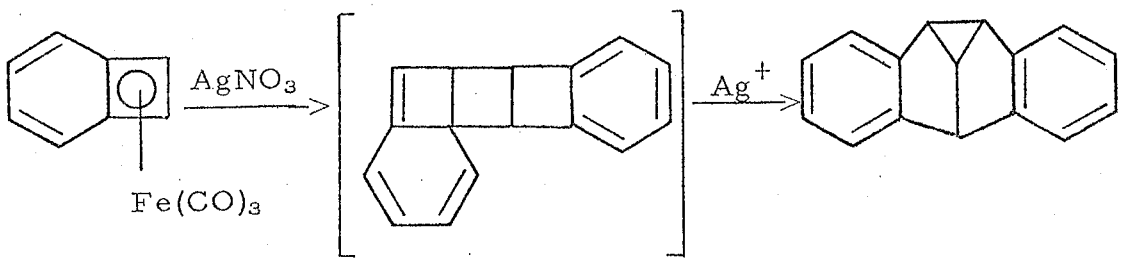
seven-membered ring proton signals in the nmr are approximately 2.0 ppm to higher field than is the tropylium ion, indicative of a paramagnetic component to the total ring current. Garratt and Vollhardt have also prepared 6, 11-methanocyclobutabenzo[1, 2-a][10]-annulene, a biphenylene analogue containing a 10π-electron ring.[184] The unusually low field resonance of the bridging methylene protons (7.55 and 9.71τ) compared to that of the unsubstituted 1, 6-methano[10]annulene (10.5τ) is suggestive of increased paramagnetism, especially near the four-membered ring. Thus, it appears that benzannelation only reduces the contribution of the reactive double bond in the four-membered ring but does not fundamentally change the nature of the bicyclic interaction.



110

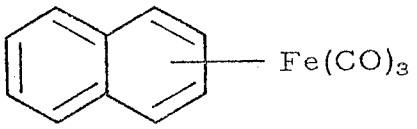
An alternative method of stabilizing fused cyclobutadiene rings is by metal complexation. Although in most cases very little can be said about the ground state aromaticity of the ligand, complexation does allow synthesis of stable derivatives of [m.2.0] bicyclic conjugated systems which can then be generated as a free species by oxidation of the metal. Benzocyclobutadiene-iron tricarbonyl

(111) has been isolated as air-stable orange prisms.[87] Oxidative decomposition with $AgNO_3$ produced metallic silver and the dimeric 113, presumably via Ag catalyzed rearrangement of the first formed 112. Professor Günther[185] has argued, based on the spin-spin



111 112 113

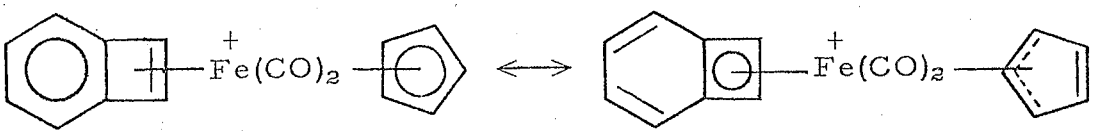
coupling constants in the ^1H nmr of 111, that considerable bond fixation exists in the six-membered ring in contrast to the enhanced(?) delocalization of the benzene ring in the iron complex of naphthalene (114). This is consistent with iron(zero)'s ten



114

electron demand and suggests that substitution of more nucleophilic electron pair donors (e.g., RN=C) for the carbonyls might generate a benzocyclobutadiene ligand which more nearly resembles the uncomplexed molecule. An alternative approach involving a

dihapto-benzocyclobutadiene iron complex was recently reported by Giering.[186] Although an nmr of complex 115 was not obtained, it seems likely that structure 115a will predominate. A chromium(zero)



115a 115b

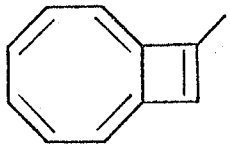
tetracarbonyl complex (116) of benzocyclobutadiene has also been reported[187] which shows a downfield shift of 0.4 ppm in the four-membered ring protons in the nmr compared to the cyclobutadiene chromium tetracarbonyl 117. This is consistent with a decrease in

116 117

the paratropicity of the system upon benzannelation but clearly other factors must be involved since a similar shift was not observed with the corresponding iron tricarbonyl complexes.

Of the (4n) + (4n) π-electron bicyclic systems with a 4n+2 π-electron perimeter even fewer examples are known. Schröder and

co-workers have prepared several cyclobutadienocycloöctatetraenes, one of which, 7-methylbicyclo[6.2.0]deca-1, 3, 5, 7, 9-pentaene (45), is decidedly more diamagnetic in both rings than appropriate monocyclic standards.[93] (See also the General Introduction to this thesis and Table V .) This interesting result certainly suggests that

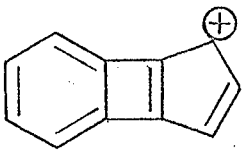


45

more (4n) + (4n) bicyclic systems involving strongly antiaromatic rings should be prepared as they are likely to be aromatic overall. Besides the cyclobutadienocyclobutadiene (butalene, 28) discussed in Part I, where it was found that the aromaticity of a benzene π configuration plus the strain in a bicyclic olefin such as 28a, b possibly outweighs the π aromaticity of 28a such that the molecule may actually prefer a diradical ground state, the 1, 4-dehydrotropylium ion 30c is an example of a molecule where such fusion might lead to an aromatic bicyclic array. In 30c (as indeed it appears in the case of anion 30a, vide supra) the extra carbon atom in one of the bicyclic bridges may allow the 1, 4 σ bond to remain intact.

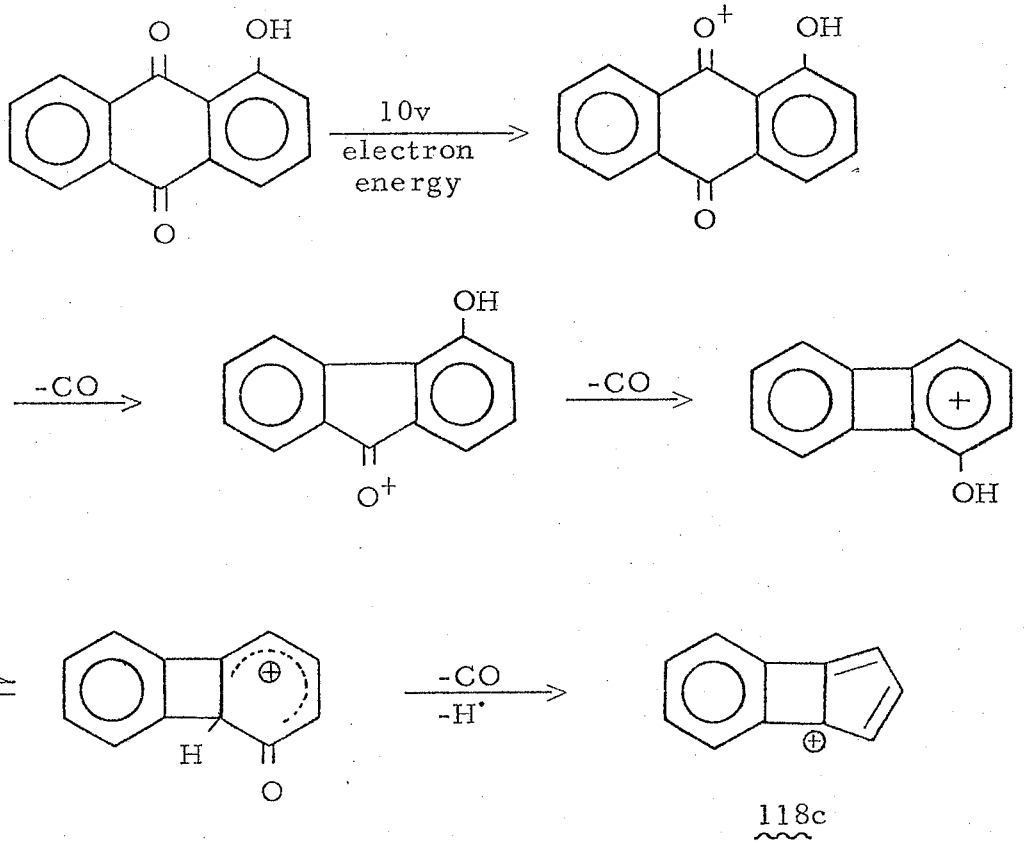
Prior to the start of my work on the dehydrotropyl systems, only one reference to a 1, 4-dehydrotropylium cation could be found.

Beynon, Lester and Williams[190] proposed the structure 118c for a stable fragment of mass 139 observed in the mass spectrum of 2-hydroxyanthraquinone. The three major peaks in the spectrum of



118c

this compound occur at masses 196, 168, and 139. As such they correspond to the extrusion of CO, CO and then a CHO radical. The loss of a neutral CO from the molecular ion of all quinones is a high yield process.[191] That the final fragment formed corresponds to loss of CHO rather than CO as in phenol is at least partly associated with the "exceptional" stability of the ion of mass 139, perhaps 118c. Beynon, et al., report that a peak of this mass occurs widely in the mass spectra of many aromatic hydrocarbons. This ion also appears to be able to lose a second electron as well since a peak of average intensity of 7% of the base peak occurs at mass 69.5 whenever m/e 139 is present (average intensity m/e 139 100% of base peak). D'Amore[76] also noted that all isomers of hydrocarbon 48 examined had virtually identical mass spectra with a strong contribution from a P-1 fragment of m/e 89, entirely similar to those C_7H_8 hydrocarbons which all give high yields of the stable tropylium ion.[191] While several alternative structures



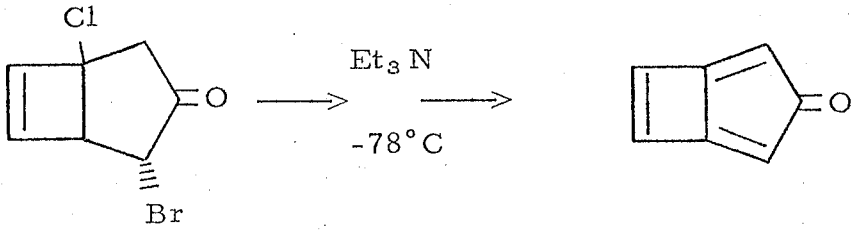
118c

for this m/e 89 ion may be imagined, among them the benzocyclopropenium ion 29c, it is possible that the stable ion is 30c based on Beynon's results. Since this time two reports have appeared

30c 29c

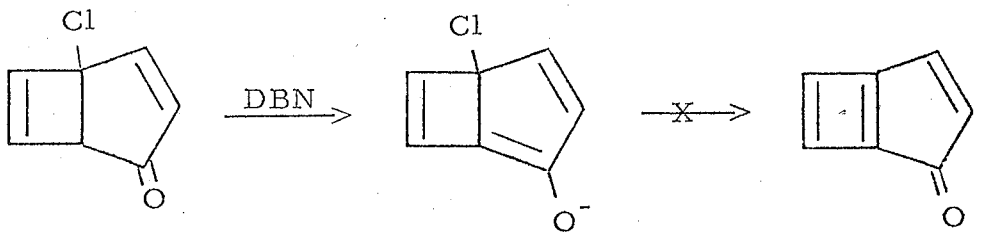
concerning 1, 4-dehydrotropones whose major dipolar resonance forms contain the 1, 4-dehydrotropylium cation.

Breslow, Oda, Sugimoto[104] have prepared a solution of what appears to be 3, 6-dehydrotropone (52) based on an nmr spectrum at -48°C. This compound, formed by elimination of HCl and then HBr from 119 with triethylamine, shows an upfield shift of 0.9 ppm in the five-membered ring and a downfield shift of 0.1 ppm in the four-membered ring in its ^{1}H nmr compared to appropriate non-aromatic but similarly strained standards (see Table XIX). Since



119 52

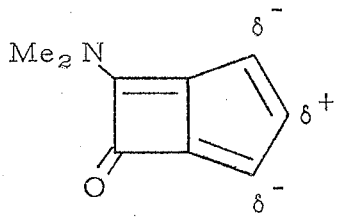
the signals due to this compound disappear from the nmr spectrum of the elimination mixture on warming to only -10°C, the only other data obtained for 52 is a uv λ_{max} of 284 nm. Although not particularly striking, the upfield shift of the five-membered ring perhaps indicates net paramagnetism in 52 and greater similarity to cyclopentadienone than to tropone, a conclusion opposite to that predicted for a 4n+2 system. A similar attempt was made to produce an isomeric 2, 5-dehydrotropone by elimination of HCl from 120. Here, while evidence exists that the anion 121 could be formed, it prefers bimolecular aldol condensation to β-elimination of Cl^-. While this latter result says very little about the relative



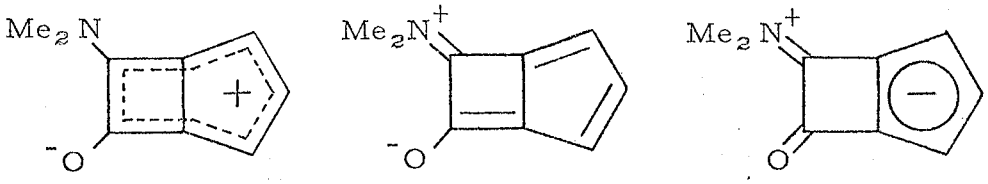
120 121 122

ground state stabilities of ketones 52 and 122, it does say that, at least in the transition state, formation of a cyclobutadiene-type interaction is unfavorable.

Dahl, Gray and Dreiding[192] have recently prepared a stable dimethylamino derivative of a third possible isomeric dehydrotropone, 2-dimethylamino-3, 7-dehydrotropone (123). The nmr

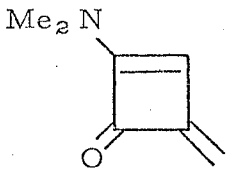


123

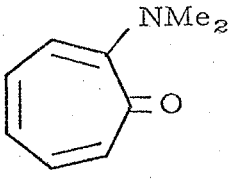


123a 123b 123c

spectrum of this compound clearly shows delocalization of positive charge into the five-membered ring ruling out a major contribution by resonance forms 123c since the C-4, 5, 6 positions alternate in chemical shift in a way consistent with δ^+ at the bridgehead and C-5 positions (see Table XIX). However, from the nmr data it is not clear what the relative importance of 123a and 123b is to the ground state in the absence of appropriate standard nmr's such as those of 124 or 125. In any case the molecule does not appear to be very paramagnetic.



124



125

Recently, the criteria by which monocyclic annulenones have been judged to be aromatic in the ground state have been criticized. Bertelli and Andrews[193] examined the proton nmr, bulk magnetic susceptibility, molecular vibrational spectra, empirical resonance energy, and dipole moment of tropone (128) together with appropriate standards. They concluded that only the abnormally low carbonyl stretching frequency of 1594 cm^{-1} gives any indication of the contribution of the dipolar, aromatic resonance form to the ground state of 128. Thus, although planar and nonalternate,[215]

Table XIX

NMR Data for Conjugated Annulenones and Appropriate Standards

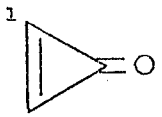
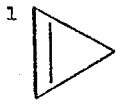
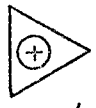
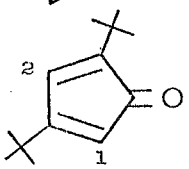
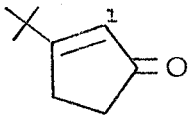
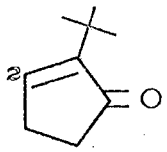
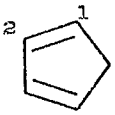
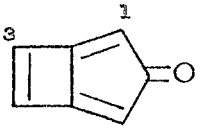
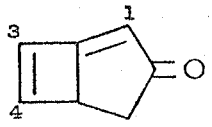
Compound		^{1}H Chemical Shift (τ, TMS 10.0τ)	Solvent	Ref.
	126	H_1, 0.92	CH_3NO_2 or CH_2Cl_2	194
		H_1, 3.0	CH_3NO_2	194
	1c	-1.1	CH_3NO_2	195
	129	H_1, 5.07 H_2, 3.50	CCl_4	196
		H_1, 4.17	CCl_4	196
		H_2, 2.78	CCl_4	196
		H_1, H_2, 3.58	CCl_4	177
	52	H_1, 3.44 H_3, 3.15	ether/Et_3N	104
		H_1, 2.52 H_3, 3.25 H_4, 4.44	ether/Et_3N	104

Table XIX (Continued)

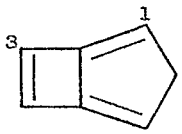
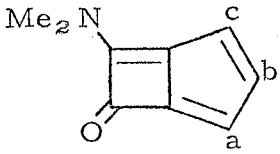
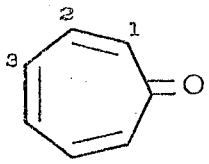
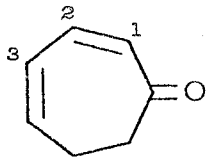
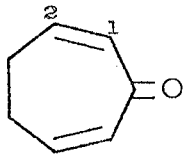
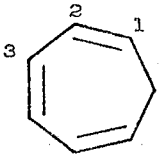
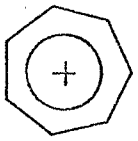
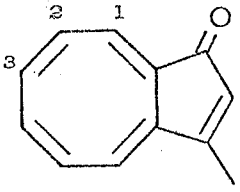
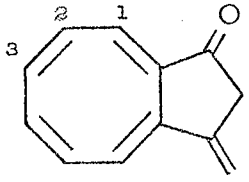
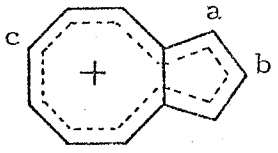
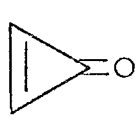
Compound		^{1}H Chemical Shift (τ, TMS 10.0τ)	Solvent	Ref.
	48	H_1, 4.92 H_3, 3.27	CCl_4	76
	123	H_a, 3.62 H_b, 2.52 H_c, 3.53	CCl_4	192
	128	H_1, 3.07 H_2, 3.45 H_3, 3.60	C_6D_6	197
		H_1, 4.20 H_2, 3.79 H_3, 4.26	CCl_4/C_6D_6	197
		H_1, 4.00 H_2, 3.38	CCl_4	198
		H_1, 4.73 H_2, 3.90 H_3, 3.50	CCl_4	199

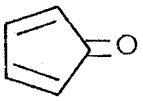
Table XIX (Continued)

Compound		^{1}H Chemical Shift (τ, TMS 10.0τ)	Solvent	Ref.
	5c	0.3	CH_3CN	63
	130	H_{1-3} 3.5-4.5	CCl_4	203
	131	H_1, 3.9 H_2, 4.3 H_3, 4.1	CCl_4	203
	37c	$H_{a,b}$, 4.12 H_c, 2.72	CH_3CN	82

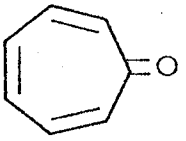
128 must be considered a polyenone.[216] Of all the remaining annulenones,[217] similar comparisons show that only cyclopropenone[200] (126) and cyclopentadienone[201] (127) exhibit ground state properties of an aromatic (or antiaromatic) nature. Indeed, from



126



127

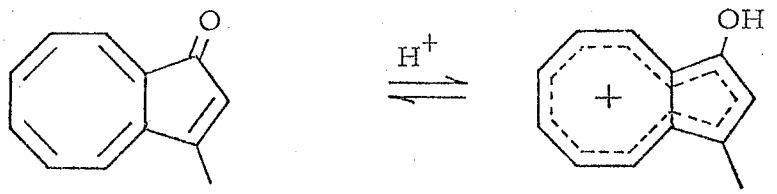


128

Table XIX, the protons of cyclopropenone are almost as deshielded as those of the cyclopropenium cation. While unsubstituted cyclopentadienone is too reactive to allow an nmr determination (dimerizes rapidly even at -80°C[202]), the stable 2, 4-di-t-butyl derivative 129 shows an upfield shift of approximately 1.0 ppm perhaps due to paratropicity. On the other hand, the supposed polyolefinic tropone shows a downfield shift of 1.0 ppm on the average and a more even charge distribution than the indicated standards. Thus, it is probably safe to say, even with Bertelli's reservations, that while the annulenones themselves are not very aromatic, their ground state properties may at least be indicative of the aromaticity to be expected of the corresponding cation. That the inverse of this statement is not true can be seen from the following example of a potentially (4n) + (4n) bicyclic π system.

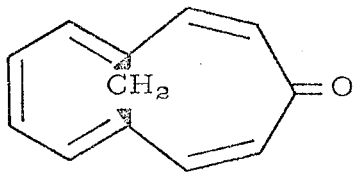
The bicyclo[6.3.0]-(11)-annulenone 130 prepared by Breslow in 1965 shows only polyolefinic properties, similar in most respects

to the non-bicyclicly conjugated standard 131 (see Table XIX).[203] Ketone 130 is very unstable to basic conditions but surprisingly



130 130a

stable in acid. The compound can be extracted from $CHCl_3$ solution with 65% H_2SO_4 and recovered unchanged on neutralization. Breslow estimates the pK_{BH^+} of the conjugate acid 130a to be -2.3. Compared to the pK_{BH^+} of fluorenone (-7.2)[204] for which recent work has indicated nonaromaticity in the ketone containing five-membered ring,[68] 130 is ~7 kcal/mole stabilized by aromaticity and almost as aromatic as Vogel's (11)-annulenone 132 (pK_{BH^+} -0.6, $\Delta\Delta H^\circ$ = 7 kcal/mole).[205] While an nmr of 130 in acid has not been



132

reported, there is every reason to believe that 130a will show diatropicity similar to the corresponding cation 37c discussed in the General Introduction to this thesis. A similar experiment with Breslow's ketone 52 would be very informative.

Therefore, since the magnetic and stability criteria of the hydrocarbon ions themselves are of primary importance as far as determination of aromaticity is concerned, it was the goal of the research presented in this second part of my thesis work to generate nmr (or esr) observable concentrations of 30a and 30c and to be able to form these ions under conditions where equilibria such as (1) or (2) could be realiably followed. The determination

$$RH + A^- \rightleftharpoons R^- + HA \qquad (1)$$

$$pK_{RH_a} = \mathcal{H}^\circ - \log \frac{[R^-]}{[RH]} - pK^\circ_{HA}$$

where $\mathcal{H}^\circ$ is an acidity function referenced to dilute aqueous solution

$$R^+ + BH \rightleftharpoons RB + H^+ \qquad (2)$$

$$pK_{R^+} = C^\circ - \log \frac{[RB]}{[R^+]} + \tfrac{1}{2}\,(pK^\circ_{BH} - pK^\circ_{B^-})$$

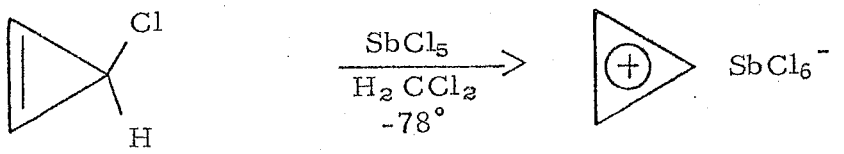
where C° is an acidity function referenced to dilute aqueous solution

of aromatic heats of stabilization for these ionic species from the pK_{RH_a} obtainable from equation (1) and the pK_{R^+} from equation (2) against a defined nonaromatic pK_{RH_a} and pK_{R^+} was illustrated in Table I of the General Introduction of this report.

I hoped to take advantage of the one-step introduction of strain and unsaturation possible in the pyrolytic formation of a bicyclo[3.2.0]heptatriene from 1,2-diethynylcyclopropanes according to the method of D'Amore and Bergman.[111] The previously employed elimination routes to bicycloheptatrienes which could be converted into 30a or c met with very little success, presumably because the intermediates were themselves highly strained, unstable, and reactive, a situation which automatically forced one to work with low yield reactions on diminishingly small amounts of materials. In addition, unlike Breslow's and Bauld's triene 50, the 1,4,6-triene 48 prepared by D'Amore does not dimerize in solution and seems to be significantly more stable. As such it appeared to be a much better entrance into systems 30 than does triene 50. However, it has been shown by subsequent research that even 48 will not serve as a source of nmr observable concentrations of 30a or c due to the great reactivity of the four-membered ring under the conditions of strong Lewis acid or base necessary to remove a hydrogen from 48. Therefore, derivatives of 48 where the ion forming reactions would go to completion faster and at lower temperature looked more promising.

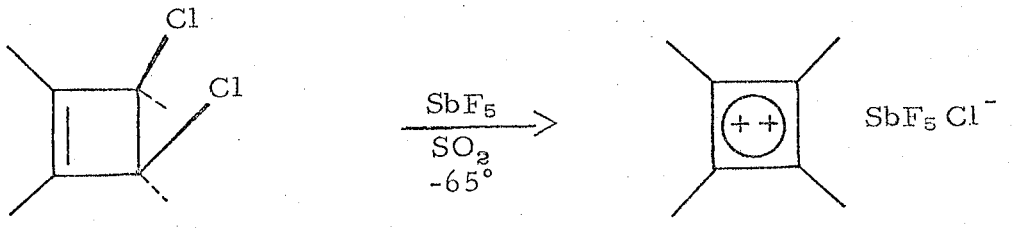
While carbon cations have been prepared by a variety of methods ranging from protonation of alcohols in H_2SO_4[206] to

hydride abstraction by Lewis acids,[207] by far the highest yields of unsaturated cations are prepared by Lewis acid catalyzed ionization of organic halides at low temperature.[208] For example, simple mixing of a methylene chloride solution of 3-chlorocyclopropene 133 with antimony pentachloride at -77° produced a 100% yield of the cyclopropenium salt according to Breslow and Groves.[195] Similarly



133 1c

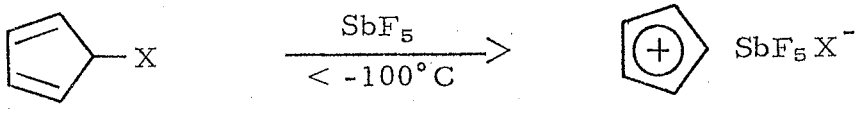
Olah was able to prepare the first potentially aromatic cyclobutenium dication by treatment of the tetramethyl dichloride 134 with SbF_5 at -65°C in SO_2 solution.[209] Recently Saunders, et al.[188] have prepared dilute solutions of the paramagnetic, apparently antiaromatic



134

cyclopentadienium cation 3c using a -200°C solid phase reaction of SbF_5 with either the bromide 135 or chloride 136. Saunders has also shown that due to the absence of localized heating in such a

method, true mixing temperatures of -100°C or lower in SO_2ClF can be obtained, allowing synthesis of unsaturated cations which normally polymerize or rearrange under more usual SbF_5 treatment.[188(b)] This latter technique should be applicable to the generation of 30c from 62b or 62c. The ^1H nmr of 30c should be

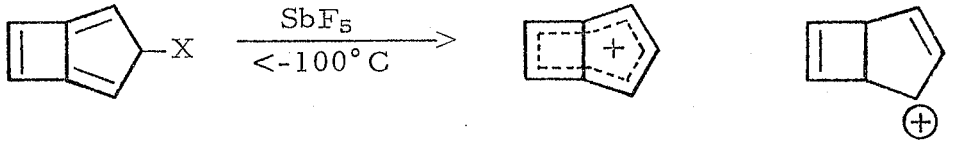


135, X = Br

136, X = Cl

3c

indicative of both the charge distribution and ring current.[63] Separation of these effects will require comparison to such ions as the tropylium cation 5c,[63] the cyclopentenyl cation 19c,[64] or the bicyclo[3.2.0]heptadienyl cation 137c generated by Saunders' technique at -120°C where it should be stable.[210] It would also be



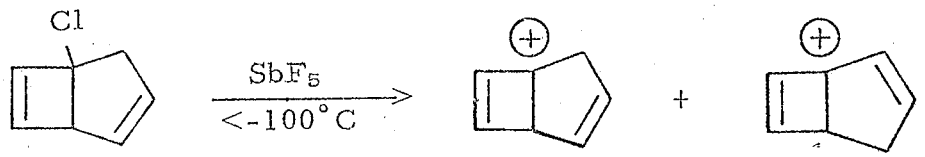
62b, X = Br

62c, X = Cl

30c

137c

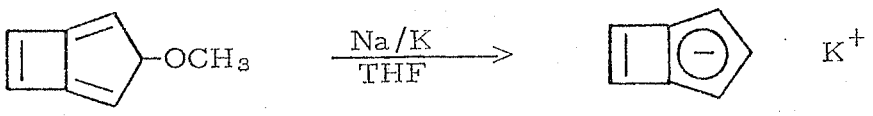
of interest to prepare cations 138c and 139c, perhaps available from Breslow's chloride 51. An independent measure of the charge



51 138c 139c

distribution in these cations could be obtained from their ^{13}C nmr[211] and quenching reactions with nucleophiles such as methanol.

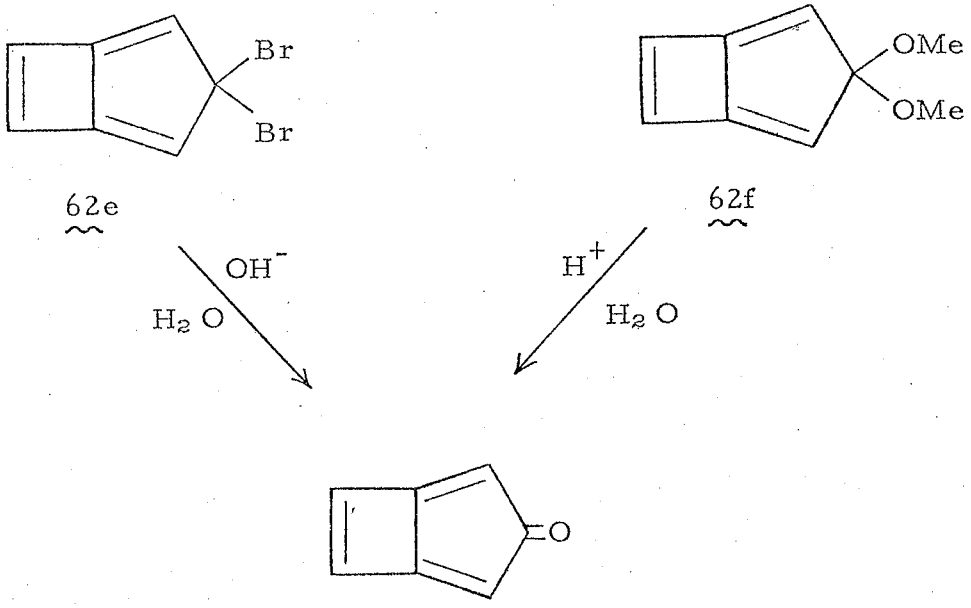
The facile anionic polymerization of D'Amore's triene 48 under the thoroughly investigated anion-forming conditions necessary to remove a proton from such a weak base ($pK_a \sim 29$, Breslow reference 103) make it extremely unlikely that 48 will serve as a source of nmr observable concentrations of 30a. A similar problem was encountered in attempts to form the possibly antiaromatic tropenide anion 5a from cycloheptatriene, only high yields of a 1, 6-addition polymer being obtained with sodium or potassium alkyls.[212] However, Dauben and Rifi were able to prepare 75-80% yields of 5a from 7-methoxy-1, 3, 5-cycloheptatriene upon reaction with excess 1:5 sodium-potassium alloy at -20°C.[212] A similar approach to 30a would require the methyl ether 62d. Although an

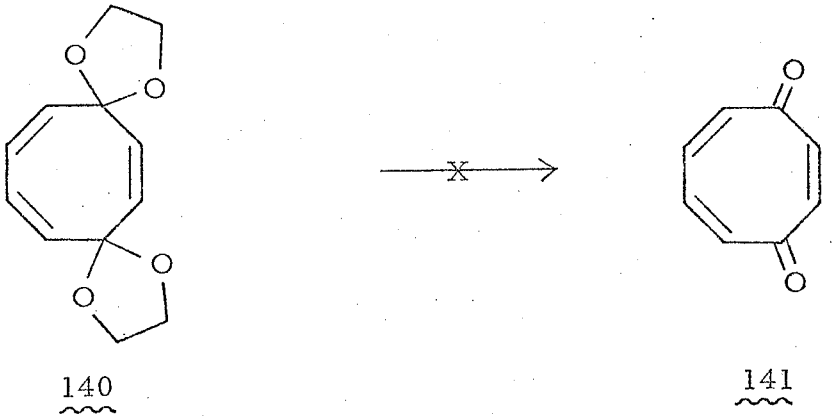


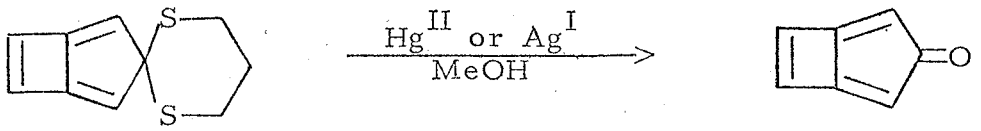
62d 30a

nmr of 5a has never been recorded, this is presumably due to the further reduction of this anion to form small amounts of the dianion radical[213] rather than due to insufficient concentrations. However, even though an esr signal was not detected at early reaction times and in the absence of contact with metallic minors, it is possible that 5a is a ground state triplet. One would not expect similar complications for 62d since there are no low lying or degenerate antibonding orbitals in the molecular orbital treatment of 30a.[76]

Since such properties as the pK_{BH^+} or the ^{13}C nmr[214] of Breslow's bicyclo[3.2.0]heptatrien-3-one (52) would be very indicative of the aromatic stabiliation and charge distribution in 30c respectively, it would be of considerable interest to generate 52 under milder conditions than the strong base used by Breslow.[104] While such compounds as the dibromide 62e and the dimethylketal 62f could conceivably be hydrolyzed to 52, the former requires hydroxylic base and the latter aqueous acid, both of which have been shown by D'Amore[76] to rapidly polymerize the unsaturated parent triene 48. Furthermore, in at least one case where hydrolysis would have generated an apparently antiaromatic dication intermediate enroute to the diketone 141, ordinary conditions of acid hydrolysis failed to cleave either ketal in 140.[218] Use of a thioketal group helps avoid both problems since mild, neutral conditions of cleavage are available using Hg^{II} or Ag^{I} ions to form insoluble alkylsulfide salts providing driving force for the reaction. Therefore one of the primary goals of this research was to synthesize 62f.

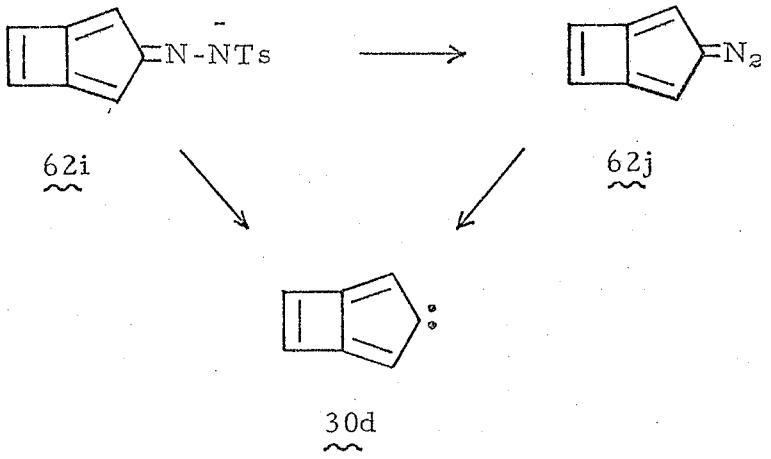

Br
Br
OMe
OMe
62e
62f
OH⁻
H₂O
H⁺
H₂O
O
52


O
O
O
O
O
O
140
141



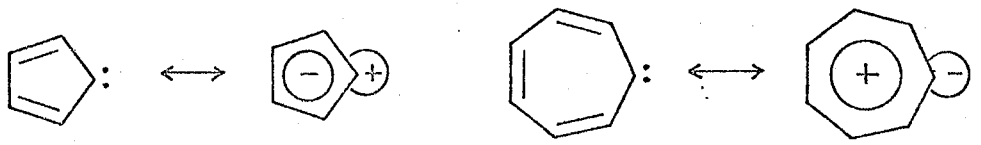
62g 52

Ketone 52 is also a possible precursor of several other interesting bicyclo[3.2.0]hepta-1, 4, 6-triene derivatives. Sodium borohydride reduction should lead to the alcohol 62h, another potential source of the cation with SbF_5.[219] Formation of a tosylhydrazone salt with a nonnucleophilic base such as LDA followed by either thermolysis or photolysis would perhaps lead to the theoretically interesting carbene 30d.[220] The extent to which 30d



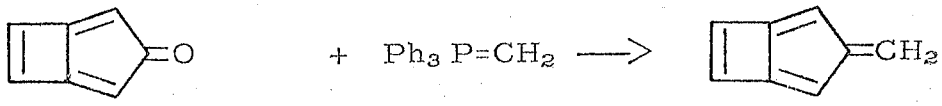
62i 62j

30d



3d 5d

resembles the reactive, electrophilic carbene 3d with a triplet ground state[221] or the relatively unreactive, nucleophilic carbene 5d with a singlet ground state[222] will provide a direct comparison of the stabilization to be expected of the delocalized anionic or cationic resonance forms. Reaction of 52 with preformed ylid reagents such as 142 may provide a route to the standard state fulvene 49 . As discussed in the General Introduction, compounds of this type provide a way of measuring the strain and magnetic environment of the neutral 3.2.0 system.



52 142 49

Theoretical Predictions for the Bicyclo[3.2.0] Systems

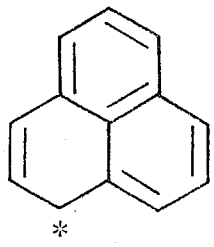
As discussed in the General Introduction and illustrated further in the previous section, there are three nonequivalent rules of thumb for prediction of aromatic stabilization in bicyclic conjugated arrays. It is probably safe to say that none of them is without exception. The first, and probably the oldest, is that a bicyclic system is aromatic if its component rings are aromatic. This rule fits the (4n+2) + (4n+2) cycles, especially the benzenoid hydrocarbons such as naphthalene by analogy to which it was derived. Certainly there are no paratropic molecules in this class. The (4n+2) + (4n) cycles are also covered by this rule, and for the most part the reactivity and paratropicity of these systems can be assigned to the antiaromatic ring. For example, benzocyclobutadiene (31) dimerizes at the cyclobutene double bond, and the paratropicity of the cyclobuteno[10]annulene 110 arises mostly from the four-membered ring as the chemical shifts of the methylene protons show. Professor Garratt has discussed these systems in terms of their component rings.[32(c)] Although perhaps really compelling evidence is lacking, it seems that many of the (4n) + (4n) fused systems are exceptions to this rule, showing in most instances enhanced diatropicity, stability or both. Nevertheless, there are (4n) + (4n) systems such as octalene 42 and the cycloöctatetraenyl-cycloheptatrienyl anion 143a which are not particularly stabilized.[91] However, it is probably fair to say that the 40-50 kcal/mole required to flatten an eight-membered ring is more than the aromaticity of a 14 π electron cycle (? 3-6 kcal/mole[33, 68]).

A molecular orbital picture for this rule would involve the use of interaction diagrams with the added stipulation that the smaller (more strongly interacting) ring orbitals do not interact with the π fragment fused to it strongly enough to significantly change the MO closed or open shell, monocyclic array.

A second rule of thumb is that a bicyclic system is predicted to be aromatic if it contains 4n+2 π electrons in total (same as containing 4n+2 π electrons on the perimeter in these systems) and antiaromatic if the total number is 4n. This rule includes all the examples discussed with the forementioned exception of the octalene-type molecules. That this rule is a simplification of Dewar's perturbational MO methods[33] was discussed earlier but is, nevertheless, surprisingly accurate.

Both of these previous rules were based on the 4n+2 rules for monocyclic systems under a bicyclic perturbation. The 4n+2 rule itself was based on the concept of closed (full) shells of π electrons. Therefore, one could propose a third rule of thumb based on a Hückel closed shell prediction in a bicyclic array. Besides the fact that Hückel's theory does not treat bicyclic systems very accurately compared to the reasonably accurate qualitative picture one has become used to in monocyclic systems (even to the point of predicting that the ground state of the cyclopentadienyl cation would be a triplet), the additional problem of a single nonbonding level occurs in some bicyclic systems. Although it was fairly clear in cases like cycloöctatetraene (6) where two degenerate nonbonding levels are produced in simple Hückel theory that both

must be filled for a closed shell system to result, the same may not be true of a single nonbonding level. A case in point is that of the tricyclic ions 144a and 144c derived from the hydrocarbon phenalene. Simple Hückel theory predicts the presence of six bonding levels and a single nonbonding orbital for the π array in 144. Here, in practice both the 12π cation 144c and the 14π anion 144a have been found to be stable, heavily delocalized, enhanced diatropic species.[223]



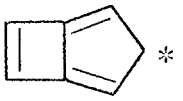
144a, * = -

c, * = +

On the other hand, for the neutral hydrocarbon bicyclo[3.3.0]-cycloöctatetraene or pentalene (32) simple HMO theory also predicts the presence of a single empty nonbonding molecular orbital and 2.45β π resonance energy versus a standard state of four ethylenes.[73] However, recently prepared alkyl substituted

pentalenes appear to be quite reactive (methylpentalene dimerizes at -140°C and evidently is not very stabilized by aromaticity). The approximately 5τ nmr ring proton absorptions of the somewhat more stable tri-t-butylpentalene confirm its polyolefinic nature. The 10π dianion of pentalene (32a), in contrast, appears to be quite stable and apparently aromatic (vide supra, General Introduction). Indeed, more sophisticated MO calculations show that the HMO nonbonding level in pentalene is in fact a bonding orbital and that the stability of the dianion compared to acyclic standards may be due to a closed shell of 10π electrons.[224]

Therefore, perhaps the one most interesting feature of the energy level diagram predicted by simple Hückel theory for the bicyclo[3.2.0]heptatrienyl systems 30 is the occurrence of a nonbonded orbital[73] (Figure XXV). Since this zero-order treatment does not take electron-electron repulsion terms into account, the same π resonance energy of 2.91β versus three isolated carbon-carbon double bonds is calculated for the anion 30a, radical 30b and cation 30c. For comparison, 2.99β is calculated for the cycloheptatrienyl cation and 2.47β for the cyclopentadienyl anion, both of which are commonly accepted to be aromatic. The implication is that both 30a and 30c will be stabilized by aromaticity. Anion 30a is predicted to be a closed shell but, like benzocyclobutadiene, a 4n π electron system overall. On the other hand, cation 30c is a 4n+2 π electron system. Thus, there is an interesting conflict of prediction here, and the synthesis of 30a and 30c would go a long



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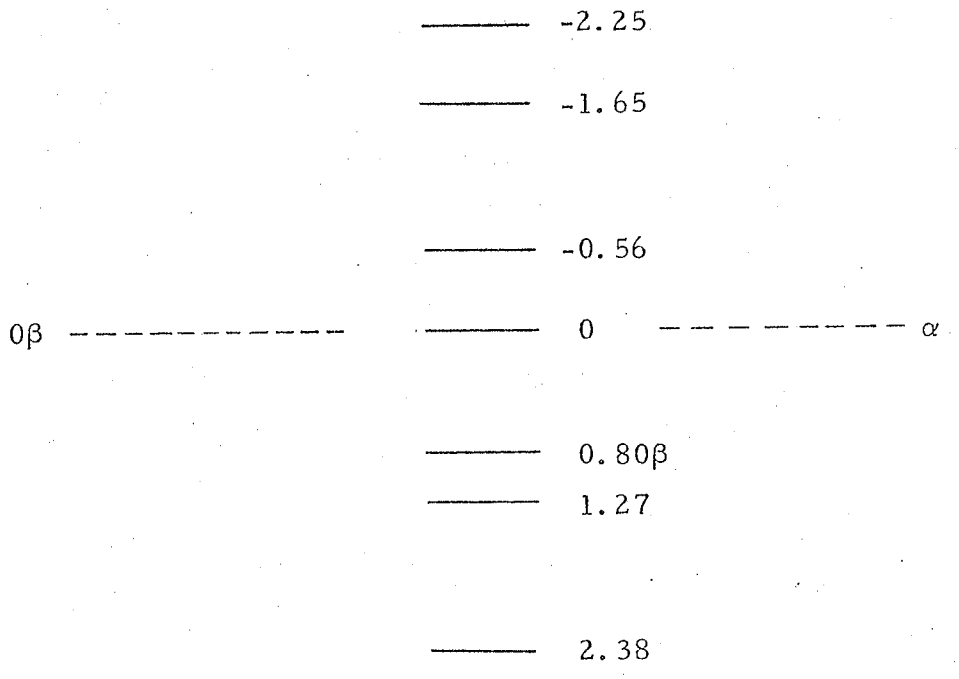
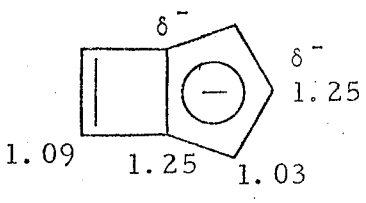
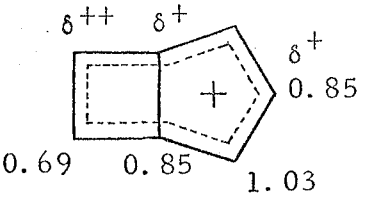




30a



30c

Charge Densities
($= 1.0 - \Sigma Nc_i$)

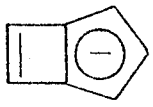
Figure XXV

HMO Treatment of 1, 4-Dehydrotropyl Systems

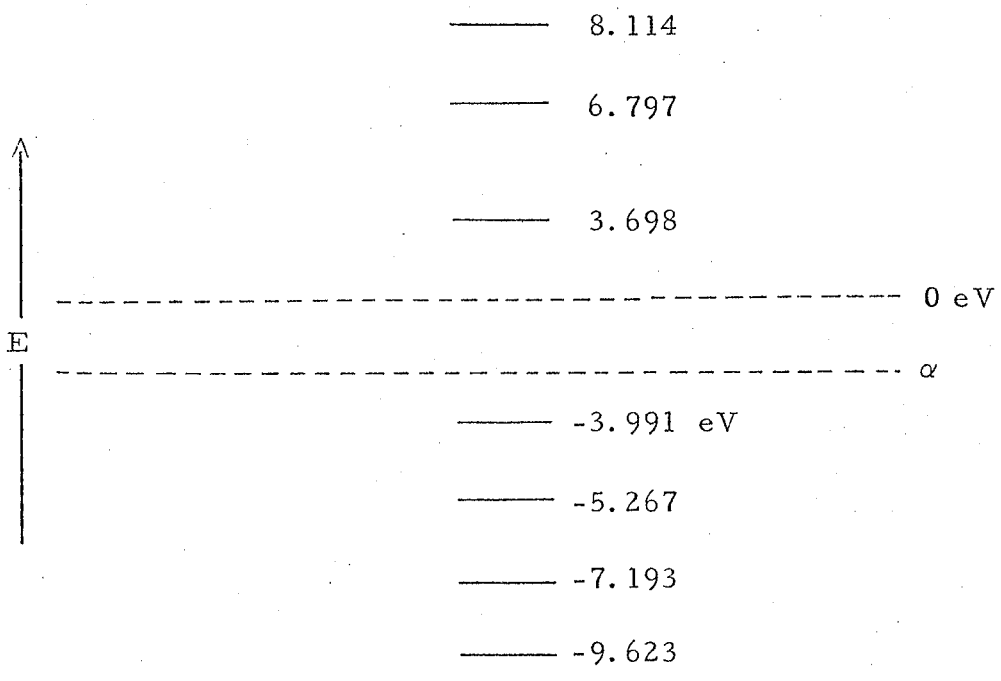
way toward clarifying our views as to aromaticity in bicyclic systems.

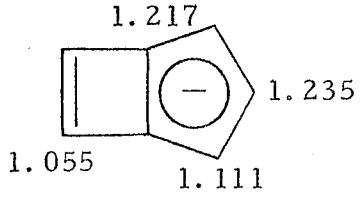
An SCF-MO calculation was performed for us on the anion 30a by Simmons[225] (Figure XXVI) which indicates that, as in pentalene, the HMO nonbonding level becomes a bonding orbital under this more elaborate iterative treatment confirming the closed shell MO prediction for 30a. A very similar charge density picture is predicted here for 30a compared to the simple Hückel prediction. Essentially, it shows a cyclopentadienyl anion and a weakly interacting double bond. However, such charge distributions fail to justify D'Amore's protonation results which point to large amounts of the negative charge at C-1 and C-5 and apparently very little at C-3.

While no calculations more advanced than simple Hückel theory are available for cation 30c, it is interesting to examine the charge density distribution predicted here in light of the recently prepared ketones 52 and 123. Most of the positive charge in this cation is predicted to lie in the four-membered ring. Continuing the analogy to component rings, Hückel theory shows 30c to be composed of a cyclobutadienyl dication with a weakly interacting allyl



30a



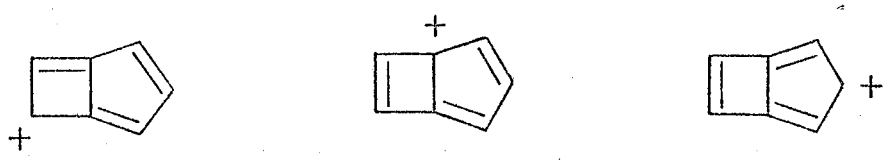


Charge Densities

Figure XXVI

SCF MO Treatment of the 1, 4-Dehydrotropyl Anion

anion. In resonance terminology, resonance forms A are predicted to be more important than B or C which in turn are much more important than D or E. This preferred charge distribution which



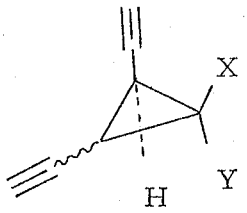
A B C

D E

maximizes aromaticity (always selecting to have an intact aromatic ring and a weakly interacting π fragment) may contribute to an explanation of why Breslow's ketone 52 appears to be less stable than Dahl's 123.

Approaches to Synthesis

As possible sources of functionalized diethynylcyclopropanes of general formula 61, I considered three major types of synthetic routes:



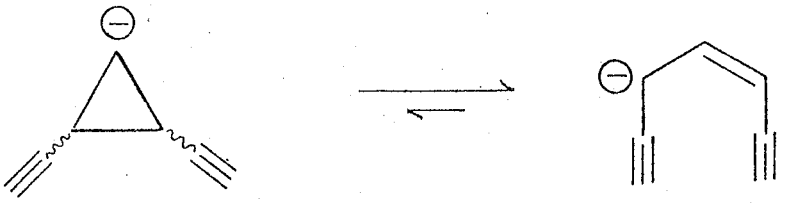
61

I. Formation of an unfunctionalized 1, 2-diethynylcyclopropane followed by substitution at the 3 position.

II. Formation of the acetylenic groups followed by creation of a functionalized cyclopropane ring.

III. Formation of a functionalized cyclopropane ring followed by formation or addition of the acetylenic groups.

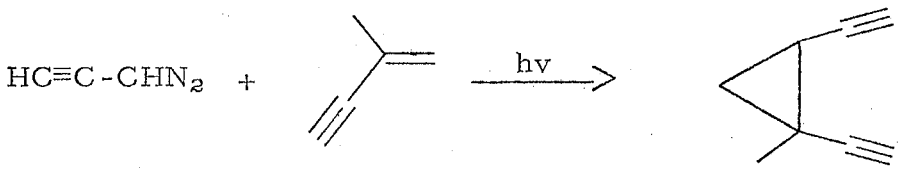
An obvious problem with the first route is that the C-3 position in D'Amore's diethynylcyclopropane 61a (x, y = H) is the least reactive in the entire molecule. Basic reagents would probably prefer to abstract the acetylenic protons, add nucleophilicity to the acetylenes (cyclization?), and abstract the C-1, C-2 propargylic protons in that order. If the formation of the acetylenic salts is not reversable, the negative charge might in fact inhibit these latter processes such that formation of a C-3 anion might be possible. However, since systems isoelectronic with the cyclopropyl anion are known to ring open very easily,[226] it is most likely that only products of 146 would be isolated upon quenching. Hydride abstraction by strong Lewis acids might also compete with electrophilic



145 146

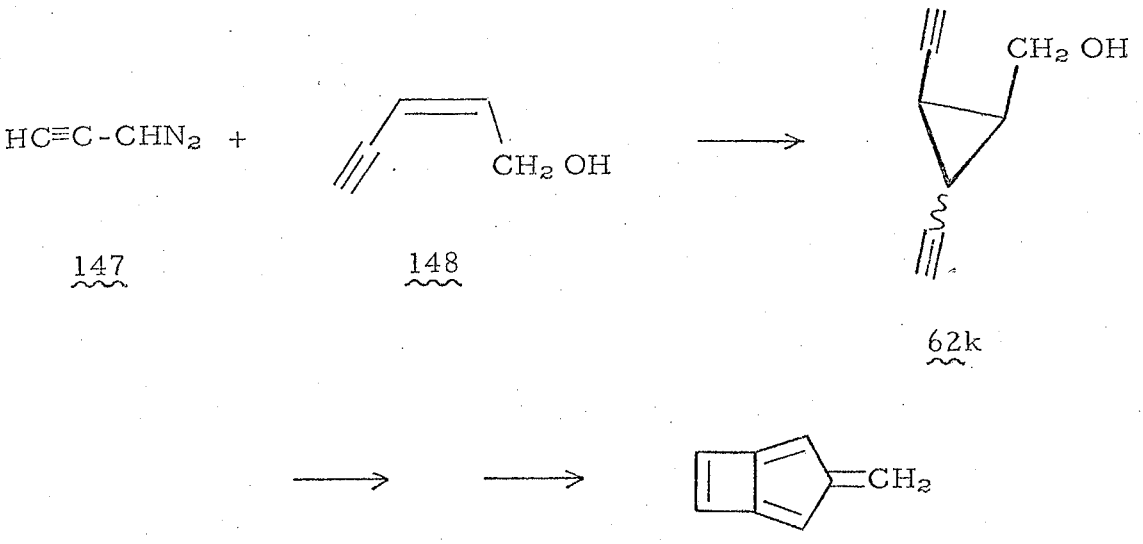
addition to the acetylenes, but abstraction of the propargylic hydrogens leads to the most stable first-formed cation. Again, ring opened products are likely to be the result. The preference of radical forming reagents for the propargylic position of acetylenes has been amply demonstrated.[227] Only in the case of a very "hot" radical abstraction might a statistical distribution of cyclopropyl radicals result. Routes based on II and III therefore seemed more likely to succeed and have the added advantage of versatility.

The first example of a diethynylcyclopropane was prepared by D'Amore and Bergman[111(a)] by direct irradiation of diazopropyne (147)[228] in an ether solution of 2-methylbuten-3-yne (148). A route to 61



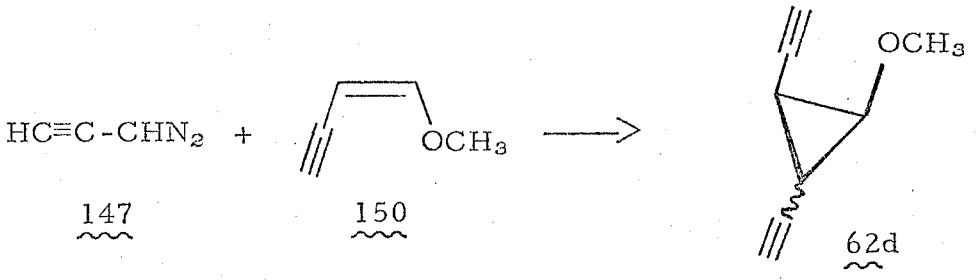
147 148 64

derivatives based on this reaction would be an example of a type II approach. Two appropriately functionalized eneynes are commercially available. The 3-penten-1-yn-5-ol (149) is a possible precursor of 49.



147 148 62k 49

The methylether 150 could provide a route to 62d. Several representative eneynes in the literature which might serve as precursors or suggest possible syntheses are summarized in Table XX



147 150 62d

By far the most versatile source of functionalized cyclopropanes is the addition of functionalized carbenes to olefins. A route to the diethynylcyclopropanes 62 based on the known 1,5-hexadiyn-3-ene (60) is thus possible. An entire range of carbenes from the photoproduced methylene and carboethoxycarbene which react very unselectively to the very mild copper catalyzed decomposition of these compounds which produce only products of addition and from the electrophilic dihalocarbenes to the nucleophilic lithium

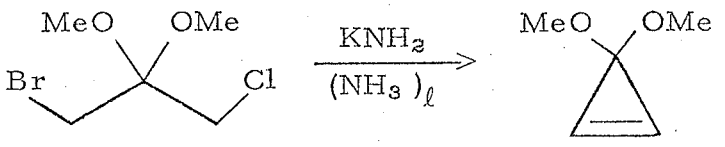
Table XX

Some Representative Eneynes from the Literature

Compound	Source	Yield	Ref.
$HC\equiv C-CH=CHCN$	$HC\equiv C-C\equiv CH$	30%	229
$HC\equiv C-CH=CH-CH_2Cl$	$HC\equiv C-CH=CH-CH_3$ tBuOCl	?	230
$HC\equiv C-CH=CH-CHO$	$HC\equiv C-CH=CH-CH_2OH$, CrO_3	50%	231
$HC\equiv C-CH=CHNMe_2$	$HC\equiv C-C\equiv CH$	60%	232
$HC\equiv C-CH=CHCl$ also -Br, -I	$HC\equiv C-C\equiv CH$	20%	233
$PhC\equiv C-CH=CHCl$	$PhC\equiv C-Cu$, $ICH=CHCl$	90%	234
$PhC\equiv C-CH=CHI$	$PhC\equiv C-Cu$, $ICH=CHI$	30%	235
$PhC\equiv C-CH=C=CH_2$	$PhC\equiv C-Cu$, $HC\equiv C-CH_2Cl$	?	236
$HC\equiv C-CH=C(OCH_3)_2$	$RC\equiv C-C\equiv C-Br$	85%	237
$HC\equiv C-CH=C(OEt)_2$	$CH_3C\equiv C-C(OEt)_3$	70%	238

carbenoids such as $LiCHClOCH_3$ are available. Also methods of generation range from the basic media of the phase-transfer catalyzed carbene addition to the thermal or photolytic decomposition of carbene complexes. These have been amply reviewed. The anticipated sensitivity of enediynes 60 (see, for example, Part I of this thesis) to bases as well as heating can perhaps be avoided by silylation of the acetylenes. Several studies have indicated, at least in the case of eneynes, that the preferred site of carbene addition will be the olefin.

A third route in Class II is shown in Figure XXV and is based on a γ (1, 3)-elimination. Gamma-eliminations produce some of the highest yields known in cyclopropane formations.[240] An example which especially interested us was that of Butler[241] in the formation of 3, 3-dimethoxycyclopropene from 1-bromo-3-chloro-2, 2-dimethoxypropane. We had previously believed that the methoxy group



would be too good a leaving group to allow γ-elimination to predominate over β-elimination here.

D'Amore and Bergman devised an alternative route to diethynylcyclopropanes in Class III.[76] Condensation of methylvinylketone with chloroacetone gave trans-diacetylcyclopropane which in turn was elaborated into trans-diethynylcyclopropane by PCl_5

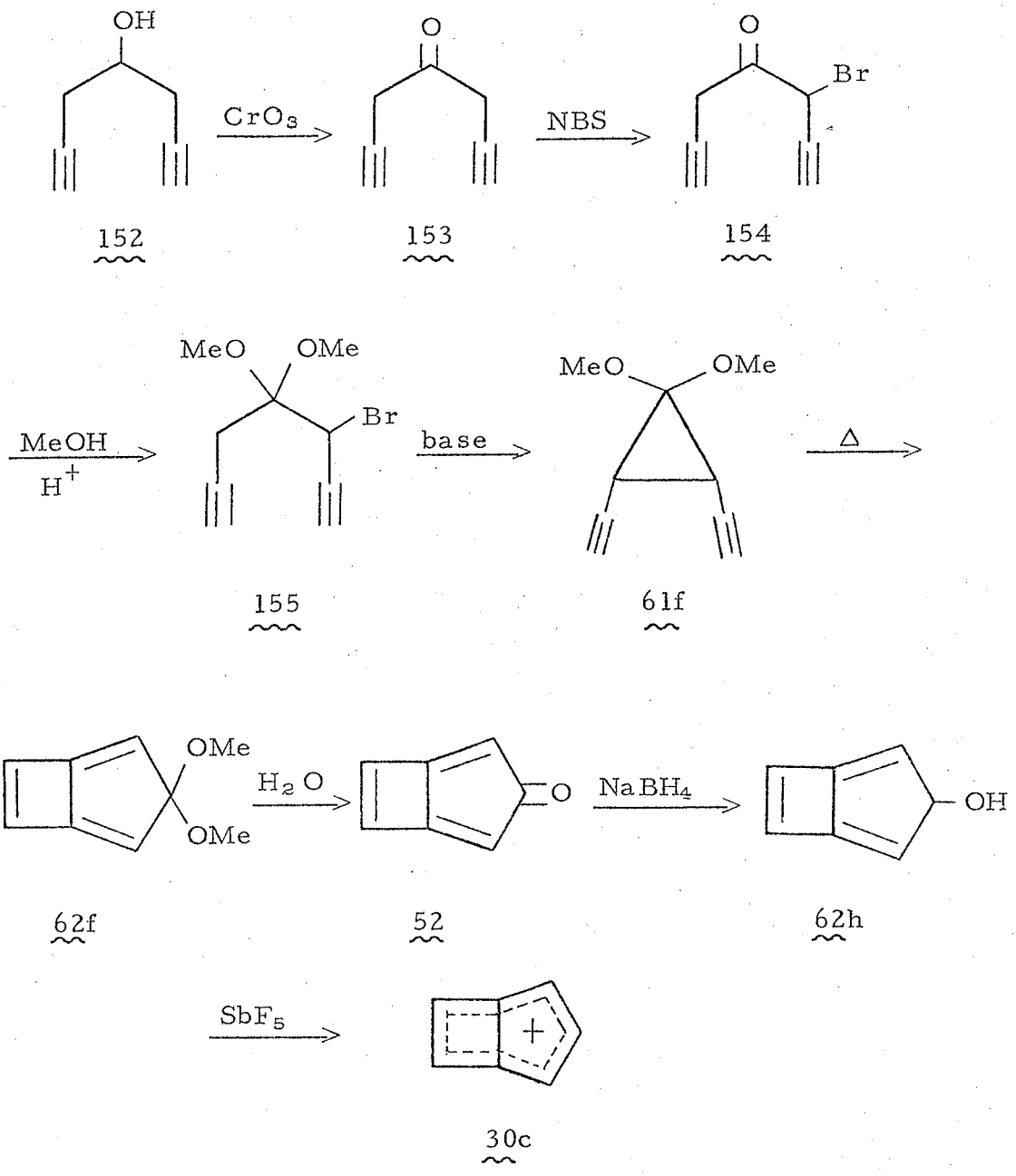
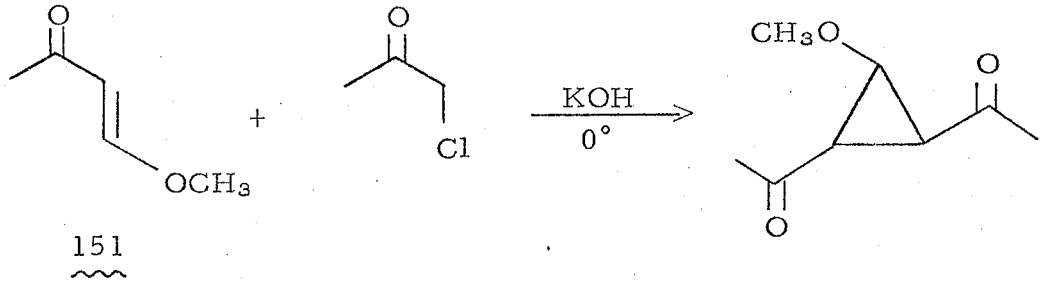


Figure XXVII

A γ-Elimination Route to Diethynylcyclopropanes

chlorination followed by KOtBu elimination of HCl. The basic conditions employed probably do not allow one to have halogen functionalization in the precursor, but methoxy groups would be acceptable. The 4-methoxy-3-buten-2-one (151) required for the synthesis of 62d by this route is commercially available. A second route in Class III based on Maier and Sayrac's[242] addition



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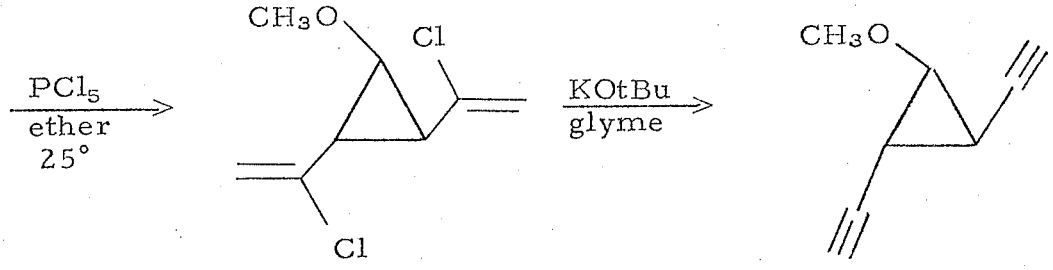
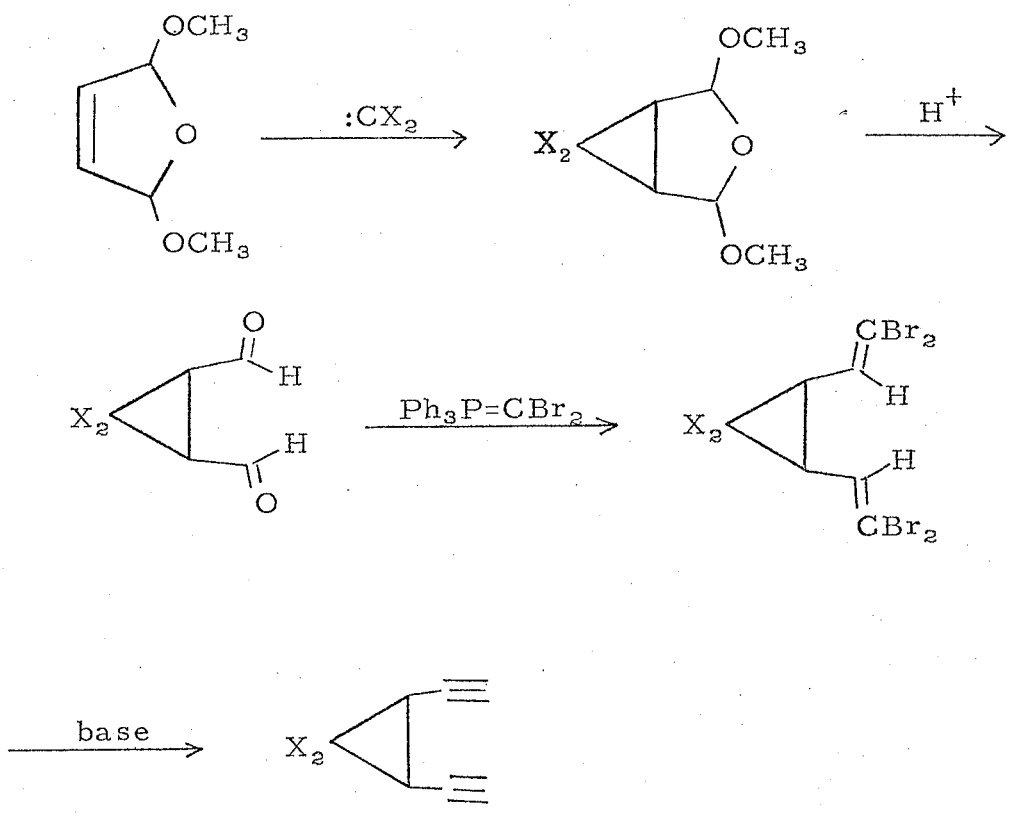


62d

of methylene to 2, 5-dimethoxy-2, 5-dihydrofuran (156) is currently under investigation by J. Bamberg in Professor Bergman's group.

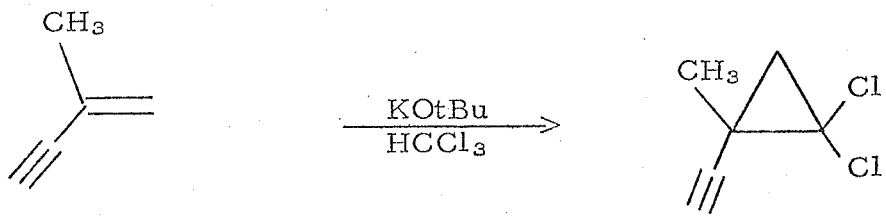


Bamberg is also interested in a direct route to functionalized bicyclo[3.2.0]heptatrienes via the readily available triene 48. The doubly allylic methylene position in 48 is now one of the more reactive cites.

Methods and Results

Attempted Carbene Additions to 1, 5-Hexadiyn-3-enes

Dichlorocarbene can be generated in the presence of olefins by the method of Doering and Hoffmann[243] via α-elimination of HCl from $HCCl_3$ with KOtBu. Using conditions suggested by Vo-Quang and Cadiot,[244] a 60% yield of the dichloroethynylmethylcyclopropane 157 was obtained from 2-methyl-1-buten-3-yne (148). Repetition of



148 157

these conditions with a 30% solution of cis- and trans-1, 5-hexadiyn-3-ene (60) in pentane, prepared by the method of Sondheimer,[131] resulted in only a tarry, black polymer in which no carbene addition products could be detected. However, since it was later found that the half-life of the enediynes 60 was only 5 minutes at -20°C with KOtBu in pentane under these conditions, it is likely that no carbene addition could have been seen even if 60% yields were possible. Substitution of the KOtBu/HOtBu complex formed by distillation of tBuOH from a potassium metal solution in tBuOH allowed the half-life of cis- and trans-60 to be increased to 30 minutes at -20°C in pentane at an initial concentration of 10%. Under these conditions, addition of two equivalents of chloroform and stirring for two hours at -20°C showed one new product in approximately 1% yield in addition to peaks in the glc trace attributable to

tetrachloroethylene, hexachlorocyclopropane, and 2, 2-dimethyl-1, 1-dichlorocyclopropane[245] by coinjection with authentic samples. No enediynes 60 were recovered in the product mixture. Attempted preparative glc isolation of this product failed to yield enough for nmr and ir analysis and a glc-ms was not obtained. All attempts to scale up this reaction failed, giving in at least one instance an explosive polymerization and the production of a carbon ash.

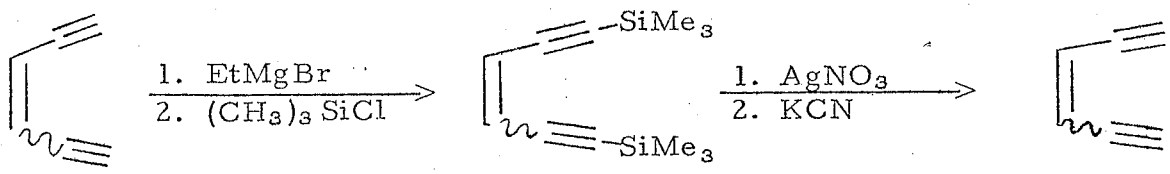
It has been suggested that aprotic media yield more reactive carbenes as far as addition to olefin is concerned.[239] An approximation of aprotic conditions was obtained using a modification of the method of Parham and Schweizer[246] to produce $:CCl_2$ from base decomposition of trichloroacetates. A mixture of enediynes as a 30% solution in pentane, dry NaH, and methyltrichloroacetate was prepared at -20°C without incident. Less than one equivalent of methanol (based on the NaH) was added dropwise by syringe with rapid stirring. After six hours at -20°C the reaction mixture was worked up by dilution with pentane and filtration of the solids yielding a small return of cis- and trans-60, a 5% yield of tetrachloroethylene but no other products by glc analysis. All other possible combinations of these reagents resulted in a rapid decomposition of the enediynes and no products of carbene addition.

Finally, dichlorocarbene was generated in refluxing benzene by thermolysis of phenyl(bromodichloromethyl)mercury by the method of Seyferth.[247] Previous experience with the enediynes and the Seyferth reagent indicated that under these conditions the half-life of the enediynes was over twice that of the mercurial.

However, after six hours reflux all of the enediynes 60 and only 75% of the mercurial had disappeared. Workup showed tetrachloroethylene and hexachlorocyclopropane by glc analysis as well as a <1% yield of two unknowns. While coinjection analysis was not done, comparison of retention times indicated that one of these materials was perhaps identical to the product found in the $HCCl_3$/KOtBu reaction. Again all attempts to isolate these compounds or increase their yield failed.

The relatively high yield of hexachlorocyclopropane in the previous reactions demonstrates that a rather large amount of $:CCl_2$ is being generated. The enediynes then are either inert toward $:CCl_2$ or are polymerizing too rapidly to provide a high concentration of carbene acceptor under these conditions. Professor Sondheimer[248] has shown that silylation of the terminal acetylenic positions of conjugated eneynes greatly increases their thermal stability. I therefore prepared the cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-enes (160) by treating an ether solution of cis- and trans-60 with three equivalents of ethylmagnesium-bromide followed by 3.3 equivalents of $(CH_3)_3SiCl$. Distillation gave a 63% yield of cis- and trans-160 based on the starting tosylate 84. Glc on Se30 showed this material to be 42% cis and 58% trans with the cis-160 eluting prior to the trans-160. In the first preparation of this material a highly silylated, base and heat stable, unidentified impurity was formed independent of the yield of the disilylenediynes 160 which conveniently served as an internal standard in the following reactions. Application of the method of Schmidt

and Arens[249] allowed quantitative removal of the silyl groups to regenerate enediynes 60.

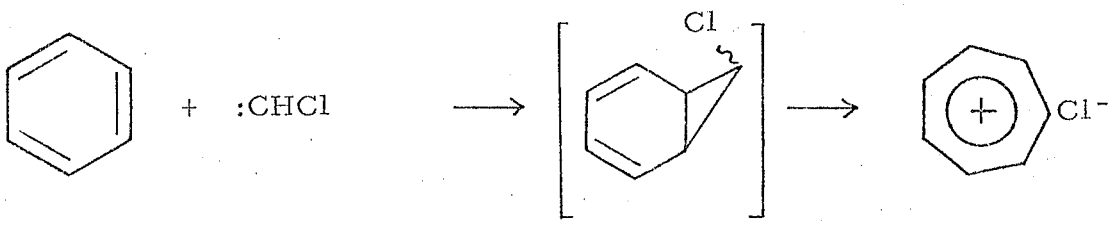


60 160 60

Application of the method of Doering and Hoffmann[243] for generation of dichlorocarbene to 1.0 gm of cis- and trans-disilyl-enediyne 160 as above resulted in a 51% decrease in the cis-isomer and an 80% decrease in the trans-compound versus the silylated internal standard. Glc analysis revealed an approximately 5% yield of two new thermally stable products with longer retention time than 160. Ir suggested chlorocarbons and nmr showed silylmethyl groups, but no other protons could be seen in a preparative glc isolated sample of these materials. On attempted scale-up this result could not be repeated, however. A virtually identical result was obtained using the method of Parham and Schweizer;[246] only here less decomposition of the starting material was observed as expected, since aprotic basic conditions do not allow cleavage of the silyl groups. In the presence of $PhHgCCl_2Br$ in refluxing benzene under argon, however, no attenuation of the cis- and trans-disilylenediynes was noted and no products of carbene addition were found. The reflux was continued to disappearance of the mercurial in the glc trace (~12 hours); the recovery of PhHgBr was 98%. Cleavage of the silyl groups from the terminal acetylenes of this

product mixture showed only cis- and trans-60 together with an approximately 10% yield of hexachlorocyclopropane. The quality of the $PhHgCCl_2Br$ prepared was checked by carrying out the addition of dichlorocarbene to cyclohexene using a procedure identical to the one above. Here a yield of 85% (literature[247(a)] 89%) of the theoretical amount of 7, 7-dichloronorcarane was obtained based on the weight of the mercurial. Therefore, I concluded that due to a combination of several unfavorable circumstances both inductive and conjugative, no dichlorocarbene addition to the enediynes was occurring even under normally very favorable conditions. The small yields of material seen in the $HCCl_3$-KOtBu reactions could conceivably be products of nucleophilic addition as well as the expected cis- and trans-1, 2-diethynyl-3, 3-dichlorocyclopropanes.

Such a situation also occurs with benzene, but reducing the electrophilicity of the carbene effects addition.[239] The addition of chlorocarbene to benzene proceeds in 20% yield to give the tropylium salt 5c presumably via the norcardiene 161,[250] a reaction

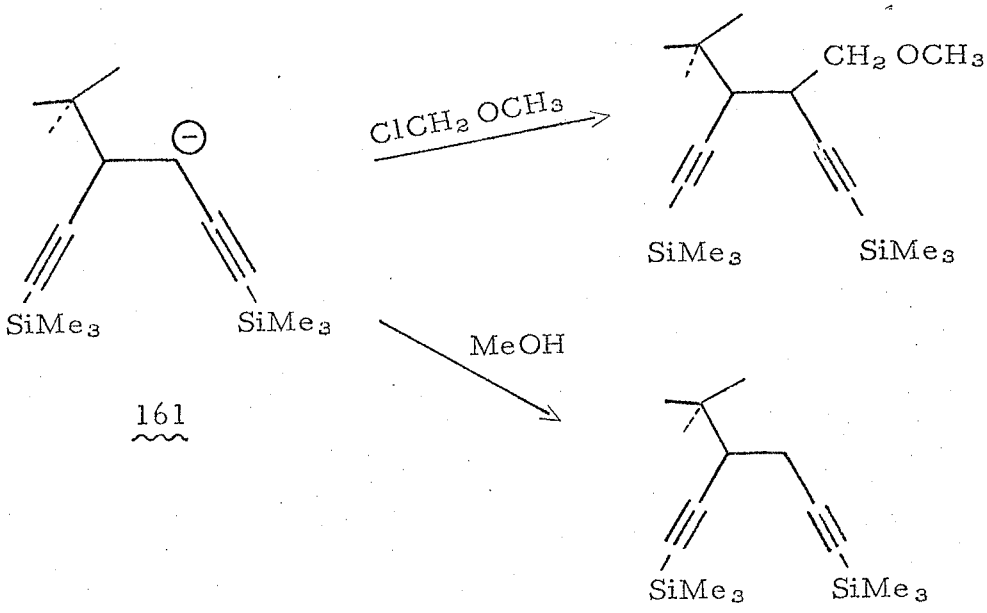


161 5c

which dichlorocarbene fails to undergo. Using the method of Closs[250] I therefore attempted the addition of chlorocarbene to the disilylenediynes 160. Methyllithium (Alfa Inorganics, from methyl iodide) in pentane was syringed slowly into a -30°C solution of methylene chloride and cis- and trans-160 also in pentane. Workup after 30 minutes at -20°C showed, however, no addition product and only small attenuations in the disilylenediynes by glc and ^{1}H nmr analysis. The procedure was checked with an excess of cyclohexene as the carbene acceptor. Here a 20% yield (based on the H_2CCl_2) of a mixture of endo- and exo-7-chlorobicyclo[4.1.0]-heptane was obtained as reported by Closs.[250] The source of the methyllithium (MeCl or MeBr) was varied and even n-BuLi (from n-BuBr) was employed without affecting the outcome of the disilyl-enediyne reaction.

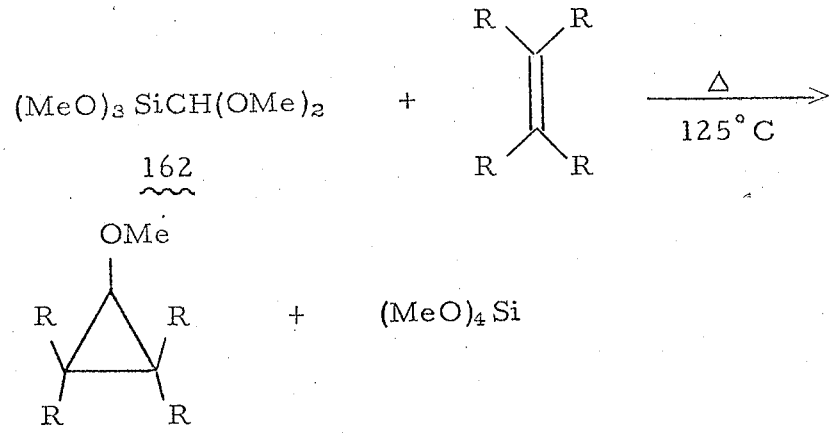
While there is some confusion in the literature as to whether chlorocarbene transfer occurs in the reaction of RLi with H_2CCl_2 in the presence of olefins via the nucleophilic carbenoid $LiCHCl_2$[251] or via the free carbene :CHCl,[250] the choice possibly depending strongly on the acceptor olefin, it is clear that alkoxycarbene transfer from reaction of RLi with Cl_2CHOR' occurs via the nucleophilic carbenoid.[252] That nucleophilic addition to the double bond of the disilylenediynes is indeed possible was demonstrated in the attempted formation of methoxycarbene by the reaction of tBuLi and $ClCH_2OCH_3$ as described by Schöllkopf and Pitteroff.[253] In the presence of cis- and trans-160, nucleophilic addition of the t-butyl anion occurred to give the propargyl anion 161. This anion could

be trapped by nucleophilic displacement of chloride ion from the chloromethylether or isolated as the hydrocarbon conjugate acid by quenching with MeOH. These compounds were isolated by

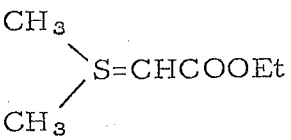


161

preparative glc and identified from their respective nmr's and mass spectral parent ions. Very little of the corresponding allenic product was obtained in either case. However, when methoxycarbene transfer to cis- and trans-160 was attempted by the method of Schöllkopf and Paust[254] via reaction of methyllithium (From CH_3I) with Cl_2CHOCH_3 no products of nucleophilic addition, carbene transfer and only minor decreases in the disilylenediynes were noted. Free methoxycarbene itself is now readily available by pyrolysis of (dimethoxymethyl)trimethoxysilane (162) as described by Atwell, et al.[255] But here again, production of the carbene in the presence of cis- and trans-160 resulted in no products of carbene addition and no appreciable destruction of the starting olefins.

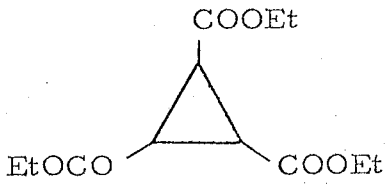


Vogel[256] overcame a similar problem with very electron deficient double bonds by using this effect to accelerate pyrazoline formation by 1, 3-dipolar addition. Repeated application of diazomethane to 160 resulted in complex mixtures of red oils showing nothing of interest in the nmr and only small decreases in both cis- and trans-disilylenediynes. However, the really successful route to cyclopropanes from olefins such as the maleate and fumarate esters with which Vogel was working is via ylide additions. Yields on the order of 80-90% are reported for these systems using ethyl(dimethylsulfuranylidene)acetate (EDSA)[257] (163).



163

Unfortunately, application of this material to the cis- and trans-disilylenediynes 160 in refluxing benzene showed no attenuation of the starting olefins versus an internal standard and only one product, identified by nmr and ir as tricarboethoxycyclopropane (164).



164

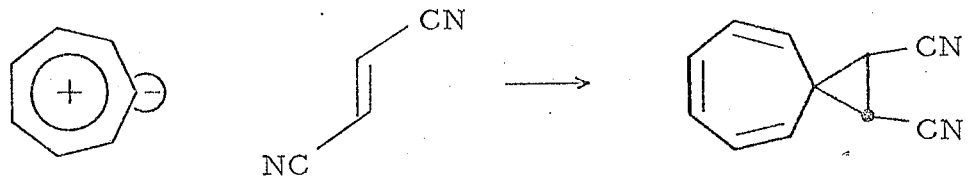
An alternative source of cyclopropanes from olefins of low nucleophilicity is via Cu catalyzed decomposition of diazomethanes. I first decomposed CH_2N_2 with CuI catalyst at room temperature in the presence of a concentrated ether solution of the cis- and trans-disilylenediynes 160. Immediate discoloration and N_2 evolution were noted but even repeated application of diazomethane did not produce any products by glc analysis and only slight reductions in the starting olefins versus an internal standard. Substitution of the ether soluble catalyst $[Ph_3P \cdot CuCl]_4$ as suggested by Moser[258] did not change this result. On the other hand, substitution of ethyldiazoacetate for diazomethane in either the CuI or soluble $Cu^{(I)}$ conditions gave large decreases in the starting cis- and trans-disilylenediynes versus an internal standard with the cis-160 disappearing twice as fast as the trans-160. Repeated application of ethyldiazoacetate until disappearance of the cis-160 showed, however, only small yields of products other than the expected diethylmaleate, diethylfumarate, and tricarboethoxycyclopropane 164. One product, present in 5% yield based on 160, was isolated by preparative glc and showed nmr and ir absorptions characteristic of a diethynylcyclopropane. The silyl groups were not cleaved from this material on treatment with $AgNO_3$/KCN and its formation could not be

repeated with an identically prepared second batch of $N_2CHCOOEt$. This product was not characterized further. Photolytic decomposition of ethyldiazoacetate in the presence of cis- and trans-160 by the method of Skell[259] gave yields of the fumarate and maleate esters as well as 164 but no attenuation in the disilylenediynes.

Thus, I have subjected the hexadiynene structure to a wide variety of carbenes and carbenoids. The high return of starting disilylenediynes 160 under most of these conditions demonstrates that, at least in the case of 160, carbene addition followed by decomposition of the cyclopropane is not responsible for the absence of product. Although trimethylsilyl substitution is known to inhibit carbene addition to vinylsilanes,[260] this effect is largely steric and is probably not the reason for no addition in the case of the hexadiynenes, since the parent 60 also is inert to dichlorocarbene from $PhHgCCl_2Br$. Use of the recently reported phase-transfer, catalyzed generation of CCl_2[261] may allow what appear to be small yields of carbene adducts in the $HCCl_3$/KOtBu case to be raised by the use of large excesses of reagent. The enediynes 60 should be fairly stable dissolved in $HCCl_3$ where only a catalytic amount of base is present. The photolytic decomposition of diazomethane was not investigated which leaves open the possibility that either the hot singlet or an equilibrated triplet methylene will effect addition, although insertion is very likely as well. Both chloro- and bromodiazomethane are available and give carbenes upon thermolysis or photolysis which are considerably more active with respect to addition and insertion than are their carbenoid ($LiCHX_2$)

counterparts. (The photostability of cis- and trans-60 has been demonstrated; see Part I of this thesis.) In the catalyzed carbene transfer reactions where at least one encouraging result was obtained, it has recently been shown that such halocomplexes of $Cu^{(I)}$ as Moser's $[Ph_3PCu^{(I)}Cl]_4$ complex do not coordinate olefins to any appreciable extent. When less tightly bound complexes such as those from $Cu^{(I)}OSO_2CF_3$ and $Cu^{(I)}BF_4$ salts were employed, however, it was seen that olefin complexes do participate in the transition state and that actually electron-deficient olefins are preferred.[262] Thus, in the latter case an intramolecular transfer of carbene may be possible.

It is clear that nucleophilic addition to the double bond of 160 is possible; the problem is to find a nucleophile as basic as tBu^- but possessing a leaving group as well so that γ-elimination can occur. The carbenoid $LiC(OCH_3)_2Cl$ is a possibility, perhaps available by MeLi displacement from $Cl_2C(OCH_3)_3$, but more likely by the action of tBuLi on $HC(OCH_3)_2Cl$. While this species has not been investigated, the very similar $LiCCl_2OCH_3$ is known to give 1-chloro-1-methoxycyclopropanes with olefins.[254] Toward a more nucleophilic carbene, I was recently impressed by the fact that cycloheptatrienylidene (165) while inert to cyclohexene or 2-butene, underwent addition to 1, 2-dicyanoethylene in a completely stereospecific fashion[163] to give the 1, 2-dicyanospirocyclopropane 166. Surely 1, 2-dicyanoethylene is an appropriate model for the enediynes. Lastly, I should like to point out what appears to be an electronic effect which disfavors electrophilic addition to central



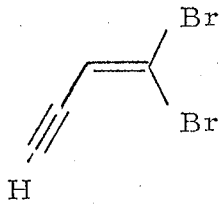
165 166

double bonds of linear conjugated olefins in favor of addition to the terminus. Doering and Roth[264] while investigating the $Cu^{(I)}$ catalyzed addition of diazomethane to 1, 3, 5-hexatriene found a 2.5/1 preference (corrected for a 2/1 statistical factor) for the terminal olefinic bond. Such a preference is reasonable based on even the simple 'particle-in-a-box' model of linear olefins wherein at longer chain lengths (greater numbers of electrons), the maximum charge density is found to approach the ends of the conjugated chains.[265]

Preparation of Eneynes

When it became apparent that routes to diethynylcyclopropanes 61 based on hexadiynenes would be difficult, I became interested in adding propargyl carbene as prepared by Gramas[228(b)] from photolysis of diazopropyne (147) to substituted butenynes. It has been amply demonstrated by D'Amore,[76] Vo-Quang,[244] and others that such olefins as the 2-methylbuten-3-yne are susceptible to electrophilic carbene addition. Besides the 3-penten-1-yn-5-ol (149) and the 1-methoxy-1-buten-3-yne (150) commercially available and the various eneynes in Table XX from the literature, I succeeded in preparing

1, 1-dibromobuten-3-yne (167) and β-ethynyl-1, 3-dithia-2-methylene-cyclohexane (168) by ylid addition to propargyl aldehyde.



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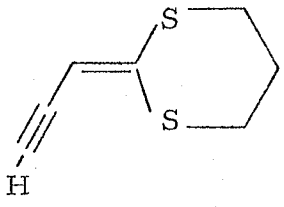

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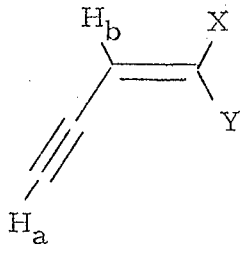
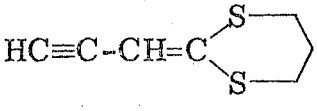
Propargyl aldehyde was prepared in 50% yield by oxidation of propargyl alcohol by the method of Sauer, et al.[132(a)] as described in Part I of this thesis. Using a reagent suggested by Corey and Fuchs[266] prepared by Zn elimination of Br_2 from carbontetrabromide in the presence of triphenylphosphine, the ylid addition product 1, 1-dibromobuten-3-yne was obtained in 61% isolated yield after silica gel chromatography. Glc analysis showed only one major impurity (approximately 5% of the mixture) identified by nmr and ir as the allenic dibromide $H_2C{=}C{=}C{=}CBr_2$. The nmr and ir spectra of dibromide 167 were consistent with the proposed structure and are summarized in Tables XXI and XXII together with similar data for other eneynes. This eneyne is conceivably a source of 61b by reduction either before or after propargyl carbene addition. As it is, 167 is possibly a source of the interesting carbene 30d by metal-halogen exchange or ketone 52 by basic hydrolysis.

Table XXI

^{1}H NMR Spectra of Eneynes

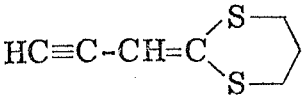


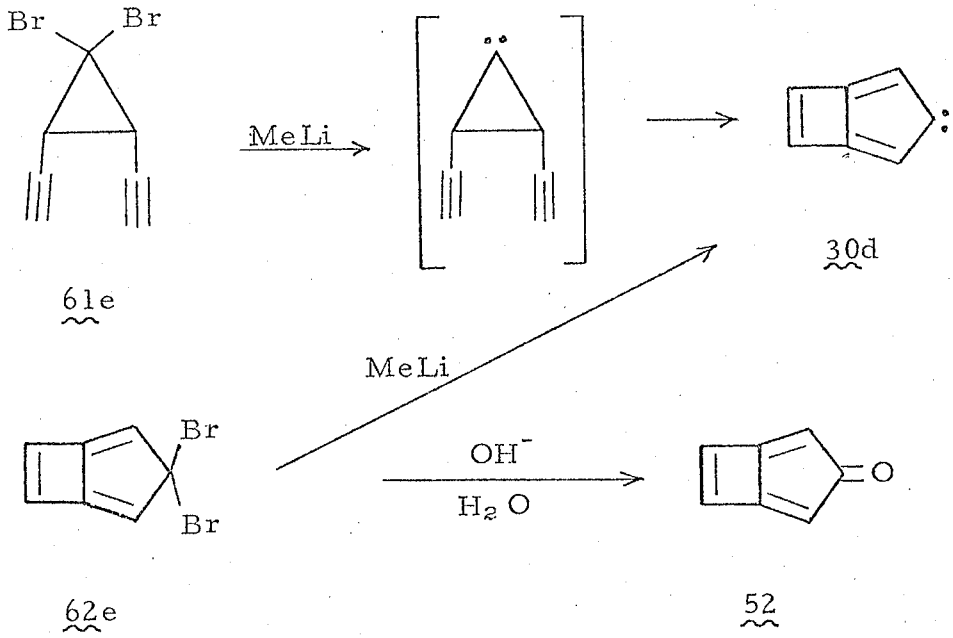
Compound	τ ($DCCl_3$)[a] H_a	H_b	Ref.
$HC\equiv C-CH=CBr_2$ **167**	6.62	3.48	this work
 **168**	6.55	4.27	this work
$HC\equiv C-CH=CHOCH_3$ **150**	6.92	3.63	this work
$HC\equiv C-CH=CHBr$ **169**	6.46	3.55	233
$HC\equiv C-CH=CHI$ **170**	6.40	3.21	233

[a]Referred to TMS at 10.0τ.

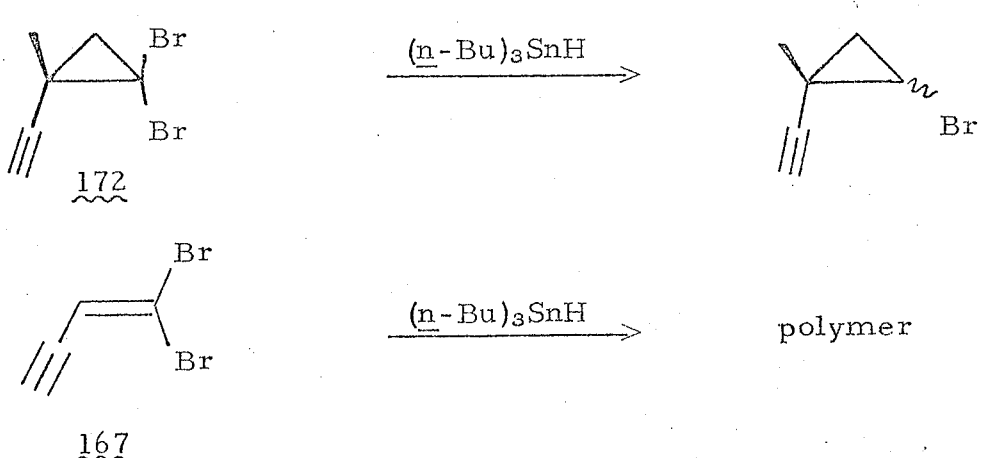
Table XXII

IR Spectra of Eneynes

Compound	ν (cm^{-1})	Ref.
$HC\equiv C-CH=CBr_2$ 167	3315 (≡CH), 2045 (C≡C), 1750 (C=C), 1475, 1390, 1130, 740	this work
 168	3300 (≡C-H), 1740 (C=C), 1415, 1295, 920, 700, 625	this work
$HC\equiv C-CH=C(OCH_3)_2$ 171	3290 (≡C-H), 2100 (C≡C), 1636 (C=C)	237
$HC\equiv C-CH=CHOCH_3$ cis-150	3310 (≡C-H), 2113 (C≡C), 1630 (C=C), 1456, 1275, 1120, 650	this work
$HC\equiv C-CH=CHBr$ trans-169	3280 (≡C-H), 2105 (C≡C), 1728 (C=C), 1581, 980	233
$HC\equiv C-CH=CHI$ trans-169	3291 (≡CH), 2101 (C=C), 1617 (?), 1566, 948	233



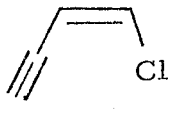
Several attempts to reduce the dibromide 167 to the bromoeneyne 169 with (n-Bu)$_3$SnH by the method of Seyferth[267] used successfully by D'Amore[76] to reduce the ethynylcyclopropane 172 gave a 10% yield of returned starting material after twelve hours stirring at 25°C but no less volatile products by glc analysis.



Use of an added AIBN catalyst resulted in a violent reaction at 40°C and substitution of the more reactive $(n\text{-Bu})_2SnH_2$ led only to polymer after twelve hours at 0°C. In neither case were any products of reduction seen. In an attempt to directly form the analogous chloride 173 by trapping the chlorocarbene from H_2CCl_2 and n-BuLi with Ph_3P and subsequent ylid addition to propargyl aldehyde according to the method of Seyferth,[268] only a vanishingly small yield of a chlorovinyl acetylene of correct molecular weight was obtained. To raise this yield, perhaps advantage could be

$$H_2CCl_2 + n\text{-BuLi} + Ph_3P \longrightarrow Ph_3P{=}CHCl$$

$$\xrightarrow{HC{\equiv}C\text{-}CHO}$$



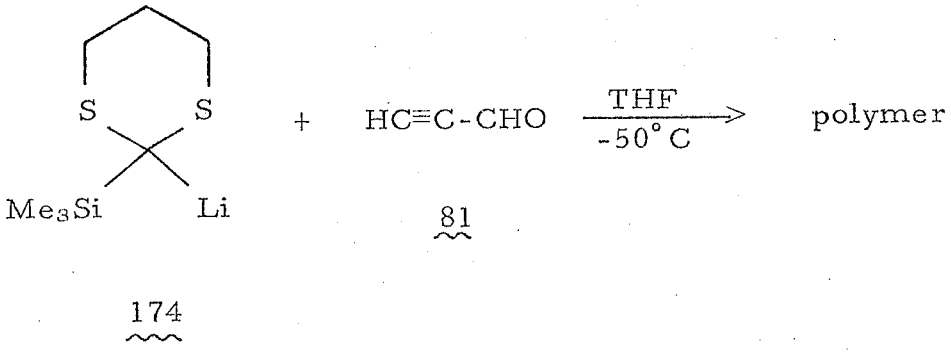
173

taken of Seyferth's suggestion that the ylid salt with HBr be isolated and the chloromethylene ylid regenerated by the action of PhLi. Alternatively, consistently high yields of chloro- and bromomethylenes have been produced by the thermal decomposition of PhHgCHXBr (X = Cl, Br) in the presence of Ph_3P and an aldehyde.[269]

As a source of the bicyclo[3.2.0]heptatrien-3-one (52), the thioketal 62g (hopefully available from pyrolysis of the diethynylcyclopropane thioketal 61g) is particularly attractive. While such compounds as the dibromide 62e and the dimethylketal 62f could conceivably be converted into 52, the former requires hydroxylic basic conditions and the latter aqueous acidic conditions, both of

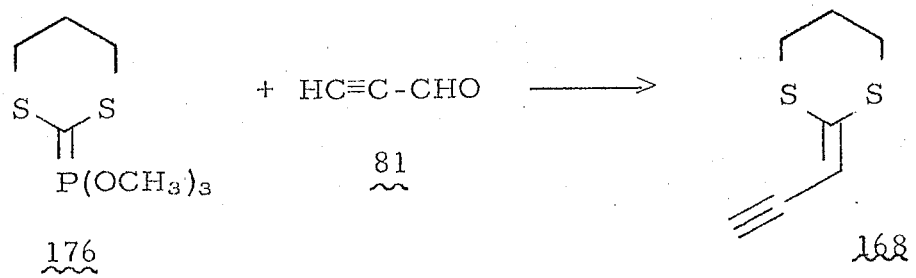
which have been shown by D'Amore[76] to rapidly polymerize the unsaturated parent triene 48. Propargyl carbene addition to the ketenethioacetal 168 would afford 61g. Therefore routes to this previously unknown eneyne were initiated.

Treatment of 2-lithio-2-trimethylsilyl-1, 3-dithiane (174), prepared as described by Jones and Lappert,[270] with propargyl aldehyde gave only polymeric material at -50°C. Recent results in



174 81

Professor Bergman's laboratory show that a major improvement in the base sensitivity of 81 can be obtained by trimethylsilylation of the acetylene. Therefore, this reaction would probably stand a better chance with 175. However, use of Corey's dithian ylide[272] 176 with the unsubstituted propargyl aldehyde at -20°C provided the expected ethynylketene thioacetal 168 in 20% glc yield based on the reported yield of the ylide. Attempts to separate this product from



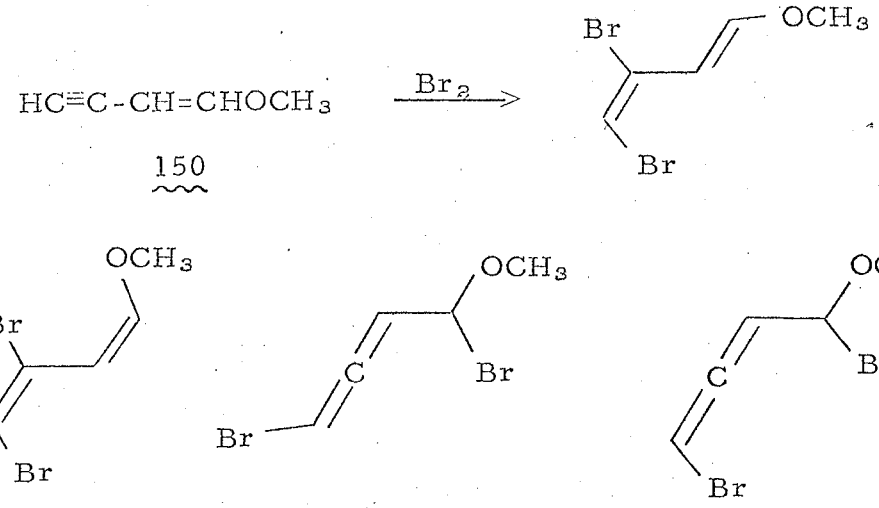
176 81 168

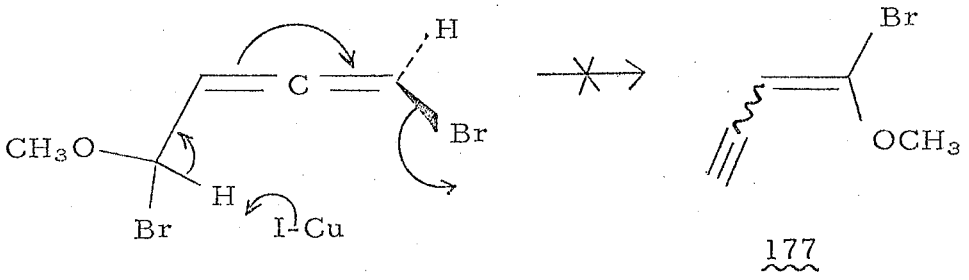
$Me_3SiC{\equiv}C\text{-}CHO$

175

the excess trimethylphosphite solvent proved to be difficult. To prepare a sample pure enough for the proposed carbene addition, it was necessary to resort to preparative glc. The nmr and ir spectral properties of 168 purified in this way are summarized in Tables XXI and XXII. The assignment of structure appears quite reasonable in light of the similar data for other eneynes in these tables. To facilitate isolation of pure 168 in large scale, perhaps advantage could be taken of Corey's suggestion that the excess trimethylphosphite be removed by 'lyophilization' followed by resolution of the thermally unstable ylide in $HCCl_3$ and addition of the aldehyde.

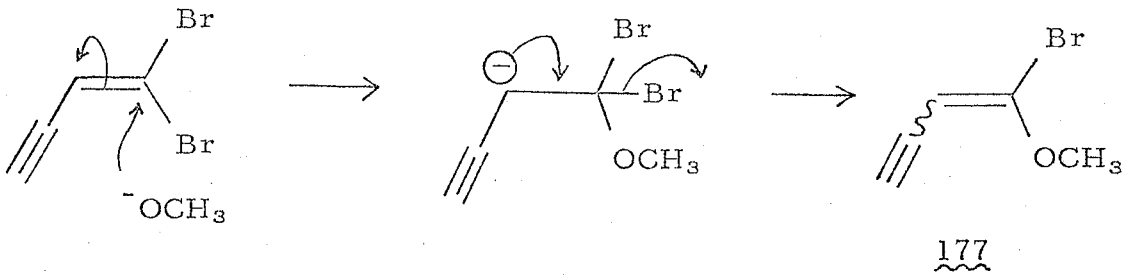
Two routes to 1-bromo-1-methoxybuten-3-yne (177) were also investigated. Addition of Br_2 to the commercially available 1-methoxybuten-3-yne (150) at -20°C in CCl_4 gave a mixture of four dibromides (four methylether peaks produced in the nmr) in roughly equal amounts.[273] However, treatment of the mixture so produced with KOtBu in diglyme[274] or heating with dry cuprous iodide in DMF[275] failed to produce any acetylenic products. There was, however, some indication that 177 was formed in an addition-elimination reaction of $NaOCH_3$ with the dibromide 167. A new glc peak of correct molecular weight was present in the largely





177

polymeric mixture but in low yield. This material was never isolated.



177

Synthesis of trans-1, 2-Diethynyl-3-methoxycyclopropane by Propargyl Carbene Addition to 1-Methoxybuten-3-yne

Diazopropyne[228] (147) was prepared as a dilute solution in diethylether or pentane essentially as described by Gramas[228(b)] from base decomposition of N-nitroso-N-propargyl urea (178). This latter compound, available from propargyl amine, was prepared as outlined in Figure XXIX at 10X the scale used by Gramas without incident. The yield of diazopropyne based on the nitroso urea was 30% when extracted into pentane and 40% with ether as determined by titration with dilute alcoholic HCl to disappearance of the 2080 cm^{-1} diazo band in the ir. These orange-red solutions were stable at room temperature over a period of several hours (half-life of a 40% solution in ether is approximately five hours as monitored by ir) giving only a brown, ether insoluble polymer. The presence of cintered glass and sharp objects was avoided, but the solutions could be dried over powdered Na_2SO_4 without decomposition. However, on one attempt to prepare a concentrated solution (~10M) in pentane by vacuum transfer from a mineral oil solution with a pentane purge, a violent explosion occurred upon warming the trap to -25°C.

1-Methoxybuten-3-yne (150) is available from Farchan and Aldrich as a 50% solution in methanol. Extraction with ether, washing with water, and distillation allowed neat 150 to be obtained as a clear, colorless liquid which quickly turned red-brown even at 0°C upon exposure to air. This material was contaminated with at least two products of MeOH addition and a product of thermal

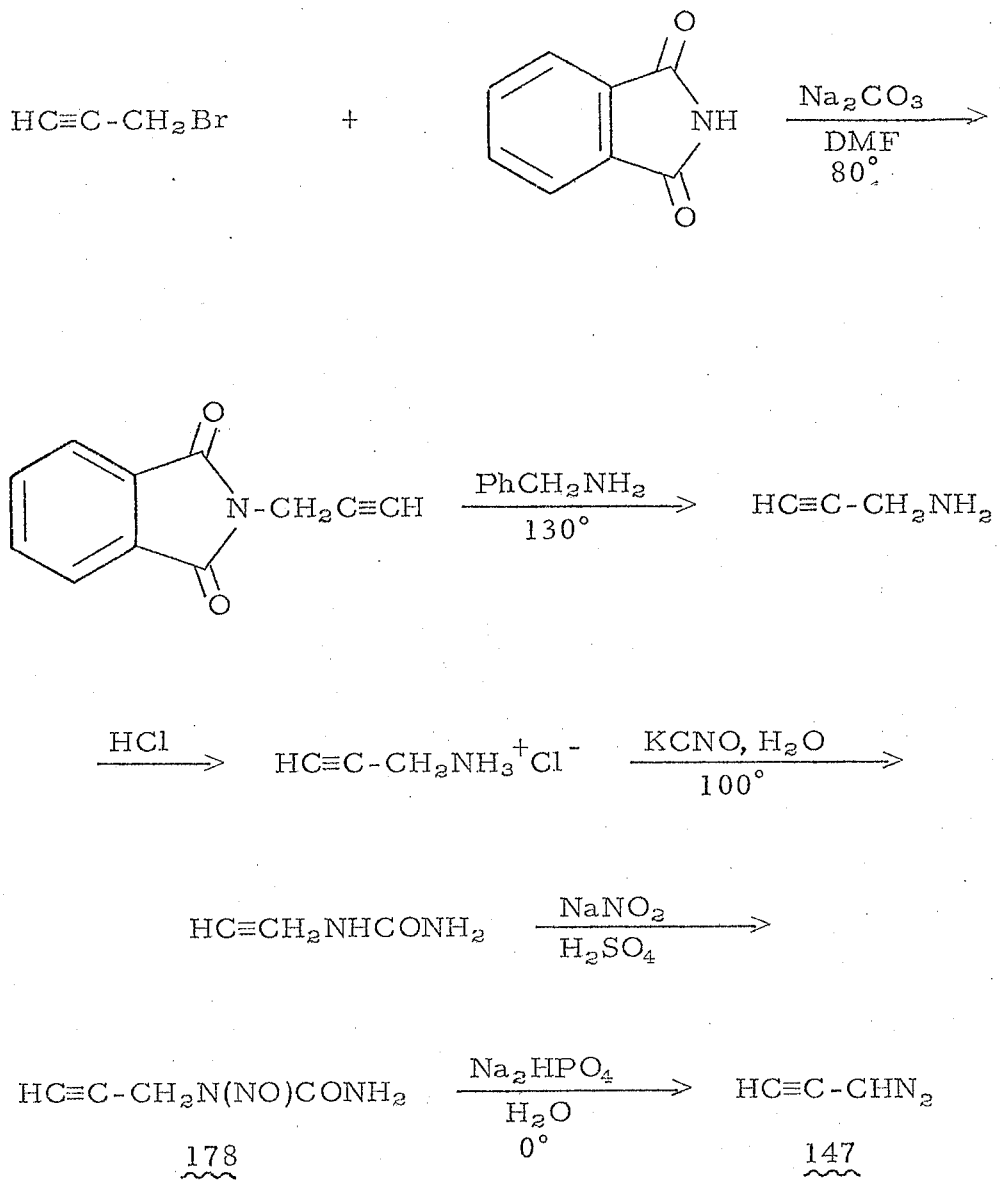


Figure XXIX

Synthetic Route to Diazopropyne

rearrangement or disproportionation to the extent of 3-5%. Careful redistillation did not reduce these impurities, but preparative scale glc on SE30 using a glass column allowed isolation of 150 with no contaminant greater than 0.1% by weight (analytical glc integrations from flame ionization detector). Analytical glc also showed that this material was only one isomer, identified by the 6.6 Hz vinyl-vinyl coupling constant in its proton nmr and the absence of a ~930 cm^{-1} band in the ir[238] as cis-1-methoxybuten-3-yne.

A degassed solution of 0.24 mole 150 and 0.12 mole diazopropyne in 250 ml olefin free ether was subjected to direct irradiation at 5°C internal temperature through a Pyrex filter with a Hanovia medium pressure Hg vapor lamp. One product of longer glc retention time than 150 was seen together with a large return of the vinyl ether after ir showed complete disappearance of the diazo band. Distillation of most of the diethylether followed by CO_2 assisted vacuum transfer[276] of the volatiles from the polymer (see Preparation 35, Note C) and preparative glc on a glass SE30 column allowed isolation of this new material as a 3/1 mixture with the methoxyeneyne. A second preparative glc isolation from a benzene solution of this crude product produced 60 mgm or 0.4% yield of a pure, air-sensitive substance of mass spectral parent ion m/e 120.

The mass spectrum of this material at 70 ev (Table XXIII) shows a pattern below m/e 90 ($C_7H_6^+$) almost identical to that reported by D'Amore[76] for the diethynylcyclopropanes 61a. The m/e 89 ($C_7H_5^+$) corresponding to loss of OCH_3 is in fact the base peak.

Other than this, however, there is very little in the fragmentation pattern to recommend a methoxydiethynylcyclopropane. But the ir spectrum is easily interpreted in terms of the terminal acetylene, cyclopropyl and methylether functions as Table XXIII shows. A 60 MHz nuclear magnetic resonance spectrum in C_6F_6 is also very revealing and nearly first order. A three proton singlet occurs in the position expected for a methylether. Two nonequivalent acetylenic protons appear as overlapping doublets, each coupled to a single propargylic proton. The methoxy-cyclopropyl-methyne proton is a doublet of doublets while the two propargylic cyclopropyl protons appear as a complex multiplet clearly composed of two nonequivalent resonances. Although a 220 MHz spectrum would have been helpful, the 60 MHz pattern for the cyclopropyl protons can be analyzed in terms of an ABX pattern as described by Abraham,[277] only slightly broadened by the small coupling to the acetylenic protons. This pattern is shown in Figure XXX and the assignment of resonances and coupling constants summarized in Table XXIV.

Since the all-cis- or the trans-3-methoxy-cis-1, 2-diethynylcyclopropane would have been expected to possess simpler spectra (AA'X), the material isolated from the propargyl carbene addition to cis-1-methoxybuten-3-yne (150) is assigned structure 61d, consistent with all the above data. The assignment of the trans stereochemistry to the ethynyl groups is also chemically reasonable since D'Amore found that the unsubstituted cis-1, 2-diethynylcyclopropane (cis-61a) is very liable to polymerization in neat form.

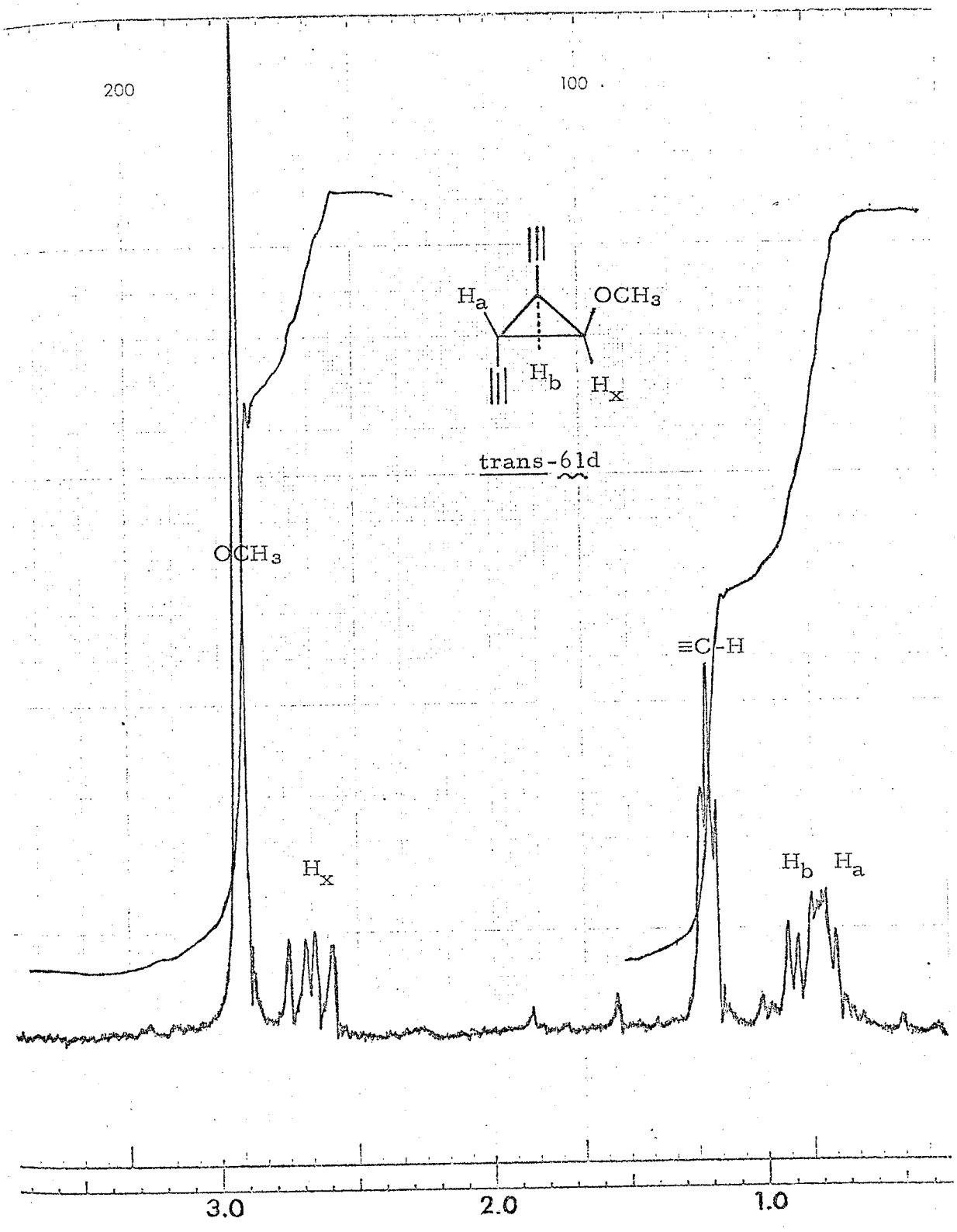
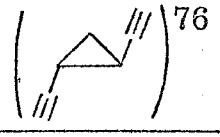


Figure XXX

60 MHz ^1H NMR of trans-1, 2-Diethynyl -3-methoxycyclopropane (61d)

Table XXIII

Infrared and Mass Spectral Data for
trans-1, 2-Diethynyl-3-methoxycyclopropane (61d)

IR Assignment[a]	ν (cm^{-1})[b]	 76
C≡C-H (stretch)	3305	(3310)
 (stretch)	3030, 2990	(3010)
O-CH_3 (stretch)	2930, 2850	
C≡C (stretch)	2120	(2140)
O-CH_3 (bend)	1450	
C≡C-H (combinational)	1220	(1220)
O-CH_3 (asym. stretch)	1122	
 (stretch)	1072	(1060)
≡C-H (bend)	650	(650)

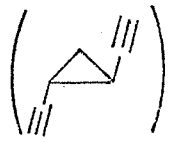
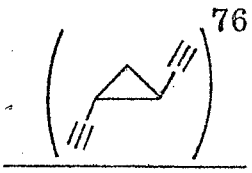
MS[c]			
m/e	Ion	% Base Peak	
121	P+1	0.6	
120	P	5	
105	$C_7H_5O^+$ (-CH_3)	39	
91	$C_7H_7^+$ or $C_6H_3O^+$	87	
90	$C_7H_6^+$ or $C_6H_2O^+$	55	(16)
89	$C_7H_5^+$ (-OCH_3)	100	(100)
77	$C_6H_5^+$	87	

Table XXIII (Continued)

MS[c] (Continued)



76

m/e		% Base Peak	(52)
63	$C_5H_3^+$	16	(52)
51	$C_4H_3^+$	49	(32)
39	$C_3H_3^+$	30	(38)

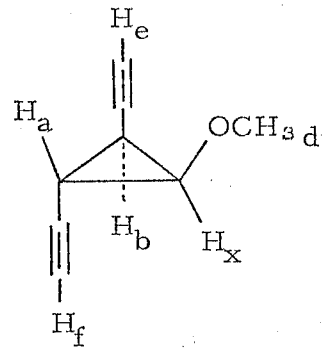
[a]Assignments based on tables in reference 83.

[b]Calibrated versus polystyrene.

[c]At 70 ev electron energy.

Table XXIV

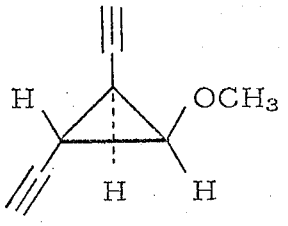
^{1}H NMR Data for trans-1, 2-Diethynyl-3-methoxycyclopropane (61d) in C_6F_6



trans-61d

Proton	τ*	mult.	J (Hz)
d	7.07	singlet	—
x	7.32	dd (ABX)	J_{bc} = 5.0 J_{ac} = 4.0
b	9.20	ABX	J_{ab} = 5.5
a	9.10	ABX	J_{ab} = 5.5
e, f	8.78	d	J_{ec}, J_{df} = 1.0

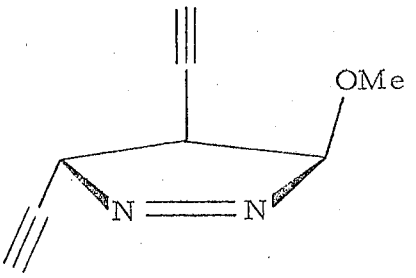
*External TMS at 10.0τ.



trans-61d

Compound 61d was stable neat under vacuum at 25°C but readily polymerized in air. The addition of propargyl carbene is usually interpreted in terms of the triplet since nonstereospecific addition is observed.[228] Here, since cis-diethynyl configurations are less stable and highly reactive, the presence of only one product cannot be taken as evidence for a singlet carbene addition.

In the course of this work it was discovered that the photoproduct 61d could be produced by allowing the diazo compound to stand in a concentrated solution of the methoxyeneyne 150 followed by injector port pyrolysis at 150°C. In one instance a 5% glc yield of 61d was obtained based on the diazopropyne. No evidence in the nmr or ir could be obtained, however, for what must have been at least a 5% yield of pyrazoline 179 even after three days at 0°C at which time ir showed >90% disappearance of the diazo band. The pyrolytic yield of 61d proved to be erratic (0-5%) either by sealed tube heating at 150°C or injector port pyrolysis. Consistently higher yields of the diethynylcyclopropylmethylether were



179

obtained by photolysis of the pyrazoline containing solutions in a manner entirely similar to that described above followed by preparative glc isolation of 61d. However, the added labor required to prepare solutions of diazopropyne in neat methoxyenyne 150 (extraction of diazopropyne from pentane solutions by equilibration with the pentane insoluble methoxyeneyne at 0°C) made this route less valuable than it might seem based on the ten-fold increase in yield.

Application of either of the above methods to the 1,1-dibromoeneyne 167 and the ethynylketenthioketal 168 led to no detectable products of propargyl carbene addition from glc analysis. The state of purity and the amount of starting material available in the attempted addition to 167 make it likely that as little as 0.1% yield could have been seen in the glc trace. It is perhaps not surprising that this addition does not occur considering the electron deficient nature of such a double bond. Seyferth's experiments with dichlorocarbene from a variety of sources show that addition to

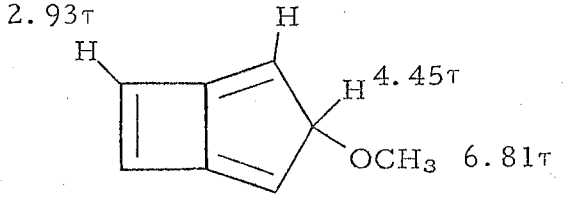
1,1-dichloroölefins is as much as 100X slower than addition to cyclohexene in competition experiments.[278] On the other hand, yields of as high as 60% have been reported for dichlorocarbene additions to keteneacetals.[279] That no products were seen with 168 is perhaps due to the fact that only small amounts of this acetal could be prepared so that experiments where the acetal was the virtual solvent could not be run. Also, since the purity of 168 obtained from even preparative glc was not high due in part to the thermal instability (products unknown) of this compound, it is possible that a 1% yield of propargyl carbene addition would have gone undetected.

Formation of 3-Methoxybicyclo[3.2.0]hepta-1,4,6-triene by pyrolysis of 61d

Since D'Amore obtained the highest yields of triene 48 under conditions of flow pyrolysis at 300-350°C, the atmospheric pressure flow pyrolysis apparatus pictured in Figure XIV was equilibrated at 310°C at the center giving an average temperature of 305°C across a 20 cm hot zone. The 3-methoxy-1,2-diethynylcyclopropane 61d as a 10% solution in 0.4 ml hexafluorobenzene or d_8-THF was vaporized into the hot quartz tube with a 60 ml/min flow of dry helium under which conditions a residence time in the hot zone of 10 sec was estimated. The complete disappearance of the cyclopropane was confirmed by glc analysis but only a 5% yield of what could conceivably be a dimeric product was noted. However, upon opening this sample to air, a brown polymer began forming

indicating the presence of some very reactive material. Nmr of a vacuum-transferred, sealed sample of this material showed a virtually quantitative yield of an olefinic methylether with a proton resonance pattern entirely similar to that reported for 48 (see Figure XXXI). Introduction of a sample of this solution into the batch analyzer of the mass spectrometer produced a spectrum practically identical to that obtained for 3-methoxy-1, 2-diethynyl-cyclopropane (61d) superimposed on the solvent (d_8-THF), at least confirming that the product is an isomer of 61d. Again the loss of OCH_3 produced the major fragment, m/e 89. Upon attempted determination of an ir spectrum, the compound decomposed so that only broad C-H absorption was seen.

Solely on the basis of the nmr spectrum, the structure of this new compound was assigned as 62d. The rather low field



62d

absorptions for the methoxy methyne proton in 62d and those on the four-membered ring may indicate significant polarization of the C-O ring bond. A corresponding downfield shift of the methyne proton of tropylmethylether 180 is not observed perhaps due to a

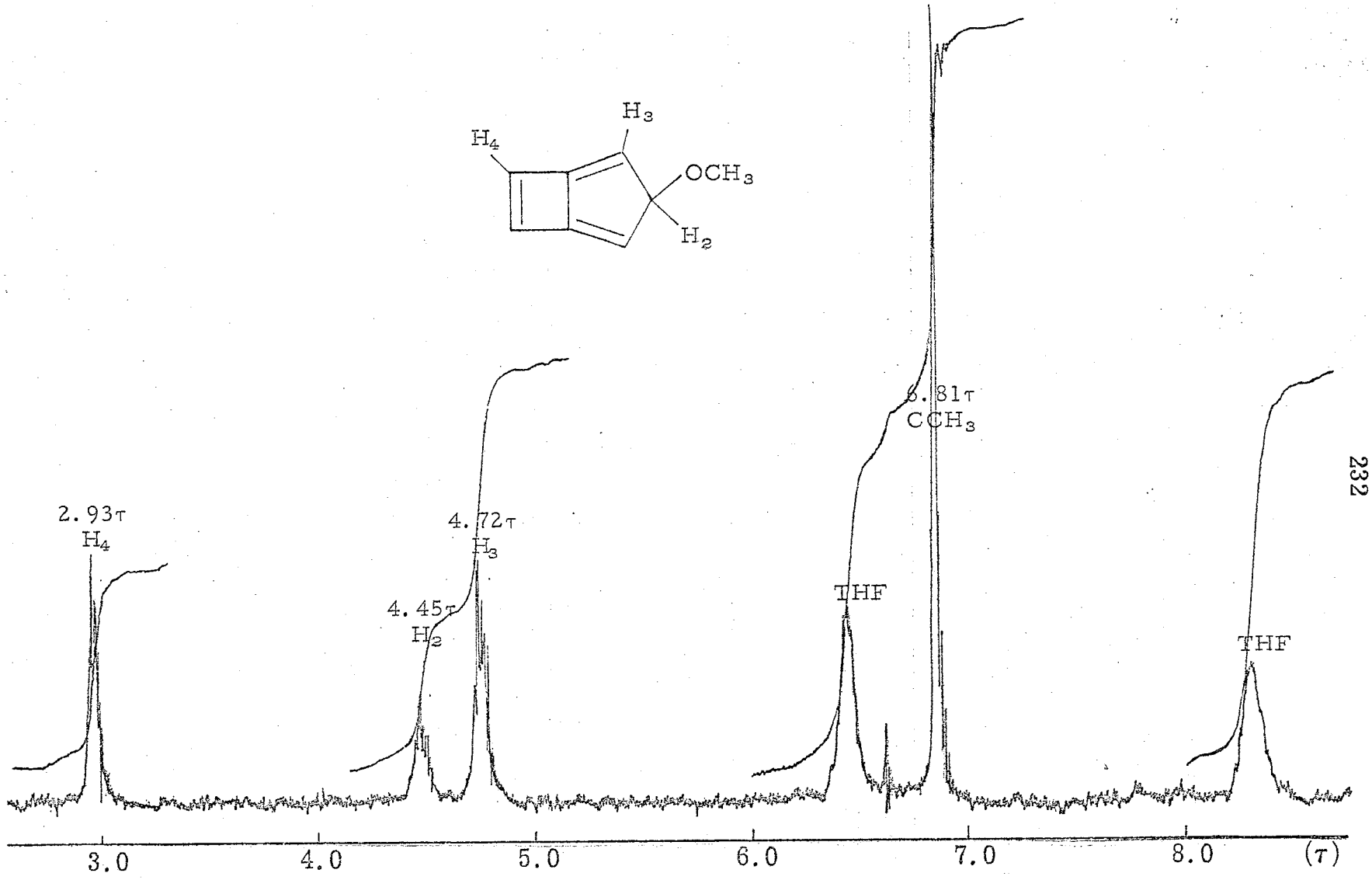
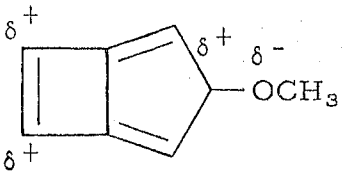


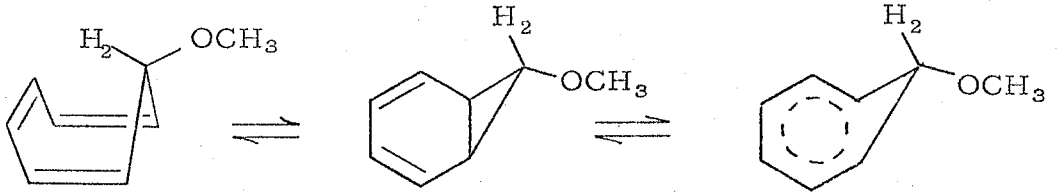
Figure XXXI

60 MHz ^{1}H NMR of 3-Methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d)



62d

contribution from B or C, since each isomer would be expected to cause an upfield shift in H^2 (see Table XXV) to the extent that it is in equilibrium with A. A similar equilibrium in 62d would not be expected.



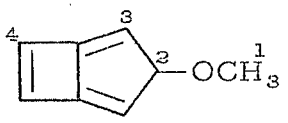
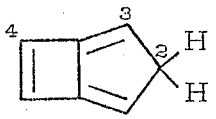
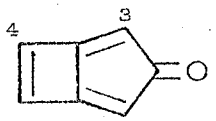
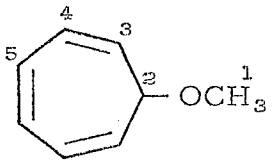
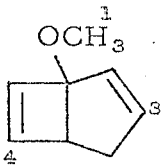
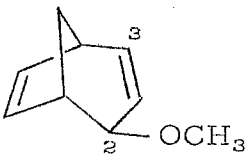
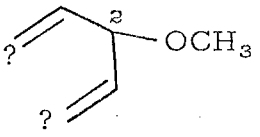
A B C

180

An indication of the activation energy required to convert 61d into 62d can be obtained from the fact that at an oven temperature of 275°C, one pass under atmospheric flow conditions, contact time approximately 10 seconds, was sufficient to rearrange only 46% of the methoxycyclopropane. Assuming uncatalyzed simple first order kinetics and an A factor of $\log^{-1}$ 15.5 as determined by D'Amore for the rearrangement of trans-1,2-diethynylcyclopropane (61a), an activation energy of 40 kcal/mole can be estimated.[76]

Table XXV

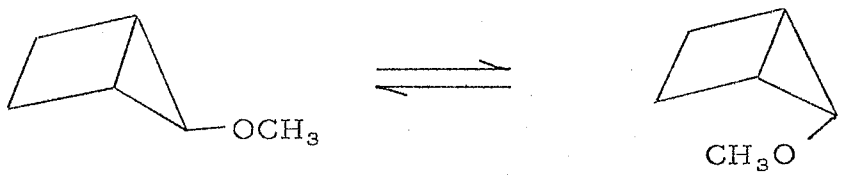
^{1}H NMR Data[a] for 3-Methoxybicyclo[3.2.0]heptatriene 62d with Appropriate Models

Compound	Chemical Shift (τ, TMS 10.0τ)	Solvent	Reference
	H_1, 6.81τ H_2, 4.45 H_3, 4.72 H_4, 2.93	THF-d_8	this work
	H_2, 6.62τ H_3, 4.92 H_4, 3.27	CCl_4	76
	H_3, 3.44τ H_4, 3.15	ether/ Et_3N	
	H_1, 6.65τ H_2, 6.84 H_{3-5}, 3.5-4.7	CCl_4	this work
	H_1, 6.76τ H_3, 4.13 H_4, 3.77	CCl_4	280
	H_2, ~6.7τ H_3, 4.72	DME	281
	H_2, 5.4τ[b]	CCl_4	

[a]Some of these assignments have not been rigorously established. A consistent assignment only is implied.

[b]Calculated from the tables given in reference 140.

Compared to the 44 kcal/mole E_a found for 61a, the OCH_3 π donor group accelerates the presumably diradical cyclopropane ring cleavage by 4 kcal/mole. Such an acceleration is not unexpected based on the 9 kcal/mole lower activation energy for cleavage of chlorocyclopropane to chloropropene compared to cyclopropane itself.[282] This weakening of the 2, 3 σ bond in 1-substituted cyclopropanes by π donors has been discussed in terms of the Walsh orbitals by Hoffmann.[283] Both Fellenberger, et al.,[284(a)] and Tufariello, et al.,[284(b)] have observed a 9-10 kcal/mole lower activation energy for the interconversion of exo- and endo-181 than in appropriate all hydrocarbon bicyclo[2.1.0]pentane systems.



exo-181 endo-181

Attempted Formation of the 1, 4-Dehydrotropyl Anion 30a by Ether-Cleavage Reduction of 3-Methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d)

Both Breslow, et al.,[103] and D'Amore and Bergman[76] were apparently able to form small concentrations of the 1, 4-dehydrotropyl anion 30a by KOtBu removal of a proton from trienes 50 and 48, respectively. Upon quenching these solutions in which no spectral evidence of an anion such as 30a was seen, reprotonation

evidently led in both cases to 50 which dimerized to a mixture of syn- and anti-95 in approximately 5% overall yield. D'Amore[76] was able to prepare as much as a 30% yield of dimers 95 by treatment of 48 with potassium. If 30a is postulated as an intermediate here, it must rapidly abstract a proton from solvent or 48 to form 50, since no nmr of an anion was observed and since dimers 95 were present in high yield even before quenching with methanol. While it is conceivable that dimers could arise from intermediate radicals 48a or 30b (see Figure XXXII), the fact that only the dimers 95 , known to arise from 50 from other work, are formed strongly implicates the anion 30a as the major pathway for reaction. The remainder of the product was polymeric, also possibly arising from trapped 30a.

It is clear from the kinetic assumptions made in Figure XXXII that if a better leaving group than $\dot{H}$ or H^- were available to a reversibly formed bicyclo[3.2.0]heptatriene radical anion, higher initial concentration of anion 30a might be obtained. In such a case, even with addition/polymerization and hydrogen abstraction/dimerization reactions competing for triene, a sufficient concentration of 30a for spectroscopic observation might remain after complete reaction of all trienes. If hydrogen abstraction from solvent by either 30b or 30a is a problem, use of perfluorinated ethers instead of THF may provide a solution.

That such an approach is reasonable can be seen by analogy to the successful generation of the possibly antiaromatic tropyl anion 5a from 7-methoxycyclohepta-1, 3, 5-triene (180) by Dauben and

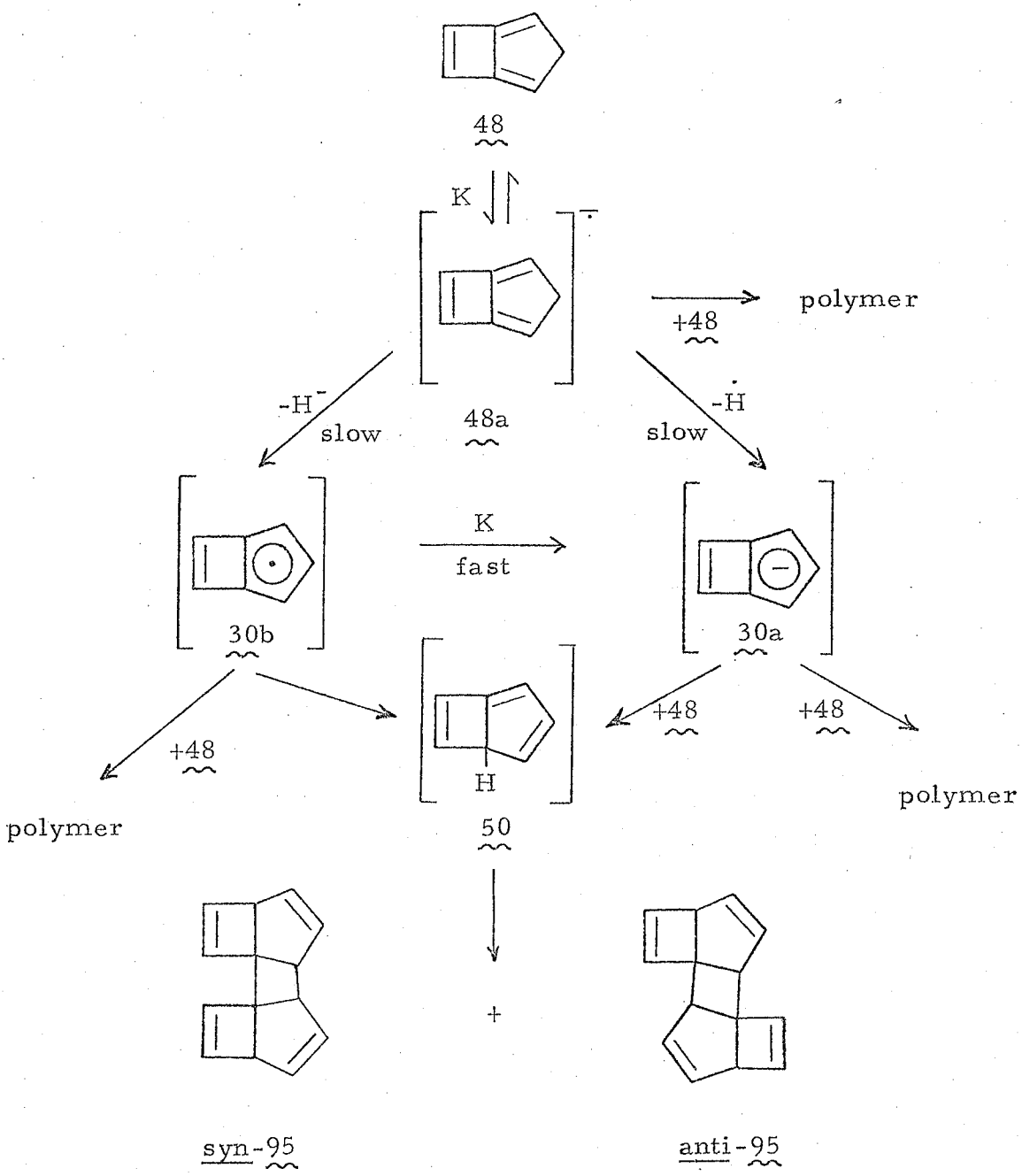


Figure XXXII

Reaction of Bicyclo[3.2.0]hepta-1, 4, 6-triene (48) with Potassium

Rifi.[285] While reaction of cycloheptatriene with bases such as phenylsodium or shaking with reducing agents such as sodium-potassium alloy led only to polymer and no products of 5a upon quenching either with D_2O or CO_2, slow addition of tropylmethylether 180 in THF to an excess of sodium-potassium alloy in THF at -20°C produced a deep blue, diamagnetic solution of the anion as seen by an 80% yield of dimeric and trapped products upon workup by carbonation. Similar conditions to the above were applied to the 3-methoxybicyclo[3.2.0]heptatriene 62d in d_8-THF.

While Dauben and Rifi stipulate 12 hours for the addition of the ether, I found that the deep blue solutions of 5a could be generated much more rapidly than this. With triene 62d long addition times were not possible with the techniques employed due to polymerization in the syringe. However, it was clear from the first drop in what must be reasonably dilute conditions that whatever intermediate is first formed is very reactive. One drop of a 5% solution of 62d in d_8-THF (~200 μl) generated a yellow color in 0.2 ml d_8-THF at -20°C containing rapidly stirred excess 1:5 Na/K alloy. This color over a period of approximately 10 seconds gave way to a brown, finely divided precipitate. Continued addition over 30 minutes led to considerable brown precipitate and no nmr signal due to unreacted 62d, anion 30a or any other product. Workup with methanol as described by D'Amore gave no returned starting material, triene 48, dimers 95, or any other product by glc and nmr analysis. From this one must conclude that either the anion 30a was never formed or if formed the increased reactivity of the

methoxybicycloheptatriene compared to 48 led only to addition polymer product. Not surprisingly, identical results were obtained when a 5% solution of 62d in d_8-THF was allowed to contact a potassium mirror at -40°C except that here the disappearance of the methoxybicycloheptatriene was not immediate but occurred over 12-24 hours due undoubtedly to polymeric coating of the mirror. In this latter experiment, no esr signal was seen either when in contact with the mirror or after decantation.

Thus, while it is not clear whether or not 62d cleaves to 30a faster than 48 does, addition/polymerization is still the major pathway of reaction. One way to avoid this problem is to achieve conditions of effective high dilution of 62d. D'Amore devised an apparatus (Figure XXXIII) which may allow slow vacuum transfer of solutions of 62d in THF or DME in flask C into a stirred mixture of Na/K alloy in THF in flask A at -78°C. Under such conditions, an extremely small amount of 62d is exposed to excess Na/K and already formed 30a. Abstraction/dimerization will complete with further anion formation but at least chain polymerization of 62d initiated by 30a, 30b or the initially formed radical anion will be minimized. Since the solution containing 62d need only be warmed briefly to fill flask B with vapor, very long reaction times can be achieved. D'Amore failed to produce large yields of dimers 95 from reaction of 48 with napthalene radical anion or lithiumdicyclohexylamide in such an apparatus. However, reaction with Na/K alloy over 24 hours was not investigated.

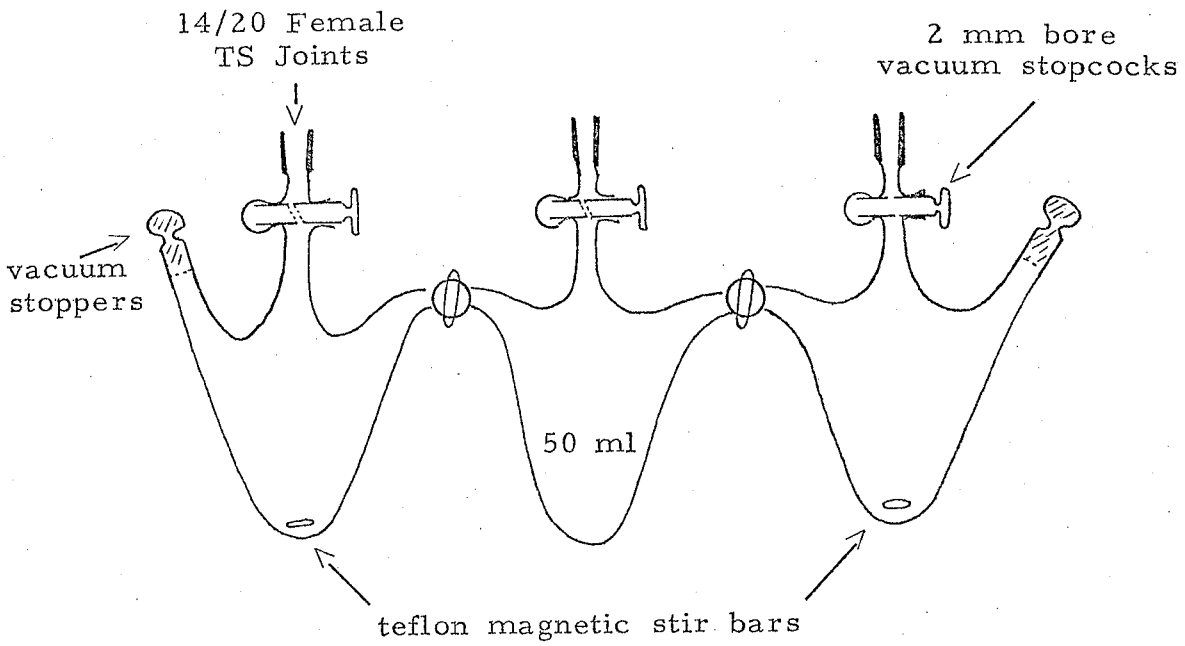


Figure XXXIII

Apparatus for High Dilution Experiment

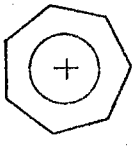
An alternative approach which has been used successfully to counter polymerization of conjugated olefins in anion forming reactions is to stabilize the anions by complexation of the counter ions with low molecular weight tertiary amines.[286] Use of equimolar amounts of crown ethers is another possibility.[287] High dilution of 62d could also be used in such an approach either with the apparatus in Figure XXXIII or with more usual methods employing large amounts of solvent. The latter can be employed to give nmr concentrations of 30a by precipitation of the salt with added hexane as described by Yasuda, et al.,[286] for sodium and potassium salts of the anions from the labile pentadienes and cycloöctadienes.

Advantage could also be taken of the gas phase reaction of a low flux of 62d with a relatively high flux of alkali metal in an apparatus such as that described by Klabunde.[288] Since the products in such an apparatus are condensed out of the gas phase as a soft matrix at 77°K, reaction of the anions or radicals formed initially in the gas phase with unreacted 62d in the condensed phase is discouraged due to immobility. Added to this, the high dispersion of metal atoms and clusters in the solid solution formed makes it likely that complete reduction of 62d to anions will occur either upon aging at -77°K or upon thawing. These suggestions have not been pursued due to the difficulty of obtaining 62d by the methods described in the previous sections.

Attempted Formation of the 1,4-Dehydrotropyl Cation 30c by Reaction of Bicyclo[3.2.0]hepta-1,4,6-triene (48) and 3-Methoxybicyclo[3.2.0]hepta-1,4,6-triene (62d) with Lewis Acids

Stable solutions of carbon cations (carbonium ions)[289] in nmr observable concentrations have been generated by hydride abstraction, protonation of alcohols, ethers, esters for example by strong protic acids, and electrophilic displacement by Lewis acids on organic halides.[290] The aromatic tropylium ion 5c, a particularly stable example of a free carbon cation, has been generated by all these methods and many more besides.[291] In contrast, formation of the potentially antiaromatic cyclopentadienyl cation 3c required use of the strong Lewis acid antimony pentafluoride and very

3c

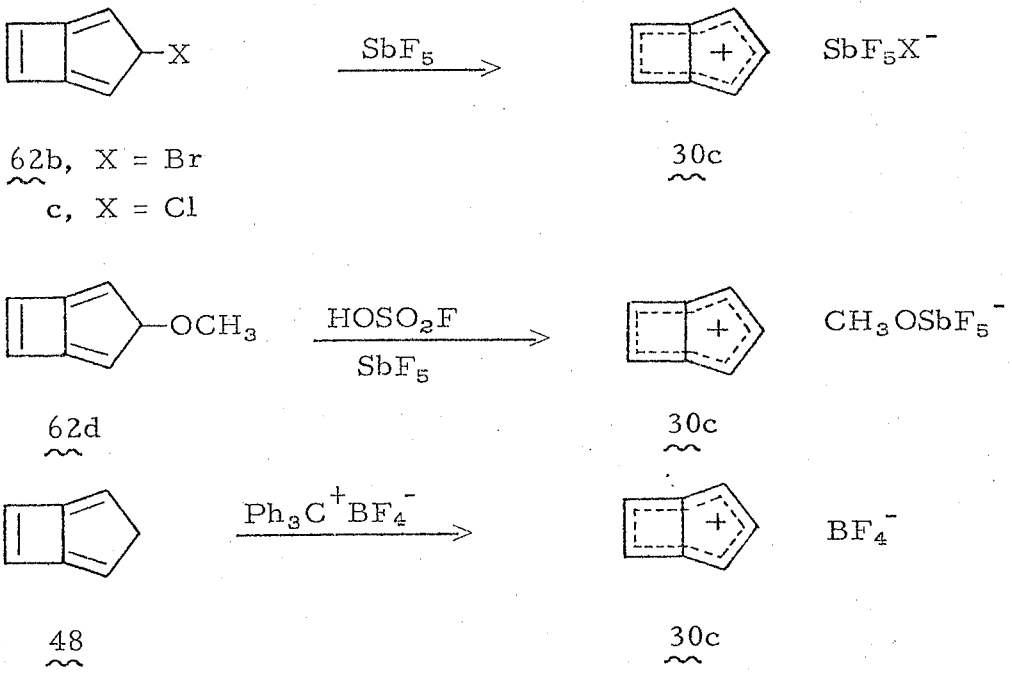


5c

critical conditions with cyclopentadienyl iodide or bromide.[188] In addition to the fact that formation of ions such as 3c is considerably more endothermic than formation of 5c, such processes as addition/-polymerization complete effectively with ionization even in stabilized unsaturated systems such as allyl.[292] For this reason, the low activation energy for halide abstraction by SbF_5 which allows

reasonable rates of ionization even at 70°K and the low affinity of such reagents for the electrons in carbon-carbon double bonds makes allylic halides ideal precursors of conjugatively destabilized carbon cations.[208, 188] In addition, the low nucleophilicity of anions such as SbF_6^- allow the complexes formed to be reasonably ionic.

While, as discussed in the General Introduction to this thesis and in the Introduction to Part II, there is ample reason to believe that 30c will be more aromatic than 3c and for this reason far more easily formed, the expected reactivity of the double bond in the four-membered ring will make addition/polymerization processes more competitive than they are even in allyl. Nevertheless, in the absence of the ideal precursors of 30c, i.e., the bicyclo[3.2.0]-heptatrienyl halides 62b, c, I have investigated the protonation/-cleavage of the ether 62d under conditions of strong acid catalysis



62b, X = Br
c, X = Cl

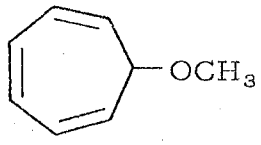
62d

48

30c

and the hydride abstraction from 48 by a presumably less stable trityl cation 182c. Under both of these conditions, addition/polymerization would be expected to compete effectively. However, as discussed in the case of anion 30a in the previous section, initial rapid generation of large concentrations of 30c may allow measurement of its properties on the small concentrations which may remain after polymerization has taken its toll to exhaustion of the precursor.

In a preliminary experiment, injection of 20 μl of an approximately 5% solution of 62d in C_6F_6 into a rapidly stirred 0.10 ml of concentrated sulfuric acid at 0°C resulted in the precipitation of a black residue. The resulting red solution was diluted with 0.9 ml concentrated sulfuric acid and a uv taken which showed a flat maximum at 270 nm and a tailing absorption to 330 nm. Since quenching this solution with water to roughly 50% acid by volume resulted in the disappearance of the red color and a new absorption at 255 nm, the 330-270 nm spectrum may be that of 30c while the 255 nm peak may be attributed to the alcohol 62h. (An identical experiment with tropylmethylether 180 resulted in the formation of a

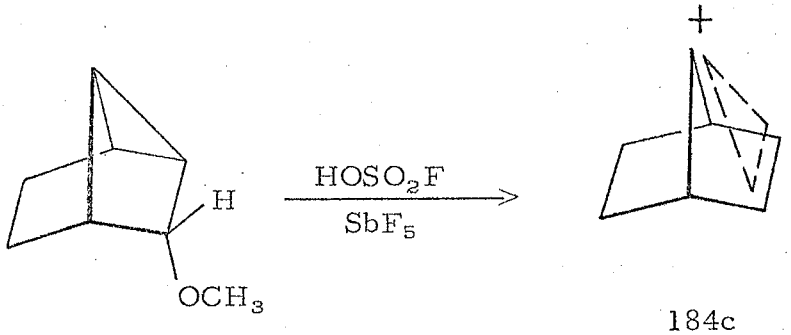


180

colorless solution, λ_{max} 275 nm identical to that reported for the

tropylium ion from tropylbromide.[17]) No attempt was made to recover an alcohol such as 62h from this experiment.

Winstein[293] has prepared nmr observable concentrations of the bicyclic bishomocyclopropenium ion 184c by use of Olah's fluorosulfonic acid/antimony fluoride reagent[294] to cleave the tricyclic ether 183. Application of this low temperature (-78°C) mixing



183 184c

technique to 62d resulted in complete disappearance of starting material at -50°C, a red-brown solution with a large amount of brown polymer, and only a small absorption at 6.25τ due to $CH_3\overset{+}{O}HSbF_5$ indicative of some cleavage to 30c.[294] No absorptions in the 0-1.0τ region expected for 30c were seen. However, when this technique was modified as suggested by Saunders[188(b)] to achieve effective temperatures of mixing much lower than -78°C with the "molecular beam" apparatus pictured in Figure XXXIV and employing only a catalytic amount of $HOSO_2F$ (<5% by volume), a strong signal at 6.2τ (3H) was observed together with definite absorption at 1.15τ (2H) and 1.70τ (?H) versus external standard TMS at 10.0τ. These signals remained even after the sample was warmed

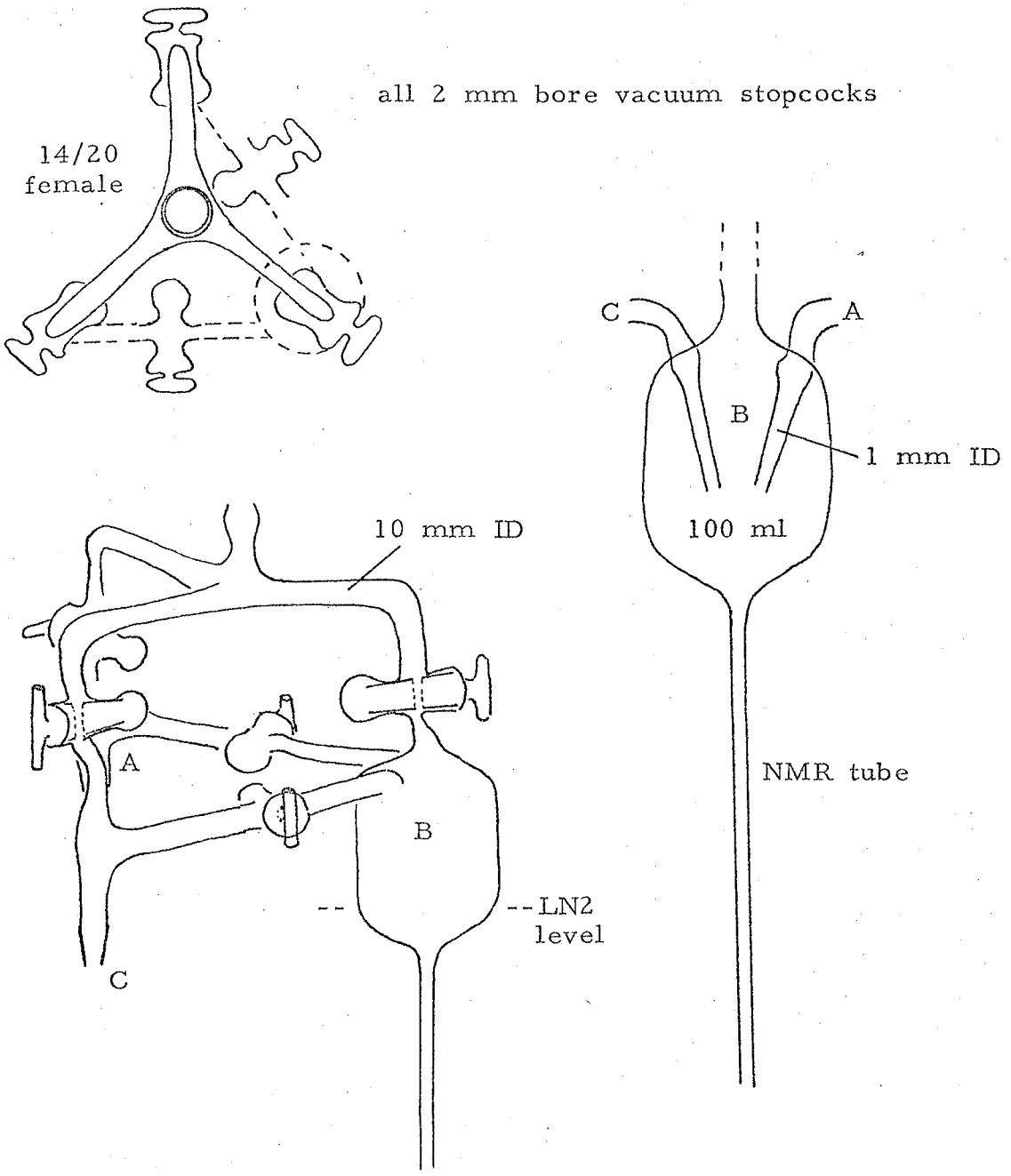


Figure XXXIV

Low Temperature Molecular Beam
Apparatus According to Saunders[118(b)]

to 25°C and are shown in Figure XXXV. An identically prepared sample of the tropylium ion (τ1.18 versus external standard TMS) from tropylmethylether is shown in Figure XXXVI for comparison.

The signal at 6.2τ is complicated even in the tropylium case but is understandable in terms of an overlapping doublet from CH_3OHSbF_5 and a triplet from $CH_3OH_2^+$. Signals similar to these but without SbF_5 complexation were observed by Olah in the $SbF_5/HOSO_2F/SO_2$ cleavage of aliphatic ethers where considerably more $HOSO_2F$ was present.[294] The large signal at τ-0.2 is probably due to $HOSO_2F$ and $HOSO_2FSbF_5$ in good agreement with the τ-0.4 reported by Olah for the 1:1:1 $SbF_5/HOSO_2F/SO_2$ mixture. The signal at τ1.8 is conceivably due to $H_2OSbF_5^+$ but also contains contributions from the hydroxylic protons of the $CH_3OH_2^+$. A large proportion of this signal broadens and disappears on warming to 25°C with a simultaneous upfield shift of 0.1τ in the τ-0.2 absorption due to exchange. Under these conditions it is possible to confirm the likelihood that absorptions due to a carbon cation occur at 1.7τ.

The pattern visible at 1.15τ is more clearly resolved and integrates for 2H based on 3H for the CH_3OHSbF_5 signal. Two absorptions are clearly seen, separated by 3.5 Hz. If this represents a coupling constant, then it is larger than any of the estimated coupling constants in 48 or 62d. But since flattening of the 3-C upon ionization moves the attached hydrogen into the plane of the C^2-H bond, it is not unreasonable that an increase of $J_{H2,3}$ from 2 to 3.5 Hz should occur. This argues that the 1.15τ signal is due

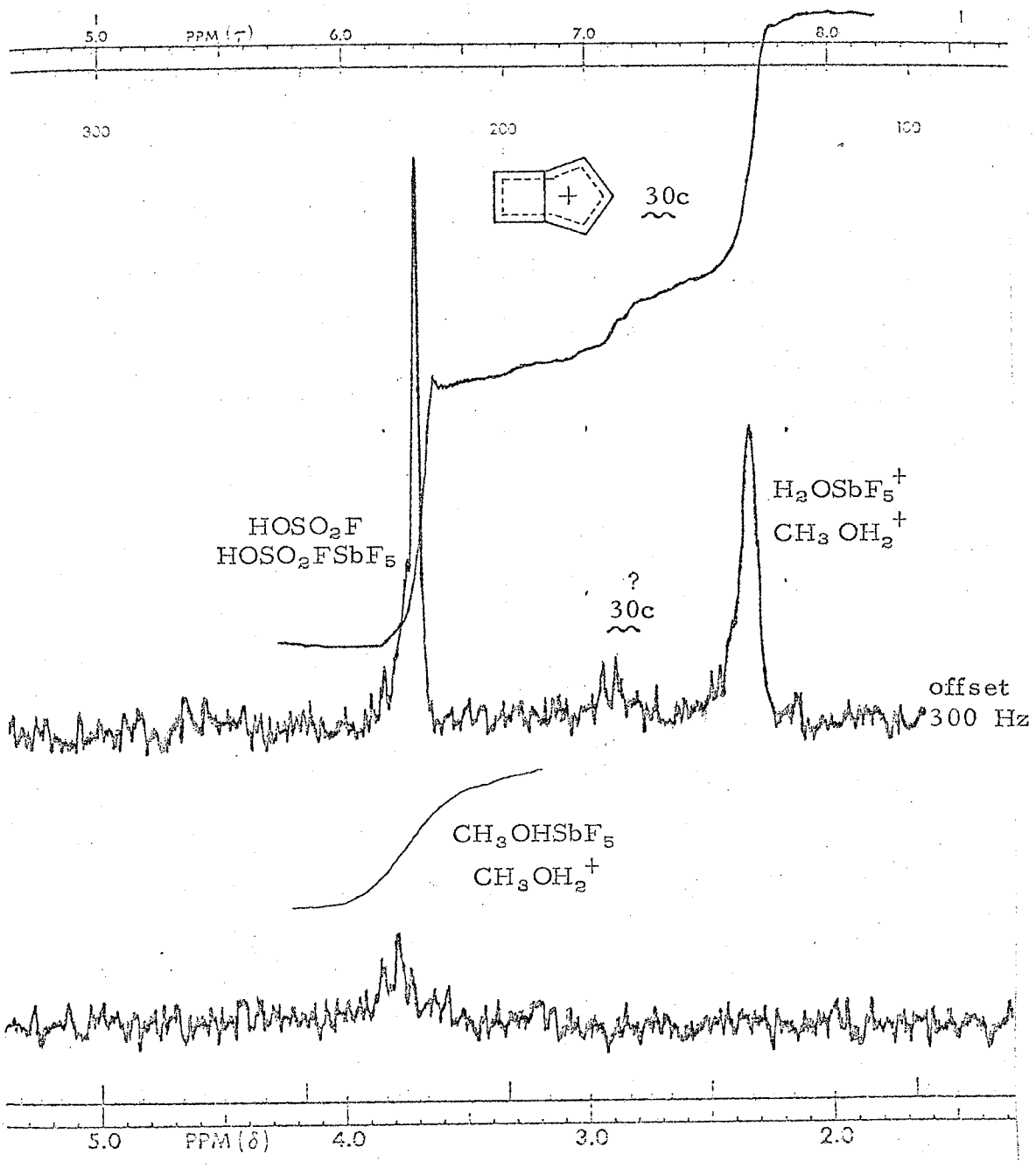


Figure XXXV

^{1}H NMR of 3-Methoxybicyclo[3.2.0]heptatriene (62d) in $SbF_5/HOSO_2F$

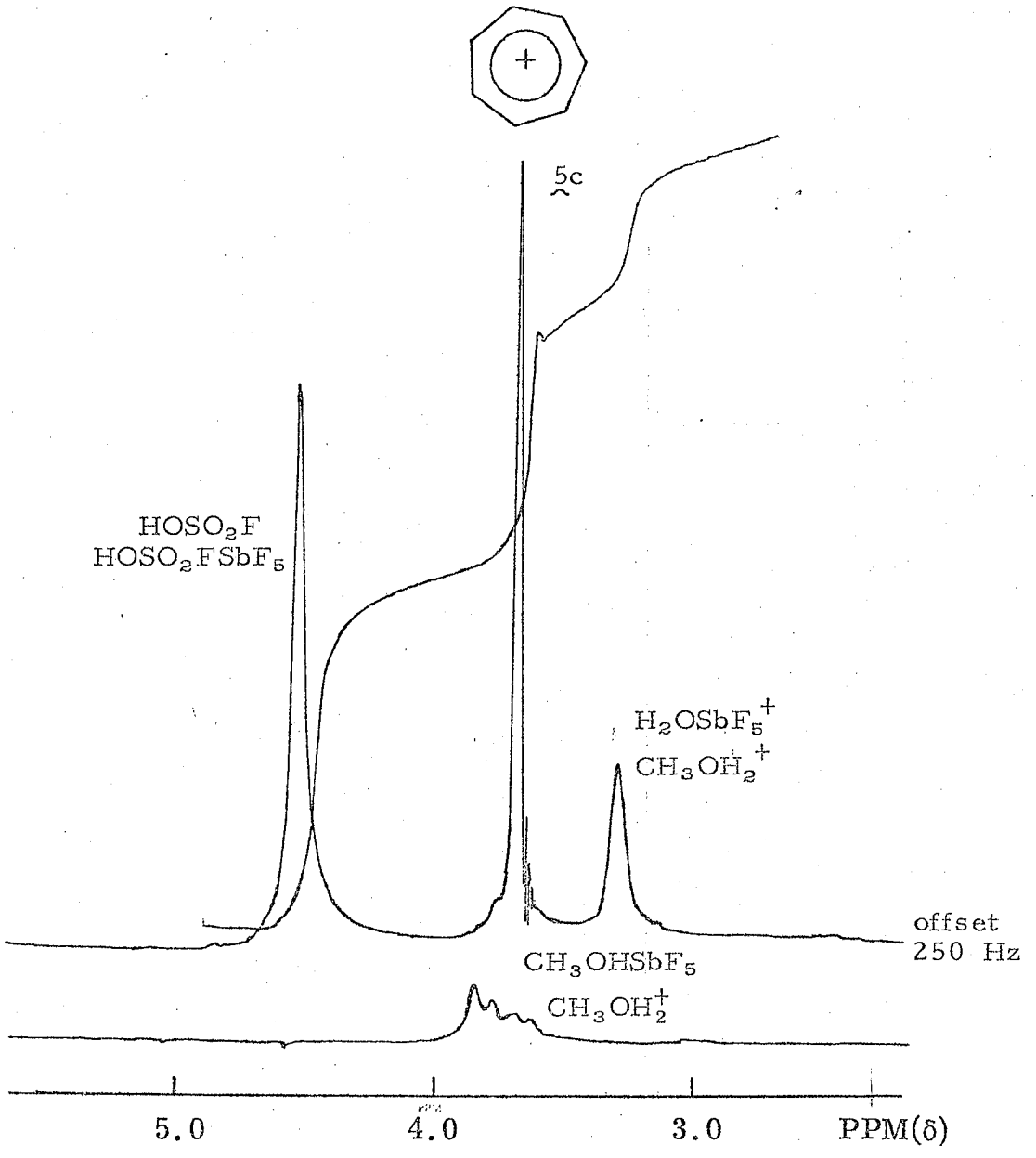
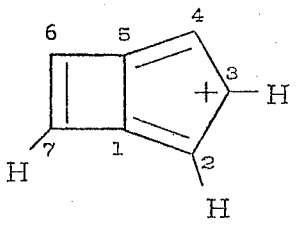


Figure XXXVI

^1H NMR of 7-Methoxycyclohepta-1, 4, 5-triene (180) in $SbF_5/HOSO_2F$



to the C-2 protons. However, because HMO theory places most of the positive charge on C-1, C-3 and C-6, it is equally likely that these are the C-6[6, 7] protons since no absorptions further downfield were seen. But to be fair, these data are really only suggestive and a more concentrated sample should be prepared.

When it became apparent that derivatives of the triene 48 could not be made easily by the routes envisaged, I became more interested in attempting generation of 30c from the readily available 48. My initial assumption that 48 would not serve as a source for complete study of 30c due to its reactivity under the more vigorous conditions necessary to generate cations from hydrocarbons may still be valid, however. For this reason, the many Lewis acid conditions which have been used successfully with tropylidene and even other less favorable systems such as generation of allyl cations from methyl substituted propenes[295] may not be applicable here since they generate acids upon hydride abstraction.[296] On the other hand, hydride abstraction by a less stable carbonium ion than 30a should generate nmr concentrations of the desired cation if the

relative rates of abstraction and electrophilic attack leading to polymer are favorable.

As I have already pointed out in the Introduction to Part II, 30a has an HMO delocalization energy nearly as large as tropylium (versus three ethylenes) but lacking a closed shell of electrons. This is reflected in D'Amore's calculations[76] from which a pK_{R^+} of -1 for the completely delocalized 30c can be estimated based on tropylium at +4.8 and heptatrienyl at -18.0 (see Table Ib). Thus, the triphenylmethyl(trityl)carbonium ion[297] at $pK_{R^+} = -6.63$ should be able to abstract hydride from 48.

Bicyclo[3.2.0]hepta-1, 4, 6-triene (48) was prepared by pyrolysis of trans-1, 2-diethynylcyclopropane (61a) as described by D'Amore.[76] In an initial experiment, 30 mgm of 48 in trideuteroacetonitrile (CD_3CN) was vacuum transferred into a solution of 110 mgm freshly recrystallized triphenylmethylfluoroborate ($Ph_3C^+CF_4^-$)[298] frozen in CD_3CN. Upon allowing to warm to room temperature, a bright red color developed where triene in solution contacted undissolved $Ph_3C^+BF_4^-$. After all the salt had redissolved, thorough mixing resulted in a dark red-brown solution which quickly turned black. Nmr analysis showed complete destruction of the triene 48 and the presence of triphenylmethane (PH_3CH) but no downfield absorptions in the region expected for a delocalized carbon cation. Glc analysis of the mixture after pentane/water workup confirmed the formation of a 30% yield of Ph_3CH, a 30% return of $Ph_3C^+BF_4^-$ based on the Ph_3COH recovered, but showed

no products from 48 although it is likely that these would not have survived the glc conditions.

In an attempt to observe a small steady-state concentration of cation 30c which may be forming in such a reaction, the above experiment was repeated with mixing in a low-temperature nmr probe. At -40°C I observed slow destruction of the triene but no product. At -20°C I began to see small amounts of triphenylmethane, and at 0°C, complete destruction of triene but no product other than Ph_3CH. Use of triphenylmethylhexafluoroantimonate in hopes of forming a tighter complex than is possible with fluoroborates produced an identical result. Substitution of dry, liquid SO_2 for CD_3CN in an attempt to reach lower temperatures resulted in a rapid reaction even at -70°C, forming polymeric products and again Ph_3CH.

In an effort to understand the reactions occurring here and perhaps to place an upper limit on the pK_{R^+} of 30c, this reaction was repeated with tropyliumfluoroborate.[298] When a solution of the triene 48 and $C_7H_7^+BF_4^-$ in CD_3CN was allowed to warm to room temperature a slower reaction occurred generating a red-brown solution but without the initial bright-red color seen with the trityl abstraction. Nmr showed no cycloheptatriene and no new downfield absorption. This was substantiated by glc analysis following pentane/water workup. At -40°C the disappearance of 48 was very slow; but at 0°C, 48 disappeared at approximately the same rate as in the trityl reaction at -40°C.

Comparison of these reactions with appropriate controls in the absence of 48 and extraction of known amounts of triphenylmethane and cycloheptatriene under identical workup conditions clearly show that in the case of the triphenylmethyl salts, I am observing hydride abstraction from 48 to produce 30c as an intermediate. Accepting this, it follows that the pK_{R^+} of 30c lies somewhere between -6 and +4, since no abstraction was observed in the tropylium case. Considering the extent of the reaction (roughly $\frac{1}{3}$ of the initial $Ph_3C^+BF_4^-$ remains unreacted, $\frac{1}{3}$ abstracted forming Ph_3CH, and $\frac{1}{3}$ must have initiated polymerization by electrophilic attack), it is surprising that 30c could not be observed in the nmr. Nevertheless, it is interesting to note that hydride abstraction and electrophilic addition to this strained olefin are roughly equally favored with the triphenylmethyl cation. This says quite a lot for the ease of abstraction and a relatively high pK_{R^+} for 30c.

The bright red color seen initially may be due to the cation, since it should have a low-lying bonding or nonbonding empty MO giving rise to a low excitation energy and considerable absorption in the visible region. This should be compared to the colorless tropylium solutions and salts for which a closed shell is predicted. Unfortunately, no attempt was ever made to produce this colored solution at dilute concentration in a uv cell to compare with the 330-270 nm absorption seen in the methylether 62d/H_2SO_4 experiment.

EXPERIMENTAL

General

Purification of Solvents

To remove olefins from saturated solvents such as diethylether or pentane, the solvent was passed through a silver nitrate on alumina column as described by Murray.[156] It was found that at least six liters of solvent could be freed of olefins by 300 gm of this material. The solvents were then dried over calcium hydride and distilled from sodium. In this way very pure, dry pentane, cyclohexane, diethylether and tetrahydrofuran were obtained from commercial Reagent Grade (A.C.S.) chemicals. The alcoholic solvents were prepared free of water by distillation from the magnesium alcoholate as described by Vogel.[157] The purification of the solvents hexafluorobenzene, 2, 6, 10, 14-tetramethylpentadecane (pristane), carbon tetrachloride, toluene, methanol, benzene and diphenylether used in the pyrolysis experiments is described in the Preparation concerned.

Gas-liquid Chromatography

Preparative gas chromatography was performed on a Varian Aerograph Model 90-P equipped with a thermal conductivity detector using 5 foot and 10 foot, $\frac{1}{4}$ inch and $\frac{3}{8}$ inch ID Pyrex glass columns. To avoid breakage upon installation and to increase the normal installed lifetime of such columns, the injector end was fitted with a metal to glass manufactured seal and the detector end, a Teflon sleeve connecting onto an aluminum L joint, $\frac{1}{4}$" OD (Figure XXXVII). These were coupled to the chromatograph by $\frac{1}{4}$

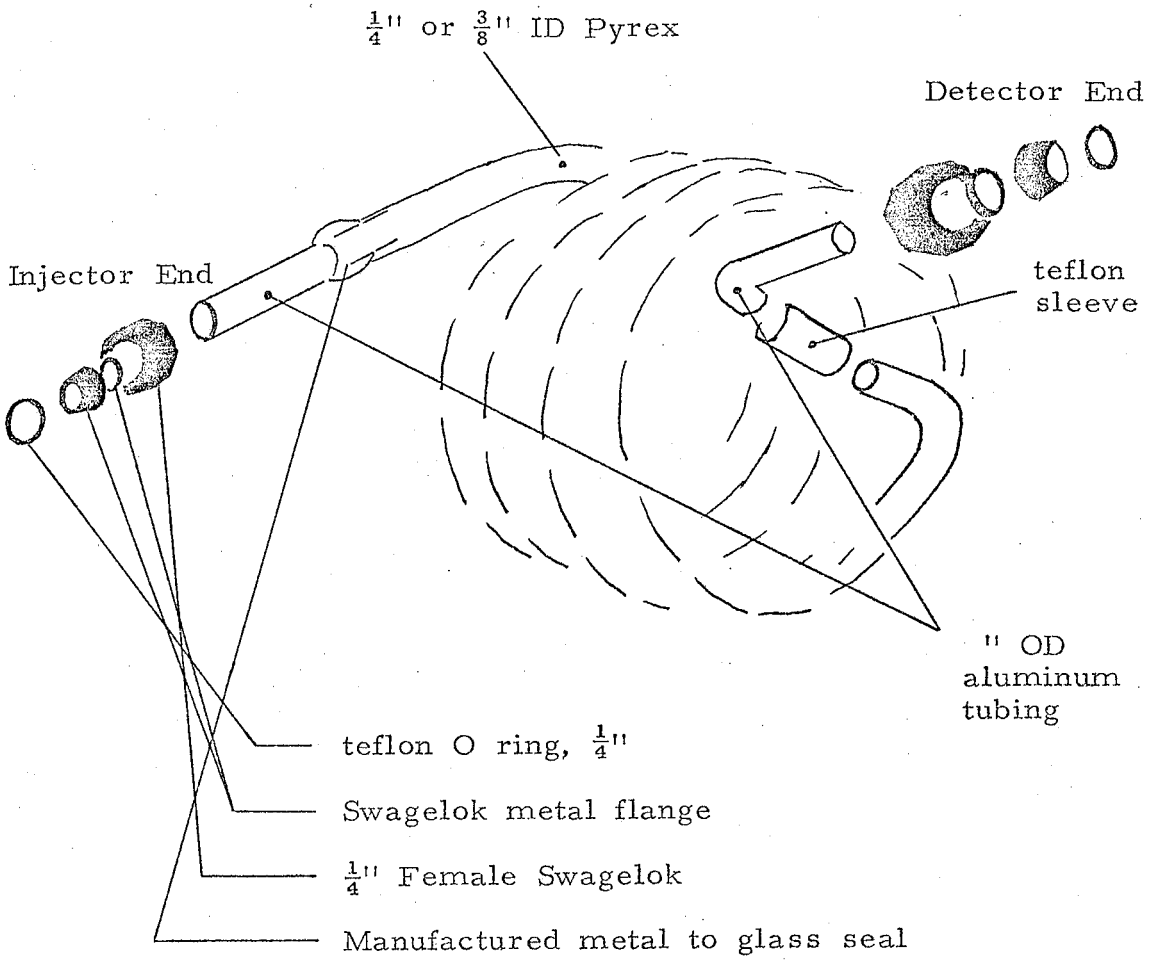


Figure XXXVII

Glass Preparative GLC Column

inch Swagelok female fittings and Teflon 'O' rings (Porter Seal Co., Glendale, California, size A-010). The solid support, Chromosorb W(AW), 60/80 mesh was obtained from Johns-Manville through Applied Science Laboratories, Inc., P.O. Box 440, State College, Penn. The various liquid phase materials were obtained from Perco Supplies, P.O. Box 201, San Gabriel, California. The procedure used for preparing the column packing was as follows.

An approximately 5% solution of the liquid (stationary) phase in tetrahydrofuran was added to the freshly screened 60/80 mesh solid support to the desired loading (20% by weight, maximum) and the solvent slowly removed on a rotoevaporator at low rpm to avoid breaking up the solid further. After all but approximately 5 ml of the solvent had been removed, the pressure was reduced further on a vacuum line (0.01 mm Hg) with periodic hand mixing until minimum weight was obtained. The material was then heated in an oven at approximately 50° short of the proposed maximum temperature limit for 12 hours. The glass columns were loaded by suction on an aspirator vacuum line, tapping with a rubber mallet to thoroughly pack. Each column was baked out with a 10 psi He flow and at the proposed temperature limit for twelve hours. The columns prepared in this manner were:

A: a 5' × $\frac{1}{4}$: glass 5% SE30, max. limit 200°C.

B: a 10' × $\frac{1}{4}$" glass 20% SE30, max. limit 200°C.

C: a 10' × $\frac{1}{4}$" glass 15% 20M Carbowax, max. 180°C.

D: a 10' × $\frac{1}{4}$" glass 20% DEGS (diethyleneglycolsuccinate), max. limit 175°C.

E: a 10' × $\frac{3}{8}$" glass 20% SE30, max. limit 200°C.

F: a 10' × $\frac{3}{8}$" glass 15% 20M Carbowax, max. limit 180°C.

G: a 10' × $\frac{3}{8}$" glass 10% UCW98, max. limit 200°C.

Analytical gas chromatography was performed on a Hewlett Packard Series 5750B Research Gas Chromatograph equipped with a flame-ionization detector and a Hewlett-Packard Model 3370A Digital Integrator. The 10 foot and 20 foot, $\frac{1}{8}$ inch OD stainless steel columns used were prepared as above but with 100/120 mesh Chromosorb W(AW) solid support and packed with a 40 psi gas flow and rapid vibration. The columns prepared in this manner were:

H: a 10' × $\frac{1}{8}$" 20% SE30, max. limit 200°C.

I: a 22' × $\frac{1}{8}$" 20% SE30, max. limit 200°C.

J: a 10' × $\frac{1}{8}$" 10% TCEP (tetracyanoethylpentaerythritol), max. limit 90°C.

K: a 12' × $\frac{1}{8}$" 15% Carbowax 20M, max. limit 200°C.

The column employed, temperature of the oven, settings and retention times measured from injection are reported in a footnote to each glc reference.

Absorption Spectra

Infrared (ir) spectra were determined on a Perkin-Elmer IR 257 Grating Spectrophotometer. The solvent and cell path length are indicated for each case. Nuclear magnetic resonance (nmr) spectra were determined on Varian A60-A, A56/60, T60, HA100

and XL 100 instruments. The instrument, solvent, temperature and reference employed are indicated for each sample. Electron paramagnetic resonance (epr) spectra were determined on a Varian U4500 series spectrometer. X-band radio frequency was used. The appropriate field in gauss, modulation and amplitude are reported for each case. Ultraviolet (uv) electronic spectra were recorded on a Cary Model 14 spectrophotometer.

Mass Spectra

All mass spectra were of glc peaks and were taken on an EAI Quad 300 Mass Spectrometer interfaced with a Hewlett-Packard 7620A Research Gas Chromatograph equipped with a thermal conductivity detector. Typically the Quad-300 was set at low range with a 0.1 sec sweep, resolution 4.5, focus 9 volts, ion energy 8 volts, electron energy 10 volts, emission 190 μa, recorder 200/200/1.0 and chart speed 20 inches/sec. The low electron energy was designed to detect parent peaks. Fragmentation was obtained by increasing this to 50 volts. The remainder of the settings were to keep the largest peak on scale using as much of the chart width as possible for maximum accuracy, assuming a 1 μl injection of an ~0.1M solution. The inlet valves were opened just prior to the sample peak's appearance on the glc trace to avoid solvent interference and to protect the detector filament. The spectra were obtained at 2-3 second intervals all across the glc peak and an average of at least seven readings reported. Deuterium enrichment is present on the front side of each peak.

Also, the intensities of the peaks on a Quad-300 seem to vary ±10% randomly. An average corrects for both the systematic and random error here. The accuracy of the measurements obtained can be judged against the measured P+1 for the parent. To avoid further pyrolysis, the detector and separator manifold were kept at 150°C. These were baked out at 250°C immediately following use.

Pyrolysis Apparatus

The atmospheric pressure flow pyrolyses were performed in the apparatus pictured in Figure XIV. A cylinder of Linde dry Helium (Union Carbide Corporation) was connected to two towers of activated 3Å molecular sieves (dried at 150°C under a 50 ml/min flow of dry nitrogen for twelve hours) with Teflon tubing, wired into position with 14 B.C. copper wire. The towers were 20 × 5 cm and contained approximately 500 gm molecular sieves. The drying towers led through Teflon tubing and a needle valve to a 25 ml 3-neck flask via a capillary bubbler. The flask connected with a 40 cm, 15 mm OD quartz tube in an oven capable of 2000°C obtained from Basic Products Corp., Watertown, Wisconsin (Type 77, Serial No. 102063, 600 watts). The exit end of the tube led directly into two U traps built to set into 15 cm × 6 cm ID dewar flasks. These were in turn connected to a third tower of activated 3Å molecular sieves and a bubble flow meter via Teflon tubing. All glass joints were of 14/20 ground glass with teflon sleeves. No grease was used in the apparatus. The procedure followed was to syringe the sample to be pyrolyzed either neat or dissolved

in a degassed high boiling solvent into the bubbler flask through a rubber septum under a previously measured 60 ml/min helium flow. The pyrolysate was collected in CO_2 ice/isopropanol cooled traps and either vacuum transferred from there or washed down at low temperature with solvent.

The low pressure, vacuum pyrolyses were performed in the apparatus pictured in Figure XV. The same quartz tube and oven described above were used together with vacuum adaptors, basically $\frac{3}{8}$" Pyrex T joints fitted with 5 mm bore vacuum stopcocks so as to allow degassing on either side of the quartz tube while access to the tube was closed off. The receiver end (B, Figure XV) led through a vacuum stopcock to a Hg manometer via a second T joint. Pear-shaped flasks were used as receivers, often with nmr tubes sealed to the tip. All joints were of 14/20 ground glass lightly greased with high-vacuum silicone grease (Dow-Corning). The procedure followed was to introduce the sample to be pyrolyzed into the pear-shaped flask on side A. The material was degassed by three freeze-thaw cycles at 0.01 mm Hg. Pyrolysis was achieved by vacuum transfer through the quartz tube at 0.01 mm Hg initial pressure. The manometer showed an instantaneous pressure as high as 0.1 mm Hg during this process. The pyrolysate was condensed at liquid nitrogen temperature in the pear-shaped flask at B. The rate of transfer could be controlled by adjusting the temperature of the evaporating sample at A. The partial pressure of the substrate could be adjusted by varying the concentration in an inert solvent of similar boiling point. In this

way as much as 10 ml of a 1.0M solution could be pyrolyzed at one time.

The liquid phase pyrolyses were conducted on an analytical scale (50 μl of solution) in sealed Pyrex tubes. The Pyrex glass tubing, 0.4 cm OD, was carefully selected for absence of striations or internal marks in the glass. This was cut into 20 cm lengths and sealed at one end by pulling and rounding off in a medium Pyrex flame. Constrictions were pulled about 5 cm from the upper end for later ease of sealing and the top edge was fire polished. These tubes were washed in acetone, dilute hydrofluoric acid, water, soaked overnight in ~5% EDTA in H_2O, MeOH, NaOH and finally with distilled water. The tubes were dried at 150°C until used. The sample to be pyrolyzed was syringed in and the material degassed by three freeze-thaw cycles at 0.01 mm Hg pressure attached to the vacuum line by the fitting described in Figure XXXVIII, A. The tubes were carefully sealed by slowly pulling and rounding off in a cooler flame and then annealed in a sooty yellow flame. The tubes were placed in a steel housing as pictured in Figure XXXVIII, B. This was immersed in a constant temperature circulating bath from Gebrüder Haake, Berlin-Steglitz, Germany, equipped with an ultrathermostat Model NB (±0.01°C accuracy, max. limit 250°C) and filled with 12 liters of Landa Ultra-Therm 330S (triaryldimethane).

The preparative scale pyrolyses were carried out in a stainless steel bomb modeled after the small scale bomb in Figure XXXVIII, B only now 200 ml in capacity. The material to be

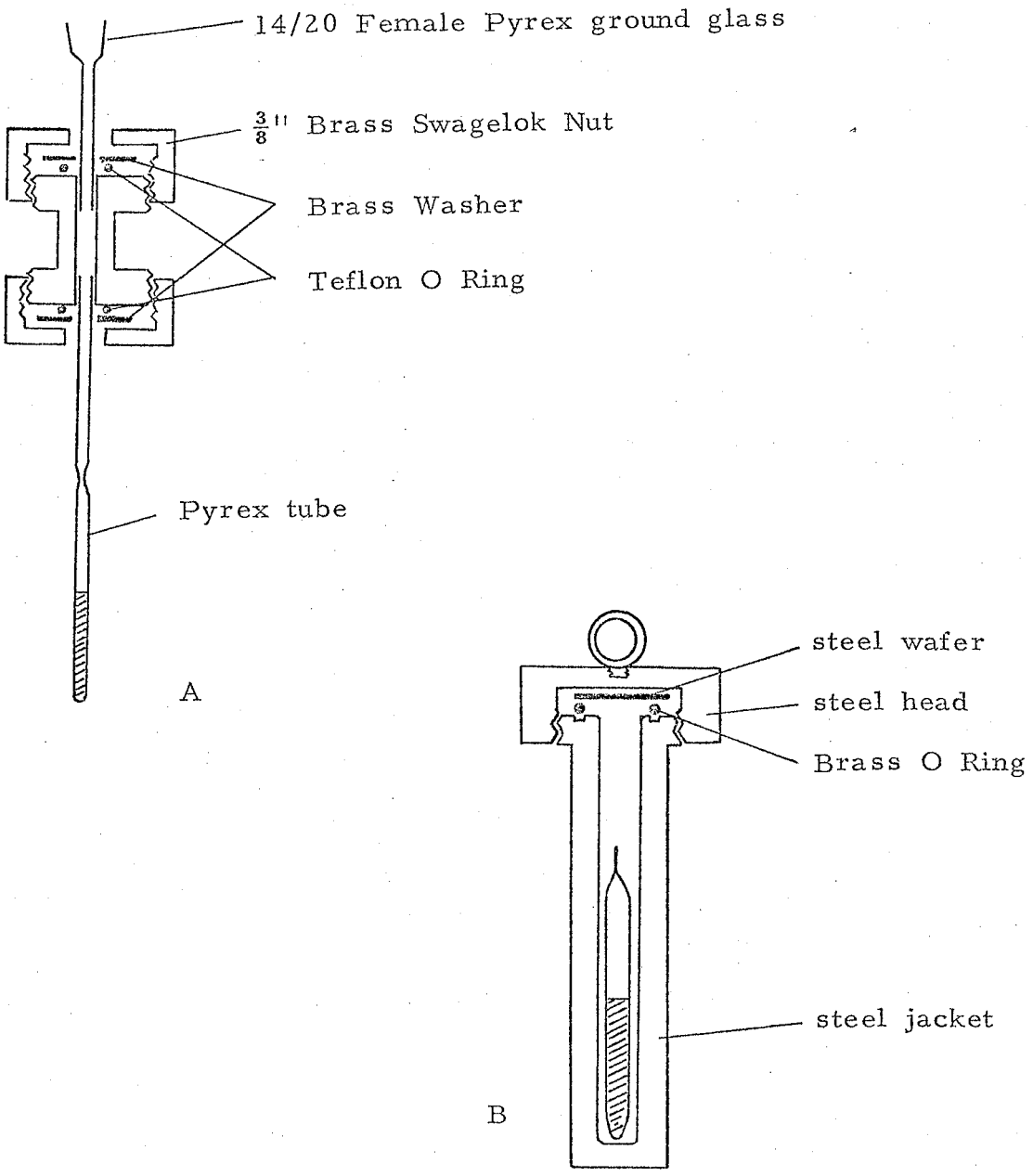


Figure XXXVIII

A. Vacuum Attachment for Pyrolysis and Nmr Tubes
B. Steel Jacket for Small Tube Pyrolysis

pyrolyzed was either placed directly into the steel chamber or in Pyrex tubes which were either sealed or open depending on the volatility of the solvent. The detailed procedure employed is described for each case under the Preparation concerned.

All temperatures were measured with an iron-constantan thermocouple versus an ice/water slush reference. The potential difference was determined with a Leeds and Northrup millivolt potentiometer, Model The thermocouple was inserted into a closed quartz $\frac{1}{4}$" ID tube and this placed between the heater wall and the quartz tube. In the liquid phase pyrolyses, the temperature inside an open steel jacket was measured directly by immersing the thermocouple into a small amount of silicone oil at the bottom of the steel well. The steady state temperature was reached within one minute. The reaction timer was begun after 30 sec dead time for both the 200° and 150° pyrolysis experiments.

Melting Points

Melting points were taken on a Hoover melting point apparatus from Arther H. Thomas Co., Philadelphia, Penn., Model 6406-H and are uncorrected.

Preparative

1.) Propiolaldehyde (81):[132] (Note A). A specially prepared 5-neck, 3-liter round bottom flask was equipped with a grease seal stirrer, a 1-liter dropping funnel with attached capillary for small droplet addition, a capillary gas inlet tube, a gas exit tube with stopcock, and a mercury thermometer. The gas exit tube was connected to three traps in series with the larger annular regions being exposed to the gas flow first to avoid clogging. The flask was charged with 112 gm (2.0 moles) propargyl alcohol (Note B), 350 ml distilled water and 135 ml concentrated sulfuric acid maintaining 20°C with an isopropanol bath. After flushing with argon, the contents of the flask were cooled to -5°C, the first trap to -15°C, and the next two to -78°C with CO_2-ice, isopropanol. The pressure was reduced to ~60 mm Hg using full pumping and regulating the argon flow through the capillary inlet tube which extended below the surface of the liquid. Vigorous stirring was begun and a previously cooled solution of 210 gm (2.1 mole) chromium trioxide (Note C) in 400 ml water and 135 ml sulfuric acid was added over 5 hours maintaining the temperature in the flask below 15°C and the pressure at ~60 mm Hg. After the addition was completed, the pressure was lowered to 20 mm Hg and the flask slowly warmed to 40°C; pumping was continued for 30 minutes. The combined contents of the last two traps weighed 64.5 gm and appeared to be relatively free of water. The first trap contained mostly water but upon addition of sodium chloride, two layers

separated yielding an additional 10 gm aldehyde. The combined aldehyde was dried overnight on anhydrous magnesium sulfate under argon at -20°C and then decanted to yield 71 gm or 65% of theoretical HC≡C-CHO; nmr (neat, 35°C, A60-A, internal TMS at 10.0τ) : 6.25τ (s, C≡C-H), 1.0τ (s, -CHO) each integrating for 1H; ir (CCl_4, 0.1 mm, microcell) : 3480 cm^{-1} (w, H_2O), 3280 (s, ≡C-H), 3030 (w), 2860 (s, CHO), 2740 (w), 2330 (w), 2105 (m, C≡C), 1890 (w), 1695 (s, C=O).

Note A: Propiolaldehyde is an extreme lachrymator and skin irritant. The compound is air sensitive but can be stored indefinitely at -50°C under argon or nitrogen. The aldehyde undergoes an explosive polymerization in the presence of base [eg., $(MeO)_3P$].

Note B: Propargyl alcohol, 97% Aldrich Chemical Co., Inc., ir and glc analyzed, used as received.

Note C: Chromium trioxide, Mallinckrodt Chemical Works, analytical reagent.

2.) 1,5-Hexadiyn-3-ol (83),[133] prepared according to the method of Sondheimer, Anirel, and Gaoni:[131(a)] To 27.0 gm (1.1 mole) fresh magnesium turnings (Note A) in a flame-dried, 5-neck, 3-liter round bottom flask equipped with a reflux condenser, 500 ml addition funnel, thermometer, grease seal stirrer and argon inlet system was added 100 ml dry diethyl ether and 0.3 gm mercuric chloride and finally ~4 gm propargyl bromide (Note B) under argon at 10°C. After completion of the initial reaction,

130 gm (1.1 mole) propargyl bromide in 600 ml dry diethylether was added dropwise with stirring while the reaction temperature was held below 15°C with a CO_2-ice, isopropanol bath. After the addition was completed, the yellow-green solution was cooled to -30°C and 40 gm (0.74 mole) distilled propiolaldehyde (Note C) in 400 ml dry diethylether added dropwise keeping the temperature below -10°C. The mixture was stirred at -20°C for one hour and then allowed to warm to room temperature at which point saturated ammonium chloride was added until hydrolysis was complete. The ether layer was separated, the water layer extracted with three 100 ml portions of ether, and the combined extracts and ether layer washed with saturated sodium chloride solution and dried over magnesium sulfate for six hours. The ether was then stripped on a rotoevaporator and the crude alcohol transferred from the polymer (Note D) and then distilled under vacuum (Note E) to give 58 gm or 83% $HC{\equiv}C\text{-}CHOHCH_2C{\equiv}CH$; nmr (neat, 35°C, A60-A, internal TMS 10.0τ) : 5.51τ (ABX_2Y, major J = 6.5, 2.0 Hz, 1H, methyne), 5.75τ (broad doublet?, 1H, hydroxyl), 7.27τ (d, J = 2 Hz, 1H, acetylenic), 7.41τ (A_2MX, J = 6.5, 2 Hz, 2H, methylene), 7.73τ (t, J = 2.7 Hz, 1H, acetylenic); nmr ($DCCl_3$, 35°C, A60-A, internal TMS 10.0τ) : 5.43τ (AMX_2Y, 1H), 6.45τ (d, 1H), 7.34τ (d, 1H), 7.39τ (A_2XY, 2H), 7.81τ (t, 1H); ir (neat, film) : 3380 cm^{-1} (s, OH), 3280 (s, ≡C-H), 2921 (m, -CH-CH_2-), 2140 (m, C≡C), 1425 (s, OH), 1210 (m, ≡C-H), 1045 (s, C-O), 660 (s, ≡C-H) indicating no allenic impurity.

Note A: Magnesium from rods, assay 99.8% min., Matheson Coleman and Bell.

Note B: Propargyl bromide, 98%, b.p. 88-90°C, Aldrich Chemical Co., Inc., ir analyzed. Used as received after drying 62 hours over 4Å molecular sieves. Stored at -10°C.

Note C: Propiolaldehyde from Preparation 1, this report. Dried 48 hours at -15°C over $MgSO_4$, distilled through a 12" Vigreux column taking the fraction distilling 53-54°, dried finally over 4Å molecular sieves for 12 hours at 0°C under argon.

Note D: The residue from this reaction and the polymer found upon attempted distillation at this point is highly explosive. Prolonged heating should be avoided. Therefore, it is recommended that when preparing acetylenic alcohols the products should be transferred from the polymeric residue at low temperature prior to any attempt at fractionation.

Note E: Distillation was carried out through a 12" vacuum jacketed Vigreux column at 1 mm Hg taking the fraction distilling at 28-30°C. An explosion shield is recommended! When the distillation was carried further after the fraction at 30° ceased, a violent polymerization of the residue occurred even under vacuum (pot at 80°C) which broke glass and left cinders of carbon. Under no conditions should air be allowed to contact hot residue.

3.) 1,5-Hexadiyn-3-ol-1,6,0 d_3: A few milligrams of sodium was added to 30 ml D_2O. To this solution was added 2.24 gm 1,5-hexadiyn-3-ol (83). The solution was stirred at 70°C for 30 minutes and then at room temperature for 24 hours. Extraction with three 10 ml volumes of ether, drying over Na_2SO_4, and removal of the solvent by rotoevaporation at 30°C gave ~2 gm deuterated alcohol DC≡C-CHODCH$_2$C≡CD; nmr (CCl_4, 30°C, A60-A, internal TMS 10.0τ) : 5.68τ (t, J = 6.5 Hz, 1H, methine), 7.54τ (d, J = 6.5 Hz, 2H, methylene).

4.) 1,5-Hexadiynyl-3-tosylate (84)[131(b)] prepared by the method of Eglington, Whiting, et al.,[134]: Recrystalized tosyl chloride (Note A), 55.7 gm (0.29 mole), was dissolved in 31.8 gm dry pyridine (Note B) by heating in a 500 ml Erlenmeyer flask equipped with a calcium chloride drying tube in a silicone oil bath at 110°C. The solution was cooled quickly to precipitate fine needles. To the stirred mixture, 25 gm (0.266 mole) 1,5-hexadiyn-3-ol (83) was added under an argon blanket by syringe at such a rate that the reaction temperature did not exceed 25°C. The brown mixture was allowed to stand in the cold at 2°C for 24 hours before workup. The excess tosyl chloride was hydrolyzed by slow addition of water while keeping the temperature at ~10°C. Following this, 400 ml ice water was added. Filtration through a medium porosity fritted glass funnel gave 69 gm crude tosylate. This material was dissolved in ether and extracted twice with saturated sodium bicarbonate to remove any tosylic acid and once with 3% hydrochloric acid to remove traces of pyridine. The ether

layer was then washed with saturated sodium chloride and dried over anhydrous magnesium sulfate for 24 hours. The ether was stripped and this material recrystallized from ether-petrol (Note C) at -78°C to give 51 gm or 78% 1, 5-hexadiynyl-3-tosylate $HC{\equiv}C\text{-}CHOTsCH_2C{\equiv}CH$; m.p. 74.5-75.0° [literature 74.5-75°, reference 131(b)]; nmr (CCl_4, 30°C, A60-A, internal standard TMS at 10.0τ) : 2.43τ (AB, 4H, aromatic), 4.90τ (AX_2Y, J ~ 6.5, 2.0 Hz, 1H, methine), 7.30τ (A_2MX, J ~ 6.5, 2.5 Hz, methylene), 7.56τ (s, methyl) on 7.63τ (d, J = 2.0 Hz, C-1 acetylenic) together integrating for 4H, 8.07τ (t, J = 2.5 Hz, 1H, C-6 acetylenic); ir (CCl_4, 10%, 0.2 mm) : 3310 cm^{-1} (s, ≡C-H), 2930 (m, -CH-CH_2-), 2150 (m, C≡C), 1920 (w), 1605 (m, aromatic), 1400 (vs, S=O), 1200 (s), 1185 (s), 1107 (m), 1007 (s), 960 (s), 905 (s), 840-740, 690-640.

Note A: Tosyl chloride from Matheson Coleman and Bell, Los Angeles, Calif. was recrystallized by the method of Pelletier.[158] In 150 ml chloroform was dissolved 100 gm tosyl chloride, m.p. 66-69°C. The solution was diluted with 750 ml 30-60 petrol to precipitate impurities. The solution was filtered, clarified with a few ml chloroform, and concentrated to 300 ml on the steam bath. Further concentration was achieved on a rotoevaporator to ~200 ml. Upon chilling in ice water, this gave 85 gm of brilliantly white needles. The crystals were collected by suction and washed with pentane. After drying 3 hrs under vacuum, a melting point was taken in a sealed capillary under argon, m.p. 67.5°C sharply.

Note B: Pyridine, spectroquality, Matheson Coleman and Bell, Los Angeles, Calif., was dried over 4Å molecular sieves for 72 hrs before use.

Note C: The tosylate was dissolved in ether at 25°C and 40-60 petrol added until faintly cloudy.

5.) 3-Tosyloxy-1, 5-hexadiyne-3-ene-1, 6-d_2 (84-d_2) was prepared as above from 2.0 gm 1, 5-hexadiyn-3-ol-1, 6, 0-d_3 (Preparation 3); nmr (CCl_4, ~10%, 30°C, A60-A, internal standard TMS at 10.0τ) : 2.44τ (AB, 4H, aromatic), 4.88τ (t, J = 6.5, 1H, methine), 7.30τ (d, J = 6.5, 2H, methylene), 7.60τ (s, 3H, tosyl methyl), and > 90% acetylenic-d_2 by nmr integration; ir (CCl_4, 10%, 0.2 mm) : 3310 cm^{-1} (w, ≡C-H), 2930 (m, -CH-CH_2-), 2605 (s, ≡C-D), 2010 (m, -C≡C-), 1920 (w), 1610 (m, aromatic), 1395 (vs, S=O), 1200 (s), 1185 (s), 1110 (s), 1007 (s), 960 (s), 910 (s), 840-740, 680 (s).

6.) Cis- and Trans-1, 5-hexadiyn-3-enes (60),[130] prepared by modification of the method of Sondheimer:[131] A. To a solution of 50 gm (0.20 mole) 3-tosyloxyhexa-1, 5-diyne (60) in 500 ml dry diethylether was added 50 gm (0.40 mole) 1, 5-diazabicyclo[4.3.0]-non-5-ene[159] (DBN, Note A) dropwise with stirring under argon. The white suspension was stirred for a further 30 minutes at room temperature and then 100 ml of ice water added. The ether layer was separated, washed with 3 × 100 ml water and dried over anhydrous sodium sulfate for 3 hrs and over activated 4Å molecular sieves overnight at -20°C. The estimated yield was 80% based on

nmr integration versus added standard cyclohexane. B. For some purposes it was necessary to have higher concentrations of the hexadiynenes and to vary the solvent. This was accomplished by vacuum transfer from an elimination of TsOH in a high boiling solvent. In 20 ml triethyleneglycol (Note B) was dissolved 10 gm (0.04 mole) 3-tosyloxyhexa-1, 5-diyne (84). This solution was placed in a 50 ml round bottom flask with a serum cap wired on to a side arm with a small magnetic stir bar inside. Following degassing by three freeze-thaw cycles with CO_2-ice, isopropanol (0.01 mm Hg final pressure), argon atmosphere was introduced from a gas bulb. To the well-stirred solution at 10°C (internal temperature, ice bath cooling), 10 gm (0.08 mole) similarly degassed DBN was syringed in slowly over five minutes maintaining this temperature. The appropriate solvent (Note C) and amount were syringed into this mixture, and the solution degassed again and frozen under vacuum. The hexadiynenes 60 and the solvent were vacuum transferred under 0.01 mm Hg pressure through anhydrous calcium chloride in an attempt to remove traces of DBN and water from the vapors into a liquid nitrogen cooled container by slowly raising the temperature of the reaction flask to 50°C with a hot water bath. If the temperature was raised too quickly or above 75°C, considerable decomposition occurred. In this way a 40% glc yield (vs. added internal standard cyclohexane) of a 60/40 mixture of cis- and trans-60 could be prepared in almost any nonreactive volatile solvent. These 1.0 to 10M solutions were explosively reactive to air or traces of base. Even under argon,

complete decomposition occurs in a few hours at room temperature. They can, however, be stored at -50°C for several days.

C. Sondheimer[131(b)] reports that cis- and trans-60 can be separated cleanly by glc and this appeared to be the case when allowance was made for the extreme reactivity of these compounds. Using the 10 foot glass 20% SE 30 column E at an oven temperature of 30°C, He flow 60 ml/min, 50 μl of concentrated solutions of cis- and trans-60 in ether, benzene, hexafluorobenzene or cyclohexane were injected slowly (over 30 sec) into a 75°C glass lined injector block. The trans-60 eluted first (after the solvent peak in the case of ether or hexafluorobenzene) at 24-26 minutes retention time from the air peak followed by the broader cis-60 at 28-32 minutes. The enediynes were collected in CO_2-ice/isopropanol cooled U-tubes (Figure XXXIX) fitted with a vacuum stopcock and topped with a $CaCl_2$ drying tube. Since the neat enediynes decompose rapidly even under these conditions to give a brown insoluble polymer, the solvent peak was also collected with the two acetylenes alternately. The first prepped material was contaminated with 5-10% of the opposite isomer and the isolated material was reprepped. In this way 1.0 gm each of cis- and trans-60, ~10% in these solvents could be prepared, each isomer > 99% free of the other by reinjection glc analysis. cis-60, nmr (C_6H_{12}, 30°C, A60-A, external TMS reference 10.0τ) : 4.20τ (s, 1H, olefinic) and 6.83τ (s, 1H, acetylenic); nmr (C_6F_6, 30°C, A60-A, external TMS reference 10.0τ) : 4.46τ (s, 1H, olefinic and 7.07τ (s, 1H, acetylenic). trans-60, nmr (C_6H_{12}, 30°C, A60-A, external TMS 10.0τ) :

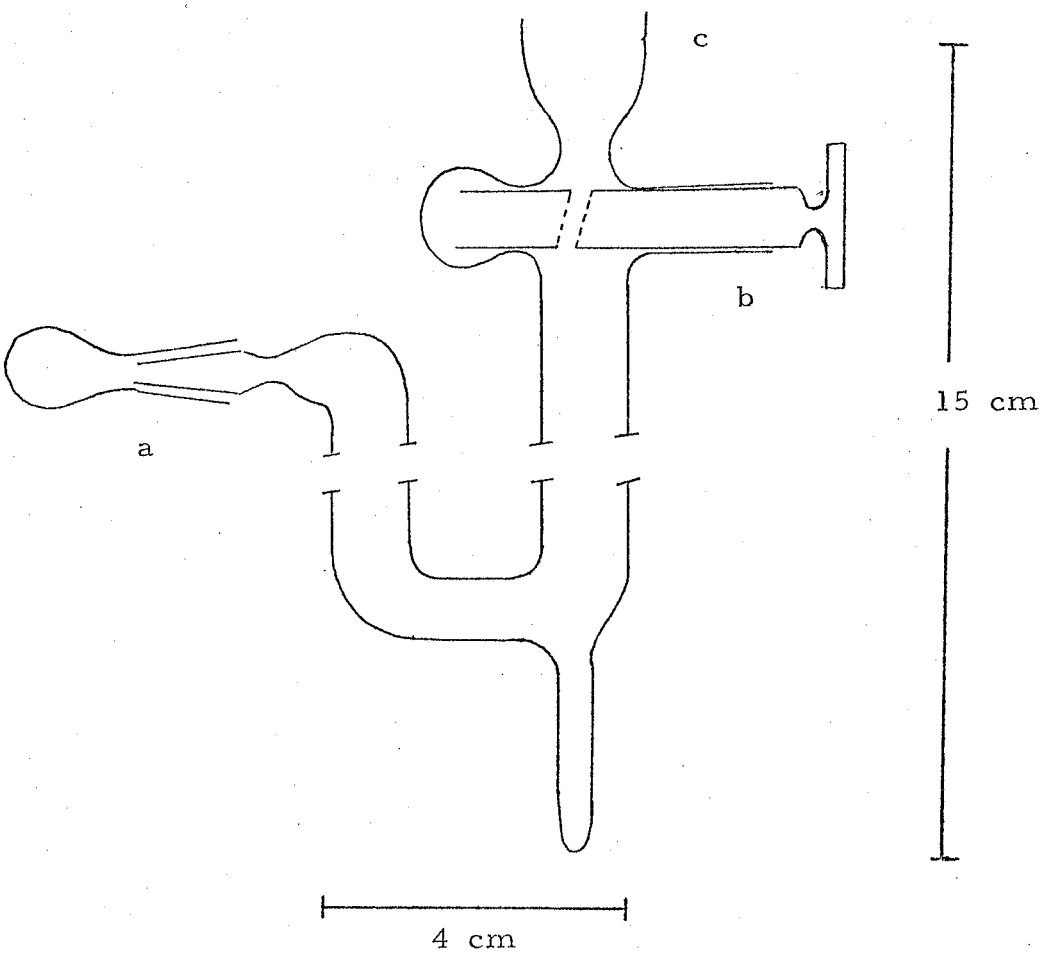


Figure XXXIX

GLC Volatile Liquid Collector

a. male 16/32 joint with female vacuum stopper
b. 3 mm bore vacuum stopcock
c. 14/20 female for vacuum line attachment

3.99τ (s, 1H, olefinic) and 6.97τ (s, 1H, acetylenic); nmr (C_6F_6, 30°C, A60-A, external TMS 10.0τ) : 4.39τ (s, 1H, olefinic) and 7.23τ (s, 1H, acetylenic). These spectra were obtained by vacuum transferring a sample into an nmr tube assembly and sealing under vacuum. All samples were manipulated by vacuum transfer and were stored at -50°C in glass stoppered flasks under argon, sealed with teflon tape where they have a half-life of approximately three weeks. The trans-60 is somewhat more stable to storage than is the cis-60. A brown, insoluble polymer is the only detectable product after this time.

Note A: 1, 5-Diazabicyclo[4.3.0]non-5-ene (DBN), Aldrich Chemical Co., Inc., Milwaukee, Wisconsin, is extremely hygroscopic. The compound was preliminarily dried over BaO and then distilled from sodium at 95-98°C, 7.5 mm Hg.

Note B: Triethyleneglycol (Matheson Coleman and Bell, gold label) was dried over $CaSO_4$ for one week and distilled under vacuum through a 12 inch Vigreux column at 5 mm Hg pressure collecting the fraction distilling at 138-140°C. The glycol was stored in a glass stoppered bottle over 4Å molecular sieves and sealed with Teflon tape.

Note C: Various solvents were employed in this study, for example, cyclohexane, benzene, hexafluorobenzene, methanol and carbon tetrachloride. All were purified before use as described under the preparation in which they are used (vide infra). In this procedure

volumes of added solvent from 0.5 to 10 ml were conviently employed. A second purge with a smaller volume of solvent generally increased the yield of recovered enediyne. After the initial vacuum transfer of approximately 1.0 ml solvent and enediynes, the generator flask was cut off from the vacuum, 0.5 ml solvent injected through the wired on rubber septum, and the material frozen and degassed as before. Vacuum transfer of this material after thorough mixing at room temperature constituted one purge.

7.) Cis- and Trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a): All attempts to prepare 60a from the deuterated tosylate 84-d_2 (Preparation 5) by the method described in Preparation 6.A resulted in only 50% retention of the acetylenic label even when care was taken to dry all reagents. In retrospect, the most likely source of the protons is waters of hydration in the DBN. This problem was circumvented by use of a triethyleneglycol route as described in 6.B. This latter method allows one to wash in and wash out acetylenic label in the same type of process. Into 10.0 ml of triethyleneglycol-0, 0-d_2 (Note A) was placed 2.0 ml of an approximately 1.0M solution of cis- or trans-1, 5-hexadiyn-3-ene (Preparation 6.B) in hexafluorobenzene (Note B) plus 30 μl DBN (Note C) as catalyst. The solution was stirred under N_2 at 25°C for 15 minutes. After degassing by three freeze-thaw cycles, the volatiles were transferred out under 0.01 mm Hg vacuum into a liquid nitrogen cooled second flask. Into this was syringed a second 10.0 ml

triethyleneglycol-0, 0-d_2 plus 30 μl DBN. This second equilibration was stirred for 10 minutes under N_2 at 25°C and the transfer process repeated. In this way a 30% yield of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 was obtained free of contamination by water, DBN or other hydrocarbons gy glc analysis (Note D). Use of 1.0 ml purges of C_6F_6 in these equilibrations allowed one to increase the yield but at the expense of concentration. To this stock solution 10.0 μl cyclohexane was added as an nmr and glc internal standard. Nmr (Note E) and mass spectral (Note F) analyses indicate that these samples are 95% d_2, 5% d_1, and 0% d_0, d_3 and d_4 and are $>$ 95% labeled in the acetylenic positions. (See also Tables IX and X in the text.) cis-60a, nmr (C_6F_6, ~4% solution, 30°C, A60-A, external standard TMS 10.0τ) : 4.46τ (s, olefinic, integration 65), 7.07τ (s, acetylenic, integration 6), 8.33τ (s, cyclohexane, integration 35); MS (electron energy 10v) : m/e 77 (amplitude 5.4), 78 (100), 79 (6.3). trans-60a, nmr (C_6F_6, ~6% solution, 30°C, A60-A, external standard TMS 10.0τ) : 4.39τ (s, olefinic, integration 105), 7.23τ (s, acetylenic, integration 8), 8.33τ (s, cyclohexane, integration 35); ms (amplitude 6.0), 78 (100), 79 (6.4). Literature[160] P+1 for m/e 76 = 6.5.

Hexafluorobenzene (Note B) was added to portions of these solutions to make 0.2M solutions for the gas-phase pyrolysis experiments. The concentration was estimated from the known amount of C_6H_{12} standard. The manipulation of these solutions was essentially the same as for the rather more concentrated solutions of Preparation 6. The mass spectra in this and the

following experiments were taken on samples stored in 5 ml pear-shaped flasks under argon, frozen in dry ice and capped with wired-on rubber septa. The samples were melted only long enough to get a representative 3 μl sample for injection onto the glc-ms.

Note A: Triethyleneglycol-0, 0-d_2 was prepared by stirring 40 gm (2.0 mole) D_2O (99.5%, Columbia Organic Chemicals Co., Inc.) with 60 gm (0.4 mole) triethyleneglycol (see Note B, Preparation 6) plus 30 μl DBN as catalyst. This 5/1 molar ratio produces 83% alcoholic deuteration in one equilibration. The D_2O/H_2O was removed under vacuum and a second 40 gm D_2O added. Repetition of this process for a third equilibration produced triethyleneglycol-0, 0-d_2, theoretically $>$ 99% dideuterated.

Note B: Hexafluorobenzene (Aldrich Chemical Co., Inc., Milwaukee, Wisconsin) was purified by preparative glc on a 10' $\times \frac{3}{8}$" glass 20% SE 30 column (E) at 80°C, 60 ml/min helium carrier flow, 50 μl injections.

Note C: DBN (1, 5-diazabicyclo[4.3.0]non-5-ene, Note A Preparation 6) is very hydroscopic, perhaps containing some tightly bound water. To assure that no H_2O was introduced into this and subsequent experiments, a 5 gm sample of DBN was equilibrated three times with 1.0 ml D_2O, followed by vacuum removal of the water.

Note D: 10' $\times \frac{1}{8}$" 20% SE 30 Column H at 80°C oven temperature, helium flow 60 ml/min at 50 psi, 1 μl injections at 120°C,

attenuation X8, range 10^3, HP 5750B with flame ionization detection. Retention time trans-60 8.11 min, cis-60 8.76 min.

Note E: Nmr analyses were performed at 60 MHz (Varian A60-A Spectrometer) with probe temperature 30°C using precision bore nmr tubes 528-PP available from Wilmad Glass Co. The values reported are averages of 10 integrations, five in each direction of scan. The reported error for the integration circuits on the Varian A60-A is ±2%, however, our data indicate an average deviation of ±5% from the mean. The integration of the remaining acetylenic protons is of course the most in error since the absolute error in the vinyl integration is of the same order of magnitude as the acetylenic signal.

Note F: The mass spectra were recorded on an EAI Quad-300 as described in the General Experimental. The accuracy of the procedure used to obtain these numbers can be judged versus the P+1 peak at m/e 77 which was reproduced to within an absolute error of ±0.2 or ±3%.

8.) Removal of acetylenic deuterium label from cis- and trans-1,5-hexadiyn-3-ene-1,6-d_2 (60a): Approximately 0.1 ml of a 0.2M solution of cis- and trans-60a (Preparation 7) in hexafluorobenzene (Note A) was vacuum transferred (Note B) into 1.0 ml of perprotiotriethyleneglycol with 30 μl DBN catalyst. Warming, followed by stirring for 15 minutes at 25°C under nitrogen, degassing and finally vacuum transfer as in Preparation 7 gave

cis- and trans-1, 5-hexadiyn-3-ene (60) free of deuterium by mass spectral and nmr analysis (See Tables IX and X) after only one equilibration. cis-60, nmr (C_6F_6, ~0.08M, 30°C, A60-A, external standard TMS 10.0τ) : 4.46τ (s, olefinic, integration 71), 7.07τ (s, acetylenic, integration 73), 8.33τ (s, cyclohexane, integration 40); ms (electron energy 10v) : m/e 76 (amplitude 100), 77 (6.6), 78 (0). trans-60, nmr (C_6F_6, ~0.12M, 30°C, A60-A, external standard TMS 10.0τ) : 4.39τ (s, olefinic, integration 120), 7.23τ (s, acetylenic, integration 119), 8.33τ (s, cyclohexane, integration 40); ms (electron energy 10v) : m/e 76 (amplitude 100), 77 (6.4), 78 (0).

Note A: See Preparation 7, Note B.

Note B: For efficient washout of label, good mixing is necessary. To assure that no enediyne condensed in the flask which subsequently did not mix with the glycol, the apparatus was thoroughly shaken.

9.) Atmospheric pressure flow pyrolysis of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a): Approximately 0.2 ml of a 0.2M solution of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a) in hexafluorobenzene (Note A) was syringed into the vaporizer of the pyrolysis apparatus pictured in Figure XIV as described in the General Experimental. Using a flow of dry helium measured to be 40 ml/min at one atmosphere, 23°C with a soap film flow meter (Note B), this solution was evaporated through a clean quartz tube (Note C) at 306°C and collected in U traps at -78°C. The contact

time in the hot zone was estimated to be 30 sec, and a partial pressure of 0.002 atm. 60 was calculated (Note D). The colorless pyrolysate was transferred from the traps under vacuum and analyzed by glc, nmr and mass spectra (Note E). Glc showed greater than 80% yield of enediynes and no adjustment in the cis-trans ratio. Nmr, however, showed extensive scrambling of label in the cis-60 but no such scrambling in the trans-60. Mass spectral analysis confirmed the retention of total label in both the cis- and trans-enediynes. cis-60, nmr (C_6F_6, ~0.08M, 30°, A60-A, external standard TMS 10.0τ) : 4.46τ (s, olefinic, integration 26), 7.07τ (s, acetylenic, integration 27), 8.33τ (s, cyclohexane, integration 34); ms (electron energy 10v) : m/e 76 (amplitude 0), 77 (7.4), 78 (100), 79 (6.8). trans-60, nmr (C_6F_6, ~0.12M, 30°, A60-A, external standard TMS 10.0τ) : 4.39τ (s, olefinic, integration 97), 7.23τ (s, acetylenic, integration 7), 8.33τ (s, cyclohexane, integration 34); ms (electron energy 10v) : m/e 76 (amplitude 0), 77 (8.2), 78 (100), 79 (6.8).

Removal of the acetylenic deuterium label by the method described in Preparation 8 followed by mass spectral analysis confirmed the scrambling seen for the cis-60 in the previous nmr and the complete absence of such scrambling in the trans isomer. cis-60, ms (electron energy 10v) : m/e 76 (amplitude 98), 77 (8.0), 78 (100.0), 79 (7.0). trans-60, ms (electron energy 10v) : m/e 76 (amplitude 100), 77 (6.4), 78 (0), 79 (0).

Note A: See Preparation 7, Note B.

Note B: A soap film manometer of the type supplied by Varian Associates for their 90-P series gas chromatograph was employed together with a stopwatch. The flow was set with the oven at 300°C before introduction of the sample.

Note C: The quartz tube was cleaned prior to every experiment by a preliminary wash with 30/60 petrol to remove grease followed by 20% aqueous hydrofluoric acid to remove polymer and finally a thorough flushing with distilled water and a rinse with 2 ml D_2O.

Note D: The tube volume was calculated assuming a diameter of 1.5 cm and a hot zone of 25 cm length to be approximately 40 cm^3. With a 40 ml/min flow rate corrected to 80 ml/min in the hot zone at 600°K, the residence time is roughly 30 seconds. Since it required approximately 10 minutes to transfer 0.2 ml of solution, a partial pressure of 60 of 0.002 atm can be estimated from its instantaneous concentration of 5×10^{-9}M in the hot zone.

Note E: See Preparation 7, Notes E and F. The percent scrambling for the nmr measurement after pyrolysis was calculated by the formula:

$$\% = \frac{2a - 2x\,(a + v)}{a + v - 2x\,(a + v)} \times 100$$

where $x = \dfrac{a_0}{a_0 + v_0}$

a = acetylenic integration in the pyrolyzed sample

v = vinylic integrations in the pyrolyzed sample

a_0 and v_0 are the initial integrations

This formula in part corrects for the initial acetylenic protons. All integrations are relative to the cyclohexane internal standard.

10.) Low pressure, vacuum flow pyrolysis of cis- and trans-1,5-hexadiyn-3-ene-1,6-d_2 (60a): Into the flask on side A of the vacuum pyrolysis apparatus pictured in Figure XV and described in the General Experimental of this report was transferred 0.2 ml of a 0.2M solution of both cis- and trans-60a in hexafluorobenzene (Note A). This solution was degassed by three freeze-thaw cycles under 0.01 mm Hg pressure and then allowed to vacuum transfer through the 450°C quartz tube, condensing the pyrolysate in the receiver flask with liquid nitrogen. Vacuum transfer of this material from the flask into an attached nmr tube followed by sealing under vacuum showed in the nmr spectrum that one pass was sufficient to cause 97% scrambling in the cis-hexadiynene (Note B). cis-60, nmr (C_6F_6, ~0.08M, 30°C, A60-A, external TMS at 10.0τ) : 4.47τ (s, olefinic, integration 39), 7.09τ (s, acetylenic, integration 37), 8.35τ (s, cyclohexane, integration 35). trans-60, nmr (C_6F_6, ~0.12M, 30°C, A60-A, external TMS at 10.0τ) : 4.40τ (s, olefinic, integration 93), 7.25τ (s, acetylenic, integration 7), 8.35τ (s, cyclohexane, integration 35). It was also seen that at this temperature the trans-hexadiynene was either 8% scrambled or had lost 16% of its acetylenic label. Analysis of these products by mass spectra as before showed that indeed 15-20% of the initial deuterium was lost in the trans-60a pyrolysis, while the cis isomer

lost less, presumably because the rearrangement is rapid and the deuterium is less easily exchanged off the vinyl positions. Removal of acetylenic label as described in Preparation 8 showed that there was indeed no scrambling in the trans-1,5-hexadiyn-3-ene (> 2% detectable) while the cis-60 was completely rearranged. These mass spectral determinations described here are completely analogous to those already reported in Preparation 9 and are summarized in Table XVI.

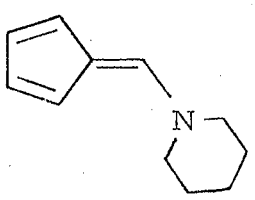
Note A: See Preparation 7, Note B.

Note B: The percent scrambling was calculated using the formula given in Preparation 9, Note E.

11.) Atmospheric pressure pyrolysis of cis- and trans-1,5-hexadiyn-3-ene (60) with a $HNMe_2$ carrier flow: A. To 5.0 ml dry triethyleneglycol (Note A) was added 1.0 gm (0.004 mole) 3-toxyl-oxy-1,5-hexadiyne (84) and the solution degassed by pumping to 0.01 mm Hg. To this was added 1.0 gm (0.008 mole) DBN (Note B) under nitrogen atmosphere and the mixture stirred for 10 minutes at 25°C. The enediynes produced were vacuum transferred from this medium in the manner described in Preparation 6.B into 1.5 ml devolatilized pristane (Note C). The yield of cis- and trans-60 was estimated to be 43% based on a cyclohexane internal standard by nmr and glc analysis (Note D). This solution was placed in the volatilizer of the atmospheric pressure pyrolysis apparatus pictured in Figure XV. A cylinder of dimethylamine

(Note E) was attached to the bubbler through a single 3Å molecular sieve tower. The cis- and trans-60 were blown out of the hydrocarbon with a flow of 60 ml/min of amine and pyrolyzed at 310°C by passage through the hot quartz tube. The products were collected at 0°C in two consecutive U traps. Small amounts of a red-brown, ether insoluble polymer found in the pyrolysis tube, and the mineral oil solution became noticeably darker as the flow of amine continued over one hour to assure complete removal of the enediynes. The dimethylamine was evaporated from the pyrolysate on a rotary evaporator with the flask at 0°C (ice bath). The red residue was taken up in 0.1 ml CCl_4. Analysis by glc (Note D) showed a large number of new products in $\ll 1\%$ yield and one major product in 3% yield, based on the recovered cyclohexane internal standard, not present in either the DBN, triethyleneglycol or the $HNMe_2$. No returned 60 was seen but perhaps the evaporative workup precluded this. Coinjection with an authentic sample of N, N-dimethylaniline (Note F) showed that this material was definitely not the major component of this product mixture. Nmr analysis of the total residue showed no aromatic protons but instead small absorptions in the vinyl and methylamine regions. The sensitivity of the analytical technique was demonstrated by the ability to see as little as 0.003 gm or 0.5% yield N, N-dimethylaniline in the pyrolysate. The glc analysis would probably show even 1/10 this amount if no interfering peaks were present. Retention time for N, N-dimethylaniline: 15.5 min; for the new product: 17.0 min (Note D). B. The above experiment was

repeated only this time a cold (25°C) quartz tube was used so there would be no pyrolysis. Immediately a bright yellow substance began to collect with the amine. The dimethylamine was stripped away as before, and the orange oil was examined by glc and nmr. Glc showed that the major product seen in A was also present here, now in ~10% yield and overall fewer products. Nmr of the crude material showed only complex olefinic absorptions and no aromatic protons. Examination of the mineral oil in the volatilizer also showed this product to be present, indicating that the yield could be even higher than 10% overall. Also present in the transferred material and to a lesser extent in the mineral oil was a small return of the trans-1, 5-hexadiyn-3-ene but no cis-41. A glc/ms of the products showed that this technique was not amenable to the very low yields of other products in this experiment; but for the major component in both A and B an m/e of 121 was seen at 20 volts, assigned to the parent, showing that this product was probably the result of nucleophilic addition of $HNMe_2$ to either cis- or trans-60 or both (Note G). A crude nmr of these products showed a pattern very similar to that obtained by D'Amore[76] for 55b.



55b

Note A: See Preparation 6, Note C.

Note B: See Preparation 6, Note A.

Note C: Pristane, 2, 6, 10, 14-tetramethylpentadecane from Aldrich Chemical Co., Inc., Milwaukee, Wisconsin, was stirred over one equal volume of concentrated H_2SO_4. The acid layer turned very black. The pristane was decanted into a separatory funnel and washed with dilute $NaHCO_3$. This acid treatment followed by a bicarbonate wash was repeated until the acid layer remained colorless. The final washed hydrocarbon was dried first over $MgSO_4$ then distilled from CaH at 8 mm Hg pressure through a simple Claisen head. The fraction distilling at 148-150°C was stored over 4Å molecular sieves.

Note D: 12' × $\frac{1}{8}$" 15% Carbowax (Column J) at 175°C oven temperature, helium flow 40 ml/min at 50 psi, 10 μl injections at 200°C, attenuation X16, range 10^3, HP 5750B gas chromatograph with flame ionization detector.

Note E: Dimethylamine, 98%, Matheson Coleman and Bell, lecture bottle used as received except for drying through the in-line molecular sieve tower.

Note F: N, N-Dimethylaniline, J. T. Baker analyzed, as a 1% solution in CCl_4.

Note G: Column J on the HP 7620A with identical settings as in Note D. The Quad-300 set at low range with a 0.1 sec sweep of

width 150, resolution 4.5, center mass 75, focus 9 volts, ion energy 8-10 volts, electron energy 20-50 volts, emission 190 μa, recorder 200/200/1.0 and chart speed 20 inches/sec.

12.) Atmospheric pressure pyrolysis of cis- and trans-1,5-hexadiyn-3-ene (60) with an H_2S carrier flow: To 0.25 gm (0.001 mole) 3-tosyloxy-1,5-hexadiyne (84) in 1.0 ml dry triethyleneglycol was added 0.25 gm (0.002 mole) DBN and the reaction mixture stirred for 15 minutes at 25°C under nitrogen. The volatiles were vacuum transferred into 5 ml devolatilized pristane (Note A) as described in Preparation 6.B. Glc (Note B) showed a good yield of cis- and trans-1,5-hexadiyn-3-ene versus an added cyclohexane internal standard. Into a 1.0 ml portion of this solution was bubbled H_2S (Note C) after passage through a drying tower containing 500 gm 3Å molecular sieves. The solution turned dark red immediately. Glc showed a slow disappearance of both cis- and trans-60 at nearly equal rates but no detectable volatile products. The half-life of the enediynes in the presence of H_2S was approximately one hour at 25°C. Following this preliminary experiment where it was clear that there would be sufficient time to volatilize 60 into a pyrolysis tube before complete polymerization and presumably without interference from "cold tube" products, the remainder of the pristane solution was placed in the volatilizer of the atmospheric pressure flow pyrolysis apparatus pictured in Figure XIV. The enediynes were transferred out of the hydrocarbon with a flow of 60 ml/min H_2S (dried by passage through a

tower of 500 gm 3Å molecular sieves, presaturated with H_2S) into the quartz tube at 410°C. The products were trapped at -78°C in two consecutive U traps. These exited through a 3Å molecular sieve tower (previously saturated with H_2S) into the exit port of an efficient hood. The H_2S was allowed to evaporate from the traps by slowly warming to -10°C in an efficient hood. The products were washed from the traps with 5 ml ether and the ether reduced on a rotoevaporator with the flask at 0°C (ice bath). Glc (Note B) showed returned cis- and trans-60 in 20 and 10% yield, respectively together with a trace of what must have been benzene, although this evidently was not confirmed by spiking. One other new product in about 0.1% yield was seen. Spiking with an authentic mixture (Note D) suggested that this product was indeed thiophenol, not present even to this extent in the control. Retention time thiophenol: 11.5 min; pyrolysis product 11.5 min, a sharp peak produced on coinjection. A glc/ms was attempted but the concentration of the product was far too low to be seen even when the entire sample was injected.

Note A: See Preparation 11, Note C.

Note B: 12' × $\frac{1}{8}$" 15% Carbowax 20M, Column K at 175°C oven temperature, helium flow 40 ml/min at 50 psi, 10 μl injections at 200°C, attenuation X8, range 10^3, display X1, HP 5750B.

Note C: Hydrogen sulfide, 99%, Matheson Coleman and Bell, dried and cleaned by passage through a tower of 3Å molecular sieves.

Note D: Thiophenol, J. T. Baker analyzed reagent, 0.004 gm (3.6×10^{-5} mole) in 5 ml ether as a glc standard.

13.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn-3-ene (60) in 2,6,10,14-tetramethylpentadecane: A solution of cis- and trans-60 was prepared by vacuum transfer into 5.0 ml pristane (Note A) as described in Preparation 6.B from 0.25 gm (0.001 mole) tosylate 84 and 0.25 gm (0.002 mole) DBN in 2.0 ml TEG. To this ~0.1M solution was added 20 μl (0.015 gm) n-octane as an internal standard. A portion of this solution was diluted with pristane to make a final concentration of 0.01M (0.0035M in cis-60 and 0.0054M in trans-60 by uv analysis, Note B). In previously washed Pyrex tubes, 3.0×0.4 cm OD as described in the General Experimental, were placed 50 μl volumes of this ~0.01M solution. The contents were degassed by two freeze-thaw cycles under 0.01 mm Hg pressure and carefully pull-sealed. Five tubes were pyrolyzed at 200°C and five at 150°C each in a steel jacket as pictured in Figure XXXVIII, B and immersed in a thermostated oil bath whose temperature had been shown to be constant for one hour previous to the pyrolysis (Note C). Two samples were kept in the bath only 30 seconds as zero point controls. The others were heated for periods of 2.5 to 40 minutes. Each sample was quenched by first cooling the steel jacket in a stream of 20°C tap water. The sample portion of the jacket was cooled to well below 100°C in less than one minute. The glass tubes were removed and frozen in CO_2 ice before breaking open and analyzing by glc (Note

D). One new product of longer retention time than cis- or trans-60 was seen in > 95% yield based on the cis-60. (See Table XXVI and Figures XVII and XVIII.) Spiking with an authentic sample showed that the new product was probably benzene, retention time 8.5 minutes. This was confirmed by nmr in a subsequent pyrolysis of 60a, vide infra (Preparation 14). No other volatile products were seen even at high sensitivity.

Note A: See Preparation 11, Note C.

Note B: Based on an estimated ϵ (λ_{max}) of 18,000 at 250 nm for 40% cis-60, 60% trans-60.[131(b)]

Note C: Constant temperature circulating bath from Gebrüder Haake, Berlin, with an Ultra-thermostat Model NB and filled with Landa Ultra-Therm 330S.

Note D: Enediynes in pristane with n-octane internal standard were analyzed on the stainless steel 10' × $\frac{1}{8}$" 20% SE30 Column H at 75°C oven temperature, helium flow 20 ml/min, injecting 1 μl 0.01M solutions with the injector port at 150°C, attenuation HP 5750 1×10^3 display X10, HP 3370A Digital Integrator: N.S. 3, S.S. 0.1 up, 0.1 down, B.L. Reset 0.2, Σ100, SC off front, 0.1 rear, flame detector 250°C. Retention time trans-60: 6.9 min from injection, cis-60: 7.5 min, benzene: 8.5 min. Coinjection with 1 μl 0.005M benzene in pristane showed a sharp peak at 8.5 min.

Table XXVI

Glc Integrations[a] from Pyrolysis of Cis- and Trans-60 in Pristane[b]

At 200°C

time (min)	trans-60	cis-60	benzene
0	9350	5721	—
2.5	6432	1981	4089
5	4572	1136	5372
10	3906	748	5479
20	2401	149	5719
40	2098	0	5896

At 150°C

time (min)	trans-60	cis-60	benzene
0	9080	5932	—
2.5	7314	5609	431
5	5882	3754	711
10	5729	2768	1504
20	5134	2520	2055

[a]Integrations relative to n-octane at 3000, see also Preparation 13, Note D.

[b]2, 6, 10, 14-Tetramethylpentadecane, initial concentration of 60 was ~0.01M.

14.) Liquid phase pyrolysis of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a) in 2, 6, 10, 14-tetramethylpentadecane: In 10.0 ml triethyleneglycol-0, 0-d_2 (Note A) was dissolved 0.25 gm (0.001 mole) 1, 5-hexadiynyl-3-tosylate-1, 6-d_2 (84-d_2, Preparation 5) and any volatiles removed by stirring under 0.01 mm Hg pressure for one hour. Nitrogen atmosphere was introduced and 0.25 gm (0.002 mole) DBN (Note B) was syringed in through a wired on rubber septum. Stirring was continued for 30 min and the deuterated enediynes vacuum transferred into a second 10.0 triethyleneglycol-0, 0-d_2 containing 100 μl DBN as catalyst. Vacuum transfer from this second equilibration as described in Preparation 7 into 1.0 ml degassed pristane (Note C) showed 1, 5-hexadiyn-3-ene-1, 6-d_2 91% d_2 by ms analysis and 93% acetylenic deuteration by nmr. cis-60a, nmr (pristane, ~0.4M, 30°C, A60-A, external TMS at 10.0τ) : 4.17τ (s, olefinic, integration 57), 6.77τ (s, acetylenic, integration 5); ms (electron energy 10v) : m/e 75 (amplitude 0), 76 (3.2), 77 (7.2), 78 (100), 79 (6.8). trans-60a, nmr (pristane, ~0.6M, 30°C, A60-A, external TMS 10.0τ) : 3.99τ (s, olefinic, integration 63), 6.95τ (s, acetylenic, integration 5); ms (electron energy 10v) : m/e 75 (amplitude 0), 76 (2.8), 77 (7.5), 78 (100), 79 (6.3). Pristane, ~50 ml, was added to the above to make a 0.01M stock into which 100 μl n-octane was placed as an internal standard. Pyrolysis of 10.0 ml samples of this solution for 5 and 10 minutes at 200°C was carried out as in Preparation 13 in sealed pyrex tubes after thorough degassing by three freeze-thaw cycles under 0.01 mm Hg pressure. Glc analysis (Note D) showed ~20% of the

initial cis-60a remaining in the 5 min sample. The volatiles were collected by bubbling dry nitrogen (Note E) through the pristane at ~40 ml/min, trapping the products in two liquid nitrogen cooled U traps in series. The trapped material in each sample was vacuum transferred into 0.3 ml CCl_4 in an nmr tube and sealed off under vacuum. Nmr showed no scrambling of label as defined by the equations in Preparation 9, Note E, in either the 5 minute or 10 minute sample although 5% in the former could probably have been seen (integration error ±3-5%). T = 5 min, 200°C, nmr (CCl_4, ~0.1M, 30°, A60-A, external TMS at 10.0τ) : 2.72τ (s, aromatic, integration 68), 3.99τ (s, trans-olefinic, integration 350), 4.16τ (s, cis-olefinic, integration 140), 6.75τ (s, cis-acetylenic, integration 10), 6.90τ (trans-acetylenic, integration 21). T = 10 min, 200°C, nmr (CCl_4, ~0.1M, 30°, A60-A, external TMS at 10.0τ) : 2.72τ (broad s, aromatic, integration 56), 3.99τ (s, trans-olefinic, integration 120), 4.16τ (s, cis-olefinic, integration 31), 6.75τ (s, cis-acetylenic, integration 2), 6.90τ (s, trans-acetylenic, integration 9). The slightly broadened singlet at τ 2.72 is typical of benzene-1, 2-d_2.[161] The glc-ms of the peak attributed to benzene-1, 2-d_2 showed 88% d_2, 8% d_1, 3.5% d_0 or 3% overall loss of label in formation. ms (electron energy 10v) : 76 (4.1), 77 (8.8), 78 (100), 79 (6.5).

Note A: See Preparation 7, Note A.

Note B: See Preparation 7, Note C.

Note C: See Preparation 11, Note C.

Note D: See Preparation 13, Note D.

Note E: CIT dry nitrogen used as is after passage through a Dow Gas Purifier available from Applied Science Laboratories, Inc., State College, Penn. (No. 14510).

15.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn--3-ene (60) in carbon tetrachloride: A. A solution of cis- and trans-60 was prepared in glc pure carbon tetrachloride (Note A) from 0.25 gm (0.001 mole) 3-toxyloxy-1,5-hexadiyne (84) in 2.0 ml dry triethyleneglycol and 0.25 gm (0.002 mole) DBN as described in Preparation 6.B. The volatiles were vacuum transferred with two 0.5 ml purges of CCl_4. Approximately 50 μl n-octane internal standard was added, and a portion of this solution diluted to 0.011M (concentration determined by uv, Note B). Into each of ten clean, dry 0.4 cm OD Pyrex tubes (Note C) was placed 50 μl of this 0.01M solution, the material degassed by three freeze-thaw cycles under 0.01 mm Hg pressure, and the tubes sealed evenly. Pyrolysis was carried out as in Preparation 13 in steel jackets (Figure XXXVIII, B) immersed in a thermostated oil bath at 150° and 200°C. The samples were quenched by submerging the steel jacket in 25°C water. The tubes were then removed, cooled in CO_2 ice, and examined by glc (Note D). One new product was seen to grow in at the expense of the cis-60 in virtually quantitative yield at 200° but in only 21% yield at 150°C. (See Table XXVII and Figures XIX and XX.) Spiking with an authentic sample showed that the new product was probably 1,4-dichlorobenzene (retention time 19.7 min,

Note D), a sharp peak being produced on coinjection. The remaining cis- and trans-60 in CCl_4 was diluted with approximately 100 ml distilled CCl_4 (Note E) to 0.01M and pyrolyzed in a stainless steel bomb (Note F) at 200°C for 5 minutes. The majority of the CCl_4 was distilled at 76-78°C through a 3 foot tantalum wire coil, vacuum jacketed column until approximately 20 ml remained. Glc analysis as before now showed three products in about 5% total yield together with a 70% glc yield of the major product. Coinjection of authentic samples suggested that the product present in 4% yield was meta-dichlorobenzene, while ortho-dichlorobenzene could possibly be present in 1% yield (Note D). Preparative gas chromatography (Note G) easily allowed isolation of the major product and its identity to para-dichlorobenzene was confirmed by ir. B. The pyrolysis of cis- and trans-60 in CCl_4 was also repeated on an analytical scale with an equal concentration of p-benzoquinone, a known radical scavenger.[146] In 25.0 ml glc pure carbon tetrachloride (Note A) was dissolved 0.0270 gm (0.00025 mole) sublimed p-quinone (Note H) to make a 0.01M solution. In each of two 4 mm OD Pyrex tubes was placed 10 μl of this solution and 10 μl of the 0.01M solution in glc pure CCl_4 prepared in Part A. These were thoroughly degassed by three freeze-thaw cycles at 0.01 mm Hg and sealed under vacuum. The results after pyrolysis of these samples, one at 200°C for 10 min and the other at 150°C for 20 min, are shown in Table XXVII and Figures XIX and XX to be practically identical with that obtained without para-quinone at similar

temperatures and times. The analytical technique employed was identical to that described in Part A.

Note A: The analytical (50 μl) samples were prepared from 10 ml glc prepped Spectroquality CCl_4, Matheson Coleman and Bell: 10' $\times$ $\frac{3}{8}$" Carbowax 20M Column (F), 50°C. Varian 90-P oven temperature, He flow 60 ml/min, 100 μl injected over 30 seconds at 100°C, detector (T_c) at 150°C.

Note B: See Preparation 13, Note B.

Note C: See General Experimental.

Note D: Analyzed by temperature programmed glc, 10' $\times$ $\frac{1}{8}$" 20% SE30 Column (H) on the HP 5750B at temperature program 85°-150°C, PII 9 min, rate 10°/min, UCI 12 min, 1 μl injections at 200°C, range 1×10^2, display X1, HP 3370A Digital Integrator as in Preparation 13, Note D. Retention time trans-60: 4.2 min, cis-60: 4.4 min, carbon tetrachloride: 5.0 min, n-octane: 8.8 min, m-dichlorobenzene: 18.6 min, p-dichlorobenzene: 19.7 min, o-dichlorobenzene: 20.1 min. Coinjection of authentic materials was done with 1 μl of the sample in question and 1 μl of a 1×10^{-4}M solution of the compound in CCl_4, avoiding contamination by first taking a sample of the pyrolysate into the syringe.

Note E: Since small impurities of higher boiling point than CCl_4 will be concentrated in such an experiment, a combination of methods short of preparative glc of 200 ml CCl_4 were used to

reduce these. One pint of Spectroquality CCl_4 was stirred over approximately 10 ml liquid mercury to remove sulfides as suggested by Perrin.[162] Considerable grey powder formed over eight hours stirring at room temperature. The liquid was filtered then passed through a column of 200 gm $AgNO_3$ treated alumina Act IV, prepared as described by Murray[156] to remove olefins and aromatics. This material was then dried over P_2O_5 and distilled from the same through a 3 foot tantalum wire column, taking the fraction distilling at 77.5-78.0°C.

Note F: A pyrolysis bomb similar to that pictured in Figure XXXVIII,B only now with a 100 ml capacity was constructed. The pyrolysis was performed by immersing the entire bomb into the Gebrüder-Haake 200°C circulating bath described in the General Experimental. Each time approximately two minutes were allowed for the material to reach 200°C before starting the timer. No specific control was performed to see if this estimated dead time was reasonable.

Note G: 10' × $\frac{3}{8}$" glass 20% SE30 Column (G), oven temperature 125=C, 50 μl injections at 150°C, Varian 90P (TC).

Note H: Approximately 5.0 gm commercial p-benzoquinone, Matheson Coleman and Bell reagent grade (ACS) was sublimed at 100°C, 0.005 mm Hg. The light yellow crystals were placed in a dark bottle and stored at 0°C.

Table XXVII

Glc Integrations[a] from Pyrolysis of Cis- and Trans-60 in CCl_4

At 200°C

time (min)	trans-60	cis-60	p-dichlorobenzene
0	6488	5301	—
2.5	3827	1995	2329
5	2101	594	3655
10	2092	0	3638
10[b]	1911	0	3993
20	1573	0	3378

At 150°C

time (min)	trans-60	cis-60	p-dichlorobenzene
0	6461	5006	—
5	6109	4536	357
10	4970	2389	941
20	4710	1798	1170
20[b]	4902	1908	1062

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[a]Integrations relative to n-octane at 10,000; see also Preparation 13, Note D.

[b]Added equal volume of 0.01M benzoquinone.

16.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn-3-ene (60) in methanol: A solution of cis- and trans-1,5-hexadiyn-3-ene (60) was prepared in 1.0 ml dry, Spectroquality methanol (Note A) from 0.25 gm (0.001 mole) tosylate 84 in 2.0 ml dry triethyleneglycol and 0.25 gm (0.002 mole) DBN as described in Preparation 6.B. The volatiles were vacuum transferred with two further 0.5 ml purges of CH_3OH. This material was diluted to 100 ml with spectroquality methanol and 50 μl n-octane added as an internal standard. Approximately 50 μl of this 0.012M solution (Note B) were placed in each of ten clean 4 mm OD Pyrex tubes as described in the General Experimental. The solutions were degassed by three freeze-thaw cycles and the tubes carefully sealed under vacuum. Pyrolysis at 150° and 200°C in steel jackets (Figure XXXVIII) as in Preparation 13 in a thermostated oil bath (Note C) followed by quenching at various times by cooling the steel container with tap water showed considerable loss of sample due to pressure breakage. In all, besides the 30 sec controls as in Preparation 13, only one sample at 200°C and two at 150°C were recovered. Since methanol interferes with the glc analysis (Note D), the samples were worked up as follows. The Pyrex tubes were removed from the steel housing and cooled in CO_2-ice. The tubes were cut open at this temperature and 50 μl pristane (Note E) added. After warming to room temperature, the contents of the tubes were each equilibrated with 1.0 ml H_2O in a 5 ml pear-shaped flask with the aid of a pipet. The pristane (upper) layer was removed by pipet and dried over a few grains of Na_2SO_4.

These extracts were analyzed directly by injection of 10 μl into the gas chromatograph (Note D). The results, summarized in Table XXVIII and Figure XXI, show a rapid disappearance of cis-60, a somewhat slower disappearance of trans-60 and the appearance again of benzene in high yield as the major product, presumably from the cis-60. The identification of the benzene was supported by coinjection of an authentic sample. Examination of the sample pyrolyzed for 20 min at 200°C at maximum glc sensitivity showed an approximately 5% yield of benzyl alcohol, identified by coinjection of an authentic sample (Note D). Anisole was expressly looked for but was not present, although as little as 0.5% yield could probably have been detected. All attempts to pyrolyze even 20 ml samples of 0.01M enediyne in methanol in sealed pyrex tubes led to pressure breakage. However, as in Preparation 15, pyrolysis of 200 ml of a 0.01M solution of 60 in Spectroquality methanol in a stainless steel bomb (Note F) for 10 min at 200°C showed a high yield of benzene, a low yield of the material attributed to benzyl alcohol, and a 40% return of trans-60 but no cis-60. The pyrolysate was concentrated by slow distillation of the methanol through a 3 foot tantalum wire coil, vacuum jacketed column until approximately 2 ml pot residue remained. The peak attributed to benzyl alcohol was isolated by preparative glc (Note G) and shown to be identical to an authentic sample of benzyl alcohol by ir.

Note A: Spectroquality methanol, Matheson Coleman and Bell, was dried by distillation from the magnesium alcoholate as described by Vogel.[157] The methanol thus prepared was pure by glc analysis (Note D).

Note B: The concentration was determined by uv based on an estimated $\epsilon(\lambda_{max})$ of 18,000 at 250 nm for 40% cis- and 60% trans-60.

Note C: See Preparation 13, Note C.

Note D: Employed a 10' × $\frac{1}{8}$" 20% SE30 Column (H) at 85°C HP 5750B oven temperature, 40 ml/min He flow, 10 μl injections at 150°C, range 1×10^2, display X1. Retention time trans-60: 4.45 min, cis-60: 4.7 min, benzene: 5.3 min, n-octane: 9.5 min, anisole: 15.8 min, benzyl alcohol: 30.6 min. Standard samples of benzyl alcohol and anisole were prepared by dissolving 0.001 gm each (reagent grade) in 10.0 ml Spectroquality methanol. 50 μl samples of these solutions, 1×10^{-3}M, were carried through the workup procedure with pristane as outlined above before coinjection analysis.

Note E: 2, 6, 10, 14-tetramethylpentadecane, see Preparation 13, Note A.

Note F: See Preparation 15, Note F.

Table XXVIII

Glc Integrations[a] from Pyrolysis of Cis- and Trans-60 in Methanol

At 200°C

time (min)	trans-60	cis-60	benzene
0	6348	5062	–
20	1277	–	5609
20[b]	671	–	8206

At 150°C

time (min)	trans-60	cis-60	benzene
0	6348	5062	–
5	5306	3666	1114
10	4464	1118	1722

[a]Integrations versus n-octane at 3000, see also Preparation 13, Note D.

[b]Preparative scale pyrolysis in a steel bomb.

Note G: Employed a 10' × $\frac{3}{8}$" 20% SE30 Column (E) at 150°C, collecting the peak at approximately 17 min retention time from injection, 50 μl injections at 200°C, detector 200°C.

17.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn-3-ene (60) in toluene: A solution of cis- and trans-60 was prepared in glc prepped toluene (Note A) from 0.25 gm (0.001 mole) e-tosyloxy-1,5-hexadiyne (84) in 1.0 ml dry triethyleneglycol and 0.25 gm (0.002 mole) DBN as described in Preparation 6.B. Approximately 50 μl n-octane was added to this 2.0 ml solution as an internal standard. Glc analysis (Note B) showed that this material was approximately 0.75M in enediynes versus the n-octane standard. A 0.10 ml portion of this solution was diluted to 7.5 ml with toluene. Into each of ten clean, dry 0.4 cm OD Pyrex tubes as described in the General Experimental section was placed 50 μl of this ~0.01M solution, the material degassed by three freeze-thaw cycles under 0.01 mm Hg pressure, and the tubes sealed evenly under vacuum. Pyrolysis was carried out as in Preparations 13-16 in a steel jacket immersed in a thermostated oil bath at 200°C. The samples were quenched at various times by submerging the steel jacket in a 20°C flow of tap water. The tubes were opened after cooling to -78°C and examined by glc (Note B). The major product was benzene in 36% yield based on the cis-60. Several other products in small yield were also seen, but there were impurities even in the glc prepped toluene visible at these high glc amplitudes which prevented proper analysis. (The glc

results for the appearance of benzene and the disappearance of cis- and trans-60 are summarized in Table XXIX and Figure XXII.) Coinjection of authentic materials showed that the methylbiphenyls and diphenylmethane were possible products. Similarly, bibenzyl was not present, although this spiking shows that a 0.0001M (or 1% yield from cis- and trans-60) concentration could easily have been seen (Note B).

Note A: Reagent grade toluene from Matheson Coleman and Bell contained large amounts of benzene and xylenes as well as several unidentified heavier products by glc analysis (Note B). No other source of toluene examined including a sample of fluorometric grade from Hartman-Leddon Co. was substantially better, however. The sulfur containing impurities were removed from one liter of toluene (MCB) by shaking with 500 ml cold, concentrated H_2SO_4, followed by a liter of water, then 500 ml 5% $NaHCO_3$, and a final liter wash of distilled water. The resulting toluene was dried over 100 gm $CaSO_4$, filtered, then over 100 gm CaH overnight. The toluene was then distilled from the CaH through a vacuum jacketed, 3 foot tantalum wire coil taking the fraction distilling at 109-111°C. This resulted in nearly a 100% reduction in most impurities, but the product was still too impure for the low yield pyrolysis anticipated. In the end, this distilled material was glc prepped on the $10' \times \frac{3}{8}''$ UCW98 Column (G) at 90°C Varian 90P oven temperature, 50 μl injections over 30 seconds at 150°C, TC detector 200°C. The collected material was stored over 4Å molecular sieves.

Table XXIX

Glc Integrations[a] from Pyrolysis of
Cis- and Trans-60 in Toluene

At 200°C

time (min)	trans-60	cis-60	benzene
0	1703	1390	—
2.5	1120	343	1848
5	851	116	3762
10	759	0	3493
25[b]	582	0	3967

[a]Integrations based on n-octane at 10,000; see also Preparation 13, Note D.

[b]Preparative scale pyrolysis in a stainless steel bomb.

Note B: Analyzed by temperature programmed glc, 10' × $\frac{1}{8}$" 20% SE30 Column (H) in the HP 5750B at 100°-200°C oven temperature, PII 17 min, rate 20°/min, UCI 20 min, 1 μl injections at 200°C, range 1×10^2, display X1, HP 3370A digital integrator as in Preparation 13, Note D. Retention time in min, trans-60: 6.2, cis-60: 6.7, benzene: 7.4, toluene: 13.6 to 14.0, n-octane: 16.3, xylenes during heat-up, biphenyls: 21.0-23.5, diphenylmethane: 25.2, bibenzyl: 33.0.

18.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn-3-ene-1,6-d_2 (60a) in hexafluorobenzene: A solution of 1,6-d_2 enediynes (60a) in 0.5 ml hexafluorobenzene (Note A) was prepared from 0.25 gm tosylate 84-d_2 by the method described in Preparation 7. Glc analysis (Note B) showed this solution to be roughly 1.0M compared to 50 μl added n-octane internal standard. Mass spectral and ^{1}H nmr analysis (Note C) showed that this material was 90% d_2 and 94% deuterated in the acetylenic positions. (See Preparation 7.) A 0.01M solution of 60a was prepared by dilution of 0.10 ml of the above to 10 ml with glc prepped hexafluorobenzene. Into an 8 mm OD nmr tube containing a 0.01 ml sample of THF-d_8 in a sealed melting point capillary was vacuum transferred approximately 1.0 ml of this solution. The frozen sample was opened to air momentarily and capped. An FT ^{1}H nmr with 90,000 transients showed that this material was detectable and a 95% acetylenic deuteration calculated (Note D). cis- and trans-60a, ^{1}H nmr (C_6F_6, FT 90,000 transients, 30°C, XL-100, THF-d_8

lock, no reference, signals in cycles from end of scan) : 428 Hz (trans vinyl, integration 8450), 421 Hz (cis vinyl, integration 7500), 158 Hz (cis acetylenic, integration 350), 145 Hz (trans acetylenic, integration 450). A second 1.0 ml of the 0.01M solution was transferred into a Pyrex tube (Note E), degassed and sealed under 0.01 mm Hg pressure. Pyrolysis for 5 minutes at 200°C showed 30% recovery of the cis-60 by glc versus the n-octane standard. FT nmr of this sample as above showed approximately 11% scrambling in the cis-60 and no scrambling in the trans-isomer by the formula given in Preparation 9, Note E. The error in this measurement is estimated to be ±5% absolute by comparison of the nmr integrations of the vinyl peaks versus the glc results. cis- and trans-60a after pyrolysis, ^{1}H nmr (C_6F_6, FT 100,000 transients, 30°C, XL-100, THF-d_8 lock, signals in cycles from end of scan) : 427 Hz (trans vinyl, integration 8925), 421 Hz (cis vinyl, integration 2240), 157 Hz (cis acetylenic, integration 240), 145 Hz (trans acetylenic, integration 400).

Note A: See Preparation 7, Note B.

Note B: See Preparation 7, Note D.

Note C: See Preparation 7, Notes E and F.

Note D: The integration of these peaks was by triangulation.

Note E: A thick wall, 7 mm OD pyrex tube was prepared 5 cm in length as described in the General Experimental. When half filled, the one sample pyrolyzed did not break.

19.) Liquid phase pyrolysis of cis- and trans-1,5-hexadiyn-3-ene-1,6-d_2 (60a) in diphenylether: A solution of cis- and trans-60a was prepared in 100 ml of devolatilized diphenylether (Note A) from 0.25 gm (0.001 mole) d_2-tosylate (84-d_2) as described in Preparation 7 to make an approximately 0.008M solution. The concentration was confirmed by comparison to an added glc internal standard of 50 μl n-octane. Nmr showed that the enediynes were 90% deuterated in the acetylenic positions (Note B). cis- and trans-60a, nmr [$(C_6H_5)_2O$, 0.01M, CAT600X, A60-A, 30°C, external standard TMS at 10.0τ]: 4.13τ (trans vinyl, integration 100-31 C^{13} satellite from solvent = 69), 4.25τ (cis vinyl, 44), 6.88τ (cis acetylenic, 6), 7.20τ (trans acetylenic, 9). The entire 100 ml of 0.01M solution of cis- and trans-60a was placed in an open Pyrex tube and degassed by three freeze-thaw cycles at 0.01 mm Hg. The unsealed tube was placed in a steel bomb under argon and pyrolyzed at 200°C for 5 minutes (Note C). The sample was quenched in 25°C tap water while still in the bomb. After cooling to 0°C, the bomb was opened and the diphenylether solution examined by glc (Note D). A 10% return of cis-60 was seen together with an approximately 55% return of the trans-60. The volatiles were recovered from the ether by passing dry nitrogen (Note E) through the solution, trapping out the volatiles in two

consecutive U traps at -78°C, protected from moisture by a post-line tower of $CaSO_4$ (anhydrous). Nmr of the recovered material obtained by vacuum transfer from the traps into an nmr tube containing 0.3 ml CCl_4 (Spectroquality) showed no rearrangement of label in the trans-60a but a 19% scrambling of label in the cis-60, nmr (CCl_4, ~1%, CAT60X, A60-A, 30°C, external standard TMS at 10.0τ) : 4.13τ (trans vinyl, integration 37.2, corrected for C^{13} satellite of airosoled diphenylether), 4.25τ (cis vinyl, 4.2), 6.88τ (cis acetylenic, 1.0), 7.20τ (trans acetylenic, 4.3). The error in this measurement and the calculation of percent scrambling by the formula in Preparation 9, Note E is estimated to be ±5% absolute.

Note A: 200 ml of diphenylether, Matheson Coleman and Bell, reagent grade, were devolatilized by heating under vacuum (0.005 mm Hg) for one hour.

Note B: See Preparation 9, Note E and Note F below.

Note C: See Preparation 15, Note F.

Note D: Employed a 10' × $\frac{1}{8}$" 20% SE30 Column (H), 100°C oven temperature, helium flow 50 ml/min, 1 μl injections at 150°C, attenuation 1×10^2, display X1. Retention time in min, trans-60: 6.5, cis-60: 7.1.

Note E: CIT pure, dry nitrogen passed through a tower of 500 gm 3Å molecular sieves, activated at 150°C.

Note F: These integrations were obtained by making 10 Xerox* photocopies, cutting and weighing. An average was taken.

20.) Photolysis of cis- and trans-1, 5-hexadiyn-3-ene-1, 6-d_2 (60a) in cyclohexane: A. A solution of cis- and trans-60a was prepared in 7 ml glc prepped cyclohexane (Note A) from 0.25 gm (0.001 mole) d_2-tosylate (84-d_2) as described in Preparation 7. The concentration was determined by uv (Note B) to be approximately 0.11M. The solution contained no benzene or other impurities by glc analysis (Note C). Nmr and ms analysis showed greater than 90% deuteration in the acetylenic positions and greater than 90% d_2 overall. cis- and trans-61a, ^{1}H nmr (C_6H_{12}, 0.11M, 30°C, A60-A, external standard TMS 10.0τ) : 3.91τ (s, trans vinyl, integration 79), 4.11τ (s, cis vinyl, integration 63), 6.73τ (s, cis acetylenic, integration 10.5), 6.90τ (s, trans acetylenic, integration 13). Into each of two 0.3 cm ID quartz tubes (Note D) was placed 0.1 ml of this solution and the contents thoroughly degassed by three freeze-thaw cycles under 0.01 mm Hg pressure. After sealing under vacuum the tubes were irradiated with 254 nm light from an unfiltered Hanovia 450 watt medium pressure lamp (Note E) cooling with a forced air flow. Irradiation was continued for 30 minutes and one hour, respectively. The material in the sealed tubes was bright yellow, but no insoluble polymer was seen. The tubes were opened after cooling to -78°C (CO_2 ice). Glc showed that roughly 50% and 75% of the cis-enediyne had been destroyed by this treatment. The only products seen were an approximately 1% yield of dimeric

material (two glc peaks, m/e 152, at retention time 7.6 and 8.5 min, Note C) in each sample. No benzene was seen, although as little as 1% yield could have been detected. The trans to cis isomer ratio, initially 1.25, was 1.15 after 30 min and 1.09 after 60 minutes from the glc integrations. Ms analysis showed overall retention of total deuterium label in both the cis- and trans-60a. Nmr showed no scrambling of label in either isomer according to the formula in Preparation 9, Note E where 3-5% could have been detected. cis- and trans-60a after 1 hr under 254 nm photolysis, 20-25°C, ^{1}H nmr (C_6H_{12}, ~0.03M, 30°C, A60-A, external standard TMS) : 3.91τ (s, trans vinyl, integration 89), 4.11τ (s, cis vinyl, integration 81.5), 6.73τ (s, cis acetylenic, integration 13.5), 6.90τ (s, trans acetylenic, integration 12.5). In an attempt to isolate the dimeric products for identification, this photolysis was repeated at 10X scale from 2.50 gm tosylate 84 and 70 ml distilled, dry, olefin free cyclohexane. No dimeric products were seen even after 3 hrs irradiation and > 90% destruction of the cis-60. B. Thinking that the dimers probably arose from a triplet excited enediyne adventitiously sensitized in the previous small scale experiments, 0.2 ml of 0.11M cis- and trans-60a in cyclohexane solvent with 0.0182 gm (0.0001 mole) added recrystallized benzophenone (Note F) was degassed and sealed in a Pyrex tube as in Part A. Irradiation at > 300 nm for 3 hours where > 99% of the light should be absorbed by the sensitizer gave a yellow solution which when analyzed as above showed a 50% return of cis-60 with no benzene or any other products. Again the trans- to cis-isomer ratio showed a reduction

indicating an approach to the photostationary state but no scrambling of label was seen by nmr in either isomer.

Note A: Spectroquality* cyclohexane, Matheson Coleman and Bell, was passed through the $AgNO_3$ on alumina column described in the General Experimental. The effluent was distilled from sodium through a 3' tantalum wire column taking the fraction distilling 80-81°C. An ultra pure sample was prepared by preparative glc using the 10' × $\frac{3}{8}$" glass 20% SE30 column (E) at 50°C oven temperature, 50 μl injections at 100°C.

Note B: See Preparation 13, Note B.

Note C: See Preparation 13, Note D.

Note D: Quartz tubes were prepared from 0.3 cm ID quartz tubing in a manner entirely similar to that described for the Pyrex tubes in the General Experimental.

Note E: Hanovia Model No. 679A36, Type L, medium pressure Hg lamp, 450 watt was mounted in a water-cooled quartz well; the air-cooled sample was taped to the outside wall.

Note F: Benzophenone, Eastman red label, was recrystallized from ethanol, water and dried under under vacuum; m.p. 48°C sharply, white needles.

21.) Cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-ene[248] (160): Ethyl magnesium bromide (Note A) was prepared from 54.5 gm (0.50 mole) ethyl bromide and 12.3 gm (0.50 mole) magnesium turnings in 200 ml dry tetrahydrofuran (THF) in a 5-neck, 2-liter round bottom flask equipped with a ground glass, grease sealed stirrer with teflon paddle, an argon blanket inlet system, pentane low temperature thermometer (-150 to +50), 1-liter addition funnel, and a water-cooled reflux condenser. To this was added an additional 200 ml dry THF (Note B) followed by approximately 0.16 mole cis- and trans-1, 5-hexadiyn-3-ene (60) in 450 ml dry diethylether (Preparation 6.A) over a 45 minute period maintaining a 5°C internal temperature with an ice bath and stirring continuously under an argon atmosphere. After the addition was completed, the dark red solution was stirred for a further 30 minutes followed by addition of 70 ml, 59.5 gm (0.55 mole) trimethylsilylchloride (Note C) over a 40 minute period with vigorous stirring at 5°C. The suspension was stirred overnight at room temperature during which time a considerable precipitate of MgClBr formed with concurrent lightening of the color of the solution. Workup was begun by addition of 100 ml saturated ammonium chloride followed by 300 ml pentane and the combined organic extracts were washed with three 100 ml portions of water and dried 12 hours over sodium sulfate. The solvent was then stripped off on a rotoevaporator (pot 25°C) to give a dark red liquid weighing 52.4 gm. Nmr showed the product together with peaks attributable to THF, ether and $(CH_3)_3SiCl$. This oil was distilled at 0.8 mm Hg through an ordinary Claisen head,

discarding a 3 gm forerun and taking the fraction distilling at 62-67°C, to give 29.7 gm of a colorless oil (Note D). Glc analysis (Note E) showed this mixture to contain 40% cis-160, 44% trans-160 and 16% of a third substance. Distilled liquid, ^{1}H nmr (CCl_4, ~10%, A60-A, 30°C, internal standard TMS 10.0τ) : 4.08τ (s, trans vinyl, 1H), 4.25τ (s, cis vinyl, 1H), 9.81τ (s, cis $SiMe_3$, 9H), 9.83τ (s, trans $SiMe_3$, 9H); ir (CCl_4, ~10%, microcell, polystyrene calibrated): 2960 cm^{-1} (s), 2900 (m), 2180 (m), 2160 (m), 2130 (m), 1250 (s). Preparative glc allowed isolation of the three components of this mixture. The identity of cis- and trans-160 was confirmed by nmr. The third substance showed only Si-CH_3 proton absorptions and an ir typical of silanes. Since it was base and air stable, this material, while not identified, served as a convenient internal standard for reactions of 160. These materials seemed to be air stable to moderate exposure and base stable in aprotic media. They were stored as a concentrated pentane solution in a glass stoppered flask at -15°C.

Note A: Ethyl magnesium bromide was prepared from ethyl bromide (Matheson Coleman and Bell) and magnesium turnings (from rods, 99.8% minimum assay, Matheson Coleman and Bell). The magnesium turnings and flask were flame dried and cooled under a flow of argon. The turnings were covered with a minimum amount of dry THF and ~1.0 ml ethyl bromide containing ~0.05 gm iodine added all at once. After the initial exothermic reaction

had subsided, the remaining bromide was added dropwise as an approximately 25% solution in THF.

Note B: The purpose of the additional THF is to keep the bis-Grignard in solution during the addition of the ether solution of the hexadiynenes.

Note C: Chlorotrimethylsilane, tech., Aldrich Chemical Co., Inc. Milwaukee, Wisconsin, freshly distilled from barium oxide and stored over 4Å molecular sieves.

Note D: An infrared lamp was used to maintain the temperature of the distillation head above 70°C so that crystallization of the trans isomer does not occur.

Note E: A 10' × $\frac{1}{4}$" glass 20% SE30 column (B) was employed at 180°C, 60 ml/min He flow in a Varian 90P (TC oven 250°C). Preparative gas chromatography was performed on a 10' × $\frac{3}{8}$" glass 20% SE30 column (E) at 180°C, 50 μl injections of a 10% solution at 200°C. Retention time in minutes: cis-160, 24.2; impurity, 30.4; trans-160, 33.5

22.) 1, 5-Hexadiyn-3-ene (60) from cleavage of the Me_3Si groups from $Me_3SiC{\equiv}C\text{-}CH^{\circ}CH\text{-}C{\equiv}C\text{-}SiMe_3$ (160): As a means of testing the feasibility of cleavage of the trimethylsilylethers by the method of Schmidt and Arens,[249] 2.2 gm (0.01 mole) cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-ene was dissolved in 21 ml dry ethanol in a 500 ml flask equipped with a magnetic stir

bar, pentane low temperature thermometer, 200 ml addition funnel, and argon blanket inlet system. At 0°C, 9.0 gm (0.054 mole) silver nitrate (Note A) was added over a 15 min period. A light yellow precipitate was formed. After cooling to -20°C, 16.8 gm (0.258 mole) potassium cyanide (Note B) in 25 ml distilled water was added allowing the mixture to come slowly to room temperature. More water was added until dissolution of the white silver cyanide precipitate. This solution was extracted with 100 ml pentane and the pentane layer dried over anhydrous sodium sulfate. Pentane was removed on a 3-foot tantalum wire coil, vacuum jacketed column at 36°C head temperature until approximately 10 ml remained in the pot. Nmr analysis showed the characteristic pattern for the cis- and trans-1,5-hexadiyn-3-ene (60) plus a considerable amount of unreacted trans-$Me_3SiC{\equiv}C\text{-}CH^{\circ}CH\text{-}C{\equiv}C\text{-}SiMe_3$ indicating that longer reaction times are needed. The pentane and enediynes were vacuum transferred away from the crystalline trans-160 which was recycled. cis- and trans-60, ^1H nmr (pentane, ~10%, 30°C, A60-A, internal standard TMS) : 4.04τ (s, trans vinyl, 1H), 4.25τ (s, cis vinyl, 1H), 6.83τ (s, cis acetylenic, 1H), 7.0τ (s, trans acetylenic, 1H); pure by glc analysis (Note C).

Note A: Silver nitrate, $AgNO_3$, Mallinckrodt analytical reagent, from Scientific Products, 1711 Red Hill Ave., Santa Ana, California.

Note B: Potassium cyanide, ACS analytical reagent, Allied Chemical Co.

Note C: See Preparation 7, Note D.

23.) Attempted addition of dichlorocarbene ($:CCl_2$) to cis- and trans-1, 6-Bis(trimethylsilyl)-1, 5-hexadiyn-3-ene (160): A: Dichlorocarbene was generated using the method of Doering and Hoffmann[243] which gave in my hands a 60% glc yield of 1-methyl-1-ethynyl-2, 2-dichlorocyclopropane from 2-methyl-1-buten-3-yne as reported by Vo-Quang and Cadiot.[244] The reaction was carried out in a 25 ml, 3-neck round bottom flask equipped with a magnetic stir bar, a wired-on rubber septum, a low-temperature pentane thermometer, and an argon blanket inlet system. To a rapidly stirred mixture of 1.0 gm (0.05 mole) bis(trimethylsilyl)hexadiynenes (160) and 0.006 mole potassium tert-butoxide (Note A) in 5.0 ml dry, olefin free pentane at 5°C (ice bath cooling) internal temperature was added dropwise 0.4 ml, 0.6 gm (0.005 mole) chloroform (Note B) by syringe. The addition was complete in 15 minutes, whereupon the brown reaction mixture was stirred for a further three hours, allowing the temperature to rise slowly to 25°C. The disappearance of the chloroform was monitored by nmr. The final mixture was taken up in 50 ml pentane and the solids removed by filtration, washing the filter with an additional 50 ml pentane. The 100 ml pentane extract was washed twice with 50 ml saturated NH_4Cl solution and then twice with 100 ml water. The organic layer was dried over anhydrous Na_2SO_4 for five hours at 10°C after which time the solvent was stripped on a rotoevaporator with the pot at 10°C. Glc (Note C) showed a 51% decrease in the

cis-160 and an 80% decrease in the trans-160 versus the internal standard, base stable silylated impurity. Two small products (< 5% yield) of material with retention times longer than the starting olefins were seen. These peaks were heat stable to 350°C at least in the injector block of the glc. Preparative glc isolation of these materials (Note C) showed that both contained silylmethyl groups but no other protons could be seen in the nmr. A crude ir suggested the possibility of chlorocarbons from a strong 650-700 cm^{-1} region. In an attempt to increase the amount of these possible $:CCl_2$ products available for analysis, this reaction was repeated at 10X the given scale. Glc showed, however, the complete destruction of cis- and trans-160 and no volatile products. The silyl groups were cleaved from any remaining acetylenes by the method outlined in Preparation 22. Vacuum transfer of the pentane solution from the workup described after thorough washing with water and reduction of the volume by distillation showed a small amount of cis- and trans-60 and one small peak in the region expected for a $C_7H_XCl_2$ species in the glc. This <1% yield was not isolated pending further experiments. B. Dichlorocarbene was generated using a modification of the method of Parham and Schweizer.[246] In a 25 ml, 3-neck round bottom flask with a magnetic stir bar, a wired-on rubber septum, an ether condenser, and an argon blanket inlet system together with a low-temperature, pentane thermometer was placed 0.575 gm of a 57% oil dispersion of sodium hydride (Note D). The oil was removed by repeated washing with pentane under argon, removing the pentane wash by

syringe. The flask and hydride were dried by a low flame and rapid passage of dry argon. To this was added 1 gm (0.005 mole) of the cis- and trans-160 in 5 ml dry, olefin free pentane and 2.42 gm (0.014 mole) dry methyltrichloroacetate (Note E) with rapid stirring under argon, cooling to 5°C internal temperature with an ice bath. To this solution was added 0.5 ml (0.0125 mole) dry methanol over an hour period, maintaining 0-5°C. The progress of the reaction was followed by observing the methyltrichloroacetate by glc (Note C). The acetate had completely disappeared after 8 hours at 0°C. Workup was initiated by addition of 20 ml dry pentane and filtration from the solids. An additional 50 ml pentane was used to wash the filter. This pentane extract was washed twice with 50 ml volumes of saturated NH_4Cl and twice with 100 ml volumes of distilled water. The organic layer was dried overnight at 0°C over anhydrous Na_2SO_4. The pentane was removed by rotoevaporation at 0°C pot, and the concentrate examined by glc (Note C). A 10% decrease in the cis-160 and a 52% decrease in the trans-160 was observed based on the silylated internal standard. The only products seen at low attenuation were a somewhat smaller yield of the unknown products observed in A. These were not isolated. Nmr confirmed the loss of starting material, mostly in the trans isomer. Workup by cleavage of the trimethylsilyl groups as above here failed to show any product of carbene addition even at the 1% level. C. Dichlorocarbene was generated from thermal decomposition of phenyl(bromodichloromethyl)mercury according to the method of Seyferth.[247] In a 50 ml, 3-neck round bottom

flask equipped with a reflux condenser, a 0-150°C thermometer, a magnetic stir bar, and an argon blanket inlet system was placed 4.41 gm (0.01 mole) phenyl(bromodichloromethyl)mercury (Note G) dissolved in 15 ml reagent grade, thiophene-free benzene (Note H). To this solution was added 2.0 gm (0.0091 mole) cis- and trans-160 in 5.0 ml benzene. The light yellow solution was stirred for one hour under an argon flow at 25°C to displace the dissolved oxygen. The temperature was then taken to 90°C to initiate benzene reflux with moderate stirring. The solution turned darker yellow and dark brown after one hour reflux under argon, while a precipitate began to form. The reaction was monitored by watching the disappearance of the phenyl(bromodichloromethyl)mercury on the glc (Note I). The reaction was terminated after twelve hours at reflux. Glc analysis (Note C) showed no attenuation of the cis- or trans-160 based on the silylated internal standard. The only products seen were tetrachloroethylene and hexachlorocyclopropane (Note J) identified by coinjection with authentic samples. The crude mixture was distilled at 0.1 mm Hg pressure through a short path taking fractions at 45-50°C, 50-53°C, and 55°-higher. The first fraction was enriched with cis-160, while the third was mostly trans-160. Nmr analysis showed no products other than the cis- and trans-160 and the impurity used as an internal standard which co-distilled. The residue was extracted with benzene and concentrated on a roto-evaporator. Redissolving this in 10% hexane until cloudiness gave 3.0 gm of a crude white solid upon cooling to -78°C. Recrystallization from the minimum benzene gave 2.85 gm or 70% of

theoretical phenylmercuric bromide, identified by mixed melting point with an authentic sample, m.p. 275-276°C.

Note A: Potassium tert-butoxide was freshly prepared from 0.234 gm (0.006 mole) purified potassium metal (see also Preparation 24, Note A) as the mono-solvate after vacuum removal of the t-butanol (see also Preparation 24, Note B). This reaction was repeated with freshly opened KOtBu from Alfa Inorganics, Ventron Corp. and sublimed KOtBu (200°C, 0.1 mm Hg) with identical results.

Note B: Chloroform, Spectroquality, Matheson Coleman and Bell, was used as received after drying over 4Å molecular sieves for two weeks.

Note C: A 10' × $\frac{1}{4}$" glass 20% SE30 column (B) was used at 210°C oven temperature, 1 μl injections at 250°C, He flow 60 ml/min for the analytical samples of silylated materials. Retention times in minutes: cis-160, 5.3; internal standard, 6.4; trans-160, 6.9; first unknown product, 9.1; second unknown product, 12.5. Preparative work was carried out on a 10' × $\frac{3}{8}$" glass 20% SE30 at 180°C. For the conditions used to analyze the silyl-cleaved samples, see Preparation 7, Note D.

Note D: Sodium hydride, NaH, as a 57% dispersion in mineral oil, Alfa Inorganics, Ventron. This reaction was repeated with commercial sodium methoxide, $NaOCH_3$, Matheson Coleman and Bell, with identical results.

Note E: Methyltrichloroacetate, $Cl_3CCOOCH_3$, was prepared by esterification of trichloroacetic acid and methanol. One pound of trichloroacetic acid (ACS grade, Matheson Coleman and Bell) was dissolved in one liter of technical methanol and 5 ml concentrated sulfuric acid added. The solution was heated to reflux for nine hours over a steam bath. Workup was accomplished by addition of one liter of distilled water. The ester separated as the bottom layer and was washed twice with 200 ml saturated sodium carbonate followed by 200 ml saturated sodium chloride. The crude ester was dried overnight over anhydrous sodium sulfate and distilled under vaccum at 20 mm Hg taking the fraction which distilled at 65°C. Analysis by glc (Note F) showed the compound to be at least 99% pure.

Note F: A 5' × $\frac{1}{4}$", 5% SE30 column (A) was used at 95°C Varian 90P oven temperature, He flow 60 ml/min.

Note G: Phenyl(bromodichloromethyl)mercury, $C_6H_5HgCCl_2Br$, was prepared by the method of Seyferth and Lambert.[247(b)] Into a dry 1-liter, 3-neck flask equipped with an argon blanket inlet system, grease sealed overhead stirrer with a teflon paddle, and a low temperature (-150° to 50°C) pentane thermometer was placed 25.0 gm (0.08 mole) phenylmercuric chloride (Alfa Inorganics, Ventron), 19.7 gm (0.12 mole) bromodichloromethane (Aldrich Chemical Co., Inc., freshly distilled from P_2O_5), and 200 ml dry tetrahydrofuran (THF). Potassium t-butoxide as the mono-solvate from 4.3 gm (0.11 mole) purified potassium (washed free of mineral oil with

dry THF) was dissolved in 75 ml dry THF and added to the above solution at -25°C (CO_2 ice-isopropanol cooling, internal temperature) over a 30 minute period with rapid stirring. The THF was then stripped off on a rotoevaporator as rapidly as possible at ~0°C pot temperature, cooling the receiver to -78°C (CO_2 ice) to speed up the process. To the grey residue was added 400 ml of cold (~0°C) reagent grade benzene and 50 ml distilled water. This mixture was thoroughly shaken in the cold and then filtered. The benzene was rotoevaporated at 10°C pot temperature with a -78°C receiver. This residue was recrystallized from hot 3/1 hexane/chloroform giving 16.85 gm or 50% theoretical $C_6H_5HgCCl_2Br$ as a first crop of white, fine needles, m.p. 108°C sharply (literature:[247] 108-110°C). As a test of the quality of this phenyl(bromodichloromethyl)mercury as well as a confirmation of its identity, 2.20 gm (0.005 mole) of this material was placed in a 25 ml round-bottom flask equipped with a reflux condenser, argon inlet system, and a thermometer. Cyclohexene, 1.23 gm (0.015 mole), glc pure, distilled from CaH, in 5 ml dry benzene was then added and reflux begun under argon. Following the reaction by glc (Note I) showed a steady increase of a single product of retention time intermediate to cyclohexene and $C_6H_5HgCCl_2Br$ and a steady decrease in the latter two. After three hours, the reaction was complete. The colorless reaction mixture was filtered leaving 1.76 gm (98% theoretical) phenylmercuric bromide. The dichlorocarbene adduct was isolated by preparative glc and possessed an ir and nmr identical to an authentic sample.

The yield was estimated by glc integration to be 85% (literature:[247(a)] 89%).

Note H: Benzene, ACS grade, thiophene free, Matheson Coleman and Bell, Los Angeles, California.

Note I: A 10' × $\frac{1}{4}$" glass 20% SE30 column (B) was employed under manual temperature programming on Varian 90P gas chromatograph. The column initially at 100°C oven temperature was raised to 170°C after 10 min in steps of 10°C every 2 min and then to 200°C after 5 min in steps of 10°C every 4 min. One μl injections at attenuation X1 were employed, injector 270°C, detector 270°C.

Note J: An authentic sample of tetrachloroethylene was obtained from Eastman-Kodak Chemical Co., red label, ACS grade used as is. An authentic sample of hexachlorocyclopropane was obtained from Professor J. D. Roberts of the California Institute of Technology.

24.) Attempted addition of dichlorocarbene ($:CCl_2$) to cis- and trans-1,5-hexadiyn-3-ene (60): A. Dichlorocarbene was generated in the presence of 60 by adaptation of the method of Doering and Hoffmann.[243] In a 50 ml, 3-neck round bottom flask equipped with a magnetic stir bar, a reflux condenser, an argon blanket inlet system, and a -25° to +150°C thermometer was placed 0.53 gm (0.014 mole) potassium metal (Note A) and approximately 10 ml tert-butanol (Note B). The tert-butanol was brought to reflux under argon with stirring. The potassium was completely dissolved

after three hours. The flask was cooled to -25°C (internal temperature, CO_2 ice-isopropanol cooling bath) and 10 ml of a concentrated solution of cis- and trans-60 in pentane from 2.5 gm (0.01 mole) tosylate 84, prepared as in Preparation 6.B, was added all at once with stirring. The solution turned black but glc analysis (Note C) showed that the enediynes were disappearing only slowly at this temperature (estimated half-life one hour at -25°C under argon). To this stirred mixture was added 1.09 ml (0.014 mole) spectroquality chloroform dropwise over 15 minutes. The reaction was stirred at -20°C following the disappearance of the $HCCl_3$ by glc. After two hours, the reaction was worked up by pouring the black solution and solids into 50 ml pentane and washing with 100 ml water. The emulsified upper layer was filtered, the filter washed with 50 ml pentane, and the entire organic layers washed with 50 ml saturated NH_4Cl and then 100 ml water. After drying overnight at 10°C over anhydrous Na_2SO_4, the pentane was reduced by slow distillation through a 3-foot tantalum wire coil, vacuum jacketed column. Glc analysis of the concentrate showed no returned 60 and several heavier products in low yield. The major product was identified as tetrachloroethylene by coinjection with an authentic sample. In similar fashion a trace of hexachlorocyclopropane was also seen. An attempt to preparatively isolate two of the other peaks in $<1\%$ yield by glc evidently failed to produce enough for nmr and ir spectra. A glc/ms was not taken. B. Dichlorocarbene was generated by modification of the method of Parkam and Schweizer.[246] In a 50 ml, 3-neck round bottom flask

attached to a vacuum line equipped with a magnetic stir bar, a soft rubber septum (wired on), and an argon blanket inlet system was placed 1.5 gm of a 57% dispersion of NaH (0.034 mole) in mineral oil (Note D). The oil was removed by repeated washing with pentane, removing the pentane by syringe. The flask and NaH was then dried under vacuum. Into this was vacuum transferred 5 ml of a concentrated solution of cis- and trans-60 in pentane, prepared as in Preparation 6.B from 5.0 gm (0.020 mole) tosylate 84. Into this was syringed 4.0 ml (0.034 mole) $Cl_3CCOOCH_3$ (Note E) and argon atmosphere introduced. The temperature was raised to -20°C (CO_2 ice-isopropanol) and stirring begun. Some discoloration was noted. To this stirred mixture was added dropwise via syringe 1.0 ml dry MeOH (0.025 mole) maintaining the temperature in the reaction flask below -20°C. The disappearance of the ester was followed by glc (Note F). After six hours the reaction was poured into 50 ml pentane and washed with 50 ml saturated NH_4Cl and then 100 ml distilled water. The pentane layer was dried overnight over anhydrous Na_2SO_4 at 0°C. The pentane was distilled through a vacuum jacketed tantalum wire coil column until approximately 5 ml remained in the pot. Glc analysis (Note C) showed a small yield of tetrachloroethylene but no other products even at low attenuation. A small yield of returned enediynes 60 was also detected. C. Dichlorocarbene was generated from the thermolysis of phenyl(bromodichloromethyl)mercury by the method of Seyferth.[247] Cis- and trans-60 were prepared from 5.0 gm (0.020 mole) tosylate 84 by the procedure described in Preparation 6.B as a solution in

10 ml benzene (Note G). The benzene and enediyne were vacuum transferred onto 4.4 gm (0.010 mole) $C_6H_5HgCCl_2Br$ in a 25 ml round bottom flask. Argon atmosphere was introduced and a reflux condenser attached. The benzene was refluxed under argon for 6 hours at which time more than $\frac{3}{4}$ of the mercurial and almost all of the enediynes 60 had disappeared via glc analysis (Note H). The reaction was worked up by vacuum transfer of the volatiles. Nmr showed a small return of starting cis- and trans-60 but no discernable products. Glc (Note C) showed a fair yield of tetrachloroethylene and the largest yield so far of hexachlorocyclopropane, confirmed by coinjection of authentic material (Note I). As well, small yields, $<1\%$ based on the hexadiynenes, of the unknowns present in the $HCCl_3$, KOtBu reaction A were also seen here. Attempts to isolate them by preparative glc also failed at these concentrations.

Note A: Purified potassium metal bar, J. T. Baker Chemical Co., was cut into small (0.2 cm) lumps under mineral oil. These were washed free of oil by five consecutive treatments with 10 ml pentane before being placed in the reaction flask.

Note B: Tert-butanol, J. T. Baker Chemical Co., ACS grade, was distilled from sodium prior to use.

Note C: A 0.2 ml aliquot was worked up by addition of 0.3 ml pentane and 0.3 ml water and extracted with a pipet. The pentane layer was dried over a few grains of Na_2SO_4 and 10 μl injected

onto the 10' × ¼" glass 20% SE30 column (B) at 125°C oven temperature (Varian 90P), He flow 50 ml/min, injector 200°C, TC detector 200°C. Retention times in minutes from the air peak: pentane, 0.8; enediynes 60, 1.5; chloroform, 3.0; tetrachloroethylene, 4.5; unknown, 6.1; hexachloroethylene, 8.0; unknown, 12.5; unknown, 13.5.

Note D: See Preparation 23, Note D.

Note E: See Preparation 23, Note E.

Note F: The ester was seen with the 10' × ¼" glass 20% SE30 column (B) at 210°C, He flow 60 ml/min, 1 μl X2. Retention time in minutes from air peak: 15.5.

Note G: Spectroquality benzene (MCB) was used as received. The yield of enediynes was estimated to be 80% by nmr analysis.

Note H: See Preparation 23, Note I.

Note I: See Preparation 23, Note J.

25.) Attempted addition of chlorocarbene (:CHCl) to cis- and trans-1,6-bis(trimethylsilyl)-1,5-hexadiyn-3-ene (160): Using the method of Closs and Closs[250] which gave a 20% yield of the endo- and exo-isomers of 7-chlorobicyclo[4.1.0]heptane from cyclohexene (Note A), 1.54 ml of a 2.33M solution of methyl lithium (Note B) in pentane was syringed slowly into 2.70 gm (0.014 mole) cis- and trans-160 in 0.45 ml (0.007 mole) dry

dichloromethane (Note C) and 5 ml pentane with rapid stirring at -30°C (internal temperature, CO_2 ice-isopropanol bath) under argon. The solution turned black during the first five minutes. Glc (Note D) showed attenuation of the dichloromethane but no corresponding decrease in the peaks due to 160 versus the internal standard sylylated unknown. After 30 minutes at -20°C, workup was accomplished by addition of 10 ml pentane, filtration to remove solids, and a wash with 20 ml saturated NH_4Cl solution then 40 ml distilled water. Concentration by rotoevaporation showed only starting material in the glc and ^1H nmr.

Note A: To check this procedure, the reaction was carried out as above on cyclohexene. Methyllithium (1.1 ml of a 2.33M solution) was syringed slowly into a -30°C solution of 0.82 gm (0.01 mole) cyclohexene and 0.43 gm (0.005 mole) dichloromethane in 5 ml pentane. Glc (Note D) showed immediate formation of two products in approximately 20% yield later shown by nmr to be a mixture of endo- and exo-7-chlorobicyclo[4.1.0]heptane as reported.[250]

Note B: Methyllithium, CH_3Li, 2.33M in pentane from CH_3I, Alfa Inorganics, Inc., Beverly, Massachusetts.

Note C: Dichloromethane, H_2CCl_2, ACS reagent grade, Matheson Coleman and Bell, Los Angeles, California; distilled dry from P_2O_5.

Note D: Approximately 0.1 ml aliquots were worked up with 0.2 ml saturated NH_4Cl by pipet. The pentane layer was injected

directly onto the 10' × ¼" glass 20% SE30 column (B) at 125°C, 60 ml/min He flow, 1 μl injections X1 at 200°C.

26.) Attempted addition of methoxycarbene (:$CHOCH_3$) to cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-ene (160): A. Methoxycarbene was generated in the presence of 160 from (dichloromethyl)methyl ether and methyllithium by the method of Schöllkopf and Paust.[254] To 1.80 gm (0.008 mole) cis- and trans-160 in 10 ml pentane was added 0.575 gm (0.005 mole) (dichloromethyl)methyl ether (Note A) and the solution cooled to -20°C with a CO_2 ice-isopropanol bath. Into this solution under argon with stirring was syringed 2.2 ml of a 2.29M solution of methyllithium (Note B). The reaction mixture turned dark immediately and the disappearance of the dichloro ether followed by glc (Note C). The reaction was stirred at this temperature for 15 minutes then allowed to warm to room temperature while stirring for ½ hour. Workup was accomplished by addition of 50 ml pentane, filtration of the solids, and a wash with 50 ml saturated NH_4Cl solution. Glc analysis (Note C) showed no decrease in the cis- or trans-160 versus the silylated internal standard and no other products. B. Methoxycarbene was generated by thermal decomposition of (dimethoxymethyl)trimethoxysilane (162) by the method of Atwell, et al.[255] A mixture of 1.80 gm (0.008 mole) cis- and trans-160 in 10 ml pentane was placed in a thick-wall Pyrex ampoule with an enclosed teflon-coated magnetic stir bar. The pentane was slowly removed under vacuum. To this was added 4.0 gm (0.02 mole) 162 (Note D) and the ampoule

degassed and sealed under vacuum. The sealed mixture was heated to 125°C for 16 hours with moderate stirring. The tube was then cooled to 0°C (ice bath) and broken open. The dark brown product mixture was then hydrolyzed by dilute hydrochloric acid and extracted with ether. The ether extract was washed with 100 ml 10% $NaHCO_3$ solution followed by 100 ml distilled water and dried over Na_2SO_4 overnight at 10°C. The filtered ether extract was then concentrated by rotoevaporation at 0°C in the pot. Glc analysis (Note C) showed no appreciable decrease in either the cis- or trans-160 versus the silylated internal standard and no new products.

Note A: (Dichloromethyl)methyl ether, Cl_2CHOCH_3, from Aldrich Chemical Co., Inc., Milwaukee, Wisconsin, was distilled dry from P_2O_5.

Note B: See Preparation 25, Note B.

Note C: The 10' × $\frac{1}{4}$" glass 20% SE30 column (B) was employed at 180°C Varian 90P oven temperature, He flow 60 ml/min, 1 μl injections at 210°C X8. Aliquots were worked up with pentane and saturated NH_4Cl before injection on the glc.

Note D: (Dimethoxymethyl)trimethoxysilane (162) was prepared by the method of Atwell, Weyenberg, and Uhlmann.[255] A mixture of 74.2 gm (0.7 mole) methylorthoformate and 2.24 gm (0.07 mole) anhydrous methanol was added to 29.5 gm (0.11 mole) hexachlorodisilane (Alfa Inorganics, Ventron, dried by distillation from BaO) over a 2 hour period. After the initial exothermic reaction, the

mixture was heated at 60-70° for an additional 10 hours with continuous removal of methylchloride and methylformate in a Dean-Stark trap. Fractional distillation on a 3-foot tantalum wire column taking the fraction boiling at 82-85°C at 20 mm mercury gave 4.8 gm crude product used as is but containing at least 80% (dimethoxymethyl)trimethoxysilane by nmr.

27.) Attempted addition of ethyl(dimethylsulfuranylidene)-acetate (163) to cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-ene (160): Using the method of Payne[257] which gave excellent reported yields with some highly delocalized olefins of low nucleophilicity, 0.8 gm (0.004 mole) cis- and trans-160 and 0.6 gm (0.004 mole) ethyl(dimethylsulfuranylidene)acetate (EDSA, Note A) were placed in 2.5 ml dry, thiophene-free benzene (Note B) and refluxed under argon. After 24 hours at reflux temperature, nmr showed 90% destruction of the ylide. Glc analysis (Note C) showed, however, no attenuation in the cis- and trans- versus the internal standard silylated impurity. One product at long retention time was also seen. This was isolated by preparative glc and identified by its nmr and ir as the known tricarboethoxycyclopropane (164), ^{1}H nmr (CCl_4, ~5%, 30°C, A60-A, external standard TMS at 10.0τ) : 5.85τ (q, 2H), 7.55τ (m, 1H), 8.6τ (t, 3H); ir (CCl_4, ~1%, microcell) : 3060 cm^{-1}, 1745, 1455, 1380, 1350, 1270, 1175, 1030, 855; probably a mixture of isomers from the nmr.

Note A: Ethyl(dimethylsulfuranylidene)acetate (EDSA) was prepared according to Payne.[257] A solution of 26.5 gm (0.159 mole)

ethylbromoacetate (Aldrich Chemical Co.) and 11.4 gm (0.184 mole) dimethylsulfide (Matheson Coleman and Bell, ACS grade) in 50 ml acetone was stirred overnight at 23°C in a stoppered flask. The 30.2 gm (84% of theoretical) hydroscopic crystals of the sulfonium bromide were isolated by filtration and washed with 100 ml acetone. These were dissolved in 105 ml $HCCl_3$, and after cooling to 5°C were treated with a mixture of 78.7 ml saturated K_2CO_3 and 10.5 ml 12.5N NaOH. This mixture was stirred at 20°C for 15 minutes, filtered to remove the salt and the chloroform layer separated and dried over anhydrous K_2CO_3. The ylide was stored at -5°C as a chloroform solution. Portions were removed and the solvent stripped before reaction. The yield was estimated by evaporation of 5 ml for an nmr sample to be 93%.

Note B: Benzene, Spectroquality, thiophene-free, Matheson Coleman and Bell.

Note C: The reaction mixture was injected directly onto the 10' × $\frac{1}{4}$" glass 20% SE30 column (B) at 200°C Varian 90P oven temperature, He flow 60 ml/min, 1 μl injections X1 at 250°C. Preparative work was performed on the 10' × $\frac{3}{8}$" glass 20% SE30 column (E) under identical conditions.

28.) Attempted Cu catalyzed addition of carboethoxycarbene ($:CHCOOCH_2CH_3$) to cis- and trans-1, 6-bis(trimethylsilyl)-1, 5-hexadiyn-3-ene (160): Carboethoxydiazomethane was thermally decomposed with the aid of a soluble copper catalyst according to the method of

Moser.[258] To 1.90 gm (0.01 mole) cis- and trans-160 from Preparation 21 as a solution in 10 ml dry pentane was added 0.3 gm $[(C_6H_5)_3P \cdot CuCl]_4$ (Note A) under argon at 23°C (water bath) with stirring until solution. This was followed by syringe injection of 8.0 ml (~0.08 mole) $N_2CHCOOCH_2CH_3$ (Note B) in 0.5 ml portions. The evolution of nitrogen was clearly evident and the reaction could be conviently followed by ir (Note C). When the diazo band at 2100 cm^{-1} decreased below the C≡C absorption, another 0.5 ml of $N_2CHCOOCH_2CH_3$ was added until a total of 8 ml was reached over a 24 hour period at 23°C. Glc (Note D) showed decreases in the starting olefins, the cis-160 disappearing almost twice as fast as the trans-160. Several products were seen. Among these diethylmaleate and diethylfumarate were definitely confirmed by preparative isolation and spectral comparison to authentic samples. By comparison to Preparation 27, tricarboethoxycyclopropane was found in <2% yield based on the $N_2CHCOOCH_2CH_3$. One product of longer retention time was also isolated, present in 5% glc yield based on the cis- and trans-160. Although the spectra were of very poor quality, nmr showed silylmethyls at 9.9τ, a multiplet at 7.6τ, a quartet at 5.8τ and a triplet at 8.7τ. Ir indicated that the peak contained carbonyl material (1740 cm^{-1}) and possibly cyclopropyl absorptions (1035 and 845). However, since the proportions of these various absorptions are grossly in error based on that expected for the 1-carboethoxy-2, 3-diethynylcyclopropane (61e), the material at best is a mixture.

Note A: The triphenylphosphene complex of cuprous chloride was prepared by dissolving 15.5 gm (0.05 mole) $(C_6H_5O)_3P$ (Eastman Organic Chemicals, Red Label, ACS grade) in 20 ml benzene (MCB, spectroquality) and adding 5.0 gm (0.05 mole) cuprous chloride (Fischer, reagent grade). After stirring overnight, the cloudy solution was filtered and most of the benzene removed by rotoevaporation at 23°C. This substance was thoroughly dried of benzene by heating to 100°C while pumping at 0.01 mm Hg pressure. Checked by ir, identical to that reported.[258]

Note B: Ethyldiazoacetate was prepared from ethylglycinate · hydrochloride ($Cl^- NH_3^+CH_2COOCH_2CH_3$, MCB) and sodium nitrite by modification of the method of Smith[299] as described by Moser.[258] Distillation under 0.05 mm Hg at 30°C yielded 82% of theoretical ethyldiazoacetate, free of ethylchloroacetate by glc (Note D). The ir spectrum was identical to that reported by Smith.

Note C: Ir analyses were carried out by removal by syringe of a 50 μl portion. This was placed on the face of a sodium chloride disk and a film spectrum taken.

Note D: The $10' \times \frac{1}{4}''$ glass 20% SE30 column (B) was employed at 200°C Varian 90P oven temperature, 60 ml/min He flow, 1 μl injections of the reaction mixture at 250°C. Retention times in minutes from the air peak: pentane, 0.5; ethyldiazoacetate, 1.4; diethylfumarate, 2.4; diethylmaleate, 2.6; cis-160, 3.7; internal

standard, 4.4; trans-160, 5.0; tricarboethoxycyclopropane, 8.8; unknown, 13.1.

29.) N-Propargyl urea (178a): N-Propargyl urea was prepared essentially by the method of Skell and Gramas.[228] To 1.0 liter of dry dimethylformamide (Note A) was added 416 gm (2.83 mole) phthalimide (Note B) and 450 gm anhydrous Na_2CO_3 in a 2-liter, 3-neck round bottom flask equipped with a 500 ml addition funnel, a grease-sealed teflon paddle overhead stirrer, a -5 to +250°C thermometer, and a nitrogen blanket inlet system. A nitrogen atmosphere was introduced by flushing and stirring the mixture for one-half hour under a steady flow. The gas flow was then reduced and the temperature raised to 60°C with a silicone oil bath. After stirring for 15 minutes at this temperature, 263 gm (2.31 mole) propargyl bromide (Note C) was added dropwise. Glc internal temperature rose to 75°C during this addition and was maintained there with the oil bath for ten hours followed by continued stirring at 26°C for a total of forty hours. The reaction mixture was then poured with stirring into one liter of ice water. The solids formed were collected by suction filtration in a coarse fritted glass funnel and washed twice with one liter of distilled water. The water washes were combined and extracted with eight pints of chloroform. This chloroform extract was used to dissolve the solids, washed with a further three liters of water, and then dried over sodium sulfate for twelve hours at 25°C. The chloroform was evaporated on a continuous feed rotoevaporator with

on-line sintered glass filtration. The remaining chloroform and any other volatiles were removed from this concentrate by vacuum drying at 0.01 mm Hg to yield 416 gm (2.25 mole) or 97% crude yield of propargylphthalimide, nmr ($DCCl_3$, ~10%, 30°C, A60-A, internal standard TMS) : 2.18τ (AB m, 4H), 5.54τ (d, J = 2.7 Hz, 2H), 7.76τ (t, J = 2.7 Hz, 1H). To this crude material in a 2-liter round bottom flask was added 513 gm (4.80 mole) dry benzylamine (Note D) and an efficient magnetic stir bar. The flask was attached to a simple Claisen-head still and nitrogen atmosphere introduced. The temperature of the pot (external) was slowly raised to 100°C with a large silicone oil bath at which point the phthalimide melted. The temperature was then taken to 150°C with vigorous stirring where the amine distilled. The propargyl amine distillate was collected over a head temperature range of 90-100°C in an ice-cooled 2-liter flask with attached $CaCl_2$ drying tube. After 2 hours, the temperature of the pot was raised to 200°C until no further distillate was obtained. Nmr of a sample of this ~130 ml amine showed less than 1% benzyl impurity. The crude amine was dried over anhydrous Na_2CO_3 overnight and then filtered and redistilled taking the 81.5-82.5°C fraction, giving in this way 105 gm (1.90 mole) or 82% very pure propargylamine, nmr (CCl_4, ~10%, 30°C, A60-A, internal standard TMS) : 6.64τ (d, J = 2.8 Hz, 2H), 7.76τ (t, J = 2.8 Hz, 1H), 8.60τ (slightly broadened singlet, 2H); ir (CCl_4, ~5%, 23°C, polystyrene calibrated) : 3370 cm^{-1}, 3285, 2920, 2845, 2110 (w), 1596, 930, 840 (broad), 650. The entire distilled amine was dissolved in 500 ml distilled water and 6N HCl added dropwise

with stirring to pH 6 (Fischer pH paper) maintaining the internal temperature below 10°C (ice bath cooling). To this stirred solution was added 350 gm (4.25 mole) potassium cyanate (KOCN, Note E) and the mixture refluxed for 30 minutes. Most of the water was distilled off through a simple Claisen-head still and 400 ml 90% EtOH added with continued reflux for 10 minutes. The hot EtOH solution was filtered and the filter washed with an additional 100 ml boiling EtOH. This solution was concentrated by distillation until crystallization. Upon cooling to 0°C a large crop of white plates formed which when filtered and washed with 100 ml cold EtOH gave 87.0 gm (0.89 mole) or 47% theoretical (based on the amine) N-propargyl urea, $HC{\equiv}C\text{-}CH_2NHCONH_2$, m.p. (white plates from EtOH) 129-130°C (literature[76] 128-129°C); nmr (CD_3COCD_3, ~5%, 30°C, A60-A, external standard TMS 10.0τ) : 3.95τ (broad mult.), 4.60τ (broad mult.) and 6.94τ (s) together integrating for 3H, 6.2τ (XY, 2H), 7.51τ (t, J = 2.5, 1H); ir (CD_3CN, ~10%, 0.1 mm, calibrated versus polystyrene) : 3475 cm^{-1}, 3370, 3270, 2930 (vw), 2105 (?), 1690, 1610, 1527, 1325, 1145, 660. Further concentration yielded an off-white second crop weighing 56 gm, m.p. 125-126°C.

Note A: Purification of dimethylformamide (DMF) was accomplished by the method suggested by Perrin.[162] Magnesium sulfate, 50 gm, was dried by heating under vacuum. DMF, 1.2 l, freshly opened ACS grade reagent, Matheson Coleman and Bell, was placed over this for twelve hours. Filtration and further drying over BaO for

twelve hours followed by a second filtration and distillation under 20 mm Hg pressure yielded a dry solvent which was stored over 4Å molecular sieves.

Note B: Phthalimide, freshly opened from Matheson Coleman and Bell, m.p. 232-234°C.

Note C: Propargyl bromide, Aldrich Chemical Co., was dried over active anhydrous $MgSO_4$ for twelve hours at 10°C in a tightly stoppered flask. Filtration followed by distillation under argon at atmospheric pressure through a 12" Vigreaux column taking the fraction distilling at 81°C yielded a dry reagent, stored over 4Å molecular sieves.

Note D: Benzylamine, $C_6H_5CH_2NH_2$, 900 gm, Matheson Coleman and Bell gold label was dried over NaOH pellets in the dark for twelve hours. The amine was filtered from the NaOH and then dried over Na chunks (washed in pentane). Distillation from sodium at 50 mm Hg pressure, taking the fraction distilling at 78°C yielded a dry reagent, stored over 4Å molecular sieves in a brown bottle.

Note E: Potassium cyanate (KOCN), 'Baker Analyzed Reagent,' J. T. Baker Chemical Co. used as received.

30.) N-Nitroso-N-propargyl urea[228(b)] (178b): N-Nitroso-N-propargyl urea (Note A) was prepared essentially as by Werner.[300] In a 3-liter beaker equipped with a large, flat magnetic stir bar and a suspended -150° to +50°C pentane thermometer was placed 48 gm

(0.49 mole) propargyl urea (178a) and 136 gm (1.97 mole) sodium nitrite. These were dissolved in 750 ml distilled water and the solution cooled to 5°C with an ice bath. A previously cooled solution of 96 gm (~0.98 mole) concentrated sulfuric acid in 500 ml water was added dropwise with stirring over two hours, keeping the internal temperature at 5°C or below. After approximately 75 ml of acid solution had been added, a yellow focculant precipitate rose to the surface and the blue solution began to evolve a red gas (NO_2). After the addition was complete, the mixture was stirred for a further hour, then saturated with NaCl and extracted with two liters of ether. The ether extract was washed with saturated Na_2SO_4 and dried over $MgSO_4$ for twelve hours. The ether was stripped with the pot at 0°C on a rotoevaporator and the product dried to constant weight on a vacuum line (0.01 mm Hg). In this way 40 gm (0.31 mole) or 67% of theoretical N-nitroso-N-propargyl urea (178b) was isolated; m.p. 69-70°C (literature[76] 69°C); nmr ($CDCl_3$, ~10%, 30°C, A60-A, internal standard TMS at 10.0τ) : 3.0-4.0τ (broad, 1H), 5.50τ (d, J = 2.5 Hz, 2H), 7.95τ (t, J = 2.5 Hz, 1H); ir ($DCCl_3$, ~0.1M, 0.1 mm, calibrated versus polystyrene): 3515 cm^{-1}, 3475, 3400, 3300, 2990, 1745, 1580, 1510, 1408, 1342, 1305, 1190, 1070, 900. This material was dissolved in 800 ml distilled water and two drops H_2SO_4 added as a preservative. The compound was stored as an aqueous solution at 5°C.

Note A: Nitroso ureas are potentially explosive, especially when dry. They are also known carcinogens. Thus, extreme care is

urged in their handling. Use of metal spatulas or exposure to any metal surface should be avoided, since this can initiate decomposition. Heat should be avoided, especially when dry. In my experience, the best way to store this material is in a slightly acidic (pH 6) aqueous solution.

31.) Diazopropyne[228(a)] (147): A. Diazopropyne was prepared as a pentane solution by the method of Skell and Gramas.[228(b)] To 225 ml NaOH, Na_2HPO_4 base buffer solution (Note A) saturated with NaCl and 50 ml olefin-free pentane cooled to 5°C in a 2-liter, 3-neck round bottom flask equipped with an addition funnel, magnetic stir bar, pentane low temperature (-150° to +50°C) thermometer and argon blanket inlet system was added 200 ml of a 0.39M solution of N-nitroso-N-propargyl urea in approximately 20 ml increments. The solution was stirred slowly to avoid foaming, maintaining the temperature below 10°C. After approximately 80 ml of the nitroso urea solution had been added, a polymer began forming on the interface of the pentane-buffer layers as evidenced by an insoluble brown foam. The pentane was removed at this time and replaced by another 50 ml and the reaction continued in this fashion, removing the pentane layer when the concentration of diazopropyne became high enough to cause polymerization until all the urea had been added. The final reaction mixture was stirred at 10°C for another hour and then allowed to warm slowly to room temperature. The combined dark orange pentane layers were dried over anhydrous Na_2SO_4 for three hours, decanted and used immediately.

The yield of diazopropyne was estimated to be 30% based on titration of a sample with 2N HCl to give propargyl alcohol. $HC{\equiv}C\text{-}CHN_2$, ir (pentane, ~5%, 0.1 mm) : 3315 cm^{-1}, 2120, 2065, 1358, 1057, 695. While such dilute solutions of diazopropyne were easily handled and did not decompose in the presence of ice or salt crystals, in general direct contact with sintered glass or sharp glass edges was avoided. Of particular note, one attempt to prepare a concentrated solution in pentane by vacuum transfer from a mineral oil solution resulted in a violent explosion upon warming the trap to -25°C. As with all diazo-compounds, skin contact or breathing the vapors should be avoided. B. An identical procedure was followed to prepare diazopropyne in olefin-free diethylether. Here a somewhat larger yield of 40% was possible. ir (diethylether, ~4%, 0.1 mm) : 3300 cm^{-1}, 3250, 3060, 2130, 2080, 670 (broad). All solutions of diazopropyne were disposed of by addition of acetic acid before discarding.

Note A: A buffered solution was prepared by dissolving 6.0 gm NaOH and 15.0 gm Na_2HPO_4 in 340 ml distilled water.

32.) 1,1-Dibromo-1-buten-3-yne (167): Using a reagent suggested by Corey and Fuchs,[266] 140 gm (0.53 mole) triphenylphosphine (Note A) and 34.2 gm (0.53 mole) freshly cleaned zinc dust (Note B) were placed in a dry 1-liter, 3-neck round bottom flask equipped with a rubber septum, a large magnetic stir bar, a reflux condenser topped with an argon blanket inlet system and a -50° to +150°C thermometer. One liter of methylene chloride

(Note C) was then added and the mixture stirred under an argon flow for $\frac{1}{2}$ hour to displace the dissolved oxygen. Ice bath cooling was initiated and 176 gm (0.53 mole) carbontetrabromide (Note D) added by syringe maintaining the reaction temperature below 28°C. After 30 minutes all the reagent had been added. The ice bath was removed and the reaction stirred overnight at room temperature. Propargylaldehyde, 14.5 gm (0.27 mole) from Preparation 1, was dissolved in 100 ml methylene chloride and the solution dried over Na_2SO_4 until clear. The Zn, Ph_3P, CBr_4 reagent was cooled to 5°C with an ice bath and the filtered aldehyde solution added dropwise with vigorous stirring. After the addition was complete (~30 minutes), the reaction mixture was allowed to warm to 23°C and stirred at this temperature for a further two hours. Workup was accomplished by removal of most of the methylene chloride by rotoevaporation and pouring the resultant into 500 ml 50% aqueous methanol and 500 ml ether. Water was added until the ether layer separated and the water layer further extracted with 3 × 500 ml ether. The combined ether extracts were washed with one liter distilled water and dried over $MgSO_4$ overnight. The ether was filtered, stripped on a rotoevaporator and the resultant chromatographed on 500 gm act III Woehm silica gel eluting with pentane. The product emerged with an R_f of 0.47 as a light yellow liquid, 34.5 gm or 61% theoretical $HC{\equiv}C\text{-}CH{=}CBr_2$, glc (Note E) showing ~5% in the ir and nmr spectra to be the allenic dibromide $H_2C{=}C{=}C{=}CBr_2$. Nmr (CCl_4, ~10%, 30°C, A60-A, internal standard TMS 10.0τ) : 3.48τ (d, J = 2.5 Hz, 1H) and 6.62τ (d, J = 2.5 Hz,

1H); ir (pentane, ~10%, 0.2 mm) : 3315, 3190 (w), 2045, 1475, 1390, 1130, 740.

Note A: Freshly opened triphenylphosphine, m.p. 79-5-80.0°C, from Matheson Coleman and Bell, used as received.

Note B: Forty grams of zinc metal dust from Mallinckrodt Chemical Works was washed with one liter 5% HCl then three times with one liter of distilled water. Drying was accomplished by washing three times with one liter of acetone and three times with one liter of ether followed by vacuum drying.

Note C: Methylenechloride, ACS reagent grade, Matheson Coleman and Bell Co., Inc., was cleaned by shaking with portions of concentrated H_2SO_4 until the acid layer remained colorless. The acid was removed by washing with water, 5% aqueous $NaHCO_3$ and then with water again. After predrying over calcium chloride, the washed dichloromethane was distilled from calcium hydride at 40°C, taking the center fraction. This was stored in a brown bottle over 4Å molecular sieves.

Note D: Carbontetrabromide, Matheson Coleman and Bell gold label reagent grade, was used as received without purification.

Note E: Analytical chromatography was performed on the $10' \times \frac{1}{4}''$ glass 20% SE30 column ( ) at 190°C Varian 90P oven temperature, 60 ml/min He carrier flow, 1 μl injections X1 at 210°C. Retention

times in minutes from air peak: pentane, 0.8; $HC{\equiv}C\text{-}CH{=}CBr_2$, 4.3; allenic impurity, 5.2; unknown impurity, 13.0.

33.) β-Ethynyl-1,3-dithia-2-methylenecyclohexane (~~): Using a reagent as suggested by Corey and Märkl,[272] 4.0 gm (0.027 mole) 1,3-dithiacyclohexan-2-thione (Note A) and 12.0 gm (0.097 mole) trimethylphosphite (Note B) were placed in a 100-ml, 3-neck round bottom flask equipped with a magnetic stir bar, reflux condenser topped with an argon blanket inlet system, -50 to +150°C thermometer, and a serum cap. This solution was stirred at 25°C for one hour under an argon flow to remove dissolved air and at 45°C internal temperature (silicone oil bath heating) for four hours to form the ylide. The disappearance of the thione and the appearance of two products in roughly 1:1 ratio as described by Corey was followed by glc (Note C). Nmr showed new absorptions in the 6.3τ region due to the $P\text{-}OCH_3$ protons of the ylide and the thionophosphate biproduct $(CH_3O)_3PS$ and only 10% contamination by a doublet at 8.55τ due to a thermal rearrangement product of the ylide. This yellow reaction mixture was then cooled to -20°C under argon (CO_2 ice-isopropanol bath) and 1.46 gm (0.017 mole) neat, dry propargyl aldehyde (Preparation 1) was syringed in slowly maintaining this temperature (roughly 30 minutes for addition). The resulting orange solution was stirred for two hours at -20°C and then allowed to warm to room temperature whereupon considerable darkening occurred, probably due to polymerization of the remaining aldehyde. Glc showed one new product of retention time shorter than the

phosphorous-containing materials. Nmr revealed in this crude product a clear doublet at 4.64τ from which a 20% yield was estimated based on the ylide. Most of the excess trimethylphosphite was distilled by CO_2 assisted vacuum transfer (Note D) and the remaining black residue chromatographed on 250 gm act III Woehm silica gel, eluting with 10% ether in pentane. After 0.8 liter of solvent, the product emerged as a light yellow, sweet smelling oil but containing considerable $(MeO)_3P$ by glc analysis. Preparative glc, however, allowed isolation of 1.3 gm pure ketenethioacetal, $HC{\equiv}C\text{-}CH{=}\overline{C\text{-}S\text{-}(CH_2)_3\text{-}S}$ as a colorless oil, nmr ($DCCl_3$, ~5%, 30°C, A60-A, internal standard TMS at 10.0τ) : 4.27τ (d, J = 2.5 Hz, 1H), 6.55τ (d, J = 2.5 Hz, 1H), 6.8-7.2 (broad multiplet, 4H), 7.8τ (m, 2^+H); ir ($HCCl_3$, ~1%, 0.2 mm, calibrated versus polystyrene) : 3300 cm^{-1}, 3030 (broad), 1740, 1415, 1295, 920, 700, 655; uv (diethylether) : λ_{max} 293 nm.

Note A: 1, 3-Dithiacyclohexan-2-thione was prepared by the method of Mills and Saunders from 2.3 gm (0.1 mole) oil-free sodium, 75 ml absolute EtOH, 5 gm (0.066 mole) CS_2 (Matheson Coleman and Bell), 10.8 gm (0.0535) trimethylene dibromide (Aldrich Chemical Co.) and H_2S from Matheson, dried by passage through a tower of 3Å molecular sieves. The crude yellow oil from this preparation was dissolved in 200 ml boiling ethanol and the solution cooled to -40°C to give 4.85 gm or 60% fine, silky yellow needles, dried under vacuum, m.p. 75-76°C, nmr ($DCCl_3$, ~5%, 30°C, A60-A,

internal standard TMS at 10.0τ) : 6.73τ (broadened triplet, J ~ 5.5 Hz, 4H) and ~7.53τ (m, 2H).

Note B: Trimethylphosphite, Matheson Coleman and Bell, gold label reagent (ACS) grade was used as received.

Note C: Analytical chromatography was performed on the 10' × $\frac{1}{4}$" glass 20% SE30 column (B) at 185°C Varian 90P oven temperature, He carrier flow 60 ml/min, 1 μl injections at 200°C, X4. Retention times in minutes from the air peak: trimethylphosphite, 1.5; β-ethynyl-1,3-dithia-2-methylenecyclohexene, 8.3; phosphorous products, 14.0, 15.5, 17.5.

Note D: See Preparation 35, Note C.

34.) 1-Methoxy-1-buten-3-yne (150): Cis-1-methoxy-1-buten-3-yne was obtained from Aldrich Chemical Co. as a 50% solution in aqueous methanol. A 100 ml portion of this solution was diluted with 500 ml distilled water and extracted five times with 100 ml portions of ether. The ether extracts were combined, washed with two portions of 100 ml saturated aqueous Na_2SO_4 and dried over anhydrous Na_2SO_4 for twelve hours at 5°C. The diethylether was distilled on a rotoevaporator with the pot at 0°C losing only a small portion of the eneyne. Glc (Note A) showed several impurities of higher boiling point. Fractional distillation through a 3-foot, vacuum-jacketed tantalum wire coil column at 50 mm Hg taking the fraction distilling at 42.0-42.5°C failed to remove all of these impurities as well as creating yet another as a thermal product

representing approximately 1% of the mixture. However, preparative scale glc (Note B) produced 150 in high purity, sufficient to see even a 0.1% yield of any product of carbene addition. The 50 ml of material prepared in this fashion remained free of rearranged or disproportionated product if stored below 0°C and used below 25°C. Analyzed by glc, nmr, and ir to be one isomer, cis-1-methoxy-1-buten-3-yne, nmr ($DCCl_3$, ~10%, 35°C, A60-A, internal standard TMS at 10.0τ) : 3.63τ (d, J = 6.6 Hz, 1H), 5.50τ (dd, J = 6.6, 2.4 Hz, 1H), 6.20τ (s, 3H), 6.92τ (d, J = 2.4 Hz, 1H); ir ($DCCl_3$, ~10%, microcell 0.01 mm) : 3310 cm^{-1}; 2950, 2865, 2113, 1630, 1456, 1388, 1271, 1120, 1024; uv (hexane) : λ_{max} 285.5 nm. Photolysis of a degassed sample sealed in a Pyrex tube with a 450 watt Hanovia No. 679A36 medium pressure Hg lamp at 10°C showed no photoproducts after 30 minutes. After one hour the material seen as a thermal product was detected but in $\ll$1% yield.

Note A: Analytical gas chromatography was performed on a 22' × $\frac{1}{8}$" 20% SE30 column (I) on the HP 5750, oven temperature 100°C, He flow rotometer 0.5 at 75 psi, range 1×10^3, attenuation X16, display X10, 1 μl injection at 150°C. Retention time in minutes from injection: cis-150, 24.3; thermal product, 36.2.

Note B: Preparative work was performed on a 10' × $\frac{3}{8}$" glass 20% SE30 column (E) on the Varian 90-P, oven temperature program 90°C to 120°C, He flow ~80 ml/min, attenuation X128, 300 μl injection over 30 sec at 125°C.

35.) 1, 2-Diethynyl-3-methoxycyclopropane (61d): A. To 250 ml of an ether solution containing approximately 8 gm (0.12 mole) diazopropyne (147) was added 20 gm (0.24 mole) glc pure 1-methoxy-1-buten-3-yne (150). (See Preparations 31 and 34.) This solution was placed in a standard quartz photolysis well and degassed for two hours with a slow flow of argon. The entire apparatus was placed in a -20°C circulating bath and photolysis carried out at 5°C internal temperature with a 450 watt Hanovia No. 679A36 medium pressure Hg vapor lamp with a Pyrex filter. The progress of the reaction was monitored by ir to disappearance of the 2080 cm^{-1} diazo band (Note A) after one hour irradiation. Glc (Note B) showed one new product of higher boiling point than the methoxyeneyne in approximately 1% yield as well as a 2% yield of cis- and trans-60 based on the diazopropyne. The thermal products of the methoxyeneyne were also seen but in much lower yield. The red-brown solution was removed from the photolysis well and most of the diethylether distilled under argon through a 3-foot, tantalum wire coil, vacuum-jacketed column maintaining the pot below 65°C. The oil remaining in the pot was vacuum transferred with CO_2 assistance (Note C). The cyclopropyl product was isolated by preparative glc (Note D), collecting the methoxyeneyne as well (to be recycled). Ir showed that the photoproduct prepared in this way contained as much as 25% methoxyeneyne. A second preparative glc isolation from a benzene solution produced 60 mgm (5×10^{-4} mole) relatively pure 1, 2-diethynyl-3-methoxycyclopropane in any appropriate solvent. Nmr ($DCCl_3$, ~5% soln., 30°C, A60-A, internal

standard TMS at 10.0τ: : 6.48τ (s, methyl) and 6.55τ (partially obscured triplet or dd, J ~ 5.2 Hz, methoxymethine) together integrating for 4H, 7.99τ (d, J = 1.0 Hz, 1H, ethynyl), 8.10τ (d, J = 1.0 Hz, 1H, ethynyl), 8.30τ (m, J ~ 5, 2, 1 Hz, 2H, propargylic methines); nmr (C_6F_6, ~5% soln., 30°C, A60-A, external standard TMS at 10.0τ) : 7.07τ (s, 3H, methyl), 7.32τ (dd, J ~ 5, 3 Hz, 1H, methoxymethine), 8.78τ (overlapping doublets, J ~ 1 Hz, 2H, ethynyls), 9.15τ (m, 2H, propargylic methines); nmr (THF-d_8, ~5% solution, 30°C, A60-A, internal standard TMS) : 6.60τ (s, methyl) and 6.5-6.7τ (m, methoxymethine) together integrating for 4H, 7.76τ (two overlapping doublets, J ~ 1 Hz, 2H, ethynyls), 8.35τ (m, J ~ 4.5, 2, 1 Hz, 2H, propargylmethines); ir (CCl_4, ~5%, microcell, 0.1 mm, calibrated versus polystyrene) : 3305 cm^{-1} (s), 3030, 2990, 2930, 2890 (sh), 2850, 2820, 2120, 1450, 1395, 1330, 1220 (s), 1185, 1122 (s), 1072, 1025, 972, 650; ms (electron energy 70 v) : m/e 121 (9.3, P+1), 120 (81.8, P), 119 (57.0), 105 (620), 91 (1380), 90 (868), 89 (1580), 77 (1400), 65 (215), 63 (255), 51 (782). While this material was relatively stable, exposure to air was avoided. The product was handled by vacuum transfer and the nmr spectra were obtained in tubes sealed under vacuum. B. In an attempt to prepare considerably more concentrated solutions of diazopropyne in methoxybutenyne solvent, diazopropyne was extracted from pentane solution into the eneyne (insoluble in cold pentane) by repeated equilibration of 6 ml of each, recycling each layer. The final 6 ml 1-methoxy-1-buten-3-yne contained the diazopropyne from 36 ml pentane. Glc (Note B) analysis of this solution showed a

substance with a retention time identical to that of the photoproduct found in A and in approximately the same yield based on the eneyne. Preparative glc isolation of this material allowed confirmation of its identity as the 1, 2-diethynyl-3-methoxycyclopropane, now apparently formed from pyrolysis of a pyrazoline in the glc injector port. Ir and nmr showed no evidence for a pyrazoline but considerable remaining diazopropyne. Upon standing at 0°C for three days, ir showed virtually 90% loss of the initial diazopropyne but no increase in the cyclopropyl product on glc pyrolysis, even at 250°C injector port temperature. Repetition of this experiment showed that the yield of 3-methoxy-1, 2-diethynylcyclopropane was very erratic by this method. Photolysis of this solution, however, as above in a Pyrex tube under argon consistently produced a 5% yield of the photoproduct, identical in all respects to the above.

Note A: A 10 μl sample was taken from the reaction mixture through a rubber septum and injected into 100 μl of Spectroquality CCl_4 in a 0.2 mm sodium chloride cavity cell.

Note B: The analytical glc work was performed on the glass 10' × $\frac{1}{4}$" 20% SE30 column (B) at 75°C Varian 90-P oven temperature, He carrier flow 60 ml/min, attenuation X2, 1 μl injections at 150°C in a glass lined injector block. Retention times in minutes from the air peak: ether, 1.0; trans-60, 2.2; cis-60, 2.6; 1-methoxy-1-buten-3-yne, 4.4; thermal product, 15.0; thermal product, 17.0; photoproduct, 21.8; thermal product, 23.0.

Note C: Engell, Kimland and Rosengren[276] described a mild method for vacuum transfer of high boiling materials which in my case proved to be an effective method for removing volatiles from polymeric material without heating. The oil from the distillation pot was placed in flask A, Figure XL and thoroughly degassed by three freeze-thaw cycles under 0.01 mm Hg. After the final degassing cycle, the apparatus was closed to the vacuum line and the oil in A allowed to melt. Liquid nitrogen cooling was begun on B and a slow (~60 ml/min) flow of CO_2 begun. The solid CO_2 condensed in B effecting a "steam distillation" of the products. The flask B was allowed to melt under continued CO_2 flow (~20 ml/min) and the distillate removed by syringe.

Note D: The photoproduct was isolated in a CO_2 ice-isopropanol, -78°C trap by preparative scale glc on the 10' × $\frac{3}{8}$" 20% SE30 column (E) at 115°C Varian 90-P oven temperature, 60 ml/min He carrier flow, 50 μl injections at 150°C over 30 seconds with the TC detector at 160°C. A solvent was vacuum transferred onto the frozen material, and then the trap was warmed to 25°C under argon. The product was removed by vacuum transfer.

36.) 3-Methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d): The quartz tube of the atmospheric pressure pyrolysis apparatus pictured in Figure XIV was equilibrated to 310°C at the midpoint for one hour. A solution of 20 mgm 3-methoxy-1, 2-diethynylcyclopropane in 0.4 ml C_6F_6 or d_8-THF (Note A) was then syringed into the vaporizor flask under a dry helium flow of 60 ml/min.

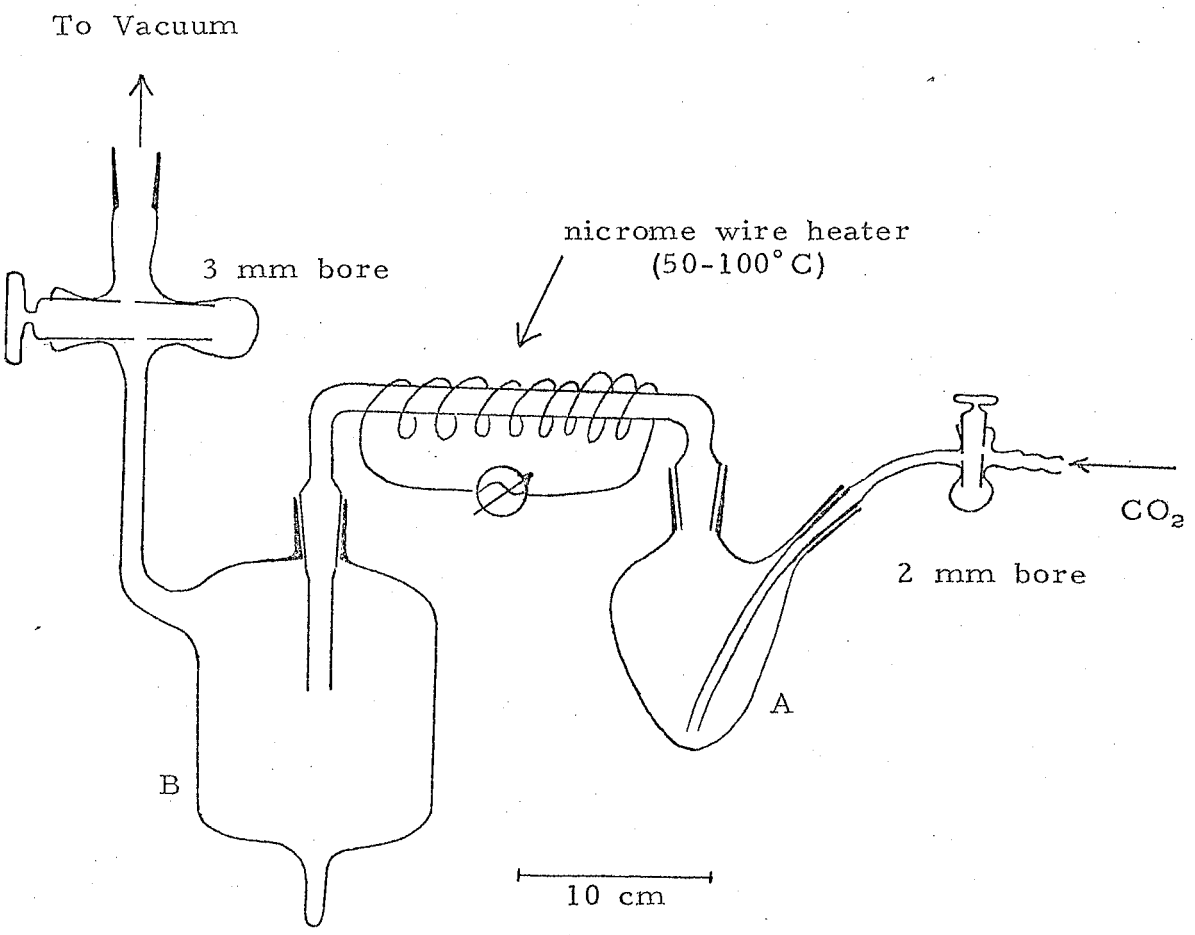

Figure XL

CO_2-Assisted Vacuum Transfer Apparatus

The pyrolysate was collected in a series of two U traps, cooled to -78°C with a CO_2 ice-isopropanol bath. A small amount of a brown, insoluble polymer formed where the hot flow first struck the cold trap. This collected material was then vacuum transferred into a 10 ml pear-shaped flask and a rubber septum installed under argon. Glc analysis (Note B) showed complete destruction of the starting material and only one new product peak in 5% yield but at much longer retention time. A crude nmr of a sample of this material showed it to be most likely a mixture of olefinic methyl ethers. A mass spectrum was not obtained although it is conceivable that this material is dimeric. Upon opening the remaining solution in the flask to air, a large amount of insoluble brown polymer formed in a few minutes. Repetition of this pyrolysis, vacuum transferring the collected product into an nmr tube and sealing under vacuum showed a quantitative yield of a new olefinic methylether, identified by comparison of its nmr with the known bicyclo[3.2.0]hepta-1, 4, 6-triene[76] as 3-methoxybicyclo[3.2.0]-hepta-1, 4, 6-triene, nmr (C_6F_6, ~5%, 30°C, A60-A, external standard TMS 10.0τ) : 3.26τ (m, 2H), 4.88τ (m, 1H), 5.00τ (m, 2H), 6.88τ (s, 3H); nmr (THF-d_8, ~5%, 30°C, A60-A, internal standard TMS 10.0τ) : 2.93τ (m, 2H), 4.45τ (m, 1H), 4.72τ (m, 2H), 6.81τ (s, 3H); ms (electron energy 70 volts) : m/e (% of base peak, 121 (0.5), 120 (4), 105 (40), 91 (75), 90 (63), 89 (100), 63 (39), 51 (23), 39 (30), corrected for background d_8-THF. These solutions were thoroughly dried by vacuum transfer onto CaH at 0°C for 10 minutes before use.

Note A: See Preparation 35; the choice of solvent depended on the use intended for the sample. Both solvents employed were dried over purified potassium metal (see Note A, Preparation 37) for 24 hours and vacuum transferred onto the glc prepped diethynylcyclopropane.

Note B: Analytical glc was carried out on the $10' \times \frac{1}{4}''$ glass 20% SE30 column (B) at 95°C Varian 90-P oven temperature, He carrier flow 60 ml/min, 5 μl injections at 150°C X1. Retention times in minutes from air peak: C_6F_6, 1.5; toluene standard, 4.3; 3-methoxy-1, 2-diethynylcyclopropane, 10.5; 3-methoxybicyclo[3.2.0]heptatriene ?, 25.5; dimeric ? products, 35.5.

37.) Reaction of 3-Methoxy[3.2.0]hepta-1, 4, 6-triene (62d) with Potassium Mirror: Using conditions employed by Katz and Garratt[302] to prepare nmr observable concentrations of the cyclononatetraenyl anion, 0.015 gm (3.85×10^{-4} mole) purified potassium (Note A), washed free of oil by pentane, was placed in bulb A of the apparatus pictured in Figure XLI. The entire apparatus was heated with a yellow, soft flame under vacuum to remove traces of moisture as well as the pentane from the potassium. A blue flame was used sparingly to distill approximately half of the potassium into a mirror on the upper end of the attached nmr or esr tube (Note B). Into the B flask of the same apparatus was vacuum transferred 0.2 ml of a d_8-THF solution containing approximately 10 mgm 3-methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d) from drying over CaH_2 (Note C). The solution was thoroughly degassed by three

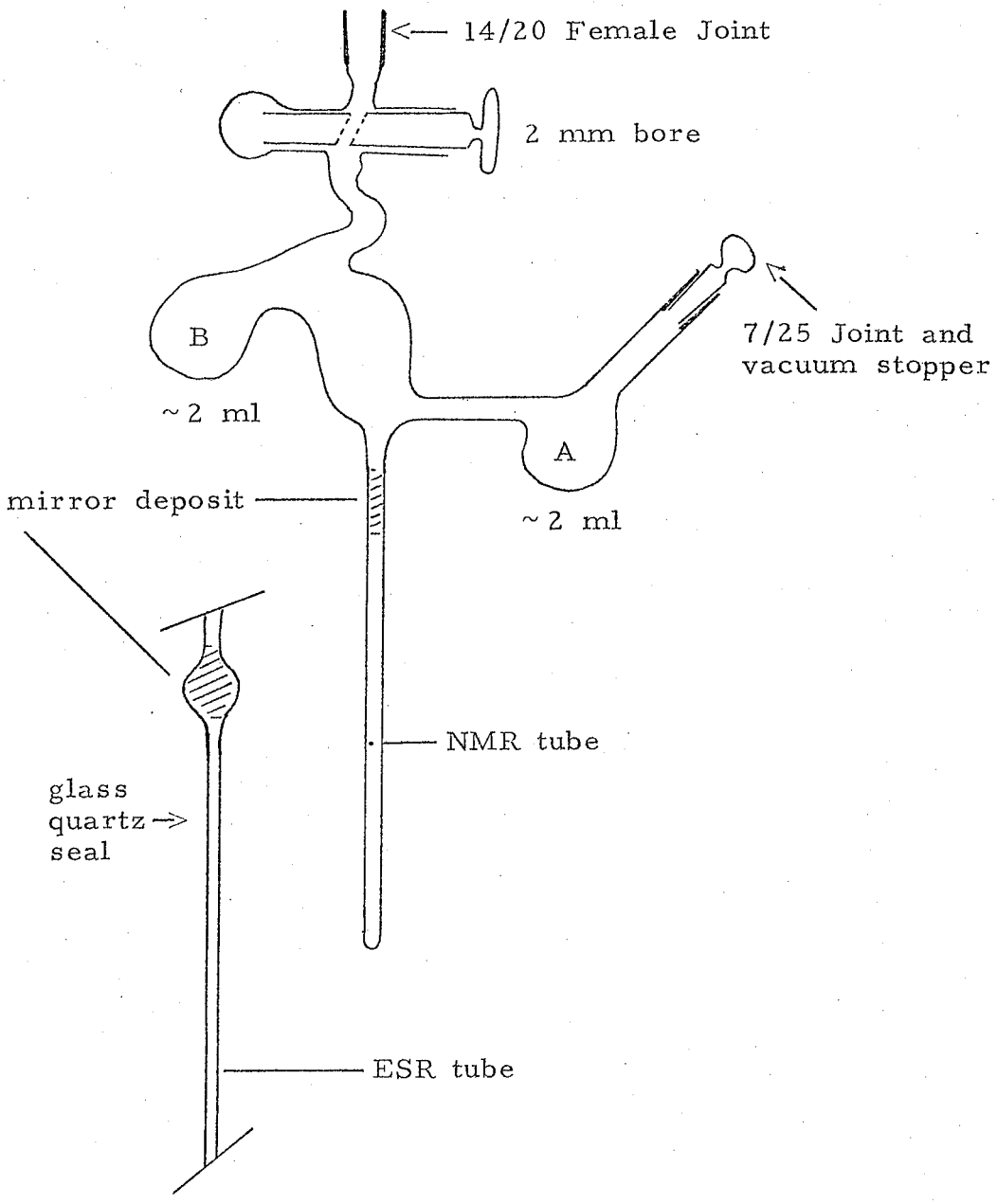

Figure XLI

Apparatus for Reaction with Metallic Mirrors

freeze-thaw cycles (LN2) and then finally pumped down to 0.001 mm Hg pressure. The stopcock (see Figure XLI) was then closed and the triene-THF solution vacuum transferred to the bottom of the nmr or esr tube. The tube was sealed under 0.001 mm Hg pressure (stopcock open) somewhere above the level of the mirror. The solution was allowed to melt by placing the entire tube in a -40°C bath. An initial nmr or esr was taken. The tube was then inverted and the solution allowed to contact the mirror at -40°C. Immediately a brown coating formed on the mirror. After one hour at this temperature, the tube was inverted and a spectrum taken. Esr showed no signal; nmr showed only a slight reduction in the intensity of the triene spectrum but no new absorptions. The tube was reinverted and allowed to stand for 12 hours over the potassium in a -50°C freezer after which time nmr showed roughly 50% destruction of the triene signals but no new products in what was now a red-brown solution with polymer coating the mirror. In the esr experiment, again no signal was observed. The solution was then placed in contact with the mirror at 25°C with vigorous shaking for two hours. This resulted in complete destruction of the triene as monitored in the nmr, the formation of a brown insoluble polymer and no esr signal. After cooling to -10°C, the tubes were broken open below the mirror and the liquid quenched with methanol. No appreciable color change was noted. Filtration and examination in the nmr and glc (Note D) showed no evidence of olefinic products. Although a standard workup with added authentic dimers was not performed, it

is estimated that as little as 5% yield of 95 could have been detected.

Note A: Purified potassium, J. T. Baker, was further cleaned of oxides and hydrocarbon by the method of Johnson.

Note B: Two experiments are described here. One employed a thick wall glass nmr tube, 0.4 cm I.D., and analysis at -40°C (A56-60). The other was completely identical except that a 20 cm quartz esr tube, 0.2 cm I.D., was employed with analysis at -40°C in a Varian V4500 X-band esr spectrometer. Both tubes were soaked in 5% aqueous EDTA, KOH for 24 hours then rinsed well with distilled water followed by acetone and drying at 150°C. Since it was very difficult to distill a mirror into an esr tube due to its small size, the mirror was actually formed in a Pyrex glass bulb above a sealed on (graded) esr tube. The esr spectra were scanned over a range of 1000 gauss centered at 3300 gauss. DPPH was employed as a standard marker in a separate sample tube.

Note C: See Preparation 36; the amounts of material quoted are based on the starting methoxycyclopropane assuming quantitative conversion in the pyrolysis at 310°C.

Note D: A 5' × $\frac{1}{4}$" glass 5% SE30 column (A) was employed at 85°C, 60 ml/min helium flow, 10 μl injections X2 at 125°C on a Varian 90P with TC detector at 150°C.

38.) Reaction of 3-Methoxybicyclo[3.2.0]hepta-1, 4, 6-triene (62d) with SbF_5 and $HOSO_2F$: The conditions suggested by Saunders, et al.,[188(b)] were modified to include a catalytic amount of fluorosulfonic acid. Into flask A of the apparatus pictured in Figure XXXIV (Note A) were placed 0.1 ml SbF_5 (Note B) and 0.01 ml of a 1:1 mixture of FSO_3H and SbF_5 (Note C) under anhydrous conditions in a dry box under nitrogen (Note D). The apparatus was attached to a vacuum line capable of 0.001 mm Hg and 0.2 ml of a C_6F_6 solution containing approximately 10 mgm (8.3×10^{-5} mole) methoxytriene 62d was vacuum transferred from drying over CaH_2 into flask C. Both solutions were thoroughly degassed by three freeze-thaw cycles. Liquid nitrogen cooling was begun to the indicated mark (see Figure XXXIV) in flask B and the stopcocks to A and C opened after closing off the apparatus to the vacuum. The transfer of the SbF_5 was assisted by a low (yellow) flame with periodic closing of the stopcock to C to maintain an even mixture in the deposit in B. After transfer of all the SbF_5 was complete, 0.2 ml SO_2 (Note E) was distilled into flask B and the entire sample allowed to melt at -78°C and flow into the attached nmr tube. The tube was then refrozen in LN2, vacuum again introduced, and the tube sealed while pumping. The sample was allowed to melt in an nmr probe at -60°C (Note F). ^1H nmr analysis showed complete disappearance of starting triene 62d and broad new absorptions at 6.12τ due to protonated CH_3OHSbF_5 (3H) and somewhat less clearly, 1.15τ (2H) and 1.70τ perhaps due to 30c. In addition, signals at 0.38τ ($HOSO_2F$) and 1.8τ (H_3O^+) were seen,

the latter interfering with the integration of the 1.7τ signal. These signals, except for a large decrease in the H_3O^+ absorption, remained unchanged upon warming. Unfortunately, this sample was lost before a quenching experiment with methanol could be performed. Although a coupling of ~4 Hz was noticed in the 1.15τ absorption, in general the amount of material present in this sample was not sufficient to obtain any structural detail.

Note A: The apparatus in Figure XXXIV was constructed according to Saunders.[188] All joints and stopcocks were lubricated with Kel-F fluorocarbon grease (3M). The only modification I desired after this initial use was the removal of a stopcock between flask A and B since it interfered with the transfer of the SbF_5 and eventually became permanently stuck anyway.

Note B: Antimony pentafluoride, SbF_5, was purchased from Allied Chemical Company and was used as received. The material was transferred with a calibrated Teflon pipet in a dry box.

Note C: "Magic acid," a 1:1 mixture of fluorosulfonic acid and antimony pentafluoride, was purchased from Aldrich Chemical Co. and was dispensed with a Teflon pipet in a dry box.

Note D: Nitrogen, CIT 99.5% pure-dry, was passed through two towers of 500 gm 3Å molecular sieves (activated at 150°C for 12 hours) and into a make-shift dry box constructed from a glove bag. The dryness of the atmosphere inside could be judged by whether or not the SbF_5 "fumed" when opened.

Note E: Sulfur dioxide gas was purchased as a lecture bottle from Matheson. The gas was dried by passage through concentrated H_2SO_4 and then a tower of anhydrous $CaSO_4$. The SO_2 was condensed out in a flask on the vacuum line where it was degassed prior to transfer into the reaction flask.

Note F: See Preparation 37, Note C.

Note G: See Preparation 37, Note A.

39.) 1-Methoxycyclohepta-2, 4, 6-triene[17(b)] (180): According to a procedure outlined by Harrison, et al.,[303] 10.0 gm (0.056 mole) recrystallized tropyliumfluoroborate (Note A) was dissolved in 200 ml absolute methanol in a one-liter Erlenmeyer flask topped with a $CaCl_2$ drying tube by heating to 70°C in a water bath. At this temperature was added 2.3 gm (0.10 mole) cleaned sodium (Note B) dissolved in 75 ml absolute methanol in one portion all at once. After cooling to 23°C, this methanol solution was diluted to one liter with distilled water and extracted with four 100 ml portions of pentane. The pentane extracts were dried over $MgSO_4$ for 12 hours, filtered, and the solvent removed by rotoevaporation to give 7.5 gm of a light yellow oil. Glc analysis (Note C) showed one major product which was isolated glc pure by preparative scale gas chromatography. Nmr (CCl_4, ~10%, 30°C, A60-A, internal standard TMS at 10.0τ) : 3.47τ (broad triplet, J ~ 3.0 Hz, 2H), 4.0τ (complex doublet of multiplets, J_{major} ~ 11 Hz, 2H), 4.68τ

(dd, J = 11, 4 Hz, 2H), 6.65τ (s, 3H), 6.85τ (m, 1H), identical to a spectrum reported by Borden.[280]

Note A: Tropyliumfluoroborate, $C_7H_7^+BF_4^-$, was prepared by the one-step procedure of Dauben, et al.,[298] from 20.0 gm (0.080 mole) triphenylmethanol (Matheson Coleman and Bell, gold label) and 12.5 ml (0.105 mole) 48% fluoroboric acid (Baker and Adamson) in 200 ml acetic anhydride titrating with cyclohexatriene (Aldrich) to a colorless solution. Precipitation with ether and recrystallization from CH_3CN gave 10.0 gm $C_7H_7^+BF_4^-$ as white plates, m.p.: 210°C (dec.); nmr (CD_3CN, 30°C, internal standard TMS at 10.0τ) : 0.60τ (s).

Note B: Purified sodium from J. T. Baker was further cleaned by the method of Newman as reported by Fieser.[304]

Note C: The 10' × $\frac{3}{8}$" glass 20% SE30 column (E) was employed at 155°C, He flow 100 ml/min, analysis by injecting 10 μl neat, preparative by injecting 100 μl neat over 15 seconds at 175°C injector port temperature, TC detector 210°C. Retention time in minutes from air peak: methoxycycloheptatriene, 19.1 min.

40.) Bicyclo[3.2.0]hepta-1, 4, 6-triene (48): 1, 2-Diethynylcyclopropane (61a) was prepared as described by D'Amore[76] as a concentrated solution in pentane. By preparative glc (Note A), 100 μl of the trans-61a was isolated and dissolved in 3.5 ml dry olefin free hexane. This solution was pyrolyzed by submitting it to two vacuum transfers through a 485°C quartz tube in the apparatus

pictured in Figure XV. Preparative glc (Note B) yielded 30 mg triene 48 as an air sensitive liquid. Solvent was transferred onto the frozen 48 in the trap before warming. Analytical glc (Note C) showed this material to be 99+% pure. Nmr (CD_3CN, ~10%, 30°C, sealed under vacuum, A60-A, internal standard TMS at 10.0τ): 3.02τ (A^2B), 4.61τ (A^2B), 6.55τ (A^2B).

Note A: Preparative glc on a glass 10' × ⅜" 20% SE30 Column (E) at 50°C Varian 90-P oven temperature, He carrier flow 60 ml/min, 300 μl injections at 75°C over 15 seconds, TC detector 150°C. Retention times in minutes from air peak: trans-1, 2-diethynyl-cyclopropane, 32-36 min.

Note B: Preparative glc on a glass 10' × ⅜" 20% SE30 Column (E) at 65°C Varian 90-P oven temperature, He carrier flow 60 ml/min, 50 μl injections at 75°C, TC detector 100°C.

Note C: Analytical glc on a 10' × ¼" glass 20% SE30 Column (B) at 55°C Varian 90-P oven temperature, He flow 60 ml/min, 1 μl injection of a 10% solution at 75°C, TC detector 100°C.

41.) Reaction of Bicyclo[3.2.0]hepta-1, 4, 6-triene (48) with Triphenylmethylfluoroborate: A. Using a modification of a procedure employed by Dauben, et al.,[305] 30 mgm (3.3×10^{-4} mole) triene 48 in 0.1 ml dry CD_3CN (Note A) was thoroughly degassed and then vacuum transferred onto a frozen solution of 110 mgm (3.3×10^{-4} mole) $Ph_3C^+BF_4^-$ (Note B) in 0.2 ml CD_3CN also thoroughly degassed in an nmr tube. The tube was sealed under

vacuum and allowed to warm to 25°C without agitation. A bright red color developed where the triene solution contacted a few crystals of the $Ph_3C^+BF_4^-$. After all the solids had dissolved, the tube was thoroughly shaken at 25°C resulting in the formation of a dark red-brown color which turned to black in a matter of seconds with precipitation of a black solid. Nmr showed complete destruction of the bicycloheptatriene 48 and the presence of Ph_3CN. No absorptions which might be attributed to a cation were seen. The tube was broken open and the contents quenched with water. Extraction with pentane and examination by glc (Note C) showed a 30% yield of Ph_3CH and a 30% yield of recovered Ph_3C^+ as Ph_3COH, yields based on the initial $Ph_3C^+BF_4^-$. B. Preparation 41.A was repeated except that the tube was recooled to -40°C in a CO_2-ice isopropanol bath before mixing. Here a red-brown color developed slowly. Nmr examination at -40°C (Note D) showed the presence of triene 48 and Ph_3C^+. Upon warming to -20°C the triene was observed to disappear with a half-life of approximately 30 minutes. A small amount of Ph_3CH was detected but again no absorptions due to the expected 30c. Quenching with water as above and extraction with pentane confirmed a 5% yield of Ph_3CH and no 48 or alcohol 62h (Note C).

Note A: Deuteroacetonitrile, CD_3CN, was purchased from Stohler Isotope Corp. and was dried for 48 hours over 3Å molecular sieves before use.

Note B: Triphenylmethyl fluoroborate, $Ph_3C^+BF_4^-$, was prepared from 10.5 gm (0.04 mole) triphenylmethanol (Matheson Coleman and Bell), 10.5 ml (0.09 mole) 48% fluoroboric acid (Baker and Adamson) and 105 ml propionic anhydride as described by Dauben, et al.[298] Recrystallization of this crude material from CH_3CN yielded orange needles, m.p. 210°C (dec.) [literature 215° (dec.)]. ^1H nmr (CD_3CN, ~10% solution, 30°C, A60-A, internal standard TMS at 10.0τ) : complex mult., 1.7τ-2.2τ in good agreement with the spectrum reported and reproduced by Farnum.[306] Quenching with H_2O and extracting with pentane showed this material to be free of triphenylmethane by glc analysis.

Note C: Analytical glc was performed on a 10' × $\frac{1}{4}$" glass 20% SE30 Column (B) at 200°C Varian 90-P oven temperature, He carrier flow 60 ml/min, 5 μl injections at 210°C att. X1, TC detector 250°C. Retention times in minutes from air peak: PH_3CH, 4.0 min., Ph_3COH, 6.0 min.

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