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PHOTOISOMERIZATION OF 3H-AZEPINES

by

BERNARD SCHMALL

**A dissertation submitted to the
Graduate Faculty in Chemistry in partial
fulfillment of the requirements for the
degree of Doctor of Chemistry,
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1972

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To Barbara
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Abstract

PHOTOISOMERIZATION OF 3H-AZEPINES

by

Bernard Schmall

Adviser: Professor Robert A. Odum

The photoisomerization of 3H-azepines substituted in the 2-position with ethoxy, amino, and dimethylamino groups was investigated. Prior photochemical studies of heterocyclic seven-membered rings containing a conjugated triene system utilized symmetrical structures which could only lead to the formation of one cyclobutene derivative.

Selectivity in the photoisomerizations of the 3H-azepines was observed at all concentrations and in all solvents and wavelengths employed. Although photochemical concerted intramolecular cycloadditions of 2-dimethylamino-3H-azepine, 2-amino-3H-azepine and 2-ethoxy-3H-azepine can lead to the corresponding 2-aza-bicyclo(3.2.0)hepta-2,6-dienes and 6-aza-bicyclo(3.2.0)hepta-2,6-dienes by orbital symmetry-allowed disrotatory processes, the only major volatile products were the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes, in all cases.

Irradiation of dilute pentane solutions of 2-dimethylamino-3H-azepine with 3000A lamps gave a brown polymer and about a 70% yield of 3-dimethylamino-2-aza-bicyclo(3.2.0)

hepta-2,6-diene. Similar reactions of 2-amino-3H-azepine in pentane or methanol and of 2-ethoxy-3H-azepine in pentane, using 2537A lamps, gave the corresponding 2-aza-bicyclo(3.2.0)hepta-2,6-dienes in 45% and 60% yields, respectively. Since the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes are obtained in synthetically useful yields, the photolysis of 3H-azepines affords a reasonable synthetic entry to the otherwise difficultly accessible 2-aza-bicyclo(3.2.0)structure.

The 2-aza-bicyclo(3.2.0)hepta-2,6-dienes are readily interconverted. Alkylation of 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one with triethyloxonium fluoroborate provided a convenient synthesis of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene in 70% yield. Treatment of this imidate ester with dimethylamine gave the dimethylamino derivative in high yield. The conversion of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene to the 3-ethoxy-derivative was effected in high yield by ethanolysis in the presence of a catalytic amount of glacial acetic acid. In a similar manner, 2-amino-3H-azepine was converted to 2-ethoxy-3H-azepine. This transformation is novel, constituting the first isolation of an imidate ester from the intermolecular acid catalyzed reaction of an amidine with an alcohol, such as ethanol.

Although the cycloreversion of cyclobutenes should be photochemically allowed by orbital symmetry theory, there were few reported cases. The photocycloreversion of 3-

dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene to 2-dimethylamino-3H-azepine was readily effected in 10% yield by irradiation with a medium pressure mercury arc through a vycor filter. Also, in accord with orbital symmetry theory, temperatures above 200° were required to effect the thermal cycloreversion of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene to 2-ethoxy-3H-azepine.

The mechanism of the photoisomerization process is discussed. One possible deciding factor for the selective nature of the reaction might be the loss of amidine or imidate ester resonance energy. The possibility that the observed selectivity of ring closure could be rationalized by consideration of the symmetry of the highest occupied molecular orbital was investigated. Excited state molecular orbitals were obtained by simple Huckel molecular orbital calculations employing a heteroatom model for the methylene carbon. The calculations were carried out over a range of parameter values for the coulomb integral for the methylene-pseudoheteroatom. A convincing argument to explain the observed selectivity on the basis of these molecular orbitals could not be developed. Application of Fukui's method of orbital interactions shows promise in leading to a consistent theory for the selective nature of these reactions.

ACKNOWLEDGEMENT

I wish to express my sincere appreciation to Professor Robert A. Odum for his inspiration, guidance, and friendship. Without his untiring patience, understanding and encouragement the completion of this research would have been impossible.

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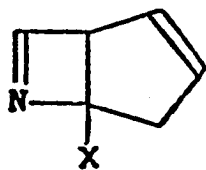
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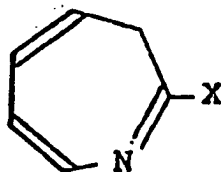
INTRODUCTION

A number of photochemical butadiene-cyclobutene interconversions contain the diene chromophore as part of a seven-membered conjugated cyclic system. Because of the constraints imposed by the ring, symmetry-allowed disrotatory closure is observed. The photochemical behavior of 1,3,5-cycloheptatriene and its derivatives have been well documented¹. However, only the photochemistry of its symmetrical heterocyclic counterparts had been reported at the inception of this thesis research. Photochemical intramolecular cycloadditions of 1H-azepines were known, and, in all cases, resulted in the formation of only one cyclobutene derivative².

In contrast, concerted intramolecular cyclization of 3H-azepines (1) might lead to at least two different bicyclo(3.2.0) isomers (2) and (3).



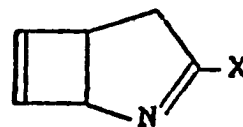
(3)



(1a) X = -NMe₂

(1b) X = -NH₂

(1c) X = -OEt



(2)

Alternatively, intramolecular cyclizations of 3H-azepines might not be concerted³. In either case, selectivity in the formation of possible photoisomers would be intriguing.

This thesis research is concerned with the photochemistry of 2-amino-3H-azepine, 2-dimethylamino-3H-azepine and 2-ethoxy-3H-azepine, and with some simple considerations of the initial interactions developing in the highest occupied orbital of the first excited state on proceeding along the reaction coordinates.

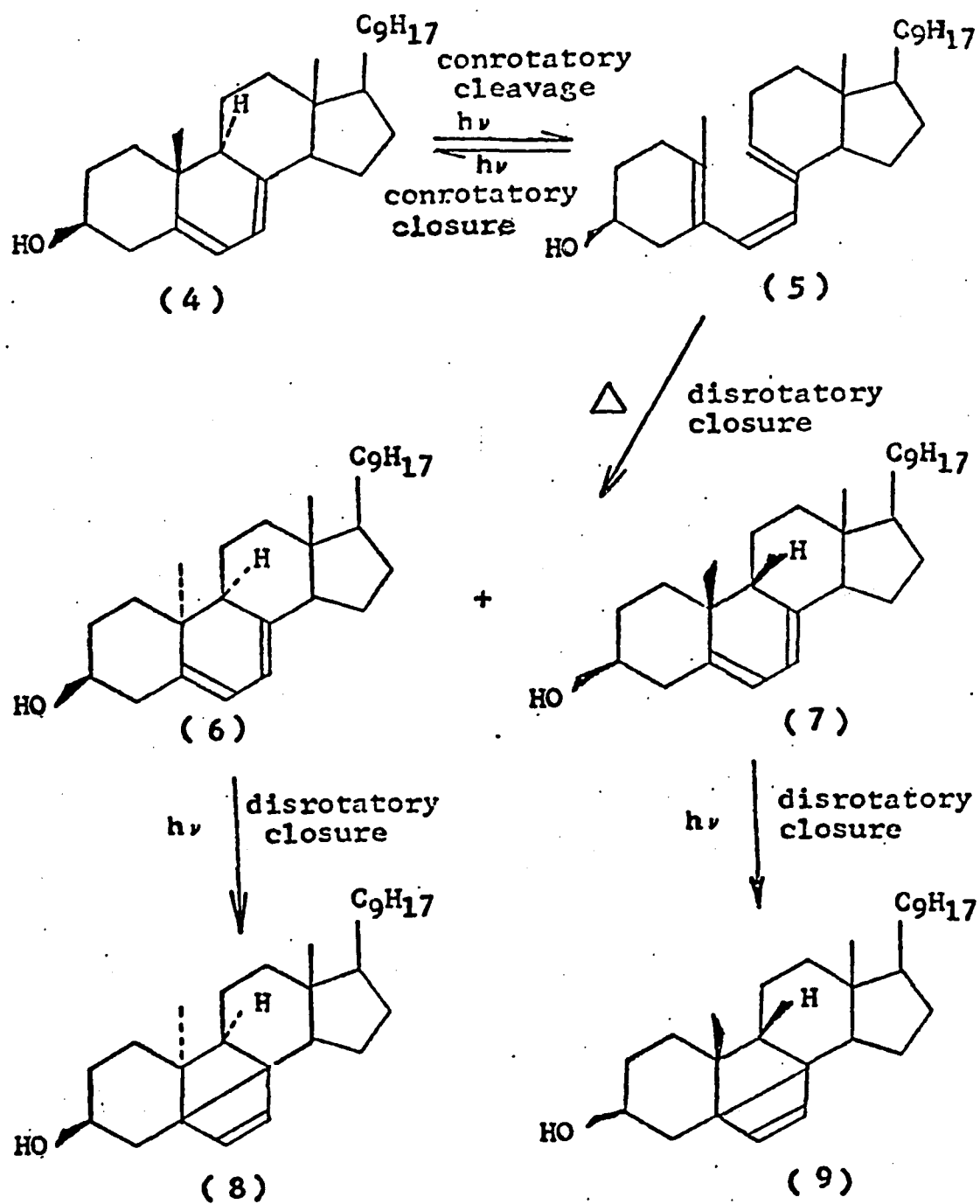
This thesis also presents a novel procedure for transforming 3H-azepines and their photoisomers containing the amidine functionality into their corresponding imidate esters.

HISTORICAL AND THEORY

- A. Early observations of intramolecular cycloaddition and cycloreversion reactions; application of the Woodward-Hoffmann electrocyclization selection rules.

In recent years, an active area of photochemical research has been concerned with the intramolecular cycloaddition and cycloreversion reactions of conjugated olefins⁴, and with the application of the Woodward-Hoffmann selection rules for such concerted processes^{5,6,7}. Intramolecular cyclization is an example of a valence isomerization^{8,9}. Valence isomerizations differ from the more usual types of rearrangements in that they do not involve migration of atoms, but only involve a reorganization of the σ and π electrons of the molecule with concomittant changes in bond angles and bond distances. Some of the earliest examples of intramolecular cycloadditions and cycloreversions were exhibited in the reactions of the steroidal vitamin D₂ series^{1,10,11} (scheme 1).

Havinga^{12,13} and Velluz¹⁴ showed that $\Delta^{5,7}$ -steroidal-dienes possessing 9,10-anti stereochemistry cleave to trienes on irradiation and Dauben¹⁵, in 1959, reported that the corresponding 9,10-syn isomers gave intramolecular cycloaddition products upon irradiation. On heating, the trienes underwent ring closure to the 9,10-syn isomers rather than reverting to the 9,10-anti isomers. Thus, reversible ring fission of 1,3-cyclohexadiene to 1,3,5-hexatriene was observed in the photochemical interconversions of ergosterol(4)



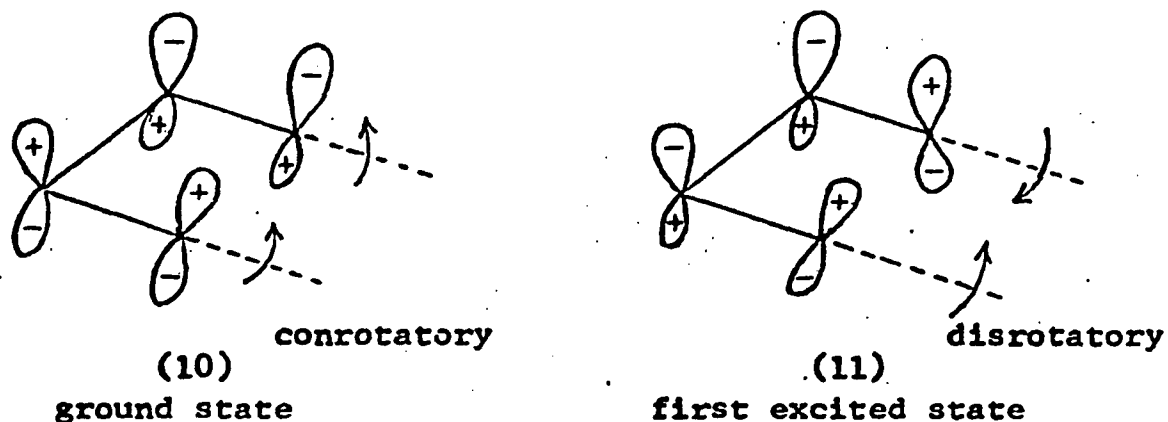
Scheme 1

Reactions of the steroidal vitamin D₂ series

and precalciferol (5). Intramolecular cyclization¹⁵ of a 1,3-diene to a cyclobutene was elucidated in the photolytic conversions of pyrocalciferol (6) and isopyrocalciferol (7) to their valence isomers (8) and (9), respectively. The 9,10-syn isomers (6) and (7) were obtained thermally from the triene (5).

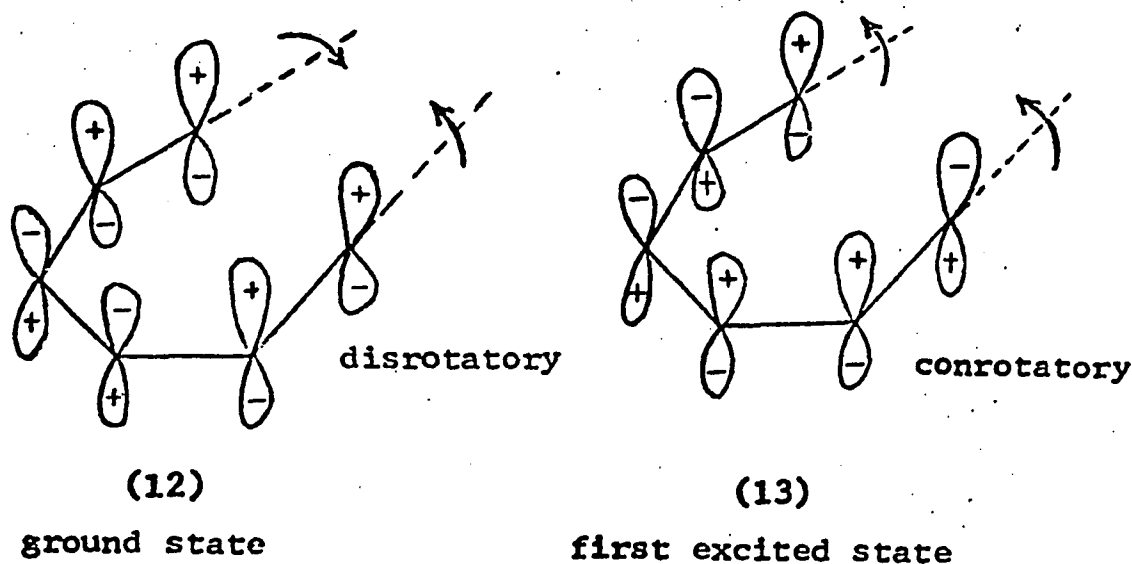
Although subtle stereochemical factors may play a controlling rule in determining the course of these valence isomerization reactions, Oosterhoff¹⁶ suggested that the differences between the stereochemical courses of the thermal and photochemical reactions of the Vitamin D₂ series might be related to orbital symmetries. In 1965, Woodward and Hoffmann⁵, as a result of their investigations of the vitamin B₁₂ system,¹⁷ formulated a theory of orbital symmetry which in the absence of secondary steric factors, controls the course of concerted reactions. They proposed that the symmetry of the highest occupied molecular orbital of an acyclic polyene determines the steric course of an "electrocyclization" reaction. Woodward and Hoffmann defined an electrocyclization reaction as one in which an acyclic system containing $k\pi$ - electrons is converted to a cyclic system by the formation of a single bond between the termini of the acyclic system, and the reverse process. These workers assigned the terms conrotatory or disrotatory to modes of closure in which rotations about each termini conform, i.e. rotate in the same direction, or do not conform, i.e. rotate

in opposite directions. Transformations of either type occur thermally or photochemically depending on the size of the linear π -system. These rotations in the highest occupied molecular orbitals of the ground and first-excited states of butadiene and hexatriene are depicted in schemes 2 and 3, respectively.



Scheme 2

Highest occupied molecular orbitals of the ground and first-excited states of butadiene



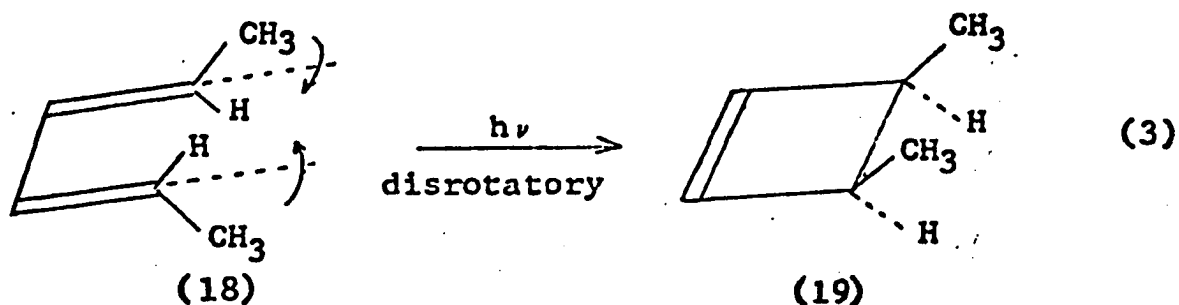
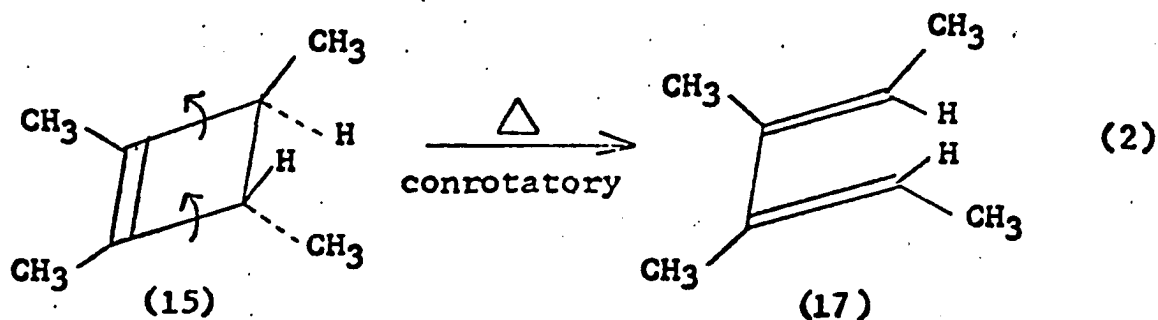
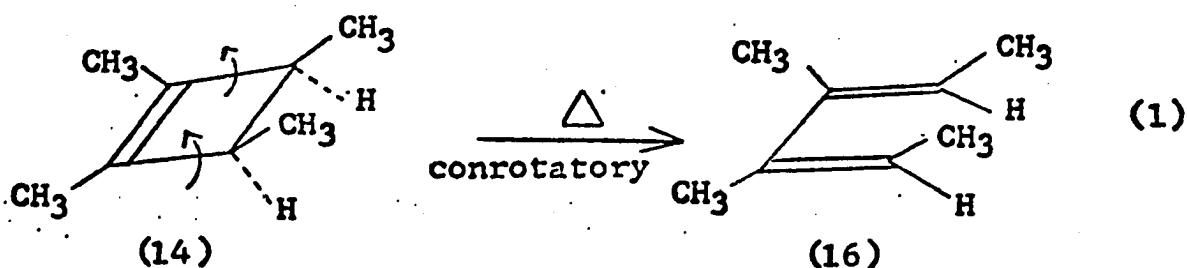
Scheme 3

Highest occupied molecular orbitals of the ground and first-excited states of hexatriene

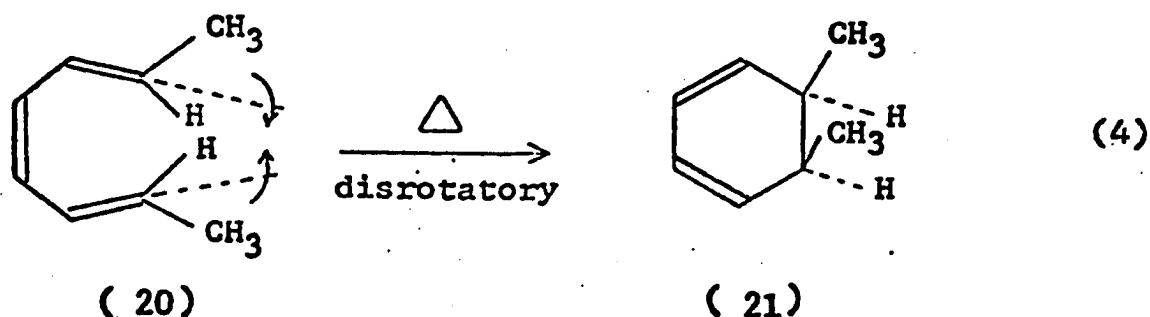
Woodward and Hoffmann⁵ stated that

"the steric course of electrocyclic transformations is determined by the symmetry of the highest occupied molecular orbital of the open-chain partner in these changes. Thus, in any open-chain system containing $4n$ π -electrons, the symmetry of the highest occupied ground-state orbital is such that a bonding interaction between the termini must involve overlap between orbital envelopes on opposite faces of the system, and this can only be achieved in a conrotatory process. Conversely, in open systems containing $(4n + 2)$ π -electrons, terminal bonding interaction within ground-state molecules requires overlap of orbital envelopes on the same face of the system, attainable only by disrotatory displacements. On the other hand, promotion of an electron to the first excited state leads to a reversal of terminal symmetry relationships in the orbitals mainly involved in bond redistribution, with the consequence that a system which undergoes a thermally induced disrotatory electrocyclic transformation in the ground state should follow a conrotatory course when photochemically excited, and vice versa." (See schemes 2 and 3.)

Polyenes containing $4n$ π -electrons undergo conrotatory closure, thermally, and disrotatory closure, photolytically. Thus, on heating, *cis*-and *trans*-1,2,3,4-tetramethylcyclobut-1-enes (14) and (15) yield stereospecifically their corresponding open-chain partners (16) and (17) by conrotatory openings¹⁸; and *trans*, *trans*-2,4-hexadiene (18) and the pyrocalciferols (6) and (7) undergo photochemical cyclization by a disrotatory closure^{6,19,20}.



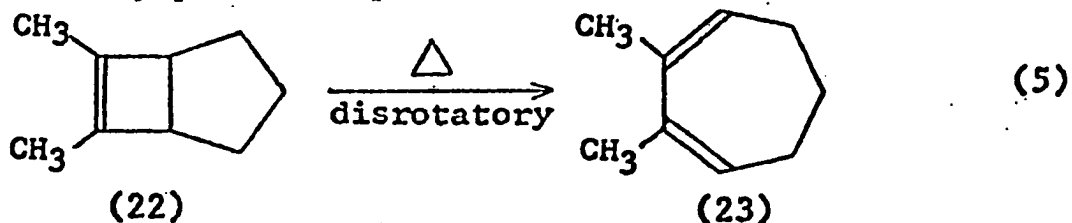
Polyenes containing $(4n + 2)$ π -electrons will undergo disrotatory closure, thermally, and conrotatory closure, photolytically. Thus, the hexatriene (20), on heating yields stereospecifically the cyclohexadiene (21)²¹ by a disrotatory



closure; ergosterol (4) and precalciferol (5) are photolytically interconverted by conrotatory modes of action; and precalciferol (5) undergoes thermal disrotatory closure to (6) and (7). Secondary steric factors prevent the pyrocalciferols (6) and (7) from undergoing light-induced ring opening to (5). Steric constraints imposed by the ring prevents a conrotatory bond movement leading from the 9,10-syn isomers 6 and 7 to (5)²².

A point of much importance is that the electrocyclicizations rules predict a favored process, but do not exclude the operation of the other under very energetic conditions. Whereas, cis-1,2,3,4-tetramethylcyclobut-1-ene (14) is converted to cis, trans-tetramethylbutadiene (16) in a conrotatory process at 200°, the dimethylbicyclo(3.2.0) heptene derivative (22) is only slowly transformed to the cycloheptene (23) in a disrotatory process²³ at 400°. The geometrical constraints of the five-membered ring makes the

conrotatory process impossible.



In 1959, Barton²⁴ suggested that the intramolecular cycloreversion (ring opening) reaction and not the intramolecular cycloaddition (bridging) reaction observed in the vitamin D₂ series was the preferred reaction for 1,3-cyclohexadienes, and generalized that rings containing $2n$ members and $(n-1)$ conjugated double bonds should lead to open chains of n -conjugated double bonds. However, Barton's rules for rings of $2n$ members did not always hold as more examples^{20,22} of bridging reactions became known. The Woodward-Hoffmann theory of orbital symmetry has elegantly resolved the different modes of valence isomerizations observed for rings containing $2n$ members and $(n-1)$ conjugated double bonds.

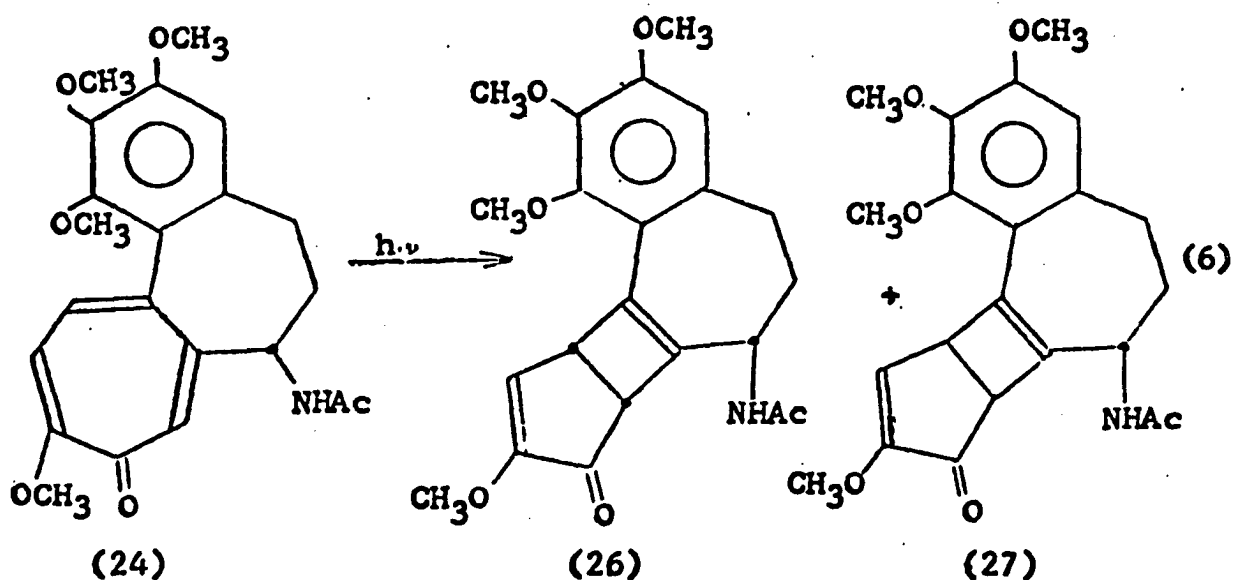
For rings containing an odd number of atoms Barton²⁴ had also suggested, that rings of $(2n + 1)$ members and n -conjugated double bonds should lead to bridging. In almost all cases this has been observed since ring opening cannot readily occur. The theory of orbital symmetry has correctly predicted the thermal and photolytic valence isomerization pathways for symmetrical 1,3,5-cycloheptatriene and symmetrical heterocyclic analogs (see discussion in sections C and F of historical). However, reports of orbital symmetry considerations of unsymmetrical seven-membered conjugated cyclic systems are rare (see discussion in section D of historical), especially from the viewpoint of predicting the preferred mode of closure between two possible butadiene-cyclobutene interconversions.

B. Rationalization of intramolecular cycloadditions in terms of "dipolar" excited states

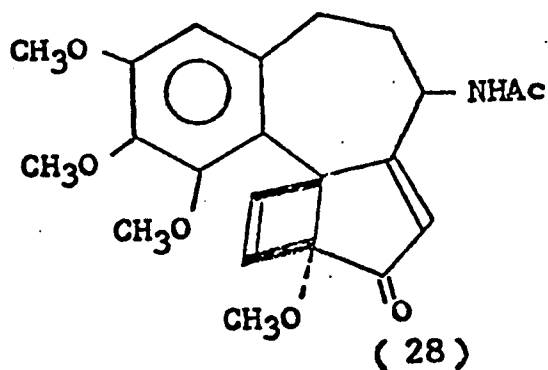
1. Tropolones

A number of early reports on intramolecular cyclizations of rings with $(2n + 1)$ members and n conjugated double bonds resulted from observations on the photochemical behavior of colchicine (24) and isocolchicine (25). These natural products contain the seven-membered tropolone ring. The spectral characteristics of enones such as the troponoids, are different from those of simple olefins, since the enones may undergo $n-\pi^*$ excitation in addition to $\pi-\pi^*$ excitation. However, the importance of $n-\pi^*$ excitation in photo-cyclization reactions is presently obscure²⁵, and, therefore, a review of the selective nature of the photoisomerizations of tropolones is informative. No attempts to apply orbital symmetry theory to the tropolones have been reported.

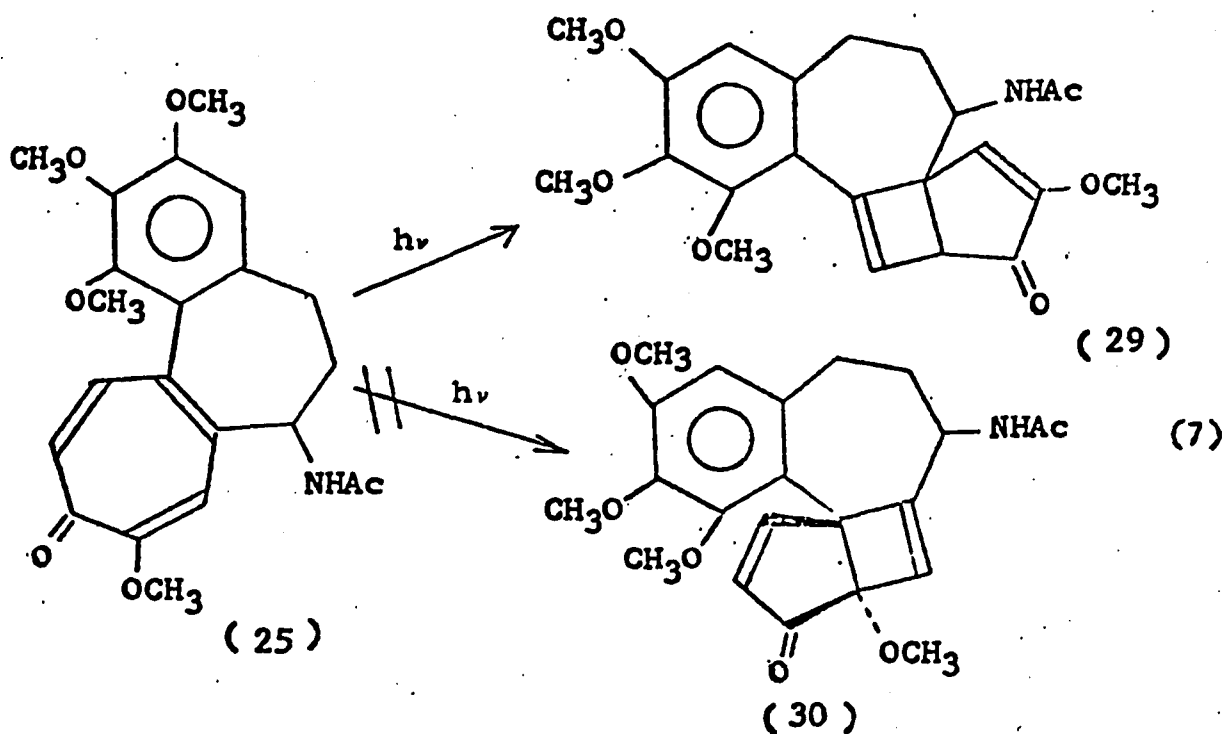
Photo-cyclization across the cycloheptatrienone ring of colchicine^{1,26,27} produces the structural isomers β -lumicolchicine (26), γ -lumicolchicine (27), and α -lumicolchicine, which is a dimer of β -lumicolchicine. The alternative



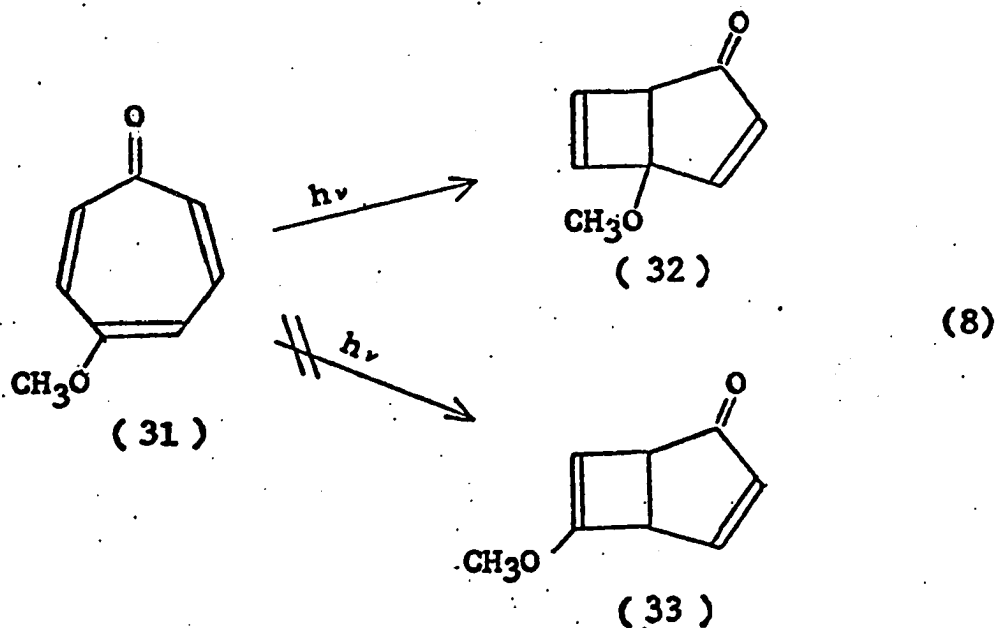
mode of intramolecular cycloaddition leading to (28) was not observed.



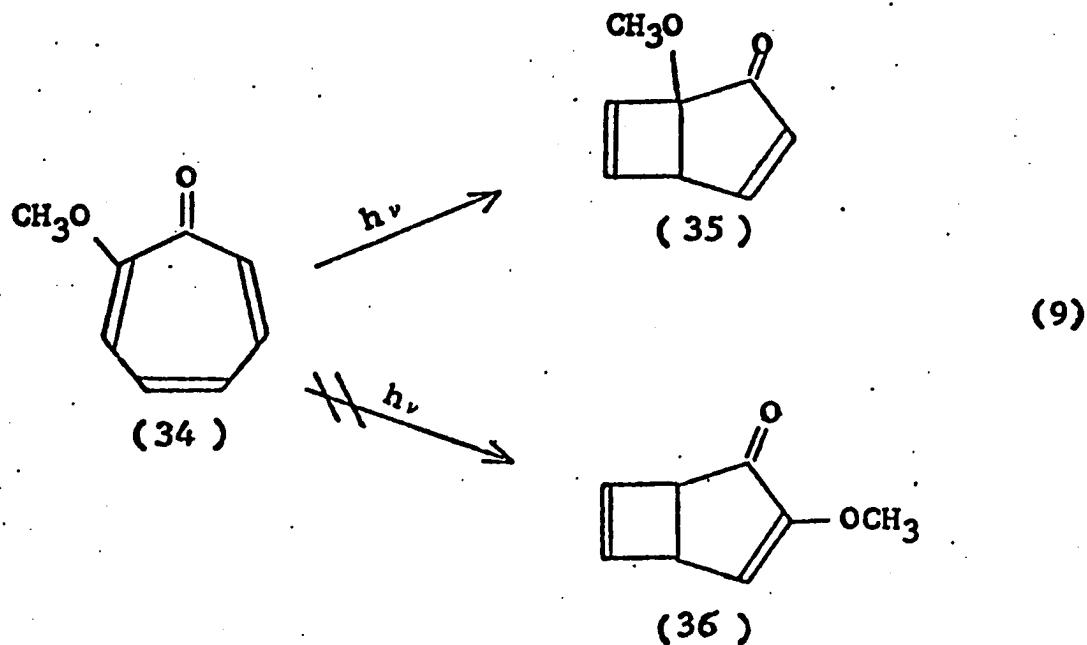
In the case of isocolchicine²⁷⁻²⁹ which has two possible modes of closure to bicyclic products (29) and (30), only the photoisomer (29) was observed.



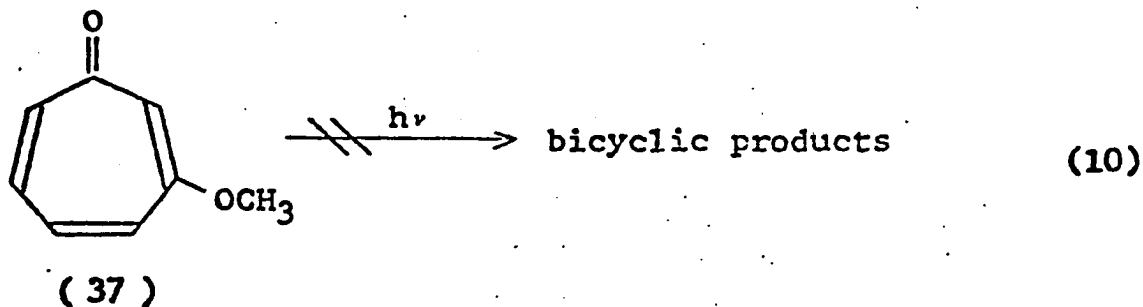
The photochemical behavior of colchicine stimulated investigations of simple tropolones^{1,27,28}. In 1960, Chapman and Pasto³⁰ reported that irradiation of γ -tropolone methyl ether (31) produced only one photoproduct (32), and



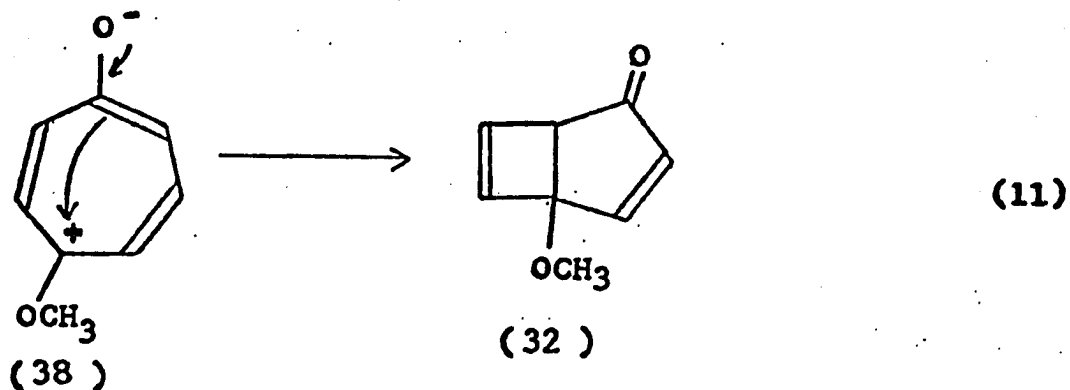
Dauben and co-workers³¹ reported that the primary photoproduct from the photolysis of α -tropolone methyl ether (34) was the bicyclic photoisomer (35). However, photolysis of β -tropolone



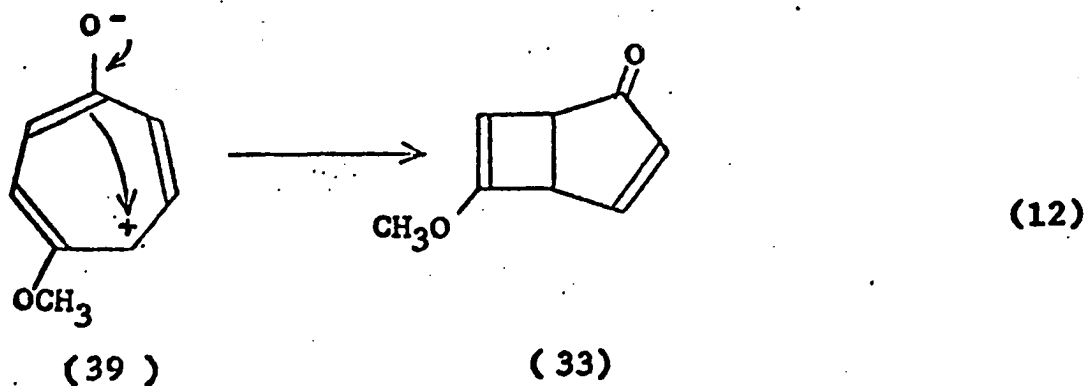
methyl ether (37) did not lead to any bicyclic products¹.



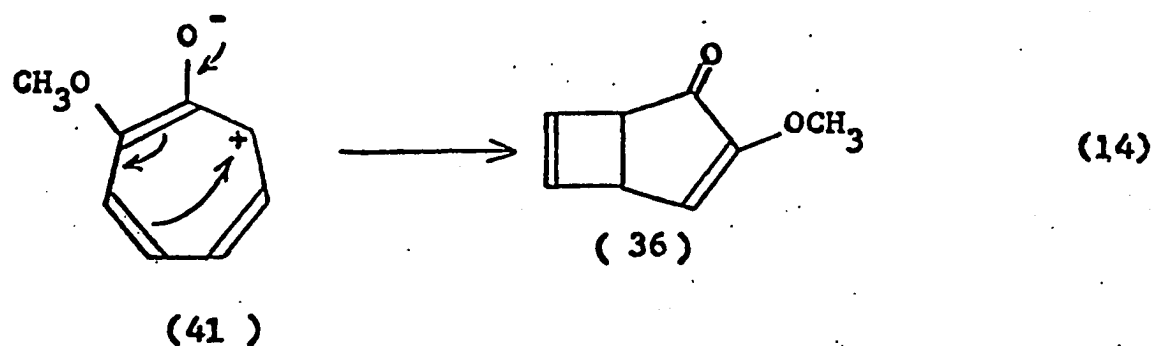
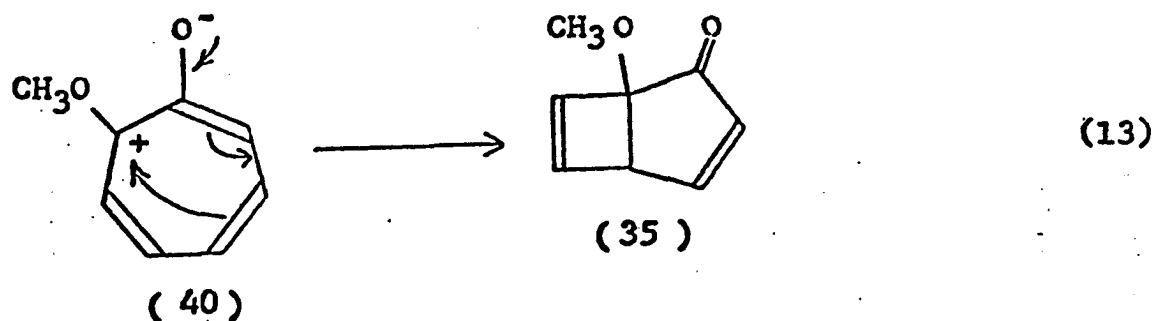
Chapman²⁸ suggested a rationalization (no implication as to the mode of electronic excitation or excited state was intended) for the preference of photoproduct 32 over 33 in the irradiation of γ -tropolone methyl ether (31). He attributed the preference for the formation of 32 to stabilization of a possible dipolar excited state by the methoxyl group, as depicted in formula (38). Such stabilization is



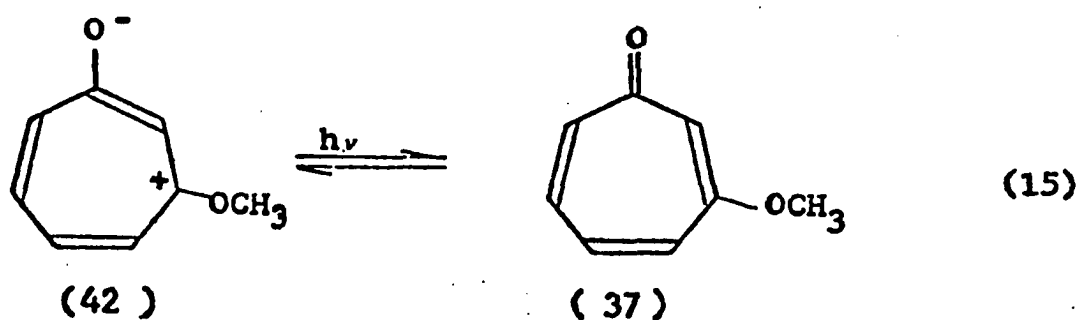
not favorable in the alternative electron distribution leading to 33, as depicted in formula (39). Similar arguments may be



evoked for the preference of 35 over 36 in the irradiation of α -tropolone methyl ether (34). In this case, collapse to photoproduct is more favorable from formula (40) than

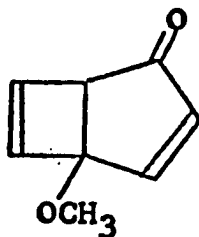


from formula (41). In the case of β -tropolone methyl ether (37) the dipolar excited state, as depicted in formula (42), can only return to the ground state, so that competitive processes occur and complex mixtures are obtained.

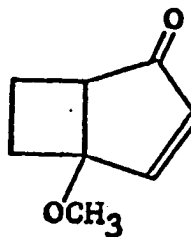


Extending the dipolar excited state concept to colchicine (24) and isocolchicine (25), the unobserved products 28 and 30 should have been preferentially formed. Although stereochemical factors may be operating in the case of colchicine this has been discounted since inspection of dreiding models of isomers 29 and 30 derived from isocolchicine indicate that both structures should possess comparable steric strain. Therefore it has been suggested that the reaction pathway followed in the irradiation of both colchicine and isocolchicine is due to electronic factors which preserves the trimethoxylstryrl entity.

Although the dipolar excited state concept is not the controlling factor in the irradiation of colchicine and isocolchicine, this concept is useful in rationalizing the products observed with the tropolone methyl ethers. There is considerable interaction of the cyclopentenone chromophore with the cyclobutene double bond as shown by the ultraviolet spectrum of 32 (obtained from γ -tropolone methyl ether) which has maxima at 243 and 328 m μ instead of the single maximum of the bicyclopentenone (43) at 215 m μ .

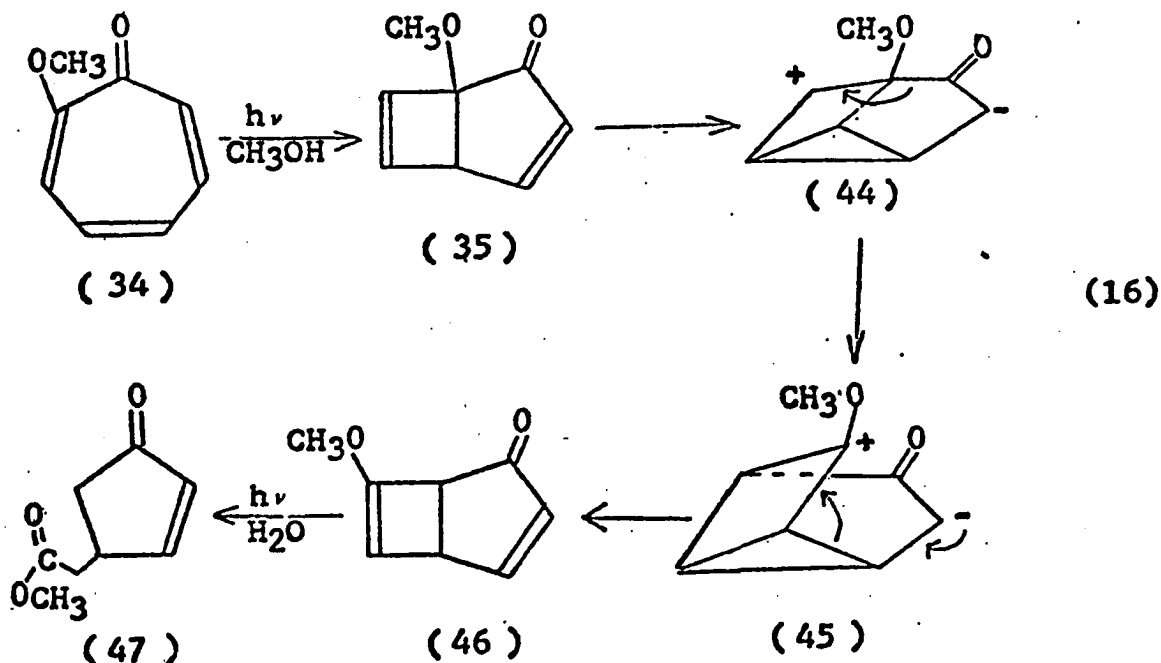


(32)

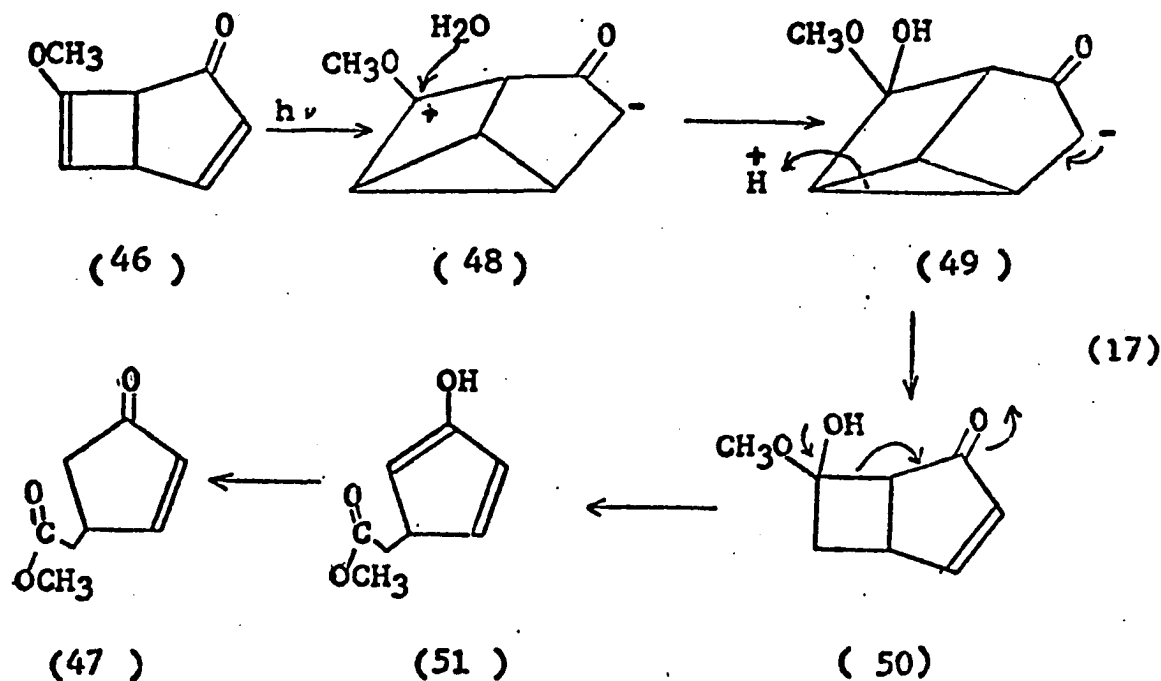


(43)

This interaction is consistent with a dipolar intermediate which can be invoked to explain the rearrangement of the primary photoproduct 35 from the photolysis of α -tropolone methyl ether (34) in methanol to a secondary product 46.

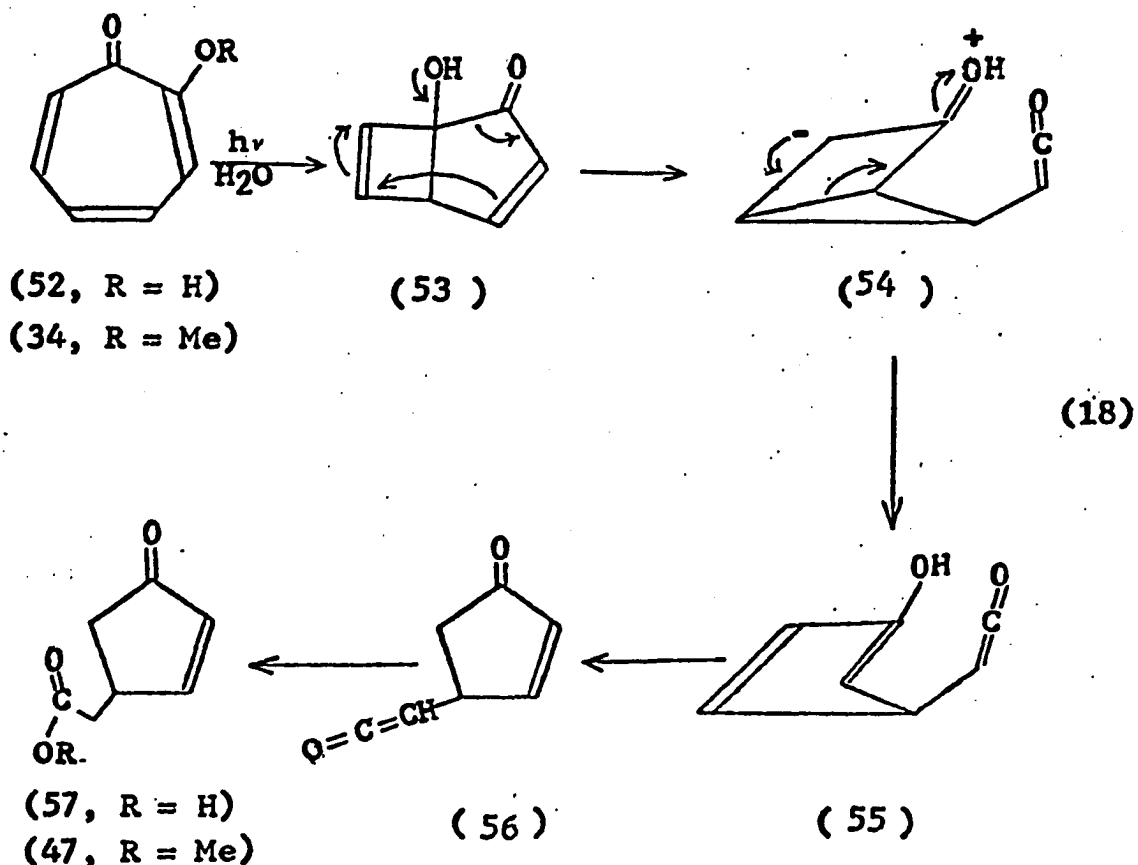


Photolysis of the secondary product 46 in water resulted in the production of the methyl ester of 4-oxo-2-cyclopentene-1-acetic acid (47). The formation of this product may be

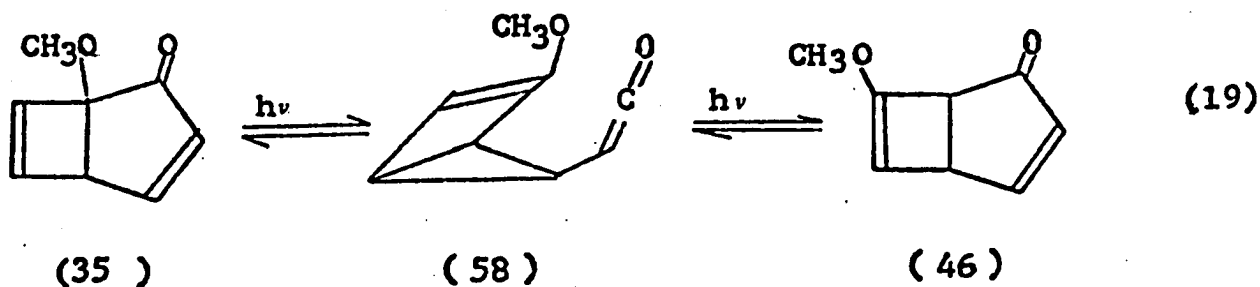


rationalized^{28,31} by an attack of water on a dipolar excited state species such as 48 in which the positive charge resides on the carbon containing the methoxyl group. This product was also observed²⁸ in a thermal acid-catalyzed reaction of 46 and water. A similar mechanism involving dipolar intermediates is plausible for this reaction.

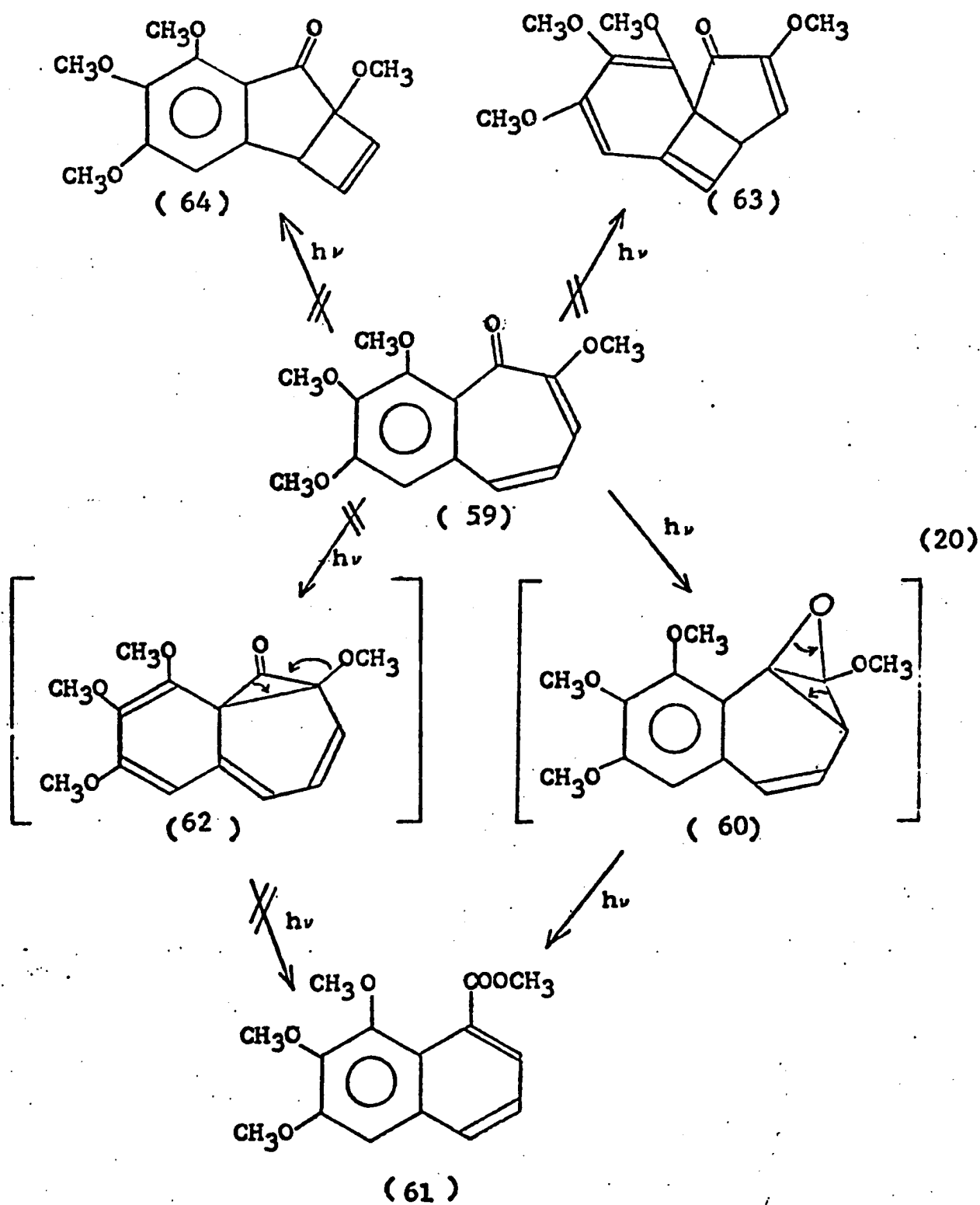
Although equations (16) and (17) conveniently rationalize the rearrangement of 35 to 46 and the formation of 47 from 34, there is evidence that other mechanisms may be operable. For example, the possibility of the intervention of a ketene intermediate must be considered since the carbonyl function is capable of $n-\pi^*$ excitation and the formation of ketenes are known examples of α -cleavage reactions due to $n-\pi^*$ excited states. However,, while a^{28,31} ketene mechanism satisfactorily accounts for the formation of 4-oxo-2-cyclopentene-1-acetic acid (57) from α -tropolone (52)



under aqueous conditions, it fails to account for the formation of the methyl ester (47) from α -tropolone methyl ether (34). Interestingly, Chapman^{32,33} has recently observed the photolytic interconversions of 35 and 46 in a neat glass at -70° . The ketene 58 a ground state intermediate, which is thermally unstable above -70° , was observed spectroscopically to be a primary photoproduct.

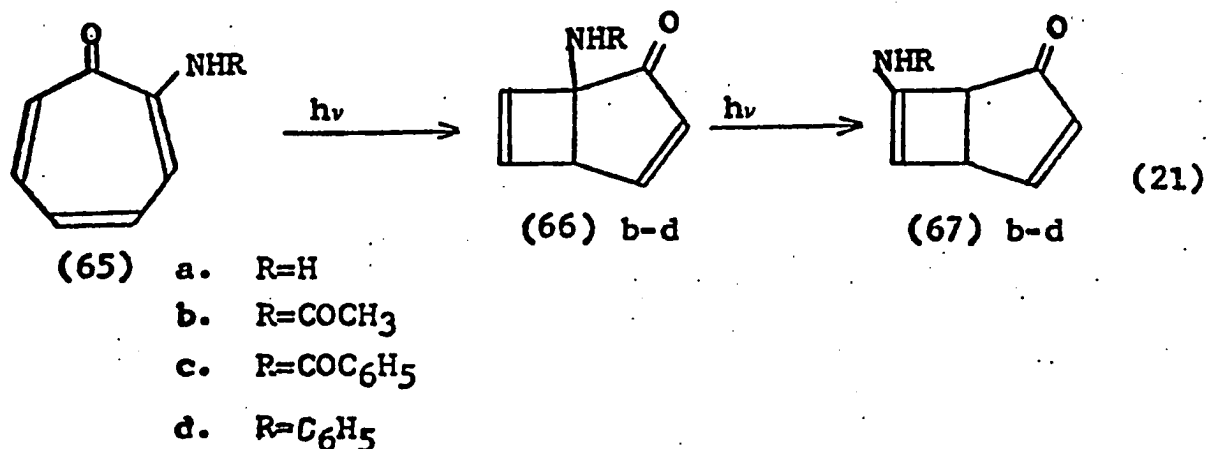


Although cyclization of tropolones to bicyclic(4.1.0) valence isomers is a possibility in light-induced reactions, the formation of norcaradiene derivatives has not been observed. The intervention of a norcaradiene intermediate was initially suspected in the photolysis of purpurogallin tetramethyl ether (59) in ethanol solution to the methyl ester (61) (equation 20), but it was finally demonstrated²⁷ that the reaction proceeded via the oxabicyclobutane intermediate (60) rather than the norcaradienone (62). Apparently the aromatic ring exerts a directive influence on the course of the reaction because contraction of the seven membered ring is favored instead of cyclization to the bicyclic(3.2.0) isomers 63 and 64. The formation of 63 is unlikely because it requires the destruction of the aromatic ring. However, a rationale for the non-observance of the expected product 64 is not as obvious.



2. 2-amino-tropones

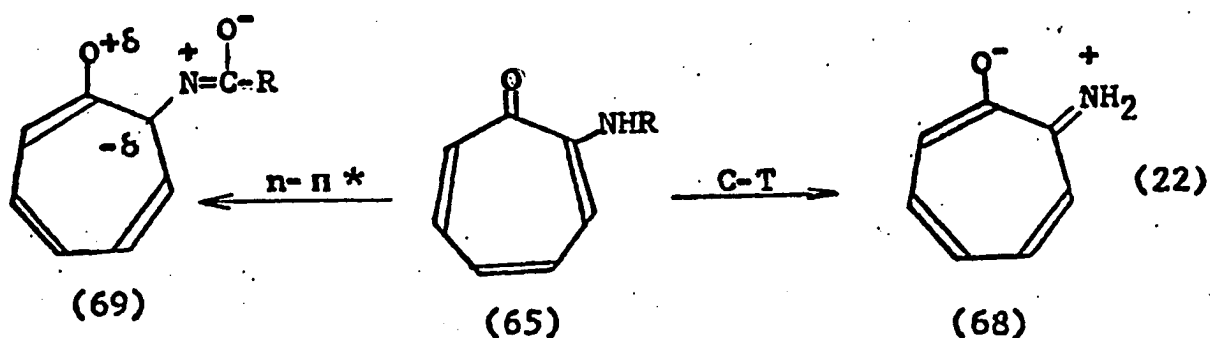
The nature of the substituent in the tropone ring has a profound influence on the photoreactions of the troponoid system. Whereas the tropolones and their methyl esters rearrange to bicyclo(3.2.0)heptadienones, irradiation of tropone and 2-chlorotropone gave photo-dimers, and 2-aminotropone (65a) afforded no isolable products²⁵. Mukai and Kimura²⁵ observed that acylation or arylation of 2-aminotropone resulted in the formation of cyclization products. Thus, irradiation of the acetylamino (65b) and



benzoylamino (65c) compounds in benzene or ethanol through a pyrex filter gave the bicyclo(3.2.0)heptadienones 66b and 66c in 87 and 71% yields, respectively. Compounds 67 are secondary photoproducts. Irradiation of 2-anilino-tropone 65d in cyclohexane gave 66d in 37% yield, while it was quantitatively recovered in ethanol. The rearrangement of 65c does not occur in aprotic or protic solvents when electron-donating substituents are in the p-position of the phenyl group. However, the photocyclization does

take place in aprotic solvents, but not in protic solvents when electron-withdrawing groups are in the p-position.

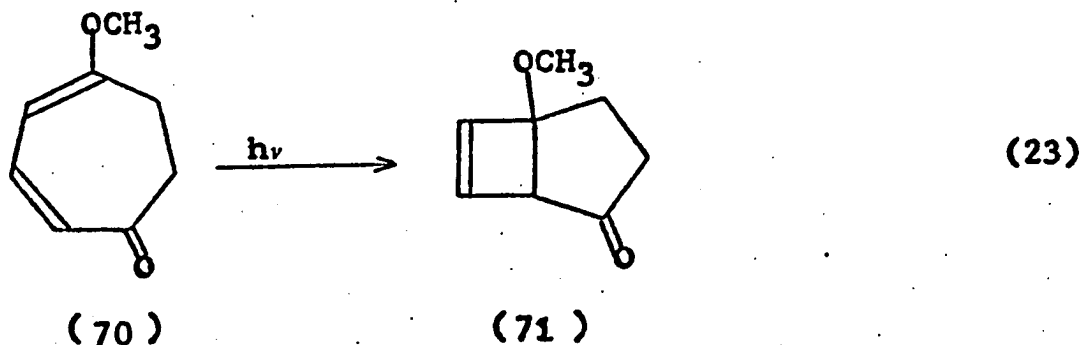
The photo-reactions of 65b-d occur more rapidly in aprotic than in protic solvents. The UV spectrum of compounds 65 provides an explanation for this effect. In protic solvents the tropones 65b-d exhibit a blue shift, while 65a exhibits a red shift. This evidence suggests that the lowest lying level of 65a is the charge-transfer state 68 which does not lead to products, while compounds 65b-d have an excited state 69 which does lead to products. Mukai and Kimura assumed the excited state to be a $n-\pi^*$ transition. However, these workers noted that "the $n-\pi^*$ band of troponoid derivatives is obscure, there is no evidence that the photo-cyclization giving 66 arises from the $n-\pi^*$ or $\pi-\pi^*$ state."



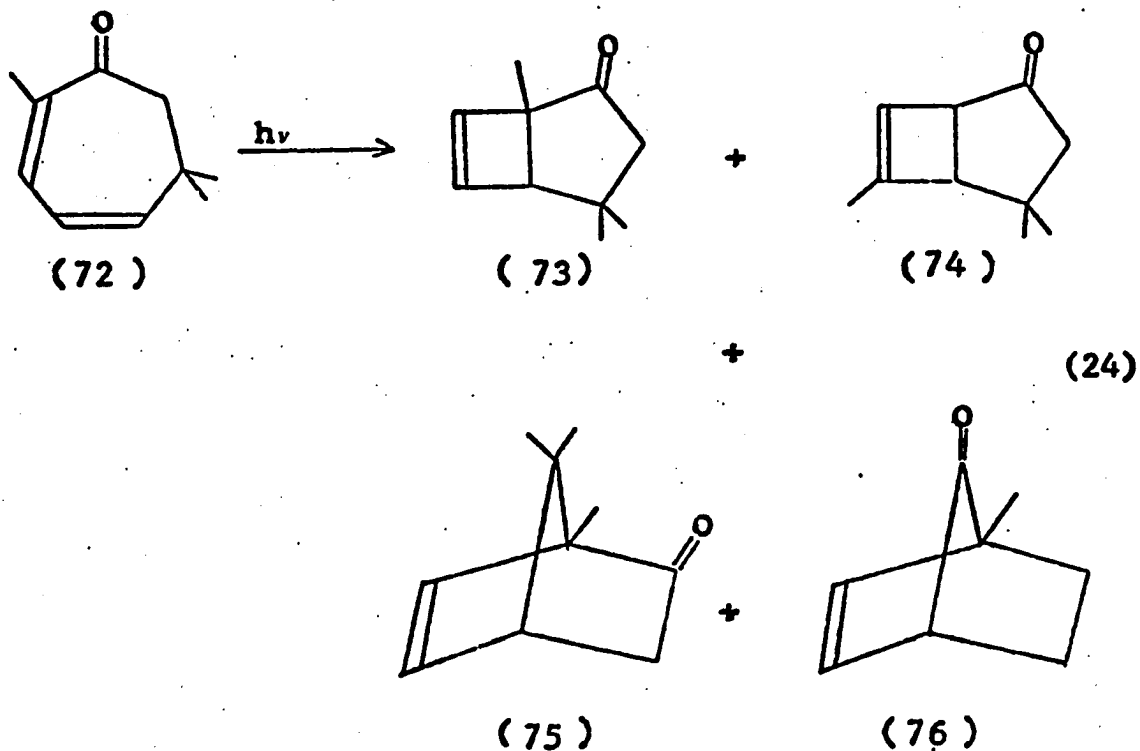
Unsuccessful attempts to quench the reaction of 65b and 65c with oxygen, isoprene or ferrocene and the observation of fluorescence from these compounds indicate that the valence isomerizations proceed by a singlet state mechanism.

3. 2,4-cycloheptadienones

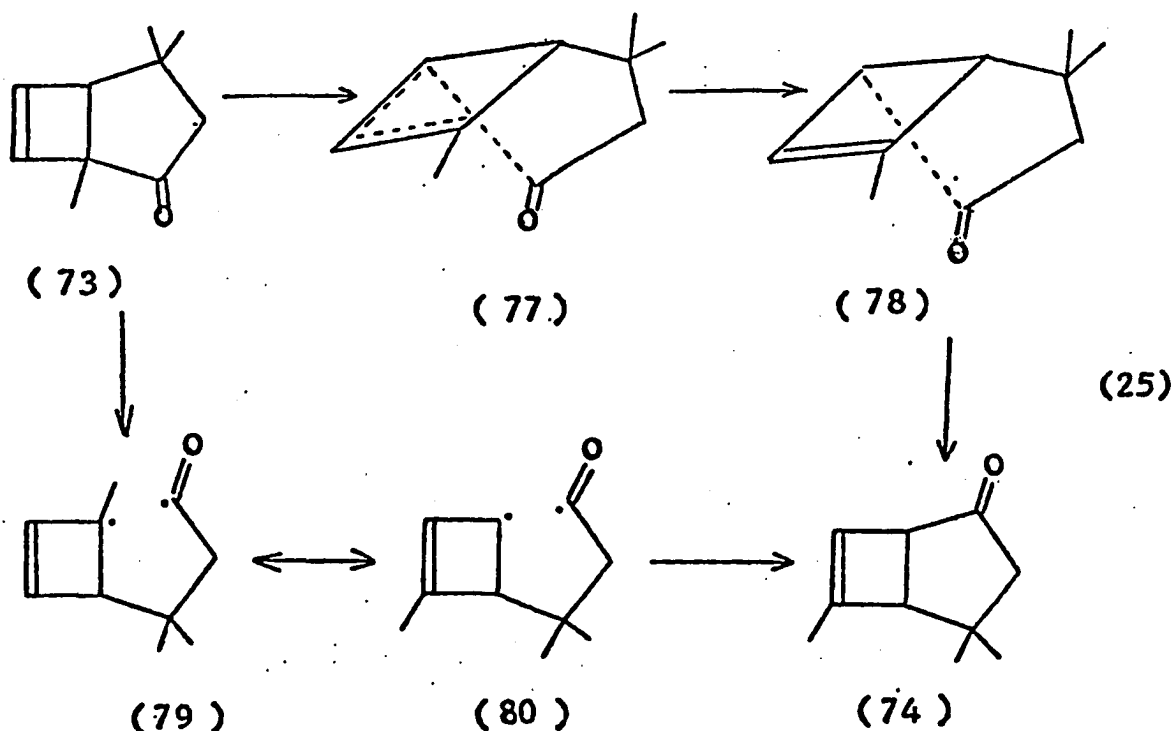
The photochemical behavior of 2,4-cycloheptadienones has also been depicted as proceeding via dipolar intermediates. However, it is difficult to rationalize the formation of all the products from a single intermediate. Irradiation^{1,34} of 5-methoxy-2,4-cycloheptadienone (70) gave the bicyclic



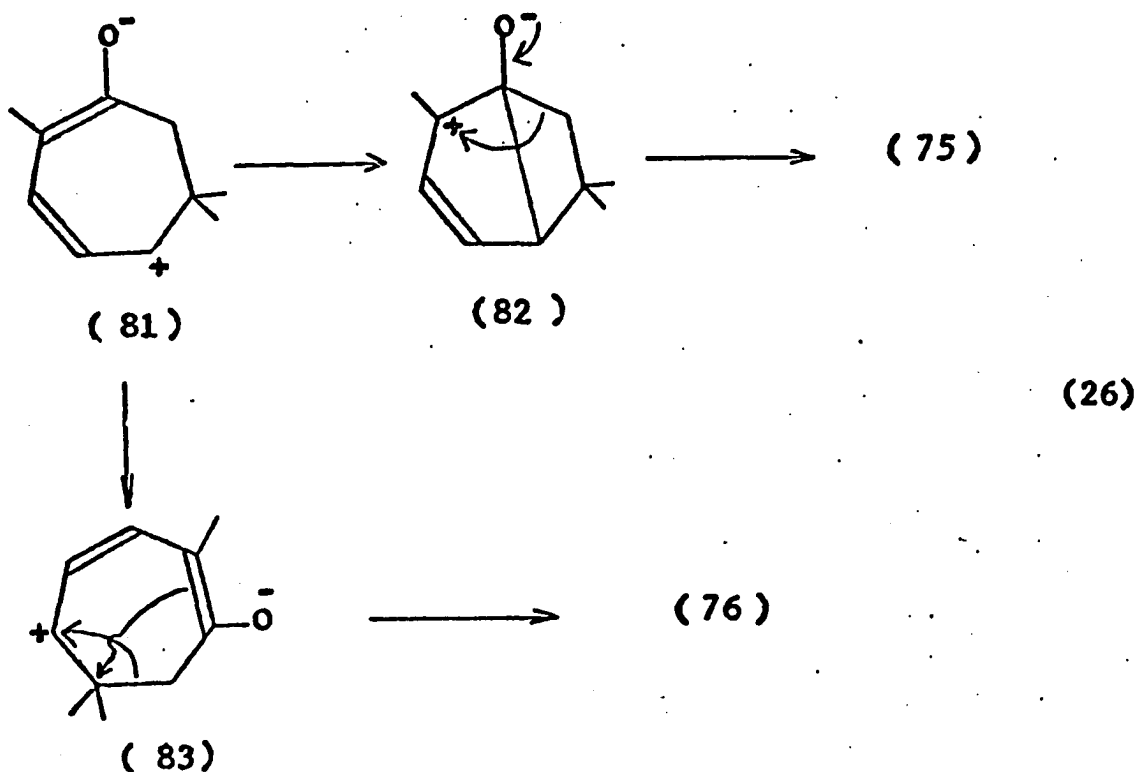
ketone 71. In the case of eucarvone (72), the reaction was more complicated, and, depending on reaction conditions, several products were obtained. Two of the photoproducts,



73 and 74, may be pictured as being formed in a concerted mechanism³⁵ or via α -cleavage to a diradical¹ (73 yields 74).

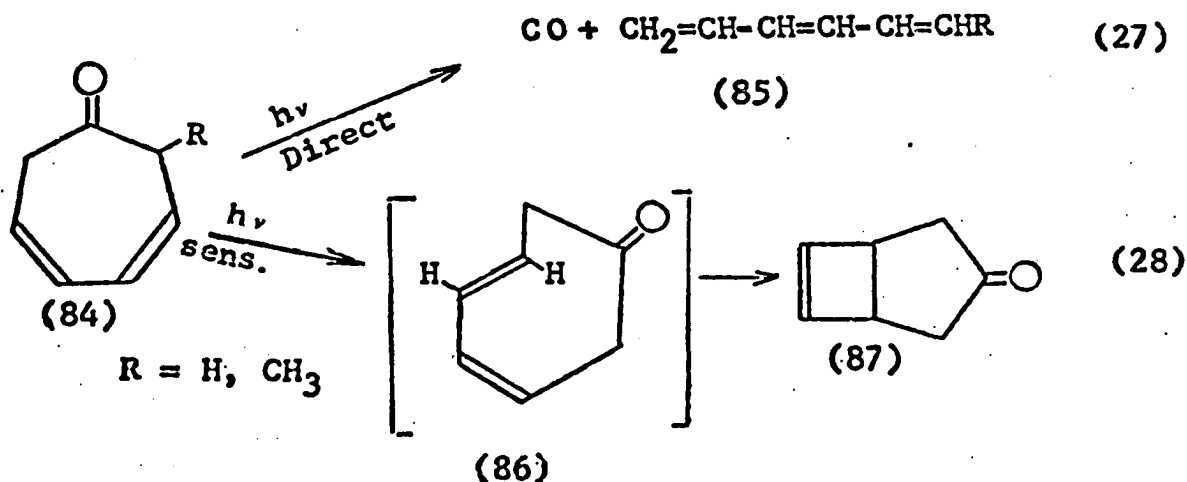


Two more products, 75 and 76, may require dipolar species^{1,10,36,37}. The complex series of reactions of eucarvone has very recently been discussed by Hart³⁸.



4. 3,5-cycloheptadienones

The 3,5-cycloheptadienones (84) are an exception to Dauben's rule that irradiation of rings with $(2n + 1)$ members and n conjugated double bonds should lead only to intramolecular cycloaddition. Chapman^{1,10,31} and Schuster³⁹



reported that these compounds undergo ring fission to form carbon monoxide and 1,3,5-trienes (85) on direct irradiation. Schuster³⁹ reported that photosensitization of 3,5-cycloheptadienone gave the valence isomer bicyclo(3.2.0)hept-6-en-3-one (87). This reaction via the triplet state is an example of conversion of a cis, cis-1,3-diene to a cis, trans isomer (86) followed by thermal conversion to a cyclobutene derivative (see discussion in section C part 1 of historical).

Chapman³¹ attributed the anomalous behavior of 84 in the direct irradiation to the lack of coplanarity of the

diene system. However, this rationale has been refuted by Mislow and Gordon⁴⁰ who reported that the two double bonds of 84 are stereochemically and spectroscopically completely equivalent because they possess a twofold axis of symmetry with respect to the diene chromophore. Schuster reported that the unusual reactivity of compounds 84 is, in fact, due to their possessing such a symmetry element, a circumstance which is absent in the 2,4-dienones. Schuster employed orbital symmetry arguments to explain the fragmentation of 84 and related the fragmentation to the decomposition of diazenes, discussed by Lemal and McGregor⁴¹.

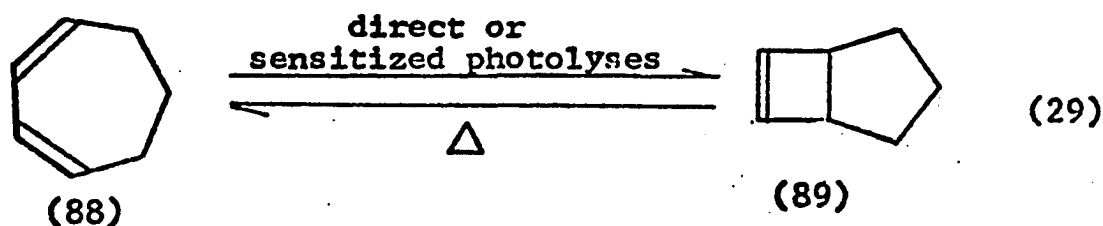
The decarbonylation reaction proceeds through the singlet excited state involving the carbonyl $n-\pi^*$ transition, since the reaction occurred on direct irradiation through pyrex filters, could not be quenched by triplet quenchers, and underwent singlet sensitization. However, there is considerable interaction between the β, γ double bonds and the carbonyl group, and therefore, mixing of the $n-\pi^*$ and $\pi-\pi^*$ transitions. This interaction is indicated in the uv spectrum of 84, which exhibits a low wavelength maximum at 213m μ .

C. Intramolecular cyclization of 1,3-cycloheptadienes and 1,3,5-cycloheptatrienes; orbital symmetry considerations

1. 1,3-cycloheptadienes

Polarized excited states are not a prerequisite for intramolecular cycloaddition reactions. The photoreactions of the Vitamin D₂ series demonstrated that cyclization occurs with six membered cyclic dienes not containing a polarizable group, and, in 1961, Dauben and Cargill⁴² reported that cyclization occurs, as well, with the parent seven membered ring, 1,3-cycloheptadiene (88).

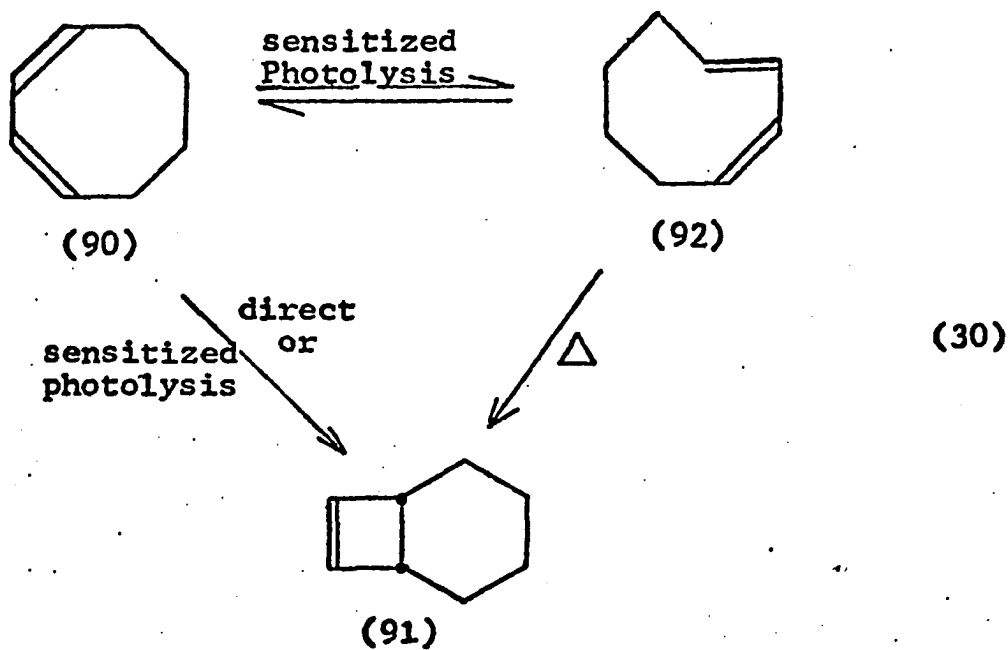
Thus, irradiation of 1,3-cycloheptadiene in ether solution with a high pressure mercury lamp for 40 hours gave bicyclo(3.2.0)hept-6-ene (89) in 42% yield. Bicyclo(3.2.0)hept-6-ene is also obtained on photosensitization of 1,3-cycloheptadiene. Frey⁴³ obtained 89 in 45% yield after



irradiating a dilute isopentane solution of 88 and acetophenone for 2 hours. Acetophenone is a triplet sensitizer, and, therefore, the reaction most likely involves a triplet pathway. The direct photolysis must then proceed by either a singlet pathway or from a vibrationally excited ground state. Intersystem crossing to the triplet state is highly unlikely for conjugated dienes due to the large energy gap

between the lowest singlet and triplet states. Orbital symmetry arguments suggest that an electronic excited state is the species responsible for the formation of 89 since the constraints of the ring requires a disrotatory closure. If the reaction involved a vibrationally excited ground state then the valence isomerization would require a thermally allowed conrotatory closure. Due to the constraints of the ring a conrotatory closure would be energetically unfavorable. The direct photolysis, therefore, probably occurs from a singlet state. The nature of the electronic state, i.e. singlet vs triplet, is not a consideration in orbital symmetry arguments. Either state may lead to the formation of 89 by a concerted disrotatory process.

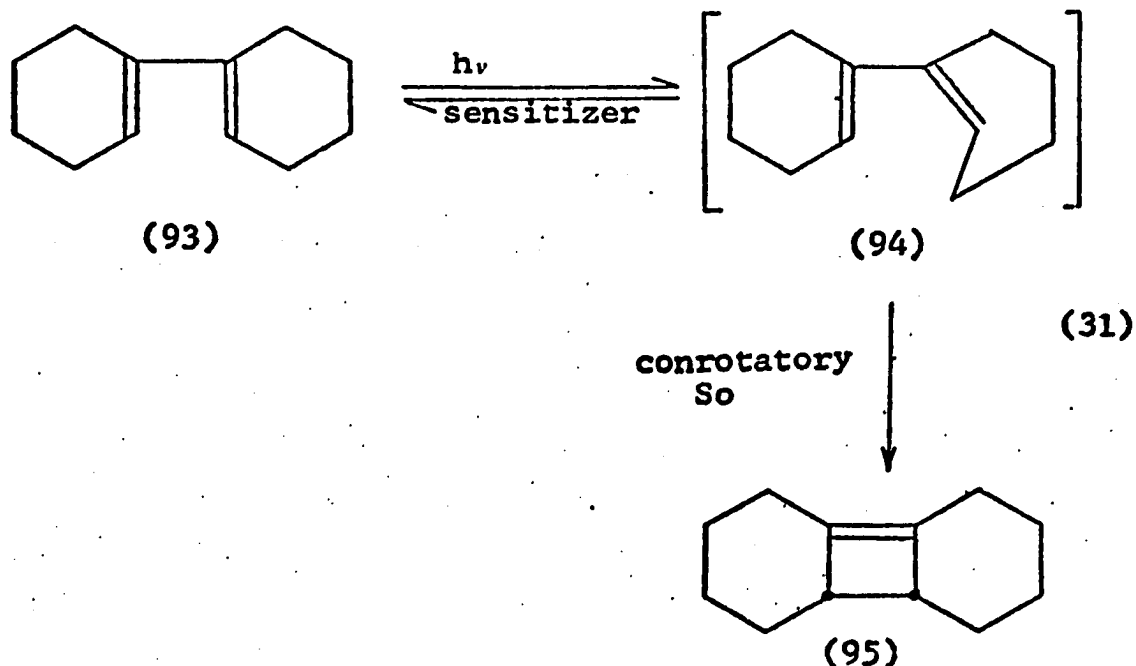
However, evidence has recently emerged which suggests that the singlet state is responsible for the formation of 89 in the direct photolysis and that a vibrationally excited ground state, vs. a triplet state, is responsible for the formation of 89 in the photosensitized reaction. Thus, in a related situation it has been reported that cis, cis-1,3-cyclooctadiene (90) is converted to bicyclo(4.2.0)oct-7-ene (91) under direct and sensitized photolyses⁴⁴. Bearing on this problem is the observation by Fonken⁴⁵ that cis, trans-1,3-cyclooctadiene (92) undergoes facile thermal isomerization to bicyclo(4.2.0)oct-7-ene (91). Liu⁴⁴ has reported that on photosensitization 90 isomerizes to the cis, trans isomer 92, which cyclizes to 91. The efficiency of the



reaction was shown to depend upon the reaction temperature. An 85% yield of 91 was obtained when the photosensitized reaction was carried out at 80°, but virtually no 91 was obtained on irradiation at 15°. Instead the cis, trans isomer 92 was obtained. Prolonged irradiation established a photostationary state between 91 and 92. On direct irradiation of 90, Liu obtained only the bicyclo isomer 91, which suggests that in such photolyses 92 is not involved as an intermediate. Although a photostationary state between 90 and 92 can be established, the composition is essentially 100% 90. Liu also studied the photosensitization of 1,3-cycloheptadiene at 20 and 80° but did not detect any cis, trans isomer of 88.

The only remaining example in which the same product is formed on direct and sensitized irradiation is the isomerization

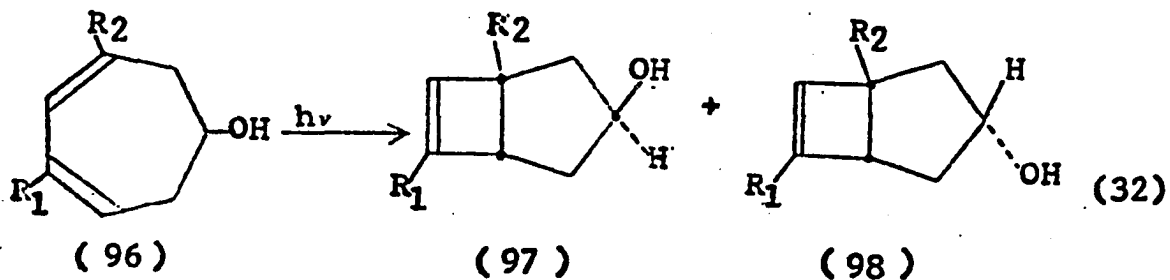
of 1,1'-bicyclohexenyl (93) to (95) reported by Dauben⁴⁶. Liu postulates that this may also take place by way of a cis, trans intermediate (94). There is a report on double



bond migration in substituted cyclohexenes in which the authors favor, among possible mechanisms, a trans-cyclohexene intermediate⁴⁷. Triplet sensitization, therefore, leads to the formation of a geometrical isomer, which undergoes a thermal conrotatory closure from a vibrationally excited ground state.

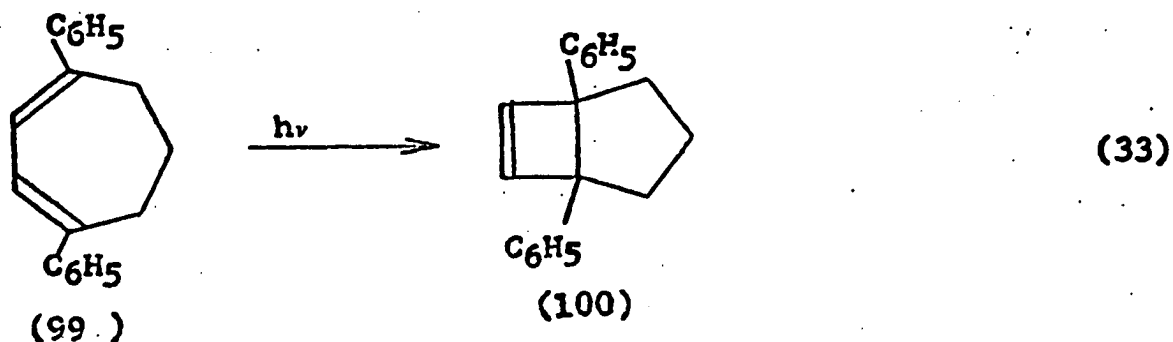
Pyrolysis of bicyclo(3.2.0)hept-6-ene (89) at 400° regenerated the starting material (88). Due to the constraints of the ring the cycloreversion must occur by a disrotatory mode. High temperatures are required since the disrotatory opening of cyclobutenes is symmetry forbidden in a thermal process, and, therefore, energetically unfavorable.

Additional examples of photoisomerization of 1,3-cycloheptadienes are known⁴⁸. Irradiation of 3,5-cycloheptadienol (96) and its methoxy derivatives gave rise to two epimeric alcohols 97 and 98, in a three to one ratio⁴⁹.



- (a , $R_1=R_2=H$)
- (b , $R_1=OMe, R_2=H$)
- (c , $R_1=H, R_2=OMe$)

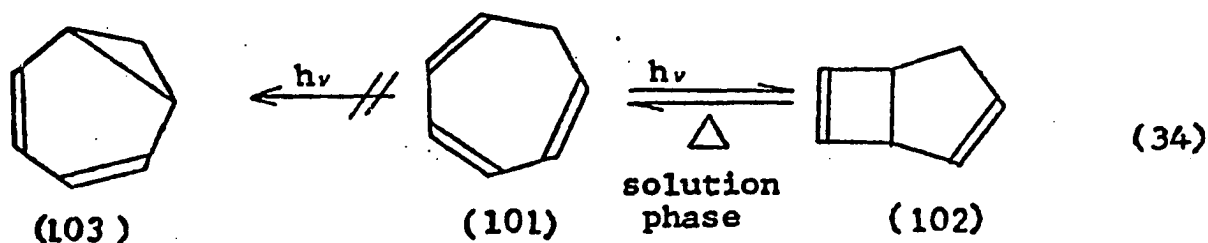
Irradiation of 1,4-diphenyl-1,3-cycloheptadiene (99) gave (100) even though the two large phenyl substituents were destined to occupy bridgehead positions in the photoproduct⁵⁰.



2. 1,3,5-cycloheptatriene

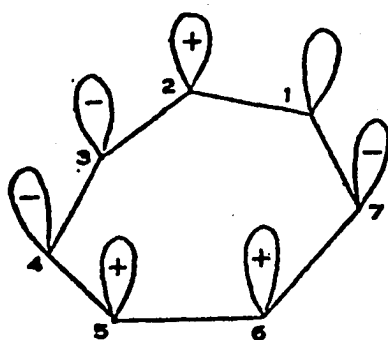
a. Solution phase photolysis:

Dauben and Cargill⁴² also studied the solution phase photolysis of 1,3,5-cycloheptatriene (101). Irradiation of 101 with a high pressure mercury lamp for 200 hours gave bicyclo(3.2.0)hepta-2,6-diene (102) in 34% yield. Pyrolysis of 102 at 200° regenerated the starting material. The formation of norcaradiene (103), a possible intramolecular cycloaddition product was not detected. Photosensitization of 1,3,5-cycloheptatriene in solution has not been reported.



The formation of only one product from 101 can be understood by use of orbital symmetry theory. Application of the Woodward-Hoffmann electrocyclization rules requires a determination of the orbital symmetry of the highest occupied molecular orbital of 1,3,5-cycloheptatriene. The Huckel molecular orbital calculation employed to obtain the molecular orbitals of cycloheptatriene should take into account the methylene group as well as the 1,3,5-hexatriene chromophore. This consideration was made by Simon⁵¹ who regarded methyl and methylene groups as heteroatoms with two electrons in his simple FMO calculation (without overlap) of 1,3,5-cycloheptatriene.

Employing a cyclic model and the coulomb and resonance parameters given on page 209 of appendix 7 (taken from Streitwieser's book)⁵², Simon obtained the eigenvalues and molecular orbitals given in table (1). The highest occupied molecular orbital for the electronically excited seven atom, eight electron π -system is ψ_5 and may be depicted as in scheme 4, in which there is a node at the methylene carbon atom. Consideration of the orbital symmetry of scheme 4 indicates that conrotatory closure across positions 2 and 7 is required for formation of the norcaradiene (103). However, due to the steric constraints imposed by the seven-membered ring a conrotatory mode of closure is prohibited, and, therefore, the formation of the norcaradiene is unlikely. On the other hand, the orbitals at positions (2 and 5) or (4 and 7) are of the appropriate orbital symmetry to permit disrotatory closure leading to the observed bicyclic isomer (102).



Scheme 4

Highest occupied molecular orbital of the first excited state of 1,3,5-cycloheptatriene in a cyclic system

Cyclic Model: $k_{67} = k_{17} = 0.7$

h77	Wave Functions	Energy Levels	Coefficients						
			1	2	3	4	5	6	7
2.0	7	+1.802	.000	.232	-.418	.552	-.552	.418	-.232
	6	+1.359	.189	-.454	.484	-.204	-.204	.484	-.454
	5*	+0.444	.000	.521	-.231	-.418	.418	.231	-.521
	4**	-0.178	.340	-.443	-.313	.386	.386	-.313	-.443
	3	-1.246	.000	.419	.522	.230	-.230	-.522	-.419
	2	-1.680	.344	-.079	-.374	-.548	-.548	-.374	-.079
	1	-2.501	.855	.306	.168	.133	.133	.168	.306

From Simon⁵¹

Eight-electron seven-atom π -system

* First excited state

** Highest ground state

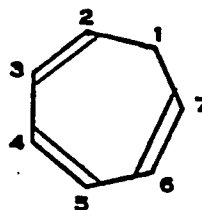


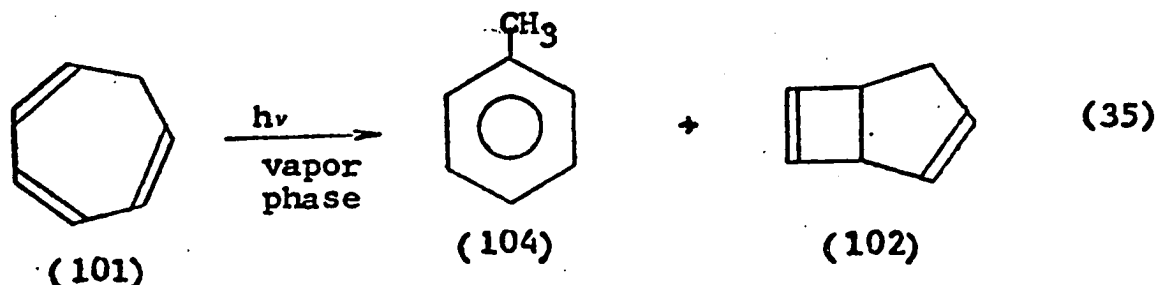
TABLE 1

1,3,5-cycloheptatriene

HMO Energy Levels and Coefficients

b. Vapor phase photolysis

The photolysis of 1,3,5-cycloheptatriene (101) has also been studied in the vapor phase. Srinivasan⁵³⁻⁵⁵ found that irradiation of (101) at low pressures gave toluene (104) as the major product and low yields (less than 5%) of bicyclo(3.2.0) hepta-2,6-diene (102). Srinivasan suggested that the formation



of the bicycloheptadiene 102 occurred by photoisomerization from an excited singlet state, but that toluene was formed by a thermal isomerization from a high vibrational level of the ground state. His suggestions were based on quantum yield studies. The quantum yields of toluene and the bicycloheptadiene were determined at 2600Å and 3130Å in the absence and in the presence of inert gases. A variety of inert gases were used and the quantum yields were determined as a function of inert gas pressure. The effect of temperature on quantum yields was also investigated. It was found that the quenching efficiencies of the inert gases increased as their molecular weights and boiling points increased. No gas appeared to exert a specific quenching effect. Thus, oxygen and nitric oxide which are usually considered to be good triplet quenchers were not as efficient as carbon dioxide, methane, or diethyl ether.

The lack of specific quenching appears to indicate that the triplet excited state is not involved in the reaction. The observed quenching is due, therefore, to either quenching of an excited singlet state or to quenching of a "hot" ground state which is formed by internal conversion from the excited singlet state. Collisions of inert gases with electronically excited and vibrationally excited cycloheptatriene molecules may lead to quenching, but in the case of deactivation of an electronic excited state a greater sensitivity to the nature of the colliding molecule is expected for the transfer of electronic energy. Xenon was found to be a better quencher than helium, although neither gas should be particularly important in electronic transfer processes since they both have all their electrons in closed shells. Since quenching efficiencies appear related only to molecular weights and boiling points, a trend which suggests very little specificity, the effect of an increase in pressure is more important in quenching vibrational energy in the ground state or the upper electronic state than quenching electronic energy. The quantum yields for both products were pressure dependent. At high pressures, the quantum yield of toluene approached zero (toluene is not observed in solution where the pressure is infinitely high); at low pressures, the quantum yield of toluene approached unity. On the other hand, the quantum yield of the bicycloheptadiene showed only a minor dependence on pressure,

increasing slightly with an increase in pressure. Since the formation of toluene and bicycloheptadiene exhibit different pressure dependencies, the states responsible for their formation cannot be the same. Assuming that only one electronically excited state is involved one of the products must arise from an excited singlet state while the other occurs from a "hot" ground state.

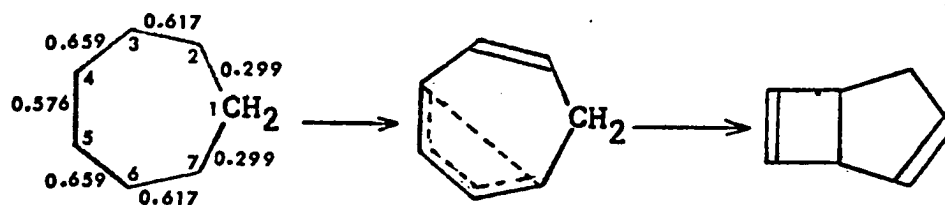
It has been shown^{54,55} that the bicycloheptadiene can be thermally converted to cycloheptatriene, but that the reverse process does not take place. This observation in conjunction with the fact that the quantum yield of 102 increases with pressure and decreases with temperature indicates that 102 evolves from an excited singlet state of cycloheptatriene. At low pressure 102 is formed from the electronically excited state, but possessing excess vibrational energy thermally reverts to cycloheptatriene. At higher pressures 102 persists because the excess vibrational energy is collisionally deactivated before reversion to cycloheptatriene can occur. On the other hand, toluene is known^{55, 56} to arise thermally from cycloheptatriene. This observation in conjunction with the dependency of quantum yield on pressure and the increase of quantum yield on increasing temperature suggests that toluene is formed from a highly vibrationally excited ground state of cycloheptatriene. At low pressure rearrangement of cycloheptatriene to toluene occurs, but at higher pressures vibrational deactivation is efficient and reversion to cycloheptatriene takes place.

Further evidence for invoking a singlet rather than a triplet excited state in reactions of 1,3,5-cycloheptatriene is comparative. The valence isomerization of conjugated dienes or trienes to cyclobutene derivatives has so far not been observed from a triplet state on direct photolysis. The lowest triplet state of cycloheptatriene is estimated⁵⁷ to be about 52 kcal and the lowest singlet state 112 kcal. Therefore, there is a large S_1 - T_1 gap which should result in inefficient intersystem crossing. (However, if the potential surface of an upper triplet state, such as T_2 , is isoenergetic with a low vibrational level of S_1 , intersystem crossing from S_1 to T_2 may occur, and, then the argument is invalid)⁵⁸.

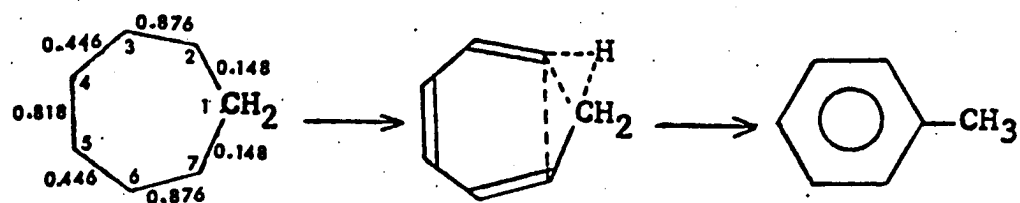
However, the assumption that the electronically excited state in the photolysis of cycloheptatriene is the singlet is subject to reservation. The lack of quenching by oxygen and nitric oxide suggests that a triplet electronic state is not involved in the reaction, but does not demand it since the rate of reaction from the triplet may be faster than the rate of quenching. Shida and co-workers⁵⁹ irradiated mercury to form Hg (^3p) in the presence of 1,3,5-cycloheptatriene vapor at different pressures and obtained a single product, toluene. Since the mercury ^3p atom is a triplet sensitizer, Shida argued that the formation of toluene must have involved triplet cycloheptatriene. Since toluene is formed in both the photosensitized and the direct irradiation, the triplet electronic state of cycloheptatriene is implicated in the direct irradiation. Shida concluded that an excited molecule of

cycloheptatriene could either isomerize into toluene or be collisionally deactivated since the yield of toluene decreased with increasing pressure of cycloheptatriene. However, Srinivasan⁵³ counter-argues that the similarity between the photosensitized and direct irradiation breaks down when the direct photolysis of cycloheptatriene to its bicyclo isomer 102 (a process which cannot occur from the vibrationally excited ground state) is taken into account.

Srinivasan⁵³ desired theoretical support for his experimental results and referred (albeit with reservations) to Simon's⁵¹ postulates which predict, as stated by Srinivasan, "that a given product will be formed from the electronic state (the choice being between an excited state and the ground state) in which the π -bonding order of double bonds which must be broken is smaller, and the free valence indices of the atoms which must enter into new bonds are larger." Simon obtained the following diagrams (scheme 5) based on his HMO calculation (see page 32), which predict the formation of toluene from a ground electronic state and bicyclo(3.2.0)hepta-2,6-diene (102) from an excited state.



First Excited State



Ground State

From Simon⁵¹ and Srinivasan⁵³

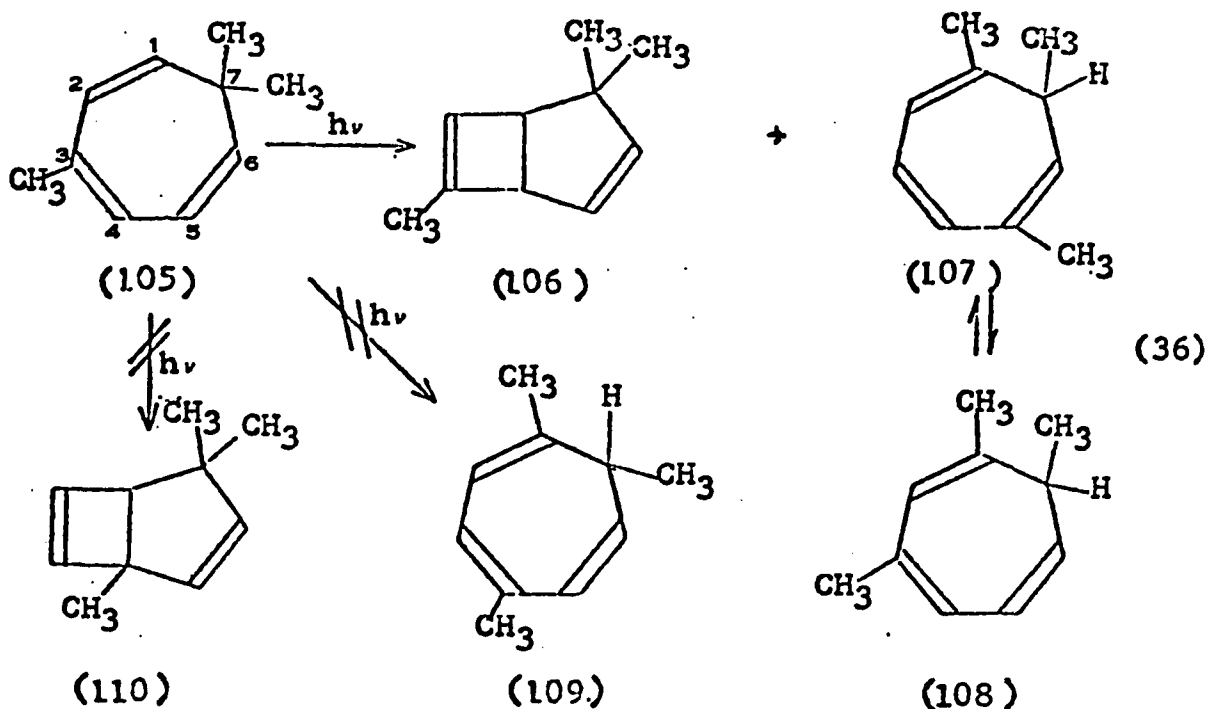
Scheme 5

Bond orders of 1,3,5-cycloheptatriene in a cyclic system

D. Stereoselectivity in intramolecular cyclization of unsymmetrical 1,3,5-cycloheptatrienes

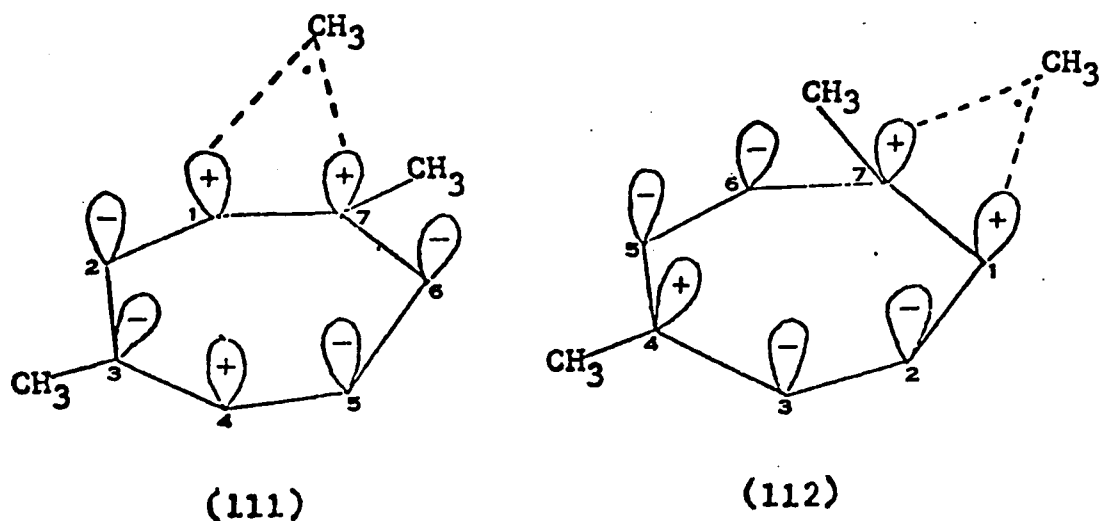
1. Trimethylcycloheptatrienes

Stereoselectivity was observed in cyclization reactions in which at least two different valence bicyclic isomers were possible in methyl substituted cycloheptatrienes. Jones and Jones⁶⁰ observed selective photoreactions with 3,7,7-trimethylcycloheptatriene (105). This compound gave the selective electrocyclization product 106 and the selective (1,7) sigmatropic methyl and methyl followed by hydrogen migration products 107 and 108 respectively.



The sigmatropic migration products are converted to other products on prolonged irradiation, possibly bicyclo(3.2.0) compounds. These selective (1,7) sigmatropic reactions are in accord with the Woodward-Hoffmann⁶¹ rules for sigmatropic migrations. Of the two possible suprafacial (1,7) methyl

migration products 107 and 109 only one product is observed, which suggests that the olefinic methyl group exerts a directive influence on the course of the reaction. Transition states 111 and 112 for 3,7,7-trimethylcycloheptatriene depicting the orbital symmetries of the first excited states were obtained by Jones and Jones from their Huckel molecular orbital calculations employing, presumably, a cyclic model for the transition state. Inspection of these transition states indicates that suprafacial (1,7) migration can take place by migration of the methyl group as in 111 to give 107 and as in 112 to give 109. (1,3) or (1,5)-migrations are not feasible since such migrations must proceed by an antarafacial mode which is prohibited by the presence of the ring. Orbital symmetry considerations of the above transition states do not readily offer a rationale for the preferential formation of compound 107. However, Huckel molecular orbital charge density calculations indicate that in transition state 111 carbon atom 3 bearing the methyl substituent has a relatively positive charge, whereas in transition state 112 it has a



Scheme 6

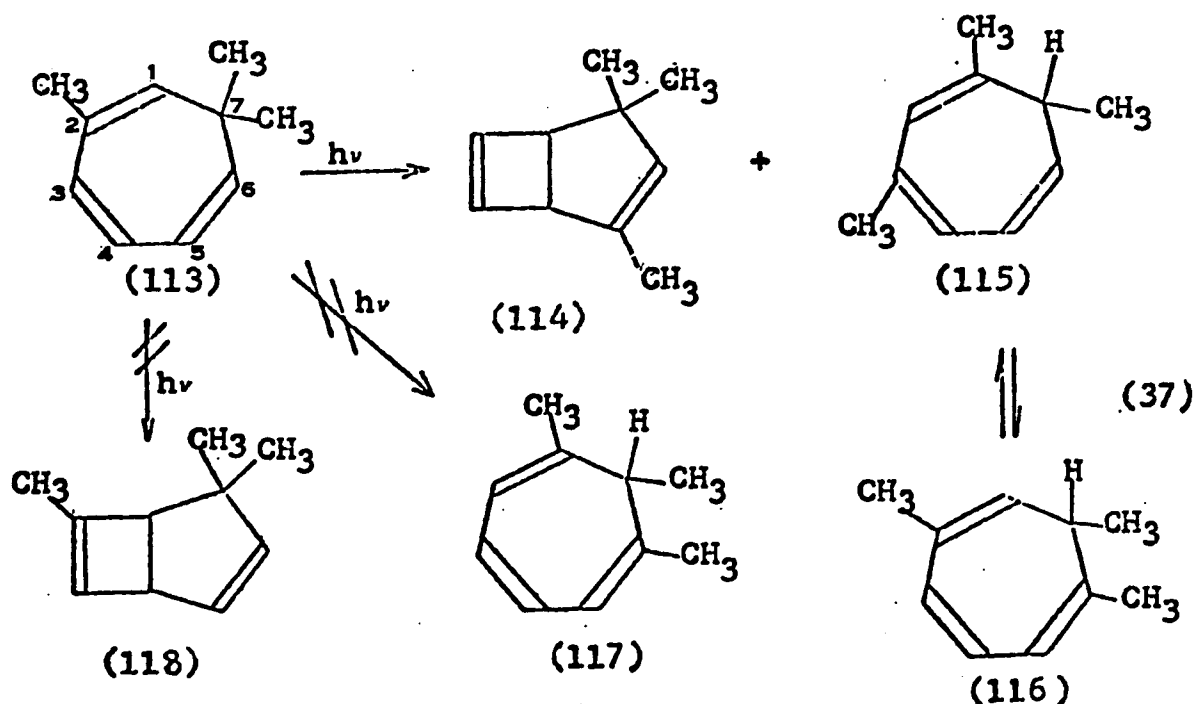
Highest occupied molecular orbitals of the first excited state of 3,7,7-trimethylcycloheptatriene

relative negative charge. The methyl group supplies electron density to C-3 by inductive and hyperconjugative effects, and, thereby increases the Coulomb integral α at that site. The Coulomb integral α represents the energy of an electron in an isolated atomic orbital. Increasing the Coulomb integral of an atom which bears a positive charge tends to stabilize any electron deficiency at that atom. However, increasing the Coulomb integral of an atom on which a negative charge resides has a destabilizing effect and raises the energy of the system. Therefore, transition state 111 should be of lower energy than 112 and compound 107 should predominate.

The stereoselectivity of the cyclization reaction of 105 cannot be readily explained by orbital symmetry considerations. Application of the Woodward-Hoffmann rules for electrocyclization reactions indicates that both isomers 106 and 110 may be formed by a disrotatory cyclization process. However, the possible cyclization product 110 was not detected. Also, considerations of HMO charge density calculations utilizing an increased value of the Coulomb integral α for the methyl substituent and of Simon's approach utilizing free valence indexes and π -bond orders to predict the formation of a given product (see page 39 of this thesis) failed to account for the predominant formation of compound 106. Therefore steric considerations were invoked to rationalize the observed selectivity in the cyclization reactions. Although Dreiding models indicates that non-bonded interactions between the

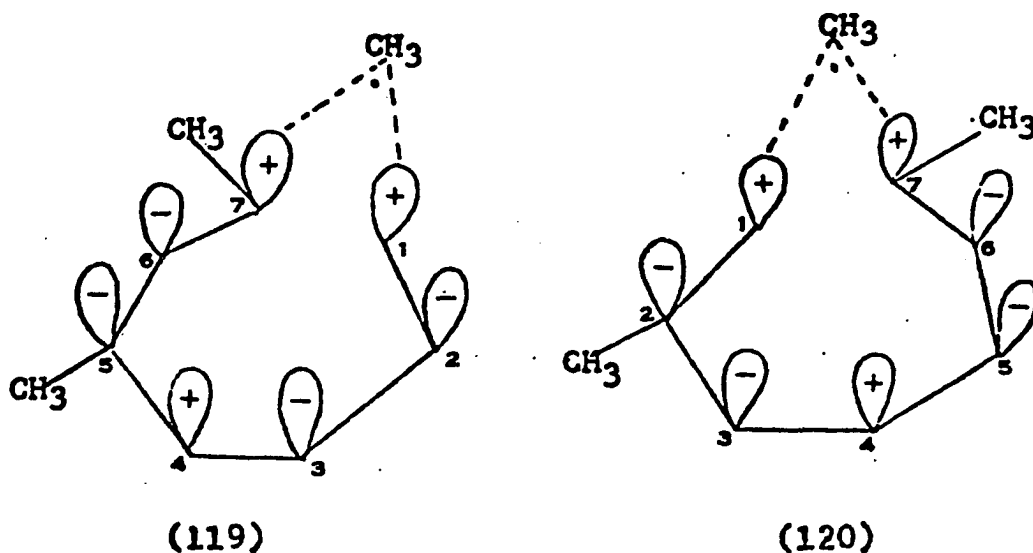
1,4-cis-methyl groups of compound 110 are not serious, there exists an unfavorable eclipsing interaction between the hydrogen and the methyl group in the bridgehead positions of 110 which is absent in 106. Furthermore, 106 is more stable relative to 110 since it bears a methyl group on the cyclobutene double bond.

In another paper⁶², Jones and Jones studied the photochemistry of 2,7,7-trimethylcycloheptatriene (113). Selective



electrocyclization and sigmatropic migration products were also observed with 113. HMO calculations were carried out by these workers who assumed that the transition state of the methyl migration reaction is composed of a radical containing seven π -electrons and a methyl radical whose σ -orbital interacts with the π -system. They employed a hyperconjugation model to describe the effect of the methyl substituents, and obtained more consistent results using a linear rather than a cyclic framework for the C-7 radical.

Consideration of transition states 119 and 120 indicates that 115 may arise from 119 and that 117 may arise from 120 via suprafacial (1,7) migrations. Transition state 119 was calculated to be 1.5-2 kcal lower in energy than 120 thereby favoring the formation of 115. Again orbital symmetry and charge density considerations do not readily offer a rationale for the stereoselectivity of the cyclization reaction. Although both isomers 114 and 118 may be formed by a disrotatory cyclization process, only 114 was observed. The preferential formation of 114 was attributed to a serious non-bonded interaction in 118 between the methyl group on the cyclobutene ring and the endo methyl of the gem-dimethyl group.

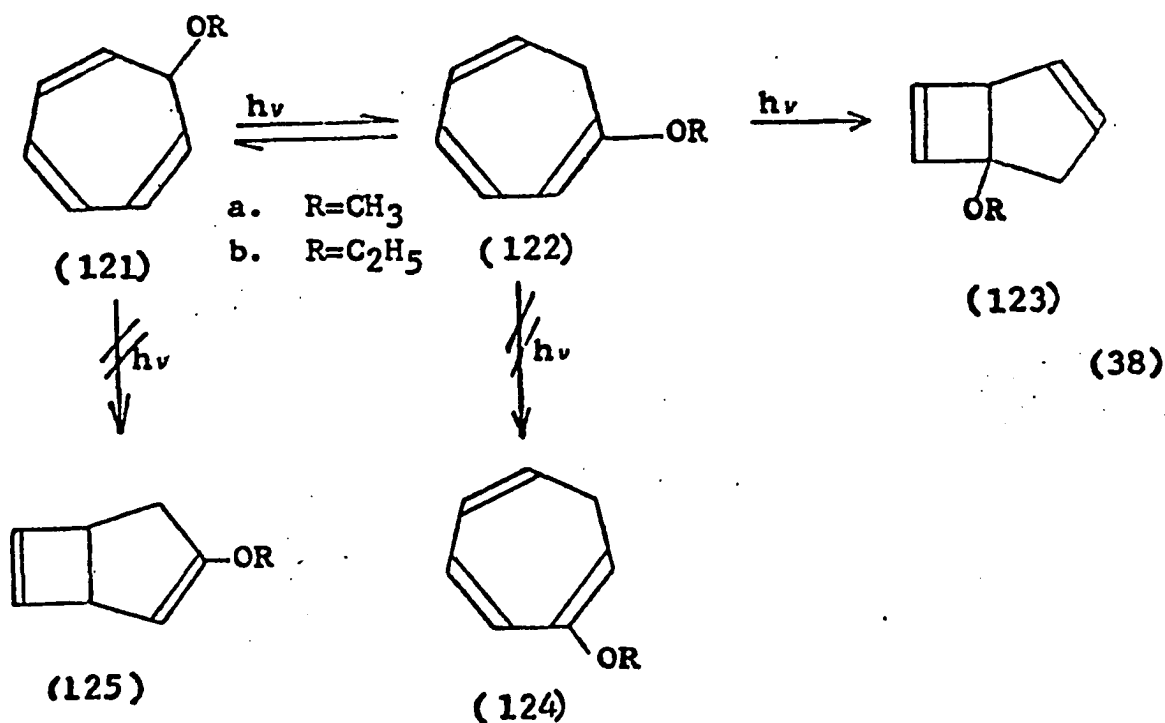


Scheme 7

Highest occupied molecular orbitals of the first excited state of 2,7,7-trimethylcycloheptatriene in a linear system

2. Alkoxycycloheptatrienes

Stereoselectivity has also been observed in alkoxy substituted cycloheptatrienes. Chapman⁵⁷ observed that the photolysis of 1-ethoxy and 1-methoxy-1,3,5-cycloheptatriene in solution and in the vapor phase was anomalous when compared to 1,3,5-cycloheptatriene itself. Thus, Chapman found that irradiation of 7-methoxy cycloheptatriene (121) or 7-ethoxy cycloheptatriene (121b) afforded in each case, via a 1-alkoxycycloheptatriene intermediate (122), a single 1-alkoxybicyclo(3.2.0)hepta-3,6-diene (123) in better than 90% yield. The 1-alkoxycycloheptatriene is the primary



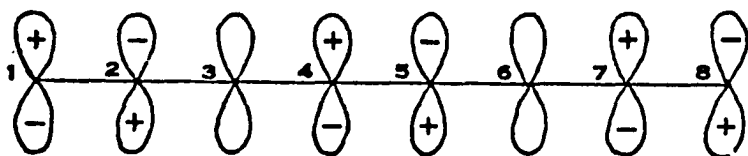
photoproduct of the reaction since a plot of concentration vs. time for this substance goes through the origin on extrapolation to zero time. A similar plot for the bicyclo compound does not go through the origin. This time delay in

the appearance of the bicyclo compound indicates that it is a secondary photoproduct. The bicyclo compound appears early in the reaction, and, therefore its formation from its 1-alkoxycycloheptatriene precursor is an efficient process. In a control experiment, irradiation of the intermediate 1-methoxycycloheptatriene (122a) rapidly established a photostationary state with 7-methoxycycloheptatriene (121a). Prolonged irradiation resulted in a displacement of the photostationary state existing and led to only one product, the bicyclo valence isomer (123a). The high yield of bicyclo compound in these photolyses and the efficiency of the process contrasts sharply with the long reaction time required to realize only a 34% yield of bicyclo compound in the photolysis of cycloheptatriene⁴². In addition, irradiation of 7-methoxy cycloheptatriene (121a) at low pressure in the vapor phase gave a mixture of products consisting of 14% (121a), 38% (122a), and 48% (123a), which contrasts conspicuously with the predominant formation of toluene in the photolysis of cycloheptatriene (only about 5% of bicyclo(3.2.0) hepta-2,6-diene was observed). The (1,7) sigmatropic hydrogen shifts of (121) and (122) are again in accord with the Woodward-Hoffmann rules for sigmatropic reactions in the cycloheptatriene system.

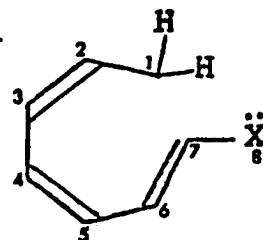
Of the two possible (1,7) hydrogen migration products, 7-methoxycycloheptatriene (121) and 2-methoxycycloheptatriene (124) from (122), only the 7-methoxy-derivative was observed. Chapman

explained the selective nature of the migration reaction by considering the orbital symmetry of the highest occupied molecular orbital for an electronically excited nine-electron, eight-atom linear π -system which includes the oxygen atom with its two electrons. Further details of the calculation were not given. This molecular orbital was depicted as in figure (126) with nodes at carbon atoms 3 and 6. Inspection of (126) indicates that the orbital symmetry of positions 1 and 7 is suitably disposed for suprafacial hydrogen migration, while transfer from position 1 to position 2 is not suprafacially favorable. Chapman did not offer any explanation for the observed selectivity in the electrocyclization reaction leading to (123). A consideration of his description of the orbital symmetry of the first excited state and application of the Woodward-Hoffmann rules for electrocyclization reactions, indicates that either of the bicyclic compounds, (123) and (125), may be formed by a disrotatory cyclization process. The reason therefore, for the observed selectivity is presently obscure.

H.



(126)

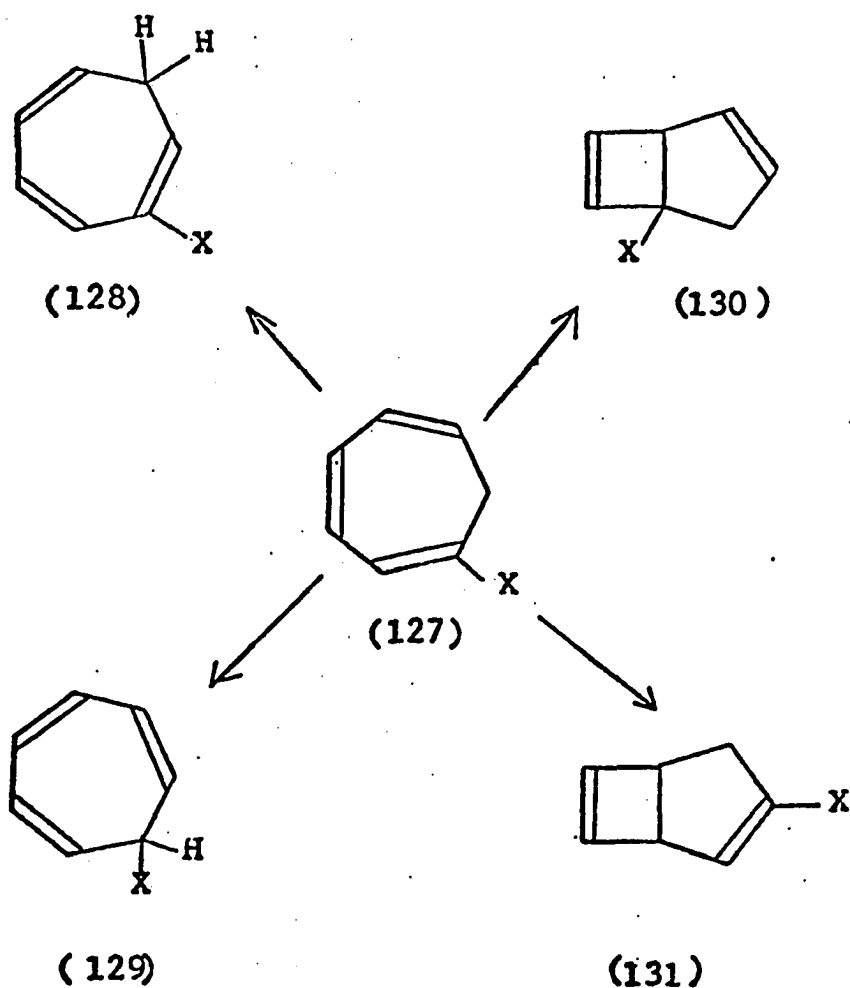


3. Photosensitization of trimethyl- and alkoxy-cycloheptatrienes

Unsuccessful attempts by Chapman⁵⁷ to photosensitize the reaction of 1-methoxycycloheptatriene (122) and by Jones and Jones⁶² to photosensitize the reactions of 2,7,7-trimethylcycloheptatriene (113) and 3,7,7-trimethylcycloheptatriene (107) with benzophenone (E_T 70 kcal/mole) and acetophenone (E_T 74 kcal/mole) and unsuccessful attempts by these workers to quench those reactions with oxygen appears to indicate that a triplet excited state is not involved in the sigmatropic and electrocyclization processes and implies that those reactions proceed only through singlet intermediates. Although the possibility that the photoproducts may arise via a vibrationally excited ground state cannot be completely ruled out, the facts that 104 is favored in solution but not in the vapor phase and that the thermal reactions⁶³ of 2,7,7-trimethylcycloheptatriene (113) leads to products different from those of the photochemical reaction, suggests that such a mechanism is unlikely.

4. 1-substituted-cycloheptatrienes

A.P. Ter Borg and co-workers⁶⁴ reported photoisomerization products and yields for a number of 1-substituted cycloheptatrienes. Their results, summarized in scheme 8 includes the 1-dimethylamino-substituent. The photochemical behavior of 1-dimethylamino-1,3,5-cycloheptatriene (127f) leading to photoproduct 130f with the substituent at the bridgehead position is analogous to the behavior of Chapman's 1-methoxy-1,3,5-cycloheptatriene in its specific mode of cyclization, albeit a small amount of the 3-dimethylamino-photoisomer (131f) was produced (a few percent of the corresponding 3-methoxy isomer may have escaped detection in Chapman's studies). As the electron donating ability of the substituent increased, the amount of cyclization product increased while the amount of the sigmatropic hydrogen migration product diminished.



(Initial) Products of irradiation (in %) of
1-substituted cycloheptatriene

Substituent				Products			
				(128)	(129)	(130)	(131)
a.	CN	..	..	100	-	-	-
b.	Ph	..	..	50	50	-	-
c.	Me	..	..	2	98	-	-
d.	SMe	..	..	-	65	35	-
e.	OMe	..	..	-	35	65	-
f.	NMe ₂	..	..	-	-	97	3

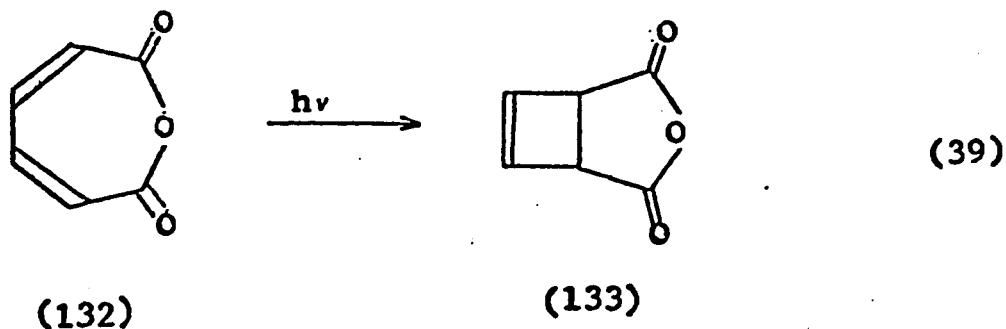
From terBorg ⁶⁴

Scheme 8

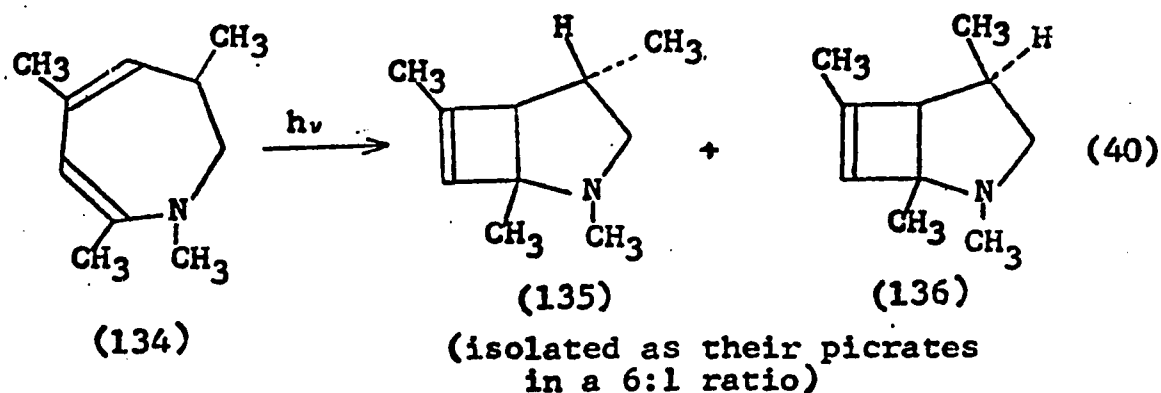
Photoreactions of 1-substituted-1,3,5-cycloheptatrienes

E. Photoisomerization of heterocyclic analogs of 1,3-cycloheptadienes; 1,2-dihydro-3H-azepin-2-ones

The photoisomerization of heterocyclic counterparts of 1,3-cycloheptadiene have been investigated. In 1961, Fonken⁶⁵ reported that irradiation of the oxygen heterocycle, muconic anhydride (132) produced the bicyclic anhydride 133, and,



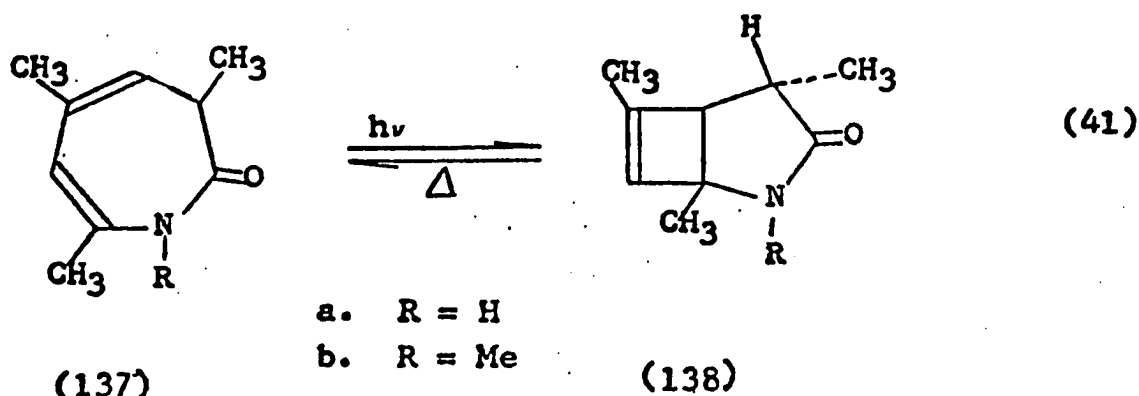
in 1963, Paquette^{66,67} reported that the nitrogen heterocycle 2,3-dihydro-1,3,5,7-tetramethyl-1H-azepine (134) undergoes photoisomerization to a mixture of two 1,2,4,6-tetramethyl-2-aza-bicyclo(3.2.0)hept-6-enes, 135 and 136, which parallels the reaction of 1,3-cycloheptadiene. In 1964,



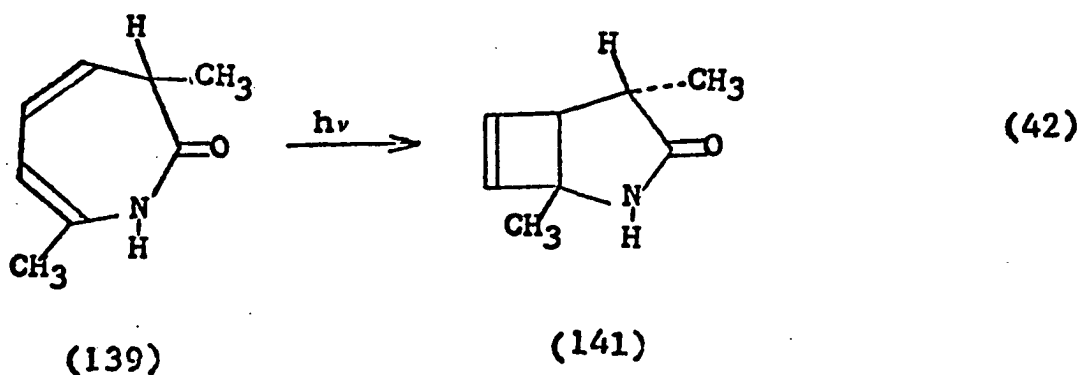
Chapman⁶⁸ and Paquette⁶⁹ reported their studies on the photochemical behavior of the dihydroazepin-2-one, 1-aza-3,5,7-trimethylcyclohepta-4,6-dien-2-one (137). The investigations of these workers were prompted by the possibility that (137)

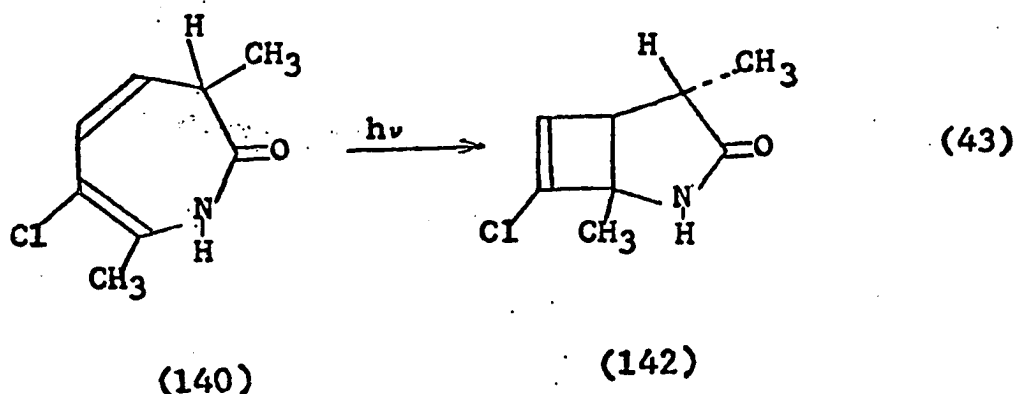
being the heterocyclic analog of 3,5-cycloheptadienone might follow the latter's decarbonylation reaction (equation 27, pg. 25) by the possibility that 137, might dimerize⁶⁹ like its homolog α - pyridone, and by the possibility that 137, which is basically a heterocyclic 1,3-cycloheptadiene, might cyclize (equation 29, page 27).

The studies of Chapman and Paquette revealed that, on irradiation, 137 undergoes the familiar electrocyclization of 1,3-cycloheptadienes. Photoisomerization of the lactams 137a and b led, in each case, to a single stereoisomer of 1,4,6-trimethyl-2-aza-bicyclo(3.2.0)hept-6-en-3-one (138).

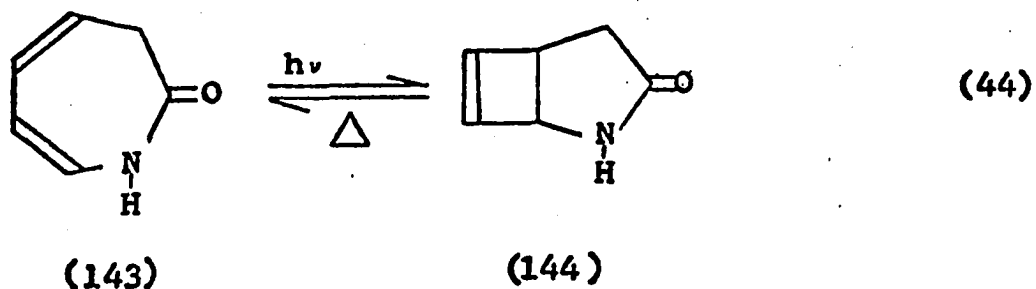


Similarly, irradiation⁷⁰ of the dihydroazepin-2-one (139) and its chloro derivative (140) in methanol gave the corresponding 2-aza-bicyclo(3.2.0)hept-6-en-2-ones (141) and (142).



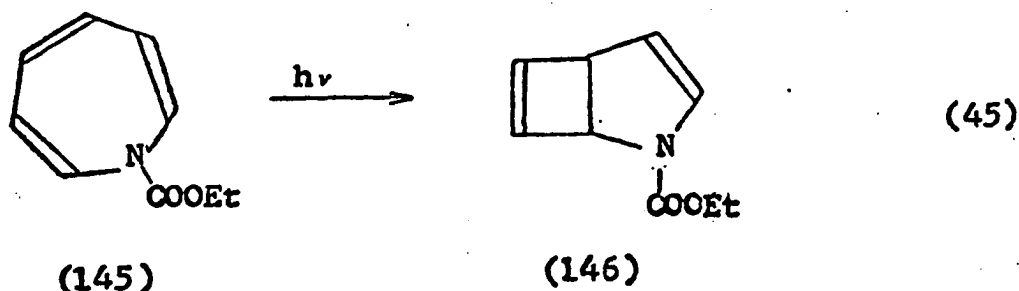


Photoisomerization has also been observed for the parent dihydroazepin-2-one. Vogel⁷¹, in 1965, reported that photolysis of 1,2-dihydro-3H-azepin-2-one (alternatively 1,3-dihydro-2H-azepin-2-one or 2,3-dihydro-1H-azepin-2-one) (143) in ether gave a 74% yield of 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144). The structure of the photoproduct was assigned on the basis of its elemental analysis, spectral properties (uv, ir, and nmr), thermal cycloreversion to starting material, and hydrogenation to 2-aza-bicyclo(3.2.0)hepta-3-one.

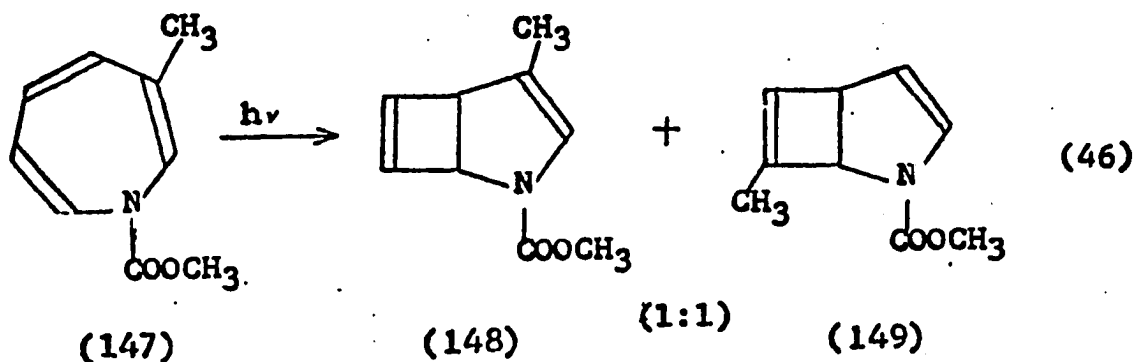


F. Stereoselectivity in the photoisomerization of 1H-azepines

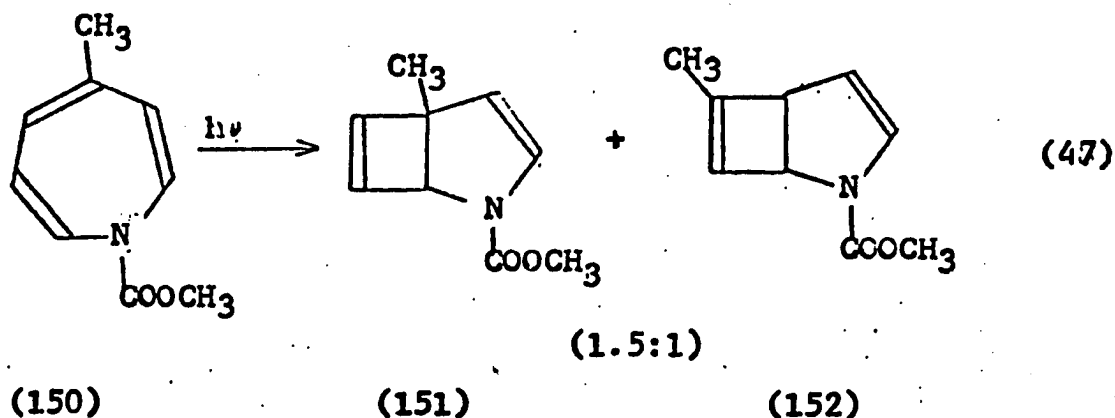
Photoisomerization has also been observed for heterocyclic analogs of 1,3,5-cycloheptatriene. Thus, Paquette² reported that photolysis of N-carbethoxy azepine (145) in tetrahydrofuran led to 2-carbetoxy-2-aza-bicyclo(3.2.0)hepta-3,6-diene (146), a reaction paralleling that of 1,3,5-cycloheptatriene. N-carbetoxy azepine is symmetrical, and,



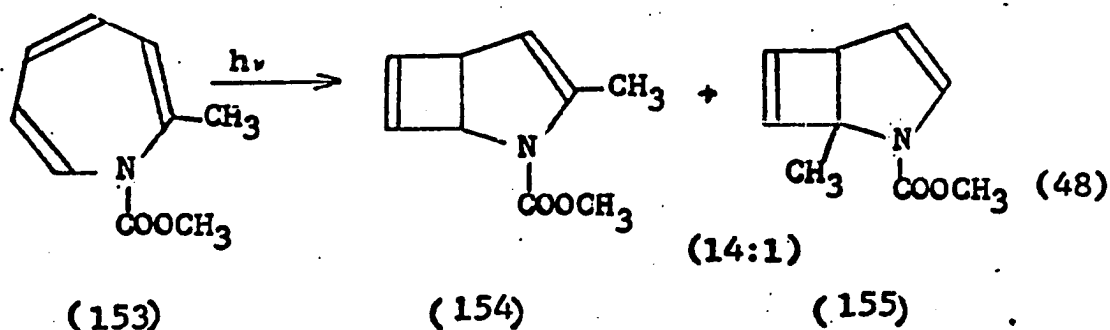
therefore can lead to only one bicyclic (3.2.0) valence isomer. In contrast, unsymmetrical substituted N-carbetoxy azepines might lead to at least two different bicyclo(3.2.0) valence isomers. Indeed, Paquette⁷² recently observed that irradiation of 3-methyl-N-carbomethoxy-azepine (147) gave a 1:1 mixture of 4-methyl-2-carbomethoxy-2-azabicyclo(3.2.0)hepta-3,6-diene 148 and the corresponding 7-methyl isomer (149). The products were formed at equal rates and they did not appear to be interconvertible. The starting material was



completely consumed. Similarly the 4-methyl derivative (150) gave a 1.5:1 mixture of the 5-methyl isomer (151) and the 6-methyl isomer (152). However, the 2-methyl derivative (153)



gave a mixture containing a 14:1 ratio of the 3-methyl isomer (154) and the 1-methyl isomer (155). Both isomers were primary photoproducts and neither was destroyed upon prolonged irradiation. Faquette invoked a steric argument to explain

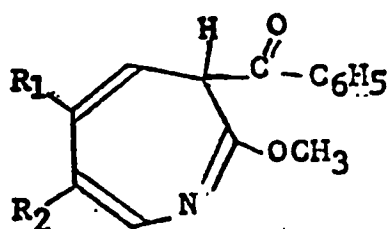


the selectivity observed in the irradiation of the 2-methyl-derivative (153). Although a methyl group in a bridgehead position is in a more hindered environment than other methyl groups, its steric interactions should not normally be the major factor in controlling the course of the reaction because 151 which contains the bridgehead group is the

predominant product of 150. Faquette attributes the selectivity observed in the cyclization of 153 to 154 to non-bonded interactions between the methyl group and the carbomethoxy group in the transition state during the disrotation process. Non-bonded interactions are not important in the photorearrangements of 147 and 150 and selectivity is not observed. Faquette on the basis of calculations of Jones and Jones^{60,62} says "These results are congruent with H₂O calculations which indicate no preference for the competitive cyclizations in the absence of polarizable substituents."

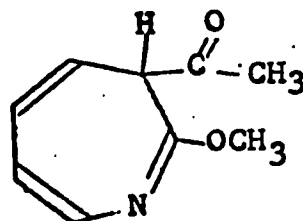
G. Photoreactions of 3H-azepines via diradical intermediates

There had been no reports on the photochemistry of 3H-azepines at the inception of this thesis research. Recently, however, Ogata and co-workers³ reported on the photolyses of a number of 3-acyl-2-methoxy-3H-azepines (156 and 157) and on a number of 3-acyl-2-amino-3H-azepines (158 and 159). At the same time, the report included work

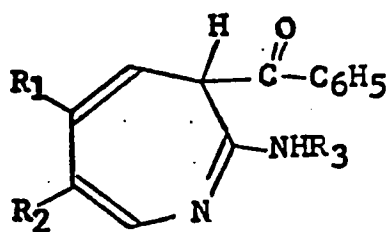


(156)

	<u>R₁</u>	<u>R₂</u>
a.	H	H
b.	Cl	H
c.	H	Cl

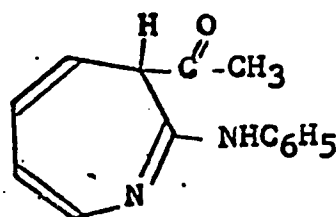


(157)



(158)

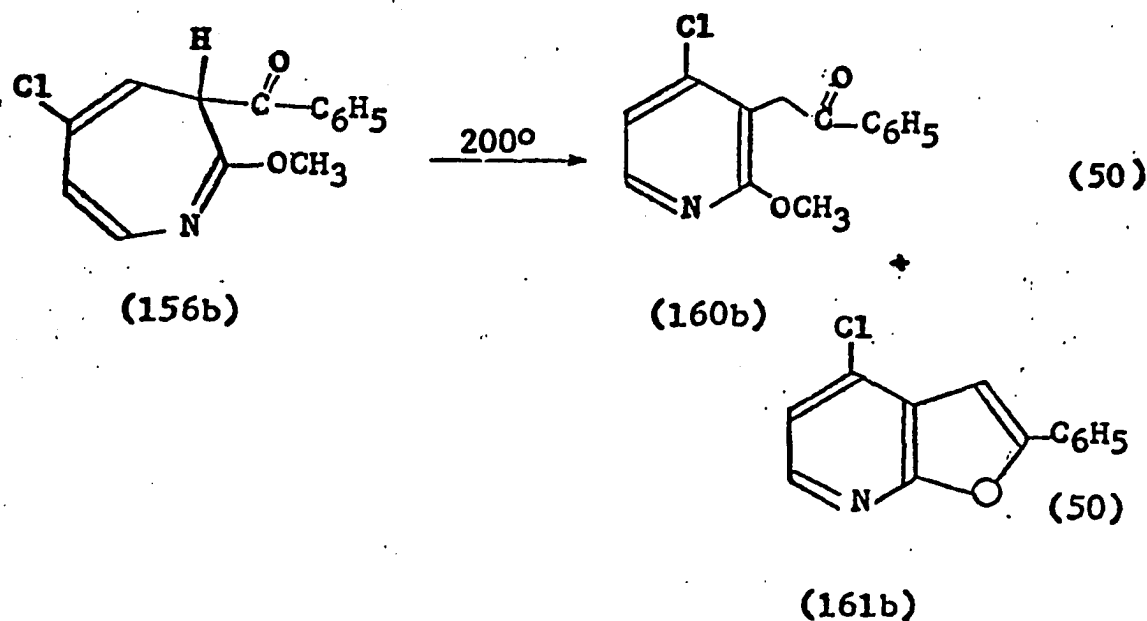
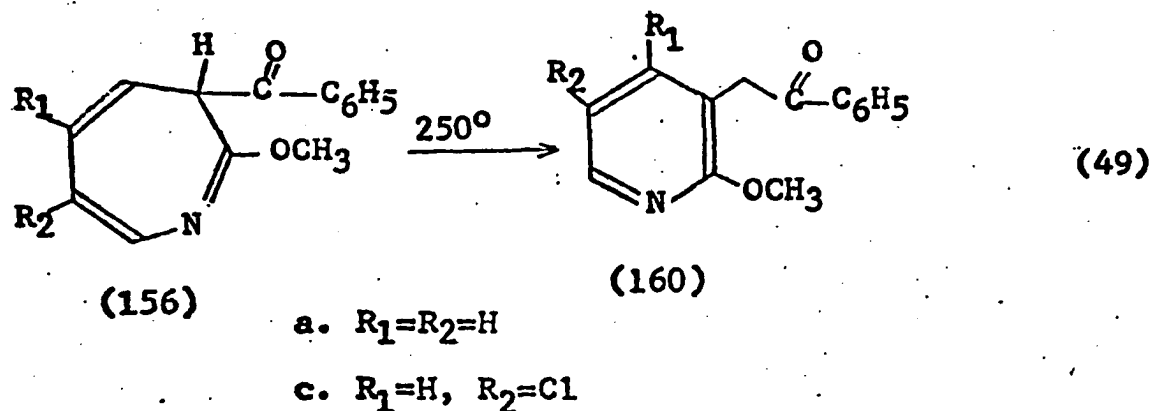
	<u>R₁</u>	<u>R₂</u>	<u>R₃</u>
a.	H	H	C ₆ H ₅
b.	Cl	H	C ₆ H ₅
c.	Cl	H	(C ₂ H ₅) ₂
d.	Cl	H	n-bu



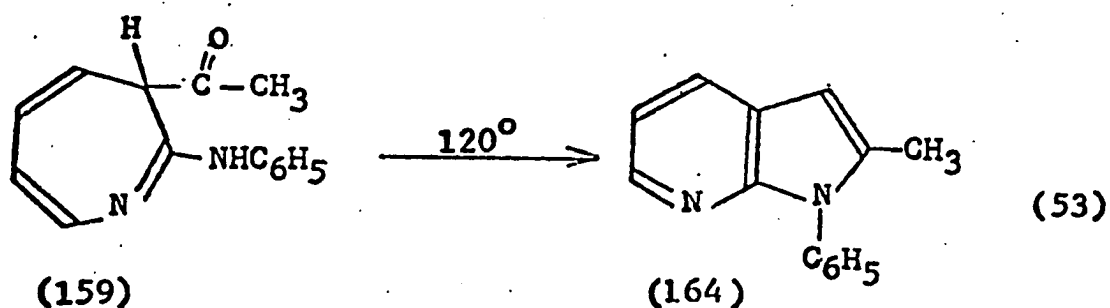
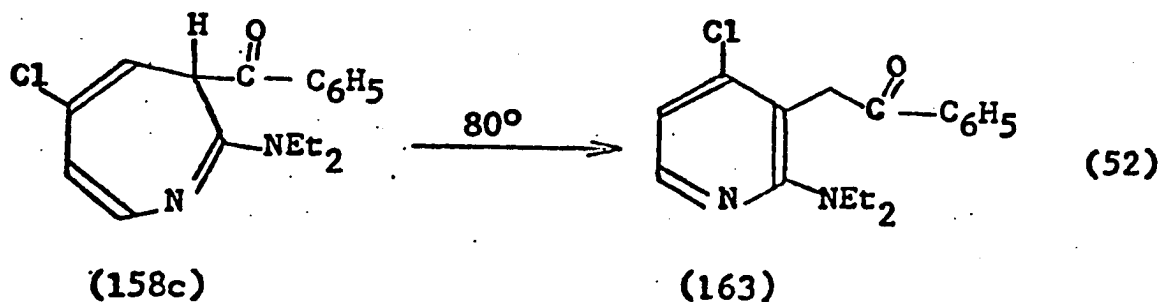
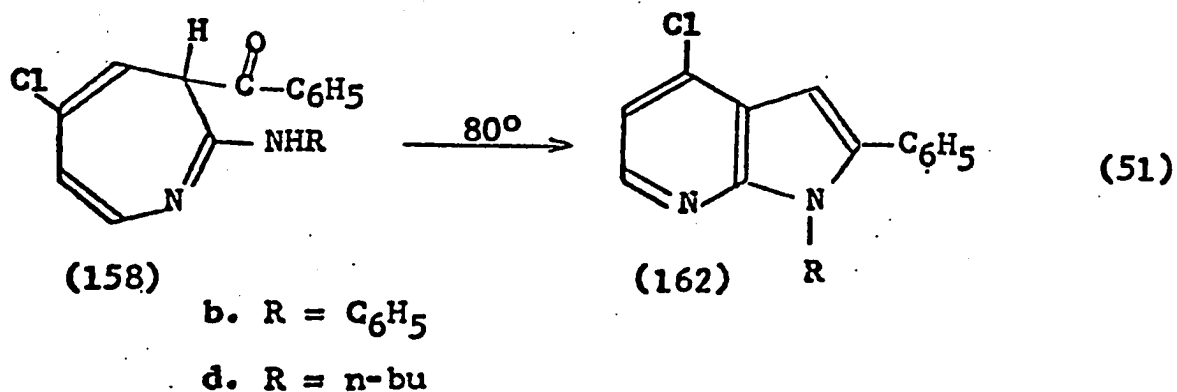
(159)

on the well documented⁷³ involvement of norcaradiene intermediates in thermal reactions and the Woodward-Hoffmann⁵ theory of orbital symmetry which permits the formation of such an intermediate by a symmetry-allowed disrotatory process. The mechanism of the photoreactions are best understood by first discussing the thermal reactions.

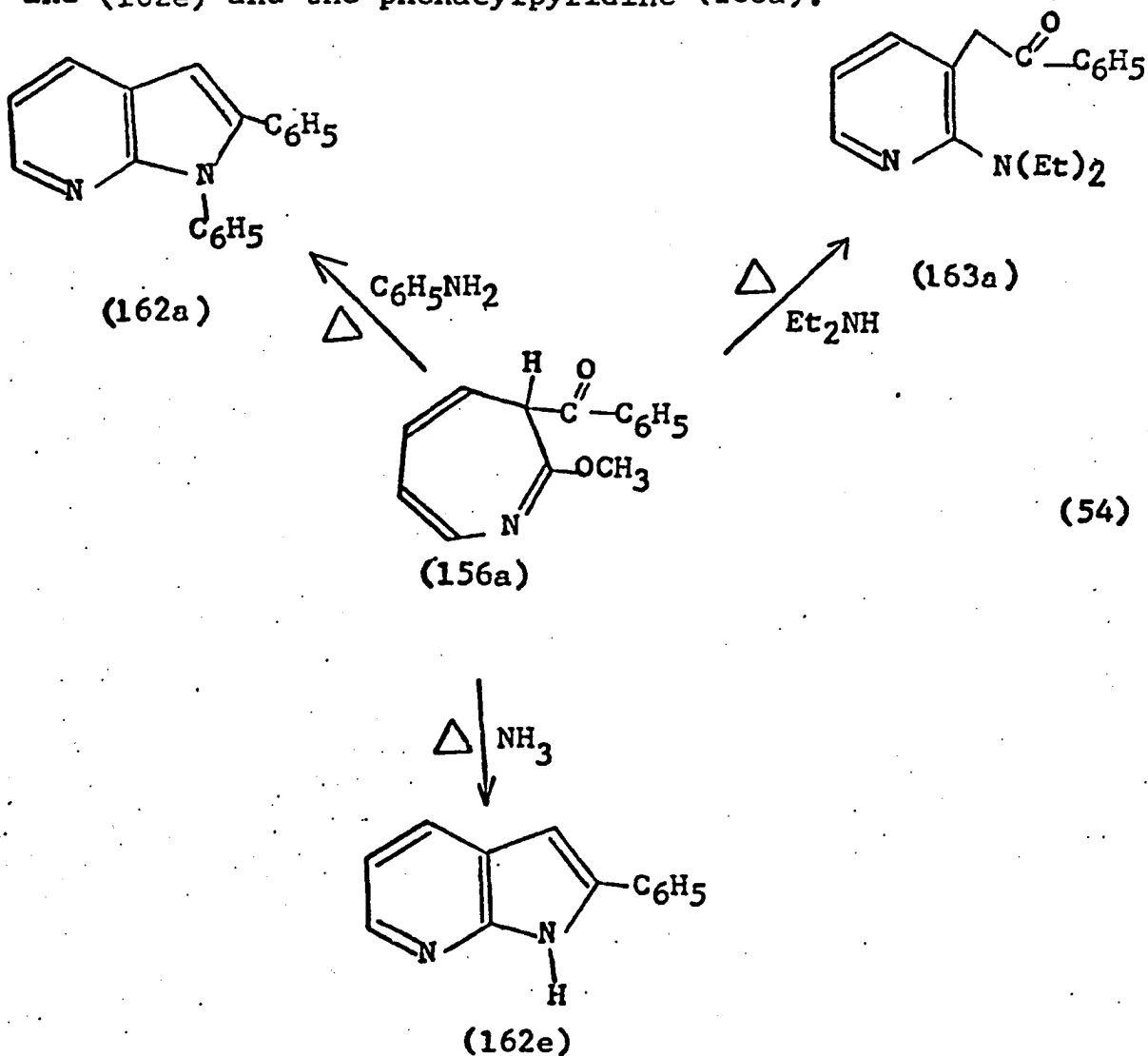
Thermolyses of the 3-benzoyl-2-methoxy-3H-azepines (156) led in low yields to various proportions of the pyridine derivatives 2-methoxy-3-phenacylpyridine (160) and 2-phenyl-furo(2.3-b) pyridine (161).



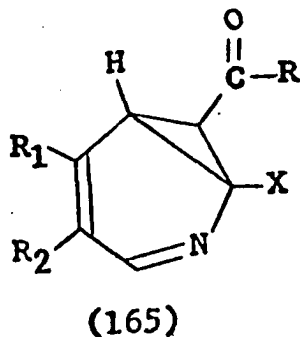
Thermolyses of the amidines (158) led to similar ring contractions but in better yields. It was noticed that the thermal rearrangements of 158 occurred more readily than those of 156, but an explanation was not offered.



Heating 156a in aniline, ethanolic ammonia or diethylamine gave the corresponding pyrrolo (2.3-b) pyridines (162a) and (162e) and the phenacylpyridine (163a).



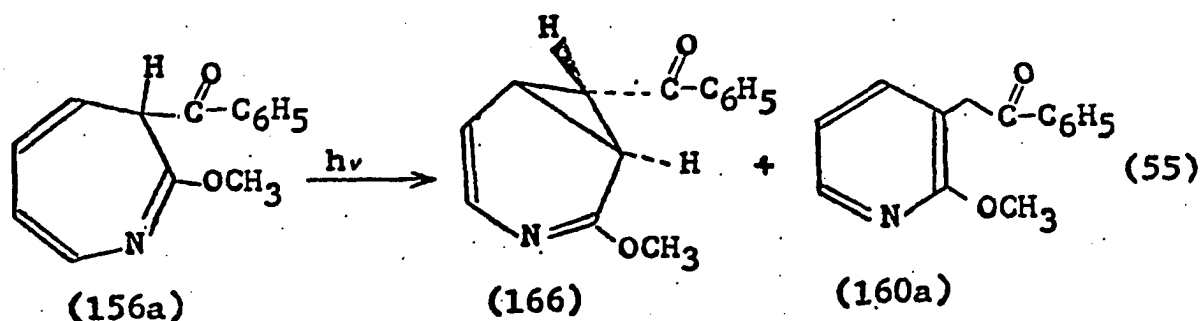
The thermal rearrangements of 156 and 158 were envisaged by Ogata as proceeding through an azanorcaradiene intermediate



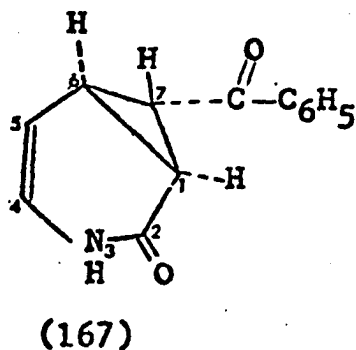
165 from which 160 and 163 are formed by cleavage of the

cyclopropane rings and hydrogen shifts. Dehydrative cyclization of 160 and 163 leads to compounds 161 and 162.

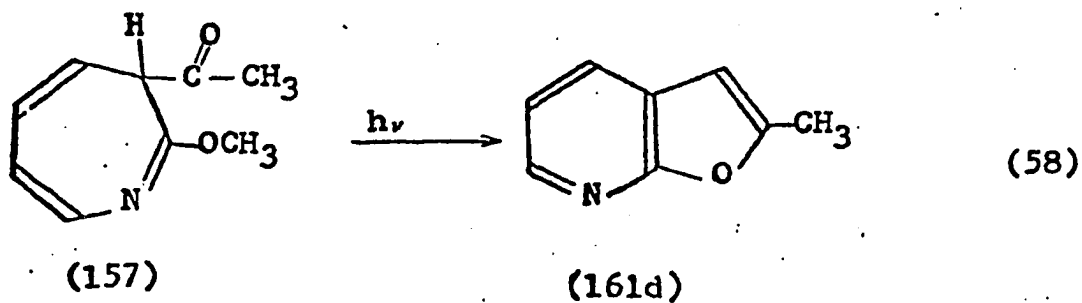
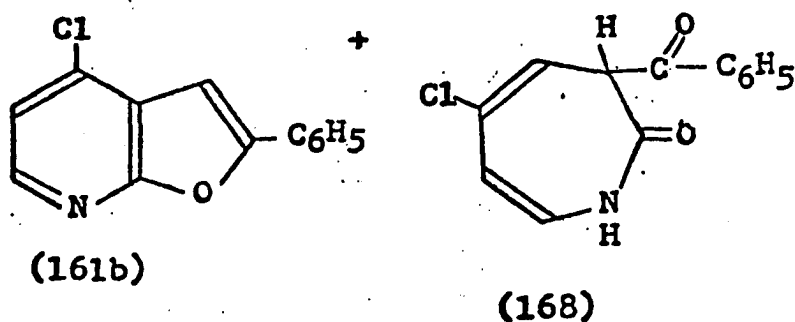
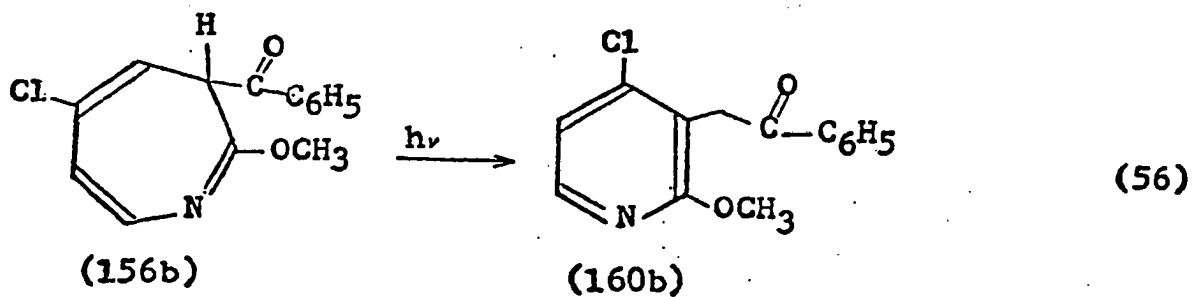
The photo-reactions gave some new products, but also some products which were identical to those obtained in the thermal reactions. Photolysis of 3-benzoyl-2-methoxy-3H-azepine (156a) in methanol gave the phenacylpyridine 160a and 7-benzoyl-2-methoxyl-3-azabicyclo(2.1.0)hepta-2,4-diene (166). The formation of these products contrasts sharply with the more characteristic cyclization reactions of cycloheptatrienes and azepines leading to bicyclo(3.2.0) derivatives. Compound 166



could not be isolated. Its assigned structure was deduced from the NMR spectrum of the crude photolysis mixture and by isolation of 7-benzoyl-3-azabicyclo(4.1.0)hept-4-en-2-one (167), which was obtained from 166 on passage through an alumina column.

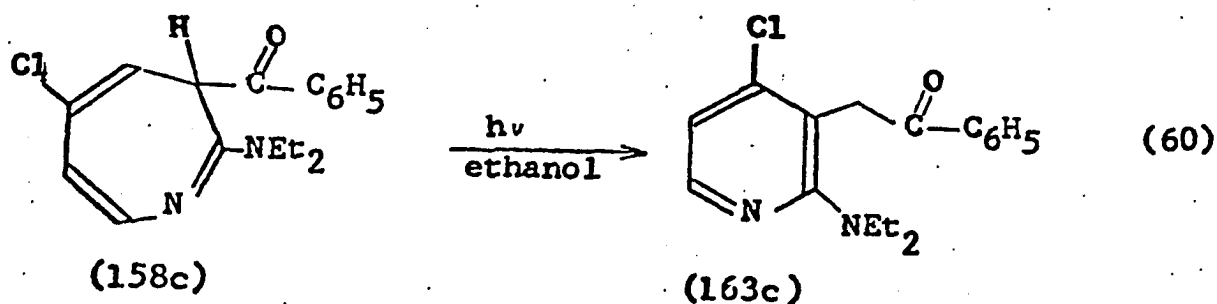
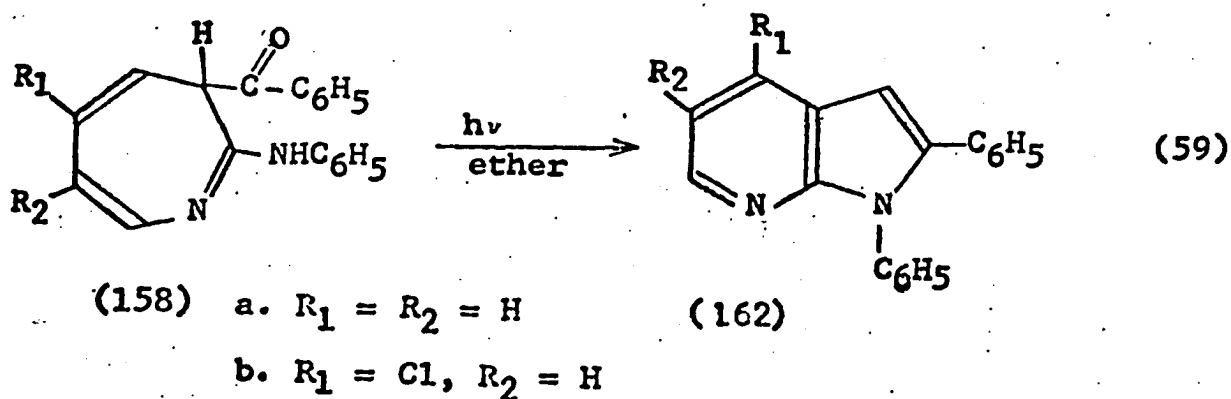


There is just one common type product, furo (2.3-b) pyridine (161), in the photolyses of 156b-c and of 157. Only 156b gave

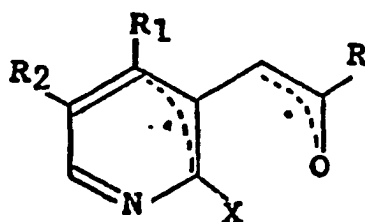


a product, of the type 160 which was observed from 156a. In the case of 156b, a unique but trivial reaction which led to the lactam 168 was also observed.

In contrast to the photochemical behavior of the imide ester 156a irradiation of the amidine 158a led only to the pyrrolo(2.3-b)pyridine 162a. Analogous photolyses of 158b and 158c gave only the pyrrolo(2.3-b) pyridine or phenacylpyridine.



In contrast to the thermal disrotatory process, photochemical symmetry-allowed conrotatory closure leading to an azanorcaradiene intermediate is subject to steric constraints. Therefore, Ogata proposed that compounds of the type 156 and 158 rearrange to the diradical 169 by β cleavage of the C₂-C₃ bond of the azepine ring. The intermediate diradical 169 can then readily form the observed photoproducts. Analogous cleavages of C-C bonds β to



(169) $X = \text{OCH}_3 \text{ or } \text{NHR}_3$

α -carbonyl groups have been reported for the reversible photoisomerization of arylaroylcyclopropanes⁷⁴.

Since products of the type 160a may be formed by photolysis of the azanorcardiene (165) in equilibrium with 156a, Ogata eliminated this possibility by nmr studies. There is still an unexplained solvent dependency for these reactions since 156 was stable to light in methylene chloride, cyclohexane, and acetonitrile.

Interestingly, the photolyses of 156 and 158 did not lead to products possessing the bicyclo(3.2.0) structure. This is in direct contrast to the expectations for 3H-azepines, if the Woodward-Hoffmann orbital symmetry rules are applied for a concerted electrocyclic-reaction, and the major reason for Ogata proposing a diradical intermediate.

STATEMENT OF THE PROBLEM

Although photochemical studies of heterocyclic seven-membered rings containing the diene chromophore as part of a conjugated system had been extensively studied, all cases reported at the inception of this thesis research were concerned with symmetrical structures. It was, therefore, the purpose of this thesis research to begin the exploration of the unsymmetrical 3H-azepine system with a view towards elucidating the nature and structure of the photolysis products and the mechanism of the reaction.

Since orbital symmetry considerations are important in any mechanistic discussion of concerted intra-molecular cyclization reactions, a further objective of this research was to obtain a description of the symmetry of the molecular orbitals of the 3H-azepine system by Huckel Molecular Orbital calculations. Additional interest in the photolysis of 3H-azepines was generated by the work of Ogata³ which indicated that photolytic reactions of 3H-azepines are not necessarily concerted.

The parent 3H-azepine is not known, but a number of 3H-azepines with heteroatoms in the 2-position are readily available⁷⁵⁻⁷⁷. Therefore the photochemistry of these compounds were studied.

RESULTS

I. General Photolyses of 3H-azepines

Irradiation of dilute pentane solutions of 2-dimethylamino-3H-azepine (1a) with 3000A lamps gave a brown polymer and about a 70% yield of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a). Similar reactions of 2-amino-3H-azepine (1b) in pentane or methanol and of 2-ethoxy-3H-azepine (1c) in pentane, using 2537 A lamps, gave the corresponding 2-aza-bicyclo(3.2.0)hepta-2,6-dienes, (2b) and (2c), in 45% and 60% yields, respectively. The identity of each product was established by elemental analysis*, ir, uv, and nmr spectroscopy and chemical synthesis. Most of the photolytic experiments to establish solvent and wavelength conditions for optimum yields were carried out with 2-dimethylamino-3H-azepine (1a). Highest yields were obtained when pentane was employed as solvent and the azepines were irradiated at wavelengths corresponding to their maximum absorptions in the ultra-violet.

A. Photolysis of 2-dimethylamino-3H-azepine (1a)

Photolyses of 2-dimethylamino-3H-azepine at all concentrations and in all solvents and wavelengths employed gave generally similar results in that only one major volatile product, 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) was formed plus almost an undetectable amount of

* Satisfactory elemental analyses were obtained for the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2a-c).

a more volatile product which was never isolated, and varying amounts of a brown polymer. The brown polymer was investigated briefly by isolation from photolyses in ether.

Elemental analysis of the brown solid indicated that it contained about 25% oxygen. This solid did not sinter at 350°. An ir spectrum (KBr pellet) of the solid material displayed broad bands centered at 3300 and 1600 cm^{-1} . The structure of this polymer was not investigated further.

Irradiation of dilute pentane solutions of 2-dimethyl-amino-3H-azepine (1a) with the Hanovia medium pressure lamp through filters, which isolated the region between 260-340 mμ gave a 64% overall yield of 2a. Initial reactions in pentane employed filter solutions absorbing wavelengths above 340 mμ in conjunction with the corex filter. However, succeeding reactions without the filter solution gave equivalent results. Photolyses of dilute pentane solutions of 1a in a Rayonet reactor with 3000 Å light gave only 2a in yields of 63-72%, based on reactant consumed. The reaction solutions were usually purged of oxygen prior to irradiation (table 2 and figure 1). In one of the experiments (table 3 and figure 2), when this was not done, a somewhat lower conversion of 1a to 2a was found; a lower mass balance of volatile materials was also observed. However, this may not be significant because the difference is of the order of magnitude of the experimental error.

Sample	Time (mins)	1 Weight of reactant	2 Weight of product	3 Sum of weights of reactant and product	4 Product yield, % (based on total reactant charged)	5 % reactant not consumed	6 Change in reactant weight	7 Product yield, % (based on reactant consumed)
control	-	3.19	-	3.19	-	100.0	-	-
1	35	2.61	0.23	2.84	7.3	81.8	0.58	39.7
2	93	2.20	0.55	2.75	17.3	69.0	0.99	55.6
3	122	2.12	0.82	2.94	25.8	66.5	1.07	76.6
4	160	1.76	1.02	2.78	31.9	55.2	1.43	71.3
5	205	1.40	1.18	2.58	37.0	43.9	1.79	65.9
6	240	1.11	1.32	2.43	41.5	34.8	2.08	63.5
7	278	1.03	1.41	2.44	44.0	32.3	2.16	64.8
8	305	0.89	1.44	2.33	45.0	27.9	2.30	62.6
9	415	0.50	1.93	2.43	60.5	15.7	2.69	71.7

TABLE 2

Photolysis (3000A) of 2-dimethylamino-3H-azepine in pentane
(oxygen purged before irradiation)

Figure 1

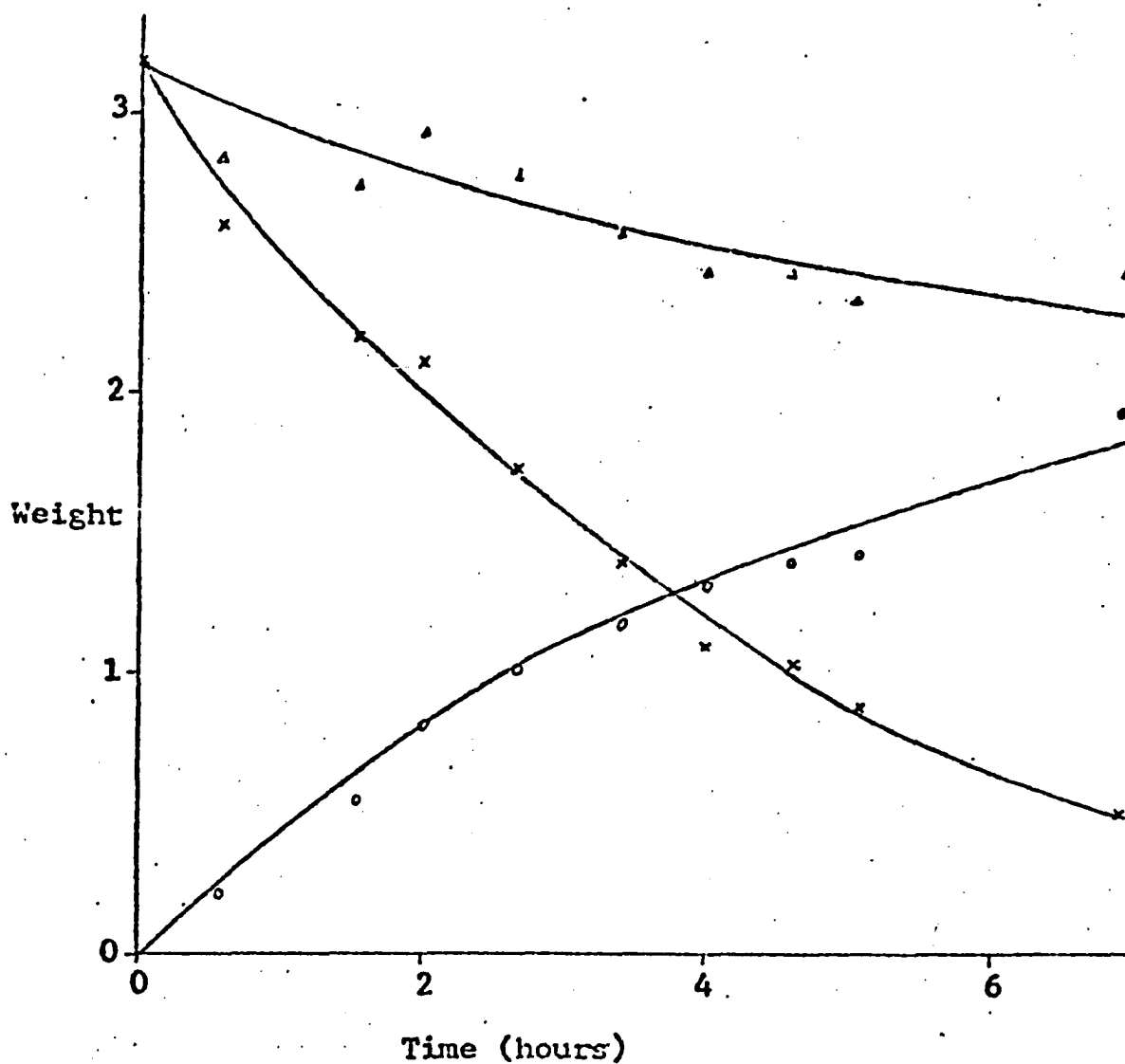
Photolysis (3000A) of 2-dimethylamino-3H-azepine in pentane
(oxygen purged before irradiation)

Plot of weights vs. time of irradiation

2-dimethylamino-3H-azepine (1a, x)

3-dimethylamino-2-aza-bicyclohepta-2,6-diene (2a, o)

Sum of 1a and 2a (Δ)



Sample	1	2	3	4	5	6	7
Time (mins)	Weight of reactant	Weight of product	Sum of weights of reactant and product	Product yield, % (based on total reactant charged)	% reactant not consumed	Change in reactant weight	Product yield, % (based on reactant consumed)
control	-	-	-	-	100.0	-	-
1	3.33	0.21	3.33	6.3	80.2	0.66	31.8
2	2.67	0.31	2.88	9.3	77.5	0.75	41.3
3	2.58	0.77	2.89	23.1	64.3	1.19	64.7
4	2.14	1.00	2.91	30.0	47.7	1.74	57.5
5	1.59	1.07	2.59	32.1	41.1	1.96	54.6
6	1.37	1.32	2.44	39.6	35.4	2.15	61.4
7	1.18	1.51	2.50	45.3	26.7	2.44	61.9
8	0.89	2.00	2.40	60.0	9.6	3.01	66.4
647	0.32		2.32				

TABLE 3

Photolysis (3000A) of 2-dimethylamino-3H-azepine in pentane
(oxygen not purged before irradiation)

Figure 2

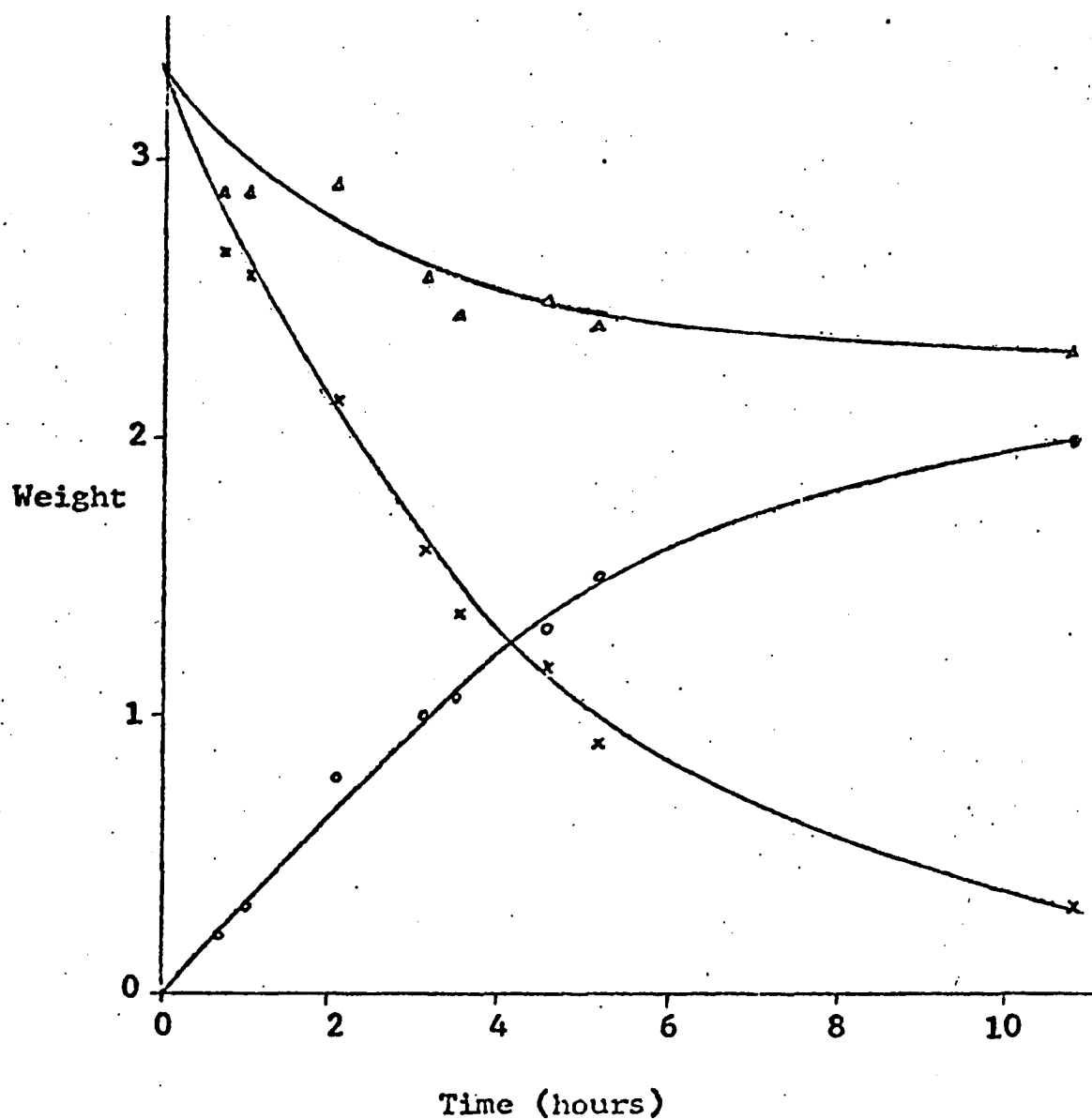
Photolysis (3000A) of 2-dimethylamino-3H-azepine in pentane
(oxygen not purged before irradiation)

Plot of weights vs. time of irradiation

2-dimethylamino-3H-azepine (1a, x)

3-dimethylamino-2-aza-bicyclohepta-2,6-diene (2a, o)

Sum of 1a and 2a (Δ)



In contrast to the reactions in pentane, irradiation of dilute ether solutions of 2-dimethylamino-3H-azepine with the Hanovia medium pressure arc gave lower yields of 2a. Irradiation through a pyrex filter absorbing wavelengths below 280 mμ or through a corex filter in conjunction with a filter solution which isolated the region between 260-340 mμ gave 2a in yields of 9% and 20%, respectively.

Photolyses of 1a in absolute ethanol were briefly studied. A Rayonet reactor with 3000 Å lamps was employed, and only 2a was obtained. The product yield was not determined.

The photolyses in ether were the preliminary experiments on the photochemical behavior of 2-dimethylamino-3H-azepine. Although product yields were not optimized, they were considerably lower than those in the pentane photolyses. The effect of wavelength in the ether photolyses served to demonstrate that higher product yields could be obtained when 2-dimethylamino-3H-azepine was irradiated at wavelengths near its maximum absorption in the ultra-violet.

B. Photolyses of 2-amino-3H-azepine (1b)

As in the case of the 2-dimethylamino derivative 1a, photolyses of 2-amino-3H-azepine (1b) at varying concentrations in all solvents and all wavelengths employed gave generally similar results in that only one major volatile product, 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b), was formed plus almost an undetectable amount of a more volatile product, and a brown polymer which was never characterized.

Photolyses of dilute pentane solutions of 2-amino-3H-azepine (1b) in a Rayonet reactor with 2537A lamps gave 40-50% yields of 2b. A brown polymer accounted for the remainder of the material; mass balances of 98% were obtained.

Photolyses of 1b in methanol solutions in a Rayonet reactor with 2537A lamps resulted in incomplete reaction. Polymer, soluble in methanol, was formed which absorbed the light and stopped the reaction. After separation of the polymeric material from the reaction mixture of 1b and 2b, the recovered material could be rephotolyzed to give a 45% yield of 2b.

Photolyses of 1b in tetrahydrofuran were briefly studied employing a Hanovia medium pressure mercury arc and corex filter which absorbed light below 260 mμ. Only a single photoproduct, 2b, was obtained. Although product yields were not optimized, considerably lower yields were experienced with the ethereal solvent.

Similar results were obtained when light of 3000A was used. Photolyses of 1b in a mixture of benzene and pentane in a Rayonet reactor with 3000A lamps gave a 45% yield of 2b (see table 4 and figure 3).

Sample	1	2	3	4	5	6	7
Time (mins)	Weight of reactant	Weight of product	Sum of weights of reactant and product	Product yield, % (based on total reactant charged)	% reactant not consumed	Change in reactant weight	Product yield, % (based on reactant consumed)
control	1.13	-	1.13	-	100.0	-	-
1	1.08	0.01	1.09	0.5	95.6	0.05	12.0
2	0.95	0.02	0.97	1.5	84.1	0.18	9.4
3	1.02	0.03	1.05	2.7	90.3	0.11	27.3
4	0.98	0.05	1.03	4.7	86.7	0.15	35.3
5	1.03	0.03	1.06	2.7	91.2	0.10	30.0
6	0.94	0.06	1.00	5.0	83.2	0.19	29.5
7	0.91	0.10	1.01	8.7	80.5	0.22	44.5
8	0.81	0.15	0.96	13.1	71.7	0.32	46.3
9	0.74	0.17	0.91	15.0	65.5	0.39	43.3
10	0.70	0.13	0.83	11.2	61.9	0.43	29.3

TABLE 4

Photolysis (3000A) of 2-amino-3H-azepine in benzene-pentane

Figure 3

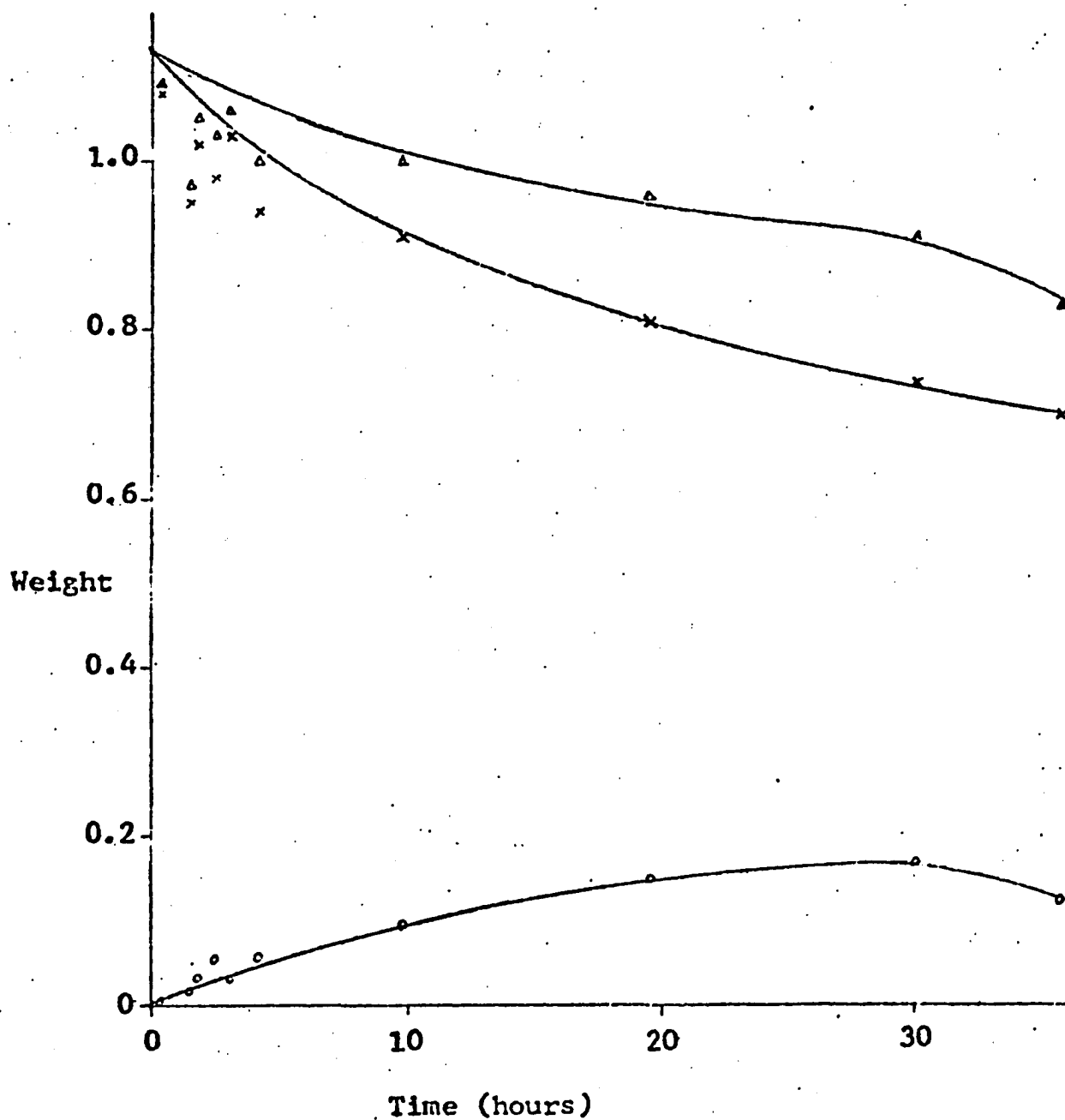
Photolysis (3000A) of 2-amino-3H-azepine in benzene-pentane

Plots of weights vs. time of irradiation

2-amino-3H-azepine (1b, x)

3-amino-2-aza-bicyclohepta-2,6-diene (2b, o)

Sum of 1b and 2b (Δ)



C. Photolyses of 2-ethoxy-3H-azepine (1c)

As in the cases of the 2-amino and 2-dimethylamino-3H-azepines, photolyses of 2-ethoxy-3H-azepine at varying concentrations in pentane gave one major volatile product, 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) plus a small amount (less than 3%) of a more volatile product and a brown polymer which were never characterized.

However, in contrast to the work with the amidines, an additional, less volatile product was formed whose yield was about one-fourth that of the major product before decreasing on prolonged irradiation. This minor product was studied in reactions employing 3000A lamps. Poor glpc resolution of this product and the major one did not permit its isolation and characterization.

The yield of the major product is wavelength dependent; it doubles on going from 3000A to 2537A light.

Prolonged photolyses of dilute pentane solutions of 2-ethoxy-3H-azepine in a Rayonet reactor with 3000A lamps resulted in the formation of 2c in 30% yield (see table 5 and figures 4 and 5). The less volatile minor product reached a maximum yield of 6% and decreased to 3% when most of the starting material had been consumed. Although the yield of the major product was about ten times that of the minor one when the reaction was terminated, it was only three times as great at its relative maximum. The minor product was not investigated further because of poor glpc resolution despite many efforts to improve separation.

Sample	Time (mins)	1 Weight of reactant	2 Weight of product*	3 Sum of weights of reactant and product	4 Product yield, % (based on total reactant charged)	5 % reactant not consumed	6 Change in reactant weight	7 Product yield, % (based on reactant consumed)
control	-	0.615	-	0.615	-	100.0	-	-
1	15	0.428	0.026	0.454	4.3	69.6	0.187	13.9
2	30	0.292	0.049	0.341	7.9	47.5	0.323	15.2
3	54	0.154	0.078	0.232	12.7	25.0	0.461	16.9
4	92	0.077	0.076	0.153	12.4	12.5	0.538	14.1
5	128	0.071	0.114	0.185	18.5	11.5	0.544	21.0
6	190	0.060	0.129	0.189	21.0	9.8	0.555	23.2
7	252	0.070	0.142	0.212	23.0	11.4	0.545	26.1
8	338	0.052	0.163	0.215	26.5	8.5	0.563	29.0

* product: 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene

TABLE 5
(continued on page 79)

Photolysis (3000A) of 2-ethoxy-3H-azepine in pentane

Sample	Time (mins)	1 Weight of reactant	2 Weight of product*	3 Product yield, % (based on total reactant charged)	4 Change in reactant weight	5 Product yield, % (based on reactant consumed)
control	-	0.615	-	-	-	-
1	15	0.428	0.005	0.8	0.187	2.7
2	30	0.292	0.019	3.1	0.323	5.9
3	54	0.154	0.030	4.8	0.461	6.5
4	92	0.077	0.026	4.3	0.538	4.8
5	128	0.071	0.029	4.6	0.544	5.3
6	190	0.060	0.014	2.3	0.555	2.5
7	252	0.070	0.021	3.5	0.545	3.9
8	338	0.052	0.015	2.5	0.563	2.7

* product: least volatile product (retention ratio 0.91)
(assumed to have same thermal conductivity as reactant)

TABLE 5

(continued from page 78)

Photolysis (3000A) of 2-ethoxy-3H-azepine in pentane

Figure 4

Photolysis (3000A) of 2-ethoxy-3H-azepine in pentane

Plots of weights vs. time of irradiation

2-ethoxy-3H-azepine (1c, x)

3-ethoxy-2-aza-bicyclohepta-2,6-diene (2c, o)

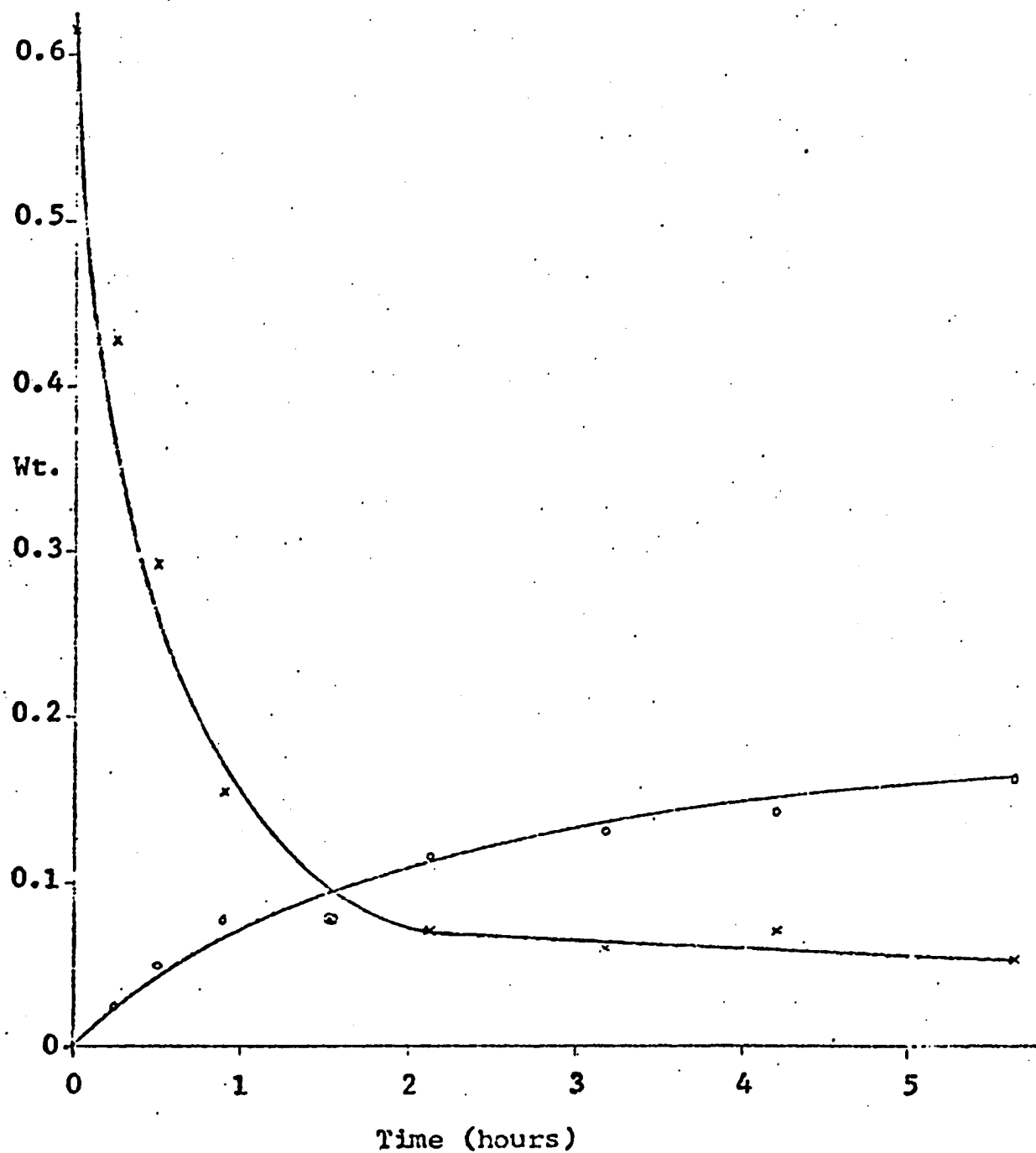
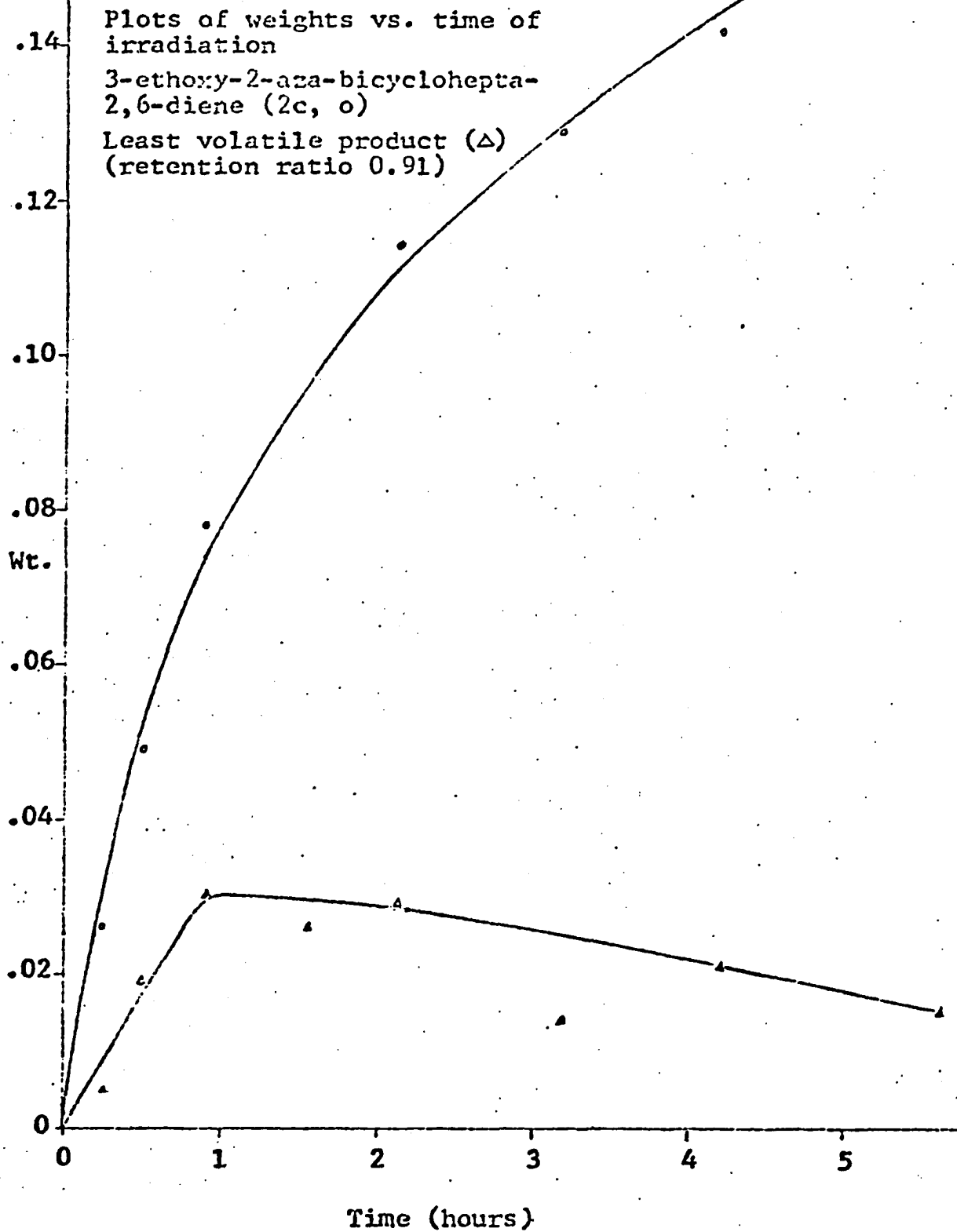


Figure 5

Photolysis (3000A) of 2-ethoxy-3H-azepine
in pentane



Photolyses of pentane solutions of 1c with 2537A lamps resulted in a 60% yield of 2c (see table 6 and figure 6). The less volatile product was not detected although it is possible that it may not have been resolved from the major one on glpc.

A photolysis reaction of 1c in pentane was carried out in which 3000A and 2537A lamps were consecutively employed (table 7 and figures 7 and 8). After irradiation with the 3000A lamps, a 30% yield of 2c was obtained. Substitution of the 3000A lamps by the 2537A lamps resulted in an increased yield (53%) of 2c (in calculating this yield, product formed on photolysis with the 3000A lamps was discounted). With the glpc column employed in this experiment, the less volatile minor product could not be detected.

Photolysis of 1c in methanol with 2537A lamps gave two products. The area ratio of the major product to the more volatile minor one was 1.5:1. Although the products were not isolated, the major product was chromatographically indistinguishable from that of an authentic sample of 2c. The minor product is probably 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2d) which is formed by the alcoholysis of the bicyclic photoproduct or by photoisomerization of alcoholated starting material. Heating the bicyclic compound in methanol gives a material with the same retention time as this minor product. This alcoholysis was studied in detail under different conditions (see page 95) and no further photolyses were done in methanol.

Sample	Time (mins)	1 Weight of reactant	2 Weight of product	3 Sum of weights of reactant and product	4 Product yield, % (based on total reactant charged)	5 % reactant not consumed	6 Change in reactant weight	7 Product yield, % (based on reactant consumed)
control	-	0.588	-	0.588	-	100.0	-	-
1	15	0.390	0.075	0.465	12.8	66.3	0.198	37.9
2	30	0.246	0.135	0.381	23.0	41.8	0.342	39.5
3	45	0.227	0.115	0.342	19.6	38.6	0.361	31.9
4	60	0.211	0.205	0.416	34.9	35.9	0.377	54.4
5	75	0.186	0.220	0.406	37.4	31.6	0.402	54.7
6	90	0.174	0.252	0.426	42.9	29.6	0.414	60.9
7	105	0.147	0.274	0.421	46.6	25.0	0.441	62.1
8	120	0.102	0.271	0.373	46.1	17.3	0.486	55.8
9	135	0.086	0.297	0.383	50.5	14.6	0.502	59.2
10	150	0.072	0.307	0.379	52.2	12.2	0.516	59.5
11	165	0.075	0.309	0.384	52.6	12.8	0.513	60.2
12	180	0.051	0.324	0.375	55.1	8.7	0.537	60.3
13	195	0.033	0.351	0.384	59.7	5.6	0.555	63.2
14	210	0.029	0.355	0.384	60.4	4.9	0.559	63.5
15	225	0.026	0.346	0.372	58.8	4.4	0.562	61.6

TABLE 6
Photolysis (2537A) of 2-ethoxy-3H-azepine in pentane

Figure 6

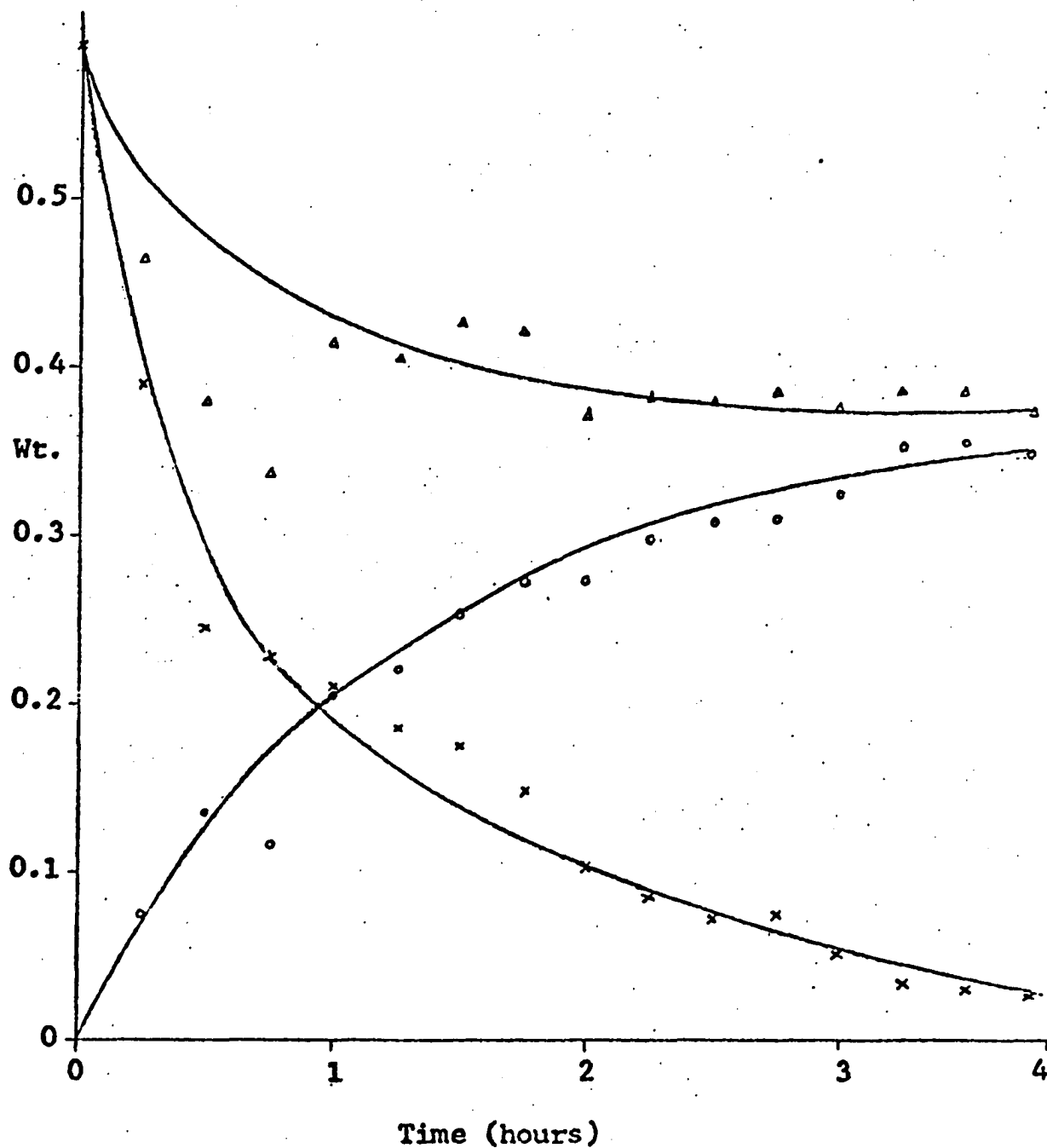
Photolysis (2537Å) of 2-ethoxy-3H-azepine in pentane

Plots of weights vs. time of irradiation

2-ethoxy-3H-azepine (1c, x)

3-ethoxy-2-aza-bicyclohepta-2,6-diene (2c, o)

Sum of 1c and 2c (Δ)



Sample	Time (mins)	1 Weight of reactant	2 Weight of product	3 Sum of weights of reactant and product	4 Product yield, % (based on total reactant charged)	5 % reactant not consumed	6 Change in reactant weight	7 Product yield, % (based on reactant consumed)
control (3000 A)	-	0.355	-	0.355	-	100.0	-	-
lamps								
1	15	0.343	-	-	-	96.6	0.012	-
2	61	0.343	*	-	-	96.6	0.012	-
3	108	0.302	0.006	0.308	1.7	85.1	0.053	11.3
4	128	0.299	0.009	0.308	2.6	84.2	0.056	16.6
5	153	0.320	0.011	0.331	3.1	90.1	0.035	31.1
6	171	0.308	0.016	0.324	4.6	86.8	0.047	34.9
7	207	0.295	0.016	0.311	4.6	83.1	0.060	27.3
8	223	0.291	0.019	0.310	5.4	82.0	0.064	29.8
9	254	0.284	0.019	0.303	5.4	80.0	0.071	27.2
control (2537 A)	-	0.284	-	0.284	-	100.0	-	-
10	15	0.274	0.003	0.277	1.1	96.5	0.010	32.0
11	47	0.265	0.012	0.277	4.1	93.3	0.019	61.1
12	82	0.238	0.016	0.254	5.6	83.8	0.046	34.8
13	142	0.237	0.026	0.263	9.0	83.5	0.047	54.5
14	208	0.223	0.033	0.256	11.5	78.5	0.061	53.6

* not detectable

TABLE 7
Photolysis of 2-ethoxy-3H-azepine in pentane

Figure 7

Photolysis of 2-ethoxy-3H-azepine in pentane

Plots of weights vs. time of irradiation

2-ethoxy-3H-azepine (1c, x)

3-ethoxy-2-aza-bicyclohepta-2,6-diene (2c, o)

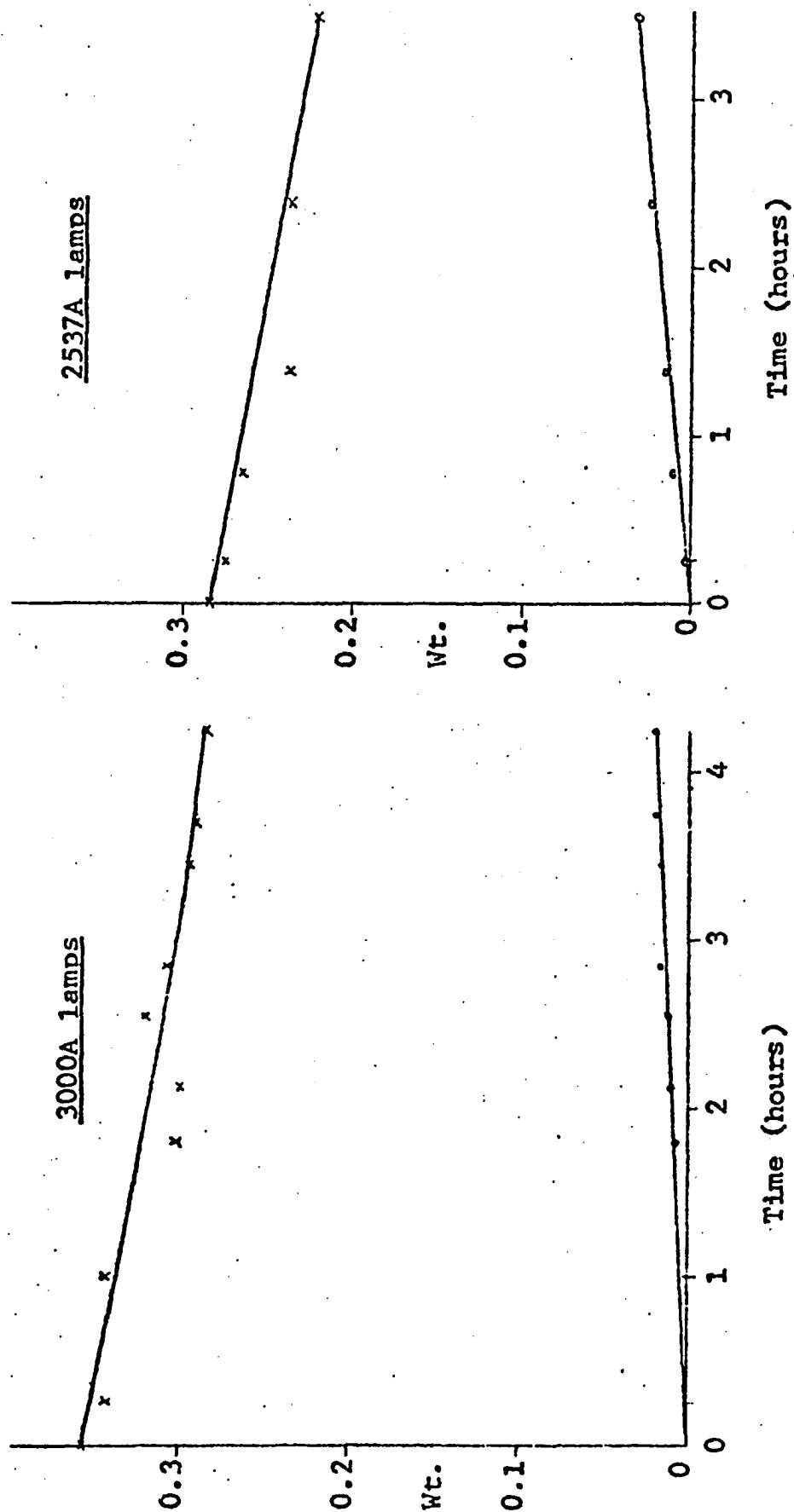
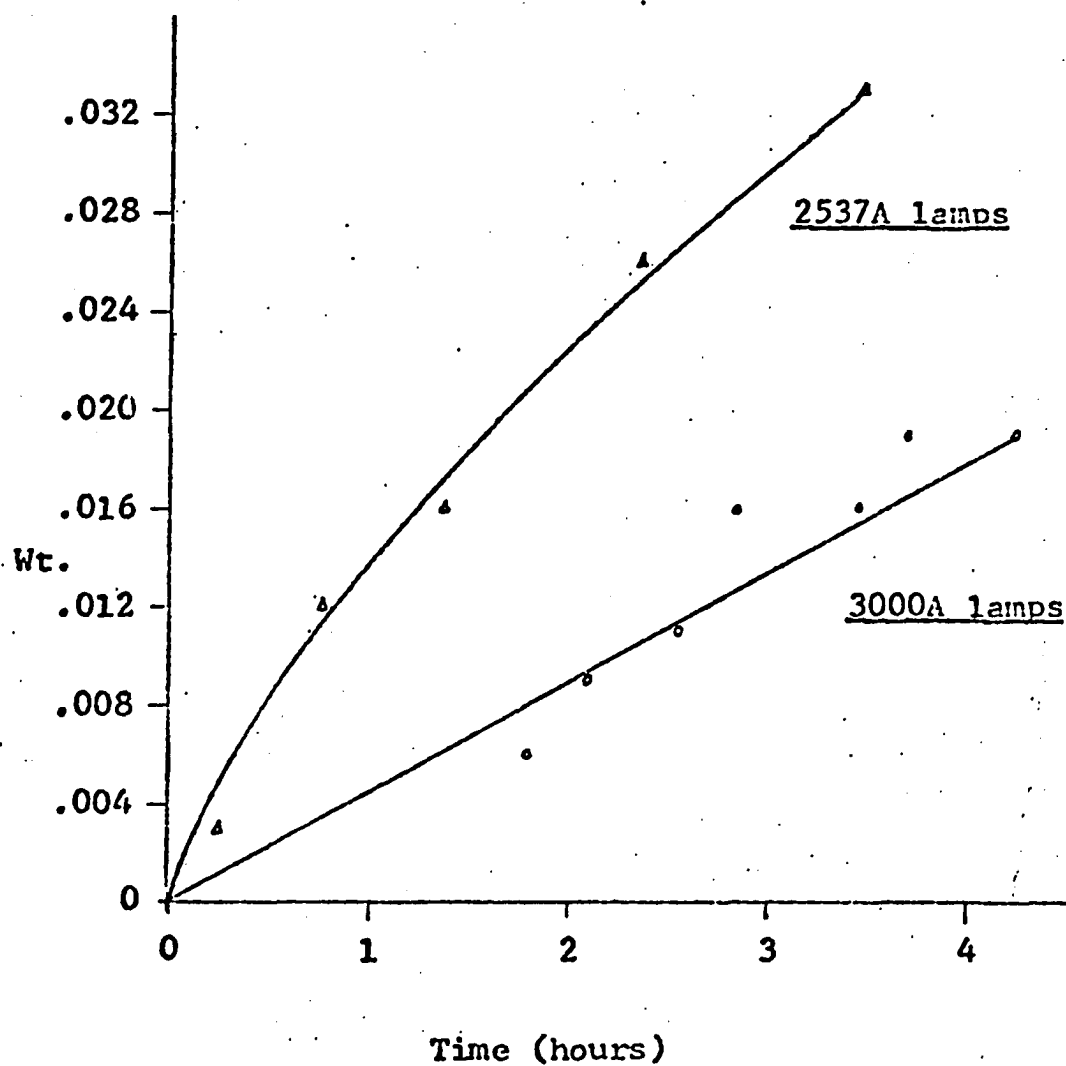


Figure 8

Photolysis of 2-ethoxy-3H-azepine in pentane

Plots of weights vs. time of irradiation

3-ethoxy-2-aza-bicyclohepta-2,6-diene (2c, o and Δ)



D. Photolytic conversion of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) to 2-dimethylamino-3H-azepine (1a)

Photolysis of dilute pentane solutions of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene with a Hanovia medium pressure arc through a corex filter for 30 minutes gave a 3% yield of product. During the course of the reaction, the corex filter was replaced by a vycor filter. As anticipated, the yield of product increased on changing filters (see table 8 and figures 9 and 10). After 30 minutes irradiation through the vycor filter a 10% yield of product was obtained (in calculating this yield, product formed on photolysis through the corex filter was discounted). Prolonged irradiation with either filter led to a decrease in product yield. For example, after one hour irradiation with the 2537A lamps conversion to product was about 4% and after two hours the conversion had decreased to 1%.

Product yield based on reactant consumed was lower when 2a was irradiated through the vycor filter. This most likely reflects a greater amount of decomposition of volatile compounds to non-volatile substances on exposure to the higher energy light.

The photoproduct, which was chromatographically indistinguishable from 2-dimethylamino-3H-azepine (1a), had an ir spectrum identical to that of 2-dimethylamino-3H-azepine. Recovered starting material was found to be pure 2a by nmr criterion.

Sample	1	2	3	4	5	6	7
Time (mins)	Weight of reactant	Weight of product	Sum of weights of reactant and product	Product yield, % (based on total reactant charged)	% reactant not consumed	Change in reactant weight	Product yield, % (based on reactant consumed)
control (corex filter)							
1	3.86	-	3.86	-	100.0	-	-
2	3.39	0.13	3.52	3.4	87.8	0.47	27.7
	3.20	0.11	3.31	2.8	82.9	0.66	16.7
control (vycor filter)							
3	3.20	-	3.20	-	100.0	-	-
4	1.87	0.34	2.21	10.6	58.4	1.33	25.6
5	1.64	0.32	1.96	10.0	51.3	1.56	20.5
6	1.45	0.22	1.67	6.9	45.3	1.75	12.6
7	1.36	0.12	1.48	3.8	42.5	1.84	6.5
8	1.44	0.07	1.51	2.2	45.0	1.76	4.0
	1.45	0.03	1.48	0.9	45.3	1.75	1.7

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TABLE 8

Photolysis of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene in pentane

Figure 9

Photolysis of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene in pentane

Plots of weights vs. time of irradiation

3-dimethylamino-2-aza-bicyclohepta-2,6-diene (2a, x)

2-dimethylamino-3H-azepine (1a, o)

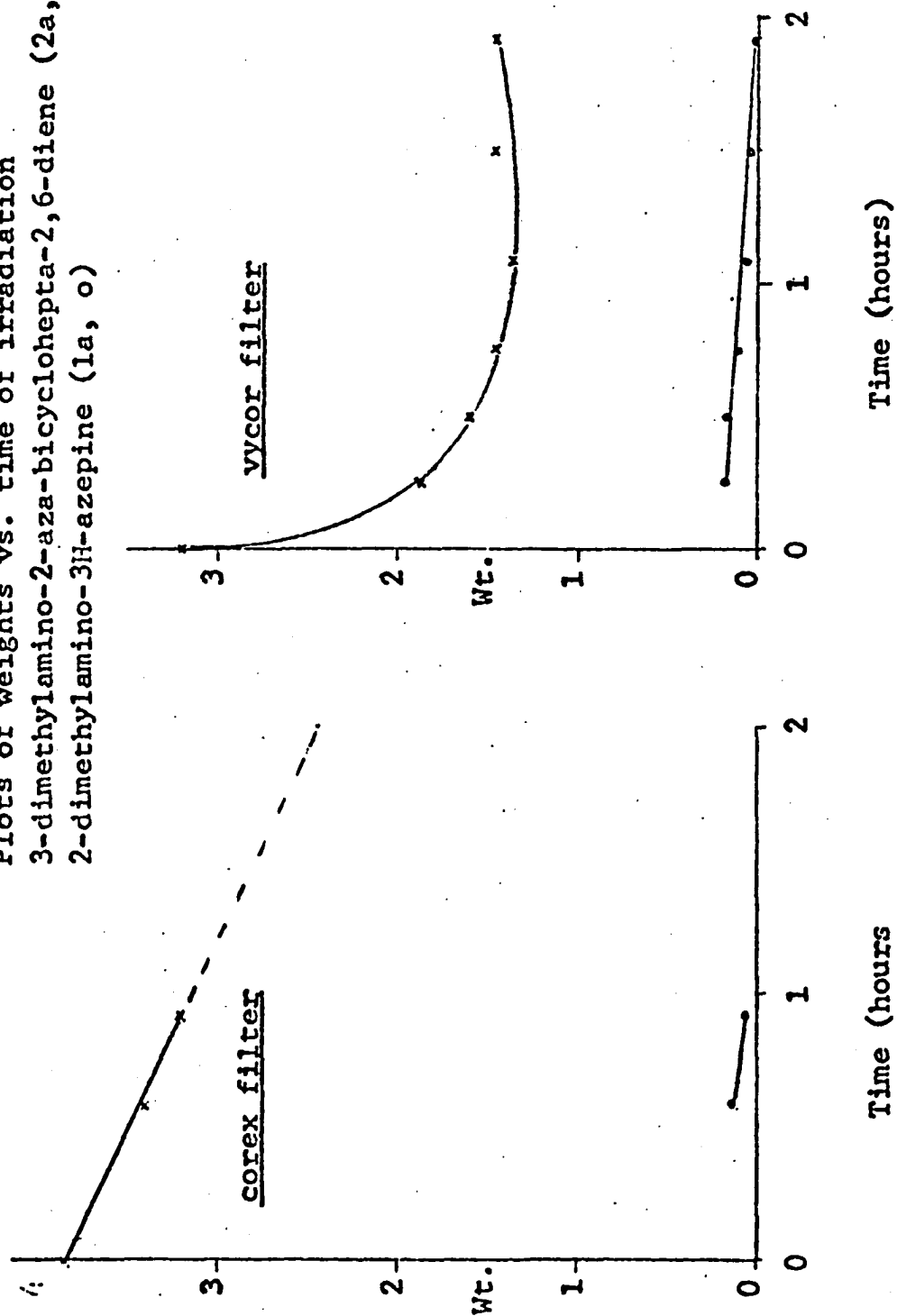
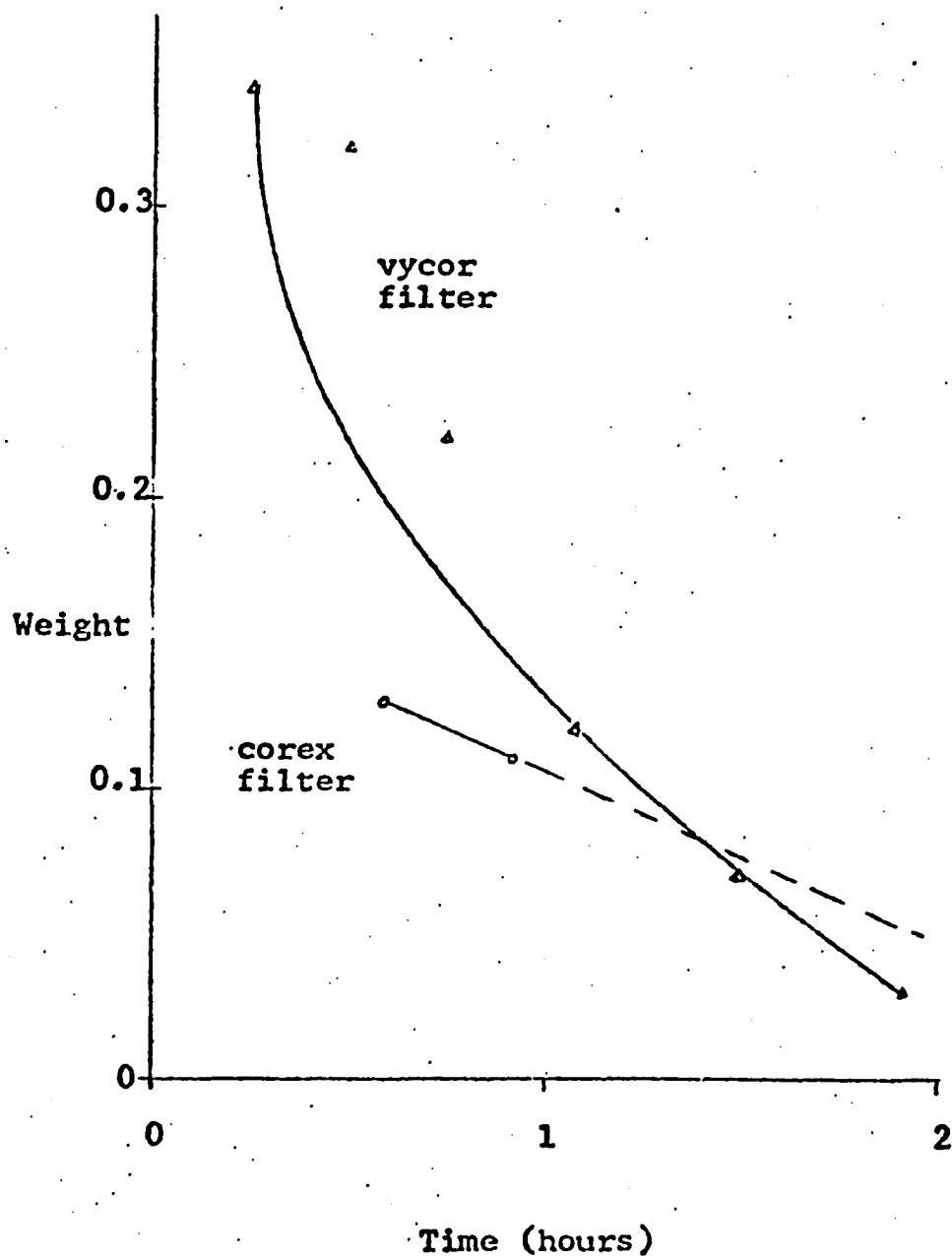


Figure 10

Photolysis of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-
2,6-diene in pentane

Plots of weights vs. time of irradiation

2-dimethylamino-3H-azepine (1a, o and Δ)



II. Chemical Transformations of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes

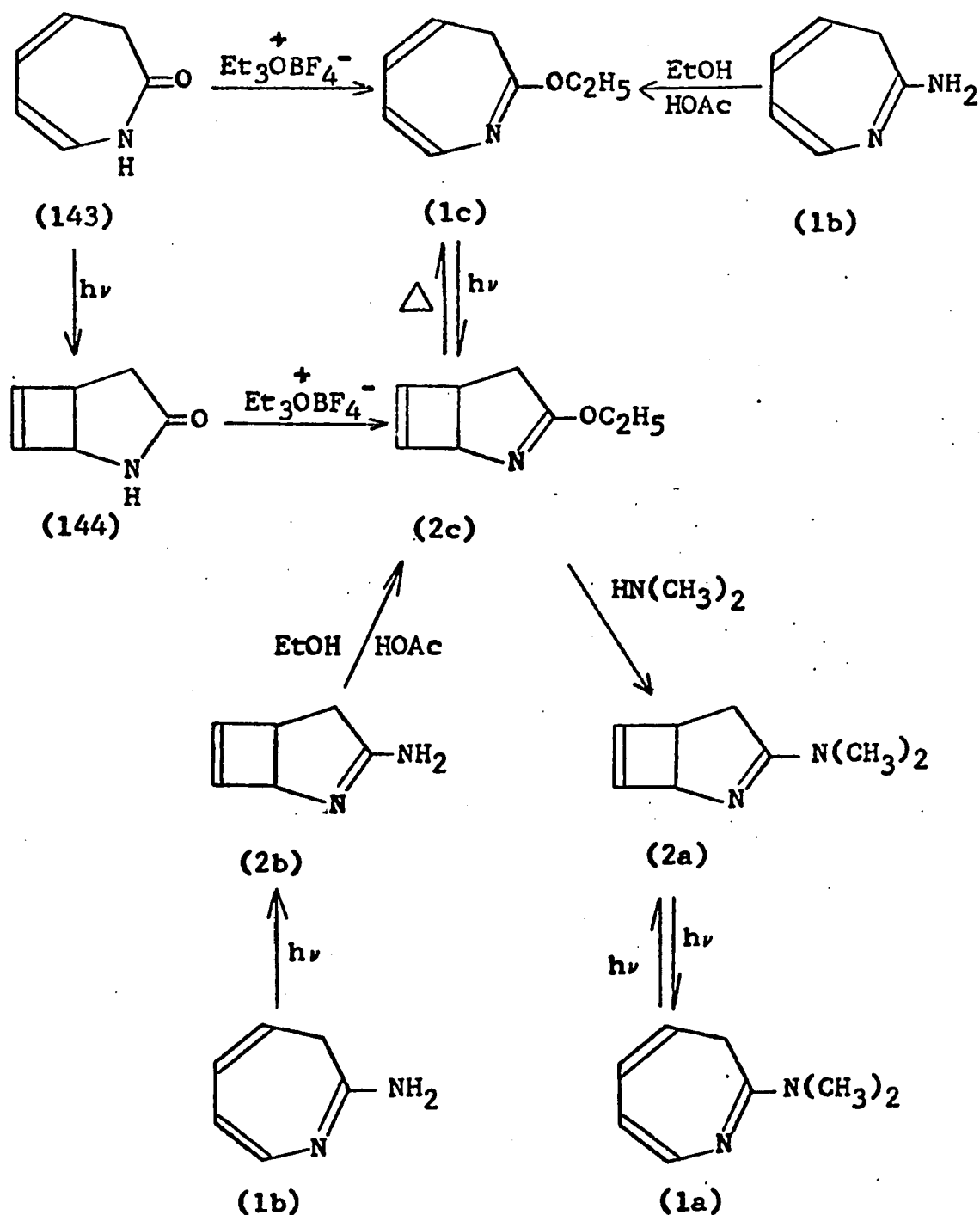
Chemical evidence for the structure of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2a-c) was obtained by their synthesis from or transformation to known compounds (scheme 9).

The structure of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) was corroborated by its synthesis from the known⁷¹ lactam 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144) (see page 54). The alkylation of 144 was effected by its in situ reaction with triethyloxonium fluoroborate; a 70% yield of 2c was usually obtained. Further evidence for structure 2c was suggested by its thermolytic cycloreversion to 2-ethoxy-3H-azepine (1c). Thermolysis of a dilute hexane solution of 2c by passage through a column of pyrex helices (300°) gave a 70:30 mixture of 1c and 2c from which 1c could be obtained in 46% yield (based on reactant consumed) by preparative VPC. The product was chromatographically indistinguishable from an authentic sample of 1c and had an infrared spectrum which was identical with that of 1c.

The structure of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) was chemically related to 2c by an aminolysis which was effected by heating 2c and dimethylamine in a sealed tube. Only one product was detected by vapor phase chromatography. The yield of this product appeared to be almost quantitative. However, only a small fraction of it was isolated. The product was identical in its spectroscopic

and glpc behavior to that product from the photolysis of 2-dimethylamino-3H-azepine. Further evidence for structure 2a was obtained by its photolytic cycloreversion in pentane to 2-dimethylamino-3H-azepine (see page 182).

The structure of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene was correlated to 2c by an alcoholysis reaction which was similar to the one reported for 2-amino-3H-azepine (see result section III on the alcoholysis of amidines). The product of the alcoholysis reaction of 2b had the same ir and nmr spectra as an authentic sample of 2c.



SCHEME 9

Correlation of the structures of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2a-c) obtained by photo-reactions and chemical transformations

III. Alcoholysis of Amidines

The conversion of the amidines 2-amino-3H-azepine (1b) and 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) to their corresponding imidate esters 1c and 2c was effected by refluxing an ethanolic solution of the amidine in the presence of a catalytic amount of glacial acetic acid (0.1 mole of acid per mole of amidine is desirable). Isolation of the products required distillation of the ethanol at atmospheric pressure since in vacuo the product and alcohol distill together. When the amidine 1b was refluxed for 5 days a 49% yield of 1c and a mass balance of 91% was realized, whereas, after heating for nineteen hours, a 14% conversion to 1c and a 95% mass balance was realized. Although the reaction time was not optimized, it appears that the reaction might be quantitative. Analysis by glpc indicated that 1c was suitably pure for photochemical studies. The transformation of 2b to 2c (see page 146) constitutes part of the structure proof for 2b.

EXPERIMENTAL

A. Materials

Reagent grade chemicals were used without further purification unless stated otherwise. When anhydrous ether or tetrahydrofuran were employed, they were either obtained from unopened containers or freshly distilled over lithium aluminum hydride. Methanol (containing ca. 0.002% formic acid), benzene (thiophene free), chloroform (containing ca. 0.75% ethanol), and absolute ethanol (200 proof) were used without further purification. Pentane from an unopened container could be employed without further purification; when purified, the hydrocarbon was washed with aqueous potassium permanganate, sulfuric acid, sodium carbonate and water to neutral pH; after drying over calcium chloride it was distilled over sodium ribbon or calcium hydride prior to use. Prepurified nitrogen (Matheson) was used without further purification.

B. Instruments and Analyses

Melting points were taken on a calibrated Reichert hot-stage or Thiele tube apparatus.

Elemental analyses were done by the Schwarzkopf Micro-analytical Laboratory, Woodside, New York.

Infra-red (ir) spectra were taken on a Perkin-Elmer model 237 Infracord and calibrated by means of a polystyrene calibration film.

Ultra-violet (uv) spectra were taken on a Cary 14 spectrometer.

Nuclear magnetic resonance (nmr) spectra were obtained on a Varian A-60 spectrometer. Tetramethylsilane was employed as an internal standard and chemical shifts are presented in δ values (probe temperature ca. 40°).

Vapor phase chromatography (gipc) was carried out on an Aerograph dual-column gas chromatograph model A-350-B utilizing a thermal conductivity detector (helium carrier gas, 150 ma filament current). A Leeds and Northrup Speedomax H recorder (chart speed 30 and 60 inches/hour, range 0 to 1 MV, response time 1.0 sec. full travel) was used in conjunction with the chromatograph. Injector and detector temperatures of about 180° and 200°, respectively were employed. Column material was packed in stainless steel columns. When reactant and photoproduct peaks were symmetrical, peak areas were determined by the method of height times base at half-height. When reactant and photoproduct peaks were unsymmetrical a planimeter (Keuffel & Esser compensating polar planimeter No. 620015) was used. Retention times were obtained by measuring the distance (in millimeters) from the air peak to that point when the peak began to appear and dividing by 25.4 mm (for the chart speed employed 25.4 mm = 1 minute). Retention times of both symmetrical and unsymmetrical peaks were measured in this manner. In cases where the air peak was masked by the solvent peak, the beginning of the

solvent peak was used as the basis for measurement. When reference is made to retention ratio, it is understood to be the ratio of the retention times of the product to that of the reactant, unless stated otherwise. Retention ratios were found useful in that they remained fairly constant (ca. $\pm$ 0.03) while individual retention times varied somewhat between experiments.

C. Photolytic Apparatus and Methods

Photolysis experiments were carried out with either a Hanovia medium pressure mercury arc (Hanovia Lamp Division, Newark, N.J.) in conjunction with Corning glass filters, or a Rayonet photochemical reactor (Southern N.E. Ultraviolet Co., Middletown, Conn.). The reaction vessels were equipped with a reflux condenser, gas inlet adapter, and a neoprene septum for removal of aliquots during the course of the reaction. The gas inlet adapter on the condenser was connected to a manifold (exiting to a mercury bubbler) through which vacuum could be applied to the system or nitrogen introduced. The reaction solution was alternately subjected to vacuum and nitrogen to remove oxygen and moisture. At the most, 50 ml of solvent was removed during the vacuum purges. The reactions were run under a blanket of nitrogen. The reaction solutions were either stirred by means of a magnetic stirring bar or refluxed over boiling stones (porcelain). Before turning on the lamps, a sample of the reaction mixture was taken as a control. During the course of the reaction, aliquots were

removed from the solution and either injected directly into the gas chromatograph or first concentrated under a current of nitrogen (a method which proved to be undesirable) or concentrated by distillation effected by gentle warming. In the latter method, the aliquot was placed in a 15 ml tapered graduated tube containing a porcelain boiling stone and was distilled to 1 ml in an oil bath, which was maintained at a constant temperature of 55°. About 1/5 of the tube was initially immersed in the oil bath. As the volume of this solution decreased, the tube was raised so that the level of the solution in the tube was always considerably above the oil level.

Hanovia - The Hanovia lamp model no. 679A-36 type L, 11" long, and filter sleeve were placed in a Hanovia jacketed quartz immersion well which was inserted into a 5-liter round bottom 3-neck flask or a cylindrical 1-liter 3-neck flask. Cooling water was circulated through the jacket of the quartz well. Filter sleeves employed were pyrex no. 7740 absorbing wavelengths below 280 mu, corex no. 9700 absorbing wavelengths below 260 mu, and vycor no. 7910 absorbing wavelengths below 205 mu.

Rayonet - Rayonet model RPR-100 equipped with sixteen RPR-lamps or model RPR-204 equipped with four RUL-lamps were used with quartz reaction vessels of 2/3 and 1½-liter capacities, respectively. Both models were supplied with lamps delivering 2537 A, 3000 A, or 3500 A light. The usual

operating temperature for the smaller model was about 35° with a fan in operation and about 70° without the fan. The larger model did not contain a fan. With the 3500 A lamps a temperature of about 42° was measured at the center of the reactor. Since the 2537 A and 3000 A lamps were usually employed, the reflux condenser was not sufficient to prevent the evaporative loss of low boiling solvents and a blower situated below the reactor was required to cool the reaction vessel to about 39°.

D. Preparation of Starting Materials

Phenyl Azide

Phenyl azide was prepared by the method given in "Organic Synthesis"⁷⁸ incorporating the modification of Doering and Odum⁷⁵ in which the ethereal extracts were washed with 2N NaOH to remove phenol and improve the stability of the product (b.p. 48.5-50.0°/16 mm; $n_D^{25.2}$ 1.5595).

2-amino-3H-azepine (1b)

Essentially, the procedure of Doering and Odum⁷⁵ was used for the preparation of 2-amino-3H-azepine. Into each of two 2-liter vacuum jacketed pyrex flasks equipped with a dry-ice condenser and a magnetic stirring bar was placed 18.0 g (0.15 mole) of phenyl azide. The flasks were filled with liquid ammonia (by condensation of the vapor) and each flask was irradiated for nine hours with four 275 watt Sylvania sunlamps. After allowing the ammonia to evaporate partially overnight, the remaining solutions were carefully transferred (and thus combined) to a 4-liter erlenmeyer flask. Before all the ammonia had evaporated from the erlenmeyer, 200 ml. of benzene was added. Additional time was allowed for the evaporation of residual ammonia, and, then the benzene extract was concentrated to 50 ml. on a rotary evaporator. After chilling, the product was filtered and sublimed (80-90°, 0.2-0.3 mm). Typically, about a 30% yield of 2-amino-3H-azepine (m.p. 90-91°) was obtained (uv spectrum in 95% ethanol $\lambda_{\max}$ 280 m μ , ϵ = 5370).

1,2-dihydro-3H-azepin-2-one (143)

1,2-dihydro-3H-azepin-2-one was prepared by the procedure of Doering and Odum⁷⁵ in which 2-amino-3H-azepine was refluxed in water until ammonia was no longer evolved. The product was usually obtained in about 90% yield (m.p. 48-49°).

2-dimethylamino-3H-azepine (1a)

The procedure of Odum and Brenner⁷⁶ was employed for the preparation of 2-dimethylamino-3H-azepine with a modification in the workup. Into each of two 2-liter vacuum jacketed pyrex flasks equipped with a dry-ice condenser and a magnetic stirring bar was placed 16.0 g (0.134 mole) of phenyl azide. The flasks were filled with liquid dimethylamine (by condensation of the vapor) and each flask was irradiated for eight hours with four 275 watt Sylvania sunlamps. After allowing the dimethylamine to evaporate partially overnight, the remaining solutions were carefully transferred (and thus combined) to a 4-liter erlenmeyer flask. Before all the dimethylamine had evaporated from the erlenmeyer, 200 ml. of anhydrous ether was added. The ethereal solution was extracted with 2N HCl and, then, the aqueous layer was repeatedly extracted with ether to remove any residual phenyl azide. The aqueous phase was neutralized with 2N NaOH, and, then extracted with ether. The ethereal extracts were dried over Na₂SO₄ and concentrated on a rotary evaporator. Distillation under vacuum gave 20.6 g (56% yield) of a light yellow liquid. The 2-dimethylamino-3H-azepine, thus obtained, was

purified by regeneration from its picrate utilizing the procedure of Odum and Brenner⁷⁶. The light yellow liquid was added to 30.8 g of picric acid (containing 10-12% water) in 580 ml. of absolute ethanol. Crystallization occurred after all the azepine was added. The yellow crystals were filtered and recrystallized from 150 ml. of 95% ethanol yielding 37.6 g of yellow crystals. The amidine was regenerated with 60 ml. of a saturated solution of lithium hydroxide in contact with 120 ml. of ether. The aqueous layer was removed and washed two times with 120 ml. portions of ether. The combined ether extracts (reddish) were washed twice with 30 ml. portions of the saturated LiOH solution and once with water, whereupon the color of the ether phase became yellow. After drying over potassium hydroxide pellets, the ether was removed on a rotary-evaporator. Careful evaporative distillation (0.05 mm, 67° maximum heating block temp.) gave 13.0 g of pale yellow 2-dimethylamino-3H-azepine (overall yield 36%) (uv spectrum in cyclohexane $\lambda_{\text{max}} = 295 \text{ m}\mu$, $\epsilon = 7460$).

2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144)

2-aza-bicyclo(3.2.0)hepta-6-ene-3-one was prepared by an adaptation of Vogel's⁷¹ method. The lactam 1,2-dihydro-3H-azepin-2-one (143) was irradiated in ether, tetrahydrofuran, methanol, or pentane with 2537 Å lamps in a Rayonet reactor. Typically 5.2645 g (0.0482 mole) of the lactam (4) in 650 ml of tetrahydrofuran (due to solubility difficulties a more dilute solution must be used when pentane is employed as

solvent) was irradiated for about 24 hours. After evaporation of solvent and sublimation of the residual reddish solid, a 68% yield of product, m.p. 78-79°, can be obtained. Recrystallization from anhydrous ether gives white crystals melting at 79-80° (lit. 83°)⁷¹. The product may contain a small amount of starting material (probably not more than 3%) since the gas chromatographic column employed to follow the reaction (8' x ¼" 20% apiezon L on chromosorb P, 60/80, regular, 170° column temperature, 200ml/min flow rate) was only useful for a qualitative indication of the course of the reaction. Quantitative work was not satisfactory because the peaks were highly unsymmetrical exhibiting considerable rounding and tailing. During the early stages of the reaction, when only a small amount of product had been formed, the retention times of starting material and product were about 5.4 and 9.2 mins, respectively. However, as the reaction progressed, the retention time of the starting material increased while that of the product decreased. At the end of the reaction the retention time of the product was 6.7 mins. Due to the poor resolution of the peaks towards the end of the reaction it is possible that a small amount of starting material was present but indistinguishable from the product peak. The ir spectrum (KBr pellet) of the product showed broad bands at 3250 and 1675 cm⁻¹. The nmr spectrum (in CDCl₃) of the product showed a one-proton singlet (broad) centered at 8.20 δ, a two-proton singlet at 6.34 δ, one-proton

multiplets centered at 4.43 δ and 3.51 δ , and a two-proton multiplet centered at 2.33 δ (lit.⁷¹; one-proton broad singlet at 8.7 δ , two-proton singlet with discernible splitting at 6.6 δ , and 1:1:2-proton multiplets at 4.6, 3.6 and 2.3 δ).

2-ethoxy-3H-azepine (1c)

1. by alkylation of 1,2-dihydro-3H-azepin-2-one (143)

2-ethoxy-3H-azepine was first prepared by Aaronson⁷⁹ utilizing Paquette's⁸⁰ method in which 1,2-dihydro-3H-azepin-2-one was ethylated by triethyloxonium fluoroborate. After fractional distillation of the product, Aaronson obtained a 52% yield of a pale yellow oil having the following properties and elemental analysis: b.p. 24-26° (0.1mm), $n_D^{25} = 1.5080$

Anal. Calcd. for $C_8H_{11}N$: C, 70.45; H, 8.08; N, 10.21.

Found: C, 70.29; H, 8.30; N, 10.45.

Essentially following Paquette's⁸⁰ procedure (1c) was obtained in about 50% yield by this worker. The spectral characteristics of 1c obtained by preparative glpc was identical to those obtained by Aaronson⁸¹. The uv spectrum of 1c in cyclohexane showed a maximum at 2600Å ($\epsilon = 5365$). The ir spectrum of 1c showed important bands at 1620 cm^{-1} (strong) and 1535 cm^{-1} (strong). The nmr spectrum of 1c was identical to the spectrum of 1c prepared by alcoholysis of 2-amino-3H-azepine (see page 106). A small amount of an impurity, 1-chloro-2,3-diethoxypropane, was usually

formed during the in situ preparation of the alkylating reagent and was often present in the product. Careful fractional distillation removed a major portion of the impurity, but its complete removal was difficult. This impurity was isolated during the preparative glpc purification of 1c employing a 12' x 3/8" 12% Apiezon L:KOH (4:1) on Chrom W, 60/80 A/W DMCS column. An infra-red spectrum (neat) of the impurity had a strong band at about 1120cm^{-1} , which suggested that the impurity may be a saturated ether. The nmr spectrum showed a six-proton triplet centered at 1.18δ , consistent with the methyl protons of the ethoxy groups, and a nine-proton multiplet centered at ca. 3.53δ , representative of hydrogens on carbon bearing an oxygen or chlorine atom. Its refractive index $n_D^{26} = 1.4237$ and low volatility are comparable to the index $n_D^{20} = 1.4246$ and boiling point $b_{14} = 69.8-70.4^\circ$ reported by Meerwein^{82,83}.

2. by alcoholysis of 2-amino-3H-azepine (1b)

A solution of 2.277g (0.0211 mole) of the amidine and 0.128g (0.00211 mole) of glacial acetic acid in 100 ml of absolute ethanol was refluxed in a 250 ml flask for five days. The solution was concentrated to 5 ml by distillation at atmospheric pressure over 0.146g (0.00106 mole) of anhydrous potassium carbonate. The product and residual ethanol was collected by careful distillation through a vigreux column. An initial fraction was collected at 35 mm

and ambient temperature using a dry-ice condenser, and a second fraction was collected at 0.5 mm and with an oil bath temperature of 85°. A semi-solid residue remained in the distillation flask which was essentially unreacted amidine. Both fractions contained product. They were combined and the ethanol was removed at atmospheric pressure yielding 1.409g (49% of theoretical) of product ($n_D^{20} = 1.5112$ after evaporative distillation at 34 mm and 28°). The product had the same infra-red spectrum as 2-ethoxy-3H-azepine obtained from the reaction of the lactam 1,2-dihydro-3H-azepin-2-one (143) and triethyloxonium fluoroborate. The nmr spectrum of the product showed a 1-proton doublet at 6.88 δ (J:7.5 Hz), a 1-proton quartet at 6.18 δ (J:7.5 Hz), a 1-proton quartet at 5.87 δ (J:5.5 Hz), a 1-proton multiplet at 5.20 δ , a 2-proton quartet at 4.09 δ , a 2-proton doublet at 2.58 δ , and a 3-proton triplet at 1.18 δ .

When the reaction, run under similar conditions, was terminated after 19 hours, a solid residue was obtained on concentration of the reaction mixture as described above. Based on unreacted amidine a 14% conversion to product and a 95% mass balance was realized. See result section on alcoholysis of amidines.

E. Photolysis Experiments

Photolyses (3000A) of 2-dimethylamino-3H-azepine (1a) in pentane

A solution of 0.584 g (0.00430 mole) of 2-dimethylamino-3H-azepine in 3 liters of pentane was irradiated with the Hanovia medium pressure mercury arc through a corex filter absorbing wavelengths below 260 mμ and a filter solution absorbing light above 340 mμ. The filter solution was prepared by dissolving 46 parts of $\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$ and 14 parts of $\text{CoSO}_4 \cdot 7\text{H}_2\text{O}$ in 100 parts of distilled water (succeeding reactions without the filter solution gave equivalent results). During the course of the reaction, aliquots were removed from the refluxing pentane solution, concentrated, and qualitatively analyzed by vapor phase chromatography (12' x 1/4" 20% Apiezon L-KOH (4:1) on Chromosorb P regular 60/80 mesh column, 200° column temperature and 80 ml/min flow rate). Both reactant and product gave symmetrical peaks. After 7 hours, the reaction was essentially complete. The glpc retention time for the starting material was 6.6 minutes and that of the photoproduct was 4.7 minutes. The retention ratio of the photoproduct to the starting material was 0.71. A small amount of another product was barely detectable at a retention time of 1.9 minutes (retention ratio 0.29). The pentane was removed from the reaction mixture by distillation at atmospheric pressure. After the solution was concentrated to 10 ml, it was placed in a 15 ml tapered centrifuge

tube. After centrifugation, the clear yellow supernatant was removed from the brownish residue and transferred to a graduated tube. The solution was concentrated to 1 ml and then transferred to a small sublimator. The pentane was removed at ambient temperature and 400 mm pressure, and the product was evaporatively distilled at ambient temperature and 0.15 mm in a closed sublimator yielding 0.372 g (64% of theoretical, better than 99% pure by glpc) of pale yellow crystals which liquefied at 5°. (Since the product is a liquid below 5°, a coolant at -10° was circulated through the condenser during the distillation.) An elemental analysis of this material was obtained.

Anal. Calcd. for $C_8H_{12}N_2$: C, 70.55; H, 8.88; N, 20.57

Found: C, 70.61; H, 9.11; N, 20.66

Purification of the product by preparative vapor phase chromatography (12' x 3/8" 12% Apiezon L-KOH (4:1) on Chromosorb W A/W DMCS 60/80 mesh column, 200° column temperature and 250 ml/min flow rate) followed by evaporative (4.7 mm, 30° heating block) or Vigreux (4.4 mm, 75° vapor, 90° oil bath) distillation yielded a colorless liquid, $n_D^{23.5}$ 1.5157, whose uv spectrum in cyclohexane exhibited an inflection at 2400-2250 Å (ϵ = 4670-6050). The ir spectrum of the product (neat and in CCl_4) showed important bands at about 3100 (weak), 3030 (weak), 1650 (weak), 1565 (weak), 750 (strong), and 700 cm^{-1} (weak) which are attributed to the cyclobutene moiety and 1605 cm^{-1} (strong) which is attributed to the carbon-nitrogen double bond. The nmr

spectrum of the product in CCl_4 showed a 1-proton doublet at 6.50 δ ($J = 2.5 \text{ Hz}$) (cyclobutene olefinic proton), a 1-proton triplet at 6.14 δ which is composed of two overlying doublets ($J = 2.0$ and 2.5 Hz) (cyclobutene olefinic protons), two 1-proton multiplets centered at 4.71 and 3.27 δ (bridgehead protons), a 6-proton singlet at 2.87 δ (methyl protons), and a 2-proton multiplet centered at 2.40 δ (methylene protons).

Similar yields of 2a were obtained when 0.518 g (0.0031 mole) of 2-dimethylamino-3H-azepine in 1.5 liters of pentane was irradiated with 3000A. lamps in a Rayonet reactor. The photolyses were quantitatively followed by glpc with 0.154 g (0.000107 mole) of n-decane as an internal standard in the reaction solution. During the course of the reactions, 10 ml aliquots were placed in 15 ml graduated tubes and concentrated by distillation. After 7-hours irradiation, a 72 $\pm$ 5% yield (based on reactant consumed) of photoproduct was obtained; 16% starting material remained (see table 2, and appendices 1 and 2). Figure 1 shows weight of product formed, weight of reactant remaining, and the sum of their weights as a function of irradiation time. In one photolysis in which the solution was not purged of oxygen prior to irradiation, a 63 $\pm$ 5% yield of photoproduct (based on reactant consumed) was obtained after 11 hours irradiation; 10% starting material remained (see table 3 and figure 2).

Photolyses (3000A) of 2-dimethylamino-3H-azepine (1a) in ether

A solution of 0.556 g (0.00408 mole) of 2-dimethylamino-3H-azepine in 4 liters of anhydrous ether was irradiated with the Hanovia medium pressure arc through a pyrex filter absorbing wavelengths below 280 mu. As in the case of the photolytic reactions of 1a in pentane, a single photoproduct was observed at a retention time of 4.7 minutes. Also, as in the pentane photolyses, a small amount of another product at a retention time of 1.9 minutes was barely detectable. The reaction was terminated after five hours due to buildup of a brown solid on the Hanovia well. The ether was removed by distillation at atmospheric pressure. After one-half of the ether was removed, 0.050 g of the brown solid was recovered by filtration through a Hersh funnel fitted with filter paper. The filtrate was further concentrated to 5 ml yielding a dark brown viscous liquid from which 0.042 g (9% yield based on starting material consumed) of a colorless mobile product and 0.065 g of starting material were obtained by preparative glpc.

The brown solid was dried in an Abderhalden (CCl_4) overnight under high vacuum. This solid did not sinter when taken to 350° . Its ir spectrum (KBr pellet) displayed broad bands centered at 3300 and 1600 cm^{-1} .

Anal. Found for solid: C, 53.02; H, 6.07; N, 13.86; ash, 2.4

Total: 75.35

O_2 by difference: 24.65

In a similar experiment, irradiation through a corex filter in conjunction with a filter solution which isolated the region 2600-3400A gave product at a retention time of 4.7 minutes, and a barely detectable amount of a minor product at a retention time of 1.9 minutes. The reaction was terminated after 3 hours. By then essentially all starting material had been consumed. The clear yellow ethereal solution was concentrated to 5 ml yielding a dark brown fluid liquid from which 0.115 g (20% yield based on starting material consumed) of 2a was obtained by preparative glpc.

The ir and nmr spectrums of the photoproduct were identical to those spectra of 2a obtained from the photolysis of 2-dimethylamino-3H-azepine in pentane.

Photolysis (3000A) of 2-dimethylamino-3H-azepine (1a) in ethanol

A solution of 0.119 g (0.00875 mole) of 2-dimethylamino-3H-azepine in 650 ml of absolute ethanol (200 proof) was irradiated with 3000A lamps in a Rayonet reactor. Only one major product (retention time 4.7 minutes) was obtained; a trace of a product with a retention time of 1.9 minutes was also observed. After 1 hour irradiation, essentially all starting material was consumed. After removal of the alcohol by distillation at atmospheric pressure, the photoproduct was isolated from the residual brown oil by preparative glpc. A product yield was not measured. The spectrum of the collected material was identical to that of 2a.

Photolyses (2537A) of 2-amino-3H-azepine (1b) in pentane

A solution of 0.152g (0.00141 mole) of 2-amino-3H-azepine in 1.5 liters of pentane was effected by warming the reaction vessel in a water bath. On cooling the reaction vessel to ambient temperature, the azepine remained in solution. The solution was irradiated for 140 minutes with 2537A lamps in a Rayonet reactor. On termination of the reaction, the solution was light brown in color and contained some brownish particles. There was no appreciable film on the wall of the reactor except at the surface of the solution. The solvent was removed on a rotary evaporator under water vacuum to yield 0.150g of a brown solid. This was sublimed at 0.15 mm and 60° (oil bath) and 0.0755g of a white sublimate was collected. The percentages of product and unreacted starting material in the sublimate were determined by glpc analysis using n-decane as an internal standard. A solution of 0.0465g of the sublimate and 0.1030g of n-decane in absolute ethanol (see appendix 4) was analyzed on a 14' x 1/8" Apiezon L-KOH (4:1) Chromosorb P regular 60/80 mesh column, 160° column temperature and 45 ml/min. flow rate. Retention times of starting material and product were 13.5 and 9.7 minutes respectively. The areas of the product, starting material, and n-decane were measured with a planimeter since the product peak was unsymmetrical and the small amount of unreacted starting material constituted a shoulder on the tail of the product peak. The area ratios of each component

relative to n-decane were calculated and by comparison with a calibration of weight ratio vs. area ratio it was determined that the sublimate was essentially product (less than 1% starting material was present). Therefore, based on reactant consumed, a 50% conversion of lb to product was obtained (see appendix 4).

In a manner similar to the above, 2-amino-3H-azepine was photolyzed for 70 minutes. After removal of the solvent the residual brown solid was sublimed to yield 0.0625g of sublimate and 0.0865g of residue. The combined weight of sublimate and residue represents a mass balance of 98%. The sublimate contained 97% product. Therefore, based on reactant consumed, a 40% conversion to product was realized. The sublimate was recrystallized from ether and resublimed to yield a white product which melted at 125-126°.

The ultra-violet spectra of the product in cyclohexane showed only end absorption. Its infra-red spectrum (0.5 mg per 100 mg KBr) showed broad absorptions at 3310, 3115, 1670, and 1600 cm^{-1} and bands at 1525 (weak), 760 (strong), and 705 cm^{-1} (weak). When the spectrum was taken in 1,4-dioxane (saturated solution, 0.10 mm cell path), the broad absorptions collapsed and bands appeared at 3450 and 3350 cm^{-1} (indicative of the NH_2 group) and 1640 cm^{-1} (carbon-nitrogen double bond). Bands at 3100, 3030, 760, and 700 cm^{-1} (indicative of the cyclobutene moiety) also appeared in the solution spectrum. The nmr spectrum of the

product in pyridine- d_5 exhibited a 3-proton doublet at 6.48 δ (due to a cyclobutene olefinic proton and the hydrogens of the amino group), a 1-proton triplet at 6.20 δ ($J = 2.5$ Hz) which may be composed of two overlying doublets (cyclobutene olefinic proton), two 1-proton multiplets centered at 4.95 and 3.23 δ (bridgehead protons), and a 2-proton multiplet centered at 2.43 δ (methylene protons). Upon washing with D_2O the olefinic proton at 6.75 δ appeared as a doublet ($J = 2.5$ Hz). An elemental analysis of the product was obtained.

Anal. Calcd. for $C_6H_8N_2$:	C, 66.64	H, 7.46	N, 25.91
Found	C, 66.91	H, 7.49	N, 25.65

Photolyses (3000A) of 2-amino-3H-azepine in tetrahydrofuran

A solution of 7.390g (0.0634 mole) of 2-amino-3H-azepine in 750 ml of tetrahydrofuran was irradiated for fourteen hours with a Hanovia medium pressure mercury arc employing a corex filter absorbing wavelengths below 260 mu. The red solution obtained was evaporated on a roto-vac, yielding a brown semi-solid mass which could not be quantitatively removed from the evaporating flask. The mass removed was transferred to a sublimator and sublimed at room temperature and 0.05 mm. A solution of the sublimate (3.08g) in tetrahydrofuran was subjected to preparative vapor phase chromatography on a 12' x 3/8" column, 12% Apiezon L-KOH (4:1), 60/80 mesh A/W DMCS Chromosorb W. Glpc conditions were 300° detector, 250° injector, 180° column, 100 ml/min flow and 100 ma current. An 0.039g fraction (retention time 10.2 mins) and an 0.12g fraction (retention time 13.9 mins) were obtained. These were shown to be 2b and 1b, respectively by mixed melting point and spectral criterion.

Photolyses (2537A) of 2-amino-3H-azepine in methanol

A solution of 2.0g (0.0185 mole) of 2-amino-3H-azepine in 650 ml of methanol was irradiated in the Rayonet reactor with sixteen 2537 A lamps. Glpc analyses were performed on a 12' x 1/4" 20% Apiezon L-KOH (4:1) Chrom P 60/80 non-acid washed column (185° column temperature and 100 ml/min flow). Injections were made without prior concentration of the

aliquots taken during the run. After 7 hours irradiation, about one-half of the starting material was consumed. Although glpc analysis after 19 hours irradiation indicated some unreacted starting material, the reaction was terminated. The solution was concentrated on a roto-vac to a few milliliters (further concentration yields a semi-solid mass) and transferred to a sublimation flask. The remaining methanol was evaporated in a sublimation vessel under water-aspirator pressure, yielding a semi-solid mass. On applying high vacuum (less than 1 mm) to remove residual methanol, splattering of material onto the wall of the flask occurred. The sublimation condenser was installed and the apparatus was completely immersed in an oil bath. Sublimation at 0.1 mm and 50° followed. The sublimate was rephotolyzed in methanol until no more starting material could be detected by glpc analysis. The reaction solution was worked up as above yielding 0.9g of product (45% yield).

Photolyses (3000A) of 2-amino-3H-azepine in benzene-pentane

A solution of 2.055g (0.0190 mole) of 2-amino-3H-azepine in 650 ml of a mixture of 450 ml pentane and 200 ml of benzene was irradiated with sixteen 3000 A lamps in the Rayonet reactor. Prior to irradiation, helium was bubbled through the stirred solution overnight to remove oxygen. In order to minimize solvent loss due to bubbling the helium through the solution, the helium was saturated with solvent by

passing it through a benzene-pentane mixture. An external standard method was employed for quantitatively determining product yields. The external standard was prepared by dissolving 0.620g of diphenyl ether in benzene in a 250 ml volumetric flask. 5 ml of this solution was pipetted into a 10 ml volumetric flask and diluted with an aliquot from the reaction mixture. The solutions thus obtained were injected without prior concentration into a 12' x 14" 20% Apiezon L-KOH 4:1 Chrom P 60/80 non-acid washed column (185° column temp., 95 ml/min flow). A planimeter was used to measure areas since the reactant and product peaks were unsymmetrical. For this experiment it was assumed that the reactant and product have similar thermal conductivities. A 45% yield of product (based on reactant consumed) was obtained after 19 hours irradiation (see appendix 3, table 4, and figure 3). Prolonged irradiation (39 hours) reduced the conversion to 30%. It was subsequently found for photolyses of 2-amino-3H-azepine in pentane at 2537 Å, that the thermal conductivities of reactant and product are not equal and therefore product yields in this experiment are probably lower than stated.

Photolyses (2537A) of 2-ethoxy-3H-azepine (1c) in pentane

A solution of 0.450 g (0.00329 mole) of 2-ethoxy-3H-azepine and 0.757 g (0.00548 moles) of trans-decalin (internal standard) in 1500 ml of pentane was irradiated with 2537A lamps in the Rayonet reactor. Aliquots taken during the run were quantitatively analyzed by glpc (14' x 1/8" 12% Apiezon L-KOH (4:1) on Chromosorb P regular 60/80 mesh column, 160° column temperature and 45 ml/min flow rate). Reaction aliquots (10 ml) were concentrated by distillation to 1 ml. Both reactant and product gave symmetrical peaks. Aliquots were removed in 15 minute intervals over a period of four hours. Retention times for the major product and starting material was 4.0 and 4.5 minutes, respectively. A minor product appeared at a retention time of 1.9 minutes. The conversion of 2-ethoxy-3H-azepine to photoproduct was about 60% based on reactant consumed (appendix 5, table 6, and figure 6); the area ratio of the major product to the minor one was about 18:1. The solvent was removed by distillation at atmospheric pressure and the photoproduct was isolated by preparative glpc. The product was then evaporatively distilled at 18 mm and 54° (heating block) yielding a colorless liquid. An elemental analysis of the product was obtained.

Anal. Calcd for $C_8H_{11}NO$:	C, 70.04;	H, 8.08;	N, 10.21
Found:	C, 70.22;	H, 8.10;	N, 10.49

The ultra-violet spectrum of the product in cyclohexane showed only end absorption. Its infra-red spectrum (neat) had characteristic absorptions at 3100 (weak), 3025 (weak), 1655 (weak), 1595 (weak), 765 (strong), and 705 cm^{-1} (weak) which are attributed to the cyclobutene moiety and 1630 cm^{-1} (strong) which is attributed to the carbon-nitrogen double bond. The nmr spectrum of the product in CCl_4 showed a 1-proton doublet at $6.37\text{ }\delta$ ($J = 2.5\text{ Hz}$) (cyclobutene olefinic proton), a 1-proton triplet at $6.20\text{ }\delta$ ($J = 2.5\text{ Hz}$) which is composed of two overlying doublets (cyclobutene olefinic proton), two 1-proton multiplets centered at 4.72 and 3.28 δ (bridgehead protons), a 2-proton multiplet centered at 2.38 δ (ring methylene protons), a 3-proton triplet at 1.27 δ (ethoxy group methyl protons), and a 2-proton quartet at 4.15 δ (ethoxy group methylene protons).

Photolyses (3000A) of 2-ethoxy-3H-azepine (1c) in pentane

A solution of 0.445g (0.00324 mole) of 2-ethoxy-3H-azepine in 1500 ml of pentane was irradiated with 3000A lamps in a Rayonet reactor. The progress of the reaction was followed by vapor phase chromatography. An external standard method was employed for quantitative analysis and equal thermal conductivities were employed on the basis of their determination in photolyses at 2537A. The external standard was prepared by dissolving 0.267g of trans-decalin to 50 ml with pentane. One ml of this solution was added to 9 ml of the reaction mixture. This solution was concentrated by distillation to approximately 0.4 ml. Injections of the concentrated solution were made on a 12' x 1/8" 8% Apiezon L-KOH (4:1) on chrom P regular 60/80 mesh column, 130° column temperature and 60 ml/min. flow rate. After 5.5 hours the reaction was terminated with 8.5% of the starting material remaining. A 30% yield of the major photoproduct was obtained, which is based on the starting material consumed and equal thermal conductivities for reactant and product (table 5, appendix 5 and figures 4 and 5). The retention time (4.0 minutes) of the major product was the same as in the previous experiment. A product which wasn't previously observed appeared at a retention time of 4.5 minutes (retention ratio 0.91). It immediately followed the product and overlapped the

starting material. The yield of this minor product reached a maximum of 6% (based on reactant consumed and assumption of equal thermal conductivities for reactant and product) after 54 minutes, then decreased to 3% by the end (5.5 hours) of the reaction. Although the area ratio of the major photoproduct to the minor one was 10:1 when the reaction was terminated, the area ratio was only 3:1 after 54 minutes of irradiation.

In an attempt to isolate the less volatile product, a number of identical reactions were run under a variety of different chromatographic procedures.

In one case, temperature programming (18' x 1/8" 8% Apiezon L-KOH (4:1) chrom P regular 60/80 column, 4°/min, duo-dial setting 18, initial temperature 60°, hold at final temperature of 130°, 45 ml/min flow rate) was employed and it was found that the minor product was actually composed of two components which could not be resolved. Although the resolution between the minor (estimated retention time 23.3 min) and the starting material (estimated retention time 25.6 min) and major product (retention time 20.5 min) was improved, there was still some overlapping. Because the glpc resolution was poor, the minor product was not investigated further. Pure 2-ethoxy-3H-azepine (1c) and its bicyclo(3.2.0) valence isomer (2c) as well as a mixture of the two, at concentrations analogous to concentrations before and after the reaction, were subjected to the above temperature programming conditions. It was found that there was no decomposition of either pure material nor any interaction between them.

Photolysis of 2-ethoxy-3H-azepine (1c) in pentane in a Rayonet reactor employing 3000A and 2537A lamps

A solution of 1.020g (0.00744 mole) of 2-ethoxy-3H-azepine in 400 ml of pentane was irradiated in a Rayonet reactor. The wavelength of light used and the intensity of the light source was varied during the course of the reaction. Aliquots were periodically removed from the reaction mixture and uniform glpc sample injections were made without prior concentration of the aliquots. Both reactant and product gave symmetrical peaks (12' x 1/4" 20% Apiezon L-KOH (4:1) on chrom P regular 60/80 mesh column, 160° column, 100 ml/min). The decrease in reactant concentration was obtained from a calibration curve of the area of the reactant vs. injection size. The calibration curve was obtained by measuring the area of the reactant at various injection sizes of the control. The slope of the calibration curve was 0.349 ± 0.016 ; the deviation represents an error of about 4.6%. Initially the reaction mixture was irradiated for about 4½ hours with 3000A bulbs. A 30% conversion (based upon starting material consumed) to photoproduct was realized (assuming that starting material and photoproduct had similar thermal conductivities) (see appendix 5, table 7 and figures 7 and 8). After 4½ hours the area of the photoproduct was approximately 0.021 and that of the starting material was 0.279. Therefore 0.070 area units of starting material were consumed ($0.349 - 0.279 = 0.070$). The conversion to photoproducts is therefore $100(.021/.070) = 30\%$. The number of bulbs supplying

3000A light was gradually increased from eight to sixteen during the $4\frac{1}{2}$ hours exposure. Eight bulbs were used for the first $1\frac{1}{2}$ hours, 12 bulbs during the following hour, 14 bulbs over the next hour and finally 16 bulbs during the remaining $\frac{3}{4}$ hour. Essentially a linear plot was obtained with change in intensity of the 3000A light. After the $4\frac{1}{2}$ hours reaction time, the sixteen 3000A bulbs were removed and replaced with eight 2537A bulbs. Irradiation was continued for an additional 3-1/2 hours. The amount of starting material was now $1.020\text{g} \left(\frac{.279}{.349} \right) = 0.816\text{g}$ in ca. 367 ml solution (had removed a total of 33 ml solution during the first $4\frac{1}{2}$ hours reaction period). Therefore, the new concentration of starting material was now .00595 moles. During the final $3\frac{1}{2}$ hours reaction time, the product area increased to 0.054 and the reactant area decreased to 0.219. Therefore, the additional photoproduct formed may be represented by an area increment of $(0.053 - 0.021) = 0.032$ and the starting material consumed may be taken as $(0.279 - 0.219) = 0.060$. Therefore, during the 2537A irradiation a $100 \left(\frac{.032}{.060} \right) = 53\%$ conversion to photoproduct was realized. There appeared to be only one photoproduct which eluted at a retention time of 4.0 minutes when 3000A light was employed. On changing to the 2537A bulbs another photoproduct (estimated to be less than 5%) appeared at a retention time of about 1.9 minutes. The solution was concentrated on a rotary evaporator to about 5 ml. Preparative vapor phase chromatography of the

concentrated solution yielded the major photoproduct. Its ir spectrum was identical to that of the imidate ester prepared by the reaction of 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one with triethyloxonium fluoroborate (see page 128).

Photolysis (2537A) of 2-ethoxy-3H-azepine (1c) in methanol

A solution of 3.96g (0.029 mole) of 2-ethoxy-3H-azepine in 650 ml of methanol was irradiated with 2537A lamps in a Rayonet reactor for 35 hours. After four hours, a peak (12' x 1/4" 20% Apiezon L-KOH (4:1) Chrom P reg 60/80, 150° column, 100 ml/min.) developed at a retention time of 3.1 minutes, which had not been observed in photolyses experiments in pentane. A considerable amount of the major photoproduct had already formed, appearing at a retention time of 4.0 minutes. A small amount (ca. 3%) of a highly volatile material occurred at a retention time of 1.9 minutes. When the reaction was terminated the area ratio of the major product to the product of retention time 3.1 minutes was about 1.5:1. The major product was chromatographically indistinguishable from an authentic sample of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c). The minor product is presumably 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2d) (see page 133).

Photolysis of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) in pentane with a Hanovia medium pressure mercury arc employing corex and vycor filters

A solution of 0.377 g (0.00277 mole) of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene and 0.0975 g (0.000686 mole) of n-decane (internal standard) in 800 ml of pentane was irradiated with the Hanovia medium pressure mercury arc. Initially a corex filter was employed, but after one hour irradiation it was replaced by a vycor filter. The photolysis was continued for an additional two hours. Aliquots were taken during the course of the reaction and, after concentration by distillation were analyzed by vapor phase chromatography (14' x 1/8" 12% apiezon L-KOH (4:1) chrom P reg 60/80, 160° column temp., 45 ml/min). The retention times of the starting material and the major product of the reaction were 10.7 and 15.3 minutes, respectively. A small amount of another product was barely detectable between the starting material and major product, during the time of irradiation when the corex filter was employed. This material disappeared on substitution of the vycor filter. Irradiation with the vycor filter produced a barely detectable amount of a highly volatile product. A 3% yield of product was obtained after one-half hour irradiation employing the corex filter (see appendix 2, table 8 and figures 9 and 10). There was a small decrease in yield on irradiation for an additional one-half hour.

In order to determine the effect of a vycor filter, the following procedure was employed. The area of the starting material relative to the area of the internal standard was 2.58 initially. After the one-hour irradiation, it was 2.14. On substitution of the vycor filter the yield of product increased. The amount of product formed on photolysis through the corex filter was discounted (see page 123 for an example of how product yields are calculated when wavelength is changed during the course of the reaction). After one-half hour irradiation through the vycor filter, a 10% yield of product was obtained. After one-hour irradiation with the vycor filter, the conversion decreased to 4% and at the termination of the reaction the percent yield had decreased to 1%. Concentration of the reaction mixture by evaporation, and, preparative glpc yielded a product which was chromatographically indistinguishable from 2-dimethylamino-3H-azepine (1a), and whose ir spectrum was that of 2-dimethylamino-3H-azepine. The starting material was recovered by preparative glpc and found to be pure (2a) by nmr criterion.

F. Chemical Transformations

Synthesis of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) by ethylation of 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144) with triethyloxonium fluoroborate

The title synthesis was essentially effected by Paquette's⁸⁰ procedure. Typically, 7.2g (0.078 mole) of epichlorohydrin was added slowly, under nitrogen, to a solution of 14.6g (0.103 mole) of boron trifluoride etherate in 60 ml of anhydrous ether in a 250 ml 3-neck flask equipped with a mechanical stirrer and a fritted tube. The epichlorohydrin was added at a rate which maintained a state of constant gentle reflux. Gelatinous material formed which crystallized on continuous stirring. After stirring for two hours at room temperature, the ether was removed under vacuum by a fritted tube and the product was washed at least four times with 60 ml portions of anhydrous ether. The triethyloxonium fluoroborate was dissolved in 30 ml of methylene chloride. A solution of 7.0g (0.064 moles) of the lactam 144 in 45 ml of methylene chloride was added to the alkylating reagent, while the temperature was maintained between 10-15°. After stirring at room temperature for two hours, the solution was allowed to stand overnight under nitrogen. The solution was cooled below room temperature and decomposed by the careful addition of 16.0g of 50% aqueous potassium carbonate. The material which precipitated was filtered. The filtrate was placed in a separatory funnel and the organic layer was removed, dried over magnesium sulfate, and filtered. The methylene chloride

was distilled at atmospheric pressure and the residual oil was distilled through an 18" Vigreux column at 67° vapor and 3.5 mm to yield 6.0g (69%) of colorless distillate. This liquid was subjected to preparative vapor phase chromatography. Evaporative distillation (54° at 18 mm) of the material collected from the gas chromatograph yielded a colorless liquid (b.p. 86° at 41 mm, n_D^{21} 1.4701). The infra-red spectrum (neat) of the product showed absorptions at 3100 (weak), 3025 (weak), 1655 (weak), 1630 (strong), 1595 (weak), 765 (strong) and 705cm^{-1} (weak). Its nmr spectrum in CCl_4 showed a one-proton doublet at 6.37 δ (J: 2.5 Hz) and a one-proton triplet at 6.20 δ (J: 2.5 Hz), one proton multiplets centered at 4.72 and 3.28 δ , a two-proton multiplet at 2.38 δ , a two-proton quartet at 4.15 δ , and a three-proton triplet at 1.27 δ . Its uv spectrum in cyclohexane showed only end absorption.

Although the elemental analysis of 2c obtained by photolysis of 1c was satisfactory, the elemental analysis of 2c obtained in the alkylation reaction consistently indicated a carbon content about 1% below the calculated amount.

Anal. Calcd. for $\text{C}_8\text{H}_{11}\text{NO}$: C, 70.07 H, 8.02 N, 10.21

Found: C, 68.96 H, 8.20 N, 10.53

Careful vapor phase chromatography indicated a small shoulder on the front side of the 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) peak. The retention time of this shoulder was essentially indistinguishable from a small amount of an

impurity which usually was formed during the triethyloxonium fluoroborate alkylation of 1,2-dihydro-3H-azepin-2-one (143) to 2-ethoxy-3H-azepine. This impurity was isolated during the preparative glpc workup of 2-ethoxy-3H-azepine and was assigned the structure 1-chloro-2,3-diethoxypropane based on its infra-red and nmr spectra and refractive index (see page 105). Meerwein^{82,83} extensively studied the formation of triethyloxonium fluoroborate by the reaction of epichlorohydrin and boron trifluoride etherate in excess diethyl ether, and Topchiev⁸⁴ had discussed the formation of tertiary oxonium fluoroborates including the work of Meerwein. Considering the discussions of Meerwein and Topchiev it is not unreasonable that a small amount of 1-chloro-2,3-diethoxypropane could be formed under the experimental conditions employed for the in situ alkylation of 1,2-dihydro-3H-azepin-2-one (143) and of 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144), and in fact, 1-chloro-2,3-diethoxypropane could be sometimes seen as a contaminant in the nmr spectra of (2c). Approximately 5% of 1-chloro-2,3-diethoxypropane would be required as a contaminant in 2c in order to reduce the carbon content of 2c from 70.07 to 68.96. The shoulder on the peak of 2c was estimated to be about 5% of the total area.

Thermal conversion of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) to 2-ethoxy-3H-azepine (1c)

A solution of 0.357 g (0.0026 mole) of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene in 25 ml. of hexane was added dropwise in twenty minutes to a vertically mounted pyrolysis column (6' x 0.75" column packed with pyrex helices). The column was preheated to 315° and swept by a stream of dry nitrogen (40 ml./min.) both before and during the course of the reaction. The material exiting from the column was collected in a receiver which was immersed in a dry-ice-isopropanol bath. After the addition was completed, the column was washed with 25 ml. of hexane. The pyrolysate and washings were combined and the hexane was removed by distillation at atmospheric pressure. The residual oil was evaporatively distilled at 18 mm and 50° yielding 0.164 g of a colorless liquid. Preparative vapor phase chromatography (14' x 1/8" 12% Apiezon L-KOH (4:1) on Chromosorb P reg. 60/80, 160° column temp., 45 ml/min.) of this liquid gave 0.029 g of starting material and 0.108 g (30% yield) of product. The ir and nmr spectra of the product were identical to an authentic sample of 2-ethoxy-3H-azepine.

Synthesis of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) by the aminolysis of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) in dimethylamine

A solution of 0.645 g (0.0047 mole) of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene and 1 ml. of liquid dimethylamine was sealed in a Carius tube (pyrex brand glass, Corning no. 8640, 200 mm. length, 8 mm. I.D., 10 mm. O.D.) and heated in an oil bath at 50° for 13 hours. The tube was opened and the dimethylamine was allowed to evaporate. Analysis by glpc indicated the formation of only one product. The starting material was completely consumed. Although only a fraction of the product was isolated, the yield of this product appeared to be almost quantitative. A fraction of the residual brown oil was evaporatively distilled yielding 0.11 g of a colorless liquid. The product had the same ir and nmr spectra as the product from the photolytic reaction of 2-dimethylamino-3H-azepine in pentane.

Conversion of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) to 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) by ethanolysis

A solution of 0.222 g (0.00206 mole) of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene, 0.06 g (0.001 mole) of glacial acetic acid, and 60 ml. of absolute ethanol in a 100 ml. flask was refluxed for three days. After cooling, 0.056 g (0.001 mole) of potassium hydroxide was added to the solution. A fraction of the solution was distilled at 46 mm. The distillate containing ethanol and product was fractionated

by distillation at atmospheric pressure. The residual oil was subjected to preparative vapor phase chromatography. (14' x 1/8" 12% Apiezon L-KOH (4:1) on Chromosorb P reg. 60/80, 160° column temp., 45 ml/min.) yielding 0.032 g of product. The ir and nmr spectra of this product were identical to an authentic sample of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene. See result section on alcoholysis of amidines (page 95).

Possible synthesis of 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2d) by methanolysis of 3-ethoxy-2-aza-bicyclo(3.2.0) hepta-2,6-diene (2c)

A solution of 0.0670 g (0.00048 mole) of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene in 10 ml. of methanol was refluxed in a 25 ml. flask for eight hours. The reaction was followed by vapor phase chromatography. The glpc column and conditions were the same as those employed in the photo-reaction of 2-ethoxy-3H-azepine in methanol (see page 125). Essentially all starting material was consumed. A single product was obtained, which was not isolated. This product, presumably 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene, had the same retention time (3.1 mins.) as a volatile product from the photo-reaction of 2-ethoxy-3H-azepine in methanol.

Possible synthesis of 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2d) by methanolysis of 3-amino-2-aza-bicyclo(3.2.0) hepta-2,6-diene (2b)

A solution of 0.111 g (0.00103 mole) of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene and 12 ml. of methanol (containing 0.002% formic acid) were refluxed in a 25 ml. flask. The reaction was followed by vapor phase chromatography. The glpc

column and conditions were the same as those employed in the photoreaction of 2-ethoxy-3H-azepine in methanol (see page 125). A single product was obtained, which was not isolated. This product, presumably 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene, had the same retention time (3.1 mins.) as a volatile product from the photo-reaction of 2-ethoxy-3H-azepine in methanol.

Attempted synthesis of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) by ammonolysis of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c)

A solution of 0.326 g (0.00238 mole) of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene, 1 ml. of tetrahydrofuran, and 0.5 ml. of liquid ammonia was sealed in a Carius tube (Pyrex brand glass, Corning no. 8640, 200 mm. length, 8 mm. I.D., 10 mm. O.D.) and heated in an oil bath at 44° for 24 hours. The tube was opened and the ammonia was allowed to evaporate. The residual brown oil which was analyzed by glpc was only starting material.

Attempted hydrolysis of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) to 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144)

A solution of 0.565 g (0.00413 mole) of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene in 20 ml. of water was placed in a 50 ml. flask and heated. The imidate ester (2c) appeared to dissolve when the temperature approached 75°, but the solution became cloudy again and at 90° a yellow oil separated. Prolonged refluxing for four hours resulted in a

red oil which was soluble in chloroform but was not characterized.

A mixture of 0.20 g (0.00146 mole) of the imidate ester (2c) and 3ml. of water was sealed in a Carius tube and heated. Two immisible layers were always present throughout the course of the reaction. After 35 minues (52°) the aqueous layer was cloudy and after two hours (68°) a white solid-like material appeared at the interface. The temperature was maintained at 68° for an additional ten hours. When the reaction was terminated the aqueous-layer was yellow and the oil-layer was a yellowish-brown. The tube was opened and the contents extracted with chloroform. The organic phase was separated, dried over sodium sulfate and filtered. The chloroform was removed on a rotatory evaporator yielding a viscous liquid which was not investigated further because the desired product is a solid.

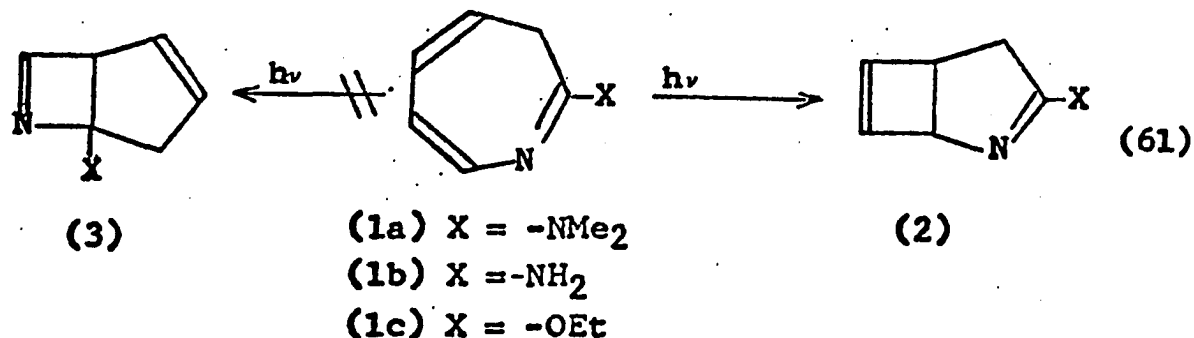
Attempted hydrolysis of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) to 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144)

A solution of 0.215 g(0.002 mole) of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene and 3ml. of water was heated in a 10 ml. flask. During the course of heating the reaction mixture to reflux, ammonia was detected by hydrion paper placed at the exit of the reflux condenser when the temperature reached 70°. After refluxing for fourteen hours, the reaction mixture was cooled in an ice-water bath, acidified with 2N HCL, and extracted five times with 3 ml. portions of chloroform. The organic phase was separated, dried over sodium sulfate, and filtered. The chloroform was removed on a rotatory evaporator yielding a yellow liquid which was not investigated further because the desired product is a solid.

DISCUSSION

I. Nature of the Photoproducts

Photochemical concerted intramolecular cycloadditions of 2-dimethylamino-3H-azepine (1a), 2-amino-3H-azepine (1b) and 2-ethoxy-3H-azepine (1c) should lead to the corresponding 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2) and 6-aza-bicyclo(3.2.0)hepta-2,6-dienes (3) by disrotatory processes. Conrotatory closure leading to azanorcaradiene structures should be sterically unfavorable because of the constraints imposed by the seven-membered ring. Sigmatropic rearrangement products should be unimportant since the 3H-azepine structure is the more stable tautomer^{75,85}. The experimental results are in accord with these views. However, selectivity leading to the predominant formation of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2) was observed in the photoisomerizations.



a. Spectroscopic Evidence for Structure

The ultraviolet spectrum of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2) showed only end absorptions in cyclohexane. The high energy of these transitions indicates disruption of the conjugation of their respective isomeric precursors

and suggests bridging of the rings. Therefore, there can be no conjugated double bonds, which indicates the absence of ring cleavage products or the formation of azanorcaradiene compounds.

The infra-red spectra of these 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2) are in accord with their proposed structures, exhibiting absorptions at about 3100 (weak), 3030 (weak) 1650-1670 (weak), 1600-1630 (strong), 1565-1600 (weak), 760 (strong) and 700 (weak) cm^{-1} . The absorptions at 3100, 3030, 1650-1670, 1565-1600, 760 and 700 cm^{-1} are consistent with a cyclobutene moiety.

Vogel⁷¹ reported bands for the bicyclic lactam 2-aza-bicyclo(3.2.0)hepta-6-ene-2-one (144) at 3122, 3050, and 1562 cm^{-1} which he attributed to cyclobutene⁸⁶. Bands at 3070, 1640 and 730 cm^{-1} have been assigned by Paquette⁶⁹ to a cyclobutene fused to a five membered ring in the same manner as Vogel's compound. Dauben and Cargill⁴² reported that bands at 3020, 1560 and 735 cm^{-1} which appear in the spectrum of bicyclo(3.2.0)hepta-6-ene (89) were characteristic of cyclobutene and in accord with the generalization of Lord and Evans⁸⁷. Weaker bands at 1625 and 1670 cm^{-1} have been assigned by Wiberg⁸⁶ as overtones of methylene vibrations. Interestingly, the 1-azetine structure has been reported¹⁰² to have similar absorptions at 3060, 3000, 1600, 810 and 760 cm^{-1} , and, therefore cannot be excluded by this data.

The band at 1605 cm^{-1} in 2a is indicative of the carbon-nitrogen stretching vibrations of the amidine chromophore. The amidine 1a displays two strong absorption bands between

1500 and 1600 cm^{-1} . Such bands have been attributed to the carbon-nitrogen stretching vibration in mono- and disubstituted amidines⁸⁸. Characteristically, 2-dimethylamino-3H-azepine (1a) and 2-diethylamino-3H-azepine display bands at 1510 and 1560 cm^{-1} ^{75,76}. The lower absorption band disappeared when 2-diethylamino-3H-azepine was hydrogenated⁷⁵. Therefore this band must be due to the conjugated system. After hydrogenation there was a strong absorption at 1600 cm^{-1} . Analogously, on passing from 1a to 2a the lower absorption band disappeared and an intense band appeared at 1605 cm^{-1} indicating disruption of the conjugation between the amidine chromophore and the ring double bonds. Therefore, it is reasonable to assume that the absorption at 1605 cm^{-1} is due to the carbon-nitrogen double bond. Again, the 1-azetine structure has a reported¹⁰² absorption at 1600 cm^{-1} . Therefore the ir spectra does not conclusively distinguish between the two possible structures.

The structures of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2) are unequivocally assigned on the basis of their nmr spectra. Although their nmr spectra do not permit a first order analysis, proton assignments are possible. These compounds exhibit a one-proton doublet at 6.36-6.40 δ , a one proton triplet at 6.11-6.20 δ , two one-proton multiplets in the range of 4.71-4.95 δ and 3.23-3.28 δ , and a two-proton multiplet at 2.38-2.43 δ .

The one-proton doublet at 6.36-6.40 δ and the one-proton triplet at 6.11-6.20 δ are assigned to the olefinic protons

of the cyclobutene ring. Dauben⁴², Vogel⁷¹, Chapman^{57,68}, and Paquette^{67,69,70} reported resonance positions for cyclobutene olefinic protons at 6.08-6.60 δ , which is in accord with our observations. Cyclopentene protons not adjacent to nitrogen were at 5.18-5.87 δ . Thus the cyclopentene structure expected for compounds 3a-c would not fit the data.

In addition, the olefinic protons at 6.36-6.40 δ and 6.11-6.20 δ have spin coupling constants of 2.5 Hz. The fact that one proton appears as a doublet while the other appears as a triplet (or two overlying doublets) is evidence for long range coupling for one of the protons. The magnitude of the coupling constant is very significant because coupling constants of cis-olefinic protons increase with ring size^{57,89-91}. The cyclobutene protons reported by Dauben, Vogel, and Chapman had a coupling constant of 2.5-3.7 Hz. This is in agreement with our observed coupling constants. In contrast, the coupling constants of cyclopentene protons were reported to be in the range of 5.4-7.0 Hz. Therefore, the photoproducts can only contain a cyclobutene ring on the basis of the chemical shift and coupling constants of the olefinic protons. This would again eliminate any possibility that the products were 6-aza-bicyclo(3.2.0)hepta-2,6-dienes (3).

The one-proton multiplets in the range of 4.71-4.95 δ and 3.23-3.28 δ are assigned to the ring junction protons. Similar protons in bicyclo(3.2.0)hepta-2,6-dienes and

2-aza-bicyclo(3.2.0)hepta-6-ene-3-ones absorb at 3.09-4.88 δ . When two bridgehead protons were present, the one on carbon adjacent to nitrogen resonated at the lower field position. These bridgehead protons were effected by long range coupling and are generally broad multiplets. This is in complete accord with our observations of broad complex multiplets in the range of 4.71-4.95 δ and 3.23-3.28 δ . The one at 4.71-4.95 δ can be assigned to the proton adjacent to the nitrogen atom. Only the 2-aza-bicyclo(3.2.0)hepta-2,6-diene (2) has two bridgehead hydrogens. Therefore, this also excludes the 6-aza-bicyclo(3.2.0)hepta-2,6-diene (3).

The two-proton multiplet at 2.38-2.43 δ is due to the methylene protons. The complexity of the multiplet is due to the non-equivalency of these protons, as well as possible long range coupling. Methylene protons in bicyclo(3.2.0)hepta-2,6-dienes and their aza-analogs are reported to have methylene protons which absorb in the region 2.30-2.70 δ ^{42,57,67-71}. Thus, this portion of the nmr spectra does not help us to distinguish between the two possible structures 2 and 3.

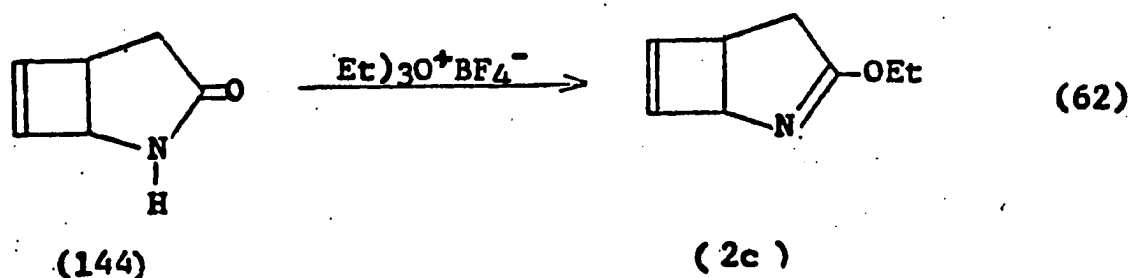
Thus, on the basis of elemental analysis and spectroscopic evidence the 2-aza-bicyclo(3.2.0)hepta-2,6-diene (2) structure can unequivocally be assigned to the photoproducts of the 3H-azepines (1). The ultra-violet spectra of compounds 2 rules out any conjugated systems; the infra-red spectrum shows the cyclobutene and amidine or imidate ester elements in the structure; and the nmr requires the 2-aza-bicyclo(3.2.0)hepta-2,6-diene assignments.

b. Chemical Evidence for Structure

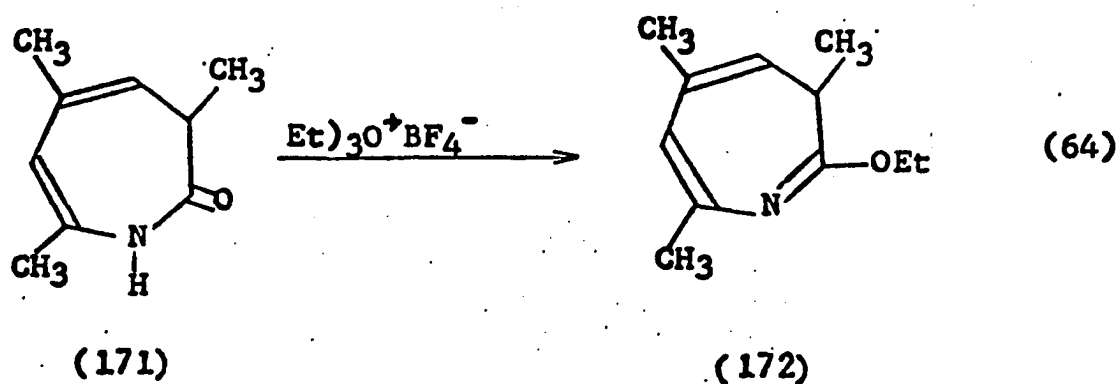
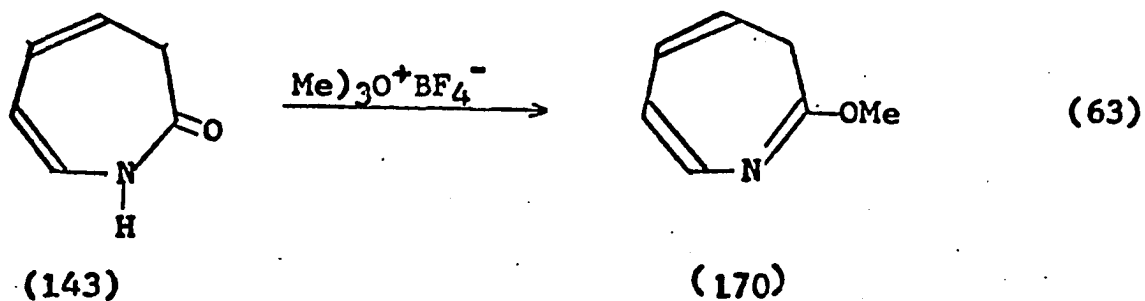
The structural assignments for the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2a-c) are supported by chemical transformations. In each case the identity of the synthetic compound was established by spectroscopic evidence. The uv, ir, and nmr. spectra of the synthetic products were identical to those spectra of those products obtained from the photoreactions.

1. 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c)

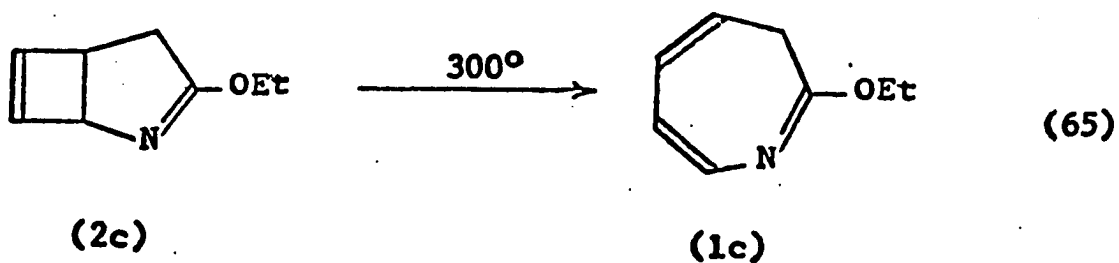
The structure of 2c was confirmed by alkylation of its lactam 2-aza-bicyclo(3.2.0)hepta-6-ene-3-one (144) whose structure is known⁷¹ (see page 54).



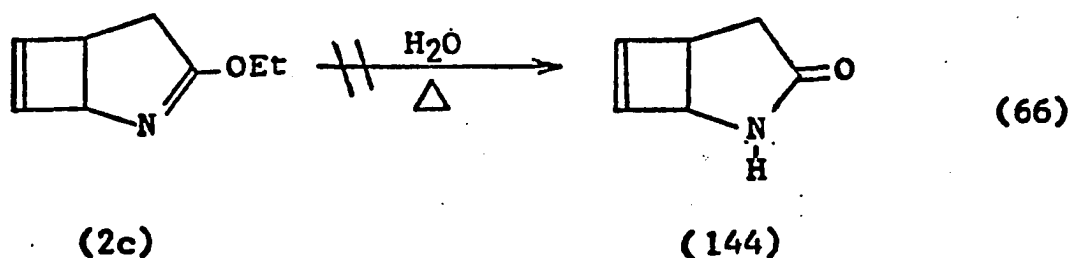
Similar alkylation reactions were carried out by Vogel⁷¹ and Paquette⁸⁰. Vogel reported that methylation of 1,2-dihydro-3H-azepin-2-one (143) with trimethyloxonium fluoroborate gave 2-methoxy-3H-azepine (170) and Paquette found that triethyloxonium fluoroborate treatment of 1,3-dihydro-3,5,7-trimethyl-2H-azepin-2-one (171) afforded 2-ethoxy-3,5,7-trimethyl-3H-azepine (172).



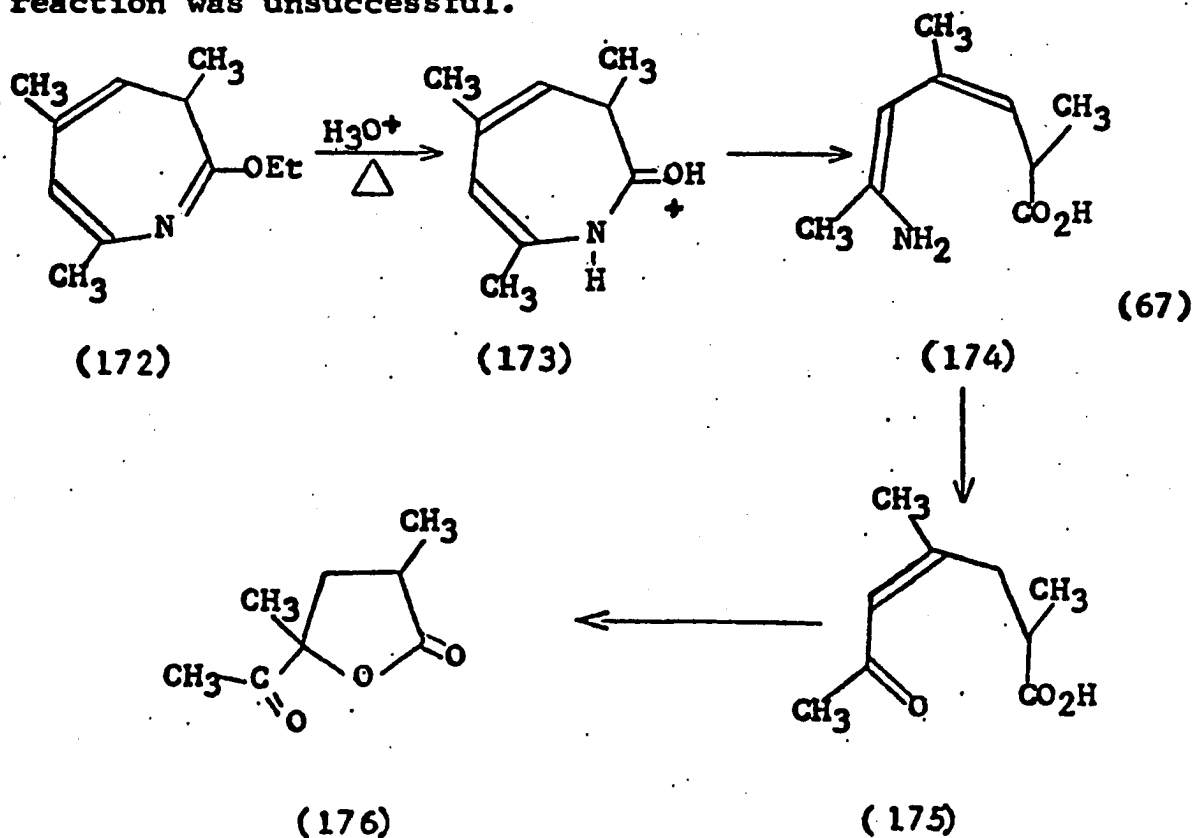
Further evidence for 2c was suggested by its thermolytic cycloreversion to 2-ethoxy-3H-azepine (1c). This thermal rearrangement is expected for the valence tautomeric structure 2c (see page 182).



A cursory attempt to hydrolyze 2c to its lactam (144)

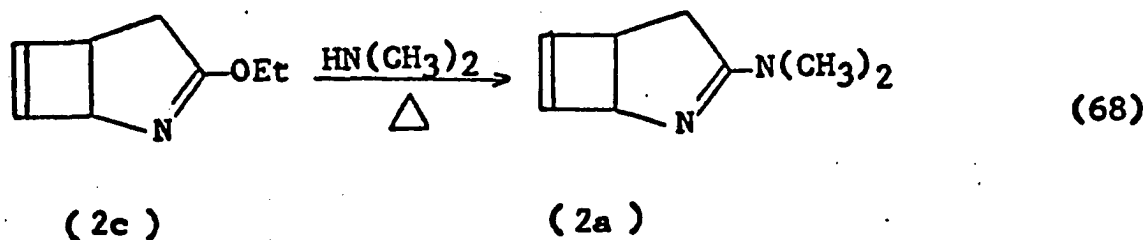


failed to produce the desired result. The hydrolysis of imide esters is well documented^{92,93}. Acidic solutions of imide esters yield the corresponding esters and ammonium salts⁹². Sometimes amides, instead of esters are the products⁹². However, the hydrolysis of 2c was carried out in a neutral medium since it had been reported that in the presence of acid, the imide ester 2-ethoxy-3,5,7-trimethyl-3H-azepine (172) rearranges^{80,94,95} via the conjugate acid of the lactam (171) to the furanone (176). Still the reaction was unsuccessful.

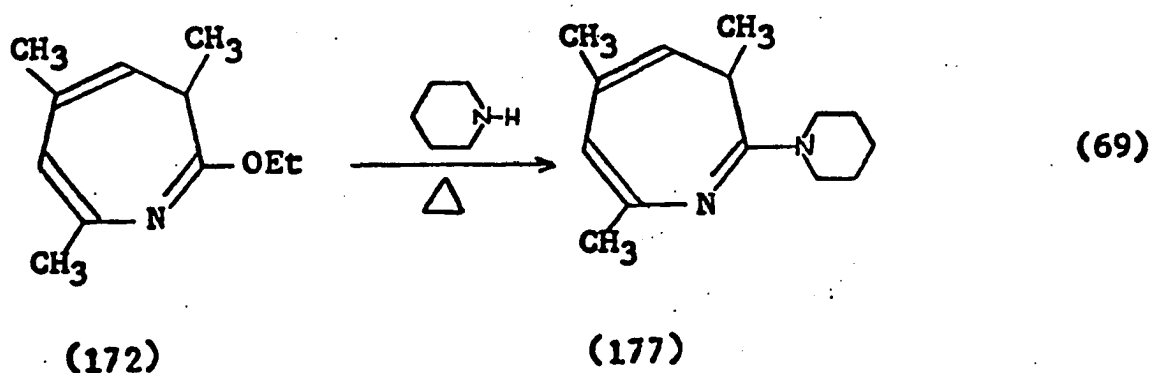


2. 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a)

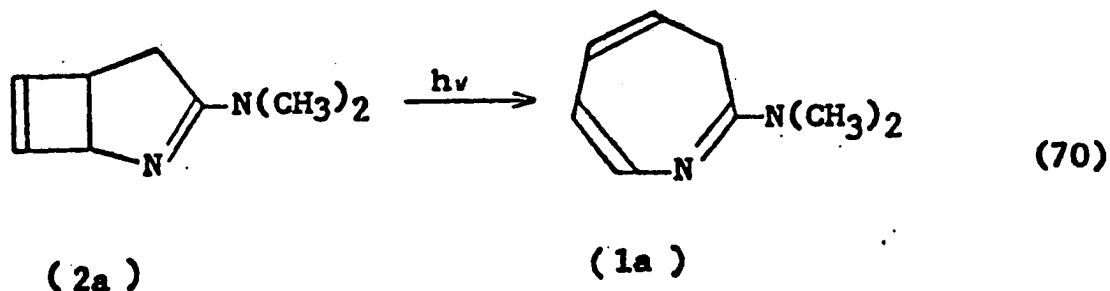
After relating the structure of 2c to that of the known lactam 144, the structure of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) was confirmed by aminolysis of 2c.



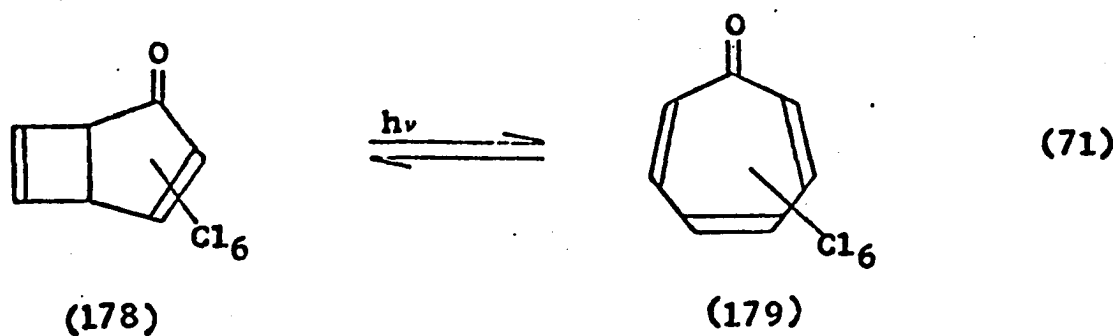
The conversion was anticipated by analogy with the known conversion of 2-ethoxy-3,5,7-trimethyl-3H-azepine (172) to 2-piperidino-3,5,7-trimethyl-3H-azepine (177)^{80,94}.



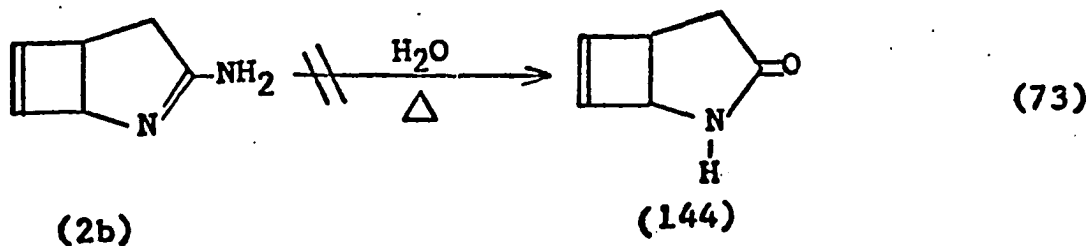
Further evidence for structure 2a was obtained by its photolytic cycloreversion in pentane, a rearrangement expected for the tautomeric structure 2a (see page 182).



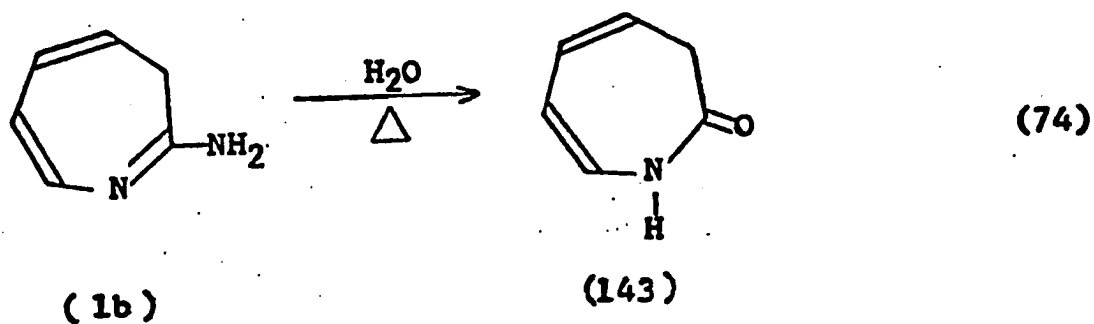
Only recently, the first example of a photochemical cycloreversion reaction of a fused four and five membered ring was reported. Thus, Scherer⁹⁶ obtained hexachlorotropone (179) by the direct photoisomerization of hexachlorobicyclo(3.2.0)hepta-3,6-dien-2-one (178).



A survey attempt to hydrolyze 2b to its lactam (144) failed to produce the desired result, albeit in a similar



reaction, Doering and Odum⁷⁵ converted 2-amino-3H-azepine (1b) to the lactam 1,2-dihydro-3H-azepin-2-one (143) in 90% yield by refluxing an aqueous solution of 1b in the absence of acid.



II. Effect of Reaction Conditions

Selectivity in the photoisomerizations of the 3H-azepines was observed at all concentrations and in all solvents and wavelengths employed. In all cases, the only major volatile products were the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes (2). Yields of 70%, 45%, and 60% were generally obtained for 2-dimethylamino-3H-azepine, 2-amino-3H-azepine, and 2-ethoxy-3H-azepine, respectively. A small amount of a more volatile product was usually detected in all of the photolyses but was most evident (less than 3%) in the case of 2-ethoxy-3H-azepine. No other products were detected by vapor phase chromatography except on photolysis of 2-ethoxy-3H-azepine when an uncharacterized product of lower volatility than 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) was found in a ratio of 1:3 to 2c after 54 minutes of irradiation. However, this product decreased rapidly on prolonged irradiation while the yield of 2c increased. A brown polymer accounted for the remainder of the material in the photolyses of the 3H-azepines.

A. Concentration

Dilute solutions of the azepines were required in order to achieve reasonable conversions in the photolyses. Concentrations of 0.001 to 0.03 molar were employed. At these concentrations there was no noticeable effect of concentration on product yields. Generally irradiation times of 3 to 7 hours were required for concentrations below

0.003 molar; about 15% starting material was unreacted. At the higher concentration levels longer irradiation times were required due to considerable buildup of brown polymer which interfered with the photoisomerization process by increasing the optical density of the solution or by forming a thin film of absorbent at the surface of the vessel. However, the photoisomerization could be taken practically to completion on rephotolization of the reaction mixtures after the polymeric material was removed.

B. Solvent

Photolyses of the 3H-azepines were extensively studied in pentane. Survey photolyses were conducted in ether, tetrahydrofuran, benzene, ethanol and methanol. Generally, highest yields of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes were obtained in pentane. When 2-ethoxy-3H-azepine was photolyzed in methanol, glpc analysis indicated the formation of two products. Although the products were not characterized, the major product was chromatographically indistinguishable from that of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c), and the minor more volatile product was chromatographically indistinguishable from the solvolysis product of methanol and 2c. Alcoholysis⁹² of imidate esters as the free bases leads on heating to alkoxyl exchange. Therefore, the minor product, presumably 3-methoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2d), may be formed either by alcoholysis of the 2c photoproduct or by photoisomerization of ester exchanged starting material, and, therefore, methanol is not a suitable solvent in this system.

C. Wavelength

Photolyses of the 3H-azepines were studied with 2537A and 3000A light. Generally highest yields of the 2-aza-bicyclo(3.2.0)hepta-2,6-dienes were obtained when the azepines were photolyzed at wavelengths near their maximum absorptions in the ultra-violet. Quantitative studies on the formation of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) indicated that the yield of 2c is wavelength dependent; it doubles on going from 3000A to 2537A light. An explanation for this behavior is not readily apparent.

III. Mechanism of the Photoisomerization

A. Early mechanistic theories for photo-electrocyclizations related to cycloheptatriene-like molecules

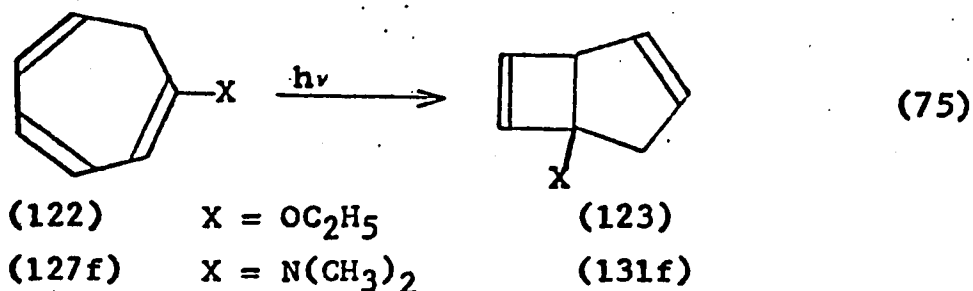
In our discussion of the literature we covered in detail a number of examples of all the known intramolecular photocyclization reactions of conjugated seven-membered ring compounds and their aza-analogs. In all cases, except one, the formation of the photoproducts could be explained by applying the orbital symmetry rules for concerted electrocyclizations. The one exception was the 3H-azepines studied by Ogata (see page 58). These compounds isomerized via diradical intermediates. The products of the photocyclization of the 3H-azepines (I) are readily explained by a concerted mechanism, and differ from the types of products reported by Ogata.

A number of the compounds encountered in the literature survey exhibited stereoselectivity in their photoisomerizations. Various mechanisms were considered to account for the direction of cyclization. A "dipolar" excited state mechanism was put forth by Chapman to rationalize the selectivity observed for the troponoids and their methyl esters (see page 11). Jones and Jones reported that orbital symmetry considerations did not offer a rationale for the stereoselectivity observed in the photoreactions of trimethylcycloheptatrienes, and, therefore invoked a steric argument to explain his observations (see page 41).

Paquette, likewise, invoked a steric argument to explain the selectivity observed in the photocyclizations of 1H-azepines (see page 55). Chapman observed selectivity in the photocyclizations of 1-alkoxycycloheptatrienes, but did not offer any reasons for his observations (see page 46).

B. Photoisomerization of 3H-azepines

The predominant formation of the 2-aza-bicyclo(3.2.0) hepta-2,6-dienes (2) from 2-substituted 3H-azepines is in direct contrast to the observations of Chapman and terBorg (see pages 46 and 50) in which only the bridgehead isomers 1-ethoxybicyclo(3.2.0)hepta-3,6-diene (123) and 1-dimethylaminobicyclo(3.2.0)hepta-3,6-diene (131f) were obtained from the photolyses of the corresponding cycloheptatrienes 122 and 127f.



C. HMO calculations; Orbital symmetry considerations

The construction of molecular models do not readily allow for a steric rationale for the observed selectivities in the 3H-azepine and cycloheptatriene systems. Therefore, the symmetry of the highest occupied molecular orbital was

considered to determine whether disrotatory closure to the alternative 6-azabicyclo(3.2.0)hepta-2,6-dienes (3) is symmetry allowed. An important question is why the photoisomerization exhibits the direction of selectivity it does at all in view of the observation of Chapman that only 1-ethoxybicyclo(3.2.0)hepta-3,6-diene (123) was obtained from the photolyses of 1-ethoxy-cycloheptatriene (122).

Descriptions of the symmetries of the molecular orbitals of the 3H-azepine and cycloheptatriene systems were determined by simple Huckel molecular orbital calculations (see appendices 6 and 7 for a description of the method and definitions of terms). The simple HMO method was employed since the method described in "Conservation of Orbital Symmetry"⁷ should not require more sophisticated calculations when applied to the question of whether a mode of ring closure is allowed.

One of the main values of the Huckel method lies in the facility with which it can be used to generalize chemical phenomena in a qualitative manner. In the case of hydrocarbons, the success of the Huckel theory depends to a large extent on the equivalence of all the α and β terms. When heteroatoms are introduced these equivalencies no longer hold. Therefore, Huckel calculations on molecules involving heteroatoms give much poorer agreement with experimental properties than do similar calculations on hydrocarbons. However, we were not concerned with the prediction of absolute physical

properties. Rather we desired to employ molecular orbital calculations in a qualitative way to look at the symmetry of the orbitals undergoing cyclization, and, thus, determine whether the unobserved cyclization products in the 3H-azepine and cycloheptatriene systems are symmetry allowed. For this purpose, the equivalency of the α and β terms of the carbon atoms, for a given system, is not an unreasonable assumption, and the α and β terms of the heteroatoms can be studied over a range of parameter values. In this regard, the Huckel method may be applicable to our problem. However, we recognize that it is dangerous to extrapolate from one type of molecule to another. As Dewar⁹⁷ has cautioned, "the fact that a given choice of Huckel parameters works well for one set of compounds cannot be taken as a justification for using them indiscriminately for compounds of other kinds."

The choice of a molecular orbital model, cyclic vs. linear, as well as the selection of a suitable model for σ - π interactions is important for a reasonable description of the orbital symmetries of the 3H-azepine and cycloheptatriene systems. The appropriate selection of models and parameters must be carefully considered before higher order molecular orbital calculations are undertaken, and, any mechanistic speculation on the selective nature of reactions based on the coefficients that are obtained from a simple HMO calculation are, at best, tenuous.

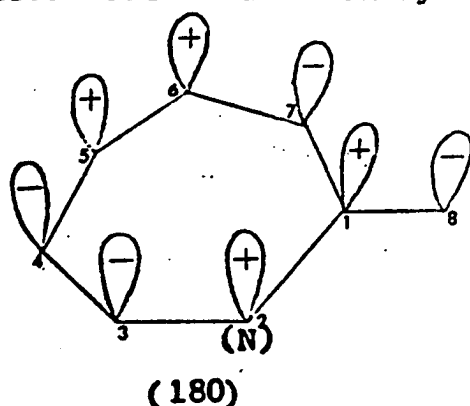
The HMO calculations employed to obtain the molecular orbitals of 3H-azepines should take into account possible σ - π interactions of the methylene group with the azaheptatriene chromophore. This problem is discussed in appendix 7. The HMO calculations were carried out employing a heteroatom model for the methylene carbon. Parameters for the coulomb and bond integrals suggested by Streitwieser⁵² for a methyl heteroatom were assigned to the methylene carbon. Similar parameters were employed by Simon⁵¹ in his HMO calculation of 1,3,5-cycloheptatriene (see page 32), and Srinivasan⁵³ referred to Simon's calculation in his discussion on the photochemical behavior of 1,3,5-cycloheptatriene in the liquid and vapor phases (see page 39).

D. Orbital symmetry considerations of 3H-azepines employing a cyclic model

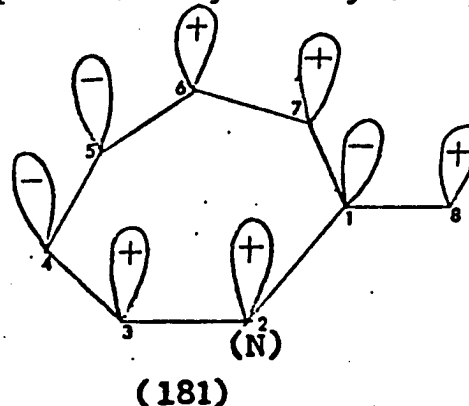
In initial HMO calculations, energy levels and coefficients were obtained for the 3H-azepine system employing a ten-electron eight-atom cyclic heteroatom model for the azepine system (table 9, appendix 8). The parameters used for the coulomb integral were $h_{gg} = 2.0$ and $h_{77} = 2.0$, and those for the resonance integral were $k_{18} = 0.8$, $k_{67} = k_{17} = 0.7$ and $k_{22} = 0.5$ (see appendix 7 for a discussion of the parameters for nitrogen, oxygen, and the methylene group). The electrons of the methylene-pseudo-heteroatom were considered to interact weakly with the π -system, and, a large Coulomb parameter $h = 2$ was used to reflect this (see quote on page 207, appendix 7). The orbital symmetry for the highest occupied molecular orbitals of the ground and first excited states are depicted in figures 180 and 181 of scheme 10, respectively. Inspection of figure 181 indicates that photochemical disrotatory closure across either termini 1,4 or 3,6 is symmetry allowed.

Scheme 10

Highest occupied molecular orbitals of the ground and first excited states of 2-ethoxy-3H-azepine in a cyclic system



Highest ground state
 $h_{77} = 0, 1/2, 1, \text{ or } 2$



First excited state
 $h_{77} = 0, 1/2, 1, \text{ or } 2$

However, experimentally preferential closure was across the 3,6 termini. Although there are uncharacterized products in all of the reactions, especially with 2-ethoxy-3H-azepine, they never account for more than a fourth of the product, and, therefore, do not alter the basic observation of selectivity in the photoisomerization.

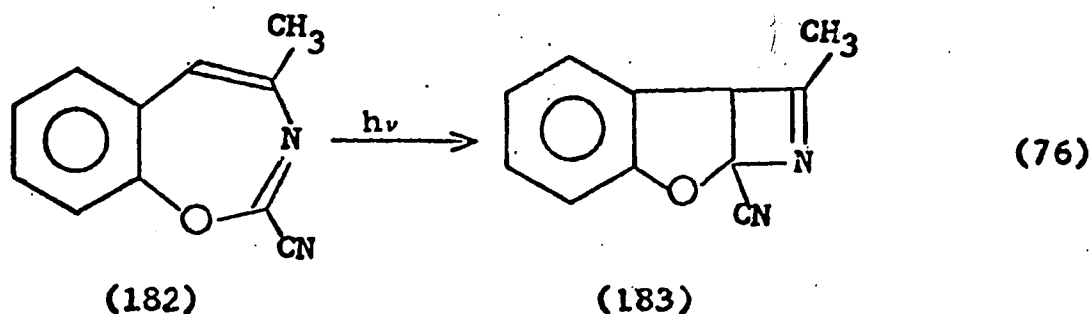
One of the possible deciding factors for the selective nature of the reaction might be due to loss of amidine or imidate ester resonance energy. Since the loss of resonance energy should not be as important with imidate esters as with amidines, the uncharacterized product in the photolyses of 2-ethoxy-3H-azepine may well be the isomer with the ethoxy group in the bridgehead position.

E. Possible structural factors that may influence reaction selectivity

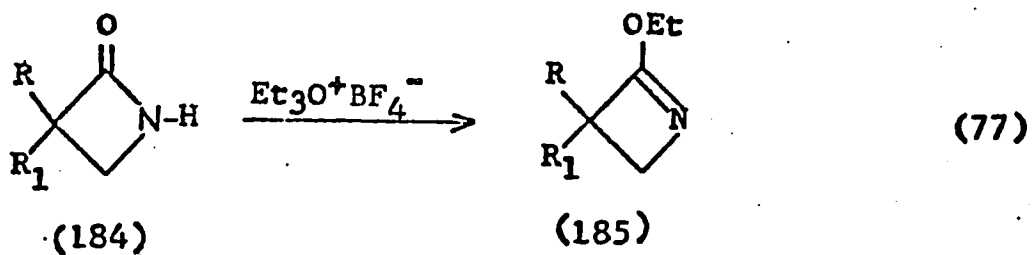
Another possible rationale is that the unique structural feature of 6-aza-bicyclo(3.2.0)hepta-2,6-dienes (3), the 1-azetine system (a four-membered ring containing a carbon-nitrogen double bond), can not exist.

When this research was initiated, Fowden and Bryant⁹⁸ believed they had a 1-azetine derivative but it was not adequately characterized. Reports⁹⁹ on the preparation of the 1-azetine structure by the reaction of glyoxal with amino acids could not be reproduced¹⁰⁰.

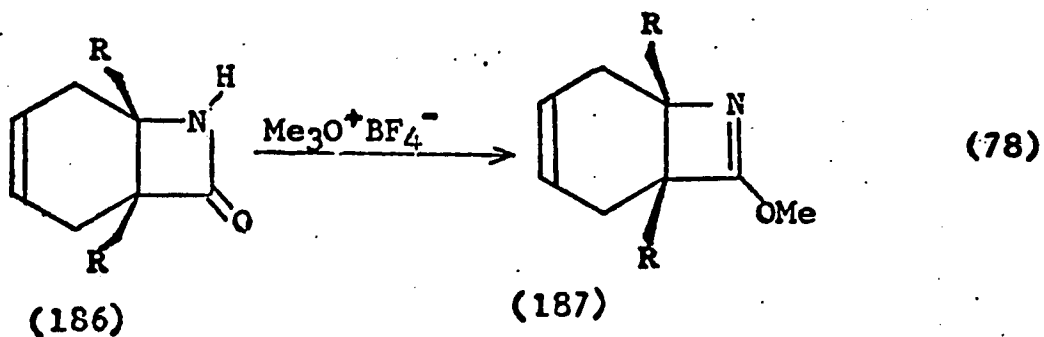
However, a number of 1-azetine compounds have recently been synthesized by photolytic and non-photolytic procedures. Thus, irradiation of the 1,3-oxazepine (182)¹⁰¹ gave the 1-azetine derivative 183, and, alkylation of the



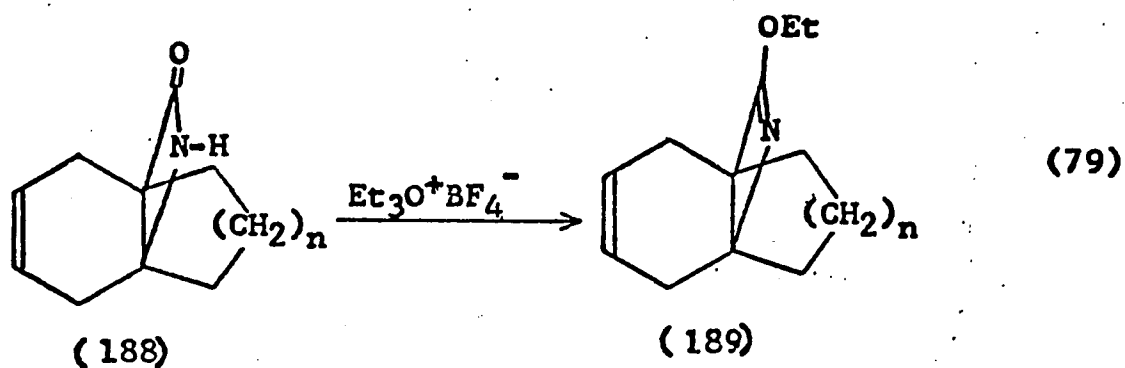
azetidin-2-ones (184)^{102,103}, (186)¹⁰⁴, and (188)¹⁰⁵ with trialkyloxonium fluoroborates gave the 1-azetines 185, 187, and 189, respectively.



- a. $R = R_1 = n\text{-C}_3\text{H}_7$; b. $R = \text{C}_6\text{H}_5$, $R_1 = \text{C}_2\text{H}_5$;
 c. $R = R_1 = \text{C}_6\text{H}_5$.



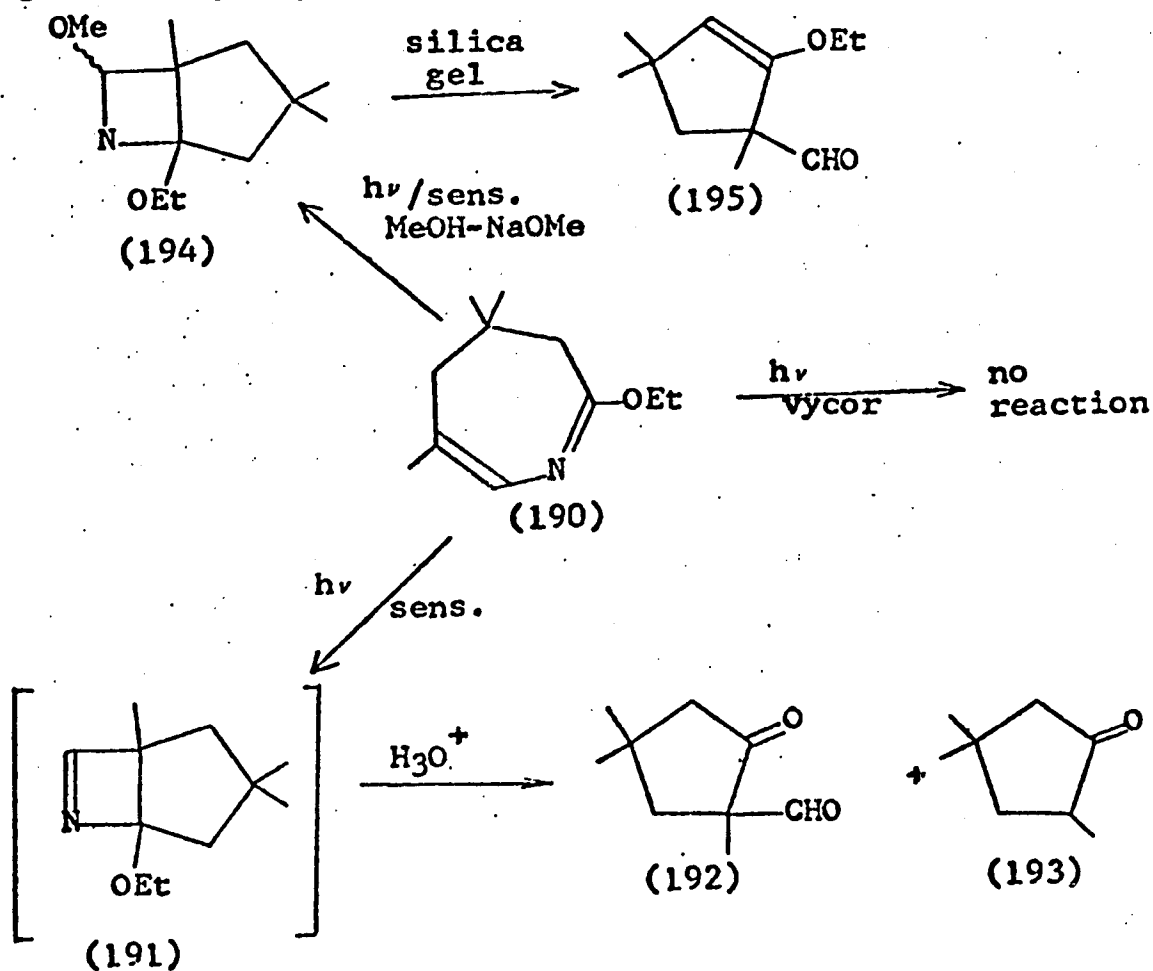
- a. $R = \text{H}$; b. $R = \text{CH}_3$



- a. $n = 1$; b. $n = 2$; c. $n = 3$

However, in the formation of the 1-azetine compound 183 by light-induced electrocyclization an alternative intramolecular cycloaddition reaction path did not exist and the formation of the 1-azetine structure did not require the concomitant loss of amidine or imidate ester resonance energy.

Very recently, the light-induced cyclization of a dihydro-3H-azepine to an unstable 1-azetine structure was reported¹⁰⁶. Photosensitization of 4,5-dihydro-2-ethoxy-4,4,6-trimethyl-3H-azepine (190) gave an unstable product which could not be isolated. However, acid hydrolysis of the oil gave the cyclopentanone derivatives (192) and (193) which



Scheme 11

(191)

Scheme 11

hyl-

Photo-reactions of 4,5-dihydro-2-ethoxy-4,4,6-trimethyl-3H-azepine

suggests that the unstable oil is 1-ethoxy-3,3,5-trimethyl-7-aza-bicyclo(3.2.0)hept-6-ene (191). Compound 193 is formed by a reverse aldol condensation of 192. Further evidence for 191 was obtained by trapping it with sodium methoxide to produce 194. This product is hydrolyzed to the cyclopentene (195) during silica gel chromatography.

Therefore, 1-azetine structures may be formed by a variety of methods and even in a photochemical reaction in which imide ester resonance energy is destroyed.

Therefore, although the deciding factor for the selectivity observed with 3H-azepines may be the loss of imide ester or amidine resonance energy, when there are two possible modes of closure, further considerations of the highest occupied molecular orbital (HOMO) in the excited state may offer another rationalization.

F. A second look at orbital symmetries in cyclic systems

1. Orbital symmetry considerations of 1-ethoxycycloheptatriene employing a cyclic model

In order to compare the orbital symmetry of our system to that of Chapman's, calculations were made for 1-ethoxycycloheptatriene employing a cyclic model (atom 2 being carbon instead of nitrogen, i.e., $h_{22} = 0$) and the parameters used in the 2-ethoxy-3H-azepine calculation. Table 10 gives the results of the calculation. The orbital symmetry obtained is the same as that for 2-ethoxy-3H-azepine (see figure 181 of scheme 10). Disrotatory closure across either termini 1,4 or 3,6 is permitted for 1-ethoxy-cycloheptatriene.

Therefore, the reasons for the observed selectivities in the photoisomerizations of the 3H-azepines and 1-ethoxycycloheptatriene are not apparent from these calculations. Interestingly, Chapman reported similar results for 1-ethoxycycloheptatriene in which a linear model was used for the molecular orbital calculations, but further details were omitted (see page 48).

2. Effect of changing the coulomb parameter h

The orbital symmetry depicted in figure 181 may be misleading, and other orbital symmetry schemes based on other parameters for the methylene-pseudoheteroatom may provide a better rationale for the observed modes of closure. Because the heteroatom model for the methylene carbon of

conjugated seven-membered cyclic systems may not weigh the contributions of the methylene group properly, a range of values for the h parameter of the coulomb integral of this group was studied. The h parameter was varied from 0 to 2. The interaction of the electrons of the methylene group with the π -system decreases as h increases (see appendix 7, page 209). In all cases, for both the 3H-azepine and cycloheptatriene systems photochemical disrotatory closure across either termini 1,4 or 3,6 is symmetry allowed, and, figure 181 describes all cases.

G. Non-applicability of correlation diagrams

So far in our discussion, we have only considered, in accord with the Woodward-Hoffmann electrocyclization rules, that the highest occupied molecular orbital of the reactant can determine the course of a concerted cyclization reaction. However, the safest procedure for determining whether a process is symmetry allowed is to follow the participating orbitals of both the reactant and product along the entire course of the reaction⁶. This is readily done, when symmetry elements (e.g. two-fold axis, plane of symmetry, etc.) are present, by the use of the orbital and state correlation diagrams as shown by Longuet-Higgins and Abrahamson¹⁰⁷. This method cannot be readily employed for the 3H-azepine and cycloheptatriene derivatives since symmetry elements are absent.

H. Bond order considerations in cyclic systems

1. Overall-bond orders

Another approach to this type of problem was first used by Simon who employed bond orders to determine the preferred electronic state (ground vs. excited) in the photoisomerization of 1,3,5-cycloheptatriene to toluene and bicyclo(3.2.0)hepta-2,6-diene, and suggested that the preferred product is that for which the π -bonding order of bonds being broken is smaller (see page 39). Jones and Jones also considered π -bond orders to rationalize the selectivity of substituted cycloheptatrienes (see page 43). Extension of Simon's criterion to the azepine system does not permit a consistent rationale for the observed selectivities. Since Jones and Jones did not give any details of their calculation, we also applied this criterion to additional cycloheptatrienes and had similar results.

Considerations of overall- π bond orders of bonds being broken in cyclic models of 2-ethoxy-3H-azepine and 1-ethoxycycloheptatriene indicates essentially equivalent bonding character for the 5-6 and 1-2 bonds, and, therefore, do not rationalize the experimental observations (table 13).

Alternatively, one may look at the π -bond order of bonds being made during the isomerization process. The greater the bond order of the central bond of the butadiene moiety the more bonding character already inherent in the

bond destined to become the double bond of the cyclobutene type ring. However, it was found that the 2-3 and 4-5 bond orders have essentially equivalent bonding character for both the azepine and cycloheptatriene models (table 13). Therefore, when viewed in this manner, the π -bond orders of new π -bonds being formed also do not rationalize the experimental results.

2. HOMO bond orders

Some precedent has been established for consideration of the π bonding order of only the highest occupied molecular orbital (HOMO) as a measure of bonding character. Hammond and coworkers¹⁰⁸ have noted that HMO calculations indicate an enhanced bond order for the central bonds of conjugated dienes on excitation and suggested that this may account for the characteristic photosensitization reactions of butadiene. Daudel and coworkers¹⁰⁹ reported that the photochemical cis-trans interconversions of stilbene may be due to a decrease in the central bond order in its lowest excited state. Although Zimmerman¹¹⁰ has noted the limitations of using only the highest occupied molecular orbital of the first excited state to predict bonding characteristics and has cautioned that a safer approach is to consider overall-bond orders, overall-bond orders failed to provide a rationale for the observed selectivities in the azepine and cycloheptatriene. Therefore, the HOMO bond orders were considered.

The HOMO bonding order of the 5-6 bond is about two to three times weaker than the 1-2 bond and the 4-5 bond has a more enhanced central bond character than the 2-3 bond, for both the azepine and cycloheptatriene systems (table 14). Both trends favor closure across the 3-6 termini in accord with the observed selectivity in the azepine system but not in accord with the observed selectivity in the cycloheptatriene system. Therefore HOMO bonding orders fail to predict observed selectivities.

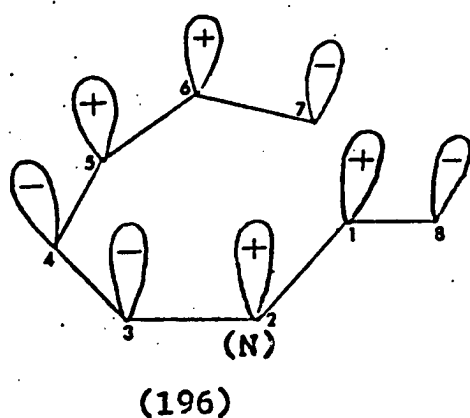
I. Linear systems

1. Orbital symmetry considerations in linear systems

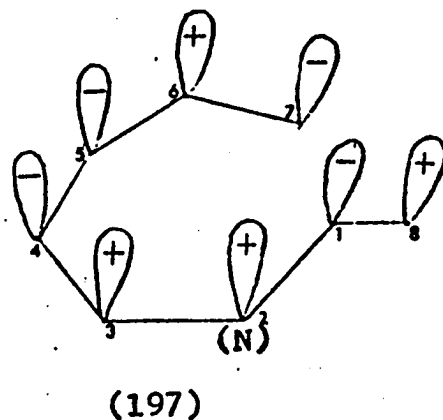
As in the case of electrocyclization reactions, orbital symmetry plays a central role in determining the course of sigmatropic reactions. Woodward and Hoffmann⁶¹ suggested that selectivity in sigmatropic rearrangements "may be explicable in terms of a preference for processes with the maximum degree of linear conjugation in the transition state." In this regard, Jones and Jones⁶² in their rationale of the selective sigmatropic photoreactions of 2,7,7-trimethylcycloheptatriene (113) noted that "the most consistent results are obtained using a linear rather than a cyclic model for the C-7 radical" (see page 44). A linear model was also employed by Chapman⁵⁷ in rationalizing the photo-induced sigmatropic hydrogen migrations of 7-methoxycycloheptatriene (121) and 1-methoxycycloheptatriene (122) (see page 48). Since linear models have been successfully

employed for sigmatropic reactions they were considered for the electrocyclizations of azepines and cycloheptatrienes.

The results of calculations on linear models are given in tables 11 and 12 for 2-ethoxy-3H-azepine and 1-ethoxycycloheptatriene. These linear models were obtained by setting $k_{17} = 0$, while maintaining the parameters $k_{67} = 0.7$, $k_{18} = 0.8$, $h_{22} = 0.5$ (for the 3H-azepine system), and $h_{77} = 0, 1/2, 1$ or 2 . Scheme 12 depicts the orbital symmetry for the highest occupied molecular orbitals of the ground and first excited states of the 3H-azepine and cycloheptatriene systems, when $h_{77} = 1/2, 1$, or 2 . Inspection of figure 197 indicates that photochemical disrotatory closure across either termini 1,4 or 3,6 is symmetry allowed.



Highest ground state
 $h_{77} = 1/2, 1$ or 2



First excited state
 $h_{77} = 1/2, 1$ or 2

Scheme 12

Highest occupied molecular orbitals of the ground and first excited states of 2-ethoxy-3H-azepine and 1-ethoxycycloheptatriene in a linear system

The changes which occur in the coefficients of the HOMO in the first excited states of 2-ethoxy-3H-azepine and 1-ethoxycycloheptatriene as h_{77} is varied from 0 to 2 is shown in schemes 13 and 14, respectively.

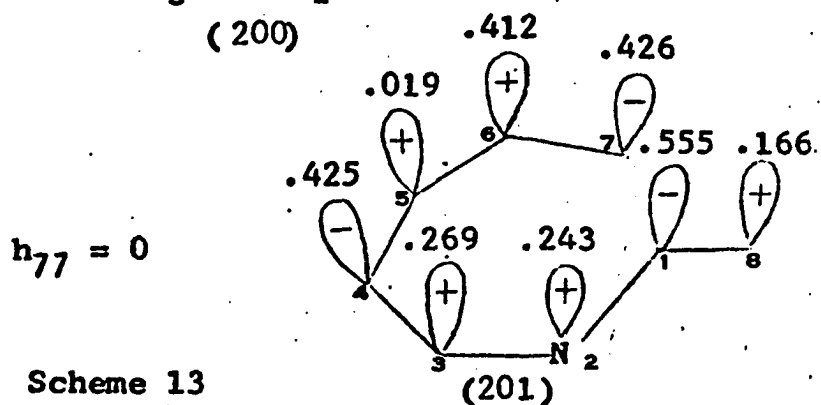
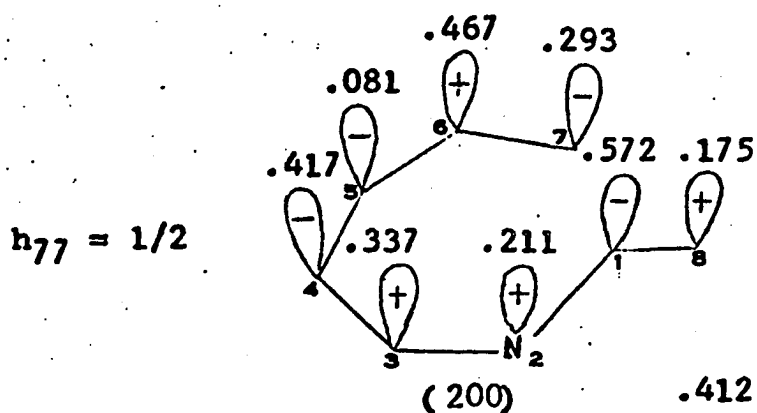
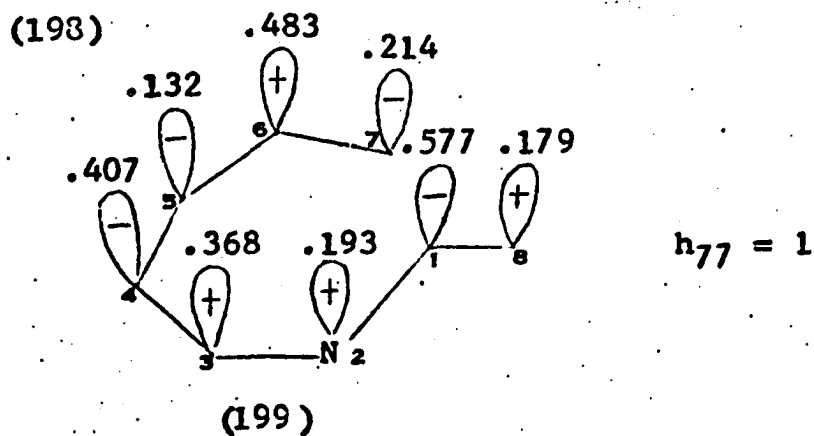
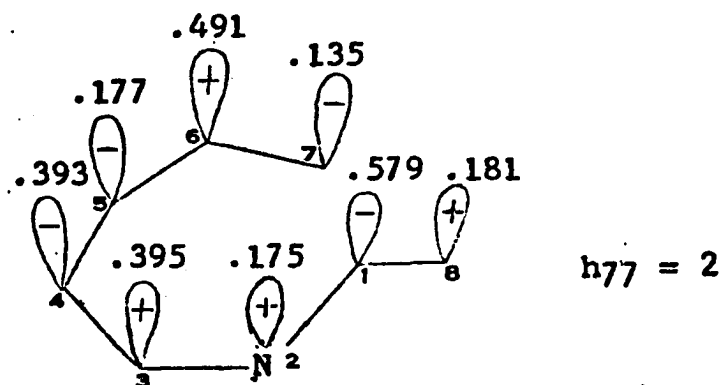
There is a new effect with the linear model in that a node develops between the 4 and 5 carbon atoms (figure 201 of scheme 13) or is very close to atom 5 (figure 205 of scheme 14) as h_{77} approaches zero. This effect is considered in Section L of the Discussion. It should be noted that the total symmetry of orbitals 3-6 does not permit it to be a valid molecular orbital for butadiene, and, therefore, does not represent the electrocyclization reaction center. This would be in accord with the closure of 1-ethoxycycloheptatriene, but not for the 3H-azepines.

2. Overall-bond orders in linear systems

Consideration of overall π -bond orders for linear models of the 3H-azepine and cycloheptatriene systems indicates essentially equivalent bonding character for the 5-6 and 1-2 bonds and for the 4-5 and 2-3 bonds (table 13, appendix 9), and, therefore, do not rationalize the experimental observations.

3. HOMO-bond orders in linear systems

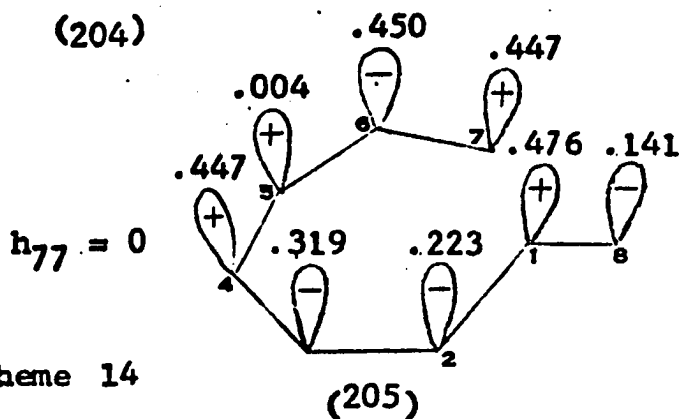
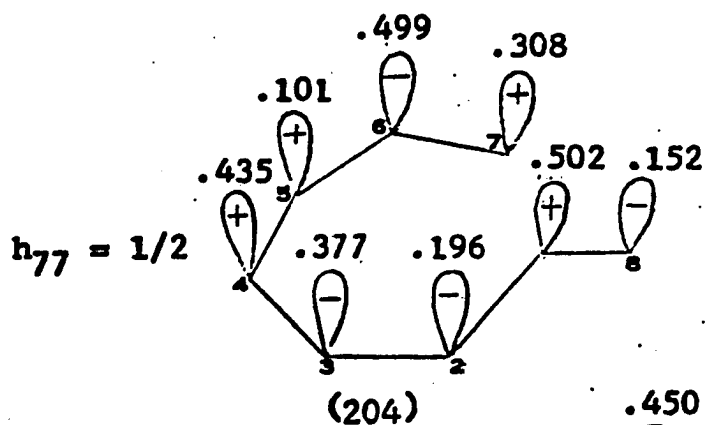
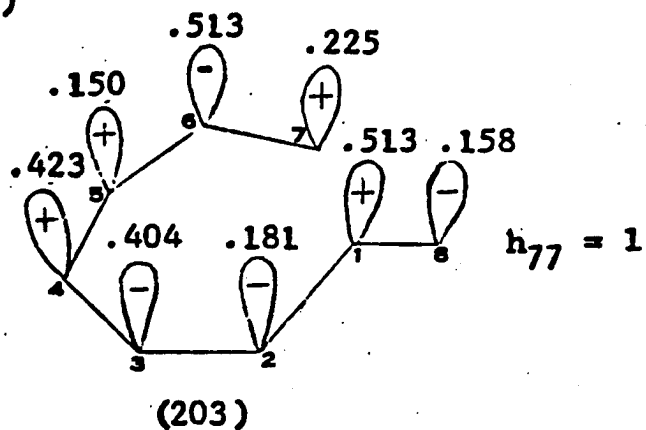
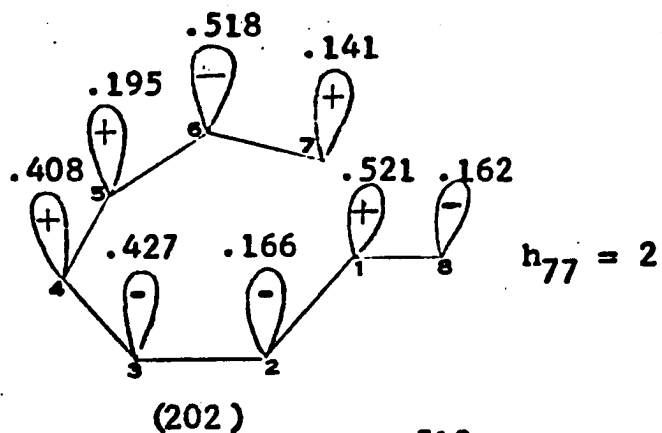
However, consideration of HOMO π -bond orders indicates that, when h_{77} is less than 1, the 1-2 bond has less bonding character than the 5-6 bond. While a node develops between the 4-5 bond, the bonding character of the 2-3 bond remains



Scheme 13

Effect of h_{77} on coefficients in linear system

Highest occupied molecular orbital of first excited state of 2-ethoxy-3H-azepine



Scheme 14

Effect of h_{77} on coefficients in linear system

Highest occupied molecular orbital of first excited state of 1-ethoxycycloheptatriene

high. This would be in accord with the closure of 1-ethoxycycloheptatriene, but not for the 3H-azepines.

J. Summary of results of orbital symmetry and bond order considerations in cyclic and linear systems

It is worthwhile noting that h_{77} has been varied over a reasonable range; at a value of 2 the contribution of a methylene group is essentially one expected for a heteroatom and at a value of zero it is essentially that expected for a carbon $2p_z$ orbital. It is reasonable to expect that the methylene contribution is actually someplace in between.

Therefore, orbital symmetry considerations and both overall- and HOMO bond orders of cyclic and linear systems do not offer a rationale for the selectivities of the combined systems.

This conclusion, however, is based on a simple Huckel molecular orbital calculation. It is possible that a different conclusion might be obtained by employing Hoffmann's extended Huckel method in which sigma as well as pi orbitals are considered.

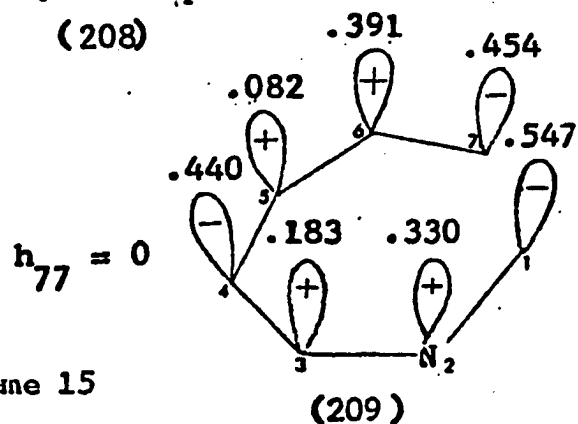
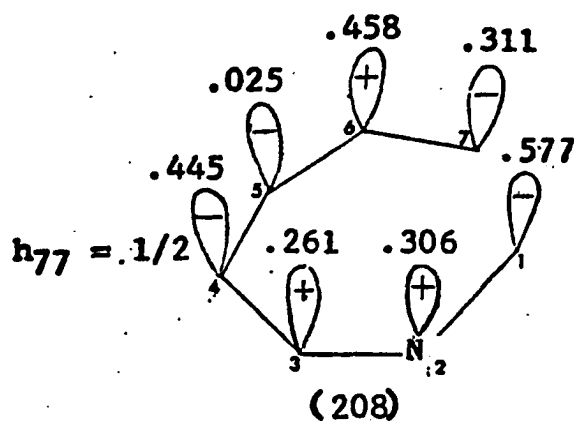
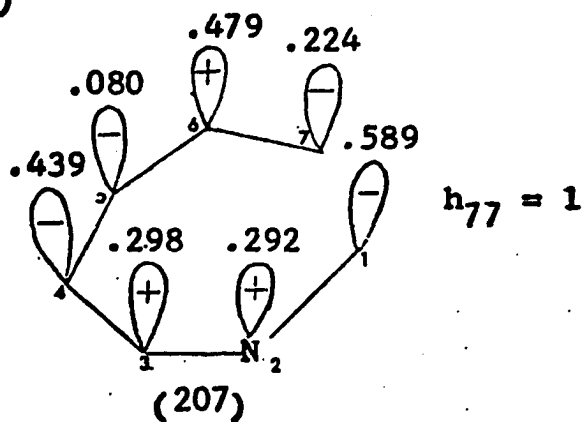
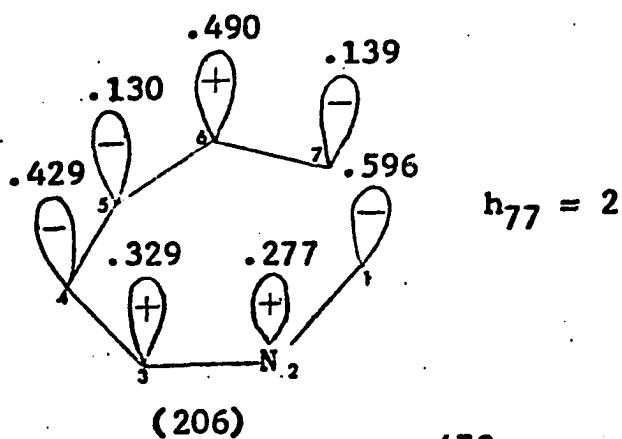
K. Orbital symmetry considerations of the parent 3H-azepine and cycloheptatriene in linear systems

Although, the HMO calculations performed do not offer a direct rationale for the selectivity in the 3H-azepine and cycloheptatriene systems, another look may offer an insight into some of the factors influencing the course of these reactions.

As discussed previously, there is some precedent for employing a linear model in these systems. It is only for a linear model that there is a greater tendency for closure

in the direction observed for 1-substituted cycloheptatrienes. In this regard, results of analogous calculations for the parent 3H-azepine parallel those of its derivatives.

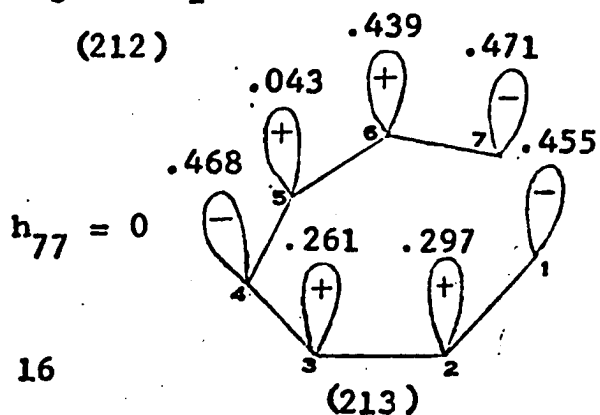
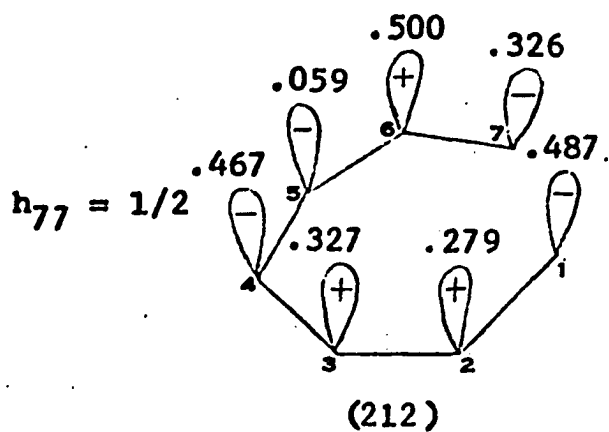
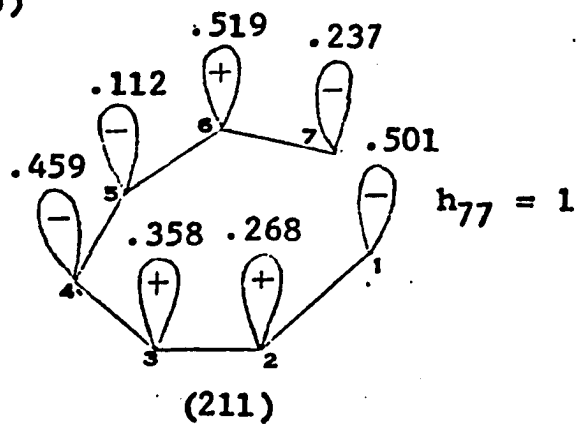
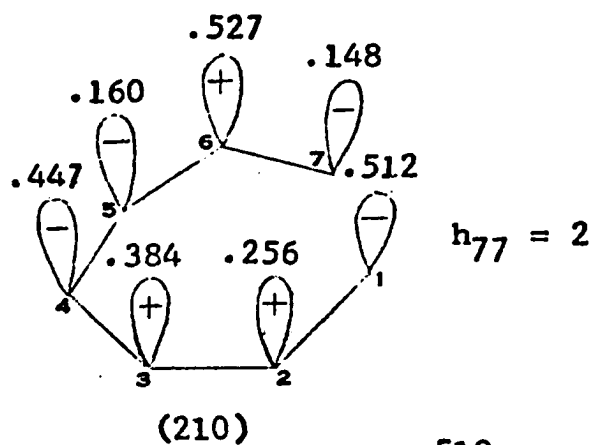
Scheme 15 shows the orbital symmetry of the HOMO of the first excited state as h_{77} is varied from 0 to 2. Therefore, the ring substituent is not required for nodal formation. Interestingly, when viewed by a linear model, cycloheptatriene, itself, shows a node between the 4-5 bond as h_{77} approaches zero (scheme 16). It may be that this is the normal condition for 3H-azepine, cycloheptatriene, 1-substituted cycloheptatriene, and 2-substituted 3H-azepines. Unfortunately, one is again forced to invoke the loss of resonance energy in order to explain the photoisomerizations of 2-substituted-3H-azepines.



Scheme 15

Effect of h_{77} on coefficients in linear system

Highest occupied molecular orbital of first excited state of 3H-azepine



Scheme 16

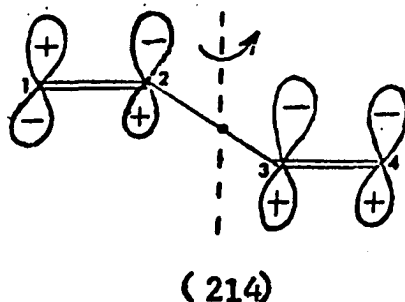
Effect of h_{77} on coefficients in linear system

Highest occupied molecular orbital of first excited state of 1,3,5-cycloheptatriene

L. An application of Fukui's method of orbital interactions

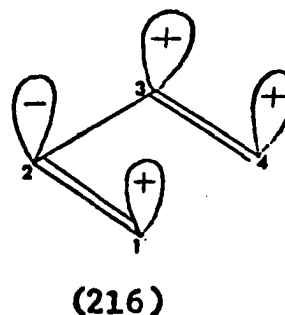
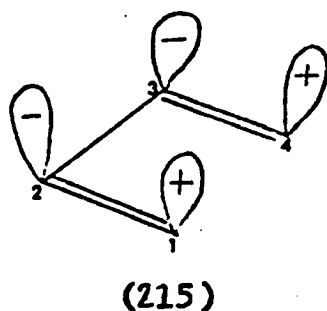
An important question may be asked. Arbitrarily assuming that the orbital diagram of figure 201 (see page 168) is a fair approximation of the symmetry of the highest occupied orbital of the first excited state of the cycloheptatriene system, can orbital symmetry considerations alone predict selectivity on ring closure? We will attempt to answer this question here.

In our orbital symmetry discussion, we never explicitly considered the inner lobes while we discussed the terminal lobes of the dienes which may undergo closure. However, they were implicitly under consideration because each orbital had to be a proper molecular orbital. The reason for this is due to a fundamental quantum mechanical principle. As Woodward and Hoffmann have pointed out⁷ "no molecular orbital may be at the same time symmetric and antisymmetric with respect to any existing molecular symmetry element. Thus, the orbital (214) is symmetric under rotation by 180°



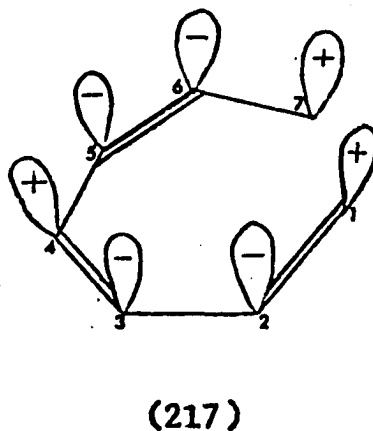
if atoms 2 and 3 are viewed, but antisymmetric if 1 and 4 are considered; it is not an acceptable molecular orbital of

butadiene." In the case of the first excited state of butadiene, the orbital (215) is allowed because it is



symmetric to a plane of reflection bisecting the reaction center. Orbital (216) is not allowed. The first excited state molecular orbital of butadiene is a priori orbital (215).

However, this a priori symmetry criterion may not be so evident when the diene is part of a more extensive conjugated system. A molecular orbital may be envisaged whose overall symmetry satisfies this criterion, but whose diene parts do not. The molecular orbital depicted in figure (217) is symmetric to a plane of reflection, and, therefore, satisfies this criterion as does its diene part, 1-4. However, its



diene part, 3-6, is both symmetric and antisymmetric to a

plane of reflection, and, therefore, does not meet this criterion. Therefore, the diene part is not a valid representation of a butadiene electrocyclization.

However, unless the diene parts in question are uniquely independent of the molecular orbital as a whole, this criterion may be deceiving. In our discussion we have tacitly assumed that we can consider the diene parts of an orbital as being independent of the orbital as a whole. Since viewing only a part of a molecule is, at best, an approximation, it is desirable to consider some precedent for doing so.

Fukui^{111,112} has put forth the concept that the orbital interactions between the HOMO (highest occupied molecular orbital) of one reactant and the LUMO (lowest unoccupied molecular orbital) of the other can determine the steric course of cyclic reactions of conjugated molecules. He stated that:

"a majority of chemical reactions should take place at the position and in the direction of maximum overlapping of the HOMO and the LUMO of the reacting species; in reacting species possessing a singly occupied molecular orbital (SOMO), this plays the part of the HOMO or of the LUMO, or of both."

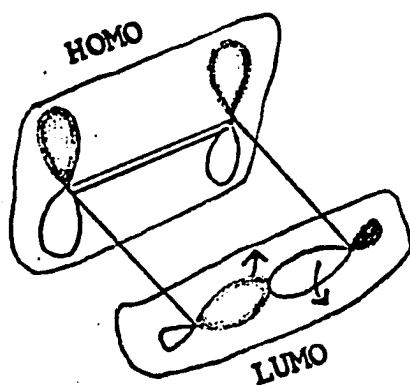
His method leads to the same predictions for the stereospecificity of concerted reactions as the Woodward-Hoffmann method.

In a number of examples discussed by Fukui, the reaction center did not encompass all the atoms of the molecule, or

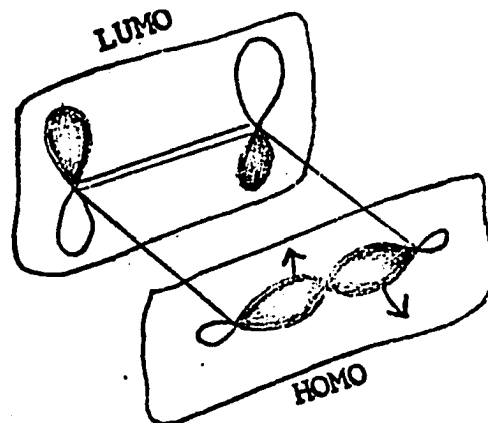
even of a conjugated system. Fukui¹¹¹ stated that his method involves:

"an approximation in which a molecule is partitioned into parts so that each part involves the one-half portion of a reaction center. These parts may be treated as if they were different molecules. Since in ordinary chemical reactions the configurational change takes place only in a limited portion near the reaction center and the remaining part is almost left unchanged, this approximation is usually very effective."

As an example of Fukui's orbital interaction method, consider the thermal ring opening of cyclobutene to butadiene. The process is illustrated in scheme (17). The overlapping of the HOMO-LUMO interaction leads to a conrotatory opening.



(218)



(219)

Scheme 17

The mode of the HOMO-LUMO interaction in the thermal ring-opening of cyclobutene

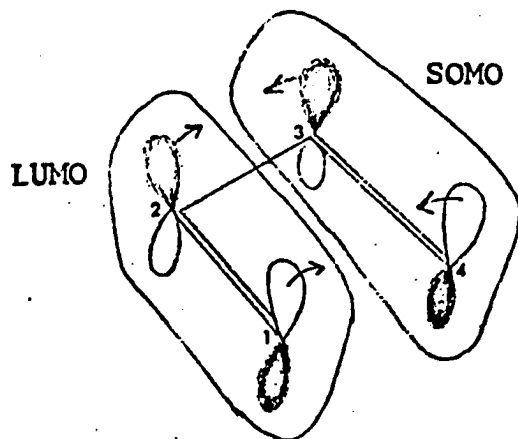
Fukui¹¹² has explained that

"the reaction may be initiated by the mutual charge-transfer interaction between the π -bond and the σ -bond to be broken. This interaction will take place between the HOMO and LUMO of each bonding region. The HOMO is bonding and the LUMO is antibonding. The charge transfer to the antibonding LUMO from the bonding HOMO will cause the weakening, and accordingly the stretching of both bonds. This principle is most easily understood if the diatomic case is thought of. An increase in bond length will cause a lowering of the LUMO level and an elevation of the HOMO energy, so that the charge transfer is further facilitated. Such interactions may be assisted by vibrational motion. As the reaction proceeds, the donor character of the C = C π -bond and the acceptor character of the C - C σ -bond become distinct, and the contribution of interaction (218) of scheme (17) becomes more important than that of (219)."

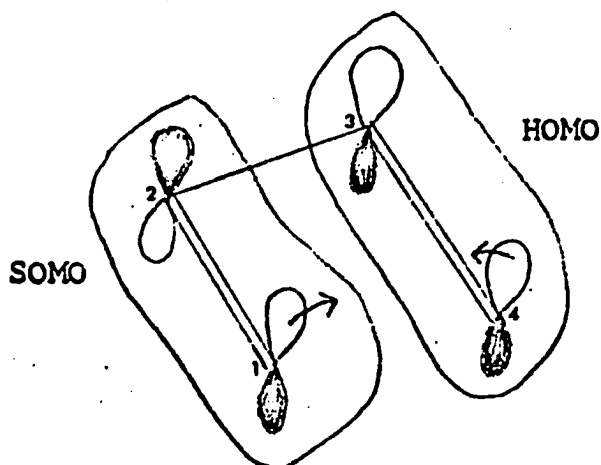
In the photochemical cyclization of butadiene to cyclobutene, the orbital interaction is between the SOMO and LUMO levels as depicted in scheme (18). The effective overlapping of the SOMO-LUMO interaction leads to a disrotatory cyclization. The mode of closure of both lobes of the SOMO and LUMO are taken into account. Taken together, the SOMO and LUMO yield an orbital pattern identical to that of the first excited state of butadiene.

Scheme 18

The mode of the SOMO-LUMO interaction in the photochemical ring closure of butadiene



Application of Fukui's method to the molecular orbital depicted in figure (217) indicates that the diene part, 1-4, can undergo an SOMO-LUMO interaction. Cyclization will occur by a disrotatory mode as shown in scheme (18). The diene part, 3-6, cannot undergo orbital interaction of its ethylene moieties since one is an SOMO while the other is an HOMO, as shown in figure (220). Since the SOMO, in this case, plays the role of the HOMO, the other orbital is required to be a



(220)

LUMO. It should also be noted that the total symmetry of orbitals 1-4 do not permit it to be a valid molecular orbital for butadiene, and, therefore, does not represent the electrocyclization reaction center.

Applying the orbital interaction method to the symmetry scheme of figure (201) closure across positions 3-6 can readily be recognized as the orbital scheme in figure (220), and, as such should not allow a disrotatory closure. It is worthwhile reemphasizing that the symmetries of the orbitals represented by the diene orbitals 3-6 readily reveals that it is not a proper molecular orbital for isolated butadiene. One is tempted to apply the Fukui method to 1-ethoxycycloheptatriene (122) and 2,7,7-trimethylcycloheptatriene (113). Using the linear model for 1-ethoxycycloheptatriene with $h_{77} = 0$, an orbital very similar to the one in figure (201) is obtained with the exception that a node is very close to atom 5 instead of occurring between atoms 4 and 5. This would then predict 1-4 closure as reported by Chapman.

Using Jones and Jones orbital scheme based upon a linear model (see page 45), a similar situation exists to show the selective electrocyclization of 2,7,7-trimethylcycloheptatriene (113) to 2,4,4-trimethylbicyclo(3.2.0)hepta-2,6-diene (114). The selectivity in this reaction was not apparent to Jones and Jones when applying the Woodward-Hoffmann rules to these compounds, and they invoked steric arguments to explain the course of the reaction.

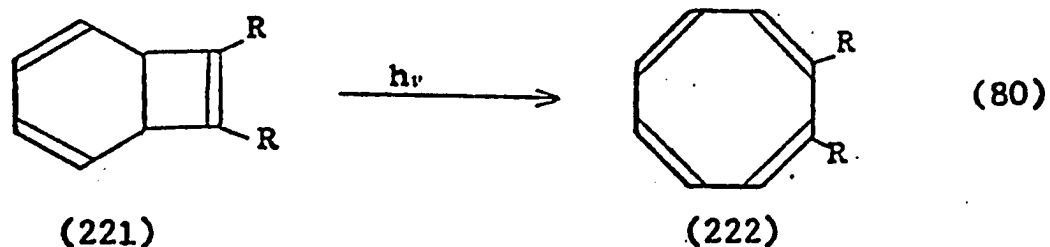
When applying the Fukui system to 3H-azepine, again using the linear model with h_{77} at 0, one would expect selective 1,4 ring closure. However, there has been no experimental test with this compound. Finally, when applying the Fukui method to the 2-substituted 3H-azepines studied in this research a linear model with $h_{77} = 0$ will again predict 1,4 closure which is contrary to the results described in earlier sections of this thesis. One would then have to invoke the same kind of arguments for selective rearrangement that were used when applying the Woodward-Hoffmann rules, that is closure across the 1,4 position would destroy amidine or imide ester resonances.

IV. Cycloreversions of 2-aza-bicyclo(3.2.0)hepta-2,6-dienes

Bicyclo(3.2.0)hept-2,6-dienes and the 2-aza analogues can only exist in the *cis* configuration. Their thermal isomerizations to cycloheptatrienes or 3H-azepines can only occur by a concerted disrotatory process or via an intermediate diradical due to constraints imposed by the seven-membered ring. In either case, the energy of activation of the isomerization will be higher than for the conrotatory isomerization of monocyclic-cyclobutenes. In a similar cycloreversion, the isomerization of bicyclo(3.2.0)hept-6-ene to cycloheptadiene, Frey⁴³ reported that a diradical mechanism would require an activation energy of 55-60 kcal/mole. Since Frey observed an activation energy of less than 46 kcal/mole, a diradical mechanism was ruled out for this reaction. Therefore, a disrotatory mechanism was proposed for the isomerization of bicyclo(3.2.0)hept-6-ene to cycloheptadiene, and, may be expected, as well, for the thermal cycloreversion of bicyclo(3.2.0)hept-2,6-dienes. The electrocyclization rules predict the favored concerted process, but do not exclude the operation of the other under very energetic conditions. Frey⁴³ reported that the energy of activation for the thermal isomerization of bicyclo(3.2.0)hepta-6-ene is about 10 kcal/mole greater than that for analogous isomerizations of monocyclic-cyclobutenes.

In contrast to the thermal reactions, disrotatory cycloreversions of monocyclic and bicyclic butenes should

be allowed photochemically. However, only one example for such a photolytic isomerization, the conversion of bicyclo(4.2.0)octatriene (221) to cyclooctatetraene (222), had been reported¹¹³ at the inception of this thesis research.



Therefore, it was desirable to provide additional examples of the photo-cycloreversion of cyclobutenes.

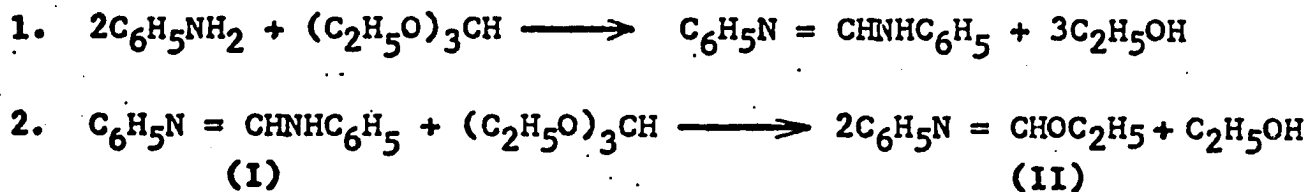
The absorption curve of 3-dimethylamino-2-aza-bicyclo (3:2.0)hepta-2,6-diene (2a) shows only end absorption. We were able to effect the cycloreversion of 2a to 2-dimethylamino-3H-azepine (1a) in 10% yield by irradiating 2a with a Hanovia medium pressure arc through a vycor filter (which transmits light above 205 mμ). It was also possible to effect the isomerization of 2a to 1a in 3% yield by irradiation with a Hanovia medium pressure arc through a corex filter (which absorbs light below 260 mμ). The formation of 1a under these conditions is probably due to a small amount of high energy light transmitted by the corex filter. Prolonged irradiation with either filter destroyed both starting material and product, which can account for the low yields of 1a obtained in these photolyses.

In contrast to the photo-cycloreversion of 2a, thermal cycloreversions were not as readily effected. Thus, temperatures above 200° were required to effect the cycloreversion of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) to 2-ethoxy-3H-azepine (1c).

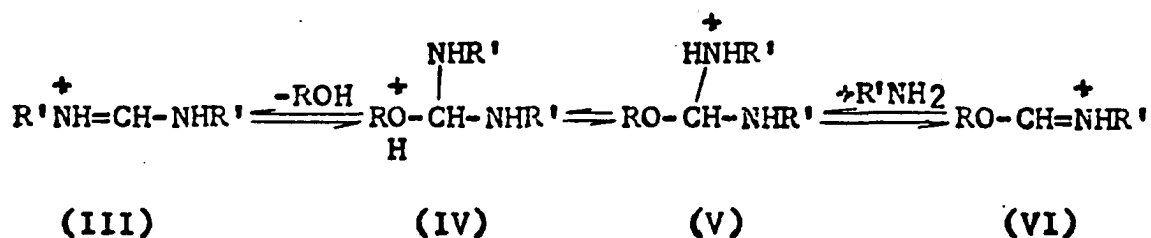
Recently, photo-cycloreversions of cyclobutenes have been reported by Scherer and Srinivasan. Scherer⁹⁶ irradiated a dilute dichloromethane solution of hexachlorobicyclo(3.2.0)hepta-3,6-dien-2-one (178) and obtained an equilibrium mixture of (178) and hexachlorotropone (see page 145). Srinivasan¹¹⁴ reported on the photosensitized photolyses of cis-3,4-dimethylcyclobutene in the vapor phase, which resulted in a complex series of reactions.

V. Alcoholysis of Amidines

In order to obtain pure 2-ethoxy-3H-azepine (1c) for photochemical studies and to prove the structure of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) the possibility of transforming amidines into imide esters was investigated. The only literature related to the alcoholysis of amidines¹¹⁵ was work by Roberts¹¹⁶⁻¹¹⁸ on the reaction of ethyl orthoformate and aromatic amines. Claisen¹¹⁹, in 1895, prepared ethyl N-phenylformimidate (II) from aniline and ethyl orthoformate. He proposed a two-step mechanism via the intermediate N,N'-diphenylformamidine (I), which was formed in good yield when the reaction mixture was heated for a short time. Prolonged heating resulted in a low yield of (II).

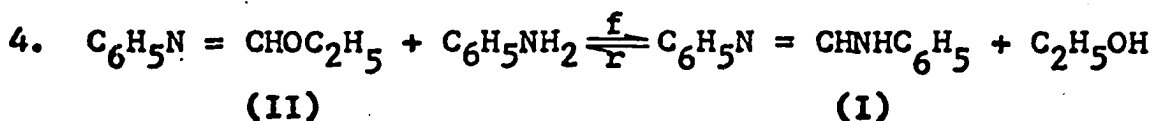
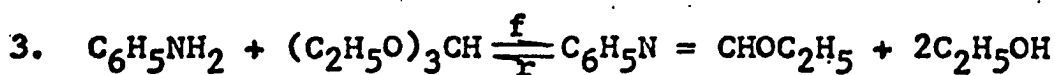


Roberts and co-workers, in the 1950's, reinvestigated this reaction and demonstrated that the second-step was dependent on acid catalysis by obtaining ethyl N-phenyl formimidate (II) in high yields when N,N'-diphenylformamidine (I) and ethyl orthoformate were reacted in the presence of aniline hydrochloride. These workers¹¹⁷ suggested a mechanism involving alcoholysis of the formamidine conjugate acid (III).



The ethanol required for the initial alcoholysis was considered to be present as an impurity in the ortho ester or formed by the acid-catalyzed hydrolysis of the orthoformate.

Roberts then proposed a mechanism consisting of two reversible steps for the acid-catalyzed reaction of aniline and ethyl-orthoformate, and explained the formation of N,N'-diphenylformamidine (I), observed by Claisen, by assuming that reactions 3f and 4f are consecutive and that step 4f is faster than 3f.



Direct evidence for the alcoholysis of amidines comes from Roberts and DeWolfe's¹¹⁶ demonstration of step 4r. Employing high dilution techniques in conjunction with ultraviolet spectrophotometry, these workers obtained evidence for the initial and final products of the reaction. The ultraviolet spectra of a reaction mixture of ethyl orthoformate and aniline in heptane were determined before and after heating.

At low aniline concentrations, the spectrum after heating indicated that ethyl-N-phenylformimide (II) and not N,N-diphenylformamidine (I) was the primary reaction product. At higher aniline concentration, N,N'-diphenylformamidine (I) is obtained by reaction of ethyl N-phenylformimide (II) with aniline. Under the conditions of the reaction N,N'-diphenylformamidine (I) does not react at all with ethyl orthoformate. However, the ultraviolet spectrum of a dilute reaction solution (hexane) of N,N-diphenylformamidine (I) and ethyl orthoformate in the presence of ethanol and a catalytic amount of acetic acid before and after heating indicated the formation of ethyl N-phenylformimide (II), thus demonstrating step 4r, and, consequently providing evidence for the alcoholysis of an amidine.

Encouraged by the possibility of converting an amidine function to its corresponding imide ester by alcoholysis, we succeeded in converting the amidines 2-amino-3H-azepine (1b) and 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) to the corresponding imide esters (1c) and (2c) in ethanol, in the presence of a catalytic amount of glacial acetic acid. This transformation is novel, constituting the first isolation of an imide ester from the intermolecular acid catalyzed reaction of an amidine with an alcohol, such as ethanol. Methods of synthesis of imides were reviewed in 1961 by Roger and Neilson⁹³. Only one method, the Pinner synthesis of imides involving reaction of an alcohol and nitrile in

the presence of anhydrous hydrogen chloride, was known to have general applicability. However, the Pinner synthesis cannot be used for the preparation of N-substituted imidates. Very recently, Suydam et al.¹²⁰ investigated the synthesis of imidates by reaction of ethyl chloroformate with amides. They suggested that the reaction appears to be generally applicable to the preparation of N-substituted imidate hydrochlorides from aliphatic amides but may be unsatisfactory when aromatic amides or N-substituted amides in which the substituent is larger than ethyl are employed. A versatile method for the synthesis of imidates from N-substituted amides is the reaction of cyclic amides with triethyloxonium fluoroborate⁸⁰. However, this procedure may suffer isomeric N-alkylation under best experimental conditions, and, may suffer contamination by non-volatile by-products during the in situ preparation of the triethyloxonium fluoroborate reagent (see page 105 of this thesis). On the other hand, ethanolysis of the N-substituted amidines 3-amino-2-azabicyclo(3.2.0)hepta-2,6-diene (2b) and 2-amino-3H-azepine (1b) (see page 95 of this thesis) gave the corresponding imidate esters (2c) and (1c) essentially free of impurities. The observation that amidines may undergo alcoholysis is timely, since considerable interest has currently been shown concerning the mechanism of acyl transfer reactions. Thus, Hand and Jenks¹²¹, in 1962 reported their studies on the mechanism of the aminolysis of imidate esters, in 1968 Schmir et al.^{122,123}

reported their studies on the hydrolysis of imidate esters, on ester aminolysis and on the alcoholysis of amides, and in 1970 Robinson^{124,125} reported his studies on the hydrolysis of amidines. In each case, the acyl transfer reaction was shown to proceed through tetrahedral addition intermediates. Conspicuous by their absence are reports on the mechanism of the alcoholysis of amidines.

Appendix 1

Determination of product yields by vapor phase chromatography

In a number of photolyses the weight of product formed and the weight of reactant remaining were followed during the course of the reaction by glpc analyses.

Calibration curves of weights vs. areas for reactant and product, relative to a standard compound, were made. The data for these curves are given in appendices 2, 3, and 5. A difference in the slopes of the calibration curves for reactant and product reflects a difference in the thermal conductivities of those substances. To obtain reproducible results in a photolysis experiment it is important to determine the calibration curve for both reactant and product at the time of the reaction and under the identical glpc conditions, and to employ concentrations similar to those in the experiment.

The weights of reactant and product in photolyses reactions were obtained by multiplying the areas of reactant and product by the respective slopes of their calibration curves.

Tables 2-8 gives the following information as a function of irradiation time:

Weight of reactant, weight of product, sum of reactant and product weights, product yield based on total reactant charged, percent reactant remaining, and product yield based on reactant consumed (weight of product/change in reactant weight).

Figures 1-10 are plots of the weights of product formed and reactant remaining during the course of a reaction.

Appendix 2

Determination* of calibration curves of weight ratio vs. area ratio of 2-dimethylamino-3H-azepine (1a) and 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) relative to n-decane

The following amounts of 2-dimethylamino-3H-azepine (1a) and n-decane were weighed directly into a 10 ml. volumetric flask and dissolved in hexane.

<u>Flask No.</u>	<u>Weight of amidine (1a)</u>	<u>Weight of n-decane</u>	<u>Weight ratio amidine/decane</u>
1	.3005	.1005	2.990
2	.2050	.1020	2.009
3	.1460	.1040	1.403
4	.1015	.1030	0.985
5	.0520	.1025	0.367
6	.0260	.1035	0.251

The solutions were analyzed with a 12' x 1/8" 8% Apiezon L-KOH (4:1) on Chromosorb P regular 60/80 mesh column. VPC conditions were 215° detector, 200° injector, 160° column, 60 ml/min flow rate.

The areas obtained and the ratio of the areas are:

<u>Flask No.</u>	<u>Area of amidine</u>	<u>Area of n-decane (attenuation 8)</u>	<u>Area ratio amidine/decane</u>
1	12.758 (att 8)	5.240	2.415
2	18.625 (att 4)	5.320	1.750
3	8.500 (att 2)	5.400	0.394
4	8.100 (att 1)	5.120	0.198
5	12.045 (att 4)	5.240	1.149
6	11.182 (att 4)	3.413	1.618

Since attenuation 4 is twice as sensitive as attenuation 8, the area determined at attenuation 4 must be divided by two etc. in computing the ratio of the area of amidine to decane.

* See appendix 1

The slope of the calibration curve of weight ratio vs. area ratio of 2-dimethylamino-3H-azepine is 1.250 ± 0.018 as obtained from the following data:

Flask No.	Weight ratio amidine/decane	Area ratio amidine/decane	Slope <u>Wt. ratio</u> area ratio	Deviation
1	2.990	2.415	1.238	.012
2	2.009	1.618	1.242	.008
3	1.403	1.149	1.221	.029
4	0.985	0.791	1.245	.005
5	0.507	0.394	1.287	.037
6	0.251	0.198	<u>1.268</u>	<u>.018</u>
Average			1.250	.018

In a manner similar to the above, the slope of a calibration curve of weight ratio vs. area ratio of 3-dimethylamino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2a) was found to be 1.495 ± 0.019 .

The calibration curves of 1a and 2a have relative errors less than 2%.

Appendix 3

Determination of calibration curves of weight vs. area of 2-amino-3H-azepine (1b) and of 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) relative to n-decane

A calibration curve of weight ratio vs. area ratio of amidine to internal standard was determined in a manner similar to that for 2-dimethylamino-3H-azepine (see Appendix 2).

VPC conditions

14' x 1/8" 12% Apiezon L-KOH (4:1) chrom P. Reg 60/80 160° column, 40 ml/min. The areas of the amidines were unsymmetrical.

The slope of the curve for 2-amino-3H-azepine is 1.054 ± 0.026 as obtained from the following data:

Weight ratio amidine/ n-decane	Area ratio amidine/ n-decane	Slope <u>Wt. ratio</u> area ratio	Deviation
2.965	2.914	1.015	.039
1.940	1.842	1.053	.001
0.956	0.874	<u>1.093</u>	<u>.039</u>
Average 1.054			.026

In a similar manner, the slope of the curve for 3-amino-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2b) is 1.436 ± 0.072 .

The calibration curves of 1b and 2b have relative errors of 2-5%.

Appendix 4

Determination of product yield for the photolyses (2537A) of 2-amino-3H-azepine in pentane

A calibration curve of weights vs. areas of reactant and product was determined in appendix 3. The slopes of the calibration curves for 2-amino-3H-azepine (1b) and 3-amino-2-aza-bicyclohepta-2,6-diene (2b) are 1.054 and 1.436, respectively.

Since

$$\frac{W_p}{W_i} = S_p \frac{A_p}{A_i}$$

$$\frac{W_r}{W_i} = S_r \frac{A_r}{A_i}$$

Where W = weight, A = area, S = slope, r = reactant, p = product, i = internal standard

then, solving these equations simultaneously gives

$$\frac{W_p}{W_r} = \frac{S_p}{S_r} \frac{A_p/A_i}{A_r/A_i}$$

For the above reaction:

Area Product	Area Decane	Area Product Area Decane	Area Reactant	Area Decane	Area Reactant Area Decane
277 ± 1	72 ± 1	3.85	3.5 ± 1	72 ± 1	.049
285 ± 0	73 ± 2	<u>3.90</u>	3 ± 1	73 ± 2	<u>.041</u>
Average 3.88			Average .045		

Substituting

$$\frac{W_p}{W_r} = \frac{1.436}{1.054} \frac{(3.88)}{(.045)} = 111:1$$

$$\% \text{ Product} = (100) \frac{117}{117 + 1} = 99\%$$

Since weight of sublimate was 0.0755g, then $.0755(.99) = .0747$ g of product, and $.0755 - .0747 = .0008$ g of unreacted starting material. Therefore, product yield =

$$(100) \frac{.0747}{.1515 - .0008} = 49.6\%$$

Appendix 5

Determination of calibration curves of weight vs. area of 2-ethoxy-3H-azepine (1c) and of 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene (2c) relative to t-decalin

A calibration curve of weight ratio vs. area ratio of imide ester to internal standard was determined in a manner similar to that for 2-dimethylamino-3H-azepine (see Appendix 2).

VPC conditions

14' x 1/8" 12% Apiezon L-KOH (4:1) chrom P. Reg. 60/80
160° column, 40 ml/min.

The slope of the curve for 2-ethoxy-3H-azepine is 1.018 ± 0.020 as obtained from the following data:

Weight ratio imide ester/ t-decalin	Area ratio imide ester/ t-decalin	Slope <u>Wt. ratio</u> <u>area ratio</u>	Deviation
2.000	1.937	1.032	.014
1.024	1.024	1.000	.018
0.522	0.495	1.054	.036
0.243	0.243	1.000	.018
2.898	2.884	<u>1.005</u>	<u>.013</u>
Average		1.018	.020

In a similar manner, the slope of the curve for 3-ethoxy-2-aza-bicyclo(3.2.0)hepta-2,6-diene is 1.028 ± 0.010 .

The calibration curves for 1c and 2c have relative errors less than 2%.

APPENDIX 6

Huckel Molecular Orbital Method¹²⁶

Molecular orbitals of a conjugated π -system may be represented, to a fair approximation, by some combination of atomic orbitals of the constituent atoms. In a linear combination of atomic orbitals (LCAO) only one-electron wave functions are considered. The number of constructable molecular orbitals of the LCAO method is always equal to the number of atomic orbitals.

The energies of the molecular orbitals are given by the Schrodinger equation.

$$H\psi = E\psi \quad (1)$$

where H is the Hamiltonian energy operator

E is the energy of the molecular orbital

ψ is the LCAO one-electron wave function

$$\psi_j = C_{j1}P_1 + C_{j2}P_2 + \dots + C_{jn}P_n \quad (2)$$

$$\psi_j = \sum_{r=1}^n C_{jr}P_r \quad (3)$$

where j is the j th molecular orbital

P_r is the π -atomic orbital for the r th atom

C_{jr} is the coefficient of the r th atomic orbital in the j th molecular orbital

The subscripts $r, s, \dots$, are generally used to represent atoms or atomic orbitals and $i, j, \dots$, are generally used to represent molecular orbitals.

We must find the best set of values for the coefficients that give the lowest energies for the molecular orbitals. The variation principle is employed, which states that

$$\epsilon = \frac{\int \psi H \psi d\tau}{\int \psi^2 d\tau} \geq E \quad (4)$$

That is, any wave function other than the correct one will yield a value for the ground-state energy algebraically higher than the true value. This expression is obtained by multiplying equation (1) through by ψ so that

$$\psi H \psi = E \psi^2 \quad (5)$$

Integration over all space then gives

$$\int \psi H \psi d\tau = E \int \psi^2 d\tau \quad (6)$$

$$E = \frac{\int \psi H \psi d\tau}{\int \psi^2 d\tau} \quad (7)$$

The set of coefficients that yields the lowest energies is found by minimizing ϵ with respect to each of the coefficients

$$\frac{\partial \epsilon}{\partial C_r} = 0 \quad (8)$$

The variation principle may be more readily understood by application to the ethylene molecule. The wave function

for an electron in a π -molecular orbital of ethylene is a linear combination of P orbitals

$$\psi = C_1 P_1 + C_2 P_2 \quad (10)$$

substituting (10) into (7)

$$E = \frac{\int (C_1 P_1 + C_2 P_2) H (C_1 P_1 + C_2 P_2) d\tau}{\int (C_1 P_1 + C_2 P_2) (C_1 P_1 + C_2 P_2) d\tau} \quad (11)$$

Expansion of these integrals yields

$$E = \frac{C_1^2 \int P_1 H P_1 d\tau + C_1 C_2 \int P_1 H P_2 d\tau + C_2 C_1 \int P_2 H P_1 d\tau + C_2^2 \int P_2 H P_2 d\tau}{C_1^2 \int P_1 P_1 d\tau + C_1 C_2 \int P_1 P_2 d\tau + C_2 C_1 \int P_2 P_1 d\tau + C_2^2 \int P_2 P_2 d\tau} \quad (12)$$

For convenience we introduce the symbols

$$H_{11} = \int P_1 H P_1 d\tau$$

$$S_{11} = \int P_1 P_1 d\tau$$

$$H_{12} = \int P_1 H P_2 d\tau$$

$$S_{12} = \int P_1 P_2 d\tau$$

$$H_{21} = \int P_2 H P_1 d\tau$$

$$S_{21} = \int P_2 P_1 d\tau$$

$$H_{22} = \int P_2 H P_2 d\tau$$

$$S_{22} = \int P_2 P_2 d\tau$$

Then

$$E = \frac{C_1^2 H_{11} + C_1 C_2 H_{12} + C_1 C_2 H_{21} + C_2^2 H_{22}}{C_1^2 S_{11} + C_1 C_2 S_{12} + C_1 C_2 S_{21} + C_2^2 S_{22}} \quad (13)$$

It can be shown that

$$H_{12} = H_{21} \quad (14)$$

and

$$S_{12} = S_{21} \quad (15)$$

Therefore

$$E = \frac{C_1^2 H_{11} + 2C_1 C_2 H_{12} + C_2^2 H_{22}}{C_1^2 S_{11} + 2C_1 C_2 S_{12} + C_2^2 S_{22}} \quad (16)$$

E is minimized by differentiating it with respect to C_1 and C_2 and setting each derivative equal to zero.

Carrying out this calculation gives for

$$\frac{\partial E}{\partial C_1} = 0 \quad (17)$$

$$C_1(H_{11} - S_{11}E) + C_2(H_{12} - S_{12}E) = 0 \quad (18)$$

$$\text{and for } \frac{\partial E}{\partial C_2} = 0 \quad (19)$$

$$C_2(H_{21} - S_{21}E) + C_1(H_{12} - S_{12}E) = 0 \quad (20)$$

Equations 18 and 20 are homogeneous linear equations which must be solved simultaneously to find the allowed values of E .

$$\begin{vmatrix} C_1(H_{11} - S_{11}E) & C_2(H_{12} - S_{12}E) \\ C_2(H_{21} - S_{21}E) & C_1(H_{12} - S_{12}E) \end{vmatrix} = 0 \quad (21)$$

Factoring out C_1 and C_2

$$C_1 C_2 \begin{vmatrix} H_{11} - S_{11}E & H_{12} - S_{12}E \\ H_{21} - S_{21}E & H_{22} - S_{22}E \end{vmatrix} = 0 \quad (22)$$

Since C_1 and C_2 are not zero, this condition can be satisfied only if the determinant equals zero. Therefore,

$$\begin{vmatrix} H_{11} - S_{11}E & H_{12} - S_{12}E \\ H_{21} - S_{21}E & H_{22} - S_{22}E \end{vmatrix} = 0 \quad (23)$$

This equation is the secular determinant for ethylene.

So far no approximations have been made beyond the original use of a linear combination function as a solution to a one-electron Hamiltonian. Further approximations are now introduced which constitute the simple LCAO or Huckel (HMO) molecular orbital method.

The terms H_{rr} , H_{rs} , and S_{rs} are called the Coulomb, resonance (bond), and overlap integrals, respectively.

The Coulomb integral represents the energy of an electron in a carbon 2p-orbital. If the Π -lattice consists entirely of carbons, we assume that all such integrals are equal, and, are denoted by the symbol α .

The resonance integral represents the energy of interaction of two atomic orbitals, and depends on the distance between the orbitals. We assume that all resonance integrals are equal for all r and s that are bonded and denote such integrals as β . The interaction energy is small for r and s which are not bonded and, in that case, H_{rs} are assumed to be zero.

Relative to the energy of an electron at infinity, both α and β are negative energy quantities.

The overlap integral is a measure of how much two atomic orbitals overlap. $S_{rr} = 1$ for normalized atomic orbitals. For r and s separated by a large distance S_{rs} is negligible. To simplify the solution of the secular determinant, the assumption is made that $S_{rs} = 0$ even when the distance between r and s is not large. This assumption, however, is not so drastic since the assumption is equivalent to treating the constituent atomic orbitals as orthogonal. This assumption has some justification since the definition of α and β are so vague that neglect of S_{rs} may be justified empirically by the success of the simple HMO procedure.

Applying these assumptions to the secular determinant of ethylene

$$H_{11} = H_{22} = \alpha$$

$$H_{12} = H_{21} = \beta$$

$$S_{11} = S_{22} = 1$$

$$S_{12} = S_{21} = 0$$

The determinant becomes

$$\begin{vmatrix} \alpha - E & \beta \\ \beta & \alpha - E \end{vmatrix} = 0 \quad (24)$$

Dividing each term by β , we obtain

$$\begin{vmatrix} \frac{\alpha - E}{\beta} & 1 \\ 1 & \frac{\alpha - E}{\beta} \end{vmatrix} = 0 \quad (25)$$

Making the substitution

$$x = \frac{\alpha - E}{\beta} \quad (26)$$

the determinant becomes

$$\begin{vmatrix} x & 1 \\ 1 & x \end{vmatrix} = 0 \quad (27)$$

Expansion of this determinant gives the polynomial equation

$$x^2 - 1 = 0 \quad (28)$$

The roots of the equation are

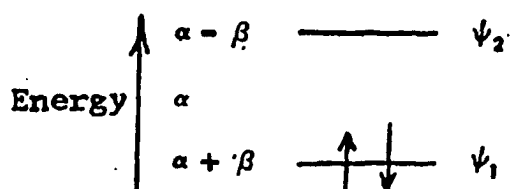
$$x = -1, x = 1$$

The energies E of the secular determinant are

$$\text{for } x = 1 \quad E = \alpha - \beta \quad (29)$$

$$\text{for } x = -1 \quad E = \alpha + \beta \quad (30)$$

Since α and β are both negative quantities the lowest energy level of the ground state is $E = \alpha + \beta$. Ethylene has two electrons in the Π -bond which are placed in this bonding orbital, ψ_1 .



The energy of the two Π -electrons in ethylene

The coefficients for the molecular orbital that corresponds to each energy is found by inserting each energy in terms of β relative to α into the original set of simultaneous equations (18) and (20) and applying the normalization condition

$$\int \psi \psi \, d\tau = 1 \quad (31)$$

which for ethylene is

$$c_1^2 + c_2^2 = 1 \quad (32)$$

Then these equations are solved for the coefficients. The case of ethylene is trivial and the reader is referred to reference 126.

Application of the HMO procedure to specific compounds involves the following operations:

1. Setting up the secular determinant
2. Expanding the secular determinant
3. Finding the roots of the characteristic equation
4. Determining the coefficients

The roots of the characteristic equation determines the energies of the molecular orbitals.

The coefficients of a molecular orbital determine the orbital symmetry of that molecular orbital.

APPENDIX 7

Huckel Molecular Orbital Calculations of 3H-azepines and cycloheptatrienes

In appendix (6) we discussed the Huckel molecular orbital method with application to the ethylene molecule.

Generalizing,

$$\psi = C_1P_1 + C_2P_2 + \dots + C_nP_n$$

and

$$\begin{vmatrix} H_{11} - S_{11}E & H_{12} - S_{12}E & \dots & H_{1n} - S_{1n}E \\ H_{21} - S_{21}E & H_{22} - S_{22}E & \dots & H_{2n} - S_{2n}E \\ \vdots & \vdots & & \vdots \\ H_{n1} - S_{n1}E & H_{n2} - S_{n2}E & \dots & H_{nn} - S_{nn}E \end{vmatrix} = 0$$

Solving this secular determinant for E gives the allowed energy levels for an electron in molecular orbitals spanning n carbon atoms.

Heteroatoms may be treated in the HMO method by appropriate changes in the empirical α and β parameters associated with each atom and bond¹²⁶.

Due to the increased electronegativity of nitrogen and oxygen terms like α_N and α_O , which represent the energy of an electron in a $2P_z$ orbital of these heteroatoms differ from the energy α of an electron in a $2P_z$ orbital of carbon. The effective nuclear charge of the atom is important in determining the magnitude of α . Along one row of the periodic table the increase in nuclear charge is not completely screened by the

additional electrons; the increasing core potential means that $\alpha_O > \alpha_N > \alpha_C$. The Coulomb integrals of heteroatoms are adjusted by expressing them in terms of α plus some multiple of β , which makes for easier incorporation of the α_N and α_O terms into the secular equation.

$$\alpha_N = \alpha + h_N \beta$$

$$\alpha_O = \alpha + h_O \beta$$

Since α and β are both negative terms, α_N and α_O are more negative (lower energy) than α .

A heteroatom is capable of donating either one or two electrons to the Π -electronic system. The contributions of two electrons by the heteroatom decreases the shielding at the heteroatom, thus, exposing the electron in the Π -system to a greater core potential. The resultant effect is reflected in the lowering of α . Reasonable agreement with experimental data has been obtained utilizing the following values for the donation of 1 or 2 electrons by the heteroatom (from Streitweiser's⁵² book).

$$\underline{\alpha + h\beta}$$

$$\alpha_{N(1)} = \alpha + 1/2 \beta$$

$$\alpha_{N(2)} = \alpha + 3/2 \beta$$

$$\alpha_{O(1)} = \alpha + 1 \beta$$

$$\alpha_{O(2)} = \alpha + 2 \beta$$

The resonance integral for carbon-heteroatom bonds are adjusted by expressing them as a multiple of β . The resonance parameter k depends on the type of carbon-heteroatom bond. Streitwieser has suggested the following parameter values for nitrogen and oxygen for use with simple LCAO theory⁵².

$$\beta_{cx} = k_{cx} \beta_{cc}$$

carbon	$k_{CC} = 1$
nitrogen	$k_{CN} = 1, k_{C-N} = 0.8$
oxygen	$k_{C-O} = 0.8$

Where k_{CC} implies carbon-carbon bond as in pyridine
 k_{CN} implies carbon-nitrogen bond as in pyridine
 k_{C-N} implies carbon-nitrogen bond as in pyrrole
 k_{C-O} implies carbon-oxygen bond as in phenol

However, various values for the k parameter which range about those suggested by Streitwieser have been used by other authors. Apparently, no simple reason can be given for the values of k .

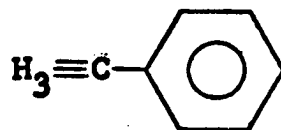
The HMO calculations employed to obtain the molecular orbitals of 3H-azepines should take into account possible σ - π interactions of the methylene group with the azahexatriene chromophore. Kier¹²⁷ concisely describes the methods for estimating the σ - π contribution to conjugated systems.

"A methyl group bonded to a conjugated system is known to have a modest effect on the π -electron system, although a π -bond of the conventional form cannot be written. There are three ways that the methyl group effect can be introduced into π -electron calculations. The methyl group can be regarded as a heteroatom group similar to NH_2 and OH , in which two " π -like" electrons are considered available to the delocalized π system. Since these are conceded to weakly interact with the system, a large Coulomb integral is used to reflect this. Similarly, the low values of the resonance integral

reflects this weak interaction.

A second way of considering the methyl group influence is to regard its effect on the attached atom of the Π -system as strictly an inductive effect through the Π -electrons. This electron enrichment of the bonded carbon core should result in a modest lowering of the core electronegativity. This in turn would be reflected by a modest lowering of the Coulomb integral for the attached carbon of the Π -system. Thus, the parameter, h , for this carbon would have a modest negative value.

The third model, known as the conjugation molecule, envisages the three hydrogen atoms functioning like a pseudo-atom with a Π -orbital which can extend the conjugation of the system to which it is attached. Thus toluene in this model, is treated by assigning a Coulomb integral value to the H_3 pseudo-atom and a resonance integral to the $H_3 \equiv C$ bond."



Streitwieser⁵² has discussed the merits of the three models proposed by various workers to take into account σ - Π interactions of methyl groups with conjugated systems.

In this thesis research, HMO calculations were carried out employing a heteroatom model for the methylene carbon. Parameters for the coulomb and resonance integrals suggested

by Streitwieser⁵² for a methyl heteroatom were assigned to the methylene carbon. The coulomb and resonance parameters

$$\begin{aligned} \alpha_{\text{CH}_2} &= \alpha + h_{\text{CH}_2} \beta & h_{\text{CH}_2} &= 2.0 \\ \beta_{\text{C-CH}_2} &= k_{\text{C-CH}_2} \beta & k_{\text{C-CH}_2} &= 0.7 \end{aligned}$$

discussed above for nitrogen and oxygen were employed in the calculations.

HMO calculations for an eight-atom Π -system involves solving an 8×8 determinant. This is most readily performed with a computer. The computer program¹²⁸ which we employed to calculate the energies and coefficients of 2-ethoxy-3H-azepine and 1-ethoxycycloheptatriene diagonalizes matrices by the Jacobi turning method, which is not effected by degenerate eigenvalues. The program was originally written in Fortran for the IBM 1620, but was readily adapted to the IBM 360 Model 40 with the appropriate internal storage.

Tables 9-12 of appendix 8 give the energies and coefficients obtained by the HMO calculations for the 3H-azepines and cycloheptatriene systems using values for the parameter h of the methylene-pseudoheteroatom over a range of 0 to 2. The interaction of the electrons of the methylene group with the Π -system decreases as h increases.

The coefficients obtained from the HMO calculations were used to compute Π -bond orders by the following formula¹²⁹:

$$\Pi \text{ -bond order} = \sum^{N_{occ}} N C_i C_j$$

where N = number of electrons in a given occupied orbital;
 $c_i c_j$ = the normalized coefficients for atoms i and j for
the occupied orbital; and the sum is taken over all of the
occupied orbitals (overall Π -bond orders). When HOMO
 Π -bond orders were computed, the sum was taken over only
the highest occupied molecular orbital.

Tables 13 and 14 of appendix 9 give the results of
the bond order calculations which correspond to the calcu-
lations in appendix 8.

For diagrammatical clarity, only the upper lobes will
be shown for molecular orbitals depicted herein.

APPENDIX 8

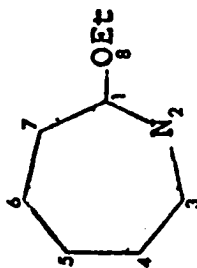
HMO Energy Levels and Coefficients of the 3H-azepine and cycloheptatriene systems

TABLE 9

2-ethoxy-3H-azepine

HMO Energy Levels and Coefficients

Cyclic Model: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = k_{17} = 0.7$, $h_{22} = 0.5$



Wave Functions	Energy Levels	Coefficients							
h77		1	2	3	4	5	6	7	8
2.0	8	.183	-.301	.494	-.560	.485	-.285	.019	-.039
	7	-.547	.458	-.275	-.101	.406	-.425	.206	-.133
	6*	-.571	.128	.442	-.352	-.263	.486	.024	.182
	5**	.279	.363	-.390	-.438	.306	.497	-.301	-.123
	4	-.265	-.498	-.125	.339	.558	.376	-.109	.294
	3	.060	.483	.548	.483	.301	.047	-.312	-.199
	2	.136	.091	.013	-.063	-.148	-.254	-.568	.749
	1	.415	.250	.128	.091	.115	.216	.659	.496
1.0	8	.175	-.296	.491	-.561	.488	-.292	.030	-.037
	7	-.552	.440	-.264	-.081	.375	-.427	.291	.132
	6*	-.567	.117	.449	-.346	-.273	.484	.038	.181
	5**	.188	.391	-.363	-.410	.341	.428	-.455	-.077
	4	-.321	-.397	.029	.432	.505	.192	-.383	.336
	3	.002	-.437	-.422	-.179	.160	.414	.633	-.003
	2	.068	.326	.385	.402	.376	.308	.296	-.505
	1	.447	.312	.168	.103	.086	.110	.265	.758

Ten-electron eight-atom π -system

* First excited state

** Highest ground state

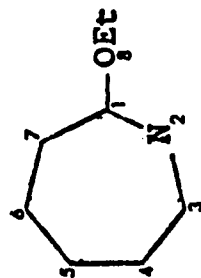


TABLE 9 (Cont.)

h77	Wave Functions	Energy Levels	Coefficients							
			1	2	3	4	5	6	7	8
0.5	8	+1.747	.167	-.291	.488	-.561	.492	-.298	.041	-.036
	7	+1.408	.553	-.425	.257	.063	-.345	.423	-.358	-.130
	6*	+0.510	-.563	.105	.457	-.338	-.285	.483	.055	.179
	5**	+0.075	.096	.410	-.332	-.385	.360	.358	-.553	-.037
	4	-1.088	.350	.185	-.241	-.447	-.246	.180	.631	-.307
0.0	3	-1.341	-.136	-.529	-.310	.114	.463	.506	.309	.165
	2	-1.865	.077	.379	.441	.443	.384	.274	.180	-.453
	1	-2.446	.440	.313	.169	.100	.100	.100	.189	.789
	8	+1.749	.148	-.280	.481	-.561	.500	-.312	.066	-.032
	7	+1.490	.550	-.403	.252	.028	-.293	.409	-.450	-.126
0.0	6*	+0.513	-.549	.073	.476	-.317	-.314	.477	.099	.175
	5**	+0.251	.050	-.435	.276	.365	-.368	-.273	.623	-.018
	4	-0.899	.375	.151	-.315	-.434	-.075	.367	.578	-.273
	3	-1.317	-.189	-.534	-.247	.209	.522	.478	.154	.222
	2	-1.853	.078	.400	.462	.457	.384	.255	.126	-.428
	1	-2.433	.434	.312	.168	.098	.069	.072	.145	.803

Ten-electron eight-atom π -system

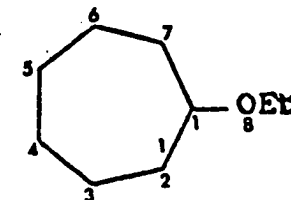
* First excited state

** Highest ground state

TABLE 10

1-ethoxycycloheptatriene
HMO Energy Levels and Coefficients

Cyclic Model: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = k_{17} = 0.7$



h_{77}	Wave Functions	Energy Levels	Coefficients							
			1	2	3	4	5	6	7	8
2.0	8	+1.813	.269	-.435	.520	-.508	.400	-.217	-.009	-.056
	7	+1.402	.482	-.451	.151	.240	-.487	.443	-.190	-.113
	6*	+0.517	.527	-.135	-.458	.371	.266	-.508	-.005	-.168
	5**	-0.121	.374	.391	-.327	-.431	.275	.464	-.312	-.159
	4	-1.146	-.306	-.526	-.297	.186	.510	.399	-.076	.286
	3	-1.675	.034	.343	.539	.561	.400	.109	-.310	-.085
	2	-2.143	.137	.062	-.005	-.072	-.150	-.248	-.546	.768
	1	-2.646	.405	.192	.104	.083	.117	.225	.682	.502
1.0	8	+1.813	.272	-.437	.521	-.507	.397	-.214	-.014	-.057
	7	+1.453	.485	-.428	.136	.230	-.470	.453	-.268	-.112
	6*	+0.517	.527	-.132	-.459	.369	.268	-.508	-.009	-.168
	5**	+0.028	.294	.412	-.305	-.403	.317	.394	-.468	-.116
	4	-1.129	-.353	-.502	-.214	.261	.508	.312	-.222	.324
	3	-1.395	.078	-.280	-.468	-.373	-.051	.301	.373	-.103
	2	-1.853	.079	.233	.353	.420	.426	.369	.368	-.430
	1	-2.435	.435	.233	.132	.087	.081	.110	.266	.801

Ten-electron eight-atom π -system

* First excited state... In figures 181 (page 156) and 197 (page 166), the signs of the coefficients are opposite to those given above.

** Highest ground state

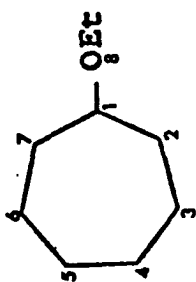


TABLE 10 (cont.)

h77	Wave Functions	Energy Levels	Coefficients							
			1	2	3	4	5	6	7	8
0.5	8	+1.813	.276	-.439	.521	-.505	.395	-.210	-.020	-.058
	7	+1.497	.484	-.405	.222	-.454	.458	-.330	-.111	-.168
	6*	+0.517	.527	-.128	.366	.272	-.507	-.014	-.079	-.351
	5**	+0.163	.213	-.282	-.379	.344	.323	-.567	-.072	.072
	4	-1.055	-.415	.058	.399	.363	-.016	-.543	.434	.357
	3	-1.214	-.070	-.472	-.126	.319	.513	.226	.187	.833
	2	-1.811	.084	.280	.485	.455	.339	.226	.187	.833
	1	-2.410	.427	.231	.083	.069	.083	.187	.833	.833
0.0	8	+1.814	.283	-.444	.522	-.503	.389	-.203	-.031	-.059
	7	+1.567	.475	-.366	.212	-.430	.462	-.419	-.032	-.107
	6*	+0.517	.527	-.116	.357	.283	-.503	-.032	-.032	-.168
	5**	+0.348	-.092	-.444	.358	-.371	-.229	.644	.578	.031
	4	-0.882	.426	.216	-.424	.138	.302	.578	.171	.305
	3	-1.174	-.206	-.405	.045	.458	.492	.171	.157	.199
	2	-1.793	.083	.297	.509	.462	.319	.157	.142	.322
	1	-2.397	.420	.229	.079	.061	.067	.142	.848	.848

Ten-electron eight-atom η -system

* First-excited state ... In figures 181 (page 156) and 197 (page 166), the signs of the coefficients are opposite to those given above.

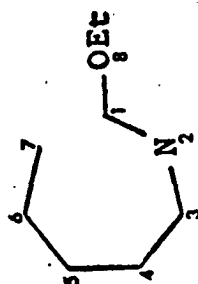
*** Highest ground state

TABLE 11

2-ethoxy-3H-azepine

HMO Energy Levels and Coefficients

Linear Model: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = 0.7$, $h_{22} = 0.5$



h77	Wave Functions	Energy Levels	Coefficients							
			1	2	3	4	5	6	7	8
2.0	8	+1.756	.189	-.299	.486	-.554	.486	-.299	.056	-.040
	7	+1.188	-.493	.486	-.328	-.097	.443	-.429	.094	.124
	6*	+0.553	-.579	.175	.395	-.393	-.177	.491	-.135	.181
	5**	-0.317	.386	.269	-.435	-.407	.306	.503	-.209	-.183
	4	-1.211	-.248	-.502	-.109	.370	.557	.304	-.270	.252
	3	-1.792	.098	.477	.519	.452	.292	.073	-.237	-.377
	2	-2.286	-.052	-.002	.048	.112	.207	.362	.887	-.146
	1	-2.390	.405	.303	.167	.097	.064	.057	.102	.830
1.0	8	+1.760	.186	-.295	.481	-.552	.489	-.309	.078	-.039
	7	+1.200	-.483	.483	-.339	-.076	.430	-.440	.140	.121
	6*	+0.582	-.577	.193	.368	-.407	-.132	.483	-.214	.179
	5**	-0.235	.385	.230	-.446	-.334	.367	.420	-.384	-.174
	4	-1.019	.242	.404	-.032	-.437	-.413	.016	.614	-.197
	3	-1.534	-.155	-.451	-.311	-.026	.271	.442	.580	.266
	2	-1.867	.054	.363	.441	.462	.421	.323	.261	-.327
	1	-2.389	.408	.303	.163	.088	.046	.023	.011	.840

Ten-electron eight-atom π -system

* First excited state

** Highest ground state

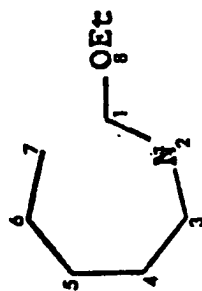


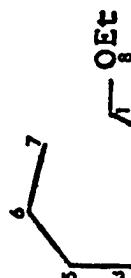
TABLE 11 (Cont.)

Wave Functions	Energy Levels	Coefficients							
		1	2	3	4	5	6	7	8
h77									
0.5									
8	+1.764	.183	-.291	.476	-.549	.492	-.318	.098	-.039
7	+1.214	-.472	.479	-.349	-.056	.417	.449	.184	.118
6*	+0.614	-.572	.211	.337	-.417	-.081	.467	-.293	.175
5**	-0.128	.379	.178	-.445	-.234	.415	.287	-.540	-.162
4	-0.807	.256	.343	-.150	-.464	-.224	.283	.647	-.171
3	-1.420	-.194	-.489	-.256	.126	.435	.491	.374	.267
2	-1.849	.066	.401	.475	.477	.406	.273	.142	-.349
1	-2.389	.408	.302	.163	.087	.046	.021	.008	.840
0.0									
8	+1.770	.178	-.284	.468	-.554	.494	-.331	.131	-.038
7	+1.238	-.452	.470	-.364	-.019	.387	.461	.261	.112
6*	+0.677	-.555	.243	.269	-.425	.019	.412	-.426	.166
5**	+0.055	-.388	-.099	.443	.075	-.447	-.050	.643	.151
4	-0.637	.300	.332	-.254	-.494	-.060	.455	.500	-.176
3	-1.373	-.212	-.506	-.230	.190	.491	.484	.247	.270
2	-1.842	.070	.414	.485	.480	.398	.252	.096	-.356
1	-2.389	.408	.302	.163	.087	.045	.021	.006	.840

Ten-electron eight-atom π -system

* First excited state
 ** Highest ground state

TABLE 12
1-ethoxy-cycloheptatriene
HMO Energy Levels and Coefficients



Linear Model: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = 0.7$

Wave Functions	Energy Levels	Coefficients							
h77		1	2	3	4	5	6	7	8
2.0	8	.255	-.421	.511	-.509	.415	-.245	.045	-.053
	7	.445	-.497	.207	.226	-.503	.433	-.092	-.108
	6*	.521	-.166	-.427	.408	.195	-.518	.141	-.162
	5**	.463	.300	-.381	-.405	.269	.479	-.195	-.215
	4	-.297	-.526	-.268	.237	.523	.326	-.247	.257
1.0	3	.095	.366	.528	.533	.380	.113	-.267	-.255
	2	-.054	-.003	.048	.112	.207	.362	.886	-.150
	1	.388	.218	.126	.078	.058	.059	.117	.871
	8	.252	-.417	.508	-.508	.418	-.254	.063	-.053
	7	.439	-.496	.218	.209	-.494	.444	-.134	-.106
1.0	6*	.513	-.181	-.404	.423	.150	-.513	.225	-.158
	5**	.456	.256	-.404	-.339	.334	.408	-.359	-.203
	4	.304	.461	.122	-.349	-.444	-.061	.554	-.226
	3	-.155	-.401	-.422	-.207	.125	.386	.616	.222
	2	.045	.245	.401	.485	.483	.394	.336	-.203
1	.392	.218	.121	.066	.036	.018	.009	.882	

Ten-electron eight-atom π -system

* First excited state ... In figures 181 (page 156) and 197 (page 166), the signs of the coefficients are opposite to those given above.

** Highest ground state

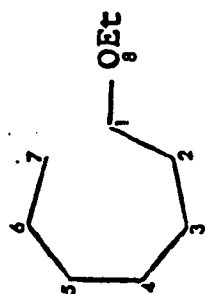


TABLE 12 (Cont.)

h ₇₇	Wave Functions	Energy Levels	Coefficients							
			1	2	3	4	5	6	7	8
0.5	8	+1.825	.249	-.413	.505	-.508	.421	-.261	.079	-.052
	7	+1.335	.433	-.495	.227	.192	-.483	.453	-.173	-.104
	6*	+0.634	.502	-.196	-.377	.435	.101	-.499	.308	-.152
	5**	-0.110	.440	.197	-.418	-.243	.391	.286	-.514	-.186
	4	-0.737	.322	.400	-.027	-.420	-.282	.211	.627	-.204
	3	-1.301	-.210	-.467	-.397	-.050	.332	.482	.421	.241
	2	-1.790	.059	.285	.452	.523	.484	.344	.186	-.225
	1	-2.356	.392	.218	.120	.066	.035	.017	.006	.882
0.0	8	+1.829	.245	-.407	.499	-.506	.426	-.273	.105	-.051
	7	+1.355	.422	-.491	.244	.161	-.461	.464	-.240	-.101
	6*	+0.705	.476	-.223	-.319	.447	.004	-.450	.447	-.141
	5**	+0.060	-.425	-.106	.432	.082	-.436	-.054	.628	.165
	4	-0.573	.374	.382	-.155	-.471	.115	.406	.496	-.210
	3	-1.243	-.239	-.499	-.381	.026	.413	.487	.275	.253
	2	-1.778	.064	.300	.469	.533	.480	.319	.126	-.232
	1	-2.356	.392	.218	.120	.066	.035	.016	.005	.882

Ten-electron eight-atom π -system

* First excited state... In figures 181 (page 156) and 197 (page 166), the signs of the coefficients are opposite to those given above.

** Highest ground state

APPENDIX 9

**Results of Bond Order Calculations for the 3H-azepine and
cycloheptatriene systems**

TABLE 13

Overall-bond orders of the first excited stateTen-electron eight-atom π -systemLinear models: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = 0.7$ Cyclic models: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = k_{17} = 0.7$

	h_{77}	Bond 12	Bond 56	Bond* order ratio 12/56	Bond 23	Bond 45	Bond** order ratio 23/45
	2	.604	.611	0.989	.680	.679	1.00
	1	.621	.592	1.05	.670	.682	0.984
	$\frac{1}{2}$	.647	.597	1.08	.651	.663	0.984
	0	.672	.638	1.05	.621	.613	1.02
	2	.590	.605	0.975	.658	.680	0.968
	1	.599	.591	1.01	.642	.675	0.952
	$\frac{1}{2}$	.611	.605	1.01	.619	.649	0.954
	0	.622	.653	0.953	.586	.594	0.938
	2	.593	.613	0.967	.655	.659	0.994
	1	.602	.607	0.992	.638	.647	0.985
	$\frac{1}{2}$	.610	.609	1.00	.618	.631	0.978
	0	.620	.613	1.01	.591	.606	0.975
	2	.582	.597	0.975	.633	.667	0.947
	1	.584	.591	0.988	.612	.654	0.935
	$\frac{1}{2}$	.587	.602	0.975	.591	.643	0.920
	0	.587	.600	0.978	.558	.613	0.912

* Ratio represents relative double bond strength of bond 12 to bond 56.

** Ratio represents relative double bond character of bond 23 to bond 45.

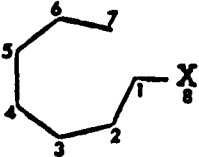
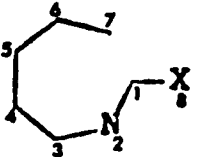
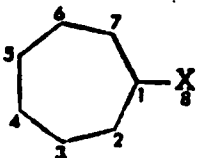
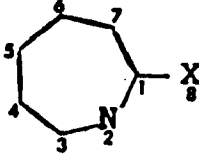
TABLE 14

HOMO-bond orders of the first excited state

Ten-electron eight-atom π -system

Linear models: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = 0.7$

Cyclic models: $h_{88} = 2.0$, $k_{18} = 0.8$, $k_{67} = k_{17} = 0.7$

	h77	Bond 12	Bond 56	Bond* order ratio 12/56	Bond 23	Bond 45	Bond** order ratio 23/45
	2	-0.0860	-0.100	0.860	.0708	.0795	0.890
	1	-0.0930	-0.0770	1.21	.0731	.0634	1.15
	$\frac{1}{2}$	-0.0980	-0.050	4.90	.0738	.0439	1.68
	0	-0.106	-0.0018	5.9	.0711	.0017	41.8
	2	-0.100	-0.0870	1.15	.0691	.0695	.990
	1	-0.111	-0.064	1.73	.0710	.0537	1.32
	$\frac{1}{2}$	-0.121	-0.038	3.18	.0711	.0337	2.11
	0	-0.135	+0.008	***	.0653	-.008	****
	2	-0.0710	-0.135	0.526	.0618	.0986	0.627
	1	-0.0700	-0.136	0.515	.0605	.0988	0.612
	$\frac{1}{2}$	-0.0670	-0.138	0.486	.0590	.0995	0.593
	0	-0.0610	-0.142	0.429	.0541	.101	0.536
	2	-0.0730	-0.128	0.570	.0565	.0925	0.611
	1	-0.0660	-0.132	0.500	.0525	.0944	0.556
	$\frac{1}{2}$	-0.0590	-0.138	0.428	.0479	.0963	0.497
	0	-0.0400	-0.150	0.266	.0347	.100	0.346

* Ratio represents relative double bond weakness of bond 12 to bond 56.

** Ratio represents relative double bond character of bond 23 to bond 45.

*** Bond 12 much weaker than bond 56.

**** Bond 23 much stronger than bond 45.

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