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Nucleophilic Substitution Reactions of Cyclopropane Derivatives

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The review is devoted to the solvolysis of cyclopropane compounds. The influence of structural and external factors on the rate and direction of the reaction are considered.
The bibliography includes 63 references.

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I. INTRODUCTION

Owing to advances in the chemistry of carbenes, particularly the development of new methods for the generation of carbenes, many cyclopropane derivatives have become available, which stimulated the study of their further reactions. The increased interest in these compounds is due to the fact that, by virtue of the unusual nature of the bonds in the strained three-membered ring, they possess a whole series of properties which distinguish them sharply from other carbocylic compounds. The solvolysis of cyclopropane derivatives is particularly characteristic in this respect—in this reaction treatment with a nucleophile as a rule entails the cyclopropyl–allyl rearrangement and not substitution.

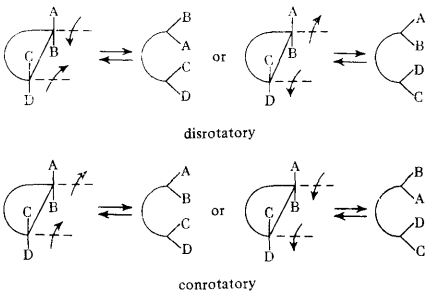
The aim of the present review is to specify the general and specific features of the solvolysis of cyclopropane derivatives.

II. THE MECHANISM OF THE SOLVOLYSIS OF CYCLOPROPANE DERIVATIVES

The specific feature of the behaviour of cyclopropane compounds in nucleophilic substitution consists in the fact that the reaction results in the formation of allyl derivatives and not substitution products. At the early stages in the relevant investigations a two-stage mechanism of the nucleophilic substitution reaction involving cyclopropane derivatives was proposed[1]: slow ionisation with formation of the cyclopropyl cation and subsequent rapid opening of the ring of the latter to give the allyl cation:

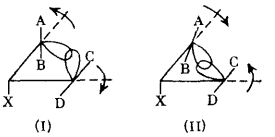


The error of this approach was demonstrated in numerous later studies. Kinetic[2,3] and quantum-chemical[4] investigations showed that the solvolysis of cyclopropane derivatives is a synchronous process involving the abstraction of an anion and the opening of the cyclopropane ring. According to the classification of Woodward and Hoffmann[5], the cyclopropyl–allyl rearrangement (opening of the three-membered ring to give the allyl cation) is an electrocyclic reaction. The authors define electrocyclic reactions as processes involving the formation of a single bond between the ends of the linear system containing k π-electrons (or the reverse process). The conversion of the cyclic form into an acyclic form and conversely can be disrotatory or conrotatory:



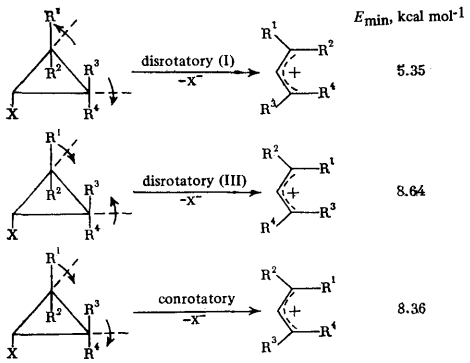
According to orbital symmetry conservation rules[5,6], thermal electrocyclic reactions are disrotatory for $k = 4n + 2$ and conrotatory for $k = 4n$. The cyclopropyl-allyl rearrangement constitutes a 2π-electrocyclic ring opening ($n = 0$). The disrotatory opening of the three-membered ring has been confirmed by quantum-chemical calculations using the MO-LCAO SCF method[7]. It has been shown[8] that the ring opening and the rotation of the methylene groups take place simultaneously; the central angle in the ring then increases from 60° to 120° and the σ-orbitals of the terminal groups are gradually converted into p-orbitals. Among all the possible structures of the $C_3H_5^+$ cation, the planar allyl cation is the most stable[4]. The energy of the cyclopropyl cation is greater by 39 kcal mol^{-1} than the energy of the allyl cation, so that there is no energy barrier to the isomerisation of the former to the latter.

In the disrotatory opening of the three-membered ring, there is a possibility of two stereochemically non-equivalent pathways—external (I) and internal (II):



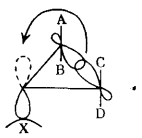
Calculations based on the principle of minimum movement[9-11] for the synchronous process involving the removal of the anion and the opening of the three-membered ring show that the two disrotatory ring opening pathways [(I) and (II)] are energetically non-equivalent: in pathway (I) there is virtually no energy barrier, while in pathway (II) there is a

considerable barrier.



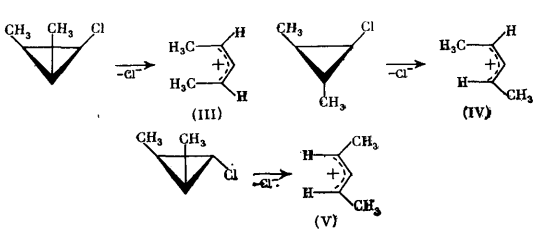
Here E_{min} is the minimum energy required for the rearrangement of the atoms in the molecular skeleton.

Calculation of the energies of the two pathways in the cyclopropyl–allyl isomerisation by the extended Hückel method[12,13] showed that substituents in the *cis*-position in the leading group rotate towards one another, while trans-substituents rotate away from one another, i.e. the disrotatory pathway (I) is followed regardless of the configuration. This result is a consequence of a secondary orbital effect in the transition state, which is due to the additional interaction of the molecular orbitals. This interaction does not lead to the formation of new bonds but lowers the activation energy for the reaction[14]:



Woodward and Hoffmann[5] note that in practice pathway (I) entails the S_N2 substitution of the leaving group X^- by the electrons of the ruptured C–C bond on the side opposite to that of the direction in which the X^- ion is eliminated.

A direct experimental confirmation of the validity of the disrotatory pathway (I) has been provided by the study of the allyl cations formed from isomeric 2,3-dimethylcyclopropyl chlorides by ^{1}H NMR.[15] The stereochemistry of the allyl cations confirms the stereospecificity of the opening of the three-membered ring. The formation of three individual 1,3-dimethylallyl cations (III), (IV), and (V) from the isomeric 2,3-dimethylcyclopropyl chlorides rules out the existence of the cyclopropyl cation as an intermediate. The disrotatory pathway (I) and the synchronous nature of the ionisation with ring opening have also been confirmed by the kinetics of the acetolysis of the isomeric 2,3-dimethylcyclopropyl chlorides [$k_{trans,trans}$(17800) > $k_{cis,trans}$(210) > $k_{cis,cis}$ (1)] [15] and 2,3-dimethylcyclopropyl toluene-*p*-sulphonates [$k_{trans,trans}$ (38000) > $k_{cis,trans}$ (460) > $k_{cis,cis}$ (2.2)].[16]



III. THE ROLE OF STRUCTURAL FACTORS IN THE SOLVOLYSIS OF CYCLOPROPYL HALIDES AND CYCLOPROPYL TOSYLATES (TOLUENE-*p*-SULPHONATES)

1. The Relative Positions of the Leaving Group and the Substituent in the Cyclopropane Ring

The fact that one of the two possible pathways in the disrotatory opening of the three-membered ring is preferred leads to different reactivities of the *cis*- and *trans*-substituted cyclopropyl halides and tosylates. According to the data in Table 1, the reactivity of cyclopropane derivatives containing substituents and the leaving group on one side of the ring is appreciably lower than the reactivity of the corresponding compounds in which the substituents and the leaving group are located on opposite sides of the ring. In the case of the *cis*-isomers ring opening is hindered by the steric interactions between the substituents in the cyclopropane ring, while in the opening of the *trans*-isomers weaker steric interactions are observed between two hydrogen atoms.

Table 1. The rates of solvolysis of isomeric 1-chloro-2,3-dipropylcyclopropanes[17] and 1-chloro-2,3-diphenylcyclopropanes[18].

2,3-Disubstituted cyclopropyl halide	Reaction conditions	k, s^{-1}
cis, cis-1-Chloro-2,3-dipropylcyclopropane	C_2H_5OH; 80°	$2.17\cdot10^{-8}$
trans, trans-1-Chloro-2,3-dipropylcyclopropane	ditto	$8.2\cdot10^{-5}$
cis, trans-1-Chloro-2,3-dipropylcyclopropane	»	$1.26\cdot10^{-6}$
cis, cis-1-Chloro-2,3-diphenylcyclopropane	CH_3COONa/CH_3COOH; 95.2°	$3.59\cdot10^{-6}$
trans, trans-1-Chloro-2,3-diphenylcyclopropane	ditto	$1.15\cdot10^{-3}$
cis, trans-1-Chloro-2,3-diphenylcyclopropane	»	$2.46\cdot10^{-4}$

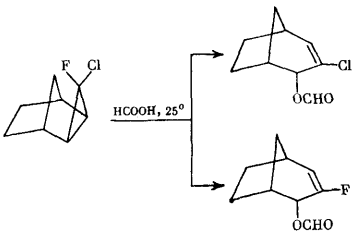
The steric repulsions of substituents in the cyclopropyl–allyl rearrangement can be so significant that *cis*-cyclopropyl halides sometimes virtually do not undergo this reaction. Thus, when a mixture of isomers of 1-chloro-2,3-dimethyl-1-phenylcyclopropane[19] or 2-aryl-1-bromo-1-fluorocyclopropanes[20] is treated with a methanol solution of silver nitrate at moderate temperatures, the *cis*-isomers remain unaltered. Under the same conditions, the *trans*-isomers undergo the cyclopropyl–allyl rearrangement. The study of the behaviour of the isomeric 2-phenylcyclopropyl halides[18,21] and cyclopropyl tosylates[12] in solvolysis showed that the *trans*-isomers react faster than the *cis*-isomers. A similar ratio of the rates has been observed also for trisubstituted cyclopropane derivatives[22,23].

Thus, in solvolysis the disrotatory ring opening of monocyclic cyclopropane systems leads to a greater ease of the elimination of the halogen in the *trans*-position with respect to the substituents in the ring.

The operation of the disrotatory pathway (I) as the only possible process involving the opening of the ring in cyclopropane derivatives has also been confirmed by the study of the solvolysis of bicyclic cyclopropane systems. The opening of a three-membered ring incorporated in a bicyclic system takes place smoothly when the leaving group is in the *endo*-position. Thus the solvolysis of *endo*-bicyclo[4,1,0]-heptyl chloride is 180 times faster than the solvolysis of the

exo-isomer[24]; *exo*-7-tosylbicyclo[4,1,0]heptane is inert under acetolysis conditions at 100 °C.[12]

The solvolysis of polycyclic asymmetric dihalogenocyclopropanes involves the hydrolytic dissociation of the *endo*-bond also in those cases where the latter is stronger than the *exo*-bond[25]:



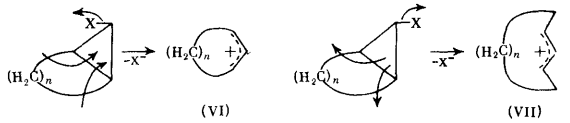
However, the elimination of the *endo*-halogen (or tosylate) is difficult in bicyclic systems with large rings. Thus in the series of bicyclo[5,1,0]octane and bicyclo[6,1,0]nonane derivatives the *exo*-isomers are found to be more reactive[26–28].

Table 2. Relative rate constants (k_{rel}) for the acetolysis of *endo*- and *exo*-bicyclo[*n*,1,0]alkyl tosylates[27].

n	0	3	4	5	6
endo	1	2500	62	3.1	3.5
exo	1	0.01	1.7	2500	10 000

Table 2 shows that the ease of the opening of the three-membered ring at the $C_{(1)}$–$C_{(n+2)}$ bond in derivatives of bicyclo[*n*,1,0]alkanes depends on the length of the bridge. The cause of this behaviour has been formulated as follows[27]: for low values of *n*, there is a possibility only of disrotatory movement in which the *cis*-allyl cation (VI) is formed, which favours the abstraction of the *endo*-halogen. With increase of *n* from 3 to 5, the stability of the cyclic *cis*-allyl cation (VI) is reduced and the reactivity of the *endo*-isomers diminishes.

The ionisation of the *exo*-isomers is sterically hindered owing to the considerable strain in the allyl cation (VII) having two *trans*-bonds. This strain is particularly large for low values of *n*; it diminishes with increase of *n*, which leads to an increase of the reactivity of the *exo*-isomers;



Thus the disrotatory opening of the cyclopropane ring incorporated in a bicyclic system takes place with elimination of the *endo*-halogen atom for small values of *n*, in contrast to the solvolysis of monocyclic cyclopropane systems. With increase of *n*, this specific feature disappears.

2. The Influence of the Nature of the Leaving Group

The ease of elimination of halogens in nycleophilic substitution at a saturated carbon atom increases from fluorine to iodine: F < Cl < Br < I.[29] The reactivity of cyclopropyl halides varies in the same series[30]. If the leaving group is a sulphonate anion (for example the tosylate anion), then cyclopropyl derivatives exhibit certain characteristic features. Acyclic alkyl tosylates are solvolysed appreciably faster than the corresponding alkyl bromides[31]. Table 3 shows that the higher reactivity of cyclopropyl tosylates compared with the corresponding halides is manifested clearly only for the *trans*-isomers. In the case of the *cis*-isomers the bromide becomes more reactive in the presence of certain β-substituents.

The greater reactivity of β-phenyl-substituted *cis*-cyclopropyl bromides has been explained[18] by the greater energy of the ground state of the bromides compared with that of the tosylates. Sliwinski et al.[3] share this view in relation to norcarane and 2,3-dimethylcyclopropane derivatives: in these compounds the steric repulsions between the *cis*-β-substituents are the leaving group are much more pronounced in the presence of the bulky bromine atom compared with the oxygen of the tosylate group, since the sulphonate residue is oriented in such a way that it is not involved in steric interaction with the β-substituent.

Table 3. The rate constants for the acetolysis (at 100 °C) of β-substituted cyclopropyl halides[3,21,32] and cyclopropyl tosylates[3,16].

Compound	k_1, s^{-1}	
	trans	*cis*
2-Methyl-1-tosylcyclopropane	$57.5\cdot10^{-7}$	$2.40\cdot10^{-7}$
1-Bromo-2-methylcyclopropane	$9.78\cdot10^{-7}$	$7.17\cdot10^{-8}$
2-t-Butyl-1-tosylcyclopropane	$13.7\cdot10^{-6}$	$2.11\cdot10^{-7}$
1-Bromo-2-t-butylcyclopropane	$16.1\cdot10^{-7}$	$14.3\cdot10^{-8}$
2-t-Butyl-1-chlorocyclopropane	$10.5\cdot10^{-8}$	$4.04\cdot10^{-9}$
2-Phenyl-1-tosylcyclopropane	$12.5\cdot10^{-6}$	$6.20\cdot10^{-7}$
1-Bromo-2-phenylcyclopropane	$82.2\cdot10^{-7}$	$20.6\cdot10^{-7}$
1-Chloro-2-phenylcyclopropane	$1.68\cdot10^{-7}$	$4.10\cdot10^{-8}$
	exo	*endo*
7-Tosylnorcarane*	$2.67\cdot10^{-4}$	$2.52\cdot10^{-2}$
7-Bromonorcarane*	$0.70\cdot10^{-6}$	$3.20\cdot10^{-2}$
7-Chlorononorcarane*	$0.40\cdot10^{-6}$	$0.15\cdot10^{-2}$
	trans, trans	*цис cis*
2,3-Dimethyl-1-tosylcyclopropane	$1.59\cdot10^{-3}$	$9.0\cdot10^{-8}$
1-Bromo-2,3-dimethylcyclopropane	$0.78\cdot10^{-3}$	$13.6\cdot10^{-8}$
1-Chloro-2,3-dimethylcyclopropane	$0.02\cdot10^{-3}$	$0.30\cdot10^{-8}$

*The values of k_1 at 200 °C are quoted.

Hausser's model[18] suffers from a number of disadvantages. Firstly, despite the high energy of the ground state of the *cis*-β-t-butyl-substituted bromide compared with the corresponding tosylate[3], the latter is more reactive (Table 3). Secondly, according to Sliwinski et al.[3], the steric strain in the ground state varies in parallel with the van der Waals radii of the leaving groups: Br (1.95 Å) > Cl (1.8 Å) > O (1.4 Å); on this basis, it was to be expected that the *cis*-chlorides would be more reactive than the *cis*-tosylates. However, kinetic results (Table 3) indicate a lower reactivity of the chlorides.

The energy of the ground state of *cis*-β-substituted derivatives of cyclopropane is probably not the only factor which determines the relative reactivities in the solvolysis of the halides and tosylates.

The next distinctive feature of β-substituted cyclopropyl halides and tosylates relative to the acyclic derivatives and unsubstituted cyclopropane derivatives is the lower sensitivity of the rate of their solvolysis to the nature of the leaving group (Table 4). In the cyclopropane series the

rates of solvolysis of the halides and tosylates differ comparatively little. One of the attempts to explain this finding was undertaken by Hausser and Uchic[18], who postulated a relation between the capacity of the leaving group for elimination and the degree of opening of the three-membered ring in the transition state. This idea was rejected by Schleyer and coworkers[3], who postulated that the degree of opening of the cyclopropane ring is independent of the nature of the leaving group. The latter workers assume[3] that the weak sensitivity to the nature of the leaving group can be explained by the fact that the same β-substituent accelerates solvolysis in different ways depending on the reactivity of the leaving group (Table 5). Comparison of the relative rate constants for the solvolysis of β-substituted cyclopropane derivatives shows that β-substituents have the greatest accelerating effect on cyclopropyl chlorides and smaller on the tosylates, which abolishes the difference between the rates of reaction of the halides and tosylates.

Table 4. Influence of the leaving group on the rate of solvolysis of acyclic aliphatic derivatives[29,31] and unsubstituted and β-substituted derivatives of cyclopropane[3,18,32,33].

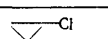
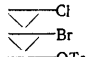
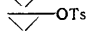
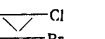
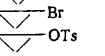
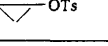
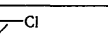
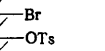
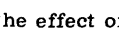
Compound	k_{rel}	Reaction conditions
t-C_4H_9Br	1	C_2H_5OH; 50°
t-C_4H_9OTs	3000	»
H_5C_6, H_3C >CHBr	1	C_2H_5OH; 50°
H_5C_6, H_3C >CHOTs	845	»
H_3C, H_3C >CHCl	1	CH_3COOH; 100°
H_3C, H_3C >CHBr	25	»
H_3C, H_3C >CHOTs	13 000	»
	1	CH_3COOH, 100°
	86	»
	231	»
	trans / *cis*	
$(CH_3)_3C$— 	1 / 1	CH_3COOH, 100°
$(CH_3)_3C$— 	16 / 35	»
$(CH_3)_3C$— 	130 / 53	»
H_5C_6— 	1 / 1	CH_3COOH, 100°
H_5C_6— 	5 / 50	»
H_5C_6—	80 / 15	»

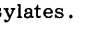
Table 5. The effect of β-substitution for different leaving groups in the compounds R—  X.[3,21,24]

R	X	k_{rel}* *trans*	k_{rel}* *cis*	R	X	k_{rel}* *trans*	k_{rel}* *cis*
$C(CH_3)_2$	OTs	330	5	C_6H_5	OTs	300	15
$C(CH_3)_2$	Br	1040	92	C_6H_5	Br	5310	11 330
$C(CH_3)_2$	Cl	5830	220	C_6H_5	Cl	9340	2 300

*In relation to the corresponding non-substituted cyclopropyl derivatives.

3. The Influence of the Nature of the β-Substituent on the Rate of Solvolysis of Cyclopropane Derivatives

As in reactions involving nucleophilic substitution at a saturated carbon atom, alkyl substituents in the β-position accelerate the solvolysis of cyclopropane derivatives. When alkyl groups are introduced in the *trans*-β-position in the cyclopropane ring, the rate of solvolysis of the halides and tosylates increases (Table 6), the acceleration becoming more pronounced with increase in the length and degree of branching of the alkyl substituent[3,30], which is consistent with the inductive effects of the alkyl groups.

Table 6. The relative rates of solvolysis of β-substituted cyclopropyl derivatives R—  X.[3,16,35]

R	X	k_{rel} *trans*	k_{rel} *cis*	Reaction conditions
H	OTs	1*	1*	CH_3COOH, 100°
CH_3	OTs	138	5.7	»
CH_2CH_3	OTs	180	7.4	»
$CH(CH_3)_2$	OTs	230	8	»
$C(CH_3)_3$	OTs	330	5	»
H	Br	1**	1**	»
CH_3	Br	630	46	»
$C(CH_3)_3$	Br	1040	92	»
H	Br	1***	1***	50% C_2H_5OH, 100°
CH_2CH_3	Br	460	20	»
$CH{=}CH_2$	Br	1770	160	»
	Br	7350	290	»

*$k = 4.16 \times 10^{-8}$ s^{-1}.
**$k = 1.55 \times 10^{-9}$ s^{-1}.
***$k = 2.18 \times 10^{-7}$ s^{-1}.

Table 7. The rates of acetolysis of β-phenylcyclopropane derivatives[12,21,32].

Compound	*t*, °C	*k*, s^{-1}
Chlorocyclopropane	150.1	$5.5 \cdot 10^{-10}$
cis-1-Chloro-2-phenylcyclopropane	150.1	$5.91 \cdot 10^{-4}$
trans-1-Chloro-2-phenylcyclopropane	150.1	$3.01 \cdot 10^{-3}$
Bromocyclopropane	160.3	$6.92 \cdot 10^{-7}$
cis-1-Bromo-2-phenylcyclopropane	119.4	$1.46 \cdot 10^{-5}$
trans-1-Bromo-2-phenylcyclopropane	119.4	$6.31 \cdot 10^{-5}$
Tosylcyclopropane	100	$4.16 \cdot 10^{-6}$
cis-2-Phenyl-1-tosylcyclopropane	108	$2.1 \cdot 10^{-6}$
trans-2-Phenyl-1-tosylcyclopropane	108	$3.2 \cdot 10^{-5}$

The accelerating effect of a *trans*-β-substituent is appreciably greater than that of a *cis*-β-substituent, which confirms the synchronous nature and the disrotatory pathway leading to the opening of the cyclopropane ring with rotation of the substituents on the outside in the case of the *trans*-isomers and on the inside for the *cis*-isomers. The steric repulsions arising in the opening of *cis*-β-substituted cyclopropyl halides and tosylates weakens the accelerating effect of the alkyl groups. The introduction of the second and subsequent *trans*-alkyl substituents is accompanied by a weaker acceleration[16].

The reactivity of cyclopropane derivatives increases also after the introduction of a phenyl substituent in the β-position (Table 7).

Under the influence of the inductive effect of the phenyl group, the rate of solvolysis of β-phenylcyclopropane derivatives should fall. The reaction is then accelerated by the +*M* effect of the phenyl group, which results in the stabilisation of the partial positive charge on the β-carbon atom in the transition state.

The change in the rate of solvolysis of cyclopropane derivatives induced by the phenyl group is greater than in the analogous substitution by the methyl group (Table 8), which can be explained by the fact that the phenyl group ensures a more effective delocalisation of the partial positive charge in the transition state. Recent studies have shown[36] that the ability of substituents to stabilise the aryl cation decreases in the sequence phenyl > cyclopropyl ≫ methyl.

Table 8. The relative reactivities of derivatives of β-methyl-[3] and β-phenyl-cyclopropanes[32,34] in the acetolysis reaction at 100 °C.

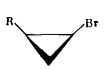
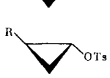
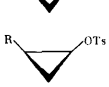
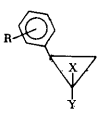
Compound	k_{CH_3}/H	$k_{C_6H_5}/H$
	630	5310
	46	1330
	138	300
	5.7	15

Table 9. The rates of solvolysis of β-arylcyclopropane derivatives



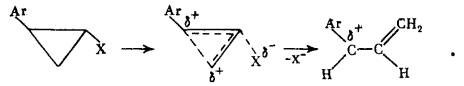
R	10^4k, s^{-1}	
	X=H, Y=OTs *, (Ref.34)	X=F, Y=Br ** (Ref.20)
H	0.305	0.89
p-CH_3	0.747	2.91
m-CH_3	0.656	1.19
m-Cl	0.0538	—
p-Br	—	0.38
m-Br	—	0.11

*Reaction conditions: CH_3COOH/CH_3COONa, 108 °C.
**Reaction conditions: CH_3OH, Ag^+, 50 °C.

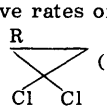
The degree of acceleration of the solvolysis of cyclopropane derivatives by β-phenyl and β-methyl groups approaches that for the α- and γ-substituted allyl halides[37], which supports the existence of a proto-allyl transition state in the solvolysis of cyclopropane systems.

The study of the solvolysis of β-arylcyclopropyl derivatives showed that electron-donating substituents in the aromatic ring accelerate and the electron-accepting substituents retard the reaction (Table 9).

The correlation between the reactivity of *trans*-2-arylcyclopropyl tosylates ($\rho = -1.75$) [34] and *trans*-2-aryl-1-bromo-1-fluorocyclopropanes ($\rho = -2.0$),[20] on the one hand, and the σ^+ constants of the substituents, on the other, permitted the conclusion that the opening of the three-membered ring and ionisation take place synchronously and that the partial positive charge in the transition state is localised at the benzyl carbon atom. The value of ρ indicates an electrophilic mechanism of the rate-limiting stage and a nearly ionic transition state:



An appreciable acceleration of solvolysis is attained when an alkoxy-substituent is introduced in the β-position in cyclopropane derivatives[17,38,39] (Table 10) by virtue of the effective stabilisation of the carbonium ion by the electrons of the oxygen in the alkoxy-group.

Table 10. The relative rates of solvolysis of β-substituted dichlorocyclopropanes  (n-C_4H_9OH; Ag^+; 80 °C) [39].

R	C_6H_5	OC_6H_5	C_4H_9	OC_4H_9
k_{rel}	0.2	0.8	1.0	20.0

4. The Influence of the Nature of the α-Substituent on the Rate of Solvolysis of Cyclopropyl Derivatives

The solvolysis of α-substituted cyclopropanes has been studied to a much lesser extent. The available literature data show that the reactivity of α-substituted cyclopropyl bromides[16,34] and cyclopropyl tosylates[32] is appreciably higher than that of the unsubstituted derivatives. Table 11 shows that the α-phenyl group stabilises more effectively the developing positive charge than the α-methyl group. The constant ρ for the series of α-arylcyclopropanes exceeds the reaction constant for the β-derivatives. According to Schleyer and coworkers[3], the high sensitivity of α-arylcyclopropyl tosylates in the solvolysis reaction to the introduction of the substituents into the aromatic ring is due to the fact that the transition state has a structure close to that of the cyclopropyl cation stabilised by the aryl group, although the solvolysis product is 2-arylallyl acetate.

The idea that the α-phenyl substituent can stabilise the cyclopropyl cation has been recently confirmed[40]: the 1-phenylcyclopropyl cation has been "captured" with the aid of the hydroborate anion before it could isomerise to the allyl cation.

Yet another argument has been adduced[34] against the existence of a transition state of the allyl type in the solvolysis reactions of α-arylcyclopropyl tosylates, namely the weak sensitivity of the solvolysis of 2-arylallyl tosylates to the introduction of substituents into the aromatic ring ($\rho = -0.4$).

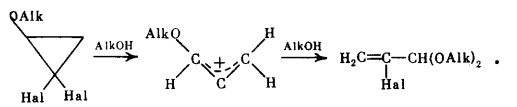
IV. THE INFLUENCE OF EXTERNAL FACTORS ON THE RATE AND DIRECTION OF SOLVOLYSIS OF CYCLOPROPANE DERIVATIVES

As shown in Section II, the solvolysis of cyclopropyl halides and tosylates leads to the formation of allyl derivatives. The charge distribution in the substituted allyl cation must be regarded as one of the factors which determine the site of addition of the anion to the allyl cation.

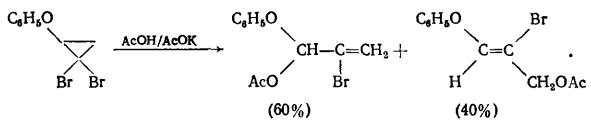
Table 11. The effect of α-methyl-[16,32] and α-phenyl-substitution[34] in the solvolysis of cyclopropane derivatives.

Compound	k_{CH_3}/H	$k_{C_6H_5}/H$	ρ (R=Ar)	Reaction conditions
	1100	390 000	−4.31(σ⁺),(108°)	CH_3COOH; 25°
	40	—	—	50% C_2H_5OH; 130°

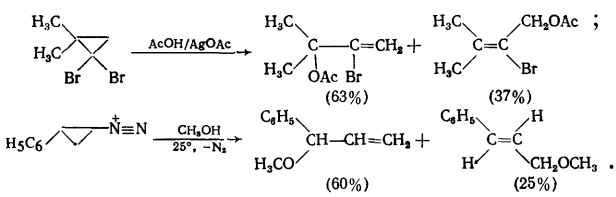
The localisation of the positive charge in the α-position relative to the substituent results in the formation of the acetals of α-halogenoacroleins in the solvolysis of alkoxydihalogenocyclopropanes[38,40,41]:



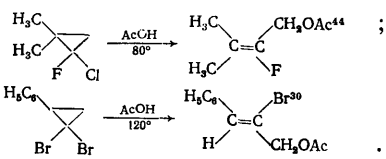
The stabilisation of the charge by the phenoxy-group is less effective owing to the conjugation of the lone electron pair of oxygen with the aromatic ring[42]:



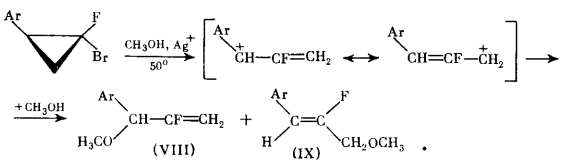
Charge control obtains also in the solvolysis reactions of derivatives of alkylcyclopropanes[30] and phenylcyclopropanes[43]:



However, in many cases the structure of the products of the solvolysis of alkyl- and phenyl-substituted dihalogenocyclopropanes is inconsistent with the charge distribution in the intermediate allyl cation:



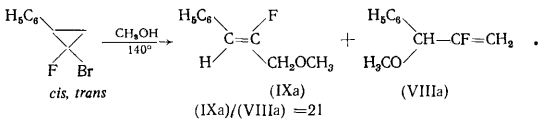
Evidently the second factor which determines the structure of the products of the solvolysis of cyclopropane derivatives is the stability of the olefins formed. It has been shown recently[20] that, under kinetically controlled reaction conditions, an allyl product with a terminal methylene group is formed preferentially:



Ar:	C_6H_5	p-$CH_3C_6H_4$	m-$CH_3C_6H_4$	p-BrC_6H_4	m-BrC_6H_4
(VIII)/(IX):	2.5	4.0	3.5	2.0	1.5

The arylallyl cation, formed as a result of the opening of the three-membered ring, reacts with methanol via both the α- and γ-carbon atoms with formation of products (VIII) and (IX) respectively. The degree of localisation of the charge on the α- and γ-carbon atoms of the allyl system, which depends on the nature of the substituent, determines the composition of the solvolysis products. The experimentally observed predominance of the yield of compound (VIII) over that of compound (IX) suggests that the charge is concentrated at the benzyl carbon atom of the arylallyl cation. The disproportion in the charge distribution increases following the introduction of electron-donating substituents into the aromatic ring and diminishes when electron acceptors are introduced.

On the other hand, under thermodynamically controlled conditions, the most stable olefins, in which the double bond is conjugated with the phenyl group (or olefins having the maximum number of substituents at the double bond), predominate:

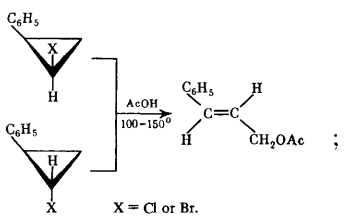


cis, trans (IXa) (VIIIa)

(IXa)/(VIIIa) =21

In the majority of studies on the solvolysis of arylcyclopropane derivatives[12,18,29,30,34] the formation of allyl products of the styrene type only has been observed, which must be attributed to the fairly severe reaction conditions (≥100–120 °C, 20–40 h).

It is remarkable that the acetolysis of *cis*- and *trans*-isomeric phenylhalogenocyclopropanes results in the formation of the *trans*-olefin only[21,22]:

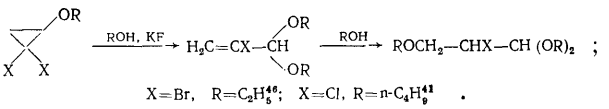


Some investigators[21] believe that the opening of the ring in *cis*-substituted halogenocyclopropanes is not subject to secondary orbital control. In other studies[45] the idea of *cis–trans* isomerisation in the allyl cation stage or of the reaction products is invoked. Bearing in mind the experimentally observed isomerisation of the *cis*-allyl cation to the *trans*-isomer[15,36], one must recognise that this view is more valid.

1. The Role of Accelerating Agents in Nucleophilic Substitution Reactions of Cyclopropane Derivatives

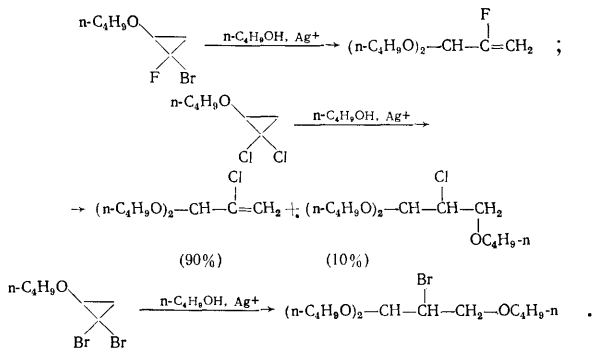
Electrophilic and nucleophilic accelerating additives are widely used in reactions involving nucleophilic substitution at a saturated carbon atom. The role of accelerating agents becomes still more marked in the solvolysis of cyclopropane derivatives, which are much less reactive than acyclic alkyl halides. Apart from the acceleration, electrophilic and nucleophilic additives can promote a further transformation of the allyl products formed.

Thus alcoholysis of alkoxy-*gem*-dihalogenocyclopropanes, accelerated by additives which generate an acid medium during the reaction (silver or alkali metal salts), is accompanied by secondary processes involving the addition of solvent molecules to the double bonds of the aryl derivatives:



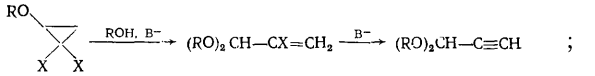
X=Br, R=C_2H_5[46]; X=Cl, R=n-C_4H_9[41] .

The ability of the dialkyl acetal of α-halogenoacrolein to combine with the alcohol is determined by the nature of the α-halogeno-group[39]:



Thus the stability of the primary products of the solvolysis of alkoxy-*gem*-dihalogenocyclopropanes in an acid medium is consistent with the +*M* effect of the halogen in the molecule of the dialkyl acetal of α-halogenoacrolein.

When an organic or inorganic base is used as the reactive nucleophile, dehydrohalogenation of the primary solvolysis product is observed:



X=Br, R=C_2H_5, B=C_2H_5ONa[46];
X=Cl, R=C_4H_9, B-t-C_4H_9ONa[38] .

The yield of the dialkoxypropyne increases both with increase of the basicity of the reactive agent (NaOH < KOH < n-C_4H_9. .ONa < n-C_4H_9OK) and with increase of its concentration[39].

The stability of the dialkyl acetal of α-halogenoacrolein in an alkaline medium varies in the same sequence as in an acid medium: the fluoro-compounds are more stable than the chloro- and bromo-derivatives (F > Cl > Br).[39]

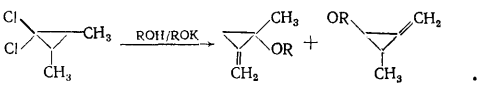
One must note that the solvolysis in the presence of strong bases proceeds with higher degrees of conversion of the primary products than in the presence of electrophilic additives. The formation of unsaturated aldehydes, enynes, and other unidentified products in solvolysis under the influence of t-C_4H_9OK has been described[47].

The cyclopropyl–allyl rearrangement, accompanied by secondary process, does not constitute the only pathway in the reactions of cyclopropane derivatives under solvolysis conditions subject to the influence of nucleophilic additives. If a strong base is used as the nucleophile then, as in the series of acyclic halogeno-derivatives, the elimination reaction competes with the substitution process.

The formation of cyclopropene from cyclopropane derivatives via β-elimination was observed for the first time by Kohler and Darling[48]. However, the isolation of the cyclopropene derivatives was not achieved for a long time owing to the instability of the three-membered ring with an *endo*-double bond. The low stability of cyclopropene and its derivatives is caused by the high strain energy of the ring[49,50]. The stability of cyclopropene compounds increases with increase of the degree of substitution, electron-donating substituents stabilising the molecule less effectively than electron-accepting substituents[51]. The high stability of polyhalogenocyclopropenes made it possible to obtain these compounds in a pure state[52].

The cyclopropenes formed under the conditions of the nucleophilic substitution reaction using highly basic additives can undergo further transformations: (a) isomerisation accompanied by the migration of the double bond outside the limits of the three-membered ring[53–55]; (b) the addition of a molecule of the nucleophile (solvent)[55] to the double bond of cyclopropene; (c) the opening of the three-membered ring with rupture of a C–C single bond in cyclopropene[39,41]. The operation of one of the above reaction pathways is determined by the structure of the initial cyclopropane or, more precisely, by the nature of its substituents.

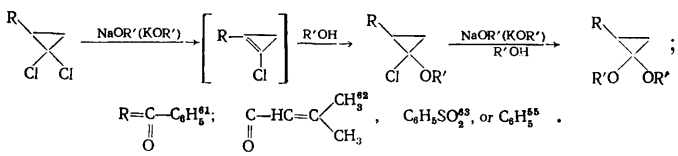
According to the data of Ampilogova et al.[56], compounds with a double bond in the three-membered ring are thermodynamically less stable than the isomeric methylenecyclopropanes. This has been confirmed experimentally by the irreversible isomerisation of alkylcyclopropenes to methylenecyclopropanes[54]. In the solvolysis of alkylhalogenocyclopropanes in the presence of strong bases the migration of the double bond outside the limits of the ring and the addition of a solvent molecule occur simultaneously in some cases[55]:



The ability of cyclopropene derivatives to undergo nucleophilic addition reactions indicates an unusual nature of the double bond in cyclopropenes, because such reactions are not characteristic of ethylenic double bonds. According to Kosai and Meyer[57], the C–H bonds in cyclopropene have an increased amount of *S*-character, while the C–C bonds have an increased amount of *p*-character. The study of the ^{13}C NMR spectra of cyclopropene derivatives led to the conclusion that the carbon–carbon double bonds in cyclopropene resemble acetylenic bonds[58]. Data for the geometry of cyclopropene (the C=C bond length is 1.3 Å [57] or 1.28 ± 0.04 Å [59]) and spectroscopic studies on substituted cyclopropenes (stretching vibrations of the C=C bond in the range 1800–1900 cm^{-1})[60] confirm the "acetylenic" properties of the cyclopropene double bond.

The elimination of the hydrogen halide with subsequent nucleophilic addition to the cyclopropene double bond under the conditions of the solvolysis of β-substituted halogenocyclopropanes under the influence of nucleophilic additives is determined by the basicity of the latter and the mobility of the hydrogen atom in the α-position relative to the substituent. Such reactions occur when strong bases (metal alkoxides) are used as nucleophiles and the cyclopropane ring has a substituent which increases the proton mobility

at the α-atom:



The dialkyl ketals of cyclopropanone formed are either stable under the reaction conditions or undergo further transformations.

In a study of the solvolysis of 2-aryl-1-bromo-1-fluorocyclopropane in deuterated methanol (CD_3OD) under the influence of potassium t-butoxide it was established[20] that the formal substitution products are not formed as a result of direct substitution of the halogen by the alcoholic residue but arise in the subsequent elimination–addition reaction.

Table 12. Degrees of conversion of 2-aryl-1-bromo-1-fluorocyclopropanes in methanolysis under the influence of t-C_4H_9OK (at 50 °C).

Reaction time, min	Conversion, %					
	H_5C_6 (F, Br)		p-CH_3–C_6H_4 (F, Br)		F_5C_6 (F, Br)	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*
10	35	17	—	—	100	100
20	60	28	—	—	—	—
30	—	—	7	4	—	—
60	80	40	17	8	—	—
90	—	—	21	12	—	—
120	92	56	29	15	—	—

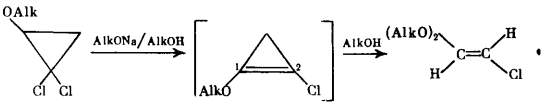
The solvolysis of aryl-*gem*-dihalogenocyclopropanes[20] in the presence of a strong base is accelerated by electron-accepting substituents and retarded by electron-donating substituents in the aromatic ring, as a result of the activation or deactivation of the benzyl proton (Table 12).

The higher reactivity of the *cis*-isomers is probably associated with the preferential *trans*-dehydrohalogenation. Similar relations between the rates of reaction of the *cis*- and *trans*-isomers have been observed in the solvolysis of 2-benzoyl-1-chlorocyclopropanes[61].

Consequently, the type of accelerating additive plays a decisive role in determining the direction of the process as a whole, the relative reactivities of the *cis*- and *trans*-isomers, and also the type of influence of the substituents in the aromatic ring on the rate of solvolysis of arylhalogenocyclopropanes. As shown above, in the presence of an electrophile (Ag^+) only the opening of the three-membered ring, accelerated by electron-donating substituents in the aromatic ring, takes place, the *trans*-isomers being more reactive than the *cis*-isomers. A strong base induces preferential reactions involving the retention of the cyclopropane ring, which are accelerated by electron-donating groups in the aromatic ring; under these conditions, the *cis*-isomer is more reactive. The cause of this sharp difference consists in the reaction mechanism; the electrophile attacks the halogen atom with formation of a carbonium ion, while the strong base attacks the mobile benzyl proton.

As already mentioned, the possibility of the solvolysis of halogenocyclopropanes with retention of the three-membered ring depends on the presence of a β-substituent activating the geminal proton. If the β-substituents are groups such as C_6H_5S [47] and OAlk,[39,41] then, under solvolysis conditions in the presence of both an electrophile and a strong base, the cyclopropyl–allyl rearrangement takes place. In the solvolysis of asymmetric alkoxy-*gem*-dihalogenocyclopropanes[39] the *trans*-isomer is more reactive in both cases.

Together with the products of the cyclopropyl–allyl rearrangement, the dialkyl acetals of *trans*-β-chloroacrolein are formed in the solvolysis of 2-alkoxy-1,1-dichlorocyclopropanes[39,41]:



The first stage probably involves the formation of 1-alkoxy-2-chlorocyclopropene, in which the $C_{(1)}$–$C_{(2)}$ bond is ruptured under the reaction conditions with addition of an alcohol molecule.

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The above analysis of the influence of various factors on nucleophilic substitution reactions in the series of cyclopropanes showed that, in contrast to the usual S_N processes, the opening of the three-membered ring, controlled by orbital symmetry, takes place, while the elimination reaction under the influence of strong bases is undergone by both the initial compounds and the primary reaction products.

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