MECHANISTIC STUDIES OF THE REACTIONS OF SOME ALLYLIC HALIDES

A thesis presented by

Mohammad Rahimizadeh

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ABSTRACT

A review of nucleophilic substitution is set forth, in which the different techniques available for the elucidation of reaction mechanism are described. Allylic solvolytic reactions are briefly summarised.

An account is given of the synthesis of several new (reactive) allylic chlorides. A chlorination method particularly useful for the preparation of very reactive or volatile allylic chlorides is described.

The solvolytic reactions (solvolyses) of 5-chloro-pent-3-en-1-yne and 3-chloro-pent-4-en-1-yne are studied and possible mechanisms are propounded. The solvolytic mechanism for the former compound is of a bimolecular type and it is suggested that the rate determining step is formation of a nucleophilically solvated ion-pair intermediate. However, for the latter compound the mechanism has a unimolecular character, and product distributions are explained by the involvement of two discrete ion-pair intermediates. It is suggested that the rearrangement and solvolysis reactions have the same ion-pair intermediate for the 3-chloro compound.

The isomerisation of 3-chloro-pent-4-en-1-yne has been studied in sulpholane at different salt concentrations. The reaction is shown to follow unimolecular kinetics in the absence of lithium chloride (chloride ion). However, lithium chloride accelerates the reaction so that the composite rate of rearrangement becomes dominated by a bimolecular process.

To my Parents

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CONTENTS

INTRODUCTION

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The chemistry of allylic compounds, which have the part-structure 1, has played an important part in the development of theoretical organic chemistry. These substances owe their importance to the high reactivity that they display in nucleophilic substitution and to the fact that they readily undergo rearrangement reactions. For this reason allylic intermediates are widely used in organic synthesis.

$$C = C - C - X \qquad (1)$$

In addition, allylic systems are found in many natural products, such as alkaloids, steroids and terpenes. Allylic systems are particularly common among the terpenes, and allylic substitution reactions are widely used in the synthesis of essential oils, vitamin A and its analogs, and other unsaturated compounds.

Rearrangements in allylic compounds have been long known.[1] A typical isomeric rearrangement is the conversion of 1-phenylallyl ester into its 3-isomer:[2]

$$PhCH(OCOR)CH = CH_2 \longrightarrow PhCH = CHCH_2OCOR \qquad (1)$$

It was first clearly recognised by Burton and Ingold[3] that such reactions may involve migration of a nucleophilic or anionic fragment from one end of the allylic system to the other. They are frequently found to accompany nucleophilic displacements in the allylic system. Rearrangement

reactions of this type belong to the class of reactions known as anionotropic rearrangement. The term anionotropy, introduced by Ingold refers to molecular rearrangement where the migrating groups are anions as $OH^{\ominus}$, $OR^{\ominus}$, $Cl^{\ominus}$ etc. Anionotopy has been redefined by Braude[4] as the migration of a group or atom in which that group or atom retains the electrons by which it was originally bound to the molecule. The equilibrium in an anionotopic system can be considered quite independently of the mechanism of the rearrangement but depends on the free energy difference (ΔG) between the isomeric structures expressed in equation (2).

$$\Delta G = - RT \ln K \qquad (2)$$

For qualitative and semiquantitative discussion it is usually sufficiently accurate to identify (ΔG) with the change in heat content and to discuss the effect of substituents attached to the carbon atoms C_1, C_2 and C_3 in terms of what is known of the stabilization energies resulting from the presence of substituents adjacent to the C_1-C_2 double bond in the first isomer and the C_2-C_3 double bond in the second isomer. For example, the equilibrium mixture of cinnamyl and 1-phenylallyl chlorides contains no detectable quantities of the latter (equation 1) and the composition of the equilibrium mixture between crotyl and 1-methyl-allyl chorides or bromides[5]:

$$(75\text{-}85)\%\ CH_3\text{-}CH{=}CH\text{-}CH_2X \rightleftharpoons CH_3\text{-}CHX\text{-}CH{=}CH_2\ (15\text{-}25)\% \qquad (3)$$

depends on the halides and the temperature. A study of the aniontropic rearrangement occurring during a displacement reaction can yield valuable information concerning the

mechanism of the latter reaction. Allylic halides display the properties of ease of nucleophilic substitution and anionotropic mobility to a high degree, and in the following sections mechanistic aspects of these reactions will be discussed with particular reference to solvolytic reactions. Isomerization reactions of allylic alcohols, esters and ethers have been reviewed by Braude, De Wolfe and Young.[4, 6, 7]

CHAPTER 1

Nucleophilic Substitution Reactions

CHAPTER 1

1 NUCLEOPHILIC SUBSTITUTION REACTIONS

Nucleophilic substitution reactions of allylic compounds are similar in many respects to the analogous reactions of saturated compounds. The allylic substitutions differ from their aliphatic analogues in the nature of the reactive intermediate and transition states involved, and the possibility of attack of the nucleophile at the γ-position of allylic system. The allylic substitution reactions can be broadly classified as being either unimolecular or bi-molecular and in addition there is a large group of reactions which do not fall under either heading and are sometimes called border-line reactions.

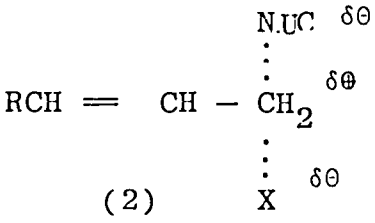
1.1 NORMAL BIMOLECULAR NUCLEOPHILIC SUBSTITUTION

This mechanism consists of one step attack in which one nucleophilic reagent displaces another (X) from its attachment to a carbon atom. The new bond is being formed at the same time as the old bond is breaking, and in the transition state, the incoming group and the leaving group are both "half bonded" to the carbon atom being attacked.

$$NUC + R - X \longrightarrow [NUC \ldots R \ldots X] \longrightarrow NUC.R + X^- \qquad (4)$$

The reactions are characterized by second order kinetics (pseudo first order where the substituting agent is in excess) and inversion of configuration if the substrate has an asymmetric carbon atom.

In order to achieve reaction, a free energy maximum associated with the transition state (2) shown below must be overcome.



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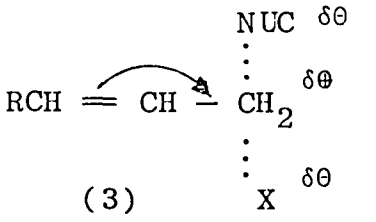


(3)

Since the transition state can be stabilized by the mesomeric release of electron from the double bond (3), SN_2 displacements of allylic halides are more rapid than those of the corresponding alkyl compounds, e.g. 3-methyl allyl chloride reacts 95 times faster than n-butyl chloride with ethanolic sodium ethoxide at 44.6° c.[9] With many simple allylic halides, bimolecular displacements proceed essentially without rearrangement. Vernon has suggested that no more than traces of products of bimolecular elimination are found when these reactions are carried out in the temperature range at which they can conveniently be studied kinetically. The rate of a bimolecular reaction is affected by substituents in the carbon chain. In the one position, substituents, whether electron releasing or withdrawing, retard the reaction by steric interference with the approach of the nucleophilic reagent. Much of the work on 2-substituted allylic halides has been done by Hatch and his co-workers.[10] Thus Hatch and Patton[11] examined the reactions of $CH_2 = CHY - CH_2Cl$ with potassium iodide in acetone, and with sodium ethoxide in ethanol. The maximum rate factor was not more than 2.5, and the observed sequence was Y = Ph>Me>H>Br>Cl.

Electron releasing substituents on the 3-carbon atom of the allylic system facilitate the direct displacement by assisting the departure of the leaving group as a negative ion. Relative rates of bimolecular substitutions of allyl and alkyl halides with ethoxide at 44.6°C. are shown in Table (1).

TABLE 1

COMPOUNDS	NUCLEOPHILE	REACTION CONDITIONS	k ALLYLIC / k SATURATED
$CH_2=CH-CH_2Cl$ $CH_3-CH_2-CH_2Cl$	$C_2H_5O^-$	ethanol 44.6°	27[a]
$CH_3-CH=CH-CH_2Cl$ $CH_3-CH_2-CH_2-CH_2Cl$	$C_2H_5O^-$	ethanol 44.6°	88[a]
$CH_2=C(CH_3)CH_2Cl$ $(CH_3)_2-CH-CH_2Cl$	$C_2H_5O^-$	ethanol 44.6°	340[a]
$CH_3-CH\ Cl-CH=CH_2$ $CH_3-CH\ Cl-CH_2-CH_3$	$C_2H_5O^-$	ethanol 44.6°	26[a]
$CH_2=CH-CH_2Cl$ $CH_3-CH_2-CH_2Cl$	$(NH_2)_2CS$	methanol 50°	167[b]
$CH_2=CH-CH_2Br$ $CH_3-CH_2-CH_2Br$	$(NH_2)_2CS$	methanol 50°	81[b]
$CH_2=CH-CH_2I$ $CH_3-CH_2-CH_2I$	$(NH_2)_2CS$	methanol 50°	57[b]

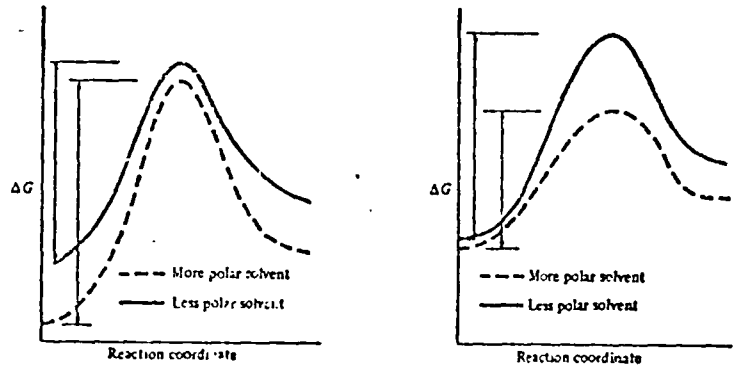
a C A Vernon, J. Chem. Soc. 4462 (1954)

b F G Bordwell, et al. J. Amer.Chem.Soc. 82,2883 (1960)

The rates of direct displacement reactions are dependent on the nucleophilicity of attacking reagent. This is determined by its solvation energy, the strength of its

bond with a carbon 2-p orbital and its steric effect.

Effects of changes in the medium on the rate of bimolecular displacement reactions are not large. The magnitude and direction of the change would be expected to depend on the relative charge densities in the starting material and in the transition state. If the starting materials have a high charge density but in the activated complex the charge is dispersed, a more polar solvent should lower the energy of the starting material more than the energy of the transition state. The result would be an increase in activation energy and a decrease in rate. This situation is shown in (fig. 1a). On the other hand, if the transition state has a higher charge density than the starting material, increasing solvent polarity should lower the activation energy and increase the rate (fig. 1b).



(a) Figure 1 (b)

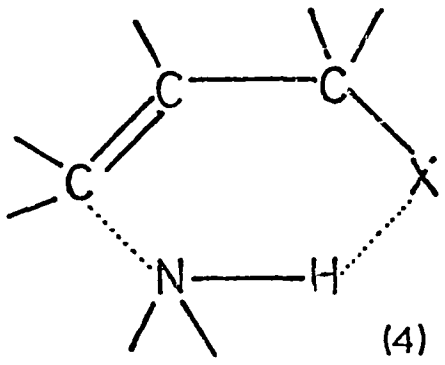
However, the predictions of rate should not be used without considering the effect which solvents may have on nucleophile and leaving group reactivity.

1.2 ABNORMAL BIMOLECULAR NUCLEOPHILIC SUBSTITUTION

In an abnormal substitution, the nucleophile attacks the 3-carbon atom of the allylic system and displaces the leaving group on the 1-carbon atom in a concerted process.

$$Y^{\ominus} + C{=}C{-}C{-}X \longrightarrow Y^{\delta-}\cdots C^{\delta+}{=}C{=}C^{\delta+}\cdots X^{\delta-} \longrightarrow Y{-}C{-}C{=}C + X^{\ominus} \qquad (5)$$

Inhibition of SN_2 attack, either by steric or by polar factors, seems to be desirable for the realization of SN_2' substitution, as in the reactions of $CH_2{=}CHCHCl\ Bu\text{-}t$ and $CH_2{=}\ CHCHCl_2$, respectively [13,16]. A number of examples exist[14] where internal hydrogen bonding may assist the formation of an SN_2'-like transition state (e.g.4).



(4)

Since it has been shown[17] that the process is not changed in rate by using N-deuteroamines instead of their proto analogues, the N-H cannot be much stretched in the transition state.

The reaction of diethylamine with α- methyl allyl chloride gives substantial isotope effects[18].

$$\frac{k_2(^{12}C_\gamma)}{k_2(^{14}C_\gamma)} = 1.057 \qquad \frac{k_2(^{12}C_\beta)}{k_2(^{14}\beta)} = 1.074$$

$$\frac{k_2(^{12}C_\alpha)}{k_2(^{14}C_\alpha)} = 1.079 \qquad \frac{k_2(^{35}Cl)}{k_2(^{37}Cl)} = 1.011$$

interpreting their result, they suggest that in the transition state considerable bonding changes are occurring involving the leaving chloride and all the three carbon atoms of the allylic system. The view is therefore supported

that a synchronous mode of displacement is under observation. Bell, Naderonero and Whiting[19] have described a rearrangement (eqn.6)

$$\text{trans-MeCHClCH=CHC}\equiv\text{CH} \xrightarrow[-HCl]{Et_2NH} \text{MeCH=CH-CH(NEt}_2\text{)-C}\equiv\text{CH} \qquad (6)$$

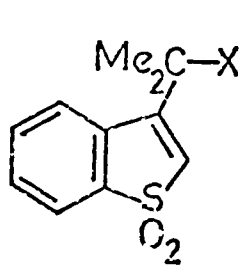
which they consider also to be of the SN_2' type; the ratio of the competing processes was found to be very dependent on the nucleophile and the solvent.

The structure of the allylic system and the nature of the reagent are both important in determining whether the SN_2' mechanism will operate. Since the formation of the transition state requires the approach of a nucleophile to an electron rich area, the mechanism rarely occurs in cases where normal bimolecular substitution is unhindered by additional substitution on the reacting carbon atom. An important comparison has been made between allylic chlorides and allylic bromides reacting with and without rearrangement by bimolecular mechanisms[20]. The results for bimolecular exchanges between radioactive bromide and chloride ions and the isomeric 1-and 3-methyl-allyl bromides and chlorides are summarized in Table 2.

TABLE 2

Compound	SOLVENT	MECH-ANISM	$\Delta S^{\neq}$ (e.u.)	$\Delta H^{\neq}$ K cal / mole	$10^6 k_2$ $mole^{-1}s^{-1}$
CH_2= CHCH(Me)Br	Me_2CO	SN_2	-19.1	15.9	379
CH_2=CHCH(Me)Br	Me_2CO	SN_2'	-17.7	18.8	14.9
$BrCH_2CH$=CHMe	Me_2CO	SN_2	-15	14.1	141000
$BrCH_2CH$=CHMe	Me_2CO	SN_2'	-19	18	5
CH_2=CHCH(Me)Cl	MeCN	SN_2	-13.9	20.8	2.87
CH_2=CHCH(Me)Cl	MeCN	SN_2'	-13.4	24.2	0.0133
$ClCH_2CH$=CHMe	MeCN	SN_2	-11.6	18.8	315
$ClCH_2CH$=CHMe	MeCN	SN_2'	-14.9	24.3	0.0053

Recently Bordwell et al. [21, 22] have re-interpreted the SN_2' reaction in terms of an ion-pair type mechanism (although objections to the re-interpretation have been advanced [75]). Bordwell checked this hypothesis by attempting to induce SN_2' reactions on substrates unlikely to give stable allylic carbonium ions, and thus favouring abnormal nucleophilic substitution, e.g. the compounds shown below, should be expected to undergo SN_1 and SN_2 reactions with reluctance, the SN_2' reaction should be



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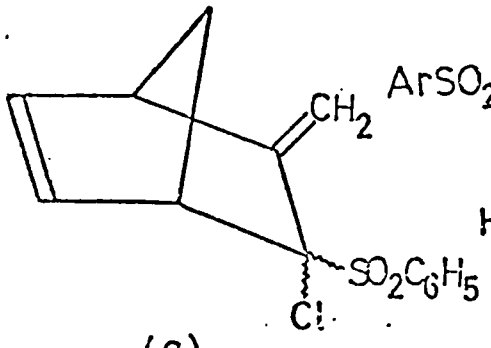

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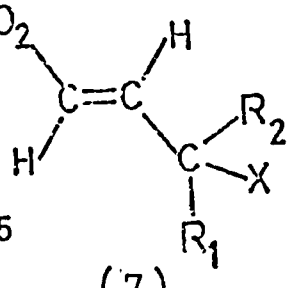
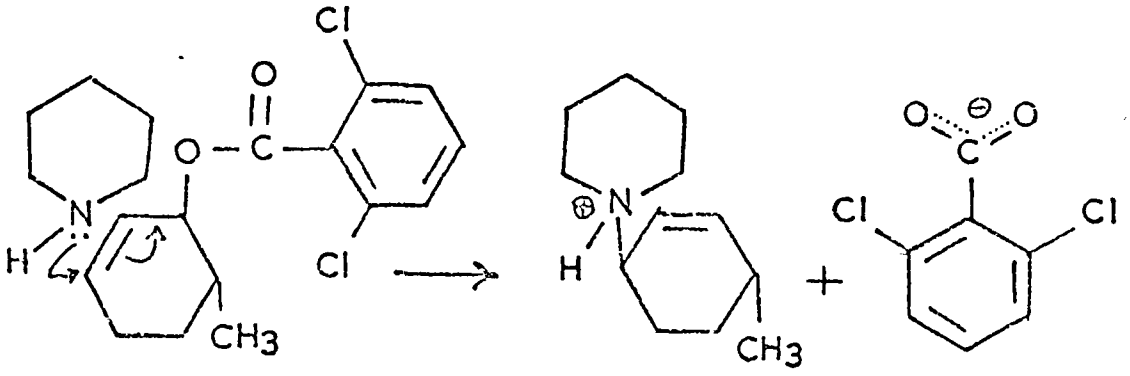


(7)

facilitated. In fact basic nucleophiles such as piperidine in benzene or sodium methoxide in methanol failed to induce any reaction. This was interpreted in terms of an ion-pair mechanism in which formation of ion-pairs was considered unlikely.

The stereochemistry of the SN_2' reaction has been studied mainly in cyclic systems [23, 24, 25, 26]. The results indicate that the leaving group and nucleophile are on the same side of the molecule in the transition state, the ring from which the dichlorobenzoate ion departs. Very recently this conclusion was reconfirmed by the same authors [26].



1.3 UNIMOLECULAR NUCLEOPHILIC SUBSTITUTION

In this mechanism, the bond to the leaving group is broken before the new bond is created, the reaction proceeding through an intermediate of somewhat the same nature as a free carbonium ion. The SN_1 mechanism of substitution occurs most readily in compounds giving rise to carbonium ions which can be stabilized by induction or mesomeric effects. Steric hindrance to nucleophilic attack is another important factor in determining whether the unimolecular or the bimolecular mechanism will operate.

The SN_1 mechanism is promoted by solvents having a high ionising power and by electrophilic catalysts such as Ag^+.

The allyl cation, $[CH_2 \cdots CH \cdots CH_2]^+$, is mesomeric. Its resonance energy should be reflected in the rate of displacement reaction on an allyl derivative to the extent to which the carbonium character is developed in the transition state. In an unimolecular reaction, therefore, it might be expected that allylic compounds would be considerably more reactive than the corresponding saturated compounds.

Although theoretical calculations indicate the resonance energy of the allyl cation to be about 18 K cal mol^{-1} measurements by electron impact of the appearance potential of this ion from allyl chloride suggest that the true value may be smaller.[27] Vernon measured the rates of solvolysis of a number of halides in moist formic acid, a solvent of high ionizing power and low nucleophilicity in which solvolysis could be assumed to occur entirely by the unimolecular mechanism. He found electron-releasing substituents on both the 1- and 3- carbon atoms greatly increased the rate of solvolysis[28]. The effects of substitution on 2-carbon atom of the allylic system appear normally to be small. This would be expected, because such groups are not conjugated or hyperconjugated with the reaction centre. Thus 2-methylallyl choride is, in formic acid, slightly less reactive than allyl chloride, whereas methyl groups in either the 1- or 3-position markedly accelerate the solvolysis. Some relative rate of solvolysis of substituted allylic halides are shown in table (3).

TABLE 3

COMPOUND	k_R/k_H
$CH_2=CH-CH_2Cl$	1.0
trans-$ClCH=CH-CH_2Cl$	3.1
Cis-$Cl\ CH=CH-CH_2Cl$	2.1
trans-t-Bu $CH=CH-CH_2Cl$	2.3×10^3
trans-$MeCH=CH-CH_2Cl$	3.6×10^3
trans-Ph $CH=CH-CH_2Cl$	5×10^5
$Me_2\ C=CH-CH_2Cl$	1.5×10^7
$MeEtC=CH-CH_2Cl$	1.2×10^7
$CH_2=CMe-CH_2Cl$	0.5
$CH_2=CH-CHCl_2$	65.5
$CH_2=CH-CHt\text{-}Bu\ Cl$	2.5×10^5
$CH_2=CH-CHMeCl$	5.7×10^3
$CH_2=CH-CMe_2Cl$	8×10^7
$MeCH=CH-CHMeCl$	1.5×10^8
Ph $CH=CH-CH\ Cl_2$	2.2×10^8

Vernon also demonstrated the pronounced dependence on solvent ionizing power of the rate of a unimolecular solvolysis. For example, the rate of unimolecular solvolysis of 1,1-dimethyl-allyl chloride and 3,3-dimethyl-allyl chloride are shown to be about 5000 times as great in 50% aqueous ethanol as in absolute ethanol.

1.4 NUCLEOPHILIC SUBSTITUTION OF BORDERLINE TYPE SUBSTRATES

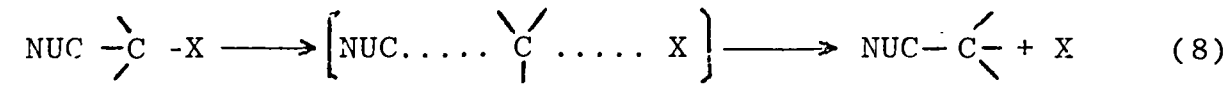
The classification of simple secondary alkyl halides, benzyl derivatives and many of allylic halides is difficult since these substrates exhibit some properties of S_N1 substrates and some properties of S_N2 substrates. Borderline behaviour can be found upon examination of stereochemistry, effect on rate and product distribution of added salts, influence of structure and of leaving group on

kinetics and products, sensitivity to solvent ionizing power and nucleophilicity and isotope effects. Hughes, Ingold and their co-workers [29,30], while recognising that borderline cases are to be represented by some sort of intermediate mechanism, have in a number of cases preferred to regard these as a mixture of SN_1 and SN_2 solvolysis, occuring simultaneously and in competition. [31,32]

Winstein, Grunwald and Jones [33] have suggested that solvolysis reactions may have a continuous spectrum of mechanisms of which the SN_1 and SN_2 mechanisms are special cases. They considered that nucleophilic interaction between the solvent and substituted carbon atom, and the electrophilic interaction between the solvent and the leaving group would, in general, both contribute to the driving force of the reaction. Those cases in which the former interaction was negligible were termed 'limiting', and correspond to the pure SN_1 mechanism of Hughes and Ingold. As there are in principle infinite gradations in the relative contributions of nucleophilic and electrophilic solvation to the driving force of the reaction, there is no sharp dividing line between the mechanisms SN_1 and SN_2.

Winstein [7] and his co-workers pointed out that a plot of the logarithm of the solvolysis rate constant against their measure of the solvent ionizing power showed a good straight line instead of curvature corresponding to the transition from SN_2 to SN_1 [34] and concluded that a single intermediate mechanism rather than two competing mechanisms was involved.

An alternative "merged mechanism" has also been described in eqn. (8).[35,36]



(8)

According to this picture, SN_1 and SN_2 mechanisms represent the two extremes of the same mechanism. So in the merged mechanism picture borderline behaviour is the result of a degree of bond formation by the nucleophile which is not as advanced as bond breaking to the leaving group, but which is significant enough to prevent formation of an intermediate carbonium ion.

The idea of gradually merging mechanisms for nucleophilic substitutions reacting was also developed by Doering and Zeiss[36], and by Streitwieser[37]. They described the change of the structural arrangement of atoms corresponding to the transition state with the change of the substituent group. The one step displacement of methyl halide in water, for example, is considered to involve no intermediate and has been described by a single transition state (fig. 2, curve 1). As the methyl group is varied structurally in a systematic series in which the energy of the free hypothetical carbonium ion is decreased continuously by increasing resonance access of electrons from the substituents to the p-orbital, the arrangement of atoms corresponding to t^{i} is transformed from a transition state to an intermediate (fig. 2, 1^{II}, 1^{III}, 1^{IV}). As the p-orbitals are filled increasingly with electrons, the stability of the carbonium ion type intermediate increases and its bonds to solvent and leaving group become longer and weaker until, in the terminal cases (I^{IV}), the bond

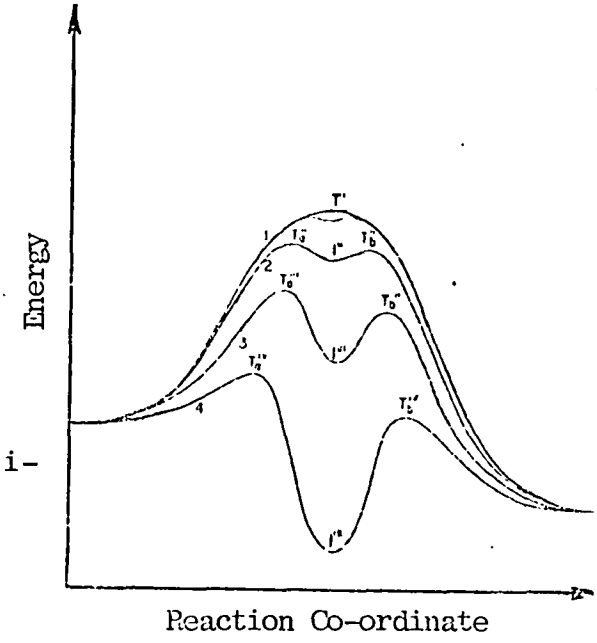


Figure 2

to the leaving group is ionic and the bond to a particular solvent molecule is non-existent. For a given nucleophile and a given leaving group, the stability of (1^{II}, 1^{III}, and 1^{IV}) will parallel the stability of the hypothetical carbonium ion obtained by ionizing RX (substrate). In extreme cases this ionization would be energetically so unfavourable that (I) would only be formed with nucleophilic assistance, in this case (1) is a transition state (fig. 2 , curve 1) and the process resembles the SN_2 mechanism.

Recently Bentley and Schleyer [38/] have proposed the formation of nucleophilically solvated ion-pair intermediates in solvolysis of primary and secondary arenesulphonates. They have also concluded that the changing character of SN_2 reactions as the magnitude of nucleophilic solvent assistance varies removes the necessity to postulate many competitive (i.e. simultaneous) SN_1 and SN_2 solvolysis reactions. However, if nucleophilic solvent assistance is small (<1Kcal/mole) it is conceivable that the overall reaction proceeds via significant proportions of both nucleophilically assisted (SN_2) and unassisted (SN_1) transition states, but the two processes blend into one another with loss of operational distinction.

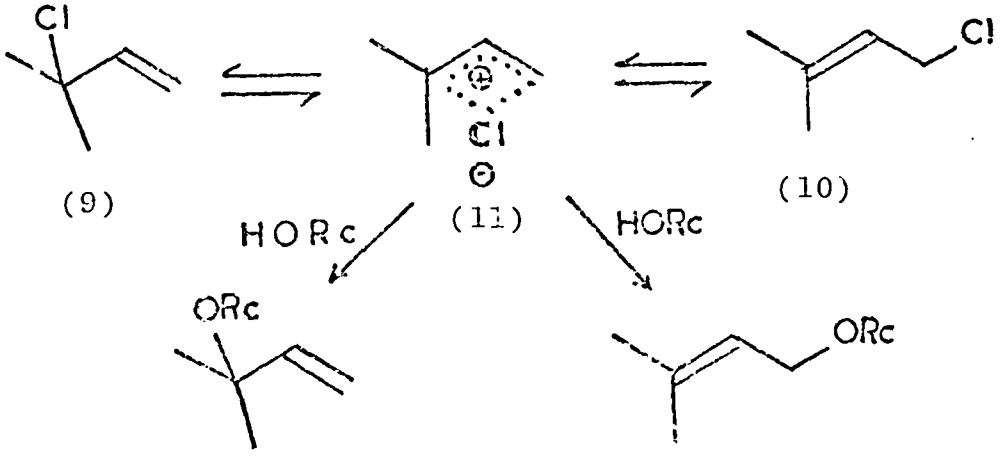
1.5. ION PAIR INTERMEDIATE IN THE REACTIONS OF ALLYLIC SUBSTRATES

Most early studies of carbonium ions involved a study of the products produced during solvolysis reactions at an asymmetric carbon. The SN_1 reaction requires the unimolecular formation of the carbonium ion as a metastable intermediate in which the carbon reaction centre becomes trigonally hybridised and the cation thus becomes planar [39]. Asymmetrically substituted alkyl groups should therefore lead to racemic products when reacting via an SN_1 mechanism. In all cases except those where very stable carbonium ions are involved, totally racemic products are not observed. In fact, the proportion of inversion usually increases as the carbonium ion formed becomes less and less stable. For example, inversion increases in the series secondary arylalkyl <tert-alkyl< Sec-alkyl. Predominant inversion can be explained in terms of lifetime effects of an intermediate.

Shielding of the carbonium ion by the leaving group was therefore invoked to explain the excess of inverted products usually observed [41]. As the leaving group departs its acquires a solvent shell which is increasingly bonded to it. During this period of time the front face of the carbonium ion is shielded from the solvent attack. Solvent molecules bound to the leaving group cannot attack the carbonium ion. If the ion is relatively unstable, rapid solvent attack will occur. This must occur from the backside unless the leaving group and its solvent shell have moved far away from the front face. If the ion is quite stable, its lifetime in a given solvent will be greater. Now the leaving group and its solvent shell have time to move farther away. This leaves a symmetric solvent

shell around the carbonium ion, and the reaction with the solvent nucleophiles may occur equally as well from either side leading to racemic product. In order to obviate the necessity of invoking shielding by the leaving group to explain products of inverted stereochemistry, Hammett[41] suggested that the product of the ionisation step was an ion-pair capable of reacting with inversion of configuration prior to dissociation.

The occurrence of ion-pairs as intermediates in solvolysis reactions was first clearly demonstrated by Young, Winstein and Goering[42], who observed that the acetolysis of 1,1-dimethylallyl chloride (9) was accompanied by a rearrangement to 3,3-dimethylallyl chloride (10). The reaction rate decreased rapidly from the initial value to that expected for the primary chloride. Added chloride ion had no effect on the rate of acetate formation, or isomerisation, indicating the absence of dissociated carbonium ions. Solvolysis of (9) in the presence of excess $^{36}Cl^-$ afforded rearranged chloride (10) containing ca 5% of the isotopic chlorine, but not the amount which corresponds to the equilibrium value.[43] Hence part of the rearranged halide must have resulted from an intramolecular rearrangement. These results were interpreted via scheme (1).

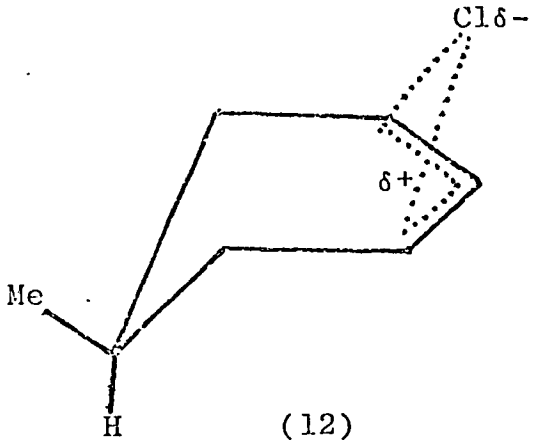


SCHEME 1

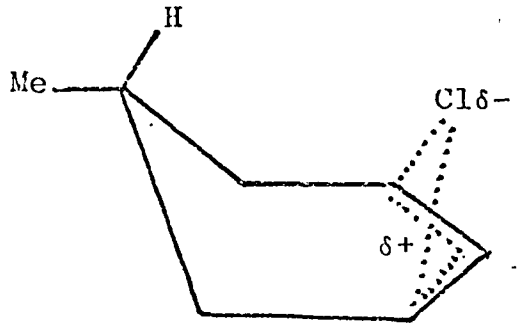
The ion pair (11) was considered an intermediate for both solvolysis and rearrangement of (9). However, the Woodward-Hoffman rules forbid the formation of this type of four membered ring transition state. An alternative route to explain their observation is the ion-pair scheme (8) which is suggested for solvolysis of 3-chloro-pent-4-en-1-yne.

Young et al.[42] proposed the term "internal return" for the recombination of ions from an ion-pair to form a covalent bond, in contrast to "external return" or mass law effect which signifies recombination of the carbonium ion and an anion from solution. The partition of the common intermediate between "return" reactions and further solvolysis reactions depends upon the nucleophilicity and ionizing power of the solvent. An increase in solvent nuclophilicity will increase the rate of reactions which involve bonding between the ion-pair and solvent. An increase in the solvation forces associated with a leaving group will also tend to facilitate further solvolysis and will relatively retard the return step. For example, in Scheme (1) when acetic acid was used as a solvent the return as measured by the rate of rearrangement was high[42]. The return step is relatively much slower than reaction with solvent in the more nucleophilic 75% aqueous ethanol[37,43]. The amount of return in absolute ethanol is zero, probably because of the greater nucleophilicity of this solvent relative to 75% ethanol towards the ion-pair intermediate.

Internal return has been investigated in the reactions of cis and trans-3-chloro-5-methylcyclohexene[44]. In both ethanol and acetic acid, the loss of optical activity of either isomer exceeds the rate of solvolysis. Each chloride solvolyses without cis-trans isomerisation. The intermediate ions(12) and (13) are symmetrical and hence incapable of sustaining optical activity.



(12)

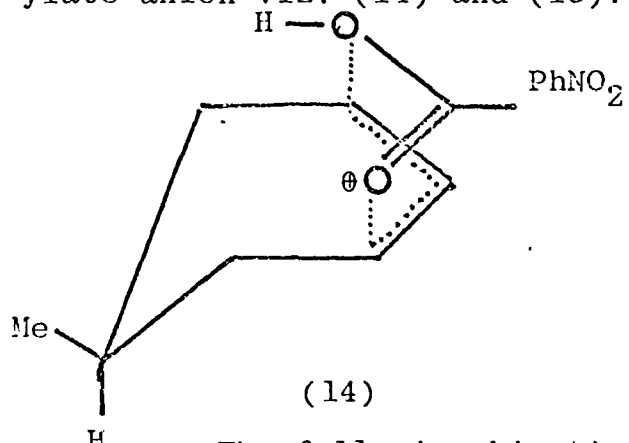


(13)

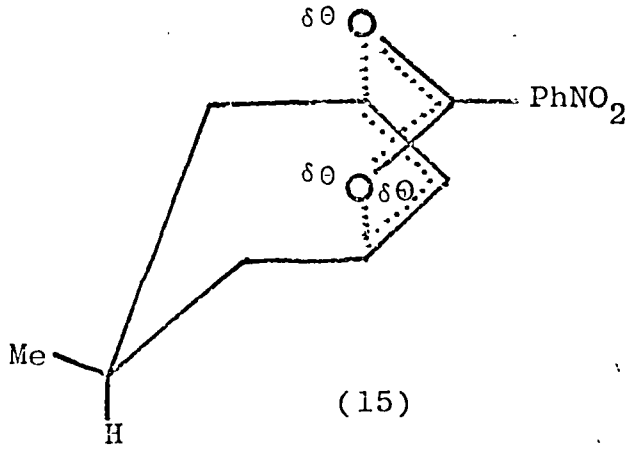
Owing to the absence of cis-trans isomerisation during racemization, the ion pairs obtained from the two isomers were given different structures; in each case the anion remained on the original side of the ring and a degree of covalent binding between it and the carbon atoms at the ends of the allylic system was invoked. If the bonding in the ion-pair were purely ionic, one would have expected relatively free rotation of each of the ions and, therefore, facile cis-trans isomerisation. However, the Woodward-Hoffman rules do not allow the formation of this type of four membered ring transition state. An intimate ion-pair instead of a four membered ring transition state might be a better choice.

Studies have also been made on the solvolysis of cis and trans-5-methylcyclohexenol hydrogen phthalates

in aqueous acetone[46], and acid catalysed and uncatalysed solvolyses of cis and trans-5-cyclohexenyl 3-p-nitrobenzoates[45]. In the acid catalysed solvolysis of the p-nitrobenzoates no internal return is found. Goering and Silversmith[45] attributed this lack of return to the absence of electrostatic bonding in the intermediate. However, as Streitweiser[37] has emphasised, the nucleophilicity of the leaving group is also important in determining the rate of return. A leaving carboxylic acid group is certainly less nucleophilic than a leaving carboxylate anion viz. (14) and (15):



(14)



(15)

The following kinetic probes are used to elucidate further the nature of ion-pair intermediates in the solvolysis reactions:

1.5.1 COMMON-ION RATE DEPRESSION

The addition of common ion salts to a solvolysis reaction can result in a so-called common-ion rate depression or mass law effect if there is return from dissociated cation and anion to neutral substrate, eqn. (9) [39, 44]. The formation of R^+ is depressed in this instance because an increase in $[X^-]$ favours the return process relative to solvent attack.

$$R\text{-}X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+ + X^- \xrightarrow{k_2} R\text{-}\overset{+}{O}S\text{H} + X^- \qquad (9)$$

1.5.2. ANION EXCHANGE

In every instance in which the common-ion rate depression has been observed, anion exchange has also been observed,[43,49] e.g. eqn. (10).

$$R\text{-}Cl \rightleftharpoons R^+ + Cl^- \overset{+^{36}Cl^-}{\rightleftharpoons} R\text{-}{}^{36}Cl + Cl^- \quad (10)$$

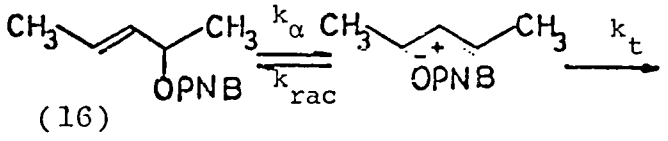
However, anion exchange and common-ion rate depression should not be equated, since anion exchange has been observed in the absence of common-ion rate depression. In these instances return from a solvent -separated ion-pair is implicated. Thus, anion exchange can also occur on solvent separate ion-pairs.

Exchange has never been detected for tight ion-pairs and appears to be quite slow for certain solvent-separated ion-pairs[50].

1.5.3 RACEMIZATION OF SUBSTRATE

The observations of a common ion rate depression and anion exchange for certain substrates but not for others was interpreted by earlier workers[39] as consistent with the SN_1-SN_2 mechanistic formulation.

However, this interpretation was shown to be incorrect by the observation that certain substrates ionize faster than they produce products even when common-ion rate depression or anion exchange is not observed. Such a result can only be due to return from some species less dissociated than a free carbocation. For example, Coering and Pombo[51] found that the optically active ester (16) in 90% aqueous acetone racemized 4 times as fast as it solvolyzed; added p-nitro-benzoate salt was shown not to interchange with carbonyl ^{18}O-labeled ester.



(16) solvolysis product (11)

The rate of ionization is equal to the overall rate of loss of optical activity (k_α) which is given by eqn. (12).

$$k_{ion} = k_\alpha = k_{rac} + k_t \qquad (12)$$

1.5.4. SPECIAL SALT EFFECT

It has long been known that the addition of non-common-ion salts to a solvolysis medium will frequently cause a rate acceleration, presumably because of an increase in ionic strength of the medium. The rate increase is normally linear with respect to the salt concentration, eqn. (13).

$$k = k_o\ (1 + b\{salt\}) \qquad (13)$$

However, certain highly reactive arene sulfonates have been observed to give a non-linear plot with added $LiClO_4$ small amounts of salts producing initially a large rate response[52]. This rate acceleration (special salt effect) was shown to result from removal of return from the solvent-separated ion-pair. Return from the tight ion-pair was not eliminated since K_α was found to respond linearly to salt concentration.

1.5.5 SOLVENT EFFECTS

The ionic dissociation of a covalent bond is a process which requires considerably more energy than homolysis, since work has to be done against an electrostatic field. This may be compensated by attractive interactions between the ions and solvent molecules (solvation energy),

consequently, ionic reactions tend almost exclusively to occur only in solution and, moreover they are very sensitive to the nature of the solvent. The greater the ability of the solvent to associate with ions the lower will be the activation energy for a heterolytic reaction of an initially neutral substrate.

One measure of solvent polarity is the dielectric constant, and a rough correlation between solvolysis rates and dielectric constant is observed[53]. A much more satisfactory measure of solvent polarity, solvent ionizing power, comes from a linear free energy relationship developed by Winstein and Grunwald, which is based on the reaction of tert-butyl chloride as a model SN_1 substrate[53]. These workers presented the following relationship:

$$\log \frac{k}{k_o} = m_{GW}Y \qquad (14)$$

where k is the solvolysis rate of tert-butyl chloride in the solvent in question, k_o is the rate in 80% aqueous ethanol, m is a measure of substrate sensitivity to solvent ionizing power and is assigned a value of unity for tert-butyl chloride. Y is thus determined by the solvolysis rates of tert-butyl chloride.

A major difference between SN_1 and SN_2 transition states is that the former closely resembles an ion-pair in which unit change is essentially wholly developed, while in the latter only partial charges have formed and they are much less concentrated, being spread over a more extended species. The SN_1 process may be expected to be the much the

more sensitive of the two to solvent ionising power and thus to be characterised by larger values of m. An m value of around 1.00 implies that the substrate solvolyses by the SN_1 mechanism. The smaller the m value the less ion-pair-like in character will be the transition state, and a purely (SN_2) solvolysis will have an m value of about 0.3.

Standard solvolysis reactions other than t-butyl chloride solvolysis have been suggested, i.e. p-methoxy-neophyl tosylate where complications due to possible ion-pair return are unimportant.[54/]

More recently Schleyer et al.[55/] have argued that "Y" values do not reflect the ability of a solvent to act as a nucleophile or to promote elimination reactions by E_2 type mechanism and that it is impossible to differentiate between these properties using tert-butyl chloride. Accordingly they solvolysed 1-adamantyl bromide in a variety of solvents; these solvolysis should have no nucleophilic solvent participation (backside attack by solvent being precluded on steric grounds) and furthermore eliminations are similarly prohibited. An excellent correlation between the data for t-butyl chloride and 1-adamantyl bromide solvolyses was obtained, confirming that t-butyl chloride solvolyses by a limiting mechanism, free from nucleophilic participation by solvent or rate-determining elimination.

A breakdown between the correlation of t-butyl chloride and 1-adamantyl bromide solvolysis is observed in aqueous trifluoroethanol solutions[56/]; (Shiner et al. had suggested earlier[57/] that trifluoroethanolysis of

t-butyl chloride involves competition between substitution and rate-limiting elimination at the ion-pair stage) and that the earlier mentioned properties of 1-adamantyl bromide made it a better standard for SN_1 limiting behaviour. By plotting log k for a series of substrates against log k for 1-adamantyl bromide for solvolysis in both aqueous ethanol and trifluoroethanol [56], it was found that for substrates reacting with significant involvement of solvent, as a base inducing elimination or as a nucleophile, the data for ethanol and trifluoroethanol could be represented by two distinct lines. On the other hand for those cases where elimination is prohibited or solvent participation excluded (e.g. 1-adamantyl chloride) a single line correlates the data for both solvent systems.

Recently Schleyer et al.[58] have suggested that hexafluoroisopropanol should be the solvent of choice for the study of limiting solvolyses, in view of its high ionising power and low nucleophilicity.

Schleyer et al recently proposed a scale of N values based on Me-OTs. This provides a good test for eqn. (15),

$$\log k/k_o = mY + \ell N \qquad (15)$$

where N is the solvent nucleophilicity and ℓ is the sensitivity to N. They claim eqn. (15) to be superior to eqn. (14) in analysing solvent effects in solvolysis.

Very recently Rappoport et al.[60] demonstrated that in all binary solvent mixtures for which N values are available except one, N and Y are nearly linearly correlated (eqn. 16). They obtained eqn.17 from eqns 15 and 16

and the relationship between m_{GW} and m of eqn. 15 which measures the sensitivity of the ionizing power when contributions due to solvent nucleophilicity are excluded, is given by eqn. 18.

$$N = aY+b \qquad (16)$$

$$\log \frac{k}{k_o} = (m + a\ell)Y+b\ell \qquad (17)$$

$$m = m_{GW} - a\ell \qquad (18)$$

1.6 ALLYLIC SOLVOLYTIC REACTIONS

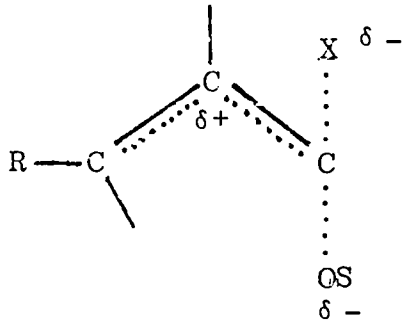
Solvolysis reactions are nucleophilic substitutions in which the solvent is the reagent. They generally exhibit first order kinetics, simply because the solvent is present in such large excess that kinetic dependence of rate on solvent concentration is not observable. Although the solvolysis of substituted allylic esters and chlorides was established as a reaction by the SN_1 mechanism, the problem of "product spreads" observed on solvolysis of isomeric allylically related compounds remainded.[7] Thus, for example, the solvolysis of 3-methylallyl chloride gives a relatively larger percentage of unrearranged 3-methylallyl alcohol than does the isomeric 1-methylallyl chloride, in buffered aqueous organic solvents. The phenomenon appears to be quite general.[7]

The traditional explanation for the rationalisation of product spreads has invoked the operation of simultaneous SN_1 and SN_2 reactions. In the above example the larger percentage of unrearranged 3-methylallyl alcohol was ascribed

to the relatively unhindered primary chloride undergoing simultaneous bimolecular attack with solvent. This process is competitive with ionisation to an intermediate (common to that produced from the isomeric 1-methylallyl chloride), which produces identical allylic related solvolysis products. The reasons for rejecting this possibility and assuming instead that one or both isomers react by a mechanism intermediate between the limiting SN_1 and SN_2 mechanisms have already been discussed.

An alternative explanation has been reported utilising the structural hypothesis of Doering and Zeiss (p.17).[36]

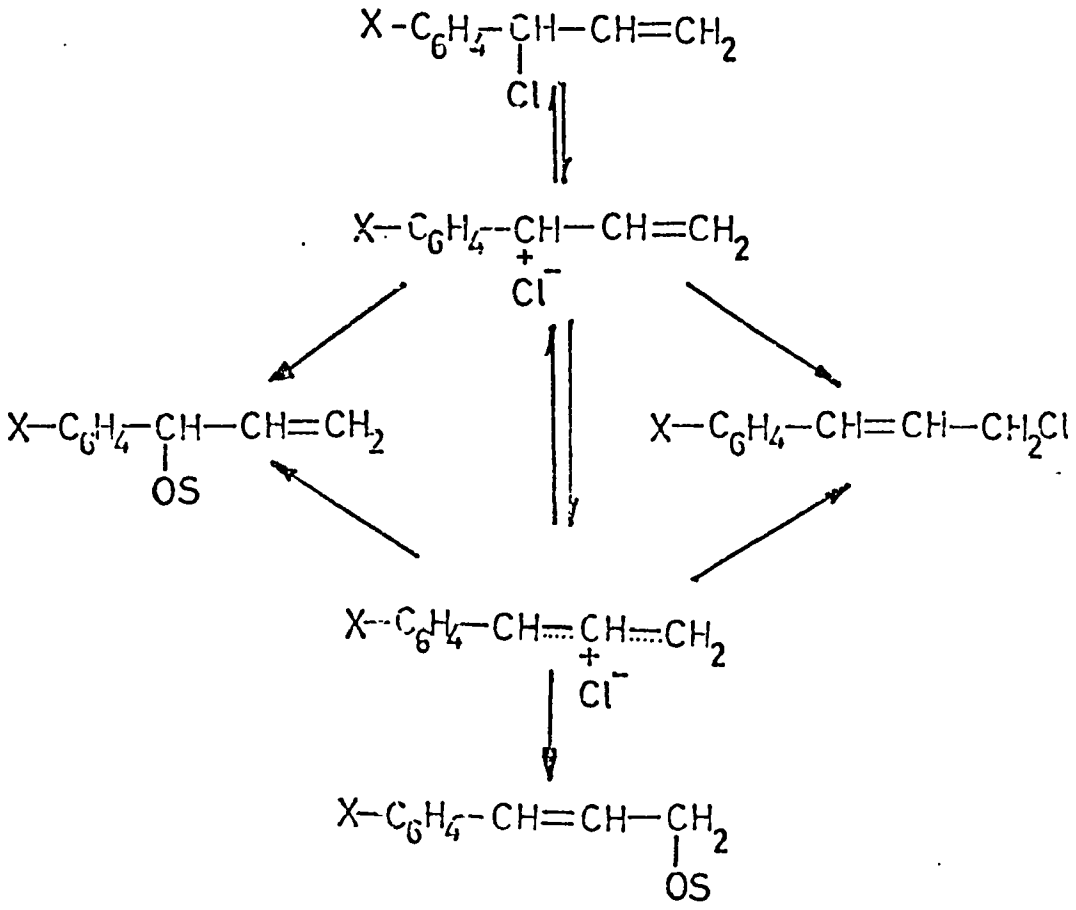
The transition state of the type (8) was proposed by Streitwieser[37] for an allylic solvolysis occurring by the SN_2 mechanism. If the nucleophilic interaction of the solvent molecule is somewhat weaker, and electrophilic solvation of the leaving group somewhat stronger, this structure can represent a highly reactive ion-pair intermediate as well as a transition state.



(8)

The problem of determining experimentally which possible carbonium-ion intermediate gives rise to solvolysis product is a complex one.[8] The mechanism of solvolytic reactions of 1- and 3-phenylallyl chloride were discussed by Shandala, Valkanas, Waight and Weinstock[61, 62, 63]. They have suggested a common ion-pair intermediate for

solvolysis and rearrangment. For the solvolytic reactions of 1-phenylallyl chloride they have suggested the following scheme.



SCHEME 2

However, Valkanas [63] considered the free phenylallyl carbonium ion to be absent from all stages of the mechanism.

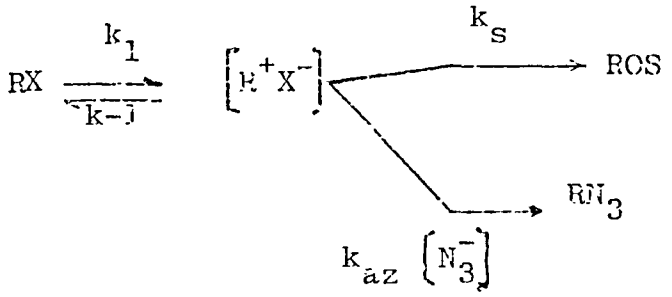
De la Mare and Vernon [43] have studied the solvolytic reaction of 1,1- and 3,3-dimethylallyl chlorides. These authors propose that the rearrangment partly occurs intramolecularly, independently of the rest of the rearrangement which follows the ionization process. However, Young Weinstein and Goering [12] prefer to regard the isomeric rearrangement and solvolysis as occuring through the same intermediate. Almost the same conclusion was drawn in the

case of crotyl and 1-methylallyl chloride.

The intermediacy of ion-pairs has also been postulated by Astin and Whiting [74], in the acetolyses of 2,4-dinitrophenolates of nerol, geraniol, linalool and ∝ - terpineol. They have also proposed [73] the existence of"Braude and Jones intermediate"for the rearrangement of 3,3-dimethylallyl, 2,4-dinitrophenyl ether to its primary isomer in acetic acid.

Sneen and his co-workers [64,65,66] have investigated the solvolysis of some allylic chlorides in aqueous solvents, in the presense of added salt capable of acting as nucleophiles (i.e. tetra-n-propylammonium azide and sodium thiocyanate),in order to determine whether allylic ion-pair intermediates could serve as substrates for nucleophilic attack. The kinetic technique paralleled that employed by Sneen and Larson [67] in the investigation of the solvolysis of (+)-2-octylmethanesulphonate competitive with added inorganic azide ion in 30% aqeuous dioxan, in that the competitive reactions in solvent ethanol ($36^{o}C$) of 1,3-dimethylallyl chloride with solvent and either tetra-n-propylammonium, azide or sodium thiocyanate were found to occur at a rate less than first order but greater than zero order in added nucleophile.

The kinetics may be forumulated in terms of the scheme shown below:



SCHEME 3

where $\dfrac{[RN_3]}{[ROS]} = \dfrac{k_{az}\ [N_3^-]}{k_s} = m\ [N_3^-]$

steady-state treatment of the above scheme gives

$$k_{obs} = \frac{k_1\ (k_s + k_{az}\ [N_3^-])}{k_{-1} + k_s + k_{az}\ [N_3^-]}$$

where k_{obs} equals the observed titrimetric rate constant.
In the absence of added salt, this reduces to:

$$k_{NS} = \frac{k_1\ k_s}{k_{-1} + k_s}$$

where k_{NS} is the rate constant in the absence of salt, whence

$$\frac{k_{obs}}{k_{NS}} = \frac{(k_{-1} + k_s)\ \ (k_s + k_{az}\ [N_3^-]}{k_s\ (k_{-1} + k_s + k_{az}\ [N_3^-])}$$

dividing through k_s affords eqn. (19)

$$\frac{k_{obs}}{k_{NS}} = \frac{(x + 1)\ (1 + m[N_3^-])}{(x + 1\ \tau_m\ [N_3^-])} \qquad (19)$$

where $x = \dfrac{k\text{-}1}{k_s}$

The use of the two added nucleophiles enabled the value of n to be fixed, and a value of x = 4.0 correlated the data with $m\{N^-_3\} = 33.0$ and $m\{SC\bar{N}\} = 6.6$.[64]

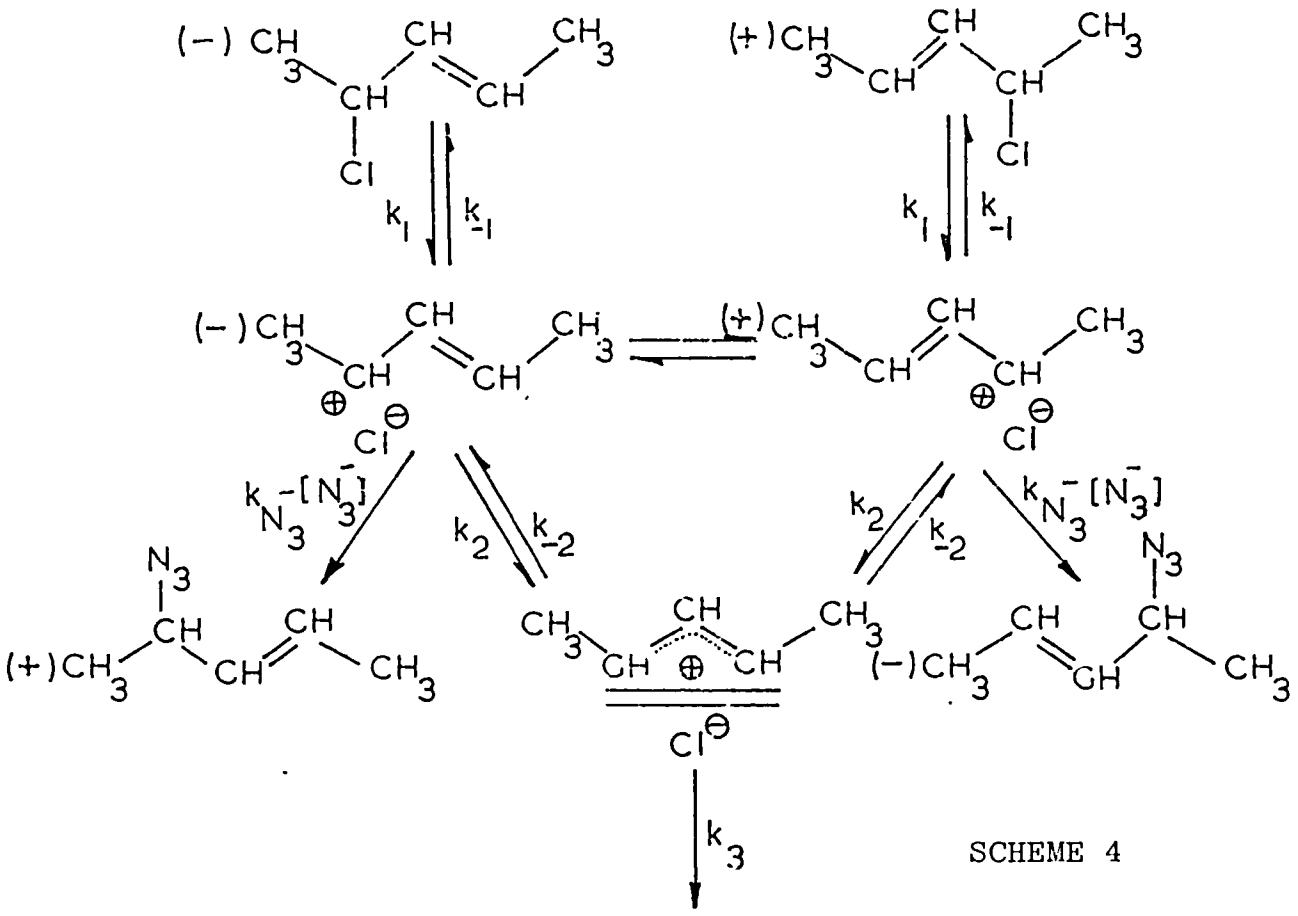
An expansion of the above scheme (3) was warranted by two further observations:

a) The solvolysis of optically active 1,3-dimethyallyl chloride in absolute ethanol at 27°C afforded racemic 1,3-dimethyallyl ethyl ether ($k_\alpha = 1.15 \times 10^{-4} sec^{-1}$, $k_t = 4.95 \times 10^{-5}$ sec^{-1}, $k_\alpha/k_t = 2.32$ unaffected by added chloride ion).

b) Reaction of levorotatory 1,3-dimethylallyl chloride at 27° in absolute ethanol in the presence of added azide ion (0.11M) afforded racemic ether and dextrorotatory 1,3-dimethylallyl azide (presumably inverted).

Thus the substitution products are formed in processes with fundamentally different sterochemical consequences, alkyl azide with maintained asymmetry and the ethyl ether with racemization, although compliance with equation (19) establishes that both products share a common intermediate.

The data were rationalised via scheme (4) which includes any asymmetric intimate ion-pair which can either serve as a substrate for azide attack, racemise via a 1,3 allylic shift, or, alternatively, react further to give a solvent-separated ion-pair which collapses to a racemic solvolysis product.



SCHEME 4

Racemic Ethers

The problem of product spreads was accounted for as the result of the relatively unselective reactions of a high-energy intermediate, the primary ion-pair[66], with solvent.

The attack of the nucleophile on the intimate ion-pair may be suggested in terms of formation of a new intimate ion-pair which collapses to give inverted product:-

$$Nuc^- + (R^{+-}X) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (Nuc^{-+}R) + X^- \overset{Fast}{\rightleftharpoons} NucR + X^- \qquad (20)$$

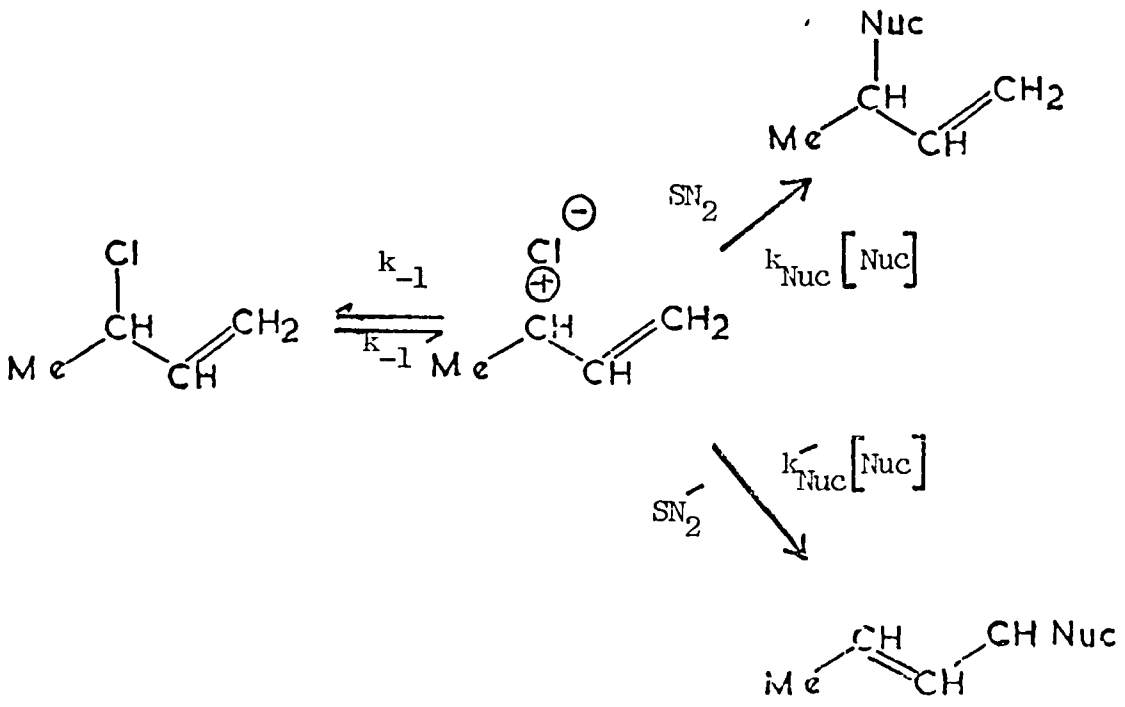
It was assumed that at low $\overline{X}$ concentrations k_{-1} is small and the reaction essentially irreversible. Precedents for this process include the observations of Streitwieser et al.[68] that during the acetolysis of

(+) - 2 - octyl tosylate, the unsolvolysed tosylate undergoes racemisation during the reaction. This was shown to be due to capture of the liberated tosylate anion by acetate-octyl ion-pair, whereupon the rate of solvolysis drifts downwards during the reaction owing to the presence of captured covalent tosylate. A further example was provided by Whiting et al.[69] The two trans-2-decalyl tosylates were acetolysed in the presence of sodium β - naphthalenesulphonate; when the reaction was interrupted before completion, the presence of covalent naphthalenesulphonate was demonstrated by u.v. spectroscopy (although it was not shown that the recovered naphthalenesulphonate had the inverted configuration).

Work done by Okamota and co-workers[70] has afforded clear evidence for the attack of anions on ion-pairs. It was found by these workers that cis-trans isomerisation and 1, 2 - rearrangement occur during the acetolysis of cis-4-t-butylcyclohexyl tosylate. They concluded that cis-trans isomerisation occurs by SN_2 attack by tosylate anion on the ion-pair intermediate and partly as a result of rotation of the 4-t-butyl -cyclohexyl cation within the ion-pair, although the evidence for this rotation was considered unconvincing. It was suggested that the 1,2 rearrangement proceeded through an intramolecular of hydride shift at ion-pair stage.

The intermediacy of intimate and solvent-separated ion-pairs has also been postulated by Borcic et al.[71], in the reaction of 1,1 and 3,3-dimethylallyl chlorides in water, ethanol and aqueous ethanol, with sodium ethoxide and sodium borohydride as a nucleophile. It was found that the

ratio of primary to tertiary substituted products increased with increasing nucleophilicities of the attacking species (i.e. $Et\bar{O} > EtOH > H_2O$). The ratio increased more rapidly for the 3,3 dimethylchloride and this was attributed to the incursion of direct SN_2 displacement on the primary chloride, in addition to displacement at the intimate ion-pair stage. Sneen and Carter [66] also invoked ion-pair intermediates in the SN_2' reaction of 1-methylallyl chloride with sodium thiophenoxide in aqueous dioxane; this was also interpreted in terms of the scheme below:



SCHEME 5.

It was assumed that the initially formed ion-pair had distributed some of its positive charge to the 3-position, and a balance of electronic and steric factors determines the

proportions of SN_2 and SN_2' products. Configurational integrity of the ion-pair is again necessary to explain the the observed syn arrangement of entering and leaving groups of an SN_2' reaction, the one example investigated[23] was interpreted as a nucleophilic substitution on the unionised substrate. This observed stereochemistry also has a theoretical justification.[72]

CHAPTER TWO

Results and discussion of synthetic work

2. RESULTS AND DISCUSSION OF SYNTHETIC WORK

Extensive studies of the synthesis, anionotropic rearrangement and solvolysis reactions of 1-phenylallyl chloride and cinnamyl chloride have been carried out by Valkanas, Waight and Weinstock. [63,73,74,75]

The aim of the research was to find a satisfactory method for synthesising the following allylic chlorides:

(16) 3-chloro-penta-1,4-diene

(17) 5-chloro-penta-1,3-diene

(18) 3-chloro-pent- 4-en-1-yne

(19) 5-chloro-pent- 3-en-1-yne

(20) 1-chloro-4,4-dimethyl-1-phenyl-pent-2-ene

(21) 3-chloro-4,4-dimethyl-1-phenyl-pent-1-ene

(22) 1-chloro-4,4-dimethyl-1-p-nitrophenyl-pent-2-ene

(23) 3-chloro-4,4-dimethyl-1-p-nitrophenyl-pent-1-ene

(24) 3-chloro-6,6-dimethyl-hept-4-en-1-yne

(25) 5-chloro-6,6-dimethyl-hept-3-en-1-yne

It was proposed to study the solvolysis and anionotropic rearrangement of these coumpounds in order to gain an insight into the nature of the intermediate species involved. The last six chlorides were of particular interest in the present investigations due to the presence of a t-butyl group which should cause normal bimolecular substitutions to be suppressed, for steric reasons, in a way analogous to that of the neopentyl halides.

Successful chlorination of allyl alcohols with more than 80% unrearranged product has been reported. [73,76] Therefore the best approach was considered to be the preparation of their corresponding alcohols, with a view to subse-

quent hydroxy-displacement. The preparation of the following allylic alcohols have been reported [78,79,80,81].

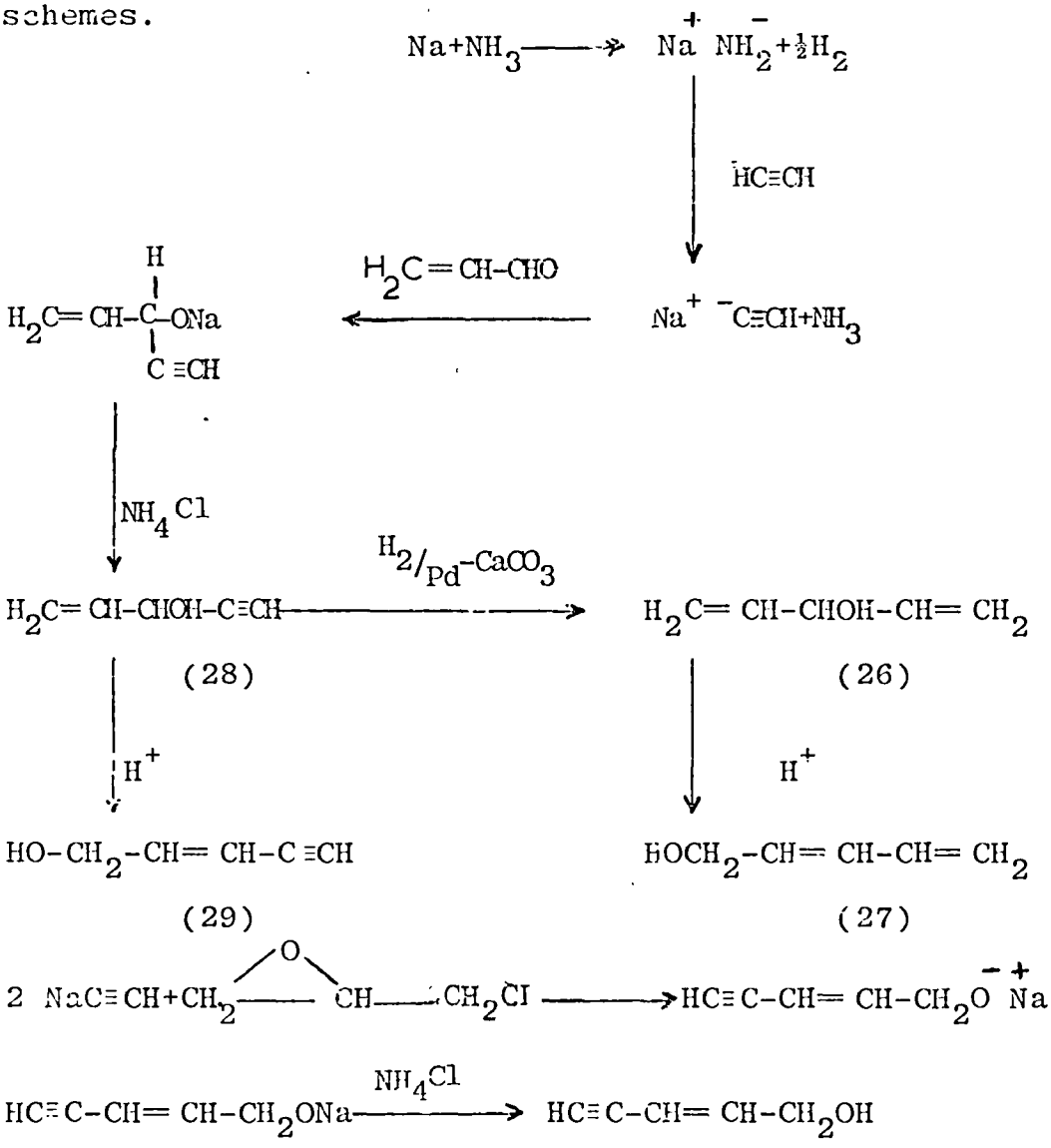
(26) Penta-1,4-dien-3-ol

(27) Penta-1,3-dien-5-ol

(28) Pent-4-en-1-yn-3-ol

(29) Pent-3-en-1-yn-5-ol

These preparations were carried out according to the following schemes.



The synthesis of the allylic alcohols 30 to 35 will be discussed and their chlorination reactions will be explained.

(30) 1-t-butyl-3-phenylallyl alcohol

(31) 1-t-butyl-3-p-nitrophenylallyl alcohol

(32) 3-t-butyl-1-phenylallyl alcohol

(33) 3-t-butyl-1-p-nitrophenylallyl alcohol

(34) 6,6-dimethyl-hept-4-en-1-yn-3-ol

(35) 6,6-dimethyl-hept-3-en-1-yn-5-ol

Several attempts were made to synthesise 3-t-butyl-1-phenylallyl alcohol (32). In the first case this compound was prepared by condensation of 4,4-dimethyl 2-pentanal and phenyl magnesium bromide in anhydrous ether. The preparation afforded a low overall yield of the required alcohol, provided that care was taken to ensure that the moisture was excluded from the reaction vessels, solvent and magnesium. The crude product of the Grignard addition was distilled, taking great care to keep the temperature of the heating bath at the minimum required to give distillation. In spite of this about 30% of the crude product remained in the distillation flask, as a dark brown polymeric residue. This method was rather long (5 steps) and resulted in very poor overall yield (3-5%). This was due to the difficulty in the preparation of pivaldehyde (which trimerized rapidly) and 4,4-dimethyl 2-pentanal.

$$\text{t-BuCl} \xrightarrow{\text{Mg}} \text{t-BuMgCl} \longrightarrow \text{t-Bu-CHO}$$

$$\text{t-BuCHO} \xrightarrow[\text{n-BuLi}]{\text{CH}_3\text{-CH=N-C}_6\text{H}_{11}} \text{t-Bu-CH=CH-CHO}$$

$$\text{t-Bu-CH=CH-CHO} \xrightarrow[(2)\text{H}_3^+\text{O}]{(1)\text{PhMgBr}} \text{t-Bu-CH=CH-CHOH-Ph}$$

An alternative route was then pursued with a satisfactory overall yield (40-42%). This method required the condensation of t-butyl-acetylene with benzaldehyde (73-78%), followed by reduction of the acetylenic bond by LAH

$$t\text{-Bu-C}\equiv\text{CH} \xrightarrow{CH_3Li} t\text{-Bu-C}\equiv\text{C}^{\ominus}\ Li^{\oplus} \xrightarrow[2\ NH_4Cl]{1)C_6H_5\text{-CHO}}$$

$$t\text{-Bu-C}\equiv\text{C-CHOH-Ph} \xrightarrow{LAH} t\text{-Bu-CH=CH-CHOH-Ph}$$

However the t-butylacetylene was prepared in moderate yield (47-50%) by dehydrochlorination of the geminal chloride (1,1-dichloro-3,3-dimethyl butane)with sodamide in liquid ammonia

$$t\text{-BuCl}+H_2C{=}CHCl \xrightarrow{AlCl_3} t\text{-Bu-CH}_2\text{-CHCl}_2$$

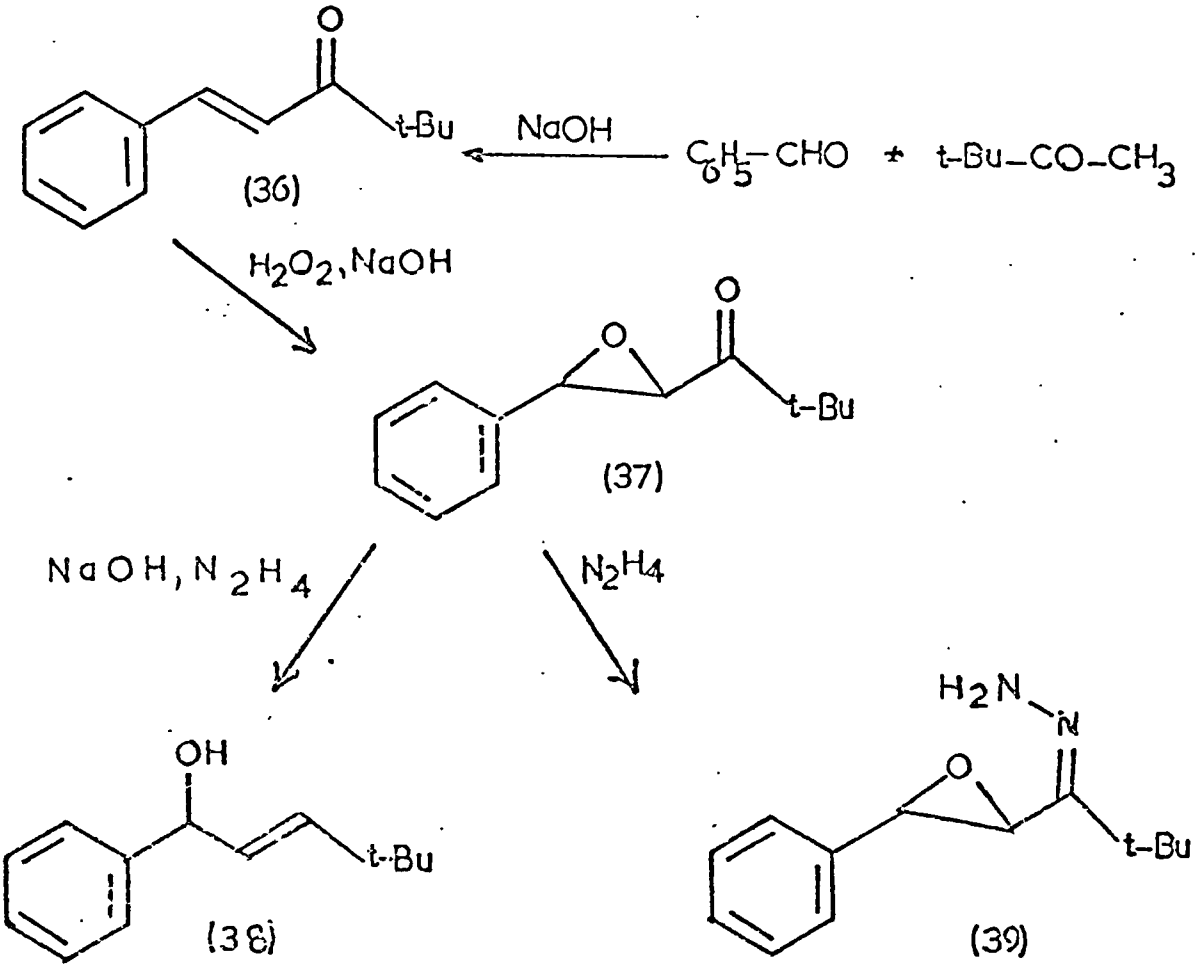
$$t\text{-Bu-CH}_2\text{-CHCl}_2 \xrightarrow{3NaNH_2} t\text{-Bu-C}\equiv\text{CNa} \xrightarrow{H_2O} t\text{-Bu-C}\equiv\text{CH}$$

The preparation of the geminal chloride was easy, provided that care was taken to ensure that moisture was excluded from the reaction vessels, solvent and aluminium trichloride. The reactions were carried out under dry oxygen-free nitrogen in a vacuum line. An alternative route to synthesize t-butyl-acetylene involved chlorination of pinacolone by phosphorous pentachloride followed by dehydrochlorination of the geminal chloride (2,2-dichloro-3,3-dimethyl butane)with potassium hydroxide in a mixture of ethanol and mineral oil as solvent.

$$t\text{-Bu-CO-CH}_3 \xrightarrow{PCl_5} t\text{-Bu-CCl}_2\text{-CH}_3 \xrightarrow{KOH} t\text{-Bu-C}\equiv\text{CH}$$

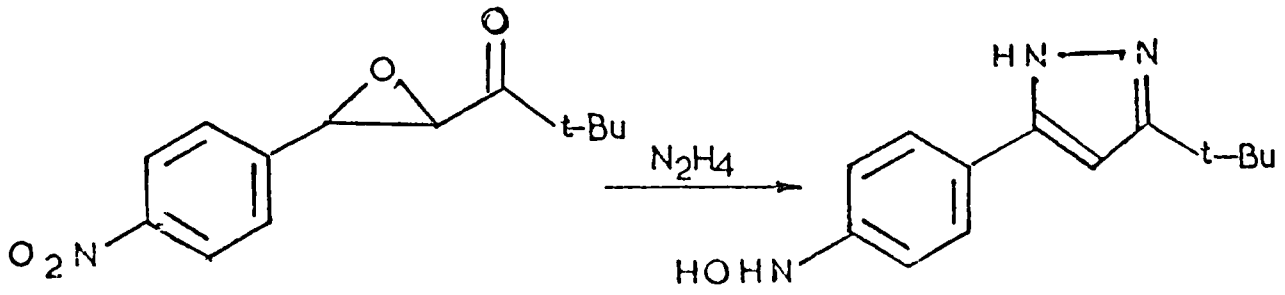
This route was convenient and gave an overall yield of 55-60%. Although the latter method of synthesis of 3-t-butyl-1-phenylallyl alcohol (condensation of t-

Butylacetylene with benzaldehyde followed by LAH reduction) was successful and had a good overall yield, it was rather time consuming. Another route to the alcohol involved the condensation of pinacolone with benzaldehyde to afford styryl-t-butyl ketone (36). The α,β -epoxyketone (37). Reduction of this α,β epoxyketone in hydrazine in the presence of sodium hydroxide afforded the required allylic alcohol (38).



The overall yield was about 20%. Attempts were not made to optimize this yield. This rearrangement involves the intermediate formation of the hydrazone of the epoxyketone (39).[77]

This collapses with extrusion of nitrogen to afford the 3-t-butyl-1-phenylallyl alcohol (38). However when the reaction was run without base, the hydrazone was isolated as the only product. This proved that the second step of reaction was base-catalysed at least in this particular system. With a nitro substituent in the para position of the aromatic ring the hydrazone reduction gave a mixture of six components, but of the four fractions examined by mass spectroscopy none was found to correspond to an allylic alcohol. NMR, IR, and mass spectral data showed that the nitro group had been reduced to an hydroxylamine and a pyrazole ring had been formed.



The formation of an hydroxylamine derivative was deduced from the observation that the compound reacted with acetone to give a nitrone.

The attempted preparation of 3-t-butyl-1-phenylallyl chloride (20) from the corresponding alcohol (32) led under all conditions to the conjugated chloride (21) (as described in pages 52 & 119).

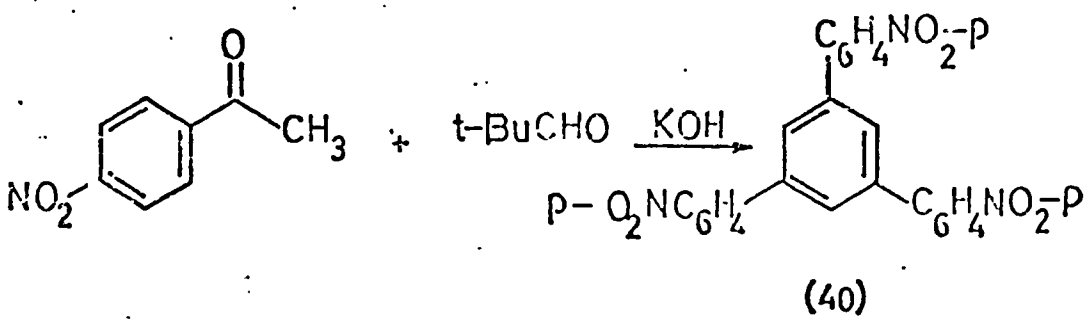
M.Y.Shandala [62] reported that an electron withdrawing substituent in the aromatic ring decreases the rate of allylic rearrangement and election-donating substituents cause an increase.

In order to decrease the rate of allylic rearrangement the preparation of 3-t-butyl 1-p-nitrophenylallyl chloride (22) was undertaken. In view of the failure of the Wharton rearrangement in this case; the preparation was tried by reaction of t-butyl-vinylmagnesium chloride and p-nitrobenzaldehyde at very low temperatures [82,83]. A mixture of seven compounds was obtained presumably because of competitive reaction of the Grignard reagent with the nitro group. It has been observed in several cases that a Grignard reagent reacts normally at the carbonyl group in the presence of a nitro group at sufficiently low temperatures, however the yields are low.

Attempts were made to prepare 3-t-butyl-1-p-nitrophenylallyl alcohol (33) from p-nitroacetophenone and pivaldehyde followed by a reduction with aluminium isopropoxide and isopropanol. [84] The pivaldehyde did not react with p-nitroacetophenone under normal aldol condensation conditions, and n.m.r. and the mass spectral data showed that the p-nitroacetophenone had undergone self-condensation to give (40), a trimeric aldol product 2,4,6-tri-p-nitro-phenylbenzene.

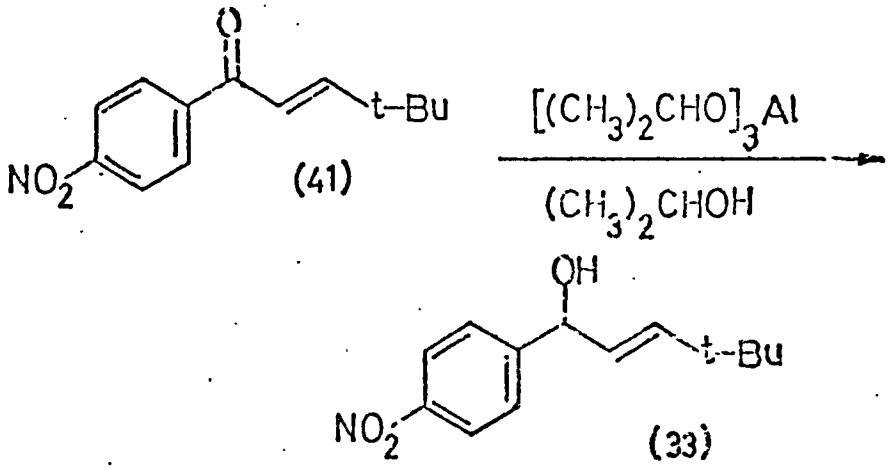
The failure of pivaldehyde to undergo condensation with p-nitroacetophenone may be due to the inductive effect of the t-butyl group which would reduce the electrophilic nature of carbonyl carbon atoms. The steric effect of the t-butyl group also may be an important factor in preventing the reaction. However, when p-nitroacetophenone was added

dropwise very slowly over a period of 5 hours to a solution of pivaldehyde and sodium hydroxide in methanol, about 43% of desired compound (41) was obtained. This slow addition of the ketone to the reaction mixture was essential in order to suppress the competitive self-condensation reaction giving rise to compound (40).



(40)

Reduction of p-nitrophenyl-t-butylvinyl ketone with aluminium isoproxide and ispropanol was successful



(41) (33)

and afforded about 65% of 3-t-butyl-1-p-nitrophenylallyl alcohol (33).

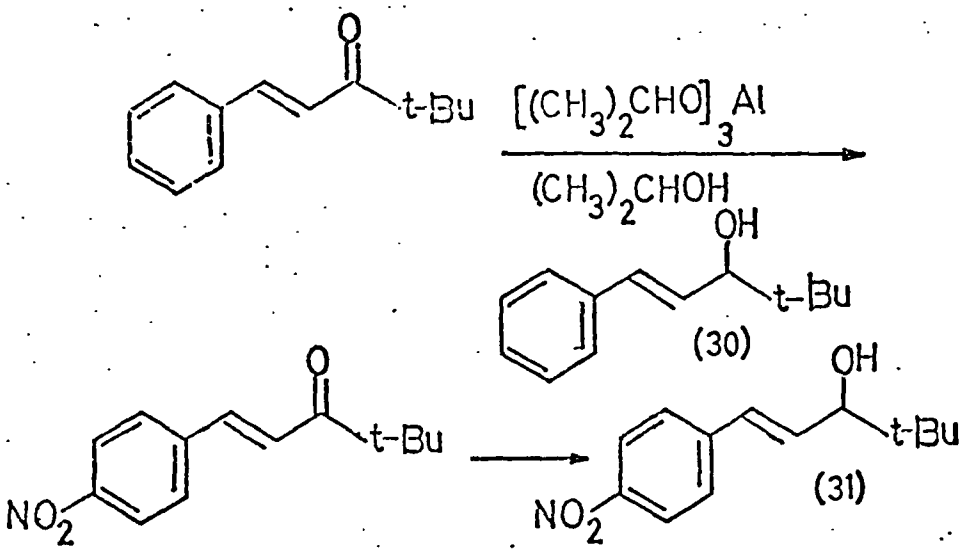
Preparation of 6,6-dimethyl-hept-4-en-1-yn-3-ol(34) from the reaction of propargyl aldehyde and t-butylvinyl magnesium bromide was successful. The reaction was carried out under dry oxygen-free nitrogen since the products in ensuing stages were thought to be air-sensitive. The yield in the formation of the t-butylvinyl magnesium bromide was 60-80%, estimated by the weight of unreacted magnesium removed at the end of the reaction. The crude product of the Grignard reaction was distilled carefully under reduced pressure. The overall yield was about 30-38%. The only side product in this reaction was a dimer of t-butylethylene.

$$t\text{-Bu-CH=CHBr} + Mg \xrightarrow{THF} t\text{-Bu-CH=CHMgBr}$$

$$HC{\equiv}C\text{-CHO} + t\text{-Bu-CH=CHMgBr} \xrightarrow[-40^{\circ}C]{THF} t\text{-Bu-CH=CH-CHOH-C}{\equiv}\text{CH} \quad (34)$$

The t-butylvinyl bromide was prepared by radically induced additions of HBr to t-butylacetylene in a reasonable yield (85). Initial attempts to prepare t-butylvinyl chloride utilising other than t-butylacetylene had failed. The Wittig reaction of $Ph_3P{=}CHCl$ with pivaldehyde was unsuccessful [86,87,88], but gave some novel ylid products which have not been investigated completely. However, judging by nmr and mass spectral data a possible structure was $Ph_3P{=}PPh_3$. The reaction of monochloroketene with pivaldehyde failed to give any of the t-butylvinyl chloride [89,90,91]. Addition of dichloroketene to unhindered aldehydes occurs in several cases. However, monochloroketene is less reactive and in the particular case of the addition to pivaldehyde, the substrate is much too hindered to react.

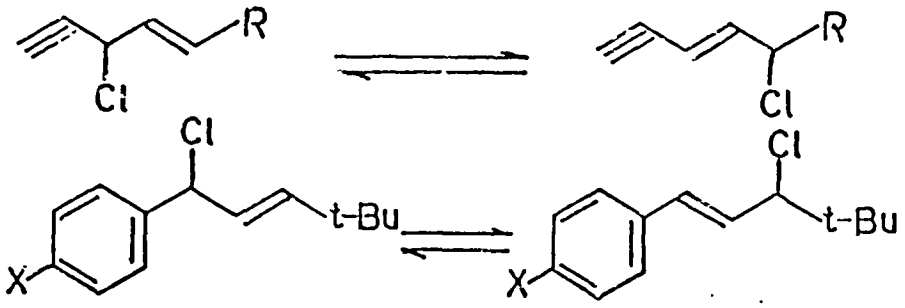
1-t-Butyl-3-phenylallyl alcohol (30) and 1-t-butyl-3-p-nitrophenylallyl alcohol (31) were simply prepared by reduction of p-nitrostyryl-t-butyl ketone (43) and styryl-t-butyl keton (36) (which were previcusly prepared in the synthesis of alcohols (32) and (33) by aluminium isopropoxide and isopropanol [84].



An alternative route to synthesize alcohol (30) was condensation of phenylacetylene with pivaldehyde followed by LAH reduction.

Attempts were made to chlorinate the allylic alcohols 16 to 25. Except for the 5-chloro-pent-3-en-1-yne (17) which is well known, [85, 86] the others (16,18 to 25) have not previously been reported. The chlorinations of the conjugated alcohols (27, 29, 30, 31, 35) were simply achieved by the use of thionyl chloride in an ethereal solution of tri-n-butylamine. [73, 76]

The unconjugated chlorides (16, 13, 20, 22, 24) however proved to be much more difficult to prepare. This is because the equilibria of the types 21 and 22 strongly favour the conjugated isomers.



(21)

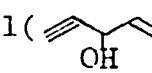
(22)

The preparation of these chlorides (16, 18, 20, 22, 24) can only succeed under non equilibrating, conditions. The possible existence of an allyl chloride similar to (18) as an intermediate in the reaction of (28) with thionyl chloride and phosphorus pentachloride was first reported by Heilbron and Jones. When the alcohols (26, 28, 32, 33, 34)[79, 80] were reacted in a cold dilute ethereal solution with thionyl chloride a mixture containing a high proportion of the conjugated chlorides resulted, as indicated by the ultra violet absorption of the product. However, when the same reactions were performed in the presence of tri-n-butylamine, whose hydrochloride is ether soluble[73], only alcohol (28) gave rise to any unconjugated chloride (18). The conjugated chlorides could be formed by abnormal bimolecular(SN_2') attacks of chloride ion on the intermediate chlorosulphinate, but the latter also rearranges intramolecularly (SN_i) to conjugated chlorides.

When a method reported by Corey[92] was applied to the chlorination of (28) a higher proportion of the unconjugated chloride was obtained and it seemed that this approach

would be promising. The reaction involves the formation of an intermediate dimethyl sulphonium halide as the halogenating species. Attempts were made to optimize the proportion of the unconjugated chloride. This was achieved by changing the published procedure slightly. The temperature of the reaction was lowered from -20°C to -70°C. However, the reaction of (28) with dimethyl sulphide (DMS) and N-chlorosuccinimide (NCS) at this temperature did not go to completion, even though the time of stirring had been trebled. Thus an excess of the chlorinating agent was added. In this case after distillation the product mixture showed two extra peaks in the n m r spectrum. When a blank reaction was performed, a side reaction between NCS and DMS which yields α-chloro-dimethyl sulphide was observed. This compound had a b.p. very close to that of 3-chloro-pent-4-en-1-yne (18) and was difficult to separate by distillation at least on a small scale. In order to increase the b.p. of this major side product diphenyl sulphide was used instead of dimethyl sulphide. In this case after distillation pure 3-chloro-pent-4-en-1-yne was obtained as shown by GLC, tlc, and n m r, it had a b.p. 72°-λ_{max} = 204, n_D^{16} = 1.4631, ε = 637 . The side reactions mentioned above did not cause any trouble in the preparation of the other chlorides.

6,6-Dimethyl-3-chlorohept-4-en-1-yne (24) was prepared in a good yield by this modified procedure together with 27% of the conjugated isomer (25). These two compounds were characterized by their physical data. The temperature of the reaction was very critical. If it was allowed to rise

above -20°C only the conjugated chlorides were obtained. It was also proved by glc that the compound (24) rearranges very easily at 0°C under the reaction conditons. It was prepared in order to attempt to study its anionotropic rearrangements. However, it had been shown by glc analysis that (24) rearranged extremely easily. It is known that anionotropic rearrangements are very sensitive to substituent effects at either the 1- or 3-positions, being facilitated by electron donating groups and inhibited by electron withdrawing groups. This type of correlation has been established by many workers [4, 93]. In particular Braude established that a methyl substituent attached to pent-4-en-1-yn-3-ol() increased the rate of rearrangement by a factor of 3×10^3 [94]. Initially chloride (24) was prepared in the hope that the steric effect of the t-butyl group would prevent bimolecular nucleophilic attack at the 3-position. However, the positive inductive effect of this group more than compensated for any steric influence. Thus rearrangement was very easy and kinetic studies were precluded.

Isolation of 3-t-butyl-1-phenyl allyl chloride (20) under even the mildest conditions failed, since this chloride rearranged very easily to afford the conjugated chloride (21) in high yield.

CHAPTER 3

Result and Discussion of Solvolytic Reactions of 3-chloro-pent-4-en-1-yne and 5-chloro-pent-3-en-1-yne

3.1 THE VINYL ACETYLENE SYSTEM

The discovery by Jones and McCombie[95] of anionotropic rearrangement involving the formation of a conjugated vinyl acetylene chromophore extended the number of systems available for study of this sort of rearrangement. The accompanying large increase in U V light absorption formed the basis of the kinetic method used by Braude and Jones.[96] They dealt particularly with oxotropy. By studying a great number of allyl alcohols Braude concluded that acid catalysis was essential for rearrangement and he postulated a mechanism involving an oxonium ion intermediate.

However, no work has been reported on the solvolytic reactions of this system. We have investigated the solvolytic reactions and rearrangements of the two isomeric chlorides, 3-chloro-pent- 4-en-1-yne and 5-chloro-pent-3-en -1-yne. This system is similar to the phenylallyl system in in many respects, but it has the advantage of being purely aliphatic in nature, thus avoiding complications arising from the presence of a benzenoid ring.[96] These compounds possesstwo distinct advantages over the simple substituted allylic systems on which a great part of the early work in this field was concentrated. The advantages derive from the fact that in one of the isomers the allylic system is in conjugation with an acetylenic bond. The 5-chloro-pent-3-en-1-yne and its normal solvolysis products absorb light at 228nm with a molecular extinction coefficient of about 12000, while the 3-chloro-pent-4-en-1-yne ε is about 637 at 204nm Since both compounds undergo solvolysis with rearrangement, the reactions can be followed by measurement

of the light absorption intensity. This enables one to employ a very low concentration of chloride and thereby avoid the need for adding bases to neutralize the acid produced on solvolysis. A large concentration of acid would catalyze the isomerization of the products.[97]

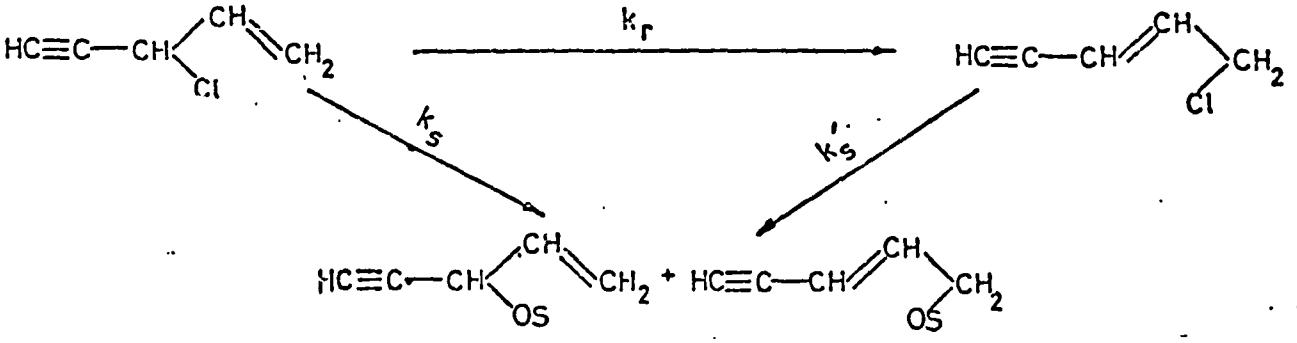
A more important point is that the final value of the light absorption intensity together with titrimetric determination of acid formed are sufficient to give a complete analysis of the products without the necessity of isolating the products or even removing the solvent.

The second advantage of the system lies in the large difference in reactivity between isolated and conjugated vinylacetylene systems. The 3-chloro-pent-4-en-1-yne has a far higher reactivity than its conjugated isomer towards unimolecular substitution, the rate constant for hydrolysis being about 60-70 times larger.

In an alkyl-substituted primary-secondary allylic system, e.g. the methylallyl chlorides, the secondary isomer is only 1.6 times as reactive as the primary.[28] Similarly in the acetylosis of 1,1-dimethylallyl chloride[98,99] the primary 3,3-isomer is formed but reacts with solvent at a rate similar to the tertiary isomer. Because of the large reactivity difference, the kinetics of the solvolysis of the unconjugated chlorides are not complicated by simultaneous isomerization followed by solvolysis of the isomer at a comparable rate to the starting material. When 3-chloro-pent-4-en-1-yne undergoes solvolysis, the reaction is accompanied by a considerable amount of isomerization, but the

5-chloro-pent-3-en-1-yne so formed is stable under the reaction conditions.

The reaction scheme is shown below:



Scheme 6

The solvolysis of both compounds was studied in a series of binary solvent mixtures in order to obtain information about effect of solvent ionizing power and solvent nucleophilicity on the product ratio and the rate constant of the reactions. The effect of added salts was also determined. For more accuracy, the reactions were followed by two methods, (a) by following the light absorption and (b) by titrating samples taken at appropriate times. Throughout the runs, very good first order rate constants were obtained. The rate constants obtained from the titration method were slightly lower than those measured spectrometrically. The differences arose because final light absorption values were a little low and titration volumes were consistently a little high. The U V errors

could arise since some solvolysis of the isomeric chloride which had formed in the rearrangement process resulted in a lower value for E_∞ than would have been the case if no solvolysis had occurred. However the difference between the titrimetric rate constants and spectrometric rate constants were within the limits of error of the measurements. In every run followed either by titration or spectrometrically, the end of the reaction was taken as the time of disappearance of 3-chloro-pent-4-en-1-yne and at that time both the final light absorption and the amount of HCl produced were measured. The rate constant obtained by either technique is the total rate constant of the reaction (k_t). By subtracting the final concentration of the HCl produced from the concentration of HCl equivalent to the initial concentration of allylchloride, the amounts of rearrangement were obtained. The rate constant of solvolysis (k_s) was calculated by multiplication of the overall rate constant (k_t) with the percentage of solvolysis. The difference ($k_t - k_s$) was the rate of isomeric rearrangement.

3.2.1 RESULTS (IONIZING POWER EFFECTS)

Tables (4) and (5) show the meanvalues for measurements of the rate of solvolysis and isomeric rearrangement of 3 chloro-pent-4-en-1-yne in various mixtures of three different binary solvent systems. The rates of reactions are very sensitive to the amount of water present in the medium and correlate quite well with the ionizing power of the medium as measured by the Y values[59b].

In fig. (3), log (k_t) is plotted against Y; the slope of line is about 0.8 which is typical of reactions in which the rate determining step is thought to be an unassisted ionization. The proportion of the rearranged isomeric chloride increases as the concentration of water in aqueous ethanol or aqueous methanol is increased while this increase causes a decrease in the relative amount of unconjugated to conjugated solvolysis product. The proportion of solvolysis to isomeric rearrangement is higher in ethanol/water than it is in aqueous trifluoroethanol, and it decreases as the concentration of water in the mixed solvent decreased. 50% aqueous ethanol has the same ionizing power as 70% aqueous trifluoroethanol, compared on the basis of Y values but has a lower nucleophilicity.[59b]

It can be seen that the total rate of reaction has not changed significantly with the lower nucleophilicity of the solvent. However, the proportion of solvolysis relative to isomeric rearrangement is greatly decreased. The close similarity of the total rates would not be expected

owing to the error involved in comparing the ionizing power of two quite different solvent systems (by means of their Y values).

TABLE 4

THE EFFECT OF SOLVENT IONIZING POWER ON THE RATE OF SOLVOLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE AT 60°C. IN AQUEOUS ETHANOL

Solvent Volume %	t-BuCl Scale Y	$k_t \times 10^3$ (Min.$^{-1}$)
90	-0.75	0.52 ± 0.03
80	0.00	2.03 ± 0.03
70	0.60	5.96 ± 0.03
60	1.12	15.7 ± 0.03
50	1.66	38.9 ± 0.03

k ± A = k ± Fractional error

TABLE 5

THE EFFECT OF SOLVENT IONIZING POWER ON THE HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE AT 50°C.

Solvent Volume %	t-BuCl Scale Y	$k_t \times 10^3 (min.^{-1})$	%R	% ROH
$CH_3CH_2OH-H_2O$				
90	-0.75	0.227 ± 0.02	15.2 ± 0.9	61.8 ± 1.3
80	0.00	0.89 ± 0.02	17.5 ± 0.9	55.8 ± 1.3
70	0.60	2.57 ± 0.02	18.7 ± 0.9	51.5 ± 1.3
60	1.12	6.64 ± 0.02	20.4 ± 0.9	49.2 ± 1.3
50	1.66	15.90 ± 0.02	21.5 ± 0.9	45.6 ± 1.3
$CF_3CH_2OH-H_2O$				
80	1.46	10.08 ± 0.02	30.3 ± 0.9	47.9 ± 1.3
70	1.66	15.57 ± 0.02	24.6 ± 0.9	43.5 ± 1.3
60	1.89	24.20 ± 0.02	20.2 ± 0.9	
50	2.33	37.66 ± 0.02	19.5 ± 0.9	
CH_3OH-H_2O				
88.3	-0.11	1.07 ± 0.02	15.7 ± 0.9	
80.9	0.30	2.26 ± 0.02	16.4 ± 0.9	
89.5	1.02	6.62 ± 0.02	20.8 ± 0.9	
50.0	1.97	39.8 ± 0.04	23.0 ± 0.9	

k ± A = k ± Fractional error

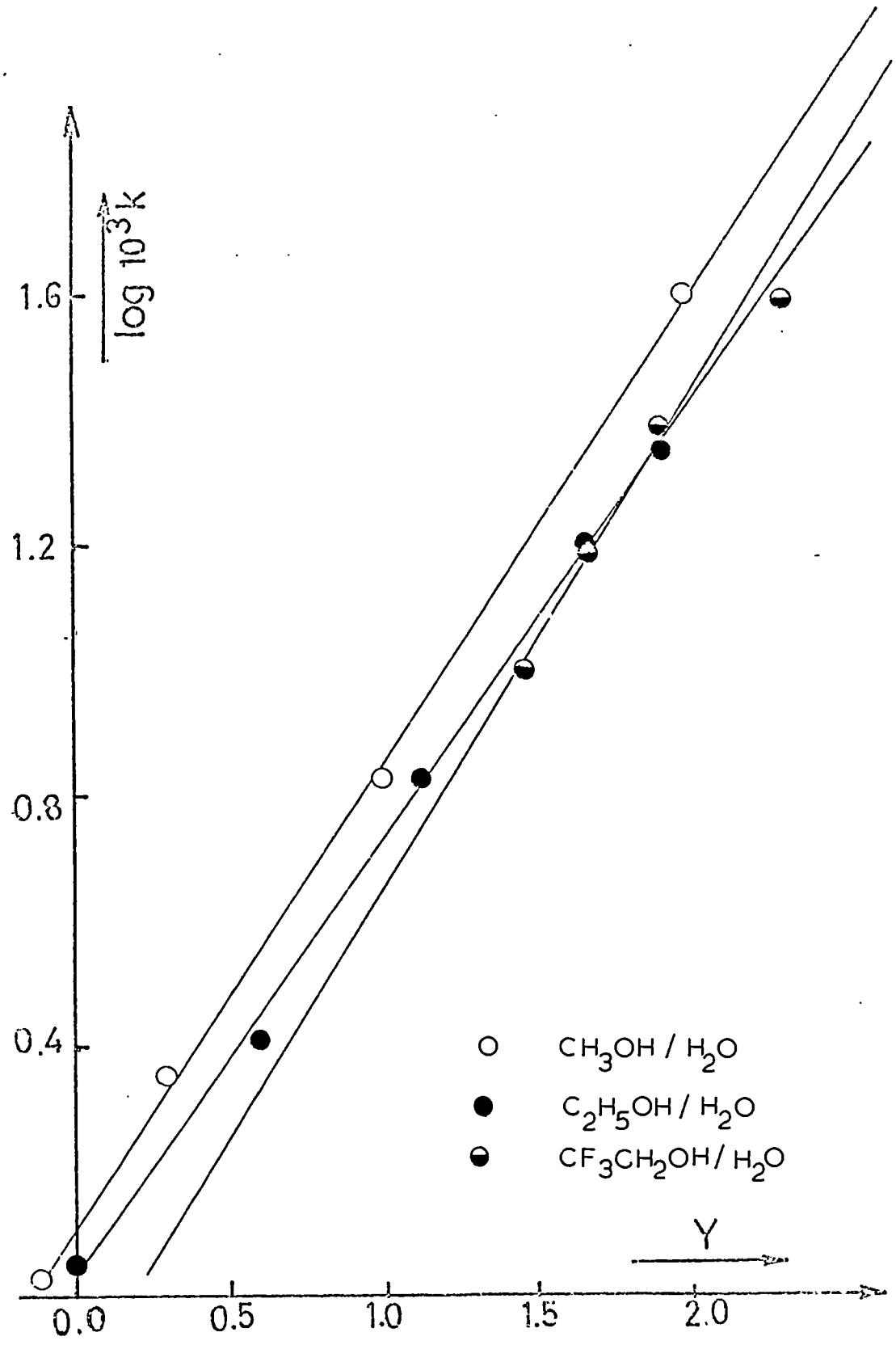

log 10³k
1.6
1.2
0.8
0.4
0.0
0.5
1.0
1.5
2.0
Y
CH3OH / H2O
C2H5OH / H2O
CF3CH2OH / H2O

Fig. 3.

3.2.2 RESULTS OF SALT EFFECT

The solvolysis of 3-chloro-pent-4-en-1-yne was carried out in the presence of different salts. Lithium salts were mainly employed because of their higher solubility in organic solvents. It was convenient to use lithium perchlorate (or sodium perchlorate) in order to ascertain the effect of increase in the ionic strength of the medium, since perchlorate ion has a low nucleophilicity and it is known that alkyl perchlorates are not stable. Tables (6) and (7) show the expected rate increase for the hydrolysis of 3-chloro-pent-4-en-1-yne, due to the effective increase in the ionizing power of the medium. The increase is of the order of magnitude predicted by theoretical treatments for a pure ionic strength effect. Both solvolysis and isomeric rearrangement rates are accelerated although not to the same extent.

It can also be seen that perchlorate ion decreases slightly the amount of secondary solvolysis products while it has caused a small increase in the amount of rearrangement.

TABLE 6

THE SALT EFFECT ON HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE IN 40% AQUEOUS ETHANOL, AT 50°C

$[LiCLO_4]$	$k_t \times 10^3$(Min.$^{-1}$)	$k_s \times 10^3$(Min.$^{-1}$)	$k_r \times 10^3$(Min.$^{-1}$)	%R	%ROS
0.00	6.64 ± 0.02	5.29 ± 0.05	1.35 ± 0.05	20.4 ± 0.9	49.7 ± 1.3
0.01	6.88 ± 0.02	5.43 ± 0.05	1.45 ± 0.05	21.0 ± 0.9	49.0 ± 1.3
0.04	7.25 ± 0.02	5.72 ± 0.05	1.52 ± 0.05	21.3 ± 0.9	47.8 ± 1.3
0.10	7.82 ± 0.02	6.14 ± 0.05	1.68 ± 0.05	21.5 ± 05	47.6 ± 1.3
0.15	8.14 ± 0.02	6.40 ± 0.05	1.74 ± 0.05	21.4 ± 0.9	45.9 ± 1.3
0.20	8.33 ± 0.02	6.54 ± 0.05	1.79 ± 0.05	22.0 ± 0.9	46.8 ± 1.3

k ± A = k ± Fractional error

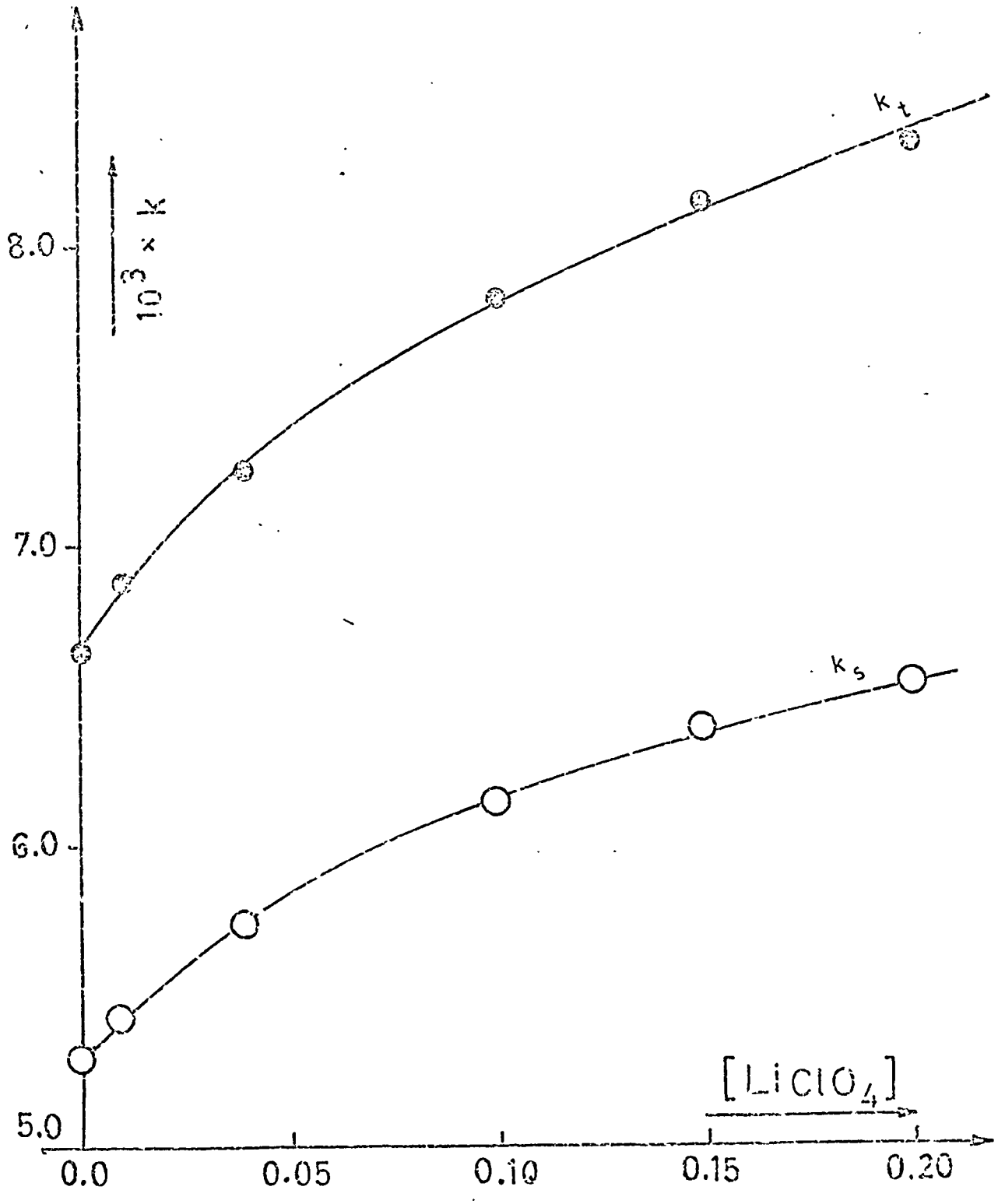


Fig. 4

TABLE 7

THE SALT EFFECT ON THE HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE IN 40% AQUEOUS ETHANOL, AT 50°C

$[NaClO_4]$	$k_t \times 10^3$(Min.$^{-1}$)	$k_s \times 10^3$(Min.$^{-1}$)	$k_r \times 10^3$(Min.$^{-1}$)	% R	% ROS
0.00	6.64 ± 0.02	5.29 ± 0.05	1.35 ± 0.05	20.4 ± 0.9	49.7 ± 1.3
0.01	6.81 ± 0.02	5.38 ± 0.05	1.43 ±).05	20.9 ± 0.9	48.0 ± 1.3
0.02	6.96 ± 0.02	5.47 ± 0.05	1.49 ± 0.05	21.5 ± 0.9	47.8 ± 1.3
0.05	7.20 ± 0.02	5.51 ± 0.05	1.69 ± 0.05	23.5 ± 0.9	47.2 ± 1.3
0.10	7.45 ± 0.02	5.68 ± 0.05	1.77 ± 0.05	24.0 ± 0.9	46.7 ± 1.3
0.20	7.95 ± 0.02	5.98 ± 0.05	1.97 ± 0.05	24.8 ± 0.9	46.1 ± 1.3

k ± A = k ± Fractional error

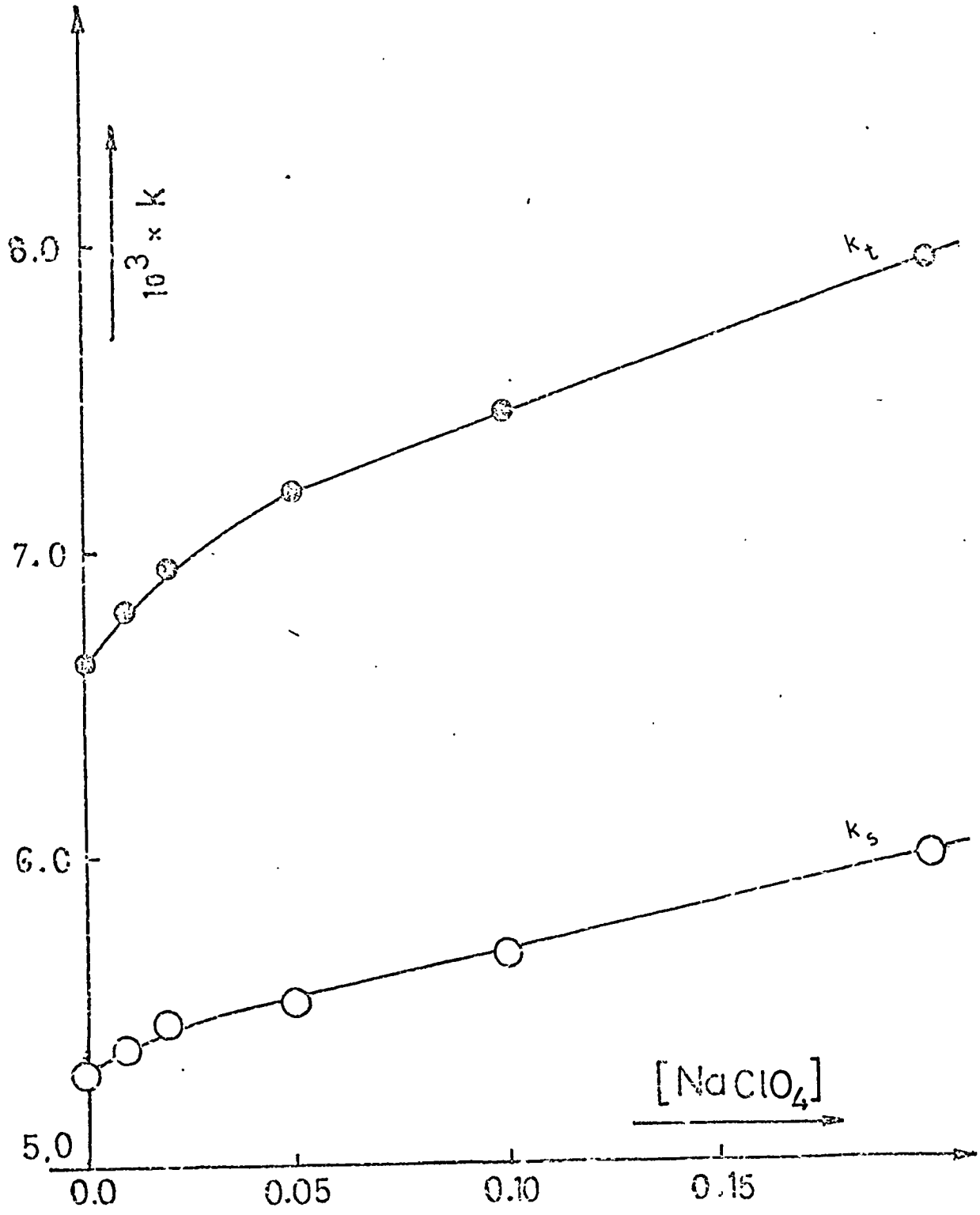


Fig. 5.

3.2.3 THE COMMON ION EFFECT RESULT

Tables (8) and (9) gives the rate constants observed for the solvolysis of 3-chloro-pent-4-en-1-yne in the presence of lithium chloride. It can be seen that lithium chloride at a concentration up to 0.15 M increases both the rate of isomeric rearrangement and solvolysis. This is due to an increase in the solvent ionizing power which more than compensates for the mass law retardation acting in the opposite direction. In order to separate these two effects and observe the influence of mass-law retardation, the effect of chloride ion was examined in a medium of constant ionic strength.

Tables (8) and (9) show that increasing lithium chloride concentration causes an increase in the amount of isomeric rearrangement and a decrease in the percentage of the solvolysis. They also indicate that the proportion of a secondary solvolysis product relative to a primary is scarcely affected as the concentration of lithium chloride increases.

TABLE 8

THE EFFECT OF ADDED CHLORIDE ION ON THE HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE in 40% AQUEOUS ETHANOL AT 50°C

[LiCl]	$k_t \times 10^3$(Min.$^{-1}$)	$k_S \times 10^3$(Min.$^{-1}$)	$k_r \times 10^3$(Min.$^{-1}$)	%S	% ROS
0.00	6.64 ± 0.02	5.29 ± 0.05	1.35 ± 0.05	79.6 ± 0.9	49.7 ± 1.3
0.02	6.65 ± 0.02	5.10 ± 0.05	1.55 ± 0.05	76.0 ± 0.9	48.4 ± 1.3
0.05	6.80 ± 0.02	5.17 ± 0.05	1.63 ± 0.05	74.0 ± 0.9	47.7 ± 1.3
0.10	7.30 ± 0.02	5.23 ± 0.05	1.97 ± 0.05	73.0 ± 0.9	47.4 ± 1.3
0.15	8.15 ± 0.02	5.84 ± 0.05	2.31 ± 0.05	71.7 ± 0.9	51.0 ± 1.3
0.20	8.10 ± 0.02	5.67 ± 0.05	2.43 ± 0.05	70.0 ± 0.9	45.2 ± 1.3

k ± A = k ± Fractional error

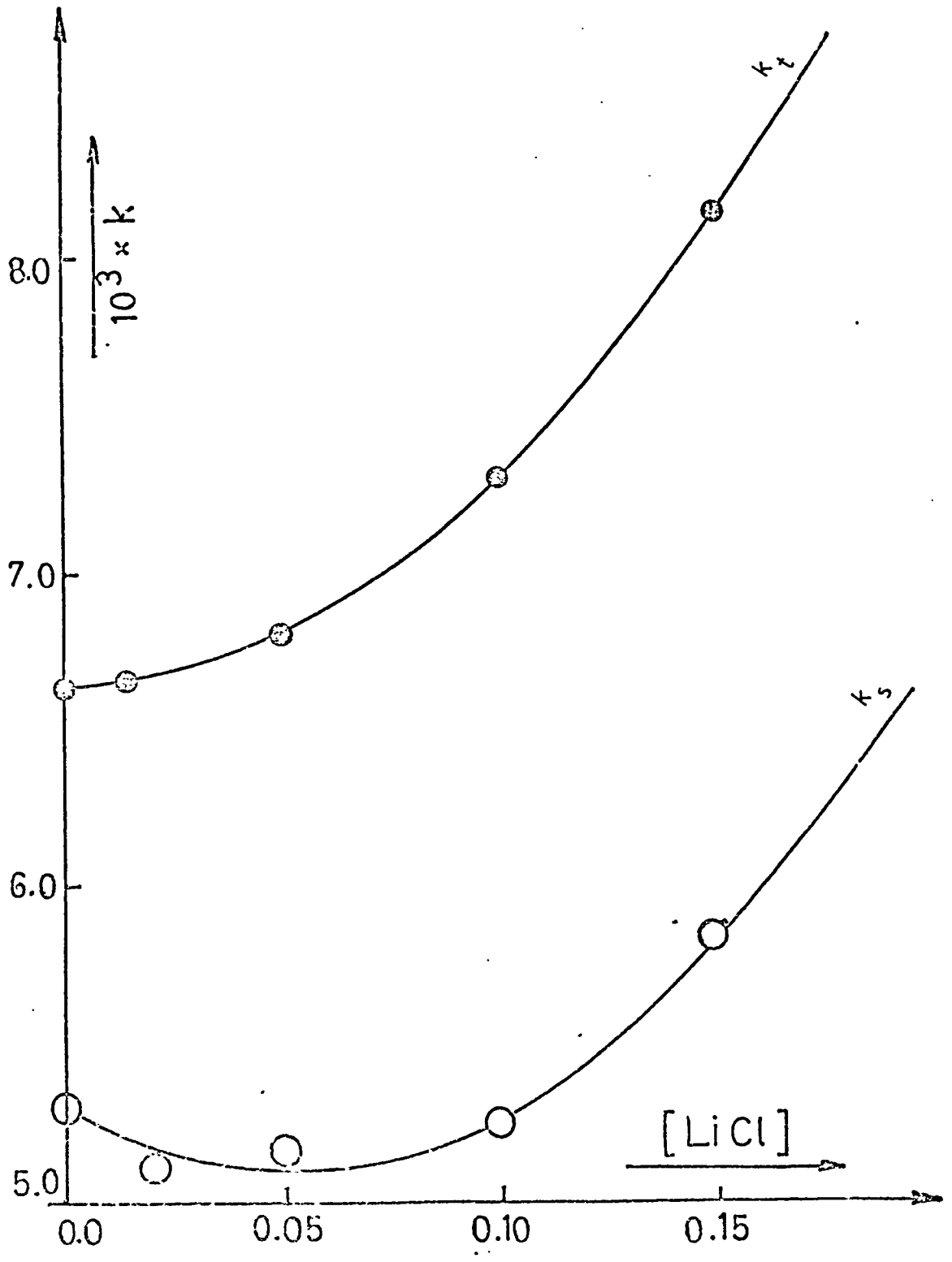


Figure 7

TABLE 9a

THE EFFECT OF ADDED CHLORIDE ION AT CONSTANT IONIC STRENGTH ($[LiClO_4] + [LiCl] = 0.15$) ON HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE IN 40% AQUEOUS ETHANOL AT 50°C.

$[LiCl]$	$k_t \times 10^3$(Min.$^{-1}$)	$k_s \times 10^3$(Min.$^{-1}$)	$k_r \times 10^3$(Min.$^{-1}$)	%S	% ROS
0.00	8.14 ± 0.02	6.40 ± C.05	1.74 ± 0.05	78.6 ± 0.9	45.9 ± 1.3
0.02	8.10 ± 0.02	6.32 ± 0.05	1.78 ± 0.05	78.0 ± 0.9	49.2 ± 1.3
0.05	8.26 ± 0.02	6.28 ± 0.05	1.98 ± 0.05	76.0 ± 0.9	50.7 ± 1.3
0.10	8.10 ± 0.02	6.02 ± 0.05	2.08 ± 0.05	74.3 ± 0.9	50.9 ± 1.3
0.15	8.15 ± 0.02	5.84 ± 0.05	2.31 ± 0.05	71.4 ± 0.9	51.1 ± 1.3

k ± A = k ± Fractional error

TABLE 9b

THE EFFECT OF ADDED CHLORIDE ION AT CONSTANT IONIC STRENGTH ($[NaClO_4] + [LiCl] = 0.1$) ON HYDROLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE IN 40% AQUEOUS ETHANOL AT 50°C

$[LiCl]$	$k_t \times 10^3$ (Min.$^{-1}$)	$k_s \times 10^3$ (Min.$^{-1}$)	$k_r \times 10^3$ (Min.$^{-1}$)	%S	% ROS
0.00	7.45 ± 0.02	5.68 ± 0.05	1.77 ± 0.05	76.0 ± 0.9	46.7 ± 1.3
0.02	7.31 ± 0.02	5.51 ± 0.05	1.80 ± 0.05	75.4 ± 0.9	46.9 ± 1.3
0.06	7.29 ± 0.02	5.44 ± 0.05	1.85 ± 0.05	74.6 ± 0.9	
0.10	7.30 ± 0.02	5.33 ± 0.05	1.97 ± 0.05	73.0 ± 0.9	47.4 ± 1.3

k ± A = k ± Fractional error

3.2.4 DISCUSSION OF SOLVOLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE

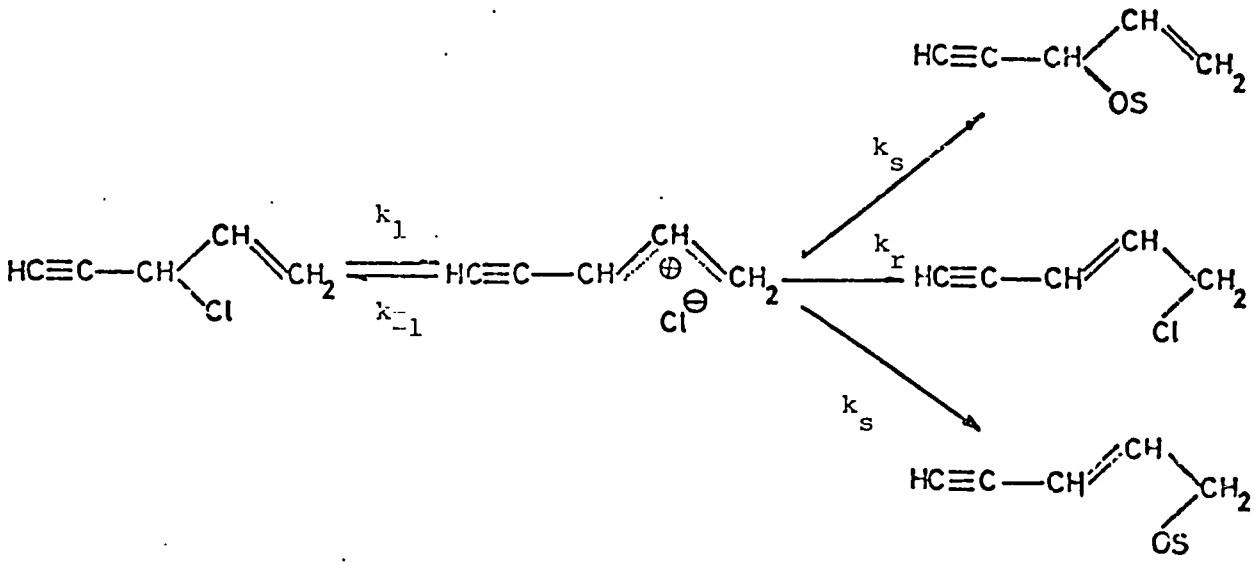
The mechanism of solvolytic reactions of the allylic compounds have already been discussed (p.29)

The results obtained in the present work for the solvolysis of 3-chloro-pent-4-en-1-yne in aqueous alcohol show that, as with the phenylallyl system and dimethylallyl system, the solvolysis occurs by the unimolecular mechanism.

Evidence that the solvolysis is unimolecular can be derived from the good correlation of the rate constants with ionizing power of the solvent (Y), in different binary solvent systems. In fig. (3) $\log k_t$ is plotted against Y, the slopes (m) of the lines are typical for unimolecular reactions. The slopes of the lines for aqueous ethanol mixtures are very similar to those of aqueous trifluoroethanol mixtures. This is a good indication that an ionization unassisted by a solvent is the rate determining step.

The salt effects are fully in agreement with a unimolecular path for the solvolysis. Lithium and sodium perchlorate increase the rate of solvolysis and rearrangement by increasing the ionic strength of the media. The effect of lithium chloride at constant ionic strength is typical of the mass-law retardation of a unimolecular solvolysis by common ion.

The product ratio data do not allow the hydrolysis to be accounted for on the basis of the simple SN_1 mechanism shown below.



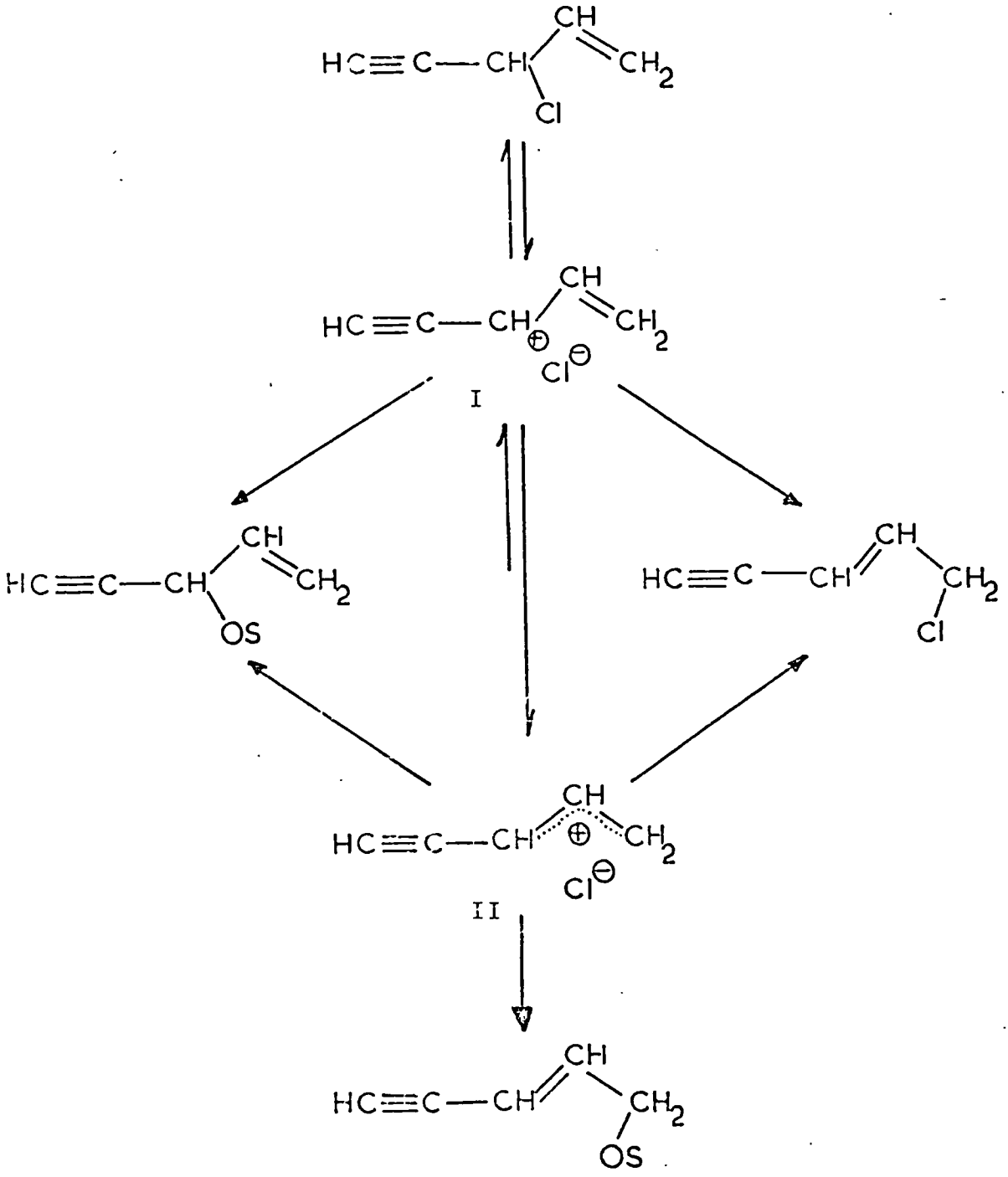
SCHEME 7

On the basis of this mechanism, one would not expect to find any variation in the product ratio with a different solvent composition. Variation of the product ratio can be easily explained by including an ion-pair intermediate in the above scheme, between the unionized allyl chloride and mesomeric carbonium ion. The variation in solvolysis product ratio together with the occurrence of an isomeric rearrangement to 5-chloro-pent-3-en-1-yne in any solvent mixture suggests that the ion-pair is formed in the rate determining step. The reactions of this ion-pair are:

(a) nucleophilic attack by the solvent to afford mostly the unconjugated solvolysis product, since in the ion-pair the departing chloride ion is closer to the 3-carbon than to the 5-carbon atom and the positive change is effectively localized at the 3-position.

(b) Isomeric rearrangement to give the isomeric chloride.

(c) Further dissociation to give the mesomeric carbonium (intermediate II) which can react further to yield the observed solvolysis products.



SCHEME 8

Scheme (8) can account for the observed variation in the product ratio. Although all solvolysis reactions have the same rate determining step, they have different product-determining steps. For this reason under various compositions of solvents we get different product ratios. In low ionizing power media, 90-80% aq. ethanol the nucleophilic attack is mostly on intermediate 1 which can yield only the unconjugated solvolysis product. Return from this intermediate is largely without allylic rearrangement.

In solvents containing more water, the ionizing power is greater, the intimate ion-pair(I) is dissociated further to give the mesomeric carbonium ion (II). Reaction of the solvent with this intermediate gives rise to isomeric solvolysis products. Return from intermediate II gives the isomeric chloride.

Table (5) shows that the ratio of the rate of rearrangement to the rate of solvolysis is not greatly affected by solvent ionizing power variation. This observation rules out the possibility of SN_i mechanism for the rearrangement process. If the rearrangement was of the SN_i type involving very little or no charge separation, the proportion of rearrangement should have been very greatly increased by decreasing ionizing power. The similar sensitivity of the isomeric rearrangement and of the solvolysis to ionizing power of the media suggests that both processes occur through common ion-pair intermediates.

An alternative route for the rearrangement is SN_2' attack of the chloride ion on the starting material. The possibility of this mechanism was rejected by observing the effect of chloride ion on the overall rate of solvolysis at constant ionic strength. Tables (9a) and (9b) show that variation of chloride ion concentration does not significantly change the overall rate. If this mechanism was involved in the rearrangement process, since it is an independent route from ionization, the total rate of reaction should have been increased.

The percentage of isomeric rearrangement increases with increasing lithium chloride concentration as it is shown in tables (8), (9a) and (9b). It therefore seems likely that the isomerization is not intramolecular in the presence of chloride ion. Evidently, chloride ion can compete with solvent molecules for intermediate II, yielding mainly 5-chloro-pent-3-en-1-yne as a result. The formation of this isomeric chloride from intermediate II by combination with added lithium chloride can further explain the slight increase in the proportion of unconjugated solvolysis products in its presence. Combination of II with chloride ion removes the only intermediate which can yield the primary solvolysis product.

The conclusion that there is a competition for the intermediate II between chloride ion, to give the isomeric conjugated chloride, and solvent, to give the primary as well as the secondary solvolysis product, is further supported by the large variation in the amount of 5-chloro-pent-3-en-1-yne formed when the reaction is carried out in media of

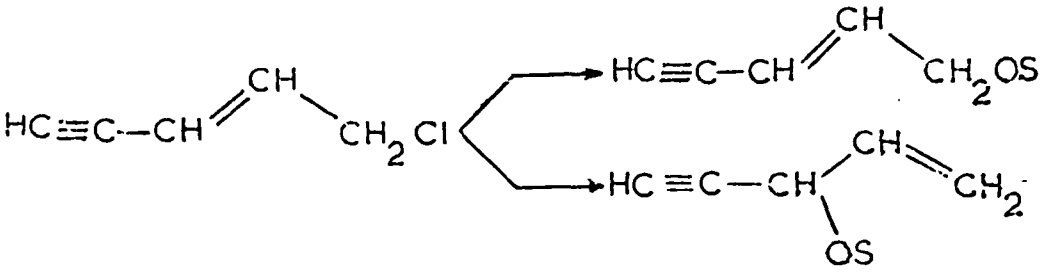
similar ionizing power but different nucleophilicity (70% TFE/H_2O and 50% EtOH/H_2O). Such large differences would not be expected if isomerisation and solvolysis were independent reactions with rather similar sensitivity to solvent ionising power.

Lithium and sodium perchlorate facilitate the dissociation of intermediate I to II. This can be due to high ionic strength or that perchlorate ion reacts with intermediate II in competition with return from intermediate II to I (k_{-2}). The primary solvolytic product can only be formed from intermediate II and the addition of a moderate amount of perchlorate ion does in fact cause a very slight increase in the proportion of it in the solvolysis product mixture.

Attempts were made to study the effect of hydroxide ion on the rate of solvolysis of 3-chloro-pent-4-en-1-yne. Difficulties arose due to a side reaction between the hydroxide ion and the allylic chloride. Formation of a carbene intermediate in the solvolytic reaction of a propargylic chloride in the presence of a base has been reported [100 & 101]. The same type of reaction could be occurring in the solvolysis of 3-chloro-pent-4-en-1-yne.

3.3.1 SOLVOLYTIC REACTIONS OF 5-CHLORO-PENT-3-EN-1-YNE IN AQUEOUS ETHANOL

The solvolysis of 5-chloro-pent-3-en-1-yne in aqueous ethanol yields two isomeric products as was expected by analogy with solvolysis of 3-phenylallyl chloride and 3-methylallyl chloride.



SCHEME 9.

Table (10) shows the mean values of the first order rate constant and the composition of products for solvolysis of 5-chloro-pent-3-en-1-yne in aqueous ethanol. The rates of reactions are not very sensitive to the amount of water present in the medium but give a good correlation with the ionizing power of the solvent (Y). In fig. (7) log k_t is plotted against Y, the slopes (m) of the lines are about 0.4 which is typical of reactions in which the rate determining step is (thought to be) a bimolecular process. Table (10) also shows that there is a decrease in the relative amount of conjugated to unconjugated solvolysis product. The energy of activation (ΔH^*) and the entropy of activation (ΔS^*) were estimated to be 22 K Cal $mole^{-1}$ and -3.0 Cal $mole^{-1}$ deg^{-1} respectively. This was

achieved by performing the reaction at two different temperatures and using equations (23) and (24).[102]

$$\log k_2/k_1 = \Delta H^*(T_2-T_1)/2.303RT_1T_2 \qquad (23)$$

$$\Delta S^* = 2.3\ R \log k + (E_A-RT)/T - 2.3\ R \log (RT/Nh)$$
$$= 4.6 \log k + (E_A-RT)/T - 59 \qquad (24)$$

The effect of lithium chloride and perchlorate on the rate of solvolysis of 5-chloro-pent-3-en-1-yne in 50 per cent aqueous ethanol are shown in tables (11) and (12) It can be seen that they behave similarly and neither of them has significant effect on the rates of solvolysis. The effect of salt on the hydrolysis product ratio was also slight. However, hydroxide ion causes an increase in the rate of solvolysis (Table 13). It can also be seen that hydroxide ion slightly decreases the amount of conjugated (primary) solvolysis product.

TABLE 10

THE EFFECT OF SOLVENT IONIZING POWER ON
THE HYDROLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE

Temp. ^{o}C	% V/V Ethanol	t-BuCl scale Y	$k_s \times 10^5$ (min.$^{-1}$)	% R´OS
50	80	0.00	3.24 ± 0.03	0.89 ± 0.05
50	70	0.60	5.74 ± 0.03	0.84 ± 0.05
50	60	1.12	8.37 ± 0.03	0.83 ± 0.05
50	50	1.66	15.3 ± 0.03	0.80 ± 0.05
50	40	2.15	24.2 ± 0.03	0.78 ± 0.05
60	80	0.00	10.5 ± 0.03	0.87 ± 0.05
60	70	0.60	17.1 ± 0.03	0.84 ± 0.05
60	60	1.12	25.7 ± 0.03	0.81 ± 0.05
60	50	1.66	42.3 ± 0.03	0.80 ± 0.05

k ± A = k ± Fractional error

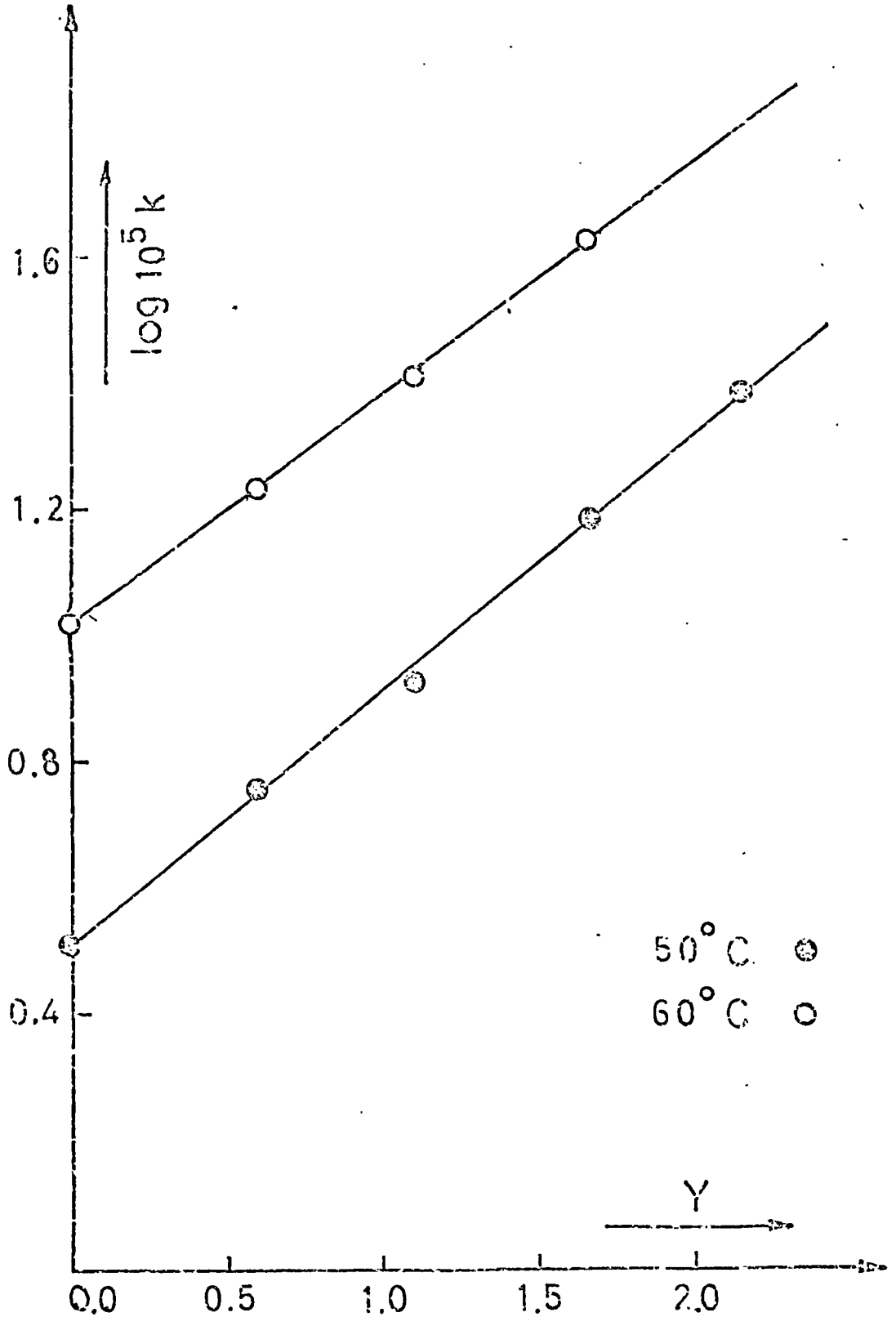


Fig. 7

TABLE 11

THE COMMON ION EFFECT ON THE SOLVOLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE IN 50% AQUEOUS ETHANOL AT CONSTANT IONIC STRENGTH

Temp. ^{o}C	$[LiCl]$, M/l	$k_s \times 10^4$ (Min.$^{-1}$)
	$[LiCl] + [LiClO_4] = 0.50$	
50	0.00	1.52 ± 0.03
50	0.20	1.50 ± 0.03
50	0.50	1.51 ± 0.03
	$[LiCl] + [LiClO_4] = 0.10$	
60	0.00	4.23 ± 0.03
60	0.06	3.81 ± 0.03
60	0.10	3.88 ± 0.03

k ± A = k ± Fractional error

TABLE 12

THE NORMAL SALT EFFECT ON THE RATES OF SOLVOLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE IN 50% AQUEOUS ETHANOL AT 50°C

Temp.°C	$[LiClO_4]$, M/l	$k_s \times 10^4$ (min.$^{-1}$)
50	0.00	1.53 ± 0.03
50	0.05	1.54 ± 0.03
50	0.10	1.52 ± 0.03
50	0.20	1.55 ± 0.03
50	0.50	1.52 ± 0.03
60	0.00	4.23 ± 0.03
60	0.02	4.24 ± 0.03
60	0.06	4.26 ± 0.03
60	0.10	4.25 ± 0.03

k ± A = k ± Fractional error

TABLE 13

THE EFFECT OF ADDED NUCLEOPHILE (OH^-) ON SOLVOLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE IN 50% AQUEOUS ETHANOL AT CONSTANT IONIC ADDED STRENGTH

Temp. °C	$[OH^-]$, M/l.	$k_s \times 10^4$ (min^{-1})	% R OS
$[OH^-] + [ClO_4^-] = 0.5$			
50	0.00	1.53 ± 0.03	0.80 ± 0.05
50	0.10	2.71 ± 0.07	0.76 ± 0.05
50	0.20	3.87 ± 0.07	0.77 ± 0.05
50	0.40	5.70 ± 0.07	0.79 ± 0.05
50	0.50	7.1 ± 0.07	0.79 ± 0.05
$[OH^-] + [ClO_4^-] = 6.752 \times 10^{-3}$			
60	0.00×10^{-3}	4.23 ± 0.03	0.80 ± 0.05
60	3.376×10^{-3}	7.80 ± 0.09	0.76 ± 0.05
60	5.064×10^{-3}	8.21 ± 0.09	0.75 ± 0.05
60	6.752×10^{-3}	9.55 ± 0.09	0.73 ± 0.05

k ± A = k ± Fractional error

3.3.2 DISCUSSION ON SOLVOLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE

It has long been known that solvolytic reactions of isomeric allylic halides can give rise to a mixture of isomeric solvolysis products but only in a few cases has the same product ratio been reported. In fact the primary isomers give a somewhat higher proportion of primary solvolysis products than secondary or tertiary halides. This has been interpreted as due to the higher efficiency of bimolecular replacement of the primary allyl halides.

In the solvolytic reactions of the 5-chloro-pent-3-en-1-yne the composition of the products is greatly different from the composition of the products of solvolysis of 3-chloro-pent-4-en-3-yne. In the case of the former isomer, at least 80% of the product was found to be an ordinary replacement product, suggesting a bimolecular mechanism for the solvolysis.

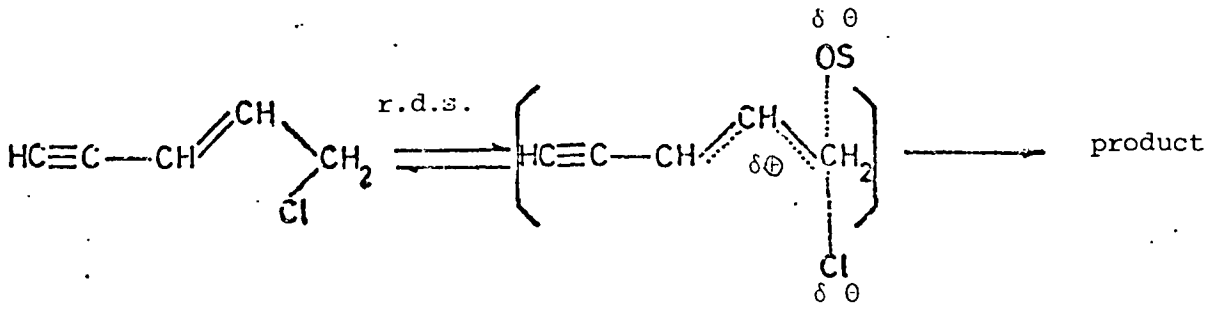
There is a very good correlation between the rate constant of the reaction and the ionizing power of the solvent (Y). Fig. (7) shows the variation of log k_t against Y. The slope of the line (m), which indicates the susceptibility of the solvolysis towards the ionizing power of the solvent, is about 0.40. This value of m is typical of reactions in which the rate determining step is thought to be a bimolecular process. The m value

is in good agreement with m values reported by Vernon et al [7], for the analogous solvolyses of allyl and 3-methyl allyl chlorides in aqueous ethanol. They have suggested a bimolecular mechanism for hydrolysis of these two compounds.

The study of the salt effect provided further evidence for bimolecularity of the solvolysis of 5-chloro-pent-3-en-1-yne. Lithium chloride and lithium perchlorate behave similarly and neither of them have a significant effect on the rate constant of the reaction, or on the product ratio.

Hydroxide ion (lyate ion) causes an increase in solvolysis rates. This confirms even further the nucleophilic assistance of the solvent in the rate determining step.

All these observations suggest strongly that the solvolysis of 5-chloro-pent-3-en-1-yne is a bimolecular process involving a nucleophile and the allylic chloride in the rate-determining step.



SCHEME 10

However, the single scheme shown above does not explain the formation of the rearranged solvolysis product, neither does it account for the small but significant variation of product ratio with ionizing power of the media.

Formation of rearranged solvolysis product can be explained by one of the following possibilities.

(1) The traditional explanation, which invokes the operation of simultaneous SN_1 and SN_2 reactions, involves the ionization to an intermediate (common to that produced from the isomeric 3-chloro-pent-4-en-1-yne), which produces isomeric solvolysis products. However this possibility can easily be rejected due to absence of any variation in the rate constant by common ion and non-common ion salt effects. The low value of m is another proof of absence of this possible mechanism.

(2) The ion-pair SN_2 mechanism, which involves rate-limiting nucleophilic attack on a preformed ion-pair intermediate, can afford some rearranged solvolysis product. This mechanism can also be ruled out by the same arguments as stated above.

(3) The abnormal bimolecular displacement - there are few well established cases of the SN_2' mechanism on substrates of the type $C{=}C\text{-}CH_2X$ although compounds of the form $C{=}C\text{-}CR_2X$ give the SN_2' product almost exclusively when they undergo bimolecular reaction at all.[8, 99] It is possible that this mechanism operates in the present system to give the observed rearranged solvolysis product. Solvolysis of 5-chloro-pent-3-en-1-yne has all the three conditions which a reaction must have before it can be classified as an ab-

normal bimolecular substitute. These are:

(1) The rates of solvolysis are proportional to the concentration of hydroxide or ethoxide ion added and the concentration of allyl chloride.

(2) The solvolysis gives isolable amounts of abnormal substitution products.

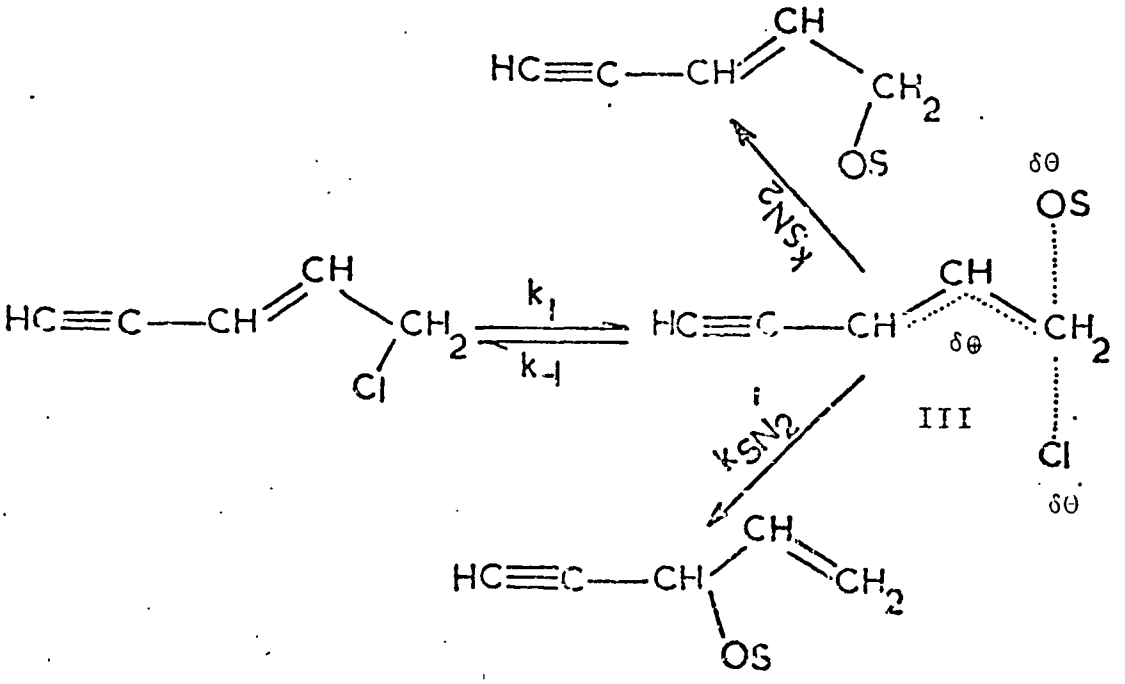
(3) It is observed that neither the starting allyl chloride nor the primary solvolysis products undergoes rearrangement under the conditions of the reaction. Although our observations fit well for the SN_2' mechanism, there have been no well established cases of the SN_2' mechanism involving simple hydroxylic solvents, e.g. water or alcohols, as substituting agents. Vernon et al[116] have studied the solvolytic reactions of methylallyl chloride in aqueous ethanol, and have reported that to observe the SN_2' reaction a much more powerful nucleophilic reagent such as the thiophenoxide ion must be used. Indeed the ethanolysis of 5-chloro-pent-3-en-1-yne in the presence of ethoxide ion gives a higher proportion of the rearranged product. One might argue that, since the formation of the transiton state of a SN_2' mechanism involves the approach of a nucleophilic substituting agent to an electron rich area, this mechanism would rarely occur in cases where normal bimolecular substitution is unhindered by additional substituents on reacting carbon atoms ($kSN_2/kSN_2' = 60000$ for 3-methylallyl chloride and 220 for 1 - methylallyl chloride).

5-Chloro-pent-3-en-1-yne is an analogue of 3-methylallyl chloride in which the methyl group has been sub-

stituted by an ethynyl group. The ethynyl group is strongly electron withdrawing while the methyl group is electron donating.[103] One can expect 5-chloro-pent-3-en-1-yne to be more susceptible than the methylallyl chloride to the SN_2' process, since the ethynyl group has reduced the election density at the double bond.

The entropy of activation for solvolysis of 5-chloro-pent-3-en-1-yne is small and negative (in 50% aqueous ethanol) suggesting an "open" or carbonium ion-like transition state (large degree of charge separation) for this reaction. The positive charge in the transition state can be stabilized by the conjugated vinyl-acetylene group.

On the basis of this explanation the following scheme for hydrolysis of 5-chloro-pent-3-en-1-yne is proposed.



SCHEME II

This mechanism is similar to the classical SN_2 mechanism except that the pentavalent species (III) is an intermediate rather than a transition state. The double bond in this intermediate is strongly polarized and a significant amount of positive charge is built up at the 3-carbon atom. The nucleophilic attack at the 3-carbon atom of this intermediate by solvent or added nucleophile can give the observed rearranged solvolysis products.

Chloride ion does not have a detectable effect on the product ratio. To explain this, one must assume that very little or no 3-chloro-pent-4-en-1-yne is produced from the nucleophilic attack of chloride ion on the intermediate (III). The unconjugated allyl chloride hydrolyses rapidly and produces a much larger proportion of the unconjugated (rearranged) solvolysis product than does the conjugated allyl chloride. This simply means that the intermediate (III) is mainly being attacked by solvent to give the solvolysis product and not by chloride ion. This occurs because the intermediate (III) is too reactive to be able to discriminate between the more reactive chloride ion present in low concentration, and the less reactive solvent which is in large excess.

The conclusion that species (III) is an intermediate rather than a transition state and can serve to some extent as a substrate for nucleophilic attack of solvents, is further supported by the small variation in the amount of rearranged solvolysis product formed with variation of the ionizing power of the medium. As the ionizing power of the solvent increases, the stability of the inter-

mediate will increase, thus it can give rise to a higher proportion of rearranged product.

CHAPTER 4

Isomerization of 3-chloro-pent-4-en-1-yne

4.1 ISOMERIZATION OF 3-CHLORO-PENT-4-EN-1-YNE

Introduction and Results

Although the isomeric rearrangements of allylic alcohols and esters have been extensively investigated, the isomerisation of allylic halides has not been thoroughly studied. Allylic bromides isomerise readily when heated [5,104], and the rearrangement has been shown to be catalysed by peroxides [104], suggesting that homolytic fission of the C-Br bond is involved in the isomerisation. The thermal rearrangement of allylic chlorides is usually much slower than that of the corresponding bromides, and is thought to proceed either through an ion-pair formed by ionisation of the C-Cl bond [42, 61], or through a four-membered ring transition state [105].

Valkanas and Waight [73] have investigated the rearrangement of the 1-phenylallyl chloride. The reaction in aprotic solvents (e.g. chlorobenzene) was found to be catalysed by hydrogen chloride as well as carboxylic acids, the rate being approximately proportional to the strength of the acid. The possibility was discussed that a halonium ion is formed. Catalysis by chloride ion in the rearrangement of 1-phenylallyl chloride has also been established by these authors.

The 3-chloro-pent-4-en-1-yne used throughout this work was prepared as described in the experimental section. It proved to be a stable colourless liquid when kept at $0^{o}C$ under argon. No rearrangement occurs when it is kept in non-polar solvents like dry ether, petroleum ether, dioxan etc. at room temperature. The most suitable solvent for study of the rearrangement of 3-chloro-pent-4-en-1-yne was found to be sulpholane: this solvent has been used in a number of investigations on allylic rearrangements. The rearrangement was followed by the spectrometric method of Braude and Jones.

3-Chloro-pent-4-en-1-yne appeared to rearrange slowly to 5-chloro-pent-3-en-1-yne in pure sulpholane. In the same solvent the effect of sodium perchlorate and lithium chloride was tested. Sodium perchlorate did not have a detectable effect on the rate of rearrangement of 3-Chloro-pent-4-en-1-yne. However, a large acceleration proportional to the lithium chloride concentration was found (Table 14). The experimental work almost certainly proves that the salt catalysis is of a bimolecular character and it is independent of another rearrangement route with unimolecular kinetics, the rate of which is given in the uncatalysed rearrangement. The reaction is pseudo-first order since the concentration of chloride ion is constant. The bimolecular rate constant, k', can be extracted from the expression $k' = \frac{k-k_o}{[LiCl]}$ where k is the observed first order rate constant and k_o is the rate constant of

rearrangement at zero lithium chloride concentration.

The bimolecular rearrangement could result either from a γ-attack by chloride ion by SN_2' mechanism or by interaction of RCl with a LiCl ion-pair. Both possibilities could contribute to a rearrangement process since lithium chloride can exist as ion-pairs at the concentration of salt used in sulpholane.[106]

A simple way of demonstrating the operation of the SN_2' mechanism is by a halide exchange reaction. By this means the amount of SN_2 attack can also be estimated by subtracting the rate of rearrangement from total ion exchange rate. Thus the isomeric rearrangement of 3-chloropent-4-en-1-yne in sulpholane in the presence of radioactive lithium chloride ($^{36}Cl^-$) was studied. The course of ion exchange was followed by measuring the activity of the organic chlorides from samples taken at appropriate times using a Beckman scintillation liquid system, as described in the experimental section. As can be seen from Table(15) the overall rate of exchange increases as the lithium chloride concentration increases and it is much higher than the rate of rearrangement.

TABLE 14

THE EFFECT OF LITHIUM CHLORIDE ON THE REARRANGEMENT OF 3-CHLORO-PENT-4-EN-1-YNE AT 60°C IN SULPHOLANE

$[LiCl] \times 10^3$ M/l	$k_r \times 10^4$ (Min.$^{-1}$)	$\frac{k-k_o}{[LiCl]} = k'$ (Min.$^{-1}$ Mole^{-1})
0.00	0.69 ± 0.05	5.44×10^{-3}
6.25	1.03 ± 0.05	5.12×10^{-3}
12.5	1.33 ± 0.05	2.94×10^{-3}
30.3	1.58 ± 0.05	2.94×10^{-3}
60.1	2.25 ± 0.05	2.60×10^{-3}
121.3	3.65 ± 0.05	2.44×10^{-3}

k ± A = k ± Fractional error

TABLE 15

THE RATE OF ION-EXCHANGE REACTIONS OF 3-CHLORO-PENT-4-EN-1-YNE AND 5-CHLORO-PENT-3-EN-1-YNE WITH RADIOACTIVE LITHIUM CHLORIDE IN SULPHOLANE

Temp. ^{o}C	Compound	$[Li^{36}Cl]$, M/l	k exchange (Min.$^{-1}$)
40	3-chloro-pent-4-en-1-yne	3.25×10^{-2}	$(5.69 \pm 0.07) \times 10^{-4}$
40	"	6.40×10^{-2}	$(6.03 \pm 0.07) \times 10^{-4}$
40	"	13.0×10^{-2}	$(6.65 \pm 0.07) \times 10^{-4}$
60	"	3.25×10^{-2}	$(2.64 \pm 0.07) \times 10^{-3}$
60	"	6.50×10^{-2}	$(2.94 \pm 0.07) \times 10^{-3}$
60	"	13.0×10^{-2}	$(3.98 \pm 0.07) \times 10^{-3}$
40	5-chloro-pent-3-en-1-yne	3.25×10^{-2}	$(4.27 \pm 0.07) \times 10^{-3}$
40	"	6.50×10^{-2}	$(4.56 \pm 0.07) \times 10^{-3}$
40	"	13.0×10^{-2}	$(5.33 \pm 0.07) \times 10^{-3}$

k ± A = k ± Fractional error

4.2 DISCUSSION AND CONCLUSION ON THE REARRANGEMENT OF 3-CHLORO-PENT-4-EN-1-YNE

the salt catalysis in the isomeric rearrangement of allylic halides has been reported by Ingold and Hughes in an attempt to establish the existence of the SN_2' mechanism. As described in the review (p. 11) England [20] examined the effect of LiBr on the rearrangement of 1-methylallyl bromide to the 3-methylallyl isomer in acetone and explained the catalysis by an SN_2' mechanism. Similar conclusions were drawn by Valkanas [63] on examining the effect of lithium chloride on the rearrangement of 1-phenylallyl chloride to the 3-phenylallyl isomer in dimethylformamide.

In the present work the effect of sodium perchlorate and lithium chloride on the rearrangment of 3-chloro-pent-4-en-1-yne to 5-chloro-pent-3-en-1-yne in sulpholane was studied. The ion exchange reactions of these two chlorides with radio-active lithium chloride (^{36}Cl) were also examined in some detail. The suggested mechanism for the rearrangement of RCl in sulpholane, in the light of the results obtained, was in good agreement with the evidence mentioned above. The results in tables and showed:

(1) The rate of ion exchange of the RCl is faster than the rate of rearrangement and that it increases as the salt concentration increases.

(2) The 5-chloro-pent-3-en-1-yne ($R'Cl$) gives a faster rate of exchange than the secondary isomer.

(3) The plot of rate constants of the rearrangement against lithium chloride concentration when extrapolated to zero salt concentration gives a figure in good agreement with that actually found for the reaction in the absence of added lithium chloride. This indicates the operation of competitive unimolecular and bimolecular pathways.

(4) Although more kinetic measurements for the rearrangement at lower salt concentrations are needed, it seems that there is a break in the plot of rate constants of rearrangement against LiCl concentration. This can be due to the association of lithium and chloride ions at higher concentrations.

All these observations strongly suggest a bimolecular mechanism for the catalysed rearrangement process. The fact that the secondary chloride has a lower rate of ion exchange than the primary isomer is in accordance with the findings of de la Mare, Vernon and England, who considered the difference in reactivity to be due to a steric effect.

The uncatalysed rearrangement of 3-chloro-pent-4-en-1-yne in sulpholane is a unimolecular process. The driving force for this reaction must be the formation of a thermodynamically more stable product ($R'Cl$). The most probable mechanism for this reaction is a SN_i mechanism possibly through a four membered ring intermediate. The SN_1' mechanism involving the formation of a free carbonium ion as the rate-determining step must be rejected on the basis that complete ionisation of the chloride in sulpho-

lane is unlikely in view of the absence of any acceleration by added sodium perchlorate.

The bimolecular rearrangement could result either from a γ attack by free chloride ion by the SN_2' mechanism or by interaction of R Cl with a LiCl ion-pair. Both possibilities could contribute to a rearrangement process since lithium chloride can exist as an ion-pair under the experimental conditions.

In the low lithium chloride concentration region (LiCl 1.25×10^{-2}M), the salt probably exists as free ions in sulpholane (at 60^{o}C) and the catalysis occurs by bimolecular attack of chloride ion at the γ-position of the allylic system. The approach of the charged ions ($Li^{\oplus}$ and $Cl^{\ominus}$) can polarise the C–Cl bond and thus facilitate the operation of this mechanism.

This conclusion is in good agreement with the work of England and Hughes [15,107]. They have reported that the SN_2 reaction of 1-methylallyl bromide is only 60 times faster than corresponding SN_2' reaction with bromide ion in acetone. However, the ratio obtained in the present work for the ion exchange reaction of 3-chloro-pent-4-en-1-yne with chloride ion ($^{36}Cl^{-}$) is even less (the SN_2 rate constant was estimated by subtracting the rate constant of rearrangement from ion exchange rate constant of RCl). The difference could be partially due to the presence of an ethynyl group, which is strongly electron withdrawing,[103] instead of a methyl group, which is electron donating, and partially due to the possible existence of LiCl ion-

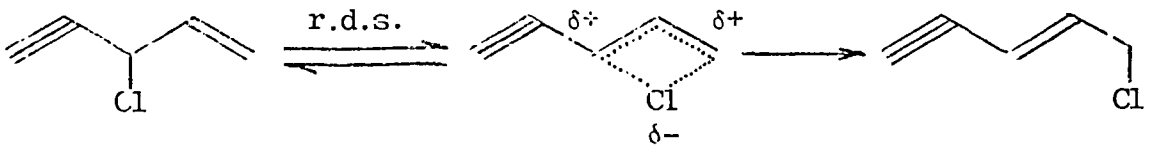
pairs even at these low salt concentrations, which interact with allylic halide giving rise to more SN_2' than SN_2 displacement.

However at higher concentrations of LiCl (LiCl 1.25×10^{-2}M) the LiCl exists as an ion pair. The ion-pair can approach easily from the chlorine side and co-ordination of the chlorine and the cation of the salt occurs. In this way a loosening of the C-Cl bond and polarisation of the α-carbon atom results. The Π-electrons of the double bond under such circumstances move towards the α-carbon and thus polarise the γ-carbon atom. The chloride ion originally with the LiCl is near the γ-carbon, thus giving an opportunity for the formation of a six-membered ring intermediate. LiCl is split off and the more thermodynamically stable 5-chloro-pent-3-en-1-yne is formed.

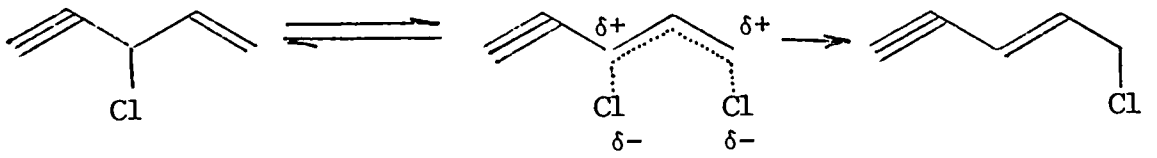
Formation of this type of six-membered ring intermediate was originally postulated in the acid-catalysed rearrangement of allylic halides by Burton[2/] and later by Valkanas[63/] in the acid and salt-catalysed rearrangement of 1-phenylallyl chloride.

Thus the isomeric rearrangement of 3-chloro-pent-4-en-1-yne in sulpholane follows the mechanisms:

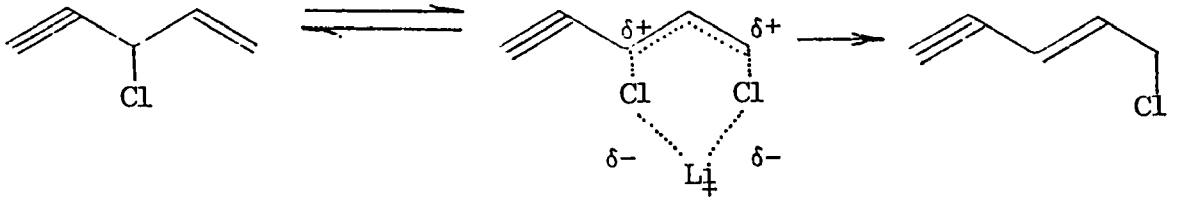
(1) $[LiCl] = 0.0$



(2) $[LiCl] < 1.25 \times 10^{-2}$



(3) $[LiCl] > 1.25 \times 10^{-2}$



CHAPTER 5

Experimental Work

5.1 PREPARATION OF SODIUM ACETYLIDE

A three necked flask, equipped with a stirrer, a gas inlet tube and an air condenser was filled with 700-800 ml of liquid ammonia. Very small pieces (0.1 g.) of sodium were introduced until the blue colour persisted. Subsequently finely powdered ferric nitrate (0.1 g.) was added. As soon as the colour of the liquid changed from dark blue to grey, sodium (23 g) was cut and at the same time introduced into the flask. The colour changed from dark blue to grey after 60 to 80 minutes stirring when the formation of sodamide was complete.

The acetylene cylinder, through a mercury safety valve, a cooled trap to condense out acetone, a Drechsel bottle containing concentrated sulphuric acid and a reversed empty drechsel bottle,was connected to the inlet tube of the reaction flask which contained the suspension of sodamide in liquid ammonia. A rapid stream of acetylene was passed in until the colour of the reaction mixture darkened (in ca. 1 hour). The formation of sodium acetylide was then complete.

5.2 PREPARATION OF PENT-1- YN-4-EN-3-OL

A solution of acrolein (0.8 mole, freshly distilled) in dry ether (50 ml) was added to a concentrated solution of sodium acetylide (0.1M) in liquid ammonia (600 ml). The reaction mixture was cooled to $-75^{\circ}C$ by means of a bath

of solid carbon dioxide in acetone. The aldehyde was added over 30-40 minutes with vigorous stirring (acrolein should not contact with ammonia vapor). At the same time acetylene was passing through the reaction mixture at a slow rate. The stirring was continued for a further 3 hours and then the cooling bath was removed and the introduction of acetylene stopped. Ammonium chloride (20 g.) was added in portions during 15 minutes; the ammonia was evaporated rapidly. Without delay ether (150 ml) was added and the mixture filtered and the solids on the filter washed thoroughly with ether (ca. 300 ml.). About half the volume of ether from the combined filtrate and washings was distilled off in order to expel any ammonia remaining, and the residual ether solution shaken with saturated aqueous sodium hydrogen sulphite. The mixture was filtered and the solids on the filter washed with ether. The ethereal solution was dried over sodium sulphate, and the drying agent was filtered off. The ether was evaporated and the residue distilled under reduced pressure.

b.p. 60-62°C/30mm, n_D^{22}=1 .4578

5.3 PREPARATION OF PENT-1-YN -3-EN-5-OL

Epichlorohydrin (0.5 mole) was added dropwise over a period of 1.5 hours to a solution of sodium acetylide (1.1 mole, see exp. I) in liquid ammonia (1 l.). During the addition, as well as for a period of 1.5 hours after, the temperature of the mixture was kept at -45°C.

The cooling bath was removed after this period and the mixture was agitated vigorously for another 3 hours. The thermometer and vent were removed, and powdered NH_4Cl (75 g .) was added in 2 g. portions with vigorous stirring The ammonia was allowed to evaporate. The reaction mixture was dissolved in water and extracted several times with ether. The extracts were dried over magnesium sulphate. The drying agent was sucked off on a sintered glass funnel and thoroughly rinsed with ether. After removal of the ether in vacuo, the residue was distilled at a very low pressure (0.1-0.5 mm) and collected in a single receiver cooled to -40^{o}. The contents of the receiver were redistilled at water pump pressure. Pent-1-yn-3-en-5-ol was obtained in a 43-48% yield; it had b.p. $94^{o}C/45$ mm Hg. $n_D^{20} = 1.496$

5.4 PREPARATION OF PENTA 1,3-DIEN-5-OL

Pent-3-en-1-yn-5-ol (4.92 g, 0.06 mole) was dissolved in dried ether (50 ml) in a hydrogenation flask and Lindlar Catalyst (300 mg) and quinoline (800 mg) were added. The mixture was hydrogenated until 1.05 molecular proportion (1410 ml) of hydrogen had been absorbed. Then the catalyst was removed and the ether evaporated under reduced pressure The pure penta-1,3-dien-5-ol was obtained after distilling of the residue, b.p. $= 120^{o}C, n_D^{20} = 1.4899$, $\lambda_{max} = 225$ ($\varepsilon = 20760$)

5.5 PREPARATION OF 1,4-PENTADIEN-3-OL

To a solution of vinylmagnesium bromide in THF (prepared by the standard procedure, P115), redistilled acrolein (10.5 ml.) was added dropwise with stirring, under nitrogen, maintaining the temperature range $-10^{o}C$ to $-5^{o}C$. The reaction mixture became greenish-yellow and was stirred for two hours longer. Cooled aqueous ammonium chloride (12g.) solution was added and a thick pale-yellow-precipitate formed. The mixture was extracted with ether, the ethereal layer was washed with water and then dried over magnesium sulphate. The ether was evaporated and the crude product was distilled under vacuum with great care, b.p. $47^{o}C$/6 cm Hg, λ_{max} 213 nm (ε676), n_D^{19} 1.4482. $\nu_{max}(Cm^{-1})$ 3320 (OH, broad), 3000 and 2900 (CH), 1645 (C=C), 1420, 1265, 1120, 1065, 1000, 938.

5.5 PREPARATION OF 1-BUTYL-3-PHENYLALLYL CHLORIDE

5.5.1 PREPARATION OF 1-t-BUTYL-3-PHENYLPROPARGYL ALCOHOL(42)

Phenylacetylene was converted into its lithium salt by adding to a solution of the alkyne (10.2g., 100 m mole) in THF (50 ml) at $0^{o}C$, one molar n-butyl lithium solution (100 ml) in ether. After stirring for 15 minutes under nitrogen, pivaldehyde (8.6g., 100 m mole) was added slowly. The solution was allowed to warm up to $25^{o}C$ and stirred for an additional two hours. Most of the solvent was removed at reduced pressure and the residue taken up in ether, which was washed with water, dried and evaporated. The residue was distilled at 84-$87^{o}C$/0.2 m m of Hg. On standing the distillate crystallized. Recrystallization from methanol/water gave pure 1-t-butyl-3-phenylpropargyl alcohol (42), m.p. 43.5-$46^{o}C$.

5.5.2 PREPARATION OF 1-t-BUTYL-3-PHENYLALLYL ALCOHOL (30)

The propargylic alcohol (42) (1.88g., 10 m mole) was refluxed with LAH(420 mg. 11 m mole) in dried THF (25 ml) for 6 hours. The intermediate was hydrolyzed by the 1:1:3 method (0.42 ml H_2O, then 0.42 ml 15% aqueous sodium hydroxide, and finally 1.26 ml of water). The aluminium hydroxide was filteredoff and washed with ether. The ethereal layer was dried over magnesium sulphate and the solvent evaporated. The residue distilled at 76-$80^{o}C$/ 0.1 mm Hg.

5.5.3 PREPARATION OF 1-t-BUTYL-3-PHENYLALLYL CHLORIDE(21)

To a well stirred solution of allyl alcohol (30) (0.7g.) in dry pyridine (2.92 ml), maintained at $0^{o}C$, a solution of thionyl chloride (3.1 ml), in dry ether (10 ml) was added dropwise, stirring was continued for 3 hours after the addition. After filtering off the precipitate the ether layer was washed with saturated aqueous sodium hydrogen carbonate solution until it was neutral. The ether layer was separated, and then dried over $MgSO_4$. After evaporating the ether, the product was distilled under reduced pressure.

b.p. 76-78^{o}C/0.1 mm Hg, λ_{max} 252.5 mm (ε 20100); NMR peaks at δ1.1 (9H.s),4.3 (1H.d), 6-6.62 (2H,m), 7.3 (5H,s).

5.6 PREPARATION OF PIVALDEHYDE

The preparation of pivaldehyde from pivalic acid did not give satisfactory results.[108] However, the following procedure was successful. t-Butylmagnesium chloride was prepared from magnesium turnings (12g.) and t-butyl chloride (55 ml.) in dry ether (175 ml.). The solution was filtered under an atmosphere of dry nitrogen and found to contain 0.37 moles of Grignard reagent as shown by titration and weighing the unreacted magnesium which was left in the reaction flask.

This Grignard solution was added dropwise with stirring to methylformate (60 ml).[109] The temperature of the reaction mixture was kept below -50^{o}C. The Grignard complex so obtained was hydrolysed with ice and sulphuric

acid (5%). (The yield was much better when the hydrolysis was done with ammonium chloride.) The aldehyde was taken up in ether. The ethereal solution was dried over potassium carbonate, hydroquinone (0.2 g.) being added to protect the aldehyde from oxidation. The yield was about 40%, based on the Grignard reagent used.

b.p. 72-75°C, n_D^{27} 1.385

5.7 PREPARATION OF 4,4-DIMETHYL 2-PENTENAL

To a solution of pure diisopropylamine (0.1 mole) in absolute ether (50 ml.) at room temperature, a solution of butyllithium (0.1 mole) in ether (150 ml.) was added with stirring. The reaction was performed under nitrogen. After a few minutes the Gilman test was negative.[110] Then at 0°C N-cyclohexyl acetaldimine, prepared from acetaldehyde and cyclohexylamine,[111] (0.1 mol in 80 ml. ether) was added slowly. After ten minutes the mixture was cooled to -70°C. The metalated Schiff's base crystallized out. Pivaldehyde (0.1 mole) in ether solution (100 ml) was added dropwise and the mixture left for 20 hours at room temperature.[112] The complex was decomposed at 0°C with a solution of oxalic acid (0.4 mole) in water (500 ml) (a small amount of hydroquinone was added). The product in ether was separated and dried over sodium sulphate. The product after the removal of solvent polymerised when distillation was attempted.

Another attempt was made with a slight modification in the last step. After the steam distillation the distillate was treated with a saturated solution of sodium bisulphate containing some alcohol to produce the adduct

of the aldehyde. The crystalline precipitate was filtered at the pump, washed with a little alcohol, followed by ether, and allowed to dry. The aldehyde was recovered by neutralization of the bisulphate adduct with dilute hydrochloric acid and extraction into ether. Infra-red bands were observed at 2980 cm^{-1}, (CH), 2880 cm^{-1} ($-\overset{O}{\overset{\|}{C}}-H$), 1700 cm^{-1}, 1650 cm^{-1}, 1490 cm^{-1}, 1390 cm^{-1}, 1370 cm^{-1}, 1125 cm^{-1}, 1060 cm^{-1}, 1020 cm^{-1}.

5.8 PREPARATION OF 3-t-BUTYL-1-PHENYLALLYL ALCOHOL (ROUTE A)

To a well stirred solution of phenyl magnesium bromide prepared from bromobenzene (0.03 mole) and magnesium (0.03 mole) in anhydrous ether (15 ml) maintained at $-20^{o}C$, a solution of 4,4-dimethyl 2-pentenal in anhydrous ether (5 ml.), was added dropwise during 30 minutes. Stirring was continued for another 2.5 hours and the complex was then decomposed with 5% sulphuric acid to avoid the formation of the gelatinous layer. The ethereal layer was separated, washed three times with water, dried over $KHCO_3$, filtered and distilled. The product had b.p. $72-77^{o}C/0.25$ mm., λ_{max} 252 nm(ε 3030). NMR peaks at δ1(9H, s), 2(1H, broad, exchanged D_2O), 5.2 (1H, m), 5.34-6 (2H,m), 7.36 (5H,m). ν max (cm^{-1}) 3300 (O-H broad), 2900 (CH), 1640 (C=C), 1600, 1490, 1450 (δCH_3), 1360 (δCH_3), 1260, 1200, 1095, 1085, 1015 1004, 878.

5.9 PREPARATION OF 1,1-DICHLORO-3,3-DIMETHYL BUTANE

In a flask was placed t-butyl chloride (1 mole, dry). This was cooled to $-40^{o}C$, and, successively

powdered anhydrous aluminium trichloride and pre-cooled ($-60^{o}C$) vinylchloride (about 10 ml) were added. The cooling bath was removed and the temperature rose gradually until the mixture turned orange after about 10 minutes.

The mixture was again cooled and the remainder of the vinylchloride (1.25 moles) added dropwise while the temperature was maintained between -35 and $-45^{o}C$. When the addition was complete, the temperature of the reaction mixture was allowed to rise to $-15^{o}C$. To this vigorously stirred mixture was added 2 N HCl (150 ml.). The organic layer was separated as quantitatively as possible and dried over anhydrous magnesium sulphate. The excess vinylchloride was removed at the water pump. The residue was used for the next step without purification.

5.9.1 PREPARATION OF t-BUTYLACETYLENE (ROUTE A)

To a vigorously stirred suspension of sodamide (3.5 moles) in liquid ammonia (1.5 l.) was added dropwise 1,1-dichloro-3,3-dimethyl butane (1 mole). The addition required about 40 minutes. Stirring was continued for a further 2 hours. Dibutyl ether (150 ml) was then added and the ammonia allowed to evaporate. Finely crushed ice (1 Kg) was added as quickly as possible. The organic layer and the gel layer in the separatory funnel were swirled twice in ice water (150 ml). The extracts were dried over a small amount of magnesium sulphate. The t-butylacetylene was distilled off from the extract under normal pressure through a Vigreux column.

n_D^{20} 1.3749, b.p. $38^{o}C$/760 mm Hg, 50-53% yield.

5.10 PREPARATION OF 2,2-DICHLORO-3,3-DIMETHYL-BUTANE

To finely powdered phosphorus pentachloride (108 g., 0.5 mole) was added pinacolone (50g. 0.5 mole) with stirring (mechanical). The reaction temperature was maintained at 0-5^{0}C. The time of addition was two hours, after which stirring was continued for nine hours. The mixture was poured on 300 g. of ice. The solid was removed by filtration, washed with water and air-dried. This amounted to 40 g. of crude dichloride. The pure dichloride was obtained by sublimation m.p. 151-152^{0}C.

There was also a liquid organic product which was taken up in ether, washed with water, 10% bicarbonate solution and water, and dried over magnesium (or sodium) sulphate. Removal of the ether layer yielded 23 g . of crude 2-chloro-3,3-dimethyl-1-butene

5.10.1 PREPARATION OF T-BUTYLACETYLENE (ROUTE B) [115]

A 2 l. three neck flask was equippedwith a thermometer, a stirrer and a Liebig condenser. The top of the condenser was connected to a distilling head permitting reflux control. The outlet from the distilling head led to a receiver immersed in an ice-bath which in turn was connected via an outlet to a vapour trap immersed in an ice bath.

A mixture of pinacolone dichloride (51.6g.), mineral oil (100 ml), and absolute ethanol (30 ml.) was added to the flask and stirred into a solution, followed by potassium hydroxide (150 g.). The stirring was started

and heat applied through a heating mantle. At a pot temperature of 110°C the KOH pellets melted to give an easily stirred fluid. At 132°C an extremely vigorous evolution of distillate began and it was necessary to lower the mantle for a short time to control the reaction. The initial head temperature reached 75°C but then subsided and was maintained as much as possible in the range of 40-60°C. After about 10-15 minutes most of the vigorous reactions had subsided, the mantle was replaced and heating & take off of distillate continued for 2 hours. The t-butylacetylene was distilled off from ethanol under normal pressure through a Vigreux column

n_D^{20} 1.3749 b.p. 38°C

5.11 PREPARATION OF 3-t-BUTYL-1-PHENYLPROPARGYL ALCOHOL

Benzaldehyde (freshly distilled, 0.25 moles) was added over 30 minutes to a suspension of lithium t-butylacetylide (0.3 moles), the temperature being maintained at -40 to -30°C Work up was carried out by the addition of saturated aqueous ammonium chloride solution(100 ml) and extraction of the aqueous layer three times with ether. The combined organic solutions were washed with a saturated ammonium chloride solution and dried over magnesium sulphate. After removing the ether and THF at the water pump, the residue was distilled through a Vigreux column. 3-t-Butyl-1-phenylpropargyl alcohol was obtained in a 63-67% yield. b.P. 84-86/0.2 mm Hg NMR peaks at δ 1.25 (9H,s), 2.69 (1,d,exchanges D_2O), 5.4 (1H,d), 7.4 (5H,m). ν_{max}(cm^{-1}) 3300 (OH,broad), 2930 (CH), 2200 (C≡C), 1490, 1450 (δCH_3), 1360 (δCH_3), 1260, 1200, 1060, 1000, 920, 860, 740, 710.

5.11.1 PREPARATION OF 3-t-BUTYL-1-PHENYLALLYL ALCOHOL (ROUTE B)

The 3-t-butyl-1-phenylallyl alcohol was prepared from 3-t-butyl-1-phenyl-propargyl alcohol by LAH reduction. (see pp. 107) b.p. 72-77°C/0.25 mm Hg, λ_{max} 252 nm (ε 3030). NMR peaks at δ1(9H's), 2(1H, broad, exchanged D_2O), 5.2 (1H,m), 5.35-6 (2H,m), 7.36 (5H,m).

5.12 PREPARATION OF PROPIOLALDEHYDE [113]

A 3-l three necked flask was fitted with a thermometer, a dropping funnel, a stirrer, a capillary tube for introduction of nitrogen near the bottom of the flask, and an exit tube attached through a manometer to three traps set in series. In the flask were placed 180 ml of 33% (by volume) propargyl alcohol (56 g . 1 mole) and a cooled solution of sulphuric acid (67.5 ml) and water (100 ml). The flask was cooled in an ice-salt mixture. While the contents of the flask were cooling, the first trap was cooled to -15° with acetone and dry ice. The last traps in series were cooled to -78° with acetone and dry ice. The pressure in the system was reduced to 40-60 mm, nitrogen was introduced through the capillary, and the mixture stirred vigorously. A solution of commercial chromium trioxide (105g) in water (200 ml) and sulphuric acid (67.5) was added dropwise during three hours maintaining a reaction temperature of 2-10°C. After the addition of chromium trioxide, the ice-bath was removed and the flask permitted

to warm up to room temperature while the pressure was gradually lowered to 14-20 mm to remove the last of the aldehyde. The condensate of the three flasks (traps) were combined and dried over magnesium sulphate, and fractionally distilled to obtain propargyl aldehyde (19 g.) b.p. 54-57°C, n_D^{25} 1,4050.

5.13 PREPARATION OF t-BUTYLVINYL BROMIDE

Through a mixture of t-butylacetylene (50g., 0.61 mole) and dibenzoylperoxide (1.2g) at 0° was passed a slow stream of dry hydrogen bromide until the absorption stopped. The resulting solution was washed with sodium bicarbonate and water and finally extracted into ether. dried over calcium chloride and the solvent removed. The residual liquid was distilled to obtain t-butylvinyl bromide (66.5 g.), b.p. 120—127°, yield 60%.

5.14 PREPARATION OF t-BUTYLVINYLMAGNESIUM BROMIDE

t-Butylvinylmagnesium bromide was prepared by the method of Normant.[114] Ethyl bromide (3drops) and iodine (one crystal) were added to magnesium turnings (1.2 g . 0.05 moles) in THF (20 ml) in a four-necked flask equipped with a stirrer, thermometer, condenser, pressure-equalising dropping funnel, and a nitrogen inlet tube. t-Butylvinyl bromide solution (ca. 0.5 ml of a solution containing vinyl bromide, 3.5 ml, 0.05 ml.) in THF (4 ml.) was added and the

mixture heated slowly until the original yellow colour had faded to a grey-green. Stirring was commenced and the remainder of the vinyl bromide solution was added during twenty minutes, thus maintaining the temperature at 55-60°. The liquid phase gradually became brown while the magnesium dissolved. The mixture was refluxed for one hour and then cooled to room temperature. The liquid was decanted from the undissolved magnesium under an atmosphere of argon.

5.14.1 PREPARATION OF 6,6-DIMETHYL-HEPT-4-EN-1-YN-3-OL

Redistilled propargyl aldehyde (3.3 ml, 0.05 mole) was added dropwise with stirring to t-butylvinylmagnesium bromide under nitrogen, maintaining the temperature in the range of -35 to -40°. The reaction mixture became greenish yellow and was allowed to stir for two hours, when it became brownish yellow. Cooled aqeuous ammonium chloride, (4 g.) solution was added cautiously and a thick yellow precipitate formed. The mixture was extracted with ether washed with water and dried over sodium sulphate. After the removal of the ether a dark yellow oil remained. This residue was distilled. A large amount of tarry material remained in the distillation flask although great care was taken to ensure that the bath temperature was the minimum required to distillation. b.p. 74-78°C/ 1 cm Hg, NMR peaks at δ 1.1 (9H,s), 2.2 (1H,m), 2.5 (1H,m), 4.8 (1H,m), 5.3-6.1 (2H, m). $\nu_{max}(cm^{-1})$ 3300 (broad, O-H +≡C-H). 2900 (CH), 2100 (C≡C), 1650 (C=C), 1480, 1460 (δCH_3), 1360 (δCH_3), 1260, 1200, 1100, 1015, 980 (δ trans CH= CH).

5.15 PREPARATION OF STYRYL -t-BUTYL KETONE (36)

In a 50 ml. flask equipped with a reflux condenser and magnetic stirrer were placed benzaldehyde (3.18 g., 0.03 moles), pinacolone (3g.), and methanol (15 ml.). A solution of KOH (1g.) in methanol (15 ml.) was added dropwise. The mixture was heated until reflux and refluxed for 5-6 minutes. After cooling the reaction mixtures was neutralized and the solvent removed. The residue was distilled under high vaccum. Styryl t-butyl ketone (36) was obtained in a 80-85% yield; it had b.p. 114°C/0.3 mm Hg.

5.16 PREPARATION OF 2-PHENYL-3-PIVALOYL OXIRANE

A solution of sodium hydroxide (1 g.) in water (6 ml.) was added dropwise to a solution of styryl-t-butyl ketone (36) (376 g.) and 35% hydrogen peroxide (6.7 ml.) in methanol (20 ml) at 25-30°C. The reaction mixture was brought slowly to reflux temperature and then allowed to cool down. The pure epoxide crystallized out on standing in the fridge as colourless needles. It had m.p.83°C. after recrystallisation from ethanol water.

5.16.1 PREPARATION OF 1-PHENYL-3-t-BUTYL ALLYLALCOHOL(38) (ROUTE C)

A suspension of epoxide(37)(0.8g.) and sodium hydroxine hydrate (8 ml. 100%) was brought to reflux temperature over 50 minutes and allowed to reflux for 5-7 minutes. The reaction mixture was cooled, neutralized, and three times extraced with benzene (15 ml.). The residue

obtained after evaporation of the solvent showed two main spots on t.l.c. which were identified as the desired allylic alcohol (38) and a pyrazol derivative. The pure 1-phenyl-3-t-buty-allylalcohol was obtained by column chromatography with silica gel. Elution with 20% ether-light petroleum ether yielded 35% of the allylic alcohol.

5.17 PREPARATION OF p-NITROPHENYL-t-BUTYL-VINYL KETONE (37)

A solution of P-nitro-acetophenone (1.65 g.) in methanol (100 ml) was added dropwise over five hours to a solution of pivaldehyde (1.2 g.) and sodium hydroxide (0.6 g.) in methanol (25 ml.) at room temperature. The reaction mixture was stirred for two or three hours longer and then neutralized. Organic compounds were extracted into ether. The residue obtained after evaporating of the solvent showed two main spots on t.l.c. which were identified as the starting material and the desired ketone (41). The residue was applied to a silica gel column. Elution with 20% ether-light petroleium ether yielded 45% of the pure p-nitophenyl-t-butyl-vinyl ketone.

5.17.1 PREPARATION OF 1-p-NITROPHENYL-3-t-BUTYL-ALLYL-ALCHOL (33).

A Solution of the keton (41) (1.1 g.), aluminium isoproxide (8g.), and isopropanol (7.5 ml.) in benzene (30 ml.) was heated under partial refluc until formation of acetone ceased (about 3 hrs.). After cooling, excess 2N-sodium hydroxide was added, the benzene layer separated, and the aqueous layer extracted with benzene. Evaporation of the combined benzene extracts afforded 1-p-nitrophenyl-3-t-butyl allylalcohol (33) together with a small amount of the starting

ketone. The pure allylalcohol (33) was obtained by passing the mixture so obtained down a silica gel column, eluting with 30% ether-light petroleum ether yield 80%

5.18 GENERAL PROCEDURE FOR PREPARATION OF ACTIVE ALLYLIC CHLORIDE (UNCONJUGATED)

A solution of diphenyl sulphide (0.20 mole) (or dimethyl sulphide in cases where the boiling point of the allyl chloride formed was expected to be much higher than α-chloro methyl sulphide) in methylene chloride (5 ml.) was added dropwise over 5-10 minutes at 0°C to a solution containing N-chlorosuccinimide (0.17 mole) in anhydrous methylene chloride (50 ml.) (mag. stirring, nitrogen atom.) The reaction mixture was cooled to -50 to -60°C. and the allyl alcohol (28, 32 and 34) (0.12 mole) in methylene chloride (10 ml) was added gradually over 30-40 minutes, stirring being continued for an additional 2-3 hours at this temperature.

The reaction mixture was warmed to -15-0°C depending on reactivity of the allyl chloride formed e.g. in the case of 6.6-Dimethyl-3-chlorohept 4-en-1-yne the temprature should not be more than -7 or -8), stirred for 1 hour and poured into ice-cold brine (60 ml.). After shaking and separating the mixture as quickly as possible , the aqueous phase was extracted with to 35 ml portions of ether. The combined organic phase was washed with cold brine (30 ml) and dried over magnesium sulphate. Filtration and evaporation of solvents gave the unrearranged allylic chloride.

3-Chloro-pent-4-en-1-yne (18), 3-chloro-6, 6-dimethyl-hept-4-en-1-yne (24) and 1-chloro-4, 4-dimethyl-1-phenyl-pent-2-yne (20) were prepared from their corresponding alcohols (28), (34) and (32) using the above procedure.

Compound (18), λ_{max} 204 (ε637) b.p. 72°C, n_D^{16} 1.4631, NMR peaks at δ 2.75 (1H,d, acetylenic proton), 4.95-6.1 (4H,m). $\nu_{max}(cm^{-1})$ 3350 (≡C-H, 2100 (C≡C), 1640 (C=C), 1420, 1403, 1319, 1265, 1195, 1009, 995, 947, 900, 750.

Compound (24), NMR peaks at δ 1.04 (9H,s), 2.7 (1H,d), 4.93-5.13 (1H, m), 5.45-6.2 (2H, m). ν_{max} (cm^{-1}) 3300 (≡C-H), 2970 (CH), 2100 (C≡C), 1640 (C=C), 1470 (δCH_3), 1370 (δCH_3), 1265, 1207, 980, 800, 704.

Compound (20), NMR peaks at δ 1.16(9H,s), 5.50-5.68 (1H,m), 5.8-6.5 (2H,m), 7.34 (5H,s).

5.19 PREPARATION OF CONJUGATED ALLYLIC CHLORIDES (21, 17, 19)

A solution of thionyl chloride (3.57 g.) in dried ether (10 ml.) was added dropwise to a solution of allyl alcohol (0.03 M) and tri-n-butylamine in dired ether (11 ml) during 30 minutes, while the temperature was kept below -10°C. The mixture was allowed to stir for one hour longer. The solution was then quickly washed with ice-cold water, saturated aqueous sodium bicarbonate solution (three times), and water again. It was dried over anhydrous magnesium sulphate. The ether was evaporated and the crude chloride was distilled under vacuum.

Chlorination of 1-t-butyl-3-phenyl-allyl alcohol (30), penta-1 ,3-dien-5-ol (27) and pent -3-en-1-yn -5-ol (29) with thionyl chloride and tri-n-butyl-amine as above afforded their corresponding chlorides (21), (17) and (19).

Compound (21), b.p. 76-78°C/0.1 mm Hg, λ_{max} 252.5 (20100), NMR peaks at δ 1.3 (9H, s), 4.46 (1 H,d) 6.18-6.81 (2H, m), 7.45 (5H, s).

Compound (17), n_D^{19} 1-4907, b.p. 60°C/200 mm Hg.

Compound (19), n_D^{18} 1.4863, b.p. 57°C/83 mm Hg, λ_{max} 228 (ε12000). NMR peaks at δ 2.95 (1H, d, acetylenic proton), 4.13 (2H, d, allylic proton). 5.6-6.6 (2H,m, vinylic protons). ν_{max} (cm^{-1}) 3300 (≡ C-H), 2920 (CH), 2070 (C≡C), 1630 (C=C), 1440, 1290, 1245, 1160, 960, 700.

5.20 SOLVENTS

5.20.1 WATER

Distilled water was de-ionized by passing it through two columns packed with cation exchange (Zerolit, Zeo-Karl 225, BDH) and an ion exchange Amberlite, resin IR-4B(OH) resins respectively. The dissolved carbon dioxide in water was removed by boiling.

5.20.2 ETHANOL

Absolute ethanol (99.9%, James Burrough Limited) was used after distillation without any further dehydration

5.20.3 SULPHOLANE

Sulpholane was purified by the procedure reported by Gore and his co-workers.[81] Commercial sulpholane (1 kg) was allowed to stand for 2 days over a molecular sieve (4A, 100g. freshly regenerated) with occasional shaking. After being cooled and decanted from solids the sulpholane was shaken with phosphoric oxide (32.5 g.). The decanted solvent was distilled under high vacuum. It had b.p. 119-120°C/0.2 mm Hg. The distillate was then stored over a molecular sieve in the dark. For the kinetic runs the solvent was again decanted and redistilled, only the middle fraction being used. It had m.p. 28.4°C and n_D^{30} 1.4823.

5.21 SALTS

5.21.1 LITHIUM SALTS

Commercial anhydrous lithium chloride and perchlorate were each kept for several hours at 100°C under reduced

pressure (0.2 mm.Hg.), before being used. The infra-red spectrum (nujol mull) of lithium perchlorate showed the presence of traces of water even after prolonged heating of the salt. For this reason sodium perchlorate was used where extremely dry reaction conditions were required.

5.21.2 SODIUM PERCHLORATE

Commercial anhydrous sodium perchlorate could be compltely dehydrated by heating under vacuum at 100°C, and has the advantage of being mildly hydroscopic.

5.21.3 RADIOACTIVE LITHIUM CHLORIDE

Radioactive hydrogen chloride (^{36}Cl) (200$^{\mu}$1, 2N) was added to a solution of lithium hydroxide (0.48g.) in water (10 ml). The excess of lithium hydroxide was neutralized with inactive HCl. The solvent was evaporated at the water pump and the solid then treated with ethanol (25 ml.) and the solvent evaporated again. The resulting solid was dried by heating at 100°C (0.2 mm Hg).

5.22 KINETICS

Two methods were employed to follow the kinetics in all sections of this work:

(a) Spectrometric technique

(b) Titrimetric technique

(a) Spectrometric Technique

Kinetic measurements were carried out by the method of Braude and Jones. Reactions were followed by observing the increase or decrease in absorption intensity of the medium at 228 nm associated with the formation or the disappearance of the vinylacetylene chromophore. A long-necked reaction vessel was heated in a thermostatically controlled water bath. The reaction medium was allowed to equilibrate in the flask, and a stock solution of organic chloride (0.5 ml., 0.15 $m/_l$) in cyclohexane was added. The flask was shaken vigorously, a 1.00 ml. sample was withdrawn immediately by a pipette and diluted into cold ethanol in a 10 ml volumetric flask to quench the reaction and give solutions of convenient absorption intensity. The obtical density of the solution at 228 nm was noted and taken as E_o using a Unicam (model SP 500) spectrophotometer. Other samples were taken at appropriate times in the same way.

In reaction of 3-chloro-pent-4-en-1-yne, the first order rate constants (k_t Min^{-1}) were calculated from the expression:

$$k_t = 2.303 \times \log[(E_\infty - E_c)/(E_\infty - E_t)] / t$$

for reactions of 5-chloro-pent-3-en-1-yne. the first order rate constants were calculated from:

$$k_t = 2.303 \times \log[(E_o - E_\infty)/E_t - E_\infty)]/t$$

where t is the time in minutes, and E_t and E_∞ are the observed optical densities after t minutes and at the end of the reaction (about nine half-lives) respectively.

(b) Titrimetric Method

To follow the solvolysis reactions the same apparatus was used as in the previous technique, 5 ml. samples in this case were pipetted into a flask containing absolute ethanol (10 ml.). The solution was shaken and directly titrated with sodium hydroxide using methyl red as an indicator. To calculate the rate constants the following expression was used:

$$k_t = 2.303 \times \log[T_\infty/(T_\infty - T_t)]/t$$

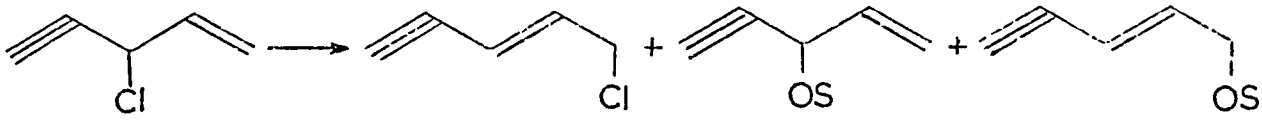
where T_t and T_∞ are the amount of hydrogen chloride produced at the time t and at a time when the reactions are complete (nine half lives).

5.22.1 DETERMINATION OF THE PRODUCT COMPOSITION

The degree of solvolysis of 3-chloro-pent-4-en-1-yne was obtained by adding a stock solution of organic chloride (0.5 ml. , 0.15 M/l in cyclohexane) to the reaction medium (25 ml.), kept at the required temperature. After about nine half-lives , determined from the kinetic run, 5 ml smaples were taken and added to ethanol (10 ml) in a conical flask. The solution so obtained was titrated

with standard sodium hydroxide (2×10^{-3} M/l) using methyl red as the indicator. The ratio of the amount of hydrogen chloride produced (T_∞) to the initial amount of organic chloride (C_o) indicated the degree of solvolysis.

The molar concentrations of reaction products were calculated in the following manner.



C_o M/l (RCl) C_1M/l (R´Cl) C_2M/l (ROS) C_3M/l (R´OS)

$$E = \varepsilon_{R'Cl} \times C_1 + \varepsilon_{ROS} \times C_2 + \varepsilon_{R'OS} \times C_3$$

$$C_o = C_1 + C_2 + C_3$$

$$T = C_2 + C_3$$

solving the three simultaneous equations for C_1, C_2 and C_3, we have

$$C_3 = \frac{E_\infty + T(\varepsilon_{R'Cl} - \varepsilon_{ROS}) - \varepsilon_{R'Cl} \times C_o}{\varepsilon_{R'OS} - \varepsilon_{ROS}}$$

$$C_2 = T - C_3$$

$$C_1 = C_o - (C_2 + C_3)$$

where C_o, C_1, C_2 and C_3 and the molar concentrations of the starting material and the products as indicated above, T is the concentration of the liberated acid, and ε_{ROS}, $\varepsilon_{R'OS}$ and $\varepsilon_{R Cl}$ are the molecular extinction coefficient of the pure secondary and primary solvolysis products and of pure 5-chloro-pent-3-en-1-yne respectively.

The overall rate constant (k_t) is given by the sum of the rate constants for the formation of the various products i.e.

$$k_t = k_{R'Cl} + k_{ROS} + k_{R'OS}$$

$k_{R'Cl}$, k_{ROS} and $k_{R'OS}$ can be obtained by multiplying k_t by the concentrations of RCl, ROS and R'OS respectively.

For solvolysis of 5-chloro-pent-3-en-1-yne, the ratio of the concentration of the conjugated and unconjugated solvolysis products ($C_{R'OS}$ and C_{ROS}) is given by the expresssion:

$$C_{ROS}/C_{R'OS} = (a_{R'OS} \times C_o - E_\infty)/(E_\infty - C_{ROS} \times C_o)$$

5.22.2 MEASUREMENT OF ISOTOPIC EXCHANGE RATES

The exchange of 3-chloro-pent-4-en-1-yne and 5-chloro-pent-3-en-1-yne with radioactive lithium chloride in sulpholane were studied using the following procedure.

The required volume of a standard solution of labelled lithium chloride in sulpholane was diluted to appropriate volume (20 ml.) with sulpholane and the reaction vessel was immersed in a thermostat at 50°C. A weighed quantity of the organic chloride was then introduced.

At various noted times a 2 ml. aliquot was withdrawn, added to hexane (10 ml.) contained in a separating funnel and the mixture shaken well and then extracted with water (2.5 ml.). The aqueous extract contained lithium chloride. The hexane layer which contained active organic chloride was dried over magnesium sulphate and filtered. After adding the

scintillator (5 ml., NE 213; Nuclear Enterprises Limited) the activity in the organic chloride was counted using a Beckman Scintillation liquid system.

First order exchange rates were calculated from:

$$k_{exch.} = 2.303 \times \log[(\lambda_\infty)/(\lambda_\infty - \lambda_t)] / t$$

where λ_∞ and λ_t are the specific molar activities finally and at time t respectively.

EXAMPLES OF KINETIC RUNS

(1) SOLVOLYSIS OF 3-CHLORO-PENT-4-EN-1-YNE

Conc. 2.65×10^{-3} M/l

Medium 70% Ethanol/Water

Temp. $50^{o}C$

Time(Min.$^{-1}$)	E	T(ml.)	$\overset{\star}{k_t} \times 10^3$(min.$^{-1}$)	$\overset{*}{k_t} \times 10^3$(Min.$^{-1}$)
0	0.103	0		
40	0.134		2.53	
175	0.222		2.64	
225		4.00		2.19
440	0.322		2.59	
475		6.75		2.24
620		7.75		2.25
665	0.367		2.58	
750	0.378		2.56	
765		8.50		2.28
790		8.55		2.25
1635		10.05		2.27
∞	0.425	10.30		
			mean k= 2.58	mean k= 2.27

$\star$ (Spectrometric rate constant), 1.00 ml of reaction mixture diluted to 10 ml. with absolute ethanol. Absorption measured in 0.2 mm cells.

* (Titrometric rate constant), 5 ml. of reaction mixture diluted to 15 ml with ethanol. It was titrated with sodium hydroxide (10^{-3} M/l).

(2) SOLVOLYSIS OF 5-CHLORO-PENT-3-EN-1-YNE

Conc. 3.37×10^{-3} M/l

Medium 70% Ethanol/Water

Temp. $60^{\circ}C$.

5 ml. diluted to 15 ml. with absolute ethanol, titrated with sodium hydroxide (10^{-3} M/l).

Time (Min.)	T(ml.)	$k_t \times 10^4$ (min.$^{-1}$)
0	0	
1221	3.10	1.70
2545	5.95	1.64
5325	9.90	1.72
7840	12.4	1.78
10915	13.9	1.69
∞	16.5	

mean $k_t = 1.71 \times 10^{-4}$

(3) ISOMERIZATION OF 3-CHLORO-PENT-4-EN-1-YNE

Conc. 2.61×10^{-3} M/l

Medium Sulpholane containing lithium chloride (3.03×10^{-2} m/l)

Temp. 60^{o}C.

1 ml. diluted to 10 ml. with absolute ethanol.

Absorption measured in 0.2 m.m. cells.

Time (Min.)	E	$k_r \times 10^4$ (Min.$^{-1}$)
0	0.067	
838	0.156	1.95
1330	0.174	1.51
2616	0.265	1.56
4160	0.343	1.52
7126	0.456	1.51
11560	0.545	1.45
17362	0.613	1.48
∞	0.657	

mean k= 1.51×10^{-4}

(4) THE EXCHANGE OF 3-CHLORO-PENT-4-EN-1-YNE WITH $Li^{36}Cl$

Conc. 1.8×10^{-2} M/l

Medium Sulpholane Containing $Li^{36}Cl(3.25 \times 10^{-2})$

Temp. $60^{o}C$

Time (Min.)	Count per min.	$k_{exch.} \times 10^{3}$ (Min.$^{-1}$)
0	60	
80	1470	2.91
145	2285	2.74
225	2997	2.52
285	3713	2.71
335	4197	2.80
657	5784	2.32
1310	6617	2.57
∞	6847	

mean $k = 2.64 \times 10^{-3}$

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