

I STUDIES IN ORGANOPHOSPHORUS CHEMISTRY

II VINYL AZIDES AS DIAZOENAMINES

by

ARVIND NATVERLAL THAKORE

B.Sc. SIMON FRASER UNIVERSITY (1969)

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF SCIENCE

in the Department
of
Chemistry

C ARVIND NATVERLAL THAKORE, 1972

SIMON FRASER UNIVERSITY

December, 1972

APPROVAL

Name: Arvind Natverlal Thakore

Degree: Master of Science

Title of Thesis: Studies in Organophosphorus Chemistry

Vinyl Azides as Diazoenamines

Examining Committee: T.N. Bell, Chairman

A.C. Oehlschlager
Senior Supervisor

L.K. Peterson
Examining Committee

D. Sutton
Examining Committee

A.M. Unrau
Examining Committee

Date Approved: January 11/73

ABSTRACT

The reaction of tertiary phosphine dichlorides and dibromides with epoxides gave vicinal dihalides. The reaction involved initial cleavage of the epoxide carbon-oxygen bond emanating from the most highly substituted epoxide carbon. Haloalkoxyphosphonium salts thus formed, underwent subsequent reaction giving vicinal dihalides and tertiary phosphine oxides. The vicinal dihalides resulting from epoxides of cyclohexenes were mixtures of cis and trans isomers in which the cis isomer is formed by backside attack of halogen at both epoxide carbons.

The reaction of electrophiles with vinyl azides was investigated. Nitrosyl tetrafluoroborate, nitryl tetrafluoroborate, acids and bromine reacted with vinyl azides at the β carbon to give 1,2,5-oxadiazoles, 2-oxo derivative of 1,2,5-oxadiazoles, amides and α -bromoketones respectively. Acetyl chloride and metachloroperbenzoic acid reacted with vinyl azide to give 2,3,5-trimethyl oxazole and 3-metachlorobenzoxy-2-butanone respectively. Reaction of dimethylacetylene dicarboxylate (DMAD) with vinyl azides in presence of aluminum chloride was also investigated. DMAD reacted with vinyl azides giving the corresponding triazoles. However, in the presence of aluminum chloride DMAD reacted with vinyl azides to give product 9b. The structural and mechanistic aspect of the formation of product 9b are discussed.

TO MOTHER
FOR HER INSPIRATION

A C K N O W L E D G M E N T S

The author wishes to express his sincere thanks to his Research Director, Dr. A.C. Oehlschlager, for guidance and advice during the course of this work.

Appreciation is also extended to:

Dr. A.M. Unrau and Dr. L.K. Peterson for inspiration and helpful discussions;

The members of room C7032 for their lively discussions and help;

And the Ogilvie Flour Co. Ltd. for providing generous support for this work in the form of a Post-Graduate Scholarship.

Table of Contents

CHAPTER I Studies in Organophosphorus Chemistry:
Reaction of Epoxides with Tertiary Phosphine
Dihalides

	Page
Abstract	iii
Introduction	1
Results and Discussions	11
(A) General Scope	12
(B) Mechanism	12
(C) Stereochemistry	21
(D) Conclusions	25
Experimental:	
(1) General	29
(2) Preparation of epoxides	29
(3) Reaction of triphenylphosphine dihalides with styrene oxide	30
(4) Reaction of triphenylphosphine dichloride with cyclohexene oxide	31

(5)	Reaction of triphenylphosphine dichloride with cyclohexene oxide in the presence of cyclopentene	32
(6)	Reaction of hexamethylphosphorus dichloride with cyclohexene oxide	33
(7)	Reaction of triphenylphosphine dibromide with cyclohexene oxide and trans-2-bromocyclohexanol	33
(8)	Reaction of triphenylphosphine dihalides with indene oxide	34
(9)	Reaction of triphenylphosphine dichloride with trans-2-butene oxides	34
(10)	Reaction of triphenylphosphine dichloride with 2 β ,3 β -cholestene oxide	35
(11)	Reaction of triphenylphosphine dichloride with 2 α ,3 α -cholestene oxide	36
(12)	Reaction of triphenylphosphine dibromide with 2 α ,3 α -cholestene oxide	37
(13)	Reaction of triphenylphosphine dibromide with 5 α ,6 α -cholestene oxide	38
	References	39

CHAPTER II Vinyl azides as diazoenamines

	Page
Abstract	iii
Introduction	44
Results and discussion	49
Conclusion	69
Experimental	70
(1) General	71
(2) Preparation of cis-2-azido cyclooctene (<u>1c</u>) and trans-2-azido-2-butene	71
(3) Reaction of trans-2-azido-2-butene (<u>1b</u>) with nitrosyl tetrafluoroborate	71
(4) Reaction of nitrosyl tetrafluoroborate with cis-2-azido cyclooctene (<u>1c</u>)	74
(5) Treatment of 2-butanone oxime and cyclooctanone oxime with glacial acetic acid and conc. hydrochloric acid	75
(6) Reaction of trans-2-azido-2-butene (<u>1b</u>) with glacial acetic acid	75
(7) Reaction of trans-2-azido-2-butene (<u>1b</u>) with acetylchloride	76
(8) Reaction of trans-2-azido-2-butene (<u>1b</u>) with acetylchloride in presence of equimolar quantity of aluminum chloride	76
(9) Preparation of 2,4,5-trimethyl oxazole	77

(10)	N.M.R. study of the complexation of trans-2-azido-2-butene (<u>1b</u>) with aluminum chloride	78
(11)	N.M.R. study of the complexation of trans-2-azido-2-butene (<u>1b</u>) with aluminum chloride in presence of acetylchloride	79
(12)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with ketene dimer	79
(13)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with allyl chloride and benzyl chloride	80
(14)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with allyl chloride and benzyl chloride in presence of aluminum chloride	80
(15)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with cyclohexene in presence of aluminum chloride	81
(16)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with carbon disulfide	81
(17)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with phenyl isocyanate	82
(18)	Reaction of trans-2-azido-2-butene with phenyl chloroformate	83
(19)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with phenyl diazonium tetrafluoroborate.	84
(20)	Reactions of trans-2-azido-2-butene (<u>1b</u>) with bromine	85
(21)	Time study of the reaction of trans-2-azido-2-butene (<u>1b</u>) with bromine	86

(22)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with metachloroperbenzoic acid	86
(23)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with nitryl tetrafluoroborate	87
(24)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with dimethyl acetylene dicarboxylate.	88
(25)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with excess dimethyl acetylene dicarboxylate	88
(26)	Reaction of trans-2-azido-2-butene (<u>1b</u>) with 1 mole of dimethyl acetylene dicarboxylate using aluminum chloride as a catalyst	89
(27)	Reaction of 1 mole of trans-2-azido-2-butene (<u>1b</u>) with 1 mole of dimethyl acetylene dicarboxylate in presence of aluminum chloride	90
(28)	Reaction of cis-2-azido-2-butene (<u>1a</u>) with excess dimethyl acetylene dicarboxylate in in presence of aluminum chloride	90
(29)	N.M.R. study on 9b	91
	References	93

List of Figures

		page
Figure I	Reactions of alcohols, ethers, ketones, acids, oximes and nitriles with triphenylphosphine dihalides	4
Figure II	Isolation of intermediate alkoxy phosphonium bromide salts	6
Figure III	Retention of configuration in alcohol to alkyl halide transformation	7
Figure IV	Reaction of triphenylphosphine and carbon tetrachloride with sugars	8
Figure V	Reaction of triphenylphosphine dihalide with styrene oxide	16
Figure VI	The coupling of H_1 , H_2 and H_3 in alkoxy phosphonium halide salt <u>3</u>	18
Figure VII	Reaction of $2\alpha, 3\alpha$ -cholestene oxide with triphenylphosphine dihalide	22
Figure VIII	Reaction of $2\beta, 3\beta$ -cholestene oxide with triphenyl phosphine dichloride	22
Figure IX	Reaction of $5\alpha, 6\alpha$ -cholestene oxide with triphenylphosphine dibromide	23
Figure X	Canonical forms of vinyl azides	48
Figure XI	Co-ordination of aluminum chloride with vinyl azides.	54

List of Tables

	page
Table I Structure of Triphenylphosphine Dihalides in Different solvents.	10
Table II Reaction of Tertiary Phosphine Dihalides with epoxides	13
Table III NMR Shifts of Vinyl methyl group <u>trans</u> and <u>cis</u> to carbomethoxy or azido groups.	67

List of Schemes

		page
Scheme I	Reaction of Triphenylphosphine Dihalides with Cyclohexene Oxide	19
Scheme II	Proposed scheme for formation of large rings	46
Scheme III	Reaction of vinyl azides with acids	51
Scheme IV	Reaction of vinyl azide with nitrosyl tetrafluoroborate	53
Scheme V	Reactions of amides with nitrosyl chloride	54
Scheme VI	Reaction of vinyl azides with acetyl chloride	56
Scheme VII	Reaction of vinyl azides with metachloroperbenzoic acid	59
Scheme VIII	Reaction of bromine with vinyl azide	61
Scheme IX	Reaction of vinyl azide with dimethyl acetylene dicarboxylate	64
Scheme X	Electrocyclic ring opening of 9a and 9b.	66

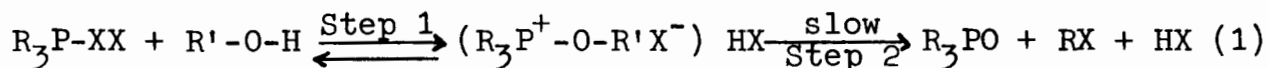
CHAPTER I
INTRODUCTION

The conversion of alkenes to vicinal dihalides through ionic halogenation invariably proceeds in a trans fashion. Only in the case of chlorination with iodo-benzene dichloride can cis halogenation be efficiently achieved¹. In this latter case the halogen is introduced from the least hindered side of the alkene. Free radical halogenation of alkenes proceeds in a stereorandom fashion². Although data are lacking one would expect the cis dihalo product formed from free radical halogenation of cycloalkenes to be that resulting from the least hindered side. We have attempted a method which would enable one to introduce cis vicinal halogens into cycloalkenes from the most hindered side of a molecular frame³. The method involves the introduction of cis halogens from the sterically most hindered side of cycloalkenes from reaction of the tertiary phosphine dihalides with epoxides, derived by epoxidation from the least hindered side of the cycloalkenes (Scheme I, Path B). The rationale for this scheme has been obtained from the work of several groups who have used tertiary phosphine dihalides as halogenating agents for alcohols, ethers, ketones and various other oxygenated functions.

The use of tertiary phosphine dihalides to convert alcohols⁴ and ethers⁵ in high yields to alkyl halides

has been known since 1954. These reagents have also been used to convert ketones⁶ to dihalides, acids⁷ to acyl halides, and oximes and amides to nitriles⁶ (Figure I).

Yields in most of these reactions range from 50-90%. The reaction with alcohols has been studied extensively by a number of workers^{4,6,8,9,10} and has been reported to proceed in most instances with inversion of configuration at the reacting carbon. The gross feature of this mechanism is depicted in Equation 1. Where kinetic data⁸ are available, this reaction is first order in phosphorus reagent and a zero order process in alcohol.



Despite this there is a marked dependence of the overall rate of reaction on the structure of the alcohol. The reactivity ratios for the sequence where R' = n-butyl; sec-butyl; and neo-pentyl are (1.0 : 0.5 : 10⁻⁵). These data rule out a rate determining reaction between alcohol and R₃P⁺XX⁻ as well as a rate determining reaction of R₃P⁺XX⁻ prior to combination with the alcohol. They are consistent with a rapid first step to form an intermediate alkoxy phosphonium halide salt which slowly decomposes to products.

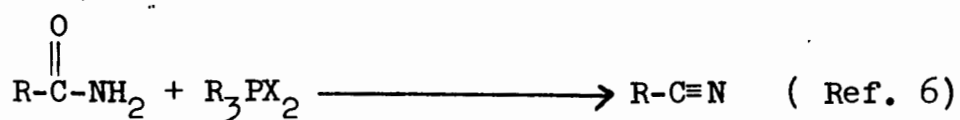
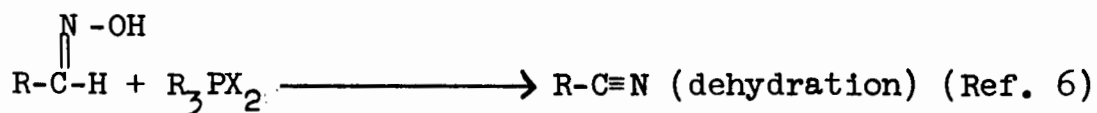
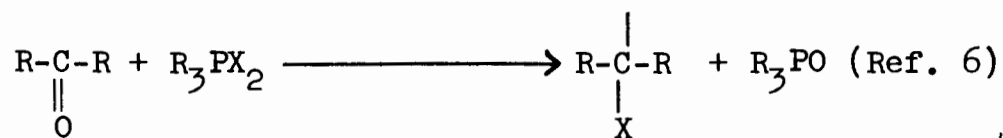
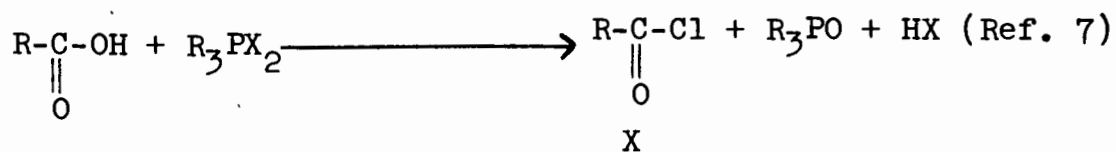
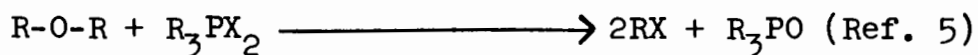
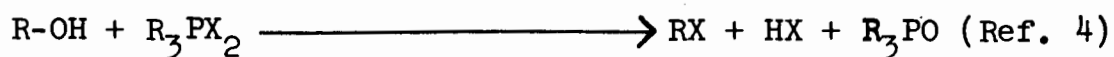


Figure I: Reactions of Alcohols, Ethers, Ketones, Acids, Oximes, and Nitriles with Triphenylphosphine Dihalides.

The first step may be either irreversible or reversible. In the latter case the rate for back reaction is required to be negligible compared to the rate of forward reaction and the rate of Step 2 (Eqn 1). Further evidence for the formation of intermediate as outlined in Equation 1 is available from the study of the reaction of $\text{Ph}_3\text{P}^+\text{BrBr}^-$ with phenol¹¹ and norbornyl alcohols⁹, where the intermediate alkoxy phosphonium bromide salts are sufficiently stable to be isolated. These salts were identified on the basis of their equivalent weights, elemental analysis and behaviour on pyrolysis (Figure II).

Retention and racemization in the alcohol to alkyl halide transformation are observed only in those cases where sometimes isolatable^{9,11,12,13} alkoxy phosphonium halide salt intermediates ionize to especially stable carbonium ions^{9,10} or where inversion at the reacting carbon centre is sterically unfavoured^{9,12} (Figure III).

Recently the pentavalent phosphorus reagent has also been used to replace the alcohol group in sugars with halogens^{14,15,16} Figure IV. This method is excellent for conversion of primary and secondary alcohols of sugars, since under the conditions used most esters, acetals and other groups are not affected by this reagent.

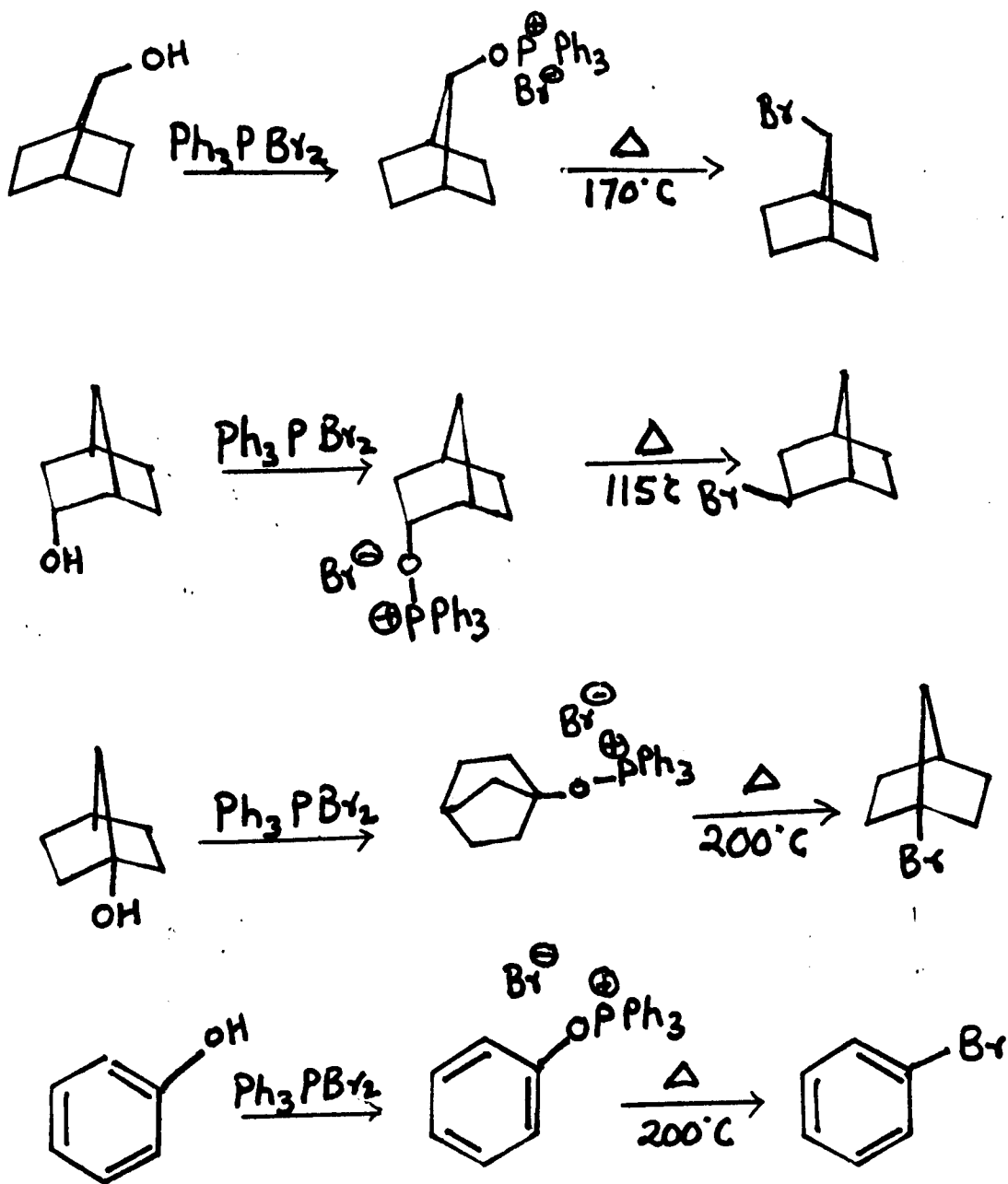


Figure II: Reactions Allowing Isolation of Intermediate Alkoxy Phosphonium Bromide Salts

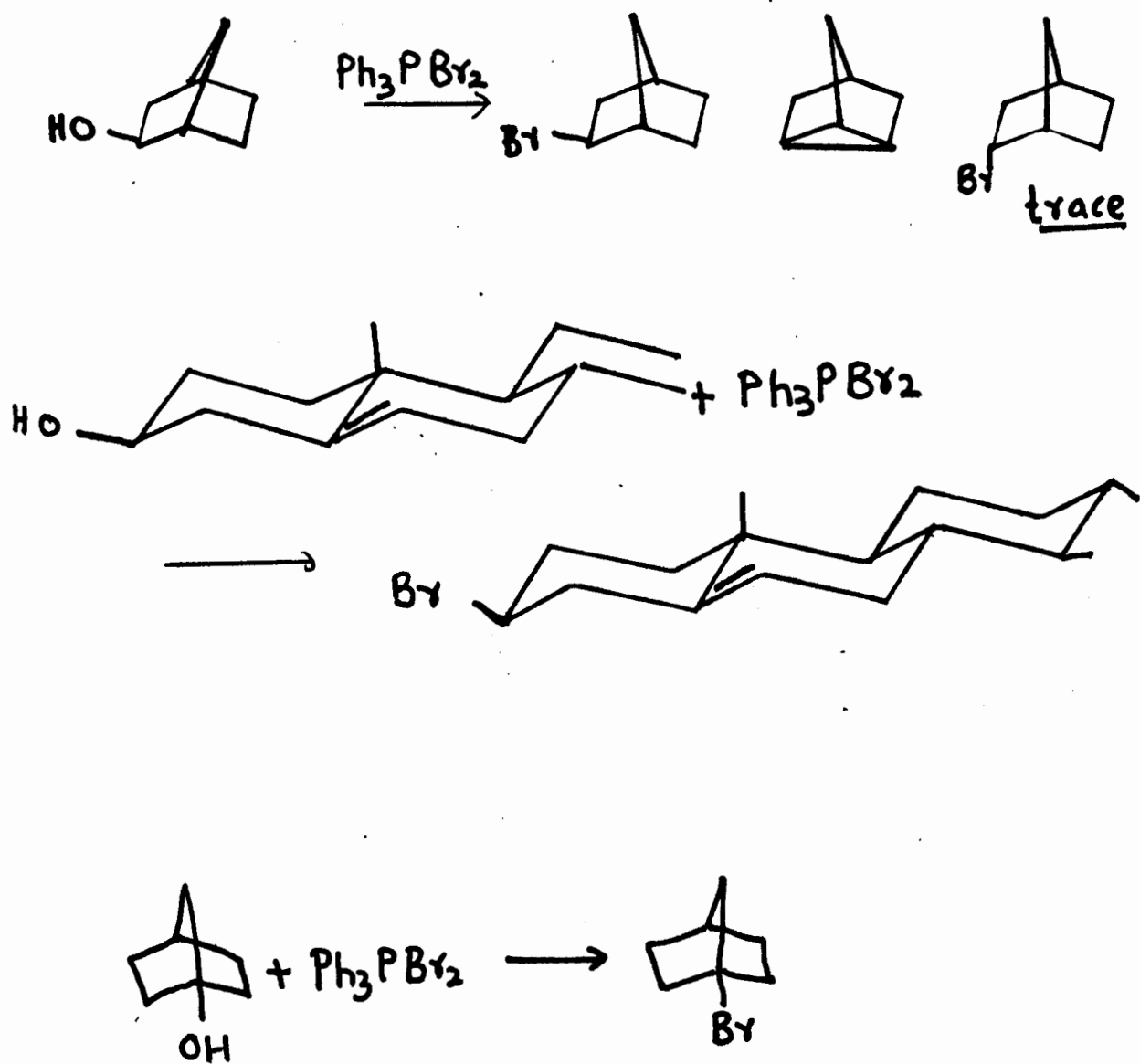


Figure III: Retention of Configuration in Alcohol to Alkyl Halide Transformation.

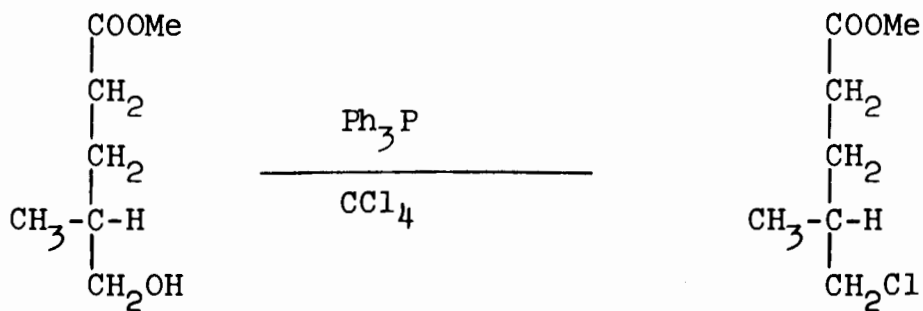
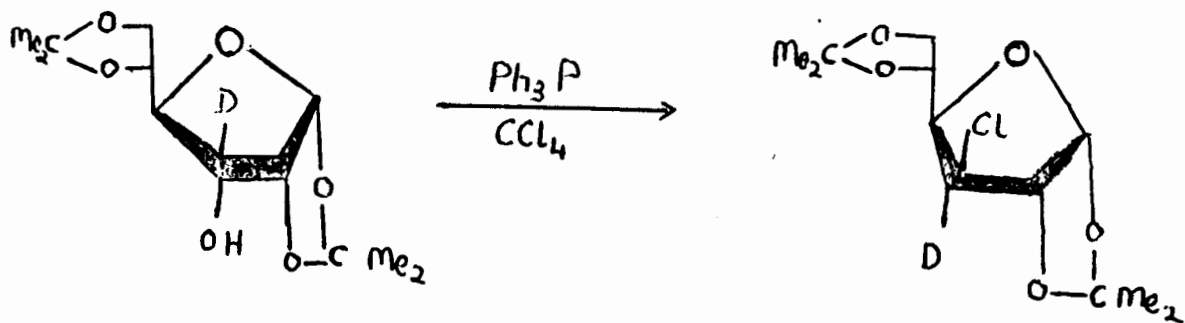
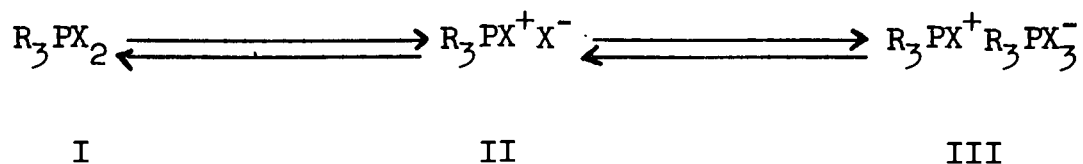


FIGURE IV Reaction of Triphenylphosphine and carbon tetrachloride with sugars

Several structures for tertiary phosphine dihalides in solution have been proposed¹⁷. By analogy with the phosphorous pentahalides the tertiary phosphine dihalides can be formulated as covalent (I) or (II, III) ionic species.



Using strong Lewis acids such as $SbCl_6$ and $AlCl_3$. Wiley and Stine^{17d} succeeded in defining unambiguously the spectroscopic properties of R_3PX^+ species. Comparing the n.m.r. and i.r. data with that obtained for R_3PX_2 (where R=phenyl or methyl) in acetonitrile it is found that R_3PX_2 exists as II in acetonitrile. Table I lists the structures of tertiary phosphine dihalides in different solvents.

TABLE I

Structure of Triphenylphosphine Dihalides in Different Solvents

Phosphorus Reagent	Solvent		
	CH ₃ CN	PhNO ₂	Liquid
Ph ₃ PCl ₂	II	I or III	
(n-C ₄ H ₉) ₃ PCl ₂	II	II	
(n-C ₄ H ₉) ₃ PBr ₂	II	II	
Ph ₃ PF ₂			I or III
(CH ₃) ₃ PF ₂			I or III
(C ₂ H ₅) ₃ PF ₂			I or III

RESULTS AND DISCUSSIONS

Scrutiny of the foregoing reports suggested a practical method of transformation of cycloalkenes^a to cis vicinal dihalide might lie in the conversion of the alkene to an epoxide followed by reaction of the epoxide with a tertiary phosphine dihalide. This work outlines the following aspects of this reaction:

- (A) General Scope
- (B) Mechanism
- (C) Stereochemistry

A. General Scope

When equimolar quantity of a variety of epoxides (Table II) were reacted with tertiary phosphine dihalides, vicinal dihalides were obtained in moderate yield. The structure and stereochemistry of the dihalide products were determined by analysis of mass spectral and n.m.r. data. In most cases studied, both cis and trans vicinal dihalides were obtained. Thus (Table II) the conversion of epoxides to vicinal dihalides is a moderately efficient and general reaction.

B. Mechanism

Since several investigations (8) have indicated tertiary phosphine dihalides exist in solution as

Reaction of Tertiary Phosphine Dihalides with Epoxides

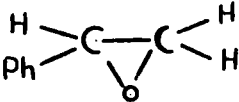
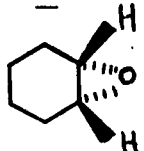
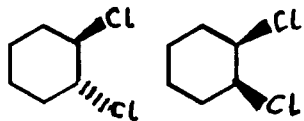
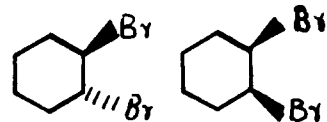
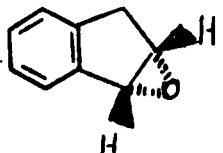
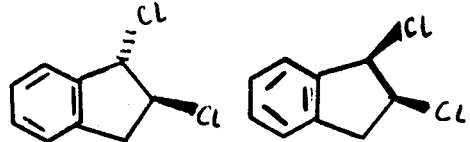
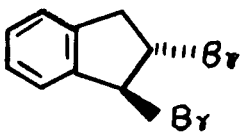
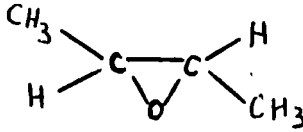
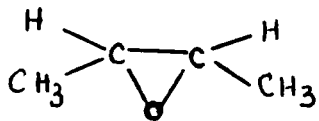
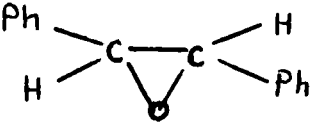
Phosphorus Reagent	Epoxide	Solvent	Products	Total Yield (Analysis method)
Ph_3PCl_2	 <u>1</u>	$\text{CH}_3\text{C}\equiv\text{N}$	$\text{PhCHCl-CH}_2\text{Cl}$ <u>2</u>	86% (isolation)
Ph_3PBr_2	<u>1</u>	$\text{CH}_3\text{C}\equiv\text{N}$	$\text{PhCHBr-CH}_2\text{Br}$	32% (isolation)
Ph_3PCl_2	 <u>5</u>	$\text{CH}_3\text{C}\equiv\text{N}$	 $\frac{\text{trans}}{50} : \frac{\text{cis}}{50}$	68% (isolation) (12%) cyclohexene formed
Ph_3PCl_2	<u>5</u>	C_6H_6	only <u>cis</u>	71% (isolation)
Ph_3P in CCl_4	<u>5</u>	CCl_4	$\frac{\text{trans}}{50} : \frac{\text{cis}}{50}$	50% (isolation)
$[(\text{CH}_3)_2\text{N}]_3\text{PCl}_2$	<u>5</u>	CHCl_3	$\frac{\text{trans}}{95} : \frac{\text{cis}}{5}$	75% (isolation)
Ph_3PBr_2	<u>5</u>	C_6H_6	 $\frac{\text{trans}}{35} : \frac{\text{cis}}{65}$	73% (g.l.p.c.)
Ph_3PBr_2	<u>5</u>	$\text{CH}_3\text{C}\equiv\text{N}$	$\frac{\text{trans}}{58} : \frac{\text{cis}}{42}$	70% (g.l.p.c.)
Ph_3PCl_2	 <u>11</u>	$\text{CH}_3\text{C}\equiv\text{N}$	 $\frac{\text{trans}}{25} : \frac{\text{cis}}{75}$	50% (isolation)

TABLE II (cont)

Phosphorus Reagent	Epoxide	Solvent	Products	Total Yield (Analysis method)
Ph_3PBr_2	<u>11</u>	$\text{CH}_3\text{C}\equiv\text{N}$	 only	50% (g.l.p.c.)
Ph_3PBr_2	 <u>12</u>	C_6H_6	$\text{CH}_3\text{CH}(\text{Br})\text{CH}(\text{Br})\text{CH}_3$ $\frac{\text{meso}}{40} : \frac{\text{dl}}{60}$	74% (g.l.p.c.)
Ph_3PBr_2	<u>12</u>	$\text{CH}_3\text{C}\equiv\text{N}$	$\frac{\text{meso}}{40} : \frac{\text{dl}}{60}$	70% (g.l.p.c.)
Ph_3PBr_2		$\text{CH}_3\text{C}\equiv\text{N}$	$\frac{\text{meso}}{44} : \frac{\text{dl}}{56}$	62% (g.l.p.c.)
Ph_3PBr_2		$\text{CH}_3\text{C}\equiv\text{N}$	$\text{PhCH}(\text{Br})\text{CH}(\text{Br})\text{Ph}$ <u>meso</u> only	60% (isolation)

halophosphonium halide salts ($R_3P^+XX^-$) initial complexation of electrophilic phosphorus with the epoxidic oxygen seemed probable. This was further supported by the work of other workers who showed that in case of alcohols (9,11) the initial attack of the electrophilic phosphorus occurred at the alcoholic oxygen. As in related epoxide openings, if this complexation is significant it would be expected to direct the initial opening reaction of unsymmetrically substituted epoxides toward the most substituted carbon. That this is indeed the case was demonstrated by following the conversion of styrene oxide, 1, to 1,2-dichlorophenylethane, 2, with triphenylphosphine dichloride in an n.m.r. probe, (Figure V). When styrene epoxide was mixed with a slight excess of triphenylphosphine dichloride in acetonitrile the quartet signals due to H_1 , H_2 , and H_3 of 1 immediately vanished and three triplets at $\delta 5.55$ ($J=5\text{Hz}$), $\delta 5.16$ ($J=7\text{Hz}$), $\delta 4.63$ ($J=5\text{Hz}$) and a doublet at $\delta 4.03$ appeared. Of these the triplet at $\delta 5.16$ ($J=7\text{Hz}$) and the doublet at $\delta 4.03$ were due to 1,2-dichlorophenylethane and increased with time until after 12 hours at room temperature they were the only resonances in the $\delta 4-6$ region. The triplets at $\delta 5.55$ and $\delta 4.63$ decreased

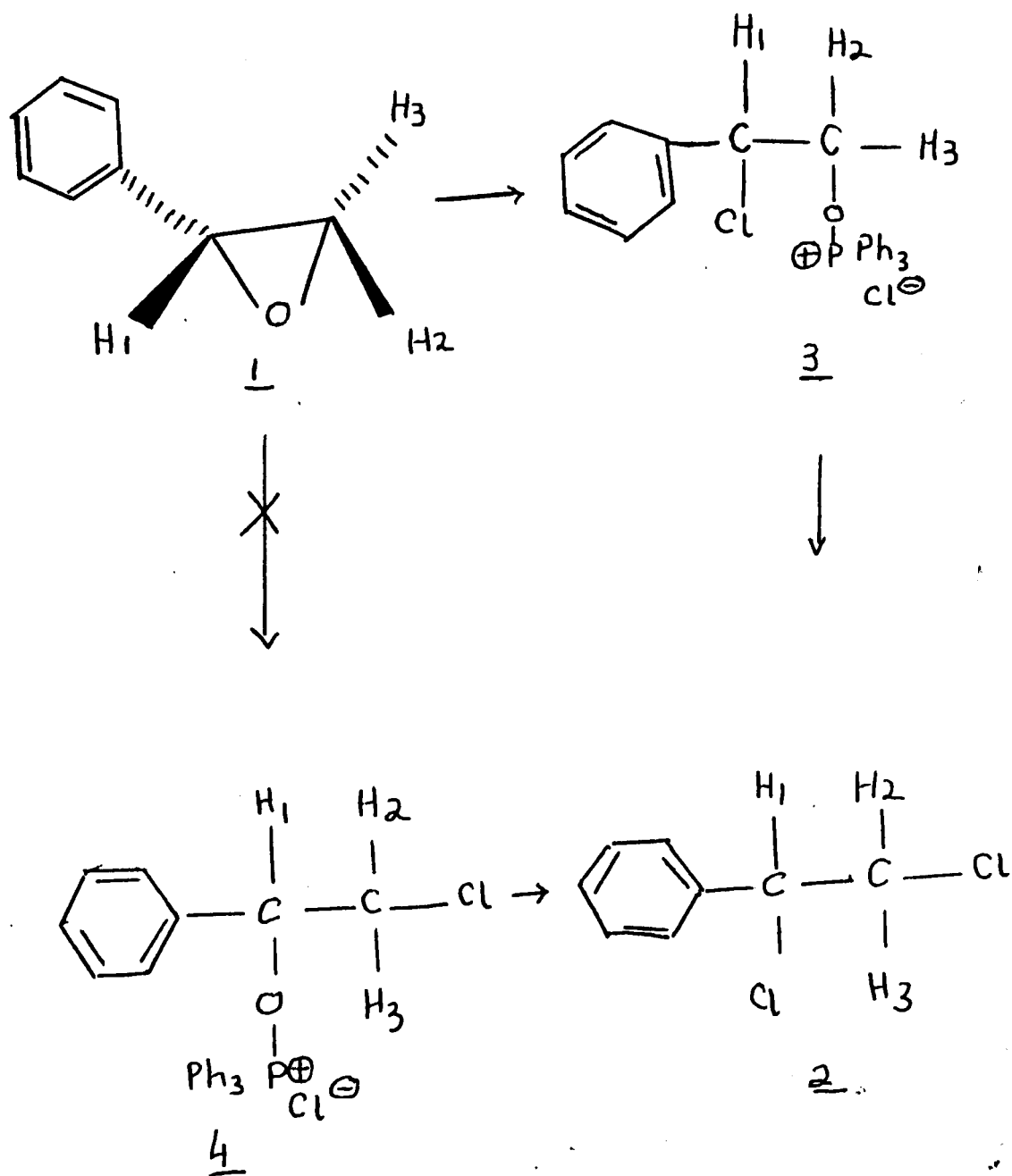
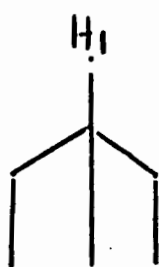
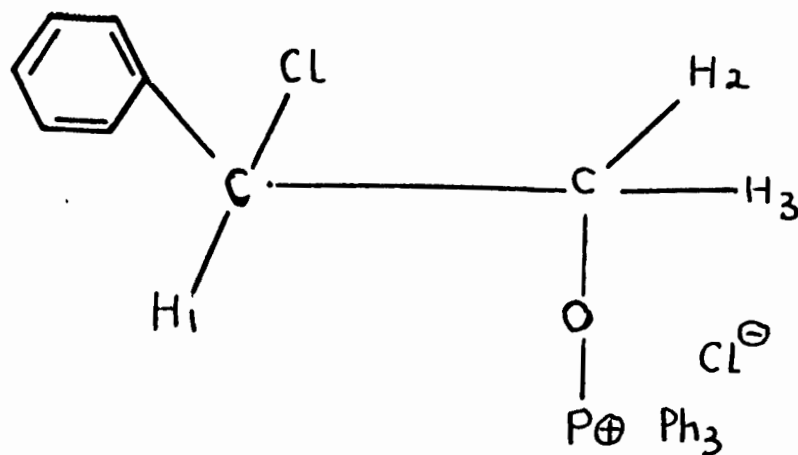


Figure V: Reaction of Triphenylphosphine dihalide with Styrene oxide.

correspondingly with time until they disappeared at 12 hours. These signals are assigned to H_1 and H_2, H_3 of 3. H_2, H_3 are observed as a triplet because the coupling of H_1 with H_2 and H_3 is very similar to P-O-CH_{2,3} coupling⁸. The alternate alkoxy phosphonium salt, 4, would be expected to give rise to a doublet (H_2, H_3) and a quartet or sextet (H_1 , Figure V).

Further support for the involvement of the alkoxy phosphonium salt, 7, was obtained from the production of the same cis-trans ratio of 1,2-dibromocyclohexanes (9:10) from the reaction of either cyclohexene oxide, 5, or trans-2-bromocyclohexanol, 6, with triphenylphosphine dibromide. (Scheme I).

The reaction of epoxides of cis cyclic alkenes with tertiary phosphine dihalides gave both cis and trans vicinal dihalides (Table II). If inversion at each epoxide carbon occurred during the second reaction as depicted in Scheme I (Path B) then one would obtain cis dihalide, where the halogens have been introduced from the most hindered side. However if the alkoxy phosphonium halide salt intermediate, 7, ionizes then the initially introduced halogen can participate as shown in Scheme I (Path A) to give trans vicinal dihalide, 10. If in this latter case Path B makes some



$J = 5 \text{ cps}$

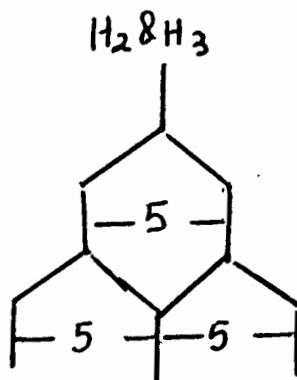
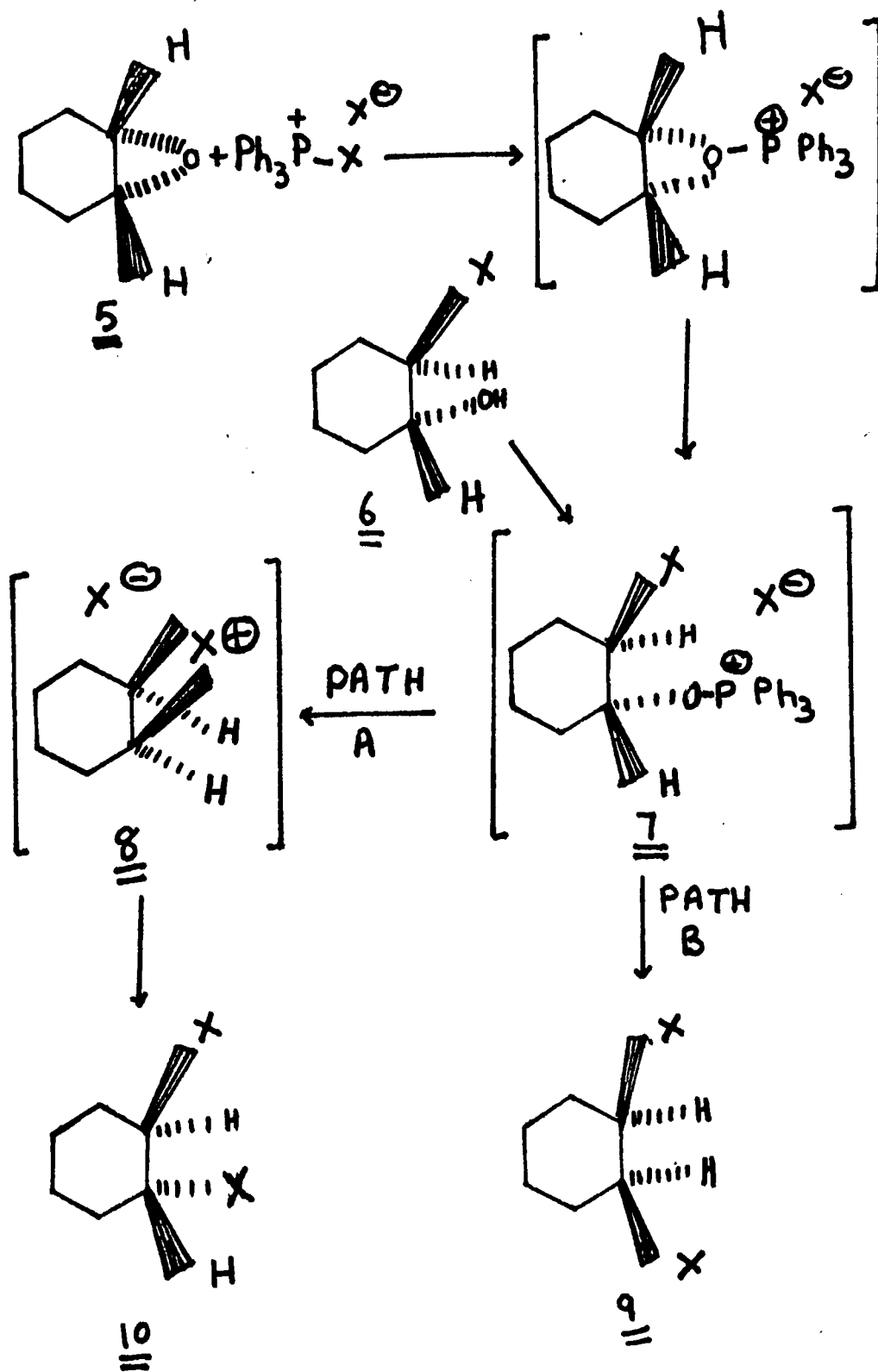


Figure VI: Interpretation of the coupling of Alkoxy Phosphonium Salt

SCHEME I



contribution the final cis : trans ratio may be subject to changes in dielectric constant of solvent and the halogens used. In the case of cyclohexene oxide, 5, which was studied in some detail, the ratio of these isomers, 9 and 10, was influenced by the dielectric constant of the solvent and the halogens used. The relative amount of trans dihalo product from 5 is increased upon changing from Ph_3PCl_2 to Ph_3PBr_2 or from Ph_3PCl_2 to $(\text{CH}_3)_2\text{N})_3\text{PCl}_2$ as well as by increasing the dielectric constant of the reaction solvent C_6H_6 , CHCl_3 , $\text{CH}_3\text{C}\equiv\text{N}$. All of these observations are compatible with the neighbouring halogen participation as outlined in Scheme I (Path A). Alkene formation was noted to be a low yield side reaction in the reaction of Ph_3PCl_2 with cyclohexene oxide, 5. Presumably the products of this reaction are $\text{Ph}_3\text{P}=\text{O}$, Cl_2 and alkene. Finally to eliminate the possibility that trans vicinal dihalide, 9, may be formed by initial deoxygenation of epoxide, 5, to the alkene followed by chlorination, the reaction of Ph_3PCl_2 with cyclohexene oxide 5 was carried out in the presence cyclopentene. In this experiment no 1,2-dichlorocyclopentane was detected. Furthermore, Ph_3PCl_2 did not react with cyclopentene under the conditions used for the conversion of epoxide to dichlorides.

C. Stereochemistry

In an attempt to determine if the cis vicinal dihalide products were formed by inversion at both epoxide carbons, the reaction of steroidal epoxides was investigated. Reaction of 2α , 3α -cholestene oxide, 14, with triphenylphosphine dibromide in dimethyl formamide (DMF) gave only 2α , 3β -dibromocholestane, 15, and 2β , 3α -dibromocholestane, 16, (Figure VIII). The reaction of 14 with triphenylphosphine dichloride gave quite unexpectedly only cholest-2-ene.

The reaction of 2β , 3β -cholestene oxide, 17, with triphenylphosphine dichloride in dimethyl formamide gave 2β , 3α -dichlorocholestane, 18, and 2α , 3α -dichlorocholestane, 19 in 1:4 ratio, (Figure VIII).

The reaction of 5α , 6α -epoxycholestane, 20, with triphenylphosphine dibromide in dimethyl formamide gave 5α , 6β -dibromocholestane, 21, and cholest-4,6-diene, 22 (Figure IX). The latter product presumably arises from diaxial dehydrobromination of 5β , 6β -dibromocholestane, 23. during work up. The absence of 5β , 6α -dibromocholestane is significant since it is the major component of the equilibrium mixture when it or 21 is refluxed in chloroform¹⁹.

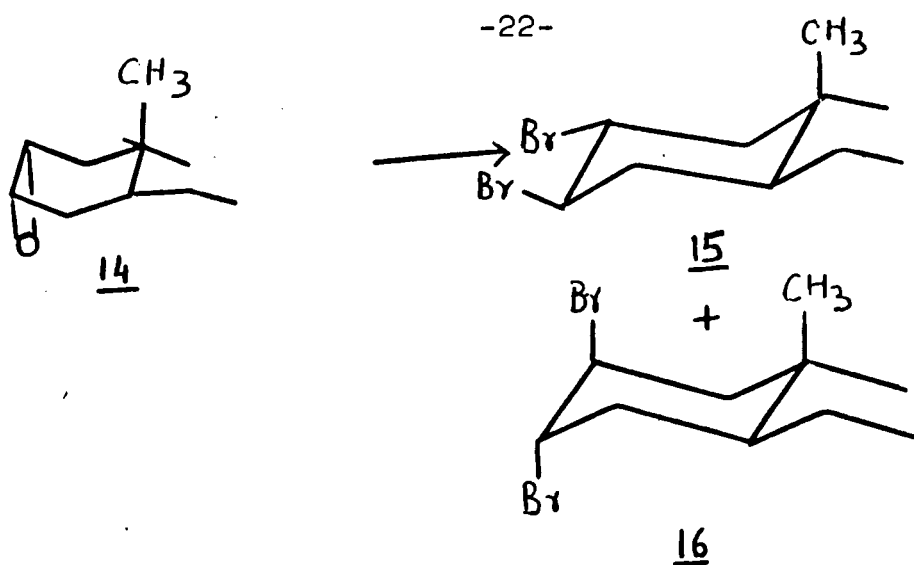


Figure VII: Reaction of $2\alpha,3\alpha$ -Cholestene oxide with Triphenylphosphine Dihalide.

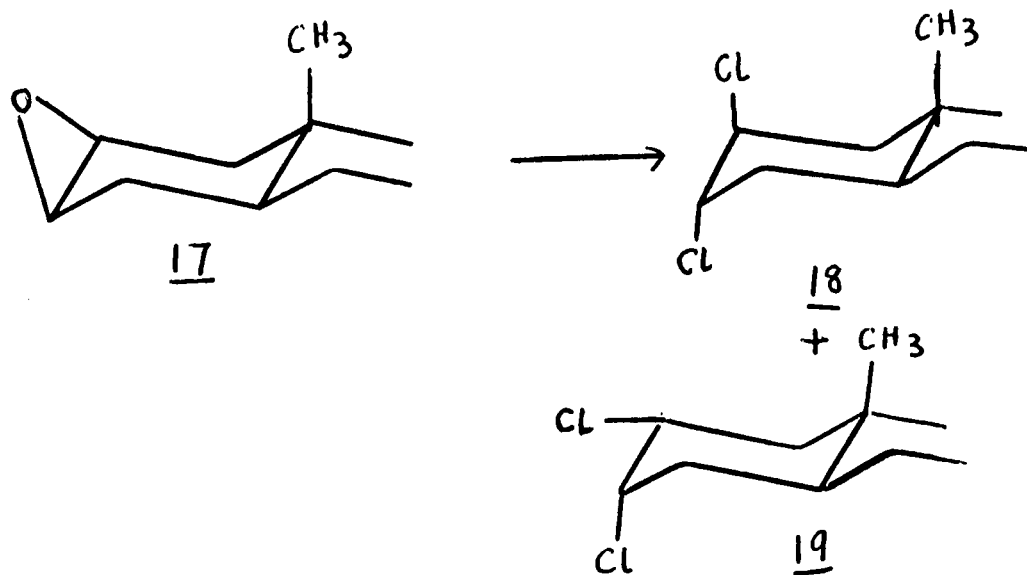


Figure VIII: Reaction of $2\beta,3\beta$ -Cholestene oxide with Triphenylphosphine Dichloride.

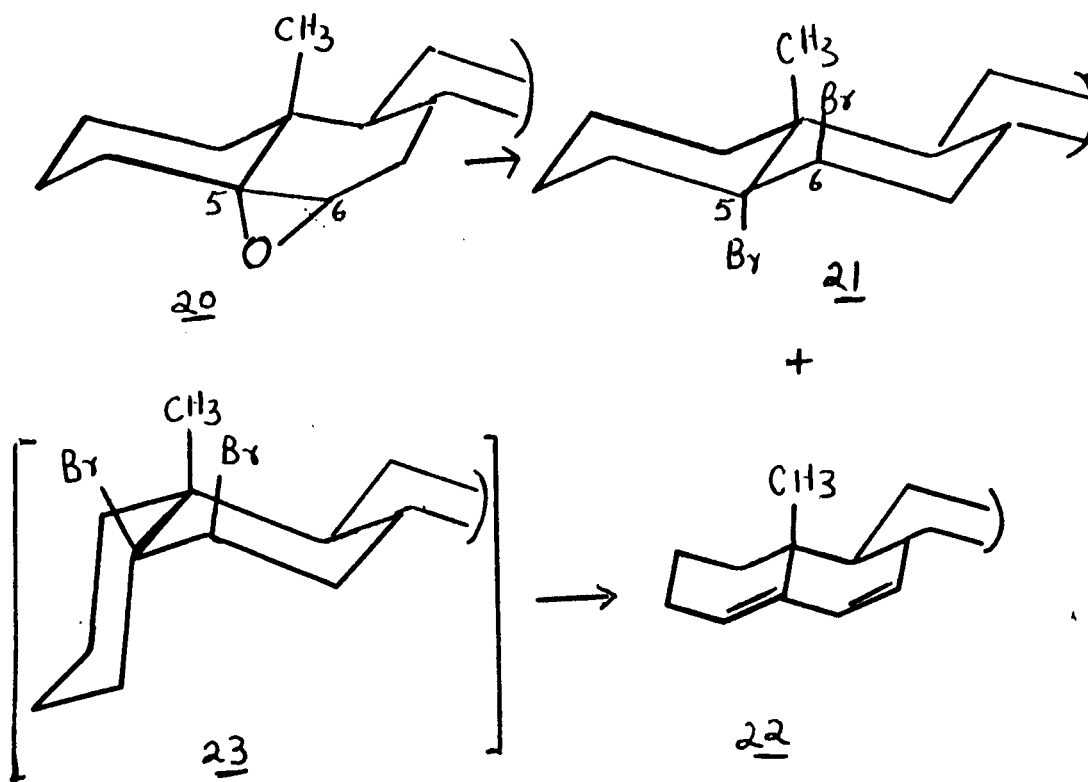


Figure IX: Reaction of 5α,6α-Cholestene oxide with Triphenylphosphine dibromide.

The presence 5 α , 6 β -dibromo isomer, 21, is consistent with SN₁ cleavage of the C₅ bond of 20 in the initial epoxide ring opening reaction.

In case of 17 the initial ring opening seems to be SN₁ type to give a 2 α , or 2 β chlorine and that the alkoxyphosphonium halide salt probably reacts by Scheme I (Path B) to give only 3 α chlorine.

CONCLUSIONS

From the data obtained in this study the following general conclusions can be drawn:

- (a) Tertiary phosphine dihalides are good reagents for the conversion of a number of epoxides to dihalides.

- (b) In cases where stereochemistry is determinable tertiary phosphine dihalides can be used as reagents to introduce cis halogens. However if such a process is sterically unfavourable as in, 14, or if the intermediate alkoxy phosphonium halide salt ionizes to a stable carbonium ion it may not be possible to introduce cis halogens. Thus our original goal of a general method of introduction of cis halogens from the most hindered side of a molecule was thwarted.

- (c)
 - (1) The reaction exhibits a marked dependency on the epoxidic carbon substituents. The initial ring cleavage takes place at the carbon which is most substituted.
 - (2) With increasing nucleophilicity of the halogens used the amount of trans dihalides and alkenes increases.

- (3) With increasing dielectric constant of the solvent the relative amount of trans dihalide, products increases.
- (4) The use of a more electron withdrawing group on the pentavalent phosphorus reagent increases the relative amount of trans dihalides.

EXPERIMENTAL

Melting points were determined using a Fisher-Johns apparatus and are uncorrected. Nuclear magnetic resonance (n.m.r.) spectra were recorded on a Varian Model A56/60 spectrometer using TMS as internal standard. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU 6E mass spectrometer. G.l.p.c. was performed on a Varian Aerograph Autoprep A-705 unit using a 6' X 1/4" 15% Carbowax 20M on 60/80 mesh Chromosorb W. Yields were determined using decalin as internal standard and are accurate to $\pm 2\%$.

Preparation of epoxides:

Styrene oxide used was obtained from Matheson Coleman and Bell, Norwood, Ohio and distilled prior to use.

The epoxides of cyclohexene, indene, cis and trans-2-butenes and trans-stilbene were prepared by reaction of the alkenes with peracetic acid (40%) in CH_2Cl_2^* containing excess Na_2CO_3 . The epoxides were isolated in (70-80%) by distillation or crystallization and were determined to be pure by g.l.p.c. and n.m.r. Trans-2-bromocyclohexanol was prepared by reaction of aqueous HBr with cyclohexene oxide.

The $2\alpha,3\alpha$ -cholestene oxide (14) was prepared by reaction of cholest-2-ene¹⁰ with perbenzoic acid in C_6H_6 . After usual workup 14 was isolated (70%) m.p., 103-104°C (lit.²⁰ m.p. 103-105°C).

The 2 β ,3 β -cholestene oxide (17) was prepared from cholest-2-ene¹⁰. The epoxide was isolated in 20% yield m.p. 89-90°C (lit.²¹ m.p., 89-90°C).

The 5 α ,6 α -cholestene oxide (20) was prepared by reaction of cholest-5-ene²² (8.1 g) with perbenzoic acid in C₆H₆. After the usual workup and five recrystallizations from acetone (20) (2g) was isolated m.p. 64-65°C (lit. m.p.²³ 74-75°C).

Reaction of triphenylphosphine dihalides with styrene oxide:

To a solution of triphenylphosphine (10 g) in 100 ml MeCN under N₂ was added an equimolar amount of Br₂ at such a rate that the temperature of the reaction did not exceed 5°C. After stirring at room temp. for 30 min. styrene oxide (3 g) was added slowly the reaction was stirred at 50°C overnight and solvent stripped in vacuo. The residue was extracted with ether, concentrated and filtered through a short column of neutral alumina (activity I). The ether eluent was concentrated and the concentrate crystallized from petroleum ether (30-60°C) to give 2.1 g (32%) of 1,2-dibromophenylethane m.p. 74-75°C (lit.²⁴ m.p. 74-75.5°C). This procedure was repeated using chlorine gas. Chromatography of the reaction mixture gave 1,2-dichlorophenylethane which was identical with a sample prepared by chlorination of styrene.

Reaction of triphenylphosphine dichloride with cyclohexene oxide:

The reaction of triphenylphosphine dichloride with cyclohexene oxide was carried out as described above in MeCN and C_6H_6 on a 0.03 M scale. After stirring overnight the solvent was removed in vacuo. Treatment of this distillate with chlorine followed by concentration in vacuo gave 10% of trans-1,2-dichlorocyclohexane. The residue was extracted with three 100 ml portions of petroleum ether (30-60°C) to separate the dichloride from the triphenylphosphine oxide which precipitated in 73% yield. The petroleum ether extract was fractionally distilled at reduced pressure (b.p. 50-60°C/10mm Hg) to give a mixture of dichlorides (63%). Analysis of this distillate by g.l.p.c. revealed two major compounds which were identified as cis and trans-1,2-dichlorocyclohexanes as described below. Chromatography of the dichloride mixture of neutral alumina gave upon elution with petroleum ether (30-60°C) trans-1,2-dichlorocyclohexane (31% b.p. 50°C/10mm Hg., lit.²⁵ b.p. 186-190°C/760mm Hg). Elution with C_6H_6 gave the cis-1,2-dichloro isomer (32% b.p. 50°C/10mm Hg., lit.²⁵ b.p. 114.4-114.5°C/50mm Hg). The n.m.r. spectra of the cis and trans-1,2-dichlorocyclohexanes were identical in the $\delta 2$ - $\delta 5$ region with those published.²⁶

The trans-1,2-dichlorocyclohexane was identical to a sample prepared by chlorination of cyclohexene.

Reaction of triphenylphosphine dichloride with cyclohexene oxide in the presence of cyclopentene:

To a soln. of 8.3 g of triphenylphosphine dichloride (6.6 g Ph_3P and 1.7 g Cl_2 in MeCN (50 ml) was added cyclohexene oxide (1g) and cyclopentene (1 g). The soln. was stirred overnight and the solvent slowly removed in vacuo. The semisolid residue was distilled (b.p. 50-60°C/10mm Hg.) to give 1.0 g (66%) of cis and trans-1,2-dichlorocyclohexanes (1:1 g.l.p.c.). No trans-1,2-dichlorocyclopentane was detected by g.l.p.c. In an independent experiment it was determined that Ph_3PCl_2 did not react with cyclopentene in MeCN soln. at room temp. for 24 hr.

Reaction of triphenylphosphine with cyclohexene oxide in carbon tetrachloride:

To a soln. of cyclohexene oxide (3 g) in 50 ml CCl_4 was slowly added triphenylphosphine (10 g). After stirring 1 hr. the solvent was stripped in vacuo and the residue was extracted with petroleum ether (30-60°C). The petroleum ether extract was fractionally distilled (b.p. 50-60°C/10mm Hg.) to yield a mixture (composition reported in Table I) of dichlorides (45%) identified by g.l.p.c. comparisons with the samples isolated above.

Reaction of hexamethylphosphorus triamide dichloride with cyclohexene oxide:

A soln of hexamethylphosphorus triamide²⁷ (4 g) in C_6H_6 (40 ml) under N_2 was treated with Cl_2 (1.7 g). The soln. was allowed to stir for 1 hr. then cyclohexene oxide (3 g) added. The reaction was stirred overnight then treated with 0.05 N aqueous HCl. The organic layer was separated dried over anhydrous $MgSO_4$ and fractionally distilled to give a mixture of cis and trans-1,2-dichlorocyclohexanes (75%) which were identified by g.l.p.c. comparisons with samples described above.

Reaction of triphenylphosphine dibromide with cyclohexene oxide and trans-2-bromocyclohexanol:

The reaction of triphenylphosphine dibromide with cyclohexene oxide and trans-2-bromocyclohexanol was carried out in C_6H_6 and MeCN on a 0.03 molar scale in the fashion described above for the triphenylphosphine dichloride reaction. Analysis of the reaction mixtures by g.l.p.c. followed by separation by column chromatography on neutral alumina gave trans-1,2-dibromocyclohexane b.p. $95-97^\circ C/15mm Hg$ (lit.²⁵ b.p. $101^\circ C/14mm Hg$) and cis-1,2-dibromocyclohexane b.p. $95-97^\circ C/15mm Hg$ (lit.²⁵ b.p. $115^\circ C/14mm Hg$). The n.m.r. and mass spectra of both compounds are consistent with the structures proposed.

Reaction of the triphenylphosphine dihalides with indene oxide:

Reaction of triphenylphosphine dichloride with indene oxide (2.5 g) in the usual manner gave, after workup, a mixture of two compounds. Chromatography of the reaction mixture on neutral alumina gave (1.5 g) cis-1,2-dichloroindane, b.p. 50°C/1mm Hg,

Calc. for: $C_9H_8Cl_2$; 226(M⁺). Found: 226(M⁺).
Elution with C_6H_6 gave 1.5 g trans-1,2-dichloroindane b.p. 50°C/1mm Hg (lit.²⁸ b.p. 108°C/15mm Hg). The n.m.r. spectrum of this isomer was identical with the published spectrum.²⁸

Reaction of triphenylphosphine dibromide with indene oxide in the usual manner gave, after workup and chromatography only trans-1,2-dibromoindane, b.p. 120°C/5mm Hg (lit.²⁸ m.p. 32°C). This sample gave n.m.r. and mass spectra identical with a sample prepared by the bromination of indene. Neither sample could be induced to crystallize.

Reaction of triphenylphosphine dichloride with cis and trans-2-butene oxides:

The reaction of triphenylphosphine dichloride with cis-2-butene oxide in the usual manner gave meso and d,l-2,3-dichlorobutanes. The meso 2,3-dichlorobutane was

identical by g.l.p.c. with a sample prepared by chlorination of trans-2-butene. The d,l-2,3-dichlorobutane was identical by g.l.p.c. with a sample prepared by chlorination of cis-2-butene.

The reaction of triphenylphosphine dibromide with trans-2-butene oxide in the usual manner gave meso and d,l-2,3-dibromobutanes. The meso-2,3-dibromobutane was identical by g.l.p.c. with a sample prepared by bromination of trans-2-butene. The d,l-2,3-dibromobutane was identical by g.l.p.c. to a sample prepared by bromination of cis-2-butene.

Reaction of triphenylphosphine dichloride with
2 β ,3 β -cholestene oxide:

To a soln. of triphenylphosphine (1 g) in 50 ml dry MeCN under N₂ was added 0.3 g Cl₂. The soln was stirred at 0°C for 1/2hr then 2 β ,3 β -cholestene oxide²¹ (0.18 g) was added. The soln was stirred at 40°C for 18 hrs then diluted with water and extracted with three 100 ml portions ether. The ether extract was washed with aqueous NaHCO₃, dried over MgSO₄, and concentrated in vacuo. The concentrate was triturated with 100 ml light petroleum (30-60°C) and the triphenylphosphine oxide precipitate which formed was removed by filtration. The filtrate was evaporated to give an oil which was chromatographed on 5 g basic alumina

(Act. III). Elution with benzene gave 18, 0.02 g, b.p. 110-112°C/760 mm Hg, (lit.¹⁹ b.p. 110-112°C/760 mm Hg) n.m.r. (CCl₄): δ 0.650 (s, 3H, C¹⁸H₃ Calcd²⁹ 0.684), 1.06 (s, 3H, C¹⁹H₃, Calcd.²⁹ 1.03) and 4.53 (m, 2H, C₂H, C₃H). Calcd for C₂₇H₁₆Cl₂: 435 Found by M.S. (M⁺): 435 Elution with benzene- chloroform (1:1) gave 0.08 g 19, m.p. 134-135°C. N.m.r.

(CCl₄): δ 0.650 (s, 3H, C¹⁸H₃, Calcd²⁹ 0.684, 0.834 (s, 3H, C¹⁹H₃, Calcd.²⁹ 0.815) and 4.53(m, 2H, C₂H, C₃H). [α]_D²⁵ + 57.3° (c=0.34, hexane).

Calcd. for C₂₇H₄₆Cl₂ : 435. Found by M.S. (M⁺) : 435.

It was independently determined that a 3α-chloro group shifted C¹⁸H₃ by δ 0.006 and the C¹⁹H₃ by δ 0.038 upfield.

From the data of Cohen et al.²⁹ for the effect of the 6β-Cl and 2β-Br the effect of a 2β-Cl was estimated to be a downfield shift of δ 0.30 on the C¹⁹H₃ and δ 0.0 on the C¹⁸H₃.

Reaction of triphenylphosphine dichloride with 2α,3α-cholestene oxide:

The reaction of Ph₃PCl₂ with 2α,3α-cholestene oxide was carried out as described above. Analysis of the reaction mixture by thin layer silica gel and n.m.r. revealed only

triphenylphosphine oxide and 2-cholestene which were identified by comparison with the authentic samples.

Reaction of triphenylphosphine dibromide with 2 α ,3 α -cholestene oxide:

To a solution of triphenylphosphine (20 g) in 100 ml dry DMF under N₂ was added 12 g Br₂. The soln was stirred at 0°C for 1/2 hr then 2 α ,3 α -cholestene oxide¹⁹ (3 g) in 200 ml of dry DMF added. The soln was stirred for 18 hrs at room temp, diluted with water and extracted with three 100 ml portions of ether. The ether extract was washed with aqueous NaHCO₃, dried over anhydrous MgSO₄, and concentrated in vacuo. The concentrate was triturated with 100 ml of petroleum ether (30-60°C) and the triphenylphosphine oxide precipitate which formed by filtration. The filterate was evaporated to give an oil (2 g) which was chromatographed on 100 g of basic alumina (Act. III). Elution with petroleum ether (30-60°C) gave 19% 2 α ,3 β -dibromocholestane (15). m.p. 142-144°C (lit.^{20,21} m.p.:142-144°C). N.m.r. (CCl₄): δ 0.828 (s, 3H, C¹⁸H₃ Calcd.²⁹ 0.73), 0.917 (s, 3H, C¹⁹H₃ Calcd.²⁹ 0.90) and 4.40 (m, 2H, C₂H, C₃H). $[\alpha]_D^{25}$ -26° (c=0.5, hexane), lit^{20,21} $[\alpha]_D^{25}$ -27°. Calcd. for C₂₇H₄₆Br : 528. Found (M⁺) : 528. Elution with benzene gave 24% 2 β ,3 α -dibromocholestane (6), m.p. 123-124°C (lit.^{20,21} m.p. 123-124°C).

N.m.r (CDCl_3) : δ 0.903 (s, 3H, C^{19}H_3 Calcd.²⁹ 0.97), 0.645 (s, 3H, C^{18}H_3 Calcd.²⁹ 0.692) and 4.66 (m, 2H, C^2H , C^3H).
[α]_D²⁵ + 75.2° (c=0.6, hexane) lit.^{20,21} [α]_D²⁵ +76°
Calcd. for $\text{C}_{27}\text{H}_{46}\text{Br}_2$: 528. Found by M.S. (M^+): 528

Reaction of triphenylphosphine dibromide with
5 α ,6 α -cholestene oxide:

The reaction of triphenylphosphine dibromide (0.05 m) with 5 α ,6 α -cholestene oxide (2g, 0.05 m) was carried out in DMF as described above. Chromatography of the dibromide fraction of basic alumina (Act. III) gave 0.6 g of cholest-4,6-diene, m.p. 82.5-84°C (lit.³⁰ m.p. 84-85°C)

Elution with C_6H_6 gave 1g of 5 α ,6 β -dibromocholestane , m.p. 110-111°C (lit.³⁰ m.p. : 110-111°C)
N.m.r (CDCl_3) : δ 1.39 (s, 3H, C^{19}H_3 , Calcd.²⁹ 1.329), 0.703 (s, 3H, C^{18}H_3 , Calcd.²⁹ 0.742) and 4.8 (m, 1H, C^6H).

REFERENCES

1. D.H.R. Barton and E. Miller, J. Am. Chem. Soc., 72, 370 (1950); Bromination with iodobenzene dibromide, although useful for selective bromination of polyenes, proceeds in a trans fashion. (M. Fryberg, A.C. Oehlschlager and A.M. Unrau, Tetrahedron, 27, 1261, 1971.
2. W.A. Pryor, "Free radicals," McGraw-Hill Book Co., Inc., New York, N.Y., 1966.
3. The closely related reaction of PCl_3 with epoxides has been reported with no mention of the stereochemical outcome; A.G.A. Rehiem, Y. Riad, and A.A. Youssef, Chem. Comm., 976, 1968.
4. D.G. Coe, S.F. Landauer and H.N. Rydon, J. Chem. Soc., 2881, 1954.
5. A.G. Anderson, Jr. and F.J. Freenor, J. Am. Chem. Soc., 86, 5038, 1964.
6. L. Horner, H. Oediger and H. Hoffmann, Ann., 626, 26, 1959.
7. A.J. Bestmann and L. Mott, Ann. 693, 32, 1966

8. G.A. Wiley, B.M. Rein, and R.L. Hershkowitz, Tetrahedron Letters, 2509, 1964.
9. J.P. Schaefer and D.S. Weinberg, J. Org. Chem., 30, 2635, 1965.
10. D. Levy and R. Stevenson, J. Org. Chem., 30, 3469, 1965.
11. J.P. Schaefer and J. Higgins J. Org. Chem., 32, 1607, 1967.
12. D.Z. Denney, A. Appelbaum and D.B. Denney, J. Am. Chem. Soc., 84, 4969, 1962.
13. L. Kaplan, J. Org. Chem., 31. 3454. 1966.
14. N.K. Kochetkov and A.I. Usov, Tetrahedron, 19, 973, 1963.
15. J.B. Lee and I.M. Downie, Tetrahedron, 23, 359, 1967.
16. C.R. Haylock, L.D. Melton, K.N. Slessor and A.S. Tracey, Carbohydrate Research, 16, 375, 1971.

17. (a) K. Issleib and W. Seidel, Z. Anorg. Chem., 281, 201, 1956 .
(b) J. Boubeau and R. Baumgartner, Z. Electrochem., 64, 598, 1960.
(c) L. Horner and H. Winkler, Tetrahedron letters, 455, 1964.
(d) G.A. Wiley and W.R. Stine, Ibid, 2321, 1967.
(e) G.S. Harris and M.R. Ali, Ibid, 37, 1968.
(f) D.B. Denney, D. Denney and B.C. Chang, J. Am. Chem. Soc., 90, 6332, 1968.

18. L. Kolditz and D. Hass, Z. Anorg. U. Allgem. Chem., 294, 191, 1958.

19. L.B. Wiesfield and H. Kwart, J. Am. Chem. Soc., 78, 635, 1956.

20. G.H. Alt and D.H.R. Barton, J. Chem. Soc., 4284, 1954.

21. D.G. Hey, G.D. Meakins and M.N. Pemberton, J. Chem. Soc., 1331, 1966.

22. J.W. Cornforth, G.P. Hunter and G. Popjak, Biochem. J., 54, 590, 1953.

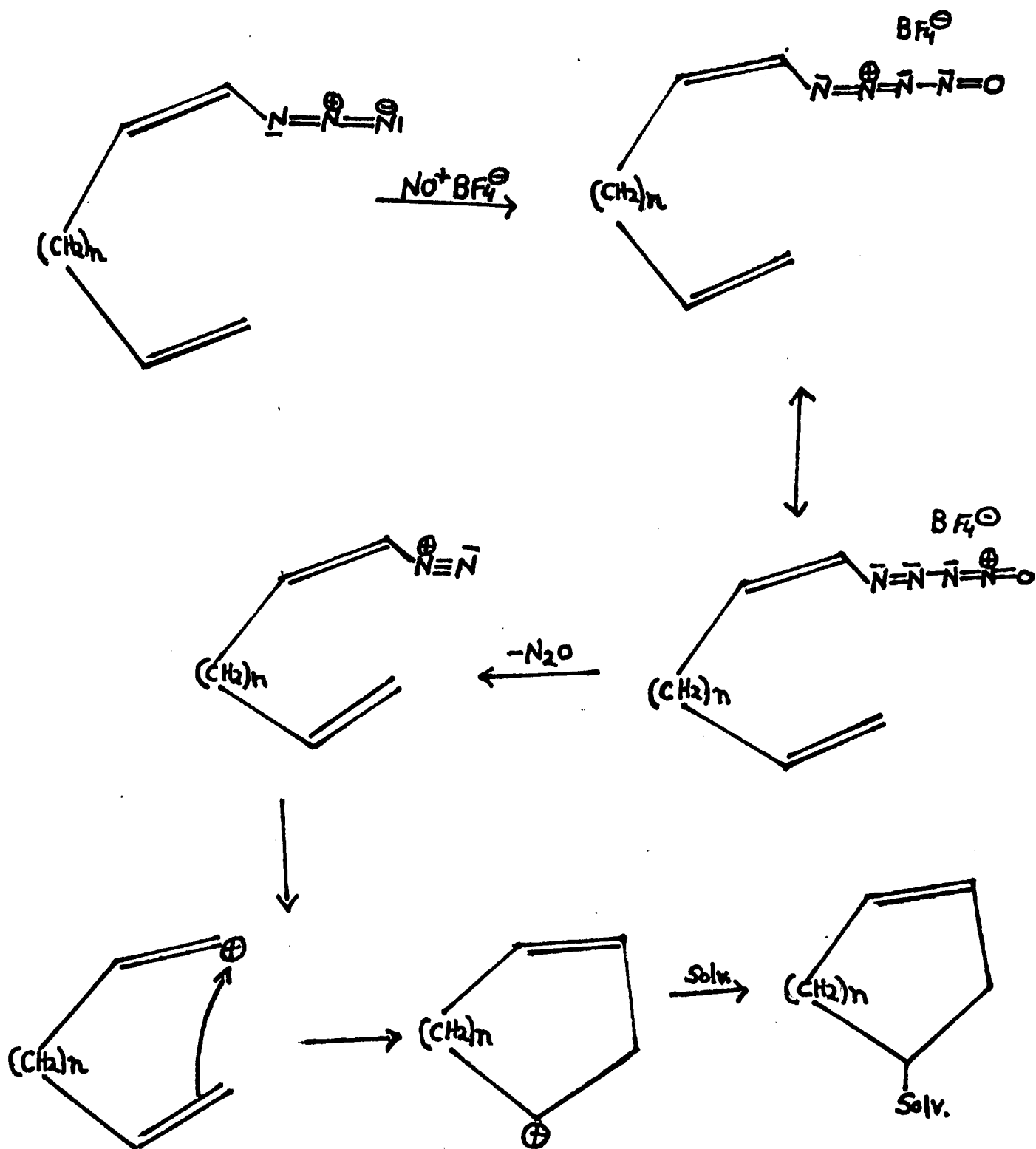
23. H.H. Gunthard, H. Hewser and A. Furst, *Helv. Chem. Acta.*, 36, 1900, 1953.
24. W.L. Loyd and L. H. Morgan, *J. Am. Chem. Soc.*, 35, 56, 1913.
25. B. Carroll, D.B. Kubler, H.W. Davies and A.M. Whaley, *J. Am. Chem. Soc.*, 75, 5382, 1951.
26. L.W. Reeves and K.O. Stromme, *Trans. Farad. Soc.*, 57, 390, 1961.
27. Procedures of V. Mark in L.F. Fieser and M. Fieser, *Reagents for Organic Synthesis*, John Wiley and Sons, N.Y., N.Y., 1967, p. 431.
28. H.R. Buys and E. Havinga, *Tetrahedron*, 24, 4967, 1968.

CHAPTER II
INTRODUCTION

In an attempt to develop new synthetic methods for preparation of large rings we chose to investigate cyclization of vinyl azides by reaction with nitrosyl tetrafluoroborate as illustrated in Scheme I. This seemed attractive because of the availability of vinyl azides¹ from olefins and the recent demonstration that aryl and alkyl azides react with nitrosyl tetrafluoroborates² to give products expected from aryl or alkyl cations. If a similar course of reaction were followed in the reaction of vinyl azides with nitrosyl tetrafluoroborate it seemed likely that the vinyl cations³ generated could be induced to react with a double bond to form a carbon-carbon bond. Such a process if it occurred intramolecularly, could lead to the formation of large rings.

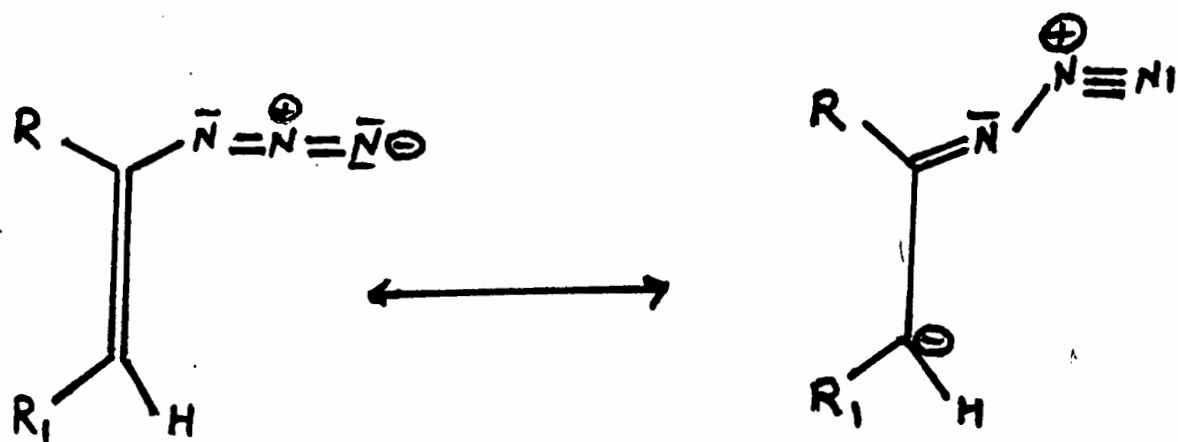
The reaction of vinyl azides with nitrosyl tetrafluoroborate, however, took a different course. Instead of the attack of NO^+ species at the terminal nitrogen of azide, the NO^+ species has been observed to attack the β -vinyl carbon. Subsequent loss of nitrogen and ring closure gave good yields of 1,2,5-oxadiazoles. This was not entirely unexpected since H.M.O. calculations⁴, infrared⁴, U.V.⁴ and n.m.r. spectra⁵ of vinyl azides, all suggest that the azide group acts as an electron donating group when in conjugation with an alkene. This would necessarily imply an increased electron density at the vicinal carbon atom of vinyl azides, Fig. X. The view that the

Scheme II



β -carbon of vinyl azides possesses significant nucleophilic character is further supported by the recent report⁶ of acid hydrolysis of vinyl azides. In acids vinyl azides rearrange irreversibly to give amides. The similarity in the ratio of amides and lactams obtained from the acid hydrolysis of vinyl azides and the Schmidt reaction of the corresponding ketones has been suggested⁶ to indicate the involvement of the same intermediate in both reactions. The proposed⁶ pathway for acid catalysed vinyl azide hydrolysis is shown in Scheme III. These properties make vinyl azides a logical choice for reactions with electrophiles. This work hence reports and discusses reactions of vinyl azides with various electrophiles.

FIGURE X



CANONICAL FORMS OF VINYL AZIDES

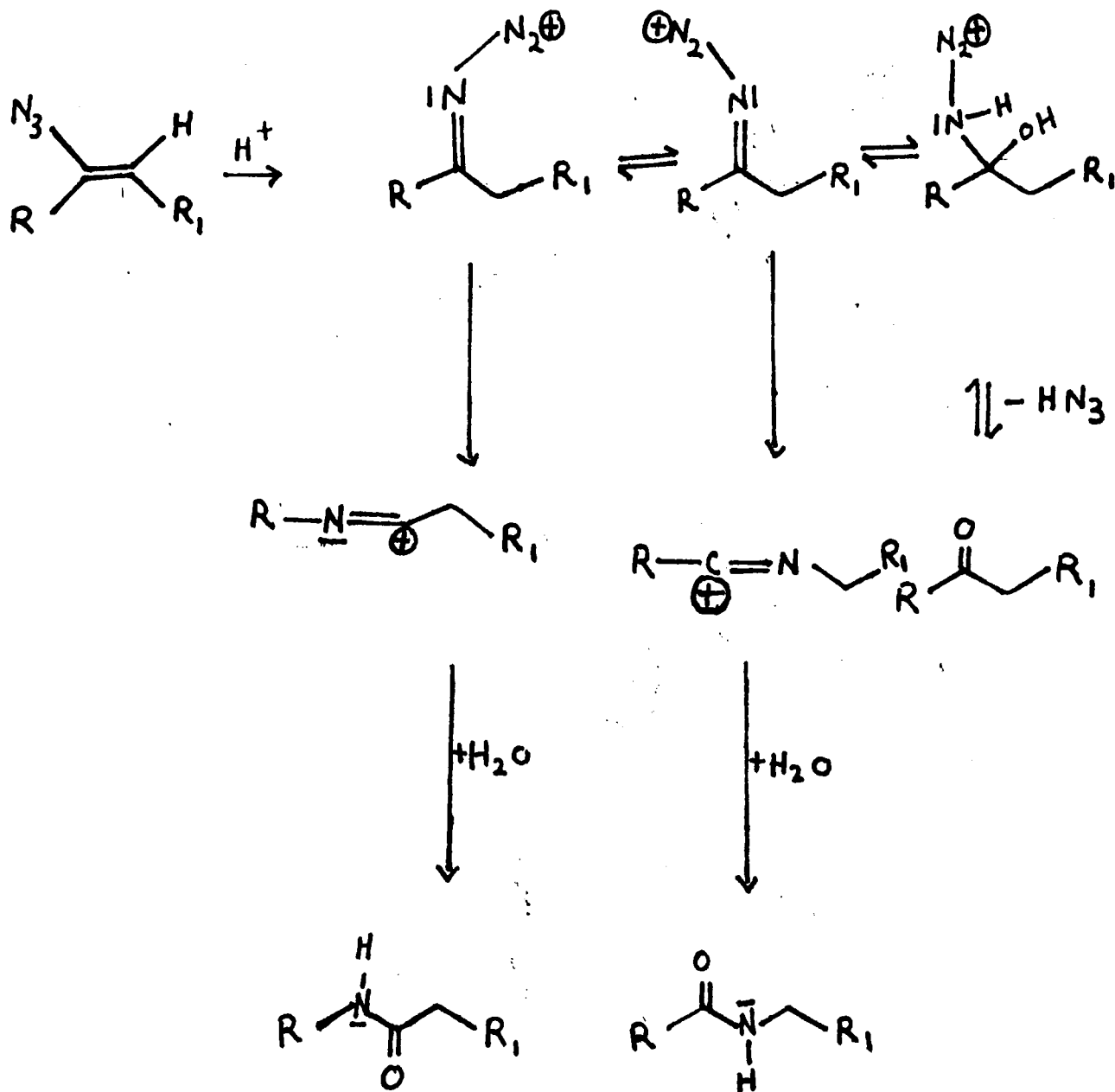
RESULTS AND DISCUSSIONS

The reaction of trans-2-azido-2-butene (1b) with nitrosyl tetrafluoroborate in acetonitrile at 0°C for 30 minutes followed by addition of water and extraction gave 80% of 3,4-dimethyl-1,2,5-oxadiazole (2a) 11% of N-ethyl acetamide (3a) and 6% of N-methyl propionamide (4a). When the same reaction was allowed to proceed for 18 hours 94% of 3,4-dimethyl-1,2,5-oxadiazole (2a)⁷ and 1% of N-ethyl acetamide (3a)⁸ and N-methyl propionamide (4a)⁸ were isolated Scheme IV.

The possibility that N-ethyl acetamide and N-methyl propionamide (4a) are precursors of the oxadiazoles was easily ruled out on the basis of literature reports^{9,10} which indicated that N-nitrosoamides formed by reaction of amides with nitrosyl chloride decompose thermally or in acid gave products outlined in Scheme V and not 1,2,5-oxadiazoles.

The reaction of cis-2-azidocyclooctene (1c) with nitrosyl tetrafluoroborate in acetonitrile at -10°C for 30 minutes gave 3,4-hexamethylene-1,2,5-oxadiazole (2b) and cyclooctyl lactam in 85% and 9% yields respectively. The production of both 3,4-hexamethylene-1,2,5-oxadiazole (2b) and cyclooctyl lactam can be rationalised according to Scheme IV which is constructed in agreement with Scheme III.

To check the possibility that the amides produced in the reaction of cis-2-azido cyclooctene (1c) with nitrosyl tetrafluoroborate arise from the backmann rearrangement of the oxime, which may be produced in the reaction, oxime of



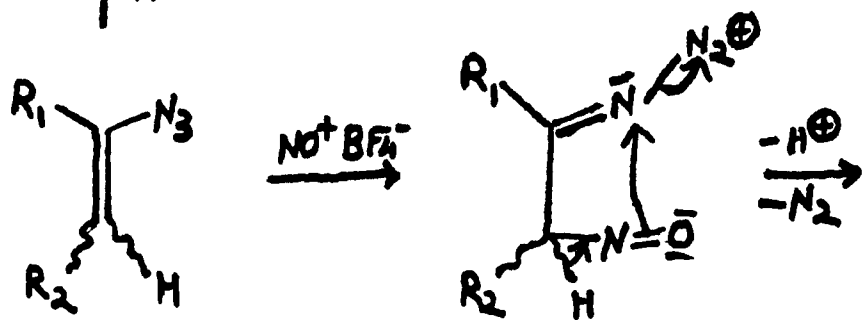
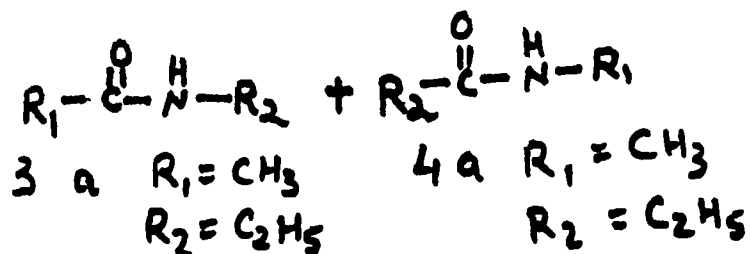
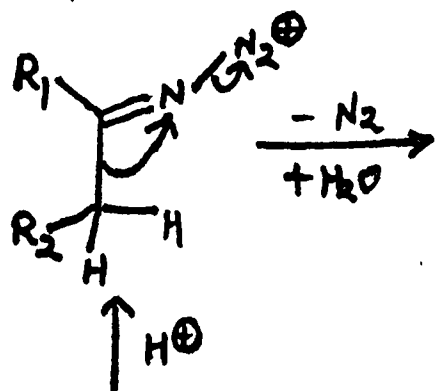
SCHEME III

2-butanone and cyclooctanone were treated with glacial acetic acid. No reaction was observed. Even the treatment with concentrated hydrochloric acid in ether at room temperature for 18 hours did not give amides. These results suggest that amides are formed via acid catalysed hydrolysis of unreacted azides during the workup of the NOBF_4 reaction (Scheme IV).

Similarly the reaction of trans-2-azido-2-butene (1b) with nitryl tetrafluoroborate in ether, at -10°C for 1 hour followed by careful distillation gave 52% yield of 3,4-dimethylfuroxan. Prolonging the reaction for 18 hours, gave after careful distillation an 84% yield of 3,4-dimethylfuroxan. The production of N-ethyl acetamide (3a) and N-methyl propionamide (4a) was negligible in the later case. This reaction has a close analogy in literature. It has been shown that in the reaction of trans-2,3-dinitro-2-butene with sodium azide the cis-2-azido-3-nitro-2-butene intermediate proceeds directly to give 3,4-dimethylfuroxan¹¹. The mechanism proposed for this conversion is in agreement with the proposed Scheme IV.

The efficiency of the reaction of vinyl azides with nitrosyl tetrafluoroborate led us to consider reaction of other potential electrophiles with vinyl azides with a view to developing new routes to small ring heterocycles.

SCHEME IV

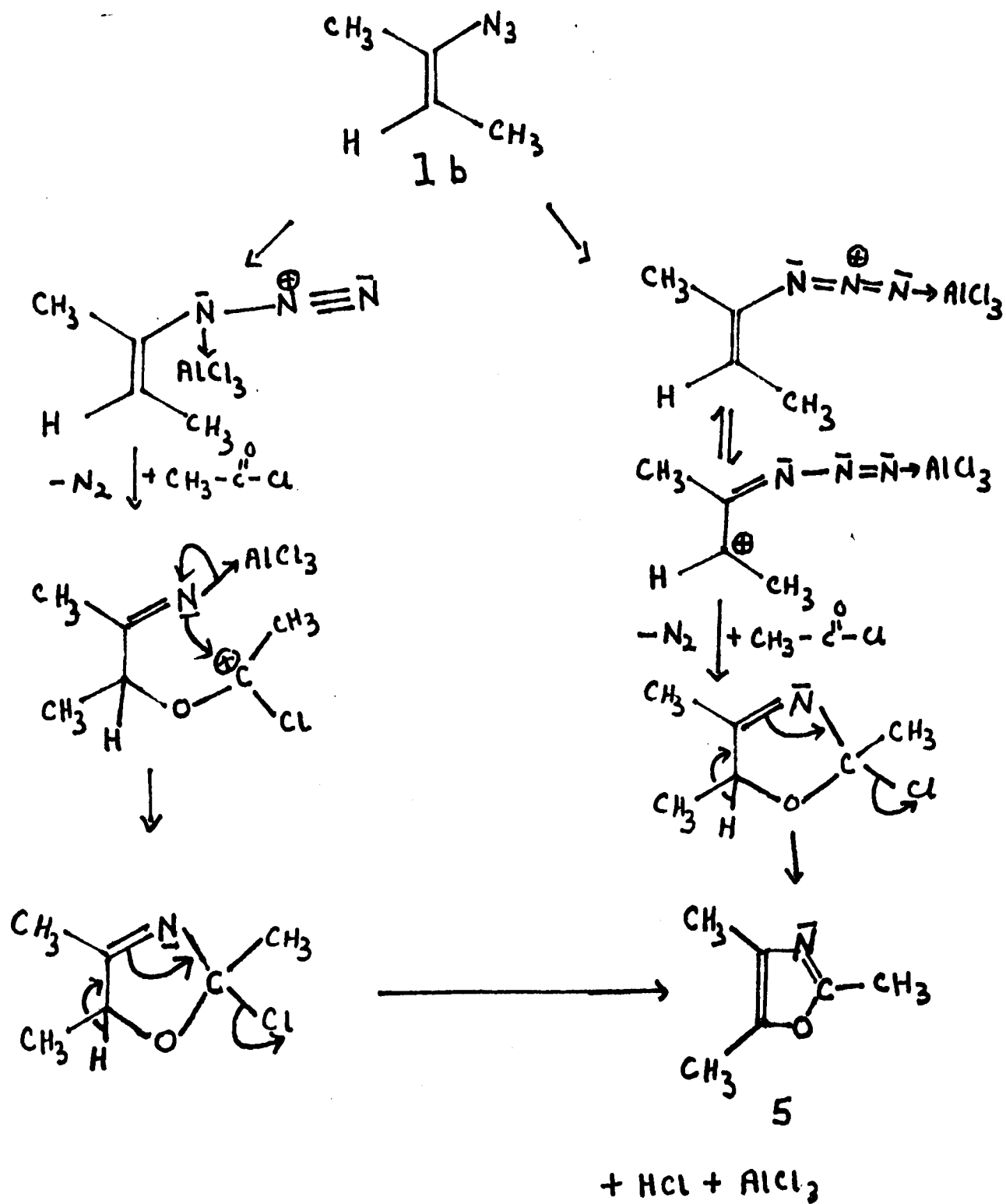


- 1 a $\text{R}_1 = \text{R}_2 = \text{CH}_3$ (trans)
 b $\text{R}_1 = \text{R}_2 = (\text{CH}_2)_6$

- 2 a $\text{R}_1 = \text{R}_2 = \text{CH}_3$
 b $\text{R}_1 = \text{R}_2 = (\text{CH}_2)_6$

Reaction of acetyl chloride with trans-2-azido-2-butene (1b) in ether at room temperature for 18 hours gave (after hydrolytic work up) as the only identifiable products N-ethyl acetamide (3a) and N-methyl propionamide (4a). In presence of one mole aluminum chloride the same reaction in ether proceeded smoothly at room temperature to give (after hydrolytic work up) a 75% yield of 2,4,5-trimethyl oxazole (5)¹² (Scheme V_I). The product obtained in this reaction is difficult to rationalise in terms of Scheme IV. A possible explanation for the course of this reaction may lie in the ability of vinyl azides to co-ordinate with Lewis acids at either the terminal or alkyl substituted azido nitrogen¹³. Such co-ordination would result in reduction of the electron density on the carbon atom of the vinyl azide (Figure XI). If such a co-ordination occurred the formation of 2,4,5-trimethyl oxazole (5) is explicable in terms of Scheme V. This reaction is analogous to that observed between azirines and benzoyl chloride¹⁴. However the possibility that azirine or chloro aziridine (the proposed intermediates for the azirine-benzoyl chloride reaction¹⁴), may be the intermediate in the present case seems quite remote because of the presence of aluminum chloride. Alternatively 1,3 dipolar cyclo addition of $\underline{\text{C}}-\text{C}=\underline{\text{N}}$ to the carbonyl bond seems an attractive possibility. However, as discussed later the reaction of dimethyl acetylene dicarboxylate with trans-2-azido-2-butene

SCHEME VI



in presence of AlCl_3 failed to give the expected cycloaddition of $\overset{+}{\text{C}}-\text{C}=\text{N}$ dipole. Hence a better description of the reaction of (1b) with acetyl chloride seems to be as outlined in Scheme VI.

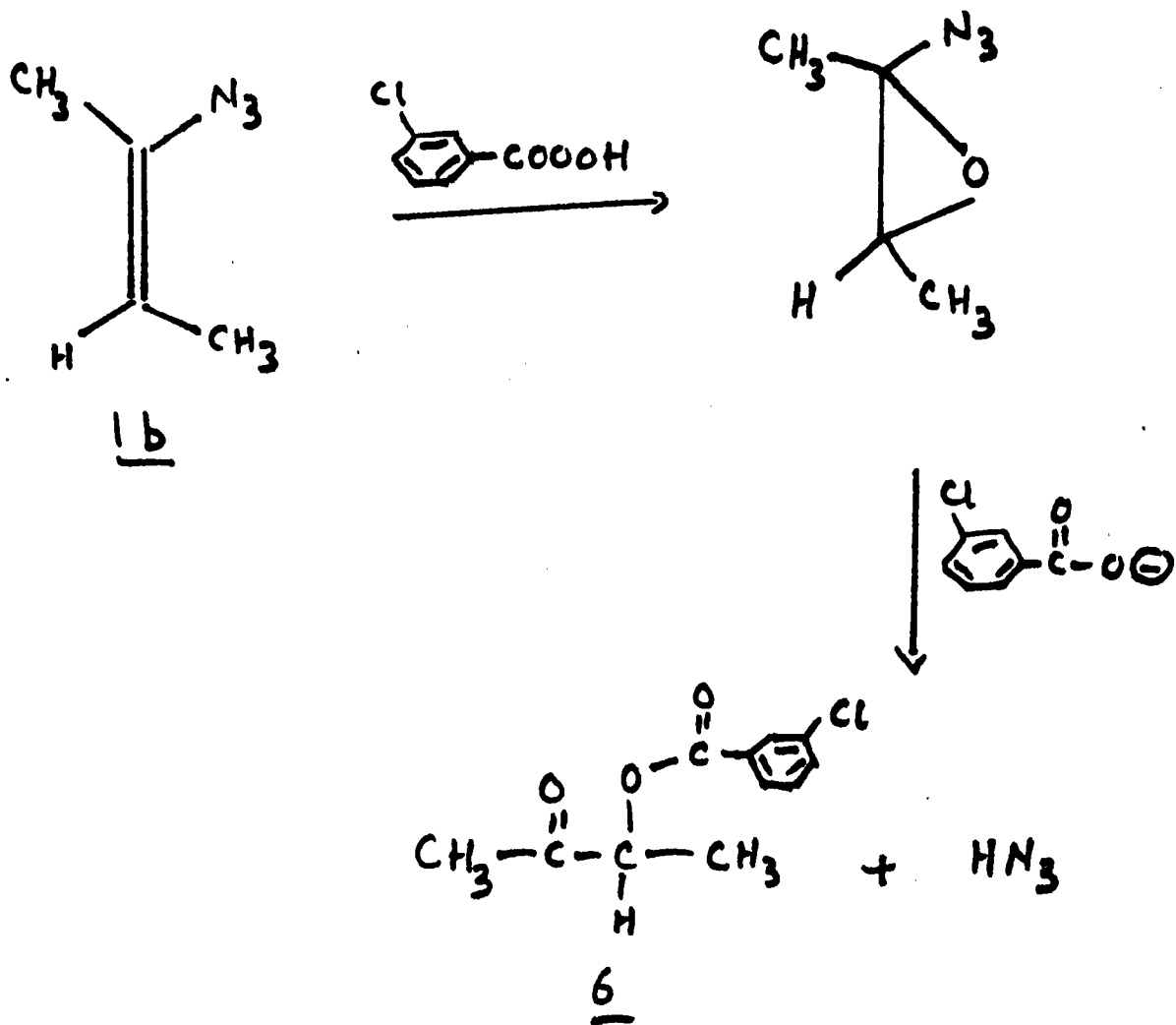
Attempts to elucidate the mechanistic path of the azide acyl chloride reaction were undertaken. A solution of aluminum chloride in deuteriochloroform was added to a solution of trans-2-azido-2-butene (1b) in an n.m.r. tube at -20°C . Under such conditions no nitrogen evolved but an azide-aluminum chloride complex precipitated. Thus while the resonances due to trans-2-azido-2-butene (1b) disappeared no new resonances were observed. Approaching the experiment in a different fashion a known amount of acetyl chloride and aluminum chloride were dissolved in dimethylsulfide, in an n.m.r. tube at -50°C . As expected the methyl resonances of acetyl chloride shifted to lower field. However addition of trans-2-azido-2-butene to this solution at -50°C , produced a slurry which precipitated. Thus these experiments only showed that aluminum chloride complexed with azide in presence or absence of acetyl chloride to give a complex which was insoluble in chloroform or dimethyl sulfide.

In an effort to extend this reaction to other electrophiles trans-2-azido-2-butene was reacted with metachloroperbenzoic acid in ether (Scheme VII). After hydrolytic work up a 43% yield of 3-chlorobenzoxy-2-butanone (6) was obtained. This product is not in agreement with the expected electrophilic

attack of an OH^+ species at the β -vinyl carbon. However if one considers the electrophilicity of the OH^+ species as compared to H^+ , NO^+ or NO_2^+ species as well as the lower nucleophilicity of β carbon of vinyl azides as compared to enamines^{5,15} it would not be difficult to visualize the production of 3-metachlorobenzoy-2-butanone (6) as a result of direct internal participation reaction as outlined in Scheme VII which has direct similarity with Scheme VI.

The reaction of trans-2-azido-2-butene (1b) with bromine proceeded smoothly at ice-methanol temperature with vigorous evolution of nitrogen, (Scheme VIII). The production of 13% yield of 3-bromo-2-butanone (7) can be easily rationalised in terms of Scheme III. However, the major product of the reaction is 31% yield of 1,3-dibromo-2-butanone (8). While it has been reported¹⁶ that in the presence of HBr a mixture of monobromo and dibromo -2-butanones equilibrate so that at 10 hours the predominant product is 1,3-dibromo-2-butanone (8), in the present case the predominance of 1,3-dibromo-2-butanone (8) is not likely dependent on this equilibration, since at 1 hour the major product was 1,3-dibromo-2-butanone (8) and not 3-bromo-2-butanone (7). In addition allowing the mixture to stand for 18 hours did not change the ratio significantly. The production of 1,3-dibromo-2-butanone (8) can thus be rationalised on the basis

SCHEME VII



of Scheme VIII. Recently Hassner²² has reported reaction of bromine with several vinyl azides and our observations are in agreement with his work.

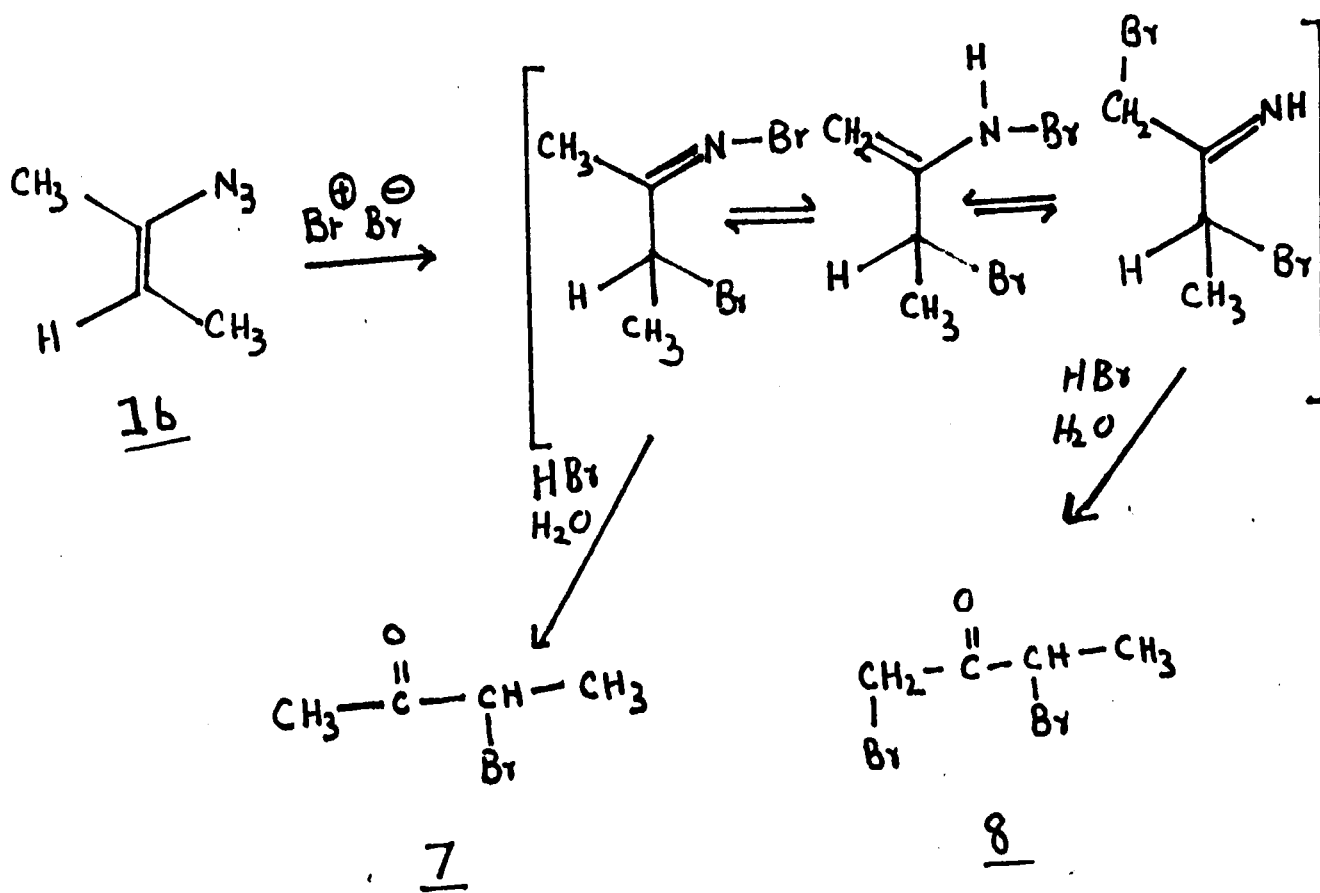
The facile reaction of acetyl chloride with vinyl azides led us to investigate the reactions of vinyl azides with ketene dimer, phenyl isocyanate, benzyl chloride, allyl chloride, carbon disulfide, phenyl chloroformate, dimethyl acetylene dicarboxylate and phenyl diazonium tetrafluoroborate. Relatively clean reaction was observed with carbon disulfide and dimethyl acetylene dicarboxylate.

The reaction of trans-2-azido-2-butene (1b) with carbon disulfide proceeded smoothly at room temperature in the presence of aluminum chloride. However when the reaction mixture was diluted with base the products underwent extensive decomposition giving a green black residue. Additional work should be done on this reaction using a resonance stabilised vinyl azide which may yield stable products.

The reaction of trans-2-azido-2-butene (1b) with dimethyl acetylene dicarboxylate gave a 1:1 or 2:1 adduct of dimethyl acetylene dicarboxylate and azide depending on the reaction procedure.

When trans-2-azido-2-butene (1b) was added dropwise to an ethereal solution containing excess of dimethyl acetylene dicarboxylate and aluminum chloride no nitrogen was evolved. The reaction gave an adduct containing one mole of trans-2-azido-2-butene (1b) and two moles of dimethyl

SCHEME VIII



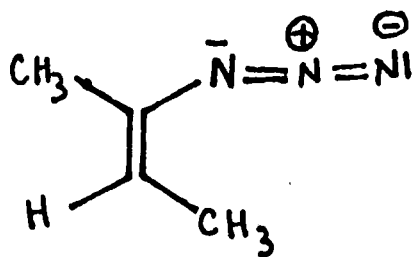
acetylene dicarboxylate. The n.m.r. spectrum of the 2:1 adduct contained four three proton singlets at δ 4.00, 3.95, 3.85 and 3.80, attributable to the four methyl groups of the ester functions, a one proton quartet at δ 3.28 ($J=7\text{Hz}$) attributable to a hydrogen geminal to a methyl group, one methyl singlet at δ 2.03 and one methyl doublet at δ 0.95 ($J=7\text{Hz}$) coupled to the one proton quartet. These data suggests two structural possibilities, 9 and 10 for the adduct. Both of these can be rationalised mechanistically (Scheme IX).

Evidence in favour of structure 9 was obtained by observation that the 2:1 adduct rearranged upon heating to 170°C . Thus heating the adduct caused it to undergo thermal rearrangement to compounds possessing vinyl methyl resonances in the n.m.r. The n.m.r spectra of the thermolysis products revealed a major component (11)¹¹ having one proton quartet at δ 6.9 ($J=7$) attributable to a vinylic proton, four three proton singlets at δ 4.10, 3.90, 3.76 attributable to four methyl groups on ester functions, a three proton singlet at δ 2.88 attributable to vinylic methyl group next to a hetero atom, and a three proton doublet at δ 1.75 ($J=7$) attributable to a vinylic methyl group geminal to the vinylic proton. This observation is clearly compatible with the electrocyclic ring opening of the cyclobutene ring in 9 but not expected of 10.

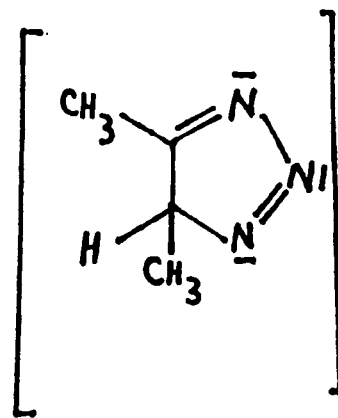
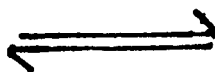
A priori one can postulate four possible dienes (11-14) arising from conrotatory opening of the two possible isomers 9a and 9b of a cyclobutene ring with the substitution in 9 (Scheme IX). It has been reported¹⁷ that a vinyl methyl group trans to carbomethoxy group resonates at higher field than the vinyl methyl of the corresponding cis isomer. The same phenomenon is observed for a vinyl methyl resonance in cis and trans-2-azido-2-butenes^{1,5} (Table III). The n.m.r. data clearly shows that the terminal vinyl methyl group of the major product resonates at higher field than the same group of the minor product. In contrast the resonance of the vinyl methyl group associated with nitrogen bearing carbon and the terminal vinylic proton, in the major product are shifted downfield relative to these resonances in the minor product. This data is in agreement with diene isomers 13, 14 where 13 is the major product and 14 the minor isomer. Thus the correct stereochemistry of the adduct 9 is deduced to be as shown in Scheme X structure 9b.

While the catalysed reaction of trans-2-azido-2-butene (1b) with excess of DMAD gave product 9b the reaction in which one mole of DMAD was added dropwise to a solution containing one mole of trans-2-azido-2-butene (1b) and

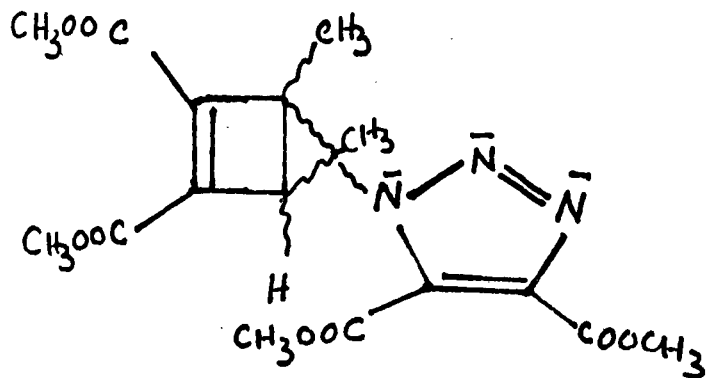
SCHEME IX



1b

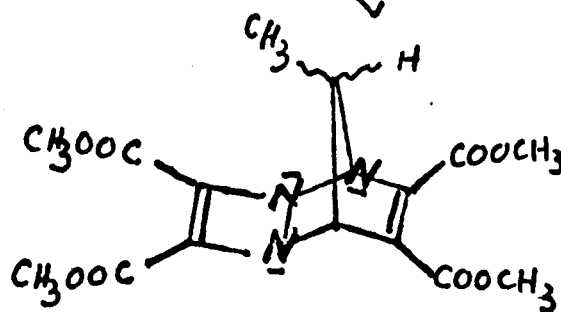
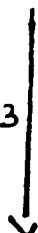


AlCl₃ | 2 DMAD



9

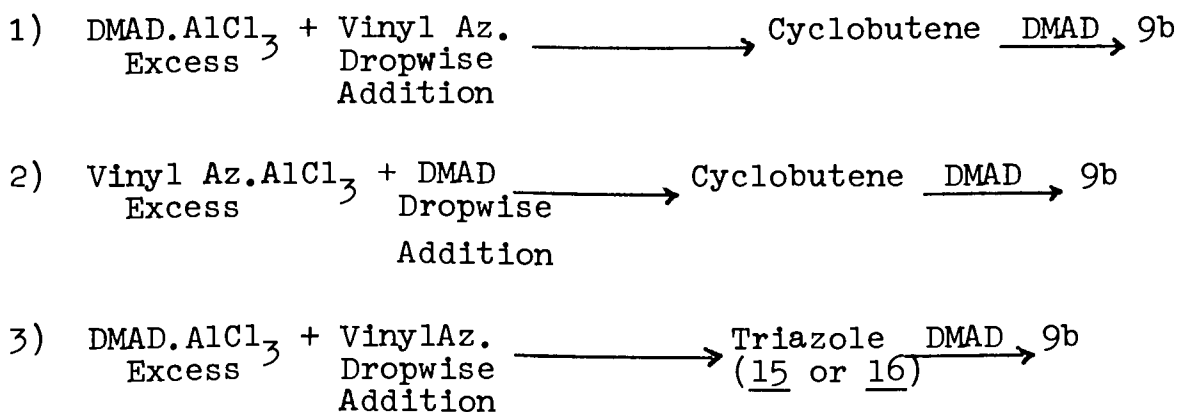
AlCl₃ | 2 DMAD



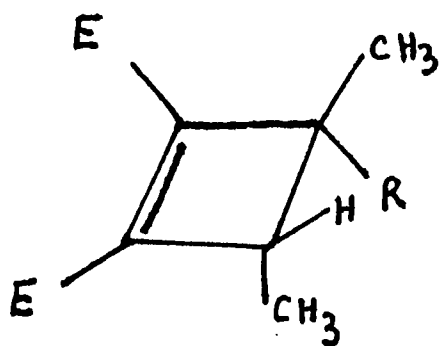
10

aluminum chloride gave only corresponding triazole¹⁸ (15). The same triazole (15) could be also obtained by mixing DMAD with trans-2-azido-2-butene (1b). However, in the latter case formation of triazole (15) is significantly slower but the yield of triazole (15) is significantly higher (90% vs 55%). The triazole (15) obtained is unreactive and attempts to synthesise product 9b by adding excess DMAD to triazole (15) in presence of aluminum chloride failed. Dropwise addition of one mole of trans-2-azido-2-butene (1b) to one mole of DMAD and one mole of aluminum chloride gave 13% of 9b and 23.5% of triazole (15). Dropwise addition of cis-2-azido-2-butene (1a) to excess DMAD in presence of aluminum chloride gave only 3% of 9b and 20% of triazole (16).

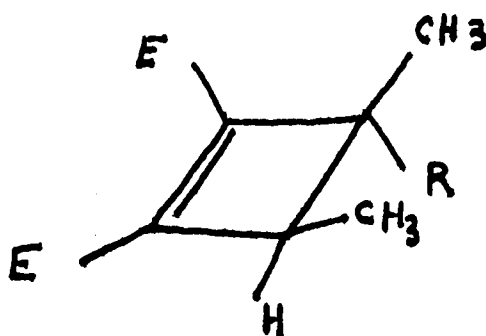
A priori four reaction paths leading to adduct 9b may be visualized as follows:



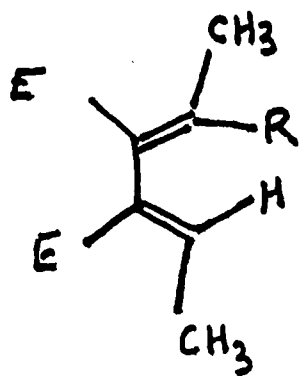
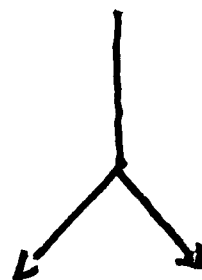
SCHEME X



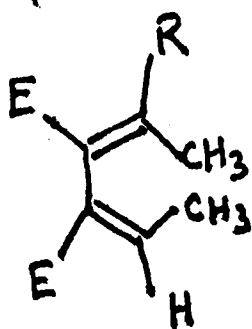
9a



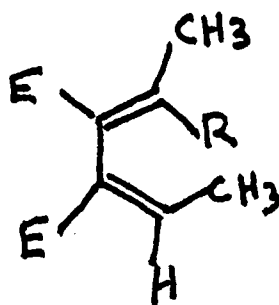
9b



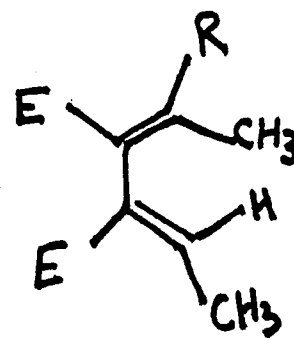
11



12



13



14

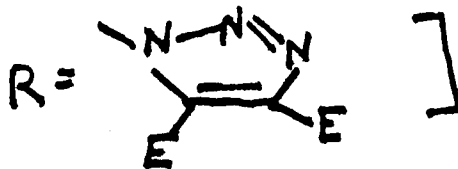
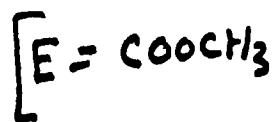
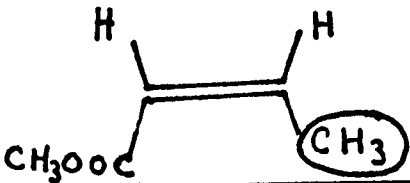
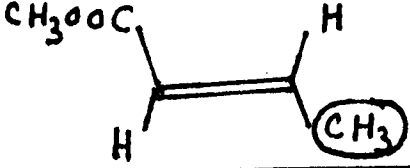
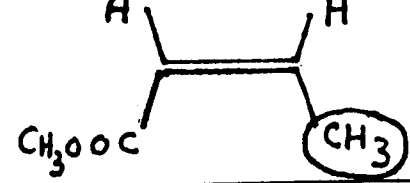
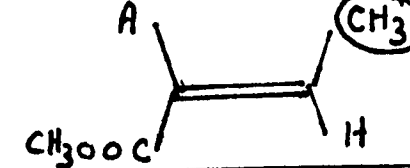
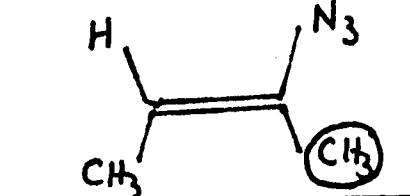
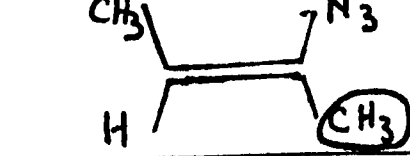
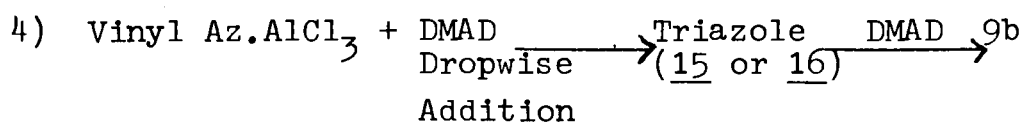
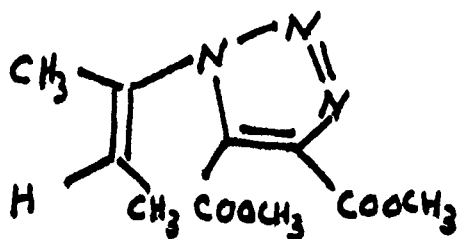


TABLE III

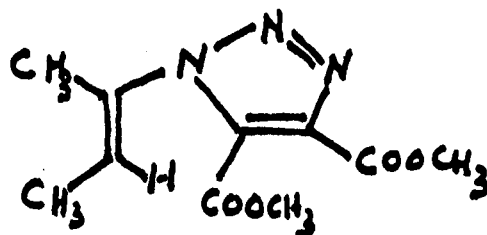
COMPOUNDS	CHEMICAL SHIFT IN δ UNITS	REL: CHEM. SHIFT CIS-TR
 <p>Chemical structure: A trans-alkene with a CH_3OOC group on the left carbon and a CH_3 group on the right carbon. Both hydrogens are pointing upwards.</p>	2.14	0.26
 <p>Chemical structure: A cis-alkene with a CH_3OOC group on the left carbon and a CH_3 group on the right carbon. The left hydrogen points up and the right hydrogen points down.</p>	1.88	
 <p>Chemical structure: A trans-alkene with an A group on the left carbon and a CH_3 group on the right carbon. Both hydrogens are pointing upwards.</p>	2.20	0.47-0.20
 <p>Chemical structure: A cis-alkene with an A group on the left carbon and a CH_3 group on the right carbon. The left hydrogen points up and the right hydrogen points down.</p>	1.73 - 2.00	
 <p>Chemical structure: A trans-alkene with a CH_3 group on the left carbon and an N_3 group on the right carbon. Both hydrogens are pointing upwards.</p>	1.95	0.23
 <p>Chemical structure: A cis-alkene with a CH_3 group on the left carbon and an N_3 group on the right carbon. The left hydrogen points up and the right hydrogen points down.</p>	1.72	



From observations described above one can easily rule out paths 2, 3 and 4 since product 9b does not arise from the addition of triazole (15) to DMAD or from dropwise addition of DMAD to trans-2-azido-2-butene (1b), and aluminum chloride. Since cis-2-azido-2-butene (1a) gives product 9b a 2+2 cycloaddition of DMAD and trans-2-azido-2-butene (1b) or cis-2-azido-2-butene is ruled out. The most reasonable explanation is that DMAD-aluminum chloride complex adds in a stepwise fashion to trans-2-azido-2-butene (1b) or cis-2-azido-2-butene (1a) to give thermodynamically most stable cyclobutene azide intermediate. This intermediate then undergoes fast 1,3-dipolar cycloaddition to DMAD giving product 9b.



15



16

The following general conclusions can be drawn from this study:

- (a) The electrophiles like H^+ , NO^+ , NO_2^+ and Br^+ attack at β -vinyl carbon of vinyl azides and where cyclisation is possible heterocycles are formed.
- (b) Aluminum chloride seems to co-ordinate with vinyl azides hence tends to modify the direction of attack of electrophiles, e.g. reaction of acetyl chloride with vinyl azide in presence of aluminum chloride.
- (c) Since the work has been done only with symmetrically substituted vinyl azides it remains to be seen whether unsymmetrical vinyl azides, react with the above electrophiles to give high yield of expected heterocycles. Preliminary work has shown that in case of unsymmetrically substituted vinyl azides the yield of products decreases while number of products increases. This is reasonable because in case of symmetrical vinyl azides several mechanisms can be written to give the same end product. However in case of unsymmetrical vinyl azide each of the mechanisms gives a different product. This possibly may be the principal limitation of these useful reactions.

EXPERIMENTAL

Infrared spectra were recorded with a Perkin Elmer S.P. 457 spectrometer, nuclear magnetic resonance (n.m.r.) spectra were obtained with the Varian A-56/60 spectrometer using tetramethylsilane (TMS) as an internal standard, and deuteriochloroform or carbontetrachloride as solvents. Melting points were taken on a Fischer-John's apparatus and are uncorrected. Ultraviolet (U.V.) spectra were recorded using Unicam Sp 800 spectrometer and mass spectra (m.s.) were taken using Hitachi Perkin Elmer RMU6E spectrometer, ionization voltage 80 e.V.

Preparation of cis-2-azido cyclooctene (1c) and trans-2-azido-2-butene

These were prepared by the method of Hassner¹⁹. cis-2-azido cyclooctene (1c) was purified by chromatography on neutral alumina (Brockmann Act. I 80 - 200 mesh) using pet ether (b.p. 30-60°C) as the eluent. Trans-2-azido-2-butene (1b) and cis-2-azido-2-butene (1a) were purified by distillation at 50°C (10mm pressure).

Reaction of trans-2-azido-2-butene (1b) with nitrosyl tetrafluoroborate

A soln of trans-2-azido-2-butene (1b, 1g, 10.3m mol.) and 10 ml of acetonitrile was stirred under dry N₂. To this soln was added nitrosyl tetrafluoroborate (1.2g, 20m mol.)

over a period of 30 min, keeping the reaction mixture at 0°C. One half of the reaction mixture was diluted with water and extracted with a three 100 ml portions of ether. The combined extract was carefully distilled to remove ether and the residue was analysed on g.l.p.c. using (15% Versamide 900 on Chrom. W, A/W. DMCS, 45/60, temp. program 50-150°C at 10°C/min, 3' X 1/8" column, 0-chlorotoluene as an internal standard). The calculations showed 80% (0.37g) yield of 3,4-dimethyl-1,2,5-oxadiazole (2a), 11% (0.1g) yield of N-ethyl acetamide (3a) and 6% (0.05g) yield of N-methyl propionamide (4a).

The other half of the reaction mixture was allowed to stir for 18 hrs after which it was extracted as above. Analysis by g.l.p.c. under the same conditions as above revealed 94% (0.45g) yield of 3,4-dimethyl-1,2,5-oxadiazole (2a) and 1% (0.0083g) of N-ethyl acetamide (3a) and N-methyl propionamide (4a).

The identity of individual peaks on g.l.p.c. was established by isolation of 3,4-dimethyl-1,2,5-oxadiazole (2a), N-ethyl acetamide (3a) and N-methyl propionamide (4a) by the following method:

A soln of trans-2-azido-2-butene (1b, 1g, 10.3 m mol) and 10 ml of acetonitrile was stirred under dry N₂. To this soln was added nitrosyltetrafluoroborate (1.2g, 20m mol)

over a period of 30 min, keeping the reaction mixture at 0°C. After 1 hr of further stirring the mixture was diluted with water and extracted with three 100 ml portions of ether. Careful removal of the ether from the combined extract followed by fractional distillation of the extract gave 80% (0.74g) of 3,4-dimethyl-1,2,5-oxadiazole (2a), (lit. b.p.²⁰ 155-156°C Found b.p. 65°C at 20 mm). n.m.r. (CCl₄): δ 2.31 (6H)^{5,7} Calc. for C₄H₆N₂O: 98 Found (M)⁺: 98⁸

The residue (0.3g) was directly chromatographed on 20 g of SiO₂ (80-200 mesh). Elution with benzene: methanol (99:1) gave 1% (0.2g) N-ethyl acetamide (3a)

ν_{\max}^{film} : 3300, 2980, 1705, 1500, 1375, 1300 and 1150 cm⁻¹,
n.m.r. (CDCl₃): δ 7.45 (m, 1H, D₂O exch.), 3.16 (quintet, 2H, J=7Hz), 1.87 (s, 3H) and 1.08 (t, 3H, J=7Hz).
Calc. for C₄H₉NO: 87. Found (M⁺): 87.

Further elution with benzene: methanol (99:1) gave 6% (0.1g) N-methyl piperonamide (4a).

ν_{\max}^{film} : 3300, 2980, 1705, 1550, 1375, 1300 and 1150 cm⁻¹;
n.m.r. (CDCl₃): δ 4.8 (s, 1H, D₂O exch.), 2.8 (d, 3H, J=5Hz), 2.0 (q, 2H, J=7Hz) and 1.6 (t, 3H, J=7.5Hz).
Calc. for C₄H₉NO: 87 Found (M⁺): 87.

Reaction of Nitrosyl tetrafluoroborate with cis-2-azido cyclooctene (1c)

To a solution of cis-2-azido cyclooctene (1c, 1g, 6.62 m mol) in 10 ml of acetonitrile under dry helium was added with stirring nitrosyl tetrafluoroborate (0.89g, 7.6m mol) over a period of 30 min. The reaction mixture was kept at 0°C for 1 hr. The mixture was diluted with water and extracted with three 100 ml portions of ether. The combined ether extract was washed with 10% NaHCO₃ soln, and the ether was removed. The red-brown residue obtained (0.85 g) was directly chromatographed on 20g of SiO₂ (80-200 mesh). Elution with benzene gave 85.4% (0.76 g) of 3,4-hexamethylene-1,2,5-oxadiazole (2b).

$\nu_{\text{max}}^{\text{film}}$: 2920, 2860, 1450, 1410, 1180, 1010 and 930 cm⁻¹;

n.m.r. (CCl₄): δ 2.88 (t, 4H, J=6Hz) and 1.60 (m, 8H).

Calc. for C₈H₁₂N₂O: 152.0950, Found (M⁺) : 152.0959.

$\lambda_{\text{max}}^{\text{MeOH}}$: 220 m μ , ($\epsilon=2,420$).

Continued elution with 99% benzene: methanol (99:1) yielded 9% of cyclooctyl lactam m.p. 72.5-73°C (lit.²¹ m.p. 72-73°C)

$\nu_{\text{max}}^{\text{kBr}}$: 3280, 2820, 1700, 1550, 1450 and 710 cm⁻¹; n.m.r.

(CCl₄): δ 6.63 (m, 1H, D₂O exch), 3.35 (m, 2H), 2.28

(m, 2H) and 1.60 (m, 8H).

Calc. for C₈H₁₅NO: 141 Found (M⁺) = 141.

Treatment of 2-butanone oxime and cyclooctanone oxime
with glacial acetic acid and conc. hydrochloric acid:

2-butanone oxime (0.5g, 5m mol) was treated with 10 ml of glacial acetic acid at 40°C for 18 hr. No reaction was observed as ascertained from g.l.p.c. Hence 2-butanone oxime (0.5 g 5m mol) was treated with 1 ml of conc. HCl, 10 ml of ether and 1 ml of acetic anhydride, for 18 hrs. Dilution with water followed by extraction with ether gave, after evaporation of the ether, only oxime.

A similar treatment of cyclooctanone oxime (0.705 g, 5m mol.) did not give reaction.

Reaction of trans-2-azido-2-butene (1b) with glacial
acetic acid

A soln of trans-2-azido-2-butene (1b, 0.5 g, 5.2m mol.) in 2 ml of ether was stirred with 3ml of glacial acetic acid at 40°C for 20 hrs followed by distillation at 27°C (15 mm Hg). The distillate was analysed by g.l.p.c. (20% S E 30 on 60/80 chromosorb W DMCS A/W temp. program 50-150°C at 10°C/min, 3' X 1/8" column). In addition to solvent and acetic acid the distillate contained 2-butanone as confirmed by mixed injection.

The oily residue after distillation was chromatographed on 20 g of SiO₂ (80-200 mesh) using benzene methanol (99:1)

as eluent to give 67% (0.39 g) of N-ethyl acetamide

$\nu_{\text{max}}^{\text{film}}$: 3300, 2980, 1705, 1550, 1375, 1300 and 1150 cm^{-1}

n.m.r. (CDCl_3): δ 7.45 (m, 1H, D_2O exch.), 3.16 (quintet, 2H, $J=7\text{Hz}$), 1.87 (s, 3H), and 1.08 (t, 3H, $J=7\text{Hz}$).

Calc. for $\text{C}_4\text{H}_9\text{NO}$: 87 Found (M^+): 87.

Further elution with benzene: methanol (99:1) gave 20% (0.1 g) of N-methyl propionamide (4a).

$\nu_{\text{max}}^{\text{film}}$: 3300, 2980, 1705, 1550, 1375, 1300 and 1150 cm^{-1}

n.m.r. (CDCl_3): δ 4.8 (s, 1H, D_2O exch), 2.8 (d, 3H, $J=5\text{Hz}$), 2.0 (q, 2H, $J=7.5\text{ Hz}$) and 1.6 (t, 3H, $J=7.5\text{Hz}$)

Calc. for $\text{C}_4\text{H}_9\text{NO}$: 87. Found (M^+): 87

Reaction of trans-2-azido-2-butene (1b) with acetyl chloride

Trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) and acetyl chloride (0.4 g, 4.16 m mol.) were stirred at room temp in 20 ml of ether. No reaction was observed as ascertained from g.l.p.c. (20% S E 30 on 60/80 chromosorb W DMCS A/W, temp program 50-150°C at 10°C/min, 3' X 1/8" column).

The mixture was heated for 18 hr at 34°C. Following the removal of ether the only products obtained (g.l.p.c.) were N-ethyl acetamide (3a) and N-methyl propionamide (4a).

Reaction of trans-2-azido-2-butene (1b) with acetyl chloride in presence of equimolar quantity of aluminum chloride:

To acetyl chloride (0.81 g, 10 m mol.) in 10 ml of dry ether was added aluminum chloride (1.4 g, 10.5 m mol.).

This was followed by dropwise addition of trans-2-azido-2-butene (1b, 1.0 g, 10.4 m mol.) during 1 hr. The evolution of N_2 was instantaneous. After stirring for additional 8 hrs the mixture was quenched with 10% $NaHCO_3$ until the reaction mixture was slightly alkaline. Continuous extraction with ether followed by solvent removal gave 1.03 g of oil. Distillation at $65^\circ C$ (15 mm Hg) gave 75% (0.8 g) of 2,4,5-trimethyl oxazole (5) which was identified by comparison with an authentic sample¹².

$\nu_{\text{max}}^{\text{film}}$: 2920, 1650 and 150 cm^{-1} ; n.m.r.

(CCl_4): δ 2.03 (s, 3H), 2.17 (s, 3H) and 2.33 (s, 3H).

Calc. for $C_4H_6H_2O$: 111. Found (M^+): 111.

Preparation of 2,4,5-trimethyl oxazole¹²

Bromine (4.0 g, 250 m mol.) was added to 2-butanone (10.0 g, 140 m mol.) and potassium chlorate (5g) in 30 ml of water. After heating at $70^\circ C$ for 1 hr in presence of a sun lamp the mixture was extracted with distilled water. Removal of ether gave a mixture of 3-bromo-2-butanone and 1-bromo-2-butanone (15 g, 100 m mol.).

This mixture of bromoketones (2.5 g, 16.4 m mol.) was refluxed at $10^\circ C$ for 4 hr in presence of acetamide (4 g, 68.2 m mol.). The reaction was quenched with water. Extraction with ether and removal of solvent

gave 1.00 g of a mixture of 2-methyl-4-ethyl oxazole and 2,4,5-trimethyl oxazole in which the later predominated. Chromatography of this mixture on 30 g of SiO_2 (80-200 mesh) using benzene as a solvent gave 2,4,5-trimethyl oxazole 95% pure. Spectroscopic data and mixed injection of this sample with that obtained in previous experiment on g.l.p.c. (20% SE 30 on 60/80 chromosorb W DMCS A/W, temp program 50-130°C at 10°C/min, 3' X 1/8" column) established the identity of 2,4,5-trimethyl oxazole (5).

N.M.R. study of the complexation of trans-2-azido-2-butene (1b) with aluminum chloride

Trans-2-azido-2-butene (1b, 56.5 mg) was weighed into two n.m.r. tubes and each cooled to -80°C. To one tube was added 0.2 cc of toluene. To the other tube was added 0.2 cc of toluene saturated with (excess) aluminum chloride. The n.m.r. spectra were taken in the temperature range of -52°C to +20°C. Below -20°C no nitrogen was evolved, and there was no change in the spectra. However, above -20°C nitrogen was evolved in the tube containing aluminum chloride and a ppt settled. Thus while the signals due to trans-2-azido-2-butene (1b) in the tube containing aluminum chloride above -20°C decreased in intensity no new signals were observed.

N.M.R. study of the complexation of trans-2-azido-2-butene (1b) with aluminum chloride in presence of acetyl chloride

Acetyl chloride (4.5 mg) was weighed into two n.m.r. tubes and each tube cooled to -55°C . To one tube was added 0.5 ml of dimethyl sulfide while to other tube was added aluminum chloride (150 mg) dissolved in 0.5 ml of dimethyl sulfide and spectra run at -55°C . As expected the methyl resonance in acetyl chloride was shifted downfield. However, on addition of trans-2-azido-2-butene (1b, 5.00 mg) to each tube, a ppt formed in the tube containing aluminum chloride. Thus, while the resonances due to acetyl chloride and trans-2-azido-2-butene (1b) decreased in intensity no new resonances appeared. At -50°C no nitrogen was evolved.

Reaction of trans-2-azido-2-butene (1b) with ketene dimer

To trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) in 10 ml of dry acetonitrile was added, freshly distilled, ketene dimer (0.5 g, 5.6 m mol.). The mixture did not react at room temp. Heating at 80°C for 18 hrs gave a dark red mixture which on analysis on g.l.p.c. (20% SE 30 on 60/80 Chrom W DMCS A/W, temp program $50-250^{\circ}\text{C}$ at $10^{\circ}\text{C}/\text{min}$, 3' X $1/8''$ column) showed presence of at least sixteen products.

The same result was obtained when trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) was added dropwise to ketene dimer (0.5 g, 5.6 m mol.) and 0.5 g aluminum chloride dissolved in 20 ml of ether.

Thermal decomposition of ketene dimer gave similar results.

Reaction of trans-2-azido-2-butene (1b) with allyl chloride and benzyl chloride

The general procedure for the reaction was to add trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) to a stirred soln of the chloride in acetonitrile. Reaction was followed by g.l.p.c. at room temp as well as at refluxing temp.

Thus the reaction of allyl chloride (0.4 g 5.2 m mol.) with trans-2-azido-2-butene (1b) at room temp did not proceed. In refluxing acetonitrile no reaction between allyl chloride and trans-2-azido-2-butene (1b) was observed.

The reaction of benzyl chloride (0.56 g, 5.2 m mol.) and trans-2-azido-2-butene (1b) in 10 ml of acetonitrile did not give any reaction either at room temp or in refluxing acetonitrile .

Reaction of trans-2-azido-2-butene (1b) with allyl chloride and benzyl chloride in presence of aluminum chloride

Dropwise addn of trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) to a stirred soln of allyl chloride (0.4 g, 5.2m mol.)

and aluminum chloride (0.3 g) in 10 ml of ether gave evolution of N_2 . After stirring for 18 hrs the slurry was quenched with 10 % $NaHCO_3$ and the organic products continuously extracted with ether. Analysis of the crude mixture after removal of solvent, on g.l.p.c. (20% SE 30 on 60/80 Chrom W, DMCS, A/W, temp program 50-250°C at 10°C/min, 3' X 1/8" column), indicated presence of N-ethyl acetamide (3a) and N-methyl propionamide (4a), and unreacted allyl chloride.

Reaction of trans-2-azido-2-butene (1b) with cyclohexene in presence of aluminum chloride

Addition of cis-2-azido-cyclooctene (1c, 0.3 g, 2.0 m mol.) to 0.1 g of aluminum chloride dissolved in 10 ml of cyclohexene gave evolution of N_2 . The mixture was heated at 60°C for 12 hrs and then extracted as before with ether. The ether extract upon evaporation gave 72% (0.214 g) cyclooctyl lactam.

Reaction of trans-2-azido-2-butene (1b) with carbon disulfide

To a soln of 0.5 g of aluminum chloride in 10 ml of carbon disulfide was added trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.). There was a vigorous reaction with evolution of N_2 . After stirring over night the soln

was neutralized with aqueous NaHCO_3 . At once the mixture turned dark green. Extraction with ether or steam distillation of this dark green mixture gave products which turned dark green on standing. Separation and collection using T.L.C. or g.l.p.c. methods gave fractions which turned dark as soon as they were collected.

Reaction of trans-2-azido-2-butene (1b) with phenyl isocyanate

Trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) was added dropwise to a soln of phenyl isocyanate (0.5 g, 4.2 m mol) in 20 ml of ether. No reaction was observed either at room temp or in refluxing ether. However, when trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) was added dropwise to a soln of phenyl isocyanate (0.5 g, 5.2 m mol.) and 0.5 g, of aluminum chloride in 20 ml of ether, there was evolution of N_2 at room temp. After stirring for 18 hrs the mixture was diluted with aqueous NaHCO_3 and continuously extracted with ether. Evaporation of solvent gave semi crystalline material which was recrystallized from ether-pet ether, to give 60% (0.3 g) of biphenyl urea m.p. 238°C (lit m.p.²³: 238°C) which was identified by comparison with an authentic sample. The mother liquor was carefully distilled to remove ether-pet ether and then distillation continued to give 13.7% (0.15 g)

yield of N-phenyl-ethylformamide.

$\nu_{\text{max}}^{\text{film}}$: 3060, 2980, 1730, 1595, 1540, 1500, 1445, 1310,
1270, 1230, 750, 690 cm^{-1} ; n.m.r.

(CDCl_3): δ 7.33 (m, 5H), 4.23 (q, 2H, $J=7\text{Hz}$), 1.30
(t, 3H, $J=7\text{Hz}$).

Calc. for $\text{C}_9\text{H}_{11}\text{NO}_2$: 165. Found (M^+): 165.

$\lambda_{\text{max}}^{\text{MeOH}}$: 238, 206.

Reaction of trans-2-azido-2-butene (1b) with phenyl chloroformate

Trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) was added to a stirred mixture of phenyl chloroformate (0.8 g, 5.1 m mol.) and aluminum chloride (0.7 g, 4.0 m mol.) over a period of 1/2 hr. The mixture was kept at -10°C throughout addition. After 18 hrs, of further stirring at room temp the mixture was neutralized with aqueous NaHCO_3 and the organic products were continuously extracted with ether. Evaporation of ether from ether extract gave 0.8 g of red brown oil which contained two products separated by preparative g.l.p.c. (20% SE 30 on 60/80 Chrom W, DMCS, A/W, at 110°C , 6' X 1/4" glass column), to give 80% (0.4 g) phenol and 18% (0.2 g) diphenyl carbonate.

Calc. for $\text{C}_{13}\text{H}_{10}\text{O}_3$: 214. Found (M^+): 214.

Reactions of trans-2-azido-2-butene (1b) with phenyl diazonium tetrafluoroborate:

Phenyl diazonium tetrafluoroborate (1.5 g, 5.2 m mol.) was dissolved in 10 ml of acetonitrile. To this was added trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.). Slow evolution of N₂ was observed. After 18 hrs, of further stirring the reaction was quenched with aqueous base and then extracted with three 100 ml portions of ether. The ether was removed from ether extract and the semi solid residue was recrystallized thrice from ether-pet ether, to give 20% (0.14 g) of N-phenylacetamide

$\nu_{\text{max}}^{\text{KBr}}$: 3270, 2980, 1700, 1592, 1480, 1430, 1365, 1320, 1260, 752, and 690 cm⁻¹; n.m.r.

(CDCl₃): δ 7.28 (m, 5H), 2.10 (s, 3H) and 8.37 (broad, 1H, D₂O, exch).

Calc. for C₈H₉NO: 135. Found (M⁺): 135.

33% (0.25 g) phenol and 40% N-ethyl acetamide (3a) and N-methyl propionamide (4a).

In a separate experiment phenyl diazonium tetrafluoroborate (1.5 g, 5.2 m mol.) was dissolved in 20 ml of acetone and to it was added trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.). After 18 hrs of stirring no reaction was observed. Slight warming decomposed phenyl diazonium tetrafluoroborate but trans-2-azido-2-butene (1b) was recovered unchanged.

Reactions of trans-2-azido-2-butene (1b) with bromine

To trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) in 20 ml of chloroform, bromine (0.8 g, 5.0 m mol.) dissolved in 10 ml of chloroform was added dropwise, while cooling the mixture in ice-methanol bath. The evolution of N₂ was instantaneous. The mixture was then allowed to stir overnight, after which it was quenched with aqueous NaHCO₃. The organic products were extracted with chloroform. Removal of solvent yielded 0.6 g of a brown oil.

Separation of the mixture by g.l.p.c. (20% SE 30 on 60/80 Chrom W DMCS A/W; 80°C; 6' X 1/4" column) gave 31% (0.4 g) 1,3-dibromo-2-butanone (8).

$\nu_{\text{max}}^{\text{film}}$: 2980, 1720, 1440, 1380, 1335, 1100, 1020 and 970 cm⁻¹;

n.m.r. (CDCl₃): δ 4.85 (q, 1H, J=7Hz); 4.23(q, (AB) 2H, J=19,12) and 1.81 (d, 3H, J=7Hz).

and 13% (0.1g) of 3-bromo-2-butanone (7). In addition 20% of N-ethyl acetamide (3a) and N-methyl propionamide (4a) were detected, as ascertained by mixed injection with authentic samples.

Time study of the reaction of trans-2-azido-2-butene (1b) with bromine:

Bromine (83 mg) dissolved in 0.3 ml of CDCl_3 was added to trans-2-azido-2-butene (1b, 53.1 mg) dissolved in 0.1 ml of CDCl_3 at -70°C . The reaction was allowed to proceed by slowly warming the tube to room temperature. Spectra were recorded at intervals, of 1/2 hr for a period of 18 hrs. Corresponding to each spectra a small portion of reaction mixture was hydrolysed and analysed by g.l.p.c. (20% SE 30 on 60/80 Chrom W DMCS A/W at 80°C ; 6' X 1/4" column). It was found that the predominant product was 1,3-dibromo-2-butanone (8) throughout the reaction.

Reaction of trans-2-azido-2-butene (1b) with m-chloroperbenzoic acid:

m-chloroperbenzoic acid (0.67 g, 3.6 m mol) was dissolved in 10 ml of ether. This soln was added dropwise to trans-2-azido-2-butene (1b, 0.35 g, 3.6 m mol.) in 30 ml of ether. The temp of the reaction vessel was maintained at -10°C throughout the addition. After 1 hr of further stirring the mixture was diluted with 100 ml of aqueous 5% NaHCO_3 and the total mixture was continuously extracted with ether. The ether extract on drying with anhyd MgSO_4 and evaporation gave 43% (0.34 g) 3-m-

chlorobenzoy-2-butanone (6).

$\nu_{\text{max}}^{\text{film}}$: 2900, 3080, 1720, 1570, 1425, 1255, 1130, 1085
and 750 cm^{-1} ;

n.m.r. (CDCl_3): δ 7.64 (m, 4H); 5.30 (q, 1H, $J=7\text{Hz}$);
2.22 (s, 3H); and 1.53 (d, 3H, $J=7\text{Hz}$).

Calc. for $\text{C}_{11}\text{H}_{11}\text{ClO}_3$: 226. Found (M^+): 226.

Reaction of trans-2-azido-2-butene (1b) with nitryl
tetrafluoroborate

To trans-2-azido-2-butene (1b, 0.5 g, 5.2m mol.)
in 20 ml of ether was added dropwise to a soln of
nitryl tetrafluoroborate (0.68 g, 5.52 m mol.) in 10
ml of ether. The whole mixture was maintained at
 -10°C throughout the addition. After further stirring
at room temp for 1 hr the mixture was distilled
carefully to remove ether. Further distillation
(b.p. $_{16\text{ mm}}$ 100°) gave 52% (0.3 g) of 3,4-dimethyl-
2-oxo-1,2,5-oxadiazole. Analysis of residue by g.l.p.c.
showed presence of 20% of N-ethyl acetamide (3a) and
N-methyl propionamide (4a).

The experiment was repeated using the same conditions
except that the reaction was allowed to stir overnight.
Direct distillation of this mixture gave 84% (0.49 g)
3,4-dimethyl-2-oxo-1,2,5-oxadiazole.

$\nu_{\text{max}}^{\text{film}}$: 2940, 1610, 1465, 1425, 1380, 1300, 1165, 1040, 995, 950, and 850 cm^{-1} ; n.m.r.

(CDCl_4): δ 2.3 (s, 3H) and 2.09 (s, 3H).

Calc. for $\text{C}_4\text{H}_6\text{N}_2\text{O}_2$: 114. Found (M^+): 114.

$\lambda_{\text{max}}^{\text{MeOH}}$: 259 $\text{m}\mu$

Reaction of trans-2-azido-2-butene (1b) with dimethyl acetylene dicarboxylate

Trans-2-azido-2-butene (1b) (0.5 g, 5.2 m mol.) and dimethyl acetylene dicarboxylate (0.7 g, 4.9 m mol.) were dissolved in 20 ml of ether. The mixture was allowed to stir for 3 days. The solvent was removed and the resulting yellow product was distilled (b.p. $_{0.1 \text{ mm}}$ 150°) to give 90% (0.99 g) of triazole (15)¹⁸.

$\nu_{\text{max}}^{\text{NaCl}}$: 2930, 1735, 1550, 1450, 825 and 810 cm^{-1} ; n.m.r.

(CDCl_3): δ 5.83 (q, 1H, $J=3.5, 0.5$ Hz), 3.98 (6H), 2.19 (quin 3H, $J=0.5$ Hz) and 1.41 (q, 3H, $J=0.5, 3.5$ Hz).

$\lambda_{\text{max}}^{\text{MeOH}}$: 217 $\text{m}\mu$

Calc. for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_4$: 239. Found (M^+): 239.

Reaction of trans-2-azido-2-butene (1b) with excess dimethyl acetylene dicarboxylate

To a mixture of dimethyl acetylene dicarboxylate (1.00 g, 7.00 m mol.) and aluminum chloride (0.5 g) in

20 ml of dry ether was added dropwise trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) and the mixture allowed to stir over night. The mixture was made weakly basic with aqueous 10% NaHCO_3 . Continuous extraction with ether gave 0.8 g of a red brown mixture. Chromatography on 20 g SiO_2 (80-200 mesh) using pet ether-chloroform as the eluent gave 0.4 g of dimethyl acetylene dicarboxylate. Elution with pet ether: chloroform, 95:5, gave 16% (320 mg) of 9b (m.p. 98-99°C).

$\nu_{\text{max}}^{\text{KBr}}$: 2950, 1725, 1655, 1500, 1440, 825 and 810 cm^{-1} n.m.r.

(CDCl_3): δ 4.00 (s, 3H); 3.95 (s, 3H); 3.85 (s, 3H);
3.80 (s, 3H); 3.28 (q, 1H, $J=7\text{Hz}$); 2.03 (s, 3H)
and 0.95 (d, 3H, $J=7\text{ Hz}$).

Calc. for $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_8$: 381. Found (M^+): 381.

$\lambda_{\text{max}}^{\text{MeOH}}$: 220m μ

Analysis: Calc; C, 50.39; H, 4.99

Found; C, 50.52; H, 5.02

Reaction of trans-2-azido-2-butene (1b) with 1 mole of dimethyl acetylene dicarboxylate using aluminum chloride as a catalyst

Trans-2-azido-2-butene (1b, 0.5 g, 5.2 m mol.) was dissolved in 20 ml of dry ether and the soln cooled to -20°C. To this was added aluminum chloride (0.8 g) followed by dropwise addition of dimethyl acetylene

dicarboxylate (0.7 g, 4.9m mol.). The mixture was warmed to room temp and after stirring over night it was diluted with aqueous 10% NaHCO_3 until it was weakly basic.

Continuous extraction with ether gave 1.00 g. of oil.

Direct chromatography on 30 g of SiO_2 using chloroform:

Pet ether (5:95) as eluent gave 55% (0.7 g) of triazole 15.

Reaction of 1 mole of trans-2-azido-2-butene (1b) with 1 mole of dimethyl acetylene dicarboxylate in presence of aluminum chloride

Dimethyl acetylene dicarboxylate (1.00 g, 7.1 m mol.) and aluminum chloride (0.95 g, 7.1 m mol.) were dissolved in 20 ml of ether. To this was added trans-2-azido-2-butene (1b, 0.7 g, 7.1 m mol.) over a period of 1/2 hr. After 18 hrs, of further stirring the mixture was diluted with aqueous NaHCO_3 and then extracted with ether. Chromatography of ether extract of 200 g SiO_2 using pet ether as eluent gave 23.5% (0.4 g) of corresponding triazole. Further elution using pet ether:chloroform (95:5) gave 13% (0.3 g) of 9b.

Reaction of cis-2-azido-2-butene (1a) with excess dimethyl acetylene dicarboxylate in presence of aluminum chloride

Cis-2-azido-2-butene (2 g, 20.8 m mol.) was added dropwise to a soln of 2.4 g of aluminum chloride and dimethyl acetylene dicarboxylate (2.5 g, 17.8 m mol.) in

20 ml of ether. After the usual work up the residual oil was chromatographed on SiO_2 (100 g). Elution with pet ether gave 0.9 g of triazole, 16.

3.95 (s, 3H), 2.21 (sextet, 3H, $J=1\text{Hz}$) and 1.85 (q, 3H, $J=1, 7\text{Hz}$).

Further elution with pet ether:chloroform (95:5) gave 3% (0.2 g) of 9b.

N.M.R. study on 9b

9b (38 mg, 0.1 m mol.) was dissolved in 0.4 ml of nitrobenzene in an n.m.r. tube. The spectra of X'' were then recorded at room temp, 153°C and 165°C . Instantaneous rearrangement was observed only at 165°C . The hot tube was allowed to cool to room temp and the final spectrum was taken of the rearranged product at room temp.

N.m.r. (PhNO_2) r.t.: δ 4.10 (s, 3H); 3.98 (s, 3H);
3.87 (s, 6H); 3.39 (q, 1H, $J=7\text{Hz}$);
2.20 (s, 3H) and 1.04 (d, 3H, $J=7\text{Hz}$)

(PhNO_2) 166°C : Major isomer (13): δ 6.75 (q, 1H, $J=7\text{Hz}$),
3.95 (s, 3H); 3.87 (s, 3H); 3.80 (s, 3H);
3.63 (s, 3H); 2.68 (s, 3H) and 1.76 (d, 3H, $J=7\text{Hz}$)

Minor isomer (14): δ 6.11 (q, 1H, $J=7\text{Hz}$); 3.9-
3.60 (12H three singlets not differentiable)
2.60 (s, 3H) and 1.85 (d, 3H, $J=7\text{Hz}$)

(PhNO_2) r.t.: Major isomer (13): δ 6.88 (q, 1H, $J=7\text{Hz}$);
4.03 (s, 3H); 3.95 (s, 3H); 3.87 (s, 3H);
3.73 (s, 3H); 2.84 (s, 3H) and 1.72
(d, 3H, $J=7\text{Hz}$).

Minor isomer (14): δ 6.20 (q, 1H, J=7Hz); 4.04 -
3.70 (12H three singlets, indistinguishable);
2.75 (s, 3H) and 1.91 (d, 3H, J=7Hz).

The n.m.r. spectra revealed the 13:14 ratio to be 87.4:12.6

Analysis: Calc; C, 50.39; H, 4.99; N, 11.02

Found: C, 50.47 H, 4.85; N, 11.12.

REFERENCES

1. A. Hassner and F.W. Fowler, *J. Org. Chem.*, 33, 2686 (1968).
2. M.P. Doyle and W. Wierenga, *J. Am. Chem. Soc.*, 92, 4999 (1970).
3. M. Hanack, *Accts. Chem. Res.*, 3, 209 (1970).
4. K. Isomura, M. Okada and H. Taniguchi, *Nippon Kagaku Zasshi*, 91, 746 (1970).
5. G. Labbé, *Chem. and Ind.*, 278 (1971).
6. A. Hassner, E.S. Ferdinand, and R.J. Isbister, *J. Am. Chem. Soc.*, 92, 1672 (1970).
7. G. Englert, *Zeit. Fuer. Anal. Chemie.*, 181, 447 (1961).
8. H.E. Ungnade and E.D. Loughran, *J. Het. Chem.*, 1, 61 (1964).
9. E.H. White and L.A. Dolak, *J. Am. Chem. Soc.*, 88, 3790 (1966).
10. A.T. Bomquist, J.R. Johnson and H.J. Sykes, *J. Am. Chem. Soc.*, 65, 2446 (1943).
11. (a) W.D. Emmons and J.P. Freeman, *J. Org. Chem.* 22, 456 (1957).
(b) G. Labbé and A. Hassner, *Angew. Chem., Int. Ed. Engl.*, 10, 98 (1971).
12. G. Theilig, *Chem. Ber.*, 86, 96 (1953).
13. G. Labbé, *Chem. Reviews*, 349 (1969).
14. F.W. Fowler and A. Hassner, *J. Am. Chem. Soc.*, 90, 2875 (1968).

15. A.G. Cook, "Enamines: Synthesis, Structure and Reactions," M. Kekker and Co., New York, N.Y., (1969).
16. C. Rappe, Arkiv. Für Kemi, 24, 73 (1965).
17. S. Bory, M. Fetizon, and P. Iaszlo, Bull. Soc. Chem. Fr., 2310 (1963).
18. G. Labbé, J.E. Galle, and A. Hassner, Tet. Lett., 4, 303, (1970).
19. F.W. Fowler, A. Hassner and L.A. Levy, J. Am. Chem. Soc., 89, 2077 (1967).
20. L.C. Behr and J.T. Brent, Org. Syn., 34, 40 (1954).
21. L. Ruzicka, M. Kobelt, O. Hafligner and V. Prelog, Helv. Chem. Act., 32. 544 (1949).
22. A. Hassner and A.B. Levy, J. Am. Chem. Soc., 93, 5469 (1971).
23. Handbook of Chemistry and Physics, 42nd Ed.; Chemical Rubber Publishing Co., New York, N.Y., (1960, 61).