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NAME OF AUTHOR/*NOM DE L'AUTEUR* Hervé Richard

TITLE OF THESIS/*TITRE DE LA THÈSE* Chemicals Transformations of N-Nitramines and C-Nitroso Compounds.

UNIVERSITY/*UNIVERSITÉ* Simon Fraser

DEGREE FOR WHICH THESIS WAS PRESENTED/*GRADE POUR LEQUEL CETTE THÈSE FUT PRÉSENTÉE* Ph. D.

YEAR THIS DEGREE CONFERRED/*ANNÉE D'OBTENTION DE CE GRADE* 1979

NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* Dr. Y.L. Chow

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CHEMICAL TRANSFORMATIONS OF N-NITRAMINES AND C-NITROSO COMPOUNDS

by

Hervé Richard

Chemical Engineer ENSC Mulhouse (Fr.),1971

AEA/DEA Organic Chemistry, Mulhouse, 1972

A THESIS SUBMITTED IN PARTIAL FULFILLMENT

OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

in the Department

of

Chemistry

SIMON FRASER UNIVERSITY

July 1979

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APPROVAL

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Degree: Doctor of Philosophy

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ABSTRACT

CHEMICAL TRANSFORMATIONS OF N-NITRAMINES AND C-NITROSO COMPOUNDS

In order to investigate the ground state and excited states of nitro and nitroso derivatives, 1) nitroamines were photolyzed under various conditions and 2) alkenyl nitroso compounds were synthesized and their decompositions studied. The products were isolated by chromatographic methods and their structures determined by spectroscopy and chemical reactions.

1) Photolysis of nitramines in neutral solvent generated nitrogen dioxide and aminyl radicals which abstracted hydrogen atoms but did not add to carbon-carbon double bonds. In dilute acidic solution, the aminyl radicals were protonated to the corresponding aminium radicals that preferentially underwent addition to π-bonds rather than hydrogen atom abstraction. Thus complex mixtures of addition products were obtained when nitramines were photolyzed in the presence of cyclohexene under nitrogen. The plethora of products is believed to arise from the complex behavior of nitrogen dioxide in solution, for example, i) nitrogen dioxide may react as an O- or N-radical, ii) nitrogen dioxide

exists in equilibrium with nitrogen tetroxide and iii) both oxides can react as oxidizing or radical trapping agents. Aminyl and aminium radicals were not trapped by carbon monoxide. In the presence of oxygen, the oxidative addition of N-nitro or N-nitrosodimethylamine to cyclohexene, 1-hexene, trans-3-hexene and various unconjugated cyclopolyenes gave 2-amino nitrate esters. Depending upon their structure, these 2-amino nitrates could undergo i) solvolysis under basic conditions resulting in the formation of 2-aminoalcohols and 2-aminoketones ii) C_1-C_2 bond cleavage assisted by the lone-pair electrons of the nitrogen giving rise to the corresponding carbonyl compounds and iii) reduction to the corresponding aminoalcohols in good yields. Dimethylaminium radical exclusively added to a trans-double bond of cis,trans,trans-1,5,9-cyclododecatriene. With cis,trans-1,5-cyclodecadiene, good yields of bicyclic amino nitrate ester were obtained; a 1,5-transannular radical cyclization mechanism is believed to operate.

2) Nitrosyl chloride reacted with 1,5-cyclooctadiene and trans,trans,trans-1,5,9-cyclododecatriene in methylene chloride by the cis-addition to give chloronitroso alkenes with cis and threo (trans) configuration, respectively. These enantiomorphic C-nitroso compounds were isolated as a single compound for the former, and a mixture for the latter, of dl and/or meso dimers, the presence of which was readily monitored by ^{13}Cnmr spectros-

copy. The former can assume a conformation to place the π-bonds of the nitroso and olefinic groups in interacting vicinity and undergo an acid catalyzed intramolecular electrophilic cyclization to give bicyclic hydroxylamines which are readily air oxidized to the corresponding nitroxide radicals. Rearrangement in acetic anhydride-methylene chloride afforded good yields of the stable bicyclic hydroxylamine acetates which served as precursors to generate the corresponding nitroxides under mild conditions. Nitrosyl chloride exclusively added to the trans-double bond of cis,trans-1,5-cyclodecadiene without regiospecificity but was believed to involve stereospecific cis-addition; this chloro-nitroso alkene also underwent acid catalyzed transannular reaction to give similar hydroxylamines that were not isolated in pure state.

"On ne voit bien qu'avec le cœur.

L'essentiel est invisible pour les yeux."

"Le Petit Prince"

Antoine de Saint-Exupéry.

To my late mother

To my father

ACKNOWLEDGEMENTS

The author wishes to express his sincere gratitude to his supervisor, Professor Y.L. Chow, for his guidance, inspiration and continued interest thoughout this work.

He also wishes to acknowledge the assistance of Dr. K.S. Pillay for numerous helpful discussions.

He owes thanks to faculty members and to fellow graduate students, especially from Dr. Chow's group for their assistance.

At a time when everything was falling apart, I am indebted to you, Leon. To Judy and John, special thanks for the moral comfort you gave me.

The author also wishes to thank the technical and support staff, Edna Cheah, Leslie Vincent, Greg Owen, Falko Tilgner, Miki Yang and especially Arthur Brooke for all the extra time.

Financial assistance from the Department of Chemistry, Simon Fraser University and the National Research Council of Canada is gratefully acknowledged.

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CHAPTER I

INTRODUCTION

I-1. The Chemistry of Secondary N-Nitramines

I-1-1. Physical properties

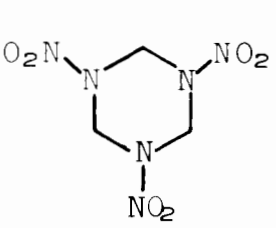
Dialkyl nitramines (R_2NNO_2) are neutral and generally colourless, low melting solids or liquids (1,4). Nitramines are prepared by two main methods: (a) catalyzed nitration (5) (Equation I-1) and, (b) nitration with cyanohydrin nitrates under basic conditions (6) (Equation I-2). Alternatively, dialkyl nitrosamines can be cleanly oxidized by peroxytrifluoroacetic acid (7) to the corresponding nitramines (Equation I-3).

[I-1] $$[R_2\overset{+}{N}H_2]^-NO_3 \xrightarrow[ZnCl_2]{Ac_2O} R_2N\text{-}NO_2 + CH_3COOH$$

[I-2] excess $R_2NH + (CH_3)_2C(ONO_2)(CN) \longrightarrow R_2N\text{-}NO_2 + CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_3 + HCN$

[I-3] $R_2N\text{-}NO \xrightarrow{H_2O_2 + CF_3COOH} R_2N\text{-}NO_2$

Although the N-NO_2 group is stable, explosive properties have been associated with many N-nitro compounds such as cyclonite or RDX (1,3,5-trinitro-1,3,5-triazacyclohexane, I-1), HMX (1,3,5,7-tetranitro-1,3,5,7-tetraazacyclooctane, I-2), nitroguanidine (I-3) and tetryl (2,4,6-trinitrophenyl nitramine, I-4).



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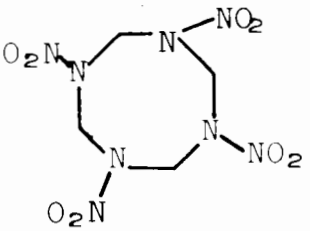

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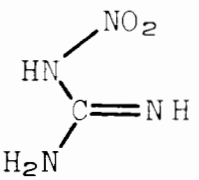

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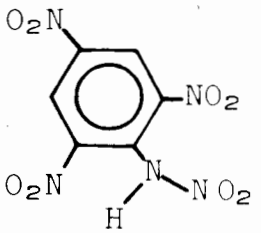


I-4

The structures of dimethylnitramine (8) and other nitramines (2) have been determined crystallographically. The nitramine portion of the molecule ($C_2N_2O_2$ atoms) was found to be planar with a relatively short N-N bond length (ca 1.3A) (8), indicating considerable resonance contribution from the $R_2\overset{+}{N}=N\bar{O}_2$ structure. They have ultraviolet spectra similar to those of nitrosamines except for the absence of a weak band in the 350 nm region in protic solvents (9,10). However a weak band near

300nm (ε ca 40) probably due to the $n \rightarrow \pi^*$ transition is observed in n-hexane (10). Recently, Harris (11) attributed the intense absorption band near 240nm (ε ca 6000) to the $\pi \rightarrow \pi^*$ transition, and also predicted existence of the slightly lower symmetry forbidden $n \rightarrow \pi^*$ transition under the strong $\pi \rightarrow \pi^*$ excitation. Application of circular dichroism to the determination of this hidden band showed the $n \rightarrow \pi^*$ transition to be near 270nm in the CD spectrum (12). The infrared spectra of dialkyl nitramines exhibit strong asymmetric and symmetric stretching bands of the nitro group at 1540-1505 cm^{-1} and at 1330-1260 cm^{-1}, respectively (13), along with other prominent bands in the regions 1130-1100 and 770-755 cm^{-1}.

I-1-2. Photochemical Reactions of N-Nitramines

The photochemistry of nitramines has been sporadically investigated in the past (10,14-18). The photochemical rearrangement of N-methyl-N-nitro-1-naphthylamine with $\lambda > 360$nm has been shown to give the o- and p-nitro derivatives by a non-radical mechanism (14). In contrast with the inertness of nitrosamines under photolytic conditions in neutral solvents (19), dialkyl nitramines undergo photodecomposition in either trifluoroacetic acid (15), n-hexane, 95% ethanol, acetonitrile (10) or in the solid state (16) to give the corresponding nitrosamines as the only detectable product. However, Lavanish (15) has reported that the irradiation of dibenzylnitramine I-5 in pentane (Scheme I-1) gave, in addition to dibenzylnitrosamine I-6,

$$Bz_2N\text{-}NO_2 \xrightarrow[\text{pentane}]{h\nu,\ N_2} Bz_2N\text{-}NO + C_6H_5CH{=}NBz + Bz_2\overset{+}{N}H_2\ \overset{-}{N}O_3$$

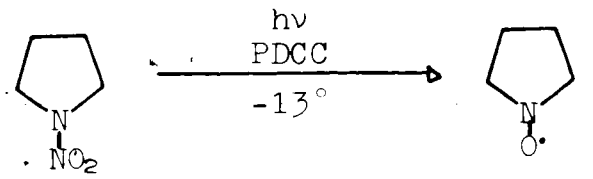
I-5 I-6 I-7 I-8

Scheme I-1

N-benzylidene benzylamine I-7 and dibenzylammonium nitrate I-8. Irradiation of I-5 in ethanol increased the yield of I-8 while irradiation in trifluoroacetic acid gave only a trace of I-8. Thermolysis of dimethylnitramine (20), diethylnitramine and N-nitropiperidine (21) in the gas phase are reported to give the corresponding nitrosamine. These reactions were proposed to proceed via fission of the N-N bond (10,15,20,21).

Bulusu et al (16) photolyzed an equimolar mixture of doubly ^{15}N labeled and unlabeled dimethylnitramine in the solid state from which an N-O bond cleavage was proposed as the primary process. It gave dimethylnitrosamine with statistically distributed ^{15}N, however no isotope crossover was observed for the unreacted starting nitramine; in light of this evidence N-N bond cleavage was rejected in the solid state.

Different results were obtained by Bodnar (17), Moon and Swanson (18) when they irradiated nine cyclic nitramines, such as N-nitropyrrolidine I-9 in 1,2-propanediol cyclic carbonate (PDCC) and in the solid state. They observed esr signals of the corresponding nitroxides, such as I-10. The absence of experi-



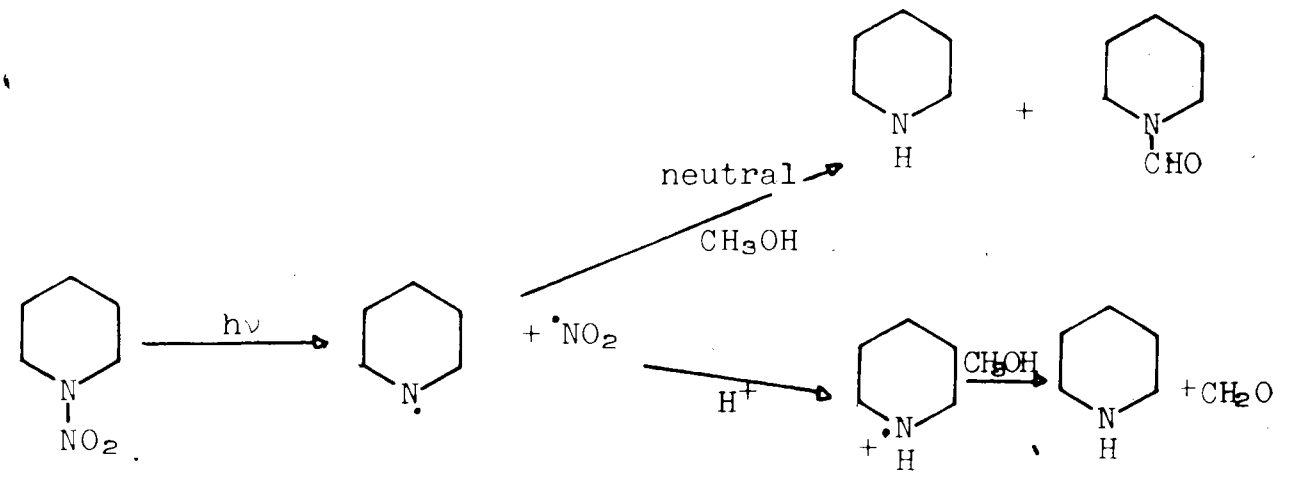
a_N 14.7 G

a_H 19.7 G

I-9 I-10

mental detail makes it difficult to evaluate the relationship of this result with previous work. It is suspected that an amine radical is oxidized by air to the stable nitroxide (22).

Finally, Chow et al (23,24) proposed aminyl (I-11) and aminium radical (I-12) intermediates (Scheme I-2), to explain the observed products during the photolysis of N-nitropiperidine I-13 in neutral or acidified methanol solutions, respectively. The quantum yield for the disappearance of I-13 in neutral methanol was measured to be 4.8 while in 0.1N-2N H_2SO_4 it was 7.0-7.8 (23). These results indicated that the photolysis occurred by short chain processes in neutral or acidic conditions.



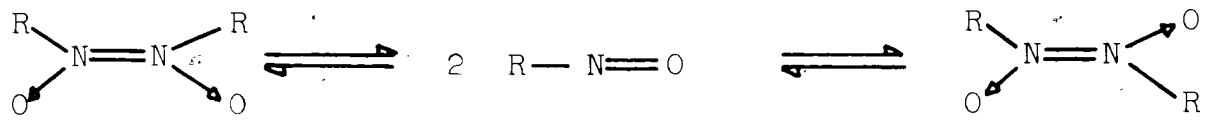
I-13 I-11 I-12

Scheme I-2

I-2. The Chemistry of Aliphatic C-nitroso compounds

I-2-1. Physical Properties

Many aliphatic C-nitroso compounds exist in the solid state as colourless dimers I-14, and when dissolved in various solvents, dissociate to different extents to a blue or green monomer I-15 (25-29). Cis (I-14a) and the generally more stable trans (I-14b) forms of the dimeric nitroso alkanes have been isolated (25),



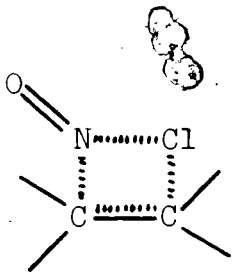
I-14a I-15 I-14b

showing that there exists appreciable double bond character in the N-N bond. Although they are all symmetrical dimers, a mixed dimer of nitroso heptane and 4-nitroso-1-octanol has been reported as an oil (30). The aliphatic C-nitroso compounds show a low intensity $n \rightarrow \pi^*$ band in the 630-790nm (ϵ ca 1-60) region. When the dimer is formed, this $n \rightarrow \pi^*$ band is replaced by a new $\pi \rightarrow \pi^*$ transition near 295nm (ϵ ca 9000) for the trans dimer I-14b and at shorter wavelenghts for the cis dimer I-14a (31). The infrared spectra of monomeric nitroso compounds showed the N-O stretching frequency in the 1539-1621 cm^{-1} region. This N-O stretching is seen at 1176-1299 cm^{-1} for the trans isomer and is replaced by two bands at higher frequencies (1323-1344 and 1330-1420 cm^{-1})

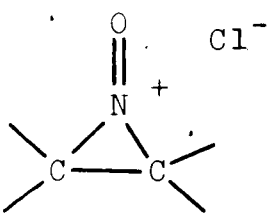
for the cis isomer (32).

I-2-2. Preparations

Aliphatic C-nitroso compounds can be prepared by numerous methods (28-29), but the most common preparation is the addition of nitrosyl chloride, nitrosyl bromide or nitrosyl formate (28, 33) to olefins. Both solvent effects and dependence on olefin structure have been observed in these reactions. Thus, cyclohexene reacts with nitrosyl chloride in liquid sulfur dioxide to give the anti-dimer of the trans-chloronitroso compound (60-80%) (34-36), but in chloroform, methylene chloride and trichloroethylene, the anti-dimer of the cis-chloronitroso compound is obtained (34). With rigid bicyclic systems, nitrosyl chloride has been shown to add in the cis fashion; eg, addition of nitrosyl chloride to norbornadiene gives the dimer of the cis-exo adduct (65%) without any observable rearrangement of the bicyclic skeleton (37). For strained olefins, a four-centered cyclic transition state (I-16) has been postulated to give the cis configuration (37,38). While a three membered nitrosonium intermediate (I-17) (37) has been postulated to give either (or both) cis and trans adducts. Nitrosyl chloride preferential-



I-16

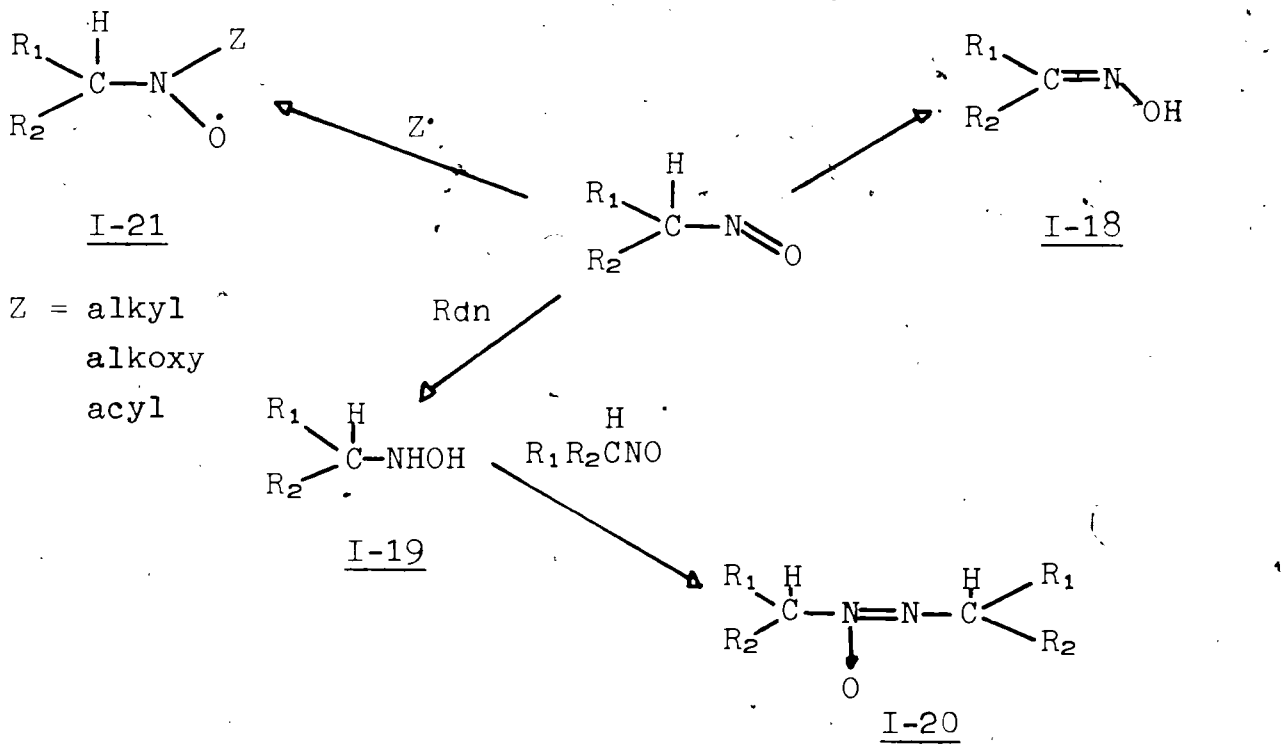


I-17

ly attacks a trans double bond rather than the cis double bond of cis,trans,trans-1,5,9-cyclododecatriene (38).

I-2-3. Reactions

Primary and secondary nitrosoalkanes which have an α-hydrogen may tautomerize to the corresponding oxime I-18. This irreversible tautomerization, which may occur with melting or in solution, competes with the reversible dimerization process and is accelerated by hydroxylic solvents, strong acids and bases, and nitric oxide (26). The rearrangement of secondary nitroso compounds catalyzed by hydrochloric acid has been shown to be a first order reaction depending only on dimer concentration (39). This strongly suggests that the rate determining step is the dissociation into monomer .



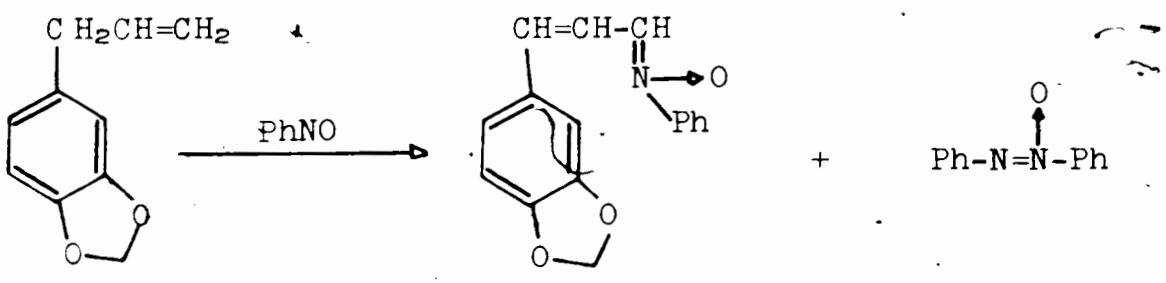
The C-nitroso group is readily oxidized to a nitro group and reduced to hydroxylamine I-19. The azoxy compounds I-20 that are usually formed (40) may arise from the condensation of the hydroxylamine with another molecule of nitroso compound.

Nitrosoalkanes react with alkyl radicals to give stable dialkylnitroxides I-21. These free radicals have characteristic esr spectra (a_N 14.3-15.7G)(41). Alkoxy (42) and acyl (43) radicals can also be trapped as reaction intermediates with nitroso compounds to form alkoxy-alkyl (a_N 26.9-29.6G) and acyl-alkyl (a_N 7.3-8.3) nitroxide radicals, respectively. These spin trapping reactions have been reviewed by Janzen (44).

I-2-4. Addition to olefins

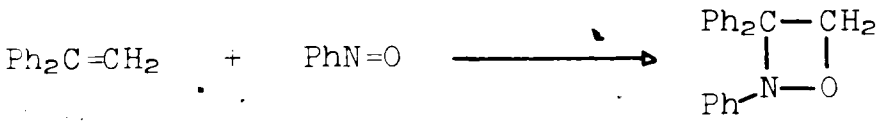
The C-nitroso group is electrophilic but not powerful enough to add to alkenes, dienes or acetylenes unless the nitroso group is activated by a vicinal electron withdrawing moiety such as phenyl (25, 26, 45-49), halogen (29, 50, 51, 52), cyano (53) and very recently acyl (53, 54).

The first account of a reaction between nitrosoarene and an olefin was reported by Alexandri (25,26) in 1910. An unsaturated nitrone I-22 and azoxybenzene I-23 were the major products isolated,



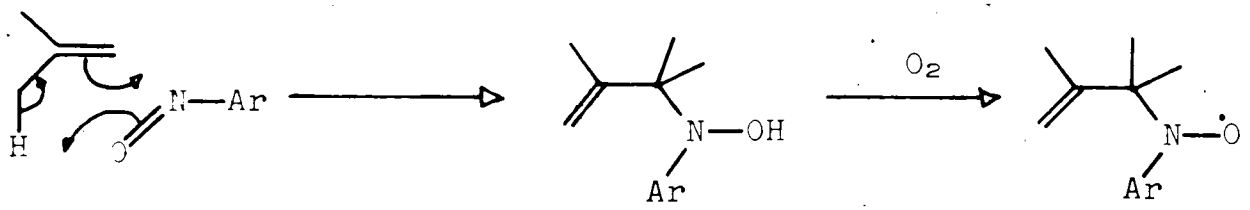
I-22 I-23

Phenylhydroxylamine is postulated as the intermediate on the basis of the formation of azoxybenzene. The reactions of nitrosobenzene with styrene and 1,1-diphenylethylene have been studied by Ingold and Weaver (45), in which 1,2-oxazetidine I-24 has been isolated.



I-24

The nitroso group of various substituted nitrosobenzenes was suggested by Sullivan (46) to undergo an addition hydrogen abstraction process ("ene" reaction) with olefins such as 2,3-dimethyl-2-butene to yield the unsaturated hydroxylamine intermediate, I-25, which was detected as its nitroxide I-26 by esr spectroscopy. Isolation and identification of several N-alkenyl-

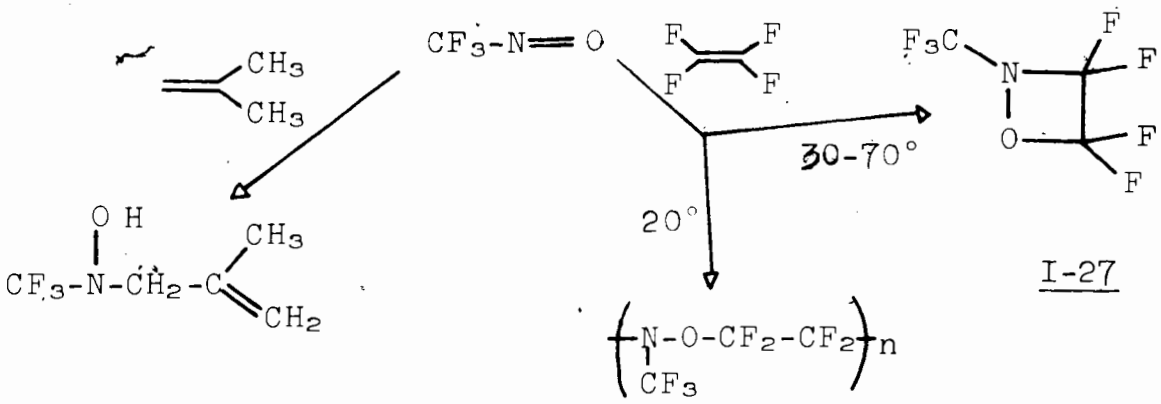


I-25 I-26

N-phenylhydroxylamines by the same method has been achieved by other groups (47,48) and further confirmed the "ene" reaction mechanism. Water et al (49) have recently shown that this reaction follows a free radical mechanism.

With aliphatic C-nitroso compounds, only perfluoronitroso alkanes are known to react with alkenes. Barr and Haszeldine (50)

claimed that perfluoro nitroso compounds and perfluoro olefins react in the dark at >30° to give 1,2-oxazetidine I-27. A 1:1 copolymer I-28 was the major product at room temperature.



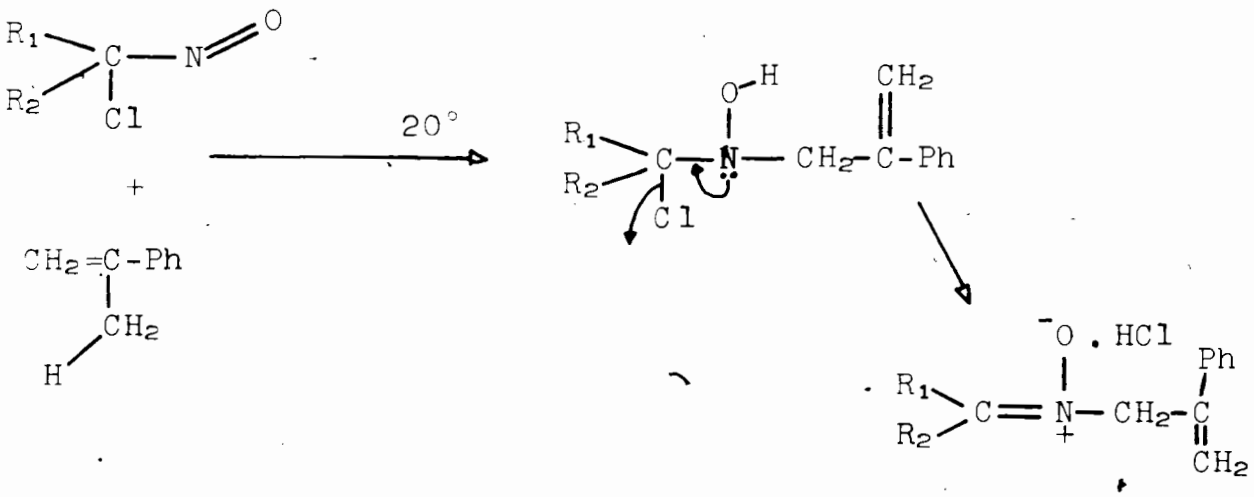
I-29

I-27

I-28

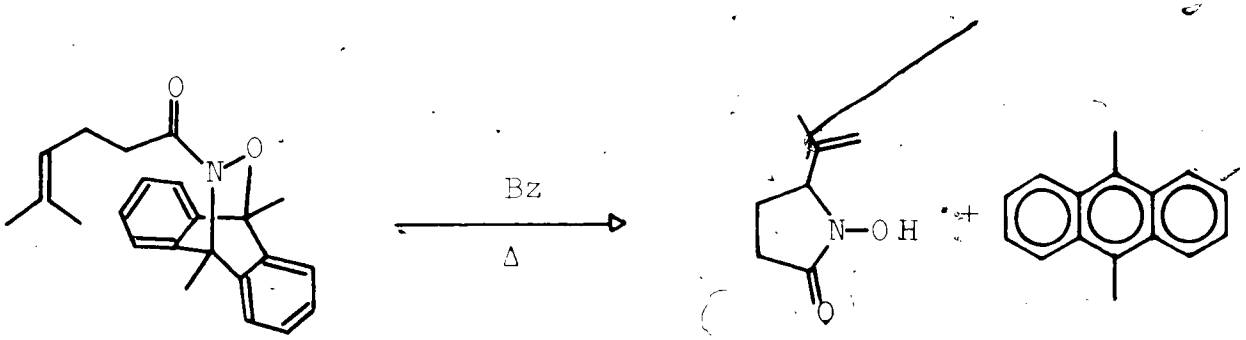
However with isobutene, the same group (51) isolated the unsaturated hydroxylamine I-29.

Recently, Schenk and de Boer (52) have shown that α-chloro nitroso compounds can also add to olefins containing allylic hydrogen and proposed an "ene" type reaction followed by the



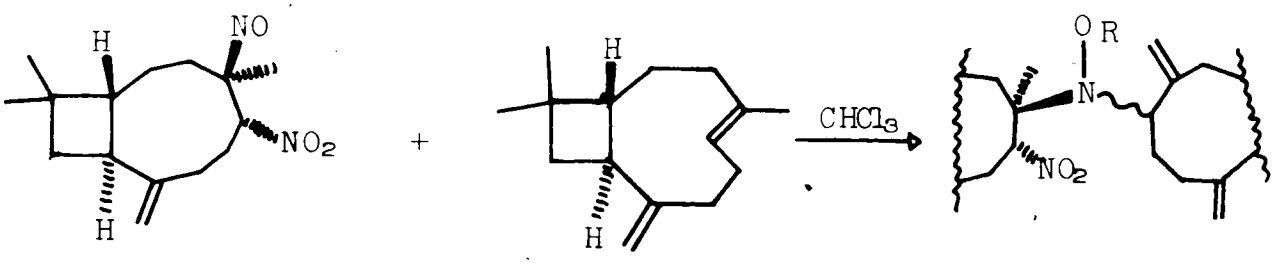
I-30

elimination of hydrogen chloride to give ketonitrone salts I-30. Very recently, Keck (54) has shown that acyl-nitroso compounds lead to intramolecular "ene' reactions. The very reactive acyl nitroso was not isolated but instead trapped with 9,10-dimethyl-anthracene (53,54) to give I-31, which when refluxed in benzene gave hydroxylamine I-32 in quantitative yield.



I-31 I-32

At present, only one alkylnitroso compound has been shown to undergo an "ene" type reaction. Roberts (55) reported that small amounts of N-alkyl-N-alkenyl hydroxylamine I-33a are formed upon reaction of caryophyllene I-34, possessing a reactive trans-trisubstituted double bond, with caryophyllene nitrosite I-35. Hydroxylamine I-33a was easily oxidized to its corresponding nitroxide I-33b. Also, the same researcher (56) found

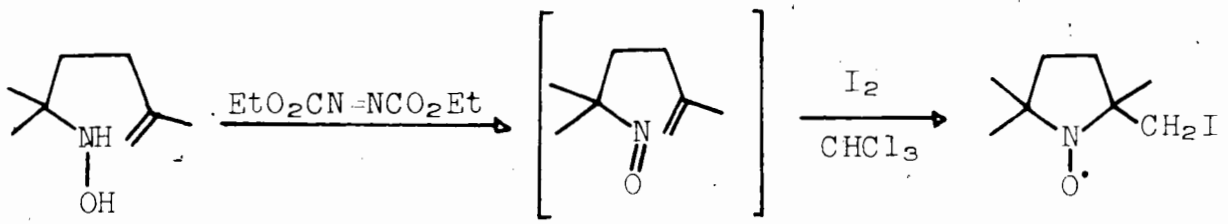


I-35 I-34

R=H , I-33a

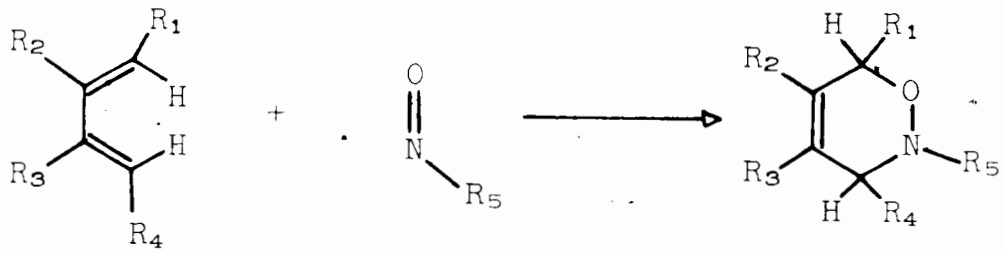
R=• , I-33b

that tertiary C-nitroso olefin I-36, generated in situ, reacts in chloroform in the presence of iodine to give a poor yield (6%) of iodo nitroxide I-37 ($g=2.0064$, $a_N=13.6$ G).



I-36 I-37

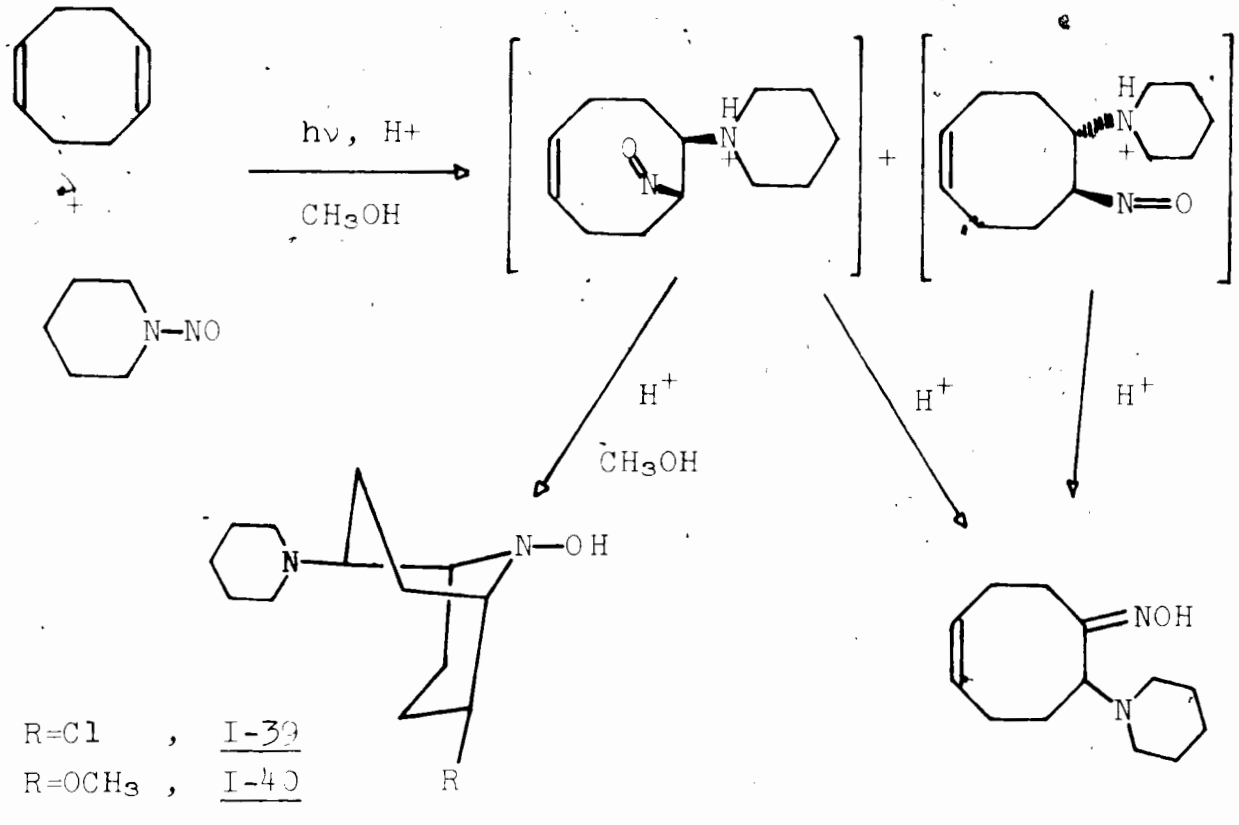
C-nitroso compounds can also react with alkyl substituted allenes (57). They can also participate in Diels Alder reactions (53,58) to give 1,2-oxazine ring compounds I-38.



I-38

Bicyclic hydroxylamines I-39 and I-40 were obtained in the photoaddition of N-nitrosopiperidine to 1,5-cyclooctadiene in methanol in the presence of hydrochloric acid or perchloric acid, respectively (59), in addition to the expected amino oxime I-41 which is known to arise from tautomerization of the

primary 1,2-addition product (19, 60,61). They were readily oxidized by alkaline hydrogen peroxide to their corresponding nitroxides,which showed an equal esr triplet with g values 2.0006-2.0007 and a_N values 15-17 G, typical of 9-azabicyclo [3.3.1] nitroxide radicals (62).



The intentions of this research can be outlined as follows:

1/ to clarify the solution photochemistry of N-nitramines in acidic,neutral and basic conditions.

2/ to investigate the trapping of aminyl and aminium radicals generated from the photolysis of N-nitramines in neutral and acidic medium, respectively, with carbon monoxide.

3/ to investigate the photoaddition of N-nitro and N-nitrosamines in the presence of an acid to various olefins. In particular, the photoaddition of N-nitro (24) and N-nitrosamine (69) in the presence of oxygen can be utilized to synthesize very cleanly amino nitrate esters. The typical and readily available olefins have been choosen for analytical reasons.

4/ to investigate the stereochemistry of the addition of nitrosyl chloride to olefins.

5/ to investigate the stereochemistry of the intramolecular electrophilic reaction of the nitroso group with a suitably located double bond.

6/ to synthesize bicyclic hydroxylamine acetates as potential precursors for the corresponding nitroxide radicals.

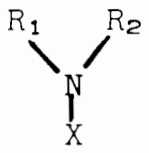
CHAPTER II

RESULTS

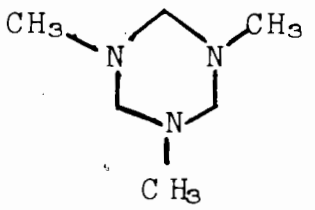
II-1. Photolysis of Nitramines

When NNOP was photolyzed in n-hexane under carbon monoxide in the presence of cyclohexene, no addition product to the cyclohexene, nor N-formylpiperidine (II-1) were detected in the crude residues. The photolysis gave piperidinium nitrate (II-2, 38%) together with NNP (33%) as the major products. The photolysis of NNOD under similar conditions gave DMF (II-3), NND and dimethylammonium nitrate (II-4) in yields of 26, 7 and 28% respectively, estimated from the nmr spectrum of the crude product (Table II-1).

Photolysis of NNOD in acetonitrile containing cyclohexene or norbornene in the presence of sodium bicarbonate or carbonate gave the same products as above. The yields of DMF (II-3) decreased to



R_1R_2	$(CH_2)_5$, X = NO_2	NNOP	
R_1R_2	$(CH_2)_5$, X = NO	NNP	
$R_1 = R_2$	CH_3, X = NO_2	NNOD	
$R_1 = R_2$	CH_3, X = NO	NND	
R_1R_2	$(CH_2)_5$, X = CHO	II-1	
R_1R_2	$(CH_2)_5$, X = $H.HNO_3$	II-2	
$R_1 = R_2$	CH_3, X = CHO	II-3	
$R_1 = R_2$	CH_3, X = $H.HNO_3$	II-4	
$R_1 = CH_3$, R_2 = H	, X = CHO	II-5	



II-6

2-3% and those of NND increased to 22 and 55% in the presence of sodium bicarbonate and carbonate, respectively. In the latter case, nitrate salt II-4 was formed in only 8% yield, as compared to a 35% yield using sodium bicarbonate.

No II-4 was formed and NND formation was low (6%) when the photolysis of NNOD was conducted in the presence of cyclohexene and sodium carbonate in n-hexane. DMF (II-3, 14%), N-methylformamide (II-5, 15%) and 1,3,5-trimethylhexahydro-1,3,5-triazine (II-6, 10%) (63,64) were the three major products. The yield of imine trimer II-6 may have been higher since it is reported to codistill with solvents (63). Compound II-5 was isolated from preparative gc and was characterized by ir, nmr and ms (65).

TABLE II-1

PHOTOLYSIS OF NITRAMINES UNDER NEUTRAL CONDITIONS

Nitramines	Solvent	[a]Olefin	Gas	NNP or NND (%)	II-4 or II-2 (%)	II-3 (%)	Remarks
NNOP	n-hexane	cyclohexene	CO	33	38	-	b
NNOD	n-hexane	cyclohexene	CO	7	28	26	c
NNOD	CH_3CN	cyclohexene	CO	22	35	2	c d
NNOD	n-hexane	cyclohexene	N_2	6	-	14	c e g
NNOD	CH_3CN	norbornene	CO	55	8	3	c e f

a more than one equivalent of the olefin was added.

b crude products isolated in percent.

c percentages calculated from nmr and/or gc analyses based on starting material.

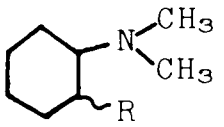
d $NaHCO_3$ (2g) present during photolysis.

e Na_2CO_3 (2g) present during photolysis.

f recovered NNOD: 6%.

g in addition, II-5 [b](15%) and II-6 (10%) were detected.

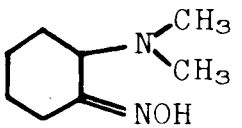
Under dilute acidic conditions, the photolysis of NNOD in the presence of cyclohexene either under nitrogen or carbon monoxide gave small amounts of mixtures of neutral compounds which were shown by gc-ms to contain more than thirty components. Among components identified were 2-cyclohexenol (II-7), 2-cyclohexenone (II-8), NNOD, a methoxycyclohexanone (II-9) and a methoxycyclohexanol (II-10). The mass spectra of the first three were identical to those of authentic samples (66). The last two compounds had correct molecular ion at m/e 128 and 130, respectively. The basic products were characterized by gc-ms analysis as dimethylaminocyclohexane (II-11, 15%), 2-dimethylaminocyloxexanol (cis and trans mixture, II-12, 28%), 2-dimethylaminocycloxexanone oxime (II-13, 24%) and 1-nitro-2-dimethylaminocyclohexane (II-14,



R = H , II-11

R = OH , II-12

R = NO_2 , II-14



II-13

22-24%). In addition there were minor amounts of two unknown compounds. The mass spectra of II-11 (64), II-12 (67) and II-13 (68) were identical to those of authentic samples, and the fragmentation pattern of II-14 was comparable with that of 1-nitro-2-piperidinocyclohexane (69).

While photolysis of nitramines in acidic conditions under inert gas gave good yields of addition products, the mixture is too complex to be useful for synthetic applications. Under an oxygen atmosphere, the $\pi \rightarrow \pi^*$ absorption band of NNOD in acidic methanol containing cyclohexene disappeared about twice as fast as comparable photolyses under nitrogen or carbon monoxide. The crude basic fraction showed strong ir absorptions at 1625, 1275 and 870 cm^{-1} (ONO_2), at 1715 cm^{-1} (C=O) and at 3420 and 1040 (C-OH). The LAH reduction of this crude basic fraction afforded 64% of a mixture of cis and trans-2-dimethylaminocyclohexanol (II-12)(67).

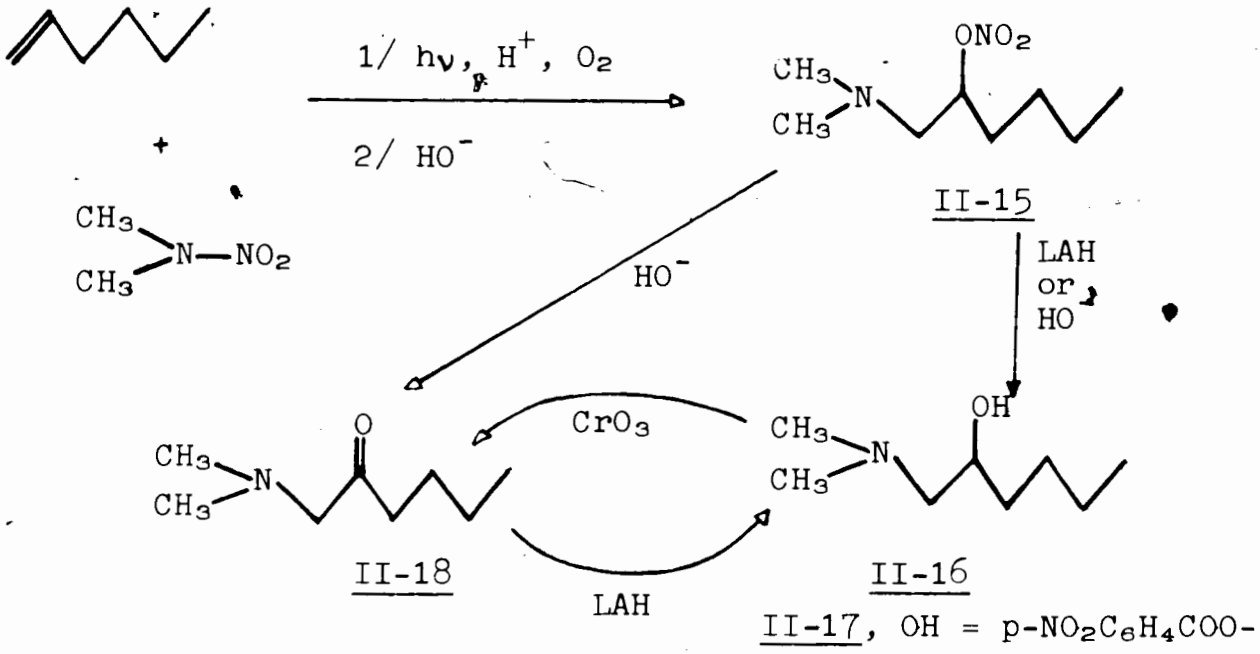
II-2. Oxidative and/or non oxidative photoadditions of N-nitro and/or N-nitrosodimethylamine to olefins

II-2-1. to 1-hexene

Photolysis of a methanolic solution of NNOD, 1-hexene and hydrochloric acid under an oxygen atmosphere exhibited a zero-order decrease of the absorption at 238 nm. The neutral fraction showed no signal for a dimethylamino moiety in the nmr but strong ir absorptions at 1625, 1280 and 860 cm^{-1} for nitrate ester as well as 1555 and 1380 cm^{-1} for nitro groups were present. This fraction was not further investigated.

The basic fraction exhibited strong ir bands at 1625, 1280 and 860 cm^{-1} (ONO_2, II-15), a medium band at 1715 cm^{-1} (C=O) and a broad band at 3400 cm^{-1} (OH). LAH reduction of the crude basic

fraction followed by preparative gc separation afforded 1-dimethyl amino-2-hexanol (II-16, 62%) as the major product (Scheme II-1). Its infrared spectrum showed bands at 3440 and 1030 cm^{-1} (C-OH) and Bohlmann bands at 2820 and 2780 cm^{-1} (70). The nmr spectrum showed a one proton multiplet at τ6.42 for the methine proton.



Scheme II-1

Treatment of II-16 with p-nitrobenzoyl chloride in tetrahydrofuran gave 1-[N,N-dimethyl]-2-[p-nitrobenzoyl] -hexyl ammonium chloride (II-17, 60%), which was characterized by ir absorptions at 1715 and 1270 cm^{-1} and by elemental analysis.

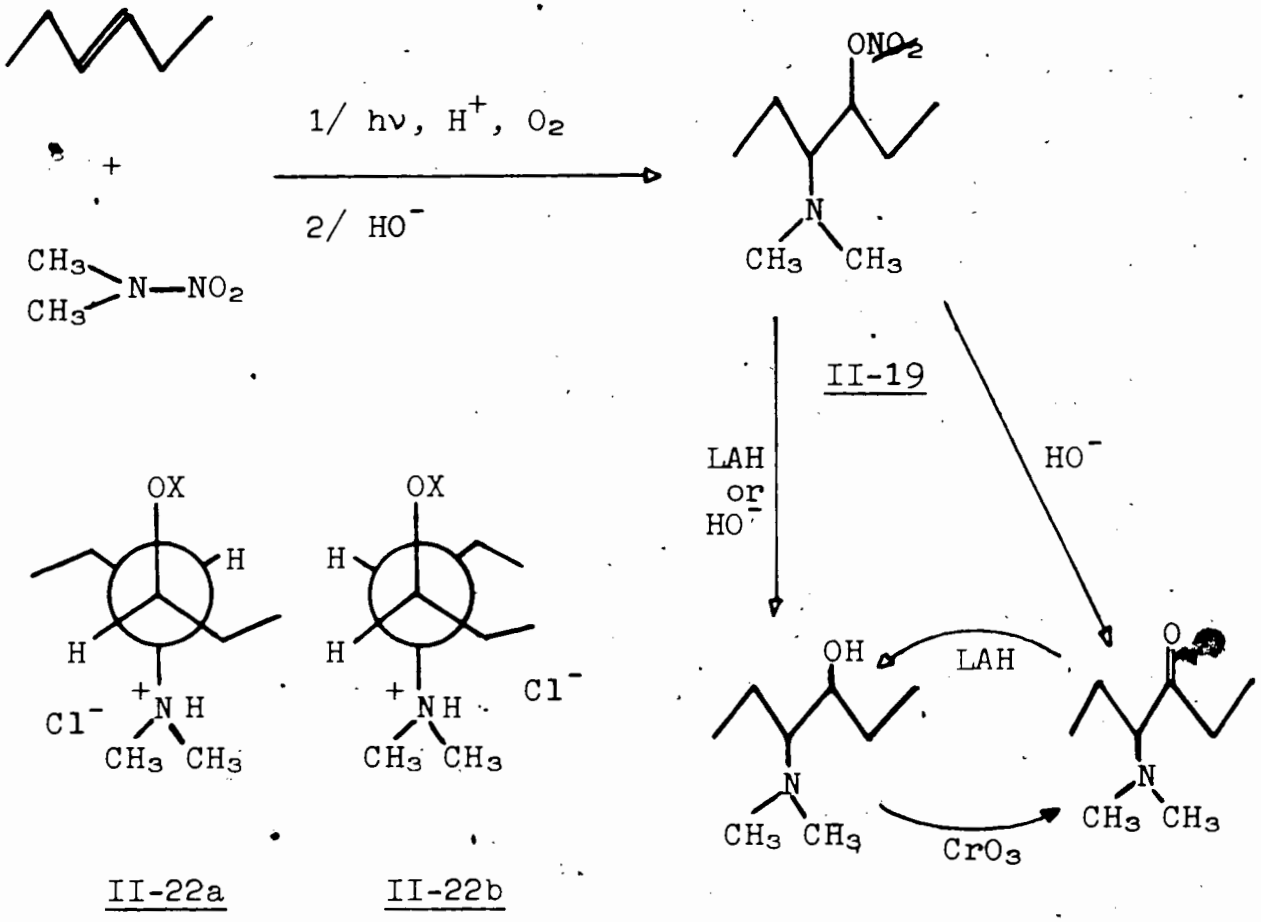
The amino nitrate ester II-15 was stable in aqueous acidic solution but was converted in basic conditions to a mixture of

amino alcohol II-16 (24 %) and 1-dimethylamino-2-hexanone (II-18, 20 %). The nmr spectrum of this mixture showed no absorptions for olefinic or aldehydic protons. The amino ketone exhibited an M^+ ion at m/e 143, ir absorptions at 1720, 2830 and 2780 cm^{-1}, and a nmr singlet at τ7.26 for the $COCH_2N$ protons. Amino alcohol II-16 oxidized with Jones' reagent to give amino ketone II-18.

II-2-2. to trans-3-hexene

Photolysis of NNOD in the presence of trans-3-hexene and hydrochloric acid under an oxygen atmosphere afforded nitrate ester II-19 as the primary product. It quickly decomposed to amino alcohol II-20 (3400 and 1045 cm^{-1}) and amino ketone II-21 (1710 cm^{-1}) during work-up, leaving only a small amount of II-19 in the crude basic fraction as shown by the weak ir bands at 1625, 1280 and 860 cm^{-1}. LAH reduction of this fraction followed by preparative gc separation afforded 4-dimethylamino-3-hexanol (II-20, 49 %) as the major product (Scheme II-2).

II-20 exhibited ir bands for a hydroxyl group (3400 and 1050 cm^{-1}) as well as Bohlmann bands (2840 and 2790 cm^{-1}). The nmr spectrum of II-20 showed a singlet at τ7.69 for a dimethylamino group and two multiplets at τ6.50 and 6.75 for the methine protons. The hydrochloride of the benzoate II-22 showed prominent ir bands at 1720 and 1275 cm^{-1} and gave a correct elemental analysis. The nmr spectrum showed two sharp singlets at τ7.03 and 7.12 for N-methyl groups. The 5:3 ratio of these two singlets pointed to a mixture of erythro II-22a and threo II-22b isomers.

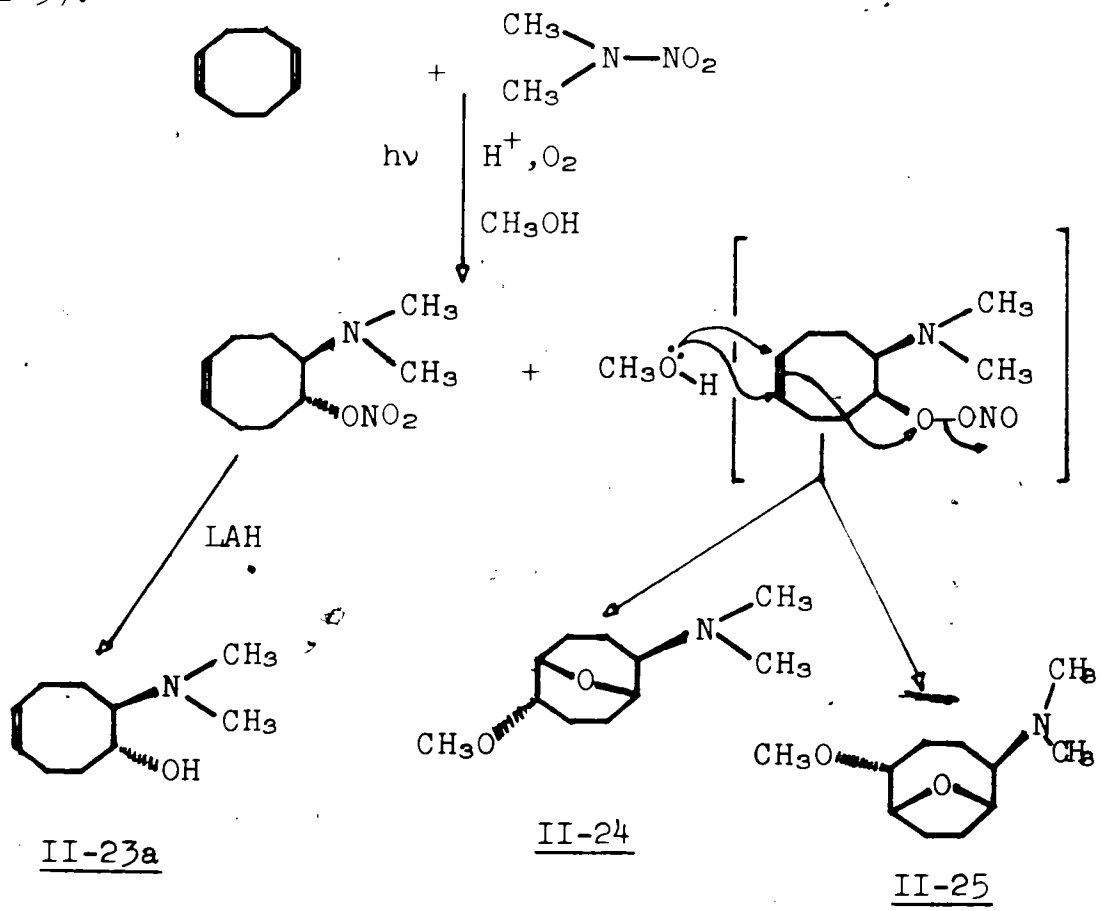


Scheme II-2

The crude basic fraction containing amino nitrate ester II-19 was readily decomposed to amino alcohol II-20 (26%) and 4-dimethylamino-3-hexanone (II-21, 25%) in aqueous basic conditions. Amino ketone II-21 showed a nmr triplet (J= 7Hz) at τ7.12 for the methine proton and a quartet (J= 7Hz) at τ7.47 for the methylene protons adjacent to the carbonyl group. Oxidation of the amino alcohol II-20 with Jones' reagent gave amino ketone II-21.

II-2-3. to 1,5-cyclooctadiene

The oxidative photoaddition of NNOD to 1,5-cyclooctadiene was carried out under the usual conditions followed by work-up to afford a basic fraction which showed strong ir bands at 1625, 1275 and 860 cm^{-1} (ONO_2) and nmr singlets at τ6.65 (OCH_3) and at τ7.71 7.74 and 7.77 (CH_3N). Reduction of the basic fraction with LAH followed by chromatography afforded trans-2-dimethylamino-5-cyclooctene-1-ol (II-23a, 48%) and a mixture of endo-2-methoxy-exo-6-dimethylamino-9-oxabicyclo[3.3.1]nonane (II-24, 12%) and endo-2-methoxy-exo-5-dimethylamino-9-oxabicyclo[4.2.1]nonane (II-25, 4%) (Scheme II-3).

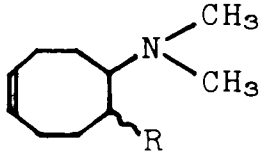


II-23a II-24 II-25

Scheme II-3

Compound II-23a was obtained as long colourless needles and was identified by direct comparison of its ir, proton nmr, gc and ms spectra with those of an authentic sample prepared by Dr. K.S. Pillay (69). Its ^{13}C nmr spectrum (Table II-7) showed expected chemical shifts and pattern. The two minor oxabicyclic compounds II-24 and II-25, as a mixture, were identified by gc relative retention times and mixed injection with an authentic mixture (69).

The non-oxidative photolysis of NNOD in the presence of COD and HCl in acetonitrile produced a yellow solution and a red oil which deposited on the walls of the photolysis vessel. This oil might have acted as a filter since the photolysis proceeded significantly slower than when NNOD was irradiated in methanol. This photolysis yielded a complex basic fraction which exhibited ir absorptions at 3010 cm^{-1} (olefin), at 3250, 1650 and 1035 cm^{-1} (C=NOH), at 710 cm^{-1} (C-Cl) and distinct bands at 1555 and 1310 cm^{-1} for a nitro group (71). Among the more than ten products shown by gc to be present, three were tentatively characterized by gc-ms analysis: namely, 1-chloro-2-dimethylamino-5-cyclooctene (II-26, 19%), 2-dimethylamino-5-cycloocten-1-ol (II-23, 32%), and 2-dimethylamino-5-cycloocten-1-one-anti-oxime (II-27, 13%).

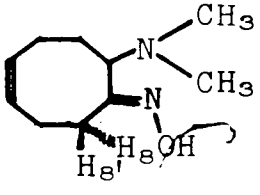


R = Cl, II-26

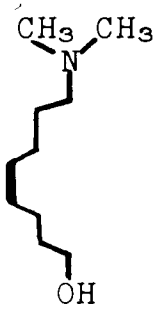
R = H, II-28

R = trans-OH, II-23a

R = cis-OH, II-23b



II-27



II-29

Compounds II-26 and II-27 were obtained from distillation of the crude basic fraction. Anti-oxime II-27, obtained as white crystals, exhibited ir bands at 2930 and 2860 cm^{-1} (CH_3N), at 3020 cm^{-1} (olefin), and at 3180, 1642, 970, 920 and 900 cm^{-1} (C=NOH). The nmr spectrum (Figure II-1) showed a double doublet at τ7.22 (J= 8.5 and 7.0Hz) for H_2, the chemical shift of which was in good agreement with that of anti-oxime of the saturated analogue (72). The signal due to the H_8 proton resonated at τ6.86 as a doublet of doublets (J= 12.0, 6.5 and 3.5Hz)(73).

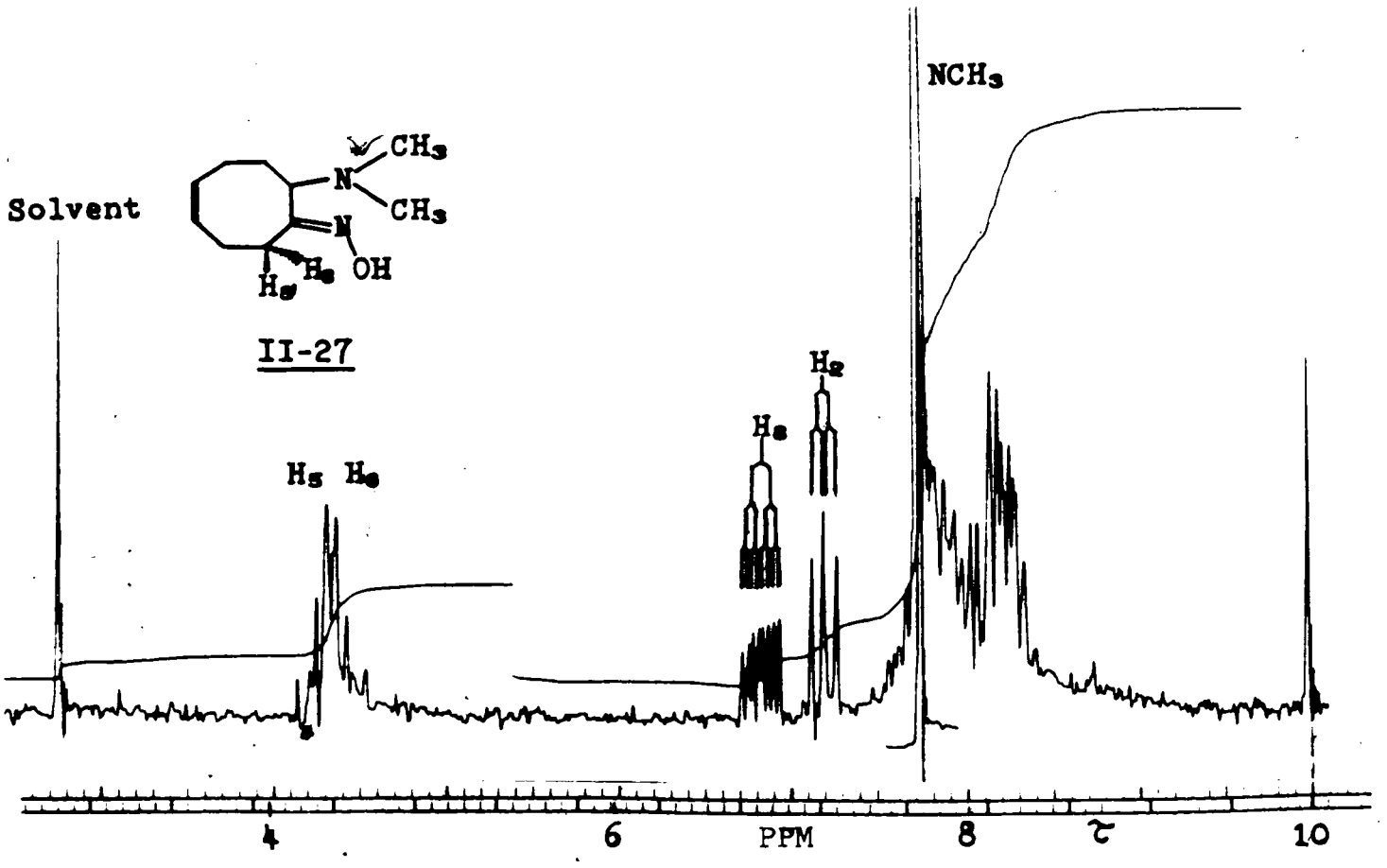


Figure II-1 nmr spectrum (100MHz) of 2-dimethylamino-5-cycloocten-1-one-anti-oxime (II-27)

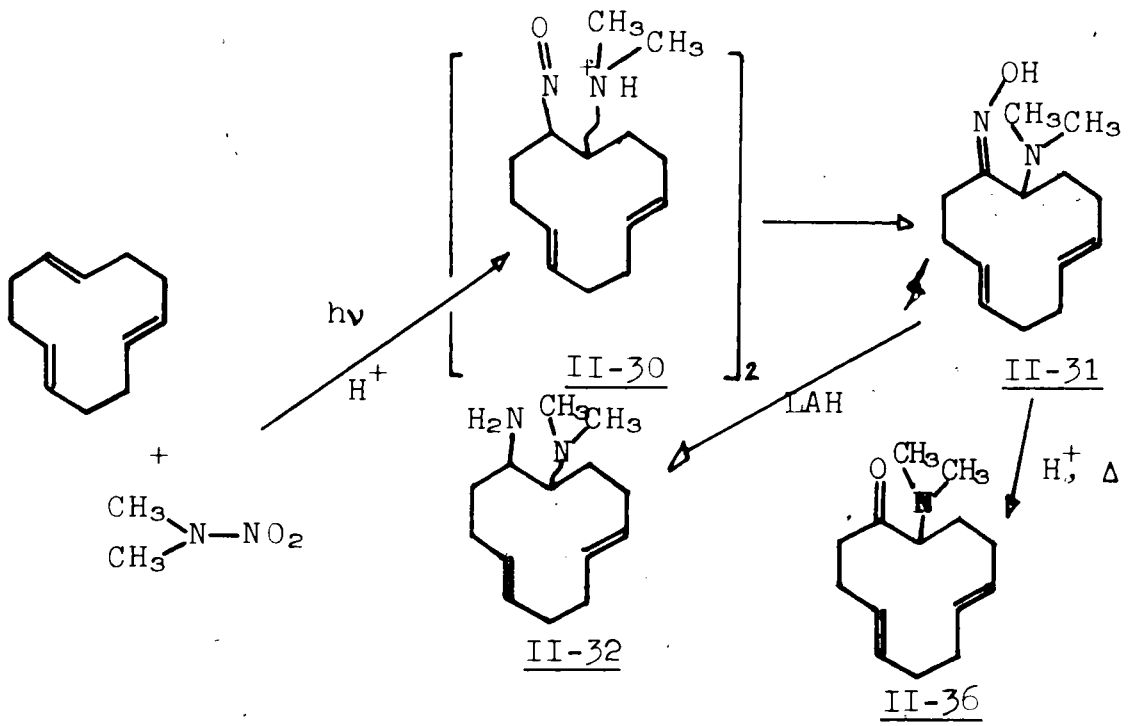
The β-chloramine II-26 was obtained as a mixture of cis and trans isomers. It exhibited ir bands at 3020 cm^{-1} (olefin), at 2870, 2830 and 2780 cm^{-1} (CH_3N) and at 710 cm^{-1} (C-Cl). The nmr spectrum showed a complex multiplet at τ5.79 for the methine protons H_1, and two equal intensity singlets at τ7.72 and 7.75 for the dimethylamino groups. Its ms revealed the M^+ ions at m/e 189 and 187 with the chlorine isotope ratio of 1:3. The mass spectrum of amino alcohol II-23 was identical to that of an authentic sample of trans-II-23a (69,74).

The LAH reduction of the basic fraction gave a mixture of four major products, namely, 5-dimethylamino-cyclooctene (II-28, 5%) cis-2-dimethylamino-5-cycloocten-1-ol (II-23b, 5%), its trans-isomer (II-23a, 21%), 8-dimethylamino-cis-4-octen-1-ol (II-29, 12%). The first three were identified by gc-ms and mixed injection (gc) with authentic samples. The fourth component, II-29, was identified from the following data; the mass spectrum from gc-ms gave the molecular ion at m/e 171 and fragments at m/e 84, 71 and 58 (100%) characteristic of a dimethylaminomethyl moiety. The proton nmr spectrum of the reduced fraction showed a triplet at τ6.40 (J= 6Hz) typical for methylene protons adjacent to a hydroxyl group and a singlet at τ7.78 (NCH_3). The ^{13}C nmr spectrum of the reduced mixture revealed absorptions at 60.8(t) and 58.5(t)ppm which were attributed to the C_1 and C_8 carbons of II-29, respectively. These values, as well as the NCH_3 signal at 44.7(q)ppm, were comparable with long chain amino alcohols II-35 and II-39 (vide infra).

II-2-4. To trans,trans,trans-1,5,9-cyclododecatriene

The non-oxidative photoaddition of NND to tttCDT in methanol under a nitrogen atmosphere was carried out and worked up in the manner well established in this laboratory. The emergence of a stong new absorption band around 300 nm in the uv spectrum was attributed to an intermediate, the dimer of C-nitroso compound II-30 (19,75).

The major product, isolated as white needles, was syn-1-oximino-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-31, 76%)(Scheme II-4). Elemental analysis and high resolution mass spectroscopy established the molecular formula as $C_{14}H_{24}NO$. The ir spectrum exhibited absorptions at 3180, 1650 and 1000-900cm^{-1} (C=NOH), at 3030 and 960 cm^{-1} (trans double bonds) and at 2780 cm^{-1} (Bohlmann). The nmr spectrum showed four olefinic protons at



Scheme II-4

τ4.91 (J= 14Hz) and a singlet at τ7.77 (NCH_3). The C_2 proton was seen at τ6.70 as a doublet of doublet (J= 7.0 and 3.5Hz). A comparison of the nmr of II-31 with that of amino ketone II-36(vide infra) showed that the C_2 proton was deshielded by 0.38ppm in amino oxime II-31 and the C_{12} proton remained at the same chemical shift, indicating the syn configuration for the oximino group(76). The ^{13}C nmr spectrum of II-31 (Table II-2) showed the expected chemical shifts. The mass spectrum of II-31 gave a strong M^+ ion peak at m/e 236, the base peak at 219 for a loss of OH, and the peaks at m/e 110, 84, 71 and 58, characteristic for dimethyl tertiary amines. The structure of amino oxime II-31 was further confirmed by its hydrolysis in 2N hydrochloric acid to an amino ketone (1715 cm^{-1}) whose spectroscopic data were identical with those of an authentic sample of II-36.

Crude amino oxime II-31 was reduced with LAH to give 1-amino-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-32 , 90%), which was shown by elemental analysis and high resolution mass spectrometry to have the molecular formula $C_{14}H_{26}N_2$. Diamine II-32 exhibited ir absorptions at 3360 cm^{-1} and the Bohlmann bands at 2820 and 2770 cm^{-1}. The ^{13}C nmr spectrum (Table II-2) showed lines at 48.7(d) and 58.5(d) ppm for the carbons attached to the amino and dimethylamino groups, respectively, in accordance with reported values (77). Its ^1H nmr spectrum (Figure II-2) showed that the C1 proton was vicinally coupled to the C_2 proton with a coupling constant of 3.5 Hz, the magnitude of which suggested that diamine II-32 might have the same configuration at C_1,C_2 as amino alcohol

Table II-2 ^{13}C nmr spectra of cyclododecadiene and dodecadiene derivatives

	II-32	II-34a	II-34b	II-37a	II-74	II-38a	II-35	II-39
C_1	48.7 d	68.4 d	69.7 d	83.5 d	48.7	69.4 d	61.6 t	61.7 t
C_2	58.5 d	59.9 d	66.6 d	58.6 d	63.3	62.8 d	59.1 t(C_{12})	59.2 t(C_{12})
C=C	131.4	133.1	133.3	132.7d(2C)	133.0	131.0	129.9(3C)	130.2
	130.9	131.2	132.8		131.8	130.6		130.0
	130.8	130.9	130.6	129.4 d	130.4	130.2		129.8
	130.3	129.6	130.1	129.0 d	128.7	128.4	129.7	129.3
[a]C_3	33.6 t	31.5 t	34.0 t	31.9 t	33.7	30.6 t(2C)	32.4 t(3C)	32.3t(2C)
[a]C_4	31.7t(2C)	31.4 t	31.8 t	31.8 t	33.4			
[a]C_7		31.2 t	31.3 t	30.0 t	31.7(2C)	27.9 t		28.7 t
[a]C_8	29.3 t	29.2 t	30.8 t	28.8 t		26.5 t	30.3 t	27.3 t
[a]C_{11}	29.1 t	26.7 t	28.7 t	27.1 t	29.4	24.5 t	28.8 t	27.2 t
[a]C_{12}	19.6 t	22.9 t	22.8 t	17.7 t	29.0	23.1 t	27.3 t	25.1 t
NCH_3	42.9 q	41.6 q	42.5 q	42.1 q	-	41.6 q	45.2 q	45.1 q

a: assigments not determined; can be all interchangeable

Table II-2 Con't

	II-31	II-36	II-75	[a] II-78	II-68	[b] II-70	[c] II-72	II-67	[d] II-71
C_1	159.6s	210.1s	158.7s	165.5s	45.7d	44.4d	50.3	37.0d	46.4
C_2	63.5d	73.0d	78.2d	57.6d	-	-	63.4	37.0d	46.4
C=C	131.3(2C)	132.4	131.5(2C)	132.7	131.9	131.7d(2C)	132.8	133.1d(2C)	133.1(2C)
	-	131.5	-	132.5	131.5	-	130.5	-	-
	131.1	130.0	131.0	129.6	130.5	130.3d	129.2	128.4d(2C)	128.1(2C)
	130.8	129.3	130.6	129.2	130.0	129.3d	126.9	-	-
[e] C_3	31.9t	39.9t	31.9t	31.8t(2C	36.6t	33.7t	33.7	31.6t(2C	31.6(2C)
[e] C_4	31.8t	32.1t	31.7t	-	32.0t	31.7t	31.9	-	-
[e] C_7	31.0t	32.0t	29.9t	31.7t	31.9t	31.5t	29.5	29.8t(2C)	29.9(2C)
[e] C_8	28.6t	31.8t	28.5t	29.1t	30.3t	29.4t	29.3(2C)	-	-
[e] C_{11}	25.7t	28.6t	27.8t	29.0t	29.8t	29.1t	-	27.9t(2C)	27.1(2C)
[e] C_{12}	18.8t	17.0t	25.4t	26.1t	29.5t	27.8t	28.9	-	-
CH_3	40.5q(2C)	41.5q(2C)	54.5q	19.4q	22.6t	22.5	-	-	-

a: 167.9s ppm for the carbonyl carbon; b: 168.9s ppm for the carbonyl carbon; c: 140.3,132.0, 128.6(2C) and 128.1(2C)ppm for the phenyl carbons, 53.5ppm for the benzyl carbon; d: 139.0, 127.7(2C), 127.5(2C) and 126.7ppm for the phenyl carbons, 65.0ppm for the benzyl carbon; e: assigments not determined, can be all interchangeable

II-34b (Table II-3).

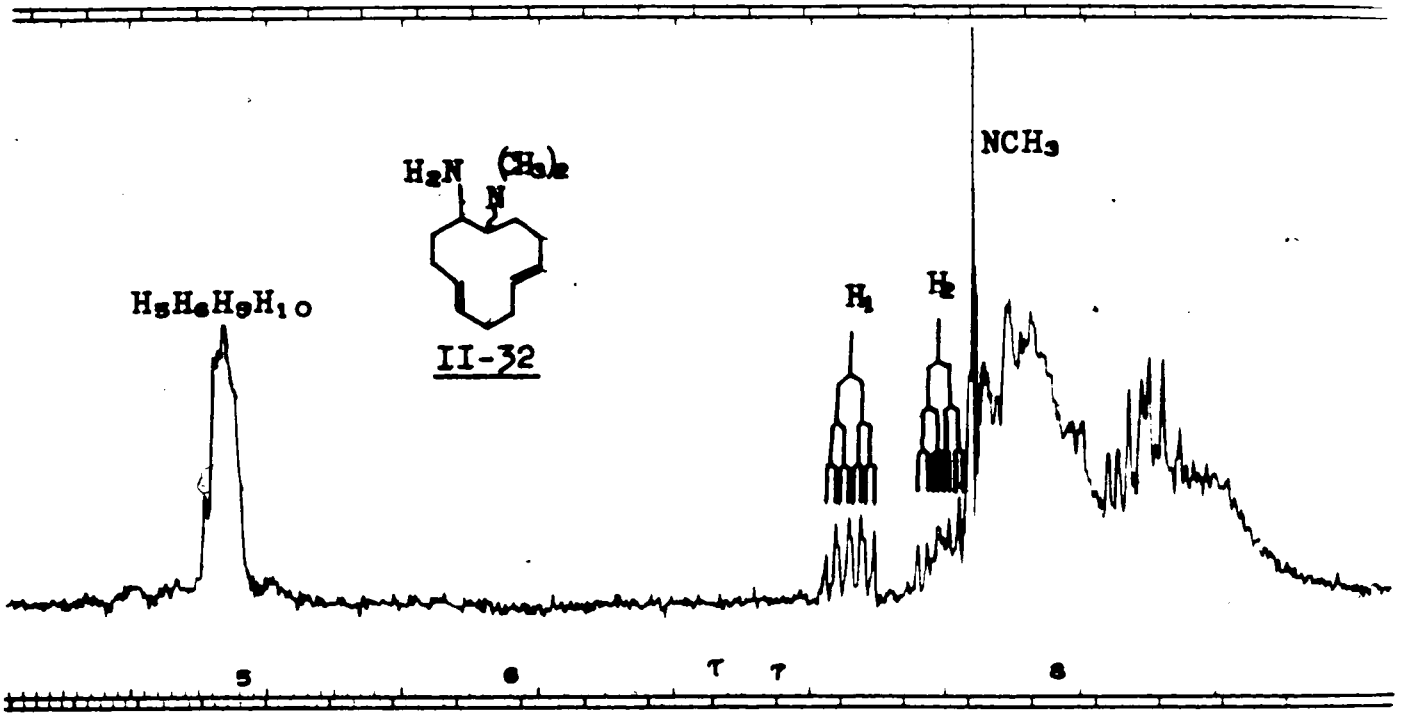
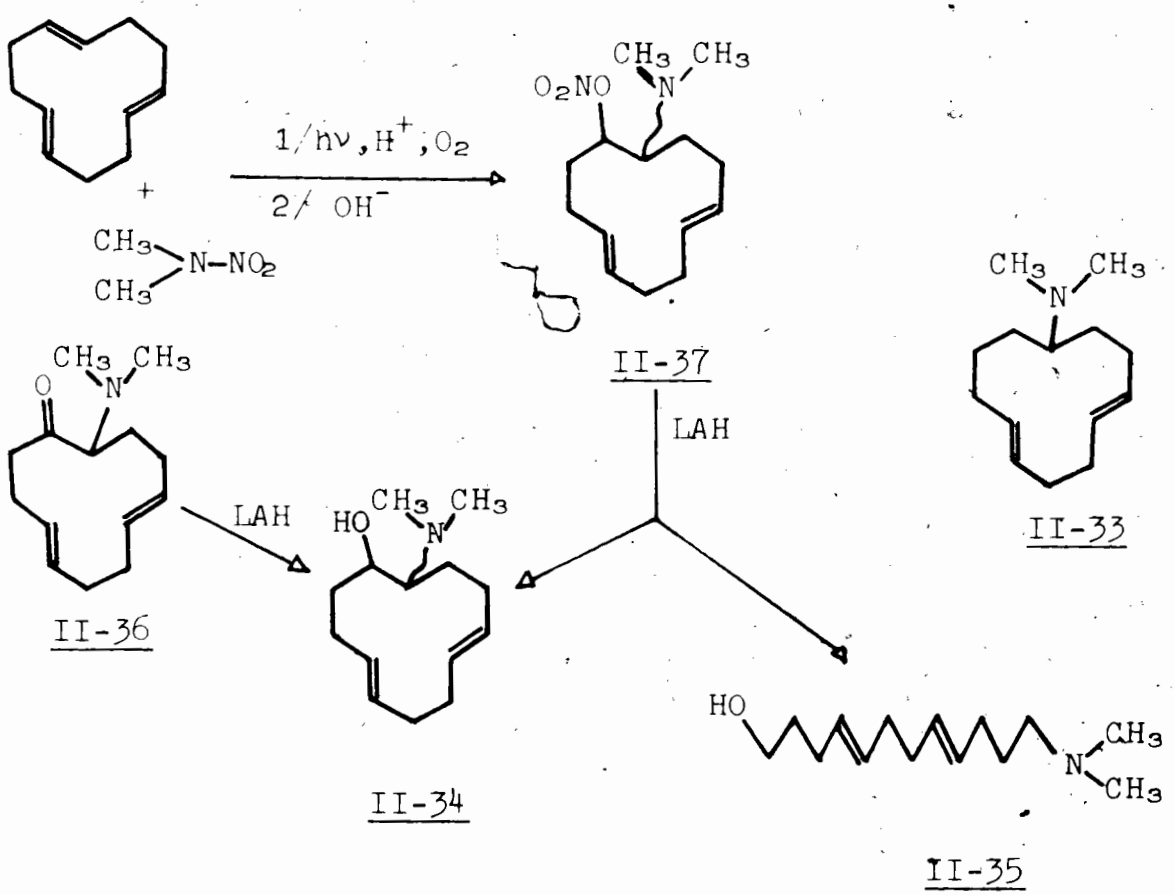


Figure II-2 ^{1}H nmr spectrum (100MHz) of 1-amino-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-32)

The oxidative photoaddition of NNOD (or NND) to tttCDT was carried out under the usual conditions followed by work-up to give neutral and basic fractions. The neutral fraction afforded tttCDT and cttCDT in the 30:1 ratio. The basic fraction exhibited strong infrared bands at 1620, 1275 and 860 cm^{-1} (ONO_2), at 1710 cm^{-1} (C=O) and 3350 and 1040 cm^{-1} (C-OH). The nmr spectrum showed multiplets at τ4.60 and 4.82 for the olefinic protons and singlets at τ7.60 (II-34a), 7.72 (II-37a + II-34b), 7.76 (II-37b + II-33)

and 7.80 (II-36) in the approximate ratio of 5:6:3:2 for the dimethylamino groups.

Reduction of the crude basic fraction with LAH, followed by extensive column chromatography afforded 1-dimethylamino-trans, trans-4,8-cyclododecadiene (II-33, 3%), the threo (trans) and erythro (cis) isomers of 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-ol (II-34a, 35% and II-34b, 12%) and 12-dimethylamino-trans,trans-4,8-dodecadien-1-ol (II-35, 24%). (Scheme II-5).



Scheme II-5

The structure of amino alcohols II-34a and II-34b was assigned on the basis of the following arguments. Their elemental analyses and high resolution mass spectra established their molecular formulae as $C_{14}H_{25}NO$. Both alcohols exhibited characteristic infrared absorption bands for a hydroxyl function and for trans double bonds (980 cm^{-1}) (78). The ^{13}C nmr spectra (Table II-2) of both the alcohols showed four olefinic carbons. The carbons bonded to the hydroxyl group (C_1) appeared at 69.7(d) and 68.4(d)ppm for II-34b and II-34a, respectively, in good agreement with literature values (77). However, the chemical shifts of the C_2 carbons exhibited 6.7 ppm difference between the two isomers indicating that II-34b (66.6, d) was deshielded while II-34a showed a normal shift (59.9, d). The ^1H nmr spectra of compounds II-34a and II-34b and partially spin-decoupled spectra are shown in Figure II-3 and Figure II-4, respectively, and their parameters are summarized in Table II-3 with those of related compounds. The coupling constants of the C_1 and C_2 protons were determined to be 7.5 and 4.0Hz for II-34a and II-34b, respectively by decoupling experiments. The mass spectra of alcohols II-34a and II-34b showed the same fragmentation patterns and differed only in the relative abundance of the various peaks (Figure II-5). In both cases, the most intense peak was observed at m/e 71 corresponding to the molecular ion C_4H_9N, along with the m/e 58 peak which were the common peaks of a dimethylaminomethyl moiety (63,69).

The amino alcohol II-35 was not detected from the basic fraction of the photolysate but obtained only after LAH reduction and

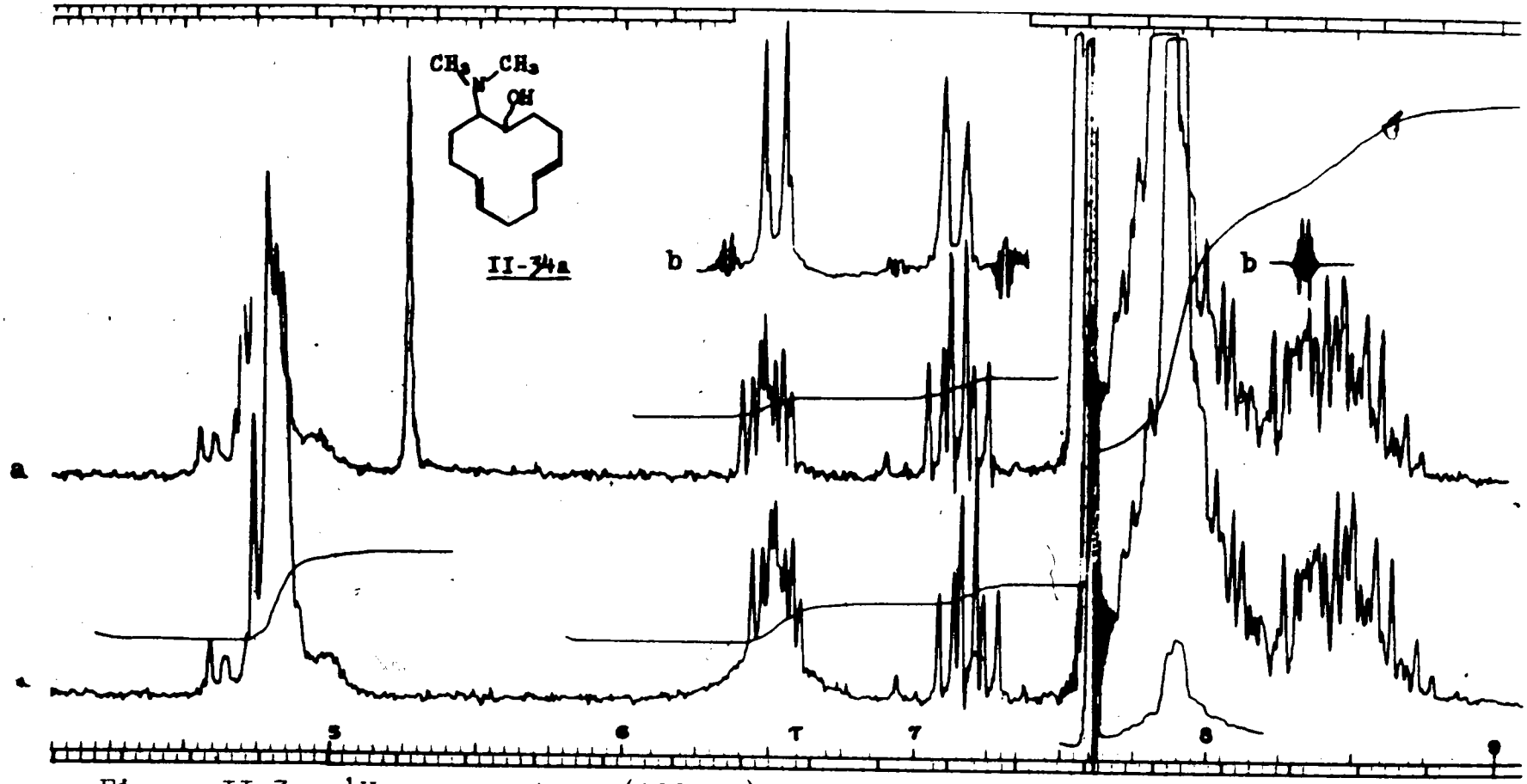


Figure II-3 ^1H nmr spectrum (100MHz) of 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-ol (II-34a);
a, D_2O exchange spectrum;
b, double irradiation of the C_3 and C_{12} protons

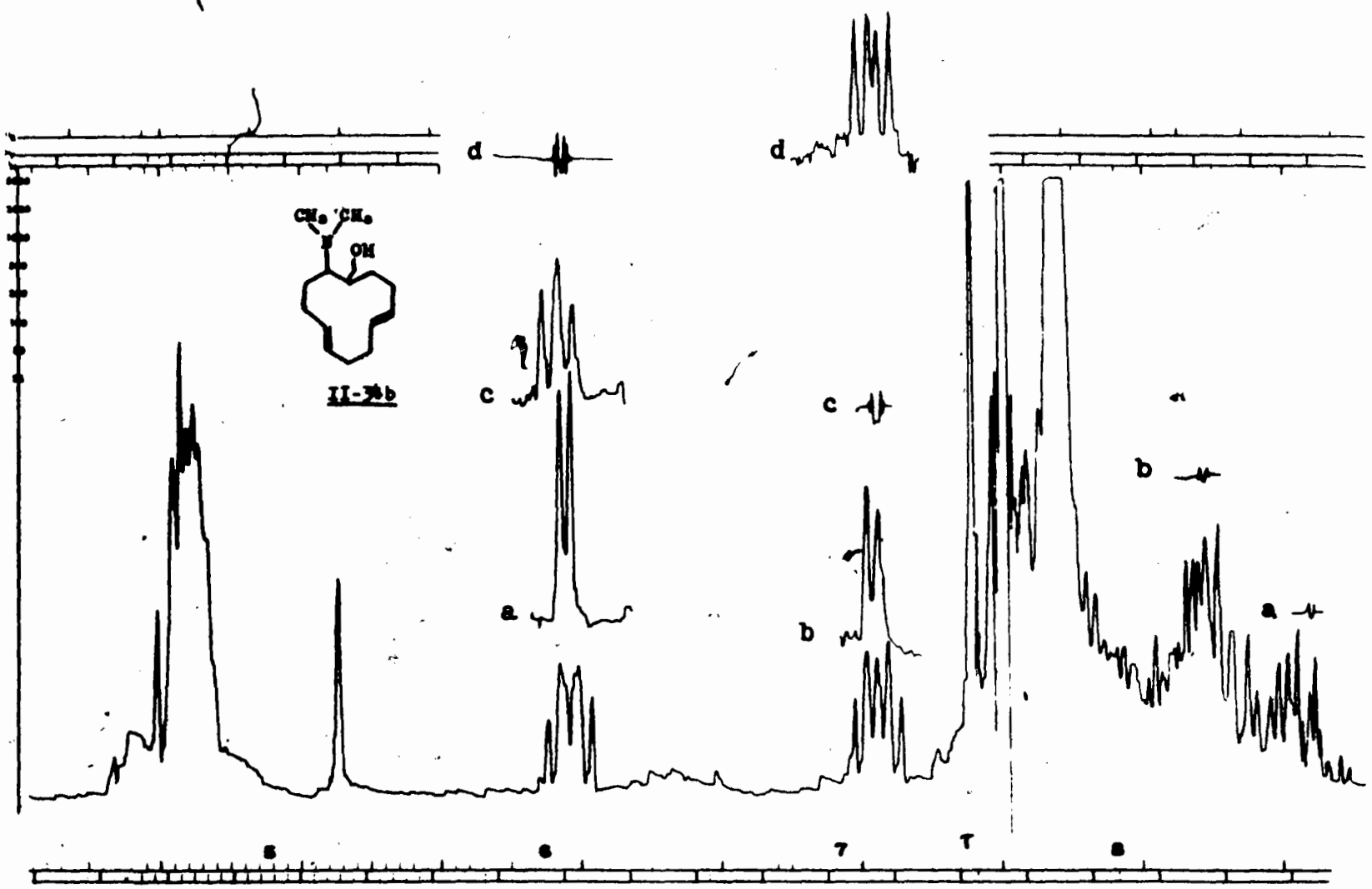


Figure II-4 D_2O exchange nmr spectrum (100MHz) of 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-ol (II-34b);

a, double irradiation of the C_3 protons;
b, double irradiation of the C_{12} protons;
c, double irradiation of the C_2 proton;
d, double irradiation of the C_1 proton.

	II-32	II-34a	II-34b	II-37a	II-38a	II-74
1	7.21(ddd)	6.53(ddd)	6.14(ddd)	a	6.44(m)	7.06(ddd)
$J_{1,12}$	9.5and4.5	6.0 and 3.5	6.6 and 4.9			6.5 and 6.0
$J_{1,2}$	3.5	7.5	4.0	7.5	6.0	2.0
$J_{2,3}$	7.5and5.5	7.5 and 5.0	7.5 and 4.5	7.5 and 4.0	6.0	7.5 and 7.0
2	7.52(ddd)	7.20 (dt)	7.25(ddd)	7.24 (dt)	7.48(q)	5.73(ddd)
5,6,9,10	4.94 (m)	4.80 (m)	4.71 (m)	4.86 (m)	4.60(m)	4.89 (m)
4,7,8,11	7.70-8.10(m)	7.91 (m)	7.90 (m)	7.82-8.50(m)	7.94(m)	7.70-8.20(m) + H_3
3,12	8.10-8.64(m)	8.00-8.80(m)	8.38-8.95(m)		8.10-8.60(m)	8.32-8.52(m) - H_3
OHorNH$_2$	8.40	6.62 (bs)	7.15 (bs)	-	7.20(bs)	8.33 (bs)
NCH$_3$	7.67 (s)	7.60 (s)	7.71 (s)	7.72 (s)	7.67(s)	-

a : hidden under H_5, H_6, H_9, H_{10} multiplet.

Table II-3 Chemical shifts (τ) and coupling constants (Hz) of cyclododecadiene derivatives

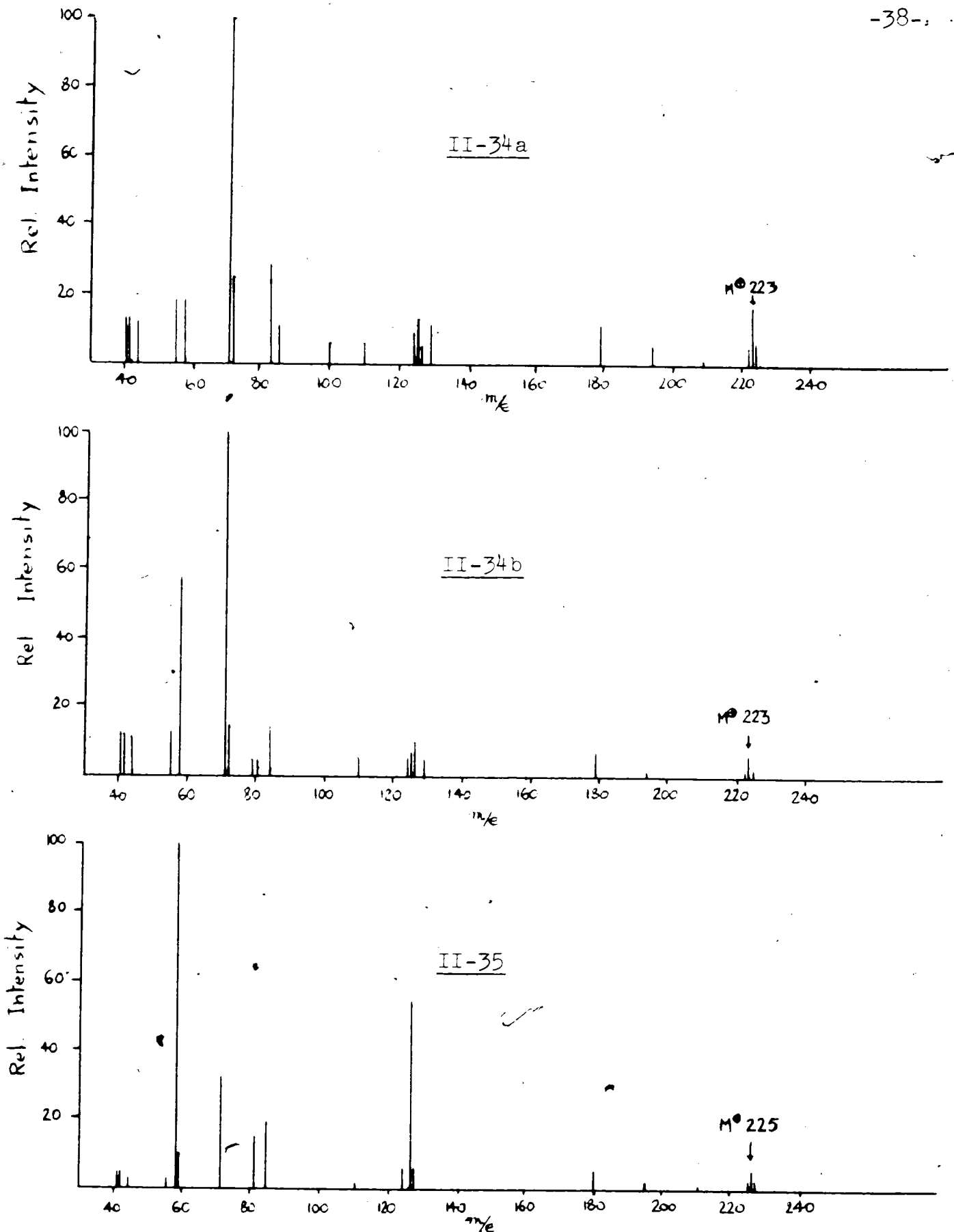
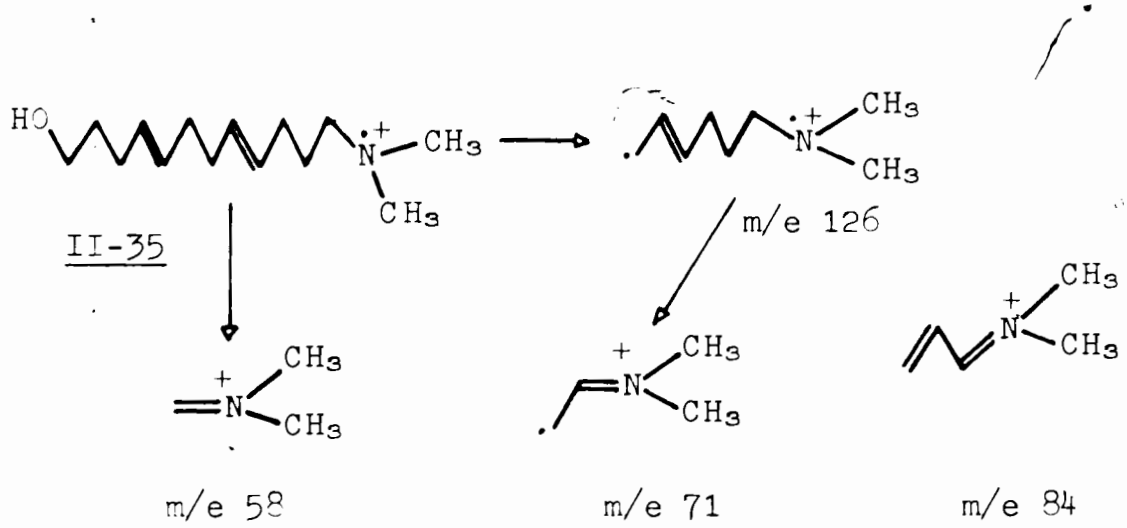


Figure II-5 Mass spectra (80eV) of 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-ols (II-34a and II-34b) and 12-dimethylamino-trans,trans-4,8-dodecadien-1-ol (II-35)

was shown by elemental analysis and high resolution mass spectrometry to have the molecular formula $C_{14}H_{27}NO$. It exhibited ir bands at 3380 and 1060 cm^{-1} (C-OH), at 3020 and 970 cm^{-1} (trans olefin), but no absorption near 700 cm^{-1} for a cis double bond(78). The ^{13}C nmr spectrum of II-35 (Table II-2) exhibited nine lines. The signal at 129.9 ppm was very intense in comparison with other peaks and was attributed to three olefinic carbons. The methylene carbons at 61.6 (t,C_1) and 59.1 (t, C_{12}) ppm were assigned by analogy with reported ^{13}C chemical shift data (77,79). The ^1Hnmr indicated four olefinic protons at τ4.56 and the CH_3N signal at τ7.78 (s, 6H); the methylene protons adjacent to the hydroxyl and dimethylamino groups were seen as simple triplets at τ6.39 and 7.03, respectively. The mass spectrum of II-35 (Figure II-5) exhibited a molecular ion peak at m/e 225 and showed mass peaks that might be derived from the fragmentation pattern as depicted in Scheme II-6. The hydrochloride of II-35 gave the correct analysis for $C_{14}H_{28}NOCl$.



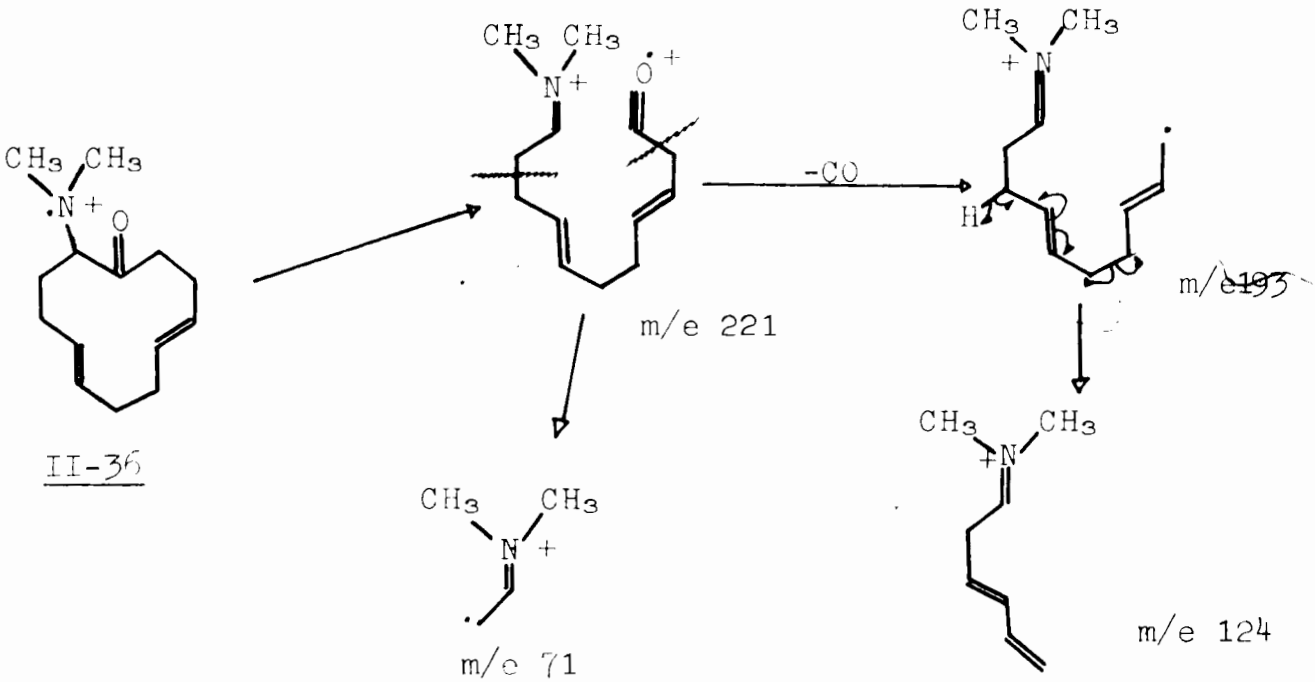
Scheme II-6

The volatile amine II-33 had a mass spectrum identical to that of a sample synthesized independently (vide infra). It codistilled with methylene chloride on a rotary evaporator. Amine II-33 showed the correct molecular ion at m/e 207 and fragment peaks typical for a dimethylamino moiety at m/e 84,71 and 58. Its infrared spectrum exhibited characteristic bands at 2850,2820 and 2770 cm^{-1} (Bohlmann) and at 3020 and 960 cm^{-1} (trans olefin), but no absorption of a cis double bond near 700 cm^{-1} (78).

Amino ketone II-36 gave correct elemental analysis and exact mass for an M^+ ion of $C_{14}H_{23}NO$. The ir spectrum of II-36 showed absorptions at 2940, 2920 and 2860 cm^{-1} (Bohlmann), at 1715-1720 cm^{-1} (C=O) and at 975 and 960 cm^{-1} (trans olefin), but not near 700 cm^{-1} (cis olefin) (78). This compound gave one spot on tlc and one peak on gc. Its proton nmr spectrum showed a sharp singlet at τ7.80 for the N-methyl groups, four olefinic protons at τ4.90 and 5.04 and a complex two protons multiplet at τ7.08 probably due to the C_2 and one of the C_{12} protons. The ^{13}C nmr signals were assigned as shown in Table II-2. The mass spectral (FigureII-6) fragmentation pattern of II-36 can be explained as shown in Scheme II-7. The methyl iodide of II-36 gave the correct analysis for $C_{15}H_{26}INO$ and ir absorption at 1715 cm^{-1} (C=O). The reaction of amino ketone II-36 with hydroxylamine hydrochloride in basic conditions gave syn-amino oxime II-31 and its LAH reduction gave a mixture containing alcohols II-34a (14%) and II-34b (72%).

The basic fraction of photolysis did not show any discernable

changes in its respective ir and nmr spectra when treated with aqueous acid or base (pH ~10). The LAH reduction of the recovered crude products gave nearly identical mixtures as those without treatment. Treatment of the crude basic fraction with sodium borohydride gave a product which showed the strong absorptions of the nitrate group but no carbonyl absorption (1715 cm^{-1}). This indi-



Scheme II-7

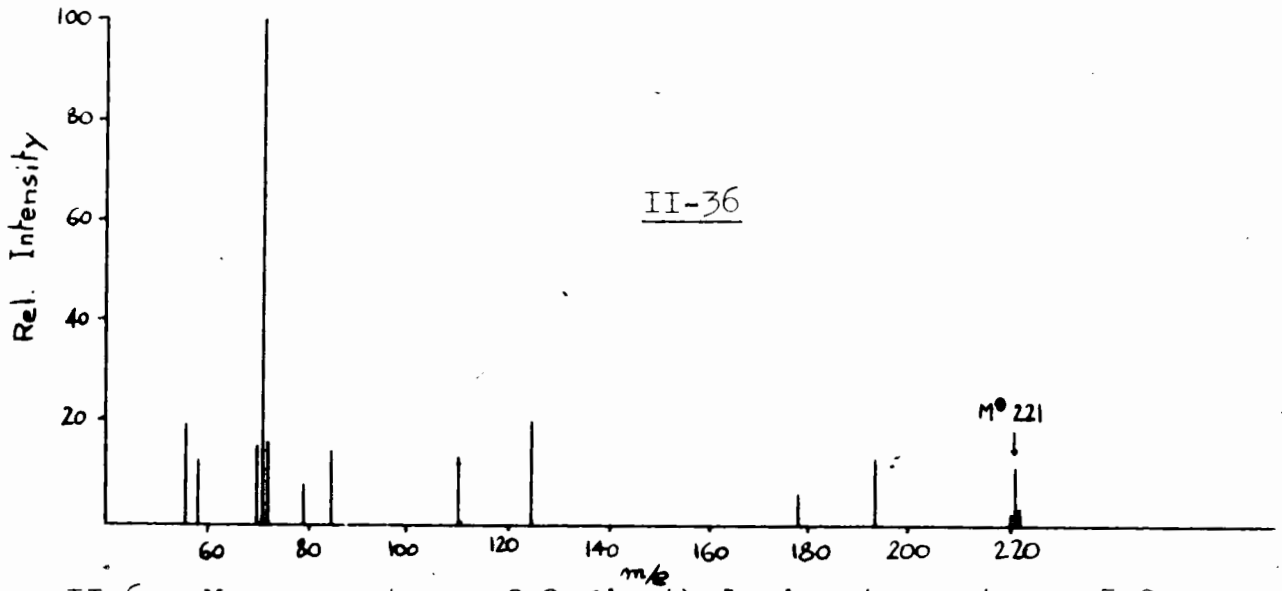


Figure II-6 Mass spectrum of 2-dimethylamino-trans,trans-5,9-cyclodecadien-1-one (II-36)

cated that the nitrate group is very resistant to this reducing agent. Chromatography of the crude product gave 1-nitrato-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-37a). The molecular ion at m/e 268 and analysis agreed with the molecular formula $C_{14}H_{24}N_2O_3$. It showed infrared absorptions at 3020 and 960 cm^{-1} (trans olefin), at 1620, 1275 and 855 cm^{-1} (ONO_2) and at 2850, 2820 and 2780 (Bohlmann bands). The ^{13}C (Table II-2) and proton (Table II-3)nmr spectra exhibited signals in consonance with II-37a. Hydrazine hydrate reduction of II-37a catalyzed with Pd/C (80) gave amino alcohol II-34a in good yields; the configuration at the C_1 and C_2 was therefore the same. This was also indicated by the large coupling constant $J_{1,2}$ = 7.5 Hz observed at the C_2 proton (τ7.24, dt, J=7.5, 7.5 and 4.0Hz), which was the same magnitude with that of II-34a (Table II-3). The mass spectrum of II-37a showed a molecular ion at m/e 268 and the (M^+-NO_2) peak at m/e 222 as the base peak.

Another fraction of the previous chromatography gave a mixture of amino alcohols II-34a, II-34b and a nitrate ester, as seen by ir bands at 1620, 1270 and 860 cm^{-1}. The nmr spectrum of this fraction exhibited singlets at τ7.60 (II-34a), 7.71(II-34b) and 7.76 in the 3:1:2 ratio; the last one was probably due to the other nitrate ester isomer II-37b. Reduction of this fraction with LAH gave a mixture which showed a nmr spectrum containing a triplet at τ6.40 (J=6.5Hz, II-35) and the singlets at τ7.60 (II-34a),7.71 (II-34b) and 7.78 (II-35) in a 2:1:1 ratio. These two ratios indicated that the unisolated amino nitrate ester II-37b was

present in the photolysate and that ca 75% of II-37b was cleaved during the LAH reduction.

The basic fraction was also reduced by hydrazine hydrate in the presence of Pd/C (80) to give a mixture of isomeric amino alcohols II-34a and II-34b in a 1:3.5 ratio as indicated by its nmr spectrum. Since under these conditions, ketone II-36 did not give alcohols, the ratio represents the ratio of nitrates II-37b and II-37a.

When pure amino nitrate ester II-37a was reduced with LAH, it yielded the open chain amino alcohol II-35 (82%) and amino alcohol II-34a (6%) in a 1:11 ratio as indicated by the intensities of the singlets at τ7.60 (II-34a) and 7.78 (II-35). Since the reduction of nitrate esters gives the corresponding alcohols without disturbing their stereochemistry (81), II-37a and II-34a were further proved to have the same configuration at the C_1,C_2 bond. Furthermore, this also indicated that II-37a was cleaved during the metal hydride reduction.

When oxidative photoaddition was carried out in the presence of a four fold and ten fold excess of NND and the crude products reduced with LAH, the yields of open chain alcohol II-35 increased significantly and those of amino alcohols II-34a and II-34b decreased (Table II-4).

Compound \ ratio tttCDT/NND	1:1	1:4	1:10
II-33	1[a] (<1[b])	8 (6)	9 (7.5)
II-35	30 (25)	54 (41)	58 (49)
II-34a	49 (41)	20 (15)	18 (15)
II-34b	15.5(13)	13 (9)	10 (8.5)

a, yields based on relative areas of all gc peaks.

b, yields estimated from total fraction and based on starting tttCDT.

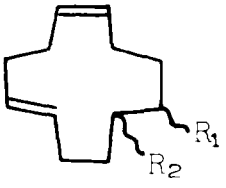
Table II-4: yields of products obtained from the photolyses of NND with tttCDT followed by LAH reduction.

II-2-5. To cis,trans,trans-1,5,9-cyclododecatriene

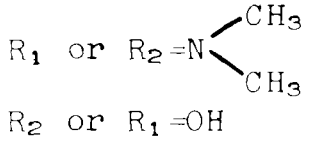
The acidic photolysis of NNOD (or NND) in the presence of cttCDT and oxygen gave a neutral fraction containing mostly the starting olefin with its tttCDT isomer (5%) indicating that isomerization took place during the photolysis.

The basic fraction exhibited strong infrared absorptions at

1630, 1280 and 980 cm^{-1} (ONO_2), at 3400 and 1035 cm^{-1} (C-OH), a medium band at 1710 cm^{-1} (C=O) and at 705 cm^{-1} (cis olefin). This fraction was immediately reduced with LAH to give a complex fraction containing low yields of II-34a, II-35 and possibly II-34b, the products from addition to the cis double bond, and 2-dimethylamino-cis,trans-5,9-cyclododecadien-1-ol (II-38a, 33%) and 12-dimethylamino-cis,trans-4,8-dodecadien-1-ol (II-39, 15%), the addition products to the trans double bond in good yields. The former group of compounds might also arise from addition to ttt CDT obtained from isomerization of the ctt CDT.



II-38a



II-39

The samples of II-38a and II-39 obtained from chromatography gave the expected ^{13}Cnmr spectra (Table II-2) as compared with the analogues II-34a, II-34b and II-35; this indicated that they are homogeous and the addition was regiospecific although the precise regiochemistry could not be obtained. The amino alcohol II-38a had a correct elemental analysis and gave a correct exact mass for $C_{14}H_{25}NO$. It showed ^{1}Hnmr comparable with that of II-34 (Table II-3) and the same mass spectral fragmentation as II-34 differing only in the relative abundance (Figure II-7).

Elemental analysis as well as high resolution mass spectro-

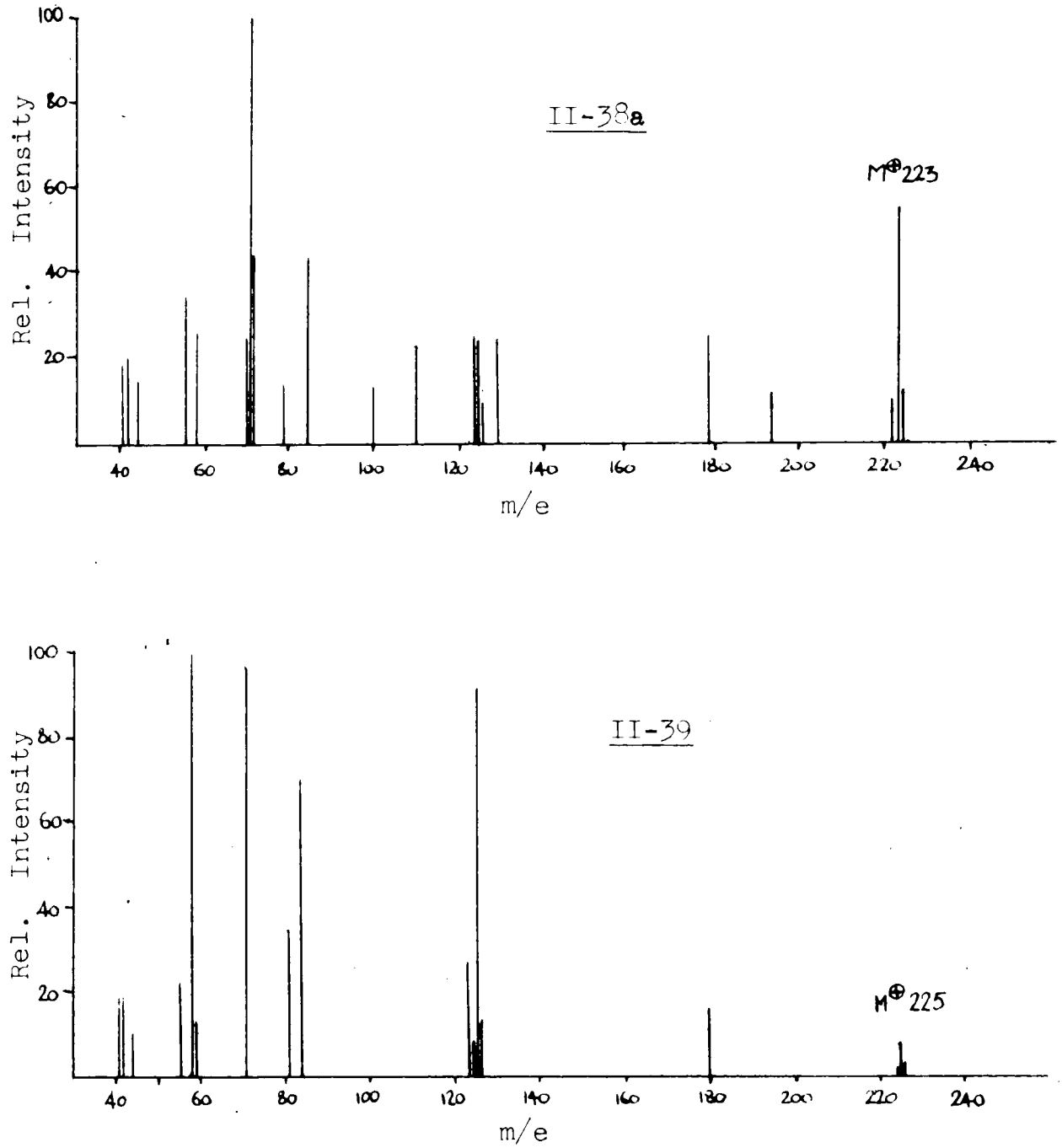


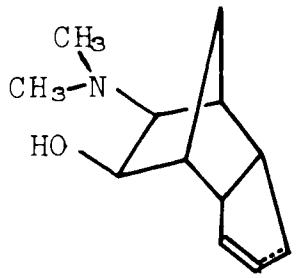
Figure II-7: Mass spectra (80eV) of 2-dimethylamino-cis,trans-5,9-cyclododecadien-1-ol (II-38a) and 12-dimethylamino-cis, trans-4,8-dodecadien-1-ol (II-39)

metry established the molecular formula of open chain amino alcohol II-39 as $C_{14}H_{25}NO$. Its infrared spectrum exhibited absorptions at 3380 and 1055 (C-OH) and at 965 and 700 cm^{-1} for a trans and a cis double bond, respectively (78). The ^{1}Hnmr and mass (Figure II-7) spectra were comparable to those II-35.

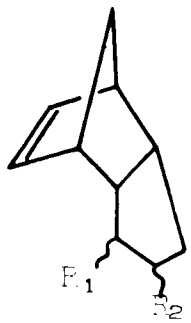
II-2-6. To endo-dicyclopentadiene

Photolysis of an acidic (HCl) methanol solution of NNOD (or NND), endo-DCPD under oxygen gave a very complex neutral fraction which was not investigated further. Neutralization at 0° followed by immediate extraction gave a crude mixture showing strong infrared absorptions at 1625, 1280 and 860 cm^{-1} (ONO_2), at 2730 and 1720 cm^{-1} (CHO) and at 3400 and 1030 cm^{-1} (C-OH). Olefinic protons were seen in the nmr spectrum at τ3.76 and 4.37 in a 1:1 ratio typical of norbornene and cyclopentene double bonds, respectively (82,83). This structural feature was also suggested by the ir bands at 3050 cm^{-1}, 750 (norbornene) and 700 cm^{-1} (cyclopentene) (84).

Immediate reduction of the crude basic fraction with LAH gave trans,cis,trans-2,4-bis-hydroxymethylbicyclo[3.3.0]oct-6-ene (II-40, 21%), exo-9-dimethylamino-endo-tricyclo[5.2.1.$0^{2,6}$]-3-decen-exo-8-ol (II-41,25%) and a compound postulated to be 4-dimethylamino-endo-tricyclo[5.2.1.$0^{2,6}$]-8-decen-3-ol (II-42, 8%); most polar compound was isolated as a mixture with II-41. Two other unidentified minor compounds were detected by gc but were not investigated further.

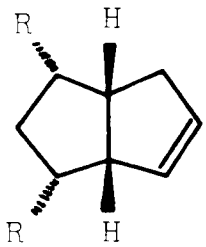


II-41



R_1 or R_2=OH
R_2 or R_1=$N(CH_3)_2$

II-42



R= CHO , II-43

R= CH_2OH, II-40

The high resolution mass spectrum of II-41 indicated a molecular ion at m/e 193.1465 in agreement with a molecular formula $C_{12}H_{19}NO$. The ir spectrum of II-41 indicated the presence of a cyclopentene double bond (708 cm^{-1}), a hydroxy group (3300 and 1070 cm^{-1}) and a dimethylamino moiety (2880, 2830, 2782 and 1030 cm^{-1}). The nmr spectrum of II-41 (Figure II-8) showed the olefinic protons at τ4.38 and 4.53, typical of a cyclopentene double bond (82,83). The endo-cis orientation of the C_8 and C_9 protons was indicated by the coupling constant of $J_{H_8-H_9}$= 6Hz (85). The C_8 endo proton was also coupled with the C_{10} *anti proton through the long range "W-plan" coupling (J=1.5Hz)(85) and with the C_1 proton (J=1.5Hz). The C_9 endo proton was weakly coupled with the

*The anti structure in this molecule is defined relative to the C_8,C_9 carbons.

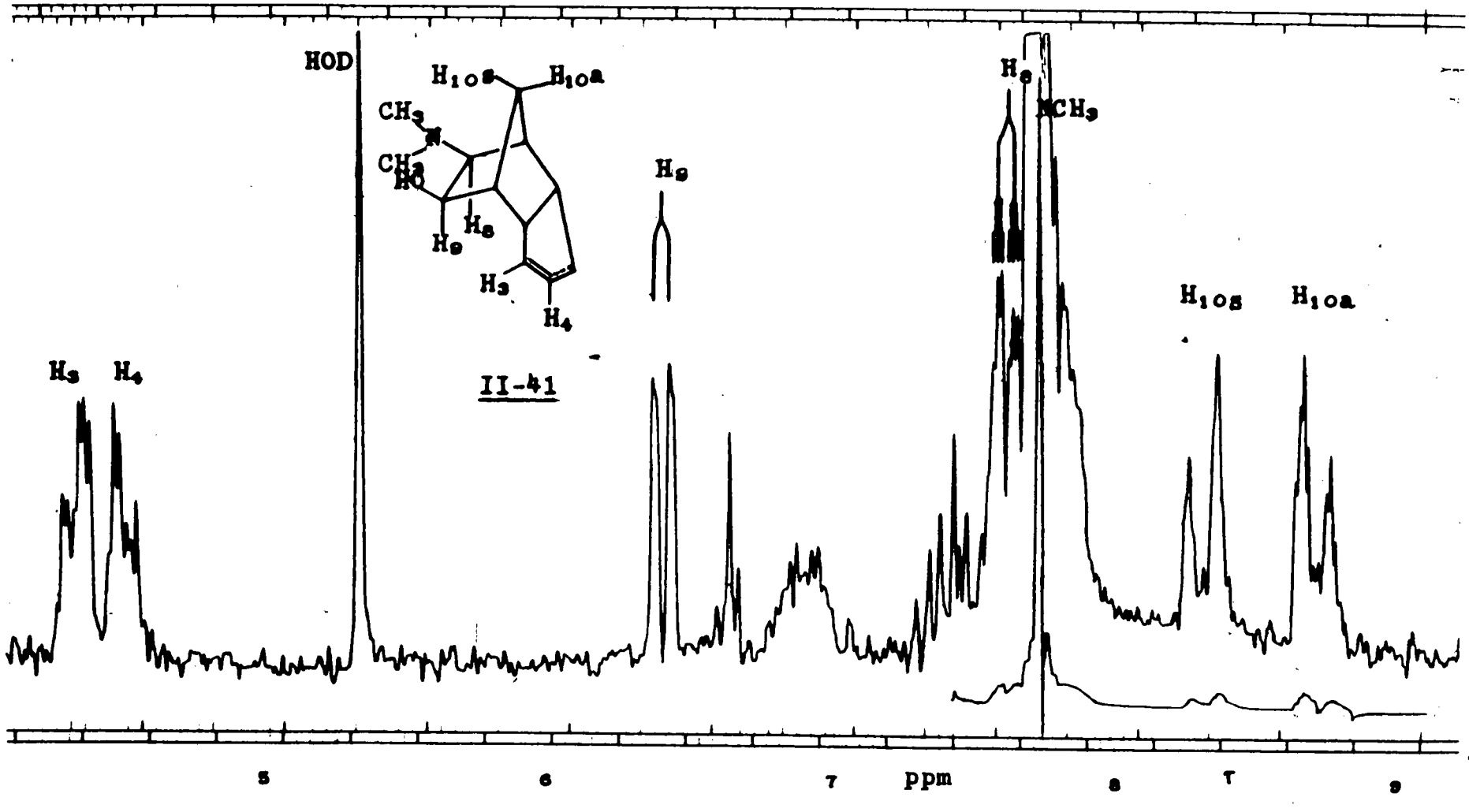
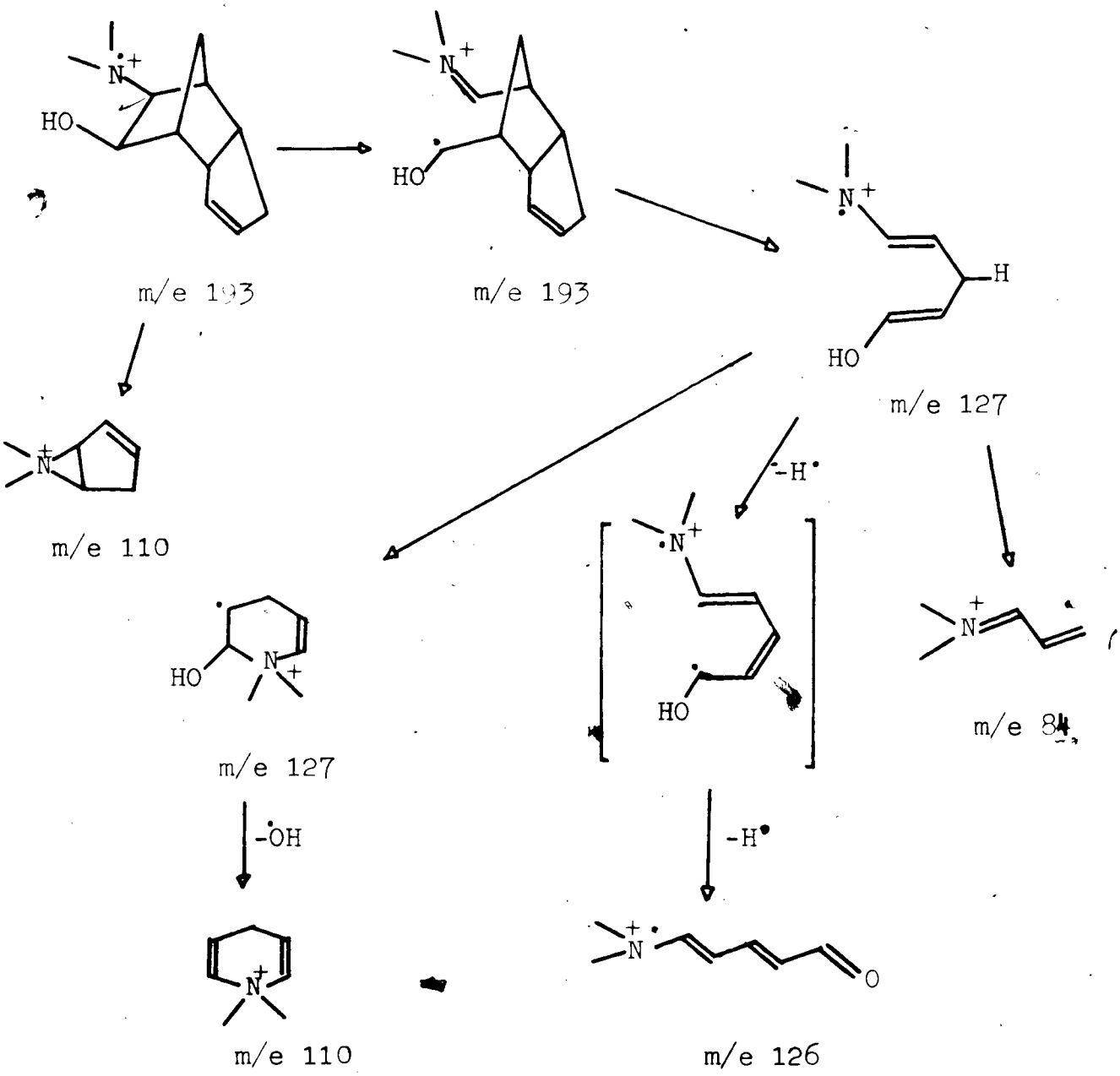


Figure II-8: D_2O exchange ^{1}Hnmr spectrum (100MHz) of exo-9-dimethylamino-endo-tricyclo [5.2.1.$0^{2,6}$]-3-decen-exo-8-ol (II-41)

C_{10} anti and C_1 protons; the last two couplings could not be measured directly but were approximated to account for the broadening observed in the C_8 axial signal. A possible mass spectral fragmentation pattern is shown in Scheme II-8 and Figure II-9.



Scheme II-8

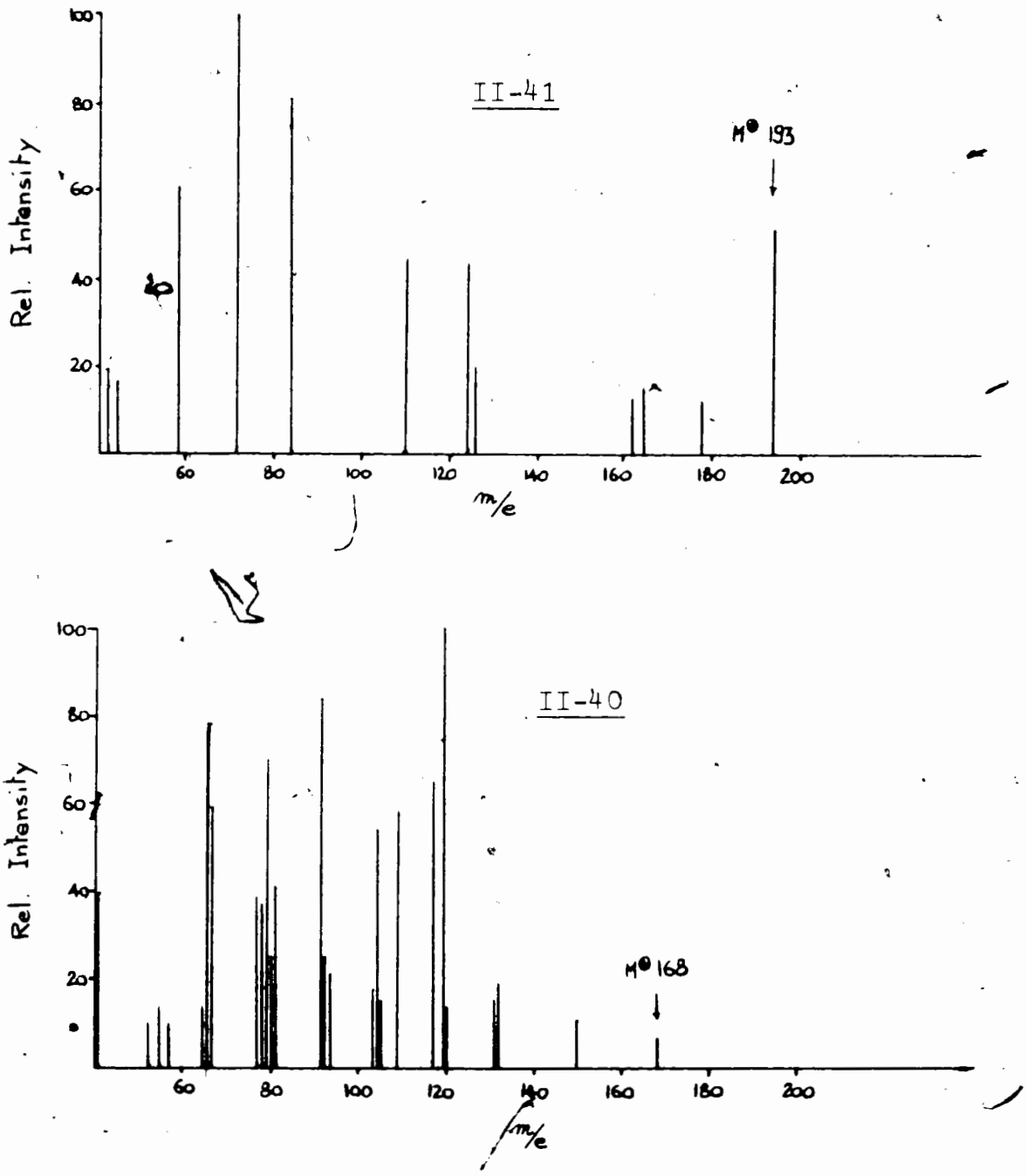


Figure II-9: Mass spectra (80eV) of exo-9-dimethylamino-endo-tricyclo[5.2.1.$0^{2,6}$]-3-decen-exo-8-ol (II-41) and trans, cis,trans-2,4-bis-hydroxymethylbicyclo[3.3.0]oct-6-ene (II-40)

The structure for II-42 is postulated on the basis of the following data obtained from a 1:1 mixture with II-41. A gc-ms showed that II-42 is an isomer of II-41 having the same M^+ at m/e 193. The nmr spectrum of this isomeric mixture contained a multiplet at τ3.80 for the double bond in norbornene (82,83) and a singlet at τ7.67 fot the dimethylamino moiety of II-42.

High resolution mass spectrometry established the molecular formula of diol II-40 as $C_{10}H_{16}O_2$. It showed ir absorptions at 3350, 1065 and 1020 cm^{-1} (C-OH); the nmr spectrum (Figure II-10) showed two exchangeable protons near τ7.7, two olefinic protonsat τ4.30 and 4.42 and two doublets (J=7Hz) at τ6.34 and 6.41 for the two non-equivalent hydroxymethyl groups. While the trans,cis,trans configuration derived from trans,cis,trans dialdehyde II-43 was assigned for II-40, the stereochemistry is not rigourously determined. The mass spectrum of II-40 (Figure II-9) showed the molecular ion at m/e 168. The presence of this compound was further confirmed by isolation of its bis-p-nitrobenzoate derivative which gave correct elemental analysis for $C_{24}H_{22}N_2O_8$.

When the crude basic fraction containing the aminonitrates was allowed to decompose under acidic conditions, (pH<2 and pH 4) the major decomposition product was found to be dialdehyde II-43 (or its epimer) in only ca 2 % and ca 4 % yields, respectively. Compound II-43 was isolated as a 3:1 mixture with an unknown product. It showed absorptions at 1720 and 2730 cm^{-1} and clear nmr doublets of the same intensity at τ0.28 (J=1.5Hz) and 0.34 (J=2.5Hz) for the aldenydes. This compound was tentatively as-

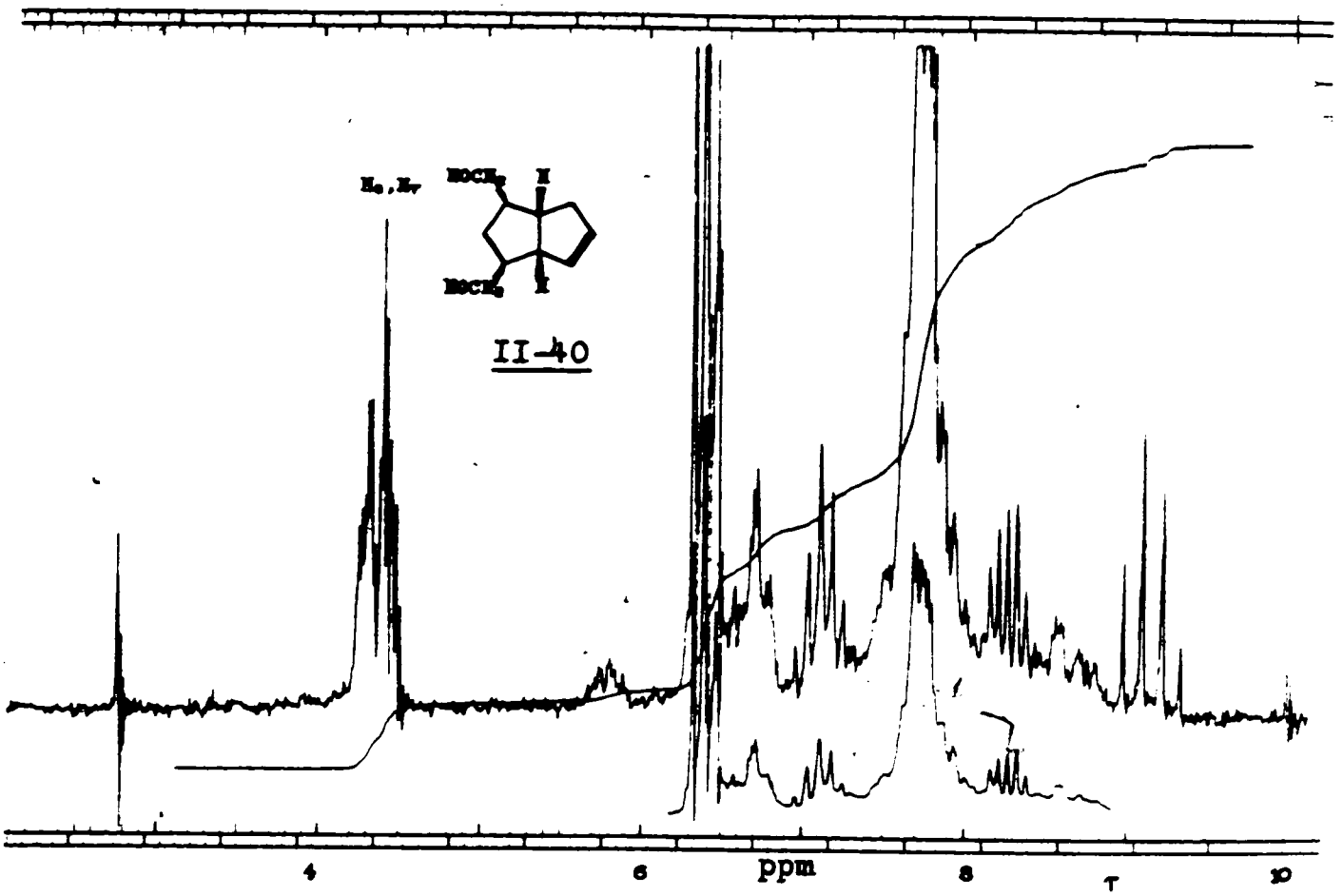


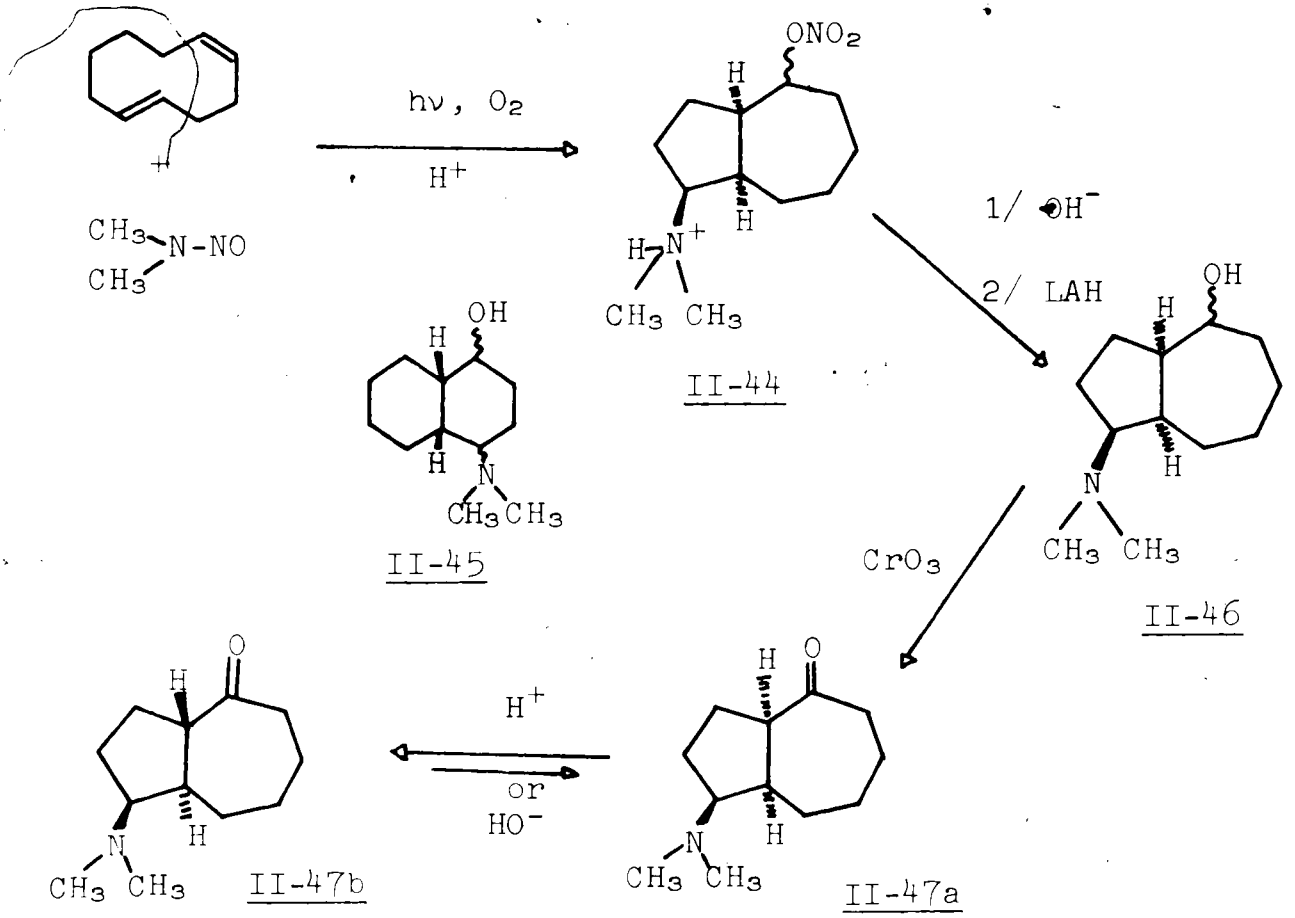
Figure II-10: ^{1}Hnmr spectrum (100MHz) of trans,cis,trans-2,4-bis-hydroxymethylbicyclo[3.3.0]oct-6-ene (II-40)

signed a trans,cis,trans configuration but epimerization may have occurred. The expected M^+ ion for $C_{10}H_{12}O_2$ at 164 was observed during gc-ms analysis. When the basic fraction was treated in basic conditions (pH 10) the resulting fraction still showed strong ir absorptions at 1625, 1280 and 860 cm^{-1} for a nitrate ester group. After LAH reduction, it yielded diol II-40 (10%) and amino alcohols II-41 (29%) and II-42 (5%) as the major products along with several other unidentified minor components.

II-2-7. To cis,trans-1,5-cyclodecadiene

Photolysis of a methanolic solution of NND in the presence of perchloric acid and 1,5-cyclodecadiene under oxygen atmosphere exhibited the expected zero-order decrease of the nitrosamine absorption at 345 nm. The photolysis resulted in the formation of saturated nitrate ester compounds (ca 78%) as the major products in addition to small amounts (ca 5%) of unsaturated products.

The perchlorate salt of the nitrate ester (32%) crystallized from the photolysate and has been tentatively identified as 2-nitrato-8-dimethylamino-cis-bicyclo[5.3.0]decane (II-44a), one of the two possible isomers at C_2 (Scheme II-10). For reasons to be discussed, it was assumed that transannular 5-7 ring closure had occurred to give a cis-fused compound as opposed to trans-fused compounds; for convenience the description of the chemistry will be based on this structure. Compound II-44a analyzed correctly for $C_{12}H_{23}N_2O_7Cl$ and exhibited the characteristic ir bands of a nitrate ester at 1605, 1290 and 890 cm^{-1}. The ^{13}Cnmr chemical



Scheme II-10

shifts of II-44a can be seen in Table II-5 along with other bicyclo[5.3.0] derivatives. While in deuterated methanol II-44a exhibited two non-equivalent CH_3 carbons at 42.0(q) and 41.8(q) ppm, it showed one peak at 42.0(q) ppm in DMSO-d_6. The 400 MHz ^{1}H nmr spectrum* (Figure II-11 and Table II-6) showed no olefinic hydrogens but a broad doublet of doublets (J= 10.4, 10.0 and ≤0.6Hz) at τ5.17 for the C_2 proton. The signal at τ7.46 for the

*We are grateful to Dr T. Nahashima from the University of Alberta, Edmonton, for the 400MHz ^{1}Hnmr spectra.

Table II-5: ^{13}Cnmr spectra of bicyclo[5.3.0]decane derivatives

	II-44a in DMSOd_6	II-44a in CD_3OD	II-46a	[a] II-46b	II-47a	[b] II-47b	[c] II-48a	II-48b
C_2	89.4 d	88.2 d	76.2 d	73.3 d	211.9 s	211.8 s	162.1	161.5 s
C_8	73.8 d	74.1 d	75.5 d	71.6 d	73.6 d	71.9 d	71.3	74.9 d
[d] C_1	45.1 d	44.8 d	51.0 d	47.5 d	54.6 d	54.6 d	40.2	48.1 d
[d] C_7	39.5	39.4 d	44.3 d	43.3 d	41.9 d	45.0 d	38.7	44.8 d
[e] C_3	32.9 t	32.5 t	38.8 t	33.9 t	42.4 t	42.9 t	31.1	32.6 t
[e] C_4	31.1 t	30.7 t	32.3 t	31.7 t	32.2 t	34.6 t	30.7	29.6 t
[e] C_5	28.8t,2C	28.2t,2C	30.2 t	26.8 t	28.0 t	28.4 t	28.4	29.3 t
[e] C_6			29.9 t	26.6 t	26.5 t	22.7 t	28.0	28.0 t
[e] C_7	27.0 t	26.7 t	28.5 t	26.0 t	24.8 t	22.2 t	27.3	26.0 t
[e] C_8	26.4 t	25.7 t	27.6 t	24.6 t	23.4 t	20.7 t	24.2	25.0 t
NCH_3	42.0 q	42.0 q 41.8 q	43.1 q	42.2 q	42.4 q	40.5 q	42.3	43.2 q

a, as a mixture with II-46a; b, as a mixture with II-47a; c, as a mixture with II-48b; d, can be interchangeable; e, can be interchangeable

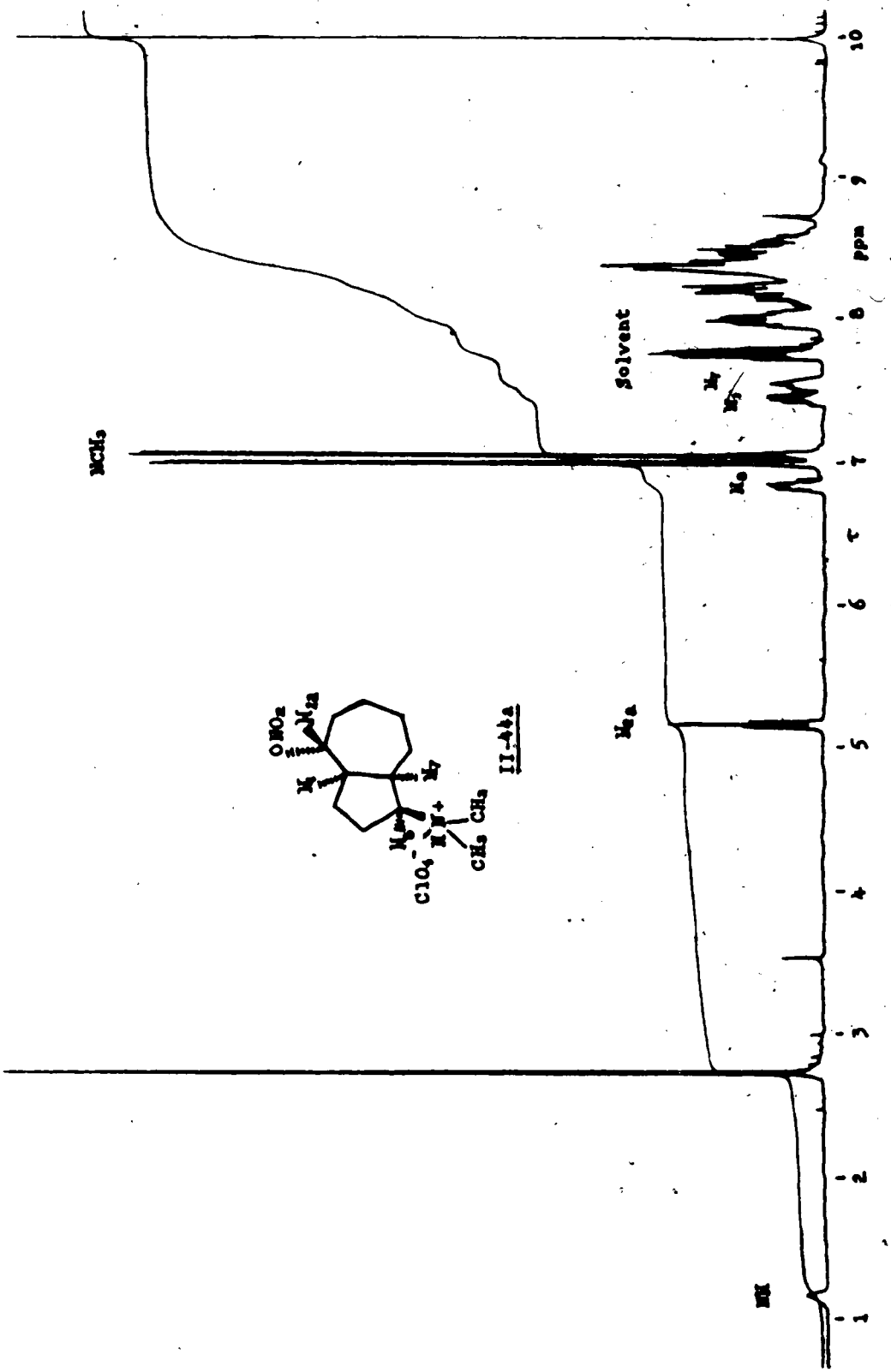


Figure II-11: ^{1}Hnmr spectrum (400MHz) of the perchlorate of 2-nitrato-8-dimethylamino-cis-bicyclo[5.3.0] decane (II-44a).

TABLE II-6

Chemical shifts (τ) and coupling constants (Hz) of the perchlorate of 2-nitrato-8-dimethylamino-cis-bicyclo [5.3.0]decane (II-44a)

Proton	τ	J
H_1	7.46(dddd)	$^{a}J_{1-7}$=12.0, J_{1-2a}=10.4, $^{a}J_{1-10}$= 9.8, $J_{1-10'}$=5.4Hz (and ≤0.5Hz)
H_{2a}	5.17(ddd)	J_{2a-1a}=10.4, J_{2a-3a}=10.0 and J_{2a-3e} ≤0.6Hz
H_3	8.01(m)	
H_4,H_5,H_6,H_{10}	8.32-8.64(m)	
H_7	7.56(m)	3 big couplings ≈10-12Hz (and small couplings ≤1Hz)
H_8	6.85(m)	2 big couplings ≈10-12Hz, 1 medium coupling ≈6-7Hz (and small couplings ≤1Hz)
H_9	8.22(m)	
NCH_3	7.015(d) 7.08 (d)	J_{CH_3-H} = 5.0Hz J_{CH_3-H} = 5.0Hz
NH	1.06(bs)	

a, may be interchangeable.

C_1 proton was analyzed as indicated in Figure II-12 and shown to possess three big and a medium coupling constants; these couplings were consistant with structure II-44a but not with the alternate structure II-45. As shown with Dreiding Models of II-44a, the C_1 proton had dihedral angles nearly zero with H_7 and H_{10}, 180° with H_{2a} and 120° with $H_{10'}$, explaining the observed coupling patterns; only one diaxial (180°) coupling of ca 10Hz should be observed with structure II-45 since all other dihedral angles are nearly 60° ($J \leq 6$Hz). Since the C_8 proton at τ6.85 showed two big coupling constants ($J_{H_8-H_7}$ and $J_{H_8-H_9} \simeq$ 10-12Hz) and one medium coupling constant ($J_{H_8-H_{9'}} \simeq$ 6-7Hz), this proton was believed to be trans to the ring juncture, placing the dimethylamino moiety cis to the ring juncture.

The lithium aluminium hydride reduction of the crude basic fraction gave mostly the two isomers at the C_2 carbon, the 8-dimethylamino-cis-bicyclo[5.3.0]-2-decanols (II-46a and II-46b) in 65 and 13% yields, respectively, in addition to 5% of an unknown product. The major amino alcohol II-46a gave the expected elemental analysis as well as the correct high resolution mass spectrum for the molecular formula $C_{12}H_{23}NO$. The ^{13}Cnmr spectrum of II-46a (Table II-5) showed eleven lines in which the C_2 and C_8 carbons resonated at 76.2(d) and 75.5(d)ppm, respectively; they were considerably deshielded in comparison with chemical shifts of 64-69 and 58-64ppm for carbons carrying a hydroxyl and a dimethylamino group, respectively (vide supra,77). As the LAH reduction of II-44a yielded alcohol II-46a, their stereochemistry

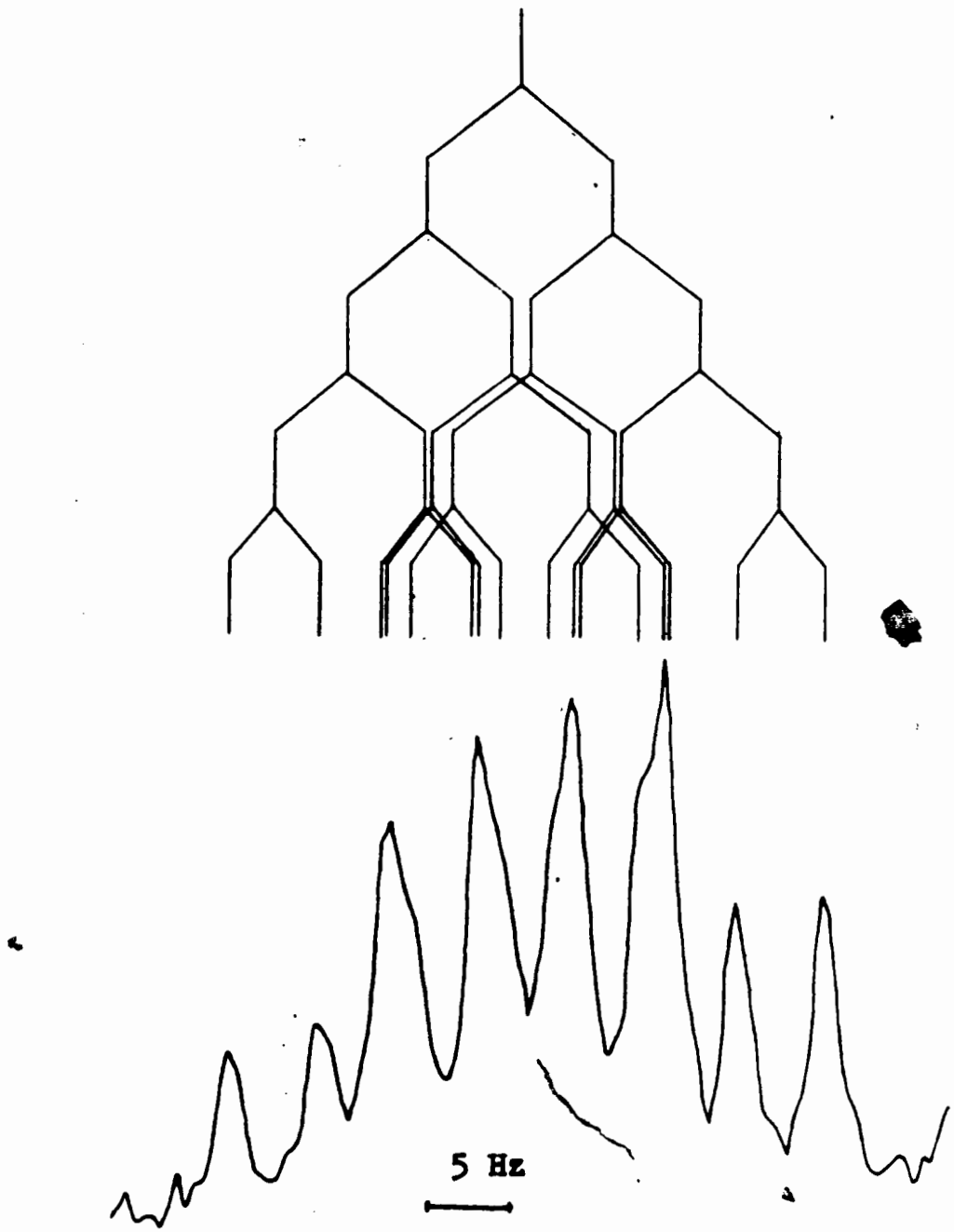


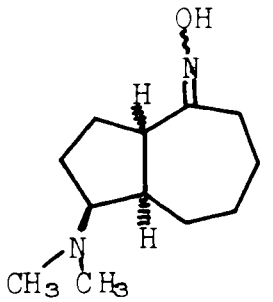
Figure II-12: ^{1}Hnmr (400MHz) expansion spectrum of the C_1 proton of the perchlorate of 2-nitrato-8-dimethylamino-*cis*-bicyclo[5.3.0]decane (II-44a).

must be identical. The minor amino alcohol II-46b was obtained as a 2:1 mixture with II-46a. The ir and 60MHz ^{1}Hnmr spectra of this mixture were very similar to those of pure II-46a. The ^{13}Cnmr signals of II-46b were obtained by mannual subtraction of those of II-46a from the spectrum of the mixture (Table II-5). Both of these isomeric amino alcohols gave the same mass fragments in gc-ms analysis of the mixture; only fragment ion intensities were different. In both cases, the most intense peak was observed at m/e 84 for $C_5H_{10}N$ and gave a molecular ion at m/e 197 corresponding to $C_{12}H_{23}NO$.

The oxidation of either alcohol II-46a or mixture of isomers II-46 with Jones' reagent (86) gave a single ketone, 8-dimethylamino-cis-bicyclo[5.3.0]-2-decanone (II-47a). It showed the correct molecular ion at m/e 195 for $C_{12}H_{21}NO$, an ir absorption at 1703cm^{-1} (C=O) and a nmr singlet at τ7.73 (NCH_3). Its ^{13}Cnmr spectrum (Table II-5) had the deshielded C_8 carbon at 73.6(d)ppm as observed in II-44 and II-46. The fact that both alcohols II-46 gave a single ketone on oxidation, unequivocally established that they were epimeric at C_2.

The bicyclic ketone II-47a, on treament either in acidic or basic solution gave a 2:3 equilibrium mixture of amino ketones II-47a and II-47b. The epimerization must have occurred at C_1 to give a trans-5,7-ring fusion in II-47b. The mixture of II-47a and II-47b could not be separated by chromatography, but showed two distinctive NCH_3 singlets at τ7.73 (II-47a) and τ7.76(II-47b) and two sets of ^{13}Cnmr signals (Table II-5).

The non-oxidative photoaddition of NND to 1,5-cyclodecadiene with a >350nm light resulted in the emergence of a new absorption band at ~300nm which increased steadily to a maximum after 7.5 hours and then decreased slowly on further irradiation. The photolysis was discontinued when the 300nm band reached its maximum intensity and the photolysate was worked-upto give a mixture consisting of ca 1:1 mixture of the two syn and anti-isomers of 2-oximino-8-dimethylamino-cis-bicyclo[5.3.0]decane (II-48)and several other unidentified minor compounds. Acid treatment of the crude photolysate gave anti-oxime II-48b (63%) and two amino ketones II-47 (22%). This indicated that the two isomers in the mixture were syn and anti-oximes and possessed the same structure otherwise.



syn , II-48a

anti , II-48b

II-48a $\xrightleftharpoons{H^+}$ II-48b

Amino oxime II-48b gave correct elemental analysis and exact mass for $C_{12}H_{22}N_2O$. Its ir spectrum showed absorptions at 3170, 955 and 910 cm^{-1} (C=NOH) and at 2820 and 2780 cm^{-1}(Bohlmann bands). The anti configuration was assigned to II-48b on steric grounds but neither ^{13}Cnmr (Table II-5) nor ^{1}Hnmr spectra were informative for structural determination. Hydrolysis of the pure amino oxime II-48b gave a 2:3 isomeric mixture of ketones II-47a and II-47b.

II-3. Transannular Electrophilic Reaction of Alkenyl Nitroso Compounds

II-3-1. Anti-dimer of cis-1-nitroso-2-chloro-5-cyclooctene

Nitrosyl chloride was prepared as a by-product in the preparation of potassium nitrate from potassium chloride and nitrogen dioxide (87) in the presence of water. Addition of a methylene chloride solution of nitrosyl chloride to 1,5-cyclooctadiene at low temperature gave a deep blue colour due to monomer II-51 (25,28) which was isolated as the dimer (or azodioxy compound) in relatively low yield (37-42%), due to its solubility and its irreversible tautomerization to the corresponding oxime chlorides II-52 (vide infra). The colourless dimer of II-51 analyzed correctly for $(C_8H_{12}NOCl)_2$. The uv absorption at 294nm (ε_{max} 6250) and the ir absorptions at 1238 and 1208 cm^{-1} indicated the anti-configuration for the azodioxyl group (31,35). The ir spectrum of II-51 also showed bands at 736 cm^{-1} (C-Cl) and 3020 cm^{-1} (olefin). The recrystallized dimer showed an eight line ^{13}Cnmr spectrum (Table II-7) indicating that the sample was homogeneous. Furthermore, each isolated crude product as well as the mother liquor of the reaction also showed this eight line pattern and other ^{13}Cnmr lines due to oximes II-52, but not for another dimer. This indicated that addition occurred stereo-

Table II-7: ^{13}Cnmr spectra of cyclooctene and 9-azabicyclic [3.3.1]nonane derivatives

	II-23a	Dimer of II-51	[a]II-52a	II-52b	[b]II-59	[c]II-60	[d]II-63	
C_1	71.1 d	67.8 d	158.8 s	160.2 s	166.9 s	59.4 d	51.6 d	C_1
C_2	65.6 d	61.0 d	56.0 d	60.2 d	59.6 d	66.7 d	71.8 d	C_2
C=C	131.1 d	131.0 d	130.6	129.4 d	129.7 d	55.2 d	47.1 d	C_5
	130.7 d	128.5 d	130.1	129.3 d	128.3 d	59.4 d	61.9 d	C_6
[e]C_3	35.3 t	35.7 t	33.9 t	36.9 t	36.2 t	27.6 t	29.1 t	[e]C_3
[e]C_4	24.0 t	27.3 t	31.9 t	25.9 t	27.1 t	23.3 t	26.6 t	[e]C_4
[e]C_7	23.8 t	21.8 t	22.3	22.8 t	21.7 t	21.6 t	24.9 t	[e]C_7
[e]C_8	21.2 t	21.6 t	21.0 t	22.1 t	21.3 t	19.4 t	18.9 t	[e]C_8
NCH_3	41.3 q					20.1 q	20.8 q	CH_3
CH_3					18.8 q	18.8 q		

a: as a mixture with II-52b; b: 167.3 s for the carbonyl carbon; c: 169.0 s and 168.4 s for the carbonyl carbons; d: 169.6 s for the carbonyl carbon; e: assigments may be interchanged

specifically to give only one product II-51, to which the cis-configuration was assigned. It also indicated that, while meso or dl dimers were possible, only one dimer, probably the more stable one was formed. The ^{1}Hnmr spectrum of the dimer of II-51 (Figure II-13) showed the C_1 and C_2 protons at τ4.57 and 5.48, respectively. Decoupling experiments (Figure II-13) indicated that they were not coupled to each other, in comparison to a large coupling constant observed for trans-II-23a (J_{1-2}=7Hz) suggesting a cis-configuration of the functional groups. The pseudo-axial orientation of the C_1 proton was indicated by a large coupling with the C_{8a} proton (J_{1-8a}=11.5Hz). The lack of big coupling for the C_2 proton signal ($W_{\frac{1}{2}}$=11Hz) suggested that it adopted a pseudo-equatorial orientation, in a staggered position with the respective C_3 protons. Such a conformation would place the chlorine in close proximity to the double bond and might cause the observed downfield shift (ca 0.25 ppm) of the olefinic protons in comparison with related compounds (τca4.45)(63).

II-3-2. Reactions of the dimer of II-51

Decomposition of a neat sample of the crude dimer of II-51 at room temperature for several weeks gave exclusively a 2:1 isomeric mixture of anti and syn chloro oximes II-52a and II-52b (Scheme II-11). The ^{1}Hnmr spectrum of the isomeric mixture exhibited the C_2 protons at τ5.68 and 5.40, respectively, as a doublet of doublets. The latter absorption was attributed to syn-oxime

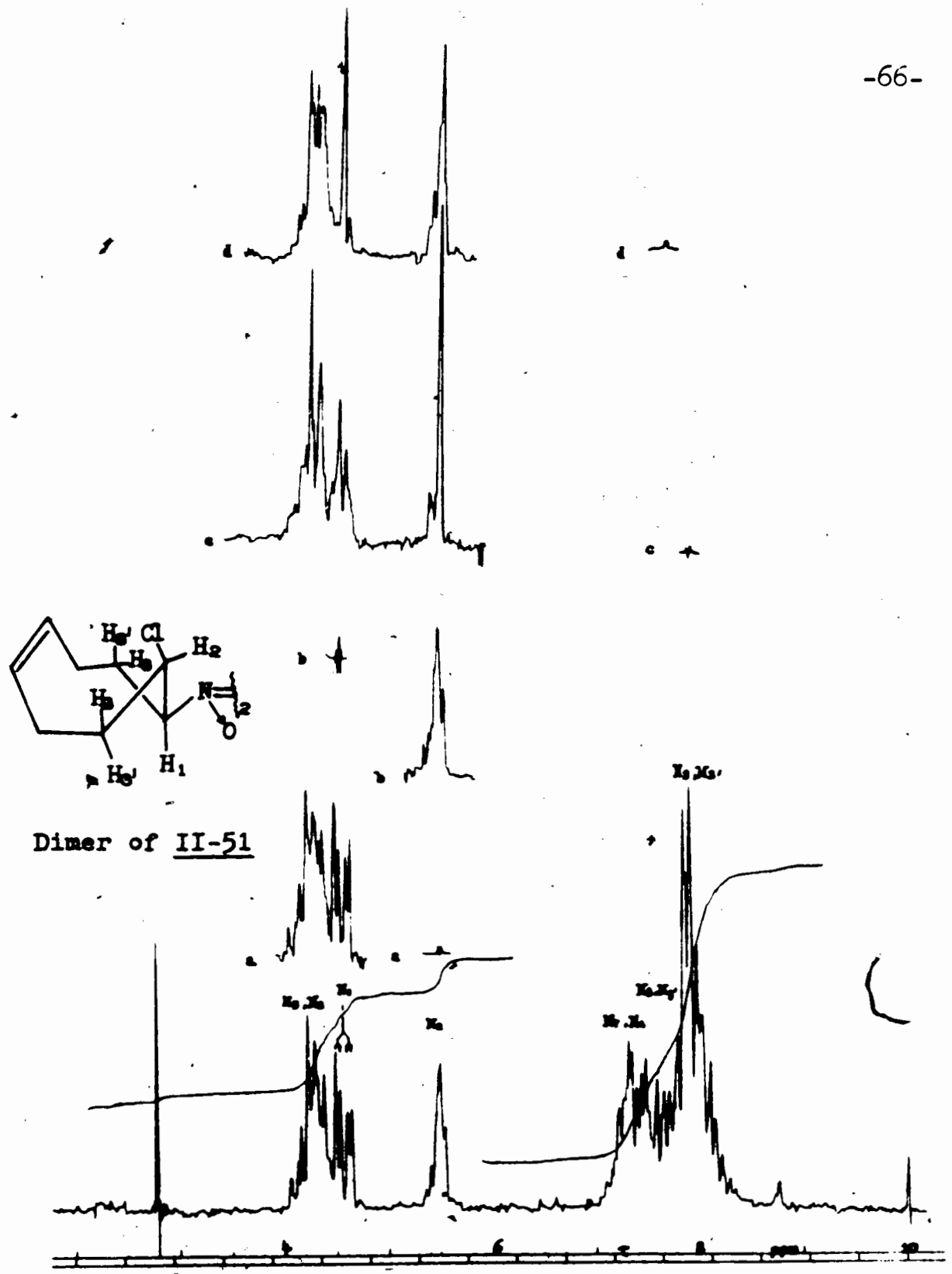


Figure II-13: ^{1}Hnmr spectrum (100MHz) of the anti-dimer of cis-1-nitroso-2-chloro-5-cyclooctene (Dimer of II-51)

a, double irradiation of the H_2 proton;

b, double irradiation of the H_1 proton;

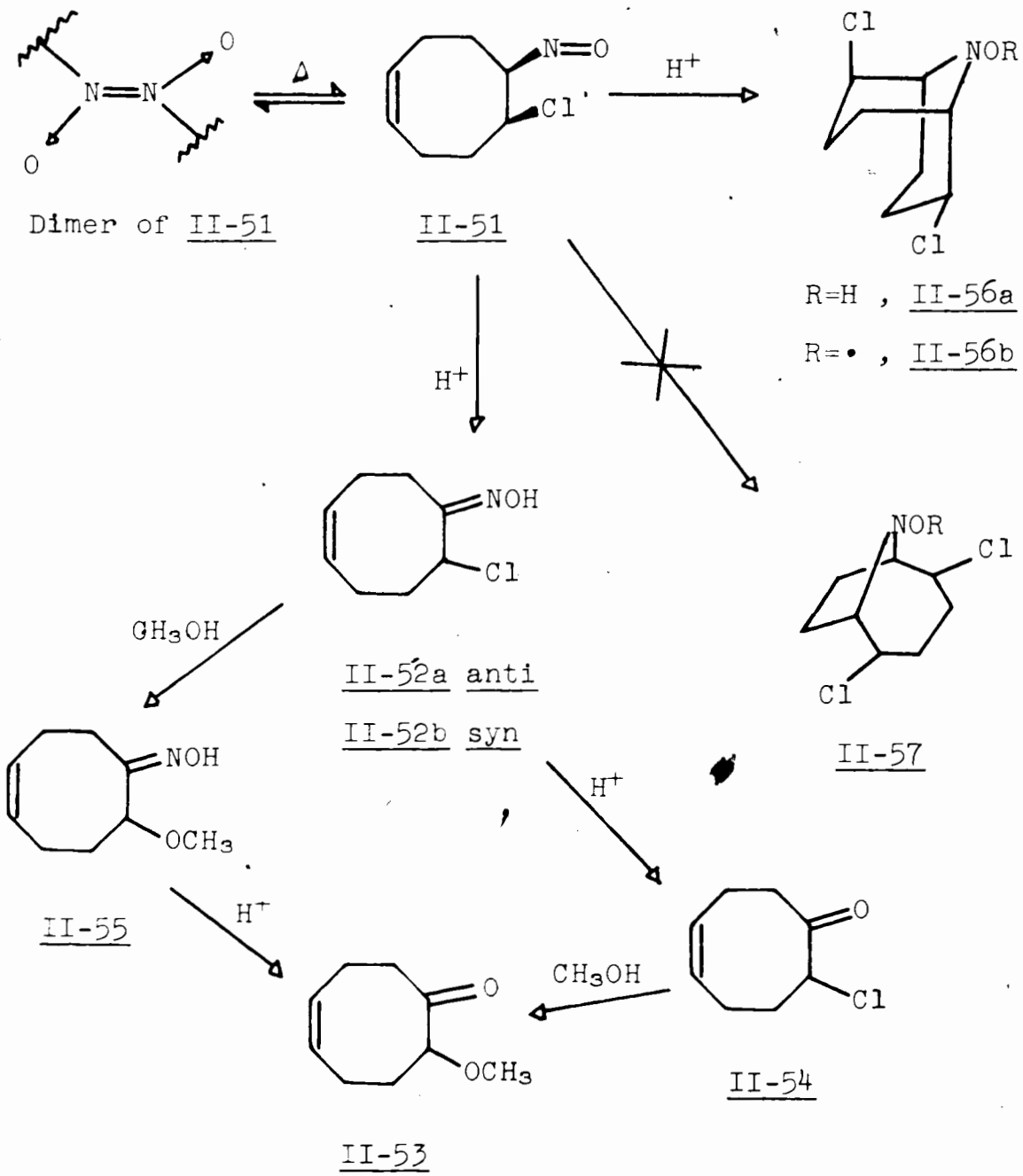
c, double irradiation of the C_3 protons;

d, double irradiation of the C_8 protons.

II-52b considering the anisotropic effect of the hydroxyl group (76). The ^{13}Cnmr spectrum of the mixture showed two sets of eight lines (Table II-7), one set of lines being relatively more intense than the other. Pure syn-1-oximino-2-chloro-5-cyclooctene(II-52b) contained the correct M^+ ion peaks at 175 and 173 and elemental analysis agreed with the molecular formula $C_8H_{12}NOCl$. The infrared spectrum exhibited absorptions at 3300, 1645, 985 and 900cm^{-1} (C=NOH); the nmr spectrum showed a doublet of doublets at τ5.40 (J=7.0 and 5.0Hz) for the methine proton, two protons multiplet for an olefinic bond at τ4.33 and an exchangeable proton at τ2.26.

(a) with hydrochloric acid: After removal of the dimer of II-51, the blue mother liquor was decomposed in methanol-hydrochloric acid to give a mixture which was characterized by gc-ms analysis as methoxy ketone II-53 (16%), chloro ketone II-54 (16%), methoxy oximes II-55 (38%), chloro oximes II-52 (6%), two unidentified products X (13%) and Y (4%) and 2,6-dichloro-9-hydroxy-9-azabicyclo[3.3.1]nonane II-56a (1%)(Scheme II-11). The two ketones II-53 and II-54 were isolated by preparative gc and their respective ir, nmr and mass spectra were in good agreement with the proposed structures (see Experiment Part). The methoxy oxime II-55 was identified by gc-ms and had a molecular ion peak at m/e 169 and an intense fragment at m/e 152 due to the loss of an OH.

Compound X was isolated by preparative gc as a colourless oil which decomposed on standing. The mass spectrum of this compound exhibited no obvious molecular ion; however it showed



Scheme II-11

fragments at m/e 162, 160 and m/e 134, 132, both with a one chlorine ratio. The ir spectrum of X exhibited absorptions at 3440, 3010, 1710 and 705 cm^{-1} suggesting the presence of a

hydroxyl group, a double bond, a carbonyl function and a chlorine atom, respectively. The nmr spectrum of X showed a two protons multiplet at τ4.46 attributed to the olefinic protons and two methine protons at τ5.70 and 6.09, the former being assigned to that geminal to a chlorine atom. No esr signal was detected for compound X.

The structure of hydroxylamine II-56a was postulated on the basis of its mass spectrum which did not show the molecular peak but base fragments at m/e 196, 194, 192 with a two chlorine pattern corresponding to a loss of OH, and fragments at m/e 132, 130 with a one chlorine pattern for a further loss of HCl. Two chlorine atoms in the molecule were in favor of a cyclized product and this was confirmed by the esr spectrum of the reaction mixture showing a broad triplet at g 2.0068 (a_N 17.2 G and line width 5.7 G) characteristic of a flexible bicyclic[3.3.1] nitroxide radical II-56b (62). The bicyclic[4.2.1] system II-57 was rejected due to the fact that rigid bicyclic[4.2.1] nitroxide radicals give well resolved patterns with hyperfine splitting constants $a_{H\alpha}$ 4.8-5.75G and aH_β -1.3+2.5G (62,88).

(b) with perchloric acid and methanol: The isolated dimer of II-51 was treated in a 1:4 mixture of methylene chloride-methanol containing small amount of perchloric acid at 40° for one day. By gc mixed injection, the neutral fraction was shown to contain chloro oximes II-52 (70%) as the major product, along with ketones II-53 and/or II-54 (1%) and methoxy oximes II-55 (15%).

A pure minor product (ca 5%) was obtained from the basic fraction. This white solid appeared to be [a] exo-2-chloro-endo-5-methoxy-9-hydroxy-9-azabicyclo[3.3.1]nonane (II-58a) based on the following spectra (Scheme II-12). Hydroxylamine II-58a had ir absorptions at 3200 and 1050 cm^{-1} (N-OH), at 1088 cm^{-1} (CH_3O) and at 910 cm^{-1} (C-Cl). The esr spectrum of II-58a showed a major broad triplet similar to II-56b and was attributed to II-58b (g 2.0073, a_N 17.5G and line width 5.5G). It is well known that hydroxylamines are easily oxidized in the presence of air to give the corresponding nitroxide radicals (89). The middle line of the triplet showed some hyperfine splitting which might be due to other radical species since the outside lines did not show any splitting. The nmr spectrum of II-58a did not show any olefinic protons at τ ca 4.5 but had a methoxy signal at τ6.64 and two multiplets at τ5.68($W_{\frac{1}{2}}$ 8Hz) and 6.02($W_{\frac{1}{2}}$ 22Hz) for the pseudo equatorial and the pseudo axial protons at C_6 and C_2, respectively. The mass spectrum had the M^+ ions at m/e 207, 205 required for $C_9H_{16}NO_2Cl$ and the base fragment at 190, 188 from the loss of an OH group.

(c) with dimethylamine hydrochloride and methanol: Since the two previous reactions yielded the oximes II-52 as the major product due to the acid-catalyzed tautomerization of the C-nitroso II-51, dimethylamine hydrochloride was chosen to react with

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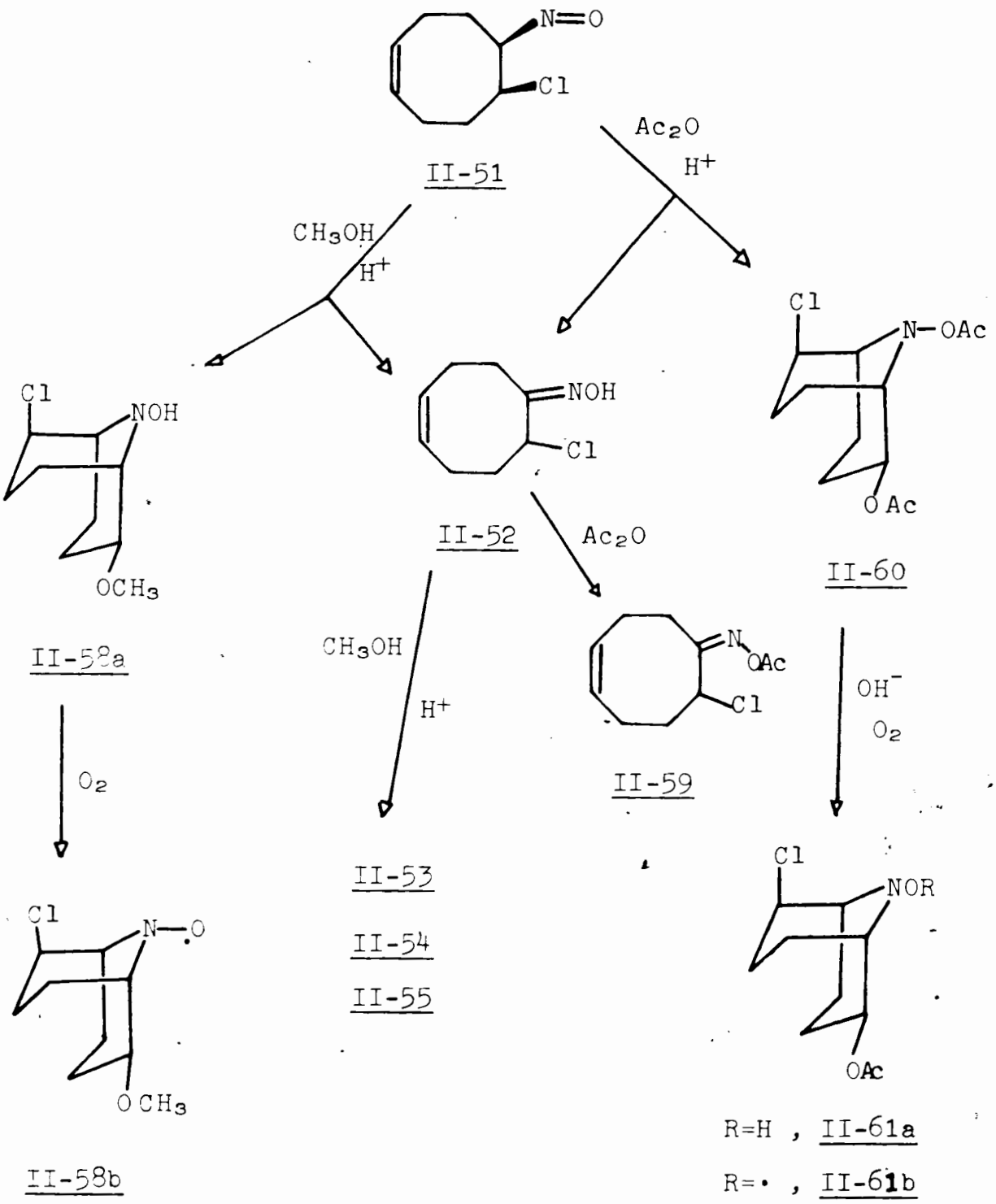
a, the exo structure in this work is defined relative to the nitrogen bridge; ie: if in a chair-chair conformation, exo corresponds to the axial position.


N=O
Cl
II-51
Ac2O
H+
CH3OH
H+
Cl
NOH
OCH3
II-58a
NOH
Cl
II-52
Ac2O
Cl
N—OAc
OAc
II-60
CH3OH
H+
N
OAc
Cl
II-59
OH−
O2
O2
Cl
N—O
OCH3
II-58b
II-53
II-54
II-55
Cl
NOR
OAc
R=H , II-61a
R=• , II-61b

Scheme II-12

II-51 in a methanol-methylene chloride solution at 40°. Analysis of the neutral fraction by tlc, ir and nmr spectra showed it contained oximes II-52 as the major product (81%), but hydroxylamine II-58a was produced in a better yield (ca 9%) than the previous reaction.

The basic fraction was found to contain only one compound assigned to 2-dimethylamino-5-cycloocten-1-one-anti-oxime (II-27 5%) on the basis of tlc, ir and mass spectra identical to those of an authentic sample.

(d) with acetic anhydride: The dimer of C-nitroso II-51, when treated in a methylene chloride solution containing acetic anhydride and acetic acid at 35-40° decomposed slowly to give a mixture of O-acetyl-2-chloro-5-cycloocten-1-one-syn-oxime (II-59 51% isolated) and endo-2,9-diacetoxy-exo-6-chloro-9-azabicyclo [3.3.1]nonane (II-60, 18% isolated) as seen in Scheme II-12. The crude hydroxylamine acetate II-60 showed an esr triplet signal, a_N 17.3G, line width 6G and g-factor 2.0068, due to a trace of nitroxide II-61b.

Oxime acetate II-59 gave correct elemental analysis for $C_{10}H_{14}NO_2Cl$. The ir absorptions of II-59 were found at 3020 cm^{-1} (olefin), 1775 and 1200 cm^{-1} (NOAc) (90), 1625 cm^{-1} (C=N) and at 770 and 750 cm^{-1} (C-Cl). Its nmr spectrum showed two olefinic protons at τ4.34 and a singlet at τ7.83 for the acetoxy group. The nmr signal for the C_2 proton was at τ5.15 (J=7.0 and 5.0Hz), slightly downfield in comparison with syn-chloro oxime II-52b (τ5.40); therefore, compound II-59 was tentatively assigned the

syn-configuration. The ^{13}Cnmr spectrum (Table II-7) showed ten lines with the expected chemical shifts.

Sublimed hydroxylamine acetate II-60 gave correct elemental analysis and exact mass for the M^+ ion $C_{12}H_{18}NO_4Cl$. It had ir absorptions at 1768 and 1726 cm^{-1}, compatible with acetates of a hydroxylamine and alcohol group, respectively. The ^{13}Cnmr spectrum (Table II-7) showed two acetoxy groups at 169.0(s), 20.1(q) and 168.4(s), 18.8(q) ppm. It did not show any olefinic carbon signal around 130 ppm but one signal at 66.7(d)ppm assigned to C_2. The intense signal at 59.4(d)ppm was attributed to two carbons, C_1 and C_6, and the signal at 55.2(d)ppm to C_5 (77).

The orientations of the chloro and acetoxy substituents were established from the proton nmr spectrum as shown in Figure II-14 and Table II-8. The lower field signals at τ4.64 and τ5.70 were assigned to geminal to the acetoxy and the chlorine group, respectively. By decoupling, the C_2 proton multiplet was shown to couple with the C_1 proton by 5Hz and the C_3 protons by 11 and 7Hz; these indicated the axial orientation for the C_2 proton. The C_6 proton had a $W_{\frac{1}{2}}$ of 8Hz indicating that this proton was in an equatorial position. It has been reported that N-methyl-endo, endo-2,6-dichloro-9-azabicyclo[3.3.1]nonane showed a multiplet at τ5.55 with $W_{\frac{1}{2}}$=17Hz for the C_2 and C_6 protons(91). Also, the 2,6-diacetyl derivative showed a broad multiplet at τ4.75-5.05 for the two CHOCOCH$_3$ protons. Such broad multiplets are regarded as evidence for axial orientation.

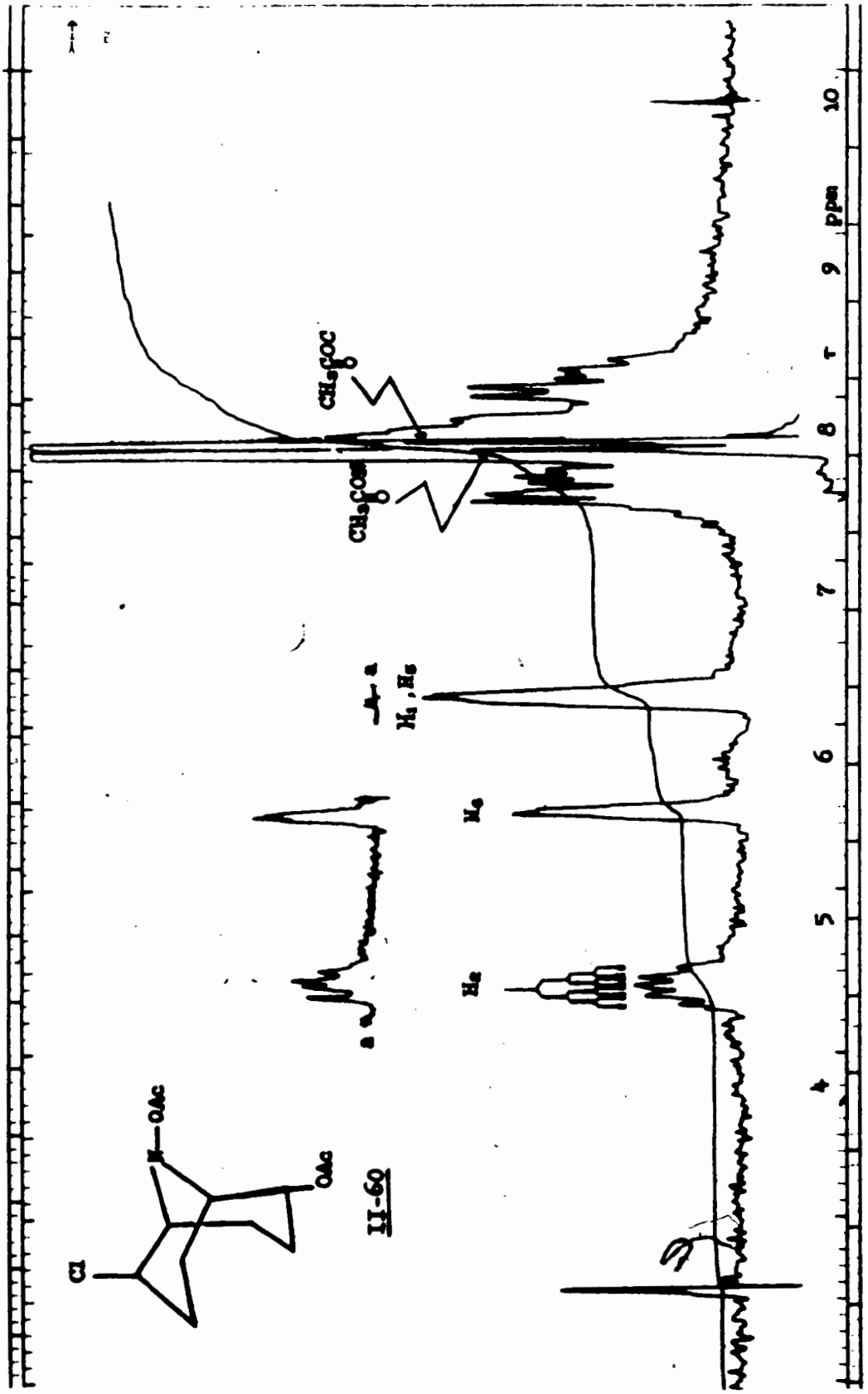


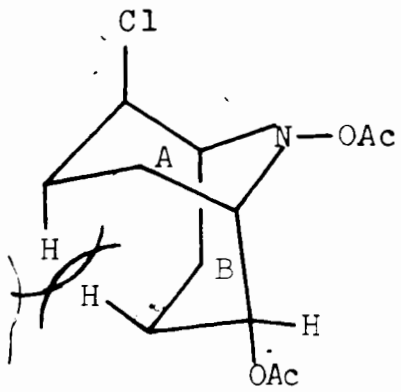
Figure II-14: ^{1}Hnmr spectrum (100MHz) of endo-2,9-diacetoxy-exo-6-chloro-9-azabicyclo[3.3.1]nonane(II-60)
a: double irradiation of the C_1, C_5 protons.

TABLE II-8

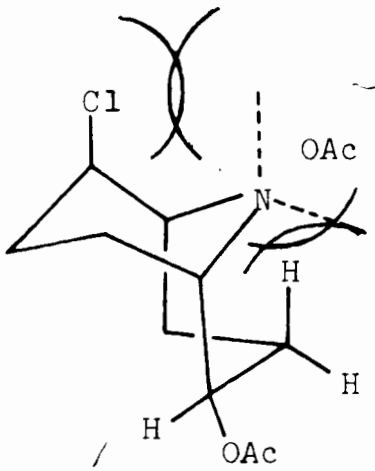
CHEMICAL SHIFTS (τ) AND COUPLING CONSTANTS (J, $W_{\frac{1}{2}}$) OF 9-AZABICYCLO[3.3.1] DERIVATIVES

Proton	II-60	II-62a	II-63
1,5	6.41(m) $W_{\frac{1}{2}}$=10Hz	6.64(m) $W_{\frac{1}{2}}$=11Hz	6.90(m) $W_{\frac{1}{2}}$=10Hz
2-exo	4.64(ddd) J_{2a-3a}=11.0, J_{2a-3e}=7.0, J_{1-2a}=5.0, J_{2a-8a}≈1.5Hz	5.48(m) $W_{\frac{1}{2}}$=20Hz	4.93(ddd) J_{2a-3a}=10.0, J_{2a-3e}=5.0, J_{1-2a}=5.0, J_{2a-8a}≈1.5Hz
3,4,7,8	7.59-8.46(m)	7.3-8.9(m)	7.5-8.4(m)
6-endo	5.70(m) $W_{\frac{1}{2}}$=8Hz	5.67(m) $W_{\frac{1}{2}}$=6Hz	5.70(m) $W_{\frac{1}{2}}$=8Hz
CH_3CON	7.87(s)	-	-
CH_3COC	7.93(s)	-	7.96(s)
NH,OH	-	~7.0Hz	7.4(bs)

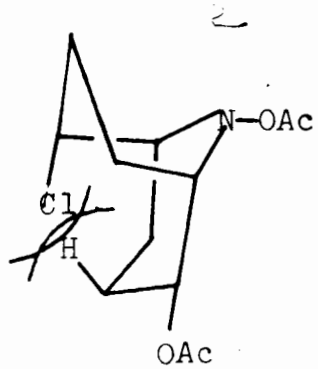
Among the three possible conformations II-60a, b and c, conformation II-60b is unlikely because of the steric crowding of the N-acetoxy group with the axial chlorine and the C_3 axial proton. Both conformations II-60a and c are possible although



II-60a



II-60b

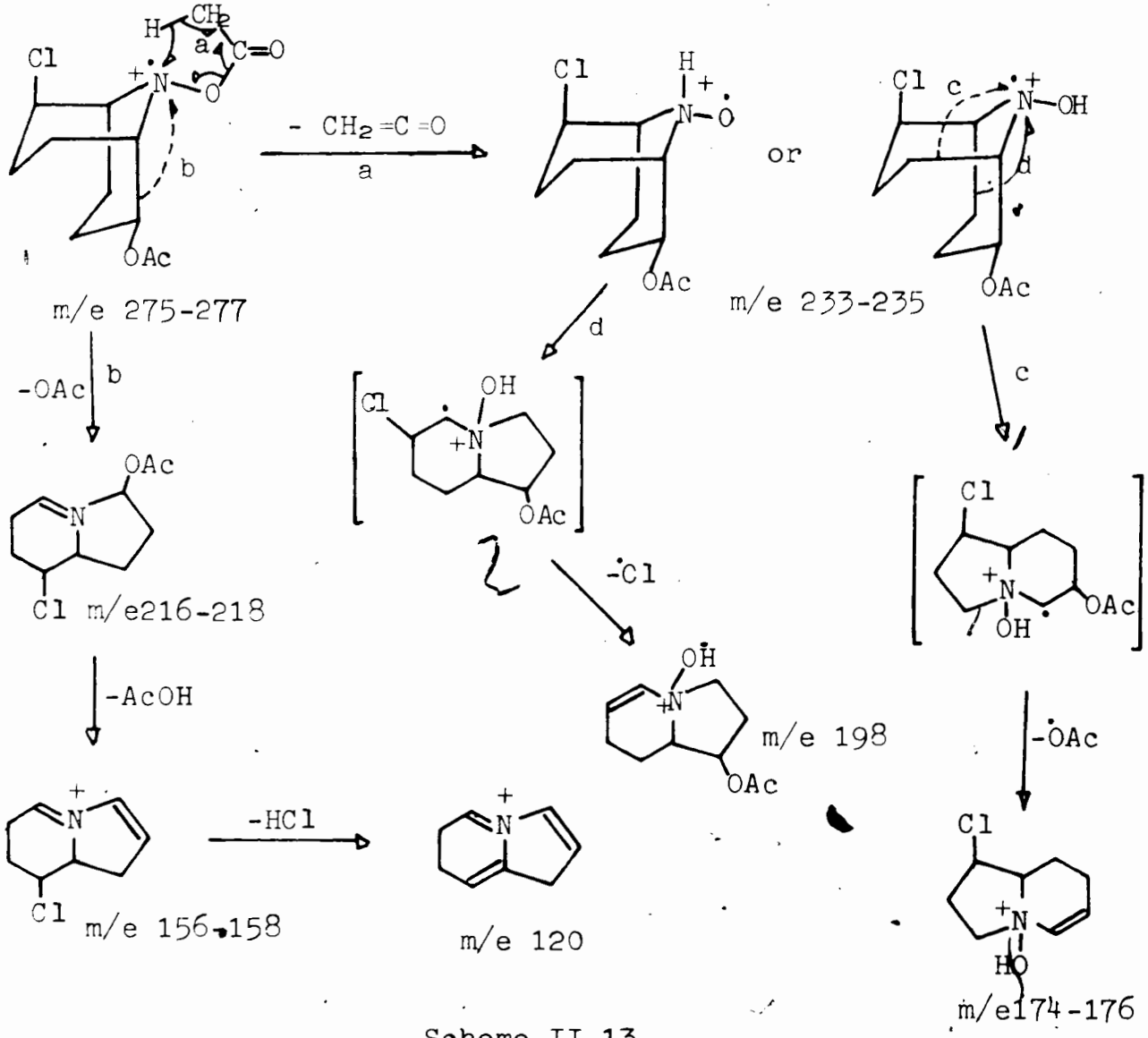


II-60c

there are interactions between the C_3 and C_7 hydrogens in II-60a and between the axial chlorine and the C_3 proton in II-60c. The former interactions can be relieved by slightly flattening the ring. The twin-chair conformation of II-60a is the only one that possesses a perfect W-plan between its C_2 and C_8 axial protons, explaining the further small coupling of the C_2 proton. Also, the multiplet due to the C_1 and C_5 hydrogens, centered at τ6.41 had a half-height width of 10Hz and a base line width of 18Hz; this indicated that II-60 was essentially in a chair-chair conformation since model compounds, with conformation of II-60a, such as

3-β-granatanol, showed the respective values of 9.0 and 16.0Hz and that of II-60c, such as 3-α-granatanol, showed the values of 16 and 28Hz(92).

Some possible mass spectral fragmentation pathways of aza-bicyclic II-60 are shown in Scheme II-13 (Figure II-15). Two pathways seemed to predominate from the molecular ion, namely, the loss of ketene (path a) and the loss of an acetoxy group (path b).



Scheme II-13

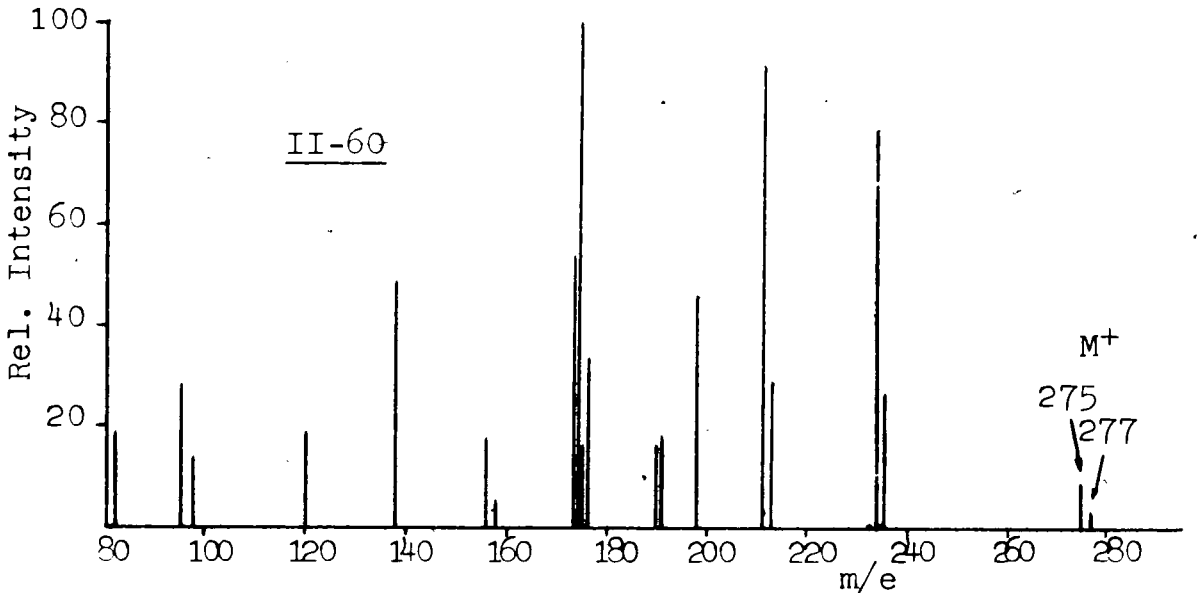


Figure II-15: Mass spectrum (80eV) of endo-2,9-diacetoxy-exo-6-chloro-9-azabicyclo[3.3.1]nonane (II-60).

Reactions of the dimer of II-51 under different conditions are shown in Table II-9. Yields were determined by isolation of the products or by proton integration in the nmr spectrum of the methyl singlets at τ7.83 (II-59) and τ7.87 and 7.93 (II-60) and of the methine protons at τ5.15 (II-59) and 5.70 (II-60). With acetic anhydride in methylene chloride as the solvent, the oxime acetate II-59 (30%) and better yields of rearranged hydroxylamine acetate II-60 (60%) were obtained.

II-3-3. Reactions of hydroxylamine acetate II-60

Pure hydroxylamine acetate II-60 did not show any esr signal in methylene chloride solution. But, when II-60 (4.54x

Conditions	% yield II-59	% yield II-60	Method of estimation
Ac_2O-AcOH in CH_2Cl_2	66	22	nmr
	51	18	isolated
Ac_2O in CH_2Cl_2	30	60	nmr
Ac_2O	50	42	nmr
Ac_2O-AcONa in CH_2Cl_2	56	37	nmr
	52	34	isolated

Table II-9: yields of products obtained from reactions of the dimer of II-51.

10^{-4} mole/l) in methylene chloride was shaken with an aerated saturated sodium carbonate solution at room temperature, a mixture was obtained that showed a triplet esr signal (Figure II-16), a_N 17.2G, line width 4.8G and g-factor 2.0073, characteristic of nitroxide II-61b (62). This signal increased drastically for the first six minutes; the increased was slight but continuous for the next two months. When this same solution was purged with nitrogen and kept free from air for one month, only a relatively slow decrease of the esr signal was observed.

Reduction of chloro hydroxylamine acetate II-60 with LAH gave endo-2,7-dihydroxy-exo-6-chloro-9-azabicyclo[3.3.1]nonane (II-62a, 85%)(Scheme II-14). The latter exhibited infrared

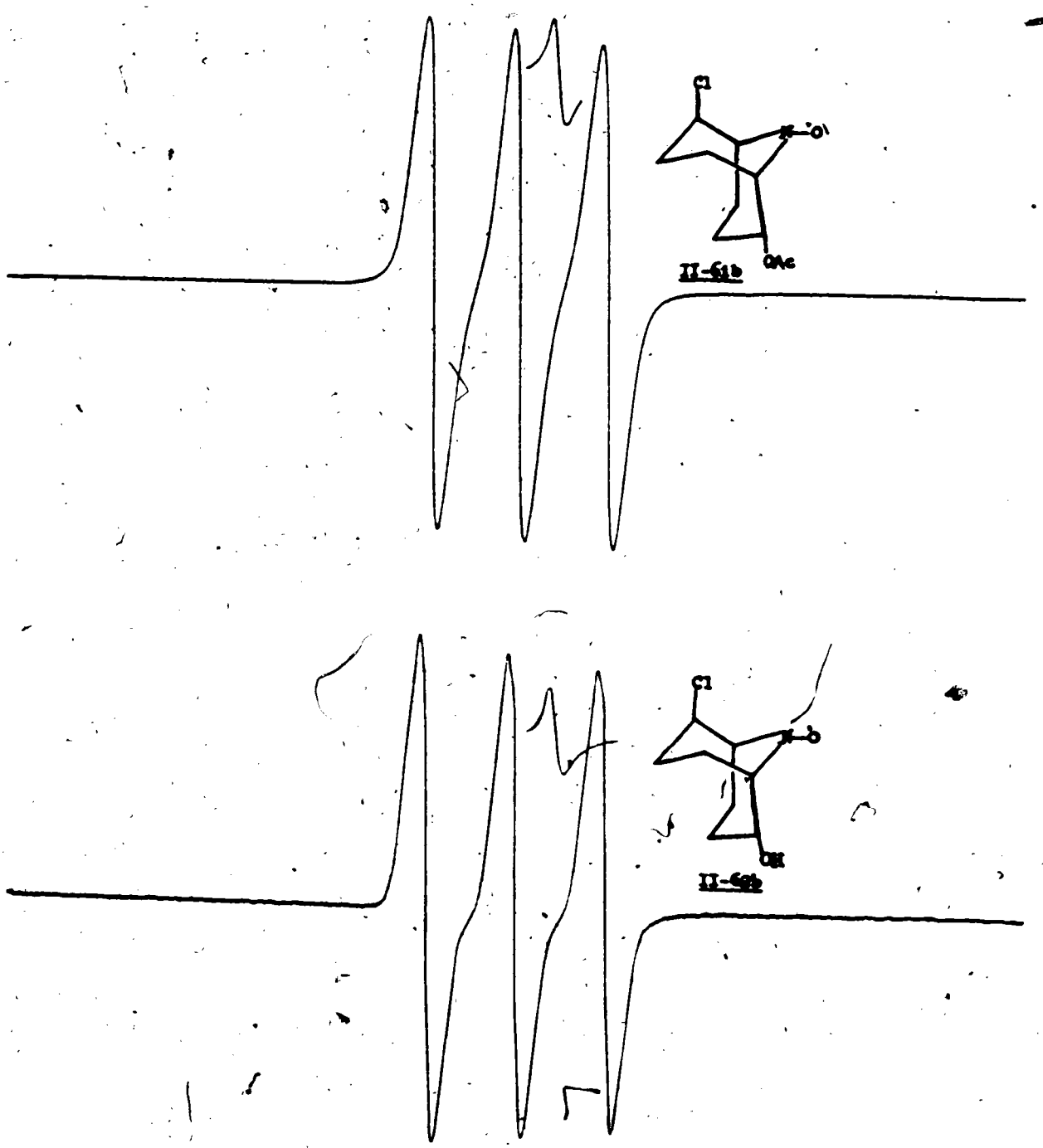
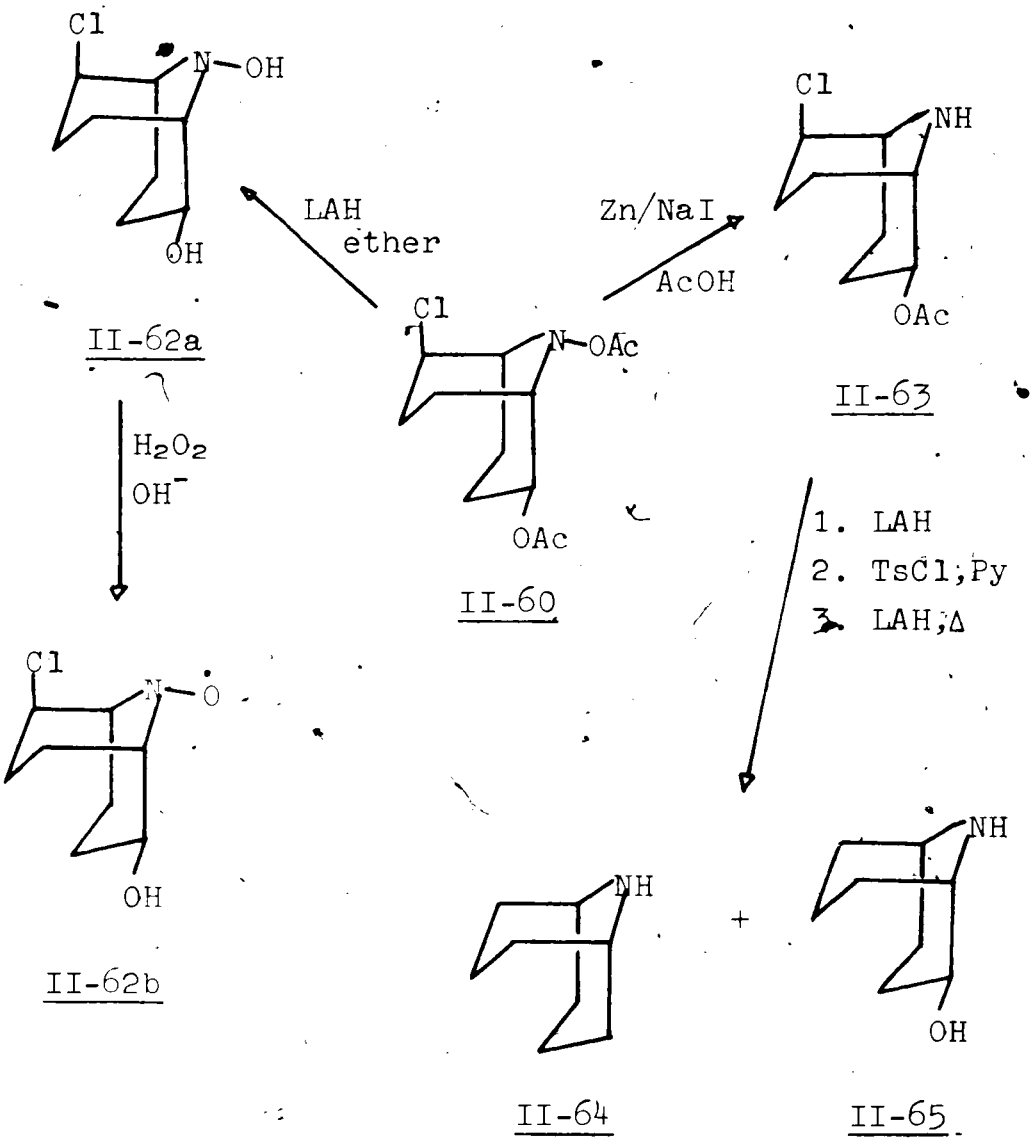


Figure II-16: esr specta of endo-2-acetoxy-exo-6-chloro-9-azabicyclo[3.3.1]nonahe nitroxyl radical (II-61b) and of endo-2-acetoxy-exo-6-chloro-9-azabicyclo[3.3.1]nonane nitroxyl radical (II-62b).



Scheme II-14

bands at 3300, 1095, 1060 and 1035 cm^{-1} (OH) and at 722 cm^{-1} (C-Cl). The ^{1}Hnmr spectrum of II-62a (Table II-8) showed a very similar pattern to that of II-60, indicating the axial

and equatorial orientations of the protons at C_2 and C_6, respectively. The mass spectrum of II-62a showed the molecular ions at m/e 193, 191 and the base fragment at 176, 174 from the loss of OH, both with a one chlorine pattern.

Hydroxylamine II-62a was oxidized with hydrogen peroxide in basic conditions to give the nitroxide radical II-62b as a yellowish solid. It exhibited in solution a strong broad esr triplet signal (Figure II-16) with a_N 17.5G, line width 5.4G and g-factor 2.0078, consistent with the 9-azabicyclic[3.3.1] structure (62).

In an attempt to remove the chlorine atom, II-60 was treated with sodium iodide and zinc in acetic acid (93). The reaction led to the reductive cleavage of the hydroxylamine to give endo-2-acetoxy-exo-6-chloro-9-azabicyclo[3.3.1]nonane (II-63, 87%)(Scheme II-14). Elemental analysis and high resolution mass spectra established the molecular formula of bicyclic amine as $C_{10}H_{16}NO_2Cl$. It had typical ir absorptions at 1735, 1370 and 1240 cm^{-1} (OAc), 3300 (NH) and 700 cm^{-1} (C-Cl). The ^{13}Cnmr spectrum was shown in Table II-7. The proton nmr of II-63 had a pattern similar to that of II-60 and II-62a as seen in Table II-8. The exo-C_2(τ4.93), C_1 and C_5(τ6.90) protons were shifted slightly upfield while the endo-C_6 proton(τ6.70) showed the same chemical shift with respect to those of II-60. This result suggested that compound II-60 had the C_6 proton far away from anisotropic effect due to the N-acetoxy group,

that is, this group oriented towards ring B as seen in II-60a. The mass spectrum of II-63 exhibited the M^+ ions at m/e 217 and 219 with a one chlorine ratio and the possible fragmentation patterns are similar to those of Scheme II-13 (path b).

The bicyclic amine II-63 was reduced with LAH, followed by tosylation with tosyl chloride in pyridine. The crude product was reduced again with LAH in refluxing ether for one day (Scheme II-14) to give a 7:6 mixture of 9-azabicyclo[3.3.1] nonane (II-64) and endo-2-hydroxy-9-azabicyclo[3.3.1]nonane (II-65). The tosylation of granatanine (II-64) afforded the tosylamide which had melting point matching that reported(94).

II-3-4. Anti-dimer of 1-nitroso-2-chloro-trans,trans-5,9-cyclododecadiene

The dimer of II-66 was prepared in 94 % yield from the low temperature addition of nitrosyl chloride to tttCDT in methylene chloride. The elemental analysis of the dimer of II-66 agreed with $(C_{12}H_{18}NOCl)_2$. Its ir spectrum exhibited absorptions at 1260 and 1220 cm^{-1} and the uv spectrum a maximum at 302 nm(ε 9400) typical of an anti-azodioxy compound (31,35). It exhibited one spot on tlc and had a sharp melting point. This compound had been prepared previously (95), but its stereochemistry was not reported. Since tttCDT had three fold axes of symmetry, addition of nitrosyl chloride would not generate regioisomers. However, it showed two sets of ^{13}C

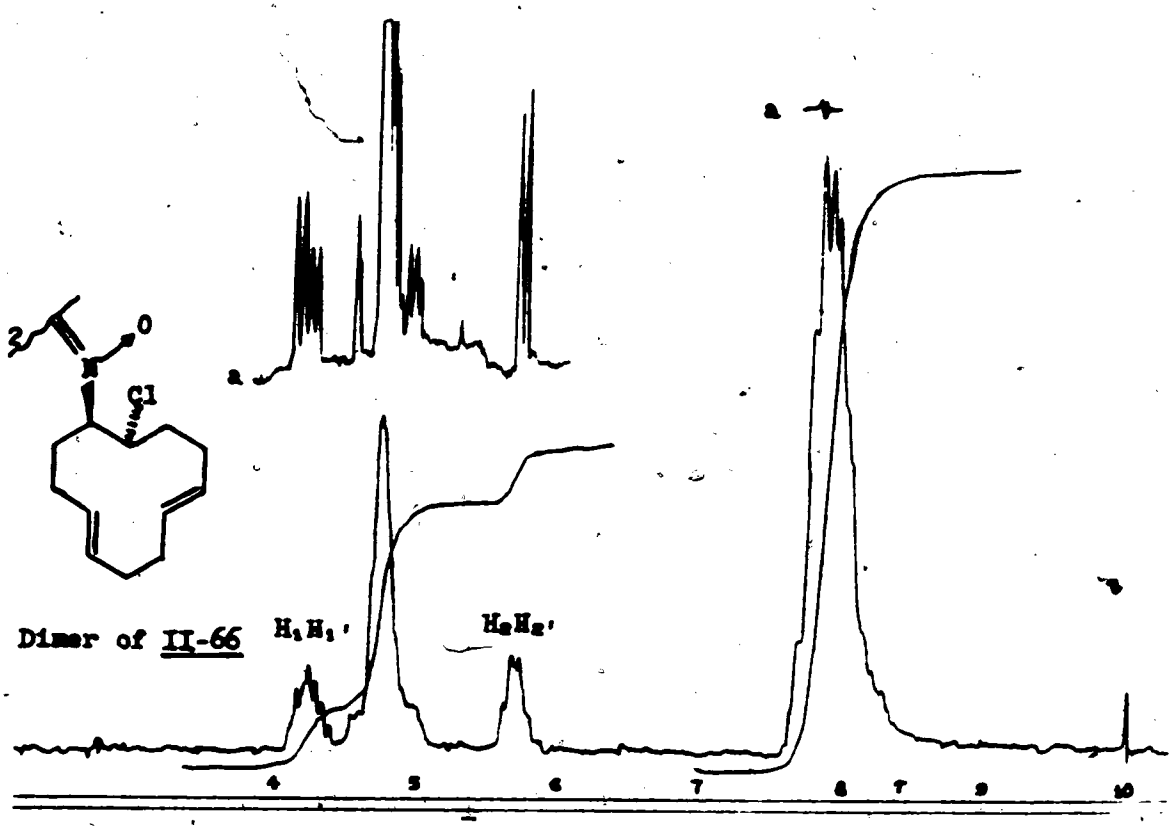
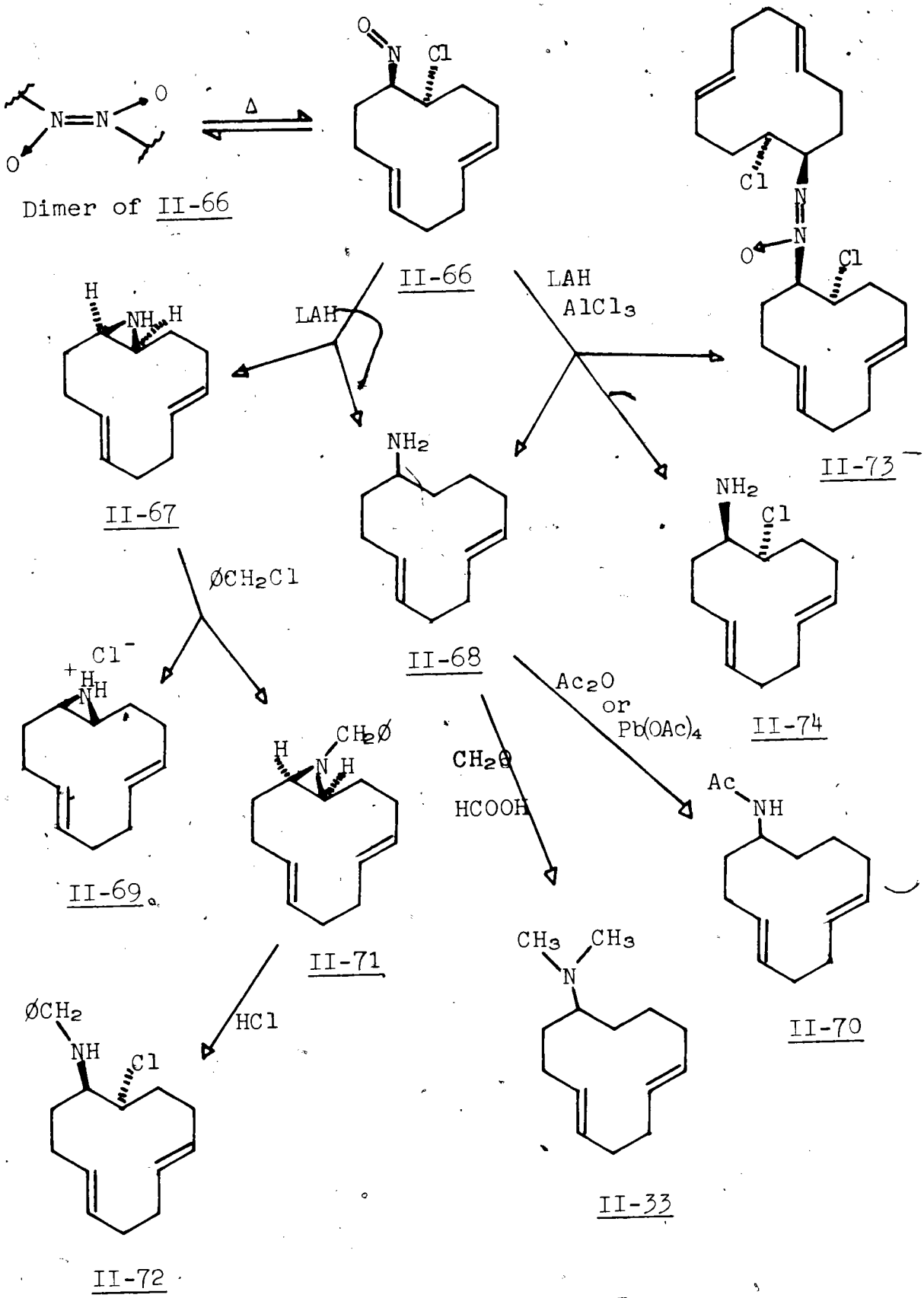


Figure II-17: ^{1}Hnmr spectrum (100MHz) of the anti-dimer of 1-nitroso-2-chloro-trans,trans-5,9-cyclododecadiene (Dimer of II-66);
a: double irradiation of the C_3 and C_{12} protons.

signals, notably at 62.7(d) and 62.6(d) ppm for the C_1 carbons and at57.5(d) and 56.7(d)ppm for the C_2 carbons. The ^{1}Hnmr of II-66 (figure II-17) showed four olefinic protons at τ4.70 and two other downfield multiplets at τ4.16 and 5.65 for the methine protons of CHN and CHCl, respectively, in agreement with reported chemical shifts (34). Spin decoupling (Figure II-17) collapsed the signal at τ4.16 to two doublets at τ4.11 (J=5.5Hz) and 4.21(J=4.5Hz) but that at τ5.65 remained as nearly superimposed doublets (J=5.0Hz). The nmr spectrum of the sample of


Dimer of II-66
Δ
II-66
LAH
LAH
AlCl3
II-67
II-68
II-73
ØCH2Cl
II-69
II-71
II-74
Ac2O
or
Pb(OAc)4
CH2O
HCOOH
HCl
II-72
II-33
II-70

Scheme II-15

the dimer indicated it to be a mixture of two isomers: mixed hydride reduction (LAH + $AlCl_3$) gave a single 2-chloroamine derivative (vide infra), indicating that the sample was a ca 1:1 mixture of dl and meso diastereoisomeric dimers, but not the isomers of threo/erythro configuration.

II-3-5. Reactions of the dimer of II-66

(a) Reduction: LAH reduction of the dimer of II-66 afforded 13-azabicyclo[10.1.0]-trans,trans-4,8-tridecadiene (II-67, 8%) and 1-amino-trans,trans-4,8-cyclododecadiene (II-68, 64%)(Scheme II-15). Both products gave the correct elemental composition and high resolution mass spectra for $C_{12}H_{19}N$ and $C_{12}H_{21}N$, respectively. The ^{13}Cnmr spectra of aziridine II-67 and primary amine II-68 are reported in Table II-2. The former showed only six lines, indicating one aziridine only with the dl or meso configuration. Amine II-68 exhibited 12 lines in its ^{13}C spectrum with the C_1 carbon at 45.7(d)ppm, in agreement with a carbon attached to an amino group (77). The ^{1}Hnmr spectrum of II-67 showed a simple pattern for the four olefinic protons at τ4.78, an unresolved multiplet at τ8.85 for the C_1 and C_2 protons and an exchangeable proton at τ9.08. The hydrochloride salt of II-67 showed two exchangeable protons at τ2.36 a multiplet at τ4.90 for the olefinic protons and a broad doublet (J=7Hz) at τ7.32 for the C_1 and C_2 protons.

The acetamide II-70 of the amine II-68 showed an ir absorption at 1635 cm^{-1}, the NCH_3 nmr singlet at τ8.04 and a ^{13}C

nmr signal for the C_1 carbon at 44.4(d)ppm (Table II-2). Further proof of the structure of primary amine II-68 was gained by methylation, using the Eschweiler-Clarke's method (96), to yield dimethylamine II-33 as the major product (57%). It was identical to an authentic sample obtained by another route (vide supra). Cyclization of II-68 by oxidation with lead tetraacetate failed to yield the azabicyclic compound; the major product being the N-acetyl derivative II-70.

Treatment of aziridine II-67 with benzyl chloride in benzene gave aziridine hydrochloride II-69 (42%) and N-benzyl-13-azabicyclo[10.1.0]-trans,trans-5,9-tridecadiene(II-71,~40%). The ^{13}Cnmr spectrum (Table II-2) of II-71 exhibited six lines for the aziridine portion and five lines for the benzyl portion. The proton nmr spectrum of compound II-71 was relatively simple; it showed the phenyl protons at τ2.78 and the benzyl protons at τ6.56 as a sharp singlet at room temperature and as a broad singlet at -55°($W_{\frac{1}{2}}$=2.5Hz). These spectroscopic data clearly proved that benzylaziridine II-71 must possess the plane of symmetry, and therefore, the meso configuration. Should II-71 have the dl configuration, the aziridine would show 12 lines ^{13}Cnmr signals and the benzyl protons would be an AB quartet due to diastereotopic nature, as observed with trans-1-benzyl-2,3-dibenzoylaziridine(97); the cis derivative showed only a broad singlet ($W_{\frac{1}{2}}$=1.5Hz) at -58°. On treatment with hydrogen chloride, the aziridine ring of II-71 was opened up to give monobenzyl chloramine II-72.

Mixed hydride reduction (LAH +$AlCl_3$) of the dimer of II-66 in refluxing ether gave 1-azoxy-2-chloro-trans,trans-5,9-cyclododecadiene(II-73, 25%), amine II-68 (7%) and threo-1-amino-2-chloro-trans,trans-5,9-cyclododecadiene(II-74, 46%) (Scheme II-15).

The azoxy derivative II-73 exhibited ir absorption bands at 1490 and 1440 cm^{-1} and two weak uv absorption bands at 354 and 290(sh)nm, characteristic of an aliphatic azoxy compound (98). Its nmr spectrum showed a broad triplet at τ5.65(J=6Hz) for the C_2, $C_{2'}$ methine protons and two other multiplets at τ5.46 and 6.40 for the CHNO and CHN protons, respectively. The ^{13}Cnmr spectrum of II-73 exhibited 20 lines with the CHNO carbon at 78.5ppm, and the C_2, $C_{2'}$ and CHN carbons at 59.0, 58.7 and 57.2 ppm, indicating one isomer only; this may arise by selective reduction of either the dl or meso isomer of II-74 or alternatively, by stereospecific condensation of one enantiomer of RR or SS-II-74 with one enantiomer of RR or SS hydroxylamine derived from the reduction of II-74. The mass spectrum of II-73 showed the M^+ ions at 422-424-426 with a two chlorines pattern.

The presence of amine II-68 was indicated by the ^1Hnmr spectrum of the reaction mixture (C_1 proton at τ7.24) and by gc peak matching with an authentic sample. The infrared spectrum of the 2-chloro amine II-74 exhibited a weak absorption around 3350 cm^{-1}(NH_2) and at 760 cm^{-1}(C-Cl). The proton nmr

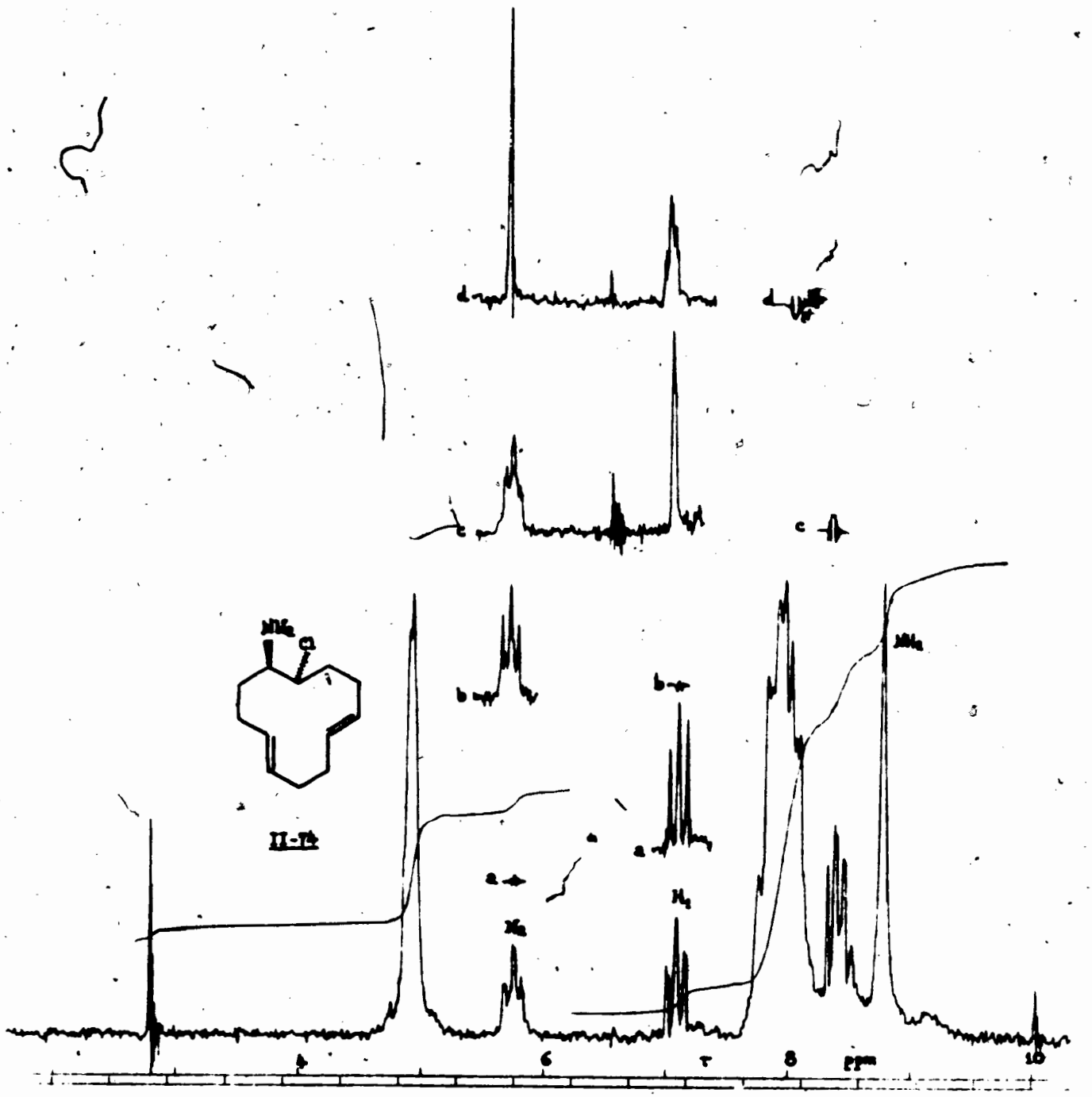
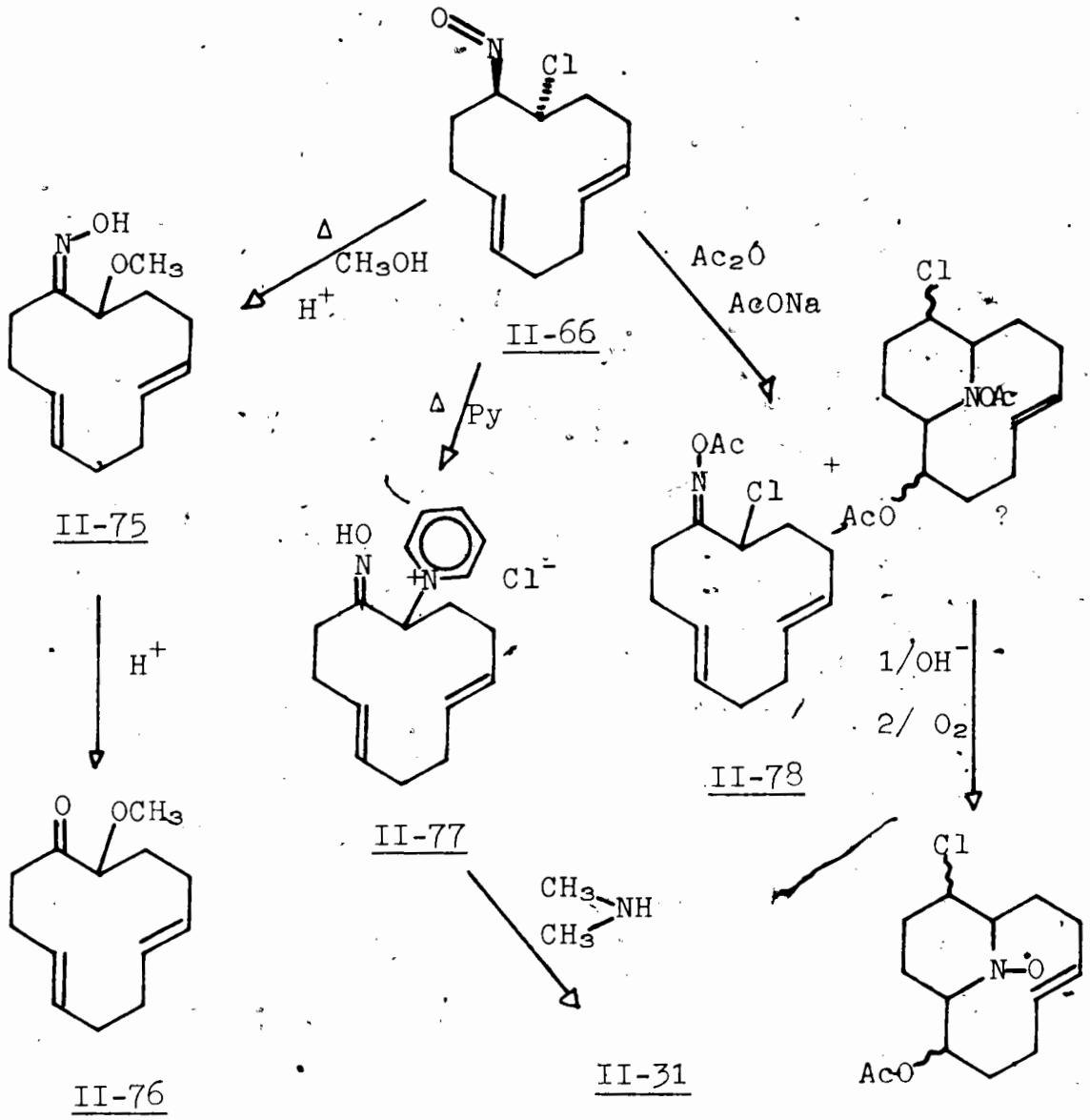


Figure II-18: ^{1}Hnmr spectrum (100MHz) of 1-amino-2-chloro-trans,trans-5,9-cyclododecadiene (II-74);
a: double irradiation of the C_2 proton; b: double irradiation of the C_1 proton; c: double irradiation of the C_{12} protons; d: double irradiation of the C_3 protons.

spectrum of II-74 and spin decoupled spectra are shown in Figure II-18. The C_1 proton (τ7.06) was vicinally coupled to the C_2 proton (τ5.73) with a small coupling constant of 2Hz (Table II-3). The meso(cis) configuration for benzylaziridine II-71 permits the determination of the stereochemistry of chloro nitroso compound II-74 as threo(trans) if the elimination of hydrogen chloride from II-74 to give aziridine II-67 is assumed to occur by trans elimination(99). No other isomeric 2-chloro amine was detected by gc of the reaction mixture. This was confirmed by the ^{13}Cnmr spectrum of the crude mixture which, after removal of the azoxy compound II-73, showed only eleven lines for II-74 (Table II-2) as well as small lines matching with those of amine II-68.

(b) with hydrochloric acid and methanol: Dimer of II-66 was treated with hydrochloric acid in boiling methylene chloride methanol solution to yield syn-2-methoxy-trans,trans-5,9-cyclododecadien-1-one oxime(II-75, 57 %) and 2-methoxy-trans,trans-5,9-cyclododecadien-1-one(II-76, 28%)(Scheme II-16). They were separated by column chromatography and identified from spectral data. The nmr spectra of II-76 and II-75 showed methoxy groups at τ6.65 and 6.72 and the C_2 protons at τ6.40(dd, J=6.5 and 4Hz) and 5.84(t, J=5Hz), respectively. The 0.56 ppm downfield shift observed for the C_2 proton for II-75 in comparison to the ketone II-76 suggested a syn configuration for the latter (76). The ir absorptions of methoxy ketone II-76 were seen at 1720 and 1098 cm^{-1} and of methoxy oxime II-75 at 3300, 1640 and



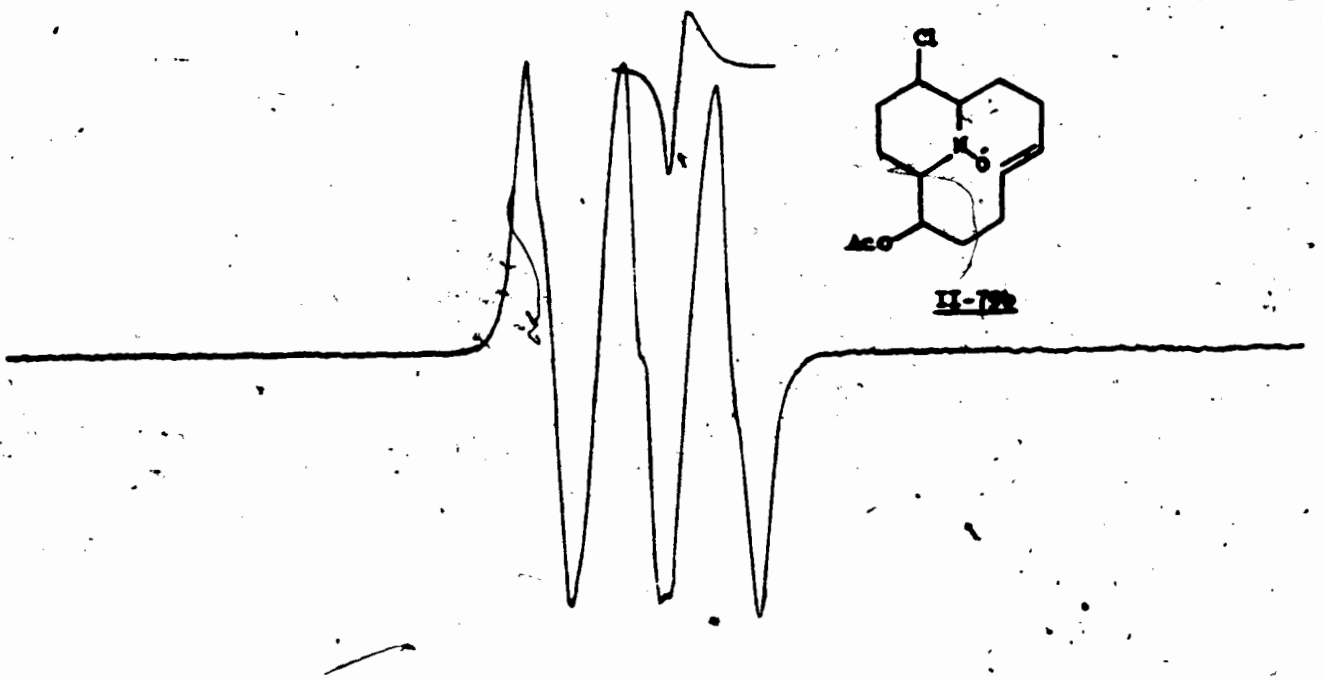
Scheme II-16

1085 cm^{-1}. Both mass spectra exhibited their expected molecular ions.

(c) with pyridine: The decomposition of a methylene chloride solution of II-66 in the presence of pyridine gave good

yields (93%) of 1-oximino-trans,trans-5,9-cyclododecadien-2-pyridinium chloride(II-77)(Scheme II-16). It exhibited ir absorptions at 1625, 1000, 770, 725 and 690 cm^{-1}. This oxime II-77 was treated with dimethylamine to give the known amino oxime II-31 (91%) prepared by another route.

(d) with acetic anhydride: The decomposition of II-66 in acetic anhydride and sodium acetate gave O-acetyl-2-chloro-trans,trans-5,9-cyclododecadien-1-one oxime(II-78,~72%) along with the starting dimer of II-66 (~10%) and unidentified minor components. The mixture also showed a broad esr triplet (Figure II-19) with a_N13.5G, line width 6.5G and g-factor 2.0068 which was attributed to nitroxide radical II-79b or isomer thereof (Scheme II-16), indicating that some cyclization might have occurred.



II-79b

Figure II-19: esr spectrum of nitroxide radical II-79b or isomer thereof.

Compound II-78 gave correct elemental analysis for $C_{14}H_{20}NO_2Cl$ and had ir absorptions at 1775, 1370 and 1202 cm^{-1} characteristic of an oxime acetate group. The ^{13}Cnmr spectrum is shown in Table II-2. The proton nmr spectrum contained well resolved multiplets at τ5.17 and 7.05 for the C_2 and one of the C_{12} proton, respectively, a singlet at τ7.80 for the acetoxy group, and four olefinic protons at τ4.82.

II-3-6. Anti-dimer of 1-nitroso-2-chloro-cis-5(7)-cyclodecene

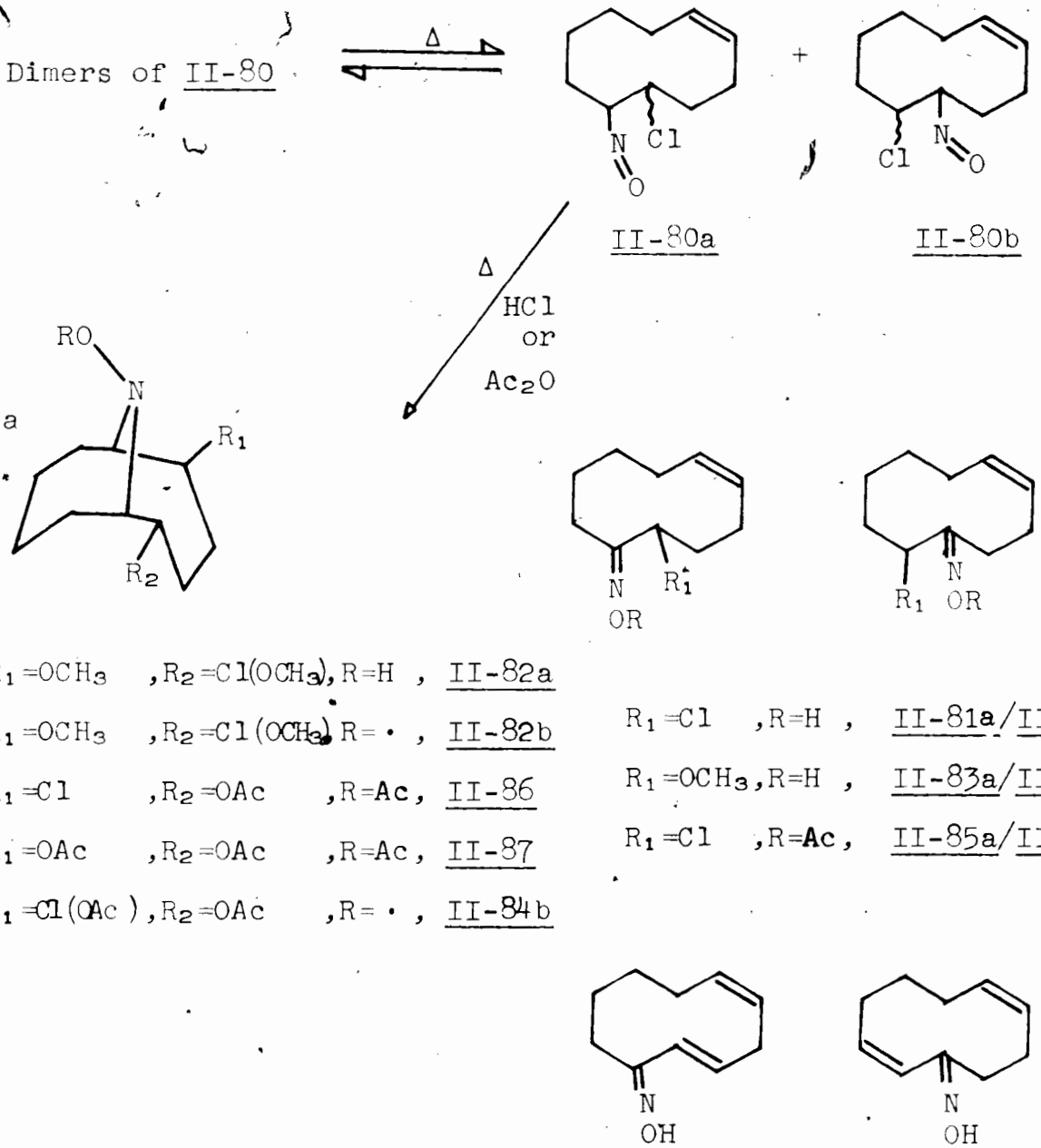
The dimer of II-80 was prepared by reaction of nitrosyl chloride with cis,trans-1,5-cyclodecadiene in a cold methylene chloride solution. The recrystallized dimer (~40%) gave a sharp melting point and had correct elemental analysis for $(C_{10}H_{18}NOCl)_2$. It showed an uv absorption band at 299nm (25,28) and four strong ir absorption bands around 1200 cm^{-1} typical of a trans azodioxy group. It also showed an ir absorption at 720 cm^{-1} for a cis double bond but not around 975 cm^{-1} for a trans double bond (100). In spite of the sharp mp, II-80 was a mixture of two different adducts, either from cis or trans addition to the trans double bond, or regioisomers of the addition to the trans double bond (II-80a and II-80b) arising from direction of the NOCl addition; it is believed to be the latter, on the basis of its treatment with anhydride leading to two isomeric acetates

II-85 (vide infra). The proton nmr of the dimeric sample exhibited multiplets for the methine protons geminal to the nitroso group and the chlorine atom at τ4.28 and 5.4, respectively. Unfortunately, due to poor solubility in solvents, the ^{13}Cnmr spectrum of the dimer of II-80 could not be taken; it yielded the lines of chloro oximes II-81 when warmed up in DMF.

II-3-7. Reactions of the dimer of II-80

(a) with hydrochloric acid: Decomposition of the dimer of II-80 in methanol-hydrochloric acid afforded a complex mixture which showed a complex esr signal of three nearly superimposed broad triplets, a_N ~15.2G and g-factor 2.0061 such as for II-82b. These data, as well as the nmr singlets at τ6.63 6.71 and 6.81 (OCH_3) indicated that cyclization had occurred giving rise to bicyclic methoxy chloro hydroxylamine derivatives which, in the presence of oxygen gave nitroxide radicals (Scheme II-17).

The major product from chromatography of the mixture was found to be 2-chloro-cis-5-cyclodecen-1-one oxime(II-81a), one of the possible regioisomeric oximes as shown by its spectral data. An exact mass determination of the M^+ ion and elemental analysis agreed with the formula $C_{10}H_{18}NOCl$. Its ir spectrum exhibited absorptions at 3250, 1620, 1000, 980 and 970 cm^{-1} (=NOH) and at 715 cm^{-1} (cis olefin)(100). The ^{13}Cnmr spectrum showed ten lines and the mass spectrum exhibited intense peaks



R_1 =OCH_3 , R_2 =Cl(OCH_3), R=H , II-82a

R_1 =OCH_3 , R_2 =Cl(OCH_3) R= • , II-82b

R_1 =Cl , R_2 =OAc , R=**Ac**, II-86

R_1 =OAc , R_2 =OAc , R=Ac, II-87

R_1 =Cl(OAc), R_2 =OAc , R= • , II-84b

R_1 =Cl , R=H , II-81a/II-81b

R_1 =OCH_3, R=H , II-83a/II-83b

R_1 =Cl , R=**Ac**, II-85a/II-85b

Z

a: or isomer thereof

Scheme II-17

expected for a one chlorine pattern. The proton nmr spectrum of II-81a consisted of a multiplet at τ4.76 for the two olefinic proton, a doublet of doublets at τ5.45(J_{2-3a}=11.0 and J_{2-3e}=4.5Hz) for the C_2 proton and a multiplet at τ6.93 for a C_{10} proton. By decoupling experiments, the last multiplet was shown to couple with a non-allylic hydrogen at τ8.39. This indicated that the cis double bond should be placed at the 5-position as in II-81a.

From the proton nmr spectrum of the mixture, another doublet of doublets at τ5.63(J=10.0 and ~5.0Hz) with similar pattern and intensity to that of the signal at τ5.45 was tentatively assigned to the methine proton geminal to the chlorine atom of the other possible isomer oxime II-81b.

Chromatography also gave a fraction as a mixture of unidentified compounds containing methoxy groups as seen by the nmr absorptions at τ6.63,6.72 and 6.78. The integration of the olefinic part of the spectrum at around τ4.6 accounted for only one proton, in comparison with an estimated total of twenty protons. This mixture was believed to be a mixture of methoxy oximes II-83 and cyclized hydroxylamines II-82a. A gc-mass analysis of the mixture showed the presence of methoxy oximes II-83, chloro oximes II-81 and two major unidentified compounds. The first unknown, compound Z (ca 24 % from the gc peak area), giving a broad gc peak, had the highest m/e peak at 165 and the 100% intensity peak at 148 for the loss of an OH. A possible structure for Z might be the diolefinic oxime giving the M^+ ion

at m/e 165 in its mass spectrum, as reported by other (101). The other unidentified compound was postulated as bicyclic hydroxylamines II-82a (Scheme II-17). The mass spectrum did not show the molecular peak but exhibited a peak at m/e197 for either a loss of CH_3OH or HCl.

(b) with acetic anhydride: Decomposition of a methylene chloride solution of dimer of II-80 containing acetic anhydride at 40-45° proceeded slowly giving the recovered dimer of II-80 (33%) and others. The esr of the remaining mixture exhibited a signal consisting of nearly superimposed triplets of one major and two minor. The major triplet had a_N14.2G, line width 4G and g-factor 2.0007 and might be attributed to a bicyclic nitroxide radical such as II-84b or isomer thereof (Scheme II-17).

The first fraction of the chromatography of the mixture afforded a 1:3 mixture (45%) of O-acetyl-2-chloro-cis-5(7)-cyclodecen-1-one oxime(II-85). The molecular formula of II-85 was ascertained by elemental analysis and high resolution mass spectrometry to be $C_{12}H_{18}ClNO_2$. The ir spectrum exhibited prominent peaks at 1775, 1205, 1000, 735 and 710 cm^{-1}. The nmr spectrum showed two olefinic protons at τ4.65 and two doublet of doublets at τ5.34 and 5.66(ratio 1:3) for the C_2 protons in the two isomers.

The second fraction isolated by chromatography afforded impure 2,11-diacetoxy-5-chloro-11-azabicyclo[4.4.1]undecane (II-86, 8%) or isomer thereof, which gave only one spot on a

tlc plate. The ir absorption of the C-acetate was shown at 1722 cm^{-1} and the N-acetate at 1765 cm^{-1}. Impure II-86 was characterized by the nmr signals at τ4.70(CHOAc), 5.48(CHCl), 6.72 for the two bridged protons and at τ7.83 and 7.96 for the N-acetate and C-acetate groups, respectively. The M^+ ions at m/e 303,305 for a one chlorine ratio had exact mass for $C_{14}H_{22}NO_4Cl$. The fragmentation pattern showed weak peaks at m/e 261,263 for the loss of ketene and had the parent peaks at m/e 244,246 for the loss of an acetate group.

The third fraction from the chromatography gave an impure triacetoxy azabicyclic compound assigned as II-87 (8%) or isomer thereof. Its ir spectrum exhibited absorptions at 1765 and 1735 cm^{-1} for acetoxy groups attached to a carbon and a nitrogen atom, respectively. The proton nmr spectrum showed a multiplet at τ4.74 for the methine protons geminal to acetoxy groups, and at τ5.27 as a broad quartet ($J \simeq 6.5$Hz) for the two bridged protons. The simplicity of this two protons pattern in the nmr spectrum might indicate that this triacetoxy compound is a symmetrical molecule as indicated by II-87. It also had two singlets at τ7.90 and 7.93 in the approximate 1:2 ratio for the N-acetate and the two C-acetate groups, respectively. The mass spectrum of II-87 exhibited the molecular ion at m/e 327, the m/e 285 for the loss of ketene and the m/e 268 for the loss of an acetate group from the molecular ion.

CHAPTER III

DISCUSSION

III-1. Photolysis of Nitramines

III-1-1. Non-oxidative photolyses

As can be seen in Table II-1, the photodecompositions of dialkyl nitramines under neutral conditions are complex. This can be explained as due to the complex behavior of nitrogen dioxide in solution (102). The photolyses of nitramines in aprotic solvents form the corresponding nitrosamines and ammonium nitrates in agreement with the results reported by others (10, 15); but NNOD also gives formamides.

Formamide II-1 is not obtained during the NNOP photolysis in n-hexane, even in the presence of carbonates and carbon monoxide, although it has been formed in methanol (23). Furthermore, formamides II-3 and II-5 are obtained in the NNOD photolyses in n-hexane. These results indicate that the formyl group must be derived from methanol in the former case and from the N-methyl groups in the latter. Furthermore, under dilute acidic

methanol solution, it has been reported that NNOP is photolytically reduced and methanol oxidized to formaldehyde (23). In view of these redox patterns, it may be assumed that the photolysis causes homolysis of the N-N bond to form dialkylaminyl radicals and nitrogen dioxide in the first step (Equation III-1). The formation of the observed products can be rationalized by the reactions outlined below.

Under neutral conditions the aminyl radicals abstract a hydrogen atom from either the solvent (Equation III-4), alkenes (Equation III-5) or from a dimethylamino moiety (eg, disproportionation Equation III-7); the last reaction gives dialkyl amines and formylidene methylamine. Subsequent trimerization or hydrolysis of formylidene methylamine gives II-6 or methylamine and formaldehyde, respectively, (Equation III-8), as previously reported (64).

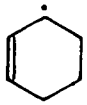
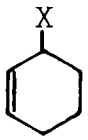
In solution, nitrogen dioxide is expected to be in equilibrium with dinitrogen tetroxide (102) under the reaction conditions (Equation III-3); both of them may act as oxidizing agents or radical trapping agents (102). Nitrosamines, which under the conditions are not photolabile (19), are suggested to be formed from amines and nitrogen tetroxide in which the nitrate anion is also formed as in Equation III-6. This nitrosation process is a well known reaction for the preparation of nitrosamides (3) and nitrosamines (103). Another possible source

[III-1] $R_2N\text{-}NO_2 \xrightarrow{h\nu} {}^{\cdot}NO_2 + R_2N^{\cdot}$

[III-2] $(CH_3)_2N^{\cdot} \rightleftharpoons (CH_3)_2\overset{+}{N}H$ (H^+)

[III-3] $2\,{}^{\cdot}NO_2 \rightleftharpoons N_2O_4$

[III-4] $R_2N^{\cdot} + SH \xrightarrow{H^{\cdot}\ \text{abstraction}} R_2NH + S^{\cdot}$

[III-5] $R_2N^{\cdot} +$  $\xrightarrow[\text{abstraction}]{H^{\cdot}}$ $R_2NH +$  $\xrightarrow{XR'}$  $+ R'^{\cdot}$

[III-6] $R_2NH + N_2O_4 \longrightarrow R_2N\text{-}NO + HNO_3$

[III-7] $2(CH_3)_2N^{\cdot} \xrightarrow{H^{\cdot}\ \text{abstraction}} (CH_3)_2NH + CH_3\text{-}N{=}CH_2$

[III-8] $CH_3\text{-}N{=}CH_2 \xrightarrow{H_2O} CH_3NH_2 + CH_2O$

[III-9] $(CH_3)_2NH + CH_2O \longrightarrow (CH_3)_2NCH_2OH \xrightarrow{Ox} (CH_3)_2NCHO$

[III-10] $CH_3NH_2 + CH_2O \longrightarrow CH_3NHCH_2OH \xrightarrow{Ox} CH_3NHCHO$

[III-11] $R_2N\text{-}NO_2 + {}^{\cdot}NO_2 \longrightarrow R_2N^{\cdot} + N_2O_4$

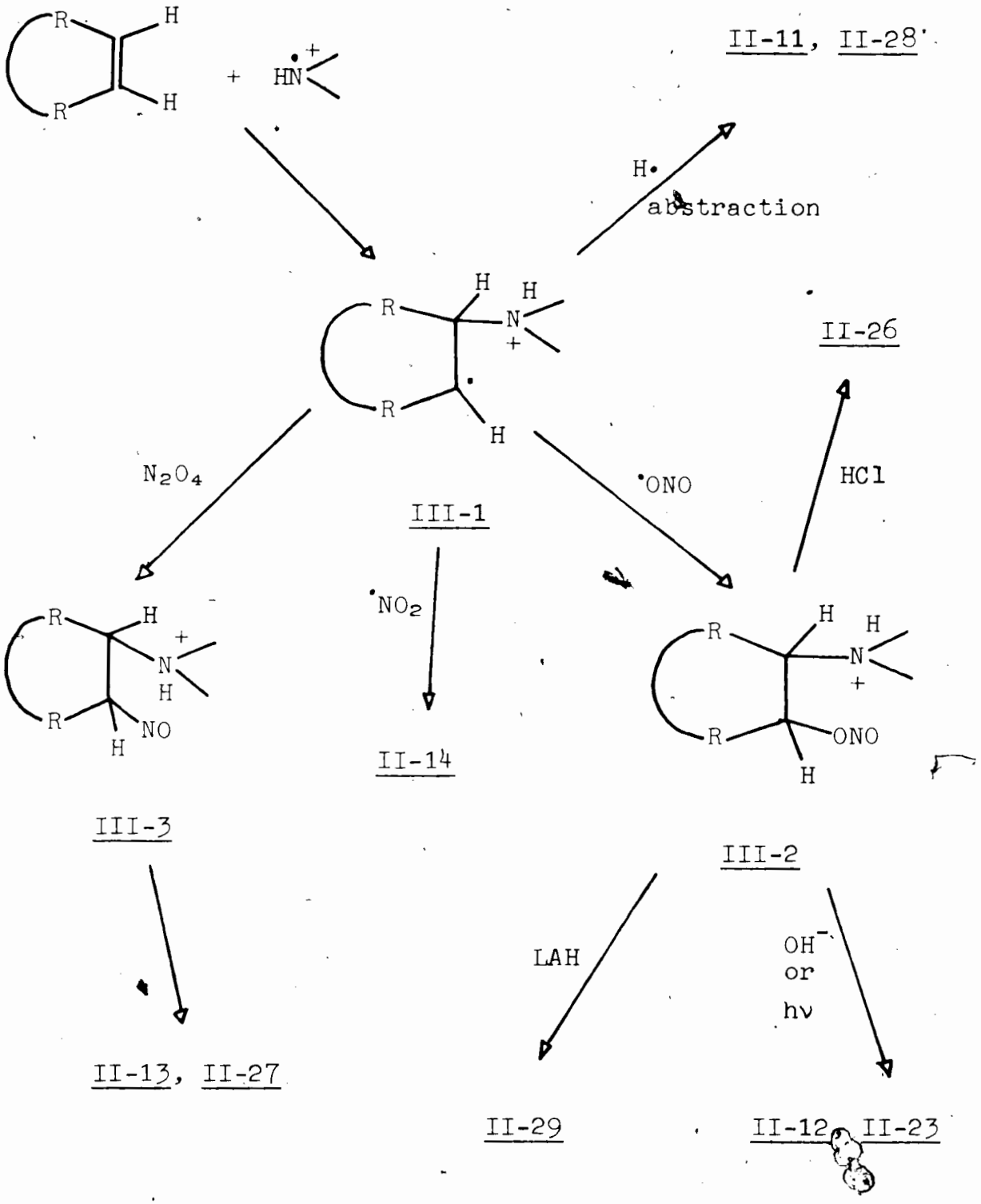
of nitrosamine might be the combination of the aminyl radical with nitric oxide, produced from secondary reactions of nitrogen dioxide with alkanes or alkyl radicals (102). However this pathway cannot account for the high yields of NND obtained in the presence of carbonates.

The formation of formamides is believed to follow the pathways shown in Equations III-9 and III-10. The first step of each reaction is a very well known process (104); the oxidation of the hydroxymethylamines to the formamides can be accomplished by nitrogen dioxide or dinitrogen tetroxide as oxidants (102). Since the quantum yield of nitropiperidine disappearance in neutral methanol has been measured to be 4.8 (23), a propagation step such as shown in Equation III-11 is proposed.

In acidic solution, aminyl radicals, whose pK_a has been reported as 6.5-7.5 (105), are protonated to give the aminium radicals (Equation III-2) which are known to add efficiently to π-bonds or abstract hydrogen atoms in the presence of olefins (19). Protonation of nitramines not expected in dilute acid (0.1-2N) since secondary nitramines are reported to be neutral species (1). Therefore, the primary photoprocess must be somewhat different from those of nitrosamine (19) and tetrazene (64,106) photolyses since in the latter aminium radicals are generated directly from excitation of proton associated nitrosamines and protonated tetrazenes.

The efficient photoaddition of nitrosamines to olefins under dilute acidic conditions and the failure to do so under neutral conditions clearly demonstrate that the photolysis of nitramines gives aminium radicals under acidic conditions and aminyl radicals under neutral conditions (23). Furthermore, neither aminyl nor aminium radicals could be trapped by carbon monoxide under our reaction conditions. However under an inert atmosphere such as nitrogen or carbon monoxide, the photoadditions of NNOD to cyclohexene or COD give a complex mixture of addition products due to two major factors. Firstly, the counter radical in the photoaddition, nitrogen dioxide, can behave as a nitrogen centered radical or as an oxygen centered radical (107), to give nitrites III-2 and nitro compounds II-14, respectively from III-1 (Scheme III-1). Secondly, the nitrites may be hydrolyzed or photolyzed (108) under the conditions to give alcohols II-12 or II-23.

Aminium radical initiated addition to olefins may be summarized as in Scheme III-1. Before reacting with by nitrogen dioxide with chloride ion to give II-26, carbon radical III-1 may abstract a hydrogen atom from the solvent to give amines II-11 orII-28. It is believed that oximes II-13 or II-27 are formed through the C-nitroso compound III-3 (19), obtained by trapping the radical III-1 with dinitrogen tetro-


II-11, II-28
H•
abstraction
II-26
N_2O_4
•ONO
HCl
III-1
•NO_2
II-14
III-3
III-2
LAH
OH⁻
or
hν
II-13, II-27
II-29
II-12, II-23

Scheme III-1

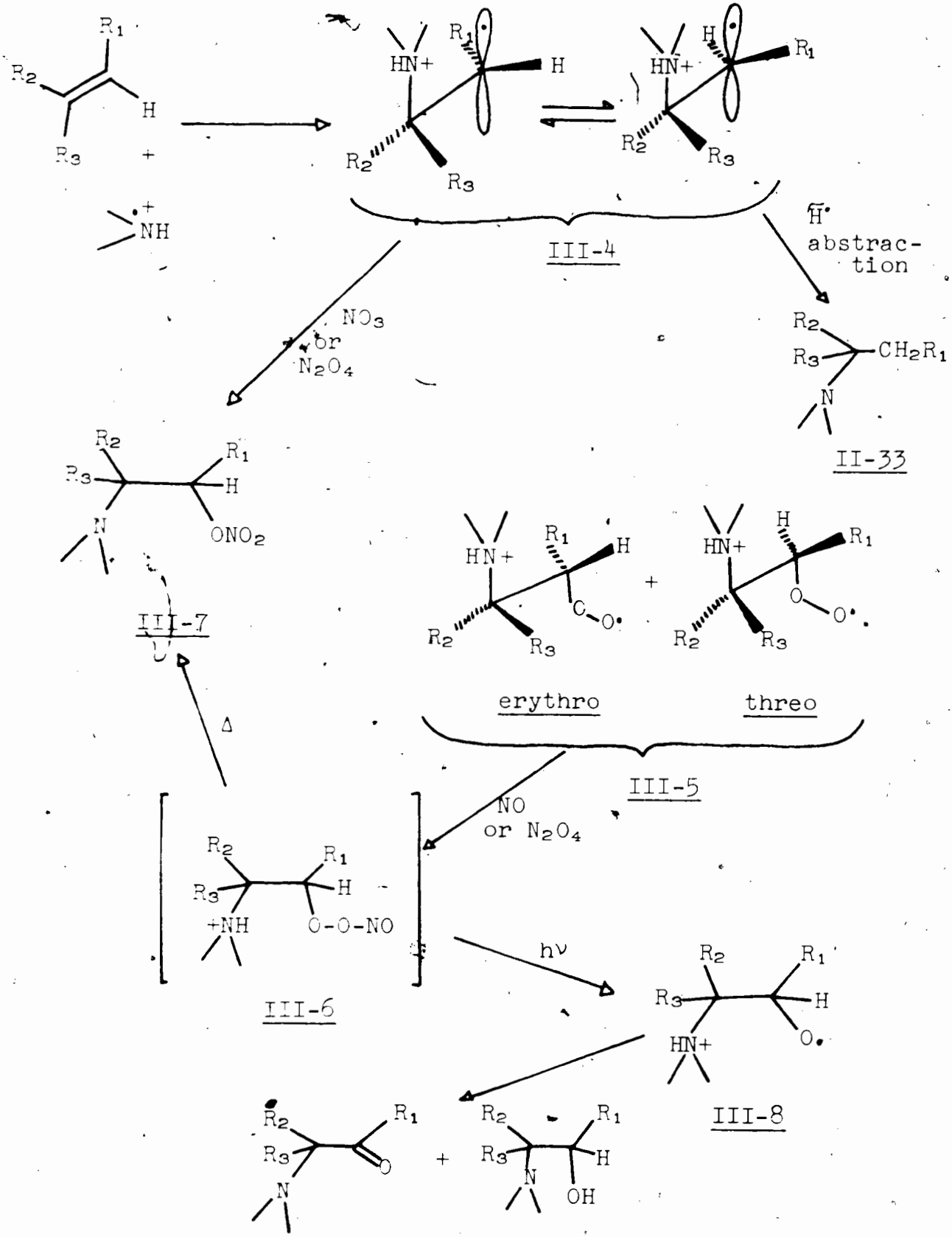
xide. In the case of the photolyses of NNOD with tttCDT or ctCDD, this last pathway accounts for 76 and 85%, respectively (vide supra). The formation of β-chloramines II-26 may be ionic in nature. As shown in Scheme III-1, the postulated nitrite ester III-2 might undergo a nucleophilic displacement by the chloride ion of the hydrochloric acid present in the photolysate to give β-chloramines II-26. It is interesting to note that in tetramethyl-2-tetrazene photolytic addition to cyclohexene in the presence of hydrochloric acid, some β-chloramines have been detected (63,64).

The formation of the open chain amino alcohol II-29 obtained after reduction of the basic photolysate fraction is believed to arise from the lithium aluminium hydride reduction of the postulated intermediate nitrite ester III-2. Obviously, the ring opening is assisted by the lone pair of electrons of the dimethylamino group and might follow a similar pathway as the one discussed with nitrate esters II-37 (vide infra).

III-1-2. Oxidative photoadditions

(a) formation of nitrate esters: The product distribution of this photoaddition is greatly simplified when run under oxygen; it gives 1-nitrato-2-amino derivatives as the primary

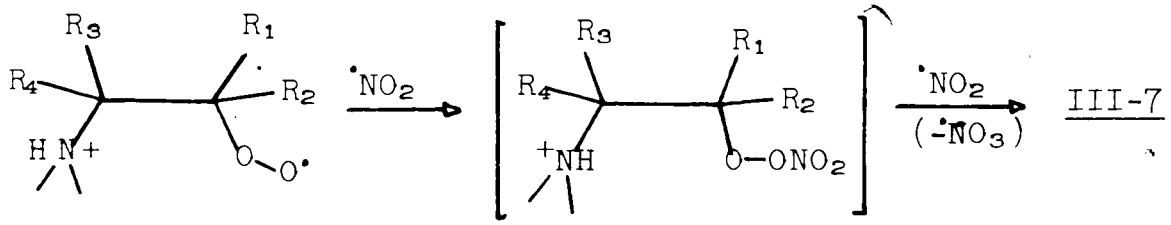
products. Aminium radicals generated during the oxidative photolysis of NNOD in dilute acidic media add preferentially to the less substituted terminus of 1-hexene to give the more stable secondary carbon radical intermediate in agreement with the non-oxidative photoaddition of NNP to 1-pentene (111). The electrophilic attack by the dimethylaminium radical on the π-bond results in the formation of intermediate carbon radicals such as III-4 (Scheme III-2). The fact that radicals III-4 are able to abstract a hydrogen atom from the solvent to give amine II-33 before it is quenched by oxygen to yield peroxyl radicals III-5 favors a stepwise process. With trans-3-hexene, the oxidative photoaddition of NNOD yielded erythro II-22a and threo II-22b in a 5:3 ratio, indicating that addition is indeed stepwise and that rotation of the carbon-carbon single bond in radicals III-4 is much faster than the subsequent step. The non-stereospecific addition of oxygen due to rapid rotation about the newly formed single bond of III-4 gave an erythro, threo mixture III-5. These radicals are further trapped by nitric oxide in the case of NND photolyses or dinitrogen tetroxide in the case of NNOD photolyses to give peroxynitrites III-6. The rate of this combination in the gas phase has been shown to be greater than $6 \times 10^8 M^{-1} s^{-1}$ (112). Although never isolated, peroxynitrites have been postulated in several instances; nitric oxide has been shown to combine under reduced pressure at room temperature with tri-


III-4
H· abstraction
NO3 or N2O4
II-33
III-7
erythro
threo
Δ
III-5
NO or N2O4
III-6
hν
III-8

Scheme III-2

phenylmethylperoxy radicals trapped in a polycrystalline triphenylacetic acid matrix to give triphenylmethyl peroxynitrite as a postulated intermediate (113). Peroxynitrite esters have also been proposed as intermediates during the reaction of t-butyl hydroperoxide with nitric oxide (114), during the photolysis of nitrite esters (115) and of nitrosamines with olefins (67) in the presence of oxygen, and during the treatment of tertiary hydroperoxides with nitrosyl chloride-pyridine (116).

As with the previous examples, peroxynitrite esters III-6 may be expected to undergo a facile rearrangement to the corresponding nitrate esters III-7 (threo and erythro), very likely by a peroxy bond scission. In the case of the photolysis with NNOD, an additional route may be mentionned, that is peroxyl radicals III-5 may combine with nitrogen dioxide to give pernitrates III-9 as possible intermediates. The peroxy nitrates formed in this way have been shown to give the corresponding ketone and nitrates as the major decomposition products (117).



III-5 III-9

An alternate source of nitrate esters III-7 may be visualized as seen in Scheme III-2. In the case of NND photolyses, the counter radical nitric oxide formed (19) may be intercepted by oxygen to give $^{\bullet}NO_3$, which combines with III-4 to yield III-7. Reaction of dinitrogen tetroxide with III-4 in the case of NNOD photolyses may also give rise to nitrate esters III-7. However, since the resulting nitrate esters of the CDT photolyses have been shown to be very stable in acidic and basic conditions, these alternate pathways do not give any photolabile or readily decomposed intermediates to explain the formation of ketone and alcohols. For this reason, the last mechanisms, if operating, are probably not the major pathways of the photolyses.

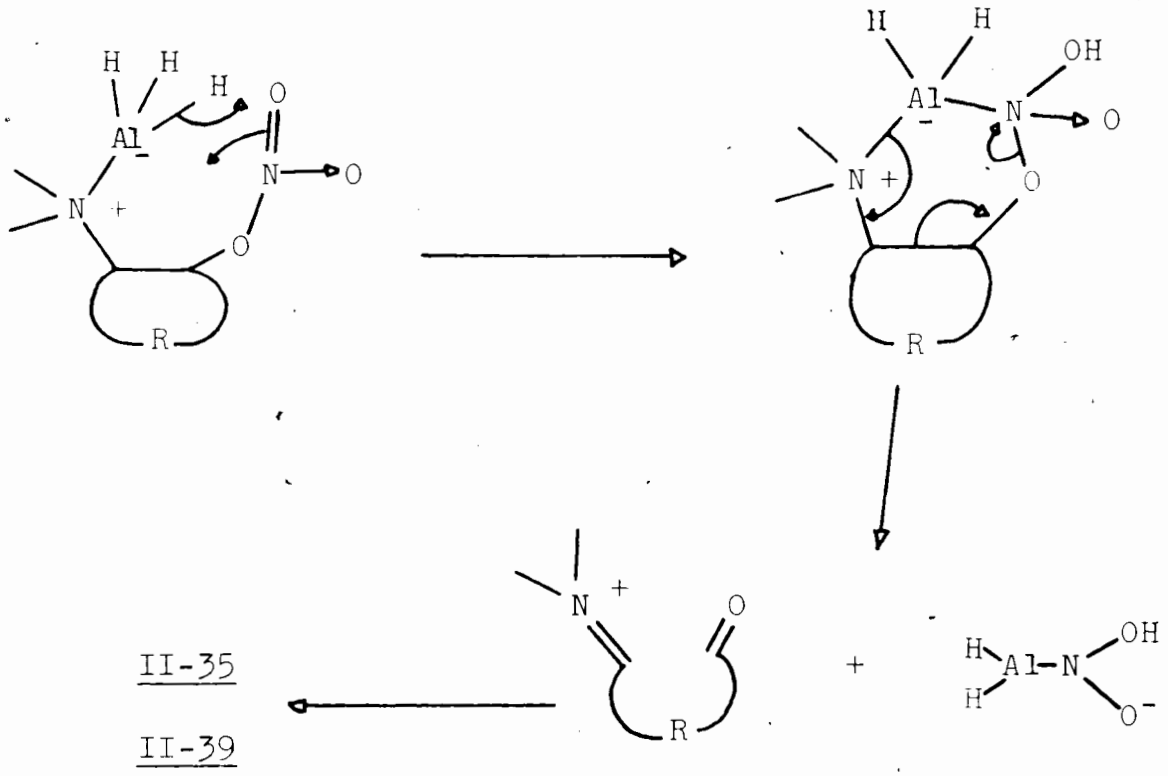
(b) formation of ketones and alcohols: To account for the formation of large quantities of amino alcohols and ketones in the photolyses with CDT, it is assumed that transient pernitrite III-6 is photolytically cleaved at the weak O-O bond to give alkoxy radicals III-8 as possible intermediates (Scheme III-2). Indeed, in analogy to the low intensity $n\rightarrow\pi^*$ uv absorption band around 340-385nm (ε20-80) for nitrite ester derivatives (118), a similar band for pernitrites III-6 may be expected in the same region. Thus, we may anticipate pernitrites to undergo secondary photolysis to generate the corresponding alkoxy radicals III-8 which may be the source of

the ketone and alcohol formation during photolysis. This is indicated by i) the ketone-nitrate esters ratio is smaller in the photolyses of NND than in those of NNOD, ii) this ratio is further reduced using excesses of NND, iii) when excesses of NND are used (Table II-4), lower yields of alcohols II-34a, II-34b are obtained after work-up as opposed to better yields of open chain alcohol II-35, which is known to arise mainly from the nitrate esters (vide infra). It is reasonable to interpret that in the presence of an excess of NND, NND acts as the internal filter to prevent the secondary photoreaction leading to lesser amount of alcohols and ketone. These results also indicate that pernitrites III-6 must have a sufficiently long life at 0° to be photodecomposed before they rearrange to the nitrate esters.

(c) LAH reduction of amino nitrate esters: The aliphatic nitrate esters II-15 and II-19 decomposed in basic conditions to give alcohols II-16 and II-20, respectively, by nucleophilic displacement or hydrolysis of the nitrate and to ketones II-18 and II-21, respectively by elimination of α-hydrogen. No β-elimination leading to olefin has been detected. These nitrate esters were easily reduced by lithium aluminium hydride to the corresponding alcohols.

Although other nitrates are reduced by LAH to give the corresponding alcohols, LAH reduction of the amino nitrate /

obtained from the oxidative photoadditions of NNOD (or NND) to the two CDT isomers causes cleavage of the C_1-C_2 bond. Such a cleavage reaction has never been observed as far as we are aware . This is assumed to be assisted by the lone pair on the nitrogen atom as depicted by the electron shifts shown in Scheme III-3. The immonium aldehyde intermediate obtained (III-10) can be further reduced to the open chain amino alcohols II-35 and II-39.



III-10

Scheme III-3

(d) Reactivity of double bond: The highly selective reactivity of the trans double bond of cttCDT has already been widely observed in ionic addition with reagents such as osmium tetroxide (119), potassium permanganate (119), diimide (120), peracids (121) and nitrosyl chloride (38). For example, with the first two reagents, cis,trans-5,9-cyclododecadien-trans-1,2-diol was obtained in excellent yields.

Although no systematic data on the relative reactivity of the cis and trans isomers of cycloalkadienes and cycloalkatrienes are available, quantitative data on the stability of the cis and trans cyclic monoolefins have been determined by direct equilibration (122) and heats of hydrogenation measurements (123)(TableIII-1); $\Delta(\Delta H^\circ)$ and $\Delta(\Delta G^\circ)$ are the

Ring size	$\Delta(\Delta H^\circ)$	$\Delta(\Delta G^\circ)$	K_{cis}/K_{trans}	% trans
8	-9.26			
9	-2.87	-4.04	232	1
10	-3.34	-1.86	12.2	24
11	-0.12	0.67	0.406	71
12	-0.41	0.49	0.517	66

Table III-1

values of the differences of heats of hydrogenation and free energies of hydrogenation, respectively, for the cis and trans cycloalkenes. For cycloalkenes of ring size larger than 10, the trans double bond becomes more stable, and the factors controlling the stabilities are substantially the same as those for open chain olefins. Although the data for the stability of cycloalkapolyenes are fragmentory, it is generally believed that the relative stabilities of cis and trans double bonds in the CDT parallel those of the cis and trans double bonds in the corresponding cyclododecene (78). It also appears (124) that tttCDT is thermally more stable that the cttCDT isomer. Dreiding Molecular Models of the cttCDT show that the cyclic system is quite flexible and that there is no visible difference in steric approach toward the cis and trans double bonds. No satisfactory explanation for preferential attack of the trans double bond by the aminium radical can be obtained from a discussion based on thermodynamic stability.

With endoDCPD, the double bond of the bicycloheptene system has been reported to be the most reactive in the radical addition of 4-chlorobenzenethiol (125), in the ionic addition of nitrosyl chloride (126), in mercuration with mercuric acetate (127) and radical reactions using the photolysis of tetramethyl tetrazene (64). These reactions occur without any skeletal rearrangement. There has been no evidence of products

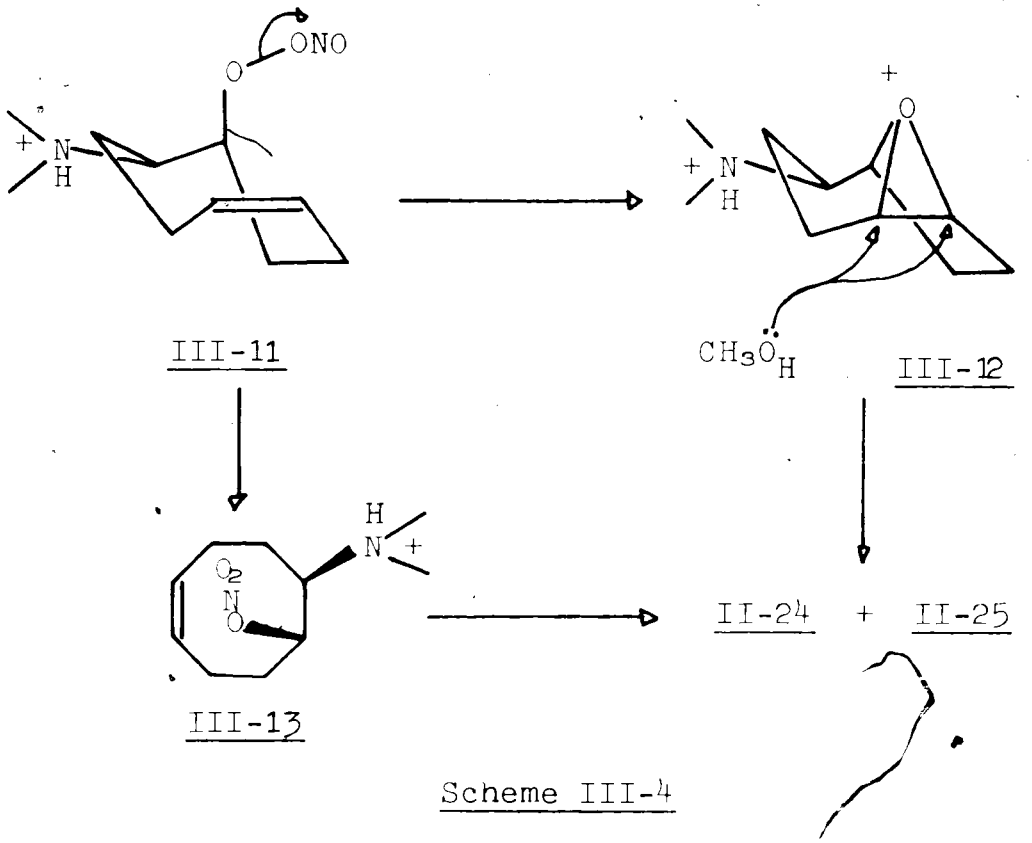
derived from attack on the double bond in the cyclopentene ring but they may have escaped detection.

Obviously aminium radicals generated from NND (or NNOD) attack the norbornene double bond as well as the cyclopentene double bond; in our conditions, the former has been found to be six times more reactive that the latter from the ratio of the yields of alcohols II-41 and II-42.

Ionic and radical additions of reagents to ctCDD (128-130, vide infra) have been shown to add selectively to the trans double bond. However, in this case, aminium radicals induced a transannular cyclization reaction; hence the initial attack of the aminium radical could not be ascertained. Nevertheless, in agreement with reported data (128-130) and with previous results with cttCDT, a selective attack at the trans double bond is believed to take place (vide infra).

III-1-3. Individual cases

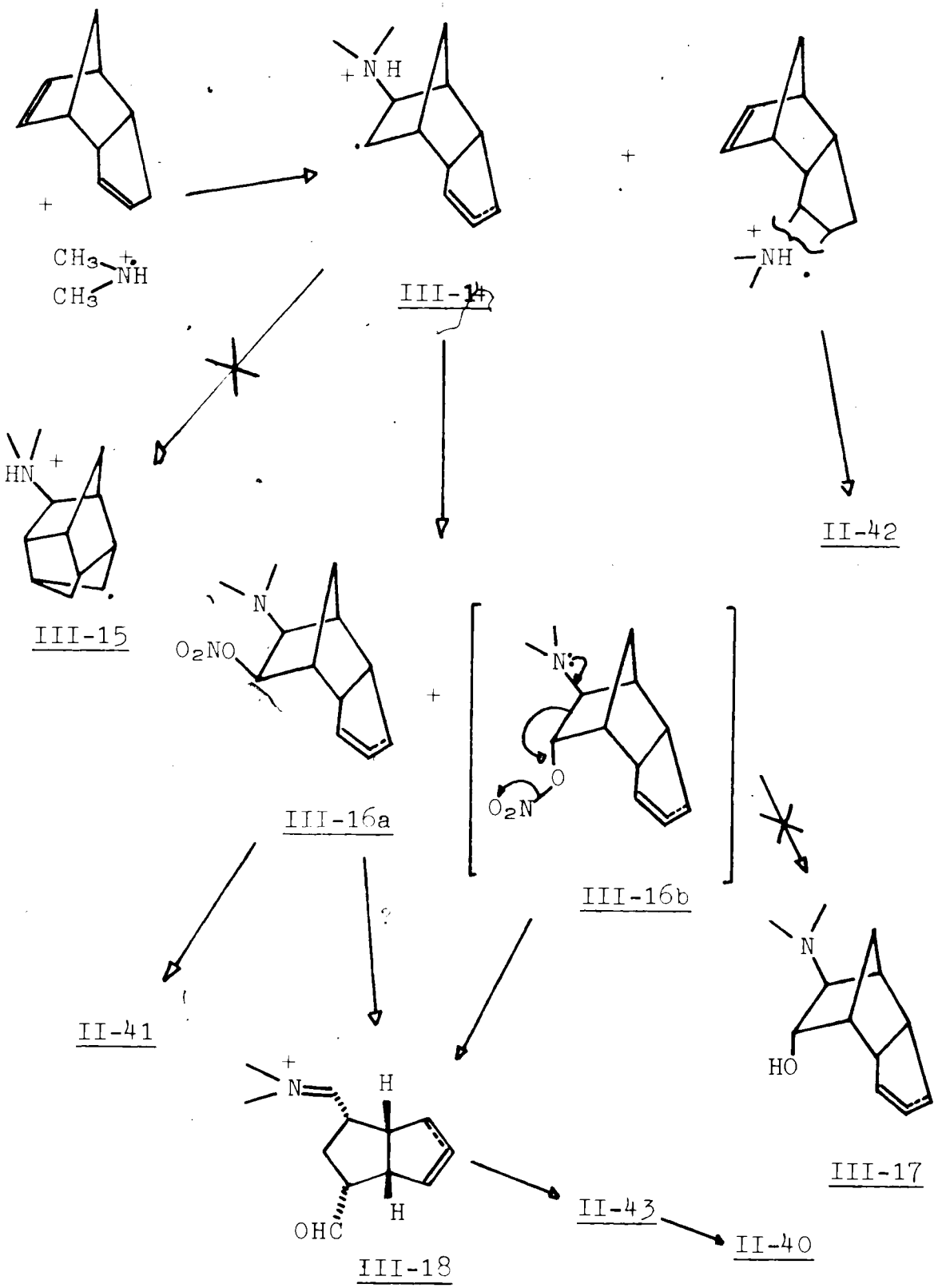
(a) Rearrangement with COD: In the oxidative addition of NNOD to COD, only trans amino alcohol II-23a of the two possible isomers can be isolated after LAH reduction. Failure to detect cis amino alcohol II-23b may be due to the facile rearrangement of cis peroxynitrite intermediate III-11 to the oxabicyclic ethers II-24 and II-25 by elimination of nitrite ion assisted by transannular π-electron migration to the electron deficient oxygen atom (Scheme III-4). This may well in-



Scheme III-4

volved the intermediacy of an oxonium ion (III-12) which solvent may attack at either C_5 or C_6 giving the oxabicyclic ethers II-24 and II-25; this transannular rearrangement has been already proposed during the oxidative photoaddition of NND to COD (69,131) and was postulated to occur through the cis nitrate ester III-13.

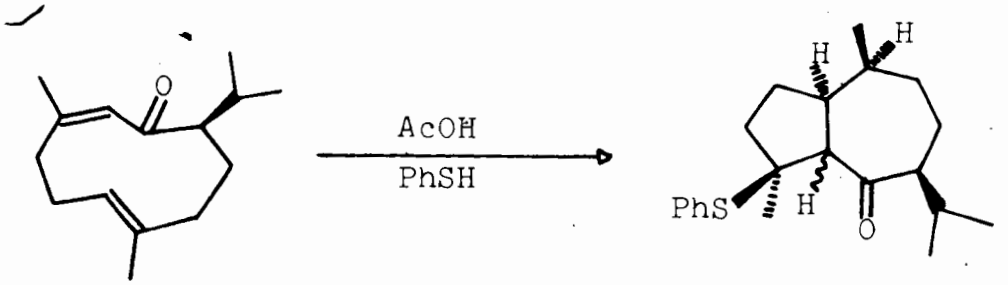
(b) Addition to endo-DCPD: From steric reasons (69,132, 133), the dimethylaminium radical is expected to approach from the exo face of the norbornene π-bond of endo-DCPD giving the exo configuration of the amine group as in III-14 (Scheme III-5)


CH3
NH
CH3
III-14
NH
II-42
HN
III-15
N
O2NO
III-16a
N
O
O2N
III-16b
II-41
N
HO
III-17
N
H
H
OHC
III-18
II-43
II-40

Scheme III-5

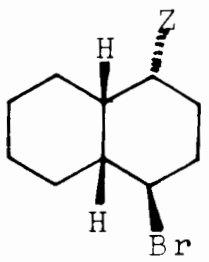
A careful examination of the product mixture did not reveal the formation of saturated compounds; this eliminated the cyclization step to III-15, although decomposition of the saturated amino nitrate ester derived from III-15 to give an olefinic content molecule is not excluded. The subsequent approach of oxygen is determined not only by the steric bulk of the amino group in the exo-9-position but also by that of the cyclopentene ring. Both exo-cis III-16a and trans nitrate III-16b (Scheme III-5) are postulated as intermediates by the following arguments. The exo-cis configuration of III-16a is easily deduced from that of amino alcohol II-41 obtained by LAH reduction. Since no trace of trans amino alcohol III-17 has been detected, trans nitrate III-16b must have been readily decomposed before reduction, in analogy to the facile cleavage of trans-2-nitrato-3-dimethylamino norbornane. That is, nitrate III-16b might eliminate nitrite ion by the electron shifts shown in Scheme III-5 to give the immonium salt III-18, the precursor of II-43, which can be reduced to II-40.

(c) Transannular cyclization with ctCDD: Cation induced transannular cyclization reactions of 1,5-cyclodecadienes (128-130,134) and their oxides (135,136) are now established to give cis decalin derivatives as the major or sole products with high stereoselectivity. In contrast, the cis,trans germacrone



III-19 III-20

III-19 is cyclized to a guaiane-type compound III-20 of undefined stereochemistry at C_5 (137); this has been interpreted as an ionic reaction but a radical mechanism with initial attack at the trans double bond cannot be excluded. Radical induced cyclizations with bromotrichloromethane and bromoform (129) have been suggested to give cis decalin III-21 and III-22, respectively, implying that initial attack is on the cis double bond. However there is no definite proof that the compounds are cis or even decalins. The aminium radical ini-



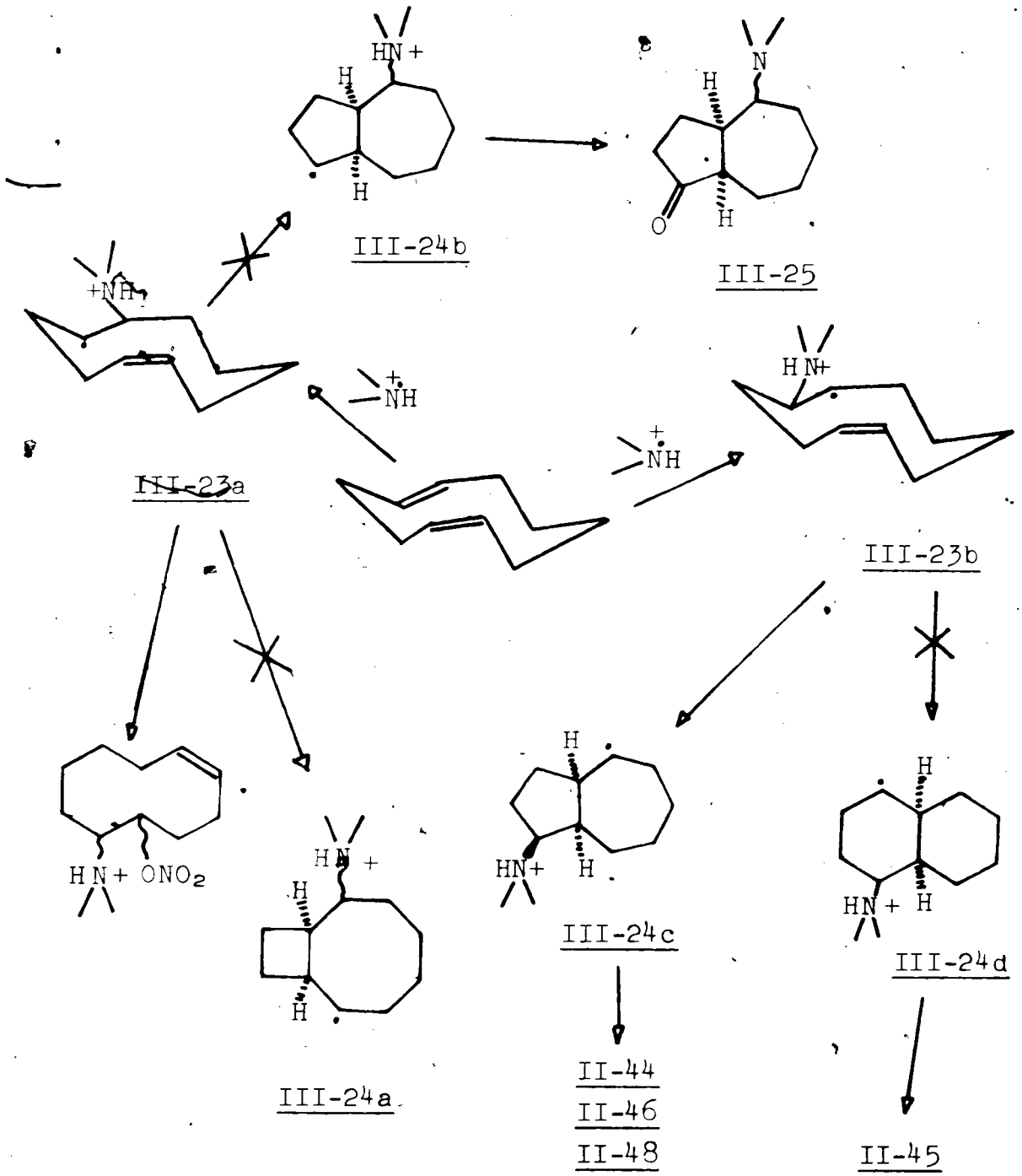
Z = CCl_3 , III-21

Z = $CHBr_2$, III-22

tiated cyclizations with ctCDD also show high stereoselectivity leading to only one compound of cis fused 5,7 bicyclic products. The cis ring fusion has been determined from the fact that the ketone II-47a can be isomerized to the more stable trans isomer II-47b; such isomerization has been reported (138-141) with analogous systems.

A dimethylaminium radical attack at the trans double bond should give rise to two different positional carbon radicals III-23a and III-23b (Scheme III-6) which, after transannular ring closure can generate four possible saturated carbon radicals III-24a-d, with the cis ring fusion. Carbon radical III-24b can be eliminated on the basis that no ir absorption band around 1745 cm^{-1} for a 5-membered ring ketone III-25 has been detected from subsequent transformations. Intramolecular radical cyclization of open chain dienes has been thoroughly investigated (24, 142-144). The direction of these cyclizations appears to be controlled by both steric (142) and electronic (144) factors yielding the kinetically more favored five-membered ring product preferentially but no four member ring. Consequently, carbon radical III-24a can be rejected. The alternative five-membered cyclization to III-24c or the six-membered cyclization to III-24d should be considered: the former pathway is preferred over the latter on the basis of the previous stereospecific cyclizations (142-144) and from the proton nmr spectrum of nitrate salt II-44a

which favors a cis fused decahydro azulene structure over a cis decalin structure.



Scheme III-6

III-2. Transannular Electrophilic Reaction of Alkenyl Nitroso Compounds

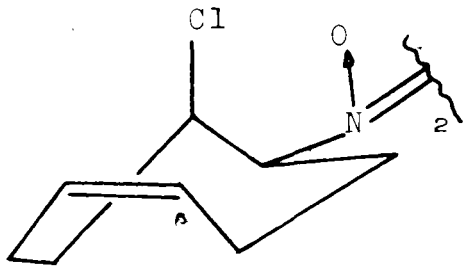
We saw in the Introduction that in principle, a nitroso group may be protonated to generate a nitrenium ion intermediate which may add intramolecularly to a strategically located π-bond. The starting C-nitroso alkene must possess a suitable configuration whereby the relevant orbitals can interact over the space. In the first step, we shall discuss the stereochemistry of the nitrosyl chloride addition to unconjugated polyenes.

III-2-1. NOCl Addition to Olefins

In spite of numerous reports on nitrosyl chloride addition to olefins (28,145), the stereochemical course of the addition remains confusing until recently when Rogić and coworkers (36) resolved the controversy over the addition of nitrosyl chloride to cyclohexene. In highly polar solvents such as sulfur dioxide, it was found that trans addition of NOCl to cyclohexene gives a pair of 2-chloronitrosocyclohexane enantiomers which dimerize homospecifically or heterospecifically to give the anti SS-SS, RR-RR (dl pair) and SS-RR (meso) nitroso dimers, respectively (36). However, in this

work, in a low polarity solvent such as methylene chloride, nitrosyl chloride adds stereospecifically to COD, tttCDT and probably ctCDD in a cis stereochemical course. This was clarified by the cis configuration of C-nitroso monomer of COD (II-51) and the threo (trans) configuration of that of ttt CDT (II-66).

Cis-chloronitroso compound II-51 dimerizes to a single dimer, either the dl or meso isomer. The cis configuration of the chlorine and azodioxy group in the dimer was established by ^{1}Hnmr. Examination of Dreiding Molecular Models suggests that the cyclooctenyl nitroso chloride dimer of II-51 exists preferentially in a twist-boat-chair conformation (III-26) with the chlorine and azodioxy group in pseudo axial and pseudo equatorial orientations, respectively, as confirmed with the methine protons of the nmr spectrum. This conformation does not lead to overlap of the π-bonds of the nitroso

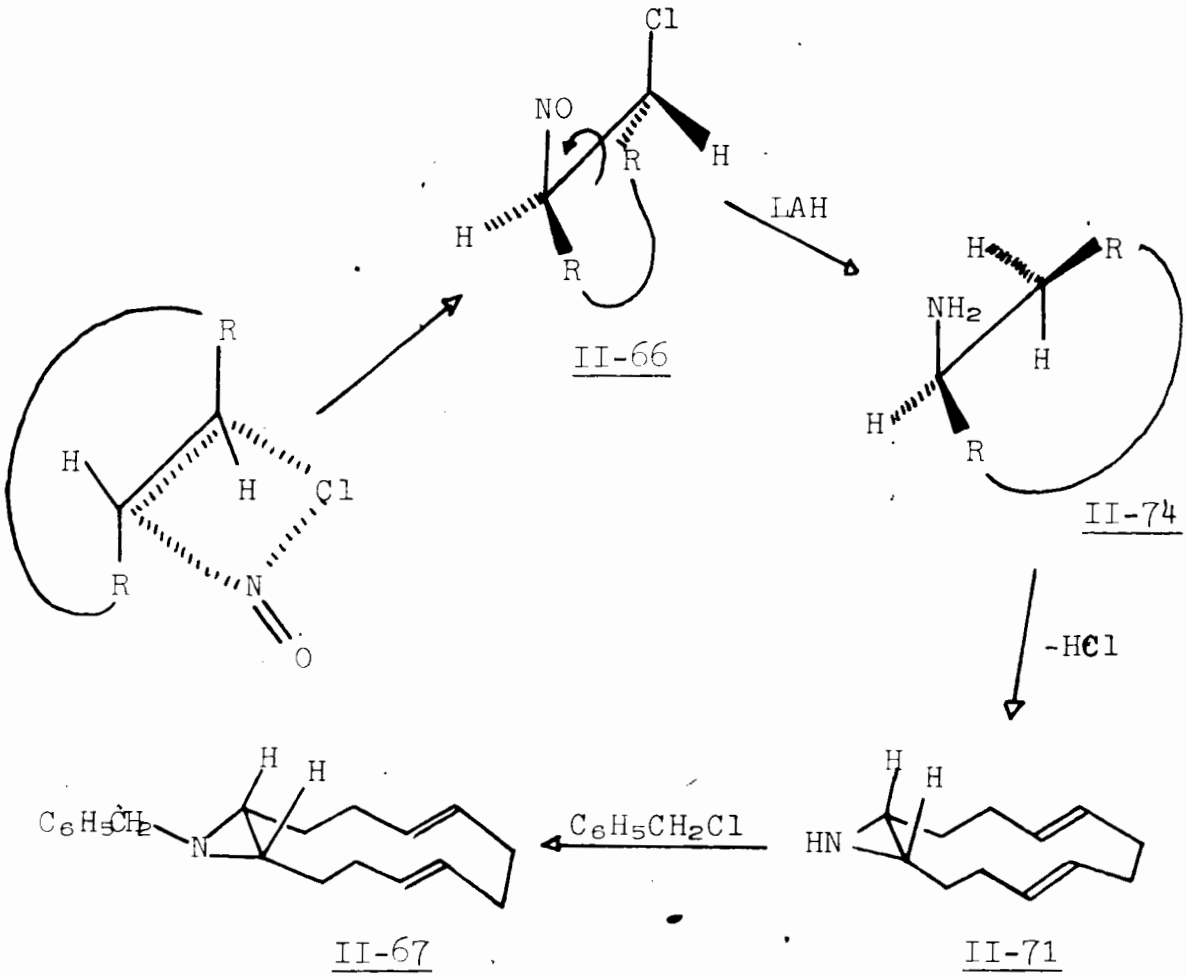


III-26

and olefinic groups, but as it will be seen later, the conformation of monomer II-51 may invert to a more favorable conformation for olefin-nitroso interaction. In any case, an assumption of the trans configuration for the dimer of II-51 does not give bicyclic hydroxylamine acetate II-60 (vide infra) with the observed configuration.

Similarly, the cis addition of nitrosyl chloride to ttt CDT in methylene chloride affords a single isomer (II-66) with the threo (trans) configuration of the chlorine and nitroso group. In this case, two dimers of II-66 are obtained, the meso and dl diastereoisomers as indicated by ^{13}Cnmr and confirmed by the chemical transformations leading to single β-chloro amine II-74. A threo (trans) configuration of II-66 was deduced from its chemical transformations to the meso benzylaziridine II-67 (Scheme III-7) and established a cis addition of nitrosyl chloride to a trans double bond of tttCDT. As proposed by Ohno (38) and Meinwald (37), a four-center transition state may operate giving the threo isomer as seen in Scheme III-7.

With ctCDD, the trans double bond is selectively attacked by nitrosyl chloride in agreement with the published results (38,95,145). However, the addition of nitrosyl chloride to the trans double bond is nonregiospecific to give two C-nitroso dimers II-80a and II-80b as indicated by the tauto-



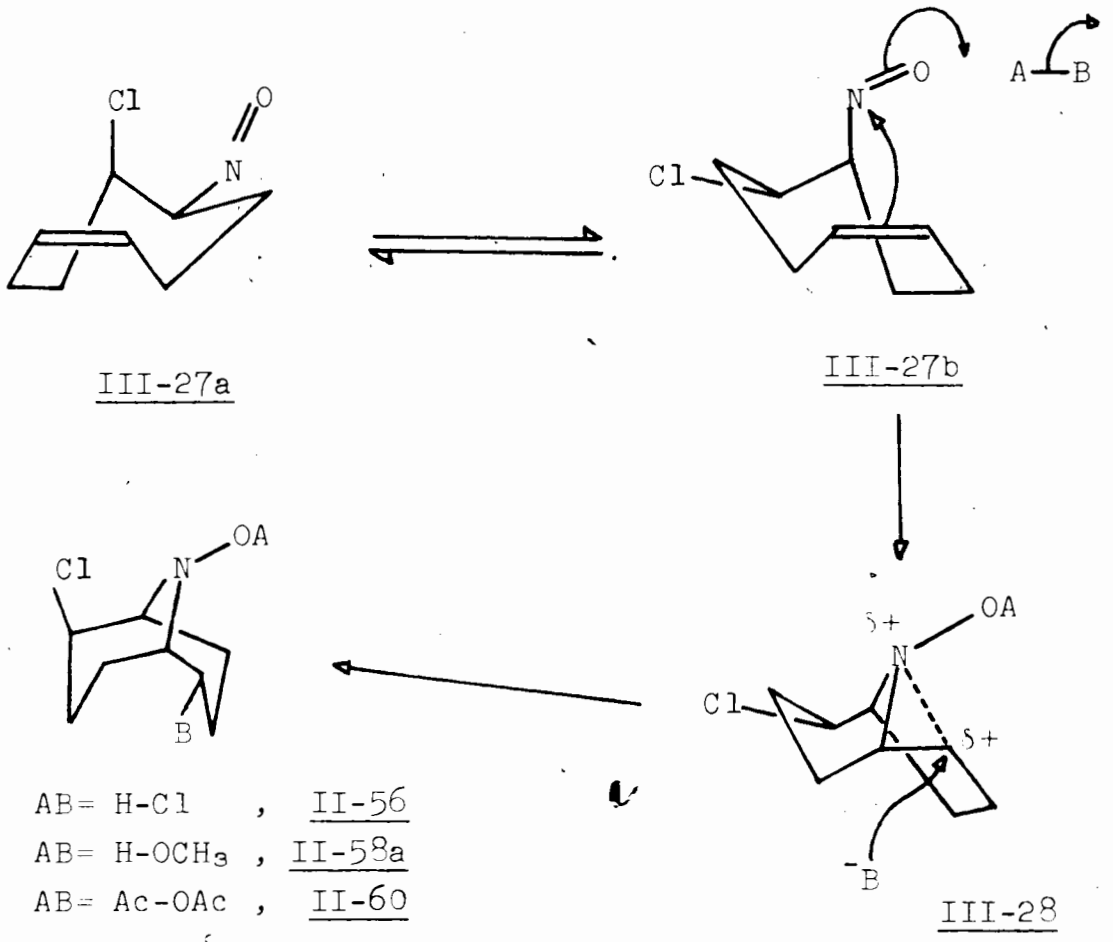
Scheme III-7

merization products II-81a and II-81b. In analogy to the addition to other olefins as discussed above, the addition to the trans double bond of ctCDD may also occur by stereospecific cis geometry but further experiments to prove this point have not been carried out.

III-2-2. Reactions of Nitrosoalkenes

Although the addition of nitroso arenes (56) and of one tertiary C-nitroso compound (49) are reported to occur by a free radical mechanism, the intramolecular reactions of alkenyl nitroso compounds described in this work are believed to take place by an ionic mechanism on the basis of the following reasons. Firstly, the reaction occurs even in the dark and is catalyzed by an acid, to give hydroxylamines but not nitroxides as the primary product. Secondly, it is well established that cyclization initiated by nitrogen centered radicals appears to favor the formation of five membered ring over those possessing six members by a kinetically controlled process (146,147); in our case, the transannular electrophilic reaction of alkenyl nitroso compounds give a six membered heterocycle rather than a five membered one.

The facile transannular reaction of chloronitroso compound II-51 can be visualized by the mechanism as depicted in Scheme III-8. In solution, under heating, the dimer of II-51 is dissociated into the monomer with conformation III-27a. The monomer, having a much smaller bulk of the nitroso group than the dimer, may be able to invert readily under the above conditions to conformation III-27b in which a transannular interaction of the nitroso and olefinic π-bonds can be easily obtained as shown in the step III-27b → III-28.



Scheme III-8

The attack of the anion from the opposite side of the nitrogen bridge in the intermediate III-28 leads to the hydroxylamines. The configuration in the latter , II-58a and II-60, is rigorously assigned from spectroscopic data and chemical transformations. If the proposed mechanism is correct, their stereochemistry indicates that the configuration of the chlorine and nitroso group of the starting C-nitroso compound II-51 must be cis.

The tautomerization of the C-nitroso compound which is also acid catalyzed competes with the transannular reaction. In the presence of proton donors such as hydrochloric and perchloric acids, the former reaction takes place overwhelmingly. This preferential tautomerization of II-51 to oximes II-52 in protic solvents may be rationalized by the steric crowding as the protonation of the nitroso group should be accompanied by increase of its size through solvation; this raises the conformation energy for III-53 and makes II-51 less likely to undergo the transannular reaction.

Chloronitroso compounds II-80a and II-80b are also capable, to a lesser extent, of assuming conformations in which the reacting nitroso and olefinic π-orbitals can be brought to overlapping proximity. However, the poorer yields of the transannular products may be due to a higher activation energy. Such a conformation is obviously not favorable for chloronitroso compound II-66. In this case, the similar type of hydroxylamine, if formed at all as judged by the esr signal of the corresponding nitroxide radical, is not present in a significant amount. Various attempts to cyclize amine II-68 during oxidation with lead tetraacetate (148), or its N-chloramine (149) have not been rewarded with success.

This acid catalyzed intramolecular reaction can also serve as an efficient route to give nitroxides indirectly

via hydroxylamines. Reports on dialkyl bicyclic nitroxide radicals possessing α-hydrogens are numerous but only in a few cases, were they actually isolated and characterized (62,150-152).This is probably due to their low yields and/or instability. They are usually non-crystalline and dimerize easily (152). On the other hand, hydroxylamine acetates such as II-60 can be easily purified and stored. Under mild hydrolysis, eg with aqueous sodium carbonate solution, they give hydroxylamines that are readily oxidized in the air to generate nitroxide radicals (89). With adequate conditions, hydroxylamine acetates can serve as stable precursors to generate nitroxides continuously for considerable period of time. Furthermore these bicyclic nitroxide radicals have been shown to be very stable and their stability can be attributed to stenic hindrance, since no double bond can be formed between the nitrogen and the adjacent carbon (150) according to Bredt's rule.

CHAPTER IV

EXPERIMENTAL

IV-1. General Techniques

Unless specified otherwise, the following experimental conditions were used.

Infrared (ir) spectra were recorded on a Perkin-Elmer 457 spectrophotometer using a Nujol mull or a liquid film of the samples. The absorption bands (cm^{-1}) are expressed as s, m, w and b for strong, medium, weak, and broad bands, respectively. An Unicam SP-800 ultraviolet (uv) spectrophotometer was used to follow the progress of the reaction; spectral bands are reported as λ_{max} nm (ε). Nuclear magnetic resonance (nmr) spectra were obtained on a Varian A 56/60 or a Varian XL-100 spectrophotometer equipped with a Nicolet 1080 computer in deuterochloroform ($CDCl_3$) solution using tetramethylsilane (TMS) as the internal standard.

Chemical shifts are reported from TMS in τ units for proton spectra or ppm for ^{13}C spectra. Coupling constants (J) and half-height widths ($W_{1/2}$) are reported in Hertz (Hz). The splitting patterns are presented as s for singlet, d for doublet, dd for doublet of doublet, ddd for double dd, t for triplet, dt for doublet of triplet, q for quartet, qui for quintet, m for multiplet, and b for broad. The D_2O exchangeable proton is indicated by D_2O exch, and the number of protons in a corresponding signal by multiples of H. The decoupling experiments were performed by Mr. Arthur Brooke, Miss Edna Cheah or by the author on the XL-100 spectrophotometer. In the ^{13}C nmr spectra, the multiplicity of the peaks observed in the off centre resonance decoupling were indicated in parentheses.

Mass spectra (ms) were taken by Mr. Gregory Owen on a Hitachi Perkin-Elmer RMU-6E instrument at an ionization voltage of 80 eV and were reported as m/e (relative abundance). The gas chromatographic-mass spectral (gc-ms) analyses were done using a Varian 1400 gas chromatograph coupled to the mass spectrophotometer. High resolution mass spectra (hrms) were performed at the University of British Columbia Mass Spectrometric Services.

Gas chromatographic (gc) analyses were performed on a F&M Model 810-19 Dual Flame Analytical Gas Chromatograph or a Varian 1200 flame ionization chromatograph using a 10% SE-30, 6ft by $^1/_8$ inch stainless steel column. Preparative gc runs were done on a Varian Aerograph Series 1700 Thermal Conductivity using a Varian Aerograph Model 20 strip chart recorder. Retention times (rt) are given in minutes (min). Where gc integration was used, the product yields were based on relative area ratio of all gc peaks without internal standard. They were further estimated with nmr and the comparison

of the two yields was believed to be less than ±3% . Thin layer chromatography (tlc) was performed on alumina or silicagel plates (0.2-0.3 mm thickness) impregnated with uv indicator, and examined by uv light and iodine vapor developer. Column chromatographic separations were performed with neutral or basic alumina (Brockmann Activity I, Fisher Scientific, 80-200 mesh), silicic acid (Mallinckrodt analytical reagent, 100 mesh), or silica gel (Baker or Fisher Scientific, 60-200 mesh).

Melting points (mp) were determined with a Fisher-Johns hot stage apparatus and were uncorrected. Elemental analyses were performed at the Department of Biology by Mr. May Kang Yang using a Perking-Elmer 240 Microanalyser. Electron spin resonance (esr) spectra were taken by Dr. K.S. Pillay or by the author on a Varian E-4 spectrophotometer. The coupling constants (a) are given in gauss (G) and the g-factor was calculated using diphenylpicrylhydrazyl radical (DPPH) as external standard.

IV-2. Chemicals

Unless otherwise stated, the anhydrous solvents used were reagent grade, distilled and stored over sodium ribbon or molecular sieves (Type 3A). The anhydrous ether used for the metal hydride reductions was distilled from lithium aluminium hydride. Reagent grade pyridine was stored over potassium

hydroxide pellets.

Concentrated sulfuric (H_2SO_4, 98%) and hydrochloric (HCl, 38%) acids were supplied by Fischer Scientific Co, trifluoro acetic acid by Matheson Coleman and Bell, glacial acetic acid by the Mc Arthur Chemical Company, and perchloric acid (70%) by Mallinckrodt Chemical Works.

Metal hydrides used were lithium aluminium hydride (LAH Alfa Products, 95%), sodium borohydride ($NaBH_4$, Fischer Scientific, 98%). The gaseous reagents except oxygen (Liquid Carbonic) and nitrogen (Union Carbide) were supplied by the Matheson Gas Company. Nitrogen was purified by scrubbing it through a Fieser solution (153) followed by concentrated H_2SO_4 and then through potassium hydroxide pellets (KOH, Fischer Scientific Co). Hydrogen peroxide (H_2O_2, 50%) was supplied by Fischer.

The commercially available olefins, 1-hexene, trans-3-hexene, cis,cis-1,5-cyclooctadiene and norbornene were supplied by Aldrich Chemical Co, cyclohexene by Fischer Scientific Co, and were distilled before used.

IV-3. General procedure of photolysis

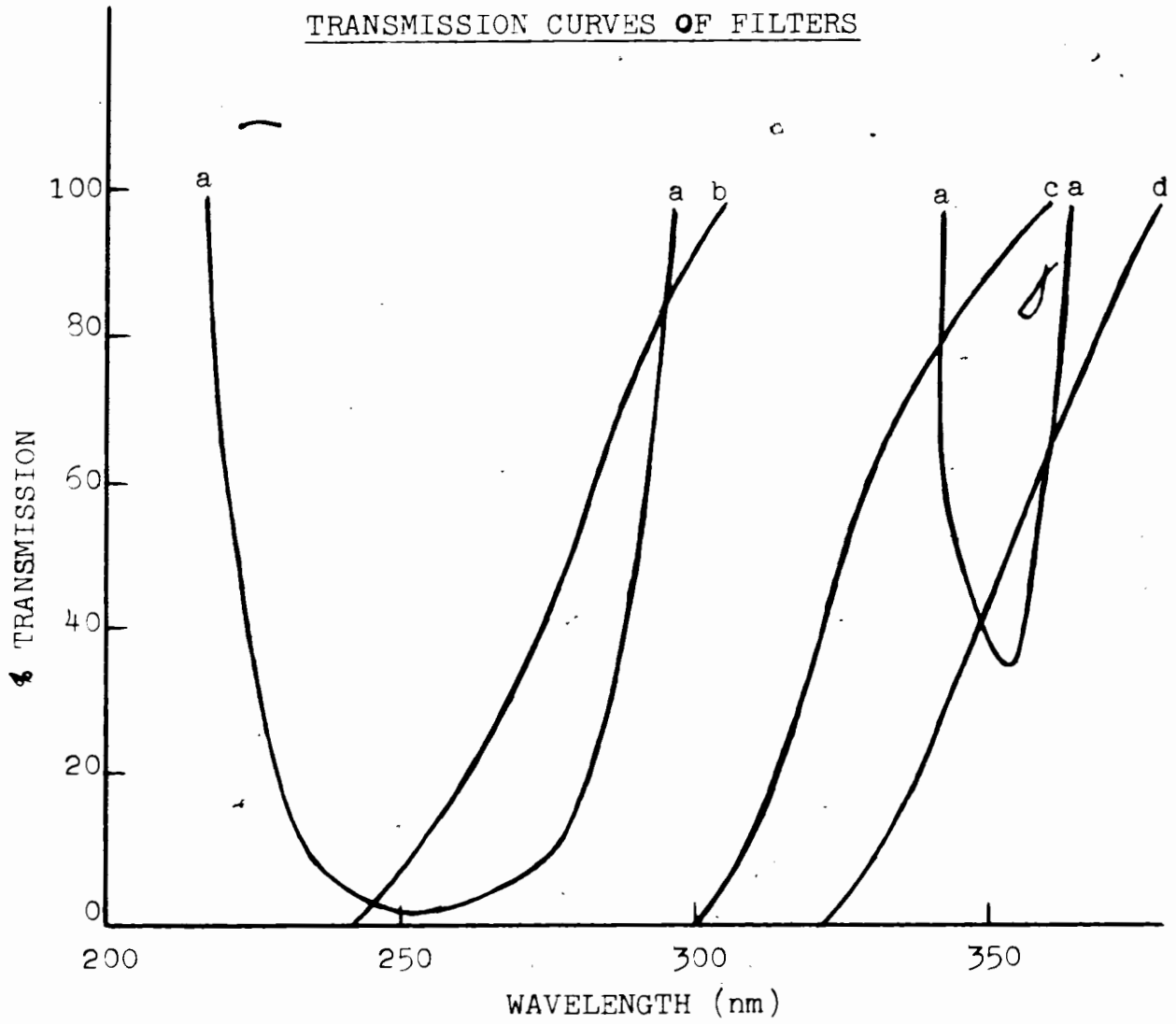
The photolyses were carried out in a previously described (154) pyrex photovessel using a quartz or pyrex cold finger. The reactants were dissolved in an appropriate solvent and were introduced into the photocell. The solution, externally cooled

to 0° by immersing the photocell in an ice bath, was stirred with a magnetic stirrer while a stream of an appropriate gas was bubbled through the solution for at least 10 minutes. The condenser was fitted with either a mercury trap or a drying tube. Unless specified otherwise, the solution was irradiated with a medium pressure mercury lamp (200W, Hanovia 654A36) placed within a cylindrical glass filter (Figure IV-1), both being placed within the lamp well of the cold finger. Other lamps, such as a 450W (Hanovia 679 A36) or low pressure (Nester Faust Model NFUV-300 or Ultraviolet Products, Inc, 100W, PCQ; 90% energy at 253.7 nm) were also used. Cooling water or filter solution I (Figure IV-1) was passed through the cooling jacket. The reaction was monitored by recording the uv spectra of properly diluted aliquots of the photolysate removed at suitable intervals. The solution was irradiated until the uv absorption at ca 240nm of the N-Nitroamine using a Corex filter (or at ca 350nm of N-Nitrosamine using a Nonex filter, see Table IV-1) had disappeared. A zero-hour control sample was kept in the dark and revealed no noticeable change at the completion of the photolysis indicating the absence of thermal reactions.

Unless otherwise specified, the solvents were removed under reduced pressure (10-20mmHg) at 10-20° using a rotary evaporator. The solutions were made basic to pH 8-10 with a saturated sodium carbonate solution. The organic phases were dried over magnesium sulfate. Unless stated otherwise, the yields were calculated from the starting limiting reagent.

FIGURE IV-1

TRANSMISSION CURVES OF FILTERS



(a) Filter solution I ($NiSO_4$, $6H_2O$ (750g) + 2,7-dimethyl-3,6-diazacyclohepta-1,6-diene (0.3g))

(b) Corex

(c) Nonex

(d) Nonex and Pyrex (2 layers).

TABLE IV-1

ULTRAVIOLET SPECTRAL DATA OF NND AND NNOD

Compound	Solvent	λ_{max} nm (ε)
NND	methanol	345 (~ 100) 230 (~ 7,500)
NNOD	n-hexane	234 (~ 5,000)
	methanol	238 (~ 6,000)
	acetonitrile	242 (~ 6,500)
NNOP	n-hexane	246 (~ 5,000)
	methanol	249 (~ 5,500)

IV-4. Purification of starting olefins

IV-4-1. trans, trans, trans-1,5,9-cyclododecatriene

The commercial product (15g), a mixture of white and yellow solid, was put in 40 ml of methylene chloride. The insoluble solid was filtrated; the methylene chloride phase was dried over magnesium sulfate and the solvent removed to yield colourless long needles (12.6g) which were recrystallized from absolute ethanol to give tttCDT as long colourless needles (10.5g) free of cis,trans,trans-1,5,9-cyclododecatriene as seen by gc

(25% Carbowax column on 60/100 Mesh Chromosorb A, 5'x$^1/_4$", 100-220° at 2°/min; rt 24.9 min) ; mp 33-4° ; ir 970 (m) and 948 (s) cm^{-1} ; nmr τ4.98 (m,$W^1/_2$ = 7 Hz, 6H) and 7.94 (m, $W^1/_2$ = 5 Hz, 12 H) ; uv (CH_3OH) λ_{max} 207.5 (ε_{max} 1130), 227 (sh, ε 7).

IV-4-2. cis,trans,trans-1,5,9-cyclododecatriene

The colourless oil was distilled twice under reduced pressure (bp 120-1° / 17 mm Hg and 115-6° / 15 mm Hg) to yield cttCDT as a colourless oil free of tttCDT, as seen by gc (25% Carbowax same as before ; rt 26.7 min) ; ir 970 (s), 948 (s) and 700 (s) cm^{-1} ; nmr τ4.6-4.9 (m,6H) and 7.92 (m, $W^1/_2$ = 5 Hz, 12H).

IV-4-3. Endo-dicyclopentadiene

Endo-tricyclo[5.2.1.$0^{2,6}$] deca-3,8-diene (or endo-DCPD, Matheson, Coleman and Bell, 95%) was distilled under reduced pressure (bp 38-9° / 2 mm Hg) to give pure endo-DCPD as a colourless solid : mp 30-1° ; ir 3050 (m), 1640 (w), 1615 (w), 755(s), 728(s), 705(s) and 678(s) cm^{-1} ; nmr τ4.05(m, H_5 and H_6), 4.52(m, H_2 and H_3) ; uv (CH_3OH) λ_{max} 206 nm (~2,000) ; nmr, identical with those of literature (82,83).

IV-4-4. 1,5-cyclodecadiene

1,5-cyclodecadiene (CDD, courtesy of Cities Service Company Cranbury, N.J.) was distilled under reduced pressure (bp 45-6° at 1.5 mm Hg) to give a mixture of two isomers as seen by its gc

on a 3 % SE-30 column (6'x$^1/_8$", 80-200° at 4° / min) : trans,trans-1,5-cyclodecadiene (rt 1.6 min, 16%) and cis,trans-1,5-cyclodecadiene (rt 2.9 min, 86%) : ir 1675(m), 975(s) cm^{-1} for a trans double bond and 1645(m), 708(s) cm^{-1} for a cis double bond (100); ^1H nmr τ4.5-6.3(m, 4H), 7.9-8.25(m, 8H) and 8.35-8.65(m, 4H) ; ^{13}C nmr ppm 134.5,132.5,126.5, 125.0, 32.7, 30.8, 28.1, 26.3, and 25.8 (2C).

IV-5. Preparation of N-nitro and N-nitroso amines

IV-5-1. N-Nitrosodimethylamine

Dimethylamine hydrochloride was treated with nitrous acid (155) to give N-nitrosodimethylamine (NND) in 65-75% yields : ir 1435(s), 1410(s), 1320(s), 1290(s), 1050(s), 850(m), and 685(s) cm^{-1} ; uv (CH_3OH) λ_{max} 345 nm (~ 100) and 230 nm (~ 7500) ; nmr τ6.18(s) and 6.93(s) in the 1:1 ratio.

IV-5-2. N-Nitrodimethylamine

The procedure of Emmons (7) was used to oxidize NND, except that 50% H_2O_2 was used in place of 90% H_2O_2. N-nitro dimethylamine (NNOD) was recrystallized from ethanol as long white needles (74%) : mp 54-5°, lit (7) mp 58° ; uv (CH_3OH) λ_{max} 238 nm (~ 6,000) ; ir ($CHCl_3$) 1510(s), 1320(s) and 1260(s);

nmr τ6.56 (t, J = 1.5 Hz) ; ms (25°) m/e (%) 91 (M^++1,20),90 (M^+,92), 74(8), 44(36), and 42(100). NNOD was free of NND as seen by gc on a 10% SE-30 column (6'x$^1/_8$", 150-250° at 4°/min) : rt NNOD = 3.6 min ; no peak at rt 1.9 min for NND.

IV-5-3. N-Nitropiperidine

The procedure of Emmons (7) was used with 50% H_2O_2 instead of 90% H_2O_2 ; the process was repeated to ensure complete oxidation of N-nitrosopiperidine (NNP) and gave N-nitropiperidine (NNOP) as a colourless oil (52%) : bp 105-6° / 25 mm Hg ; ir 1530(s), 1330(s), 1280(s) and 1240(s) cm^{-1} ; uv (CH_3OH) λ_{max} = 249 nm (~5,500) ; nmr τ6.20(m, 4H) and 8.35(m, 6H) ; gc on a 10% SE-30 column (6'x$^1/_8$", 150-250° at 6°/min) : one peak at rt 5.4 min for NNOP and no peak at rt 3.2 min for NNP.

IV-6. Preparation of nitrosyl chloride (87)

A good stream of nitrogen dioxide, generated by gently warming up a bottle (NO_2 bp 21°) was passed through two washing bottles containing wet KCl (235g KCl, 5.5 ml H_2O and 60 g KCl, 1.4 ml H_2O, respectively) to give an exothermic reaction. The red gases were dried over P_2O_5 and condensed in a receiver maintained in a dry ice-methanol bath (-78°) to yield a cherry red liquid and solid. This was further distilled at 0° (ice bath) and

collected in a graduated cylinder held in dry ice-methanol (-40°) to give NOCl as a cherry red liquid (40 ml, bp -5.5°). This liquid was either used immediately or kept in methylene chloride in the freezer for short periods of time.

IV-7. Photolysis of Nitramines

IV-7-1. Under neutral conditions, cyclohexene and CO

(a) with NNOP : A n-hexane solution (200ml) of NNOP(1.3g, 0.01 mole) and cyclohexene (2.52g, 0.03 mole) was photolyzed under carbon monoxide atmosphere for 16 hours, at which time 78% of the uv absorption at 246nm has disappeared. A dark red oil deposited on the walls of the photolysis apparatus and was removed by dissolving it every two hours with absolute ethanol. The combined ethanol solutions were evaporated to give a dark red oil (1.12g) which was shown to contain piperidinium nitrate II-2 (~38%) as the major compound by comparison with the spectra of an authentic sample : ir 3400(m,b), 2540(m,b), 2440(w,b), and 1400-1300(s,b) cm^{-1} ; nmr τ8.25(m,D_2O exch, 2H), 6.80(m, 4H) and 2.80(m, 6H). This oil was dissolved in water, the solution made basic and extracted with ether to give crude piperidine as seen by its gc, ir and nmr matching with those of an authentic sample.

The photolysate was evaporated to yield NNP (583mg, ~33%) as a yellow oil as shown by its gc (10%SE-30,6'x⅛" s.s.N_2 carrier gas inlet press. 30psi and a H_2 flame detector at 25psi,100-250° 4°/min;rt8.8min) peak matching with authentic as well as its

ir and nmr. This oil showed also some other minor components, none of them matching with N-formylpiperidine II-1 (same column and conditions ; rt 9.5min).

(b) with NNOD : A n-hexane solution (200ml) of NNOD (0.9g, 0.01 mole) and cyclohexene (1.68g, 0.02 mole) was photolyzed under carbon monoxide for 19 hours, at which time 88% of the uv absorption at 234nm had disappeared. An oil deposited on the walls and was separated by decantation from the solution. The photolysate was evaporated to give a yellow oil (153mg) which showed ir absorptions at 1625(s), 1280(s) and 870(m) cm^{-1} for a nitrate ester group, 1550(m) and 1380(m) cm^{-1} for a nitro group, 1675(s) for a carbonyl group and 3400(m,b), 1065(m) and 1025(m) cm^{-1} for a hydroxyl group.

The deposited oil was separated to a methylene chloride soluble fraction (340mg) and an insoluble fraction (175mg). The soluble fraction was found to be a mixture of NND, N,N-dimethylformamide (II-3)and II-4 as seen by its ir and nmr spectra : ir 2460(m,b), 1670(s,b), 1390-1320(s,b), 1040(m), 1022(m) and 830(m) cm^{-1} ; nmr τ 2.0(m), 7.03(s) and 7.12(s) for II-3 , 2.75 (bs, D_2O exch) and 7.21(s) for dimethylammonium nitrate (II-4) and 6.2(s) and 6.93(s) for NND; the ratio of the N-methyl peaks at τ 6.2, 6.93, 7.03, 7.12 and 7.21 was 1:1:3:3:4. Gas chromatography on a 25% Carbowax 20PTAT (6'x$^1/_8$", 120-200° at 4°/min ; rt) showed dimethylamine (3min), NND (18.3min) and II-3 (24.8min) matching with authentic samples. The insoluble fraction was

shown to contain dimethylammonium nitrate (II-4)as the major compound along with some II-3 (nmr τ7.21(s) and 7.03(s), 7.12(s) respectively).

IV-7-2. Under basic conditions

(a) with cyclohexene, CO and $NaHCO_3$: A mixture of NNOD (1.8g, 0.02 mole), cyclohexene (8.4g, 0.1 mole) and sodium bicarbonate (2g, 0.025 mole) in acetonitrile (200ml) was photolyzed under carbon monoxide for six hours, at which time 85 % of the uv absorption at 242nm had disappeared. The yellow photolysate was filtered and evaporated to give a mixture consisting of a red oil and a precipitate : ir 1670(s,b), 1440(s,b) and 1300-1400(s,b) cm^{-1}. This mixture was taken up in ether and separated into an ether soluble phase and a residue. The ether phase was dried (Na_2SO_4) and evaporated to give a red oil (440mg) consisting of NND (22%) and II-3 (2%) as seen by the following physical data : ir 1670(s), 1440(s,b), 1410(s), 1390(s), 1320(s), 1290(s),1045(s) 845(m), and 685(m) cm^{-1} ; nmr τ2.0(m), 6.20(s), 6.92(s), 7.03(s) 7.12(s) and small multiplets from 7.5 to 8.6. The four singlets were in the ratio of 10:10:1:1. The residue was dissolved partially in acetonitrile (10ml) and was filtered to give after evaporation a red oil (761mg, 35%) consisting of salt II-4 as the major product: ir 2460(m,b) and 1300-1400(s,b) cm^{-1} ; nmr τ3.1(bs, D_2O exch) and 7.21(s).

(b) with norbornene, CO and Na_2CO_3 : A mixture of NNOD (1.8g, 0.02 mole), norbornene (18.8g, 0.2 mole) and finely powdered sodium carbonate (2g, 0.025 mole) in acetonitrile (190ml) was photolyzed under CO for six hours at which time 85% of the uv absorption at 242nm had disappeared. The solvent was distilled through a Vigreau column and the distillate was trapped (170ml) in a vessel cooled in dry ice. Hydrogen chloride gas was bubbled through the distillate and the solvent was evaporated to yield a yellow oil (832mg) : ir 3300(m,b), 1650(s,b), 1545(m,b) and 1050 (m,b) cm^{-1}; nmr τ1.2(bs, D_2O exch), 6.2(s) and 6.92(s) for NND, 7.95(s) and 7.5-9.0(m). This oil was dissolved in ether. The ether solution was washed with a 10% Na_2CO_3 solution and was evaporated to yield a yellow oil (423mg) : ir 3280(s,b), 3080(m,b), 1640(s,b), 1550(s,b), 1310(m) and 1290(m) cm^{-1}; nmr τ4.2(bs, D_2O exch), 6.2(s) and 6.92(s) for NND, 7.78(bm), 8.08(s) and 7.9-9.0(m). This fraction showed one minor peak (NND, rt 10.9 min, 2%) and 1 major peak (IV-1, rt 16.7 min) on gc (10%SE-30, 6'x$^1/_8$", 100-260° at 4°/min) and was distilled (25°/0.5 mmHg) to give 2-endo-acetamido bicyclo[2.2.1] heptane (IV-1). The latter was assumed to be formed by an acid catalyzed addition of acetonitrile to norbornene (156) and was isolated as white crystals : mp 134-5° (lit.(157) mp131-2°); ir 3280(s,b), 3078(m,b), 1635(s,b), 1550(s,b), 1315(m), 1310(m) 1292(m) cm^{-1}; ms (80°) m/e(%) 153(M+,95), 138(18), 124(35), 110(42), 94(98), 82(90), 60(80) and 43(100). This solid gave one peak on gc (see above) corresponding to the major one of previous fraction (rt 16.7 min).

The residue from the photolysate (1.89g) was found to be a mixture of the following compounds as seen by its nmr : τ3.5(bs D_2O exch) and 7.21(s) for II-4, 6.20(s) and 6.92(s) for NND , 2.0(m), 7.03(s) and 7.12(s) for II-3, 6.57(t, J=1.5Hz) for NNOD. The ratio of the N-methyl peaks at τ7.21, 6.20, 6.92, 7.03, 7.12 and 6.57 was 5:18:18:1:1:4. A gc analysis (10 %SE-30, 6'x$^1/_8$", 150-250° at 4°/min; rt) showed NND (1.8min), II-3 (2.1min) and NNOD (3.6min) matching with authentic samples, and two unidentified minor components.

(c) with cyclohexene, N_2 and Na_2CO_3 : A mixture of NNOD (0.9g, 0.01 mole), cyclohexene (3.36g, 0.04 mole) and sodium carbonate (2g, 0.025 mole) in n-hexane (200ml) was photolyzed under nitrogen for 10 hours. The insoluble part (oil and solid) was decanted from the photolysate. The photolysate was evaporated to give a yellow oil (322mg) : ir 1680(s,b), 1625(m,b), 1275(m), 1260(m), 1115(s), 1000(m), 912(m) and 860(w) cm^{-1}; nmr τ2.0(m), 7.03(s) and 7.11(s) for II-3, 6.20(s) and 6.92(s) for NND, 6.81(s) and 7.82(s) for imine trimer II-6 and other multiplets at 8.35, 8.7 and 9.1 due to cyclohexyl derivatives. The ratio of the N-CH_3 at τ6.20, 6.81, 6.92, 7.03, 7.11 and 7.82 was 1:20:1:10:10:30. Gas chromatography of this mixture (25 %Carbowax 20 PTAT, 6'x$^1/_8$" 180-220° at 2°/min; rt, yields calculated from the gc peak area) showed NND (6.1 min, ~3%), II-3 (6.6 min, ~30%) and 15 unidentified peaks.

The insoluble fraction was taken up in methanol, filtrated

evaporated to give a red oil (190mg) : ir 3280(s,b), 3080(w,b), 1660(s,b), 1240(m,b) and 1040(m,b) cm^{-1}; nmr τ1.90(bs), 5.1(bs, D_2O exch) and 7.16(d, J=6Hz) for II-5, 7.03(s) and 7.11(s) for II-3, 6.20(s) and 6.92(s) for NND, and 6.56(t, J=1.5Hz) for NNOD; the doublet at τ7.16 collapsed to a singlet when D_2O was added. The ratio of the signals at τ6.20, 6.56(t), 6.92, 7.03, 7.11 and 7.16(d) was 5:2:5:4:4:15. The gc analysis of this mixture (25 % Carbowax 20 PTAT, 10'x$^1/_4$", He press.= 20psi, thermal conductivity detector; rt, yields calculated from the gc peak area) showed NND (10.3min, 19%), II-3 (10.9 min, 15%) and NNOD (25.1 min, 3%) matching with authentic samples. The major peak (19.3 min, 58%) was separated by preparative gc and showed to be N-methylformamide (II-6) by its ir, nmr and ms spectra matching with those of the literature (65).

IV-7-3. Under acidic conditions and cyclohexene

(a) with N_2 : A solution of NNOD (0.9g, 0.01 mole), cyclohexene (1.64g, 0.02 mole) and concentrated HCl (0.9ml) in methanol (190ml) was photolyzed under nitrogen for 3 hours at which time ~80% of the uv absorption at 238nm had disappeared. The work up gave a neutral fraction (160mg) and a basic fraction (790mg). The very complex neutral fraction : ir 3900(m,b), 2870(m), 1715(s,b) 1545(w), 1100(s,b) and 1050(s,b) cm^{-1}; nmr τ4.9(m), 5.3(m), 5.57(s), 5.59(s), 5.6(s), 5.68(s), 5.7(s) and 7.4-8.9(m), was analyzed by gc-ms and shown to contain >30 peaks (10 %SE-30, 100-200°/min). Some of the major peaks were tentatively assigned as the following

compounds (rt, yields calculated from the gc peak area, m/e (%)): NNOD (2.1 min, 5%) 90(M^+,100) and 42(70); 2-cyclohexenol II-7 (2.6 min, 17%) 98(M^+, 45) and 70(100); 2-cyclohexenone II-8 (3.2 min, 4%) 96(M^+, 30) and 68(100); a methoxycyclohexanone II-9 (5.0 min, 6%) 128(M^+,5) and 71(100); a methoxycyclohexanol II-10 (5.6 min, 20%) 130(M^+, 7), 98(12), 80(45), 71(74) and 57(100); unknown (12.4 min, 6%) 126(M^+?, 47), 113(100) and 81(87); unknown (20.3 min, 15%) 129(M^+?, 18), 114(32), and 69(100). Mass spectra of compounds II-7 and II-8 were matching with those of authentic samples (66).

The basic extract exhibited the following ir and nmr :ir3350 (m,b), 1660(w,b), 1552(s), 1372(m), 1160(m), 1115(m) and 1048(s); nmr : singlets at τ 7.66, 7.70, 7.72 and 7.80. The complex basic fraction was analyzed by gc-ms (10% SE-30, 6'x$^1/_8$", 100-275° at 6°/min) to give the following peaks (rt, %peak area):2.9min,15%; 4.6 min, 28% ; 5.3 min, 8% ; 6.7 min, 24% ; 7.5 min, 22% ;13.4min 3% . These peaks showed the corresponding ms peaks at the following m/e (%) : 2.9 min, dimethylaminocyclohexane (II-11) 127(M^+,38),125 (60), 97(95), 84(100), 82(98), 71(38), 58(19), 44(40) and 42(52); 4.6 min, II-12, 143(M^+,74), 128(8), 114(12), 100(20), 84(100), 71(70), 58(66), 44(38) and 42(44); unknown, 5.3 min, 170(M^+,22), 142(100), 126(66), 84(68), 71(52), 58(46), 44(38) and 42(42);6.7min 2-dimethylaminocyclohexanone oxime (II-13), 156(M^+,15), 139(100), 84(80), 71(60), 44(45) and 42(58); 7.5 min, 1-nitro-2-dimethylamino cyclohexane (II-14), 172(M^+, 86), 142(9), 126(76), 84(100), 81(54) 71(80), 58(62), 44(54) and 42(56); 13.4 min, unknown, 327-1(M^+?,2)

222(40), 125(100), 110(75), 97(75), 84(72) and 58(78). Compounds II-11 (64), II-12 (67) and II-13 (68) were matching with authentic samples. Mass spectrum of II-14 was compared with the one of 1-nitro-2-piperidinocyclohexane (69).

(b) with CO : A solution of NNOD (0.9g, 0.01 mole), cyclohexene (1.64g, 0.02 mole), and concentrated HCl (0.9ml) in CH_3OH (190ml) was photolyzed under carbon monoxide for 2.8 hours at which time 80% of the uv absorption at 238nm had disappeared. The photolysate was worked up to give a neutral fraction (176mg) shown by gc to be similar to previous neutral fractions, and a basic fraction (680mg). This basic fraction showed similar ir and nmr patterns with those of the above basic fraction, and its gc analysis showed the following peaks, rt, yields calculated from the gc peak area 2.9 min, II-11 , 15%; 4.6 min, II-12 , 28.5%; 5.3 min, 7.5%; 6.7min, II-13 ,24.5%; 7.5 min, II-14 , 24.5%.

(c) with O_2 : A solution of NNOD (0.9g, 0.01 mole), cyclohexene (1.64g, 0.02 mole) and concentrated HCl (0.9ml) in CH_3OH (190ml) was photolyzed under oxygen for 1.5 hour. The photolysate was worked up in the usual manner to yield a neutral fraction (205mg) and a basic fraction (1.52g) containing nitrate esters ; ir 3420(m,b), 1715(m), 1625(s), 1275(s), 1040(m) and 870(s) cm^{-1}. The basic fraction was immediately reduced in ether with LAH(1.5g) for one day. After the usual basic hydrolysis, a ~1:3 mixture of cis and trans-2-dimethylaminocyclohexanols (II-12, 1.04g, 64%) was obtained as seen by its ir and nmr as compared with an authentic

sample (67); the multiplets at τ6.0 and 6.7 were in the ~1:3 ratio.

IV-8. Oxidative and non-oxidative photoadditions of N-nitro and N-nitrosodimethylamine to olefins

IV-8-1. NNOD to 1-hexene, with O_2

A solution of NNOD (2.7g, 0.03 mole), 1-hexene (3.36g, 0.04 mole) and concentrated HCl (2.7ml, 0.032 mole) in methanol (200ml) was irradiated under oxygen for 3 hours. The colourless photolysate was concentrated to ca 30ml and the distillate was trapped in a vessel cooled in dry ice. Treatment of this solution with a 2,4-dinitrophenylhydrazine reagent solution (40ml) gave no precipitate. The residue was diluted with water (40ml) and extracted with ether (3x20ml). The ether extracts were washed with water (20ml) and dried. The ether was removed to give a yellow oil (89mg) which showed no NCH_3 signal in its nmr spectrum and 12 peaks on gc (20% SE-30, 140°). The fraction contained nitrate and nitro groups as seen by its ir bands at 1625(b,s), 1280(b,s), 860(m,b) (ONO_2); 1555(m,b) and 1380(m,b) (NO_2) cm^{-1}.

The aqueous acidic solution was cooled to 0°, made basic to pH 9.5-10 and immediately extracted with methylene chloride (4x50ml). The extracts were dried over sodium sulfate and evaporated to give a pale yellow oil (5.4g) : ir 2940(s), 2870(m), 2820(m) and 2780(m) [$CH_2N(CH_3)_2$] ; 1625(s), 1280(s) and 860(m)

(ONO_2) ; 1715(m) (C=O) ; 3400(w,b) and 1040(m) (OH) cm^{-1}. This crude basic fraction was immediately reduced in dry ether (60ml) at 0° with LAH (5g) for 1 hour. The solution was stirred for 1 day at room temperature. After hydrolysis (H_2O and 10 % KOH solutions) filtration and thorough washing of the inorganic residue with ether, the combined filtrate and washings were dried over sodium sulfate and evaporated to give a pale yellow oil (3.24g) which after preparative gc (30% SE-30, 20'x$^3/_8$", 120-230° at 8°/min) gave 1-dimethylamino-2-hexanol (II-16, 2.71g, 62%) as a colourless oil : ir 3440(m,b), 2940(s), 2860(s), 2820(s), 2780(s), 1270(s), 1040(s) 1030(s) cm^{-1}; nmr τ6.42(m, H_2), 6.70(s, D_2O exch, 1H), 7.75(m, 8H), 8.60(m, $W_{1/2}$=9Hz, 6H) and 9.08(m,3H); ms (50°) m/e (%) 145(M^+, 5), 128(1), 88(18), 58(100), 44(9) and 42(8); rt 9.9 min.

A solution of p-nitrobenzoylchloride (230mg, 1.24 mmole) in 1ml of dry THF was added to II-16 (180mg, 1.24 mmole) in 1.5ml of dry THF under ice cooling with stirring. A white solid separated within 5 min and the mixture was continually stirred at room temperature for 10 hours. After filtration, washing of the solid with dry THF, crude p-nitrobenzoyl derivative of II-16 (348mg, 85%, mp 184-9°) was obtained. Two recrystallizations from i-PrOH afforded white crystals (246mg, 60%) of 1-N,N-dimethyl-2-(p-nitro benzoyl)-hexyl ammonium chloride II-17 : mp 189-190°; ir 2420(m b), 1715(s), 1600(m,b),1520(s), 1350(m),1320(m), 1320(m),1270(s), 1000(m) and 720(s) cm^{-1}; nmr τ1.69(s, 4H), 4.35(bs, 1H), 6.55(m, 2H), 7.05(s, NCH_3), 8.18(m, 2H), 8.60(m, 4H) and 9.08(m, 3H); ms (150°) m/e (%) 294(M^+-HCl, 3), 293(2), 208(27), 150(41),127(19) 104(43), 84(38), 76(37), 58(100), 44(12), 42(23), 38(5) and 36(13).

Anal. Calcd. for $C_{15}H_{23}N_2O_4Cl$: C,54.46; H, 7.01; N, 8.47.

Found : C,54.75; H, 7.14; N, 8.60.

In another experiment, a solution of NNOD (0.9g, 0.01 mole), 1-hexene (1.26g, 0.015 mole) and concentrated HCl (0.9ml, 0.011 mole) in methanol (200ml) was photolyzed under oxygen with a low pressure mercury lamp (Nester Faust Model NFUV-300; 90 % of the light output at 253.7nm) through filter solution I for 4 hours. The usual work-up gave a neutral fraction (48mg) and an aqueous basic solution (pH 9-10). One twentieth of this solution was extracted with CH_2Cl_2 to give a pale yellow oil (85mg) shown to contain a nitrate ester derivative as the major compound, as indicated by its ir peaks at 1625(s), 1280(s) and 860(m) cm^{-1}. The rest was left with stirring for 1 day, extracted with CH_2Cl_2 (4x50ml) and then continuously with CH_2Cl_2 for 3 days to give two fractions (796 and 122mg, respectively) as reddish oils having similar spectra : ir 3400(s,b), 1720(s), 1040(s) and 1030(s)cm^{-1}; nmr τ 7.62(s) and 7.75(s) (NCH_3, ratio 1:1). Preparative chromatography of this mixture (30% SE-30, 20'x$^3/_8$", 100-180° at 2°/min) gave two major compounds; one was 1-dimethylamino-2-hexanone (II-18, 286mg, 20%, rt 19.5min) as a colourless oil : ir 2970(s), 2880(s) 2830(s), 2780(s), 1720(s), 1270(m), 1040(s) and 855(m); nmr τ 7.26 (s, 2H), 7.58(m, 2H), 7.62(s, NCH_3), 8.30-8.80(m, 4H) and 9.10(m, 3H); ms (80°) m/e (%) 143(M^+, 5), 114(20), 86(10), 58(100) and 42(50). the other was alcohol II-16 (348mg, 24%, rt 20.3 min) as a colourless oil, as indicated by its ir, nmr and ms spectra.

Amino alcohol II-16 (664mg, $4x10^{-3}$ mole) dissolved in acetone (5ml) was treated with Jones' reagent (2.3ml, $5x10^{-3}$ mole) (86) for two hours. After evaporation of the acetone, the residue was basified and extracted with CH_2Cl_2 to give a pale yellow oil (379mg, 59%), ir and nmr spectra of which were matching with those of amino ketone II-18.

IV-8-2. NNOD to trans-3-hexene, with O_2

A solution of NNOD (1.8g, 0.02 mole), trans-3-hexene (2.2g, 0.026 mole) and concentrated HCl (1.8ml, 0.026 mole) in methanol (200ml) was photolyzed under oxygen for 2.5 hours, at which time the reaction mixture was worked up as above to yield a neutral fraction (100mg) and a basic fraction (2.45g) ;ir 2970(s),2940(s), 2880(s), 2830(m), 2780(m) ($CHN(CH_3)_2$); 1625(m), 1280(m), 860(m) (ONO_2); 1710(s) (C=O); 3400(m,b) and 1045(m) (OH) cm^{-1}:The distillate was treated with a 2,4-dinitrophenylhydrazine reagent solution giving no precipitate. A part of the basic fraction (1.89g) was immediately reduced in dry ether (50ml) at o° with LAH (1g) for 0.5 hour, and at room temperature with stirring for 1 day. After the usual work-up, a pale yellow oil (1.28g) was obtained giving 1 major peak on gc (30 % SE-30, 100-200° at 6°/min). Purification of the oil by preparative gc afforded 4-dimethylamino-3-hexanol (II-20, 0.836g, 49%; rt 13.4 min) as a colourless oil : ir 3400(s b), 2960(s), 2940(s), 2880(s), 2840(s), 2790(s), 1125(m), 1100(m) 1050(s), 1000(s), 970(s) and 920(m) cm^{-1}; nmr τ 6.08(bs,D_2O exch, 1H), 6.50(m, H_3), 6.75(m, H_4), 7.69(s, NCH_3), 8.55(m, 4H), 8.94(m

3H) and 9.02(m, 3H); ms (60°) m/e(%) 145(M^+, 5), 116(26), 86(100), 71(33), 44(23) and 42(23).

To a solution of II-20 (64mg, 0.44mmole) in THF (1ml) was added p-nitrobenzoylchloride (82mg, 0.44mmole) in THF (1ml) to give a crude solid (87mg, 60%; mp 163-5°) which was recrystallized twice from i-PrOH to give white crystals of 4-N,N-dimethyl-3-(p-nitrobenzoyl)-hexyl ammonium chloride II-22 (42mg, 29%): mp164-5°; ir 2410(m,b), 1720(s), 1610(w,b), 1525(m), 1350(m), 1275(s), 1120(m), 1100(m),1015(m) and 720(s) cm^{-1}; nmr τ 1.70(s,4H),4.45(m,1H), 6.55(m,1H)7.03(s)and 7.12(s)(6H, ratio 5:3, NCH_3), 7.6-8.2(m, 4H) and 8.5-9.1(m, 6H); ms (120°) m/e(%) 294(M^+-HCl, 1), 293(3),265(10) 150(39), 104(40), 86(100), 76(30), 71(38), 44(25), 42(30), 38(8) and 36(17).

Anal. Calcd. for $C_{15}H_{23}N_2O_4Cl$: C, 54.46; H, 7.01; N, 8.47.

Found : C, 54.66; H, 7.08; N, 8.37.

In a separate experiment, a solution of NNOD (0.9g, 0.01mole) trans-3-hexene (1.26g, 0.015 mole) and concentrated hydrochloric acid (0.9ml, 0.013 mole) in methanol (200ml) was irradiated for 2 hours to give a neutral fraction (80mg) and an aqueous basic solution (pH 9-10). The aqueous solution was stirred at room temperature for 1 day. Methylene chloride extraction (4x50ml) and continuous CH_2Cl_2 extraction for 3 days afforded two fractions (719 and 119mg respectively) as orange oils having similar spectra : ir 3400(s,b), 1710(s) and 1050(s) cm^{-1}; nmr τ 7.69(s) and 7.79(s)(NCH_3,ratio 1:1). Preparative gc of this mixture on 30% SE-30 (same as above, 100-230°

at 6°/min) gave two major compounds. One was 4-dimethylamino-3-hexanone (II-21, 357mg, 25%; rt 14.5 min) as a colourless oil : ir 2970(s), 2940(s), 2880(s), 2830(s), 2780(s), 1710(s), 1265(m) 1045(m) and 902(s) cm^{-1}; nmr τ 7.12(t, J=7Hz, H_4), 7.47(q, J=7Hz CH_2CO), 7.73(s, 6H, NCH_3), 8.49(qui, J=7Hz, CH_2CHN), 8.93(t, J=7Hz 3H) and 9.15(t, J=7Hz, 3H); ms (80°) m/e(%) 144(M^++1, 2), 143(M^+, 1.5), 114(5), 86(100), 71(61), 58(24), 56(26), 44(35) and 42(34); the other was amino alcohol II-20 (377mg, 26%; rt 17.1 min) as shown by its ir, nmr and ms spectra.

Amino alcohol II-20 (44mg, 30mmole) in acetone (6ml) was treated with Jones' reagent (0.2ml, 42mmole) (86) to give, after evaporation of the acetone and basification, a colourless oil (23mg, 53%) showed to be amino ketone II-21 by its ir and nmr identical in all respects with those of the pure sample.

IV-8-3. NNOD to 1,5-cyclooctadiene, with O_2

A solution of NNOD (1.8g, 0.02 mole), 1,5-cyclooctadiene (2.4g, 0.022 mole) and concentrated HCl (3ml) in methanol (200ml) was irradiated under oxygen for 3.5 hours. The methanol was evaporated at 10° and the residual solution was diluted with water and extracted with ether to give an orange oil (234mg). This oil showed several spots on a tlc plate and at least 15 peaks on gc analysis (10% SE-30, 150-250° at 4°/min) and gave rise to a complex nmr spectrum containing no NCH_3 absorptions. The aqueous solution was made basic to pH 9-10 and immediately extracted with CH_2Cl_2 (5x50ml). The extract was washed with water (2x30ml), dried and

evaporated to give an orange oil (2.75g) : ir 3350(w,b), 3020 (w,sh), 2940(s), 2870(s), 2820(s), 2780(s), 1710(m), 1625(s),1275 (s), 1100(s), 1035(s), 860(s) and 735(s) cm^{-1}; nmr τ 4.38(m), 4.8(m), 6.65(s), 7.71(s), 7.74(s) and 7.77(s).

The crude basic fraction was immediately treated with LAH (2.6g, 0.068 mole) in ether (30ml) for 24 hours and the product was isolated in the usual manner to give an oil (2.43g) which showed one major and two minor spots on a tlc plate:ir 3400(s,b) 3010(m,sh), 2930(s), 2860(s), 2820(s), 2780(s),1100(s), 1045(s) and 1030(s) cm^{-1}; nmr τ 4.38(m), 6.65(s), 7.72(s) and 7.77(s). This mixture was separated by preparative gc (25 % Carbowax 20PTAT on Chromosorb A 60/80 Mesh, 10'x$^1/_4$" st.steel , 140-250°at 2°/min He pressure = 20psi, thermal conductivity detector) to afford two fractions. The first fraction (rt 31-31.5 min) was obtained as a colourless oil and was distilled at 20°/0.2 mmHg to give, after standing in fridge for 2 months, long colourless needles (mp 77-8°); the ir, ^{1}H nmr and ms spectra were identical with those of an authentic sample of trans-2-dimethylamino-5-cycloocten-1-ol (II-23a) (74, reported as an oil) : ^{13}C nmr ppm 131.1(d), 130.7(d), 71.1(d, C_1), 65.6(d, C_2), 41.3(q, NCH_3), 35.3(t), 24.0(t), 23.8(t) and 21.2(t). The second fraction (rt 36-38 min) was obtained as a colourless oil and was shown to be a 3:1 mixture of the 2 ethers, endo-2-methoxy-exo-6-dimethylamino-9-oxabicyclo[3.3.1]nonane (II-24) and endo-2-methoxy-exo-5-dimethylamino-9-oxabicyclo[4.2.1] nonane (II-25) by gc peak matching with an authentic mixture (15%)(10% SE-30, 6'x$^1/_8$, 140-250° at 2°/min, rt 15.5 and 16.0 min, respectively): ir and nmr were similar with those of authentic samples (69).

IV-8-4. NNOD to 1,5-cyclooctadiene, with N_2

A solution of NNOD (1.8g, 0.02 mole), COD (2.38g, 0.022 mole) and concentrated HCl (2.8ml) in acetonitrile (200ml) was irradiated for 10 hours under nitrogen until the uv absorption maximum at 242nm had decreased to the tenth of its initial value. A yellow solution and a red oil deposit on the walls of the photolysis vessel were separated and treated separately.

The yellow photolysate was evaporated to 10ml (20°/30 mmHg) added with water and extracted with ether (3x50ml). The ether phase was washed with water (15ml), dried and evaporated to yield an oily residue (510mg) consisting of unreacted NNOD, COD and other unknown minor compounds by its gc, ir, and nmr spectra.

The aqueous solution was made basic to pH 10 and extracted with ether (4x50ml). The ether solution was dried and evaporated to give a red oil (1.23g) : ir 3250(m,b), 3010(w), 2940(s), 2870(s), 2830(s), 2780(s), 1650(w,b), 1555(m), 1310(m), 1260(m), 1035(s), 730(m) and 710(m) cm^{-1}; the nmr spectrum exhibited weak multiplets at τ0.25, 5.8 and 6.6-7.6, strong multiplets at τ4.4 and 7.6-8.5 and singlets at τ7.72 and 7.74 in ca 1:1 ratio. The crude basic fraction showed 5 spots on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2) and was found to be a mixture of at least 10 compounds on a 10% SE-30 gc column (120-220° at 6°/min). From gc-ms analysis on a 10% SE-30 column (see above), 3 major peaks were tentatively identified (rt, yield based on relative areas of all gc peaks) : II-26 (9.1 min, 19%) m/e(%) 189(M^+, 1), 187(M^+, 3), 152(2), 110(8), 84(25), 71(100), 58(9) and 56(11); II-23 (10.1min,

32%) m/e(%) 169(M^+, 22), 140(18), 124(7), 110(24), 84(21), 71(100), 58(28), 56(45), 44(30)and 42(34); II-27 (13.5 min, 13%) m/e(%) 182(M^+, 2), 165(100), 124(19), 110(10), 84(21), 71(28), 56(20)and 42(29). This oil quickly decomposed at room temperature togive a dark brown tar. A part of the residue (60mg) was distilled atroom temperature/0.5 mmHg for two hours to give a small amount of a white solid (6mg); ir, nmr and ms were identical to those of 2-dimethylamino-5-cycloocten-1-one-anti-oxime II-27 prepared by another route (vide infra); mp 98-9° (lit(159) mp 102-3°); ir 3180(m,b), 3020(w), 2960(s,sh), 2930(s), 2860(s), 1642(w), 1172(m) 1160(m), 1140(m), 1040(m), 1025(m), 1020(m), 970(m), 920(m), 900(m) 830(m), 750(m), 730(m) and 705(m) cm^{-1}; nmr τ 2.0(bs, D_2O exch, 1H), 4.36(m, 2H), 6.86(ddd, J=12.0, 6.5 and 3.5Hz, H_{8a}), 7.22(dd, J=8.5 and 7.0Hz, H_2), 7.74(s, NCH_3) and 7.6-8.6(m, 7H); ms (80°) m/e(%) 182(M^+, 17), 165(100), 136(18), 124(25), 110(15), 97(30), 84(65), 71(87), 58(18), 56(34), 44(44) and 42(44). Continued distillation of the same sample at 40° for 3 days afforded a colourless oil (4mg) believed to be 1-chloro-2-dimethylamino-5-cyclooctene II-26 (mixture of isomers) : ir 3020(m), 2940(s), 2870(s), 2830(s), 2780(s), 1175(m), 1035(m), 730(m) and 710(s) cm^{-1}; nmr τ 4.40(m, 2H), 5.79(m, 1H) and 6.7-8.7(m, 15H, including 2 singlets at τ 7.72 and 7.75 in ca 1:1 ratio); ms (25°) m/e(%) 189(M^+, 4), 187(M^+, 12), 152(10), 124(8), 110(20), 84(29), 71(100), 58(12), 56(18), 44(16) and 42(22).

A part of these basic extracts (600mg) was dissolved in dry ether (50ml) and treated with LAH (0.5g) for 2 days followed by

basic hydrolysis to give a colourless oil (410mg) which gave 4 major spots on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2) : ir 3300(s,b), 3010(w), 2940(s), 2865(s), 2830(s), 2780(s), 1650(w), 1265(m), 1170(m), 1045(s), 1035(s), 830(m) and 730(m) cm^{-1}; nmr τ 4.50(m), 4.62(m), 5.96(bs, D_2O exch), 6.40(t, J=6Hz), 6.8-8.6 (m, including singlets at τ 7.70, 7.74 and 7.78). The following compounds, described in the order of the elution, rt, yield approximated from gc areas based on NNOD, were tentatively identified by gc-ms (10% SE-30, 6'x$^1/_8$", 80-220° at 4°/min) : i) 5-dimethylaminocyclooctene II-28, 9.7 min, 5%; m/e(%) 153(M^+,12), 138(3), 125(12), 124(9), 110(15), 84(60), 71(100), 58(12), 56(27), 44(18) and 42(21); ii) 8-dimethylamino-4-octen-1-ol(II-29) 11.9 min, 12% m/e(%) 171(M^+,10), 140(4), 126(8), 84(46), 71(32), 58(100),44(24) and 42(32); iii) II-23, 12.8 min, 26%, m/e(%) 169(M^+, 26),140(14), 124(8), 110(22), 84(59), 71(100), 58(63), 56(41), 44(34)and 42(37); iv) unknown, 15.0 min, 5%. The same mixture analyzed on a different column (20% Dowfax9N9/10%TEP,8'x$^1/_4$"copper, 210°, He press.=18psi and a thermal conductivity detector) showed 3 peaks. By the peak matching technique with authentic samples (63,160),the minor peak at 12 min was shown to be II-28, the major peak at 37 min to be trans-2-dimethylamino-5-cycloocten-1-ol (II-23a)(along with possibly II-29) and the minor peak at 48 min to be cis-2-dimethylamino 5-cycloocten-1-ol (II-23b) in the ratio of 1:8:1. Furthermore the ^{13}C spectrum of this mixture gave the peaks in the 74-35ppm region at 71.3(d), 68.1(d), 63.2(d), 60.8(t), 58.5(t), 44.7(q), 42.6(q) and 41.8(q), in addition to those at 71.0(d), 65.5(d) and 41.2(q)

for trans-amino alcohol II-23a.

The red oil deposit was dissolved in water (4oml), the pH checked (ca 1), and extracted with ether (3x50ml) to give a neutral fraction (7mg) which was not analyzed farther. The aqueous phase was made basic to pH 10 and extracted with ether (4x50ml) to give a red oil (210mg), tlc, ir and nmr of which were similar to those of the major basic fraction.

IV-8-5. NND to trans,trans,trans-1,5,9-cyclododecatriene, with N_2

A solution of tttCDT (12.96g, 0.08 mole), NND (5.92g, 0.08 mole) and concentrated HCl (8.5ml, 0.1 mole) in methanol (800ml) was irradiated with a 450 W Hanovia lamp under nitrogen for 4 hours. A new absorption (ca 300nm) appeared in the uv spectrum which decreased after 3 hours of irradiation. The photolysate was concentrated (ca 30ml) under reduced pressure and water (ca 40ml) was added. The ether extracts (4x50ml) of the acidic aqueous solution were washed with 0.5N HCl solution (2x20ml) to yield a neutral fraction (2.8g) which was shown to be tttCDT by its ir and nmr spectra.

The acidic solution was made to pH 10 and was extracted with ether (5x50ml) to give a pale yellow oil (14.4g, ~76%) which showed 1 major spot on an alumina tlc plate (8% CH_3OH-CH_2Cl_2; Rf=0.75) as II-31 : ir 3340(s,b), 3030(w), 2970(s), 2920(s), 2860(s), 2780(s), 1630(w,b), 960(s) and 890(s) cm^{-1}; nmr τ0.5(bs, D_2O exch), 4.6 and 4.9 (m, ratio 1:15), 6.7-7.0 (small m), 7.77(s), 7.92(m) and

8.1-8.5(m). Crude II-31 (150mg) was purified by column chromatography on neutral alumina (8g). Elution with 2-4% CH_3OH-CH_2Cl_2 afforded pure syn-1-oximino-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-31, 127mg) which was recrystallized from ethanol as white needles : mp 82-82.5°; ir 3180(m,b), 3030(w), 2780(s), 1650(w,b), 1170(m), 1040(m), 1015(m), 990(m), 960(s) and 890(s) cm^{-1}; ^1H nmr τ1.4(D_2O exch, 1H), 4.91(m, 4H), 6.70(dd, J=7.0 and 3.5Hz, H_2), 7.02(m, 1H), 7.77(s, NCH_3) and 7.6-8.45(m, 14H); ^{13}C nmr ppm159.6(s), 131.3(2C), 131.1, 130.8, 63.5(d,C_2), 40.5(q, NCH_3), 31.9(t), 31.8(t), 31.0(t), 28.6(t), 25.7(t) and 18.8(t); hrms (100°) m/e(%) 236.1876(M^+, 40; calcd for $C_{14}H_{24}N_2O$: 236.1889), 219.1856(100; calcd for $C_{14}H_{23}N_2$: 219.1861), 124.1127 (35; calcd for $C_8H_{14}N$: 124.1127), 110.0969(32; calcd for $C_7H_{12}N$: 110.0969), 97.0772(50; calcd for $C_5H_9N_2$: 97.0766), 84.0684(69; calcd for $C_4H_8N_2$: 84.0687), 71(63), 58.0274(38; calcd for C_2H_4NO: 58.0293), 56(40), 44(42) and 42(44). On irradiation of the broad multiplet at τ7.92(allylic protons), the signal at τ4.91(vinyl protons) collapsed to an AB quartet with a J_{AB} value of 14Hz, and the multiplets at τ6.70(H_2) and 7.02(H_{12}) showed some changes in their coupling pattern. Irradiation of the multiplet at τ6.70(H_2) changed the coupling pattern around τ8.15 and irradiation at τ8.15 ($H_3H_{3'}$) decoupled the multiplet at τ6.70 to give a broad singlet.

Anal. Calcd. for $C_{14}H_{24}N_2O$: C, 71.14; H, 10.23; N, 11.85.

Found : C, 71,29; H, 10.39; N, 11.84.

Hydrolysis of the amino oxime II-31: A 2N HCl solution(40ml) of the amino oxime II-31 (1.15g, 4.87×10^{-3} mole) was stirred at 40° for 1 week. The resultant solution was extracted with ether (3x 30ml); no residue remained after evaporation of the solvent. The aqueous phase was made basic to pH 9 and extracted with ether (3x 40ml); distillation of the solvent gave an oil (990mg) which showed 2 spots on a tlc plate. This mixture was chromatographed on neutral alumina (60g). The first fraction eluted with CH_2Cl_2 (180ml) was shown to be 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-one (II-36, 400mg, 37%) by its tlc, ir, nmr and ms comparisons with those of the authentic sample (vide infra). The second fraction, eluted with 5% methanol in CH_2Cl_2 (200ml) afforded the starting amino oxime II-31 (530mg, 46%). This last fraction was again treated with a 2N HCl solution (30ml) at 65° for 1 week. Following the previous procedure, it yielded an additional 290mg (27%) of the amino ketone II-36.

Reduction of the amino oxime II-31 with LAH : Crude amino oxime II-31 (12g, 0.051 mole) dissolved in ether (50ml) was added slowly at 0° to a suspension of LAH (8g, 0.21 mole) in 150ml of ether and left stirring for 12 hours at room temperature followed by reflux(5 hours). After the usual hydrolysis with a 20% KOH solution, extraction and drying, the extracts was evaporated to give a pale yellow oil (10.1g, 90%) showing 1 spot on a tlc plate and 1 major peak on gc (10% SE-30, 6'x$^1/_8$", 150-270° at 6°/min; rt 9.9 min). This oil was further purified by chromatography on neutral alumina to give pure 1-amino-2-dimethylamino-trans,trans-

5,9-cyclododecadiene (II-32) : ir 3360(w,b), 3020(m,sh),2920(s) 2850(s), 2820(m,sh), 2770(m), 1575(m,b), 1150(m), 1030(m), 990(s) 970(s) and 960(s) cm^{-1}; ^1H nmr(Figure II-2) τ4.94(m,4H),7.21(ddd, J= 9.5, 4.5 and 3.5 Hz,H_1), 7.52(ddd, J= 7.5, 5.5 and 3.5 Hz, H_2) 7.67(s,NCH_3),7.70-8.10(m, 8H) and 8.10-8.64(m, 6H, $2D_2O$ exch H); ^{13}C nmr ppm 131.4, 130.9, 130.8, 130.3, 58.5(d, C_2), 48.7(d, C_1) 42.9(q, NCH_3), 33.6(t), 31.7(t, 2C), 29.3(t), 29.1(t), and 19.6(t) hrms (50°) m/e(%) 222.2096(M^+, 28; calcd for $C_{14}H_{26}N_2$: 222.2096), 207.1870(12; calcd for $C_{13}H_{23}N_2$: 207.1861), 180.1752(27;calcd for $C_{12}H_{22}N$: 180.1752), 154.1485(22; calcd for $C_9H_{18}N_2$: 154.1470), 126.1292(48; calcd for $C_8H_{16}N$: 126.1282), 110.0968(23;calcd for $C_7H_{12}N$: 110.0970), 84.0814(49; calcd for $C_5H_{10}N$: 84.0813),71.0735 (100; calcd for C_4H_9N: 71.0735), 58(62) and 44(20).

Anal. Calcd. for $C_{14}H_{26}N_2$: C, 75.62; H, 11.79; N, 12.60.
Found : C, 75.88; H, 11.92; N, 12.55.

IV-8-6. NNOD to trans,trans,trans-1,5,9-cyclododecatriene, with O_2

(a) photolysis : A solution of NNOD (1.8g, 0.02 mole),ttt CDT (3.24g, 0.02 mole) and concentrated HCl (3ml) in methanol (200ml) was irradiated under oxygen for 3.5 hours. The colourless photolysate was concentrated to ca 30ml, diluted with water(40ml) and extracted with ether (5x40ml). The ether extract was washed with water (3x40ml), dried and evaporated to give a pale orange oil (720mg) which showed no NCH_3 signal in its nmr spectrum; ir 1625(m), 1270(m), 970(s), 960(m) and 945(s) cm^{-1}; nmr τ4.99

(m), 6.5(m) and 7.96(m). Preparative gc of this neutral fraction (25% Carbowax 20 PTAT on Chromosorb A 60/80, 10'x¼", 100-200° at 2°/min) afforded an unknown volatile compound (rt 5.1 min), ttt CDT (rt 31 min) and cttCDT (rt 33 min) in the 2:90:3 ratio. the last 2 compounds were identified by gc peak matching and ir comparisons with authentic samples.

The aqueous acidic solution was cooled to 0°, made basic to pH 9.5-10 and immediately extracted with ether (5x40ml). The solution was dried and the solvent was evaporated to give a yellowish viscous oil (3.7g) : ir 3350(m), 1710(m), 1620(s),1540 (m), 1275(s), 1040(m), 1025(m) and 860(s) cm^{-1}; nmr τ4.60(m), 4.82(m), 6.58(m), 7.00(m), 7.90(m), 8.35(m) and 4 singlets at τ7.60, 7.72, 7.76 and 7.80 (~ratio of 5:6:3:2).The above oil in dry ether (40ml) was added with stirring at 0° to a suspension of LAH (3.04g, 0.08 mole) in ether (40ml). The resulting mixture was stirred for 24 hours at room temperature. After hydrolysis with alternative additions of small portions of water and 10% KOH solution, filtration and thorough washing of the inorganic solid with ether, the combined filtrate and washings were dried and evaporated to give a colourless viscous oil (3.4g); gc (5% Versamid 900 on gas ChromP100/120Mesh,6'x⅛",150-270° at 10°/min) gave 3 major and 1 minor peaks; ir 3380(s,b), 3020(w,sh), 1050 (m,b), 1020(s), 985(s), 965(s) and 955(s,sh) cm^{-1}; nmr τ4.56(m) and 4.78(m) in the 4:7 ratio, 6.42(m), 7.60(s), 7.71(s), 7.78(s) 7.90(m) and 8.50(m); the ratio of the 3 NCH_3 singlets was estimated to be 5:2:4.

(b) chromatography of the basic photolysate fraction after reduction with LAH : The previous mixture (2.8g) was chromatographed on silicic acid (150g) giving 4 fractions. The first fraction (A, 23mg) eluted with CH_2Cl_2 gave 1-dimethylamino-trans,trans-4,8-cyclododecadiene (II-33; rt 10.0 min): peak matching with an authentic sample prepared by another route (vide infra) ir 3020(w), 2850(s), 2820(m), 2770(m) and 960(s) cm^{-1}; nmr τ4.86(m,4H), 7.76(s), (s, 7H), 7.89(m, 8H) and 8.33-9.0(m, 6H); ms (80°) m/e(%) 207(M^+ 27), 136(10), 124(11), 110(28), 84(97), 71(100) and 58(26). The second fraction (B, 1.1g), eluted with 2% CH_3OH in CH_2Cl_2 contained predominantly amino alcohol II-34a(85% by gc), along with amino alcohols II-34b (~6%) and II-35 (~4%). Continued elution with 3% CH_3OH in CH_2Cl_2 gave the third fraction (C, 0.5g) which contained amino alcohols II-34a, II-34b and II-35 in the gc ratio of 3:4:3. The last fraction (D, 0.8g), eluted with 4-7% CH_3OH in CH_2Cl_2, contained mostly amino alcohols II-34b and II-35 in the gc ratio of 3:11, along with minor unidentified compounds of longer retention times.

Fraction B (0.7g) was rechromatographed on silicic acid (50g) togive, on elution with 2% CH_3OH in CH_2Cl_2, a fraction (350mg) showing 1 peak on gc (rt 14.0 min). This oil was distilled at 20° 0.2 mmHg to afford a colourless viscous oil which crystalled on standing to give 2-dimethylamino-trans,trans-5,9-cyclododecadien-1-ol (II-34a): mp 20-1°; ir 3420(m,b), 3020(w,sh), 2840(s), 2820 (m,sh), 2770(m), 1020(s), 985(s), 965(s) and 955(s) cm^{-1}; ^{1}Hnmr (Figure II-3) τ4.80(m, 4H), 6.53(ddd, J= 7.5, 6.0 and 3.5Hz, H_1), 6.62(bs, D_2O exch, 1H),

7.20(dt, J= 7.5, 7.5 and 5.0 Hz, H_2), 7.60(s, NCH_3), 7.91(m, 8H) 8.0-8.8(m, 4H); ^{13}C nmr ppm 133.1, 131.2, 130.9, 129.6, 68.4(d, C_1), 59.9(d, C_2), 41.6(q, NCH_3), 31.5(t), 31.4(t), 31.2(t), 29.2 (t), 26.7(t) and 22.9(t); hrms (110°) m/e(%) 223.1933(M^+, 17; calcd for $C_{14}H_{25}NO$: 223.1936), 194.1906(5; calcd for $C_{13}H_{24}N$: 194.1908) 179.1669(11; calcd for $C_{12}H_{21}N$: 179.1674), 129.1153(12; calcd for $C_7H_{15}NO$: 129.1154), 125.1203(13; calcd for $C_8H_{15}N$: 125.1205), 84.0811(28; calcd for $C_5H_{10}N$: 84.0813), 71.0738(100; calcd for C_4H_9N: 71.0735) 58(19) and 56(19). On irradiation of the multiplet at τ8.34, the signals at τ6.53(H_1) and 7.20(H_2) collapsed to an AB quartet (J= 7.5 Hz).

Anal. Calcd. for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27.
Found : C, 75.23; H, 11.49; N, 6.60.

Fraction C (0.5g) was rechromatographed on silicic acid (30g) to give, on elution with 1-3% CH_3OH in CH_2Cl_2, a middle fraction (80mg) which was a mixture of the amino alcohols II-34b and II-35 with the gc ratio of 9:1. A further chromatography of this fraction on silicic acid (5g) gave a colourless oil (45mg) which was distilled at 20°/0.2 mmHg to give the isomer of II-34a (II-34b rt 14.5 min): ir 3420(m,b), 3030(w,sh), 2860(s), 2790(m), 1030(m) and 980(s) cm^{-1}; ^1H nmr (Figure II-4) τ4.71(m, 4H), 6.14(ddd, J= 6.6, 4.9 and 4.0 Hz, H_1), 7.15(bs, D_2O exch, 1H), 7.25(ddd, J=7.5, 4.5 and 4.0 Hz, H_2), 7.71(s, NCH_3), 7.90(m, 8H), 8.38-8.55(m,2H) and 8.55-8.95(m, 2H); ^{13}C nmr ppm 133.3, 132.8, 130.6, 130.1, 69.7(d, C_1), 66.6(d, C_2), 42.5(q, NCH_3), 34.0(t), 31.8(t), 31.3(t), 30.8(t), 28.7(t) and 22.8(t); hrms (100°) m/e(%) 223.1937(M^+, 5;

calcd for $C_{14}H_{25}NO$: 223.1936), 179.1661(5; calcd for $C_{12}H_{21}N$: 179.1674), 129.1152(5; calcd for $C_7H_{15}NO$: 129.1154), 125.1202(7; calcd for $C_8H_{15}N$: 125.1205), 84.0811(15; calcd for $C_5H_{10}N$:84.0813) 71.0727(100; calcd for C_4H_9N: 71.0735), 58.0677(53; calcd for C_3H_8N 58.0657) and 56.0521(13; calcd for C_3H_6N: 56.0500). On irradiation of the multiplets at τ8.45 and 8.85, the signals at τ6.14(H_1)and 7.25(H_2) collapsed to an AB quartet (J= 4.0 Hz). When the multiplet at τ6.14 was irradiated, the signal at τ7.25(H_2) collapsed to a doublet of doublet (J= 7.5 and 4.5 Hz) and also modified the signals at τ8.38-8.55. Irradiation at τ7.25 changed the signal at τ6.14(H_1) to a doublet of doublet (J= 6.6 and 4.9 Hz) and modified slightly the signals at τ8.55-8.95.

Anal. Calcd for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27.
Found : C, 75.35; H, 11.54; N, 6.29.

In the same way, fraction D (0.6g) was rechromatographed on silicic acid (30g) to give a second fraction (190mg) on elution with 3% CH_3OH in CH_2Cl_2. This fraction, slightly contaminated with II-34b, was rechromatographed to give a colourless oil(140mg) which was distilled at 20°/0.2 mmHg to yield 12-dimethylamino-trans,trans-4,8-dodecadien-1-ol (II-35; rt 13.3 min): ir 3380(m, b), 3020(w,sh), 2860(s), 2790(m), 1060(s), 1045(s,sh) and 970(s) cm^{-1}; ^1H nmr τ4.56(m, 4H), 6.39(t, J= 6.5 Hz, CH_2OH), 7.03(s, D_2O exch, 1H), 7.70(t, J= 6.5Hz, CH_2N), 7.78(s, NCH_3), 7.93(m, 8H), 8.38(qui, J= 6.5Hz) and 8.52(qui, J= 6.5Hz)(4H); ^{13}C ppm 129.9(3C), 129.7, 61.6(t, C_1), 59.1(t, C_{12}), 45.2(q, NCH_3), 32.4(t), 30.3(t,3C), 28.8(t) and 27.3(t);

hrms (110°) m/e(%) 225.2089(M^+, 4; calcd for $C_{14}H_{27}NO$: 225.2093) 195.1975(2; calcd for $C_{13}H_{25}N$: 195.1986), 180.1734(4; calcd for $C_{12}H_{22}N$: 180.1752), 126.1279(55; calcd for $C_8H_{16}N$: 126.1283), 84.0811(20; calcd for $C_5H_{10}N$: 84.0813), 81.0698(16; calcd for C_6H_9: 81.0705), 71.0735(33; calcd for C_4H_9N: 71.0735) and 58.0654 (100; calcd for C_3H_8N: 58.0657). On irradiation of the multiplet at τ8.38, the triplet at 6.39 collapsed to a singlet.

Anal. Calcd. for $C_{14}H_{27}NO$: C, 74.61; H, 12.08; N, 6.21.
Found : C, 74.71; H, 12.09; N, 6.19.

The hydrochloride of II-35 was recrystallized from isopropanol as white needles; mp 103-4°; ir 3380(s), 2680(s), 1065(m) and 970(s) cm^{-1}; nmr τ4.62(m, 4H), 6.37(t, J= 6.5Hz, CH_2OH), 6.45(bs, 1H), 7.05(bt, J= 7Hz, CH_2N), 7.21(s, NCH_3), 7.93(m, 8H) and 8.36(m, 4H); ms (150°) m/e(%) 225(M^+-HCl, 4), 195(5), 180(8) 126(55), 84(30), 81(33), 71(22), 58(100), 38(14) and 36(38).

Anal. Calcd. for $C_{14}H_{28}NOCl$: C, 64.22; H, 10.78; N, 5.35.
Found : C, 64.32; H, 10.41; N, 5.16.

(c) treatment of the basic photolysate fraction in acidic conditions : In a separate experiment, a solution of NNOD(1.8g, 0.02 mole), tttCDT (3.24g, 0.02 mole) and concentrated HCl (3ml) in methanol (200ml) was irradiated to give a neutral fraction (840mg) and an aqueous fraction (60ml,pH 1-2) which was divided into 3 equal parts E, F and G. Part E was immediately worked up as seen above. Parts F and G were left at room temperature for periods of 24 and 48 hours, respectively, and were worked up as

above. The 3 basic oils from E (1.35g), F (1.25g) and G (1.23g) showed identical ir spectra : 3350(w,b), 1710(m), 1620(s), 1275 (s), 1040(m), 1025(m) and 860(s) cm^{-1}. Immediate reduction of these basic fractions with LAH as described above afforded the oils E_1 F_1 and G_1, respectively, possessing similar ir spectra: 3380(s,b) 1050(m,b) and 1020(s) cm^{-1}; nmr τ7.60(s), 7.71(s) and 7.78(s). The analyses by gc on 5% Versamid 900(6'x$^1/_8$", 150-270° at 10°/min; rt, yields determined by gc/basic extracts)gave the following results: fraction E_1 (1.19g) contained II-35(13.3 min,18%),II-34a (14.0 min, 48%) and II-34b(14.5 min, 14.5%); fraction F_1 (1.11g) II-35(13.3 min, 18%), II-34a(14.0 min, 46%) and II-34b(14.5 min, 15%); fraction G_1 (1.09g), II-35(13.3 min, 16%), II-34a(14.0 min 46%) and II-34b(14.5 min, 14%).

(d) treatments of the basic photolysate fraction in basic conditions :

i/ in aqueous solution(pH 10). In a similar experiment, a solution of NNOD (1.8g, 0.02 mole), tttCDT (3.24g, 0.02 mole) and concentrated HCl (3ml) in methanol (200ml) was irradiated as described above to give a neutral fraction (800mg) and an aqueous fraction which was made basic to pH 10. This solution was divided into H (2/3) and K (1/3).Part H was immediately extracted with ether (4x60ml); the extracts were washed with water (20ml), dried and evaporated to give an oil (2.5g): ir 3350(m,b), 1710(m), 1620(s), 1275(s), 1040(m), 1025(m) and 860 (s) cm^{-1}, which was divided into 2 equal parts I and J. Fraction I was immediately reduced with LAH as described above to give a

pale yellow oil I_1. Fraction J was left at room temperature for 41 hours to give an oil which ir was identical in all respects with starting fraction J; this oil was then reduced with LAH to yield a pale yellow oil J_1. Part K was left 44 hours at room temperature and then extracted with ether (4x50ml) to give an oil which showed nitrate ester absorptions at 1620(s), 1275(s) and 860(s) cm^{-1}. This oil was reduced with LAH to yield oil K_1. All the oils I_1, J_1 and K_1 showed similar spectra : ir 3380(s,b), 1050(m,b) and 1020(s) cm^{-1}; nmr τ7.60(s), 7.71(s) and 7.78(s) and gave the followings on gc analysis (5% Versamid 900, same conditions as before; rt, yields determined by gc/basic extracts): fraction I_1 (1.17g) contained II-35(12.9 min, 20%), II-34a(13.5 min, 45%) and II-34b(14.1 min, 15%); fraction J_1 (0.96g), II-35 (12.9 min, 15%), II-34a(13.5 min, 44%) and II-34b(14.1 min, 13%) fraction K_1 (0.72g), II-35(12.9 min, 11%), II-34a(13.5 min, 42%) and II-34b(14.1 min, 11.5%).

ii/ in triethylamine : Fraction L(120mg, vide infra) was treated with 15ml of triethylamine with stirring for 3 days. After removal of the solvent, it gave an oil (108mg, 90%); ir and nmr were virtually identical with those of fraction L.

iii/ in sodium methoxide solution : Fraction L(200mg, vide infra) was dissolved in a saturated sodium methoxide solution (5ml) and left for 1 week with stirring at room temperature. Water was added (40ml) and the pH brought to 10 with a 1N HCl solution. The resultant solution was extracted with ether(3x30ml) Evaporation of the solvent gave a fraction (170mg, 85%), ir and nmr of which were identical with those of starting fraction L.

(e) chromatography of the basic photolysate fraction : A methanol solution (200ml) of NNOD (2.4g, 0.0267 mole), tttCDT (4.34g, 0.0267 mole) and concentrated HCl (4ml) was photolyzed for 5.5 hours under oxygen as described before. After the usual work-up, a neutral fraction (840mg) and a basic fraction L (4.7g) were obtained. This basic fraction L exhibited identical spectra with the previous ones, even after 5 months storage at room temperature: ir 3350(m,b), 1710(m), 1620(s), 1275(s), 1040(m) and 860 (s) cm^{-1}. From this mixture L, the following compounds were identified by peak matching on gc (5% Versamid 900, 6'x1/8", 150-265° at 6°/min) with the authentic samples (rt, ratio): II-33(11.5 min 1), II-36(13.4 min, 4), II-34a(15.5 min, 12), II-34b(15.8 min, 4) and other products (>16 min). This mixture L was shown to contain no peak corresponding to open chain amino alcohol II-35(14.8 min) by peak matching with an authentic sample.

A part(200mg) of the crude basic fraction L was reduced (24 hours) with hydrazine hydrate (4M, 5ml) in the presence of Pd/C (60mg) in methanol solution (80) and the product was isolated in the usual manner to give an oil: ir 3400(m,b), 3020(w), 2845(s), 2820(m), 2775(m), 1030(s,b) and 985 cm^{-1}. The oil was distilled under vacuum (0.2 mmHg) at room temperature to give a major fraction (83mg, ~50%) which was shown to be a mixture of isomeric alcohols II-34a and II-34b: ir 3380(m,b), 1045(m,b) and 1020(s) cm^{-1}; nmr τ4.70(m) and 4.80(m) in the 1:3.5 ratio, 6.50(m) 7.20(m), 7.60(s) and 7.71(s) in the ~4:1 ratio, 7.90(m) and 8.0-8.9(m).

A part of fraction L (2.5g) was chromatographed on silicic acid (80g). Elution with 1% CH_3OH-CH_2Cl_2 (100ml) gave a fraction (245mg) which contained a 1:1 mixture of NNOD and the amino ketone II-36 as seen by its ir: 1715(s), 1515(s), 1315(s) and 970(s)cm^{-1}, and nmr τ6.56(t, J= 1.5Hz) and 7.80(s) in the 1:1 ratio. The second fraction (345mg), eluted with 450ml of 1-3% CH_3OH in CH_2Cl_2 contained amino ketone II-36 with minor amounts of nitrate ester II-37a: ir 1715(s), 1620(s), 1275(s) and 860(m) cm^{-1}; nmr τ7.80 (s). This fraction (260mg) was rechromatographed on 15g of silicic acid with 0-1% CH_3OH in CH_2Cl_2 to yield 155mg of crystals which sublimed at 20°/0.05mmHg to give pure 2-dimethylamino-trans,trans 5,9-cyclododecadien-1-one (II-36) as white needles: mp 40-40.5° (recrystallized from methanol); uv (H_2O) λ=220nm(9200) and 278nm (90); uv (CH_3OH) λ= 307nm(90); ir 3420(w), 2980(sh,m), 2940(s), 2920(s), 2860(m), 2795(m), 1720(s,sh), 1715(s), 1710(s,sh), 1040 (s), 980(s), 975(s) and 960(s) cm^{-1}; ^1H nmr τ4.90(m, 2H), 5.04 (m, 2H), 7.08(m, 2H), 7.80(s, NCH_3), 7.60-8.26(m, 11H), 8.48(m,1H) and 8.63(m, 1H); ^{13}C nmr ppm 210.1(s, C_1), 132.4,131.5, 130.0, 129.3, 73.0(d, C_2), 41.5(q, NCH_3), 39.9(t, C_{12}), 32.1(t), 32.0(t) 31.8(t), 28.6(t) and 17.0(t); hrms (100%) m/e(%) 221.1777(M^+, 11; calcd for $C_{14}H_{23}NO$: 221.1780), 193.1828(13; calcd for $C_{13}H_{23}N$: 193.1830), 178.1591(5; calcd for $C_{12}H_{20}N$: 178.1596), 124.1119(20; calcd for $C_8H_{14}N$: 124.1126), 110.0968(13; calcd for $C_7H_{12}N$:110.0970) 84 (15), 71.0745(100; calcd for C_4H_9N: 71.0735), 58.0614(11; calcd for C_3H_8N: 58.0657) and 56(20). Irradiation at τ8.17, 8.48 or 8.63 changed the pattern of the multiplet at τ7.08. Reciprocally, on irradiation of the multiplet at τ7.08, changes were obtained at

τ8.17, 8.48 and 8.63. Irradiation of the olefinic region (τ4.95) brought changes around τ7.70 and 8.17.

Anal. Calcd. for $C_{14}H_{23}NO$: C, 75.97; H, 10.47; N, 6.33.
Found : C, 75.77; H, 10.64; N, 6.44.

The methyl iodide derivative of II-36 was recrystallized from isopropanol as white crystals: mp 241-2°; ir 1715(s), 1230 (m), 1070(m,b), 970(s), 950(s) and 865(m) cm^{-1}; nmr (D_2O) τ4.87 (m, 2H), 5.04(m, 2H), 5.88(m, 1H), 6.99(s, 9H), 7.26(m, 2H), 7.74 (m, 2H) and 8.10(m, 8H); ms (240°) m/e(%) 221(M^+-CH_3I, 18), 193 (24), 142(82), 127(53), 124(43) and 71(100).

Anal. Calcd. for $C_{15}H_{26}INO$: C, 49.59; H, 7.21; N, 3.86.
Found : C, 49.74; H, 7.09; N, 3.72.

A third fraction (590mg), eluted with 150ml of 3% CH_3OH in CH_2Cl_2, gave a mixture of amino ketone II-36 and amino nitrate esters II-37a and II-37b. Continued elution with 3-8% CH_3OH in CH_2Cl_2 afforded a mixture of amino alcohols II-34a and II-34b with minor amounts of amino nitrate esters II-37a and II-37b (1.02g). No trace of open chain amino alcohol II-35 was ever detected by gc.

The amino ketone II-36 (110mg, 5.0×10^{-4} mole) dissolved in a mixture of ethanol (5ml) and 2N NaOH solution (10ml) was treated under reflux for 4 hours with a large excess of hydroxylamine hydrochloride (400mg, 5.75×10^{-3} mole). A major part of the ethanol was removed under reduced pressure and the remaining solution was extracted with ether (3x20ml) to yield a colourless oil (95mg, 80%)

as amino oxime II-31; tlc, ir and nmr spectra were identical with those of an authentic sample prepared by another route.

Amino ketone II-36 (40mg, 1.8×10^{-4} mole) was treated with LAH (50mg) in dry ether for 12 hours. After basic hydrolysis, it yielded a colourless oil (32mg): nmr τ7.60(s,II-34a)and 7.71(s,II-34b) in a 1:6 ratio; Gc analysis (4% Versamid 900, 150-270° at 8°/min) gave the following peaks (rt, yield determined from gc peak area): II-34a (14.3 min, 15%); II-34b (14.8 min, 74%); unknown (16.3min, 8%).

(f) chromatography of the basic photolysate fraction after reduction with $NaBH_4$: The basic fraction L (2g) was treated in 20ml ethanol with an aqueous solution (20ml) of sodium borohydride (1.6g) at room temperature for 24 hours. The excess of $NaBH_4$ was destroyed slowly with a 3N HCl solution until pH 1-2. The acidic aqueous phase was made basic to pH 10 and extracted with ether (4x50ml) to yield a colourless thick oil (1.82g): ir 3350(m,b), 1620(s), 1275(s), 1040(m) and 860(s) cm^{-1}. No carbonyl absorption was detected, even after 5 months storage at room temperature.

Chromatography of this oil (1g) on neutral alumina (80g) by elution with CH_2Cl_2 gave a first fraction as a colourless oil (165 mg) which crystallized on standing in the fridge as long needles of 1-nitrato-2-dimethylamino-trans,trans-5,9-cyclododecadiene (II-37a) mp 32-3°; ir 3020(w),2970(m,sh),2930(s),2850(s),2820(m),2780(m), 1620(s),1275(s),1040(m),1005(m),985(m),970(s),960(s) and 855(s)cm^{-1} ^{1}H nmr τ4.86(m,5H),7.24(dt,J=7,5,7.5 and 4.0Hz,H_2),7.72(s,NCH_3)and 7.82-8.50(m,12H); ^{13}C nmr ppm 132.7(d,2C),129.4(d),129.0(d),83.5(d,C_1),58.6 (d,C_2), 42.1(q,NCH_3), 31.9(t), 31.8(t), 30.0(t), 28.8(t), 27.1(t) and 17.7(t); ms(80°) m/e(%) 268(M^+,1.5),222(100),206(18),192(4),

178(6),124(14),110(8),91(10),84(16),79(33),71(62),58(18)and 56(24).

Anal. Calcd. for $C_{14}H_{24}N_2O_3$: C, 62.66; H, 9.01; N, 10.44.

Found : C, 62.52; H, 9.18; N, 10.01.

A second fraction (53mg) was shown to contain a 1:1 mixture of II-37a and NNOD as indicated by its ir and nmr: τ6.56(t, J=1.5Hz) and 7.72(s) (ratio 1:1). Third fraction (158mg) contained mostly nitrate ester II-37a contaminated with some amino alcohol II-34a as seen by its ir: 3400(w,b), 1620(s), 1275(s), 1040(m) and 855(s) and the nmr singlets at τ7.60 and 7.72 (ratio 1:9). Further elution with CH_2Cl_2 gave a mixture (175mg) of alcohols II-34a and II-34b and postulated nitrate ester II-37b as shown by its ir: 3340(m,b) 1620(s), 1270(s), 1040(s,b) and 860(m) cm^{-1}, and by the nmr singlets at τ7.60, 7.71 and 7.76 (ratio 3:1:2). No nitrate ester II-37a was detected by tlc. This fraction was treated with LAH to yield an oil (141mg) as a mixture of II-34a, II-34b and II-35 ir 3340(m,b) and 1040(s,b) cm^{-1}; nmr τ6.40(t, J= 6.5Hz),7.60(s), 7.71(s) and 7.78(s) in the 2:1:1 ratio. Subsequent fractions (390mg), eluted with 0-10% CH_3OH in CH_2Cl_2 consisted of mixture of amino alcohols II-34a and II-34b.

Amino nitrate ester II-37a (85mg, 3.17×10^{-4} mole) was added slowly to a stirring suspension of LAH (100mg) in ether at 0°and was stirred at room temperature for 24 hours. After the usual work-up, the ether solution was distilled to give a colourless oil (63mg) which was showed to be a mixture of the 2 amino alcohols II-34a and II-35 as seen by its nmr spectrum: τ4.56(m), 4.80(small m), 6.39(t, J= 6.5Hz), 6.58(bs, D_2O exch), 7.20(small

m),7.60(s) and 7.78(s) in the 1:11 ratio, 7.93(m) and 8.30-8.65(m) and its gc (10%SE-30, 100-230° at 8°/min; rt, %): II-35 (9.3 min 82%) and II-34a(10.0 min, 6%).

Using Kuhn's procedure (80), 142mg ($5.3x10^{-4}$ mole) of amino nitrate ester II-37a were treated with hydrazine hydrate (4M,4ml) in the presence of Pd/C (50mg) in methanol solution at room temperature for 24 hours. The usual work-up (see above) afforded a colourless oil (88mg, 74%) which exhibited no ir absorptions typical of nitrate ester group and was distilled under vacuum (0.2mmHg, 40°) to give a major fraction (II-34a, 66mg, 56%) as indicated by its tlc, ir and nmr spectra identical with those of the pure sample.

IV-8-7. NND to trans,trans,trans-1,5,9-cyclododecatriene, with O_2

(a) NND,tttCDT in the 1:1 ratio : A methanol solution (200ml) of NND (1.48g, 0.02 mole), tttCDT (3.24g, 0.02 mole) and concentrated HCl (3ml) was photolyzed in the presence of oxygen for 2.5 hours. The colourless photolysate was concentrated under reduced pressure at 10°, diluted with water (30ml) and washed with ether (4x50ml). The ethereal washings gave 500mg of neutral material which was shown to be tttCDT as the major compound (gc, ir and nmr). The aqueous phase was made basic to pH ~9.5 and was immediately extracted with ether (4x60ml) to give a basic fraction (4.02g, ~84%): ir 3430(m), 1715(m,b), 1630(s), 1280(s), 1045(m, b), 970(m,b) and 860(s) cm^{-1}; nmr τ4.8(m), 6.5(m), 7.0(m), 7.60

(s), 7.71(s), 7.77(s), 7.80(s), 7.90(m) and 8.4(m). the 4 last singlets had an approximate ratio of 1:4:1:1.

Immediate reduction of this crude basic fraction with LAH (2.0g, 0.053 mole) in dry ether (60ml), followed by basic hydrolysis (see above), afforded a colourless oil (3.58g, ~80%) whose gc, ir and nmr were similar to those of NNOD oxidative photolysis with tttCDT: nmr τ4.56(m) and 4.78(m) in the 3:4 ratio and singlets at τ7.60, 7.71 and 7.78 in the approximate 4:1:4 ratio. The gc analysis of this oil (4% Versamid 900, 6'x$^1/_8$", 150-270° at 8°/min) by peak matching with authentic samples afforded the following compounds (rt, yields calculated from the gc peak area) II-33 (9.2 min, 1%), II-35 (14.0 min, 30%), II-34a (14.7 min, 49%) and II-34b (15.2 min, 15.5%).

(b) with excess NND : In a separate experiment, a solution of NND (2.96g, 0.04 mole), tttCDT (1.62g, 0.01 mole) and concentrated HCl (6ml) in methanol (200ml) was irradiated under oxygen until the uv absorption at 345nm had decreased to the $\frac{3}{4}$ of its initial value (1 hour). The photolysate was worked up in the usual manner to give a neutral fraction (162mg) and a basic fraction (1.9g) whose ir and nmr were similar to previous ones. A part of the basic fraction (0.4g) was immediately treated with LAH (350mg) in dry ether (20ml), followed by basic hydrolysis to give a colourless oil (312mg): ir 3400(s,b), 3020(w,sh), 1060(s), 1040(m) and 980(s) cm^{-1}; nmr τ4.58(m) and 4.80(m) in a 3:2 ratio, 6.1(bs, D_2O exch), 6.39(t, J= 6.5Hz), 7.20(m), 7.60(s), 7.71(s), 7.78(s) 7.90(m) and 8.1-8.9(m); the ratio of the 3 NCH_3 singlets was

estimated to be 3:3:7; gc (4% Versamid 900, 150-260° at 10°/min, rt, yields calculated from the gc peak area): II-33 (5.3min, 8%) II-35 (8.7min, 54%), II-34a (9.0min, 20%) and II-34b (9.2min,13%).

In an identical manner, the photolysis of NND (3.7g, 0.05 mole), tttCDT (0.81g, $5x10^{-3}$ mole) and concentrated HCl (7.5ml) in methanol (200ml) was carried out under oxygen until the uv absorption at 345nm had decreased to the $^{89}/_{100}$ of its initial value (1.2 hours). It yielded a neutral fraction (191mg) and a basic fraction (1.28g). This basic fraction (1.1g) was treated with LAH as above to give, after basic hydrolysis a colourless oil (0.81g, ~82%): nmr τ4.58(m) and 4.80(m) in the 3:2 ratio, 6.39(t, J= 6.5Hz), 6.65(bs, D_2O exch), 7.60(s), 7.72(s), 7.76(s) 7.78(s), 7.90(m) and 8.1-8.9(m); the ratio of the 4 NCH_3 singlets was ca 2:1:1:6; gc (4% Versamid 900, 150-260° at 10°/min, rt, yields determined from the gc peak area): II-33 (5.3min, 9%), II-35 (8.7min, 58%), II-34a (9.0min, 18%) and II-34b (9.2min,10%).

IV-8-8. NNOD to cis,trans,trans-1,5,9-cyclododecatriene, with O_2

A solution of NNOD (0.9g, 0.01 mole), cttCDT (1.62g, 0.01 mole) and concentrated HCl (1.5ml) in methanol(200ml) was irradiated in the presence of oxygen for 2.5 hours. The photolysate was evaporated and the residue was cooled to 0°, taken up in H_2O(30ml), and the aqueous solution extracted with ether (4x50ml) to give a neutral fraction (310mg) as a pale yellow oil: ir 970(s), 948(m)

and 700(s) cm^{-1}; nmr τ4.8(m) and 7.9(m). The gc analysis (10% SE-30, 6'x$^1/_8$", 100-290° at 8°min) by peak matching with authentic samples afforded the following compounds (rt, yields relative to total volatile fraction): tttCDT (6.4min, 5%) and cttCDT(6.6min, 92%).

The aqueous portion was made basic to pH 9-10 and extracted with ether (5x60ml) to yield an oil (1.92g, ~80%): ir 3400(m,b), 1710(m), 1630(s), 1280(s), 1035(m,b), 980(m), 860(m) and 705(m) cm^{-1}; nmr τ4.60(m), 6.5(m), 7.3-8.5(m), 7.60(s), 7.67(s), 7.70(s), 7.73(s) and 7.80(s). This fraction was added to a mixture of LAH (1.5g) in ether (50ml) and stirred for 20 hours at room temperature. This was treated with KOH (40% aqueous, 2ml) and water(5ml) at 0°, refluxed for 20min, cooled and filtered. The remaining white solid was further washed with ether. The ether solutions were combined, dried and evaporated to yield a colourless oil (1.56g, ~70%): ir 3380(s,b), 2930(s), 2880(s), 2780(s), 1035(s, b), 985(s) and 710(m) cm^{-1}; nmr τ4.60(m), 6.40(t, J= 6.5Hz), 6.80(m), 7.40(m), 7.50-8.50(m) and singlets at 7.60, 7.67, 7.74 and 7.78 in the approximate ratio of 1:7:2:5. Analysis of this oil by gc (4% Versamid 900, as above, 150-270° at 8°/min) showed a mixture of at least 6 compounds as shown below, in the order of rt and corrected relative yields from starting NNOD: II-35 (14.0min, 1%), II-34a (14.5min, 2%), II-38a and possibly II-34b (14.9min, 33%), II-39 (15.3min, 15%), unknown (16.2min, 6%) and postulated II-38b (16.8min, 14%). These compounds were identified by peak matching with authentic samples.

The reduced basic fraction (1.1g) was chromatographed on a silicic acid column (55g) and gave, on elution with 2.5-15% CH_3OH in CH_2Cl_2, different fractions of mixtures as analyzed on 4% Versamid 900 column. Fractions 8-11 (2.5% CH_3OH in CH_2Cl_2, 221mg) contained II-38a (90%) and II-34a (8%) and was further chromatographed on silicic acid to yield 2-dimethylamino-cis,trans-5,9-cyclododecadien-1-ol (II-38a) as a white solid: mp 31-4°; ^{13}Cnmr ppm 131.0, 130.6, 130.2, 128.4, 69.4(d, C_1), 62.8(d, C_2), 41.6(q NCH_3), 30.6(t, 2C), 27.9(t), 26.5(t), 24.5(t) and 23.1(t). This solid was sublimed at room temperature (0.2mmHg) to give white crystals of II-38a: mp 43-5°; ir 3400(s,b), 3000(m,sh), 2930(s) 2855(s), 2820(m,sh), 2780(m), 1055(m), 1030(s), 1010(m), 985(s) and 705(m) cm^{-1}; ^1H nmr τ4.60(m, 4H), 6.44(m, H_1), 7.20(bs, D_2O exch, 1H), 7.48(q, J= 6.0Hz, H_2), 7.67(s, NCH_3), 7.94(m, 8H) and 8.1-8.6(m, 4H); hrms (80°) m/e(%) 223.1935(M^+, 55; calcd for $C_{14}H_{25}NO$: 223.1936), 194.1919(12; calcd for $C_{13}H_{24}N$: 194.1908), 179.1674(25; calcd for $C_{12}H_{21}N$: 179.1674), 129.1155(25; calcd for $C_7H_{15}NO$: 129.1154), 124.1110(26; calcd for $C_8H_{14}N$: 124.1126), 110.0958(21; calcd for $C_7H_{12}N$: 110.0969), 84.0824(42; calcd for $C_5H_{10}N$: 84.0813), 71.0752(100; calcd for C_4H_9N: 71.0735), 58(27) 56(35), 44(14) and 42(21).

Anal. Calcd. for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27.
Found : C, 75.41; H, 11.31; N, 6.28.

Fractions 12-15 (155mg), eluted with 3-5% CH_3OH in CH_2Cl_2, were shown to be a mixture of II-38a and probably II-38b in the

ratio of 7:3 as seen by gc: nmr τ4.60(m), 6.50(m), 6.70(s, D_2O exch), 7.48(m), 7.67(s) and 7.74(s) in the ratio of 2:1, 7.95(m) and 8.1-8.6(m). The last fractions, 17 and 18 (69mg, colourless oil), eluted with 15% CH_3OH in CH_2Cl_2 were found to contain mostly 12-dimethylamino-cis,trans-4,8-dodecadien-1-ol (II-39), with a trace amount of II-38a: ir 3380(m,b), 3000(m,sh), 2925(s) 2842(s), 2775(s), 1055(s,b), 1040(s,b), 965(s) and 700(w) cm^{-1}; ^1H nmr τ4.60(m, 4H), 6.40(t, J= 6.5Hz, 2H), 6.82(s, D_2O exch,1H) 7.68-7.82(m, 2H), 7.78(s, NCH_3), 7.94(m, 8H) and 8.39(m, 4H); ^{13}C nmr ppm 130.2, 130.0, 129.8, 129.3, 61.7(t, C_1), 59.2(t,C_{12}), 45.1(q, NCH_3), 32.3(t, 2C), 28.7(t), 27.5(t), 27.2(t) and 25.1(t); hrms (80°) m/e(%) 225.2094(M^+, 7; calcd for $C_{14}H_{27}NO$: 225.2092), 180.1745(17; calcd for $C_{12}H_{22}N$: 180.1752), 126.1243(92; calcd for $C_8H_{16}N$: 126.1283), 84.0817(70;calcd for $C_5H_{10}N$: 84.0814), 81.0696 (34; calcd for C_6H_9: 81.0704), 71.0746(98; calcd for C_4H_9N:71.0735) and 58.0674(100; calcd for C_3H_8N: 58.0657). An analytical sample of II-39 was obtained on distillation (20°, 0.2 mmHg).

Anal. Calcd. for $C_{14}H_{27}NO$: C, 74.61; H, 12.08; N, 6.21.
Found : C, 74.55; H, 11.78; N, 6.24.

IV-8-9. NND to cis,trans,trans-1,5,9-cyclododecatriene, with O_2

A methanol solution (200ml) of NND (1.628g, 0.022 mole), cttCDT (3.24g, 0.02 mole) and concentrated HCl (3ml) was irradiated under oxygen for 5 hours. The solution was distilled under

reduced pressure, and the residue was treated with water (30ml) and extracted with ether (4x60ml). The ether extracts were washed with water, dried and evaporated, leaving an oil (338mg) which was shown to be mostly CDT by its ir and nmr. Gas chromatography (20% Dowfax 9N9, 10% TEP on Chromosorb P60/80, 8'x¼" copper, 100-220at2°/min, He inlet pressure at 20 psi) gave the following compounds (rt, yields based on total volatile fraction): tttCDT (22.8min, 5%) and cttCDT (24.6min, 85%).

The aqueous solution of the photolysate was then made basic to pH 10 and extracted with ether (4x60ml). The ether solution was dried and evaporated to give an oil (3.96g, ~93%): ir 3350(m,b) 1700(m,b), 1625(s), 1275(s), 1035(m,b), 975(m,b), 860(s) and 705 (m) cm^{-1}; nmr τ4.62(m), 6.3(m) and 7.3-8.8(m). A part of this basic fraction (300mg) was treated with LAH (500mg) in the usual fashion to give, after hydrolysis, a colourless oil(248mg), which ir and nmr were identical with those of oxidative photoaddition of NNOD to cttCDT. The gc analysis of this oil (4% Versamid900, same conditions as above) showed the presence of the following compounds (rt, corrected relative yields from starting NND): II-35 (14.0min, 2%), II-34a (14.5min, 3%), II-38a (14.9min, 35%), II-39 (15.3min 21%), unknown (16.2min, 7%) and II-38b (16.8min, 12%).

IV-8-10. NNOD to endo-dicyclopentadiene, with O_2

A solution of NNOD (1.8g, 0.02 mole), endo-DCPD (2.64g, 0.02 mole) and concentrated HCl (3ml) in methanol (200ml) was

photolyzed under oxygen for 5 hours. The solvent was evaporated and the residual solution (30ml) was diluted with water (30ml). Extraction with ether (4x60ml) gave a neutral fraction (830mg) as a yellow oil which showed 12 peaks (10% SE-30, 180°); ir 3400(m,b) 3050(w), 1765(m), 1735(m,b), 1640(s,b), 1550(s), 1370(s), 1280(s), 1090(s,b), 1065(s,b), 850(s) and 715(m) cm^{-1}; nmr τ0.3(m), 4.0-4.8(m), 5.0-6.5(m), 6.65(bs) and 7.1-8.8(m).

The aqueous mother liquor was made basic to pH 9.5 at 0° and immediately extracted with ether (5x60ml) to yield a reddish oil (2.7g): ir 3400(s,b), 3050(w), 2730(m), 1720(s), 1625(s), 1280(s), 1030(s,b), 860(s), 740(m) and 700(m) cm^{-1}; nmr τ-0.12(m), 3.76(m), 4.37(m), 6.69(m), 7.40(m), 7.66(s), 7.69(s, D_2O exch), 7.72(s), 7.76(s, D_2O exch), 7.81(s) and 8.40(m). After ether extraction (4 hours), the aqueous phase was further extracted with CH_2Cl_2 (2x 50ml) to give an additional basic fraction (430mg) as a brown oil: ir 3340(m,b), 3050(w), 1715(s,b) and 1040(s,b) cm^{-1}; nmr τ-0.10 (m), 3.79(m), 4.17(m), 4.40(m), 6.68(m), 7.22(m) and 7.75(m). The ether extracts (2.4g) were immediately treated with LAH (2g) in the usual way for 12 hours to give, after basic hydrolysis, a yellow oil (1.7g): ir 3380(s,b), 3040(w), 2940(s), 2880(s), 2830 (sh), 2780(s), 1345(m), 1255(m), 1040(s,b), 740(m) and 695(m) cm^{-1}; nmr τ3.77(m) 4.40(m) 6.3-6.8(m) 7.25(m) 7.6-8.0(m) 7.67(s) 7.77(s) and 8.2-8.8(m). The ratio of the signals at τ3.77 to 4.40 and 7.67 to 7.77 was 1:6. This oil was shown by gc on 4% Versamid 900 (6'x $^1/_8$", 100-270° at 8°/min) to contain the following compounds in order of increasing retention time: 14.0 min (unknown, ~1%), 15.6

min (II-42, 8%), 16.3 min (II-41, 25%), 17.3 min (II-40, 21%) and 18.3 min (unknown, ~2%). Chromatography of a portion of this mixture (1.3g) on silicic acid (80g) and elution with increasing methanol concentration in CH_2Cl_2 afforded several fractions: A (0-2%, 150mg), B (2%, 133mg), C (3-5%, 239mg) and D (5-50%, 220mg). Fraction B gave one spot on a tlc plate and one single peak on gc (4% Versamid 900, see above, rt 17.3 min) and on distillation at room temperature (0.05 mmHg) yielded trans,cis,trans-2,4-bis-hydroxymethylbicyclo[3.3.0]oct-6-ene (II-40) as a colourless oil: ir 3350(s,b), 3050(m), 1620(w), 1065(s), 1020(s) and 760(s) cm^{-1}; nmr (Figure II-10) τ4.30(m, 1H), 4.42(m, 1H), 5.78(impurity), 6.34(d, J= 7Hz, 2H), 6.41(d, J= 7Hz, 2H), 6.70(m, 1H), 7.09(m, 1H), 7.5-8.0(m, 7H, 2 D_2O exch H), 8.28(m, 1H) and 8.6-9.2(impurity). hrms (70°) m/e(%) 168.1146(M^+, 7; calcd for $C_{10}H_{16}O_2$: 168.1150), 150.1001(11; calcd for $C_{10}H_{14}O$: 150.1044), 136.0891(14; calcd for $C_9H_{12}O$: 136.0888), 132.0937(19; calcd for $C_{10}H_{12}$: 132.0939), 131.0859(16; calcd for $C_{10}H_{11}$: 131.0860), 119.0856(100; calcd for C_9H_{11}: 119.0860), 117.0706(64; calcd for C_9H_9: 117.0704), 109.0657(59; calcd for C_7H_9O: 109.0653), 105.0706(54; calcd for C_8H_9: 105.0705), 91.0541(84; calcd for C_7H_7: 91.0547), 79.0554(70; calcd for C_6H_7: 79.0548) and 66(78). On irradiation of the multiplet at τ7.72, the multiplets at 4.30 and 4.42 became a ABXY type spectrum (J_{AB} = 6Hz, J_{AX} = J_{BY} = 2Hz), the doublets at τ6.34 and 6.41 became singlets and changes occured in every other multiplets.

II-40 (50mg, $3x10^{-4}$ mole) was heated with p-nitrobenzoyl chloride (200mg, $1.1x10^{-3}$ mole) in pyridine (3ml) on a steam bath

until the solid was dissolved (0.5 hour). The reaction mixture was poured into ice-water and the resulting solid was filtered and washed thoroughly with sodium carbonate solution and with water: (65mg, 46%, mp 121-130°). It was recrystallized three times from isopropanol to give the bis-p-nitrobenzoate of II-40 as a white solid: mp 131-2°; ir 1712(s), 1610(m), 1530(s), 1350 (s), 1280(s), 1100(m) and 725(s) cm^{-1}; nmr τ1.78(m, 8H), 4.20 (m, 1H), 4.38(m, 1H), 5.56(d, J= 7Hz, 2H), 5.63(d, J= 7Hz, 2H), 6.54(m, 1H), 6.96(m, 1H), 7.4-7.7(m, 3H), 8.12(m, 1H), 8.42(m, 1H) and 8.81(m, 1H); ms (200°) m/e(%) 466(M^+, 2), 167(31), 150 (46), 132(100), 120(40), 104(43), 91(47) and 65(30).

Anal. Calcd. for $C_{24}H_{22}N_2O_8$: C, 61.80; H, 4.75; N, 6.01.
Found : C, 61.54; H, 4.79; N, 5.88.

Fraction D as a yellow oil showed one spot on a tlc plate and a single peak on gc (4% Versamid 900, see above) matching with the major peak (rt 16.3 min) of the basic mixture. This oil was distilled at 25°/0.05 mmHg to afford a colourless oil of exo-9-dimethylamino-endo-tricyclo[5.2.1.$0^{2,6}$]-3-decen-exo-8-ol (II-41): ir 3300(m,b), 3040(m), 2950(s), 2930(s), 2880(s), 2830 (m), 2782(m), 1610(w), 1245(m), 1090(m), 1070(s); 1050(s), 1030 (s), 910(m), 742(s) and 708(s) cm^{-1}; nmr (Figure II-8) τ4.38(m, H_3), 4.53(m, H_4), 6.41(ddd, J= 6.0 and <1.0Hz, H_8), 6.66(m, H_7), 6.8-7.0(m, 3H, 1 D_2O exch H), 7.45(m, 1H), 7.63(dt, J= 6.0 and 1.5Hz, H_9), 7.77(s, NCH_3), 7.87(m, 2H), 8.33 and 8.73 (AB quartet, J_{AB} = 10Hz, 2H); hrms (70°) m/e(%) 193.1465(M^+, 51; calcd for

$C_{12}H_{19}NO$: 193.1466), 178.1227(13; calcd for $C_{11}H_{16}NO$: 178.1232), 164.1440(15; calcd for $C_{11}H_{18}N$: 164.1439), 162.1281(13; calcd for $C_{11}H_{16}N$: 162.1283), 127.0994(20; calcd for $C_7H_{13}NO$: 127.0997), 125.0841(43; calcd for $C_7H_{11}NO$: 125.0841), 110.0973(45; calcd for $C_7H_{12}N$: 110.0970), 84.0814(81; calcd for $C_5H_{10}N$: 84.0813), 71.0733 (100; calcd for C_4H_9N: 71.0735) and 58.0674(62; calcd for C_3H_8N: 58.0656).

The column was washed with a 2:1 mixture of 0.05 N HCl solution and methanol. The washing was filtered and was evaporated. The aqueous solution was made basic to pH 10 with a 10% KOH solution and extracted with ether (3x40ml) to afford an oil (320mg) which was shown to contain the major amino alcohol II-41 and postulated amino alcohol II-42 in the 1:1 ratio by gc analysis (4% Versamid 900, see above, rt 16.3 and 15.6 min, respectively): ir 3400(s,b), 3050(w), 2960(s), 2870(s), 2830(m), 2780(m), 1350(m), 1255(m), 1065(s), 1045(s), 1030(s), 735(m) and 695(m) cm^{-1}; nmr τ3.80(m) 4.45(m), 5.90(m), 6.39(m), 6.60-7.30(m), 7.67(s), 7.77(s) and 8.15-8.8(m). The intensity ratios of the multiplets at τ3.80 to 4.45 and of the singlets at τ7.67 to 7.77 were nearly 1:1.

IV-8-11. NND to endo-dicyclopentadiene, with O_2

A solution of NND (1.628g, 0.022 mole), endo-DCPD (2.64g, 0.02 mole) and concentrated HCl (3ml) in methanol (200ml) was irradiated in the presence of oxygen for 5 hours. The bulk of methanol was removed. The residual solution (15ml) was diluted with water (25 ml) and extracted with ether (4x60ml) to give an oil (620mg) which was

shown to be a complex mixture by its gc (10% SE-30, 100-220° at 6°/min): ir 3340(m,b), 3035(w), 1730(m,b), 1650(s), 1555(s), 1380(s), 1280(s), 1100(s,b), 950(s) and 850(s) cm^{-1}.

Half the aqueous solution (pH<2) was stirred for 7 days at room temperature and extracted with ether to give an oil (35mg) which showed 3 major spots on a tlc plate (alumina, CH_2Cl_2), ir absorptions at 1720(s) and 2730(m) cm^{-1} and a nmr signal at τ0.3 (m) for an aldehyde moiety, along with ir absorptions at 1630(s), 1280(s) and 865(m) cm^{-1} for a nitrate ester group, and 3420(m,b), 3060(m), 1020(m,b) and 710(m) cm^{-1}. Gc-ms analysis of this oil (10% SE-30, 100-280° at 6°/min) showed 1 major component (rt 5.1 min, 53% based on gc peak areas) tentatively assigned as dialdehyde II-43 which exhibited ms peaks at m/e (%) 164(M^+, 6), 146(12), 136 (18), 117(28), 108(84), 79(100), 66(55), 41(42) and 39(55). The other unknown component (rt 8.1 min, 21%) exhibited ms peaks at m/e(%) 147(M^+?, 12), 119(22), 117(18), 105(26), 91(70), 79(72), 66(45), 41(100) and 39(64). The same acidic aqueous solution was made to pH 3-4 with a saturated Na_2CO_3 solution. This solution was stirred at 30-45° for 12 hours and extracted with ether to give extracts A (65mg). The aqueous phase was further stirred at 70-85° for 1 day and extracted with ether to give extracts B (122mg). Both neutral extracts A and B showed ir and nmr very similar to the previous neutral fraction; in particular, better resolved nmr doublets for the aldehyde protons at τ0.28(d, J = 1.5Hz) and τ0.34(d, J = 2.5Hz) with equal intensities. The gc of these 2 fractions A and B on a 10% SE-30 column (see above) showed the major peak at rt 5.1 min (72% and

65%, respectively). The same aqueous solution was further made basic to pH 10 with a 10% KOH solution and was left 2 days with stirring, at which time it was made acidic to pH 3 with a 3N HCl solution and extracted with ether to give another neutral fraction (131 mg): ir 3400(m,b),3050(w),1720(s,b),1550(m),1090(s) and 1032 (s); nmr τ3.52(m), 3.8(t,J=2Hz), 5.6-8.8(m). This fraction contained 1 major compound as seen by its gc (10 SE-30,100-280° at 6°/min. A gc-ms of this peak on the same column (rt 7.4 min, 90% of gc peak areas) gave m/e(%) 164(M^+, 20), 136(12), 123(17), 119(11) 99(68), 91(32), 66(100) and 39(42) which did not match with the one of previous dialdehyde II-43.

The other half of the aqueous solution was basified to pH 10 and left at room temperature with stirring for 2 days. It was extracted with ether to give a basic fraction (960mg) which still contained ir absorptions at 1625(s), 1275(s) and 860(m) cm^{-1} for nitrate ester groups. It was reduced in the usual manner with LAH (1g) to give, after basic hydrolysis, a neutral fraction(126mg, II-40) and a basic fraction (694mg) which showed 1 major,1 medium and several minor peaks by gc (10% SE-30, 100-280° at 6°/min). The gc-ms of the basic fraction gave the following peaks that were described in the order of rt, yield based on gc peak areas, m/e(%): 5.5 min, 2%, unknown, 179(M^+?, 10), 150(8), 109(21), 84 (100), 71(74), 58(37) and 42(90); 6.3 min, 6%, unknown, 191(17), 162(10), 135(9), 120(9), 97(34), 84(100), 71(57), 58(33), and 42(70); 6.9 min, 14%, postulated II-42, 193(M^+, 38), 176(28), 164(15),126(86), 109(75), 84(100), 71(92) and 58(76); 7.3 min,

68%, II-41, 193(M^+, 28), 178(12), 164(10), 162(9), 127(32), 125 (36), 110(39), 84(100), 71(61), 58(48) and 42(38); 9.1 min, 3%, unknown, 209(M^+?); 9.6 min, 3%, unknown, 209(M^+?). The peaks at 6.9 min and 7.3 min matched with a 1:1 mixture of II-42, II-41, respectively.

IV-8-12. NND to cis,trans-1,5-cyclodecadiene, with O_2

A solution of perchloric acid (70%, 4ml) in methanol (80ml) was added in a photovessel at 0° to a solution of NND (2.04g, 0.0276 mole) and CDD (3.13g, 0.023 mole) in methanol (100ml). This solution was irradiated under oxygen for 8 hours. The photolysate was concentrated to 60ml (10°/15mmHg). This solution deposited a yellow oil on cooling. A small portion of this oil showed ir absorptions at 1640(s,b), 1280(s) and 870(s,b) cm^{-1} (ONO_2) as well as 1000-1130(s,b) cm^{-1} (ClO_4^-). The photolysate was further concentrated to 30ml (10°/15mmHg) and was added to water (50ml). The aqueous solution was extracted with ether (4x40ml). The ether extract was washed with water (3x30ml), dried and evaporated to give a pale yellow oil (262mg) which showed no NCH_3 signal in its nmr spectrum and exhibited ir absorptions at 1625(s), 1280(s) and 865(s) cm^{-1} (ONO_2) and 1550(s) and 1372(s) cm^{-1} (NO_2). The aqueous phase was made basic to pH 10 and extracted with ether (4x50ml) to give a basic fraction (4.6g): ir 3300(w,b), 2930(s), 2880(s), 2820(s), 2770(s), 1703(w), 1625(s), 1550(m), 1280(s), 1040(m) and 865(s) cm^{-1}; nmr τ4.5-5.3(m), 6.63(m) and 7.5-9.0(m) including a broad singlet at τ7.75.

This basic fraction was immediately stirred with LAH (5g) in dry ether (80ml) for 1 day at room temperature. After the usual basic hydrolysis, a colourless oil was obtained (3.7g, ~83%) consisting of major cyclized amino alcohols II-46a and II-46b: ir 3380(s,b), 2930(s), 2860(s), 2830(s), 2790(s), 1350(m), 1265(m), 1035(sh), 1025(s), 910(m) and 865(m) cm^{-1}; nmr, no signal below τ6.0, τ6.3-6.9(m, partially D_2O exch) and 7.5-9.0(complex m) including a broad singlet at τ7.75. The gc analysis of this oil (10 SE-30 on Chromosorb S 80/100, 6'x$^1/_8$"stainless steel, 100-255° at 6°/min, He at 18 psi, and a H_2 flame detector) showed 1 minor (6% rt 9.9 min, unknown), 1 major (78%, rt 14.1 min, II-46a) and 1 medium peak (16 % rt 14.4 min, II-46b), the last 2 overlapping. This oil (3.4g) was chromatographed on a basic alumina column (150g) to give, on elution with 1% CH_3OH in CH_2Cl_2, several fractions: A (306mg, several spots on a tlc plate), B (700mg, mostly II-46 by gc), C (1.35g, mostly II-46a by gc); the last fraction D was eluted with 2-10% CH_3OH in CH_2Cl_2 (300mg, a 7:13 mixture of II-46a:II-46b by gc, vide infra).

Fraction B was rechromatographed on 150g of basic alumina to afford a middle fraction (395mg) giving 1 peak on gc (rt 14.1 min). This oil crystallized on standing. Sublimation of the solid (40° 0.05 mmHg) yielded 8-dimethylamino-cis-bicyclo[5.3.0]-2-decanol (II-46a) as white crystals: mp 54-5°; ir 3390(s,b), 2930(s), 2860(s), 2830(s), 2790(s), 1350(m), 1265(m), 1205(m), 1025(s), 910(m) and 865(m) cm^{-1}; ^1H nmr τ6.50(bt, J= 8.5Hz, H_2), 7.75(s, NCH_3), 7.8-8.9(complex m, 16H, including a D_2O exch peak at τ7.96); ^{13}C nmr ppm 76.2(d), 75.5(d), 51.0(d), 44.3(d), 43.1(q, NCH_3), 38.8(t),

32.3(t), 30.2(t), 29.9(t), 28.5(t) and 27.6(t); hrms (70°) m/e(%) 197.1781(M^+, 59; calcd for $C_{12}H_{23}NO$: 197.1780), 182.1539(6; $C_{11}H_{20}NO$: 182.1545), 180.1761(4; calcd for $C_{12}H_{22}N$: 180.1753), 179.1660(4; calcd for $C_{12}H_{21}N$: 179.1673), 168.1378(7; calcd for $C_{10}H_{18}NO$: 168.1388), 110.0946(13; calcd for $C_7H_{12}N$: 110.0969), 84.0817(100; calcd for $C_5H_{10}N$: 84.0813), 71.0721(73;calcd for C_4H_9N: 71.0735) and 58.0654(64; calcd for C_3H_8N: 58.0657). On irradiation at the broad triplet at τ6.50 changed to a broad singlet.

Anal. Calcd. for $C_{12}H_{23}NO$: C, 73.04; H, 11.75; N, 7.10.

Found : C, 73.25; H, 11.68; N, 7.25.

An acetone solution (4ml) of amino alcohol II-46a (250mg, $1.27x10^{-3}$ mole) was treated with a red solution of CrO_3-H_2SO_4 in water (8N)(0.66ml, $1.4x10^{-3}$ mole) for 1.5 hours at room temperature. A few drops of methanol were added to the green solution to destroy the excess of the Jones' reagent. The acetone was evaporated and the residue was basified and immediately extracted with CH_2Cl_2 (3x40ml) to give a clear oil (199mg, 81%) as 8-dimethylamino-cis-bicyclo[5.3.0]-2-decanone (II-47a): ir 2935(s), 2870(s), 2825(m), 2780(m), 1703(s), 1160(m), 1040(m) and 865(m) cm^{-1}; ^1H nmr τ7.0-7.9(m, 7H), 7.73(s, NCH_3) and 8.05-8.9(m, 11H); ^{13}C nmr ppm 211.9 (s), 73.6(d), 54.6(d), 42.4(t and q, 3C?), 41.9(d), 32.2(t), 28.0(t) 26.5(t), 24.8(t) and 23.4(t); ms (20°) m/e(%) 195(M^+, 20), 110(7), 84(41), 71(100), 56(12) and 42(11).

Cis-amino ketone II-47a (35mg) was treated with a 2N HCl solution (5ml) for 2 days at 50°. After basification and ether extraction, a colourless oil (26mg, 75%) was obtained and shown to be a

~2:3 mixture of amino ketones II-47a and II-47b by its ^{1}H nmr (2 singlets at τ7.73 and 7.76).

Fraction D, obtained as a colourless oil, showed 2 peaks (10 %SE-30, see above). This mixture was postulated to be a 7:13 mixture of the isomeric alcohols II-46a(rt 14.1 min) and II-46b (rt 14.4 min): ir spectrum similar with ir of pure amino alcohol II-46a; ^{1}H nmr τ6.2-6.8(m, partially D_2O exch), 7.5-8.9(m) and 7.75(s); ^{13}C nmr ppm 76.2(d), 75.5(d), 73.3(d), 71.6(d), 51.0 (d), 47.5(d), 44.3(d), 43.3(d), 43.1(q), 42.2(q), 38.8(t), 33.9(t), 32.3(t), 31.7(t), 30.2(t), 29.9(t), 28.5(t), 27.6(t), 26.8(t), 26.6(t), 26.0(t) and 24.6(t). The underlined chemical shifts were lower in intensity in comparison to others and matched with those of amino alcohol II-46a. The gc-ms (10%SE-30, 100-255° at 6°/min) of this mixture afforded the following mass: II-46a(rt 14.1 min): m/e(%) 197(M^+, 37), 182(4), 168(5), 110(12), 84(100), 71(89) and 58(68); II-46b(rt 14.4 min): m/e(%) 197(M^+, 6), 182(3), 168(2), 154 (8), 110(6), 84(100), 71(80), 58(80) and 44(28).

This fraction (100mg) was oxidized in acetone (2ml) with a solution of CrO_3-H_2SO_4 (0.3ml, see above) for 3 hours at room temperature. After the usual work-up, a basic fraction (71mg, 70%) was shown to be crude II-47a, as seen by its tlc, gc, ir, ^{1}H and ^{13}C nmr spectra matching with those of II-41a.

In a separate experiment, a solution of NND (1.48g, 0.02 mole), CDD (2.45g, 0.018 mole) and perchloric acid (70%, 3ml) in CH_3OH (200ml) was photolysed under oxygen as described above. After irradiation (2.5 hours), the photolysate was concentrated to 30ml and

water (50ml) was added, resulting in an oil depot. The entire fraction was extracted with ether (3x40ml). The ether extract was washed with water (2x30ml), dried and evaporated to give an oil (440mg) identical to previous neutral fraction. The photolysate was filtered to afford a white solid (1.97g, 32%) which was recrystallized twice from ethanol to give the perchlorate of 2-nitrato-8-dimethylamino-cis-bicyclo[5.3.0]decane (II-44a): mp 154-154.5°; ir 3090(s,b), 1605(s), 1290(s), 1280(s), 1060-1100(s,b), 970(s), 930(m), 890(s), 760(m) and 620(s) cm^{-1}; 400 MHz ^{1}Hnmr ($CDCl_3$) (Figure II-11) τ1.06(bs, D_2O exch, NH), 5.17(ddd, J=10.4,10.0 and ≤0.6Hz, H_2), 6.85(m, H_8), 7.015(d, J=5.0Hz, NCH_3), 7.08(d,J=5.0Hz, NCH_3), 7.46(dddd, J=12.0,10.4,9.8 and 5.4Hz, H_1), 7.56(m,H), 8.01 (m, 2H), 8.22(m, 2H) and 8.32-8.64(m, 8H); ^{13}Cnmr (DMSO-d_6) ppm 89.4(d,C_2), 73.8(d,C_8), 45.1(d), 42.0(q,NCH_3), 39.5, 32.9(t), 31.1 (t), 28.8(t,2C), 27.0(t) and 26.4(t); (CD_3OD) ppm 88.2(d,C_2), 74.1 (d,C_8), 44.8(d), 42.0(q,NCH_3), 41.8(q,NCH_3), 39.4(d), 32.5(t), 30.7(t), 28.2(t,2C), 26.7(t) and 25.7(t).

Anal. Calcd. for $C_{12}H_{23}N_2O_7Cl$: C, 42.05; H, 6.76; N, 8.17.

Found : C, 42.11; H, 6.71; N, 8.14.

Perchlorate II-44a (400mg) was added to water (5ml), the solution made basic and extracted with ether to give a colourless oil (242mg,85%) as the free base of II-44a: ir 3400(w,b), no carbonyl absorption, 1620(s), 1280(s) and 860(s) cm^{-1}. This fraction was immediately treated with LAH (200mg) in dry ether, overnight. After the usual work-up, a colourless oil (148mg,75%) was obtained whose ir and gc(10%SE-30, 100-240° at 10°/min, 1 peak at rt7.6min) were matching with those of pure alcohol II-46a.

IV-8-13. NND to cis,trans-1,5-cyclodecadiene, with N_2

A solution of NND (3.552g, 0.048 mole), CDD (5.44g, 0.04 mole) and concentrated HCl (4.4ml) in methanol (180ml) was irradiated under nitrogen. The photolysis was stopped when the emerging peak at ca 300nm was most intense (7.5 hours). The yellow photolysate was neutralized immediately with anhydrous sodium carbonate. No precipitate was obtained. The photolysate was concentrated to a small volume under vacuum and 50ml of ether was added. No precipitate was obtained. The solution was concentrated to give a yellow paste, to which 50ml of Brine solution was added, and was extracted with CH_2Cl_2 (3x50ml). The extracts were washed with Brine solution (3x30ml) and evaporated to give an orange oil (6.86g) which showed 1 major and several minor spots on a tlc plate: ir 3180(m,b), 3050(m,b), 2930(s), 2870(s), 2820(s), 2780(s), 1640(w,b), 1265(m), 1210(w), 1185(m), 1040(m), 1030(m), 960(m), 915(m), 860(m) and 703(m) cm^{-1}; nmr no olefinic proton, multiplets at τ7.0 and 8.5, at τ 7.74(bs, N-CH_3), an exchangeable proton at τ-0.05(b), 2 singlets at τ6.20 and 6.93 for starting NND. ^{13}C nmr indicated that this fraction contained 2 major compounds, postulated as syn and anti-oximes II-43, in relatively equal amounts as seen by the height of the following peaks: ppm 162.1, 161.5, 74.9, 71.3, 48.1, 44.8, 43.2 (2C), 42.3(2C), 40.2, 38.7, 32.6, 31.1, 30.7, 29.6, 29.3, 28.4, 28.0, 28.0, 27.3, 26.0, 25.0 and 24.2. All the underlined chemical shifts matched with pure anti-oxime II-48b isolated in the following work-up.

Acid base extraction of this mixture (5.5g) afforded a neutral fraction (yellow oil, 207mg) containing starting NND and olefinic material as indicated by its ir and nmr spectra. The basic fraction (yellow oil, 4.98g, ~75%) showed 1 major, 2 medium and 1 minor spots on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2): ir 3170(m,b), 3050(m,b), 2940(s), 2870(s), 2830(s), 2780(s), 1703(m) 1640(w,b), 1270(m), 1210(m), 1190(s), 1040(s), 1030(s.), 960(s), 915 (m), 860(m) and 703(m) cm^{-1}. Its nmr spectrum showed a broad singlet at τ-0.04, multiplets at τ6.8-8.8 and a strong and a weak singlets at τ7.74 and 7.78, respectively.

Chromatography of a portion of this mixture (4g) on neutral alumina (400g) and elution with CH_3OH in CH_2Cl_2 afforded different fractions (%CH_3OH, volume eluant, weight): fraction A(1%, 111, 95mg) B(1%, 200ml, 300mg), C(1%, 50ml, 300mg), D(1%, 350ml, 700mg), E(1-3% 800ml, 300mg), F(6%, 300ml, 580mg), G(10%, 300ml, ~1.2g) and H(15-20%, 600ml, 300mg). Fractions A, B and C contained amino ketones II-47 and showed 1 major spot on a tlc plate and singlets at τ7.73 and 7.76 in the ratio ~2:3. Fraction B was rechromatographed on 50g neutral alumina to yield a mixture of amino ketones II-47 (232mg) as a colourless oil: 1 spot on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2, Rf 0.75), 1 peak on gc (10%SE-30, 6'x$^1/_8$", 80-240° at 6°/min, rt 14.5 min); ir 2935(s), 2870(s), 2825(m), 2780(m), 1703(s) and 1040(m) cm^{-1}; ^1H nmr τ7.1-7.95(m, 4H), 7.73(s) and 7.76(s)(ratio ~2:3, NCH_3) and 8.0-9.0(m, 11H); ^{13}C nmr ppm 211.9(s), 211.8(s) 73.6(d), 71.9(d), 54.6(d), 54.6(d), 45.0(d), 42.9(t), 42.4(t), 42.4(q), 41.9(d), 40.5(q), 34.6(t), 32.2(t), 28.4(t), 28.0(t),

26.5(t), 24.8(t); 23.4(t), 22.7(t), 22.2(t) and 20.7(t). All the underlined chemical shifts were the lowest in height and matched with pure amino ketone II-47a. This fraction formed crystals in the freezer, but melted at room temperature.

Fraction D contained a mixture of amino ketones II-47 and amino oximes II-43: 2 spots on a tlc plate; ir 3180(w,b), 1703(s) 1640(w,b), 1040(m) and 1030(m) cm^{-1}; nmr τ7.74(s) and 7.76(s) in the ~2:1 ratio. This fraction D was treated with 40ml of an aqueous 2N HCl solution for 5 days to give, after basification and ether extraction, a fraction (628mg), which was shown to be a ~2:3 mixture of II-47a and II-47b by its tlc (1 spot); ^{1}H nmr, singlets at τ7.73 and 7.76 in the ratio ~2:3; ^{13}C nmr, similar to those obtained above.

Fraction E showed 3 spots on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2) corresponding to a mixture of II-47(Rf 0.75), II-43a?(Rf 0.40) and II-43b(Rf 0.25). The major spot (Rf 0.40), assumed to be II-43a could not be isolated in another chromatography of this fraction (170mg) on neutral alumina (25g). Recovery of all the fractions yielded an oil E_1(125mg) which gave only a faint spot at Rf 0.40, but the spot at Rf 0.25 became the most intense.

Fractions E_1 and F were treated with 2N HCl solutions in the same fashion as fraction D(see above) and gave 2 fractions (58mg and 420mg, respectively), each of them giving 1 spot on a tlc plate matching in Rf value with ketones II-47: ir 1703 cm^{-1}; nmr τ7.73(s) and 7.76(s) in the ~2:3 ratio.

Fraction G was rechromatographed on 150g neutral alumina to

give a major fraction (794mg) which showed only 1 spot on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2, Rf 0.25). This colourless sticky oil (500mg) was dissolved in ethyl acetate and crystallization occurred to give 3 crops of anti-2-oximino-8-dimethylamino-cis-bicyclo[5.3.0] decane (II-48b) as colourless plates (425mg): mp 116-116.5°; ir 3170(m,b), 3050(m), 2820(m), 2780(m), 1650(m) 1030(s), 1005(m), 955(s), 910(s) and 860(s) cm^{-1}; ^1H nmr τ -0.41(bs, D_2O exch, 1H), 6.93(m, 1H), 7.14(m, 1H), 7.74(s, NCH_3), 7.85(m,1H) and 8.14-8.72(m, 12H); ^{13}C nmr ppm 161.5(s), 74.9(d), 48.1(d), 44.8(d), 43.2(q, NCH_3), 32.6(t), 29.6(t), 29.3(t), 28.0(t),26.0(t) and 25.0(t); hrms (110°) m/e(%) 210.1732(M^+, calcd for $C_{12}H_{22}N_2O$: 210.1732), 193.1702(89; calcd for $C_{12}H_{21}N_2$: 193.1705),165.1375(12; calcd for $C_{10}H_{17}N_2$: 165.1391), 148.1103(26; calcd for $C_{10}H_{14}N$: 148.1126), 122.0961(9;calcd for $C_8H_{12}N$: 122.0970), 110.0932(16; calcd for $C_7H_{12}N$: 110.0970), 84.0814(66; calcd for $C_5H_{10}N$: 84.0813) 71.0738(100; calcd for C_4H_9N: 71.0735), 58(20), 56(37)and42 (36).

Anal. Calcd. for $C_{12}H_{22}N_2O$: C, 68.53; H, 10.54; N, 13.32.
Found : C, 68.57; H, 10.55; N, 13.36.

Fraction H was also shown to be II-48b as seen by its tlc, ir and ^{13}C nmr spectra. The pure oxime II-48b (99mg) was treated with a 2N HCl solution at 50° for 36 hours. The solution was made basic and extracted with ether to give a ~2:3 mixture of ketones II-47 (75mg, 80%) as seen by its ^1H and ^{13}C nmr spectra similar to those of the previous mixture.

IV-9. Transannular Electrophilic Reaction of Alkenyl Nitroso Compounds

IV-9-1. Preparation of anti-dimer of cis-1-nitroso-2-chloro-5-cyclooctene

A methylene chloride solution (20ml) of nitrosyl chloride (~3.27g, ~$5x10^{-2}$ mole) was added in 0.5 hour to a solution of COD (10g, $9.26x10^{-2}$ mole) in CH_2Cl_2 (20ml) at -10° and left with stirring at -10° for 0.5 hour. To the dark blue solution was added cold hexane (100ml) but no solid precipitated. The solution was immediately concentrated to 40ml under reduced pressure (20 mmHg at 10°). A solid was obtained, filtered, washed thoroughly with hexane and dried in a dessicator over calcium chloride. This crude white solid (2.56g, ~30%, mp 99-101°) was recrystallized from a 1:4 mixture of $CHCl_3$:hexane to give colourless needles of the anti-dimer of cis-1-nitroso-2-chloro-5-cyclooctene (dimer of II-51); mp 104.5-105°; one spot on an alumina tlc plate; uv (CH_2Cl_2) λ 294nm (6250); ir 3020(m), 1238(s), 1208(s), 775(m), 752(m) and 736(s) cm^{-1}; ^1H nmr τ4.06-4.40(m, 4H), 4.57(dd, J= 11.5 and 4.0 Hz, 2H), 5.48 (m, $W_{\frac{1}{2}}$ = 11 Hz, 2H) and 7.1-8.2(m, 16H); ^{13}C nmr ppm 131.0(d), 128.5(d), 67.8(d), 61.0(d), 35.7(t), 27.3(t), 21.8(t) and 21.6(t); ms (110°) m/e(%) no M^+, 176(1.5), 175(2), 174(3), 173(2), 158(4) 156(9), 138(13), 120(10), 107(42), 91(46), 79(100), 67(42), 53(20), 41(33) and 39(29). On irradiation at τ7.89, the multiplet at τ5.48 collapsed to a singlet and small changes were seen at τ4.57. On irradiation at τ7.78, the double doublet at τ4.57 collapsed to a

singlet and small changes were seen at τ5.48. Irradiation at τ7.36 brought changes of the olefinic signals at τ4.2 but none for the multiplets at τ4.57 and 5.48. Irradiation at τ4.57 or at 5.48 caused no change in the respective signal nor in the olefinic signal at τ4.2.

Anal. Calcd. for $(C_8H_{12}NOCl)_2$: C, 55.34; H, 6.97; N, 8.07.
Found : C, 55.23; H, 6.93; N, 8.07.

The blue mother liquor was washed with water (40ml), with a sodium carbonate solution (30ml), then with water. The organic phase was dried and evaporated to afford a mixture of yellow oil and solid. Hexane (10ml) was added to this residue to give a second crop of dimer of II-51 (564 mg, 7%; mp 98-102°); the tlc and ir were identical with those of dimer II-51. The solution was evaporated to give starting COD (4.3g) as the major product along with oximes II-52 as indicated by tlc analysis (vide infra).

In another experiment, a 34% solution of NOCl in CH_2Cl_2 (0.88g, 4.63×10^{-3} mole) was added in 15 min to a solution of COD (0.5g, 4.63×10^{-3} mole) in CH_2Cl_2 (15ml) and left at -10° with stirring for 0.5 hour. Cold hexane (50ml) was added and the resulting dark blue solution was concentrated to ca 30ml to give a white solid (196mg, ca 24%, mp 98-101°), the ^{13}C nmr spectrum of which exhibited signals due to dimer of II-51 and syn-oxime II-52b in an approximate ratio of 9:1. The mother liquor was concentrated to ca 10ml to yield a second crop of solid (165mg, ca 20%, mp 95-8°) consisting of dimer of II-51, syn- and anti-oximes II-52; the ratio of

the respective signals in the ^{13}C nmr spectrum was estimated to be 7:2:1. The mother liquor was evaporated to give a dark blue oil (222mg) consisting of oximes II-52a and II-52b, COD and dimer of II-51 as seen by the ^{13}C nmr spectrum of the mixture and matching with authentic samples; an approximated ratio of 8:4:4:3 was attributed to the respective signals of the 4 components of the mixture.

IV-9-2. Reactions of the dimer of II-51

(a) neat sample : A crude dimer of II-51 (0.45g) was left at room temperature for 2 months to give an orange oil which did not show the spot at Rf = 0.9 corresponding to the dimer of C-nitroso II-51 on a tlc plate (alumina, CH_2Cl_2) but another spot at Rf=0.1 for a mixture of isomeric oximes II-52 : ir 3280(s,b), 3020(m), 1640(m), 1155(m), 990(s), 900(s), 755(s) and 680(s) cm^{-1}; ^1H nmr τ0.95(bs, D_2O exch, 1H), 4.33(m, 2H), 5.40(dd, J= 7.0 and 5.0Hz, $\frac{2}{3}$H, syn-II-52b), 5.68(dd, J= 8.0 and 4.0Hz, $\frac{1}{3}$H, anti-II-52a) and 6.9-8.1(m, 8H); ^{13}C nmr ppm 160.2(s), 158.8(s), 130.6, 130.1 129.4(d), 129.3(d), 60.2(d), 55.9(d), 36.9(t), 33.8(t), 31.8(t), 25.9(t), 22.8(t), 22.2, 22.1(t) and 20.9(t); the underlined chemical shifts were relatively more intense than the other lines. This fraction was sublimed to give syn-1-oximino-2-chloro-5-cyclooctene (II-52b, 23mg) as a colourless oil; one peak on gc (see above, rt 17.3 min); ir 3300(s,b), 3020(m), 1645(m), 1225(m), 1215(m), 1165(m) 1155(m), 985(s), 900(s), 755(s) and 670(m) cm^{-1}; nmr τ2.26(bs, D_2O exch, 1H), 4.33(m, 2H), 5.40(dd, J= 7.0 and 5.0Hz, 1H), and 7.0-8.1(m, 8H); ms (100°) m/e(%) 175(M^+, 3), 173(M^+, 5), 158(34), 156 (88), 138(94), 120(100), 93(56), 84(66), 79(96) and 67(58). On irra-

diation at τ7.90, the double doublet at τ5.40 collapsed to a singlet and changes occured at τ4.33.

Anal. Calcd. for $C_8H_{12}NOCl$: C, 55.34; H, 6.97; N, 8.07.
Found : C, 55.50; H, 6.97; N, 8.38.

(b) with HCl : A methylene chloride solution of NOCl(0.02 mole) was added in 10 min to a solution of COD (4.54g, $4.2x10^{-2}$ mole) in 20ml CH_2Cl_2 at -10° and was kept 1 hour at room temperature. Methanol (50ml) was added and the solution concentrated to 20ml. A white solid was obtained, filtered and washed with ether to give dimer of II-51 (268mg, mp 102-4°) which showed tlc, ir and nmr spectra identical to an authentic sample. To the blue mother liquor was added 0.2ml of concentrated HCl and the mixture was stirred overnight at room temperature. The blue colour persisted. The mixture was then heated at ca 45° until the blue colour disappeared (2 days). Water (50ml) was added to the solution and the methanol removed under vacuum. The remaining solution was extracted with CH_2Cl_2 (3x40ml) to give a dark red oil (2.86g): ir 3370(m,b), 3040 (m), 1715(m,b), 1640(m,b), 1565(m), 1110(m) and 1022(m); nmr τ2.5 (bs, D_2O exch), 4.37(m), 5.2-6.5(m), 6.61(s), 6.64(s), 6.71(s) and 6.9-8.4(m); esr (CH_2Cl_2) triplet (1:1:1), a_N 17.2G, line width 5.5G, g 2.0068±0.0006. The gc-ms analysis of this complex mixture (10% SE-30, 6'x$^1/_8$", 100-250° at 6°/min) and the preparative gc (20% SE-30, 20'x$^3/_8$", 250°) showed the following compounds as seen on Chart IV-1; compounds II-53, II-54 and X were isolated using the latter column and compound II-52 was matching with an authentic sample using the former column. Esr of X did not show any signal.

CHART IV-1

Compd	rt (min)	gc	m/e(%)	ir (cm^{-1})	nmr (τ)
II-53	[a] 11.6	[a] 32	154(M^+,96)126(33)110(96) 87(100)84(81)79(94)68(91) 67(91)58(80) and 53(46)	3020(m)1710(s)1204(s) 1100(s)1070(s)980(m) 882(s) and 735(s)	4.36(m,2H),6.24(dd,J= 6.0and2.5Hz,1H),6.61 (s,3H),6.94-7.17(m,2H), 7.48-8.54(m,6H).
II-54			160(M^+,6)158(M^+,81)132(7) 130(23)123(61)118(36) 116(91)96(84)81(91)79(68) 68(92)67(89) and 54(100).	3020(m)1703(s)1243 (s)885(s)776(s) and 735(s).	4.40(m,2H),5.58(t,J= 5.5Hz,1H),6.86-7.32 (m,2H),7.40-8.22(m, 6H).
X	13.2	13	162(M^+?,6)160(M^+?,15)134 (25)132(79)97(91)79(100) 67(91) and 54(99).	3440(s,b)3010(m)1710 (s)1360(s)1220(m) 1050(s)705(s)660(m).	4.46(m,2H),5.70(m,1H) 6.09(m,1H), 7.3-8.3 (m,~11H).
II-55	16.3	38	169(M^+,7)152(87)137(49) 120(90)109(55)94(72)79 (89)67(100) and 41(78).		
II-52	17.3	6	175(M^+,2)173(M^+,8)158(22) 156(65)138(74)120(76)79 (100)67(86) and 41(89).	vide	supra
Y	18.8	4	172(M^+?,2)150(6)107(20) 105(20)91(28)79(100)67 (42)53(55)41(42)and39(30)		
II-56a	21.6	1	M^+not observed,196(10) 194(68)192(100)(M^+-OH) 158(6)156(18)132(26)130 (72)94(45)53(35)and41(52)		

Chart IV-1, note a: compounds II-53 and II-54 gave 1 peak on a 10% SE-30 column (6'x$^1/_8$") but 2 peaks on a 20%SE-30 column (20'x$^3/_8$"): II-53 (rt 37.2 min) and II-54 (rt 39.9 min) in equal ratio.

(c) with $HClO_4$ and CH_3OH : A suspension of the dimer of II-51 (200mg) in a 1:4 mixture of CH_2Cl_2:CH_3OH (25ml) containing 2 drops of perchloric acid (70%) was stirred at room temperature for 1 day. As the tlc analysis showed no change, the mixture was heated at 40° for 1 day when no spot for the dimer of II-51 (Rf=0.9) was detected. The solution was evaporated, water (20ml) was added and the resulting solution was extracted with CH_2Cl_2 (3x20ml) to yield a colourless oil (170mg): ir 3250(s,b), 3020(m), 1700(w,b), 1642(m,b), 1020(s), 990(s), 925(s), 782(s) and 725(s) cm^{-1}; ^1H nmr τ0.7(D_2O exch), 4.3-4.7(m), 5.40(m), 6.61(s), 6.67(s) and 6.85-7.20(m). By gc peak matching with authentic mixture (10%SE-30, 6'x$^1/_8$", 100-250° at 6°/min), the following compounds were identified (rt, yield from starting monomer II-51): ketones II-53 and/or II-54 (11.6 min, 1%), methoxy oxime II-55 (16.3 min, 15%) and chloro oximes II-52 (17.3 min, 70%). This oil exhibited the following ^{13}Cnmr spectrum to that of a mixture II-52a and II-52b: ppm 160.2(s), 158.8(s), 130.6, 130.1, 129.4, 129.3, 60.2(d), 56.0(d); 37.0, 33.9, 31.9, 26.0, 22.8, 22.3, 22.2 and 21.0; the lines of the underlined chemical shifts were more intense than the other lines.

The aqueous phase was made basic to pH10 and extracted with CH_2Cl_2 (3x20ml) to afford a white solid (10mg) giving 1 major spot on a tlc plate (alumina, 4% CH_3OH in CH_2Cl_2, Rf 0.4) and tentatively

assigned as exo-2-chloro-endo-5-methoxy-9-hydroxy-9-azabicyclo [3.3.1]nonane II-58a: ir 3200(m,b), 1265(m), 1102(m), 1088(s), 1050(m), 910(s), 840(m), 725(s), 653(m) and 630(m) cm^{-1}; nmr τ5.68(m, $W_{\frac{1}{2}}$ = 8Hz, 1H), 6.02(m, $W_{\frac{1}{2}}$ = 22Hz, 1H), 6.46-6.76(m, 2H), 6.64(s, OCH_3) and 7.5-8.85(m, 9H); ms (90°) m/e(%) 207(M^+, 2), 205(M^+, 6), 190(39), 188(100), 176(6), 174(20), 170(27), 160(7), 158(22), 120(21), 112(28), 71(46) and 41(41); esr (CH_2Cl_2): major triplet, a_N 17.5G, line width 5.5G, g 2.0073±0.0006. This signal was attributed to nitroxyl radical II-58b. It also contained medium bands around the central band of the triplet.

(d) with dimethylamine hydrochloride and CH_3OH :A solution containing dry dimethylamine hydrochloride (93.4mg, $1.146x10^{-3}$ mole), dimer of II-51 (200mg, $5.75x10^{-4}$ mole) in a 2:1 mixture of CH_2Cl_2-CH_3OH (30ml) was stirred under nitrogen for 2 hours at 0°, 15 hours at room temperature and 5 hours at 40°, at which time the starting dimer disappeared as shown by tlc analysis. The solvent was partially removed, water (20ml) was added and the solution was extracted with CH_2Cl_2 (4x30ml). The methylene chloride phase was dried and evaporated to give a neutral fraction (185mg) which, on a tlc plate (alumina, 2% CH_3OH in CH_2Cl_2) gave a major spot corresponding to II-52 (Rf 0.5) and a medium spot corresponding to II-58a (Rf 0.3). The spectra of the mixture were: ir 3260(s,b), 3020(m) 1650(m,b), 1550(m,b), 985(s,b), 905(s), 900(s), 760(s), 740(s), 720(m) and 670(m) cm^{-1}; nmr 3.2(bs, D_2O exch), 4.32(m), 5.4(m), 5.7(m), 6.0(m), 6.65(m), 6.7(s) and 7.1-8.2(m); the multiplets at τ4.32, 5.4, 5.7, 6.0, 6.55 and 6.7 were in the ratio of 20:9:1:1:

2:3. Esr of this mixture in CH_2Cl_2 gave a broad triplet: a_N 15.1G line width 4G, g 2.0087±0.0008. The aqueous phase was made basic to pH 10 and extracted with CH_2Cl_2 to give II-27 (11mg, 5%): mp 98-9°; tlc, ir and ms spectra were identical with those of an authentic sample prepared by another route (vide supra).

The above neutral fraction (170mg) was stirred with Ac_2O (1g) and zinc powder (1g) in CH_2Cl_2 (10ml) at room temperature under nitrogen for 1 day, then at 35-40° for 12 hours. The zinc was removed by filtration. The solution was poured into ice (15g) made basic to pH 10 and extracted with CH_2Cl_2 to give a yellow oil (190mg) which showed ir absorptions at 1770(s,b) and 1200(s,b), and a nmr signal at τ7.83(s) for an O-acetyl oxime group. This mixture was chromatographed on silicagel (15g) and elution with 0-0.5% CH_3OH in CH_2Cl_2 afforded a major fraction (II-59, 164mg); the tlc, ir and nmr spectra were identical with those of an authentic sample. The following fractions (32mg), eluted with 2% CH_3OH in CH_2Cl_2 could not be purified but showed a triplet esr signal: a_N 13.8G, line width 3.5G, g 2.0075±0.0005.

(e) with Ac_2O and AcOH : To a solution of the crude dimer of C-nitroso compound II-51 (400mg, 1.15×10^{-3} mole) in CH_2Cl_2 (20ml) purged with nitrogen and cooled in an ice-bath, was added a methylene chloride solution (5ml) of acetic anhydride (2.4g, 2.3×10^{-2} mole) and acetic acid (28mg, 0.46×10^{-3} mole). The mixture was stirred at 0° under nitrogen for 5 hours, then 3 days at room temperature. As a tlc analysis (alumina, CH_2Cl_2) of the mixture showed a large spot for starting material dimer of II-51 (Rf 0.9)

the reaction mixture was heated at 35-40° until a tlc analysis showed the absence of the dimer of II-51 (5 hours). The yellow solution was poured into ice (30g), was made basic to pH 9.5 and immediately extracted with CH_2Cl_2 (3x50ml). The extract was further washed with a 10% Na_2CO_3 solution (2x20ml), then water(30ml) and dried. Removal of the solvent gave a yellow oil(461mg) showing one minor and 2 major spots on a tlc plate (silicagel, 4% CH_3OH in CH_2Cl_2): ir 3400(w,b), 3020(m), 1770(s,b), 1735(sh), 1630(w,b), 1370(s), 1240(s), 1200(s,b), 1035(m), 1002(s), 925(s) and 770(m) cm^{-1}; nmr τ4.2-4.8(m), multiplets at τ5.12, 5.67 and 6.40 in a 3:1:2 ratio, 6.9-8.3(m), 7.83(s), 7.90(s) and 7.95(s); the ratio of the singlets was approximatively 6:1:1.

This mixture was chromatographed on silicagel (20g). The first fraction (13mg), eluted with CH_2Cl_2, was COD, impurity in the starting material dimer of II-51. The next 4 fractions, eluted with 0.5 to 1% CH_3OH in CH_2Cl_2 were crude II-59 (251mg, 51%) as a colourless oil, which crystallized on standing in the freezer but melted at room temperature. Distillation of this oil at room temperature (0.2 mmHg) afforded O-acetyl-2-chloro-5-cycloocten-1-one-syn-oxime (II-59): ir 3020(m), 1775(s,b), 1625(m,b), 1370(s), 1200(s,b), 1002(s), 980(m), 925(s,b), 770(m) and 750(m) cm^{-1}; ^1H nmr τ4.34(m, 2H), 5.15(dd, J= 7.0 and 5.0Hz, 1H), 6.88-8.10 (m, 8H) and 7.83(s, CH_3); ^{13}C nmr ppm 167.3(s), 166.9(s), 129.7 (d), 128.3(d), 59.6(d, C_2), 36.2(t), 27.1(t), 21.7(t), 21.3(t) and 18.8(q); ms (60°) m/e(%) M^+ not observed, 211(6), 209(8), 175(19), 173(52), 138(37), 120(100), 91(73), 79(96), 67(68) and 43(88); ms (70°, 10eV) no M^+. On irradiation of the multiplets at τ4.34

and 5.15, small changes were observed between τ7.30 and 7.68 and between τ7.52 and 8.10, respectively. On irradiation at τ7.50, multiplet at τ5.15 became a broad singlet and the multiplet at τ 4.34 changed to an AB quartet ($J_{AB} \simeq 12$Hz). On irradiation at τ7.85, the double doublet at τ5.15 collapsed to a sharp singlet.

Anal. Calcd. for $C_{10}H_{14}NO_2Cl$: C, 55.69; H, 6.54; N, 6.50.
Found: C, 55.53; H, 6.63; N, 6.81.

The fractions eluted with 2-4% CH_3OH in CH_2Cl_2 afforded crude II-60 (145mg, 18%) as a yellow thick oil which crystallized on the freezer. This oil in chloroform showed the esr spectrum of a broad triplet (1:1:1) which was assigned to endo-2-acetoxy-exo-6-chloro-9-azabicyclo[3.3.1] nonane nitroxyl radical (II-61b): a_N 17.2G, line width 5.7G, g 2.0068±0.0006. Sublimation of this solid at 65° (0.2 mmHg) afforded pure endo-2,9-diacetoxy-exo-6-chloro-9-azabicyclo[3.3.1] nonane (II-60) as white crystals: mp 79-83°; ir 1768(s), 1726(s), 1370(s), 1246(s), 1232(s), 1213(s), 1200(s), 1032(s), 955(m), 900(m), 880(s), 790(m) and 738(m) cm^{-1}; ^1H nmr (Figure II-14) τ4.64(5 broad lines, possibly ddd J = 11.0, 7.0 and 5.0Hz, with further small coupling < 1Hz, H_2), 5.70(m, $W_{\frac{1}{2}}$ = 8Hz, H_6), 6.41(m, $W_{\frac{1}{2}}$ = 10Hz, H_1 and H_5), 7.59-8.46(m, 8H), 7.87(s, NOAc) and 7.93(s, COAc); ^{13}C nmr ppm 169.0(s), 168.4(s), 66.7(d, C_2), 59.4(d, C_1 and C_6), 55.2(d, C_5), 27.6(t), 23.3(t), 21.6(t), 20.1(q), 19.4(t) and 18.8(q); hrms (80°) m/e(%)277.0880 and 275.0903(M^+, 2 and 5.5; calcd for $C_{12}H_{18}NO_4Cl$: 277.0894 and 275.0925), 235.0815 and 233.0800(27 and 78.5; calcd for $C_{10}H_{15}NO_3Cl$: 235.0789 and 233.0819), 218.0782 and 216.0811(30 and 88; calcd for $C_{10}H_{15}NO_2Cl$: 218.0761 and 216.0791), 198(44), 176.0646 and

174.0685(33 and 100; calcd for $C_8H_{13}NOCl$: 176.0656 and 174.0685), 158(8), 156(20), 138.0930(46; calcd for $C_8H_{12}NO$: 138.0919), 120.0809(24; calcd for $C_8H_{10}N$: 120.0813), 96.0576(29; calcd for C_6H_8O: 96.0576) and 43(94). On irradiation of the multiplet at τ6.41, the multiplet at τ4.64 became a broad double doublet (J= 11.0 and 7.0, with further small coupling < 1Hz) and changes occurred at τ5.70 and 7.6-7.8.

Anal. Calcd. for $C_{12}H_{18}NO_4Cl$: C, 52.27; H, 6.58; N, 5.08.
Found : C, 52.57; H, 6.61; N, 5.17.

A solution of II-60 (ca 0.5mg) in CH_2Cl_2 (4ml) did not show any esr signal. This solution was shaken with saturated sodium carbonate solution (1ml) in the esr tube and the spectrum was immediately recorded. A strong signal (triplet, 1:1:1, a_N 17.2G, line width 4.8G and g 2.0073±0.0005) was observed, which initially increased drastically. After 6 minutes the signal increased only slightly. The esr spectrum was taken at regular intervals after vigourous mixing. The intensity of the signal did not change significantly after several months, even after keeping this solution under nitrogen for several weeks.

(f) with Ac_2O in CH_2Cl_2 : A methylene chloride solution (5ml) of freshly distilled acetic anhydride (562mg, 5.75×10^{-3} mole) was added to a solution of the dimer of II-51 (100mg, 2.87×10^{-4} mole in CH_2Cl_2 (7ml). The solution was stirred under N_2 at room temperature for 10 hours, then at 35-40° for 10 hours. Although some dimer of II-51 still remained (alumina tlc, CH_2Cl_2

Rf 0.9), the reaction mixture was dumped into ice (20g) and was worked up as before. A colourless oil (118mg) was obtained and shown to contain dimer of II-51, II-59 and II-60 as judged by tlc analysis (silicagel, 4% CH_3OH in CH_2Cl_2, Rf 0.85, 0.7 and 0.6, respectively); ir 1770(s,b) and 1740(sh) cm^{-1}; nmr : multiplets at τ5.15 (II-59), 5.48 (II-51) and 5.70 (II-60) for the methine protons in the ratio of 1:2:2 and the singlets at τ7.83 (II-59) and 7.87, 7.93 (II-60) in the ratio of 1:2:2. This fraction was redissolved in CH_2Cl_2 containing acetic anhydride (500mg). The mixture was stirred at 45-50° under nitrogen for 1 day until no dimer of II-51 remained. The same work-up, as described above, gave a slightly yellow oil (129mg) containing oxime acetate II-59 (30%) and hydroxylamine acetate II-60 (60%) as seen by its tlc, ir and nmr spectra compared with those of authentic samples. The yields, based on monomer II-51 were determined using the nmr integration ratio of the methine protons at τ5.15(II-59) and 5.70(II-60).

(g) with neat Ac_2O : A solution of the dimer of II-51 (100mg, 2.87×10^{-4} mole) in freshly distilled acetic anhydride(5ml was stirred under nitrogen at room temperature for 7 hours and at 35-40° for 8 hours. After the usual work-up (see above), a colourless oil was obtained (155mg), which was composed of oxime acetate II-59 (50%) and hydroxylamine acetate II-60 (42%) as seen by its tlc, ir and nmr spectra: ir 1765(s,b) and 1745(s, sh) cm^{-1}; nmr τ5.15(II-59) and 5.70(II-60) in the 8:7 ratio.

(h) with Ac_2O and AcONa : A methylene chloride solution (10ml) of dimer of II-51 (400mg, 1.15×10^{-3} mole) was added to a suspension of fused sodium acetate (800mg) in CH_2Cl_2 (15ml) containing freshly distilled acetic anhydride (2.25g, 2.3×10^{-2} mole). The mixture was stirred under nitrogen at 40-45° until dimer of II-51 disappeared (2 days) as checked by a tlc analysis. After the usual work-up, a colourless oil (576mg) was obtained and was shown to be a 3:2 mixture of O-oxime acetate II-59 and hydroxylamine acetate II-60 as seen by its nmr spectrum: τ5.15 for II-59 and 5.70 for II-60 in a 3:2 ratio. Column chromatography of this mixture on 20g silicagel (see above) yielded II-59 (260mg, 52%) and II-60 (217mg, 34%); ir and nmr spectra of both compounds were identical with those of respective authentic samples.

IV-9-3. Reactions of hydroxylamine acetate II-60

(a) with LAH : An ether solution (5ml) of II-60 (50mg, 1.82×10^{-4} mole) was added at 0° under nitrogen to a suspension of LAH (200mg) in ether (10ml) and stirred at room temperature for 6 hours. The mixture was hydrolyzed with alternate portions of water and 40% KOH solution, filtered and the white solid further washed with ether. The combined ether extracts were dried and evaporated to yield a colourless oil (29mg, 85%) giving 1 major spot on a tlc plate (alumina, 4 % CH_3OH in CH_2Cl_2, Rf 0.2). Sublimation of this oil at 80° (0.2 mmHg) gave endo-2,7-dihydroxy-exo-6-chloro-7-azabicyclo[3.3.1] nonane (II-62a) as a white solid: mp 126-9°; ir 3300(s,b), 1255(s), 1095(s), 1060(s), 1035(s), 990(m), 960(m), 930(m), 905(s), 830(m)

and 722(s) cm^{-1}; nmr τ5.48(m, $W_{\frac{1}{2}}$ = 20Hz, H_2), 5.67(m, $W_{\frac{1}{2}}$=6Hz, H_8), 6.64(m, $W_{\frac{1}{2}}$ = 11Hz, H_1 and H_5) and 7.3-8.9(m, at least 1 D_2O exch H, 10H); ms (80°) m/e 193 and 191(M^+, 2 and 8), 176 and 174(35 and 100), 157(9), 156(15), 155(22), 140(40), 118(22), 112(22), 98(21), 96(26), 82(23), 80(21) and 67(25).

Hydroxylamine II-62a (10mg) was added to a solution consisting of water (1ml), hydrogen peroxide (30%, 1ml) and 1N NaOH solution (2 drops). The mixture was kept at 40° for 2 hours. NaCl was added to the solution. Extraction with CH_2Cl_2 afforded II-62b as a yellowish solid (5mg): ir 1260(m), 1020(m,b), and 800(m,b) cm^{-1}; esr (CH_2Cl_2) triplet (1:1:1), a_N 17.5G, line width 5.4G, 2.0078±0.0005.

(b) with Zn/NaI : The procedure of Schnider et al(93) was used. To an acetic acid solution (80%, 3.5ml) of II-60 (190mg, 6.9 $x10^{-4}$ mole) and sodium iodide (175mg, $1.17x10^{-3}$ mole) was added zinc dust (1.05g) in small portions and the mixture was stirred at room temperature for 36 hours and at 35-40° for 2 hours. The residual zinc was removed by filtration and the solid washed with an 80% acetic acid solution (5ml). The combined filtrates were concentrated and CH_2Cl_2 was added (10ml). An inorganic white solid was obtained and removed from the solution by filtration. The heterogeneous solution was made basic to pH 10 and extracted with CH_2Cl_2 (3x40ml). The extract was washed with saturated Na_2CO_3 solution (20ml), then with water (20ml). The solvent was dried and removed to give crude II-63 (131mg, 87%) as an orange oil. Distillation of this oil at room temperature (0.5mmHg) afforded a colour-

less oil of endo-2-acetoxy-exo-6-chloro-9-azabicyclo[3.3.1] nonane (II-63): ir 3300(m), 1735(s,b),1370(s), 1240(s,b), 1100(m), 1032 (s), 922(s), 895(m), 882(m), 798(m), 775(m), 740(s), 700(s) and 575(s) cm^{-1}; ^1H nmr τ4.93(b qui, J + 10.0, 5.0 and small coupling < 1Hz, H_2), 5.70(m, $W_{\frac{1}{2}}$ = 8Hz, H_6), 6.9(m, $W_{\frac{1}{2}}$=10Hz, H_1 and H_5), 7.4(bs, D_2O exch, NH), 7.96(s, CH_3) and 7.5-8.4(m,8H); ^{13}C nmr ppm 169.6(s), 71.8(d, C_2), 61.9(d, C_6), 51.6(d, C_1),47.1 (d, C_5), 29.1(t), 26.6(t), 24.9(t), 20.8(q) and 18.9(t);hrms(70°) m/e(%) 219.0836 and 217.0869(M^+, 2 and 7; calcd for $C_{10}H_{16}NO_2Cl$: 219.0840 and 217.0869), 182.1180(52; calcd for $C_{10}H_{16}NO_2$:182.1181), 176.0659 and 174.0685(28 and 79; calcd for $C_8H_{13}NOCl$:176.0656 and 174.0686), 159.0639 and 157.0660(28 and 82; calcd for $C_8H_{12}NCl$: 159.0629 and 157.0658), 122.0969(100; calcd for $C_8H_{12}N$:122.0969), 96.0811(48; calcd for $C_6H_{10}N$: 96.0814), 94.0654(38;calcd for C_6H_8N: 94.0656), 82.0665(40; calcd for C_5H_8N: 82.0657),80.0511(71;calcd for C_5H_6N: 80.0500), 69.0576(48; calcd for C_4H_7N: 69.0579)and 43 (52). On irradiation of the multiplet at τ6.90, the multiplet at τ4.93 became a broad double doublet (J = 10.0 and 5.0Hz) and the signal at τ5.70 was modified. Irradiation of the multiplets at 4.93 and 5.70 brought changes of the multiplet at τ6.90.

Anal. Calcd. for $C_{10}H_{16}NO_2Cl$: C, 55,17; H, 7.41; N, 6.44.
Found : C, 55.29; H, 7.48; N, 6.72.

An ether solution (20ml) of bicyclic amine II-63 (120mg, 5.52×10^{-4} mole) was treated with LAH (150mg) for 16 hours at room temperature and hydrolyzed with portions of water and 40% KOH

solution in the usual manner. The ether extract was dried and evaporated to give a colourless oil (47mg) showing 2 spots on a tlc plate (alumina, 8% CH_3OH in CH_2Cl_2), probably a mixture of endo-2-hydroxy-exo-6-chloro-7-azabicyclo[3.3.1] nonane (IV-2) and II-65: ir 3300(s,b), 1055(s), 1035(s), 830(m) and 715(m) cm^{-1}; ms (80°) m/e(%) 177 and 175(M^+ IV-2, 1 and 3), 141(M^+ II-65, 17), 140(12), 123(44), 122(30), 96(34), 94(100), 82(57), 68(29) and 54(26). The ^1H nmr spectrum did not show a signal for an acetate group at τ 7.96 but showed only a weak absorption for a methine proton at τ 5.70. The solid, after filtration, was further continuously extracted with ether for 1 day to give another fraction (7mg) of mixture IV-2 and II-65.

This mixture of IV-2 and II-65 (40mg) was treated in pyridine (1.5ml) with an excess of p-nitrosulfonyl chloride (213mg) at 0° for 0.5hour. The mixture, after being kept in fridge for 10 hours was poured into ice (10g) and extracted with ether. The ether extract was washed with a 0.5N HCl solution, then water, to yield, after drying and evaporating, an orange oil (62mg): ir 3450(m,b), 3040 (w,b), 1595(s), 1484(m), 1350(s,b), 1190(s), 1170(s), 1160(s), 1100(s), 960(s), 920(s), 840(s), 815(s), 712(s) and 660(s) cm^{-1}; nmr τ2.26(m) and 2.67(m) in a 1:1 ratio, 5.2-7.3(m), 7.52(s), 7.55 (s) and 7.93-8.9(m).

This fraction was treated with a large excess of LAH (150mg) in ether (20ml) for 1 day under reflux. The same work-up as above gave a colourless oil (34mg): ir 3350(m,b) and 1055(m) cm^{-1}, as a mixture of 9-azabicyclo[3.3.1] nonane (II-64) and endo-2-hydroxy-9-azabicyclo[3.3.1] nonane (II-65) as seen by a gc-ms on a 10 SE-30%

column (6'x$^1/_8$", 110°): II-64 (rt 4.9 min, 43%) m/e(%) 125(M^+,49), 96(87), 83(41), 82(100), 69(28) and 68(34); II-65 (rt 7.2 min,36) m/e(%) 141(M^+, 1), 123(62), 122(28), 108(18), 95(25), 94(100), 82 (19), 68(15), 67(18), 55(13), 54(28), 41(13) and 39(13). This mixture showed 2 spots at Rf 0.15 for II-64 and Rf 0.02 for II-65 on a tlc plate (alumina, 2 % CH_3OH in CH_2Cl_2). Column chromatography of this mixture on basic alumina (3g) afforded a fraction (7mg) eluted with 4-8% CH_3OH in CH_2Cl_2. This fraction was treated with p-toluenesulfonyl chloride in pyridine to give 9-tosyl-azabicyclo [3.3.1] nonane as a light brown solid: mp 152-5° (lit(94) mp 154-6°); ms (100°) m/e(%) 279(M^+, 8), 236(21), 155(49), 124(11), 95(15), 91(80) and 82(57).

IV-9-4. Preparation of anti-dimer of 1-nitroso-2-chloro-trans, trans-5,9-cyclododecadiene

A solution of nitrosyl chloride (8.3ml, 0.18 mole)in methylene chloride (50ml) was added to a solution of tttCDT (32.4g, 0.2 mole) in CH_2Cl_2 (250ml) at -10° in a period of 20 min.The mixture immediately became green and was brought to room temperature slowly, at wich time addition of methanol (500ml) afforded a white precipitate. Filtration and washing of the solid with methanol afforded the crude dimer of chloro nitroso compound II-66(39.02g, 94 % mp 127-132°) contaminated with tttCDT. Recrystallization from a 4:1 mixture of ether:CH_2Cl_2 gave the anti-dimer of 1-nitroso-2-chloro-trans,trans-5,9-cyclododecadiene (II-66) as a white solid giving 1 spot on a tlc plate: mp 133-4° (lit (95) mp 125-5.5°);

uv (ether) λ_{max} = 302 nm(~9400); ir 3020(m), 1260(s), 1220(s), 1180(s) 1130(m), 990(s), 975(s), 965(s), 770(s), 740(s) and 650(s) cm^{-1}; ^1H nmr (Figure II-17) τ4.16(m, 2H), 4.70(m, 8H), 5.65(m, 2H) and 7.70-8.3(m, 24H); ^{13}C nmr ppm 133.3, 133.1, 133.0(2C), 129.2, 129.0, 128.9, 128.5, 62.7(d), 62.6(d), 57.5(d), 56.7(d), 33.0(t,2C) 31.6(t,2C), 31.3(t,2C), 28.4(t) 28.1(t, 4C) and 27.7(t); ms (130°) m/e (%) M^+ not observed, 212(1), 210(2), 161(51), 119(32), 91(60), 79 (97), 67(100), 54(55) and 41(67). On irradiation between τ7.8 and 8.12, the multiplet at τ5.65 collapsed to 2 nearly superimposed doublets (J=5.0Hz), the multiplet at τ4.16 to 2 doublets, τ4.11 (J=5.5Hz) and τ4.21(J=4.5Hz), and the multiplet at τ4.70 changed its pattern.

Anal. Calcd. for $(C_{12}H_{18}NOCl)_2$: C, 63.29; H, 7.97; N, 6.15.

Found : C, 63.36; H, 8.19; N, 6.25.

IV-9-5. Reactions of the dimer of II-66

(a) with LAH : Crude dimer of II-66 (10g) in ether (200ml) was added to a suspension of LAH (8.5g) in ether (50ml) at 0° and was stirred under reflux for 4 days. After hydrolysis with a 10% KOH solution, the ether phase was filtered and was extracted with a 0.5N HCl solution (2x60ml). The ether solution was evaporated to give a neutral fraction (1.05g) which consisted of tttCDT as the major compound, as seen by its ir and nmr spectra. The aqueous phase was made basic to pH11 with a 10% KOH solution. The precipitate was filtered, washed with water and dried in dessicator over

calcium chloride to give a white solid (5.2g, mp 82-90°) which gave a negative Beilstein flame test and was shown to be a mixture of II-67 and II-68 as seen by tlc; ir 3400(m), 3025(m), 1620(s), 1550(s,b), 985(m), 970(s), 960(s) and 720(m) cm^{-1}; nmr τ4.80(m), 7.2(m) and 7.75-9.2(m).

The mixture (1.8g) was chromatographed on a silicagel column (70g). Elution with 7% CH_3OH in ether afforded 13-aza-bicyclo[10.1.0]-trans, trans-4,8-tridecadiene (II-67, 130mg), as white needles: mp 75-7°; ir 3170(s,b), 3025(m), 1380(m), 1350(m), 1290(m), 1250(m), 1030(w), 970(s), 950(m), 900(m), and 740(m) cm^{-1}; ^1H nmr τ4.78(m, 4H), 7.77-7.84(m, 4H), 7.9-8.2(m, 8H), 8.6-8.9(m, 2H) and 9.08(bs, D_2O exch, 1H); ^{13}C nmr ppm 133.1(d), 128.4(d), 37.0(d) 31.6(t), 29.8(t) and 27.9(t); hrms (80°) m/e(%) 177.1499(M^+, 6; calcd for $C_{12}H_{19}N$: 177.1517), 176.1448(17; calcd for $C_{12}H_{18}N$: 176.1439), 162.1269(14; calcd for $C_{11}H_{16}N$: 162.1283), 148.1136(16; calcd for $C_{10}H_{14}N$: 148.1126), 134.0948(17; calcd for $C_9H_{12}N$: 134.0969), 122.0972(24; calcd for $C_8H_{12}N$: 122.0969), 80.0664(39; calcd for C_6H_8: 80.0626), 69.0701(100; calcd for C_5H_9: 69.0705), 68(63), 54(31) and 41(32). This solid was sublimed at 25°, 0.5mm Hg to give white needles: mp 78-78.5°.

Anal. Calcd. for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90.
Found : C, 81.71; H, 10.66; N, 7.91.

Aziridine II-67 (35mg, $2x10^{-4}$ mole) in dry benzene (2ml) was treated with benzyl chloride (249mg, $2x10^{-3}$ mole) under reflux for 6 hours. The solution was evaporated and the resulting oil

was treated with ether to yield 13-azabicyclo[10.1.0]trans,trans-5,9-tridecadiene hydrochloride as a white solid(II-69,19mg,46 %); mp 193-7°(d); ir 2725(m,b),2680(m,b),2500(w,b),1120(m),990(m),978(m),966(s) and 898(m)cm^{-1}; nmr τ2.36(bs,D_2O exch,2H),4.90(m,4H), 7.32(bd,J=7Hz,2H) and 7.6-8.6(m,12H). The filtrate was evaporated to give a yellow oil(29mg) consisting of N-benzyl-13-azabicyclo [10.1.0]trans,trans-5,9-tridecadiene(II-71) contaminated with benzyl chloride: ir 3030(m),1600(w),1495(m),1262(m),1120(m),1100(s),1070, 1028(s),968(s),722(s) and 692(s)cm^{-1}; nmr τ2.74(s,impurity),2.78(s, 5H),4.88(m,4H),5.50(s,impurity),6.56(s,$CH_2\phi$),7.7-8.26(m,8H) and 8.54-8.96(m,4H). This oil was refluxed in benzene(2ml) containing benzyl chloride(250mg) for 12 hours. The solution was evaporated and the excess of ϕCH_2Cl was distilled under reduced pressure(0.5 mmHg) to yield II-71(22mg,~42 %from starting II-67) as the only product: 1 spot on a tlc plate(silicagel,2%CH_3OH in CH_2Cl_2,Rf 0.55); ^{1}Hnmr τ2.78(s,5H),4.88(m,4H),6.56(sharp s,$CH_2\phi$),7.7-8.26(m,8H)and 8.5-8.9(m,4H); (-55°) similar spectrum, no AB quartet for τ6.52(bs, $W_{\frac{1}{2}}$=2.5Hz,$CH_2\phi$); ^{13}Cnmr ppm 139.0,133.1(2C),128.1(2C), 127.7(2C), 127.5(2C), 126.7, 65.0($\underline{C}H_2\phi$), 46.4(2C, CHN), 31.6(2C), 29.9(2C) and 27.1(2C); hrms(40°) m/e(%) 267.1976(M^+, 32; calcd for $C_{19}H_{25}N$: 267.1987), 266.1901(28; calcd for $C_{19}H_{24}N$: 266.1908), 200(13), 187(12), 176.1442(50; calcd for $C_{12}H_{18}N$: 176.1439), 172(30), 159.1041(90; calcd for $C_{11}H_{13}N$: 159.1048), 134.0967(43; calcd for $C_9H_{12}N$: 134.0969), 117(15), 91(100; calcd for C_7H_7: 91.0548) and 41(23). This oil taken up in ether (5ml) was treated with hydrogen chloride gas repeatedly to afford precipitates (25mg). The solid was treated with a saturated Na_2CO_3 solu-

tion. Extraction with ether yielded a mixture showing two spots in tlc analysis (silicagel, 2% CH_3OH in CH_2Cl_2, Rf 0.55 and 0.75, respectively). This mixture was separated by preparative tlc to give 1-N-benzylamino-2-chloro-trans,trans-5,9-cyclododecadiene (II-72, 12 mg, Rf 0.75): ir 3400(w,vb), 3025(m), 1580(w), 1260(m) 1080(m), 985(s), 970(m), 958(s) 800(m,b), 750(s) and 698(s) cm^{-1}; ^{1}Hnmr τ2.80(m, 5H), 5.12(m, 4H), 5.88(m, $W_{\frac{1}{2}}$= 18Hz, H_2), 6.24(AB q J_{AB}= 13.5Hz, $\Delta\delta$= 28Hz, $C\underline{H_2}\emptyset$), 7.50(m, $W_{\frac{1}{2}}$= 22Hz, H_1) and 7.86-9.16 (m, 13H including an exch H at τ8.84); ^{13}Cnmr ppm 140.3, 132.8, 132.0, 130.5, 129.2, 128.6(2C), 128.1(2C), 126.9, 63.4(C_2), 53.5 ($\underline{C}H_2\emptyset$), 50.3($C_1$), 33.7, 31.9, 29.5, 29.3 and 28.9; hrms(40°) m/e (%) 303.1756 and 305.1729(M^+, 22 and 8; calcd for $C_{19}H_{26}NCl$: 303.1754 and 305.1724), 268.2067(24; calcd for $C_{19}H_{26}N$: 268.2066) 241(8), 146.0972(26; calcd for $C_{10}H_{12}N$: 146.0970), 133.0889(100; calcd for $C_9H_{11}N$: 133.0891), 106(7), 91.0543(61; calcd for C_7H_7: 91.0548) and 41(8); and N-benzylaziridine II-71 (4mg, Rf 0.55), as seen by its ^{1}Hnmr spectrum matching with authentic.

Elution with 10-20% CH_3OH in ether afforded 1-amino-trans, trans-4,8-cyclododecadiene (II-68, 1.03g) as white needles: mp 93-7°; ir 3350(m,b), 3280(m,b), 3030(w), 1610(m), 1560(m,b), 1480(s), 1435(s), 975(s), 970(s) and 960(s) cm^{-1}; ^{1}Hnmr τ4.90 (m, 4H), 7.23(bt, J=10Hz, H_1), 7.74-9.2(complex m, 16H including a D_2O exch broad singlet at τ8.17, NH_2); ^{13}Cnmr ppm 131.9, 131.5, 130.5, 130.0, 45.7(d, C_1), 36.6(t), 32.0(t), 31.9(t), 30.3(t), 29.8(t), 29.5(t) and 22.6(t); hrms (80°) m/e(%) 179.1672(M^+, 31; calcd for $C_{12}H_{21}N$: 179.1673), 150.1278(28; calcd for $C_{10}H_{16}N$:

150.1283), 136.1124(43; calcd for $C_9H_{14}N$: 136.1127), 122.0977 (46; calcd for $C_8H_{12}N$: 122.0970), 110.0985(43; calcd for $C_7H_{12}N$: 110.0970), 96.0809(88; calcd for $C_6H_{10}N$: 96.0813), 83.0750(94; calcd for C_5H_9N: 83.0735), 82.0676(92; calcd for C_5H_8N: 82.0656), 70.0653(80; calcd for C_4H_8N: 70.0656), 69.0586(83; calcd for C_4H_7N: 69.0578), 56.0517(100; calcd for C_3H_6N: 56.0500) and 43(89). On sublimation of this solid (40°, 0.5 mmHg), white needles were obtained: mp 98-101°.

Anal. Calcd. for $C_{12}H_{21}N$: C, 80.38; H, 11.81; N, 7.81.
Found : C, 80.11; H, 12.03; N, 7.53.

The benzoyl derivative of II-68 was recrystallized twice from methanol to give fine needles: mp 186-186.5° (lit(161)mp 197-8°); ir 3300(m,b), 1630(s), 1600(w), 1375(m), 1305(m), 960(s) and 695(s) cm^{-1}; nmr τ2.28(m, 2H), 2.62(m, 3H), 4.30(bs, D_2O exch, NH), 4.80 (m, 4H), 5.84(m, 1H) and 7.62-9.02(m, 14H); ms(180°) m/e(%) 283 (M^+, 16), 162(22), 148(10), 133(10), 122(61), 105(100), 77(65), 67(20), 57(12) and 41(19). The N-acetyl derivative of II-68 was prepared adding excess acetic anhydride to an aqueous solution of the amine. After neutralization of the mixture, a solid was obtained and recrystallized from ethanol to give 1-acetamido-trans,trans-4,8-cyclododecadiene (II-70): mp 120-3°; ir 3270(s,b), 3080(m,b), 3030(w), 1635(s,b), 1560(s,b), 1375(s), 1305(s), 1230(m), 990(m), 975(s), 970(s), 765(m) and 740(m) cm^{-1}; ^{1}Hnmr τ4.90(m, 4H), 6.12 (m, 1H), 7.68-9.10(m, 16H including a D_2O exch H) and 8.04(s, 3H) ^{13}Cnmr ppm 168.9(s), 131.7(d, 2C), 130.3(d), 129.3(d), 44.4(d),

33.7(t), 31.7(t), 31.5(t), 29.4(t), 29.1(t), 27.8(t), 22.8(q) and 22.5; ms(130°) m/e(%) 221(M^+, 75), 178(26), 162(100), 133(69) 125(66), 79(76), 60(98), 43(90) and 41(65).

Anal. Calcd. for $C_{14}H_{23}NO$: C, 75.97; H, 10.47; N, 6.33.

Found : C, 76.10; H, 10.66; N, 6.02.

Using Eschweiler-Clarke's method (96), II-68 (50mg) was refluxed for 12 hours in a solution of formic acid (98% aqueous, 1ml) and formaldehyde (37% aqueous, 1ml). Dilute HCl (1N, 2ml) was added and the solution evaporated near dryness under reduced pressure. This residue was made basic with a 40% KOH solution at 0° and extracted with ether (2x20ml). The ether phase was dried and evaporated to give a colourless oil (26mg, ~57%). Analysis by gc on a 10% SE-30 column (100-220° at 4°/min) showed 1 major component (II-33, rt 5.1 min, ~90% of all gc peaks) and several minor ones. Compound II-33 was identical in all respects with the authentic sample.

Using Nagata's procedure (148), lead tetraacetate (7.92g, 1.79×10^{-2} mole) was added under nitrogen to a suspension of amine II-68 (800mg, 4.47×10^{-3} mole) and dry potassium carbonate (1.23g, 8.94×10^{-3} mole) in 50ml of dry benzene and the mixture was stirred vigourously for 1.5 hours at 30-35°. The yellow solution containing K_2CO_3 solid was stirred with a cold saturated solution of K_2CO_3 (6ml). The benzene layer was separated by centrifuge. The lower layer and brown solid were extracted several times with ether and centrifuged. The combined organic solutions were extracted with a 20% aqueous cold tartaric acid solu-

tion (2x30ml) to give an aqueous acidic and an organic phase. The aqueous acidic phase was made to pH 9.5 with a saturated K_2CO_3 solution and extracted with ether (3x40ml). The combined basic extracts were dried over anhydrous K_2CO_3 and filtered. Acetic anhydride (4ml) was added to the solution at 0° under nitrogen. The mixture was stirred at 0° for 6 hours and was washed with a saturated Na_2CO_3 solution (3x30ml). The ether phase was dried and evaporated to give a yellow oil (210mg) containing the acetamide II-70 as the major compound as seen by its irand gc peak matching with authentic (10% SE-30, 200°, rt 5.1 min). The organic phase was further washed with a 10% Na_2CO_3 solution and the organic layer was dried. Filtration and removal of the solvent afforded a red oil (570mg) which was shown to be a mixture of 2 unknown minor and 1 major (II-70) components as indicated by gc (10% SE-30, 100-220° at 6°/min, rt(%)): 9.4 min(15%), 9.7 min(7% and 11.3 min(71%, matching with authentic II-70): ir 3300(m,b), 3030(w), 2980(m), 2920(s), 2850(s), 1740(s,b), 1650(s,b), 1540 (m,b), 1230(s,b), 1020(m,b) and 970 cm^{-1}. A partial separation of this mixture (250mg) was achieved on silicagel preparative plate (0.5 mm thickness) using 1% CH_3OH in ether as eluant and afforded 2 fractions. The bottom fraction, as a colourless oil (105mg, Rf 0.45) had ir, nmr and ms spectra identical to those of acetamide II-70. The top fraction (34mg, Rf 0.85) was obtained as a colourless oil: ir 3370(m,b), 3030(w), 2980(m,sh), 2920(s), 2850(s), 1730(s,b), 1670(s,b), 1550(s), 1440(s), 1370(s), 1240(s) 1020(m) and 970(s) cm^{-1}; nmr τ4.86(m) and 7.85(s) in a 4:3 ratio and 7.6-9.0(m); ms(130°) m/e(%), no definite M^+, 176(30), 162(28)

149(48), 109(55), 95(70), 79(76), 67(88), 55(72) and 43(100). This fraction was not analyzed further and became red orange on standing inside the freezer.

(b) with a 1:1 mixture LAH:$AlCl_3$: Using a Soxlet extractor, the dimer of II-66 (0.5g, $1.1x10^{-3}$ mole) was added to a refluxing ether suspension of LAH (0.274g, $7.2x10^{-3}$ mole) and aluminium chloride (0.96g, $7.2x10^{-3}$ mole). After the complete addition of the dimer of II-66 (11 hours), the solution was externally cooled to 0° and water (6ml) and 40% KOH solution (4ml) were slowly added. The solid was filtered and extracted 2 more times with ether. The combined ether extracts were dried and evaporated to give a white semi-solid (0.41g): ir 3400-3150(w,b), 3025(w), 1590(w,b), 990 (s), 972(s), 962(s), 814(m), 765(m) and 640(m) cm^{-1}; nmr τ4.87 (m), 5.52-5.84(m), 6.85-7.42(m) and 7.6-8.9(m); a gc analysis (10% SE-30, 150-240° at 8°/min) showed the following peaks (rt, yields calculated from the gc peak area): azoxy II-73 (2.4 min, 15%), amine II-68 (3.7 min, 10%) and chloro amine II-74 (4.0 min 65%). Amine II-68 was matching with an authentic sample (vide supra). This mixture was sublimed at room temperature (0.5mmHg) to give a first fraction, 1-azoxy-2-chloro-trans,trans-5,9-cyclododecadiene (II-73, 85mg), as a white solid: 1 peak on gc (rt 2.4 min, see above); recrystallized from ether, mp 111-3°; uv(CH_3OH) λ_{max} 354nm(~26), 290nm(sh,~21); ir 1490(s), 1440(s), 1380(m), 1332(m), 1265(s), 1120(s,b), 990(s), 970(s), 962(s), 865(m), 805(s) and 690(m) cm^{-1}; ^{1}Hnmr τ4.84(m, 8H), 5.46(m, 1H), 5.65(bt, J=6Hz, 2H), 6.40(m, 1H) and 7.65-8.60(m, 24 H); ^{13}Cnmr

ppm 133.6, 133.4, 132.7, 132.4, 130.0(2C), 129.4, 128.5, 78.5, 59.0, 58.7, 57.2, 34.1, 33.8, 31.8(3C?), 29.7, 29.5, 29.1, 28.7, 28.2 and 24.5; hrms(115°) m/e(%) 438.2205, 440.2181 and 442.2138 (M^+, 4,2.5and1; calcd for $C_{24}H_{36}N_2OCl_2$: 438.2205, 440.2175 and 442.2145), 421.2170, 423.2131 and 425.2141(14, 9 and 2.5; calcd for $C_{24}H_{35}N_2OCl_2$: 421.2178, 423.2147 and 425.2118), 349.2616(33; calcd for $C_{24}H_{33}N_2$: 349.2644), 208(25), 178.1357(84; calcd for $C_{12}H_{18}O$: 178.1358), 124.0879(50; calcd for $C_8H_{12}O$: 124.0888), 123.0814(59; calcd for $C_8H_{11}O$: 123.0810), 109.0656(92; calcd for C_7H_9O: 109.0653), 95(58), 67(100) and 41(83). A gc analysis of the remaining solid (same column and conditions) indicated the presence of compounds II-68 (rt 3.7 min) and II-74 (rt 4.0 min) in a ratio of 1:7; its ^{13}Cnmr spectrum exhibited strong lines at ppm 133.0, 131.8, 130.4, 128.7, 63.3(C_2), 48.7(C_1), 33.7, 33.4, 31.7(2C), 29.4 and 29.0 for chloro amine II-74b and small lines matching with those of authentic amine II-68. By further fractional sublimation of this solid (room temperature, 0.1mmHg), a fraction was shown to contain 1-amino-2-chloro-trans,trans-5,9-cyclododecadiene (II-74 , 17mg) as white needles: 1 peak on gc (rt 4.0 min, see above); mp 44-5°; ir 3400-3300(w,b), 3015(w), 1600(w,b), 990(s), 973(s), 962(s) and 760(s) cm^{-1}; nmr (Figure II-18) τ4.89(m, 4H), 5.73(ddd, J= 7.5, 7.0 and 2.0Hz, H_2), 7.06 (ddd, J= 6.5,6.0 and 2.0Hz, H_1), 7.70-8.20(m, 10H), 8.32-8.52 (m, 2H) and 8.33(bs, D_2O exch, NH_2); hrms(30°) m/e(%) 213.1295 and 215.1252(M^+, 9 and 3; calcd for $C_{12}H_{20}NCl$: 213.1284 and 215.1255), 178.1601(43; calcd for $C_{12}H_{20}N$: 178.1596), 132(5),

130(13), 117.0343 and 119.0318(40 and 14; calcd for C_5H_8NCl: 117.0345 and 119.0316), 96.0812(30; calcd for $C_6H_{10}N$: 96.0814), 79(15), 67(14), 56(42) and 43(100). On irradiation at τ8.42 or 7.99, the multiplets at τ7.06 and 5.73 collapsed to doublets (J= 2.0Hz), respectively. Irradiation of the signals at τ5.73 or 7.06 caused the respective multiplets to change to doublet of doublets (J= 6.5 and 6.0Hz and J= 7.5 and 7.0Hz, respectively).

A mixture of chloro amine II-74 and amine II-68 (51mg, 1:5 ratio as seen by gc, see above) dissolved in methanol (2ml) was treated with a saturated sodium methoxide solution (1ml) for 4 hours at room temperature. The solution was made to pH 9-10 with a 1N HCl solution and was extracted with ether to give an orange oil (44mg): ir 3350(m,b), 3025(m), 1710(m,b), 1640(m,b), 1260(s) 1025(m,b), 970(s,b), 910(m), 860(m), 810(s) and 732(s) cm^{-1}; nmr τ4.86(bm), 5.70(bm), 6.3(m), 6.7(m) and 7.0-9.2(complex m); a gc analysis of this mixture on a 10% SE-30 column (100-220° at 6°/min) gave the following peaks matching with authentic samples (rt, gc peak area): unknown(3.2 min, 3%), amine II-68(4.3min, 17%), chloro amine II-74 (5.0 min, 16%), unknown(5.2 min, 15%), aziridine II-67(5.4 min, 10%), unknown(9.6 min, 12%), unknown (20.1 min, 21%). This oil was not analyzed further.

(c) with HCl : To a hot solution of dimer of II-66 (1g, $2.2x10^{-3}$ mole) in CH_2Cl_2 (3ml), a methanol (10ml) solution containing 0.1ml of concentrated HCl was added. A white solid precipitated and was dissolved by heating with additional CH_2Cl_2 (7ml).

The slightly green solution was left with stirring at 45-50° for 3 days at which time a tlc analysis (alumina, 0.5 % CH_3OH in CH_2Cl_2) of the solution showed only a faint spot for starting dimer of II-66 (Rf 0.9). The yellow solution was concentrated, water(15ml) was added and the resultant solution extracted with CH_2Cl_2 (3x 60ml). The solution was dried and evaporated to give a viscous orange oil (891mg) containing II-75 and II-76 as shown on a tlc plate (alumina, 0.5 % CH_3OH in CH_2Cl_2), Rf 0.2 and 0.65, respectively: ir 3350(s,b), 3035(w), 1720(m), 1550(w), 1122(m), 1100(s) 1080(s), 975(s) and 965(s) cm^{-1}; nmr τ1.55(bs, D_2O exch), 4.83(m), 5.84(t, J=5Hz), 6.40(dd, J=6.5 and 4.0Hz), 6.65(s), 6.72 (s) and 7.2-8.3(m). The ratio of the signal at τ6.40 to 5.84 and 6.65 to 6.72 was 1:3. A gc on a 3% SE-30 column (130-220°at 3°/min) gave 2 major peaks: II-76 (rt 4.7 min, 21%) and II-75 (rt 7.3min, 63%), along with other minor components. This mixture(700mg) was chromatographed on neutral alumina (60mg). The first fraction eluted with CH_2Cl_2 afforded 2-methoxy-trans,trans-5,9-cyclododecadien-1-one (II-76, 72mg) as a colourless volatile oil: ir 3400 (w,b), 3035(w), 1725(sh), 1720(s), 1715(sh), 1130(m), 1098(s), 1080(m) and 970(s) cm^{-1}; nmr τ4.82(m, 4H), 6.40(dd, J=6.5 and 4.0Hz, H_2), 6.65(s, OCH_3) and 7.35-8.15(m, 12H); ms(25°) m/e(%) 208(M^+, 93), 176(13), 120(46), 111(47), 81(71), 79(76), 68(100), 67(86), 58(51), 55(41) and 41(50). The second fraction, eluted with 0-1% CH_3OH in CH_2Cl_2 , was a mixture of II-75 and II-76 as seen by tlc analysis. The third fraction, eluted with 1-2% CH_3OH in CH_2Cl_2 afforded syn-2-methoxy-trans,trans-5,9-cyclododecadien-1-one oxime (II-75, 365mg) as a colourless oil: 1 spot on a tlc

plate; ir 3330(s,b), 3030(w,sh), 1640(w,b), 1120(m), 1085(s,b) and 965(s) cm^{-1}; ^{1}Hnmr τ1.56(bs, D_2O exch, 1H), 4.80(m, 4H), 5.84(t, J=5Hz, H_2), 6.72(s, OCH_3), 7.35(m, 1H) and 7.6-8.3 (m, 11H); ^{13}Cnmr ppm 158.7(s), 131.5(2C), 131.0, 130.6, 78.2(d), 54.5(q), 31.9(t), 31.7(t), 29.9(t), 28.5(t), 27.8(t) and 25.4(t) ms(80°) m/e(%) 223(M^+, 27), 206(100), 174(41), 169(45), 139(78), 79(71), 67(84) and 41(76). On irradiation at τ8.20, the triplet at τ5.84 collapsed to a singlet.

(d) with pyridine : To a dimer of II-66 (1g, 2.2×10^{-3}mole) solution in CH_2Cl_2 (10ml) was added pyridine (0.5g, 6.3×10^{-3}mole) in CH_3OH (20ml) under nitrogen. The heterogenous mixture was stirred under nitrogen at room temperature for 1 day. A white solid, due to dimer of II-66, was still present and the solution was heated to 35°. The reaction was followed by tlc until the starting dimer was consumed (3 days). The solvent was removed under reduced pressure to give a semi-solid (1.25g) which was washed with ether to give a white solid (1.23g, 93%) of 1-oximino-trans,trans-5,9-cyclododecadien-2-pyridinium chloride (II-77): mp 190-4°(d); ir 3120(s,b), 1625(m), 1290(m), 1140(m), 1010(s), 998(s), 980(s), 970(s), 960(s), 895(m), 820(m), 770(s), 725(s) and 690(s) cm^{-1}; nmr (D_2O) τ1.0-2.0(m, 5H), 4.58(m, 5H), 6.8-7.35(m, 2H) and 7.5-8.6(m, 10H). A part of this solid (860mg) was dissolved in water (20ml) and added to an aqueous solution of dimethylamine(20%,20ml). The reaction mixture became cloudy upon stirring for 0.5 hour. The turbid solution clarified on addition of a saturated Na_2CO_3 solution (pH 10). Extraction with CH_2Cl_2 (3x50ml) afforded a thick

oil (645mg, 91%), tlc, ir and nmr which were identical with those of authentic amino oxime II-31.

(e) with Ac_2O : Anhydrous sodium acetate (1g) and dimer of II-66 (0.5g, $1.1x10^{-3}$ mole) were added to acetic anhydride (15ml) under nitrogen. The mixture was kept under nitrogen with stirring for 2 days at room temperature and 3 days at 45°. The reaction mixture was poured into ice (50g) and stirred for 2 hours. This solution was made to pH 9 and extracted with CH_2Cl_2 (3x60ml) to give a yellow oil (481mg). This oil showed 1 major (II-78), 1 medium (dimer of II-66) and several minor spots on a tlc plate (silicagel, 1 % CH_3OH in CH_2Cl_2): ir 3030(w), 1775(s), 1640(m), 1205(s), 1000(s), 980(s), 965(s), 950(s), 925(s) and 740(m); nmr τ4.81(m), 5.16(m), 6.7-7.15(small m), 7.0-8.0(m) and 7.79(s); esr (CH_2Cl_2): broad major triplet(1:1:1), a_N 13.5G, line width 6.5G, g 2.0068±0.0008. This mixture (450mg) was chromatographed on a silicagel column (40g) and afforded a middle fraction(301mg), eluted with CH_2Cl_2, which crystallized in the freezer. Recrystallisation from methanol afforded O-acetyl-2-chloro-trans,trans-5,9-cyclododecadien-1-one oxime (II-78) as white crystals: mp 49-49.5°; ir 3030(w), 1775(s), 1635(m), 1370(s), 1202(s), 996(s), 978(s), 960(s), 924(s), 878(m), 803(m), 765(m) and 718(m) cm^{-1}; ^{1}Hnmr τ4.82(m, 4H), 5.17(bt, J=6Hz, H_2), 6.7-7.4(m, H_{12a}), 7.6-7.9(m, 11H) and 7.80(s, CH_3); ^{13}Cnmr ppm 167.9(s), 165.5(s), 132.7, 132.5, 129.6, 129.2, 57.6(d), 31.8(t, 2C?), 31.7(t), 29.1(t), 29.0(t), 26.1(t) and 19.4(q); ms(60°) m/e(%) M^+ not observed, 212(11), 210(32), 192(8), 174(99), 79(62), 67(78) and 43(100). On

irradiation at τ7.82, the multiplet at τ5.17 collapsed to a singlet and the multiplet at τ4.82 became an AB quartet (J_{AB}=16Hz).

Anal. Calcd. for $C_{14}H_{20}NO_2Cl$: C, 62.33; H, 7.47; N, 5.19.
Found : C, 61.99; H, 7.51; N, 5.22.

Attempts to isolate minor components of the mixture were unsuccessfull.

IV-9-6. Preparation of anti-dimer of 1-nitroso-2-chloro-cis-5(7)-cyclodecene

A methylene chloride solution (20ml) of nitrosyl chloride (3.27g, 0.05 mole) was added in 10 min to a solution of CDD (9g, 6.62×10^{-2} mole) in CH_2Cl_2 (80ml) at -10°. The solution was stirred at -10° for 1 hour, then at room temperature for 3 hours. The original green emerald colour disappeared and deposited a solid. Addition of methanol (100ml) precipited more solid. The mixture was filtrated and the solid washed with methanol to yield dimer of II-80 as a white solid (1.27g, 13%, mp 143-4°). The mother liquor was concentrated to 30ml to give more solid (3.18g, 32%, mp132-8°). Both fractions gave 1 spot on a tlc plate (alumina, CH_2Cl_2, Rf 0.85) and were recrystallized from CH_2Cl_2 to give the anti-dimer of 1-nitroso-2-chloro-cis-5(7)-cyclododecene (dimer of II-80) as fine white needles: mp 150-1°; ir 3008(m), 1258(s), 1212(s), 1200(s), 1192(s), 1183(s), 1155(m), 770(s), 738(m) and 720(s)cm^{-1}; nmr τ4.28(ddd, J=9.0, 6.5 and 2.5Hz, H_1), 4.45(m, 2H), 5.4(b dt J=9.0 and 4.0Hz, H_2), 7.3-8.1(m, 8H) and 8.44(m, 4H); ms(135°,

15eV) m/e(%) M^+ for dimer not observed, 203 and 201(M^+ monomer, 1 and 2), 186(13), 184(40) 166(60), 135(90), 93(88), 81(75), 79 (10), 67(100) and 55(50); uv(CH_2Cl_2) λ_{max}= 299nm (ϵ=7960); ^{13}Cnmr (DMF) dissolved at 60° (decomposition); the major peaks matched with chloro oxime II-81. Irradiation at τ7.9 brought changes of the multiplets at τ4.28 and 5.4 to 2 broad doublets (J≃ 9.0Hz).

Anal. Calcd. for $(C_{10}H_{16}NOCl)_2$: C, 59.55; H, 8.00; N, 6.95.
Found : C, 59.20; H, 7.80; N, 6.98.

IV-9-7. Reactions of the dimer of II-80

(a) with HCl and CH_3OH : A suspension of dimer of II-80 (500mg) in a 1:2 mixture CH_2Cl_2-methanol containing 1 drop of concentrated HCl was stirred at reflux (60°) for 36 hours, at which time all the solid dissolved. Acid-base extraction of the reaction mixture afforded a neutral (464mg) and a basic (33mg) fractions. The neutral fraction had the following physical constants: ir 3300(s,b), 3008(m), 1650(w,b), 1100(m,b), 1020(m),1000 (s), 980(s), 970(s), 955(s), 770(s) and 720(m) cm^{-1}; nmr τ4.72(m), 5.45(dd, J=11.0 and ~5Hz) and 5.63(dd, J=10 and ~5Hz) in the 1:1 ratio, 6.63(s), 6.71(s), 6.8(s), and 7.2-8.8(m); esr (CH_2Cl_2) overlapping triplets in which the major had a_N 15.2G and g-value 2.0061±0.0010. This fraction was distilled at 30° (0.2 mmHg) to give a white paste (290mg) having similar ir and nmr spectra to that of the above mixture and 2 major spots on a tlc plate (silicagel, 4% CH_3OH in CH_2Cl_2). They were separated by chromatography on silicagel (15g). Elution with 0.5-1% CH_3OH gave a solid (186mg) which was sublimed (25°/0.2 mmHg) to give 2-chloro-cis-5-cyclodecen-

1-one oxime (II-81a): mp 94-5°; ir 3250(s,b), 3005(w), 1620(w, b), 1433(s), 1000(s), 980(s), 970(s), 910(m), 765(m), 715(m) and 625(m) cm^{-1}; ^{1}Hnmr τ0.99(s, D_2O exch, OH), 4.70(m, 2H), 5.45(dd, J=11.0 and 4.5Hz, H_2), 6.93(m, 1H), 7.41-8.29(m, 7H) and 8.39(m, 4H); ^{13}Cnmr ppm 160.2(s), 133.4(d), 128.0(d), 55.6(d), 33.0(t), 29.4(t), 25.3(t), 24.9(t), 24.6(t) and 22.5(t); hrms(100°) m/e(%) 203.0881 and 201.0932(M^+, 3 and 8; calcd for $C_{10}H_{16}NOCl$: 203.0891 and 201.0920), 186.0865 and 184.0887(20 and 57; calcd for $C_{10}H_{15}NCl$: 186.0864 and 184.0893), 166.1252(100; calcd for $C_{10}H_{16}NO$:166.1232 148.1125(55; calcd for $C_{10}H_{14}N$: 148.1126), 91.0546(51; calcd for C_7H_7: 91.0547), 79.0530(44; calcd for C_6H_7: 79.0548) and 67.0538 (49; calcd for C_5H_7: 67.0548). On irradiation at τ5.45, changes at τ7.68-8.10 were observed. On irradiation at τ8.06, the doublet of doublets at τ5.45 collapsed to a doublet (J=11.0Hz) and the multiplet at τ4.70 became a poorly resolved doublet (J=13Hz). Irradiating between τ7.68-8.06 failed to give clear results on the multiplet at τ5.45 due to side band effects. On irradiation at τ8.39, the multiplet at τ6.93 became an ill resolved doublet (J≈14Hz).

Anal. Calcd. for $C_{10}H_{16}NOCl$: C, 59.55; H, 8.00; N, 6.95.
Found : C, 59.71; H, 8.14; N, 7.05.

Oxime II-81a (50mg) was treated in a 2N HCl solution (5ml) for 3 days. The solution was made to pH 10 and extracted with CH_2Cl_2 to yield an oil whose nmr still showed a doublet of doublets at τ5.45 for II-81a but not at τ5.63 for II-81b.

The second fraction was eluted with 2-4% CH_3OH in CH_2Cl_2

gave a colourless oil (72mg) showing 1 major spot on a tlc plate but exhibiting several methoxy absorptions in its nmr spectrum; ir 3300(s,b), 3005(w), 1710(w), 1650(w), 1090(s,b), 945(s,b), 915(s,b), 880(m), 735(s), 715(m) and 665(w) cm^{-1}; nmr τ0.73(bs), 4.34-4.86(m, $^1/_{20}$ of total proton integration), 6.63(s), 6.72(s) and 6.78(s) in the 2:1:2 ratio, and 6.80-8.90(m).

A gc-ms of the original reaction mixture on a 10% SE-30 column (100-230° at 6°/min) showed the following compounds (rt, yield calculated from the gc peak area), m/e(%): CDD (4.0 min,7%) 132(M^+, 48) and 104(100); unidentified(6.8 min, 9%), 180(M^+,38), 106(82) and 77(100); unidentified Z(9-10.5 min, ~24%), 165(M^+?,8) 148(100), 91(46), 79(48), 67(55) and 41(65); II-83(13.3 min, 13%) 197(M^+, 6), 180(60), 148(46), 71(72) and 41(100); II-82a?(14.3min) no M^+, 197(21), 180(78), 165(88), 148(100) and 84(97); II-81 (14.6 min), 203 and 201(M^+, 5 and 15), 186(22), 184(67), 166(100 148(50), 91(52), 79(51), 67(62) and 41(61). The last 2 peaks were overlapping and gave a 40% total yield.

(b) with Ac_2O : A CH_2Cl_2 solution (20ml) of freshly distilled acetic anhydride (2.04g, $2x10^{-2}$ mole) and dimer of II-80 (403mg, $1x10^{-3}$ mole) was stirred under nitrogen at 40-50° for 3 days, at which time the pale green solution turned to a yellow colour. The resultant reaction mixture was poured into ice (30g) and was made to pH 10. The methylene chloride was further washed with a 10 % Na_2CO_3 solution (2x20ml), then with water (30ml) and dried. Removal of the solvent gave a pale brown paste (517mg)

which gave, on a tlc plate (silicagel, 1% CH_3OH in CH_2Cl_2), 2 major spots, ie, dimer of II-80 with Rf 0.9 and II-85 with Rf 0.75 and 2 minor spots, ie, II-86 with Rf 0.5 and II-87 with Rf 0.3. It was taken up in a 1:1 mixture of CH_2Cl_2-ether to yield a white precipitate which was shown to be dimer of II-80 (107mg, 33%, mp 144-5°) as seen by its identical ir spectrum. The filtrate was dried and evaporated to give an oil: ir 1765(s,b), 1740(s,b), 1630(m,b), 1390(m), 1368(s), 1250(s), 1235(s), 1210(s), 1200(s), 1180(s), 1150(m), 1120(s,b), 1000(s,b), 935(m), 892(m), 768(s) and 715(s) cm^{-1}; nmr τ4.2-4.8(m), 5.2-5.8(m), 6.8(m) and 7.0-8.9(m), 7.79(strong s), 7.92(weak s) and 7.97(weak s); esr, 3 overlapping triplets(1:1:1) (1 major and 2 minors) in which the major triplet had a_N 14.2G, line width 4G and g 2.007±0.001. This mixture was chromatographed on silicagel (30g). The first fraction eluted with CH_2Cl_2 gave an oil (147mg, 45%) which was distilled (25°,0.2mm Hg). to give a 1:3 mixture of O-acetyl-2-chloro-cis-5-cyclodecen-1-one oxime (II-85a) and its isomer O-acetyl-2-chloro-cis-7-cyclodecen-1-one oxime (II-85b) as a colourless oil: ir 3000(m), 1775(s,b), 1630(m,b), 1260(m), 1205(s,b), 1175(s), 1000(s), 935(s), 890(s), 735(s) and 710(m) cm^{-1}; ^{1}Hnmr τ4.65(m, 2H), 5.34(dd, J=12.0 and 4.5Hz, $\frac{1}{4}$H), 5.66(dd, J=11.0 and 5.0Hz, $\frac{3}{4}$H), 7.2-8.14(m, 11H), 7.74(s) and 7.76(s) in the approximate 1:3 ratio; ^{13}Cnmr ppm 166.2, 166.1, 131.8, 131.7, 127.5, 127.3, 54.2, 51.5, 34.9, 33.6, 31.3, 28.0, 27.8, 26.5, 24.2, 23.8(2C?), 23.5(2C?), 21.6, 21.3 and 19.4; hrms(70°) m/e(%) 246.1079 and 244.1105(M^++1, 4 and 10; calcd for $C_{12}H_{19}NO_2Cl$: 246.1074 and 244.1105), 243.1040(M^+, 1; calcd for $C_{12}H_{18}NO_2{}^{35}Cl$: 243.1026), 201.0928(66; calcd for

$C_{10}H_{16}NO^{35}Cl$: 201.0921), 184.0890(65; calcd for $C_{10}H_{15}N^{35}Cl$: 184.0893), 166.1236(65; calcd for $C_{10}H_{16}NO$: 166.1232), 148.1128 (100; calcd for $C_{10}H_{14}N$: 148.1127), 135.1175(85; calcd for $C_{10}H_{15}$: 135.1174), 93.0707(85; calcd for C_7H_9: 93.0704), 67.0555(94; calcd for C_5H_7: 67.0548) and 43(91).

Anal. Calcd. for $C_{12}H_{18}ClNO_2$: C, 59.14; H, 7.44; N, 5.75.
Found : C, 58.89; H, 7.55; N, 5.60.

Elution with 0.5-2 % CH_3OH in CH_2Cl_2 gave a solid fraction (27mg, 8 %) as 2,11-diacetoxy-5-chloro-11-azabicyclo[4.4.1]undecane (II-86), or isomer thereof: ir 1765(s), 1722(s), 1245(s), 1202(s), 1192(s), 1125(m), 1040(m), 1015(m), 950(m), 850(m), 788(m), 755 (m), 730(m) and 715(m) cm^{-1}; nmr τ4.70(bt, J=9.0, 9.0 and <1Hz), 5.48(m, 1H), 6.72(m, 2H), 7.7-8.6(m, ~12H), 7.83(s, 3H) and 7.96(s, 3H); hrms(80°) m/e(%): 305.1219 and 303.1237(M^+, 2 and 7; calcd for $C_{14}H_{22}NO_4Cl$: 305.1208 and 303.1238), 263.1084 and 261.1148(3 and 8; calcd for $C_{12}H_{20}NO_3Cl$: 263.1102 and 261.1132), 246(36), 244.1110(100; calcd for $C_{12}H_{19}NO_2{}^{35}Cl$: 244.1104), 226.1444(96; calcd for $C_{12}H_{20}NO_3$: 226.1443), 220(26), 218(77), 208.1345(31; calcd for $C_{12}H_{18}NO_2$: 208.1338), 184.0891(36; calcd for $C_{10}H_{15}N^{35}Cl$: 184.0893), 166.1219(31; calcd for $C_{10}H_{16}NO$: 166.1232), 148.1113(43; calcd for $C_{10}H_{14}N$: 148.1126) and 43(92). On irradiation at τ7.95, the broad triplet at 4.70 became a doublet (J = 9.0Hz). This white solid, although giving 1 spot on a tlc plate could not be recrystallized to give an analytically pure sample.

Further elution with 2% CH_3OH in CH_2Cl_2 (30ml; followed in the column because of a yellow ring) gave an orange oil which was sublimed to give 2,5,11-triacetoxy-11-azabicyclo[4.4.1]undecane (II-87, 30mg, 8%) or isomer thereof: ir 3450(m,b), 1765(s, b), 1735(s,b), 1240(s,b), 1190(s,b), 940(m,b), 890(m), 860(m)and 810(m) cm^{-1}; nmr τ4.74(m, 2H), 5.27(bq, J ≃ 6.5Hz, 2H), 7.7-8.8 (m, ~12H), 7.90(s, 3H) and 7.93(s, 6H); ms(80°) m/e(%) 327(M^+,2), 285(33), 268(100), 226(36), 208(22), 166(31), 148(28), 96(25), 67(24) and 43(62); esr: 1 major (1:1:1) broad triplet with g 2.0089, a_N 14.3 G and possibly 2 minor broad triplets with g 2.0063 and 2.0045, a_N for both 14.5 G.

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ADDENDUM

LIST OF ABBREVIATIONS

NNP	N-nitrosopiperidine
NNOP	N-nitropiperidine
NND	N-nitrosodimethylamine
NNOD	N-nitrodimethylamine
COD	cis,cis-1,5-cyclooctadiene
tttCDT	trans,trans,trans-1,5,9-cyclododecatriene
cttCDT	cis,trans,trans-1,5,9-cyclododecatriene
ctCDD	cis,trans-1,5-cyclodecadiene
endo-DCPD	endo-dicyclopentadiene
LAH	lithium aluminium hydride