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THE CHEMISTRY
OF
ENDO TRIAZOLINES

A THESIS

Presented to

The Faculty of the Graduate Division

by

Robert Howard Hill, Jr.

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

in the School of Chemistry

Georgia Institute of Technology

November, 1972

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THE CHEMISTRY

OF

ENDO TRIAZOLINES

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Leon N. Zalkow
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GLOSSARY OF ABBREVIATIONS

c	complex (NMR)
d	doublet (NMR)
e.u.	entropy units
g	gram
G.L.C.	gas-liquid chromatography
IR	infrared
i.u.	integration units
l.	liter
M^+	molecular ion in mass spectrum
m	multiplet
m/e	mass to charge ratio
mg	milligram
min	minute
ml	milliliter
nm	nanometers
NMR	nuclear magnetic resonance
q	quartet (NMR)
rt	retention time
s	singlet (NMR)
t	triplet (NMR)
T.L.C.	thin layer chromatography
uv	ultraviolet

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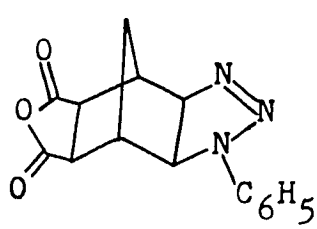
SUMMARY

Previous reports[26,28,31] from this laboratory have shown that exo triazolines, such as 40, decompose under pyrolysis conditions to give predominantly endo aziridines, such as 41. These workers proposed the formation of a diazoimine intermediate (38) to explain their observations. In this work is presented the successful synthesis of an endo triazoline. The results of several unsuccessful attempts to prepare this compound are also presented.



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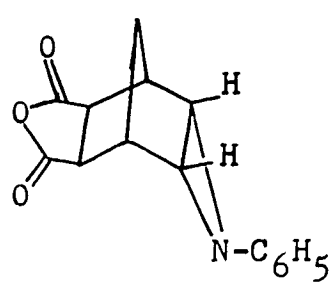

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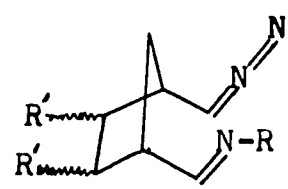

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The synthesis of endo triazoline (89) involves the preparation of two key intermediates, endo amine (80) and diazoamine (88). The latter compound was cyclized to the endo triazoline with sodium ethoxide and an ethanolic silver nitrate solution. Photolysis of 89 gave endo aziridine (92). Pyrolysis of 89 produced endo aziridine (92), exo aziridine (91), imine (94) and additionally a significant amount of

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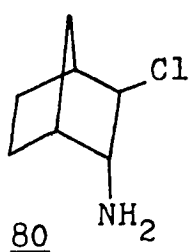
polymeric material. The formation of the exo aziridine (91) provides excellent evidence for the formation of a common intermediate, such as 38, in triazoline pyrolyses.



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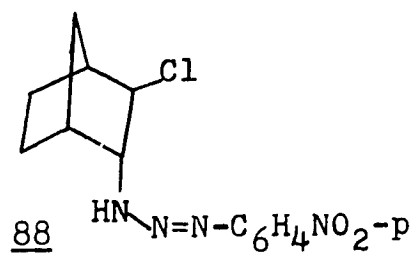

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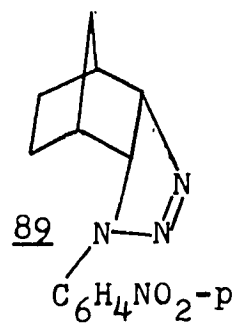

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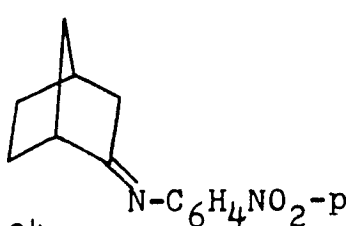

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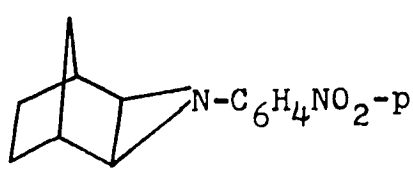

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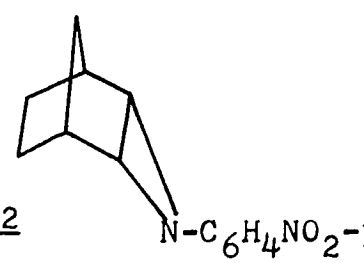

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A new mechanism has been proposed to explain the diverse results of triazoline pyrolyses. A concerted formation of a diazoimine has been postulated, which subsequently loses nitrogen to form a triplet carbene which then may add to the imine to form aziridines. A concerted imine formation from a triazoline has also been proposed. A diazonium betaine has been proposed to explain the formation of certain ionic products observed in some pyrolyses. Additionally the unexpectedly predominant formation of endo

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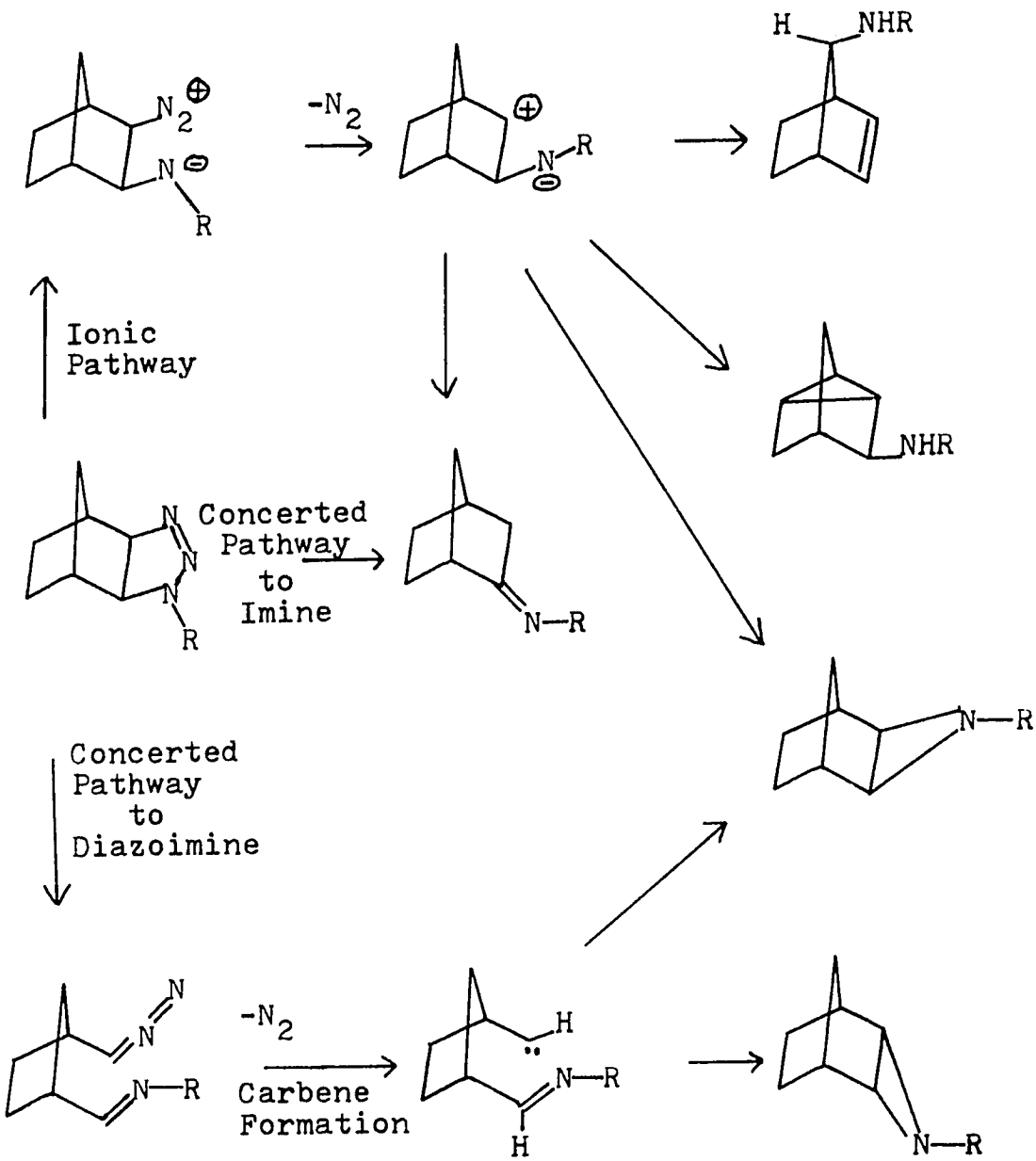
aziridines, such as 41, from the pyrolyses of certain triazolines containing anhydride or ester functions, such as 40, has been explained as the result of an exceedingly large field effect exerted by the anhydride function.



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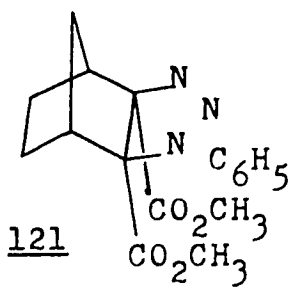
In supplemental study, exo triazoline (121) was prepared and its chemistry studied. Photolysis of 121 gave exo aziridine (122). Unexpectedly pyrolysis of 121 did not



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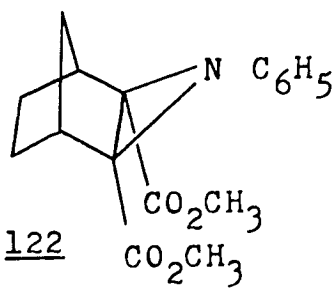

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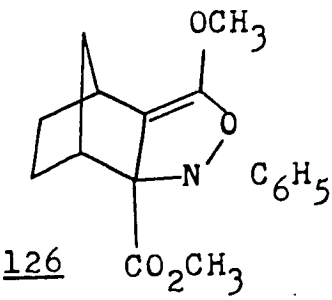

126

produce 121, but instead an unstable compound, postulated to be isoxazoline (126). Although the structure of 126 could not be conclusively established, infrared, NMR, and mass spectra provide excellent evidence for this compound.

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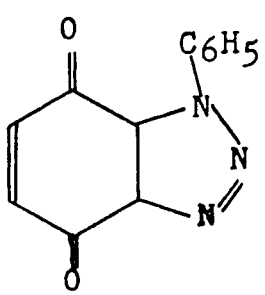
CHAPTER I

INTRODUCTION

Some eighty years ago Michael discovered that phenyl azide reacts with acetylene derivatives producing 1,2,3-triazoles[1]. This marked the beginning of study into the chemistry of azide addition products. Twenty years later, the first triazoline (1) was prepared by the reaction of phenyl azide with p-benzoquinone[2]. The team of Alder and Stein in 1931 found that norbornylene and its derivatives gave exo-Δ^2-1,2,3-triazolines (2) when reacted with phenyl azide[3]. These workers also recognized that phenyl azide



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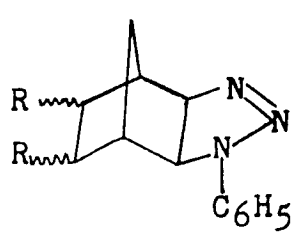

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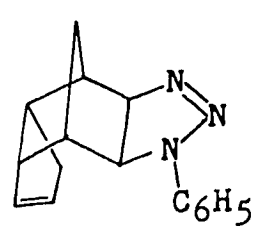

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reacted readily only with strained double bonds and this reaction was later used as a diagnostic test for strained alkenes. This was appropriately demonstrated by the fact that the strained double bond of dicyclopentadiene added phenyl azide to produce (3) while there was no reaction at the unstrained double bond[3]. In further investigations,

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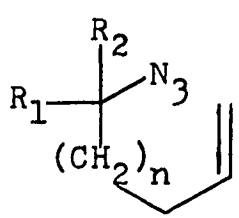
Alder and Stein were unable to obtain a triazoline from phenyl azide and cyclohexene[4]. Thus azide addition to unstrained double bonds received little attention until thirty years later when Logothetis reported that unstrained olefins (4) reacted with azide functions which were present internally and removed three or four carbons[5]. Scheiner has recently demonstrated that other unstrained double bonds under controlled conditions also react the azide moiety[6]. Several other types of "activated" olefins have been found to readily add azides, including enol ethers, enamines, and allenes[7,8].



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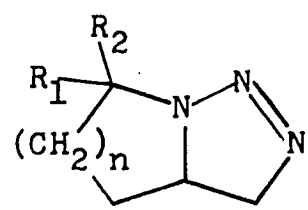

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Comparison of the rates of addition of phenyl azide at 25° to various olefins (Figure 1) also revealed that electron-donating or electron-withdrawing substituents on the double bond enhance the rate of azide addition[9]. Thus polarization of the olefin must play a key role in the mechanism of the addition. The rate of addition has also been shown to be influenced by steric factors[7]. While one carboxylate group enhanced the rate of addition, two groups

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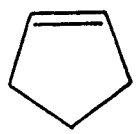
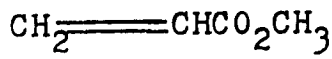


$19 \times 10^8 k_2$

6



$99 \times 10^8 k_2$

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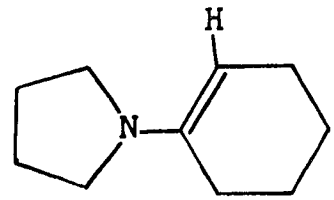


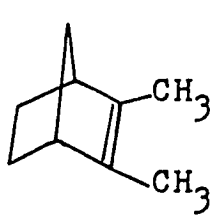
$99{,}300 \times 10^8 k_2$

8

Figure 1. Rates of Addition of Phenyl Azide to Various Olefins

caused a decrease in this rate. This was attributed to the fact that when two carboxylate functions are present, the approach of the azide is sterically hindered.

Azide addition to various norbornenes takes place only in an exo orientation. This was demonstrated by Alder and Stein, who found that while santene (9) added phenyl azide in an exo fashion, when this position is hindered to azide attack by a syn methyl group at C-7, as in apobornylene (10), the reaction failed[4]. The endo approach to norbornene appears to be blocked by the endo hydrogens at



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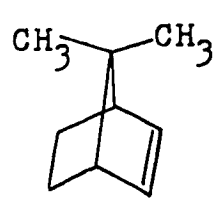

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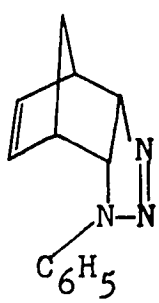
C-5 and C-6. Although norbornene has been shown to add phenyl azide only in the exo position[10], norbornadiene does not follow this rule. McLean and Findlay have isolated the first endo triazolines (11 and 12) from a norbornadiene and phenyl azide reaction mixture via fractional crystallization[11].



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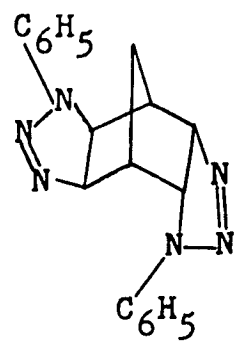

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The azide-olefin addition is one of a large group of reactions known as "1,3-dipolar cycloadditions"[7,9]. These reactions are regarded as concerted additions. Scheiner and co-workers found various aryl azides add to norbornene with large negative entropies of activation ($S^{\neq}$ = -29 to -32 e.u.), which are indicative of highly ordered transition states of a concerted reaction[12]. Substitution of the azide moiety with electron-withdrawing groups enhances the rate of addition[12]. This is explained by the unbalanced transition state (Figure 2) in which partial charges are developed on the N-1 nitrogen and the C-5 carbon. Electron-withdrawing substituents can stablize this transition state by delocalization of the partial negative charge at N-1.

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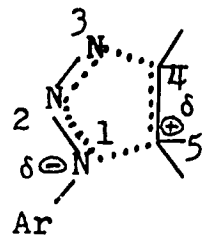
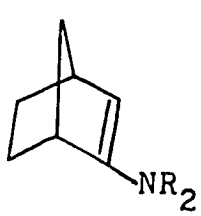


Figure 2. Transition State of an Azide Addition to an Olefin

Further support for the transition state has been provided by the orientation effects of substituted olefins. Thus the products of the reactions of phenyl azide with enamine (13) and ester (7) were the corresponding triazolines (14 and 15)[13,14].



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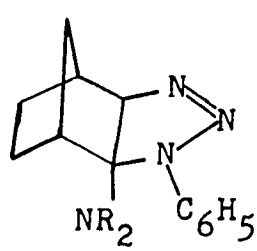

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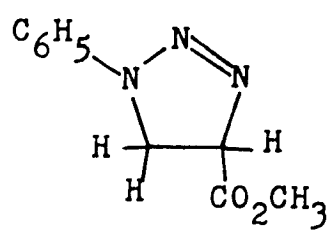

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Although the classic preparation of triazolines is via the azide-olefin pathway, there are at least two other reported methods. Diazomethane has been found to undergo a "1,3-cycloaddition" with anils to yield triazolines[15] (Figure 3). A unique synthetic pathway to this moiety,

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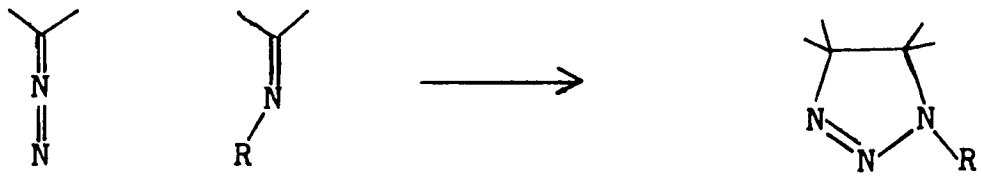

Figure 3. Triazoline Formation from Diazomethane and an Anil

reported by Heine and Tomalia, involved the isomerization of aziridines to triazolines[16] (Figure 4).

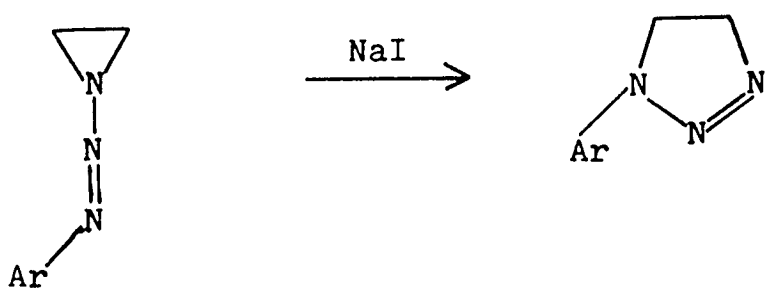

Figure 4. Triazoline Formation from Azirdine Isomerization

The great interest in Δ^2-1,2,3-triazolines arises from the fact that decomposition reactions, i.e. photolysis, pyrolysis, lead in many cases to substituted aziridines. Aziridines constitute a very interesting, useful group of compounds and have been extensively studied[17]. The biological properties and industrial uses of aziridines make any good synthetic pathway to this moiety important. In recent times two of the most publicized uses

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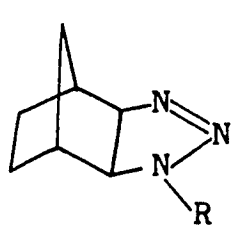
of these heterocycles have been as chemosterilants and as anti-cancer drugs[17]. The physiological effects of aziridines probably arise from the alkylating abilities of these compounds. It has been suggested that alkylation occurs at the nucleic acids, RNA and DNA, but also possibly involved are enzymes, their cofactors, and other cellar components[17a]. Aziridines also have many industrial applications, including uses in textiles, plastics, adhesives, coatings, photography, and many others[17b].

The stability of any given triazoline depends markedly upon the nature of the N-substituent. When R is a substituted phenyl group as in 16a, the triazoline is usually stable and can be isolated[12]. The presence of an electron-withdrawing group on the phenyl substituent decreases the thermal stability of these compounds[18].



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a. R=substituted phenyl
b. R=$PhSO_2$, PhCO, CN, picryl, tosyl

Investigators have shown that strong electron-withdrawing groups, as in 16b, so destablize the triazoline structure that nitrogen is immediately lost and the triazoline cannot be isolated[9,19,20].

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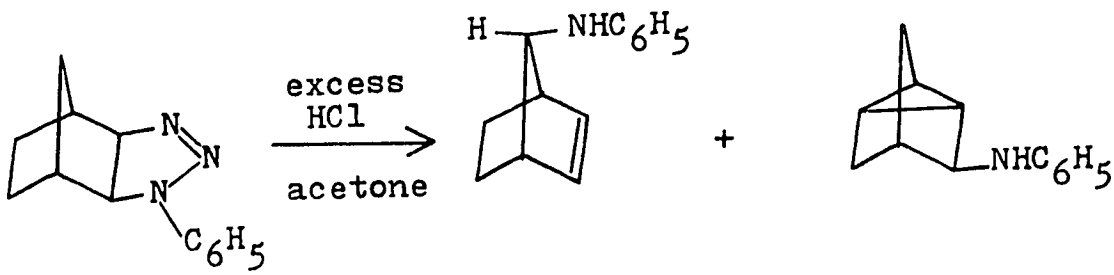
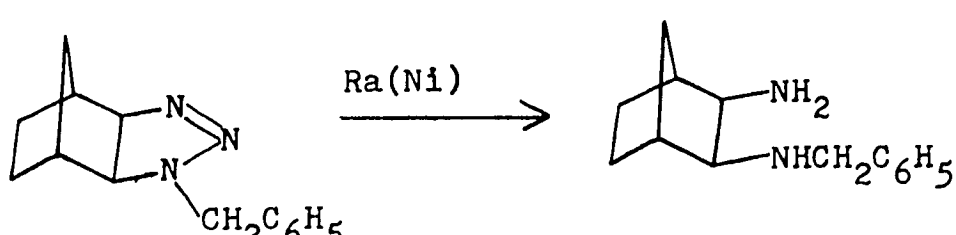
The chemistry of stable and unstable Δ^2-1,2,3-triazolines is an area of high interest and active research. As demonstrated by the example of McDaniel and Oehlschlager[18], triazolines are known to be acid sensitive, losing nitrogen immediately even at room temperature[9,21] (Figure 5). Hydrogenation of triazolines usually results in diamines, as in



17 18 19

Figure 5. Triazoline Decomposition in Acid Media

the case of the N-benzyl triazoline (20) (Figure 6)[21].



20 21

Figure 6. Hydrogenation of a Triazoline

Triazolines have been shown to decompose under photolytic conditions to substituted aziridines[17,20,22-24].

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Probably one of the most interesting of all reactions of the triazoline is its thermal decomposition. Pyrolysis of these N-substituted triazolines usually yields a variety of products including amines, imines, and aziridines[3,9,18,20,24-28]. Recently McDaniel and Oehlschlager[18] have investigated the pyrolysis of the phenyl azide adduct of norbornene (17). These workers isolated five products in various ratios depending upon the solvent used (Figure 7). It was also shown that the rate of decomposition of 17

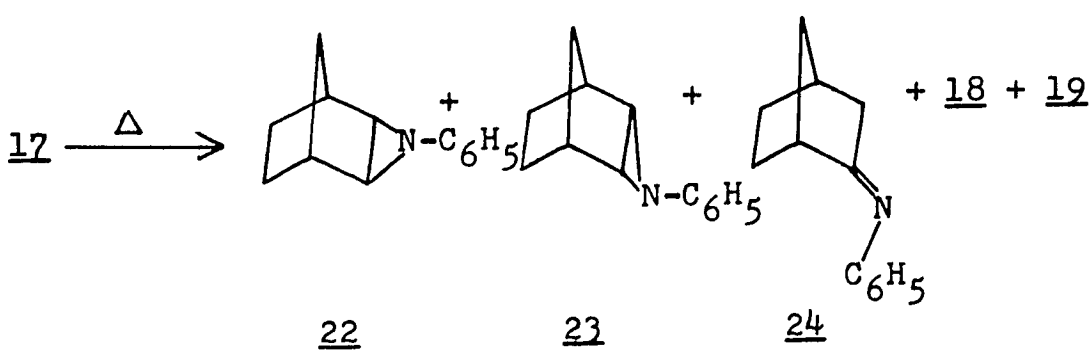
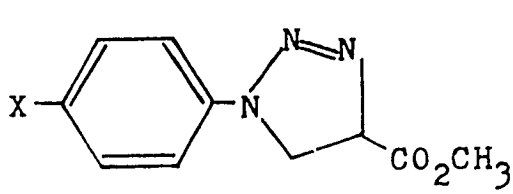


Figure 7. Pyrolysis of the N-Phenyl Adduct of Norbornene

increases as the polarity of the solvent is increased (i.e. from decalin to nitrobenzene). To be contrasted with these results is the report of Huisgen and co-



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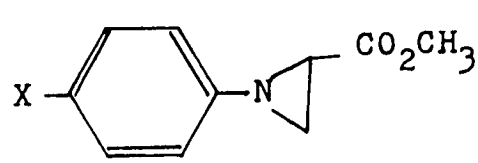

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workers[29], who found that pyrolyses of the *para* substituted phenyl triazolines (*25*) proceed at rates independent of the polarity of the solvents used to yield only aziridines (*26*).

Typical of the many diverse results observed in triazoline pyrolyses is the very recent report of Rengaraju and Berlin[30]. These workers have reported that the N-phosphorolated triazolines (*27* and *28*) decompose to yield the imines (*29* and *30*) (Figure 8). These results are examples of the few reported cases of 3,2-*endo*, *endo* group migrations in the norbornyl system.

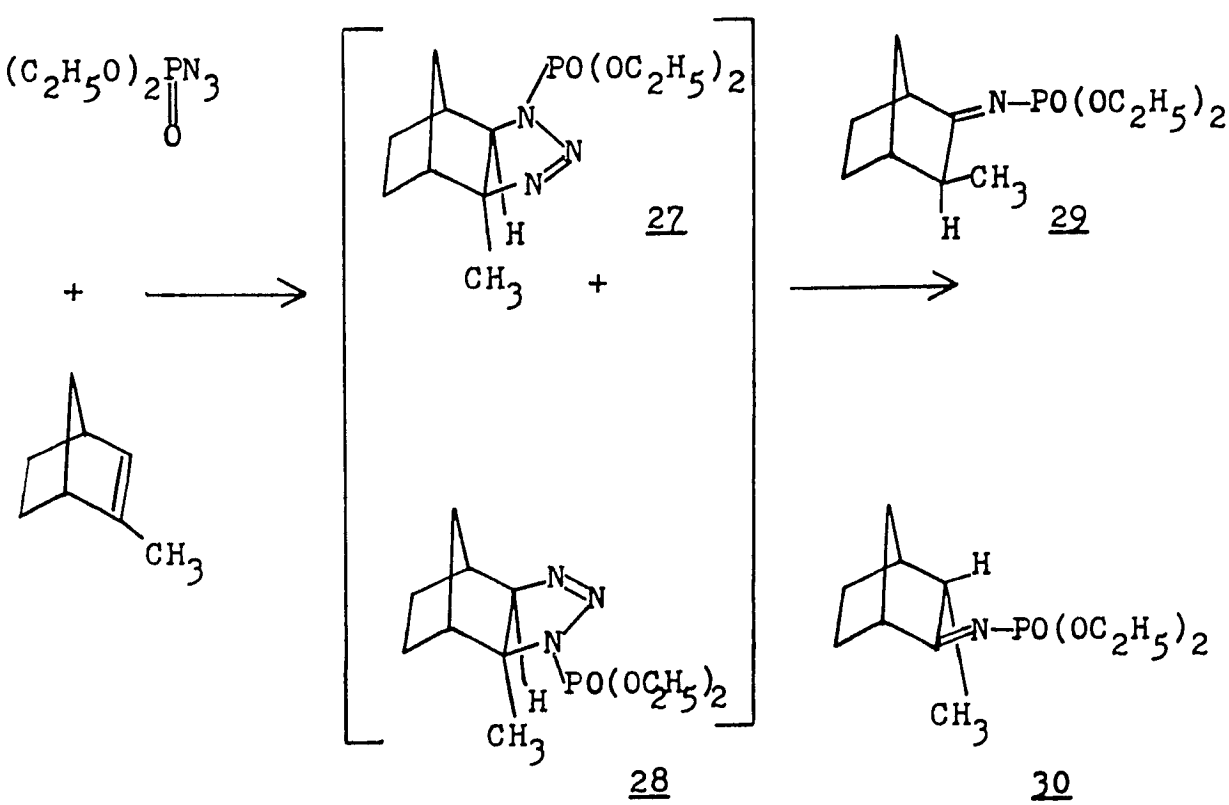

Figure 8. Decomposition of N-Phosphorolated Triazolines

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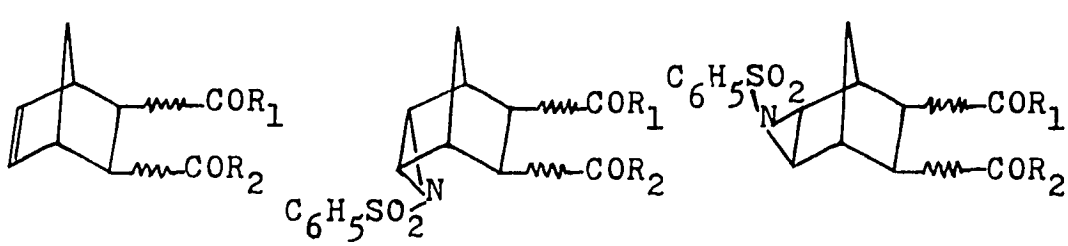
Zalkow et al.[26-28,31] have reported that benzenesulfonyl azide in refluxing carbon tetrachloride appeared to add to cis-endo (31a) and cis-exo (32a) anhydrides and cis-exo dimethyl ester (32b) in a manner which was an apparent violation of Alder and Stein's "exo addition rule"[32]. The principal products of each reaction were the endo aziridines (33a, 34a, and 34b, respectively), in contrast to the reaction of benzenesulfonyl azide with norbornene which yields exclusively the exo aziridine[20,33]. The cis-endo dimethyl ester (31b) and benzenesulfonyl azide in refluxing carbon tetrachloride produces the exo aziridine (35b). Photolysis of the endo and exo anhydrides and endo and exo dimethyl esters with benzenesulfonyl azide yields almost exclusively the exo aziridines in each case.



31a: endo anhydride $R_1=R_2=O$

31b: endo ester $R_1=R_2=OCH_3$

32a: exo anhydride $R_1=R_2=O$

32b: exo ester $R_1=R_2=OCH_3$

33a: endo anhydride $R_1=R_2=O$

33b: endo ester $R_1=R_2=OCH_3$

34a: exo anhydride $R_1=R_2=O$

34b: exo ester $R_1=R_2=OCH_3$

35a: endo anhydride $R_1=R_2=O$

35b: endo ester $R_1=R_2=OCH_3$

36a: exo anhydride $R_1=R_2=O$

36b: exo ester $R_1=R_2=OCH_3$

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Investigation of the mechanism of this reaction has revealed that a nitrene formation from azide decomposition is not involved[28]. It has also been shown that the formation of an endo triazoline is unlikely[4,7]. This leads to the conclusion that the endo aziridines must have arisen from unstable exo triazolines. A mechanism has been proposed involving the diazoimine intermediate 38 in Figure 9[18,25,27,28], which accounts for the formation of the endo aziridines. Support for this type of carbon-carbon bond cleavage is found in a report by Fusco and others[34], who have isolated diazoalkanes and imines from triazoline

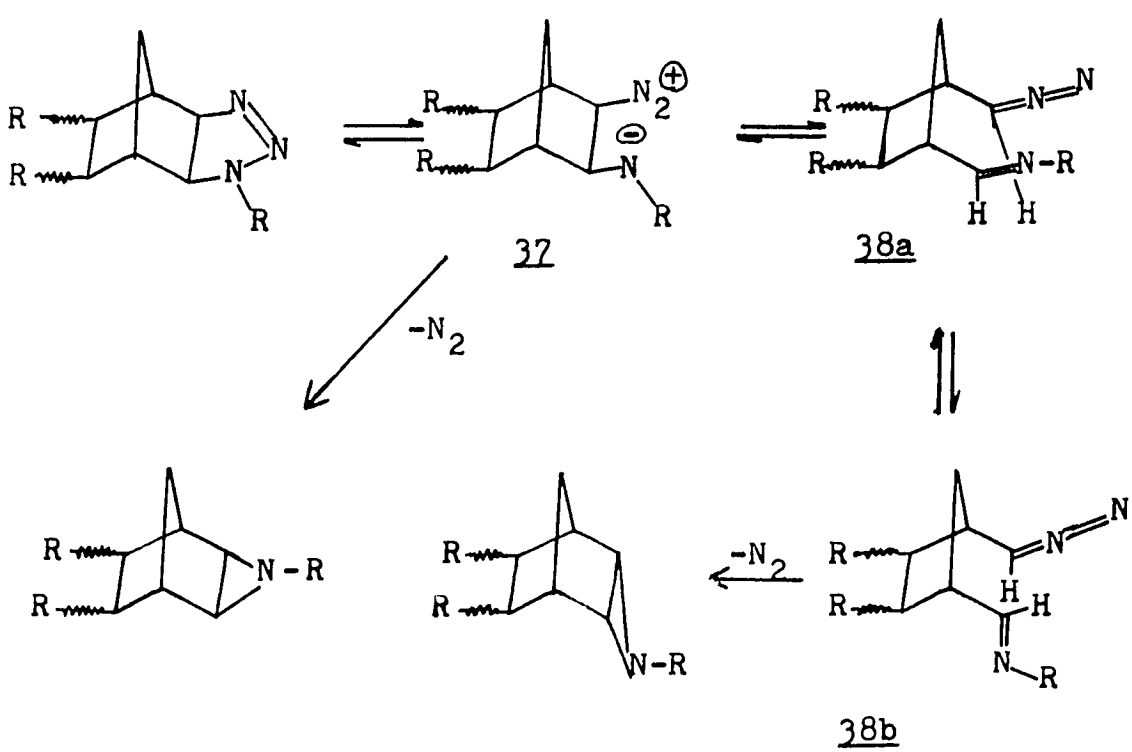

Figure 9. Mechanism of Triazoline Decomposition

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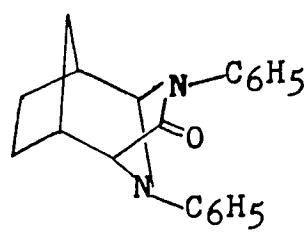
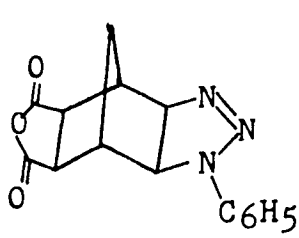
decompositions. Baldwin and his coworkers[25] have also demonstrated evidence for this kind of cleavage when 39 was isolated from pyrolysis of triazoline (17) in the presence of phenyl isocyanate. The report of Zalkow and



39

Hale[28] that triazoline (40) decomposes under pyrolytic conditions in decalin to produce endo aziridine (41) and exo aziridine (42) in a 54:46 ratio also supports the above proposed mechanism. Carpenter et al.[35] have reported that



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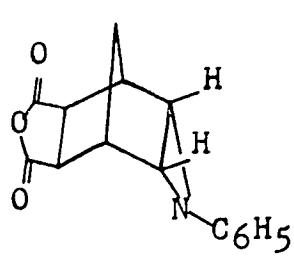

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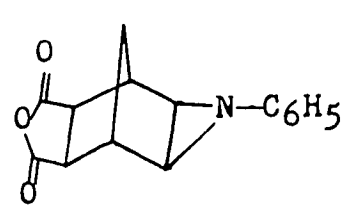

42

the fluorinated triazoline (43) under different pyrolysis conditions decomposed by two different pathways. Pyrolysis over glass beads yields an aziridine (44), while pyrolysis over nickel balls produces difluorodiazomethane and the

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corresponding imine (46).

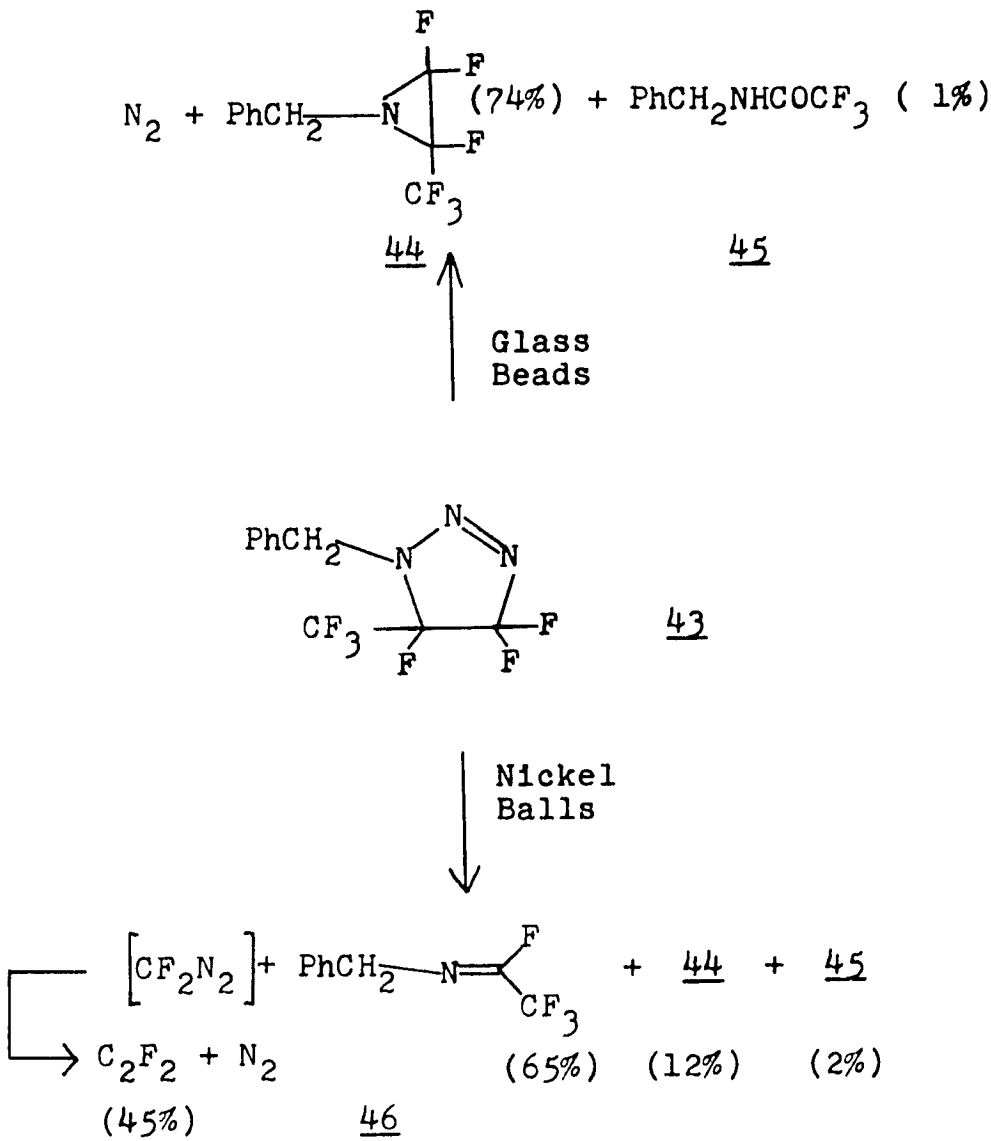

Figure 10. Triazoline Decomposition by Different Pathways

The results presented above are certainly interesting, but they bring up certain unanswered questions. Among these questions is, for instance, why do the products re-

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sulting from a certain triazoline pyrolysis differ so markedly from those products resulting from another structurally similar triazoline under similar pyrolysis conditions? Or more specifically, why does 17 produce aziridines, imine, and other amines, while 40 produces only aziridines? Or why do some triazolines decompose thermally to produce only imines? A second question which should be considered is, could the inability to isolate certain "unstable" triazolines be linked directly to the mechanism involving a diazoimine intermediate? Thirdly, if heterocyclic cleavage to a diazonium-betaine intermediate (37) is important in triazoline decomposition, then why are only aziridines observed in some cases, and not other products resulting from cationic rearrangement? If indeed a diazoimine intermediate (38) is involved as in the proposed mechanism discussed above (Figure 9), then by what mechanism are the products formed from this diazoimine? Lastly, in the case of the norbornyl triazolines, if exo triazolines under pyrolytic conditions produce endo aziridines, then will endo triazolines give rise to exo aziridines? Unfortunately, endo triazolines (47) have not been reported. One of the purposes of the present study was to devise a synthetic route to the endo triazoline and to study the chemistry of this compound. This study was to further elucidate the mechanism by which endo aziridines are derived from exo triazolines. The research presented in this work includes the

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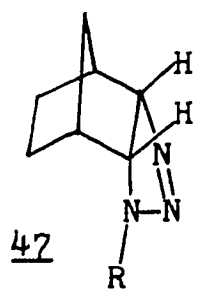
successful synthesis of an endo triazoline and an investigation of its chemistry. The discussion of the results also attempts to clear up the unanswered questions which have been raised above.



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CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Melting points were determined on a Thomas-Hoover capillary melting point apparatus or on a Fisher Microstage Melting Point apparatus and were uncorrected. Infrared spectra were recorded on a Perkin Elmer 237B spectrophotometer. Solids were in the form of potassium bromide pellets, while liquids were taken as thin films between sodium chloride plates, or as solutions in carbon tetrachloride or chloroform in matched 0.1 mm sodium chloride cells. All spectra were marked with a band at 1601 cm^{-1} of a polystyrene film as reference. Nuclear Magnetic Resonance (NMR) spectra were recorded on a Varian Associates Model A-60 spectrometer using solutions containing tetramethylsilane (TMS) as an internal standard. Mass spectra were taken using a Varian Associates Model M-66 mass spectrometer equipped with a gas-liquid chromatography interface*. Ultraviolet spectra were obtained with a Jasco Model M-66 ORD/UV-5 spectrophotometer. Gas-liquid chromatography (GLC), analytical and preparative, was performed on an F & M Model 400 and Model 402 Biomedical gas chromatograph with a hydrogen flame detector. The analytical columns

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*The author wishes to sincerely thank Mr. George Turner for the operation of the mass spectrometer.

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were glass (6 ft. x 1/8 in. inside diameter) and were bent in a U shape. The preparative column was glass (4 ft. x 1/2 in. inside diameter), fitted with a stream splitter and was bent in a U shape. The relative peak areas were measured by the cut and weigh method. Photolyses were carried out with either a 200 or 400 watt Hanovia mercury lamp through a quartz filter. Diazomethane was generated from EXR-101 obtained from E. I. Dupont Nemours, Inc., Gibbstown, New Jersey. Microanalyses were performed by Alfred Bernhardt, Microanalytical Laboratories, Mulheim, West Germany and Atlantic Microlabs, Inc., Atlanta, Georgia. Low pressure hydrogenations were carried out on a Parr Hydrogenation Apparatus.

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CHAPTER III

EXPERIMENTAL

Attempted Nitrene Addition to Bornylene

N-Aminophthalimide (48)

N-Aminophthalimide (48) was prepared by the method of Drew and Hatt from phthalimide and hydrazine in ethanol[36]. The product had the same properties as those previously reported; ν_{max}^{KBr} 3340,3260,1780,1715 cm^{-1}; M^+ at m/e of 162 (Calc'd for $C_8H_6N_2O_2$: m/e of 162).

Attempted Reaction of an Amino-Nitrene[37] with Bornylene

Bornylene (14.7 g) was dissolved in 50 ml of methylene chloride at 0°. N-Aminophthalimide (1.0 g) was introduced to this solution. To this suspension was added 2.8 g of lead tetraacetate over a five minute period. The solution immediately turned yellow upon first addition of the lead tetraacetate. The solution was stirred an additional ten minutes at ice bath temperature and then for one hour at room temperature. After this time, the lead salts were filtered and the solution was stored overnight in the freezer. Upon concentration of the solution a precipitate (441 mg) appeared and was removed by filtration. The remaining solution was chromatographed on 68 g of basic alumina, using benzene to ethyl acetate to methanol. The

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precipitate was identified as phthalimide by infrared analysis. Bornylene (7.5 g) and phthalimide (0.15 g) were recovered from the chromatography.

Several other unidentified oils were isolated, but were judged not to be the desired product as indicated by the absence of any aromatic protons in their NMR spectra.

Azide Addition to 54 and 61

Reaction of Phenyl Azide and Dimethyl Bicyclo {2,2,1} hepta-2,5-diene-2,3-dicarboxylate (54)

A solution of phenyl azide (42.1 mM, 5.0 g) and the diene (54) (54.7 mM, 11.4 g) {1:1.3 ratio} in 30 ml of cyclohexane was refluxed for two hours under nitrogen on a steam bath. The solution turned to a dark red color after 5 minutes refluxing. After reflux, the solution was allowed to stand for four days. The solution separated into two phases, the top, a clear yellow color and the lower, a dark brown-red color. The upper layer was removed by pipette. Part of the remaining lower layer, 2.0 g, was boiled in hot ether and filtered. White crystals precipitated from the ether and were filtered (m.p. 120-123°). After recrystallization from ether, the melting point was 126-127°. This compound was identified as dimethyl 1-phenyl -1,2,3-triazole-4,5-dicarboxylate (60) (rpt.[1] 126-127°); ν_{max}^{KBr} 1720 cm^{-1}; δ ($CDCl_3$), 7.54 (5H,s), 3.99 (3H,s), 3.90 (3H,x); M^+ at m/e of 261 (Calc'd for $C_{12}H_{11}N_3O_4$: m/e of 261);

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$\varepsilon_{240} = 8150.$

Preparation of Benzyl Azide

Benzyl azide was prepared according to the reported procedure[38] from benzyl chloride and sodium azide; ν_{max}^{neat} 2195 cm^{-1}; δ ($CDCl_3$), 7.15 (5H,s), 4.07(2H,s).

The Reaction of Benzyl Azide with Norbornadiene (61)

This reaction was carried out several times using various ratios of benzyl azide to norbornadiene. In Table 1 are shown the moles of each reactant in a given experiment and the amount of crystalline product.

Table 1. The Reaction of Benzyl Azide and Norbornadiene

Experiment No.	I	II	III	IV	V
10^2x Moles Benzyl Azide	3.76	3.76	3.76	3.76	3.76
10^2x Moles Norbornadiene	2.89	3.76	4.89	7.52	15.4
Amount of Crystalline product (g)	4.39	4.10	3.40	1.10	0.71

A typical procedure is described below. Into a refluxing solution of 3.5 g (0.038 m) of norbornadiene in 10 ml of cyclohexane was added drop-wise 5.0 g (0.038 m) of benzyl azide in 5 ml of cyclohexane. The solution was refluxed for two and one-third hours (total reflux time after start of addition of the azide) and allowed to stand at room temperature for two days. A brown precipitate (4.1 g) formed and was removed by filtration. This solid

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was boiled in ether and filtered to give 2.4 g of undissolved solid. Boiling this solid in ether gave 1.6 g insoluble part. The filtrate was concentrated and 0.3 g of solid was collected by filtration. Similar operations on the latter solid gave white needles from ether, m.p. 154-156°, which were identified as the anti-di-exo triazoline (67); ν_{max}^{KBr} 3050,2940,1465,1445,995,700 cm^{-1}; δ ($CDCl_3$) 1.15 (2H,m), 2.60 (2H,m), 3.22 (2H,d,J=9Hz), 4.31 (2H,d,J=9Hz), 4.61 (2H,d,J=15Hz), 4.90 (2H,d,J=15Hz), 7.30 (10H,s); M^+ minus two moles of molecular nitrogen at m/e of 302 (Calc'd for $C_{21}H_{22}N_6-2N_2$; m/e of 302); Anal.: 70.45% C, 6.3% H, 23.32% N. (Calc'd: 70.39% C, 6.15% H, 23.46% N).

Another compound (m.p. 168-170°) was isolated from the 1.6 g of insoluble solid from above via fractional crystallization from carbon tetrachloride, then n-hexane and ether. This was identified as the syn-di-exo triazoline (68); ν_{max}^{KBr} 3050,3030,2975,2920,1490,1475, 1350,1120,1105,1000,725 cm^{-1}; δ ($CDCl_3$), 1.10 (2H,m), 1.97 (1H,m), 3.00 (2H,d,J=9Hz),* 3.08 (1H,m), 4.48 (2H,d,J=9Hz)** 4.48 (2H,d,J=15Hz),** 4.79 (2H,d,15Hz), 7.27 (10H,m); M^+ minus two moles of molecular nitrogen at m/e of 302 (Calc'd for $C_{21}H_{22}N_6-2N_2$: m/e of 302); Anal.: 70.28% C,

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*The multiplet at δ 3.08 lies under one of the doublet signals.

**The doublet with J=9Hz falls between the doublet with J=15Hz.

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6.38% H, 23.39% N (Calc'd: 70.39% C, 6.15% H, 23.46% N).

The ratio of I to II was found to be 2.2 to 1 based on the amounts of each recovered.

Attempted Cyclopentadiene Addition to 69 and 71

1-Benzyl-1,2,3-Triazole-4,5-Dicarboxylic Acid

1-Benzyl-1,2,3-triazole-4,5-dicarboxylic acid was prepared from acetylene dicarboxylic acid and benzyl azide by the method of Wiley, Hussung and Moffat[39];

ν_{max}^{KBr} 2500,1760 cm^{-1}.

1-Benzyl-1,2,3-triazole (69)[39]

1-Benzyl-1,2,3-triazole was prepared by decarboxylation of the 4,5-diacid according to the usual procedure;

ν_{max}^{KBr} 3100,1600 cm^{-1}.

Attempted Addition of Cyclopentadiene (59) with 1-Benzyl-1,2,3-Triazole

To freshly prepared cyclopentadiene[40] (2.0 g) at -78° was added 4.9 g of 1-benzyl-1,2,3-triazole in 100 ml of ether. After several minutes, the starting triazole precipitated from solution. The solution was allowed to warm to room temperature and then was refluxed for ten minutes.

As the solution cooled, the triazole again precipitated. The mixture was refluxed once again for eight hours on a steam bath and then placed in the freezer overnight. No solid had formed after this time and the solution was

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then cooled in dry ice. The starting triazole (4.2 g) crystallized.

2-Imidazolone-4-Carboxylic Acid

The 2-imidazolone-4-carboxylic acid was obtained by Hilbert's[41] method from tartaric acid and urea; ν_{max}^{KBr} 3130, 3000,1740,1660 cm^{-1}; M^+ at m/e of 128 (Calc'd for $C_4H_4N_2O_3$: m/e of 128).

2-Imidazolone (71)

Using Duschinsky and Dolan's procedure[42], the 2-imidazolone-4-carboxylic acid (2.00 g) and 6.00 g of copper powder was heated at 265° overnight under vacuum in a water cooled sublimator. The next morning, the 2-imidazolone (0.82 g) was removed from the sublimator (62% yield). The compound had the same properties as previously reported; ν_{max}^{KBr} 3400,3140,2750,1645 cm^{-1}.

Attempted Diels-Alder Reaction of 2-Imidazolone (71) and Cyclopentadiene (59)

To 3.1 g of freshly prepared cyclopentadiene[40] was added 1.0 g of 2-imidazolone in 100 ml of 95% ethanol. This was allowed to stand at dry ice temperature with stirring for two hours. The dry ice was then removed and the flask gradually warmed to room temperature and was allowed to stand overnight. The solution was partially evaporated and a precipitate (629 mg) formed. Infrared analysis showed the solid to be the 2-imidazolone. Further concentrations gave more 2-imidazolone (240 mg).

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In another attempt to complete the Diels-Alder reaction, 0.401 g of 2-imidazolone and 1.0 g of dicyclopentadiene were placed in a sealed tube and heated to 175° for eight hours. After cooling to room temperature, the sealed tube was further cooled by dry ice and then opened. The mixture was washed from the tube with ethanol and the precipitate was filtered (60 mg). Infrared showed this to be 2-imidazolone. Further concentrations also gave the starting material (162 mg).

In still another attempt, 0.628 g of 2-imidazolone and 1.0 g of freshly prepared cyclopentadiene was placed in a sealed tube and heated to 140° for fifteen hours. Cooling, opening, and rinsing the contents from the tube gave a solution and precipitate. Infrared analysis showed the precipitate to be 2-imidazolone.

Synthesis and Chemistry of endo Triazoline (89)

Reaction of Norbornene with Nitrosyl Chloride

The dimer (76) was prepared as previously described[43]. A solution of 95 g of norbornene (75) in 1125 ml of chloroform was cooled to -75° in a dry ice-acetone bath. Nitrosyl chloride was slowly bubbled into the rapidly stirred solution and a bright blue color appeared. Soon a white precipitate was observed and as the reaction neared completion, the brown color of excess nitroxyl chloride was seen. The gas inlet tube was removed and the solution was allowed to

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stir for an additional thirty minutes. The white solid was removed by filtration with suction and washed twice with hexane. After drying overnight on the filter, the product (76) was recrystallized by dissolving in a minimum amount of hot chloroform and then adding an equal amount of hexane. The crystals were filtered from the hot solution (product crystalizes upon addition of hexane) and a second crop was obtained from the filtrate after it cooled giving a total yield of 50-56%; m.p. 155-156° (rpt.[43] 155.5-156.5°); ν_{max}^{KBr} 1615,1385,1230,670 cm^{-1}; $M^+/2$ at m/e of 159 (25%, Calc'd for $(C_7H_{10}ClNO_2)/2$: m/e of 159).

3-Chloronorcamphor Oxime (77)

A suspension of the dimer (76) (100 g), and urea (40 g) was refluxed in 500 ml of isopropyl alcohol until the solid disappeared (2-3 hours) according to the procedure of Miller[44]. The solution was allowed to cool and the alcohol was removed in vacuo. To the residual oil was added 600 ml of water and the mixture was extracted with four 100 ml portion of chloroform. The combined chloroform extracts were washed with four 100 ml portions of chloroform. The combined chloroform extracts were washed with four 100 ml portions of water, then dried over sodium sulfate. Removal, in vacuo, of the chloroform gave a quantitative yield of the desired oxime (77) as an oil (rpt.[44] m.p. 62-67°); ν_{max} film 3250,1675,1450 cm^{-1};

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M^+ at m/e of 159 (50%, Calc'd for $C_7H_{10}ClNO$: m/e of 159); δ ($CDCl_3$) 4.40 and 4.25 (Total area of both, 1H {ratio of 30/70 respectively}, d,J=2.0 Hz), 3.53 and 2.96 (Total area of both, 1H {ratio of 70/30 respectively}, m),2.58 (2H,m), 2.88-1.10 (6H,c).

Attempted Catalytic Reduction of the 3-Chloronorcamphor Oxime (77)

A solution of 2.0 g of the 3-chloronorcamphor oxime in 100 ml of methanol over 0.2 g of 5% rodium on alumina was placed in a 500 ml hydrogenation bottle which was shaken at 56 psi hydrogen pressure in a Parr Apparatus overnight. The resulting solution was filtered, 150 ml of dry ether was added to the filtrate and hydrogen chloride was bubbled into the latter for ten minutes. The solution, which had turned a deep yellow color was evaporated, in vacuo, and ether was added to the residual oil. Some precipitate resulted and the ether was decanted from the solid-oil mixture. Acetone was then added to this oily mixture and a precipitate formed. This solid was filtered and dried in air. This compound was not the desired amine hydrochloride and no further attempt was made to identify it; ν_{max}^{KBr} 3400,3125, 1625,1405 cm^{-1}; $\nu_{max}^{CCl_4}$ 2950,1090 cm^{-1}

Acetylation of 3-Chloronorcamphor Oxime (77)

A solution of the oxime (2.0 g) in 4.0 ml of acetic anhydride and 4.0 ml of dry pyridine was allowed to stir at

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room temperature overnight. The solution was then poured into an equal volume of ice water and an oil precipitated. The water-oil mixture was extracted three times with chloroform; the chloroform layer was then extracted sequentially with 10% aqueous HCl, with 5% aqueous $NaHCO_3$, with water, and finally dried over sodium sulfate. Removal of the chloroform in vacuo gave 2.3 g (92%) of an oil which was the desired oxime acetate (78); ν_{max}^{film} 1770,1660 cm^{-1}; $M^+ - C_2H_3O_2$ at m/e of 142 (48%), shows no molecular ion (Calc'd for $C_9H_{12}ClNO_2$: m/e of 201); δ (CCl_4), 4.34 (1H, overlapping d, J=2.5Hz), 3.48 and 3.03 (total area of both, 1H {60/40 ratio respectively},m), 3.57 (1H,m), 2.10 and 2.07 (total area of both, 3H,s), 2.05-1.10 (6H,c); Anal.: 53.70% C, 6.01% H, 17.70% Cl, 7.01% N (Calc'd 53.73% C, 5.97% H, 17.64% Cl, 6.97% N.)

A special note of caution must be included here. 3-chloronorcamphor oxime acetate as well as the 3-chloronorcamphor oxime p-nitrobenzoate, both caused dermatitis in individuals who came in contact with these agents. One co-worker exposed through accidental contact with the acetate developed such a severe case of dermatitis on both hands and arms that he was unable to work in the laboratory for several weeks. It is possible that these compounds sensitize the skin in some manner, since this author, himself, upon initial contact with these substances had no

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adverse effects. At a later time when in contact with these compounds, he experienced severe itching for several days. Since these compounds are heretofore unknown species, due caution should be exercised, particularly in light of the above effects.

Attempted Catalytic Reduction of the 3-Chloronorcamphor Oxime Acetate (78)

Into a 500 ml hydrogenation bottle was placed 0.50 g of the chlorooxime acetate in 50 ml of methanol. To this was added 0.16 g of 5% rhodium on carbon. (CAUTION: While adding the catalyst, the dust-methanol vapor mixture ignited.) This bottle was placed in a Parr Apparatus and hydrogenated overnight under 56 psi of hydrogen. The catalyst was then removed by filtration and the solvent was removed in vacuo. The solution was blue in color until the solvent was completely removed and at that time the solid obtained was light, white green (0.5 g). Recrystallization from methanol-chloroform (1:2) gave 78.3 mg of a solid which could not be dissolved in deuterochloroform or trifluoroacetic acid; ν_{max}^{KBr} 3400,3125,1625,1405 cm^{-1} (these were the only bands); δ (D_2O) 4.95 (broad hump); mass spectrum shows solid loses hydrogen chloride. Different spectra were observed at different temperatures. At 100° probe temperature, m/e 205 is the highest mass observed, while at 150° m/e is the highest detectable ion.

This compound was dissolved in water and made basic

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with sodium bicarbonate, then sodium hydroxide. This water layer was extracted with four 20 ml portions of ether and the ether layer was dried overnight with sodium sulfate. The solvent was removed in vacuo to give 40 mg of a pale yellow oil. This oil was dissolved in carbon tetrachloride and its infrared spectrum was taken. The spectra showed no N-H absorption and therefore this was not the desired product, but rather the same unidentified product isolated from the attempted catalytic reduction of the 3-chloronorcamphor oxime; ν CCl_4 2950,1090 cm^{-1}.

Attempted Sodium Borohydride Reduction of the Oxime Acetate (78)

The oxime acetate (1.0 g) was dissolved in 15 ml of absolute ethanol, to which was added 0.4 g of sodium borohydride in 10 ml of absolute ethanol. This solution was stirred for one and three quarter hours and then poured into 25 ml of water. The water layer was extracted twice with 25 ml portions of ether and the ether was dried over sodium sulfate. The drying agent was filtered and the ether was removed in vacuo to give an oil. This crude product was identified as syn and anti norcamphor oxime. Analysis by g.l.c. with 3% SE-30 on Gas Chrom Q,100/200 mesh column at a column temperature of 130° showed the syn and anti oxime esters, which appeared at 6.3 and 7.2 minutes initially, had disappeared and a single peak appeared at 1.3 minutes. This compound had the same retention time as norcamphor

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oxime prepared from norcamphor[45]; ν_{max}^{neat} 3350 cm^{-1}; $\nu_{max}^{CCl_4}$ 3590,3250,2950,1680 cm^{-1}; δ ($CDCl_3$) 9.20 (1H,b), 3.52 (0.6H,s),2.88 (0.4H,s), 2.48 (1H,s), 2.33-1.10 (8H, complex); M^+ at m/e of 125 (Calc'd for $C_7H_{11}NO$: m/e of 125): Norcamphor oxime from norcamphor: ν_{max}^{neat} 3350 cm^{-1}; $\nu_{max}^{CCl_4}$ 3590,3250,2950,2865,1675 cm^{-1}; δ ($CDCl_3$) 9.20 (1H,b), 3.53 (0.1H,s), 2.88 (0.9H,s), 2.51 (1H,s), 2.32-1.20 (8H,c).

Hydroboration of 3-Chloronorcamphor Oxime Acetate (78)

Hydroboration of oxime esters have been previously reported[46]. The hydroboration apparatus used was similar to Brown's as reported in Organic Reactions[47]. Solvents and reagents were prepared according to Brown's procedure.

Into a solution of 4.1 ml (32.6 mM) boron trifluoride etherate in 10 ml of dry diglyme was added drop-wise 0.93 g (24.4 mM) of sodium borohydride in 35 ml dry diglyme over a one-hour period. The generated diborane was swept by a stream of nitrogen into a tetrahydrofuran solution containing 1.7 g of the oxime acetate. After complete addition of the borohydride solution to the boron trifluoride, the generator was heated gradually to 60° for one hour to drive off excess diborane. The generator was then disconnected and the tetrahydrofuran solution was stoppered and stirred for 20 hours. Water (5 ml) was cautiously added, the first drops of which brought about a vigorous reaction. All

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bubbling ceased after a few minutes and the solution was stirred for an additional hour, after which the solvent was then removed, in vacuo, to give the white borate ester. To this product was added 20 ml of 10% hydrochloric acid and the solution was refluxed for one hour, then allowed to cool to room temperature. The addition of 20 ml of 20% potassium hydroxide (basic to litmus) gave a milky white solution which was extracted with three 70 ml portions of ether. The combined ether extracts were dried over sodium sulfate overnight and filtered. Hydrogen chloride (excess) was bubbled into the ether solution and a white, flocculent precipitate immediately formed. The solid (0.2 g) (17%) was collected by filtration and washed several times with dry ether. The white flakes, m.p. 195-200°, were identified as the desired amine hydrochloride (80). ν_{max}^{KBr} 3400,2925, 1960,1590,1570,1495,1475 cm^{-1}; δ (CF_3CO_2H-$CDCl_3$) 7.08 (3H,b), 3.63 (2H,m), 2.50 (1H,m), 2.32 (1H,m), 2.0-1.0 (6H,c), absorption at 7.08 disappears upon addition of deuterium oxide; M^+-HCl at m/e of 145 (67%) (Calc'd for $C_7H_{12}ClN \cdot HCl$-HCl at m/e of 145); Anal.: 45.95% C, 7.23% H, 7.49% N, 39.09% Cl (Calc'd for $C_7H_{12}ClN \cdot HCl$: 46.17% C, 7.20% N, 38.94% Cl).

The salt was dissolved in water and basification of this solution with solid potassium hydroxide gave the free amine which was extracted from the basic solution with ether. Filtration (after drying over sodium sulfate) and removal of

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the solvent, in vacuo, gave the amine as a clear oil; $\nu_{max}^{CHCl_3}$ 3380,3300,1610 cm^{-1}; deuterated amine (sample from NMR) $\nu_{max}^{CHCl_3}$ 2215,2105,1645 cm^{-1}; δ ($CDCl_3$) 3.36 (1H,t,J=3.5Hz), 3.20 (1H,t,J=2.5 Hz), 2.23 (2H,c), 2.03-1.00 (8H,c); deuterium oxide added, all absorptions were the same except amine hydrogens disappeared from the region 2.03-1.00 (6H,c).

Attempted Etherification of the 3-Chloronorcamphor Oxime

The oxime (3.5 g) was dissolved in ether and to this was added freshly prepared diazomethane (~ 2 g). Two drops of boron trifluoride etherate were added to the solution and the next day the solution was evaporated. The residue was analyzed by g.l.c. on a 3% SE-30 on Gas Chrom Q, 100/120 mesh column, at a column temperature of 130°. There were two compounds present in this residue. 3-Chloronorcamphor oxime (82%) was identified by comparison of its retention time (2.3 min.) with that of an authentic sample and also by mixed injection with an authentic sample. The minor product (18%) was identified as 3-chloronorcamphor by comparison of its retention time (0.9 min.) with that of an authentic sample (prepared by the method of Meinwald et al[43]) and also by mixed injection with the authentic sample; residue ν_{max}^{neat} 3250,1755 cm^{-1}; 3-Chloronorcamphor ν_{max}^{neat} 1755 cm^{-1}.

p-Nitrobenzoate of 3-Chloronorcamphor Oxime (79)

The oxime (5.86 g) was dissolved in a solution of

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100 ml of anhydrous ether and 10 ml of chloroform, to which was added 7.58 g of p-nitrobenzoyl chloride. After stirring for thirty minutes, a flocculent, yellow precipitate appeared. After an additional thirty minutes of stirring, the solvent was removed in vacuo and the solid then washed with 100 ml of 10% sodium bicarbonate, then collected by filtration. Washing the product with 100 ml of water, drying in air and recrystallizing from 95% ethanol gave 7.6 g of the p-nitrobenzoate oxime (79) (67%), m.p. 175-176°; ν_{max} KBr 1750,1660,1530 cm^{-1}; M^+ at m/e of 308 (just detectable, Calc'd for $C_{14}H_{13}ClN_2O_4$: m/e of 308); δ ($CDCl_3$), 8.25 (4H,m), 4.53 (2H,overlapping d,J=2Hz), 3.70 and 3.29 (total area of both, 1H {40/60 ratio respectively},m), 2.72 (1H,m), 2.47-1.30 (6H,c); Anal.: 54.45% C, 4.36% H, 11.35% Cl, 9.27%N (Anal. Calc'd for $C_{14}H_{13}ClN_2O_4$: 54.47% C, 4.24% H, 11.48% Cl, 9.07% N.)

Hydroboration of 3-Chloronorcamphor Oxime o-p-Nitrobenzoate (79)

Sodium borohydride solution (1.86 g) in 70 ml of dry diglyme was added drop-wise to boron trifluoride etherate (8.2 ml) in 25 ml of dry diglyme. The diborane was swept by nitrogen into a 125 ml tetrahydrofuran solution of 7.9 g of the p-nitrobenzoate. The hydroboration was conducted as previously described (see p. 33). Excess diborane was destroyed by adding 10 ml of water to the tetrahydrofuran solu-

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tion and stirring for one hour. The tetrahydrofuran was removed, in vacuo, and the borate ester was hydrolyzed with 10% hydrochloric acid (40 ml) for two hours. The acid layer was extracted three times with 50 ml portions of chloroform, then made basic to litmus with excess potassium hydroxide. The basic layer was extracted five times with 40 ml portions of ether. The ether solution was dried over sodium sulfate, filtered and acidified with gaseous hydrogen chloride to give the amine hydrochloride (80) as a white precipitate (1.787 g; 41.3%).

The above reaction was scaled up, using 75 g of the p-nitrobenzoate, 75 ml of boron trifluroide etherate, 9.1 g of sodium borohydride in 500 ml of diglyme. The crude product (14 g) from this reaction was of poor quality (yellow) and could not be used in subsequent reactions. This crude salt was purified by dissolving in water, basifing to litmus and extracting with ether. The ether solution was then extracted with dilute acid and the acid layer extracted with chloroform. The acid layer was then basified and extracted with ether. The ether layer was washed once with water, dried over sodium sulfate, filtered and acidified with gaseous hydrogen chloride to give a white precipitate (2.0 g). The purity of this product was of good quality and could be used in other experiments. Several repeated scale-ups of this hydroboration gave variable results and in some cases the above purification had to be repeated again.

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Diazonium Coupling of p-Nitrobenzene Diazonium Chloride (87) with Amine Hydrochloride (80)

Purified p-nitroaniline (180 mg, 1.30 mM, recrystallized from water, m.p. 147-148°) was dissolved in 1.5 ml of 12 M HCl and 3 ml of water with heating. The temperature of the solution was adjusted to 0° by external cooling in ice bath and by the direct addition of ice to the solution. To this solution was added 96.5 mg of sodium nitrite in 2 ml. of water which previously was cooled to 0° by adding ice and chilling in an ice bath. The diazonium salt solution was stirred for 15 minutes at 0° (adding ice occasionally to insure adequate cooling), then suction filtered onto 15 g of ice to give a pale yellow solution which was poured into 20 ml of a saturated sodium acetate solution cooled in an external ice bath. The pH of this solution was adjusted to 5.6-6.0 (specific range pH paper) by addition of solid sodium acetate trihydrate then transferred a portion at a time, by Pasteur pipette, to amine salt (500 mg in 25 ml of water). A yellow precipitate formed immediately. After complete addition, sodium chloride (20 g) was added and the mixture stirred for one hour and allowed to warm to room temperature. The precipitate was removed by filtration, air dried (234 mg; 61%) and identified as the coupled product (88) (m.p. 112-115° with bubbling); ν_{max}^{KBr} 3380, 1600,1500,1320,1250 cm^{-1}; δ $CHCl_3$ 3315 cm^{-1}; M^+-Nitrogen at m/e of 266 (4%) (Calc'd for $C_{13}H_{15}ClN_4O_2-N_2$: m/e of 266);

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δ ($CDCl_3$), 8.21 (2H,d,J=9Hz), 7.26 (2H,d,J=9Hz), 4.26 (1H,m), 3.89 (1H,t,J=2.5Hz), 2.54 (2H,m), 2.22-1.10 (6H,c); Anal.: 52.97% C, 5.13% H (Calc'd 52.89% C, 5.09% H).

A modified procedure involved using the free amine instead of the salt. The free amine was generated from the amine salt (500 mg) by dissolving the salt in water, basifying with a potassium hydroxide, extracting with ether, washing the ether with water, removing the ether in vacuo, to give the amine which was rinsed into a flask with water. (The amine is partially soluble in water.) The coupling was then carried out as previously described. The product was the same as above (324 mg, 81%).

Repetitions of this experiment produced variable results as to the appearance of the precipitate. At times only small amount of precipitate appeared immediately, but upon allowing the aqueous solution to sit at room temperature for several hours an additional large amount of the product appeared.

Attempted Cyclization of the Diazoamine (88)

To 20 mg of the diazoamine was added 10 ml of dimethyl t-butyl amine. The solution immediately turned a deep wine red. The solution was refluxed for four hours with no visible change in color and was then poured into water. This mixture turned to a pale yellow color and was extracted with ether. The ether was dried and then removed in vacuo, to produce a residue which was submitted for NMR. The NMR

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spectrum showed this compound to be the starting material.

Preparation of the endo p-Nitrophenyl-Triazoline (89)

The diazoamine (88) (90 mg, 0.307 mM) was dissolved in 20 ml of absolute ethanol and heated to 60° with stirring. To this was added 0.353 ml via hypodermic syringe of a 1.08 N solution of freshly prepared sodium ethoxide in absolute ethanol. The solution immediately turned a deep wine red. The temperature was maintained for thirty minutes at 60°, then a solution of 53 mg (0.307 mM) of silver nitrate dissolved in 15 ml of absolute ethanol was added. After complete addition, the solution was bright yellow in color, obscured somewhat by a brown precipitate. After stirring for an additional ten minutes, the solution was allowed to cool and filtered through a fine sintered glass filter. The brown precipitate was washed twice with small portions of absolute ethanol and discarded. The solvent was removed, in vacuo, from the bright yellow filtrate to leave a brown-yellow solid. Chloroform was added to this solid and the solution was swirled to dissolve soluble material. A brown precipitate in this solution was filtered through a fine sintered glass filter and washed with chloroform until the wash solution was colorless. The brown solid was discarded. The filtrate was concentrated, in vacuo, and the residual solid was triturated with carbon tetrachloride. The desired triazoline dissolved in the carbon tetrachloride and the remaining solid was removed by filtration. The carbon tetra-

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chloride solvent was removed in vacuo and the triazoline (89) appeared as yellow crystals (49 mg; 64%), m.p. 120-130° with bubbling. Recrystallization from ethanol gave orange crystals, m.p. 135-138° with bubbling; ν_{max}^{KBr} 1595, 1500,1378,1320 cm^{-1}; M^+-N_2 at m/e of 230 (84%) (Calc'd for $C_{13}H_{14}N_4O_2-N_2$: m/e of 230); δ ($CDCl_3$), 8.15 (2H,d,J=9Hz), 7.27 (2H,d,J=9Hz), 5.09 (1H,d of d,J=5.50Hz and J=12.0Hz), 4.02 (1H,d of d,J=4.25Hz and J=12.0Hz), 2.80 (2H,m), 1.65-0.75 (6H,c); Anal.: 60.37% C, 5.53% H, 21.59% N (Calc'd: 60.45% C, 5.46% H, 21.69% N).

Preparation of the exo p-Nitrophenyl Triazoline

The exo triazoline was prepared in the classic manner[12] by adding p-nitrophenyl azide to norbornene in refluxing petroleum ether. The yellow crystals melted at 164-165° (rpt.[12] 164-165°); ν_{max}^{KBr} 1595,1500,1375,1320 cm^{-1}; δ ($CDCl_3$) 8.30 (2H,d,J=9Hz), 7.38 (2H,d,J=9Hz), 4.77 (1H,d,J=9Hz), 3.79 (1H,d,J=9Hz), 2.90 (2H,s), 1.90-0.91 (6H,c); M^+-N_2 at m/e of 230 (23%) (Calc'd for $C_{13}H_{14}N_4O_2-N_2$: m/e of 230).

Photolysis of the exo Triazoline (90)

The exo triazoline was photolyzed in acetone in the same manner as the endo triazoline. The product was the same as the exo aziridine, 77, reported by Scheiner[23], m.p. 121-122° (rpt[23] 121-122°); ν_{max}^{KBr} 1590,1500,1385,1325 cm^{-1}; δ ($CDCl_3$), 8.10 (2H,d,J=9Hz), 6.95 (2H,d,J=9Hz), 2.57 (2H,s), 2.42 (2H,s), 1.73-1.06 (5H,c), 0.87 (1H,d,J=9.5Hz);

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M^+ at m/e of 230 (10%) (Calc'd for $C_{13}H_{14}N_2O_2$: m/e of 230).

Photolysis of the endo Triazoline (89)

A stream of nitrogen was bubbled through a solution of endo/exo (2:1) triazolines[note 1] (300 mg) in 250 ml of acetone in a photolysis unit for 10 minutes. This solution was then photolyzed at 5° for 6 hours through a quartz filter using a 200 W. Hanovia lamp. Nitrogen was continuously swept through the system during the entire photolysis.

The acetone was then removed in vacuo to give a dark brown oil. Gas chromatography on 10.8% SE-30 on Gas Chrom Q at a column temperature of 230° showed two products in a 2:1 ratio with retention times of 4.8 and 5.3 minutes respectively. The minor product at 5.3 min. was the exo aziridine (91), identified by comparison on g.l.c. with an authentic sample and by comparison of the NMR of the dark brown oil with that of an authentic sample.

The major product (4.8 min.) was collected as a yellow solid by preparative gas layer chromatography on 15% SE-30 on chromosorb W at column temperature of 200°C at 12.0 minutes retention time. Reinjection showed this corresponded to the major product at 4.8 minutes on the analytical column and did not contain the minor product. The yellow solid melted at 90-92° and was identified as the endo aziridine (92); ν_{max}^{KBr} 2960,1590,1497,1345,1325, 1285 cm^{-1}; δ ($CDCl_3$), 8.06 (2H,d,J=9Hz), 6.95 (2H,d,J=9Hz), 2.93 (2H,t,J=2Hz), 2.49 (2H,c), 2.05-1.21 (6H,c); M^+ at m/e

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of 230.0835 (4%) (Calc'd for $C_{13}H_{14}N_2O_2$: m/e of 230.0969).

Note 1: The mixture of the endo and exo triazolines (89 and 90) was obtained in the following manner. Hydroboration of 80 g of the 3-chloronorcamphor oxime p-nitrobenzoate (79) gave 14.0 g of very impure amine hydrochloride (80). This product was purified in a manner previously described to give 1.8 g of amine hydrochloride (80) (see p. 37, 2nd paragraph, hydroboration of the p-nitrobenzoate (79)). The product from this purification was coupled with the p-nitrobenzene diazonium chloride to yield the diazoamine chloride (90%). This product was closed to the triazoline by the previously described method in 89% yield. The NMR spectrum of this product indicated that this was a mixture of both endo and exo triazolines in a 2:1 ratio. The large scale hydroboration was carried out previously on at least two other occasions and the products of those purifications after subsequent reactions resulted in only endo triazoline. It is noteworthy that the infrared spectrum of this mixture was identical to that previously reported for the pure amine hydrochloride (80) and also the infrared spectrum of the diazoamine obtained from this mixture was identical to that previously described for the pure endo diazoamine (88).

Pyrolysis of the endo and exo Triazolines

Into separate pyrex tubes were placed 20 mg of the endo triazoline (89) and 20 mg of the exo triazoline (90),

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each in 3 ml of freshly distilled decalin. As much of each triazoline as possible was dissolved in the decalin by warming on a steam bath. The two tubes were then placed in an oil bath and maintained between 165°-170°C. Fifteen minutes after initial insertion of the tubes, the nitrogen evolution as evidenced by bubbles ceased, but heating at this temperature was continued for a total of two hours. Analysis of g.l.c. on a 3% XE-60 on Gas Chrom 100/200 mesh column at column temperature of 190° and flow rate 120 ml/min. gave the endo aziridine (92) at rt 8.6 min., the imine (94) at rt 9.6 min., and exo aziridine (96) at rt 10.8 min. The percentages of each were obtained by cutting and weighing the paper corresponding to each peak and are shown in Table 3. All products were identified by comparison with authentic samples.

After heating for two hours, the decalin solution of the exo triazoline was a clear, yellow color. The decalin solution of the endo triazoline was yellow but contained a brown gum on the bottom. From each of the pyrolysis solutions was removed one ml of decalin for reference purposes. To the remaining portions of each solution was added one ml of chloroform and each solution was heated on a steam bath. This procedure had no visible effects on the brown gum contained in the endo triazoline pyrosolate (i.e. did not dissolve this gum). G.l.c. of the two solutions before and after addition of chloroform gave the same ratio of pro-

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ducts. It is worth noting that the exo triazoline solution also formed a brown gum after sitting overnight in the freezer (after addition of the chloroform). It was also observed that the imine product in both reactions began decomposing after sitting overnight in the freezer, as evidenced by the gradual disappearance of the imine peak at rt 9.6 min. and the appearance of a p-nitroaniline peak at rt 5.0 min. retention time in the g.l.c.

The endo and exo aziridines (92 and 91) were identified by injection of authentic samples of each. The imine was identified by the observation that this product decomposes into p-nitroaniline (identified by g.l.c.) and norcamphor and also by injection of a sample of imine prepared by refluxing norcamphor, p-nitroaniline and p-toluenesulfonic acid in benzene. The imine could not be isolated from this reaction mixture and decomposed very rapidly during various attempted methods of purification.

Preparation and Chemistry of 119 and 121

Preparation of Dimethyl Bicyclo-{2,2,1}-hepta-2,5-diene 2,3-Dicarboxylate (54)

To 52.3 g of freshly distilled cyclopentadiene at -78° was added 90 g of dimethyl acetylene dicarboxylate. The addition was carried out slowly, as the reaction was extremely vigorous once initiated. The reaction although

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slow to start was over in a matter of seconds and completion was indicated by the red color of the solution. Vacuum distillation of the reaction mixture gave 73.0 g (68%) of the product (54) at 78° and 0.8 mm (111° at 2mm) (rpt.[48] 134-135°/10-11 mm) and 16.9 g of the dimethyl acetylene dicarboxylate; ν_{max} film 2980,2945,1710,1625 cm^{-1}; δ (neat) 6.92 (2H,t,J=2Hz), 3.88 (2H,m,J=2Hz), 3.70 (6H,s), 2.3-1.9 (2H,q of t,J=1.5Hz); M^+ at m/e of 208 (Calc'd for $C_{11}H_{12}O_4$: m/e of 208).

Preparation of Dimethyl Bicyclo-{2,2,1}-2-heptene, 2,3-Dicarboxylate (116)

The diene (54) (34.7 g) was dissolved in 110 ml of acetone and to this was added 1.75 g of 5% palladium on carbon. This solution was allowed to stir under hydrogen at atmospheric pressure. Uptake of hydrogen was followed closely and at the approximate value calculated for hydrogenation of one double bond, the rate of uptake slowed down. At this point the hydrogenation was stopped and the solution was filtered. The acetone was removed and the remaining oil was distilled under a vacuum to give the desired product (116) (23.5 g; 67%) at 86° and 0.5 mm (rpt.[48] 132-133°/12 mm); ν_{max} film 1720,1615 cm^{-1}; δ (neat) 3.70 (6H,s), 3.23 (2H, unresolved m), 2.0 to 1.0 (6H,c); M^+ at m/e of 210 (Calc'd for $C_{11}H_{14}O_4$: m/e of 210).

Preparation of Phenyl Azide[49]

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Into one-liter distilling flask was placed 300 ml of water and 55.5 ml of concentrated hydrochloric acid. The flask was surrounded by an ice bath and the magnetic stirrer turned on. Into a long stemmed dropping funnel was placed 33.5 g of phenyl hydrazine and this was added drop-wise to the solution in the flask. The tip of the funnel was above the solution during this addition. This measure prevents clogging of the stem by the salt. The phenyl hydrazine hydrochloride was formed as white plates in the solution. After complete addition the solution was stirred until the temperature dropped to 0^{o} and then 100 ml of ether was added. While stirring was continued, the end of the dropping funnel was placed into the solution. Into the dropping funnel was placed a solution of 25 g of sodium nitrite in 40 ml of water and this was added drop-wise to the acid solution. The rate of addition was controlled such that the temperature never rose above 5^{o}. The addition requires about forty-five minutes.

After complete addition of the sodium nitrite, the reaction mixture was steam distilled until about 400 ml of distillate was obtained. The ether fractions were combined and dried over calcium chloride. After removal of the ether, the residue was subjected to vacuum distillation and the product was 20 g (55%) of phenyl azide; ν_{max}^{neat} 2130, 2095 cm^{-1}.

Preparation of Bicyclo-{2,2,1}-2-heptene-1,2-dicarboxylic Acid (117)

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The diacid (117) was prepared from the dimethyl ester (116). Into 25 ml of 95% ethanol was dissolved 3.5 g of potassium hydroxide. To this solution was added 5 g of the dimethyl ester. This mixture was refluxed for twenty minutes and then allowed to cool. The solution was then acidified with diluted sulfuric acid and potassium sulfate precipitated out of solution. The solution was filtered and the filtrate was diluted with water. This aqueous solution was then filtered to give 4.3 g of the crude product. After recrystallization from water 2.8 g of the diacid (117) was obtained (66%); m.p. 213-214° (rpt.[49] m.p. 212°); ν_{max}^{KBr} 2500,1695,1622 cm^{-1}; M^+ at m/e of 182 (Calc'd for $C_9H_{10}O_4$: m/e of 182).

Preparation of Bicyclo-{2,2,1}-2-heptene-2,3-dicarboxylic Anhydride (118)[47]

To 2.5 g of the diacid (117) was added 8.4 g of acetic anhydride (six fold excess). This mixture was refluxed for one and one-half hours. The excess acetic anhydride and other volatile materials were removed in vacuo to give a brown solid. Recrystallization from n-hexane gave 1.5 g (68%) of the anhydride (118); m.p. 92-94° (rpt.[50] 98-99° from ligroin); ν_{max}^{KBr} 1827,1777,1603 cm^{-1}; M^+ at m/e of 164 (Calc'd for $C_9H_8O_3$: m/e of 164).

Preparation of 3-Phenyl-3,4,5-triazatricyclo-{5,2,1,$0^{2,6}$}-4-decene-2,6-dicarboxylic Anhydride (119)

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To 1.2 g of the anhydride (118) in 8 ml of ethyl acetate was added 0.87 g of phenyl azide. After one day of stirring, white crystals precipitated from the solution. At this time the solution was filtered and after successive concentrating of the remaining solution, 1.6 g (76%) of a white solid was isolated which melted at 150-152°. Recrystallization from ethyl acetate-n-hexane (1:1) gave the triazoline (119); m.p. 152-154° (rpt.[4] 154°); ν_{max}^{KBr} 1870,1780,1590 cm^{-1}; M^+ minus molecular nitrogen at m/e of 255 (Calc'd for $C_{15}H_{13}N_3O_3-N_2$: m/e of 255).

Photolysis of 3-Phenyl-3,4,5-triazatricyclo-{5,2,1,$0^{2,6}$}-4-decene-2,6-dicarboxylic Anhydride (119)

Into 8 ml of acetone was dissolved 0.16 g of the triazoline (119). The reaction mixture was placed in a pyrex tube and photolyzed for 3 hours with a 200 watt Hanovia lamp. The solution was kept at a constant temperature of +10° ±1°. After completion of the reaction, the acetone was removed to leave 0.14 g of residue. Recrystallization from n-hexane-ethyl acetate (1:1) gave crystals melting at 157-159° (rpt.[22] m.p. 161-162°) which corresponded to the exo aziridine (120); ν_{max}^{KBr} 1845,1775 cm^{-1}; M^+ at m/e of 255 (Calc'd for $C_{15}H_{13}NO_3$: m/e of 255).

Pyrolysis of 3-Phenyl-3,4,5-triazacyclo-{5,2,1,$0^{2,6}$}-4-decene-2,6-dicarboxylic Anhydride (119)

Into 50 ml of decalin was dissolved 0.5 g of the

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triazoline (119). This solution was then placed in a constant temperature oil bath at 163° ±2° for 2 hours (plus an additional hour to allow the decalin to reach this temperature). After the pyrolysis, g.l.c. on 3.8% UCW-98 on Chromosorb S at 200° showed the product to be identical by mixed injection with the exo aziridine (120) prepared by the photolysis of the triazoline. The decalin was removed in vacuo and the solid was recrystallized from n-hexane-ethyl acetate (1:1). The data for this product was identical to the aziridine derived by photolysis of the triazoline (119).

Preparation of Dimethyl-3-phenyl-3,4,5-triazatricyclo-{5,2,1,$0^{2,6}$}-dec-4-ene-2,6-dicarboxylate (121)

Into 10 ml of ethyl acetate was dissolved 10 g of the dimethyl ester (116). To this solution was added 5.6 g of phenyl azide. This was stirred at room temperature. After fifteen days a precipitate which had formed was filtered off and the remaining solution was returned for further reaction. The solid (5.5 g) had a melting point of 134-142°. After one recrystallization from n-hexane-ethyl acetate (1:1), were obtained 4.0 g (26%) of a white crystal compound melting at 147-149°. The yield through successive filterings over a three months period was 76%. This was identified as the triazoline ester (121); ν_{max}^{KBr} 1740, 1598 cm^{-1}; δ ($CDCl_3$) 7.23 (5H,m), 3.82 (3H,s), 3.50 (3H,s),

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3.12 (1H, unresolved m), 2.88 (1H, unresolved m), 2.60-1.6 (2H,c), 1.58 (2H, unresolved m), 1.35 (2H, unresolved m); $M^+ - N_2$ at m/e of 301 (10%) (Calc'd for $C_{17}H_{19}N_3O_4 - N_2$: m/e of 301) (see Table 3); ε_{298}=7840, ε_{285}=7130; Anal.: 62.16% C, 5.95% H, 12.75% N (Calc'd: 62.06% C, 5.82% H, 12.77% N).

Photolysis of Dimethyl 3-Phenyl-3,4,5-triazatricyclo-{5,2,1,$0^{2,6}$}-dec-4-ene-2,6-dicarboxylate (121)

Into 22 ml of acetone was dissolved 1.0 g of the triazoline (121). This was then photolyzed with a Hanovia 200 watt U. V. lamp in a pyrex tube for three hours. The reaction was kept at a constant temperature of 10° ±1°. After completion of the photolysis, g.l.c. analysis showed that there was only one product. Recrystallization from n-hexane-ethyl acetate (1:1) gave the exo aziridine (122) as white plates; m.p. 106-109°; ν_{max}^{KBr} 1725,1590 cm^{-1}; δ ($CDCl_3$) 7.30-6.73 (5H,c), 3.77 (6H,s), 2.77 (2H,m), 2.20-0.5 (6H,c); M^+ at m/e of 301 (Calc'd for $C_{17}H_{19}NO_4$: m/e of 301) (see Table 3); Anal.: 67.58% C, 6.31% H, 4.58% N (Calc'd: 67.83% C, 6.36% H, 4.65% N).

Attempted Esterification of 120

The aziridine (120) was dissolved in methanol and ether and esterified with diazomethane. The solution was allowed to sit overnight. Gas layer chromatography showed that only about 20% of the anhydride (120) was converted to the dimethyl ester (122). The mixture was then esteri-

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fied three additional times and analyzed by g.l.c. on 3% XE-60 on Gas Chrom Q at 200°. About 25% of the dimethyl ester was produced. Attempted esterification of the aziridine anhydride with diazomethane and a few drops of boron trifluroide etherate gave a brown gum. Analysis by g.l.c. on 3% XE-60 at 215° showed that the anhydride was no longer present, but the product was not the dimethyl ester. The dimethyl ester from previous esterifications was still present. The mixture chromatographed on Activity I, neutral alumina. A white oil was isolated and shown by g.l.c. to be the new product; $\nu_{max}^{CHCl_3}$ 2915,1740,1710, 1595 cm^{-1}. This oil turned purple upon sitting overnight. This compound could not be identified due to lack of material.

Pyrolysis of Dimethyl 3-Phenyl-3,4,5-triazatricyclo-{5,2,1,$0^{2,6}$}-dec-4-ene Dicarboxylate (121)

The dimethyl triazoline ester (121) was pyrolyzed many times. Below are representative examples of variations of these pyrolyses by method A which gave significant results.

(a) Into a two-neck 500 ml round bottom flask was placed 2.0 g of the triazoline and 200 ml of decalin. This mixture was warmed on a steam bath until all of the dimethyl ester dissolved. The flask was then placed in an oil bath. at 162° ±2° for three hours. After removal from the oil bath, the flask was placed on a steam bath and a short

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vigreux column was placed on the flask. Into the side arm was inserted a fine capillary gas inlet tube and this tube was connected to a nitrogen supply. Onto the column was placed a distilling head and the decalin was removed by vacuum distillation (∿0.1 mm) using a minute nitrogen flow through the system to prevent bumping. The vigreux column helps break the frothing action of the decalin. Heating on the steam bath was necessary to complete the distillation. The residue, a yellow oil, had a very bad odor. This was chromatographed on 80 g of silica gel. The fifth fraction (eluted with 50 ml benzene) gave a very small amount of yellow oil which had the following infrared: ν_{max}^{neat} 2120,1720,1695,1630,1595 cm^{-1}. (The first two fractions were benzene, while the third and fourth fractions contained decalin.) This material decomposed over a period of two hours. The isolation of this material lead to several subsequent pyrolyses in attempts to isolate a larger quantity of this yellow oil.

(b) The triazoline (3.2 g) was dissolved in 250 ml of decalin and placed in an oil bath at 100° and stirred magnetically. The temperature was then slowly raised and infrared spectra were taken periodically at 100°, 120°, 140°, and 165°. None of the infrared spectra showed bands in the region between 2200 to 2000 cm^{-1}, however, a band at 1650 cm^{-1} did appear at 165°. At 165° the triazoline began to evolve nitrogen and the temperature was held at this

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point for three hours. Removal of the decalin (0.1 mm) in vacuo as described in (a) gave the yellow oil. Chromatography of this residue on 81 g of silica gel gave the same compound (about 1 mg) as before with a characteristic band at 2120 cm^{-1} in the infrared region. An attempt to store this compound in the freezer until further spectra could be obtained was futile as the compound decomposed (no 2120 cm^{-1} in infrared).

(c) Into 200 ml of decalin was dissolved 3.0 g of the triazoline. After pyrolysis for three hours, the decalin was removed in vacuo. Chromatography of the residue on 80 g of silica gel again gave the desired compound in the fourth fraction (50 ml fractions) (ν_{max} neat 2120 cm^{-1}). After taking the infrared spectrum, the oil was washed with 2-propanol into a volumetric flask and its ultraviolet spectrum was taken. The concentration was not known and was estimated at 1 mg/2 ml; ε_{233}=1237, ε_{238}=1520, ε_{244}=1646, ε_{251}=1329. To this oil was added an excess of benzoic acid. Chromatography on 10 g of alumina gave nothing, due to small size of the sample.

(d) Into 400 ml of freshly distilled decalin was dissolved 6.0 g of the dimethyl triazoline ester. The pyrolysis was carried out as previously described at 165° ±2° overnight (seventeen and one-half hours). The solution was analyzed by g.l.c. on a column of 3% OV-17 on Gas Chrom Q, 100/120 mesh, 6 ft., 1/8 inch, at a column

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temperature of 200° and flow rate of 80 ml/min. Integration of all peaks by the cut and weigh method gave the following results:

Retention Time in Minutes	Abundances
2.9	2.31%
3.7	4.62%
6.1	6.15%
8.6	74.7 %
11.8	2.31%
14.2	3.08%
16.1	5.38%
18.4	1.54%

This solution was stored in the freezer for use at a later time. Mixed injection showed that the exo aziridine (122) was not present. The above decalin solution was processed by the following procedures.

(1) The decalin was removed in vacuo as previously described from 200 ml of the above solution and the residue (3 g) was chromatographed on 385 g of Merck acid-washed Alumina, Activity I. Continuous elution with pet ether, then benzene and finally chloroform afforded only 0.3 g of material which g.l.c. showed to be impure. The unrecovered material could be removed from the alumina only by continuous soxhlet extraction with 95% ethanol. Analysis of the extracted material by g.l.c. showed the major product was no longer present.

(2) The decalin was removed in vacuo from 40 ml of the above solution and the residue when analyzed by g.l.c. still contained the major product. Thin layer chromato-

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graphy on silica gel G with ethyl acetate: pet ether: benzene (1:1:8) gave two bands (rt=0.44, rt=0.59). Analysis of these bands by g.l.c. showed the major product was present in only one or two per cent. Instead there were two products with rt 1.6 and rt 1.9 on g.l.c. These were not identified due to lack of material.

(3) The decalin was removed in vacuo from 20 ml of the above solution and the residue was chromatographed on a thin layer of aluminum oxide G. This was eluted with chloroform-cyclohexane (1:9). The t.l.c. plate was cut into sections, which were washed with ether, filtered, and analyzed by g.l.c. G.l.c. showed the major product present in 69% abundance (62% before t.l.c.) in one of the fractions. This fraction was subjected to t.l.c. and eluted with chloroform-cyclohexane. The t.l.c. plate was separated into bands and scraped into flasks. Due to lack of time, the compound was not washed from the alumina until the next morning. At this time, analysis of all bands by g.l.c. showed the major product was no longer present and, still further, the decomposition products, previously observed (see (2)), were not present.

(4) The decalin was removed from 20 ml of the above solution and the residue was subjected to preparative g.l.c. on 3% OV-17 on Gas Chrom Q at 200° column temperature. Thirty minutes after injection a yellow oil was trapped and submitted for mass spectral determination. The tabu-

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lated spectrum of this compound (126) is shown in Table 4. Reinjection on an analytical column of 3% OV-17 showed this to be one sharp peak at 11.0 minutes. M^+ at m/e of 301; $\nu_{max}^{CCl_4}$ 2980,1725,1660 cm^{-1}. Further attempts to isolate this compound by preparative g.l.c. analysis brought unfruitful results as well as some undesired side effects. The compound during preparative g.l.c. was significantly vaporized and had a very bad odor. Breathing of this vapor caused headaches, dizziness and nervousness, thus this method of collection was abandoned.

(e) The triazoline dimethyl ester (7.0 g) was dissolved in 467 ml of decalin and pyrolyzed at 168° ±2° for four and one-half hours as previously described. The decalin was removed in vacuo from 40 ml of the pyrosolate and the residue was submitted for gas chromatograph-mass spectrograph determination. The spectra were collected from the sample passing through a glass column of 3% SE-30, (one-fourth of an inch diameter, six feet lone). The following was observed:

Retention Time	Column Temperature	M^+ at m/e of
4.0 minutes	160° to 250°	299
7.6 minutes	160° to 250°	299 (main product)
9.0 minutes	160° to 250°	299 (main product)
10.5 minutes	160° to 250°	299
11.5 minutes	250°	299
15.0 minutes	250°	299
18.0 minutes	250°	299
20.0 minutes	250°	299
†20.0 minutes	250°	299 (main product)

†This spectrum was taken on a stainless steel column of 3% SE-30 (one-eighth of an inch diameter and four feet long).

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Due to the unusual results above, it was decided to check the recorders used for the above mass spectra. Therefore the solid triazoline was submitted for mass spectral determination by direct application onto the probe. The spectra were run under identical conditions using:

(1) a flat bed recorder;

(2) a statos recorder at the speed of a typical GC-MS run;

(3) flat bed and statos recorders simultaneously.

All spectra were essentially identical except for some variations in peak intensities. The first ion observed was at m/e 301 (loss of nitrogen from the molecular ion).

An acetone solution of the triazoline (121) was submitted for GC-MS determination on a 3% SE-30 stainless steel column (1/8" diameter, 4 ft. long). The results are shown below.

Column Temperature	Injector Temperature	Retention Time	m/e Observed	Ratio
225	250	10 min.*	297/299	48/52
225	300	4 min.*	299/301	50/50
225	300	6+3/4 min.*	299/301	53/47
200	300	10 min.*	299/301	60/40
200	300	11+3/4 min.*	299/301	55/45
200	300	15 min.	299/301	65/35
200	300	17+3/4 min.	299/301	65/35

*Indicates main product.

None of the above spectra had m/e at 286 or 272. Usually observed was m/e of 268 and next was the base peak at m/e of 240.

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Method B:

Into the lower bulb of a distillation tube was placed 230 mg of the triazoline. The compound was heated slowly at 0.15 mm in a hot box distillation apparatus. At 80° the triazoline melted to a clear solution, which turned bright yellow as it began to bubble. After ten minutes of heating, the tube was removed from the system and carbon tetrachloride was added and transferred to an NMR tube. Starting triazoline crystallized and the liquid was removed by pipette from the solid. The reaction was followed by NMR by observing the change in chemical shifts and integration of the methoxyl ester groups. The methoxyl ester groups of the triazoline appear at δ3.84 and δ3.52 and each integrate for three protons ($CDCl_3$). The results of this pyrolysis and other runs of this pyrolysis using variable conditions are shown in Table 5. The mass spectrum of run D is shown in Table 6. The IR and NMR spectra of run D showed the following: ν_{max} neat 2940,1725,1705,1650 cm^{-1}; δ (CCl_4) 7.40-6.52 (39 i.u.,c), 5.75 (5.6 i.u.,b), 3.84 (13.0 i.u., s), 3.69 (21.0 i.u.,s), 3.52 (21.0 i.u.,s), 3.30-09 (60.0 i.u.,c).

Into a distillation tube was placed 200 mg of the triazoline. This solid was heated in a hot box distillation apparatus at 0.0018 mm. At 98° a white solid was noticed in the upper part of tube and at 105° an apprecia-

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ble amount of crystals had formed and the pyrolysis was stopped after thirty minutes. The solid had a melting point of 148°-150° and the infrared spectrum was identical to that of the starting triazoline (121).

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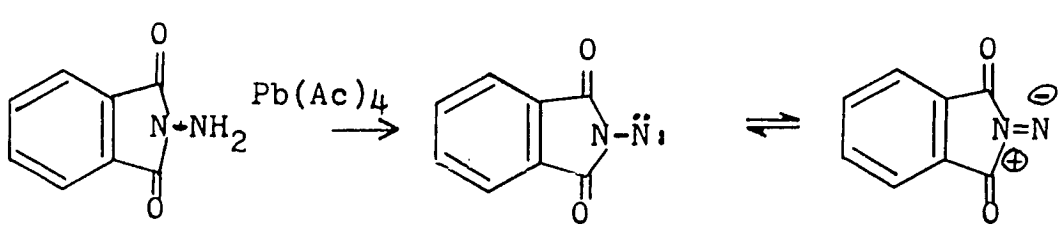
CHAPTER IV

DISCUSSION OF RESULTS

As stated in the introduction, one of the goals of this work was to devise a synthetic route to the heretofore unknown *endo* triazoline (*47*). An analysis of the synthetic problem illustrated that *endo* approach of an electrophile, such as an azide, to norbornene is highly hindered[4,10]. Indeed this steric interference is so great that when the *exo* approach is blocked by substituents on the methylene bridge, as in the case of apobornylene (*10*), there is no azide addition at all[4]. This hindrance was further substantiated by results from this laboratory.



48 *49a* *49b*

Figure 11. Formation of an Amino-Nitrene

The oxidation of N-aminophthalimide (*48*) produces an amino-nitrene (*49*) which adds stereospecifically to olefins yielding aziridines[37]. N-aminophthalimide was treated with lead tetraacetate in the presence of bornylene. It

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was hoped that the hindrance of the methyl groups would force the nitrene to add to the *endo* face of the bornylene to produce aziridine (50) which, as visualized in Figure 12, might be converted to the triazoline (53). This was

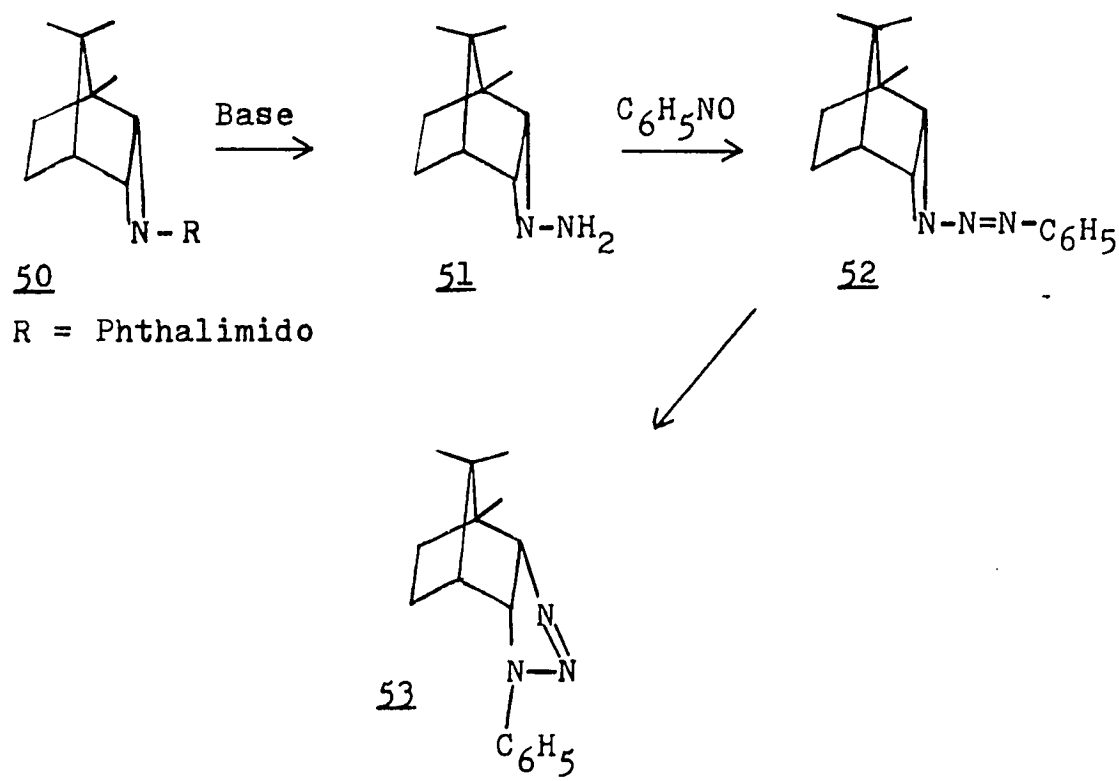

Figure 12. Proposed Synthetic Route with an Amino-Nitrene

not the case. Phthalimide, identified by m.p and infrared analysis, precipitated from the solution and further chromatography of the remaining mixture gave bornylene, phthalimide and several oils. Analysis of the NMR spectra of these oils showed that they contained no aromatic protons, thus ruling out the possibility of the presence of aziridine (50). Thus the steric hindrance of the *endo* side of

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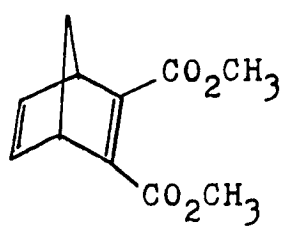
the bicyclo{2,2,1}skeleton was again dramatically demonstrated.

Another approach to the problem was suggested by the work of McLean and Findlay[11] who isolated two endo triazolines (11 and 12) from norbornadiene and phenyl azide. The diene (54) was readily available from cyclopentadiene and dimethyl acetylene dicarboxylate. It was



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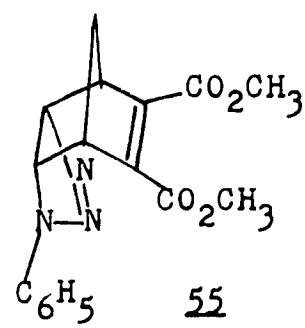

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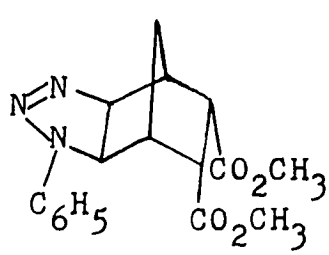

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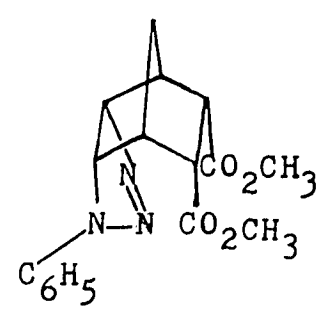

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hoped that the phenyl azide would react with the unhindered, electron rich double bond of the diene to yield the endo triazoline (55), which could then be selectively hydrogenated to 56. This triazoline would be valuable in comparative pyrolysis studies since the exo equivalent (57) is available. Phenyl azide and the bicycloheptadiene (54)

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were refluxed in cyclohexane for two hours under nitrogen. Upon work up of the reaction mixture, white crystals were isolated (m.p. 120-123°), which upon recrystallization gave a sharp melting solid, 126-127°. The infrared spectrum showed an ester band at 1720 cm^{-1}; the NMR spectrum showed two ester methoxyl singlets at δ3.90 and δ3.99 and one singlet at δ7.54 which integrated for five aromatic pro-

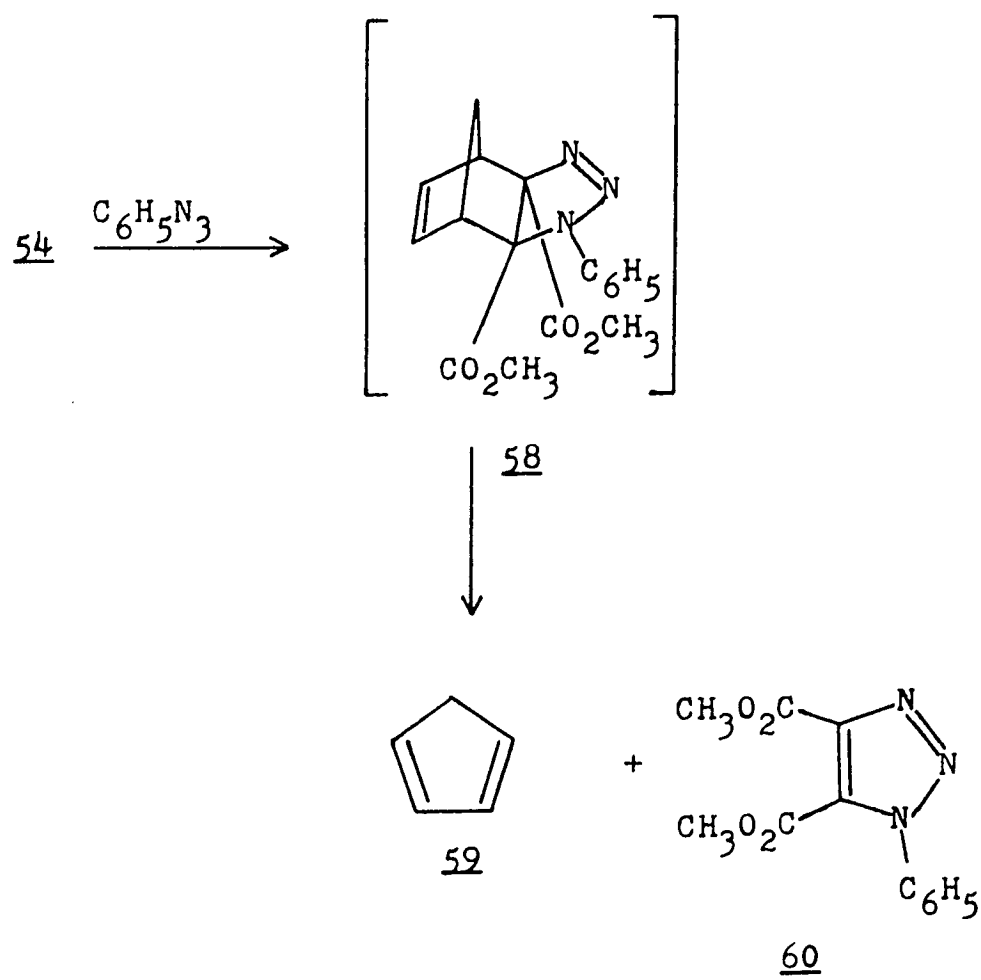

Figure 13. Retro Diels-Alder Reaction of Phenyl Azide and 54

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tons. The mass spectrum indicated the presence of a molecular ion at m/e of 261, corresponding to $C_{12}H_{11}N_3O_4$ while the ultraviolet spectra had a band at 240 mμ with an absorbtivity of 8150. On the basis of the above data this compound was identified as dimethyl 1-phenyl-1,2,3-triazole-4,5-dicarboxylate (60)[1]. This product could be derived from addition of the azide across the ester double bond of the diene followed by a retro Diels-Alder reaction (Figure 13). This triazole was the only crystalline product which could be isolated. It would be expected that the azide would add preferentially to the unsubstituted electron rich double bond rather than the hindered electron deficient double bond. Apparently at the reflux conditions of the reaction, the theremodynamically controlled product was favored or was the only product which would crystallize.

Again utilizing the approach of endo addition to a diene, benzyl azide was added to a refluxing solution of cyclohexane and norbornadiene. It was reasoned that if benzyl azide did add to the diene producing an endo triazoline, which upon hydrogenation, photolysis and finally hydrogenolysis of the benzyl group could produce an unsubstituted aziridine (65) (Figure 14). Diazonium coupling of this aziridine would yield an intermediate (66) which could then be isomerized to the endo triazoline (47) by Heine and Tomalia's procedure.[16]

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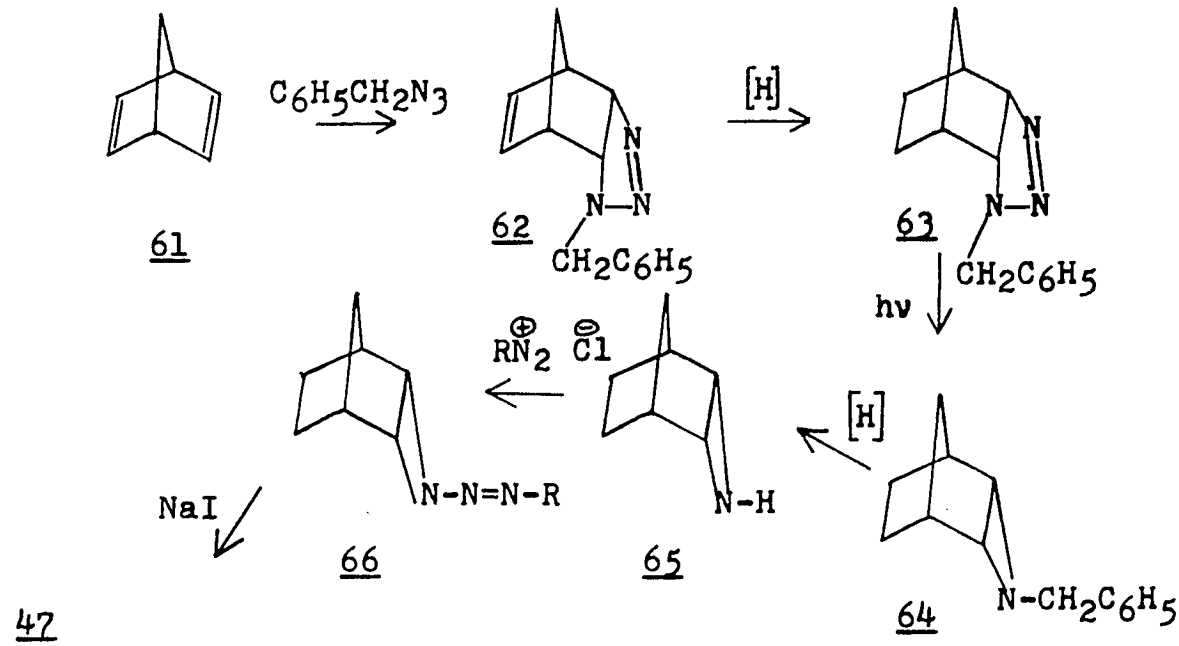

Figure 14. Proposed Synthesis with Norbornediene and Benzyl Azide

Various ratios of benzyl azide to norbornadiene were used. In each case, the same two products were isolated via fractional crystallization. The first compound crystallized as white needles from ether (m.p. 154-156°). There were no significant bands in the infrared region. The NMR spectrum showed two methylene bridge hydrogens as a multiplet centered at δ1.15, two bridgehead protons as a multiplet centered at δ2.60, two hydrogens as a doublet with J=9 Hz at δ3.22, two hydrogens as a doublet with J=9 Hz at δ4.31, two benzylic hydrogens as a doublet with J=15 Hz at δ4.61, two benzylic hydrogens as a doublet

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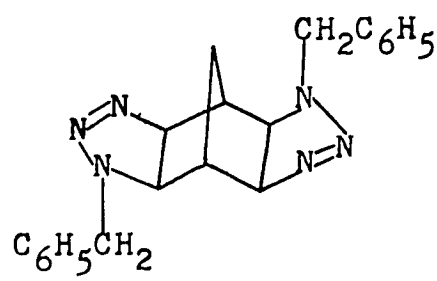
with J=15 Hz at δ4.90 and ten aromatic hydrogens as a singlet at δ7.30. The first observed ion in the mass spectrum was at m/e of 302, which corresponded to a di-triazoline adduct of norbornadiene and benzyl azide which had lost two moles of nitrogen. Analytical data was consistant with $C_{21}H_{22}N_6$, which is the formula of a di-triazoline adduct. On the basis of the above data, the new compound was identified as the anti-di-exo-triazoline (67).



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The second compound, isolated by the fractional crystallization, melted at 168-170°. The infrared analysis showed no significant bands. Nuclear Magnetic Resonance analysis showed two methylene bridge protons as a multiplet centered at δ1.10, one bridgehead hydrogen as a multiplet at δ1.97, two hydrogens as a doublet with J=9 Hz at δ3.00, one bridgehead proton at a multiplet centered at δ3.08, two allylic hydrogens as a doublet with J=9 Hz at δ4.48, two benzylic hydrogens as a doublet with J=15 at δ4.48, two benzylic hydrogens as a doublet with J=15 Hz at δ4.79, and ten aromatic hydrogens as a multiplet centered at δ7.27.

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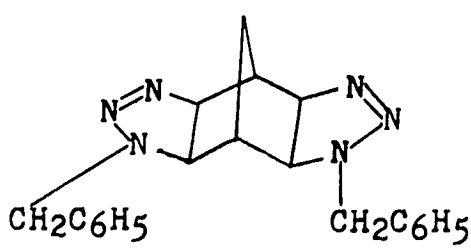
In mass spectrum the highest observed ion was at m/e of 302 which corresponds to $C_{21}H_{22}N_2$. Elemental analysis was consistent with $C_{21}H_{22}N_6$, which corresponds to a di-triazoline adduct of norbornadiene and benzyl azide. On the basis of the above data, the compound was identified as the syn-di-exo-triazoline (68). The ratio of 67 to 68 was 2.2 to 1 based on the amounts of compounds recovered from the reaction mixture.



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The results of the above experiment were not surprising, since McLean and Findlay reported a low yield for the endo-triazoline (11). The bulk of the azide substituent was increased when the benzyl azide was used in the place of phenyl azide, thus further decreasing the possibility of the endo addition.

The unfruitful results of the earlier proposed syntheses lead to an entirely new approach. It was reasoned that if the azide function would not add to the endo face of the bicyclic molecule, then this function must be incor-

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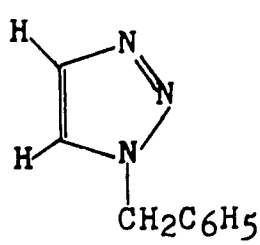
porated within the molecule by other means. The pathway visualized would involve a Diels-Alder reaction of cyclopentadiene with some moiety which could be converted to the desired product.

Freshly prepared cyclopentadiene was refluxed with 1-benzyl 1,2,3-triazole (69)[39] for eight hours in an attempt to prepare endo-triazoline (70). When the mixture was cooled with dry ice, the starting triazole was recovered



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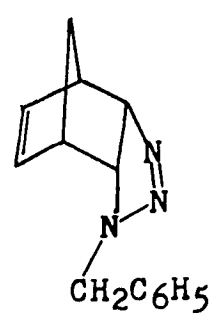

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unreacted. The results of this experiment were as expected since in order for the reaction to occur, the resonance stabilization of the triazole must be overcome. Clearly this was very unlikely, but it was felt that this route must be conclusively ruled out.

Another pathway was devised using 2-imidazolone (71) and cyclopentadiene (59) as in Figure 15.

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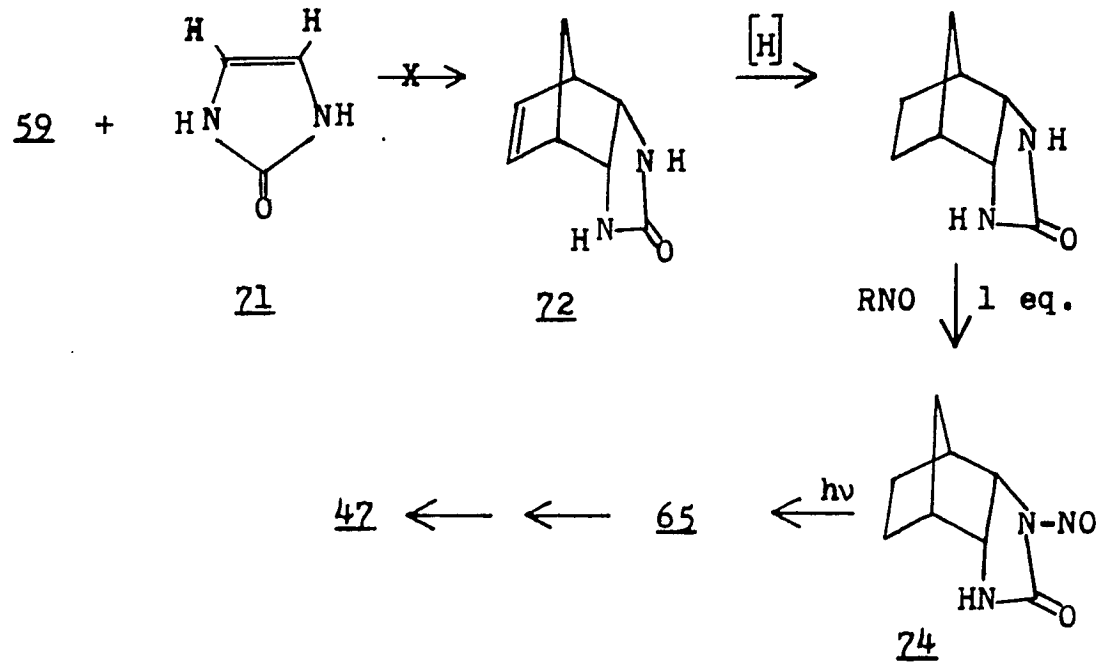

Figure 15. Proposed Diels-Alder Synthesis with 2-Imidazolone

2-Imidazolone 4-carboxylic acid was prepared according to Hilbert's[41] procedure from urea and tartaric acid. The carboxylic acid was decarboxylated by a reported method[42] to give 2-imidazolone. Freshly prepared cyclopentadiene and the imidazolone in 95% ethanol was stirred at room temperature overnight. The starting material was recovered from the mixture unchanged. In another attempt to make this reaction go, dicyclopentadiene and 2-imidazolone were heated to 175° in a sealed tube for eight hours. Upon washing the content from the tube, a precipitate was obtained. This was the starting material. In a modification of the above procedure, freshly prepared cyclopentadiene and the

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imidazolone were heated at 140° for fifteen hours in a sealed tube. Once again the starting material was obtained unchanged. The failure of the Diels-Alder reaction was not unexpected, since the imidazolone is a poor dienophile. It was hoped however that the sealed tube reaction conditions would be vigorous enough to overcome this problem.

With the failures of the preceding pathways, it was obvious that an entirely novel pathway to an endo triazoline must be devised. The envisioned route would involve an intermediate which would contain an endo amino moiety

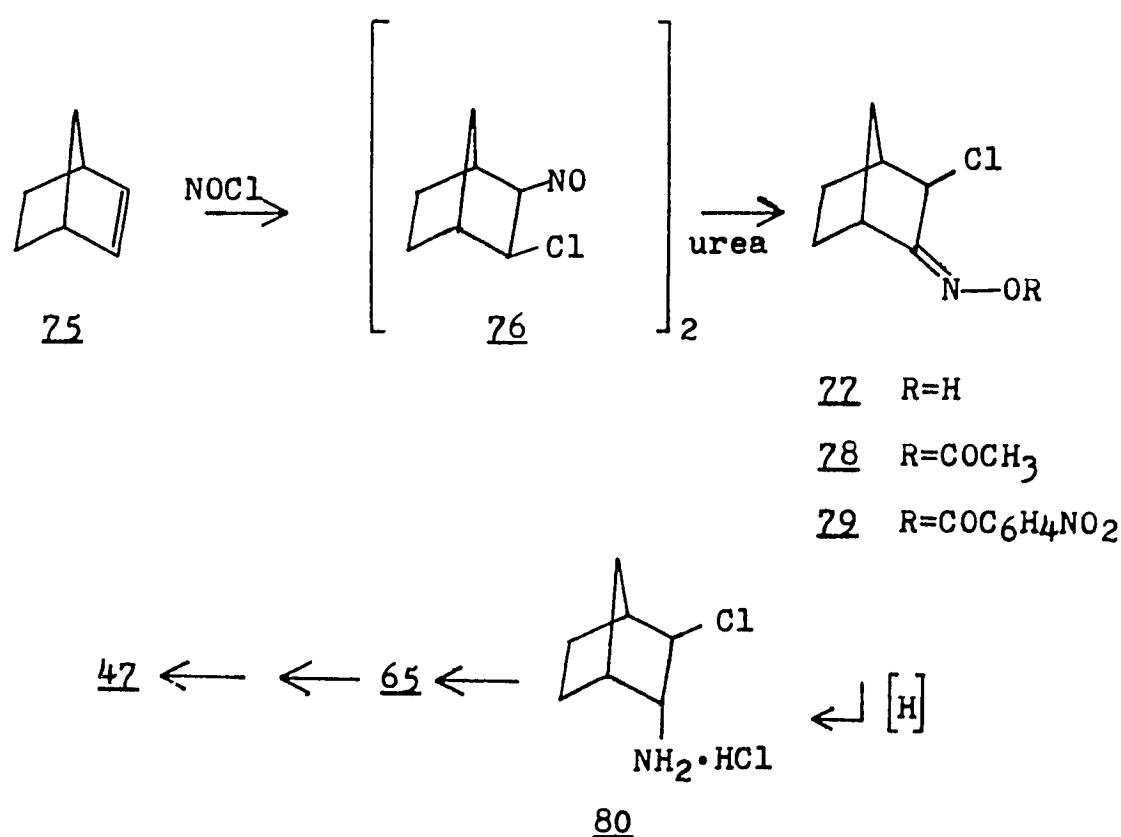

Figure 16. Proposed Scheme with 2-Chloronorcamphor oxime

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as well as exo substituent on the alpha-carbon, which might be displaced by this endo group. This amino compound could be prepared from an imine or oxime. A search of the literature revealed that 3-chloronorcamphor oxime (77) was readily available. Thus Figure 16 involving the above precursor was proposed.

The nitrosyl chloride dimer (76) was prepared by the method of Meinwald, et al.[43] and isomerized to the 3-chloronorcamphor oxime (77) by Miller's procedure[44] using urea as a catalyst. The next step met with some difficulties. Attempted hydrogenation of this oxime in methanol with 5% rhodium on alumina at 56 psi gave an unidentified oil shown not to be the desired amine hydrochloride (80) as demonstrated by the absence of the amino hydrogens in its infrared spectra.

It was decided to acetylate the oxime, since there were reports that while oxime esters reduce to amines under mild conditions, oximes required more vigorous conditions. The oxime was stirred with an excess of acetic anhydride and pyridine (1:1) at room temperature overnight. The oxime acetate (78) was isolated as an oil which showed characteristic bands in its infrared spectrum at 1770 cm^{-1} (ester) and 1660 cm^{-1} (oxime double bond).

The NMR spectrum showed a hydrogen geminal to a chlorine as a doublet with J=2.5 Hz at δ4.34, one bridgehead proton in two different environments as two multiplets

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centered at δ3.48 (0.6 proton) and δ3.03 (0.4 proton), one bridgehead proton as a multiplet centered at δ3.57, three protons of an acetyl group in two different environments as two singlets at δ2.10 and δ2.07, and a complex region between δ2.05 and δ1.10 which integrated for six protons. The mass spectrum showed no molecular ion, but did show a m/e of 142 (48%), an ion formed from the loss of an acetoxy group from the unobserved molecular ion. The oxime acetate was dissolved in methanol and hydrogenated at 56 psi using 5% rhodium on carbon catalyst. Once again, upon work up of the mixture, the unidentified solid, previously isolated from hydrogenation of the oxime, was the product. The failure of these catalytic methods was possibly due to the steric bulkiness of the environment around the oxime double bond which would not allow the molecule to be properly absorbed onto the surface of the catalyst for hydrogenation. At this point, attempts to effect catalytic hydrogenation were abandoned in favor of chemical reductions. To the oxime acetate in ethanol was added sodium borohydride in ethanol. After nearly two hours, the reaction was worked up to give an oil which was identified as a mixture of <u>syn</u> and <u>anti</u> norcamphor oxime (82) by infrared, NMR, and mass spectra and also by mixed injection with an authentic sample[45] on g.l.c. This product probably originated from the oxime acetate by cleavage of the acetyl group, followed by dehalogenation, and finally reduction of the intermediate

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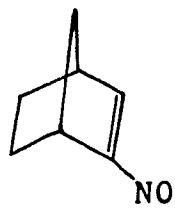
nitroso compound (81).



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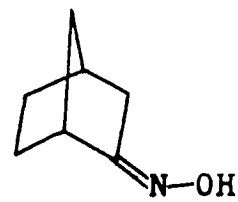

82

It was decided that other hydride reductions would lead to the same results and thus another reagent was sought. A literature survey revealed that oxime esters had been successfully reduced to primary amines by Feuer and Braunstein[46] with diborane. The oxime ester (78) was subjected to hydroboration in tetrahydrofuran at room temperature overnight. The excess diborane was destroyed with water, the resulting white borate ester hydrolyzed with 10% hydrochloric acid for one hour, then the solution was made alkaline and extracted with ether. The combined ether extracts were dried, hydrogen chloride was bubbled into the ethereal solution and a white, flocculent precipitate appeared. This was identified as the endo amine hydrochloride (17%) (78). The infrared spectrum of the salt showed bands at 1590, 1570, 1495 cm^{-1}, which are characteristic of amine salts. The NMR spectrum of this salt in trifluoroacetic acid and chloroform revealed a broad hump for three amine hydrogens centered at δ7.08, which disappeared upon addition of deu-

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terium oxide, two hydrogens as a multiplet centered at δ3.63, one bridgehead proton as a multiplet centered at δ2.50, one bridgehead proton as a multiplet centered at δ2.32, and six hydrogens in a complex pattern in the region between δ2.0 and δ1.0. The mass spectrum of the amine hydrochloride showed a m/e of 145 which corresponded to $C_7H_{12}ClN \cdot HCl$ minus HCl. Analysis of the white solid was consistent with the formula of the amine hydrochloride $C_7H_{12}N \cdot HCl$.

The free amine was obtained by treating the salt with an alkaline aqueous solution and then extraction with ether. The infrared spectrum of the oily primary amine showed bands at 3380 cm^{-1} and 3300 cm^{-1}. The infrared spectrum of the free amine which had been treated with deuterium oxide had two bands at 2215 cm^{-1} and 2105 cm^{-1}. These bands were assigned to the N-D stretch of the deuterated amine. The NMR spectrum of the amine showed one hydrogen as a triplet centered at δ3.36 with J of 3.5 Hz, one hydrogen as a triplet centered at δ3.20 with J of 2.5 Hz, two bridgehead protons as a multiplet centered at δ2.23, and eight protons in a complex pattern between δ2.03 and δ1.00. The amino protons were in the complex region between δ2.03 and δ1.00 and disappeared upon addition of deuterium oxide (the region then integrated for six protons). The two hydrogens at δ3.36 and δ3.20 were very close and appeared as two side by side triplets. However, the

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latter triplet is more likely a quartet and one of its peaks is underneath the triplet at δ3.36. Observation of the general peak ratios leads to the same conclusion as seen in Figure 17.

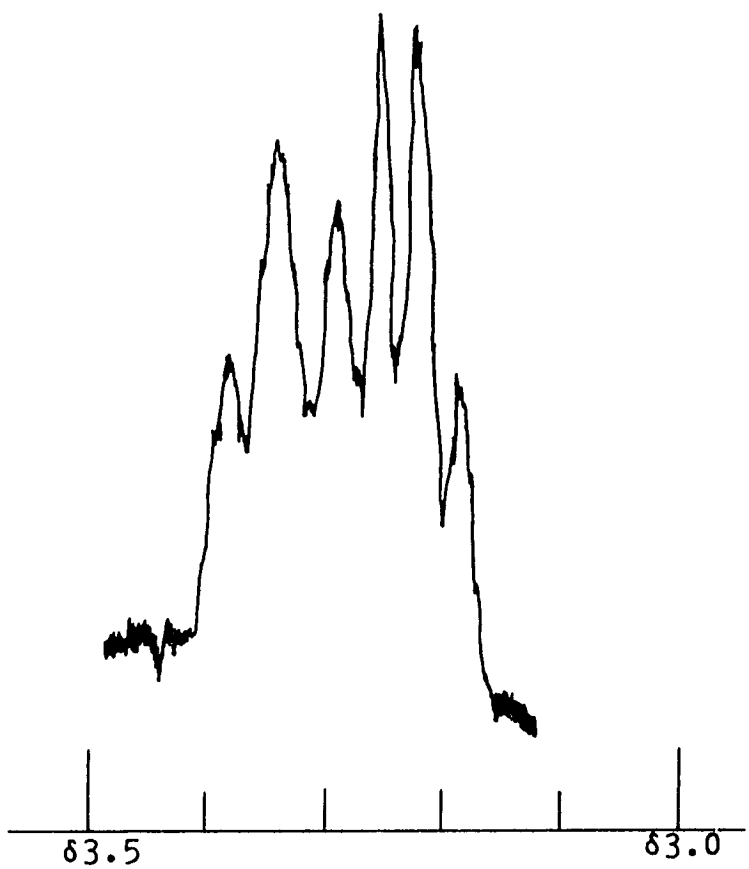

Figure 17. NMR of endo Amine Hydrochloride (80) of the δ3.5-3.0 Region

The stereochemistry of the amine and chlorine should be discussed at this point. The chlorine of the 3-chloro-norcamphor oxime has been shown to be exo[43,44]. Thus the

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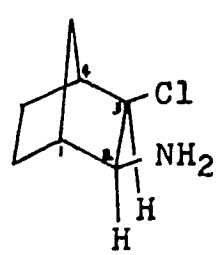
NMR spectrum of 3-chloronorcamphor oxime showed the C-3 proton as two doublets (a doublet for the syn form and a doublet for the anti form) with a J of 2 Hz. This is consistent with that expected for an endo proton coupling with an anti C-7 proton[43]. The conditions of the acylation reaction as well as that of the hydroboration reaction would not alter the stereochemistry of this chlorine, hence only the configuration of the amino groups is in question after these transformations, that is, only two products are possible, 80 and 83. It would be predicted a priori that the approach of the diborane would most likely be from the exo side of the molecule, thus producing 80.



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As mentioned above, the NMR splitting patterns exhibited by the C-2 and C-3 protons of the free amine are complicated by the fact that they overlap, i.e. that they are very close. Be that as it may, it is perhaps of some use to predict the chemical shifts and multiplicities of these protons in each compound, 80 and 83. The shifts of the exo and endo C-2 hydrogens of norbornane have been reported[51]. Data for a rigid system similar to that of the norbornane is available

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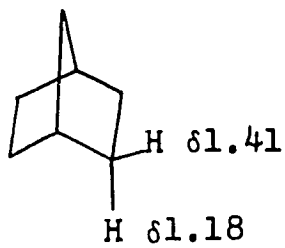

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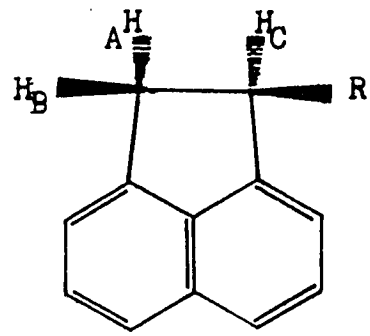

85

for 85 in Table 2[52]. From the above data it is possible

Table 2. Chemical Shifts of 85

R	H_A	H_B	H_C
H	3.36	3.36	3.36
Cl	3.90	3.63	5.73
NH_2	3.68	2.92	4.80

to predict the relative shifts of the C-2 and C-3 protons of the two compounds in question using Equation N. Thus we are able to predict for 83 that the C-2 proton will be

$$\delta \cong B + G \pm S \qquad \text{Equation N}$$

where B = base value from norbornane
G = relative shift due to the geminal substituent
S = relative shift due to the shielding or deshielding by alpha substituent

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at δ3.16 and the C-3 proton will be at δ3.87. For 80 the proton at C-2 will be at δ3.12 and the proton at C-3 will be at δ3.11. Obviously the predicted values for 80 more closely correspond to that observed for the product of the hydroboration. For 83 the predicted coupling pattern would be a doublet of doublets for each proton with $J_{2,3}$= 6-7 Hz[52] and $J_{2,7}$= $J_{3,7}$= 2 Hz[43]. The pattern predicted for 80 would be a triplet for the C-2 proton with $J_{1,2}$= $J_{2,3}$= 4.0 Hz[18,52] and a quartet for the C-3 proton with $J_{3,7}$= 2 Hz[40] and $J_{2,3}$= 4.0 Hz[18,52]. Once again the observed complex pattern more nearly fits structure 80. All of the above predictions certainly lead one to favor the endo amine as the product of the hydroboration. Yet due to the closeness of the two shifts it is not possible to conclusively identify 80 as the amine. Conclusive proof however is found in the fact that this amine was ultimately converted to the desired endo triazoline (88) by an intramolecular displacement of the exo chloro group (see later in text).

The low yield of the hydroboration of the oxime acetate lead to consideration of possible variables which might increase this yield. The most obvious variable was the substituent attached to the oxime. In Feuer and Braunstein's paper[46], oxime ethers were also readily reduced. Therefore an attempt was made to prepare the methyl ether of the chlorooxime by addition of diazomethane. The oxime (77) was dissolved in ether and to this was added an ex-

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cess of diazomethane. Two drops of boron trifluoride etherate were added as catalyst for this reaction. This solution was worked up and g.l.c. analysis showed two compounds to be present, the oxime (77) (82%) and 3-chloronorcamphor (18%). The 3-chloronorcamphor was compared with a genuine sample prepared by Meinwald et al.'s method[43].

The failure to make an ether derivative of the oxime lead to consideration of using another ester grouping. The oxime was dissolved in anhydrous ether and to this was added p-nitrobenzoyl chloride. From this reaction mixture was isolated the p-nitrobenzoate of 3-chloronorcamphor oxime (79) (m.p. 175-176°). The infrared spectrum showed an ester carbonyl band at 1750 cm^{-1} and a carbon-nitrogen double bond at 1660 cm^{-1}. The molecular ion of this ester was just barely detectable at m/e of 308 in the mass spectrum. NMR analysis was also consistent with the syn and anti forms (40/60 respectively) of 79. There were four aromatic hydrogens as a multiplet centered at δ8.25, two protons as overlapping doublets with J=2 Hz at δ6.53, one allylic bridgehead hydrogen as two multiplets (40:60) centered at δ3.70 and δ3.29, one bridgehead as a multiplet centered at δ2.72 and a complex region between δ2.47 and δ1.30 containing six hydrogens. The analytical data was consistent for $C_{14}H_{13}ClN_2O_4$.

The hydroboration of the p-nitrobenzoate (79) was carried out in the same manner as previously described for

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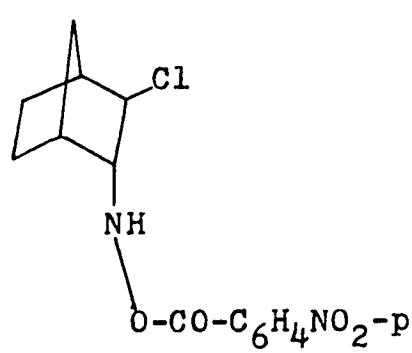
the oxime acetate. The only difference in work up of this reaction was that after acid hydrolysis, the water layer was extracted three times with chloroform to remove the p-nitrobenzyl alcohol. The acidic layer was then made alkaline and extracted with ether. The amine was precipitated as the salt in the usual manner, and the amine hydrochloride was isolated in 41% yield. The product was of the same high quality as that previously obtained from the oxime acetate (78).

At this point there should be a brief discussion of some difficulties with this particular reaction. Upon scaling up this reaction, the yield and quality of product were significantly decreased. This product would not couple in its impure state and had to be extensively purified before use in this reaction. (See later in text for discussion of coupling reaction.) The cause of the problems are not known and can only be postulated. Perhaps the best guess would be that the p-nitrobenzyl hydroxylamine (86)



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is carried over into the diazo coupling reaction and this can significantly interfere with this coupling or this can couple itself with the aryl diazo salt.

The successful preparation of the endo amine hydrochloride (80) demonstrated that this new pathway illustrated in Figure 16 was feasible. At this time, it was decided to deviate slightly from the scheme in Figure 16. Heine and Tomilia[16] have reported the coupling of aryl diazonium salts with unsubstituted aziridines. Why could not the amine hydrochloride be coupled with an aryl diazonium salt in the same manner? Thus a modified scheme was devised as illustrated in Figure 18.

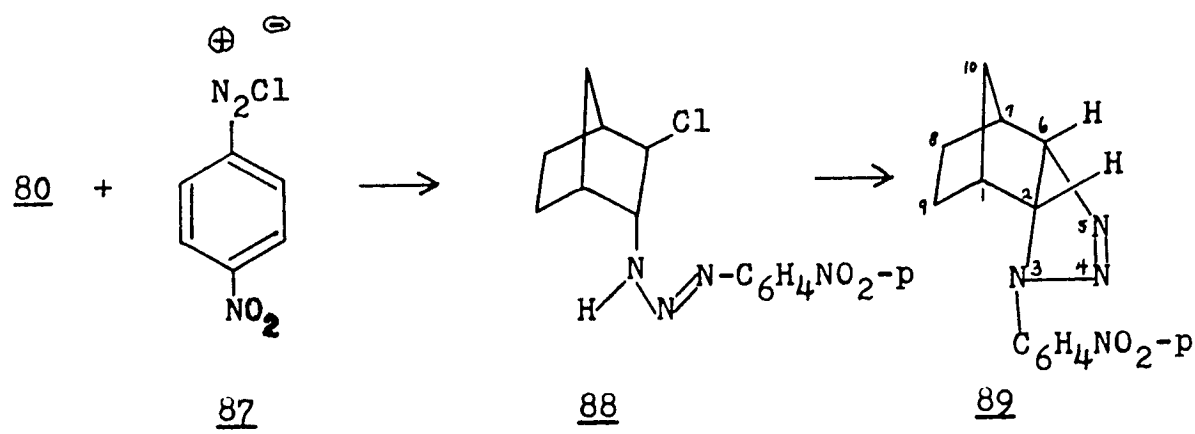

Figure 18. Proposed Synthesis of endo Triazoline (89)

The diazonium salt (87) of p-nitroaniline was prepared at 0° in the usual manner[16]. The diazonium solution was poured into a saturated sodium acetate solution. The

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pH of this solution was adjusted to 5.6-6.0 by addition of solid sodium acetate trihydrate. This buffered solution was then added a portion at a time to the amine hydrochloride (80) in water. A yellow precipitate immediately formed. After complete addition of the diazo solution, the mixture was stirred for one hour and the solid was filtered off. The yellow product was air dried (61%) and had a m.p. 112°-115° with bubbling. The infrared spectrum was consistent with that expected for the coupled product (88) showing a secondary amine at 3380 cm^{-1} (in KBr) and at 3315 cm^{-1} (in $CHCl_3$). The ion of highest mass in the mass spectrum was the molecular ion minus molecular nitrogen at m/e of 266. It is worth mentioning that the overall appearance of the mass spectrum of 88 is similar to that of the endo triazoline (89), perhaps indicating that the diazoamine closes to the triazoline and then fragments as does 89. The NMR spectrum contained two aromatic hydrogens as a doublet with J of 9 Hz at δ8.21, two aromatic protons as a doublet with J of 9 Hz at δ7.26, a complex multiplet for one proton centered at δ4.26, one proton as a triplet with J of 2.5 Hz at δ3.89, two bridgehead protons as a complex multiplet centered at δ2.54 and six hydrogens in a complex region between δ2.22 and δ1.10. Elemental analysis of this compound showed the structure was consistent with a $C_{13}H_{15}ClN_4O_2$ formula.

Mention should be made of the fact that a modified

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procedure using the free amine in the place of the salt gave an 81% yield. This was expected since the free amine is more nucleophilic than the salt.

The last step in the development of the synthesis was to close the diazoamine to the desired endo triazoline by intramolecular nucleophilic displacement of the chloride. Preliminary experiments showed that the anion (Figure 19),

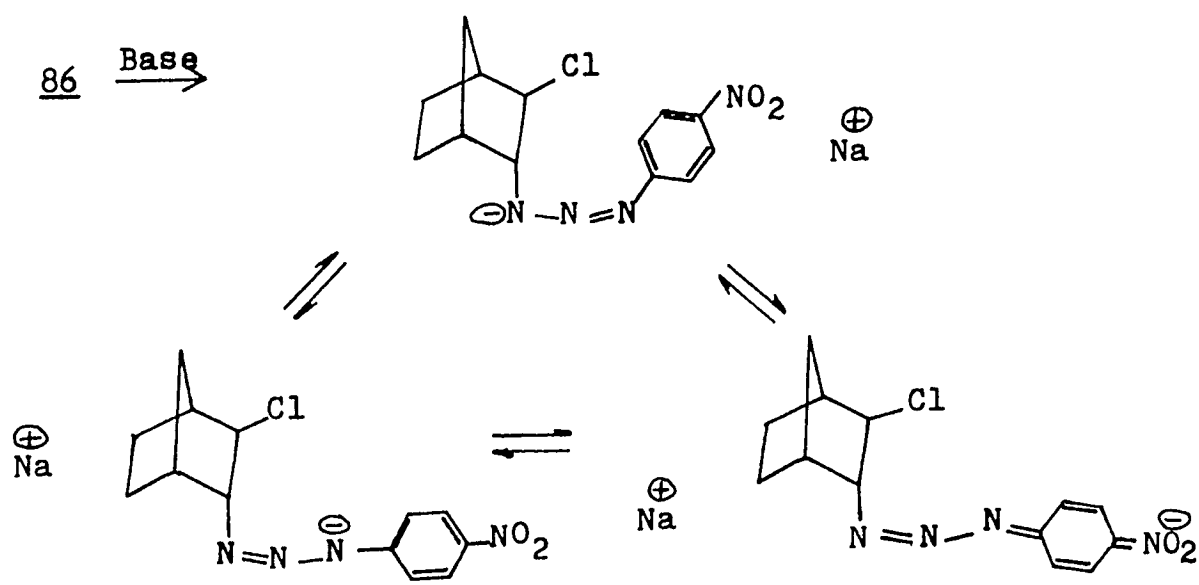

Figure 19. Anion of 86

which was recognized by its deep red color, was easily formed by treatment with a strong base, such as a tertiary amine or sodium hydride. However, it was further recognized that this anion was exceedingly stable, since the charge was

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largely delocalized. After refluxing this solution at 80° for eight hours, there was still no change in color. Thus it appeared that some additional driving force was required for the cyclization of this chlorodiazoamine. A consideration of some fundamental principles lead to the consummation of the synthesis when the endo triazoline was finally isolated.

The diazoamine (88) was dissolved in absolute ethanol and heated to 60°. To this was added slightly more than one equivalent of freshly prepared sodium ethoxide. The solution immediately turned a deep wine red, indicative of the anion formation. This solution was stirred for thirty minutes and then one equivalent of a solution of silver nitrate in ethanol was added. The color of the resultant solution after the completed addition was yellow, thus indicating a change had taken place. The solution was filtered several times and eventually upon complete work up, a yellow solid was isolated (64%; m.p. 120-130° with bubbling). Recrystallization from ethanol gave orange crystals, m.p. 135-138° with bubbling.

The infrared spectrum contained the characteristic bands for a nitro grouping at 1500 cm^{-1} and 1320 cm^{-1}. The mass spectrum showed as the ion of highest mass a m/e of 230 which corresponds to the triazoline (89) minus molecular nitrogen. The NMR spectrum shows two aromatic protons as a doublet with J of 9 Hz at δ8.15, two aromatic

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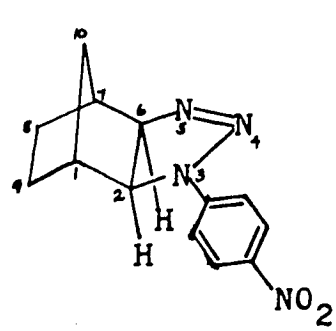
protons as a doublet with J of 9 Hz at δ7.27, one allylic proton as a doublet of doublets with J's of 5.50 Hz and 12.0 Hz centered at δ5.09, one proton as a doublet of doublets with J's of 4.25 Hz and 12.0 Hz centered at δ4.02, two bridgehead protons as a complex multiplet centered at δ2.80 and six hydrogens in a complex region between δ1.65 and δ0.75. The elemental analysis of the triazoline was consistent with that predicted for $C_{13}H_{14}N_4O_2$.

The clue to the identification of the endo triazoline is the NMR spectrum. The two protons which appear as doublets of doublets demonstrate that the triazoline function is indeed endo. The large coupling constant of 12 Hz is indicative of the cis exo C-2 and C-6 protons. These protons are also coupled with bridgehead hydrogens at C-1 and C-7 with J values of 4.25 and 5.50 respectively. Had the C-2 and C-6 protons been endo, the coupling constants with the bridgehead protons would have been near zero[50]. The NMR spectrum of the endo triazoline (11) isolated by



90

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McLean and Findlay[11], correlates well with the spectrum of 89. These workers have reported that their endo triazoline (11) also displays two doublets of doublets for the C-2 and C-6 protons. In contrast to the endo triazolines, the NMR of the exo triazoline (90) shows the C-2 and C-6 protons as doublets, each with J values of 9 Hz[12].

The use of silver nitrate in ethanol as a reagent to effectuate the cyclization of the triazoline has not been previously reported. This reagent has been widely used in qualitative organic chemistry to classify compounds known to contain halogen[69]. The ability of the silver ion to react with alkyl halides, in fact, was the reason for its selection in this reaction. From a mechanistic viewpoint, this reaction must involve the interaction of the silver ion with the chloro grouping. This complexing may lead either to eventual formation of a carbonium ion and then attack by the negatively charged nitrogen or possibly by

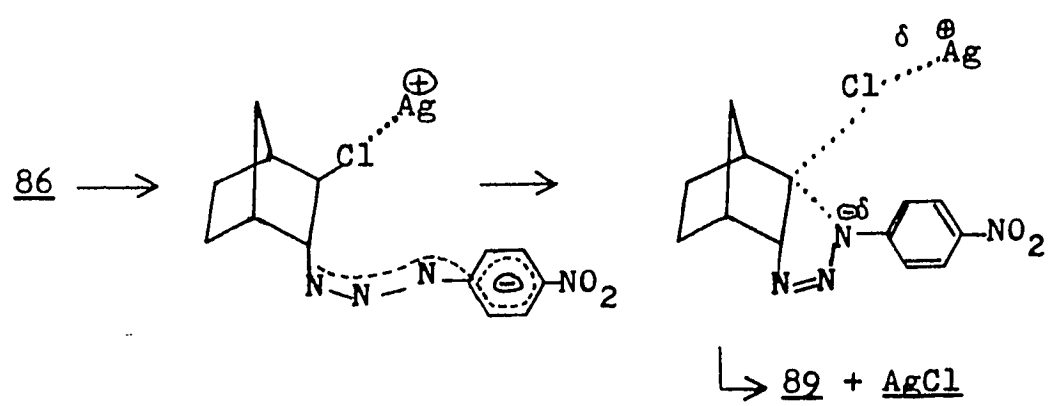

Figure 20. Silver Cation Interaction with Anion of 86

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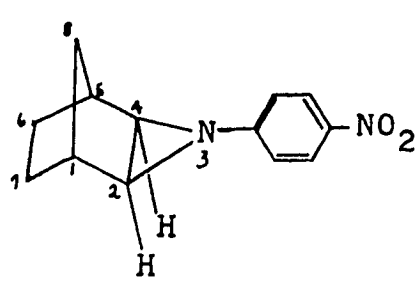
the anion displacement of the chloro group, which was at the same time being pulled by the silver ion (Figure 20). The silver nitrate was obviously necessary to make the reaction proceed, since the delocalization of the anion was so great that there was not enough nucleophilic character at any one site to displace the chlorine.

The study of the chemistry of this endo triazoline began with its photolysis. A mixture of the endo and exo triazolines (89 and 90) (2:1, respectively) was photolyzed in acetone for six hours at -5°. There were two products (2:1) by g.l.c. analysis. The minor product was identified as the exo aziridine (91) by comparison on g.l.c. with an authentic sample and by comparison of the NMR of the mother liquor with that of the authentic sample.

The major product was collected by preparative g.l.c. Reinjection of this sample showed that it was indeed pure and was the major product. This yellow solid was identified as the endo aziridine (92). The infrared spectrum contained bands at 1500 cm^{-1} and between 1350 cm^{-1}



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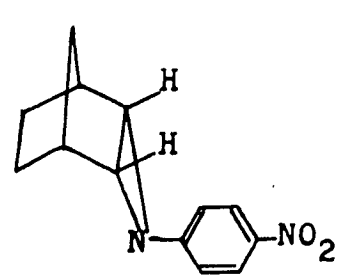

92

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and 1300 cm^{-1}, in the region expected for an aromatic nitro group[70]. The NMR spectrum contained two aromatic hydrogens as a doublet with J value of 9 Hz at δ8.06, two aromatic hydrogens as a doublet with a J value of 9 Hz at δ6.91, two aziridine ring protons as a triplet with J of 2 Hz at δ2.93, two bridgehead protons as a multiplet centered at δ2.49, and a complex region for six hydrogens between δ2.03 and δ1.21. The mass spectrum showed a molecular ion at m/e of 230 for $C_{13}H_{14}N_2O_2$.

It is perhaps worth an aside to point out a rather distinct pattern which is observed in the mass spectra fragmentation patterns of aziridines in the norbornane

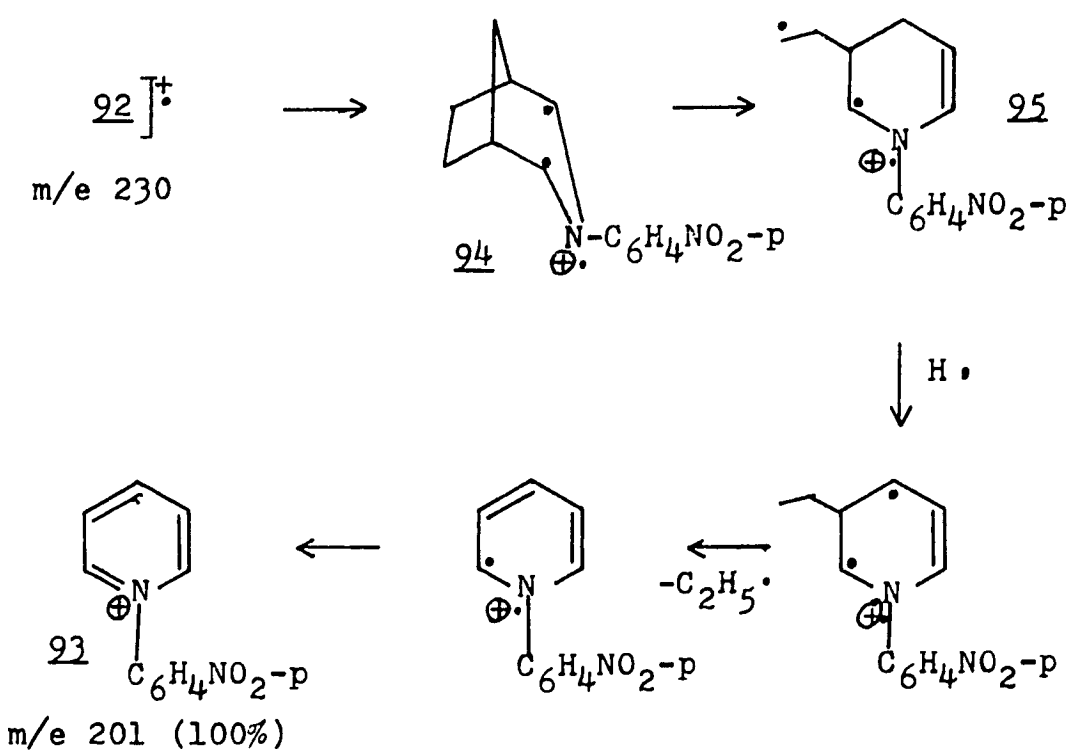

Figure 21. Proposed Ion (93) for m/e 201 From the Mass Spectrum of 92.

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series, such as 91 or 92. Almost always the first significant ion (usually the base peak) observed after the molecular ion is that ion resulting from loss of an ethyl radical. This ion in many cases is so intense that it is often the base peak of the spectrum. Thus for exo and endo aziridines 91 and 92, the base peaks are at m/e 201 and this ion probably corresponds to a pyridinium structure (93). The significance of this observation is that it may be used as a diagnostic tool to distinguish between these types of aziridines and their corresponding isomeric imines and enamines. Thus in the mass spectrum* of the imine (94) the loss of an ethyl group is only a minor pathway, ~12% (the base peak was the molecular ion). Probably the high intensity of the ion resulting from the loss of an ethyl group is a result of the large amount of ring strain within the tricyclic {3,2,1,$0^{2,4}$} system. Further support for this observation is that the base peak for the aziridine (122) is also the result of loss of an ethyl radical.

Analysis of the NMR spectrum is again the key to the identification of endo aziridine (92). The triplet observed for the protons on the carbon attached to nitrogen is characteristic of endo aziridines[18,26,53]. This is in contrast to the NMR spectrum of the exo aziridine (91) in which the

*The imine was so unstable that this mass spectrum was contaminated by norcamphor and p-nitroaniline. This spectrum was provided by Dr. Samuel K. Gabriel.

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two endo hydrogens on the aziridine ring appeared as a singlet at δ 2.42 and the anti C-8 proton appeared at δ 0.87 as a doublet with J=9.5Hz. The high field position of the anti C-8 proton is characteristic of exo aziridines[18,54].

Mention should be made of the mixture of endo and exo triazolines (89 and 90) used in the photolysis. This mixture was prepared from the amine hydrochloride which had been isolated from a large scale hydroboration of the p-nitrobenzoate oxime (79). The product from this reaction was impure. Two subsequent purifications of this product gave the amine hydrochloride used to prepare the above mixture. It is interesting that in no other repetitions of the hydroboration were such mixtures isolated. These results demonstrated that the hydroboration of the p-nitrobenzoate oxime was not stereo-specific, although the extent to which the exo amine was formed was not known.

The concluding study of the chemistry of the endo triazoline was most significant. The endo triazoline (89) and the exo triazoline (90) were each pyrolyzed in decalin at 165-170° for two hours. The results of the g.l.c. analysis of each pyrolysate are summarized in Table 3.

The solution of 90 after the pyrolysis was a clear, yellow solution, while the solution of 89 was yellow and contained a brown gum on the bottom of the tube. An attempt to dissolve the brown gum in chloroform had no visible effects and g.l.c. of chloroform solution of each pyrolysate

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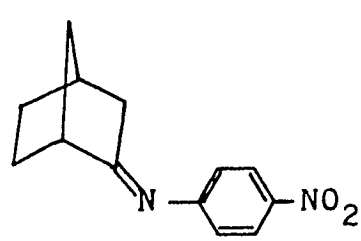
Table 3. Pyrolysis of Triazolines 89 and 90

TRIAZOLINE	ENDO AZIRIDINE (92)	IMINE (94)	EXO AZIRIDINE (91)	TOTAL* G.L.C. AREA
Exo (90)	8.8%	42.3%	48.5%	100%
Endo (89)	17.5%	48.2%	34.4%	21%

*See page 98 for explanation.

showed no change in product ratios. The solution of 90, after sitting overnight in the freezer, was also found to contain a brown gum. The imine (94) in each reaction began to decompose after sitting overnight as indicated by the gradual disappearance of the imine peak and the appearance



94

and increase of a p-nitroaniline peak by g.l.c. It is perhaps important to point out that all products from the pyrolysis of 90 would be expected to be g.l.c. volatile as was demonstrated by the work of McDaniel and Oehlschlager[18] and also that of Hale and Zalkow[28].

The results of this pyrolysis are indeed signifi-

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cant and correlate well with earlier observations of similar pyrolysis of exo triazolines[18,27,28,31,53]. The exo triazoline (90) gave as a minor product the endo aziridine (92) (8.8%). These results were very similar to those reported by Zalkow et al.[53] in the pyrolysis of the N-carbomethoxy triazoline (95) (Figure 22). As mentioned

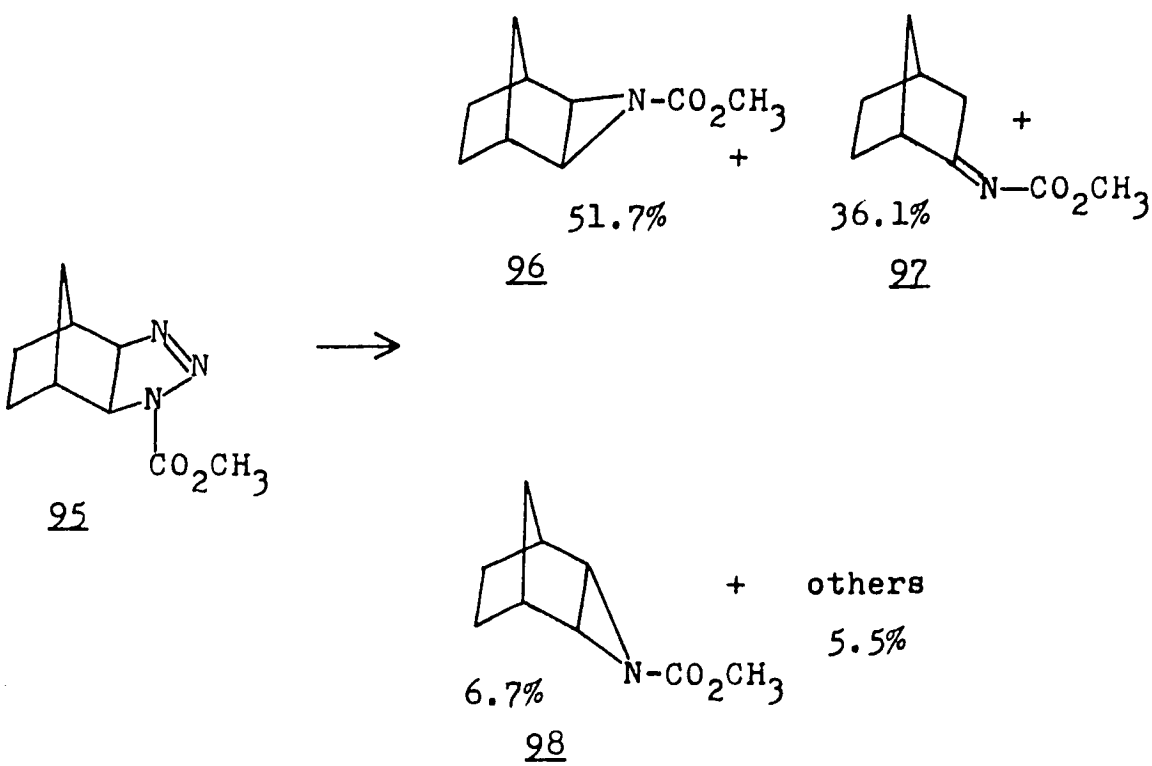

Figure 22. Pyrolysis of N-carbomethoxy Triazoline (95)

in the introduction, McDaniel and Oehlschlager[18] have found that the pyrolysis of the N-phenyl triazoline (17) also produces an endo aziridine (23) in 9% yield. Of even more importance, Zalkow and Hale[28] have recently reported that the endo aziridines, 33a, 34a, and 34b were the predominant

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products from the reaction of benzenesulfonyl azide and the corresponding olefins, 31a, 32a, and 32b respectively. These workers have shown that these products arise from unstable exo triazolines. The formation of the endo aziridines has been explained by the formation of the diazoimine intermediate (38) shown in Figure 9 of the introduction. The diazo and imine functions have a choice of conformations which may be assumed. Obviously loss of nitrogen from conformers 99b or 99d could readily result in formation of an endo aziridine, while loss of nitrogen from conformers 99a or 99c would result in the formation of the exo aziridine.

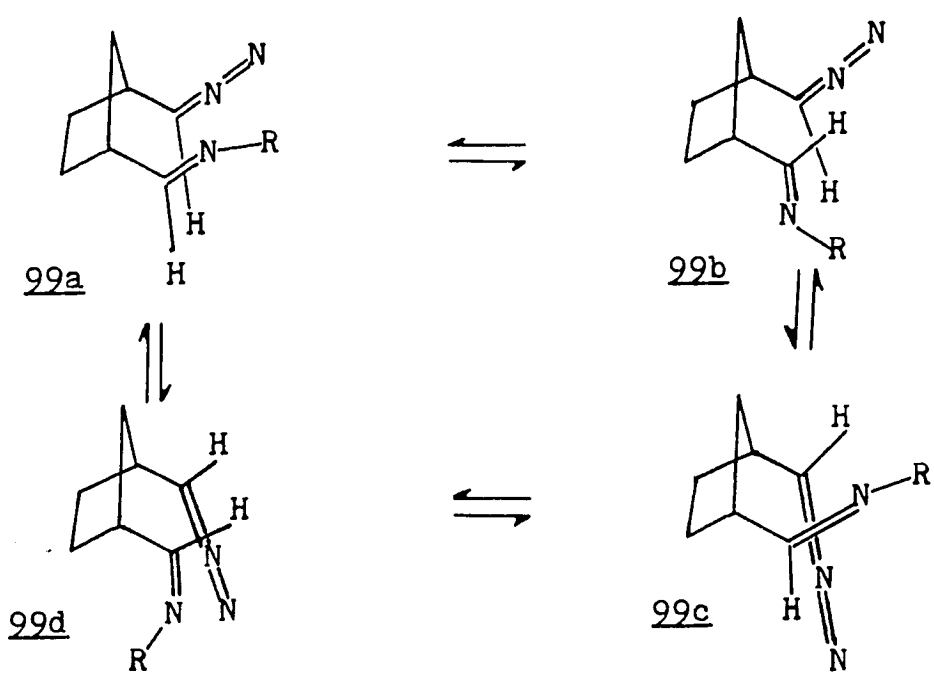

Figure 23. Conformations of Diazoimine (99)

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The results of the pyrolyses of the endo and exo triazolines (89 and 90) are interesting and certainly provide very definitive evidence for a common intermediate, namely the diazoimine (99), which can produce both endo and exo aziridines (92 and 91). Perhaps before proceeding to the theoretical implications of these results, it should be pointed out that the ratio of 92 to 91 is only an apparent one, as indicated by the Total G.L.C. Area in Table 3. The numbers in this column represent the total area of all g.l.c. peaks of each triazoline pyrolysis mixture relative to the other. Thus for every 100 units of area for the exo triazoline pyrosylate, there were only 21 units of area for the endo triazoline mixture. Since equal amounts of each triazoline were used in this pyrolysis study and the conditions of pyrolysis for each triazoline were identical, then it follows that both should have the same area in g.l.c. for equal injections. Obviously this was not the case and it therefore logically follows that at least part of pyrosylate of 89 was not g.l.c. volatile. The observation of the formation of an insoluble brown gum in the bottom of the reaction vessel of 89 explains the disappearance of volatile components, since that which does not dissolve cannot be found in the solution injected on the g.l.c. This leads us to the question of identification of this gum. Aziridines have a common, elementary property and that is the ability to be readily attacked and opened

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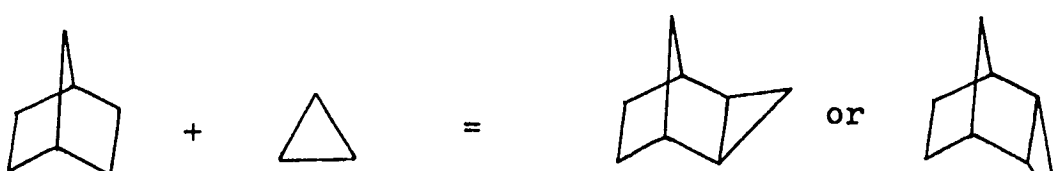
in either acid or strong basic media. In fact, this high reactivity alone makes aziridines in general a very important group of compounds, since they may be reacted with themselves to produce polymers[17]. The high reactivity of aziridines can be attributed to the release of a large amount of ring strain energy. The ring strain energies of alicyclic molecules are usually additive[55]. Thus it may be predicted that the ring strain for the aziridines, 91 and 92, should be around 46 kcal/mole (Figure 24). The



18.4 kcal/m + 27.6 kcal/m = 46.0 kcal/m

Figure 24. Predicted Ring Strain for Bicyclic Aziridines

assumption is made that the ring strain of cyclopropanes and aziridines are not very different. This large ring strain energy indicates that the aziridines under consideration should be highly susceptible to ring opening.

Further consideration of the pyrolysis mixture in question reveals that there are nucleophilic agents present. Thus the aziridines in question must be attacked from the back side. The exo aziridine is much less sus-

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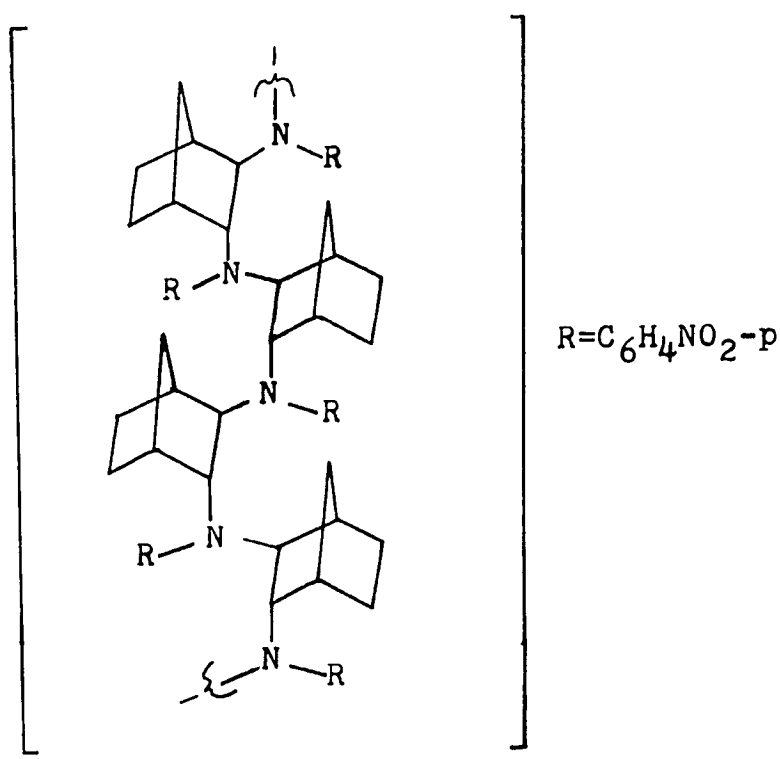
ceptible to back side attack due to steric hinderance. However, the endo aziridine, being a highly strained species, and being readily attacked from the exo face of the molecule, would be rapidly opened by nucleophilic attack. All of the above arguments suggest that the endo aziridine (92) reacts with itself to form the brown gum, which must be the resulting polymer of this aziridine shown as 100 below. The degree of polymerization noted



100

in the pyrolysis of 89 may suggest the production of a large amount of endo aziridine. It should be pointed out here that the endo triazoline was observed to lose nitrogen between 135-138°. This means that the temperature of the pyrolysis was about thirty degrees higher than that needed

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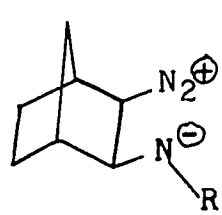
to accomplish the decomposition. This may also account for the high degree of polymerization observed. Also the fact that nitrogen liberation was observed for only the first fifteen minutes of the two-hour pyrolysis, probably indicates that the triazoline had completely decomposed at that point and thus the additional heating time would have contributed to the formation of polymer. Perhaps also a factor in this side reaction is that the p-nitrophenyl substituent, being a strong electron withdrawing group, would facilitate the ring opening reaction by delocalization of any negative charge involved in the polymerization.

At this point it is felt that new consideration should be given to the proposed mechanism in Figure 9 in light of recent concepts. In the mechanism proposed by Zalkow and others,[18,25,28,53] the first step is the heterolytic cleavage of the N-3, N-4 bond to produce a diazonium betaine (101). Evidence for this process is based on the observation that the thermal decomposition of triazolines



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is accelerated in more polar solvents[5,18,24]. Investigations have also shown that electron withdrawing groups at N-3 accelerate the reaction rate[18,56]. The second step in this proposed mechanism is the cleavage of the carbon-carbon bond to give the diazoimine intermediate (99). Extensive evidence has been provided supporting the formation of 99. First, Zalkow and others[18,25,28] have demonstrated that endo aziridines arise from exo triazolines. Secondly, Fusco et al.[34] have reported the isolation of an imine and a diazo compound from the pyrolysis of a triazoline. McDaniel and Oehlschlager reported that the phenyl triazoline when pyrolyzed in an infrared cell produced an absorption band at 2175 cm^{-1}.[18] These workers attribute this band to the diazonium betaine (101) or the diazoimine intermediate (99). These workers point out that the diazoimine (99) would be expected to have a finite existence since the 1,3-dipolar addition of diazoalkanes and imines proceeds only at a moderate rate[57]. It is indeed interesting that a similar observation was made in this laboratory, when the triazoline (121) was pyrolyzed. A yellow oil was trapped which showed bands in the infrared region at 2120,1720,1695 and 1630 cm^{-1}. (These results will be discussed in more detail in a later section.) The real significance of these results is that an accompanying band at 1630 cm^{-1} was observed, indicative of an imine double bond. Although these results lend credence to the

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diazoimine structure, it must be pointed out that the yellow oil could not be conclusively characterized.

Perhaps just as significant are the results of this work in which an exo aziridine (91) was produced from the pyrolysis of an endo triazoline (89). This surely indicates that a common intermediate is involved in these types of reactions.

At this point, let us stop to consider other pathways which might lead to endo aziridines from exo triazolines or to exo aziridines from endo triazolines. All of the supporting evidence may also be interpreted in terms of two possible concerted mechanisms. Both of these processes would be expected to involve disrotatory ring openings in accordance with the Woodward-Hoffmann Rules of orbital symmetry[58]. The first process would be a retro of a 1,3-cycloaddition which is thermally allowed for a system of three pairs of electrons (i.e. six electrons) (Figure 25). The second possible pathway is an electro-

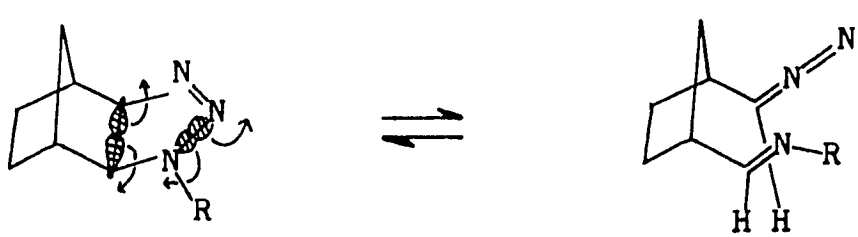

Figure 25. Retro 1,3-Cycloaddition of a Triazoline

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cyclic ring opening which is thermally allowed for a system of three pairs of electrons (Figure 26).

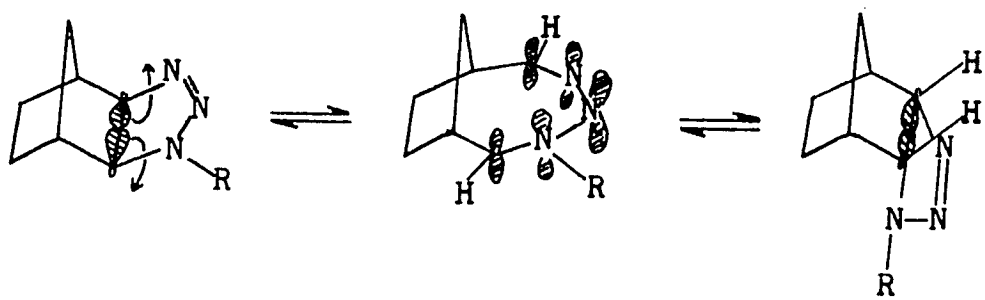

Figure 26. Electrocyclic Ring Opening of a Triazoline

Both mechanisms seem equally plausible on a theoretical basis, however the reported observations of the formation of diazoalkanes and imines from triazolines[34,35] [59,60] lead one to favor the pathway shown in Figure 25. Furthermore, if the exo triazoline is indeed transformed to an endo triazoline by the pathway in Figure 26, it should be observable by NMR temperature studies, since the endo triazoline would be expected to have a finite existence. This should particularly be true for triazoline which gives predominantly endo aziridine. This has not been observed. Also, had an endo triazoline been involved in the reactions in question, in cases where polar products, such as 18 and 19, are observed, it would be expected that comparable endo polar products would have been seen, i.e. 102

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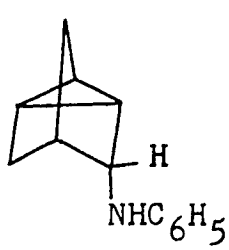
and 103. Such products have not been reported. Reconsideration of the observations by earlier workers[18,20,24,25-28,31,53] in light of the possibility of the concerted process in Figure 25 leads one to the conclusion that in some cases this concerted pathway is in competition with the heterocyclic cleavage which produces 101. That the rate of reaction increases with the polarity of the solvent suggests that indeed the ionic mechanism becomes prominent when there are solvent molecules which stabilize charge separation. Zalkow and Hale[28a] reported that triazoline



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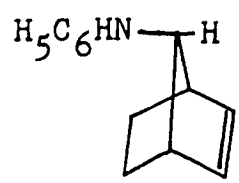

103

40 when pyrolyzed in diethylene glycol diethyl ethyl gave a complex mixture of products, while pyrolysis in decalin gave only aziridines (exo:endo; 46:54). Thus while the ionic mechanism is in operation in polar solvents, it would seem that the nonionic or concerted mechanism becomes the favored pathway in non-polar solvents. That there occurs a decrease in rearrangement products upon going from polar to a non-polar solvent, further indicates that the concerted process is the route of choice in non-

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polar solvents. Thus a higher endo:exo aziridine ratio would be expected from an exo triazoline in non-polar solvents. This is, in fact, what is observed. Furthermore, all of the previously reported substituent effects are also in accordance with this concerted mechanism. Thus strong electron withdrawing groups, such as benzenesulfonyl facilitate the concerted pathway as demonstrated by the high ratio of endo to exo aziridines[28]. Poorer electron withdrawing groups, such as phenyl[18] encourage the reactions to proceed by the ionic pathway. The diazonium betaine (101) in a non-polar solvent would be expected to lose nitrogen rapidly and result in a greater amount of exo aziridine and other more polar products, due to formation of a norbornyl cation (in the case of an exo triazoline) and thus a smaller endo:exo aziridine ratio. The concerted mechanism is also seen to be in agreement with the observation that the endo:exo aziridine ratio increases as the temperature of the pyrolysis increases[28].

If one accepts all of the above arguments, it is more than pertinent to consider by what mechanism are the products of these reactions formed, i.e. how are the products formed from the diazoimine? It is well known that diazoalkanes decompose under photolytic and pyrolytic conditions to form carbenes[61,62]. There is no reason to assume that the diazoalkane portion of the intermediate should deviate from normal behavior. Under normal pyrolysis conditions,

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the diazoalkane would be expected to decay to a triplet carbene, which would selectively add to the imine to produce the endo and exo aziridines. Obviously this accounts for the results of the reactions of benzenesulfonyl azide with the norbornene derivatives. However, this triplet carbene cannot adequately explain the formation of imine in some instances or the formation of other polar products in other instances. In the case of the N-phenyl adduct of norbornene (17), the polar products obviously arise via some type of ionic mechanism, probably the diazonium betaine or a dipolar intermediate. However, in cases where imine is the only other product besides aziridines such as in the results in this work, it becomes questionable as to whether an ionic mechanism is involved. This is particularly true in light of the work of Saunders, Schleyer and Olah[63] who showed that Wagner-Meerwein rearrangements and 6,2-hydride shifts in the 2-norbornyl cation are much more rapid than 2,3-hydride shifts. To

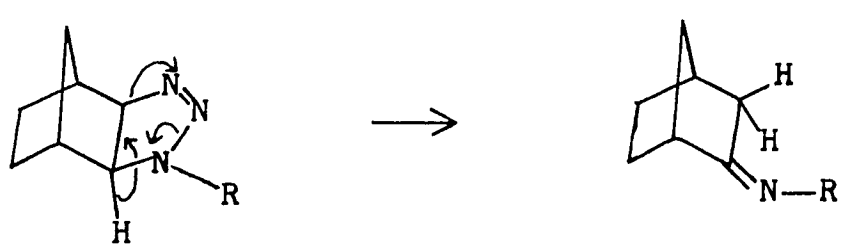

Figure 27. Concerted Formation of Imine

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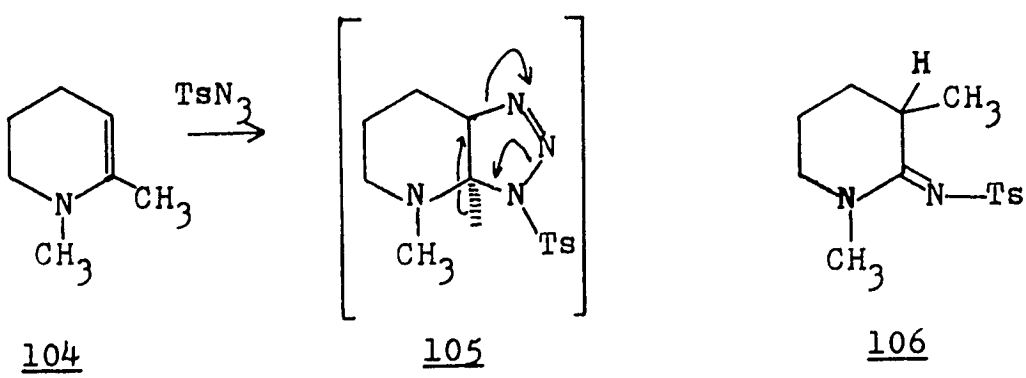
account for the imine formation, a concerted nitrogen loss and hydrogen shift may be postulated, as shown in Figure 27. A similar concerted mechanism involving the migration of a methyl group has been proposed by Richie and Rosenberger to account for the cyclic amidines from tosyl azide and several nitrogen heterocycles[59]. These workers found for example that tosyl azide and 1,2-dimethyl-2-piperideine (104) gave amidine (106) (Figure 28).



104 105 106

Figure 28. Reaction of a Tetrahydropyridine with Tosyl Azide

Bushell and Wilder[64] have reported an endo, endo-2,3-hydride shift, thus suggesting that the concerted migration pictured in Figure 32 is not unlikely. Perhaps, however, even more significant are the recent results of Rengaraji and Berlin[33]. These workers reported 3,2-endo, endo migrations when triazolines 27 and 28 decomposed to imines 29 and 30 respectively.

Thus we have now been able to account for all of the observed products in this and previous works. Perhaps

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we should now point out some general features in these triazoline decomposition processes. First benzenesulfonyl azide adds to norbornene derivatives rapidly to yield only aziridines (except in one case where some imine[20] was formed at higher temperatures). Unstable exo triazolines have been assumed to be involved although they have never been detected. The inability to isolate these unstable triazolines is certainly linked to the nature of the decomposition process. Obviously the retro 1,3-cycloaddition to the diazoimine takes place almost immediately, indicating that the equilibria for cycloadditions, involving a benzenesulfonyl group, lie very far to the left. The diazoalkane portion then decomposes to a carbene and adds selectively to form only aziridines. As we move through the spectrum of triazoline substituents, we begin to see a general trend. An electron-withdrawing group such as p-nitrophenyl under pyrolysis conditions gives aziridines and imine, but no other products. We now see that the retro 1,3-cycloaddition reaction to give diazoimine is in competition with the concerted reaction which yields imine. If we consider the results of the N-phenyl substituted triazoline (17), we see that aziridines, imine and other more polar products are observed. At this point, we begin to see an ionic process in competition with the concerted processes (Figure 34). As the electron-withdrawing power of the triazoline substituent increases, the

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likelihood of a retro 1,3-dipolar addition also increases. Thus a clear pattern has emerged and is summarized in Figure 29. These pathways account for the observed products

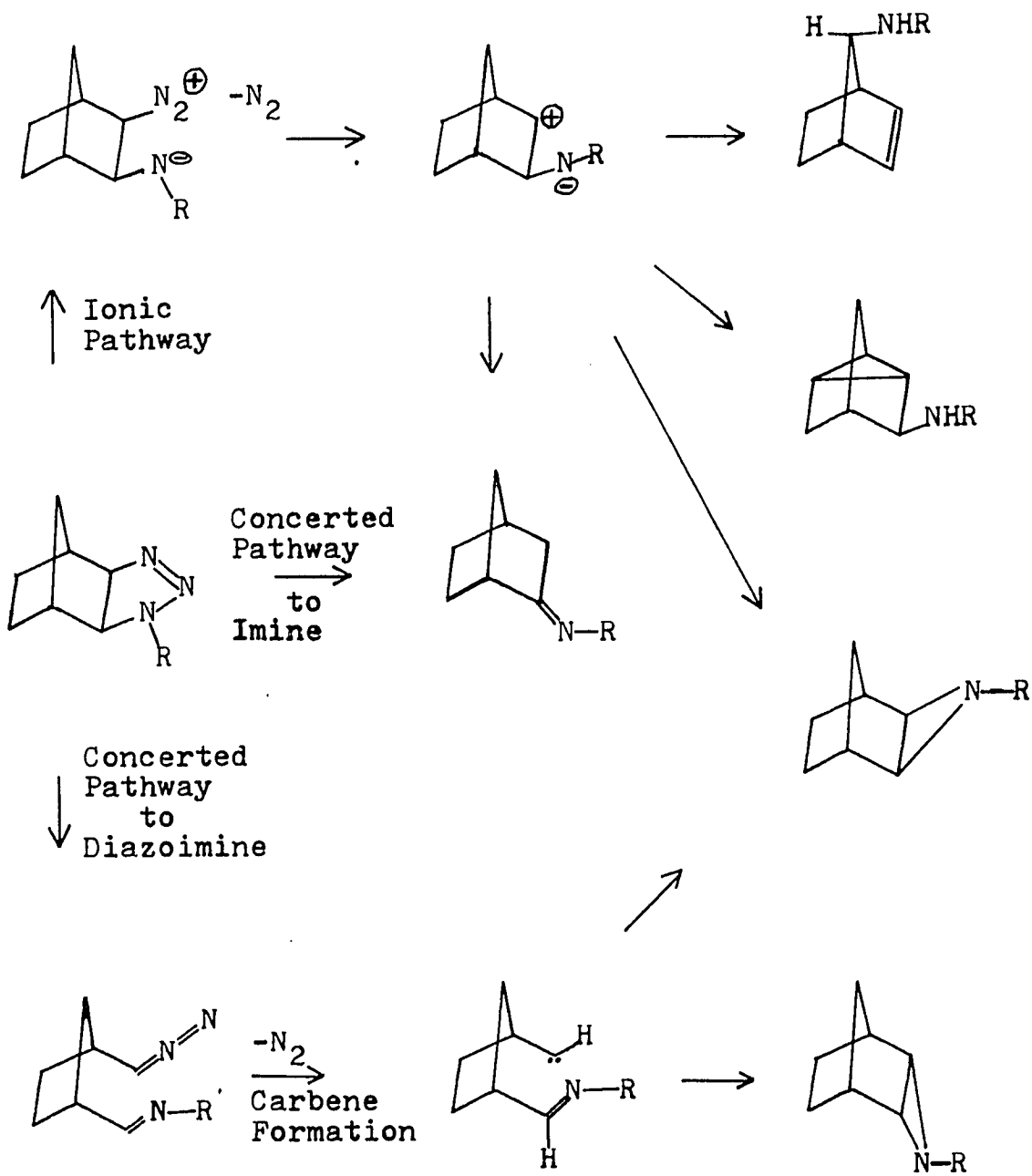

Figure 29. Summary of Mechanisms in Operation in Triazoline Pyrolysis

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and the observed solvent and substituent effects and perhaps answer many of the questions raised in the introduction.

The observations of Zalkow and co-workers[25-28,31] that norbornene derivatives react with benzenesulfonyl azide to give quantitative yields of only aziridines, is certainly strong evidence for a concerted reaction as well as demonstrating that the intermediate diazoalkane decomposes to a carbene. Had an ionic intermediate been involved (such as the norbornyl cation), it would be expected that at least some of the product would be imine (111) or a rearrangement product (110). Furthermore, had the diazo-group been involved in an attack on the imine group (108), it would be predicted that at least part of the product would have been imine. An explanation for predominance of the endo aziridine in the above cases has not been postulated as of this date.

Zalkow et al.[31] suggested that the anhydride function played a unique role in the above reactions, but later concluded that this was not the case when he found that the exo dicarbomethoxy derivative (32b) of the anhydride also gave predominantly endo aziridine (34b)[28]. It is interesting that the triazoline (40) under pyrolytic conditions in decalin also gave only aziridines and predominantly the endo aziridine (41)[28]. Oehschlager and McDaniel have shown that from a similar pyrolysis of triazoline (17), the endo

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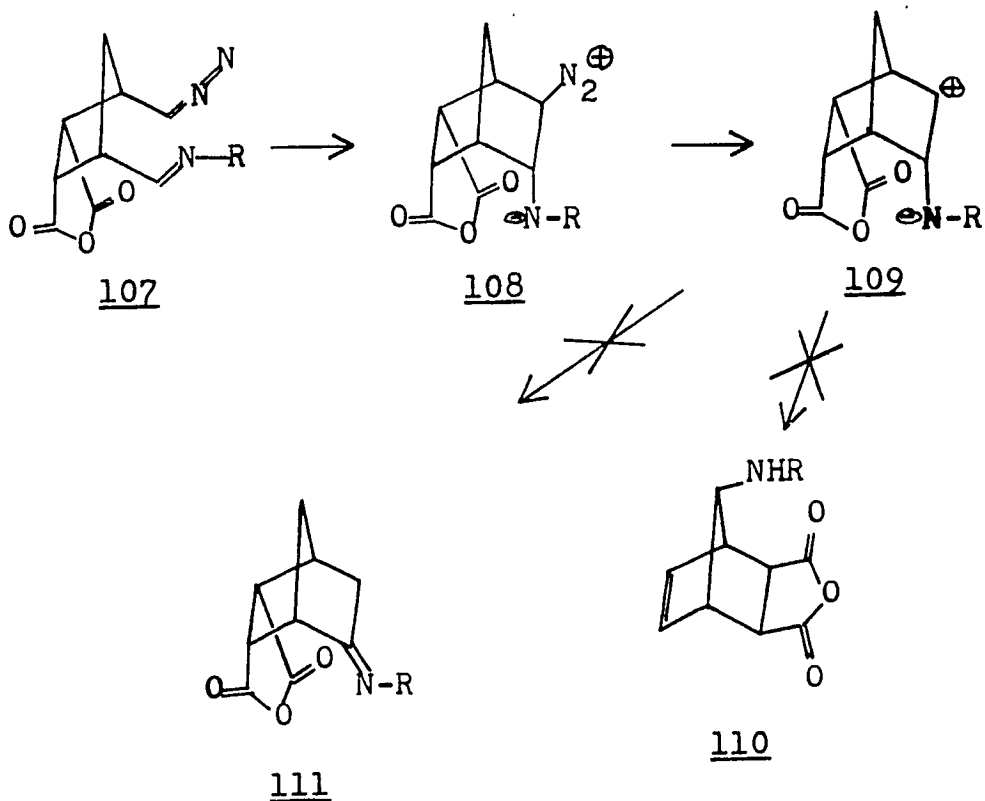

Figure 30. Expected Products from an Ionic Intermediate

aziridine is only a minor product[18]. This certainly is good evidence that the nitrogen substituent is not a major factor in the high endo/exo ratio in the cases previously described.

After consideration of the proposed intermediate diazoimine, it is worthwhile suggesting that indeed the reason for the unusual production of the endo aziridine is a very strong field effect exhibited by the anhydride or carbomethoxy groups. This field effect exerts a very real and dynamic influence on the proposed diazoimine inter-

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mediate. To explain this field effect one must accept, for the moment, the existence of this pathway which might lead to the observed endo and exo aziridine. Clearly if the imine portion of the intermediate alines itself with the dipole created by the anhydride in a head to tail fashion (i.e. negative to positive center), the conformation achieved will be 113b. If the imine is in this configuration when the diazoalkane loses nitrogen to form a carbene, the product observed will be the endo aziridine. Indeed further evidence for the field effect of the anhydride groups is present in the results of Zalkow and Oehlschlager[26] who reported that the relative rates of nitrogen evolution in the thermal reactions of benzenesulfonyl azide with norbornene, 32a, and 31a are 100:10:1 respectively. Gray and Heitmeier have also attributed the difference in rates of epoxidation of 32a and 31a (3.2 to 1, respectively) to field effects[65]. The magnitudes of the field effects in question are demonstrated in earlier results. The reaction of benzenesulfonyl azide and norbornene, which produced a quantitative yield of the exo aziridines[20,66], indicates that steric hindrance of the endo face of norbornene is so great that little or no endo aziridine may be formed without the influential field effect of the anhydrides or ester groupings. Secondly it demonstrates that even with the greatly increased steric bulk with the substitution of the endo anhydride grouping for the endo hydrogens, the

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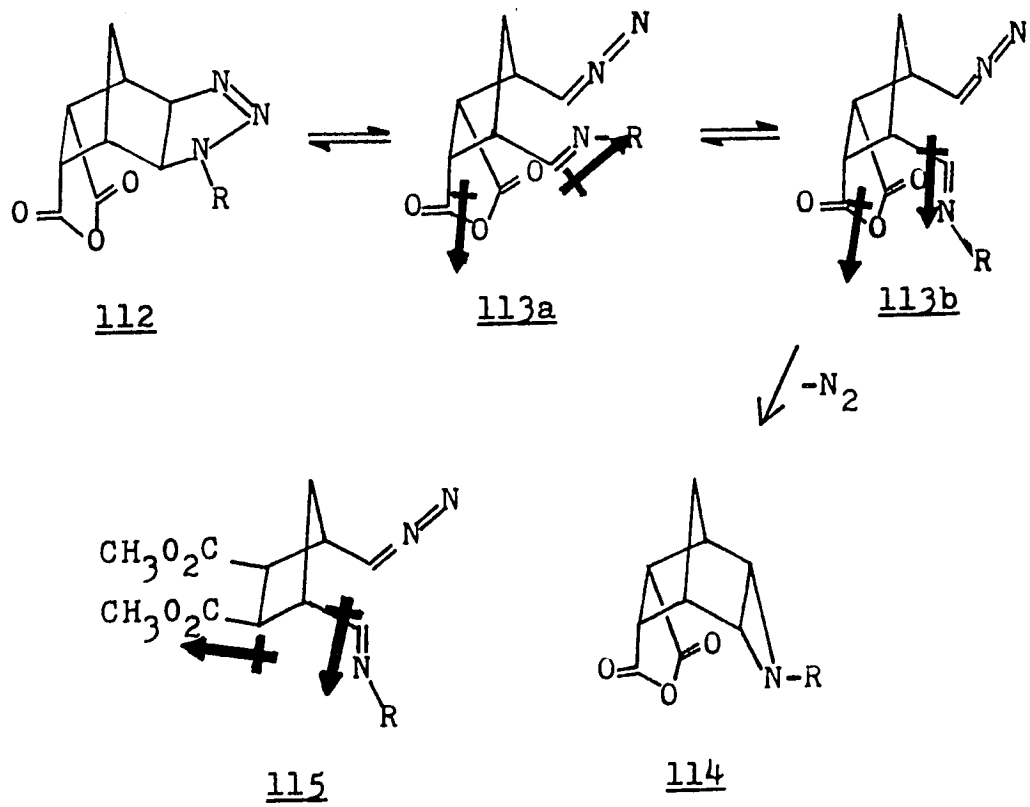

Figure 31. Illustration of Field Effect Producing High Endo to Exo Ratios

field effect is so strong that the endo aziridine prevails. Significant, however, is the fact that steric factors are too much to overcome in the case of the endo dimethyl ester (31b), which upon reaction with benzenesulfonyl azide gave a 1:99 endo to exo aziridine ratio.

In studies concurrent with the synthesis of the endo triazoline, it was felt desirable that more definitive evidence be provided for the carbon-carbon bond cleavage in the proposed mechanism. Pursuant to this end, the scheme in

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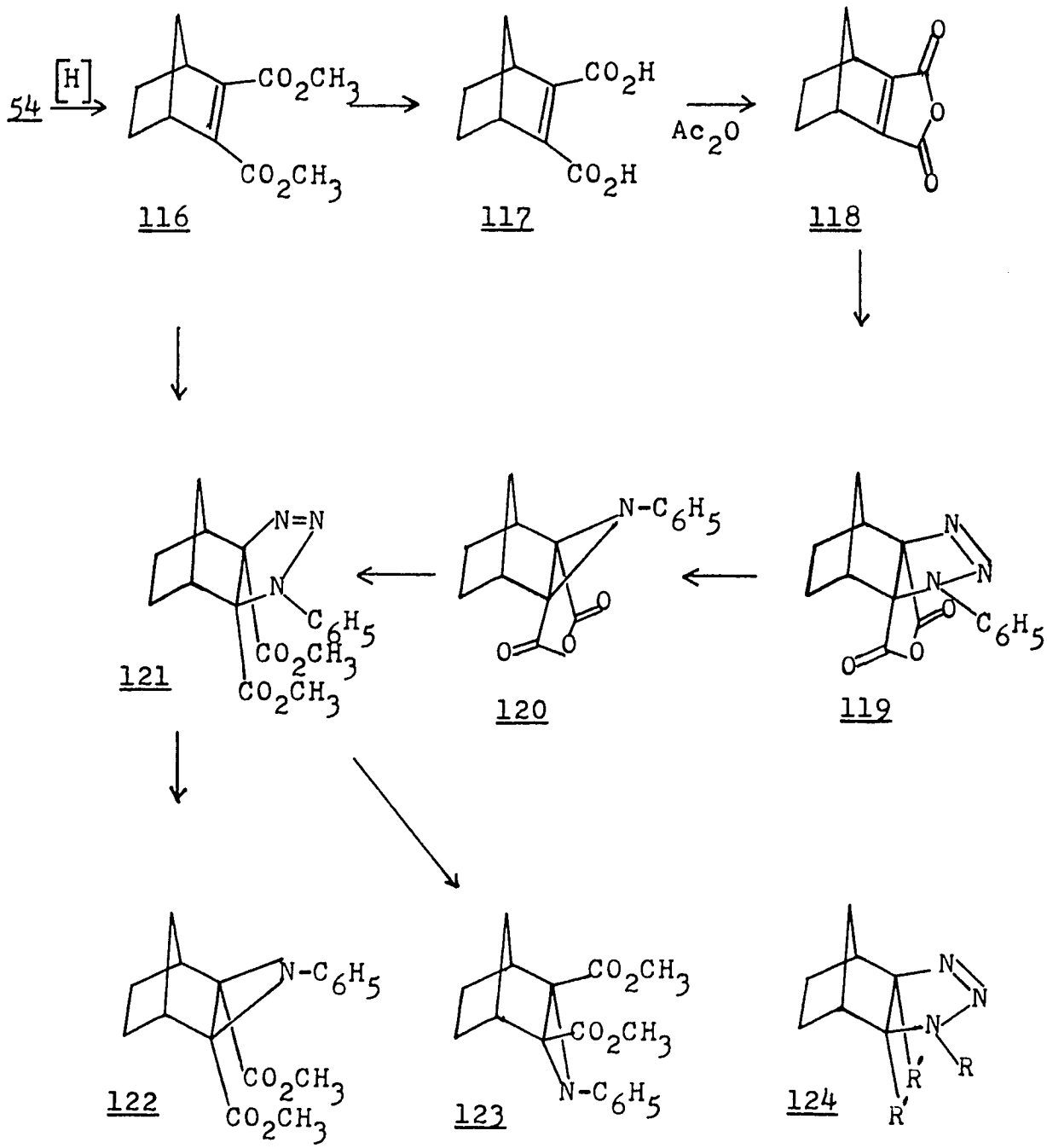

Figure 32. Proposed Scheme for Providing Evidence of Carbon-Carbon Bond Cleavage

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Figure 32 was devised to provide this data and also to provide a study of the chemistry of the 2,6-substituted tricyclic system (124).

The diene ester (54) was prepared by the Diels-Alder reaction of dimethyl acetylenedicarboxylate and cyclopentadiene. Selective hydrogenation of 54 on 5% palladium on carbon at atmospheric pressure gave the dihydro ester (116). Saponification of 116 produced the diacid (117) which was converted to the anhydride (118) by refluxing 117 in excess acetic anhydride. The reaction of anhydride (118) and phenyl azide in ethyl acetate gave a triazoline (119). The photolysis of 119 produced the aziridine anhydride (120) previously reported by Scheiner[22]. The triazoline (119) was then pyrolyzed in decalin at 163° ±2° for two hours. After pyrolysis, g.l.c. analysis showed the only product to be aziridine (120). This aziridine was isolated and had properties identical to the aziridine obtained by photolysis

The dimethyl ester (116) was reacted with phenyl azide in ethyl acetate and from this mixture was isolated the dimethyl triazoline ester (121). This compound had a melting point of 147-149° and showed an ester band in the infrared region at 1740 cm^{-1}. The NMR spectrum ($CDCl_3$) showed five aromatic hydrogens as a multiplet centered at δ7.23, three methoxyl protons as a singlet at δ3.82, three methoxyl protons as a singlet at δ3.50, one bridgehead

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proton as a multiplet centered at δ3.12, one bridgehead proton as a multiplet centered at δ2.88, two protons in a complex pattern between δ2.60 and δ1.6, two hydrogens as a multiplet centered at δ1.58, and two hydrogens as a multiplet centered at δ1.35. The mass spectrum had no molecular ion, but the highest ion observed was M^+ minus nitrogen. This compound also showed two bands in the ultraviolet region at 298 nm and 285 nm with absorbtivities of 7840 and 7130, respectively. The elemental analysis was consistent with $C_{17}H_{19}N_3O_4$, the formula of triazoline (121).

The triazoline ester (121) was photolyzed in acetone for three hours. G.l.c. analysis showed there was only one product and recrystallization of the photolysis residue gave the exo aziridine (122) (m.p. 106-109°). The infrared spectrum showed an ester band at 1725 cm^{-1} and the mass spectrum showed a molecular ion at m/e 301. The NMR spectrum had five aromatic protons in a complex pattern between δ7.30 and δ6.73, six methoxyl protons as a singlet at δ3.77, two bridgehead protons as a multiplet centered at δ2.77, and six protons in a complex pattern between δ2.20 and δ0.5. The analytical data was consistent with $C_{17}H_{19}NO_4$. In order to correlate the dimethyl aziridine ester (122) with the known aziridine (120), the latter aziridine was treated with diazomethane. Analysis by g.l.c. showed that twenty per cent of the anhydride (120) had been converted to 122. Additional treatments with diazomethane

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had very little effect on the remaining anhydride. In order to further esterify this anhydride, boron trifluoride was added to diazomethane solution. Further g.l.c. analysis showed that the anhydride was no longer present, but now a new product was present which was not the dimethyl ester. Chromatography of this mixture gave a small amount of this new compound which showed two carbonyl bands at 1740 cm^{-1} and 1710 cm^{-1}. This compound could not be identified due to lack of material.

The last part of the study involved the pyrolysis of the triazoline ester (121). As shown in Figure 32, it was visualized that there would be two products, the exo aziridine (122) and the endo aziridine (123). The results of the pyrolyses of this compound were not as expected and in fact neither aziridine was produced. The triazoline (121) was dissolved in decalin and pyrolyzed for three hours at 162° ±2°. The decalin was removed in vacuo and the residue was chromatographed on silica gel. From this chromatography was isolated a small amount of yellow oil which showed bands in the infrared at 2120, 1720, 1695, and 1630 cm^{-1}. This material decomposed over a period of two hours as evidenced by disappearance of band at 2120 cm^{-1}. Consideration of the proposed mechanism of triazoline decomposition at once leads to the conclusion that the yellow oil was the diazoimine intermediate (125). The infrared spectrum observed was consistent with such a

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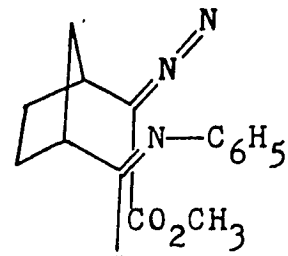
structure.



125

The pyrolysis was repeated and as the temperature of the oil bath was slowly increased, infrared spectra were taken periodically until 165° was reached. None of the infrared spectra showed bands between 2200-2100 cm^{-1}, however, a band at 1650 cm^{-1} appeared at 165°. At this temperature the triazoline began to evolve nitrogen. After three hours at 165°, the decalin was removed and the residue was chromatographed on silica gel. Once again the compound with the infrared band at 2120 cm^{-1} was isolated. This compound was placed in freezer until further spectra could be obtained, however upon further investigation this compound had again decomposed (no band at 2120 cm^{-1}). The pyrolysis was again repeated and the products chromatographed and then the infrared and ultraviolet spectra were taken. The infrared spectrum again showed the band at 2120 cm^{-1} and the UV spectrum showed absorptions at 233, 238, 244, and 251 nm, however the concentration of the solution could only be estimated. It had

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been hoped that the UV spectrum would have demonstrated the presence or absence of a band similar to that observed for a diazoacetic ester ε_{249} of 10,050[67]. Thus once again no definite conclusions could be drawn from the data collected. Further attempts to isolate the oil were abandoned.

Another pyrolysis was carried out as before and the products analyzed by g.l.c. The mixture was found to be 75% of one compound and seven minor products made up the remaining 25%. Mixed injection showed that the exo aziridine (122) was not present in the pyrolysis mixture. The pyrosolate was chromatographed on alumina. Only about 10% of the weight of the residue added to the column was recovered upon elution, and this did not correspond to the major component of the reaction product. The unrecovered material could only be removed by continuous extraction and g.l.c. analysis showed that the major product was no longer present. The major reaction product was also found to decompose upon t.l.c. on silica gel or aluminum oxide. The pyrolysis residue was subjected to preparative g.l.c. and the major component was isolated as an honogeneous yellow oil. The infrared spectrum showed an ester band at 1725 cm^{-1} and a double bond at 1660 cm^{-1}. The mass spectrum of this compound (126) is shown in Table 4 and is compared to the mass spectrum of triazoline (121) and aziridine (122). From this data, it is now possible to postulate a structure for the major product. In Table 4, it may be seen that

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Table 4. Mass Spectra of 121, 122 and 126

MASS	301	287	286	273	272	270	258	244	243	242	241	240
121	10		1	17	62		24	2	19	100	13	8
122	28			31	100	10	15		2	14	1	1
126	13	6	27	2	1	6	1	6	19	100	15	

MASS	215	214	210	183	182	180	139	130	119	118	107	105
121	13	61	9	10	29	7	6	10	11	7	6	5
122	7	38	2	2	9	1		2	1	1		1
126		1	6	5	14	4	27	14	1	2	30	6

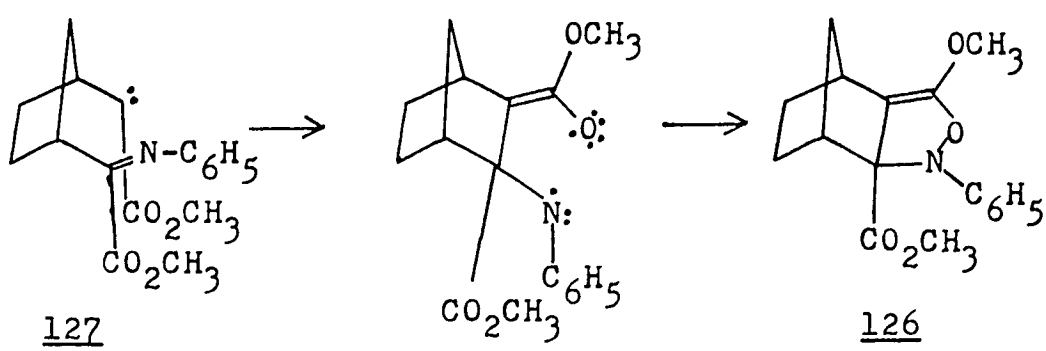
MASS	104	93	91	80	79	78	77	76	67	65	59	57
121	18	6	10	4	24	8	56	3	5	4	12	6
122	3		2	1	10	6	23	2	2	3	6	
126	23	6	6	9	41	17	81	6	6	6	15	3

MASS	55	53	52	51	50	43	41	39	28	18	17	15
121	6	3	2	13	2	6	8	6	13	47	16	8
122	1	3	3	10	2		3	4	1			
126	8	7	6	26	6	6	9	9	4			

SAMPLE CONDITIONS:

	PRESSURE	PROBE TEMP.	ANALYZER TEMP.
121	6×10^{-7}	80°	125°
122	1.2×10^{-6}	70°	130°
126	1×10^{-6}	90°	125°

m/e 301 is the first observed ion and corresponds to the loss of nitrogen from the parent compound (121). The next major ion observed in the various spectra of the major compound (126) is m/e 286. This ion corresponds to loss of a methyl group from m/e 301. The absence of this ion in the spectra of 121 and 122 indicates that these compounds do not have labile methyl groups. It is also of significance that 121 and 126 both show their base ions at m/e 242 (see page 124). Consideration of these ions leads to the postulation of isoxazoline (126) as the major product in question. This product could have



127 128 126

Figure 33. Formation of Isoxazoline (126)

arisen from the diazoimine intermediate (125) which decomposed to a triplet carbene (127). The carbene would add to form 128. From 128, the predicted product would be 126, since this pathway allows a choice between formation of a three membered ring and a five membered ring. The formation of the three membered ring would not be favored since

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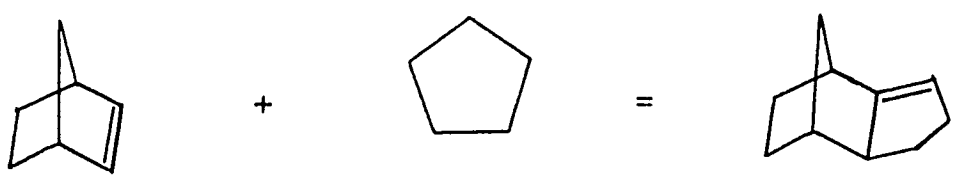
there is a large energy difference in ring strain of the two possible products. This energy difference can be estimated as 17.7 kcal/m from Figures 34 and 24. The data presented thus far are certainly consistent with 126. This compound being an enol ether would probably be unstable. The infrared spectrum would show an ester band and a strong double bond band.



22.8 kcal/m + 6.5 kcal/m = 29.3 kcal/m

127

Figure 34. Ring Strain Energy for a Tricyclic-{5,2,1,$0^{2,6}$}-decene

A discussion of the mass spectral fragmentation pattern of this compound also supports the above structure (126). The m/e 286 corresponding to loss of a labile methyl from the molecular ion is readily explained by 129. This loss is not observed in 121 and 122 because the methyl groups of the carbomethoxy groups are not readily lost and further because the bicycloheptane portion of the molecule does not easily rearrange to lose a methyl radical. The base peak of 126 was observed at m/e of 242 and undoubtedly

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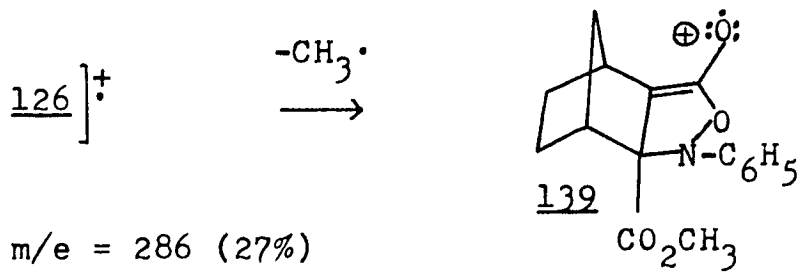

Figure 35. Mass Fragmentation of 126: m/e 286

represents loss of a carbomethoxy radical to form the exceeding stable ion (130). The abundance of this ion is due to the great stability of the aromatic ring created from loss of the ester group. This ion is also the base peak of

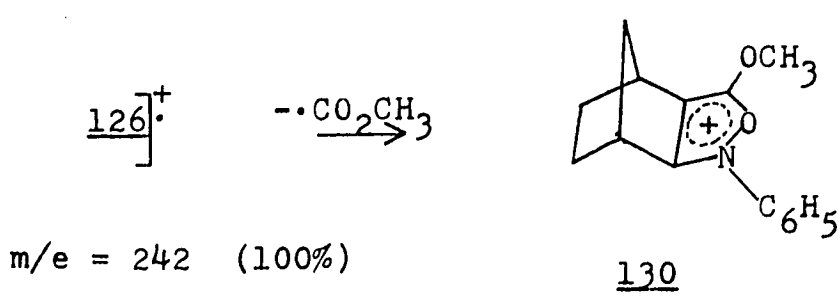

Figure 36. Mass Fragmentation of 126: m/e 242

the triazoline (121). The appearance of an ion at this m/e value in the spectrum of aziridine (122) is possibly due to a different ion (132), since the formation of 130 from the molecular ion of 122 would involve the breaking of a strong carbon-nitrogen bond and rapid rearrangement to the isoxa-

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zoline (126). Ester alkoxy radical cleavage similar to that in Figure 37 (i.e. 131) has been reported for pyrrole carboxylic esters[67].

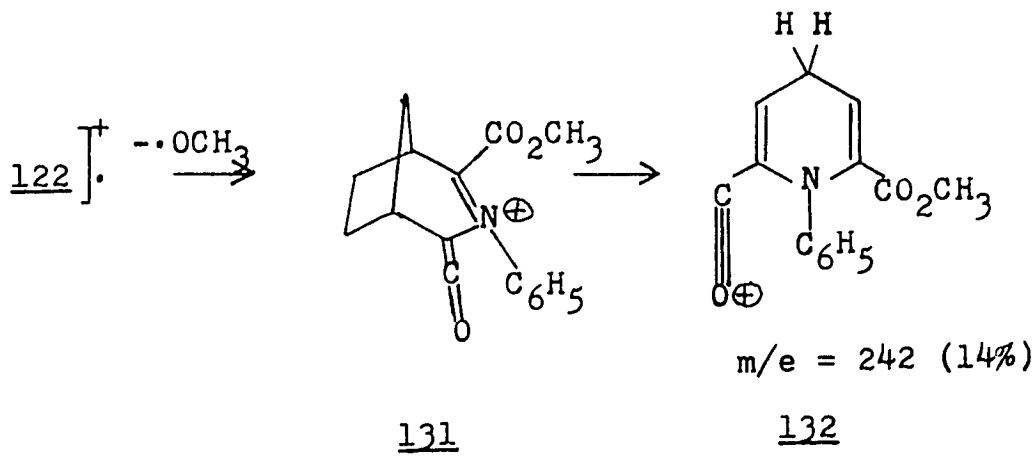

Figure 37. Mass Fragmentation of 122: m/e 242

The base peak of the aziridine (122) is probably due to ion 134

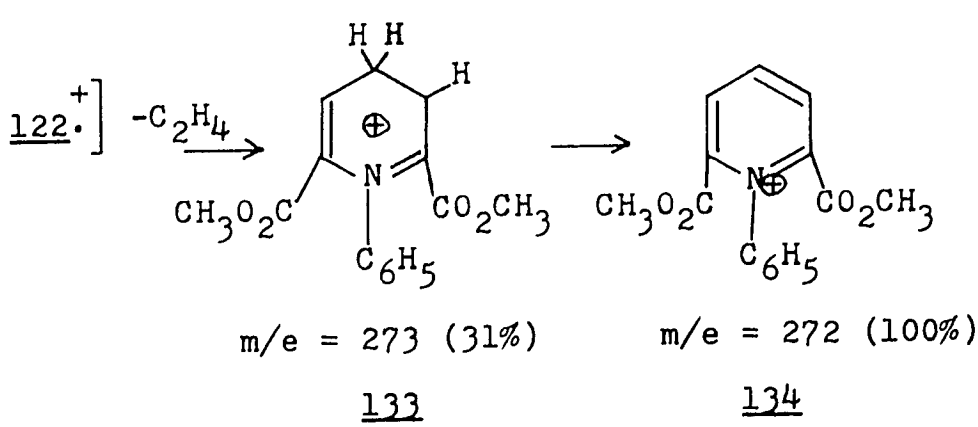

Figure 38. Mass Spectrum of 122: m/e 272

Perhaps the most significant feature in the mass

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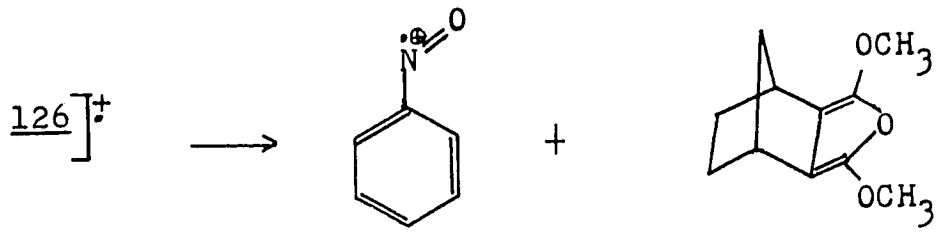
spectrum of the isoxazoline (126) is the appearance of the radical ion of nitrosobenzene (135) at m/e 107. This indeed



m/e = 107 (30%)

135 136

Figure 39. Mass Spectrum of 126: m/e 107

indicates that the nitrogen and oxygen are bonded in the parent compound. Predictably no such ion appears in the spectrum of the aziridine, and further this ion appears only to a small extent in the triazoline spectrum since m/e 107 must be derived from the molecular ion of the parent isoxazoline.

Other attempts to again isolate this compound by preparative g.l.c. gave unuseful results and undesirable side effects. The compound as it passed through the g.l.c. was vaporized and released into the air. Breathing of the vapor caused headaches, dizziness and nervousness in this individual and thus this method of collection was abandoned.

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Further efforts to elucidate the structure of 126 by use of a gas chromatograph-mass spectrometer interface (GC-MS) gave surprising and puzzling results. In each spectra the highest observable ion was at m/e 299. This corresponds to loss of molecular nitrogen from the triazoline (121) and further loss of two hydrogen atoms. Since under ordinary g.l.c. conditions, the highest observed ion was at m/e 301, the ion at m/e 299 must have arisen from dehydrogenation on the gas chromatograph before entering the mass spectrometer. It is worth noting that this phenomenon was observed on both glass and metal columns, which perhaps indicates that this process could have taken place within the injection port. It was also found that direct injection of triazoline (126) on the GC-MS gave surprising results showing m/e values of 297, 299, and 301. From all of the above results, it became evident that this method of analysis was unreliable for this reaction.

In an attempt to produce additional evidence for the elusive isoxazoline (126), a second mode of pyrolysis was tried . The solid triazoline was placed into the lower bulb of a distillation tube and pyrolyzed under vacuum at various temperatures for variable amounts of time. The resulting pyrolysis mixture had the distinctive foul odor of the compound previously isolated and upon sitting at room temperature, starting triazoline crystallized from

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this oil. Addition of carbon tetrachloride and removal of solids gave samples which were submitted for NMR analysis. The results of the NMR spectra of the different runs are shown in Table 5. The methoxyl protons of the triazoline (121) were used as reference to follow the pyrolysis. As can be readily seen, the methoxyl protons at δ3.84 began to immediately decrease while a new absorption appeared at δ3.69 and began to increase. The methoxy group at δ3.52 remained unchanged. These results can be rationalized in terms of the increasing production of the isoxazoline (126). The new methoxyl group is that one attached to the double bond in 126. The mass spectrum of run D in Table 5 was consistent with that previously observed for 126 (see Table 4) and is shown in Table 6. The abundance of m/e 272 is probably due to the presence of the starting triazoline. The infrared spectrum of run D also contained the ester band at 1720 and 1650 cm^{-1}. With all of the above evidence for 126, it should be pointed out that an unexplained absorption in the NMR spectra of run B, C and D also appeared at δ5.75 (4.5 i.u. in run D).

Further attempts to purify this mixture by vacuum distillation of the pyrosolate gave an oil which was quite different from the mother liquor in the NMR and is shown as run E. At this point, this pyrolysis study was abandoned, principally because of the purification difficulties encountered and also because of the adverse effects on the

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personal health of this researcher. It is thought very important to emphasize that further studies of this pyrolysis must be done with adequate ventilation and due caution, since the physiological effects of the products are not known.

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Table 5. Pyrolyses of Triazoline 121 in the Absence of Solvent

Pyrolysis Conditions				NMR RESULTS		
RUN NUMBER	TEMP.	TIME	PRESS	CHEMICAL SHIFT	INTEGRATION	H'S
START	0	0	0	3.84 3.52		3.0 3.0
A	80°	10 min.	0.15 mm	3.84 3.69 3.52	16 4 20	2.4 0.6 3.0
B	89-102°	60 min.	0.15 mm	3.84 3.69 3.52	10 11 21	1.5 1.5 3.0
C	102°	95 min.	0.15 mm	3.84 3.69 3.52	10 15 21	1 2 3
D	114°	330 min.	2.1-1.4 mm	3.84 3.69 3.52	13.0 21.0 21.0	2.0 3.0 3.0
E	124° 177°	95 min.	0.0025 mm	3.84 3.75 3.69 3.55 3.52	10* 30* 15* 5* 10*	2 6 3 1 2

* These values were estimated

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Table 6. Mass Spectrum of the Product from Run D in Table 5

MASS	301	286	273	272	270	242	214	182	139	107	104
Relative Abundance	14%	28%	10%	30%	6%	100%	11%	12%	22%	20%	10%

Sample Conditions:

Pressure	Probe Temp.	Analyzer Temp.
1×10^{-6}	70^{o}	125^{o}

CHAPTER V

CONCLUSIONS

The endo faces of norbornenes and norbornadienes are highly hindered as exemplified by the results reported here.

A synthesis of an endo triazoline (89) was devised involving the endo amine (80). This amine was coupled with an aryl diazonium chloride to give a variety of endo triazolines. The diazoamine (88) was cyclized with a base and silver nitrate to the endo triazoline (89). The reagent used to effectuate the cyclization perhaps has utility in other similar closure reactions.

Pyrolysis of 89 gave imine (94), endo aziridine (92) and exo aziridine (91). The formation of the exo aziridine (91) from the endo triazoline and the formation of the endo aziridine (92) from exo triazoline (90) provide excellent evidence for the existence of a common intermediate, namely the diazoimine previously proposed by Zalkow and others (Figure 29).

A new mechanistic pathway has been formulated, utilizing the diazoimine formation, to explain the varied results encountered in triazoline pyrolyses. The new mechanism actually consists of three independent paths, which a given triazoline may follow depending upon its substitution and the conditions of the pyrolysis. First a concerted

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disrotatory ring opening to form a diazoimine has been proposed to explain particularly those cases in which the sole products of pyrolysis are aziridines. The diazo part of this intermediate upon formation, subsequently decomposes to a triplet carbene which can then selectively add to produce only aziridines. In those cases where pyrolysis produces only imine, a concerted imine formation is proposed. In those cases producing both aziridine and imine, both concerted paths are in competition. In pyrolyses where more polar products, i.e. amines and rearrangement products, are observed along with aziridines and imine, a third ionic path begins to compete. This path involves the formation of a diazonium betaine which decomposes to a dipolar ion, from which are derived various products. These mechanisms are consistent with the solvent and substituent effects observed for these pyrolyses.

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CHAPTER VI

RECOMMENDATIONS

The conditions of the hydroboration of the oxime esters, 78 and 79, should be maximized in order to increase the yield of the endo amine (80). Perhaps the yield could be improved by variation of the ester moiety on the chloro oxime.

Certainly the most vital experiments should be the attempted preparation of other endo triazolines (47). Variation of the aryl diazonium salt in the coupling reaction with the amine (80) should produce other endo triazolines. The pyrolyses of other endo triazolines must be studied and the results correlated with the mechanistic proposals set forth in this work (see Figure 29).

The mass spectra of various endo aziridines should be studied to further substantiate the proposal of this work that the fragmentation pattern of these aziridines could be a diagnostic tool in the identification of these compounds.

The preparation of many endo aziridines by photolysis of endo triazolines should be quite valuable particularly in light of the fact that these compounds probably easily polymerize (from the results of this work, see page 100) and thus could be of some industrial utility.

Further experiments should be devised to isolate and

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conclusively identify the proposed diazoimine formed in the pyrolyses of these triazolines. Triazoline (121) would seem to be a good candidate for this study, particularly in light of the results presented here (see pages 116-133) and also because α-diazoesters are particularly stable, thus making isolation more likely. Possibly ESR studies of the pyrolysis of 121 could demonstrate the presence of a triplet carbene derived from the diazoimine (125).

Lastly the proposed compound (126) must be better characterized. It must again be pointed out, however, that any work with this compound must be in closed systems, due to the physiological effects previously noted (see page 128).

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APPENDIX

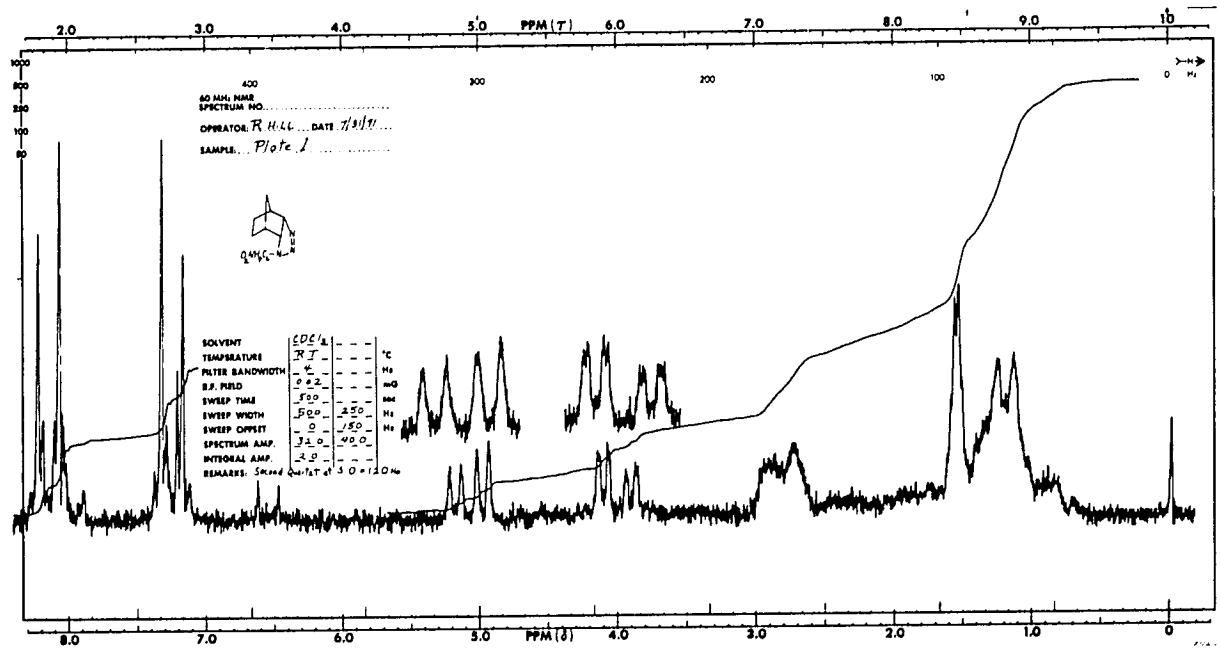

Plate 1. NMR Spectrum of endo Triazoline (89)

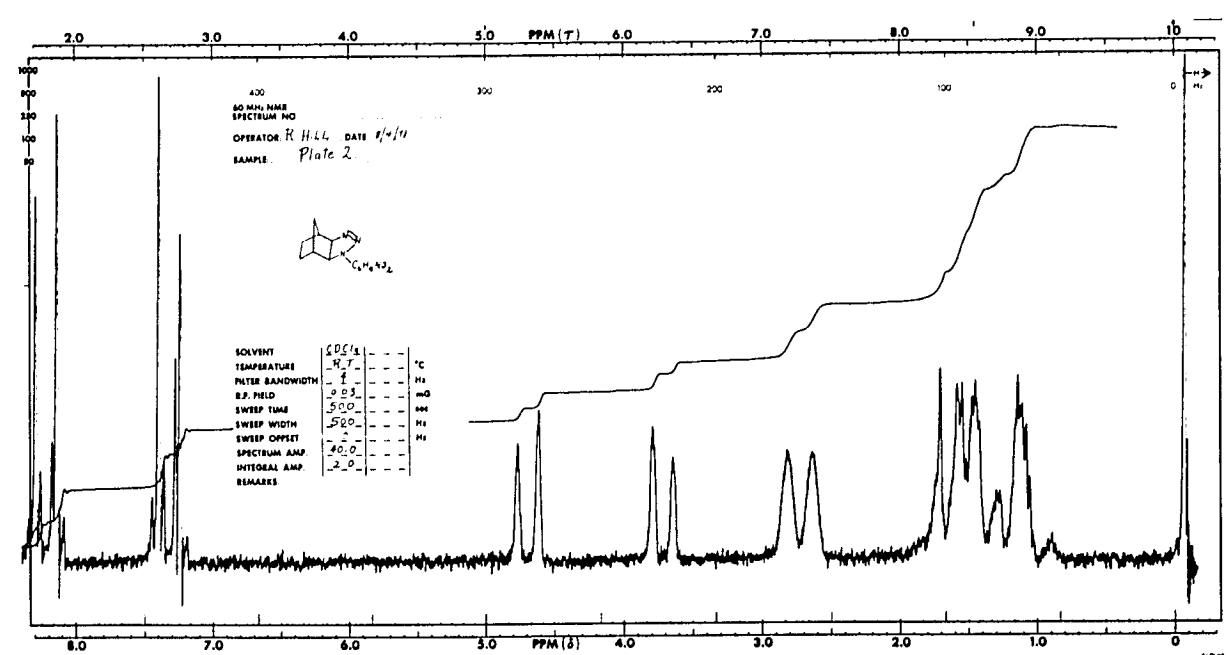

Plate 2. NMR Spectrum of exo Triazoline (90)

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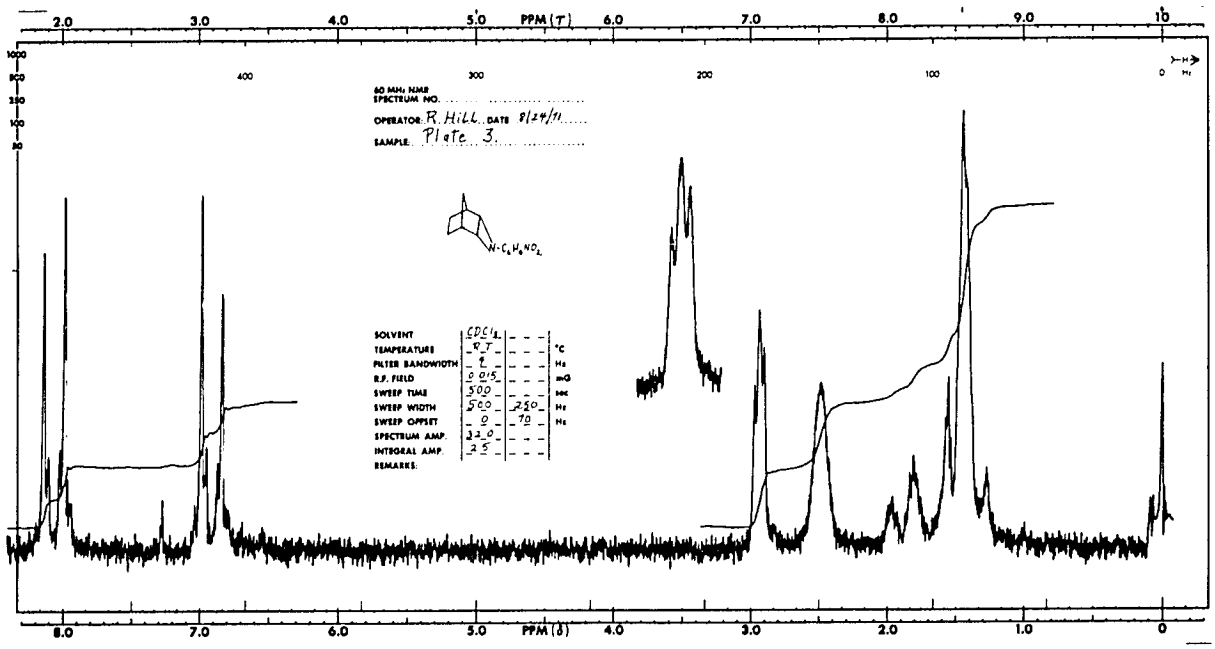

Plate 3. NMR Spectrum of endo Aziridine (92)

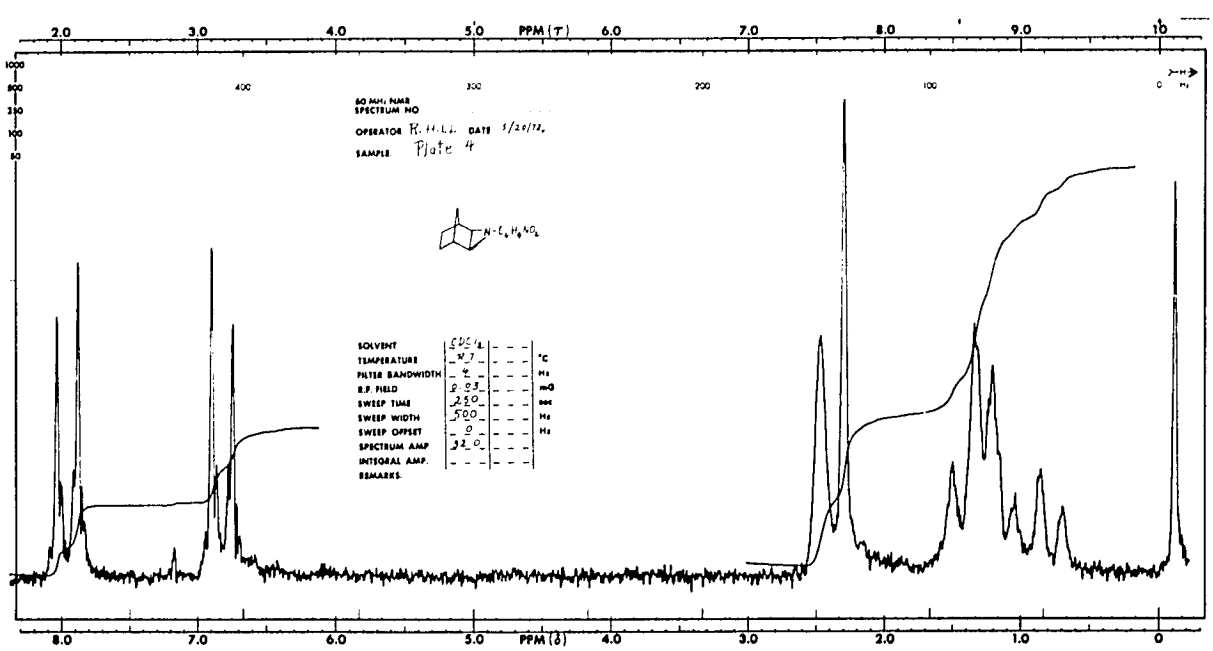

Plate 4. NMR Spectrum of exo Aziridine (91)

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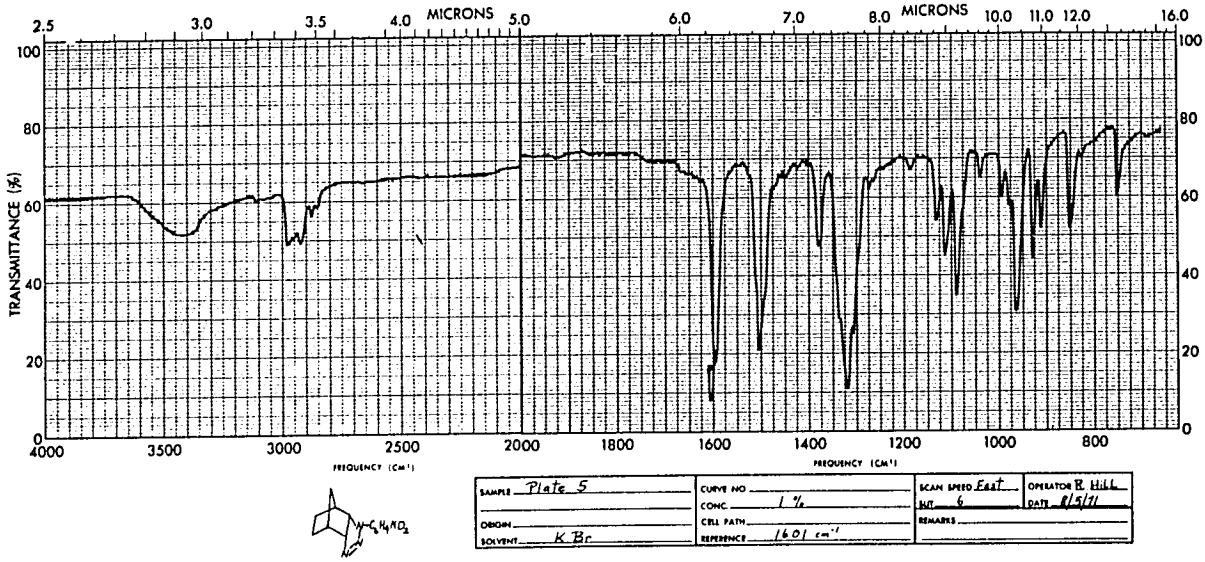

Plate 5. Infrared Spectrum of endo Triazoline (89)

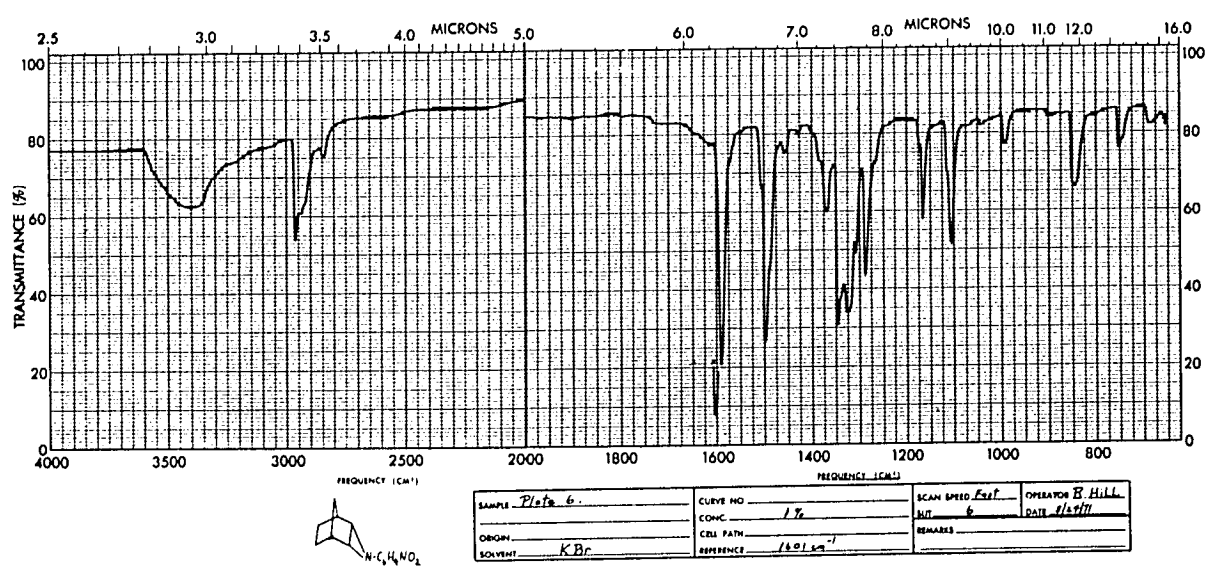

Plate 6. Infrared Spectrum of endo Aziridine (92)

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VITA

Robert H. Hill, Jr. was born in Indianapolis, Ind., on August 5, 1945. His parents moved to Savannah, Ga. when he was about two months old. He grew up in this city and graduated from Savannah High School in May, 1962. He attended Armstrong Junior College for two years and transferred to Georgia State College in Atlanta, Ga. in 1964. Two years later he received the Bachelor of Science degree with a major in chemistry. In September, 1966, Bob began his graduate studies at the Georgia Institute of Technology in the School of Chemistry.

During his studies at Georgia Tech, Bob met Carol Scruggs. The couple was married on July 12, 1969 and in March of 1971 they became the proud parents of a daughter, Tracy Michelle.

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