Synthesis and Matrix Isolated Photolysis of 2,3-Dimethylbicyclo[2.2.0]hexa-2,5-diene-1,4-dicarboxylic Acid Anhydride: A Potential Precursor to 2,3-Dimethyl-1,4-dehydrobenzene

Thesis by

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To Janet

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ABSTRACT

The synthesis of the first member of a new class of Dewar benzenes has been achieved. The synthesis of 2,3-dimethylbicyclo[2.2.0]hexa-2,5-diene-1,4-dicarboxylic acid and its anhydride are described. Dibromomaleic anhydride and dichloroethylene were found to add efficiently in a photochemical [2+2] cycloaddition to produce 1,2-dibromo-3,4-dichlorocyclobutane-1,2-dicarboxylic acid. Removal of the bromines with tin/copper couple yielded dichlorocyclobutenes which added to 2-butyne under photochemical conditions to yield 5,6-dichloro-2,3-dimethylbicyclo[2.2.0]hex-2-ene dicarboxylic acids. One of the three possible isomers yielded a stable anhydride which could be dechlorinated using triphenyltin radicals generated by the photolysis of hexaphenylditin.

Photolysis of argon matrix isolated 2,3-dimethylbicyclo-[2.2.0]hexa-2,5-diene-1,4-dicarboxylic acid anhydride produced traces whose strongest bands in the infrared were at 3350 and 600 cm^{-1}. This suggested the formation of terminal acetylenes. The spectra of argon matrix isolated E- and Z-3,4-dimethylhexa-1,5-diyne-3-ene and cis- and trans-octa-2,6-diyne-4-ene were compared with the spectrum of the photolysis products. Possibly all four diethynylethylenes were present in the anhydride photolysis products. Gas

chromatograph-mass spectral analysis of the volatiles from the anhydride photolysis again suggested, but did not confirm, the presence of the diethynylethylenes.

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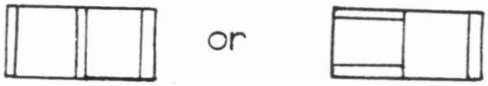
I. INTRODUCTION

1,4-Dehydrobenzene exists in the ground state as either a closed shell species, butalene (1) or as a diradical, *p*-benzyne (2). This dichotomy also exists for the 1,3-dehydrobenzenes (*m*-benzynes) 3 and 4 but apparently not for 1,2-dehydrobenzene (*o*-benzyne) which has been shown to behave chemically as a molecule with a reactive triple bond. Extensive work has been carried out by Bergman and coworkers to elucidate the structure and reactivity of 1,4-dehydrobenzene (1-5).



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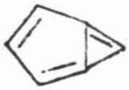

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The goal of this thesis work was to unambiguously generate 1 and determine the relationship between the two forms 1 and 2.

Theoretical treatments of the 1,4- and 1,3-dehydrobenzenes have focused chiefly on the singlet-triplet energy difference in the diradical. There has been only a minor effort to determine local energy minima corresponding to 1 and 3. The earliest theoretical treatment of butalene was a simple molecular orbital calculation by Roberts, Streitwieser, and Regan (6). They reported that a structure corresponding to 1 would have delocalization energy of 1.06β. This was greater than the predicted delocalization energy for cyclobutadiene, 0β, and spawned an effort to synthesize simple derivatives. The closed form of m-benzyne was reported to have an even greater delocalization energy, 2.39β.

In 1968 Hoffman carried out extended Huckel calculations of the energies of a number of dehydroaromatics including the 1,3- and 1,4-dehydrobenzenes (7). These calculations, which used an idealized benzene geometry, showed that there was some small positive overlap between the 1,3-dehydro centers in m-benzyne but that the overlap between the 1,4-dehydro centers in p-benzyne was small and negative. The ordering $n_1 - n_2 < n_1 + n_2$ of the interaction of the half-filled orbitals implied that the transition between the open form of p-benzyne and the bicyclohexatriene was not an allowed reaction. According to these calculations, the para isomer was more stable than the meta.

Theoretical interest in the dehydrobenzenes increased in the seventies. Whilhite and Whitten carried out large scale configuration interaction calculations on the benzynes in 1970 (8). They found that for both meta and para isomers the ground state was a triplet but that as the amount of configuration interaction increased, the difference between the singlet and triplet levels decreased. These calculations suffered from the severe restriction that the planar hexagonal benzene geometry was maintained throughout. Indeed, one might expect that geometry optimization would stabilize the singlet more than the triplet.

In 1974 Dewar and Li used a MINDO/3 program to calculate heats of formation of all three dehydrobenzenes (9). Two significant predictions emerged after inclusion of configuration interaction: 1) the meta and para isomers were singlets and 2) the meta isomer was comparable in energy to the ortho and was primarily nonradical in nature. The energies of the meta and para isomers were examined as a function of the distances between the dehydro centers. While only a single minimum was found for m-benzyne, two minima were found for p-benzyne. These minima corresponded to the structures 1 and 2, and 2 was about 35 kcal/mole lower in energy than 1. The barrier to isomerization of 1 to 2 was estimated to be 5 kcal/mole.

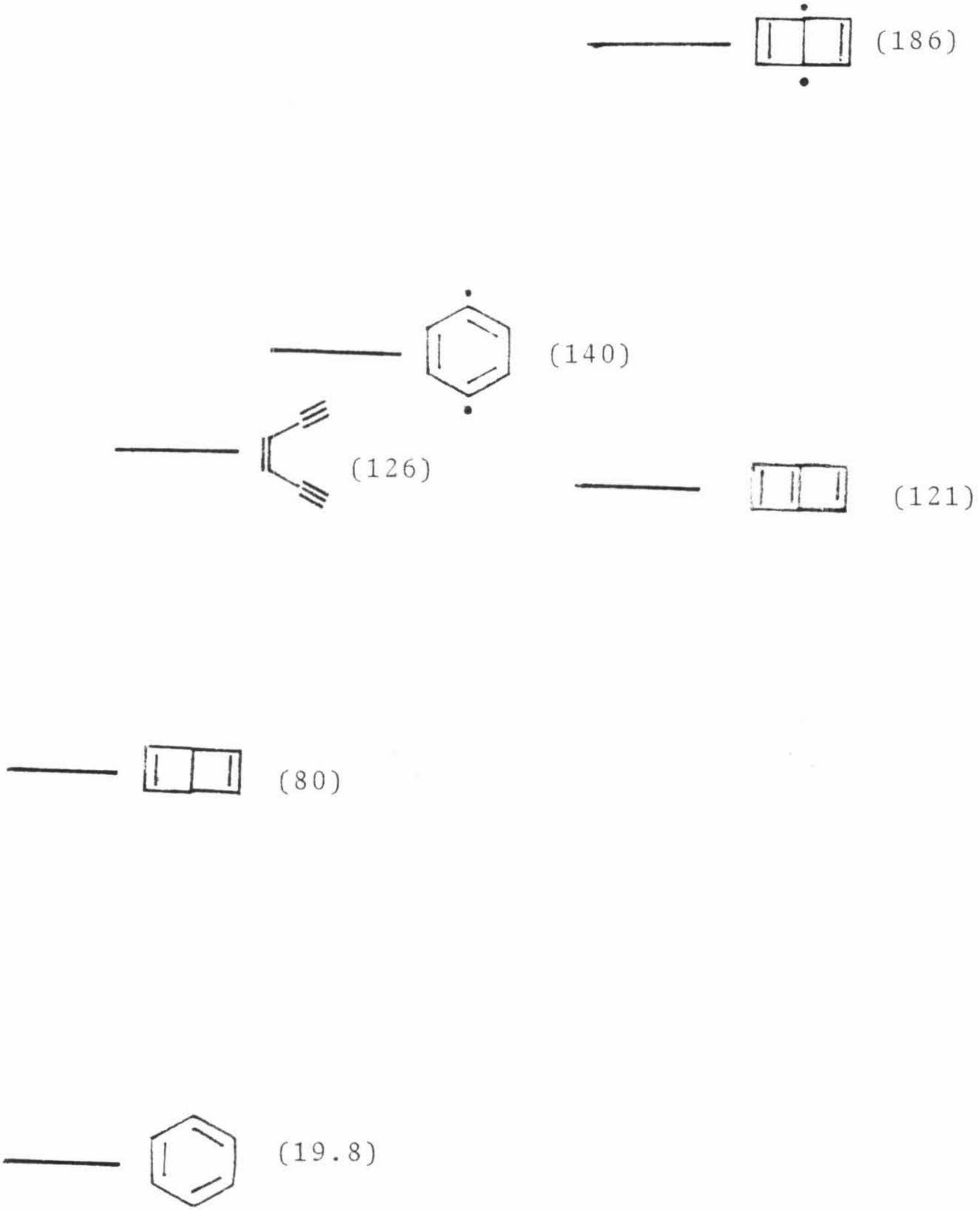
The most extensive calculations to date have been the ab initio calculations of Noell and Newton (10) which used an extended basis (4-31G) and then treated the singlet states with the generalized valence bond (GVB) formalism. They found that the ground states of all three benzyne isomers were singlets and that the energy order was ortho $<$ meta $<$ para. In the para case a limited search for a second minimum corresponding to a bicyclic structure was carried out both at the 4-31G level and using GVB. The 4-31G level showed a minimum only 5 kcal/mole above the open form whereas the GVB calculation showed a bicyclic structure almost 80 kcal/mole above the diradical. The authors indicated that the second value could easily be too large by a factor of two but did not comment on the reliability of the first value.

Using the results of the Noell and Newton calculation and some experimentally determined heats of formation, the energy diagram shown on the next page may be constructed showing the relationship between benzene and some of the dehydrobenzene structures. The heats of formation for benzene (11), Dewar benzene (12), and o-benzyne (13) have been determined experimentally. The values for the cis-diethynyl ethylene 5 and p-benzyne 1 were derived by applying values from Benson group additivity tables to the reaction:

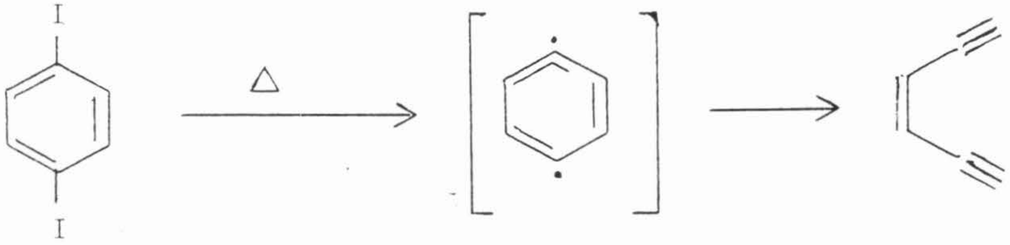
$$\text{benzene} \longrightarrow \text{1,4-dehydrobenzene} + H_2$$

(1). The value of 140 kcal/mole for the heat of formation of 1 by this simple method agrees with the value of 141 kcal/mole predicted by Noell and Newton. The high limit on the energy of the bicyclic structure was obtained by simply removing two hydrogens from Dewar benzene without allowing any interaction. The low limit was obtained by permitting the full strength of a double bond to be realized without the imposition of additional strain and without any destabilization due to the formation of two cyclobutadiene rings. Both the Noell and Newton calculation (assuming that the 80 kcal/mole value is indeed too high by a factor of two) and the Dewar calculation place the bicyclic structure about 35 kcal/mole above the open form. If this value is added to our accepted value of 140 kcal/mole for the heat of formation of the diradical a value of 175 kcal/mole is obtained for the heat of formation of the bicyclic structure. This is only 10 kcal/mole lower than the Dewar benzene 1,4-diyl.

Heats of Formation (kcal/mole) of Benzene and Its 1,4-Dehydro Derivatives

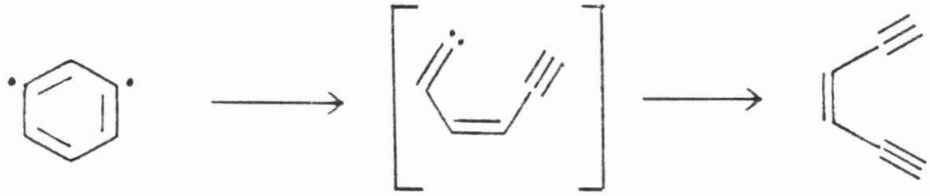


Early attempts to generate the 1,3- and 1,4-dehydrobenzenes employed methods which had been successful in generating 1,2-dehydrobenzene in the gas phase. Fisher and Lossing reported in 1963 that thermal decomposition of either 1,3- or 1,4-diiodobenzene in a reactor coupled to a mass spectrometer resulted in the formation of a species having m/e = 76. On the basis of its ionization potential (IP) of 9.46 eV, this species was identified as the diethynylethylene 5. This 9.46 eV IP was thought to be in agreement with the expected value for 5 and to be too low for a benzene-like structure.



2 5

Since the product from both isomers had m/e = 76 and a 9.46 eV IP, the possibility existed that the meta isomer isomerized to the para under these conditions. It is significant to note that no dimer was observed in the decomposition of the 1,3- or 1,4-diiodobenzenes but a dimer of m/e = 156 was observed in the thermal decomposition of 1,2-diiodobenzene. Unless a significantly higher barrier exists for the isomerization of meta to ortho benzyne than for the isomerization of meta to para benzyne, it was reasonable to expect observation of some dimer from isomerization of the m-benzyne. The diethynyl ethylene may have arisen from a cleavage of the m-benzyne itself.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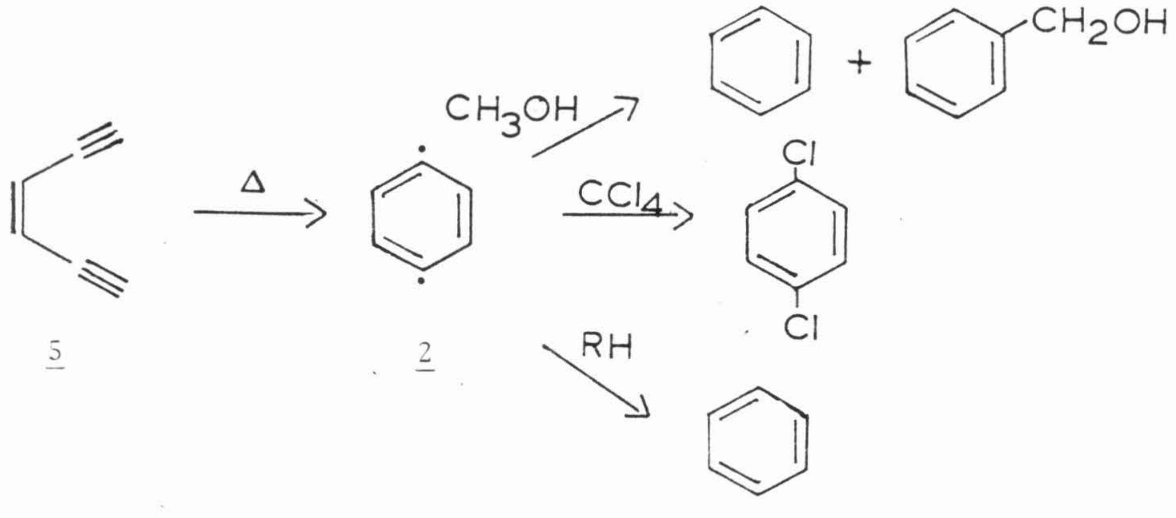
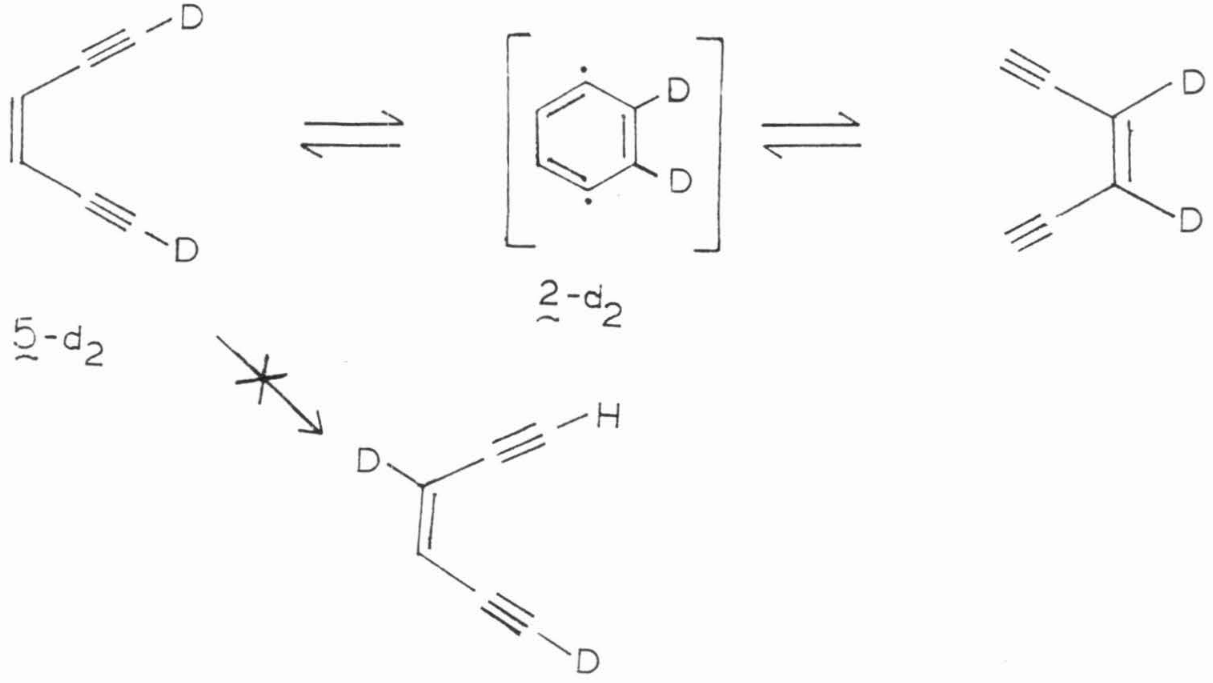
The photochemical decomposition of the 1,3- and 1,4-benzene diazonium carboxylates was reported two years later by Berry et al. (15, 16). The optical spectra and the mass spectra were measured as a function of time. The optical spectra displayed broad and flat continua. The mass spectra of the species obtained from the 1,3- and 1,4-benzene diazonium carboxylate flash photolyses were different from those obtained from the photolysis of the 1,2- isomer and from other known C_6H_4 isomers including the diethynyl ethylene 5. The mass spectra of the species produced from 1,3- and 1,4-benzene diazonium carboxylates also differed significantly from each other, indicating that the 1,3- and 1,4-dehydrobenzenes formed under these conditions did not interconvert. It is difficult to compare the results of this study with those of Fisher and Lossing (14) because different methods were used to generate the species of m/e = 76. These studies remained the only reported attempts to generate p-benzyne until the seventies (17).

In 1972 Bergman and Jones discovered that pyrolysis of 5 in hydrocarbon solvents at 200°C led to the formation of benzene (1). Pyrolysis of 5 in carbon tetrachloride produced 1,4-dichlorobenzene and pyrolysis in methanol produced benzyl alcohol and benzene. Since proton transfer to a substituted cyclobutadiene has been shown to occur readily to produce a cyclobutene methyl ether (18), and abstraction of a hydrogen atom from methanol by a radical is expected to occur at the carbon, it was evident that the species generated under these conditions behaved as a diradical.

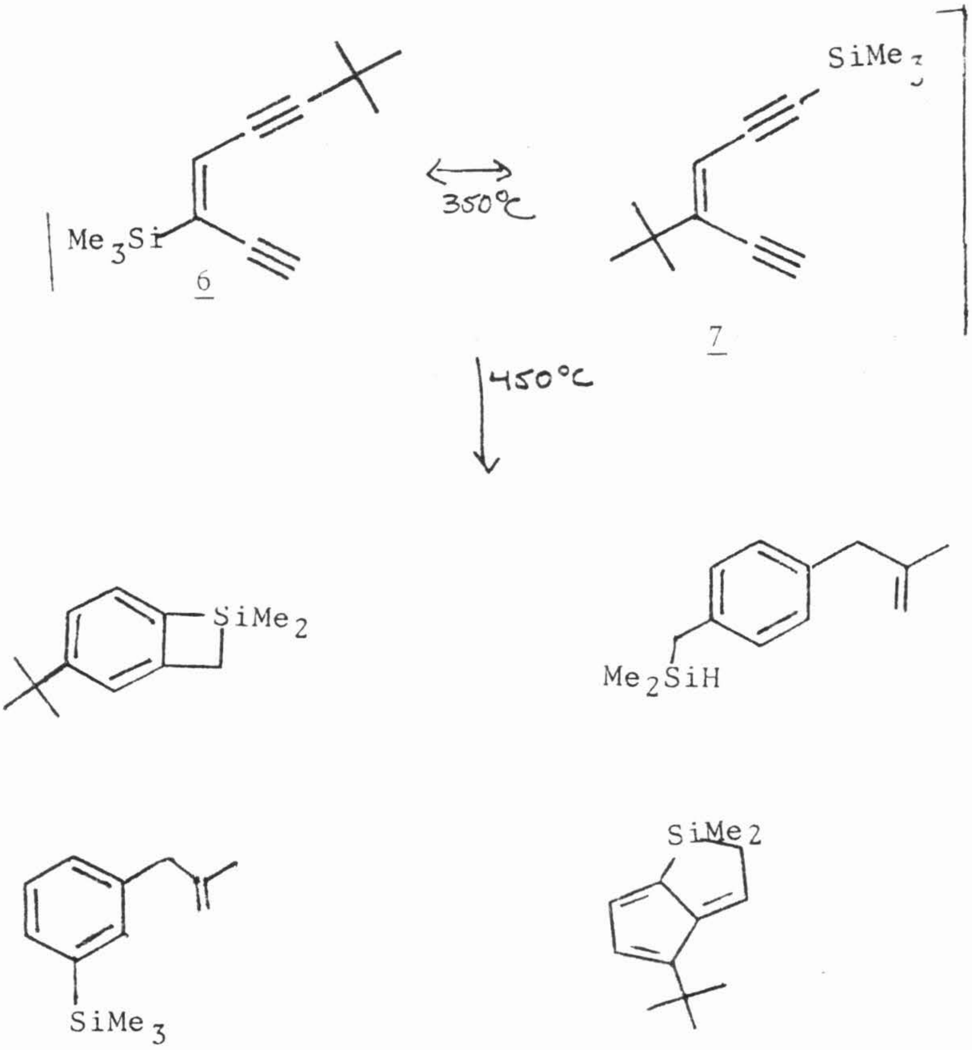


Furthermore, gas phase pyrolysis in a nitrogen flow system at 200°C of specifically labeled 5-d$_2$ resulted in pairwise scrambling of the deuteriums. This implied that a symmetrical intermediate, *p*-benzyne, was involved.



Recent elegant work by Lockhart and Bergman argued convincingly that this diradical was a singlet (5a, 5b). Under the pyrolytic conditions employed no products of 1,3 substitution were observed that might have implicated a *m*-benzyne intermediate.

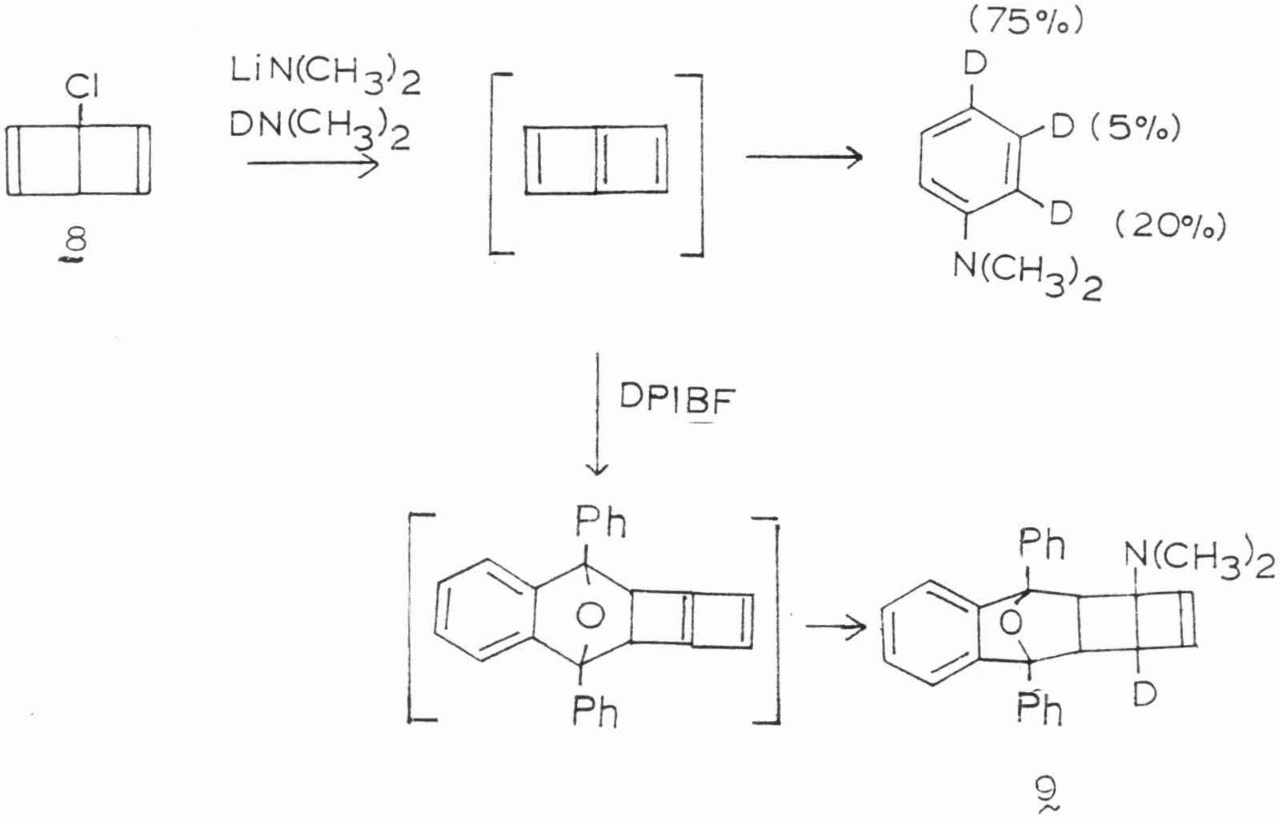
This result contrasted with the findings of Johnson and Bergman (3). They discovered that if the diethynylethylene substituted with a trimethylsilyl group and a *t*-butyl group (6) were pyrolyzed at 300°C, rearrangement to the isomeric diethynylethylene *7* occurred, presumably via a *p*-benzyne intermediate. However, if the pyrolysis temperature was raised to 450°C, a wide variety of products was observed. One of these products, *m*-methallyltrimethylsilylbenzene, was ascribed to the intermediacy of a *m*-benzyne. This *m*-benzyne clearly behaved as a diradical as did the 1,3-dehydronaphthalene generated by Billups *et al.* (19).

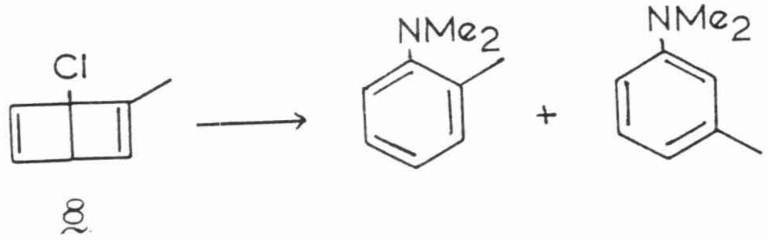


The *p*-benzynes and *m*-benzyne generated by Bergman and coworkers via the pyrolyses of diethynyl ethylenes behaved as diradicals. Breslow *et al*. (20) and Washburn *et al*. (21) generated 1,4- and 1,3-dehydrobenzenes respectively at low temperatures by dehydrohalogenation in strong base. These dehydrobenzenes were trapped in the reaction media in a manner which suggested the intermediacy of the closed forms 1 and 3.

Breslow and coworkers found that reaction of the 1-chlorobicyclo [2.2.0] hexa-2,5-diene 8 with lithium dimethylamide in dimethylamine in the presence of tetramethylenediamine (TMEDA) at -35°C led to dimethylaniline. Use of N-deuterated dimethylamine ($DNMe_2$) resulted in the formation of a complicated mixture of undeuterated as well as mono-, di-, and trideuterated dimethylanilines. Addition of diphenylisobenzofuran (DPIBF) to the reaction mixture permitted the isolation of an adduct, 9. This result was interpreted as a firm indication that part of the reaction proceeded via butalene, 1. There was no evidence for the intermediacy of a diradical or the production of dimethylaminofulvene, the product of reaction between 5 and dimethylamine (22).

Reaction of lithium dimethylamide with 1-chloro-2-methylbicyclo [2.2.0] hexa-2,5-diene in dimethylamine led to the expected *o*- and *m*-toluidines with no *p*-toluidine detected. When the reaction was carried out in deuterated

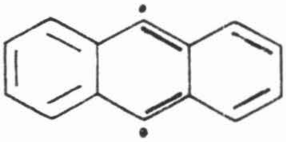

Cl
LiN(CH3)2
DN(CH3)2
8
(75%)
D
D (5%)
D (20%)
N(CH3)2
DPIBF
Ph
O
Ph
Ph
O
Ph
N(CH3)2
D
9


Cl
8
NMe2
+
NMe2

dimethylamine almost 35% of the reaction products were d_0. The absence of p-toluidine-d_0 and the high proportion of o-toluidine argued in favor of a direct replacement of chlorine. No trapping experiments with DPIBF were reported.

If butalene was an intermediate in the dehydrochlorination of the chloro-Dewar benzene, trapping of the butalene by the DPIBF must have occurred at a rate faster by a factor of ten than trapping of the butalene by dimethylamine because of the difference in concentration between the dimethylamine as solvent and the DPIBF. Furthermore, trapping of the butalene by DPIBF must have occurred at or close to the diffusion controlled limiting rate. For example, if we assume a pre-exponential of only log A = 13 (23) and the 5 kcal/mole energy barrier calculated by Dewar, the unimolecular rate constant for rearrangement of 250°C would be close to $10^8 M^{-1} s^{-1}$. Since the diffusion controlled rate constant for a bimolecular reaction is close to 10^9 and the concentration of the DPIBF can be estimated to be 0.5 M, the rates of disappearance of butalene by the two routes were competitive. This may indicateeither that the barrier to rearrangement is much higher than calculated or that butalene simply was not an intermediate in the reaction.

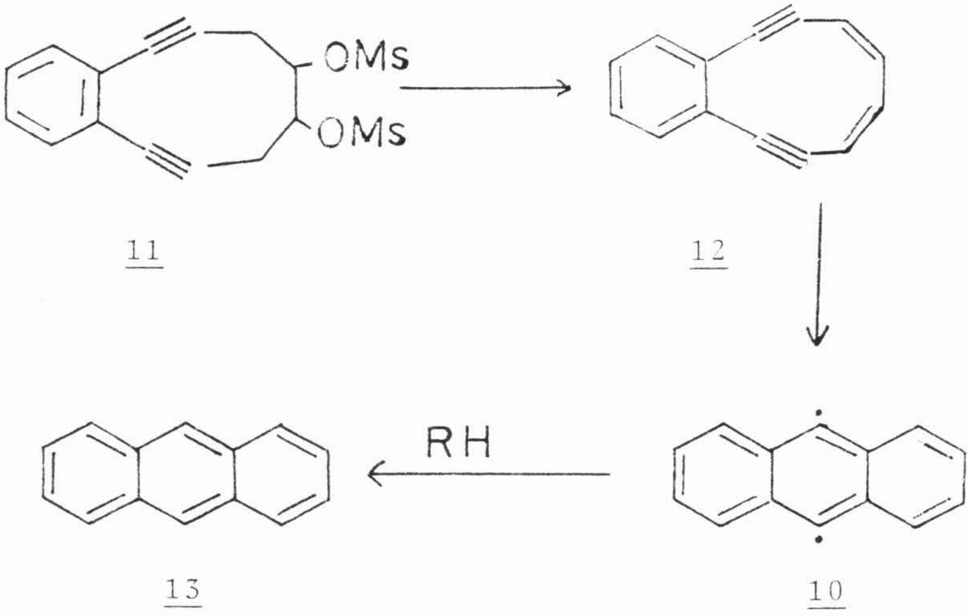
Breslow's results imply that the closed form of p-benzyne did not isomerize to the open form under the dechlorination reaction conditions. Danby *et al*. (24) and Chapman et al. (25) showed that under widely different low temperature conditions a derivative of the open form, 10, was trapped as a diradical without evidence of isomerization to the closed form.

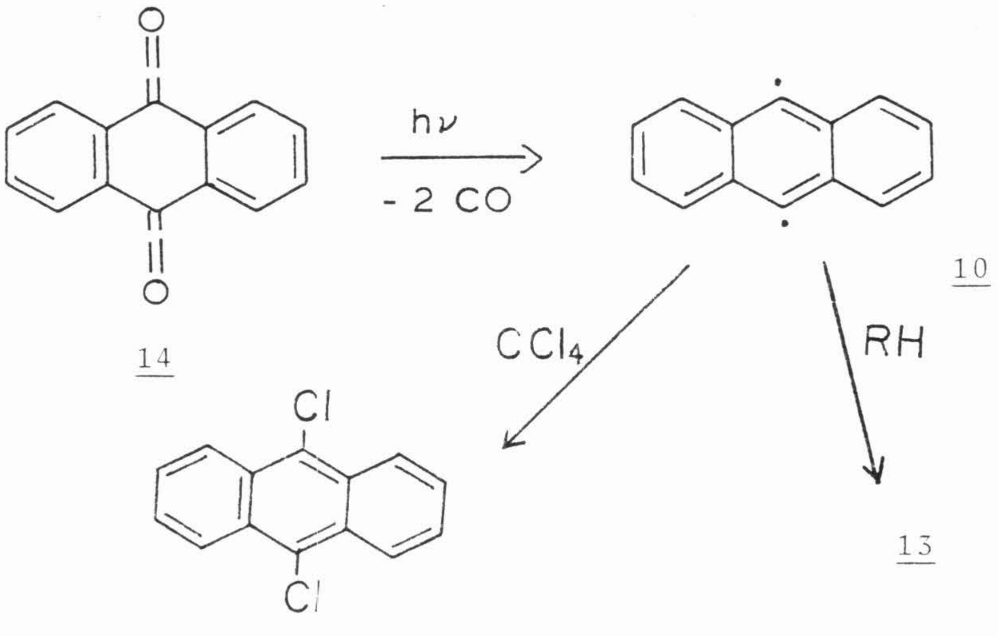


10

Danby et al. (24) showed that elimination of two molecules of mesylic acid from the dimesylate 11 resulted not in the formation of 12 but instead in the formation of anthracene 13. This likely involved the intermediacy of 10 which reacted as a diradical. Although the conditions of the elimination were not specified, they undoubtedly were not as severe as the pyrolysis conditions used by Bergman as described above.

An attempt to generate 10 directly at low temperature was reported by Chapman et al. (25). Irradiation of the bisketene 14 led to a product which possessed an ultraviolet absorption spectrum similar to anthracene and could be trapped with hydrocarbons to produce anthracene and by carbon tetrachloride to yield 9,10-dichloroanthracene. An ESR signal was not observed and Chapman et al. concluded

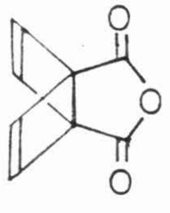

OMs
OMs
11
12
RH
13
10


hν
- 2 CO
10
14
CCl4
RH
Cl
Cl
13

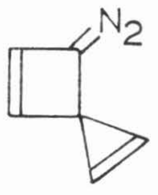
that the dehydroanthracene was a singlet.

In both of these studies no products suggested the intermediacy of the closed forms. Apparently the closed form of 1,4-dehydrobenzene must be generated with the 1,4 bond already formed.

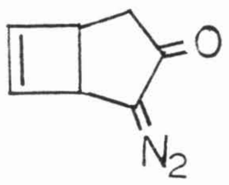
Matrix isolation techniques, which were successful in trapping many reactive intermediates such as cyclobutadiene, offered a method to study the low temperature photochemical generation of butalene. A possible approach was to construct the butalene fragment containing an extrudable group. Alternatively a precursor might be constructed which would require a ring expansion or contraction to achieve the butalene framework. Three possible precursors are shown below:



A

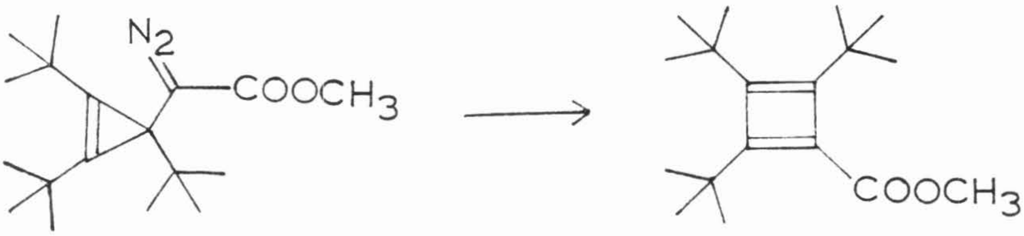


B



C

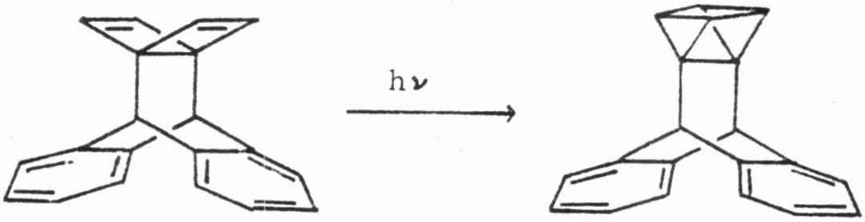
Precursor A was considered likely to be successful because of the large number of precedents in cyclobutadiene chemistry and because a rational plan for its synthesis existed. The possible precursor B was attractive because ample precedent existed for the ring expansion of small spirocyclic rings adjacent to carbenes (27), including the ring expansion of 15 to yield the cyclobutadiene 16.



15 16

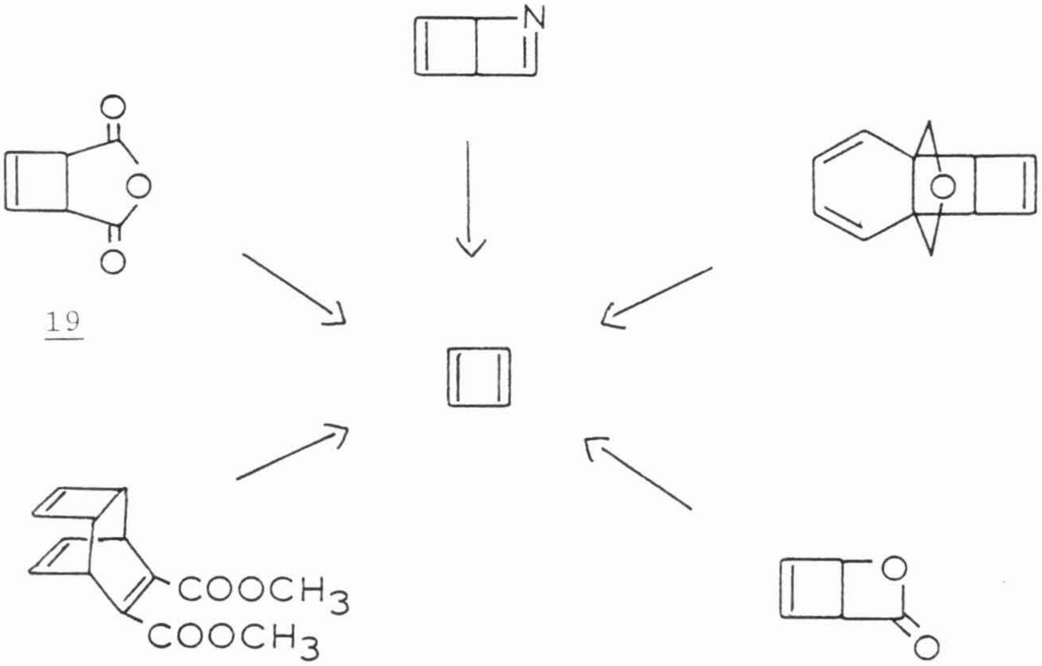
Synthesis of this type of precursor presented difficulties, however. Small, unsaturated, spirocyclic systems are uncommon and our strategy for the synthesis of B required the intermediacy of cyclobutenylidenes, whose chemistry was incompletely understood. The third type of precursor, C, required that a hydrogen shift occur in the last step in the formation of butalene. Recent work showed that benzocyclobutenylidene did not hydrogen shift to form benzocyclobutadiene (28) and the parent cyclobutenylidene did not rearrange to cyclobutadiene.

The most promising precursor was therefore the first, which required a photochemical elimination to produce butalene in the final step. The choice of the extrudable group was determined both by synthetic and photochemical considerations. One potential photochemical precursor was the Dewar benzene <u>17</u> synthesized by Johnson and Bergman (3). Johnson, Bergman, and Maier (30) found that instead of extruding anthracene upon photolysis, <u>17</u> rearranged to a new compound which was tentatively identified as a prismane derivative <u>18</u>.



<u>17</u> <u>18</u>

Some successful photochemical precursors to cyclobutadiene are shown on the next page (26). All related butalene precursors except for the anhydride analogous to <u>19</u> required the construction of a [2.2.2] propelladiene which was a very difficult synthetic objective. An anhydride precursor was therefore chosen.



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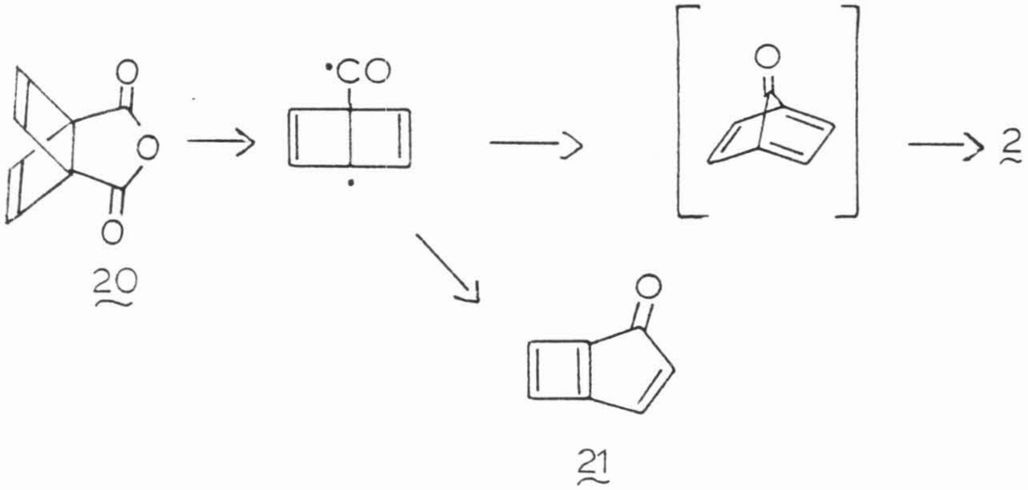
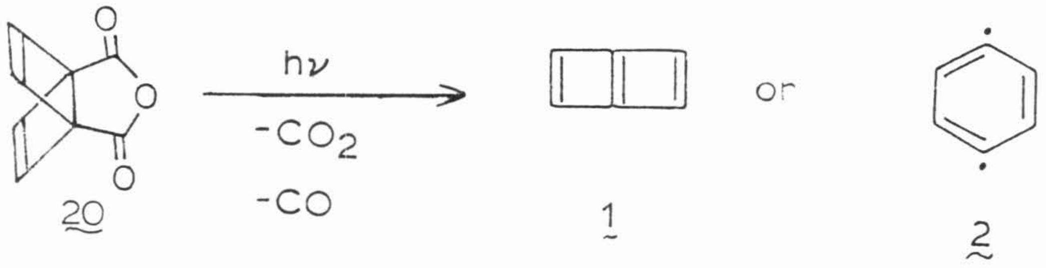
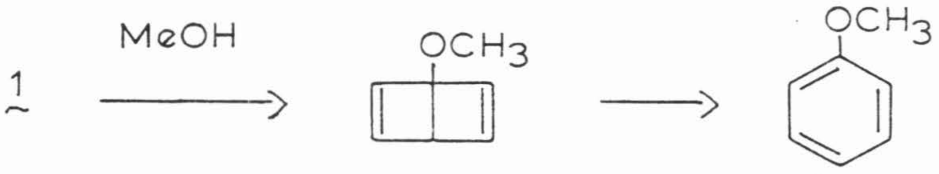
Cyclobutene anhydrides have been demonstrated to be suitable precursors for both the parent and substituted cyclobutadienes (26). Based on the photochemistry of the cyclobutene anhydrides, however, two potential drawbacks to the use of the analogous 1,4-Dewar benzene anhydride 20 existed. First , the tendency of these anhydrides to ring expand to cyclopentadienones varied from substrate to substrate. If the Dewar anhydride 20 followed this route the dehydrocycloheptatrienone 21 would be formed. Although the synthesis of 21 was not the goal of the project, its appearance would be interesting since 21 itself is of theoretical interest.

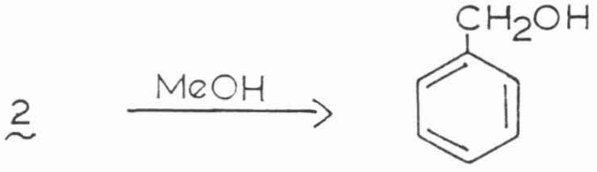


The second problem was more serious. All of the cyclobutene anhydrides previously prepared had absorption maxima at low wavelength and their molar absorption coefficients were less than several hundred. For example, the unsubstituted cyclobutene anhydride displayed a maximum at 228 nm with $\epsilon = 670$. The tetraalkyl substituted cyclobutene anhydrides displayed maxima close to 240 nm (26). The necessity of photolyzing at low wavelengths posed a serious problem if the products of the photolysis of the anhydride 20 were photochemically labile.

Ideally cleavage of the anhydride would yield observable amounts of butalene which could be trapped by methanol to yield anisole. This would provide unambigous evidence for the presence of the closed form of 1,4-dehydrobenzene.



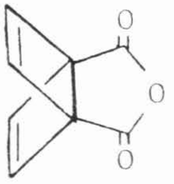




II. PREPARATION OF BYCYCLOHEXADIENE DERIVATIVES

1. Selection of Synthetic Route

The bicyclohexadiene derivatives 20 and 22 were unknown at the outset of this work. Although there were a number of methods available for the synthesis of Dewar benzenes, none were straightforward in their application to this system.



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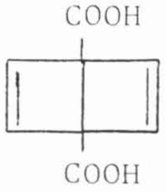
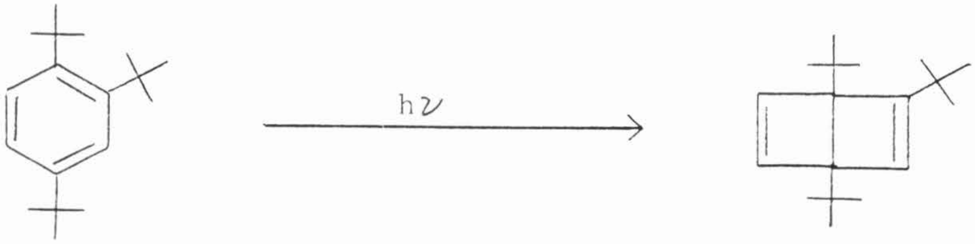
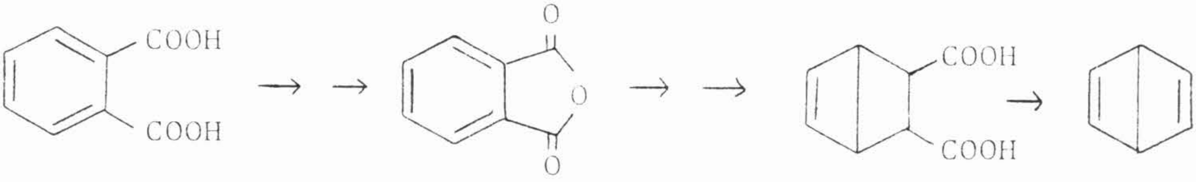


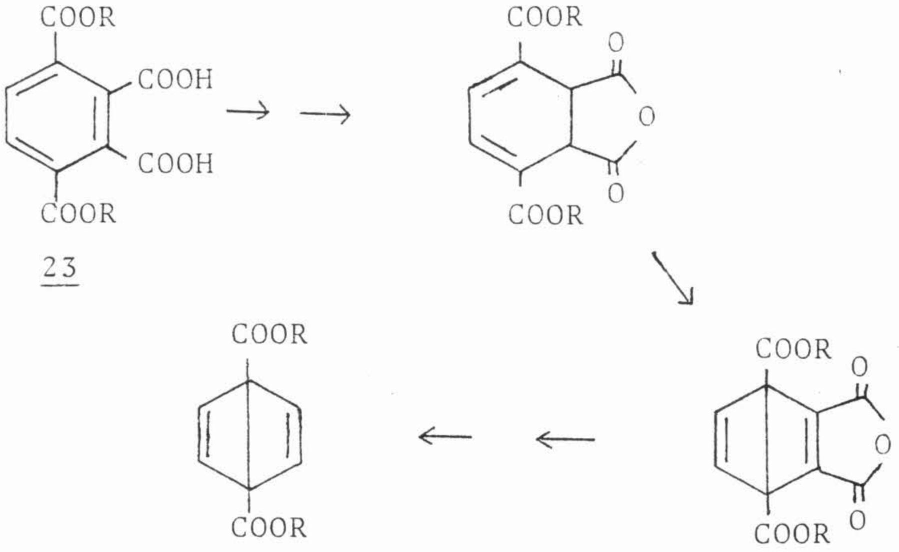
22

The earliest report of Dewar benzenes was made in the early 1960's by van Tamelen and Pappas (31a). They discovered that irradiation of benzene derivatives with bulky substituents in ortho positions led to the formation of Dewar benzenes. One year later they reported the first synthesis of unsubstituted Dewar benzene (31b):



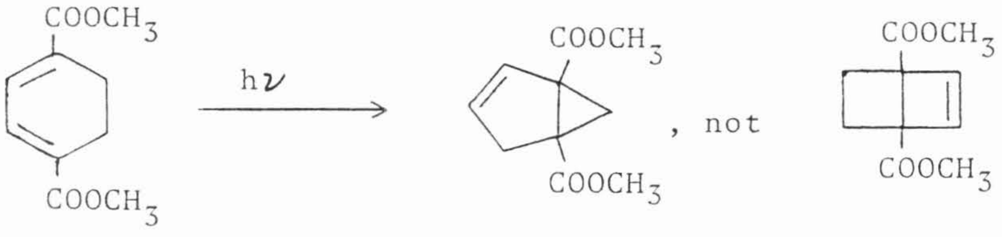


Adaptation of this first route to our system was obviously impractical, but the second held some promise. For example, if the tetraacid 23 could be synthesized with the carboxyls in the para positions clearly differentiated in some manner, it might be possible to carry out an analogous synthesis:



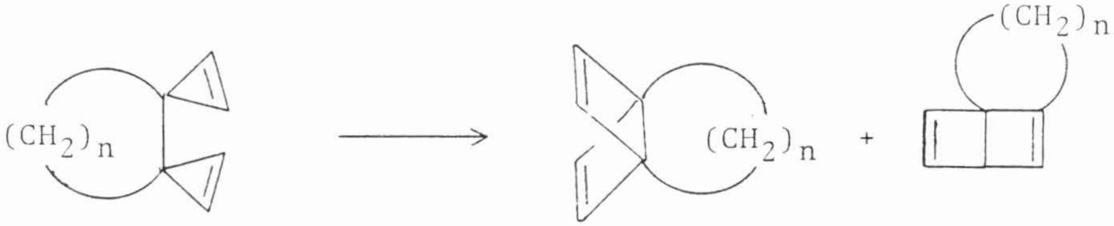
23

The photochemistry of 1,3-cyclohexadiene derivatives is imperfectly understood. The diester 24 was shown to rearrange to the bicyclo [3.1.0] hexene 25 instead of rearranging to the expected bicyclo [2.2.0] hexene 26 (32). This precedent made any route that depended on the photochemistry of a hexadiene a poor synthetic risk.



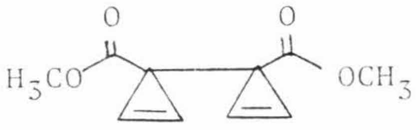
24 25 26

Another possible route employed the known silver ion catalyzed rearrangement of bicyclopropenyls 27 to Dewar benzenes (33):



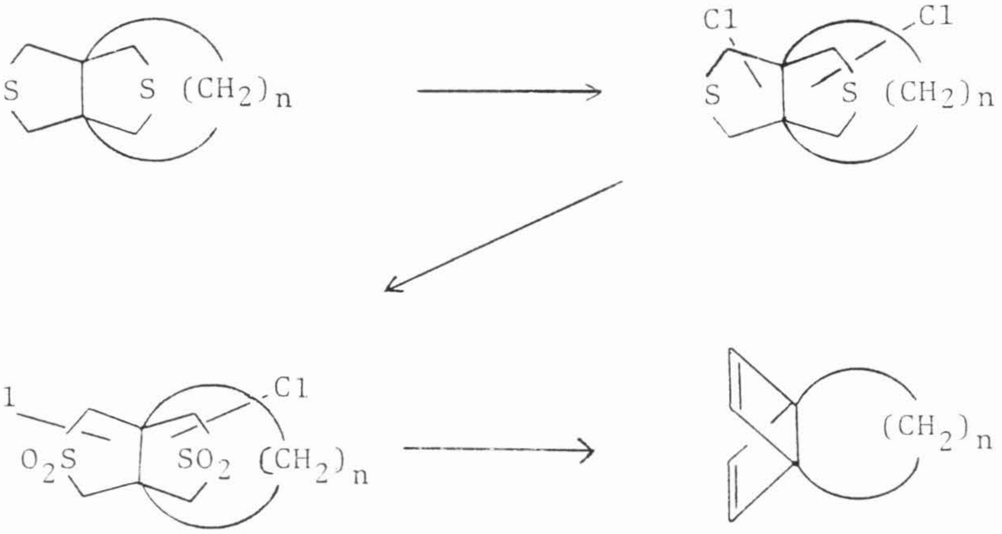
27

This route, which was briefly investigated, had two drawbacks. Firstly, cyclopropenes with carboxylic acid derivatives in the 3- position were uncommon and the methods used for their generation could not be applied readily to the synthesis of the required bicyclopropenyl 28. Secondly, the route to 20 via the bicyclopropenyl 28 or a derivative was long and required a number of transformations on thermally sensitive Dewar benzenes.

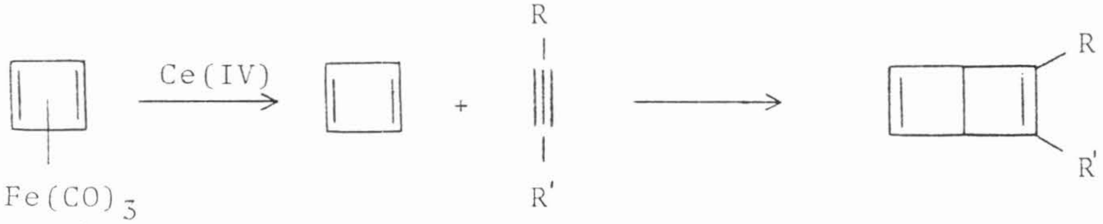


28

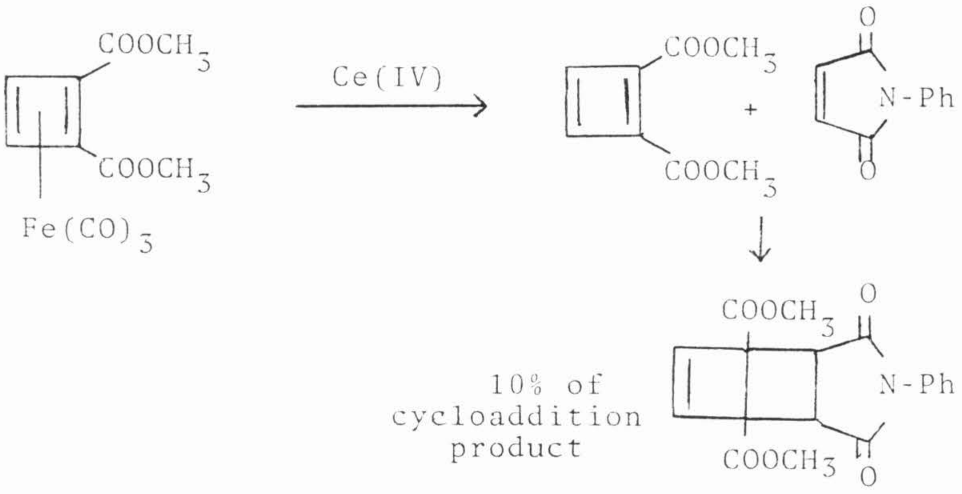
Since bridged Dewar benzenes are rare, it is necessary to mention the only other reported synthesis. Weniges and Klessing were able to obtain methylene bridged Dewar benzenes in very low overall yield by the route shown below (34):



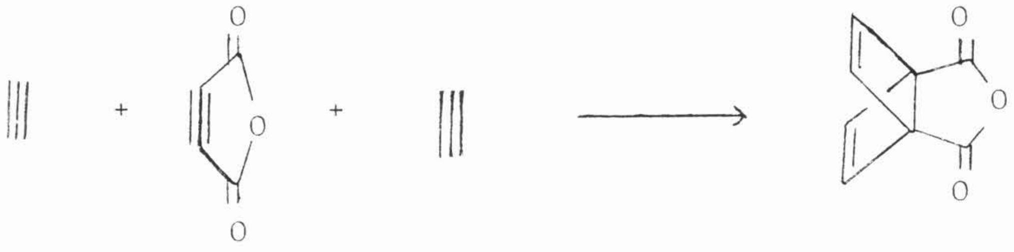
The final published method we considered was to try to trap the free cyclobutadiene 29 by acetylene to give the Dewar benzene 22-ester. This route had been applied with great success by Pettit in the synthesis of several Dewar benzenes (35):



However, 1,2-disubstituted cyclobutadienes tend to add a dienophile at the side opposite the substituents to the exclusion of 1,2-addition. The cyclobutadiene 29 was shown to add at the 1,2-position about 10% of the time but only with the most reactive dienophiles. With less reactive olefins only dimerization of the cyclobutadiene was observed (36). Although the cyclobutadiene complex 30 was available in large quantities (36, 37), this method was unacceptable because of the low overall yield in the cycloaddition and the additional steps required to transform the dienophile into a doubly bonded species.

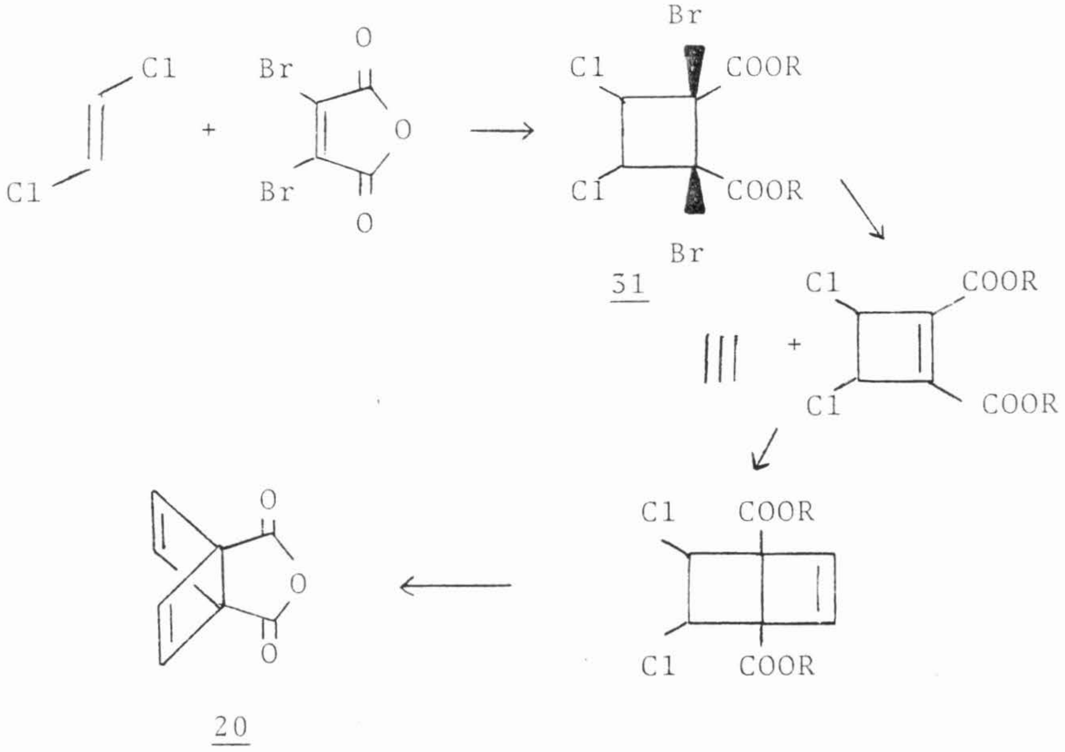


The route we decided to pursue was conceptually very simple. Addition of acetylenes in the hypothetical [2 + 2 + 2] cycloaddition would produce the desired anhydride:



20

Substitution of acetylene equivalents for the acetylenes made the reaction sequence recognizable. The projected synthetic outline is shown below:



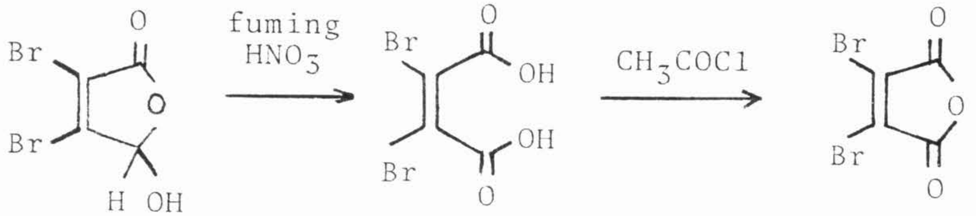
There was precedent for all of the required steps in this synthesis. Photochemical addition of maleic anhydride and its derivatives to olefins and acetylenes was well documented (38). The photochemical addition of 2-butyne to dimethylcyclobutene-1,2-dicarboxylate was also known (39). Ring closure of carboxylic acids to yield anhydrides had been accomplished by a number of methods (40). Vicinal dichlorides were often used as precursors to double bonds (41).

These final transformations would have to be carried out under mild conditions because of the anticipated thermal lability of the bicyclohexene and bicyclohexadiene skeletons.

The 1,2-dibromo-3,4-dichlorocyclobutane-1,2-dicarboxylic acid <u>31</u> (R = H) and dimethylesters <u>31</u> (R = CH_3) were known but available only after a difficult hydrolysis of the related cyclic imide (42). Substitution of dibromomaleic anhydride for dibromomaleimide in the photochemical addition to dichloroethylene provided a much more direct route to the desired cyclobutane diacid. Furthermore, Roberts had shown that the addition of dichloromaleic anhydride to dichloroethylene proceeded in satisfactory yield (36).

2. Construction of the First Cyclobutane Ring

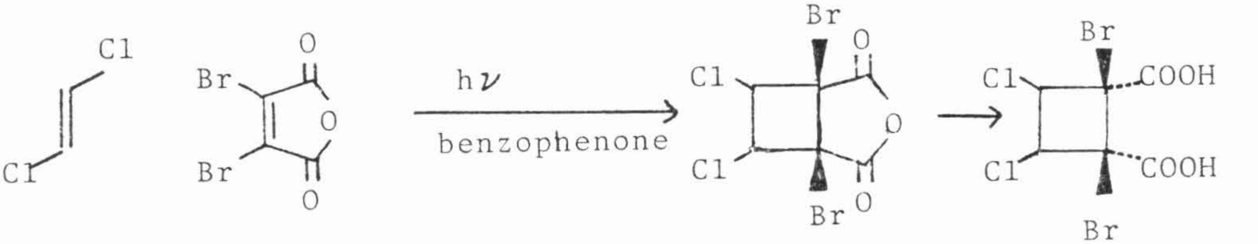
Dibromomaleic anhydride was prepared from mucobromic acid by oxidation with fuming nitric acid followed by treatment of the crude dibromomaleic acid with acetyl chloride (43, 44):



The photochemical cycloaddition of dibromomaleic anhydride to dichloroethylene was accomplished by irradiating the anhydride through Pyrex in dichloroethylene solution using benzophenone as sensitizer. This method permitted preparation of about one hundred grams of crude diacid free of benzophenone and organic polymers from sixty grams of dibromaleic anhydride. The crude diacid was approximately 60% *trans*-**31** (R = H) and 40% a three to one mixture of *syn*- and *anti*-*cis*-3,4-dichloro-1,2-dibromocyclobutane diacids. This ratio was independent of the stereochemistry about the dichloroethylene double bond because the dichloroethylene isomerized quickly under the photochemical conditions. If dibromoethylene were used in place of dichloroethylene, the photoaddition did not occur.

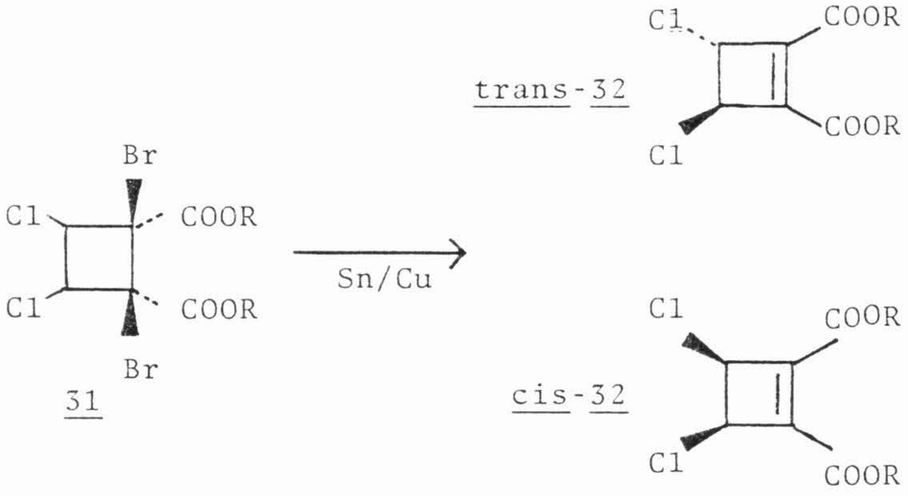
The diacids **31** (R = H) were purified by either of two methods. In the early stages of this work, they were converted to a mixture of dimethyl esters by diazomethane and used directly in the debromination step without further purification (see below). Later, when it became necessary to work with pure *cis*- or *trans*-dichlorocyclobutenes **32** (R = H), the crude diacids **31** (R = H) were treated with an excess of thionyl chloride to form the anhydrides **34**. The stereoisomeric anhydrides could be separated by fractional distillation at 0.025 mm. Regeneration of the diacids **31**

(R = H) was accomplished by dissolution in wet chloroform from which the diacids precipitated after a short period. Stereoisomerically pure diesters 31 (R = CH_3) could be synthesized by treating the purified diacids with an ethereal solution of diazomethane.



34   31 (R = H)

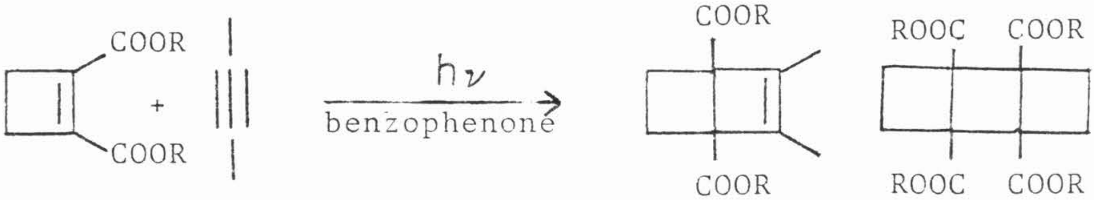
Removal of the bromines from the diesters 31 (R = CH_3) was examined first. Trialkyl tin hydrides (45) and tin/copper couple (46) both produced the desired dichlorocyclobutenes 32 (R = CH_3) upon reaction with the diesters 31 (R = CH_3). The tin/copper couple reaction was superior in ease of preparation and product isolation. Debromination of the crude diesters by tin/copper couple in THF at 20°C gave a mixture of the dimethyl cis- and trans-3,4-dichlorocyclobutene-1,2-dicarboxylates 32 (R = CH_3) which could be separated by chromatography on silica gel. Treatment of the stereoisomerically pure dichlorodibromocyclobutane 31 (R = CH_3) with tin/copper couple afforded the corresponding cyclobutene diesters 32 (R = CH_3) in high yield.



Alternatively, the crude diacids 31 (R = H) could be debrominated to give cyclobutene diacids. Purification of the mixture of diacids was difficult and the mixture was carried forward to the next step. The use of the acids purified by distillation allowed us to prepare the stereoisomerically pure cis- and trans-cyclobutene diacids. The cis-diacid 32 (R = H) was obtained as a crystalline solid from chloroform but the trans-diacid resisted efforts to force it to crystallize.

3. Construction of the [2.2.0] Bicyclohexene Skeleton

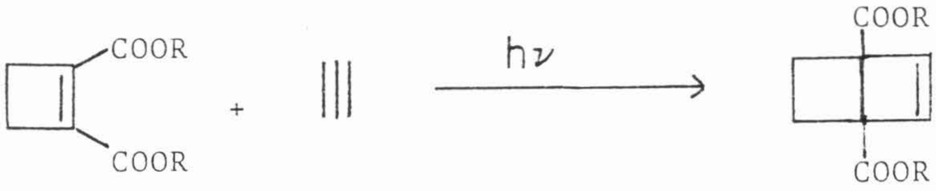
After successful preparation of both the cis- and trans-dichlorocyclobutene diacids and their dimethyl esters the construction of the bicyclohexene skeleton was the next goal. Seebach had reported that the dimethylcyclobutene-1,2-dicarboxylate 35 (R = CH_3) would add to 2-butyne to yield bicyclohexene 36 (R = CH_3) when irradiated through Pyrex in the presence of benzophenone (39). However, even when 2-butyne was used as the solvent, the yields were low because of extensive dimerization.



35 36 37

We repeated this reaction with similar results. We also found that 35 (R = $Si(CH_3)_3$) would add to 2-butyne to give the corresponding bicyclohexene 36 (R = $Si(CH_3)_3$) as well as the dimer. Both products were easily hydrolyzed to the diacids.

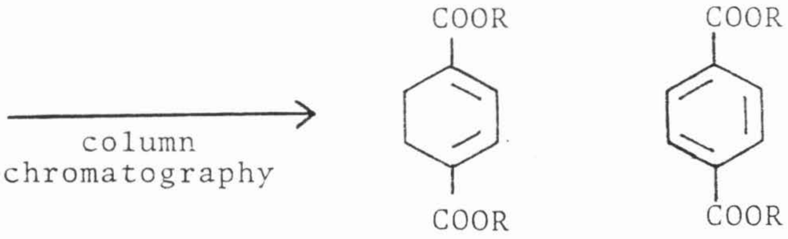
We constructed a large scale low temperature photolysis apparatus and attempted the cycloaddition of 35 (R = CH_3) to acetylene. An NMR spectrum of the crude reaction mixture indicated that some bicyclohexene 38 had been formed, but chromatography yielded a mixture of the cyclohexadiene and the benzene isomers. D. Owsley informed us that he had attempted the same reaction and that the bicyclohexene had a half-life of 5 minutes at 40°C (47). We elected at this point to continue our synthesis using 2-butyne, anticipating that the two methyl groups would provide extra thermal stability (39).



35

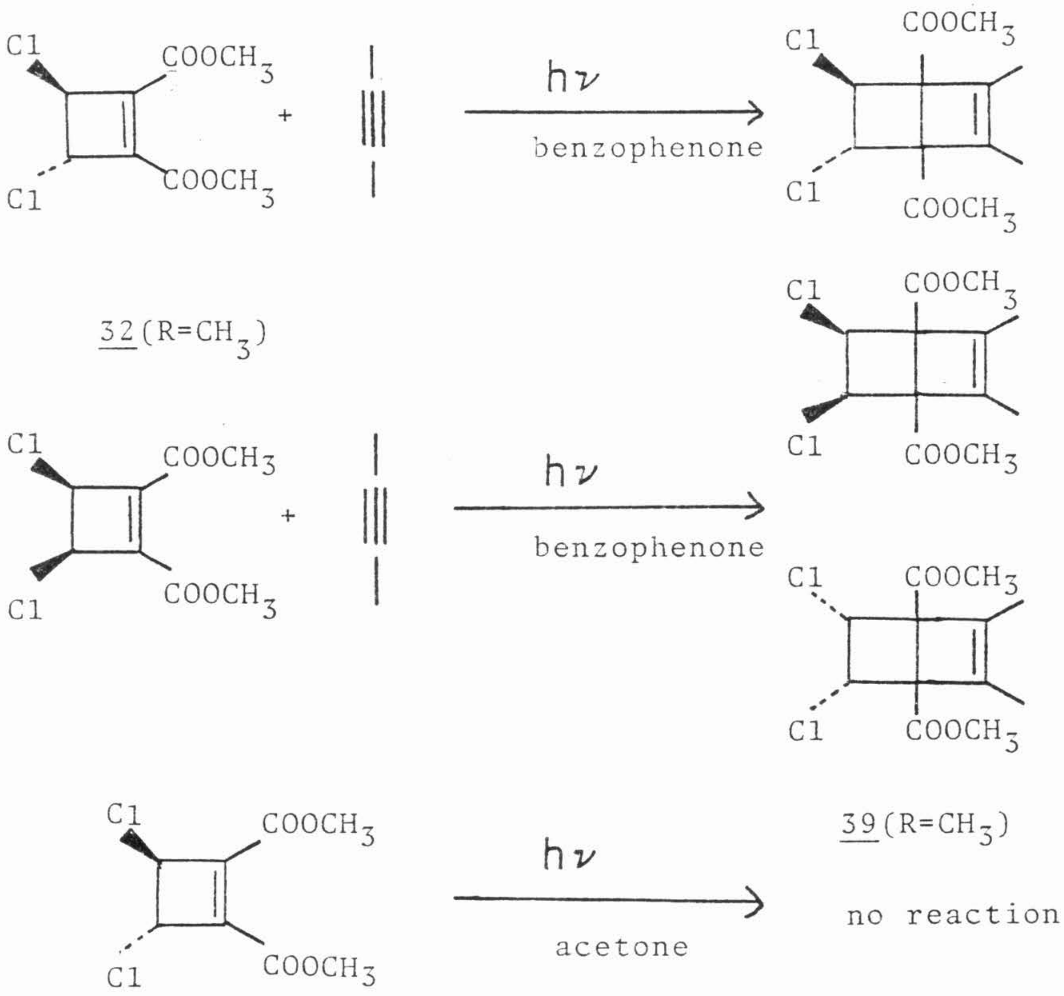
38

38



We were delighted to discover then that irradiation of the dimethyl 3,4-dichloro-1,2-dicarboxylate 32 (R = CH_3) through Pyrex in carefully degassed 2-butyne or 2-butyne-acetone mixtures led to the formation of the dimethyl 5,6-dichlorobicyclohex-2-ene-1,4-dicarboxylate 39 (R = CH_3)

in high yield. There was no evidence for dimer formation. Irradiation of the dichlorocyclobutenes 32 (R = CH_3) in acetone under conditions identical to those employed for the photochemical cycloaddition did not result in any dimerization detectable by NMR. The inclusion of benzophenone in the photolysis mixture shortened the times required for complete conversion to the bicyclohexene.



32 (R=CH_3)

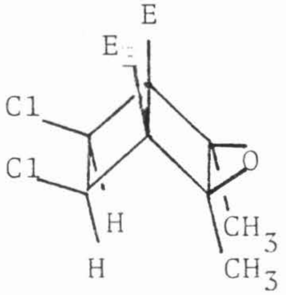
39 (R=CH_3)

The trans-dichlorocyclobutene 32 (R = CH_3) produced a single product upon irradiation in 2-butyne which could be separated from the benzophenone by column chromatography. This compound had a distinctive NMR spectrum consisting of a doublet of doublets (δ 4.05, 5.05 ppm) and two pairs of singlets (δ 1.8, 3.8 ppm). If the cis-cyclobutene 32 (R = CH_3) were used, two different bicyclohexene diesters were produced in an approximate ratio of 1:3. They were separable by column chromatography. The proton NMR spectrum of the major isomer consisted of three singlets in a ratio of 1:3:3 at δ 5.05, 3.7, and 1.88 ppm. The minor isomer was distinguished from the major isomer by an upfield shift of 0.64 ppm in the absorption of the protons α to the chlorines.

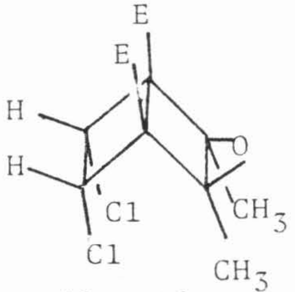
Irradiation of the cyclobutene diacids 32 (R = H) in 2-butyne or acetone/2-butyne mixtures in the presence of a large amount of benzophenone (~ 10-20% w/w) resulted in the formation of corresponding bicyclohexene diacids 39 (R = H). The trans-diacid could be purified by diluting the reaction mixture with ether, extracting with aqueous sodium bicarbonate, reacidifying, and extracting with ether. The crude diacid could be recrystallized from hot chloroform. The two cis-diacids 39 (R = H) were formed in about the same ratio as the two cis-diesters above, and were easily separated because the minor (upfield) isomer crystallized in the bottom of the photolysis vessel during the irradiation. At the end of the irradiation, the diacid was simply filtered and washed quickly with acetone and ether. The major (downfield) isomer was recovered from the filtrate using the method described for the <u>trans</u>-diacid.

We attempted to determine the stereochemistry of the <u>cis</u>-bicyclohexenes <u>39</u> (R = CH_3) by measuring the proton NMR spectra of a mixture of the two isomers in the presence of a lanthanide shift reagent, Eu(fod)$_3$. Successive additions of aliquots of a 0.75 <u>M</u> solution of Eu(fod)$_3$ caused a shift in the position of all three types of protons. We had hoped that the ratio of the shifts of the carbomethoxy-protons and the α - chlorocyclobutane protons would be different for the two isomers (48). Instead, the ratios were almost identical (minor <u>cis</u>-<u>39</u> (R = CH_3):major <u>cis</u>-<u>39</u> (R = CH_3) = 2.34:2.20). Likewise, a very small difference in ratios was measured for the carbomethoxy protons versus the allylic methyl protons (minor:major = 1.07:1.00). If <u>trans</u>-<u>39</u> (R = CH_3) were treated with successive additions of Eu(fod)$_3$, the downfield doublet moved more rapidly relative to the absorption of the carbomethoxy protons than did the upfield doublet. We could not make a case for the stereochemistry of the 2-butyne addition on the basis of these results.

Reaction of each of the *cis*-dichlorobicyclohexenes with *p*-nitroperbenzoic acid in chloroform at 50°C yielded a single product whose structure was assumed to be the epoxide from *exo* attack on the double bond. These epoxides are shown below:



40-syn

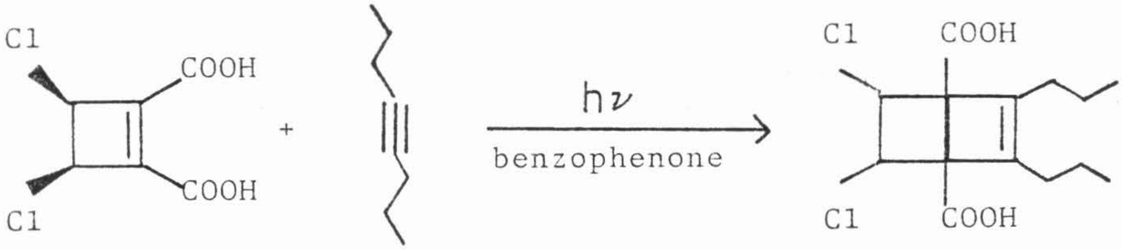


40-anti

(E = COOCH$_3$)

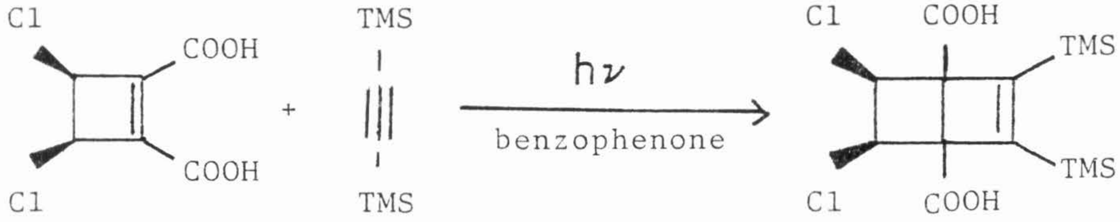
We hoped to be able to determine the stereochemistry of these epoxides by measuring the enhanced integration relative to added TMS of the *endo*-methyl groups when the protons α to the chlorines were irradiated with a second magnetic field. Molecular models indicated that the distance between the protons α to chlorines in *40-anti* was 2.5 Å and that an enhancement of 5-10% in the integrated intensity could be expected (49). No enhancement could be observed on Caltech's EM-390 using the decoupler as the irradiating field. The only change in integrated intensities occurred at the strongest field for the minor isomer. However, instead of the methyl peak area increasing, the TMS peak decreased in size. This was reproducible over several scans; the significance of this result is unknown.

Several other acetylenes were found to add to the *cis*- cyclobutene diacid *32* (R = H) under the conditions employed for the 2-butyne addition. Increasing the steric bulk of the acetylene substituents increased the proportion of the minor (upfield) isomer in the photolysis mixture. Thus the *cis*-dichlorocyclobutene diacid *32* (R = H) added to 4-octyne in good yield to give an almost 50:50 mixture of the upfield and downfield isomers *41*. The *cis*-cyclobutene diacid *32* (R = H) added reluctantly (only about 50% yield by NMR) to bis-trimethylsilylacetylene to give a single isomer whose chemical shift of the α-chloro proton corresponded to the upfield isomer *42*.



cis-*32*

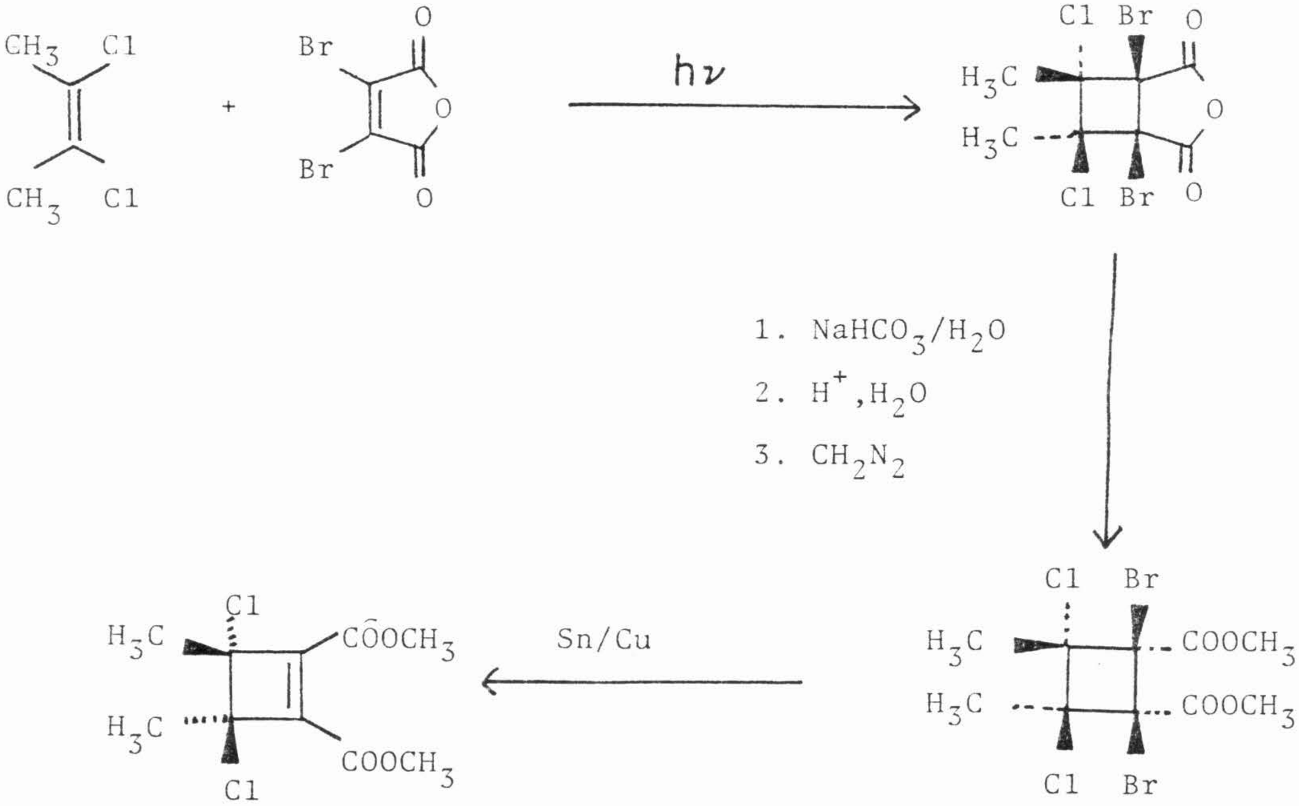
41



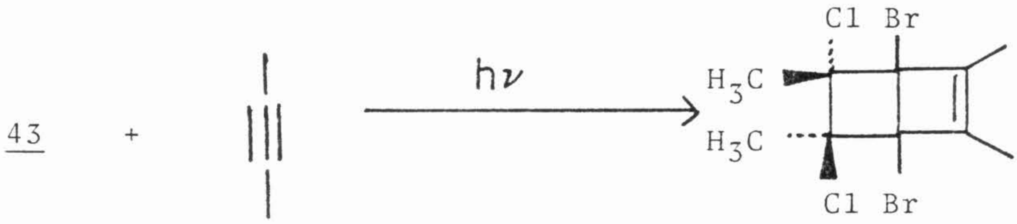
42

One possible explanation for these results was that when the substituents on the triple bond were small, i.e. methyl, the interaction between the chlorine substituents and the incoming acetylene was offset by the growing repulsion between the carboxyl or ester groups and the chlorines, and so the acetylene added on the side syn to the chlorines. However, when the acetylene became large, the chlorine and acetylene interaction dominated, and the trend was reversed. This analysis implied that the minor cis-bicyclohexene 39 (R = H, CH_3) had the chlorines anti to the carbonyls.

We also pursued the possibility of constructing bicyclohexene 44 on the assumption that an additional two methyl groups would provide even more stability against ring opening. The dimethyl 3,4-dichloro-3,4-dimethyl cyclobutene-1,2-dicarboxylate 43 was constructed in a sequence analogous to the one described above for the preparation of 32 (see next page). However, neither direct nor sensitized irradiation induced cyclobutene 43 to add to 2-butyne. The products of the photolysis obtained in the presence and absence of 2-butyne were similar by NMR and TLC. Determination of the structures of these products was not pursued further.



43

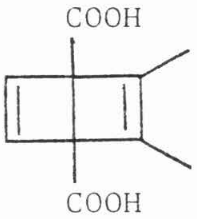


44

(not detected)

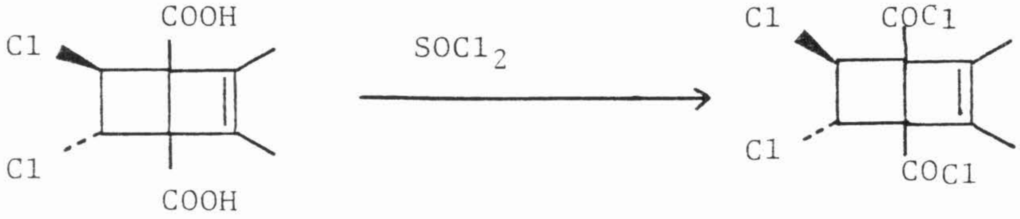
4. Closure of the Anhydride

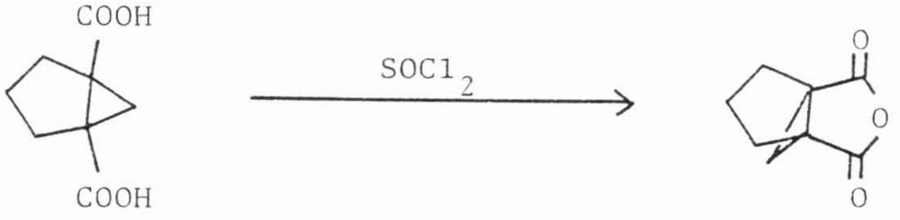
Closure of the anhydride could be accomplished before or after dechlorination of the bicyclohexene diacid. Since we believed that the Dewar diacid 45 would be thermally sensitive, we decided to close the anhydride before dechlorination if possible.



45

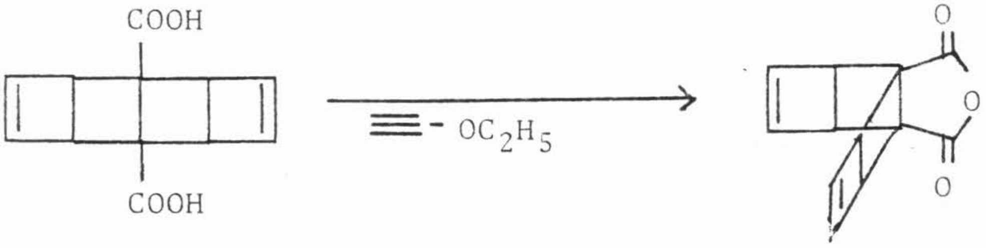
Initial attempts were made by treating the *trans*-bicyclohexene diacid (*trans*-39 (R = H)) with thionyl chloride. Use of excess thionyl chloride led to the formation of the acid chloride, in contrast to the result we obtained when the [3.1.0] bicyclohexene 46 was treated with thionyl chloride under the same reaction conditions.





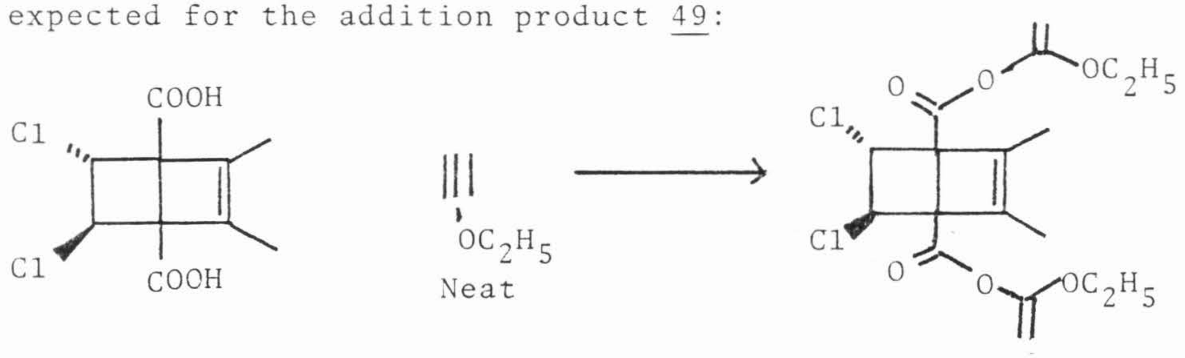
46

Gunther Maier communicated his results using neat ethynyl ethyl ether in the formation of the anhydride from the tetracyclic acid 47 (50):



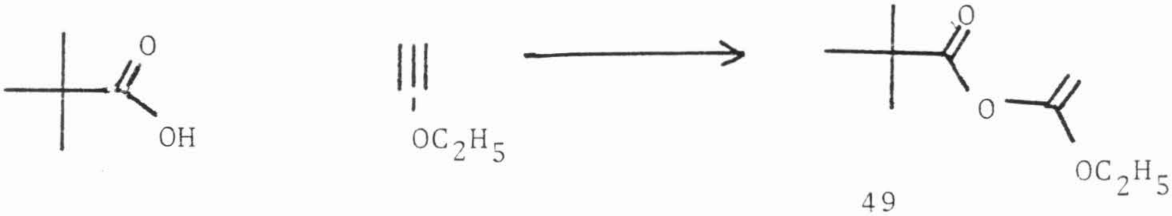
47

When the *trans*-bicyclohexene diacid *trans*-39 (R = H) was allowed to react with ethynyl ethyl ether under similar conditions a waxy solid was obtained that displayed strong bands in the infrared at 1760 and 1670 cm^{-1} and complicated multiplets in the NMR spectrum centered at δ 1.3 and 4.8 ppm in addition to the resonances expected for the bicyclohexene skeleton. Two features of the spectral data were curious. The IR band at 1670 cm^{-1} was very intense for a cyclobutene stretch and the proton NMR absorptions seemed to belong to the bicyclohexene fragment. Water was added to a solution of the solid in THF-d_8 in an NMR tube. Peaks appeared which were consistent with the formation of ethyl acetate. We began to suspect that the solid was the simple bis addition product 48 of ethynyl ethyl ether to the diacid 39. This was corroborated by our observation that pivalic acid treated with a large excess of ethynyl ethyl ether was transformed into a single product (analyzed by VPC) whose spectral data were those expected for the addition product 49:



trans-39 (R = H)

48

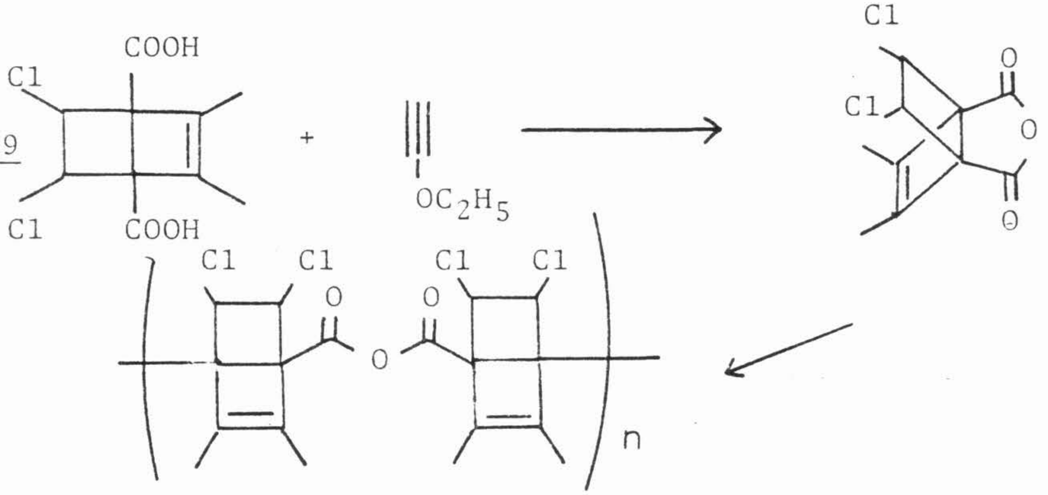


49

Once the identitiy of this bis addition product had been established it was easy to stop its formation. Treatment of the diacid trans-39 (R = H) with a slight excess of ethynyl ethyl ether in an NMR tube resulted in the formation of a new product with proton NMR resonances for the ring protons at δ 4.24 and 4.75 ppm (cf. trans-39 (R = H), which displayed resonances for the ring protons at δ 4.08 and 4.95 ppm). As the sample stood at room temperature these peaks decreased in size and were replaced by broad multiplets centered about δ 4.9 and 4.1 ppm. If the reaction were monitored by IR, the carbonyl absorption for the diacid disappeared while anhydride bands at 1850 and 1790 cm^{-1} grew. After a short period of time, these began to diminish and were replaced by new anhydride bands at 1810 and 1750 cm^{-1}. We were unable to obtain the anhydride trans-49 pure and free of the second formed anhydride.

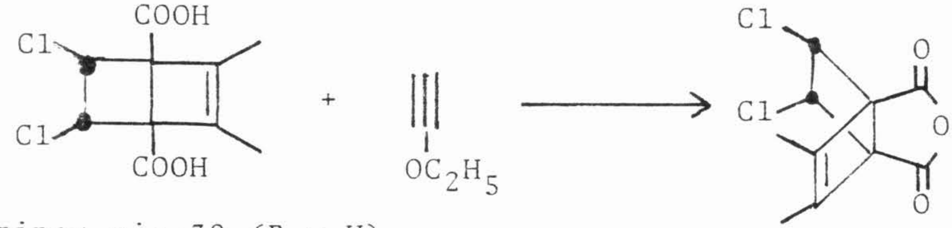
Our attention then turned to the cis-diacids 39 (R = H). Much to our dismay the major (downfield) cis isomer was found to exhibit behavior analogous to the trans-39 (R = H) upon reaction with ethynyl ethyl ether but even more rapidly. We were able to demonstrate that the bicyclohexene skeleton had not been altered by allowing the new anhydride from the major cis-39 (R = H) to stir in sodium bicarbonate solution followed by reacidification and reisolation of major _cis_-_39_ (R = H) in greater than 80% yield.

Both the NMR and IR data were consistent with the sequence shown below. Closure of the bicyclohexene diacid _39_ (R = H) occurred, but for the _trans_ and major _cis_ isomers the strained anhydride was unstable under the reaction conditions and produced an unstrained anhydride which was probably polymeric in nature.



39

Fortunately, the minor _cis_-bicyclohexene diacid _39_ (R = H) was found to react with one equivalent of ethynyl ethyl ether in chloroform to yield a stable anhydride _49_.

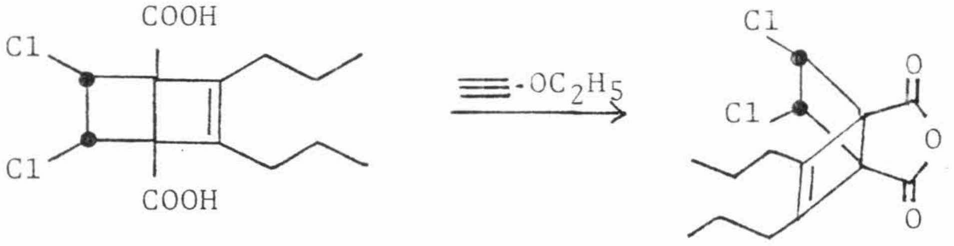


minor _cis_-_39_ (R = H)

_49_

The anhydride 49 could be purified by sublimation at 115°C and less than 0.001 mm or by chromatography on silica gel and was stable towards polymerization in a variety of solvents. Anhydride 49 was conveniently prepared in 100-150 mg batches for the dechlorination step which is discussed in the next section. The yield of anhydride after chromatography was routinely 80%.

The upfield 2,3-dipropylbicyclohexene diacid 41 and the bis-trimethylsilylbicyclohexene diacid 42 both formed a stable anhydride upon addition of one equivalent of ethynyl ethyl ether to a chloroform suspension of the diacid.



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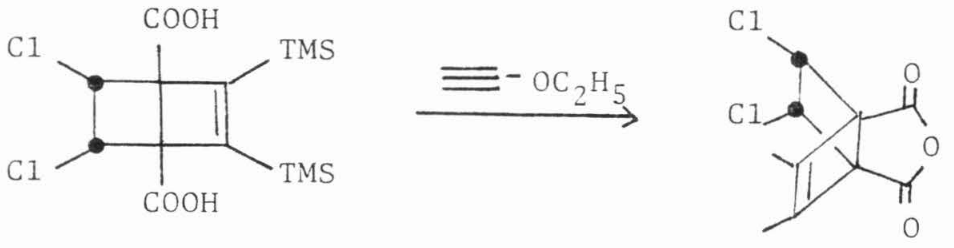


42

5. Dechlorination of Vicinal Dichlorides to Yield the Bicyclo [2.2.0] hexa-2,5-diene

The dechlorination reaction proved to be the most difficult step in the synthesis. The low reactivity of cyclobutyl chlorides combined with the thermal instability of the product and the presence of other easily modified functional groups made many of the more traditional methods of dechlorination fail. The dechlorination was attempted both before and after closing the anhydride. Early investigations were carried out using the 3,4-dichloro-1,2-dimethylcyclobutane anhydride 50 as a model (64). After we developed methods of producing large quantities of the bicyclohexene diesters and diacids 39 (R = CH_3, H) and the anhydride 49 efforts were concentrated on those materials. A listing of the reagents used is presented in Table I.

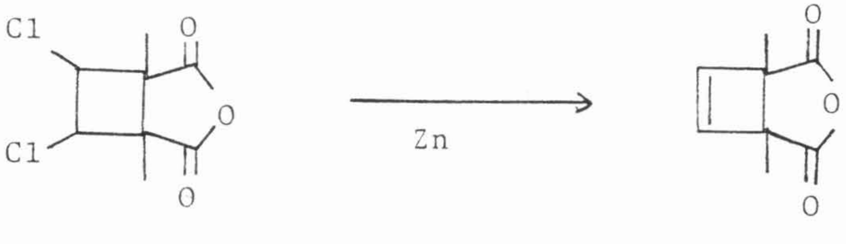
Since zinc has often been employed as a dehalogenation reagent, its use was surveyed first. Standard methods for activating the zinc include washing with dilute acid, formation of a zinc/copper couple, or preparation via the Riecke method (51). The first two forms of zinc proved to be inactive towards both the model anhydride 50 and the mixture of bicyclohexene diacids 39 (R = H) in refluxing THF. Use of the separated isomers did not affect this result.

Table 1. Reagents Surveyed to Effect Dechlorination of Vicinal Dichlorides

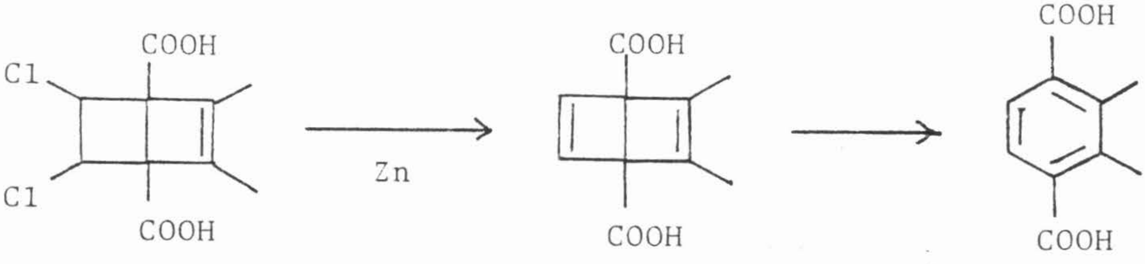
Na
Na/Hg
Li
Li/1% Na
Rieke Mn
Mg
Rieke Mg
Zn (HCl activated)
Zn/Cu
Rieke Zn
Cr(II)

$\text{NaNaphth}^{\dot{-}}$
Na/NH_3
n-Butyllithium
t-Butyllithium
NaI/acetone
CpFe(CO)_2^{-}
$[\text{CpFe(CO)}_2]_2$
$(\text{n-C}_4\text{H}_9)_3\text{SnH}$
$(\text{n-C}_4\text{H}_9)_6\text{Sn}_2$
$(\text{CH}_3)_6\text{Sn}_2$
$(\text{C}_6\text{H}_6)_6\text{Sn}_2$
$[\text{CpCr(NO)}_2]_2$
$[\text{CpMo(CO)}_3]_2$

A more reactive form of zinc, Rieke zinc, was prepared by the addition of sodium naphthalide in THF or dimethoxyethane to a solution of anhydrous zinc chloride in the same solvent (52). This preparation was unsatisfactory in the reaction with anhydrides because the large amounts of naphthalene complicated the work-up. A more satisfactory result was obtained by centrifuging the fine suspension, removing the supernatant, and resuspending the pelleted zinc. This sequence was carried out under argon and repeated until an acceptably low level of naphthalene remained. Alternatively, the Rieke zinc was prepared by refluxing pieces of potassium in a THF solution of zinc chloride (51). Rieke zinc prepared by either of these methods was found to dechlorinate the model anhydride 50 to yield 51 in yields ranging from 40-70% as assayed by NMR spectroscopy. The zinc also dechlorinated the diacids 39 (R = H). However, under the conditions required for dechlorination (reflux in THF) the product Dewar benzene 45 was unstable. At short reaction times only a fraction of the diacids were found to react even in the presence of a large excess of zinc. During the long reaction times required for more complete conversion, the Dewar benzene ring opened to 52 (53). The reactivity of the vicinal cyclobutane dichlorides towards the zinc was not increased by changing the halide counter ion or by changing the ratio of zinc chloride to to reducing agent in the preparation of the zinc. Addition of potassium iodide to the reaction mixture also had no effect (51).



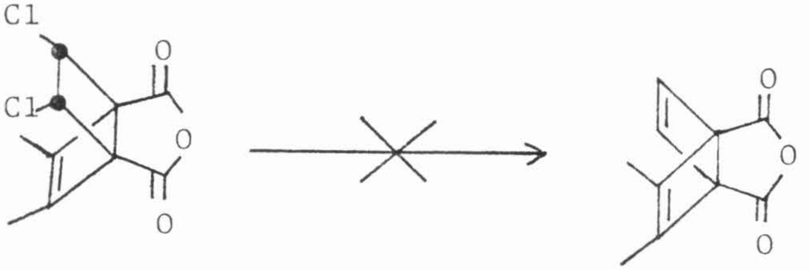
50 51



39 (R = H) 45 52

The bicyclohexene dimethyl esters 39 (R = CH_3) proved to be unreactive to Rieke zinc in refluxing THF. The major cis-bicyclohexene dimethyl ester 39 (R = CH_3) also was not dechlorinated by zinc/copper couple even in THF or methanol under reflux for several days.

After we found that one of the cis-bicyclohexene diacids 39 (R = H) would form a stable anhydride, we attempted to dechlorinate it with Rieke zinc. When the reaction was carried out in an NMR tube at 60°C, a small new peak was observed in the NMR spectrum at δ 6.9 ppm. This was consistent with the formation of the desired anhydride 53. However, when the reaction was repeated on a preparative scale, only disappearance of starting material was observed with no evidence for the desired product.



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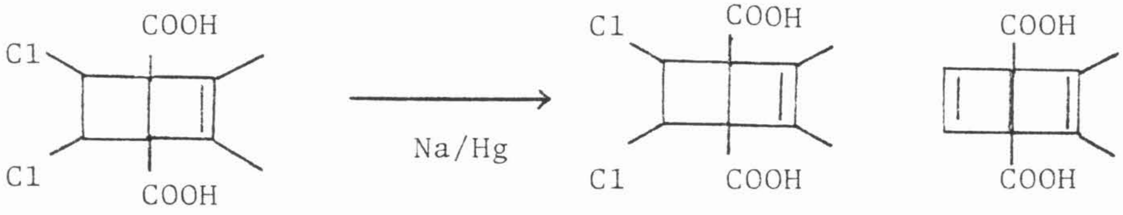
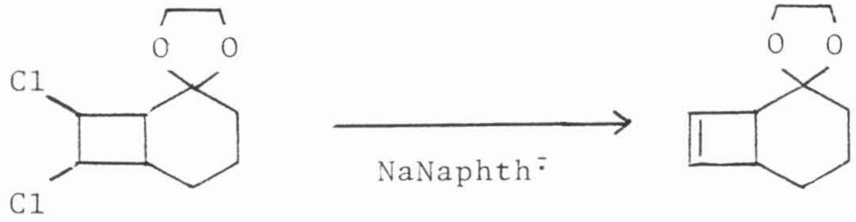
Magnesium, both in the form of turnings and Rieke magnesium, did not dechlorinate the dichlorocyclobutane anhydride 50 (54). Rieke manganese was also unreactive towards anhydride 50. Sodium, lithium, and lithium with 1% sodium did not dechlorinate bicyclohexene diacids 39 (R = H). Sodium amalgam reacted with the anhydride 50 and the diesters 39 (R = CH_3) to produce an uncharacterizable mixture of products, but did react with the bicyclohexene diacids 39 (R = H) to produce some of the desired Dewar diacid 45. Efforts to optimize the yield of the Dewar diacid by changing the strength of the amalgam, the reaction temperature, and the solvent failed to improve the situation. We did not obtain a conversion of 39 (R = H) to 45 in yield greater than about 30% at any time.



39 (R = H) 39 (R = H) 45

The use of several anions was examined. The obvious Finkelstein reaction (NaI/acetone) was attempted on the model anhydride 50 with no success. Alkyllithiums appeared to cause ring opening of the anhydride 50 and gave an unmanageable product mixture with the bicyclohexene diacids 39 (R = H). Reaction of $CpFe(CO)_2^{-1}$ with 50 produced none of the desired product 51 and instead appeared to give material in which the anhydride had opened.

Although sodium naphthalide in THF was used successfully in the dechlorination of the vicinal dichloride 54 to give 55 (55), neither reaction of sodium naphthalide with 50 nor with the bicyclohexene diester 39 (R = CH_3) gave any of the desired products.



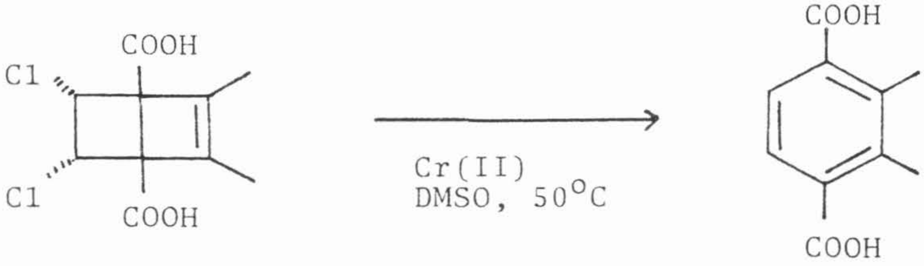
54 55

Considerable effort was spent on the reaction of the bicyclohexene diacids 39 (R = H) and their sodium or lithium salts with sodium in ammonia (56). In the crude NMR spectrum of the product mixture, in addition to the Dewar diacid at δ 6.9 ppm and starting material, resonances at around δ 6.0 ppm were observed. Very little of the Kekule diacid 52 was formed. The anomalous protons at δ 6.0 ppm were ascribed to a cyclohexadiene moiety formed by reduction of the central bond. Cleavage of strained carbon-carbon bonds bearing carbomethoxy groups often occurs upon reduction with sodium in ammonia(57a) or under the conditions of the acyloin condensation(57b).

The last class of reagents was metal complexes which would abstract a chlorine without attacking or reducing the carbonyls. Complexes containing a metal-metal bond were examined. $[CpMo(CO)_3]_2$ and $[CpFe(CO)_2]_2$ did not dechlorinate the dichlorocyclobutane 50 upon photolysis (58).

Kochi has demonstrated that solutions of Cr(II) in dimethylformamide or dimethylsulfoxide reacted with organic halides at room temperature to produce organic radicals and with vicinal dihalides to produce high yields of olefins (59). Although attempts to dechlorinate the model anhydride 50 using Cr(II) were unsuccessful, we did find that the major cis-bicyclohexene dicarboxylic acid 39 (R = H) was dechlorinated in low yield to give the Kekule diacid after work-up. The dechlorination occurred under thermal conditions where we would have expected to isolate some of the Dewar diacid based on the results with zinc. The reaction could be carried out to complete conversion but still low yield if a large excess of Cr(II) were used and the reaction mixture heated at about 50°C.

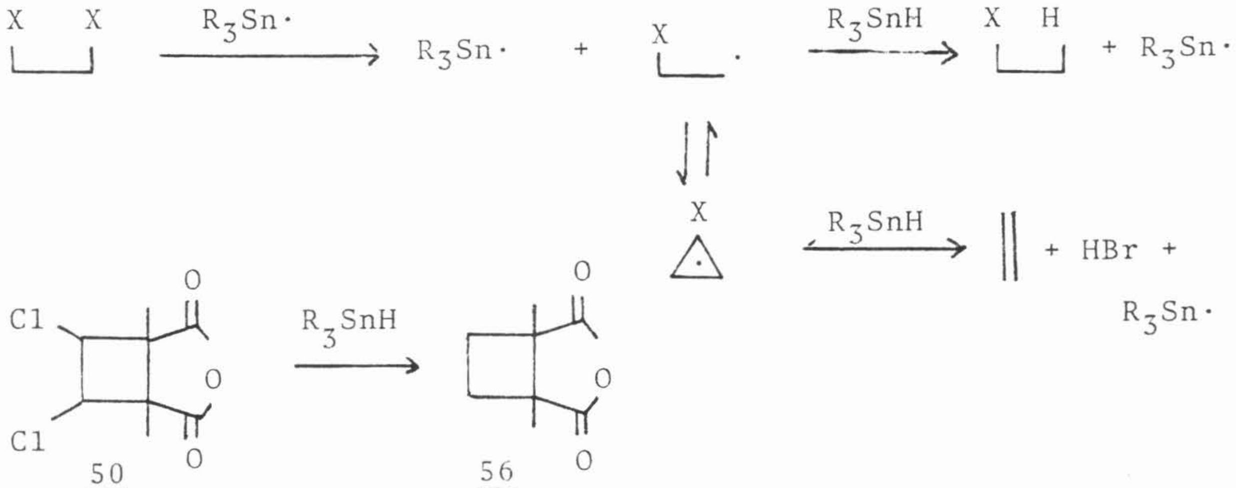
In order to enhance the reactivity of the Cr(II), Kochi added ethanolamine, which formed a complex with the Cr(II) as evidenced by a color change from blue to purple. We observed the same color change upon addition of the diacid. The addition of ethanolamine did not affect the course of the reaction.



major cis-39 (R = H)

52

We next examined the use of tin centered radicals because of their compatibility with a wide variety of functional groups. Trialkyltin and triaryltin hydrides had been previously shown to debrominate vicinal dibromides to yield olefins (60). Vicinal dichlorides reacted with tin hydrides but yielded the saturated hydrocarbon instead (60). The postulated mechanism for this transformation is as follows: Reaction of a trialkyltin hydride with a vicinal dihalide is initiated by the generation of a trialkyltin radical. The trialkyltin radical then abstracts a halogen and produces a α-halo radical. This radical may react in two possible ways. It can react with tin hydride to produce an alkene or a haloalkane. When X = Br, the alkene is produced, presumably via the bridged complex. When X = Cl, production of the haloalkane is favored. As expected, reaction of anhydride 50 with tri-n-butyltin hydride failed to produce any of the unsaturated anhydride 51, but yielded the saturated anhydride 56.



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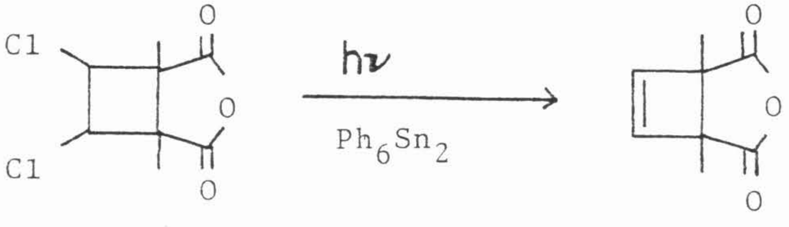
We reasoned that if a convenient source of trialkyltin or triaryltin radicals which was not also a hydride source were found this might effect dechlorination of the vicinal dichlorides.

Hexamethyldisilane and hexamethyldigermane were known to react upon photolysis with 1,2-dibromoethane to produce ethylene (61). Forrest and Ingold had used the photolysis of hexamethylditin to produce trimethyltin radicals, which were trapped by trithiocarbonates (62). We explored the photolysis of hexamethylditin and hexaphenylditin in the dechlorination of the anhydride 50 to yield the cyclobutene anhydride 51. Our initial experiments using various solvents were very encouraging. Irradiation of a solution of hexaphenylditin and 50 in THF-d_8 produced a 50% yield of 51 after 75% of the starting material had been consumed.

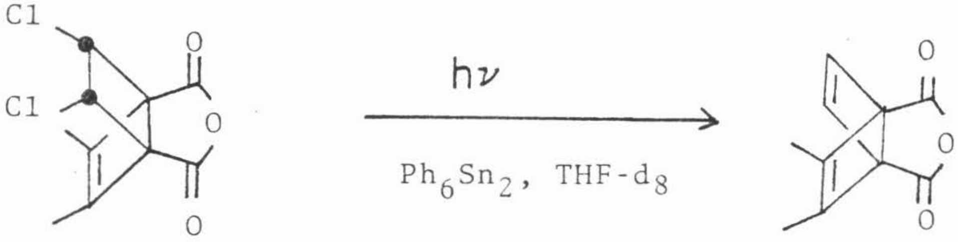
Irradiation in benzene-d_6 produced only 18% yield of the cyclobutene 51 with 50% of the starting cyclobutane 50 consumed. Irradiations in dichloroethylene, chlorobenzene, and acetonitrile were found to produce none of the desired cyclobutene. The low solubility of the hexaphenylditin was a problem in all solvents tested.



50 51

Hexamethylditin, which was miscible with both benzene and THF, was tested as a photochemical source of trimethyltin radicals. In contrast to the case with the hexaphenylditin experiments, benzene-d_6 proved to be the better solvent. In benzene-d_6 using an excess of hexamethylditin, the starting material 50 was totally consumed within two hours of photolysis and a 40% yield of the desired cyclobutene was obtained, as analyzed by NMR spectroscopy. Addition of benzophenone or acetophenone as sensitizers resulted in destruction of the sensitizer and lower yields of the desired product.

Work was then intensified on the synthesis of the target anhydride 53 from the stable dichloroanhydride 49. Irradiation of a THF-d_8 solution of hexaphenylditin and 49 gave a small peak in the NMR spectrum at δ 6.9 ppm, which was distinguishable from the hexaphenylditin peaks. Use of the diacid 39 (R = H) instead of the anhydride 49 gave evidence only for ring opening to the Kekule form 52.



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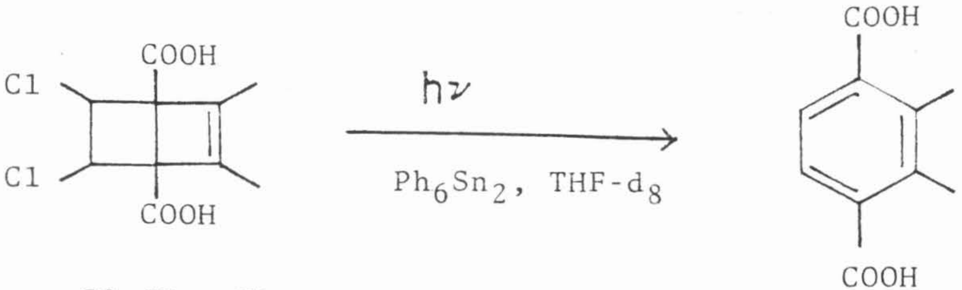
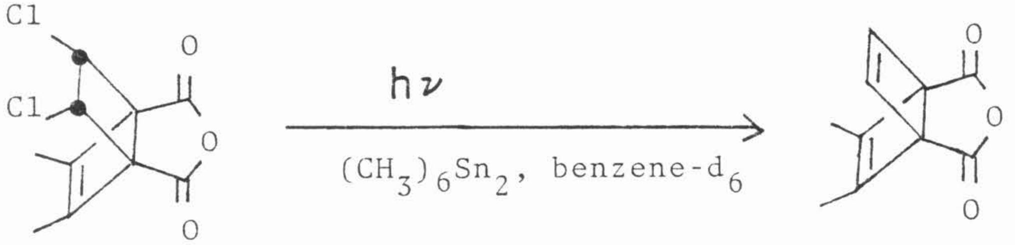


39 (R = H)

52

Irradiation of 49 in the presence of a large excess of hexamethylditin in benzene-d_6 gave clear indication that the anhydride 53 was being formed. After 1.75 hours of photolysis, the anhydride 53 was formed in 70% yield as assayed by NMR spectroscopy after correcting for unreacted starting material. The best procedure for isolating the anhydride 53 was to vacuum transfer the volatiles (which included 53) and chromatograph them in an inert atmosphere on silica gel, eluting first with petroleum ether and then with diethyl ether. The diethyl ether was removed carefully to leave the anhydride 53.



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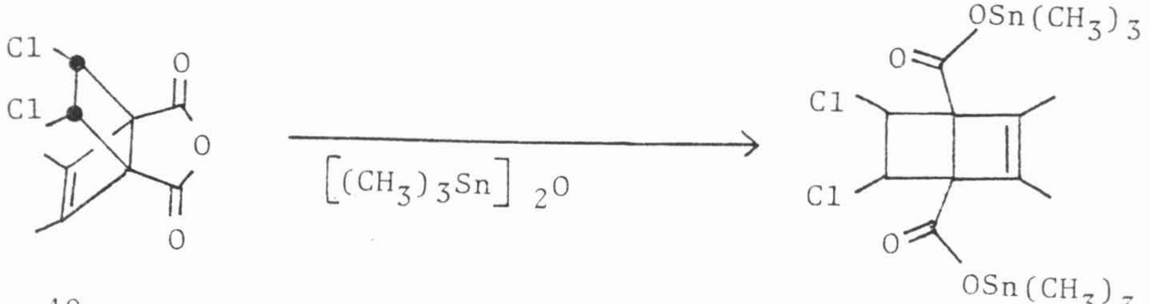
53

This procedure required large excesses of hexamethylditin or the photolysis simply became too slow with respect to decomposition of the product. Further complicating this procedure was the finding that in the presence of large excesses of hexamethylditin, the anhydride 49 was transformed into a new compound distinguishable in the NMR spectrum by a shift of about 0.33 ppm downfield for the protons α to the chlorines. The IR spectrum of this new compound (obtained only in the benzene/hexamethylditin reaction mixture) had a carbonyl band at 1690 cm^{-1}. This was consistent with the trimethylstannyl ester 57 which may have arisen from the reaction of a possible hexamethylstannoxane impurity in the hexamethylditin. Efforts to remove this stannoxane by distillation or sublimation were unsuccessful.



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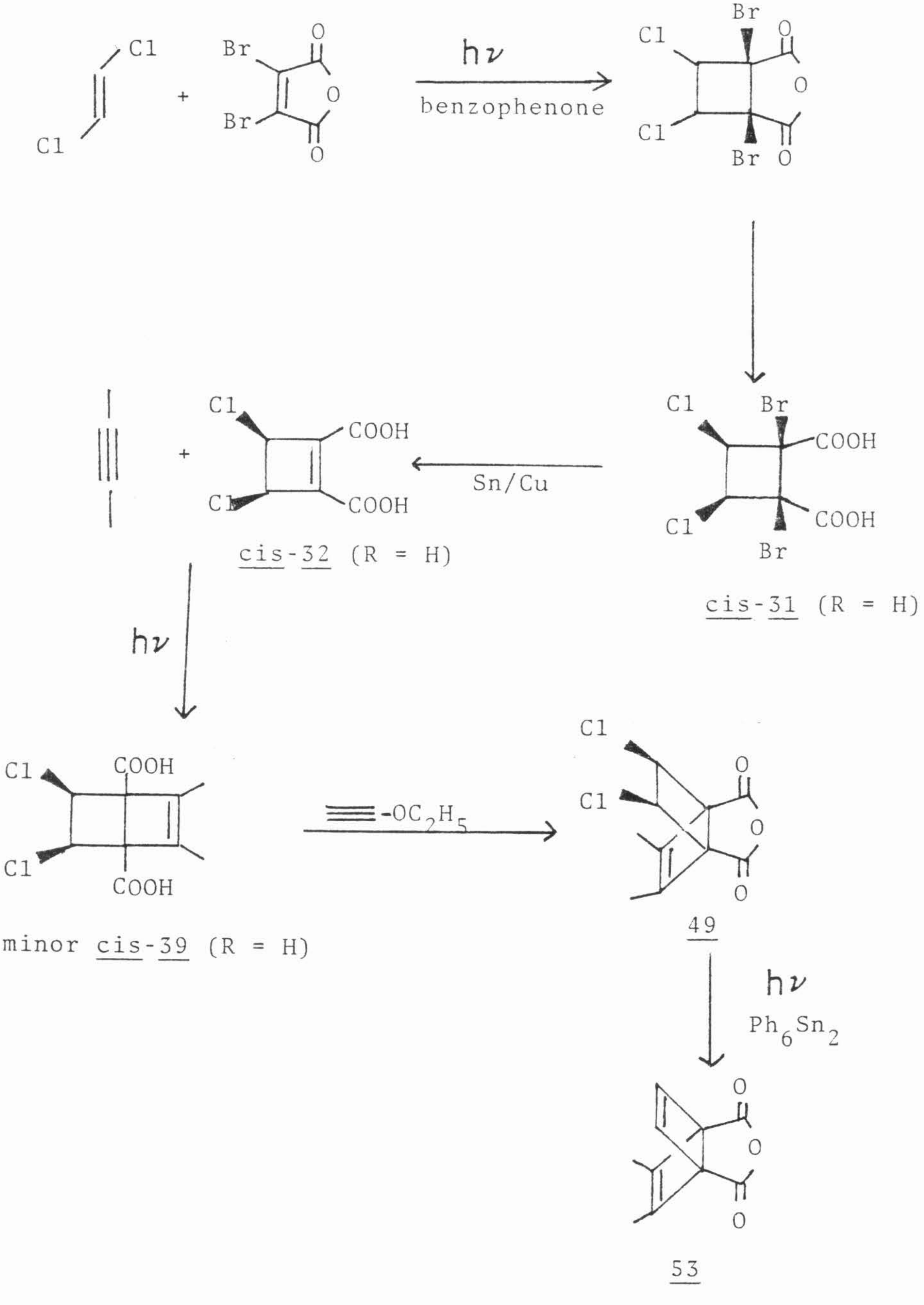
As mentioned previously, photolysis of hexaphenylditin and anhydride 49 in THF-d_8 produced a variety of products as evidenced by the number of new methyl groups appearing in the NMR spectrum. The reaction was much cleaner in benzene-d_6, although much slower due to the low solubility of the tin compound in benzene. Reducing the concentration of the anhydride from about 100 mM to less than 5 mM allowed us to use the clean hexaphenylditin photolysis in benzene-d_6 as the method of preparing 53. Thus, large scale preparations of about 0.5 mmoles of 49 were carried out in benzene. Work-up was very simple. After the NMR spectrum indicated that photolysis was complete, the anhydride was digested with a cold sodium bicarbonate solution and the reaction mixture was extracted repeatedly with chloroform and ether to remove any tin compounds. It was then reacidified and extracted with ether. Removal of the ether yielded the crude Dewar diacid 45 in about 60% yield. Reclosure of the diacid to the anhydride was achieved at room temperature using ethynyl ethyl ether in chloroform. Chromatography of the anhydride on silica gel in chloroform removed any remaining tin compounds. After removal of the chloroform, the anhydride 53 was obtained in about 25% overall yield from 49.

The anhydride 53 was a colorless solid which polymerized rapidly when allowed to warm above 30°C in the solid state. It was volatile enough to be vacuum transferred at room temperature and 0.001 mm Hg from a flask to an NMR tube. It was therefore suitable for matrix isolation studies (see Chapter III).

There remained, however, one final surprise. Our original source of hexaphenylditin was Alfa, who stopped supplying it. When we switched to a sample supplied by Pfaltz and Bauer, the dechlorination reaction simply ceased to work. Upon photolysis a complex mixture of new methyl groups appeared in the NMR spectrum. The reaction was magically restored by the addition of about 0.5 equivalents of triethylamine to the photolysis mixture. Reexamination of the NMR spectra of the reactions using

Alfa hexaphenylditin showed that triethylamine had been present in trace amounts as an impurity left behind from its synthesis. The role of the triethylamine in the reaction mechanism has not been demonstrated.

Shown on the next page is a summary of the successful synthesis of the anhydride 53.


hν
benzophenone
Sn/Cu
cis-32 (R = H)
cis-31 (R = H)
hν
minor cis-39 (R = H)
≡-OC2H5
49
hν
Ph6Sn2
53

6. Experimental

General. Nuclear magnetic resonance spectra were recorded on Varian A-60, A-56-60, or EM-390 Spectrometers. All chemical shifts (δ, in parts per million) were measured using internal tetramethyl silane (TMS) as a standard (δ 0.00 ppm) or by measuring the chemical shift of the peak relative to the peak arising from the residual protons in the NMR solvent. Infrared spectra were recorded on a Beckman IR 4210 or a Perkin Elmer 283 Spectrophotometer. Ultraviolet spectra were recorded on a Varian Cary 18. Mass spectral analyses were performed by the Caltech analytical laboratory.

Mucobromic acid was obtained from Aldrich Chemical Co. and dichloroethylene from Pfaltz and Bauer. Hexamethylditin and hexabutylditin were purchased from Alfa. Hexaphenylditin was obtained from Alfa and Pfaltz and Bauer. 2-Butyne and 4-octyne were supplied by Farchan. Chloroform was spectrophotometric grade. Alkyllithiums were purchased from Alfa. Diethyl ether was anhydrous grade from Mallinkrodt. All other chemicals were reagent grade.

All manipulations requiring an inert atmosphere were carried out in a Vacuum Atmospheres Recirculating Dri-Lab or on a high vacuum line. Tetrahydrofuran (THF) and benzene were distilled from sodium benzophenone dianion and stored in the dry box. THF-d_8 and benzene-d_6 were also distilled from sodium benzophenone dianion prior to use. The benzene used in the hexamethylditin and hexaphenylditin photolyses was kept free of tetraglyme, which was often added in our laboratory in order to speed formation of sodium benzophenone dianion. Petroleum ether (30 - 60°) was stirred over sulfuric acid and potassium permanganate, and allowed to stand over calcium hydride before distillation from sodium benzophenone dianion.

The descriptions of reactions which follow are necessarily incomplete because the research notebook which contained the original notes was stolen. I have tried to reconstruct the specific preparations that led to the synthesis of the title anhydride in as great detail as possible. Since I remembered successful experiments best, the quoted yields are accurate to within 5%.

Dibromomaleic anhydride 33 (44). Mucobromic acid (200g = 0.77 mole) was dissolved in 125 ml of fuming nitric acid and heated with an oil bath at 65°C overnight. The solid dibromomaleic acid was filtered and dried in a dessicator over KOH. The crude diacid was then dissolved in acetyl chloride (200 ml) containing 3 drops of H_2SO_4 and heated over a hotplate at 65°C until crystals of dibromomaleic anhydride formed. The crude anhydride was allowed to cool, collected, filtered, and sublimed (0.050 torr, 75°C, cold finger at 0°C) to yield dibromomaleic anhydride (150g, 0.58 mole, 75%). IR (THF) 1850, 1790 cm^{-1} (C=O), 1625 cm^{-1}(C=C).

<u>1,2-Dibromo-3,4-dichlorocyclobutane-1,2-dicarboxylic acids 31 (R = H)</u>. Dibromomaleic anhydride (60g, 0.23 mole) and benzophenone (10g, 0.05 mole) were dissolved in approximately 1200 ml of 1,2-dichloroethylene. The solution was placed in an immersion well and degassed by bubbling nitrogen through the solution for 20 min. The nitrogen stream was then slowed and the solution irradiated through Pyrex with a Hanovia 450W medium pressure mercury arc lamp. The solution was cooled by a water bath which was in turn cooled by a coil containing circulating ethylene glycol from a Formabath. The temperature of the bath was maintained at less than 25°C. Aliquots were withdrawn from the solution at intervals and the disappearance of dibromomaleic anhydride was monitored by vapor phase chromatography (VPC). The reaction was typically greater than 95% complete within 10 hours. After the disappearance of the dibromomaleic anhydride, the dichloroethylene was removed by rotary evaporation and recovered by maintaining the cooling coils in the rotary evaporator at -20°C by means of a Formabath. The crude dark oil was dissolved in ether and stirred vigorously while saturated sodium bicarbonate was added. Stirring was continued for several hours and the layers were separated. The aqueous layer was extracted with ether and then acidified with 25% HCl until the dark solution

became cloudy. The cloudy solution was saturated with NaCl and then extracted repeatedly with ether. The organic layers were combined, dried over magnesium sulfate, and evaporated to yield 105g of crude diacid **31** (R = H) as a mixture of isomers in about a 6:3:1 *trans*:major *cis*:minor *cis* ratio. The crude diacids could be treated with an ethereal solution of diazomethane to produce a mixture of diesters **31** (R = CH_3).

The isomeric diacids **31** (R = H) could be separated by treatment of the crude material with thionyl chloride and then fractional distillation of the anhydrides. The anhydrides were distilled through a 4 inch Vigreaux column at 0.025 torr. Major fractions distilling at about 80°C (mostly *trans*) and 115°(mostly major *cis*) were collected. The pot residue consisted of almost entirely the minor *cis* isomer and was not purified. These fractions were dissolved in ethanol free chloroform containing one equivalent of water. After a few minutes the solution warmed and the predominate isomer precipitated in about 95% purity. The yield of the isolated diacids was about 50% of theoretical. The NMR spectra of the acids agreed with those previously reported (42). *Trans*-**31** (R = H), ^1H-NMR (Ac-d_6) δ 5.12 (d, J = $9H_3$), 4.75 (d, J = $9H_3$) ppm. Lit.: δ 5.15 (d, J = $9H_3$), 4.79 (d, J = $9H_3$) ppm. *Cis*-**31** (R = H), ^1H-NMR (Ac-d_6) δ 5.45 (s, 2H) ppm. Lit.: δ 5.42 (s, 2H) ppm.

Cis-3,4-dichlorocyclobutene-1,2-dicarboxylic acid (cis-32 (R = H)). Cis-1,2-dibromo-3,4-dichlorocyclobutane-1,2-dicarboxylic acid (980 mg, 2.64 mmoles) and tin/copper couple (180 mg, 3 mmoles) were weighed out in a dry 50 ml round bottom flask equipped with a stir bar. THF (25 ml) was added and the reaction mixture was stoppered and then allowed to stir overnight. The reaction mixture was then concentrated on a rotary evaporator and diethyl ether (25 ml) was added. The precipitated tin halide was removed by filtration. The filtrate was dissolved in an additional 50 ml of ether and transferred to a 125 ml Erlenmeyer flask. Fifty ml of a 10% sodium bicarbonate solution was added and the mixture allowed to stir for 1 hour. The two phase mixture was filtered to remove a gelatinous precipitate and the aqueous layer was acidified by the dropwise addition of 25% HCl. The aqueous layer was saturated with NaCl and extracted four times with 50 ml of diethyl ether. The combined ether extracts were dried over $MgSO_4$. The ether was removed by rotary evaporation to leave a yellow oil. The oil was triturated with chloroform and cis-32 (R = H) crystallized in two crops. The diacid (435 mg, 2.06 mmoles, 78%) was used in subsequent reactions without further purification. ^1H-NMR(Ac-d_6) δ 5.45 (s, 2H) ppm. IR(KBr) 1690 cm^{-1} (C=O).

The cis- dimethyl ester 32 and the trans-32 (R = H, CH_3)

were prepared from the appropriate dibromodichlorocyclobutane 31 in similar yield. Trans-32 (R = CH_3) had been prepared previously (42). Cis-32 (R = CH_3) ^1H-NMR (Ac-d_6), δ 5.53 (s, 2H) 3.92 (s, 6H) ppm. IR ($CHCl_3$) 1710 cm^{-1} (C=O). Precise mass: 237.984, calc. for $C_8H_8Cl_2O_4$: 237.980. Trans-32 (R = CH_3) ^1H-NMR ($CDCl_3$) δ 4.80 (s, 2H), 3.88 (s, 6H) ppm. IR ($CHCl_3$) 1710 cm^{-1} (C=O). Trans-32 (R = H), ^1H-NMR (Ac-d_6) δ 4.97 (s, 2H) ppm. IR (thin film) 1690 cm^{-1} (C=O).

Cis-5,6-dichlorobicyclo[2.2.0]hex-2-ene-1,4-dicarboxylic acid 39 (R = H). Cis-3,4-cyclobutene-1,2-dicarboxylic acid 31 (R = H) (1g, 4.7 mmole) was placed in a 250 ml Pyrex tube (15mm inner diameter) and dissolved in about 1 ml of acetone. Benzophenone (200 mg, 1.16 mmole) was added, and the tube was topped with a vacuum stopcock. The solution was degassed with three freeze-pump-thaw cycles and then dry, degassed 2-butyne was distilled into the tube *in vacuo*. The 2-butyne/acetone solution of the cyclobutene and benzophenone was then irradiated in a water bath cooled by a Formabath next to a Hanovia 450W lamp in an immersion well for twelve hours. The tube was then opened, the crystals scraped from the sides of the tube, and the contents of the tube filtered through a medium fritted glass filter. The crystals were collected and washed quickly with 2 ml of acetone and 2 ml of ether.

These crystals were the "upfield" bicyclohexene diacid 39 (R = H) (approximately 300 mg, 1.1 mmole, 24%). ^{1}H-NMR (Ac-d_6) δ 4.72 (s, 2H), 1.82 (s, 6H) ppm.

The "downfield" bicyclohexene diacid was isolated from the filtrate contaminated with about 5% of the "upfield" isomer by diluting the filtrate with diethyl ether and washing it with a 10% sodium bicarbonate solution. The ethereal solution was then reacidified with 25% HCl, saturated with NaCl, and extracted repeatedly with diethyl ether. The ether layers were combined, dried over $MgSO_4$, and then evaporated to give the crude major bicyclohexene diacid (800 mg, 3.01 mmoles, 64%). The diacid could be recrystallized from chloroform to give this "downfield" isomer free of the "upfield" isomer. ^{1}H-NMR (Ac-d_6) δ 5.26 (s, 2H), 1.88 (s, 6H) ppm.

The trans-bicyclohexene diacid 39 (R = H) was prepared from the trans-cyclobutene diacid 32 (R = H) and 2-butyne in a manner similar to the one described above. ^{1}H-NMR (Ac-d_6) δ 4.99 (d, J = 4.5 Hz, 1H), 4.35 (d, J = 4.5 Hz, 1H), 2.84 (broad s, 6H) ppm.

The bicyclohexene diesters 39 (R = CH_3) could be prepared from the cyclobutene diesters 32 (R = CH_3) and 2-butyne in a manner similar to the one described above or by treating the bicyclohexene diacids with thionyl chloride followed by methanol. The bicyclohexene diesters

39 (R = CH_3) had the following properties:

Minor *cis*-bicyclohexene diester *39* (R = CH_3) as an impure oil: ^{1}H-NMR ($CDCl_3$) δ = 4.41 (s, 2H), 3.72 (s, 6H), 1.74 (s, 6H) ppm. IR ($CDCl_3$) 1730 cm^{-1} (C=O).

Major *cis*-bicyclohexene diester *39* (R = CH_3) ^{1}H-NMR δ 5.05 (s, 2H), 3.68 (s, 6H), 1,82 (s, 6H) ppm, IR ($CDCl_3$) 1730 cm^{-1} (C=O), precise mass: 292.026, calc. for $C_{12}H_{14}Cl_2O_4$: 292.026.

Trans-bicyclohexene diester *39* (R = CH_3) solid: ^{1}H-NMR ($CDCl_3$) δ = 5.02 (d, J = 4.5 Hz, 1H), 4.04 (d, J = 4.5 Hz, 1 H), 3.76 (s, 3H), 3.67 (s, 3H), 1,8 (s, 6H) ppm, IR ($CDCl_3$) 173 cm^{-1} (C=O), precise mass: 292.026, calc. for $C_{12}H_{14}Cl_2O_4$: 292.026.

Epoxides 40 from cis-39 (R = CH_3). An amount of each of the *cis*-*39* (R = CH_3) isomers was placed in an NMR tube along with an excess of *p*-nitroperbenzoic acid. The mixture was dissolved in dichloromethane. The NMR tube caps were secured with parafilm, and the tubes were heated in an oil bath at 50°C. The solutions were checked by NMR and were heated for 24 hours until all the starting material had been consumed. Work-up was accomplished by washing the reaction mixture with sodium thiosulfate solution until no yellow color was produced. The organic layer was separated and chromatographed to separate the epoxide from some methyl *p*-nitrobenzoate produced in the reaction. The epoxides were obtained in low yield and used directly in the nuclear Overhauser experiment after dissolution in $CDCl_3$ and carefully degassed. Epoxide from minor cis-39 (R = CH_3): ^1H-NMR ($CDCl_3$) δ 4.70 (s, 2H), 3.72 (s, 6H), 1.6 (s, 6H) ppm. Mass spectrum shows parent + 1 at m/e = 309. Epoxide from major cis-39 (R = CH_3): ^1H-NMR ($CDCl_3$) δ 5.2 (s, 2H), 3.72 (s, 6H), 1.70 (s, 6H) ppm.

Nuclear Overhauser Experiments

	Integration			
	minor		major	
Irradiating Field (mG x 10)	CH_3	TMS	CH_3	TMS
0.0	69	117	49	86
0.4	68	117	49	88
0.8	60	91	50	88

Integration is expressed in arbitrary units and is the average of three determinations. For a given field strength, the integral did not vary by more than 2 units over the three integrations.

Lanthanide Shift Experiments

The NMR spectra of the bicyclohexene diesters 39 (R = CH_3) were measured after the addition of successive aliquots of 0.75 M $Eu(fod)_3$. The data are displayed in the following figures (Figure 1, Figure 2).

Figure 1. About 10 mg of trans - bicyclohexene ($R = CH_3$) was placed in an NMR tube and dissolved in 350 l of $CDCl_3$. Aliquots of 0.75 M $Eu(fod)_3$ were added. The shift of the protons to the chlorines is plotted vs the average shift of the carbomethoxy protons. The lines have no theoretical significance.

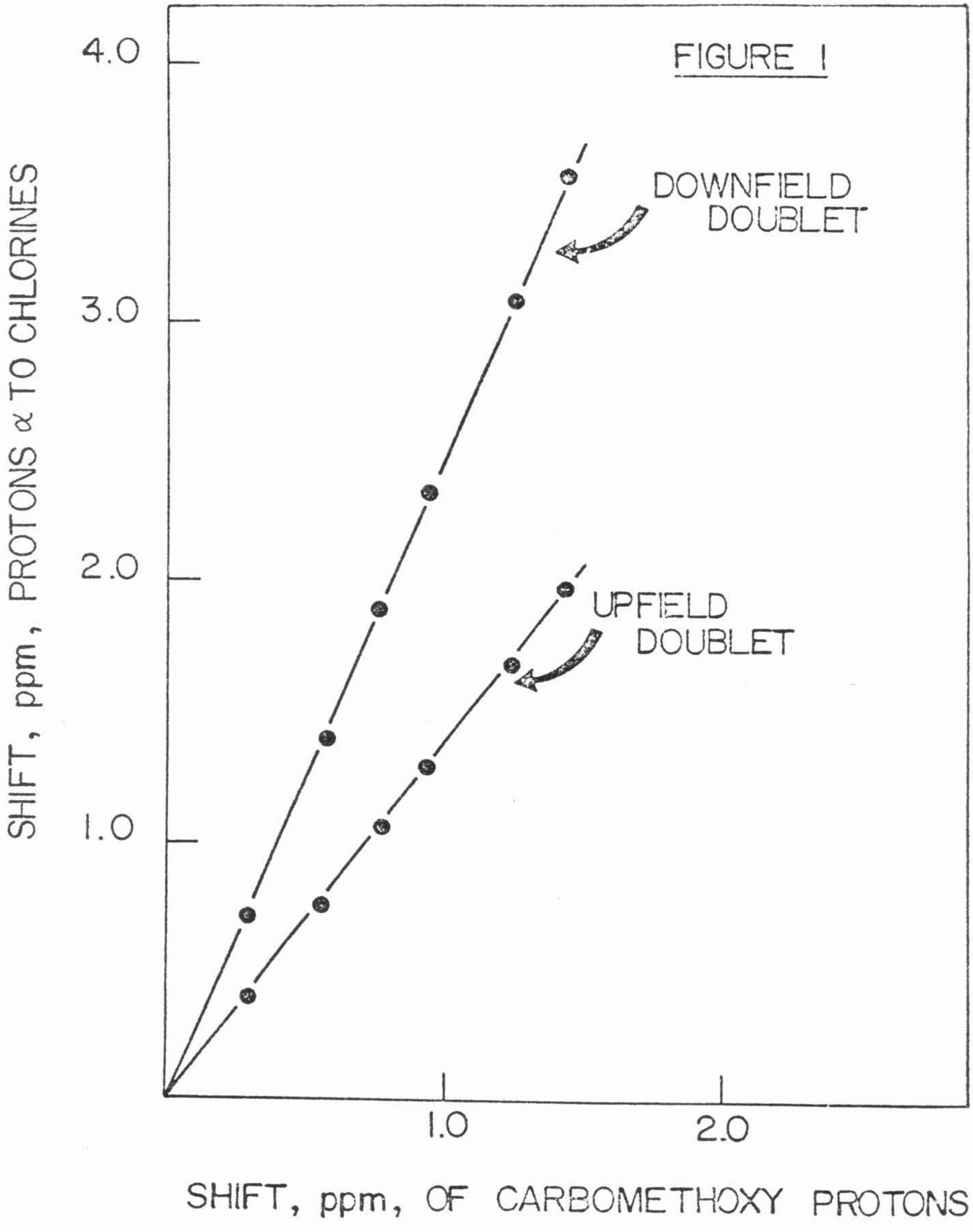


FIGURE I
DOWNFIELD DOUBLET
UPFIELD DOUBLET
4.0
3.0
2.0
1.0
1.0
2.0
SHIFT, ppm, PROTONS α TO CHLORINES
SHIFT, ppm, OF CARBOMETHOXY PROTONS

Figure 2 . 10 mg of the major *cis*- bicyclohexene 39 (R = CH_3) was placed in an NMR tube. A solution of 5 mg of the minor *cis* - bicyclohexene 39 (R = CH_3) in 350 1 of $CDCl_3$ was added to the tube. Aliquots of 0.75 M $Eu(fod)_3$ were added. The shift of the protons to the chlorines and the shift of the allylic methyl protons is plotted *vs* the shift of the carbomethoxy protons as the amount of $Eu(fod)_3$ in the solution increased.

The lines have no theoretical significance.

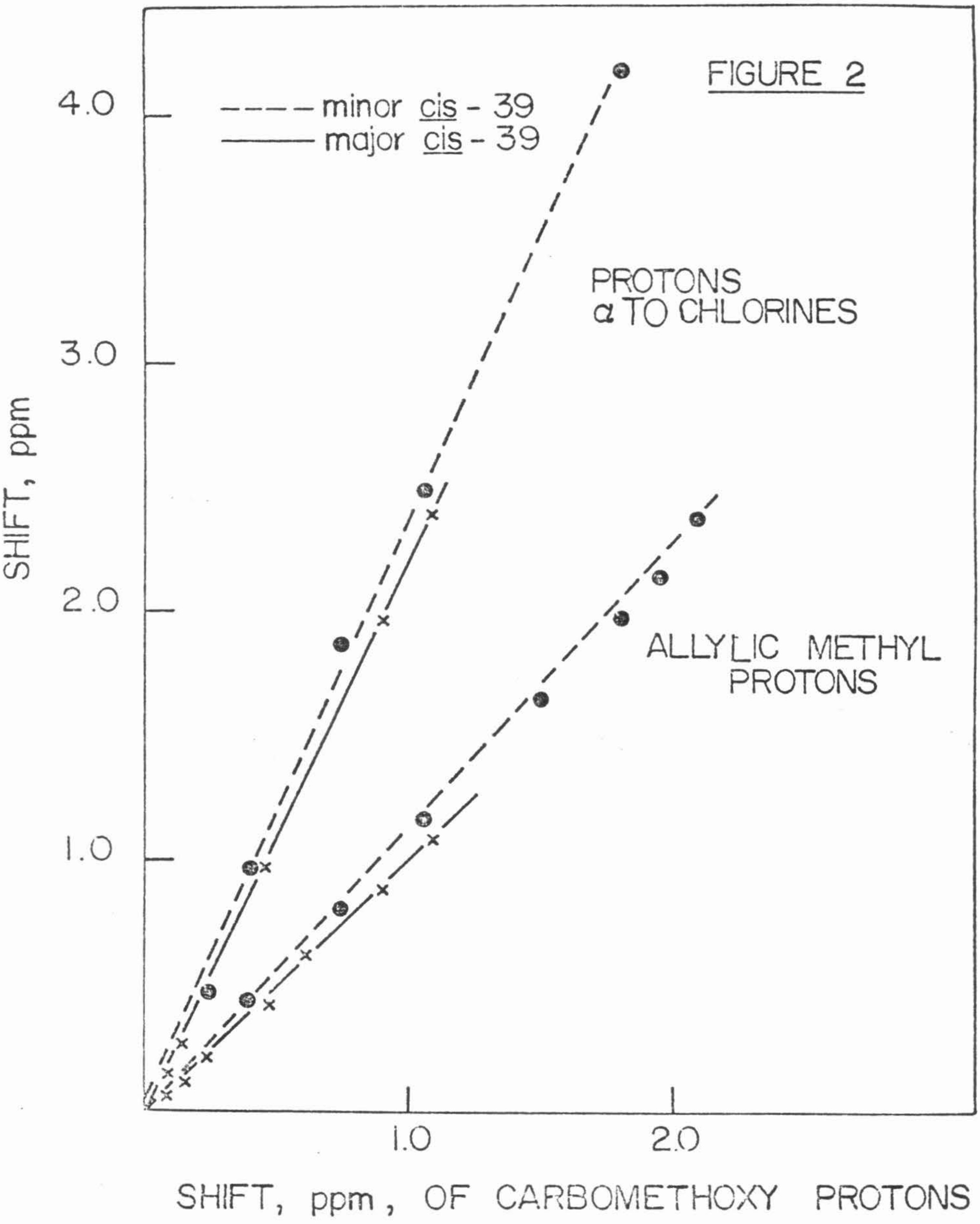


FIGURE 2
---- minor cis - 39
—— major cis - 39
PROTONS
α TO CHLORINES
ALLYLIC METHYL
PROTONS
4.0
3.0
2.0
1.0
1.0
2.0
SHIFT, ppm
SHIFT, ppm, OF CARBOMETHOXY PROTONS

5,6-Dichloro-2,3-dimethylbicyclo[2.2.0]hex-3-ene-1,4-dicarboxylic acid anhydride 49. Minor cis-5,6-dichloro-2,3-dimethylbicyclo[2.2.0]hex-3-ene-1,4-dicarboxylic acid (103 mg, 0.38 mmoles) was placed in a 25 ml flask equipped with a magnetic stir bar. 10 Ml of chloroform were added, and the flask was capped with a septum. Ethynyl ethyl ether (41 μl, 0.44 mmoles) was added via syringe and the reaction mixture was allowed to stir overnight. The reaction mixture was then chromatographed on silica gel using chloroform as eluent. The chloroform was evaporated to yield the anhydride 49 (85 mg, 0.34 mmoles, 91%) as a colorless solid which decomposed at temperatures above 125°C without melting. ^{1}H-NMR ($CDCl_3$) δ 4.62 (s, 2H), 1.84 (s, 6H) ppm. ^{1}H-NMR (benzene-d_6) δ 3.83 (s, 2H), 1,18 (s, 6H) ppm. IR ($CDCl_3$) 1855, 1792 cm^{-1}. Precise mass: 245.987, calc. for $C_{10}H_8Cl_2O_3$: 245.985. The anhydride could be sublimed at 115°C, 0.001 torr with substantial decomposition.

Dechlorination reactions - general procedures. The reagents surveyed for the dechlorination were listed in Table 1. The model anhydride 3,4-dichloro-1,2-dimethylcyclobutane anhydride 50 was prepared from dimethylmaleic anhydride and 1,2-dichloroethylene as described by Steinmetz et al. (63). Dechlorinations of the anhydride 50 were monitored by IR or NMR spectrocopy, since the product was clearly distinguishable. After one experiment, the product was isolated by VPC and shown to be the 1,2-dimethylcyclobutene anhydride 51 by comparison of its ^{1}H-NMR and IR data with literature data (64). ^{1}H-NMR (CCl_4) δ 6.44 (s, 2H), 1.44 (s, 6H) ppm, IR (THF) 1775, 1840 cm^{-1}. Lit.: ^{1}H-NMR (CCl_4) δ 6.43 (s, 2H), 1.44 (s, 6H) ppm, IR (KBr) 1772, 1840 cm^{-1}. The reactions were usually attempted on the mixture of isomers produced in the synthesis of 50 since we believed at the outset of this work that all of the isomers produced in the photolysis of dibromomaleic anhydride and 1,2-dichloroethylene would be usable throughout the synthesis. Initial attempts at the dechlorination of the bicyclohexene diacids 39 (R = H) were made on the mixture of acids for the same reason. Later attempts were made on the purified trans or major cis isomers because they were in the greatest supply. The minor cis isomer was saved for the formation of the stable anhydride 49. Dechlorination of the bicyclohexene diacids 39 (R = H) was monitored by NMR. Both the peaks at about δ 6.5 ppm for the bicyclohexadiene and the peaks for the ring opened material at about δ 7.5 and 2.5 ppm were sought.

2,3-Dimethylbicyclo[2.2.0]hexa-2,5-diene-1,4-dicarboxylic acid anhydride 53.

A. Hexamethylditin method. In an inert atmosphere a solution of freshly chromatographed 49 (20 mg, 0.08 mmoles) was dissolved in about 1.5 ml of benzene-d_6 and added to an NMR tube containing hexamethylditin (400 mg, 1.1 mmoles) and irradiated with a Hanovia 450W lamp through Pyrex. The course of the reaction was followed by ^{1}H-NMR spectroscopy. The peak at δ 3.83 ppm was gradually consumed and replaced by a peak at δ 6.1 ppm. When the starting material was gone, the yield of new product was 50% by NMR analysis. The contents of the tube were transferred into a small flask under an inert atmosphere. The flask was attached to a U-tube and vacuum stopcock. The apparatus was taken from the dry box and the contents of the flask were distilled into the U-tube under a dynamic vacuum leaving only a small residue. The apparatus was then returned to the dry box and the volatiles were chromatographed on silica gel (5 g) using pentane (30 ml) and then diethyl ether (30 ml) as eluents. The diethyl ether was removed *in vacuo* at about 100 torrs to leave a small (<2 mg, 14%) amount of the desired anhydride 53. Anhydride 53 prepared by this method often contained small amounts of tin compounds and grease. ^{1}H-NMR (benzene-d_6) δ 6.0

(s, 2H), 1.35 (s, 6H), IR (benzene-d_6) 1780 cm^{-1}, possible weak band at 1840 cm^{-1}.

B. Hexaphenylditin method. In the dry box a saturated solution of hexaphenylditin (7.0 ml) in benzene (approximately 20 mM at 20°C) was added to a flask containing anhydride 49 (100 mg, 0.37 mmoles) Triethylamine (40 μl, 28 mmoles) was added and the contents of the flask were thoroughly mixed. The contents of the flask were poured into two photolysis tubes and the tubes were topped with ground glass stoppers. The tubes were then taken from the dry box and photolyzed in a water bath with a 450W Hanovia lamp. The tubes were taken back into the box at intervals and the course of the reaction was monitored by NMR. During the photolysis the methyl group at δ 1.18 ppm was replaced by a new one at δ 1.35 ppm. Yields were greater than 80% as judged by NMR. After the starting material had been consumed, the solutions were poured into a flask containing 10% sodium bicarbonate and diethyl ether cooled with an ice salt bath. The mixture was allowed to stir for two hours at 0°C and then the layers were separated. The aqueous layer was washed at least four times with cold chloroform and ether. The aqueous layer was then acidified with cold 25% HCl, saturated with NaCl and extracted repeatedly with diethyl ether. The ether extracts were combined, dried over $MgSO_4$, and evaporated to leave about 40 mg (60%) of crude diacid. ^{1}H-NMR (Ac-d_6) δ 6.8 (s, 2H), 1.72 (s, 6H) ppm. These samples contained some tin compounds and some ($<5\%$) of the ring opened benzene 52 as well as some of the starting acid 39. The acetone-d_6 for the NMR was removed by a slow stream of N_2 and then the solid was suspended in chloroform. The suspension in chloroform was then treated with a slight excess of ethynyl ethyl ether and then chromatographed on silica gel using chloroform as eluent. The chloroform was then evaporated by a stream of N_2 to leave 53 as a clear waxy solid (20 mg, 30%), free of tin compounds and ring opened material, but still contaminated by a small amount of 49 ($<5\%$). ^{1}H-NMR ($CDCl_3$) δ 6.85 (s, 2H), 1.85 (s, 2H) ppm, IR ($CDCl_3$) 1840, 1780 cm^{-1}. MS parent peak at m/e = 176. UV (isooctane) very weak absorption at 260 nm, increases to end absorption with a possible shoulder at 225 nm ($\epsilon \approx 600$ cm^{-2}/M)

If this compound were allowed to stand in the solid state at temperatures greater than 30°C, the solid became opaque quite rapidly. This new solid would not dissolve in any organic solvents. An infrared spectrum in KBr showed bands at 1780, 1720, and 1680 cm^{-1}. The solid was then dissolved in 10% $NaHCO_3$ overnight. The $NaHCO_3$

solution was acidified with 25% HCl, saturated with NaCl, and extracted with diethyl ether. The ether extracts were combined, dried, and evaporated on a rotary evaporator. The residue dissolved in acetone-d_6. NMR (ac-d_6) δ 7.65 (s, 2H), 2.52 (s, 6H) ppm. This NMR spectrum is identical with that of 2,3-dimethyl-1,4-dibenzoic acid 52 produced by the Cr(II) reduction of 39. The structure of the Cr(II) reduction product was confirmed by its conversion to its dimethyl ester and comparison with the literature NMR. Compound 52-dimethyl ester: ^{1}H-NMR (CCl_4) δ 7.48 (s, 2H), 3.8 (s, 6H), 2.41 (d, 6H) ppm. Lit. (CCl_4): δ 7.55 (s, 2H), 3.88 (s, 6H), 2.48 (s, 6H). M.P. = 65-66° (Lit.: M.P. = 65-66° (39)).

Dimethyl trans-3,4-dichloro-3,4-dimethylcyclobutene-1,2-dicarboxylate 43. This cyclobutene was prepared via a sequence analogous to 32 (R = CH_3). 2,3-Dichloro-2-butene was prepared by the method of Scharf and Laux (65) from methyl ethyl ketone. Dibromomaleic anhydride (10 g) and benzophenone (2 g) were dissolved in the 2-butene (20 ml) and irradiated under N_2 until all of the dibromomaleic anhydride had been consumed according to VPC analysis. The solution was digested with $NaHCO_3$ solution and extracted with ether. The ether layers were combined, dried over $MgSO_4$, and evaporated to leave a black oil. The black oil was redissolved in ether and heated with an ethereal solution of diazomethane. A very low yield of dimethyl 1,2-dibromo-<u>trans</u>-3,4-dichloro-3,4-dimethylcyclobutane-1,2-dicarboxylate was obtained. ^{1}H-NMR ($CDCl_3$) δ 3.77 (s, 3H), 3.69 (s, 3H), 2.18 (s, 3H), 2.07 (s, 3H), IR ($CDCl_3$) 1740 cm^{-1} (C=O). The mass spectrum showed no parent peak at m/e = 424; instead peaks at m/e = 395 ($-OCH_3$), m/e = 345 (-Br) were present.

This ester was then treated with tin/copper couple in the same manner as described for <u>32</u> to produce, again in low yield, <u>43</u>. ^{1}H-NMR ($CDCl_3$) δ 3.85 (s, 6H), 2.00 (s, 6H) ppm, IR ($CDCl_3$) 1725, 1650 cm^{-1}. The mass spectrum showed a large peak at m/e = 231 which is equal to the parent peak (266) minus a Cl (35).

The cyclobutene <u>43</u> was irradiated in the presence of 2-butyne under conditions which had been successful in the addition of <u>32</u> to 2-butyne. No adduct was isolated. In contrast to the photolysis of <u>32</u> in acetone-d_6, irradiation of <u>43</u> in acetone produced a complicated set of products. These were not investigated further.

<u>Preparation of cis-5,6-dichloro-2,3-di-n-propylbicyclo-[2.2.0] hex-3-ene-1,4-dicarboxylic acid 41 and its anhydride.</u> <u>Cis</u>-cyclobutene <u>32</u> (R = H) was placed in an NMR tube along with benzophenone. Acetone and 4-octyne were added and after the solids dissolved, the tube was degassed and sealed and then irradiated with a Hanovia 450W lamp enclosed in

a Pyrex immersion well. During the irradiation two new singlets grew in at about δ = 5.1 and 4.5 ppm in the NMR spectrum. Evaporation of the solvent as described for the 2-butyne adducts gave a black solid which had an NMR spectrum consistent with a mixture of isomers of 41. Treatment of the crude diacid with ethynyl ethyl ether followed by chromatography on silica gel gave an anhydride [IR ($CDCl_3$) 2850, 1790 cm^{-1}] which consisted of a single isomer [^{1}H-NMR δ 4.62 (s, 2H), 2,18 (t, J = 6 Hz, 4H), 1,54 (multiplet, 4H), 0.98 (t, J = 7Hz, 6H) ppm] contaminated with an unidentified material absorbing at about δ 1.5 in the NMR spectrum.

5,6-Dichloro-2,3-bistrimethylsilylbicyclo[2.2.0]hex-2-ene-1,4-dicarboxylic acid 42 and its anhydride. *Cis*-cyclobutene 32 (R = H) was dissolved in a mixture of acetone-d_6 and bistrimethylsilylacetylene containing benzophenone in an NMR tube. The mixture was irradiated with the Hanovia lamp until the starting material had been consumed. As the starting material peak at δ 5.53 ppm disappeared, a new peak at δ 4.65 ppm increased in size. This was assigned to the bicyclohexene diacid 42, which was isolated as an impure brown solid in about 50% yield in the manner described for the 2-butyne adduct to cyclobutene 32. ^{1}H-NMR ($CDCl_3$) δ 4.67 (s, 2H), 0.29 (s, 18H), IR ($CDCl_3$) 1720 cm^{-1} (C=O). This material was transformed into an anhydride without further purification. To a magnetically stirred suspension of <u>42</u> (27 mg, 0.067 mmoles) in 5 ml of $CHCl_3$ in a 10 ml flask capped with a septum was added 8 μl of ethynyl ethyl ether via a syringe. The mixture was allowed to stir overnight and then was chromatographed on silica gel using chloroform as eluent. The chloroform was evaporated to yield 15 mg (0.039 mmole, 59%) of the anhydride as an impure white solid. ^1H-NMR ($CDCl_3$) δ 4.68 (s, 2H), 0.30 (s, 18H) ppm, IR ($CDCl_3$) 1850, 1790 cm^{-1}. The mass spectrum showed no parent peak. The base peak was at m/e = 327, which corresponded to the parent (362) minus a Cl (35).

III. MATRIX ISOLATION PHOTOLYSIS OF 2,3-DIMETHYLBICYCLO-[2.2.0]HEXA-2,5-DIENE-1,4-DICARBOXYLIC ANHYDRIDE

1. Matrix Isolation Methodology

Matrix isolation techniques have been employed with great success in the study of reactive species for over fifty years (65). In the last decade organic chemists have made increasing use of matrix isolation to study reactive organic species such as cyclobutadiene (26) and o-benzyne (66). The technique is simple in concept. Matrix isolation involves trapping of a molecule within a rigid cage of chemically inert atoms or molecules at a low temperature. The rigid cage prevents diffusion of the molecules into contact with each other while the low temperature of the matrix prolongs the lifetime of labile molecules.

Matrix host materials must satisfy several requirements. They must not react with the isolated species, they must not absorb in the spectroscopic regions to be studied, and they must have a very low vapor pressure (less than 10^{-5} torr) at the desired temperature. The final requirement eliminates hydrogen and helium as possible materials because they do not form solids at easily attainable temperatures. The other noble gases, neon, argon, krypton, and xenon, as well as dinitrogen, are all used routinely.

The melting points (T_m) of these are given below as well as the temperatures at which the solids have vapor pressures of 10^{-3} torr:

Table 2

Gas	T_m (°K)	T(P = 10^{-3} torr, °K)
Ne	25	11
Ar	84	39
Kr	116	54
Xe	164	74
N_2	64	34

At temperatures of 0.3 T_m the matrix is considered rigid. Between 0.3 T_m and 0.5 T_m annealing, or the local reorganization of matrix atoms to the most stable crystal structure occurs. Above 0.5 T_m diffusion sets in and the trapped species are free to move and interact with each other. The temperature at which the matrix solid has a vapor pressure of 10^{-3} torr is an important parameter because that temperature can be maintained only for brief periods or the matrix will be lost to evaporation. At this temperature the low temperature is more difficult to maintain because of the increased pressure in the system. An examination of Table 2 shows that 0.5 T_m and T(P = 10^{-3} torr) are roughly comparable. This imposes a constraint on experimental design in that diffusion processes cannot always be followed to completion.

The matrices can be described as crystalline, microcrystalline, or glassy. Since the conditions of the matrix formation (see below) would not be expected to favor single crystal growth, the structure of the matrix is more likely to be glassy or microcrystalline. In the glassy model, the matrix atoms are arranged randomly in a non-close packed array. The spectral absorption lines of a trapped species would be broad because of the variety of sites available. In a microcrystalline model small crystals are formed during the formation of the matrix in a close packed array with the trapped species occupying boundaries. This model predicts sharp spectral lines, which are indeed observed. Often warming the matrix to 0.5 T_m causes a degradation in the quality of the spectrum. This could be due to the formation of aggregates of the trapped species or degradation of the matrix from a microcrystalline form to a glassy form.

A few comments should be made about the term "isolation." The argon atom has a van der Waals diameter of 3.75 Å. In a crystal an argon atom has twelve nearest neighbors. If the species to be studied has a diameter comparable to argon it can occupy one of the argon sites. The probability of not finding another trapped species as a nearest neighbor can be expressed as:

$P = (1 - r)^{12}$

where P is the probability (x 100 = percent isolation) and r is the mole ratio of trapped species to argon. If the species to be studied has a molecular diameter three times that of argon, the number of nearest neighbors is now 122 and the probability of not having another trapped species as a nearest neighbor is:

$P = (1 - r)^{122}$

For example, if r = 1/500, which is a typical concentration, then the trapped species occupying one site is 98% isolated, but the species with the larger diameter is 78% isolated. This simple model can only be used as an approximate guide, since it assumes spherical molecules. It does point out the difficulty in truly isolating large molecules.

With this in mind, we can turn to the experiment itself. The experiments are relatively simple in form and are described below. The equipment required for matrix isolation work is the following:

1) A good vacuum system for mixing the sample with the argon and to evacuate the cryogenic apparatus. This system must be capable of maintaining 10^{-6} torr.
2) A refrigeration unit capable of holding the temperature at 10°K.
3) A shroud which can accommodate the cooling rod and

sample holder, maintain vacuum, and is compatible with some spectrophotometer.(Figures 3,4)

A schematic diagram of the entire system used in our experiments is shown below (Figure 5). The sample holder is connected to the refrigerator by a copper block and maintains thermal contact with the spectroscopic window through indium. A thermocouple as close as possible to the window allows the experimentalist to monitor the temperature of the window. Ideally, the thermocouple is mounted in the window, but in practice it is often mounted on the copper block. A small heating coil is wrapped around the copper block adjacent to the sample holder. The temperature of the window is regulated by the application of a current in the coil.

The experiments are carried out by reducing the pressure in the system and cooling the window to the desired temperature. The sample is then admitted to the evacuated manifold and diluted with the matrix gas. The gases are thoroughly mixed using magnetic stir bars. The matrix is then prepared by allowing a slow flow (less than 10 nmole/hour) of gas into the shroud through a nozzle which is directed at the window. The window is maintained at a temperature slightly below 0.3 T_m to permit some reorganization of the atoms as they strike the window but not high enough to permit the matrix to become a glass. If the temperature of the

TOP VIEW OF SHROUD

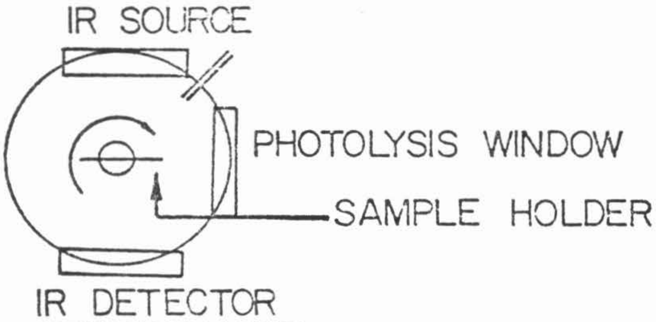


FIGURE 3

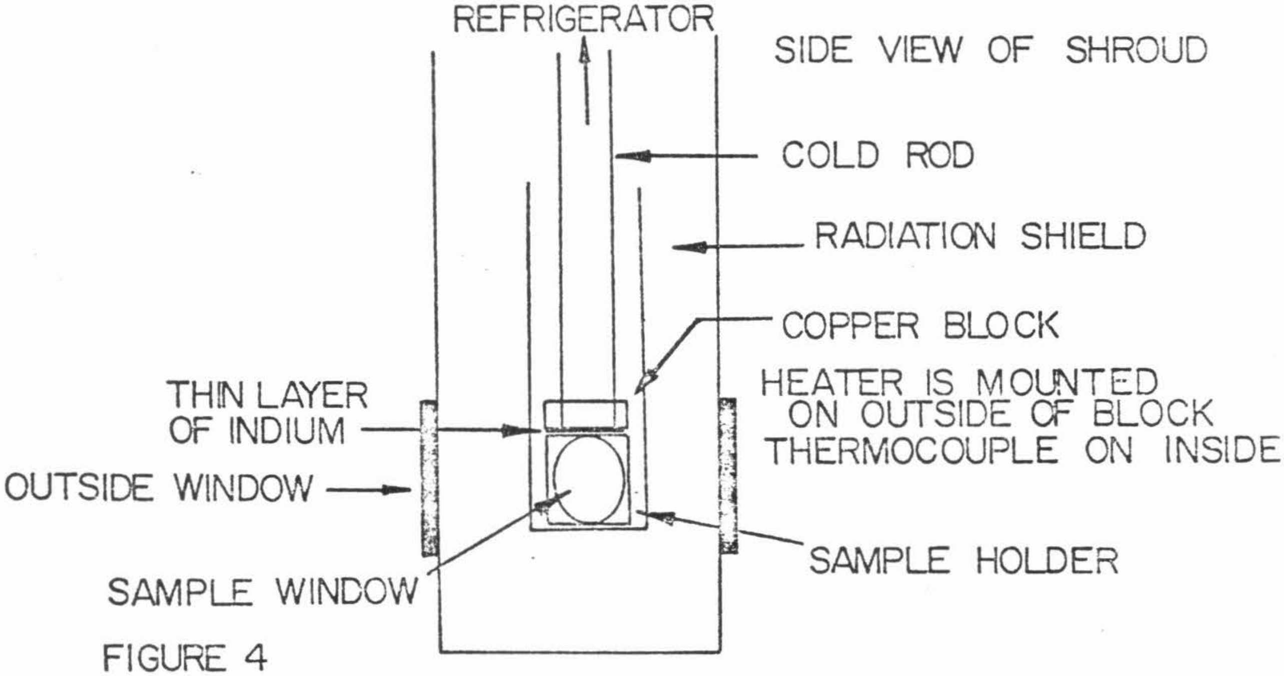
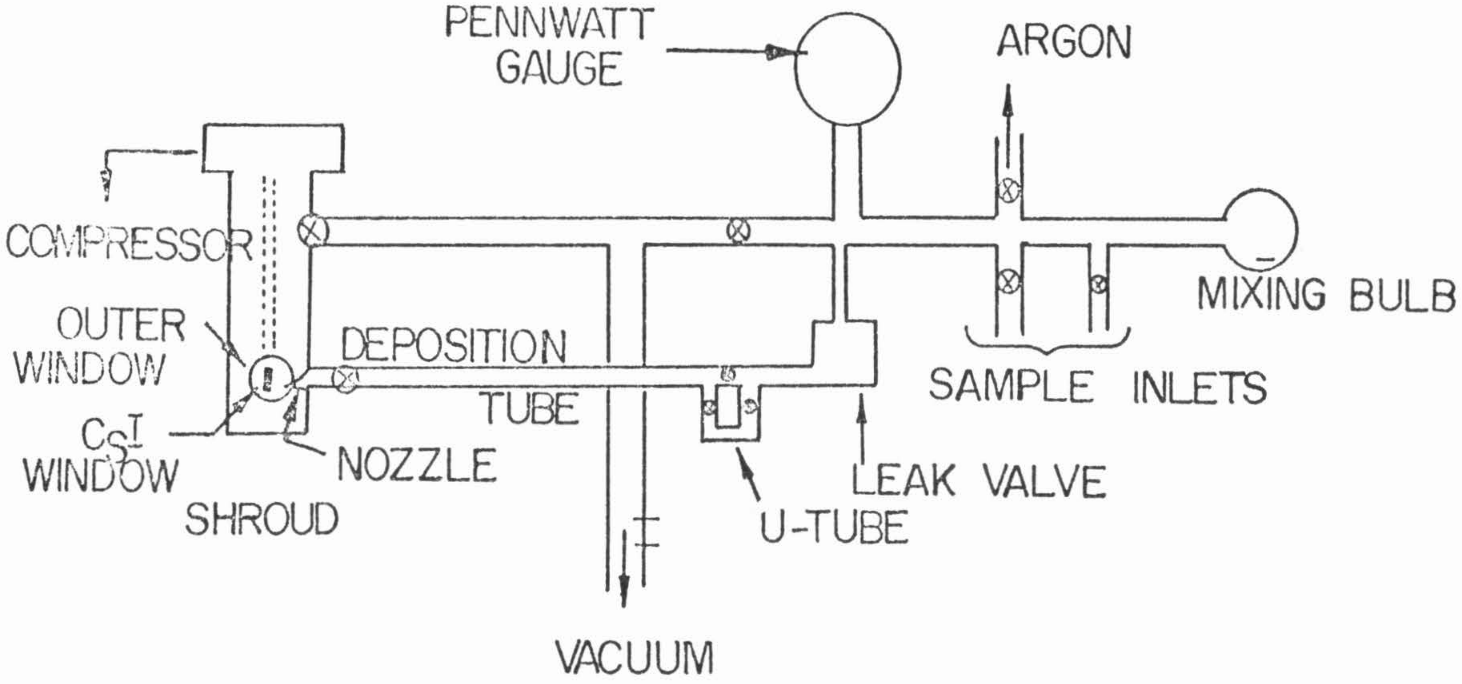


FIGURE 4



SCHEMATIC OF MATRIX
ISOLATION SYSTEM

FIGURE 5

window is too low, the matrix does not "stick" and falls off. If the flow rate is too fast, the window will not be able to maintain the temperature of the growing matrix below 0.3 T_m and diffusion may occur during deposition.

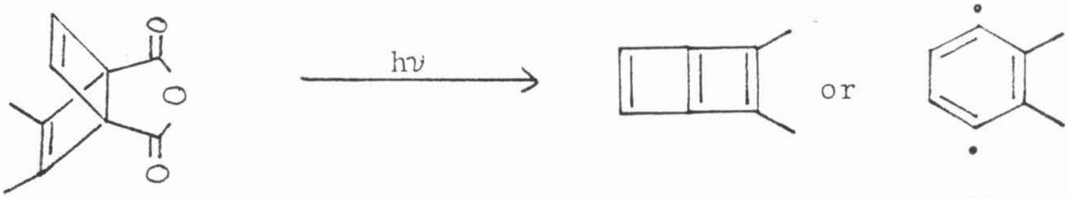
After the matrix is formed, the temperature is slowly lowered, usually to the limit of the refrigerator. The sample is now ready for spectroscopic study.

If the sample is relatively nonvolatile (vapor pressure less than 0.1 mm Hg), different methods must be used to introduce it into the matrix. The most efficient way to mix the sample with the argon prior to deposition is to include a U-tube in the gas handling system immediately after the leak valve. This insures the greatest possible mixing. If the sample is extremely nonvolatile, the sample must be heated until it reaches the shroud and mixing must occur inside the shroud and on the growing matrix surface. In these cases the ratio of matrix host to sample remains undetermined and the extent of isolation can only be judged qualitatively by the sharpness of the spectral lines. The quality of the spectral lines can be changed by changing the ratio of matrix gas flow or by changing the temperature of the sample during volatilization. Finding the optimum conditions for a particular sample is an inexact and tedious exercise.

Reactive species can be produced by pyrolysis of the sample before it is deposited on the window or by photolysis within the matrix. The cyclobutadiene and o-benzyne work mentioned earlier (26,66) used the photolytic method. In practice this is easy to carry out. The shroud is at least four-sided and one of the sides contains a quartz window. The matrix window can be rotated so that it is directly in front of this window.

2. Photolysis of 53

We herein report our attempt to generate 2,3-dimethyl-p-benzyne 56 or 2,3-dimethylbutalene 57 in an argon matrix by photolysis of the Dewar anhydride 53.



53 57 56

Matrix isolated samples of anhydride 53 were prepared by allowing a slow stream of argon (about 0.09 mmoles/minute) to pass over solid 53 in a u-tube before deposition on a cesium iodide window cooled to 21°K. After the deposition was complete the window was cooled to 11°K. The extent of isolation was judged qualitatively based on the sharpness of the infared lines. Extent of isolation was a function of sample surface area, temperature, volatization during deposition, and rate of argon flow.

The infared spectrum of the anhydride is shown in Figure 6. Peaks marked with an X were probably due to impurities in the sample (The relative size of these peaks varied from sample to sample and they remained unchanged after photolysis). Spectra were recorded on a Perkin-Elmer 621 Infared Spectrometer.

The UV absorption of the anhydride was weak at wavelengths greater than 260 nm and reached a maximum at about 225 nm (ϵ= 600 cm^2/mole in isooctane). As a consequence, lamps with a high output in the region below 250 nm were required.

Irradiation of the matrix isolated anhydride caused the disappearance of the bands attributed to the anhydride and the appearance of the bands characteristic of CO_2 (2340, 662 cm^{-1}) and CO (2140 cm^{-1}). This photochemical decomposition of the anhydride was slow and several days were required to decompose greater than 75% of the sample. The formation of CO_2 and CO versus anhydride disappearance is shown in Figure 7.

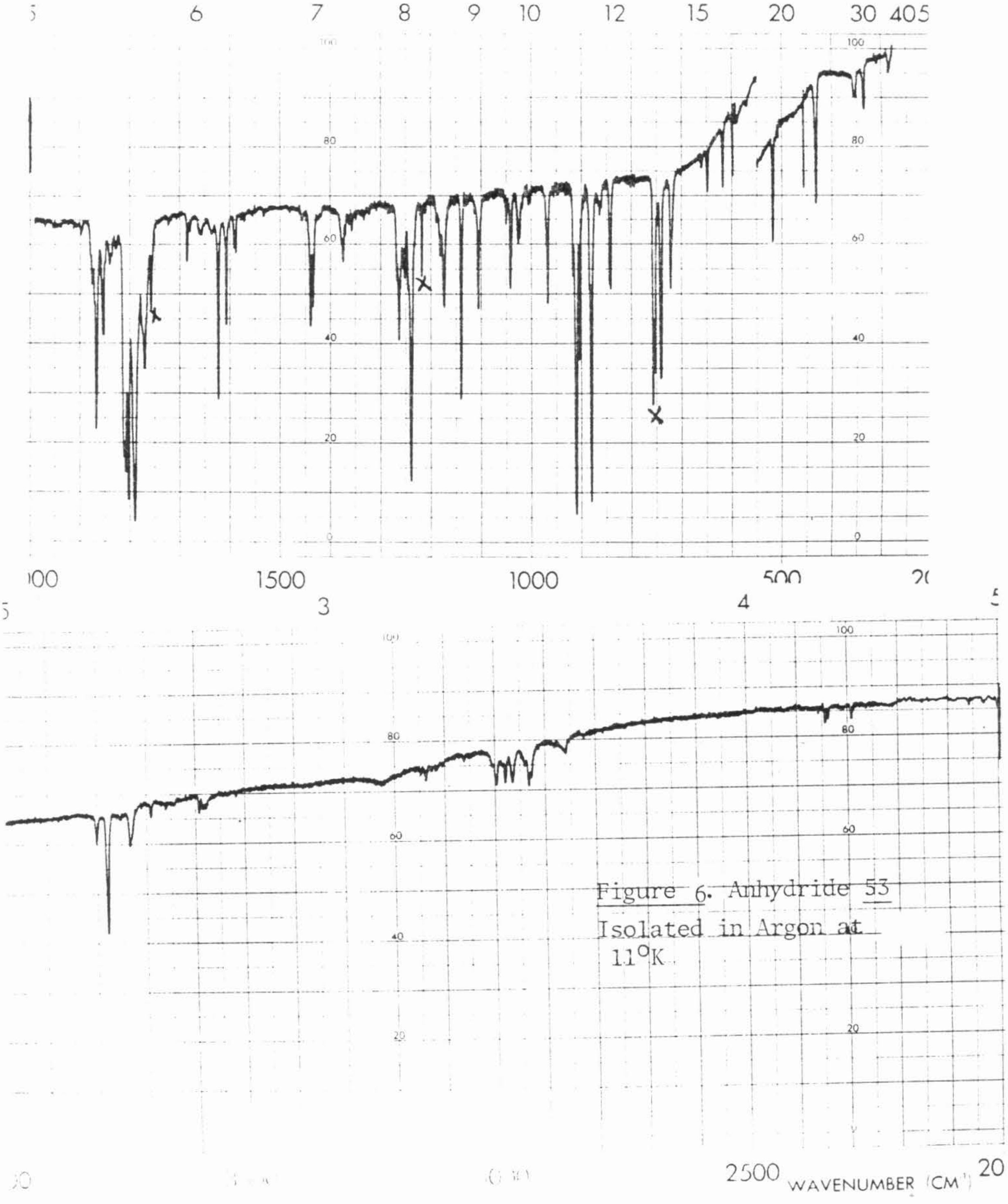


Figure 6. Anhydride 53 Isolated in Argon at 11°K

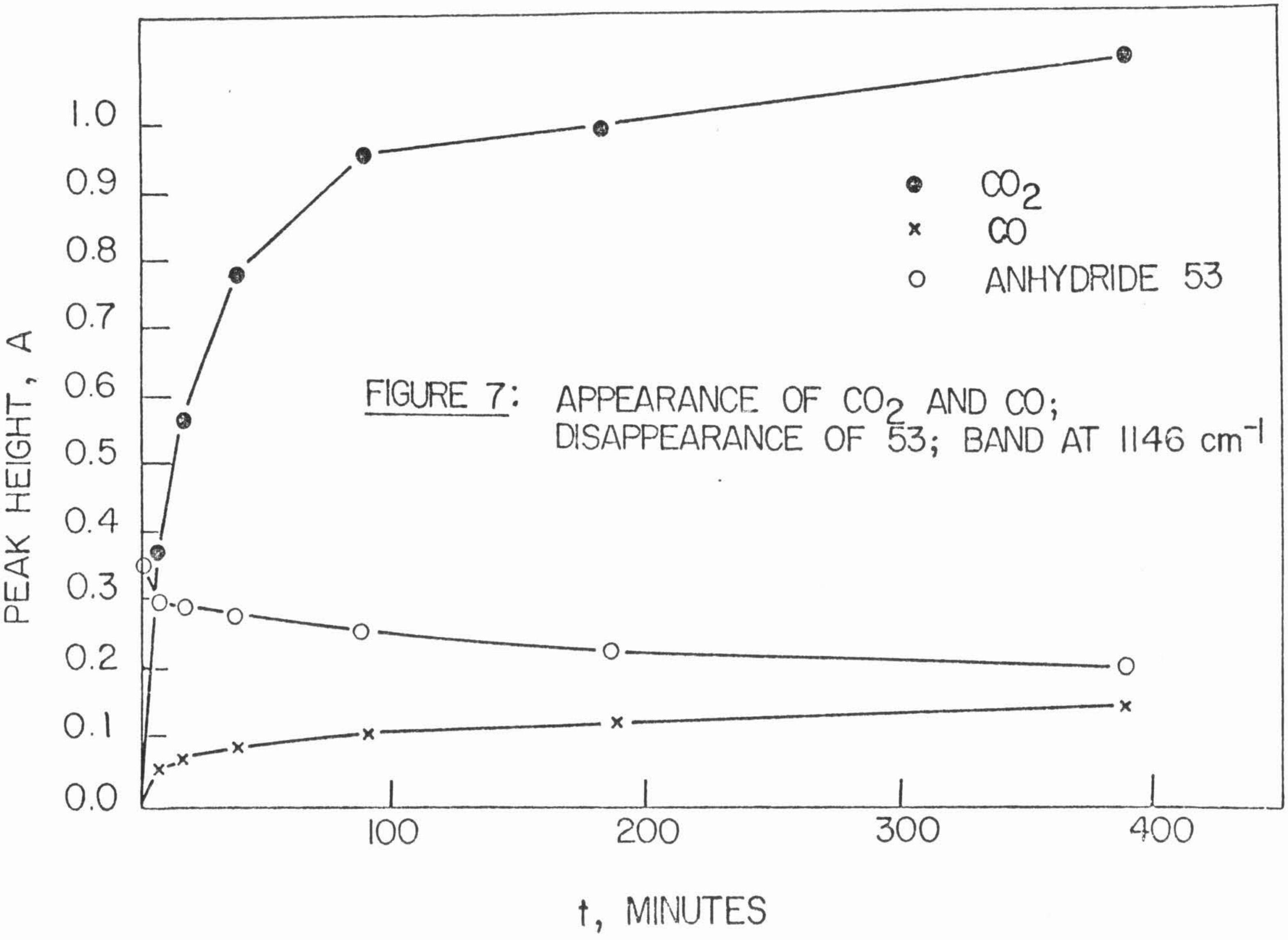


FIGURE 7: APPEARANCE OF CO_2 AND CO; DISAPPEARANCE OF 53; BAND AT 1146 cm^{-1}

The rate of disappearance of the anhydride decreased soon after photolysis was initiated. This could have been due to either imperfections in the matrix structure which caused light scattering, or to the formation of an internal filter of photoproducts.

New bands appeared during the earliest stages of the photolysis at about 3350, 931, 834, 600, and 481 cm^{-1}. All of these peaks were very small. In one experiment after 400 minutes of irradiation, the largest of the new peaks at 637 cm^{-1} was only 6 units from the baseline (scale of 100). The new peaks exhibited different time behavior. The peaks at ~3350 and ~600 cm^{-1} increased monotonically at similar rates while the 937 and 834 cm^{-1} peaks reached maxima at 87 and 17 minutes respectively. The 481 cm^{-1} peak also increased monotonically but at a different rate from the 3350 and 600 cm^{-1} peaks. These observations are demonstrated graphically in Figure 8. After long photolysis times (over one thousand minutes) other peaks became discernible (Table 3). The spectrum after irradiation for 1300 minutes is shown in Figure 9. Warming the matrix at 38°K did not cause the disappearance of the new bands.

Attempts to increase the size of the product peaks by using larger amounts of material or by preparing the matrix in thin layers and photolyzing after the deposition of each layer were unsuccessful.

Several species which might have given distinctive

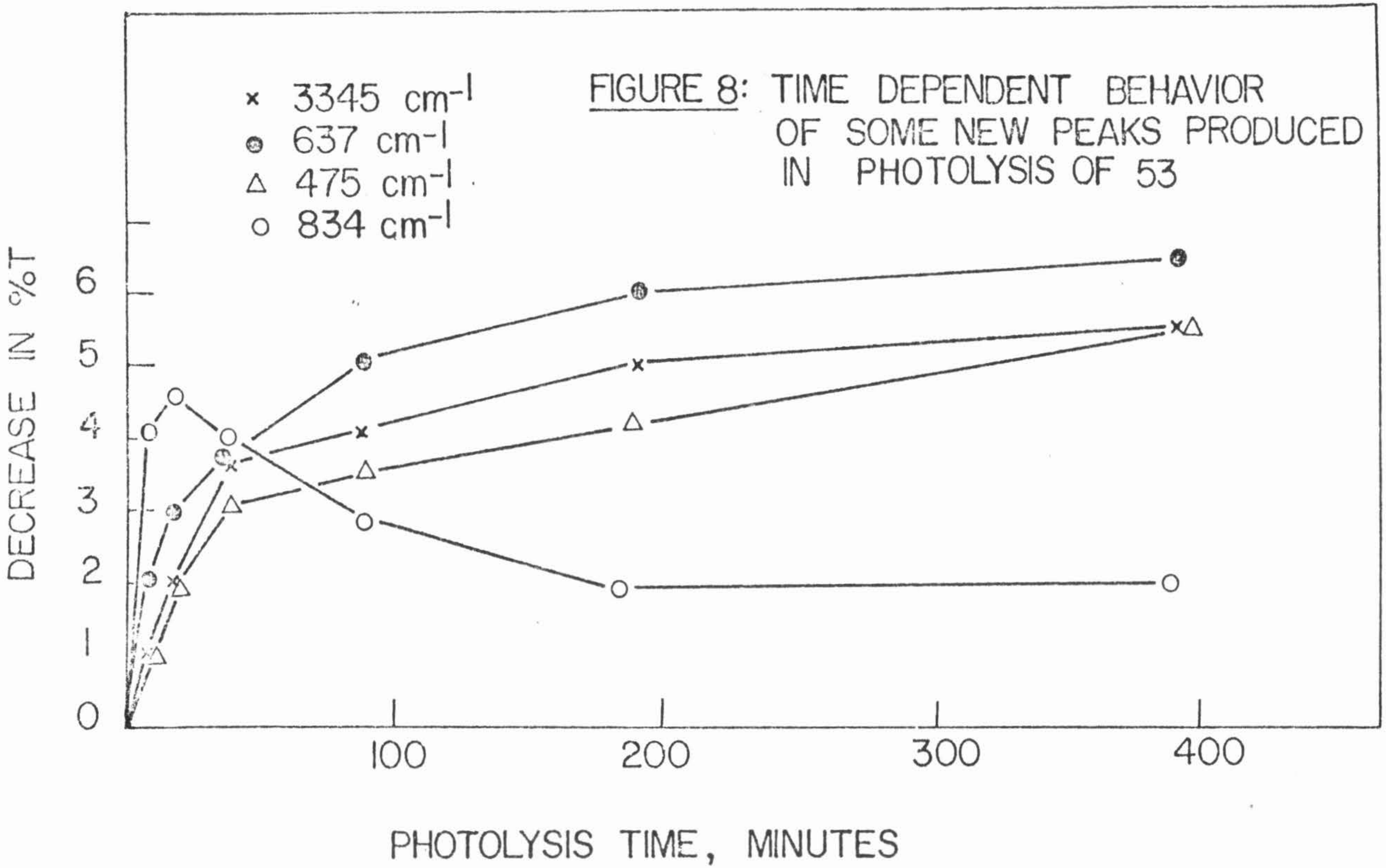


FIGURE 8: TIME DEPENDENT BEHAVIOR OF SOME NEW PEAKS PRODUCED IN PHOTOLYSIS OF 53

Table 3. Possible New Peaks (cm^{-1}) Arising From Photolysis of 53

3345
3335
1477
1445
1249
1096
937
839
632
606
475
438

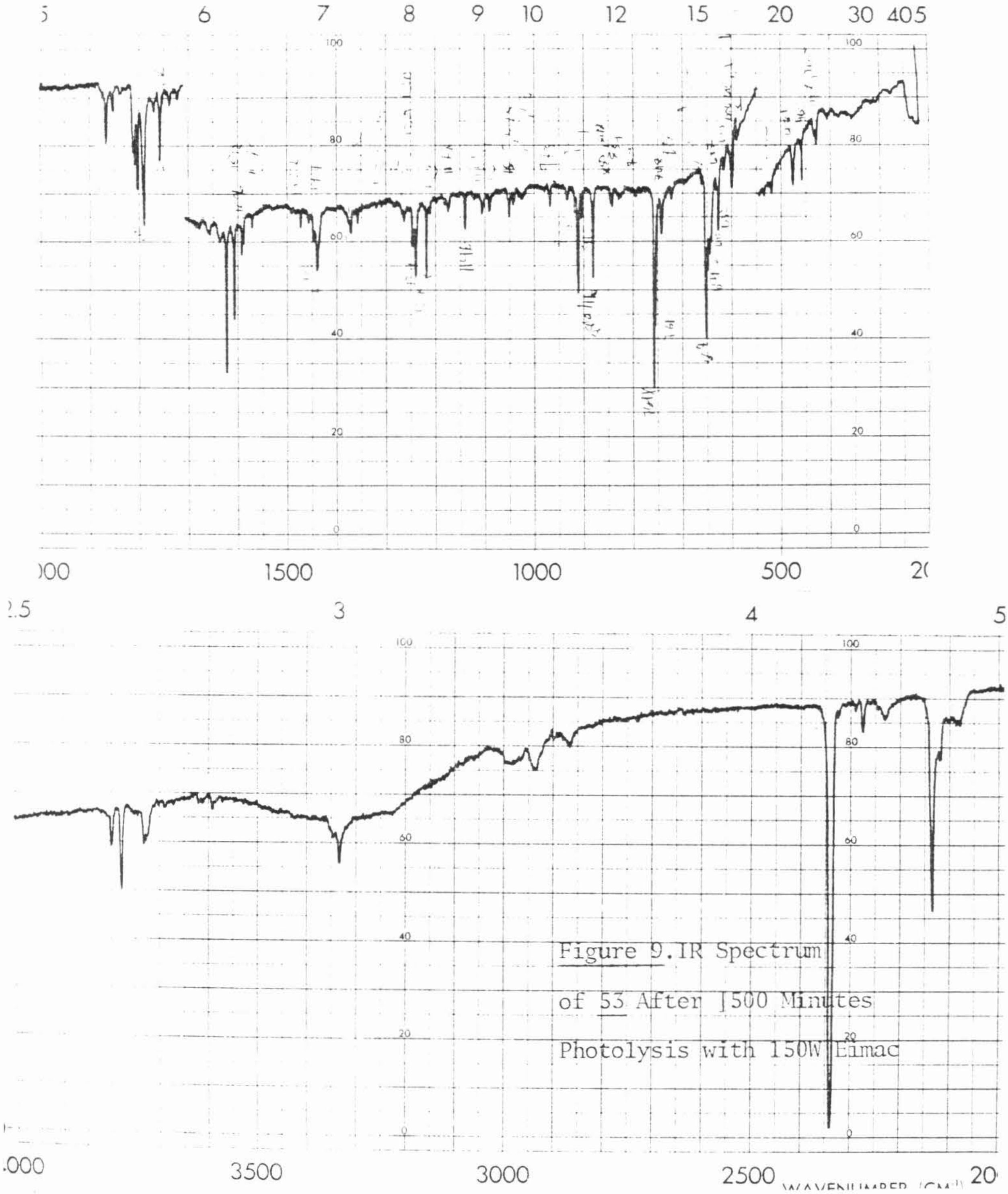
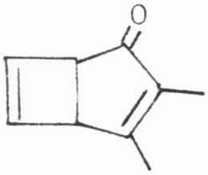
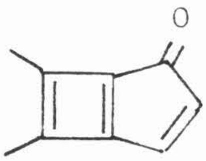


Figure 9. IR Spectrum of 53 After 1500 Minutes Photolysis with 150W Eimac

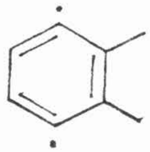
infared bands had they been formed are shown below. No



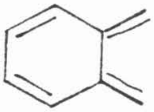
58



59



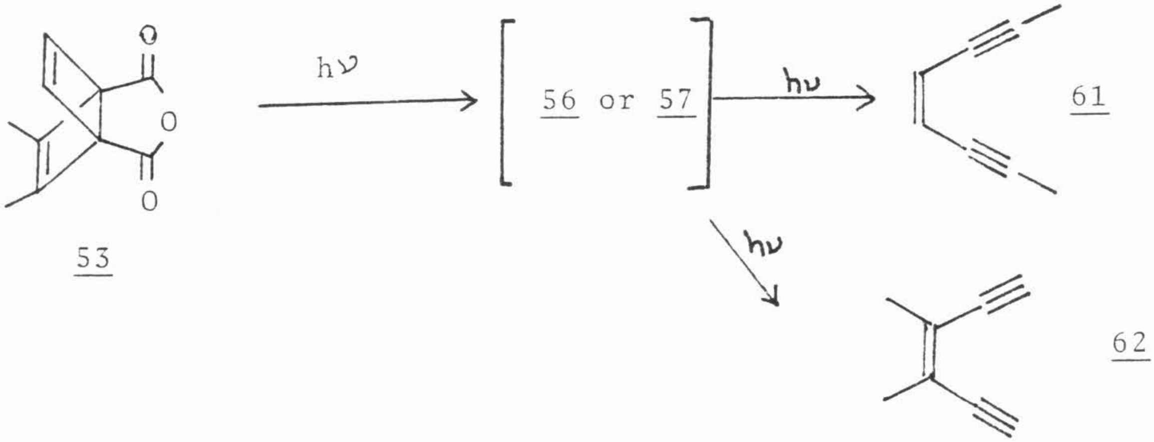
56



60

new carbonyl peaks were observed, thus eliminating 58 and 59 as final products. No new strong bands were observed to grow between 700 and 800 cm^{-1} where 56 would be expected to absorb (72) and the strong out-of-plane bending modes of 60 at 870 cm^{-1} were not detected (73).

The bands which arose at 3350 and 600 cm^{-1} suggested the formation of a terminal acetylene. A reasonable mechanism for the photochemical decomposition of the anhydride 53 via p-benzyne is shown below. This mechanism is analogous to earlier diethynylethylene work by Bergman and coworkers (1,2,4,5) and includes a terminal acetlyene cis-62 (70) as an end product.



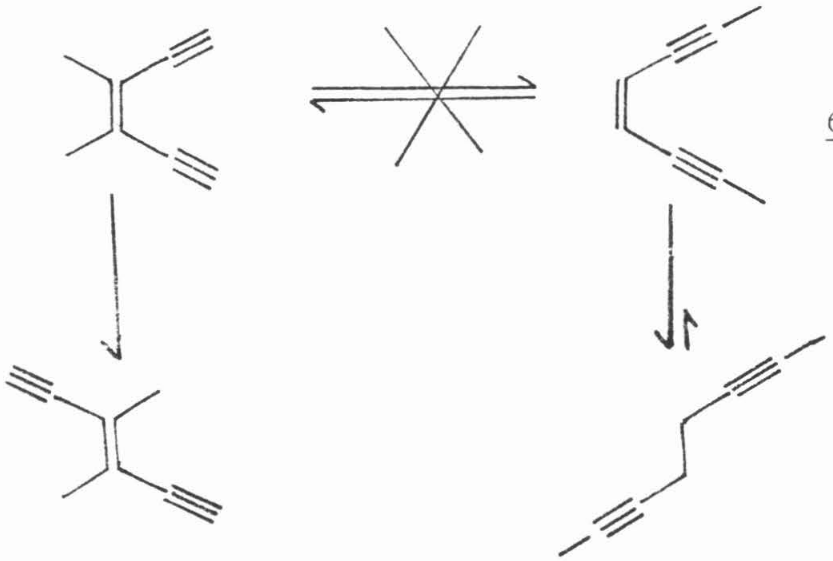
Matrix isolation of cis and trans-62 showed that the new peaks at 3350 and 600 cm^{-1} correlated well with both of these compounds. The isomeric diethynylethylenes cis and trans-61 were also prepared and isolated in an argon matrix. The new band at 937 cm^{-1} in the anhydride photolysis correlated with a strong band of trans-61 but the strongest bands in cis-61 were obscured by bands in the starting anhydride (Table 4).

In one experiment, the volatiles from the anhydride photolysis were pumped into a trap at 77^{o}K. Thin layer chromatography on silica gel showed strong fluorescent quenching spots consistent with the presence of cis and trans-61 and weak spots with R_f's identical to cis and trans-62. VPC showed traces of at least six compounds, four of which were consistent with 61 and 62. Gas chromatography-mass spectrometry analysis was difficult, because of the small amounts of material. The results were consistent with but did not unequivocally prove the formation of 61 and 62.

Table 4. Correlation of New Peaks with 61 and 62

Wavenumber	cis-61	trans-61	cis-62	trans-62
3345				x
3335			x	x
1477				
1445	x	x	x	
1249			x	x
1096			x	x
939		x		
834				
637			x	x
606			x	x
475			x	
438				

The mechanism shown above accounts for the formation of *cis*-*61* and *cis*-*62* but does not predict the *trans* isomers. IR analysis showed that irradiation of matrix isolated *cis*-*61* and *cis*-*62* produced *trans*-*61* and *trans*-*62* respectively, as did solution photolyses (1, 71). *Cis*-*61* and *cis*-*62* did not interconvert. Photolysis of *trans*-*61* produced trace amounts of *cis*-*61* but irradiation of *trans*-*62* produced no *cis*-*62* as determined by IR. During the irradiation of the *cis* isomers the concentration of the *trans* isomer reached a maximum value. Since the *trans* isomers were not converted to the *cis* isomers, this was probably not a photostationary state, but rather the *trans* isomers produced in the photolysis acted as an internal filter. All the diethynylethylenes had UV spectra showing absorption peaks at about 2650 Å.



62

61

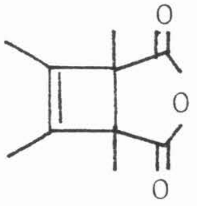
In summary, photolysis of anhydride 53 in an argon matrix at 11°K resulted in the appearance of bands in the infrared attributable to carbon dioxide and carbon monoxide as bands assigned to the anhydride decreased in intensity. Numerous very weak bands appeared during the course of the photolysis. The observation that the bands exhibit different time behavior suggested that numerous photochemical processes may be taking place, but because the new bands were very weak we were unable to assign structures to any of the intermediates or end products with certainty. Judging from the strengths of the bands in the authentic diethynylethylenes, we could estimate that 5% or less of the anhydride was being transformed into *cis* and *trans*- 62.

3. Experimental

Matrix isolation experiments were carried out at the IBM Research Laboratory in San Jose, California, in collaboration with Drs. J. Pacansky and R. D. Miller. The cryogenic equipment was manufactured by Air Products and was called a Displex. This unit included a compressor and expander connected to a copper block which could accommodate a sample holder. The refrigerant was helium under pressure. The high vacuum shroud was built by the IBM machine shop and was equipped with two cesium iodide windows, one quartz window, and sample inlet systems. The vacuum system consisted of a fore-pump and a single stage diffusion pump capable of attaining pressures of a out 10^{-6} torr. Pressures in the system were measured with thermocouple and ionization gauges. The gas handling system had a capacity of approximately 3 liters. Pressures greater than 0.2 torr in the system were measured with a Pennwalt gauge. Samples were admitted to the shroud through a leak valve. Solid samples were placed in a U-tube in the deposition line immediately after the leak valve. A schematic of the entire system has been shown earlier (Figure 5).

Matrix isolated samples were prepared by allowing a slow stream of argon (5-8 x 10^{-2} mmoles/minute) containing the sample into the vacuum shroud through a nozzle directed at a cesium iodide window cooled to 21°K. A total of 14-17 mmoles of argon was deposited. Assuming that an even matrix was laid, this produced matrices approximately 1 mm thick. This estimate was obtained from the amount of argon deposited, the surface area of the window (about 3 cm^2), and the density of solid argon (1.77 g/cm^3 (72)). This estimate was too large because not all of the sample condensed on the window.

In test experiments using the model anhydride 63 (73) which was of comparable molecular weight to 53, we found that 5 mg (0.027 mmoles) of anhydride were deposited during a typical experiment. If 17 mmoles of argon from the gas handling system were used, this corresponded to a mole ratio of 63 to argon of about 1:600.



63

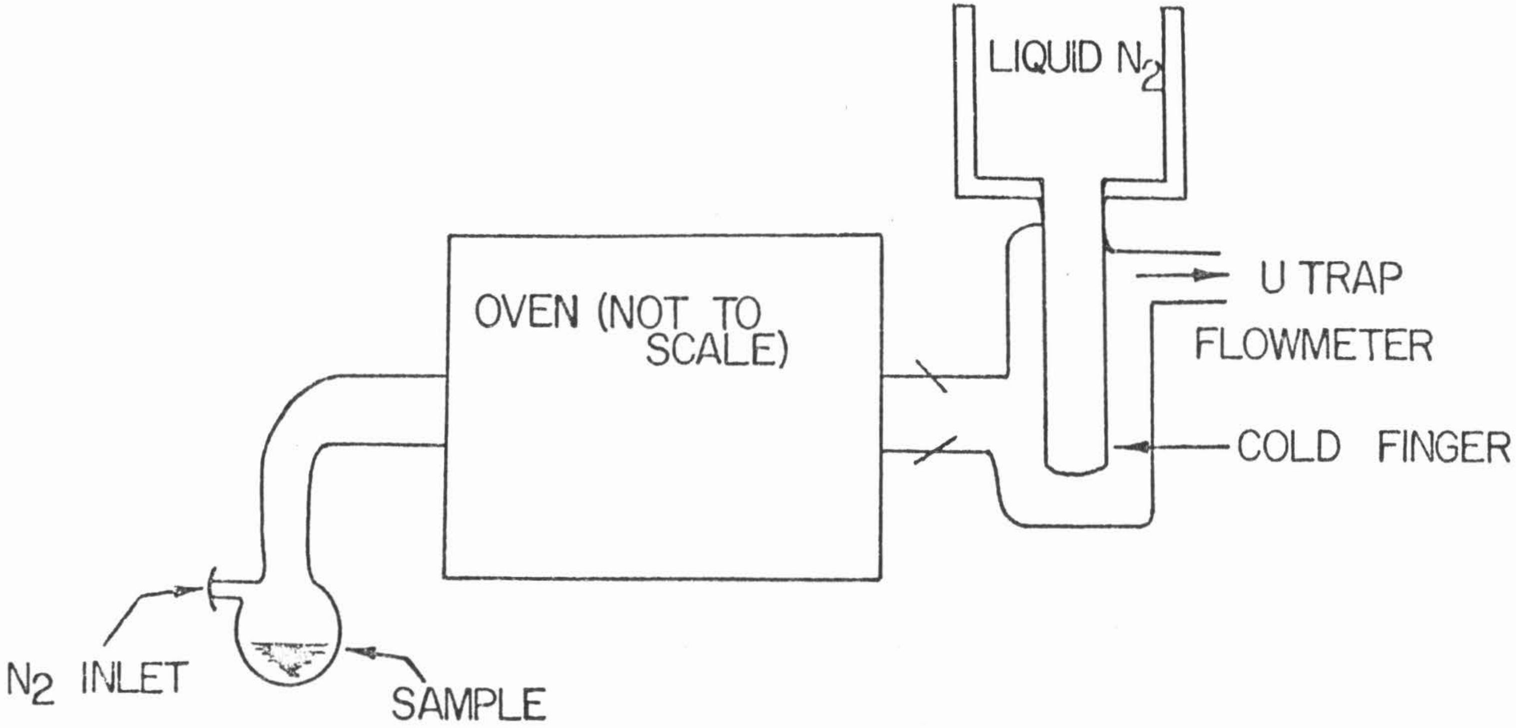
The ratio of 53:argon varied from experiment to experiment but was probably in the 1:500 range. This implied that 53 was about 70% isolated.

Photolyses were carried out with a 150W Eimac lamp (Varian), a 1500W GE street lamp, or a 500W Eimac lamp in conjunction with a monochromator. The light was passed through a water filter and then collected with a quartz lens before striking the sample. No differences except for the rate of disappearance of the anhydride and appearance of CO_2 and CO were observed between the use of the first two lamps. Using the third lamp, the flux of monochromatic radiation at 220±10 nm was not sufficient to cause any change in the spectrum of the anhydride or production of CO_2 or CO over the course of an hour. The 150W Eimac lamp was the most efficient.

Anhydride 53 was prepared as described in Chapter II and chromatographed immediately before use. It was placed in the U-tube in chloroform solution. The chloroform was removed by a stream of nitrogen and evacuation of the tube to less than 10^{-5} torr for about 30 minutes. During the evacuation the U-tube was cooled to 0°C to prevent any loss of the anhydride.

Anhydride 63 was prepared as described previously (73) and added as a solid to the U-tube prior to deposition.

The diethynylethylenes cis- and trans-62 were prepared by the method of Lockhart (74). The diethynylethylene cis-61 was prepared from cis-62 by pyrolysis in a nitrogen flow system developed by G. C. Johnson (30) and shown below.



PYROLYSIS APPARATUS
DESIGNED BY G.C. JOHNSON

The temperature of the pyrolysis tube was measured with a chromel/alumel thermocouple taped to the center of the tube. The temperature was maintained with a differential temperature controller. Complete conversion of cis-62 to cis-61 was obtained when the oven temperature was 270°C with a flow rate of about 60 ml/min. The Pyrex tube had an internal diameter of 2 cm and was 40 cm long. Thus the residence time of gases in the flow tube was about 2 min.

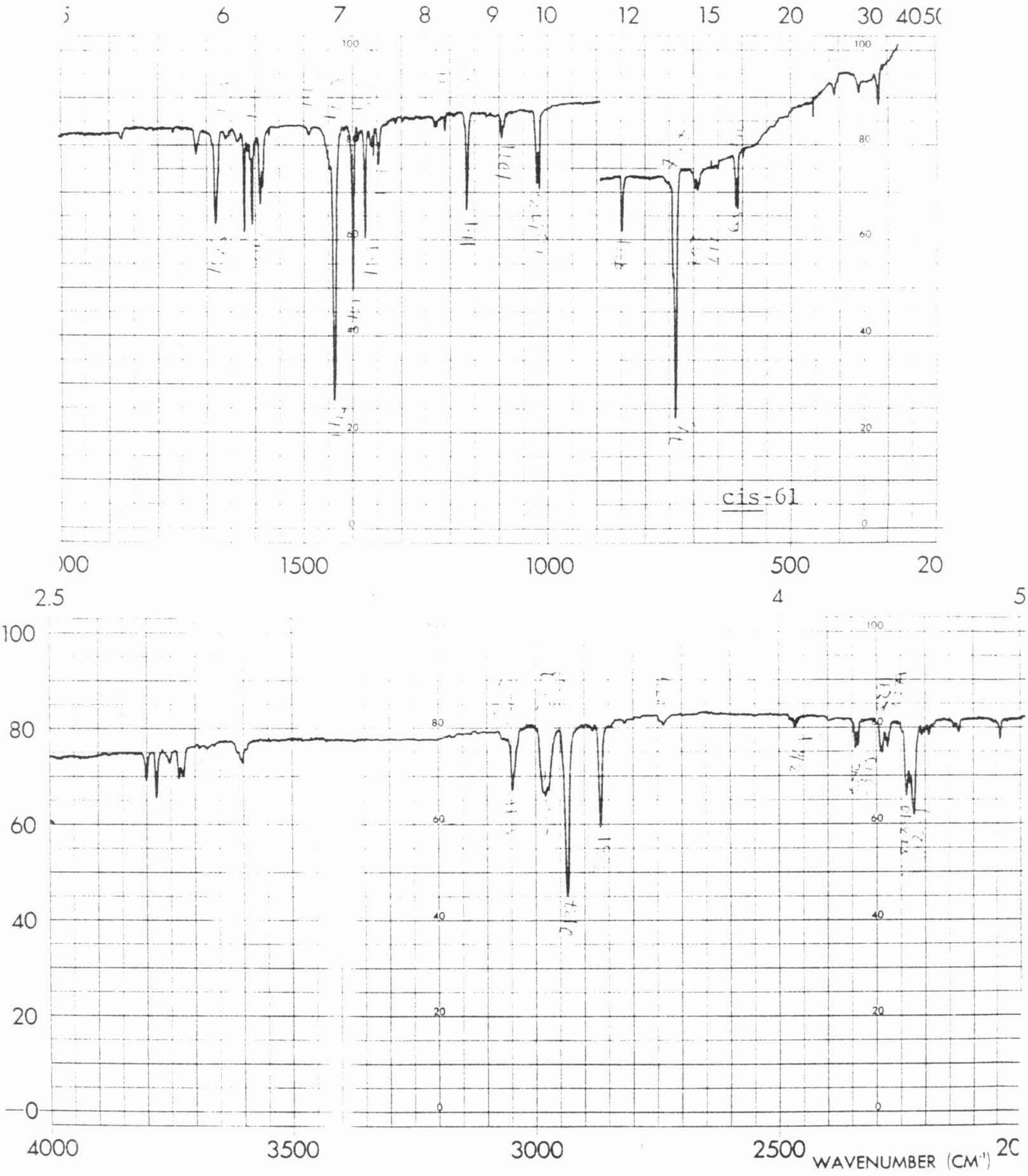
Trans-61 was prepared by photolysis of dilute solutions (about 1 mM) of cis-61 in degassed pentane with a Hanovia 450W lamp through Pyrex in an immersion well (71).

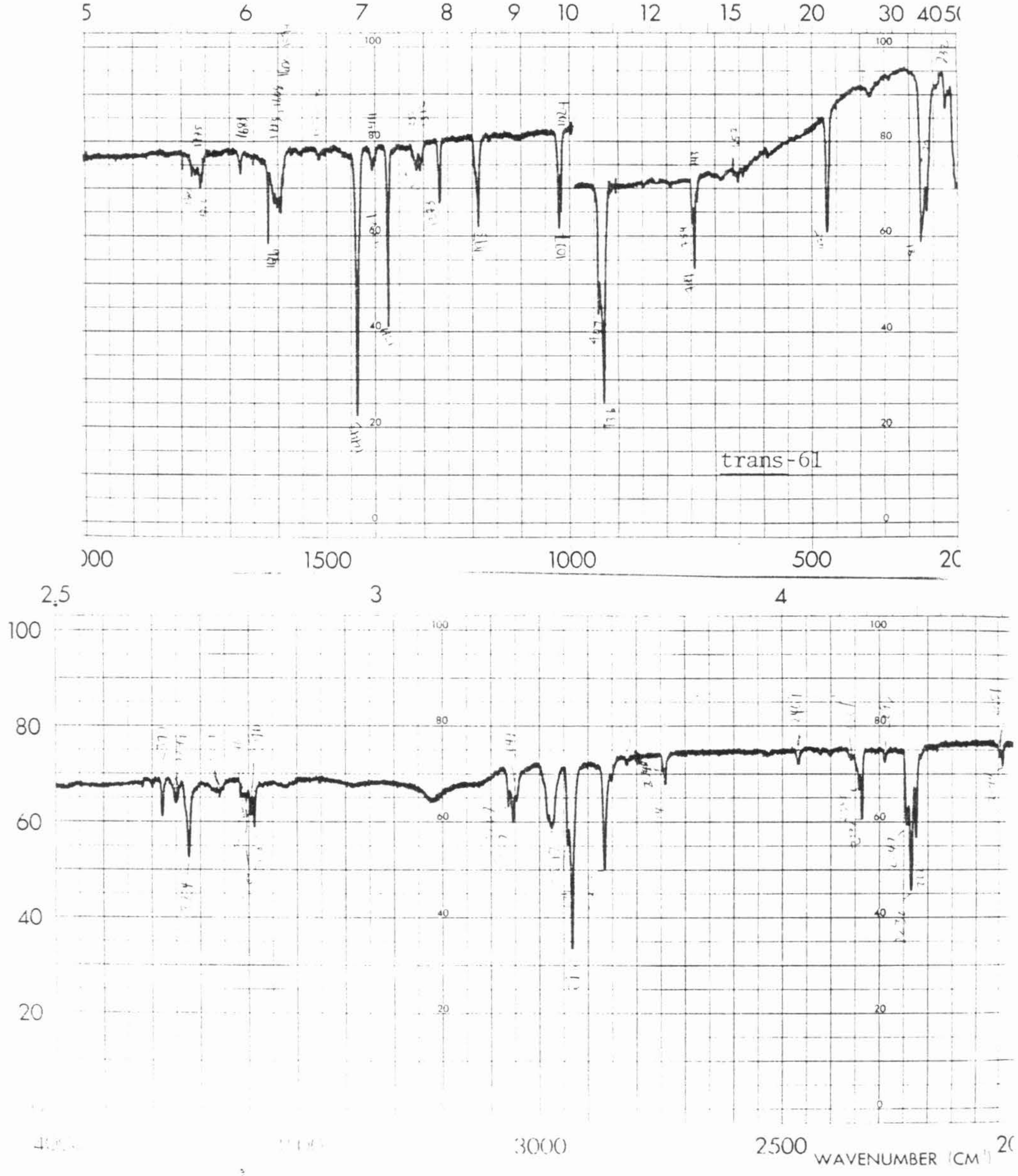
All diethynylethylenes were purified by vapor phase chromatography using a HP 5720 gas chromatograph equipped with a thermal conductivity detector. Cis- and trans-62 were collected on a 6 ft x 0.25 in glass column packed with 10% SE-30 on Chromasorb W at 60°C (injector port = 100°C, detector = 120°C), Cis- and trans-61 were collected on the same column at 80°C. The collector was maintained at -78°C for all collections.

While still in their GC collection tubes which had been dried as carefully as possible, the purified samples of the diethynylethylenes were placed in a bulb which fit onto the gas handling system. The bulb was flushed quickly with nitrogen and placed onto the gas handling system. The outside of the bulb was cooled with liquid nitrogen and the sample was degassed with four freeze-pump-thaw cycles. The vacuum was shut off from the gas handling system and the diethynylethylene was allowed to warm and fill the system. A final pressure of about 0.3 torr was usually observed. The sample was then diluted with argon (about 100 torr) and the sample was then ready for deposition. Deposition was carried out as described for 53 except for the use of the U-tube.

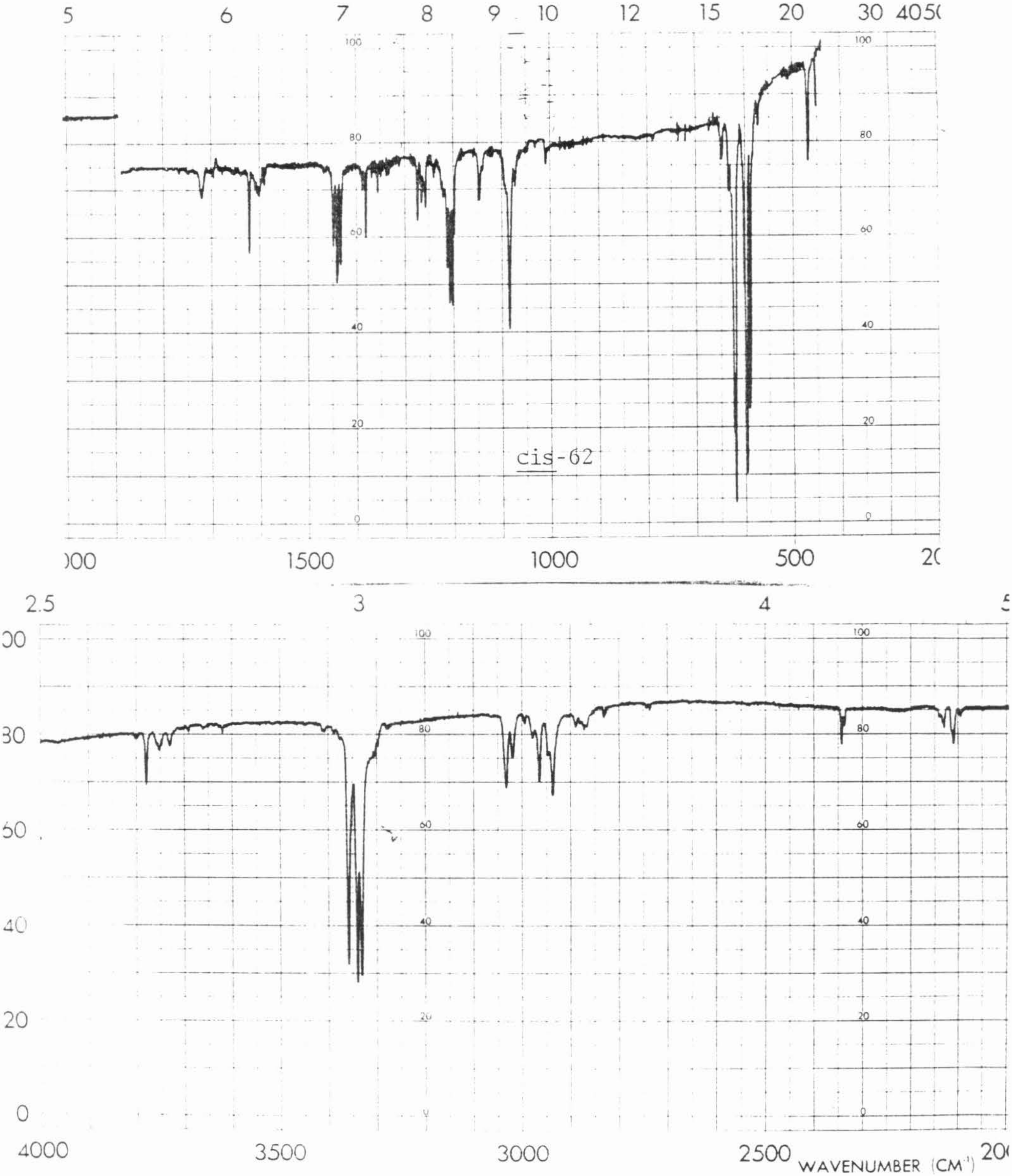
VPC and GC-MS analyses of the volatile products were carried out by T. Lockhart at the University of California, Berkeley, California.

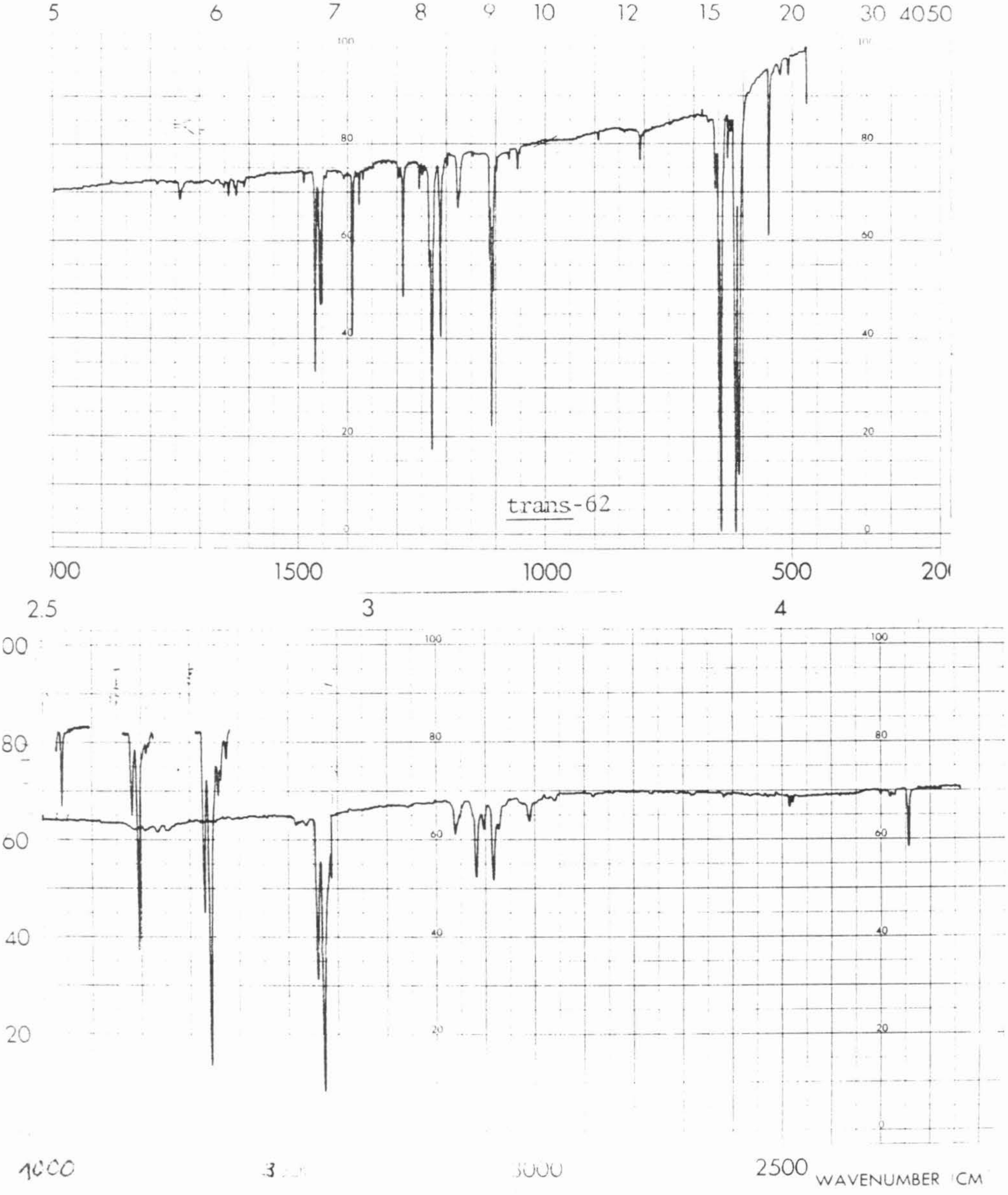
Infrared spectra of cis- and trans- 61 and 62 isolated in an argon matrix at 11°K are shown on the following pages.


cis-61
6
7
8
9
10
12
15
20
30
4050
100
80
60
40
20
0
1500
1000
500
20
2.5
4
5
100
80
60
40
20
0
4000
3500
3000
2500
WAVENUMBER (CM⁻¹)


5
6
7
8
9
10
12
15
20
30
40
100
80
60
40
20
0
1500
1000
500
2,5
3
4
100
80
60
40
20
3000
2500
WAVENUMBER (CM⁻¹)

trans-61


5
6
7
8
9
10
12
15
20
30
4050
100
80
60
40
20
0
cis-62
000
1500
1000
500
20
2.5
3
4
5
00
80
60
40
20
0
100
80
60
40
20
0
4000
3500
3000
2500
WAVENUMBER (CM⁻¹)
200


trans-62
5
6
7
8
9
10
12
15
20
30 4050
100
80
60
40
20
0
000
1500
1000
500
200
2.5
3
4
00
80
60
40
20
4000
3000
2500
WAVENUMBER CM

REFERENCES

1. R. G. Bergman and R. R. Jones, J. Am. Chem. Soc. 94, 660 (1970).
2. R. G. Bergman, Acc. Chem. Res. 1973, 25 (1973).
3. G. C. Johnson and R. G. Bergman, Tet. Lett., 2093 (1979).
4. G. C. Johnson, J. J. Stofko, T. P. Lockhart, D. W. Brown, and R. G. Bergman, J. Org. Chem. 44, 4215 (1979).
5. T. P. Lockhart, C. B. Mallon, and R. G. Bergman, submitted for publication.
6. J. D. Roberts, A. Streitwieser, Jr., and C. M. Regan, J. Am. Chem. Soc. 74, 4579 (1952).
7. R. Hoffmann, A. Imamura, and W. J. Hihre, J. Am. Chem. Soc. 90, 1499 (1968).
8. D. L. Whilhite and J. L. Whitten, J. Am. Chem. Soc. 93, 2858 (1970).
9. M. J. S. Dewar and W.-K. Li, J. Am. Chem. Soc. 96, 5569 (1974).
10. J. O. Noell and M. D. Newton, J. Am. Chem. 101, 51 (1979).
11. S. W. Benson, Thermochemical Kinetics, 2nd Edition, John Wiley and Sons, New York, N. Y. (1976).

12. N. J. Turro, B. Ramamurthy, and T. Katz, Nouveau Journal de Chemie 1, 363 (1978).

13. S. K. Pollak and W. J. Hehre, Tet. Lett. 1980, 2483 (1980).

14. I. P. Fisher and F. P. Lossing, J. Am. Chem. Soc. 85, 1018 (1963).

15. R. S. Berry, J. Clardy, and M. E. Schaefer, Tet. Lett. 1965, 1003 (1965).

16. R. S. Berry, J. Clardy, and M. E. Schaefer, Tet. Lett. 1965, 1011 (1965).

17. R. Hoyos de Rossi, H. E. Bertello, and R. A. Rossi, J. Org. Chem. 35, 3328 (1970), found no products attributable to a p-benzyne intermediate in the decomposition of a 2-nitrobenzene-1-diazonium-4-carboxylate.

18. G. Maier and W. Sauer, Angew. Chem. Int. Ed. 14, 1048 (1975).

19. W. E. Billups, J. Buynak, and D. Wolf, J. Org. Chem. 44, 4218 (1979).

20. R. Breslow, J. Napierski, and T. C. Clarke, J. Am. Chem. Soc. 97, 6275 (1975); R. Breslow and P. L. Khanna, Tet. Lett. 1977, 3229 (1977).

21. W. N. Washburn, J. Am. Chem. Soc. 97, 1615 (1975); W. N. Washburn and R. Zahler, ibid. 98, 7827 (1976); W. N. Washburn and R. Zahler, ibid. 98, 7828 (1976).

22. R. R. Jones, California Institute of Technology Ph. D. Thesis (1976).

23. Log A = 13 is an estimate. The A factor in the ring opening of bicyclohexane is 10^{13}.

24. N. Danby, G. U. Kim, J. A. Salun, K. W. Shelton, S. Takada, and S. Masamune, Chem. Comm. 1971, 1576 (1971).

25. O. L. Chapman, C.-C. Chang, J. Kolc, J. Am. Chem. Soc. 98, 5703 (1976).

26. G. Maier, Angew. Chem. Int. Ed. 13, 425 (1974).

27. K. Wiberg, California Institute of Technology Seminar, March 10, 1976, reported that

28. H. Durr, H. Nickels, L. A. Pacala, and M. Jones, Jr., J. Org. Chem. 45, 973 (1980).

29. O. Chapman, California Institute of Technology Seminar, March 25, 1976.

30. G. C. Johnson, California Institute of Technology Ph. D. Thesis (1979).

31. a) E. E. van Tamelen and S. P. Pappas, J. Am. Chem. Soc. 84, 3789 (1962). b) E. E. van Tamelen and S. P. Pappas, ibid. 85, 3297 (1963).

32. H. Prinzbach, H. Hagemann, J. H. Hartenstein, and R. Kitzing, Chem. Ber. 98, 2201 (1965).

33. I. J. Landheer, W. H. de Wolf and F. Bickelhaupt, Tet. Lett. 1975, 349 (1975).

34. K. Weniges and K. Klessing, Chem. Ber. 107, 1915 (1974).

35. L. Watts, J. D. Fitzpatrick, and R. Pettit, J. Am. Chem. Soc. 87, 3253 (1965); P. Reeves, T. Devon, and R. Pettit, J. Am. Chem. Soc. 91, 5890 (1969).

36. B. W. Roberts, private communication to D. W. Brown; B. W. Roberts, G. Berens, F. Kaplan, R. Rimerman, and A. Wissner, J. Am. Chem. Soc. 97, 7076 (1975).

37. D. W. Brown and R. G. Bergman, unpublished results.

38. J. D. Coyle, Chem. Rev. 78, 97 (1978).

39. D. Seebach, Chem. Ber. 97, 2953 (1964).

40. The authors in reference 32 used acetyl chloride to form a bicyclo[3.1.0]hexane-1,3-dicarboxylic acid anhydride. A long listing of methods is presented in reference 41.

41. C. A. Buehler and D. E. Pearson, Survey of Organic Syntheses, Volume 1, John Wiley and Sons, New York, N. Y. (1970).

42. E. K. G. Schmidt, Chem. Ber. 107, 2440 (1974).

43. H. Simonis, Chem. Ber. 32, 2084 (1899).

44. O. Diels and M. Reinbeck, Chem. Ber. 43, 1271 (1910).

45. D. W. Brown, California Institute of Technology Candidacy Report (1977).

46. P. Dowd and L. K. Marwaha, J. Org. Chem. 41, 4035 (1976).

47. D. Owsley, personal communication to D. W. Brown.

48. Shelby Sherrod, California Institute of Technology Ph.D. Thesis (1972).

49. J. H. Noggle and R. E. Schirmer, Nuclear Overhauser Effect: Chemical Applications, Academic Press (1971).

50. G. Maier, personal communication to D. W. Brown and R. G. Bergman.

51. R. D. Rieke and S. J. Uhm, Synthesis 1975, 452 (1975).

52. R. T. Arnold and S. T. Kulenovic, Syn. Comm. 7, 223 (1977).

53. The identity of 52 was confirmed by an independent synthesis and comparison with literature spectral data on the dimethyl ester. See the Experimental section for details.

54. R. K. Summerbell and R. R. Umhoefer, J. Am. Chem. Soc. 61, 3016 (1939). Rieke Mg was prepared after R. D. Rieke and S. E. Bales, J. Am. Chem. Soc. 96, 1775 (1974).

55. C. G. Scouten, F. E. Barton, Jr., J. R. Burgess, P. R. Story, and J. F. Garst, J. Chem. Soc. Chem. Comm. 1969, 78 (1969).

56. E. L. Allred, B. R. Beck, and K. J. Vorhees, J. Org. Chem. 39, 1426 (1974).

57. a) P. G. Gassman and X. Creary, J. Chem. Soc. Chem. Comm. 1972, 1214 (1972); b) J. J. Bloomfield, R. A. Martin, and J. M. Nelle, J. Chem. Soc. Chem. Comm. 1972, 96 (1972).

58. D. L. Morse and M. S. Wrighton, J. Am. Chem. Soc. 98, 3931 (1975), found that irradiation of metal carbonyl complexes containing a metal-metal bond led to the cleavage of the metal-metal bond followed by abstraction of a halogen from CCl_4. The complexes in this study were chosen simply because they were readily available.

59. J. K. Kochi, D. M. Singleton, and L. J. Andrews, Tet. 24, 3503 (1968) and references therein.

60. H. G. Kuivila, Acc. Chem. Res. 1, 299 (1968).

61. H. Sakurai, "Group IVB Radicals" in Free Radicals, Volume II, ed. by J. K. Kochi, J. Wiley and Sons, New York, N. Y. (1973).

62. D. Forrest and K. U. Ingold, J. Am. Chem. Soc. **100**, 3868 (1978).

63. K. Schenck, W. Hartmann, O. Steinmetz, Chem. Ber. **96**, 498 (1963).

64. H. D. Scharf and J. Mattoy, Lieb. Ann. Chem. **1977**, 772 (1977).

65. H. D, Scharf and F. Laux, Synthesis **1970**, 582 (1970).

66. S. Cradock and A. J. Hinchcliffe, Matrix Isolation: A Technique for the Study of Reactive Inorganic Species, Cambridge University Press, Cambridge (1975). The discussion in the text of the thesis draws heavily upon this reference.

67. O. L. Chapman, K. Mattes, C. L. McIntosh, J. Pacansky, G. V. Calder, and G. Orr, J. Am. Chem. Soc. **95**, 6134 (1973).

68. We have observed the bending modes of *o*-xylene at 740 cm^{-1}, of toluene at 725 cm^{-1}, and of benzene at 680 cm^{-1}. The phenyl radical has its strongest absorption at 710 cm^{-1}.

69. K. L. Tseng and J. Michl, J. Am. Chem. Soc. **99**. 4840 (1977).

70. *Cis* and *trans* refer to the relationship of the ethynyl substituents about the double bond.

71. C. B. Mallon, research report to R. G. Bergman. *Cis*- and *trans*-**61** prepared by the method in this thesis had NMR spectral characteristics identical to those reported by Mallon.

72. C. Kittel, *Introduction to Solid State Physics*, 5th Edition, J. Wiley and Sons, New York, N. Y. (1976).

73. R. Criegee, U. Zirnfibl, H. Furrer, D. Seebach, and G. Freund, Chem. Ber. *97*, 2942 (1964).

74. T. P. Lockhart, California Institute of Technology Ph.D. Thesis, to be submitted.