Physical Chemistry

Theoretical study of bimolecular elimination (E2) reactions. Possibility of *syn* E2 elimination in the series of 2-R-2-R'-1-halocyclopropanes

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Reactions of the methoxide ion with substituted halocyclopropanes, which result in E2 elimination, have been studied by the semiempirical quantum-chemical AM1 method. The transition states corresponding to *trans* and *cis* routes have been localized. The energetic predominance of the *trans* route over the *cis* route is reduced by 2.6 kcal mol^{-1} on going from 1-chloropropane to chlorocyclopropane because of the features of cyclopropane geometry. It has been demonstrated that, in the gas phase, *cis* elimination may predominate over *trans* elimination for a particular stereoisomer of 2-cyano-2-methyl-1-halocyclopropanes due to weakening of orbital interactions and Coulomb repulsion between the cyano group and the MeO^- anion in the *trans* E2 transition state.

Key words: AM1 method; transition states; nucleophilic elimination (E2) reaction; halocyclopropanes.

Bimolecular nucleophilic substitution (S_N2) and elimination (E2) reactions, which are among the most typical reactions in organic chemistry, have been well studied experimentally in solutions. To understand the reaction mechanism more completely, studies in the gas phase, which make it possible to obtain information on the reactivity typical of a molecule in the absence of a solvent, are required. Quantum-chemical calculations of transition states of reactions provide one possible methods for pursuing these studies. Most of the theoretical calculations have been devoted to the S_N2 reaction mechanism (see, for example, Ref. 1 and references therein).

By contrast, theoretical studies on E2 elimination reactions are scarce.[2–9] One of the factors hindering these calculations is the complexity of the determination of the E2 reaction coordinate. Moreover, *anti*, *gauche*, and *syn* conformations are possible in the E2 transition

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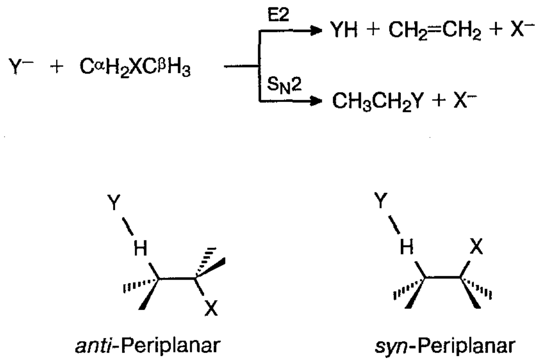
state. All of the results of calculations provide evidence that *anti* elimination always predominates over *syn* and *gauche* E2 elimination, which is in agreement with qualitative concepts of theoretical organic chemistry (Scheme 1).

Scheme 1



The *anti*-periplanar route is favorable for two reasons: (a) the overlapping of orbitals of the carbanion lone electron pair formed on the β carbon atom with the antibonding $\sigma^*(C^\alpha{-}X)$ orbital is more efficient (see Ref. 10); this orientation of interacting orbitals is favorable also for the occurrence of hyperconjugation effects;[11] (b) steric interactions are weaker in the staggered conformation. Eclipsed bonds are present in the *syn*-periplanar transition state and, therefore, this state is unstable due to the interactions between these bonds and the electrostatic interaction between Y^- and the dipole of the C—X bond.

Both *ab initio*[4,5,8—10] and semiempirical[2,3,6,7] calculations have been performed only for acyclic systems. In the case of planar cyclic systems, the *anti* route is realized for conformations intermediate between staggered and eclipsed in which the torsion angle between the C—Hal and $C{-}H^\beta$ bonds is 30—40°.[12] The question arises whether *syn* E2 elimination may predominate over *anti* E2 elimination in the gas phase if the factors determining the preference of the *anti* pathway over the *syn* pathway are reduced. Previously (see, for example, Refs. 12—14), it was demonstrated that, under particular conditions, *syn* elimination predominates.

In this work, the results of quantum-chemical calculations by the AM1 method (see Ref. 15) are reported for E2 elimination using the reaction of MeO^- with 2-R-2-R′-1-halocyclopropanes (R = R′ = H, Me; R = Me, R′ = C≡N; halogen is Cl or Br) as an example. The study involves a comparison of the energy of the *cis* and *trans* approaches of a nucleophile (a base) to an acyclic molecule and the analogous cyclopropane as well as to different substituted halocyclopropanes. In addition, the ion-dipole complexes formed at the first stage of the reaction were calculated. The suitability of analogous calculations for anions was demonstrated previously.[16] The validity of the AM1 method for predicting regioselectivity was confirmed by studies of the E2 reaction for simple ethane derivatives performed by this method.[6] A comparison of the results of *ab initio* and AM1 calculations for the gas-phase reaction between methoxide ($Y = MeO^-$) and chloroalkane as well as between ammonia and alkylhydroxonium[10] demonstrated the complete agreement with the obtained prediction about the competition between E2 and S_N2.

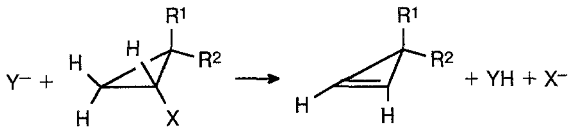
Calculation procedure

All calculations were performed on a PC-AT 386 computer using the AMPAC program.[17] The AM1 version with full optimization of geometric parameters in the PRECISE mode (see Ref. 15) was used. The transition states were first localized by the reaction coordinate method[18] and then refined by minimization of the norm of the gradient.[19] The points of minima and transition states on the potential energy surface were confirmed by calculations of normal vibration frequencies in the FORCE mode.

Results and Discussion

In the gas phase, ion-molecular reactions proceed normally through an ion-dipole complex. In the reaction between MeO^- and 2-R-2-R′-1-halocyclopropanes (**1**—**6**), formation of a number of complexes (Scheme 2) is possible; however, we have studied only those reactions that lead to the E2 transition state. The energies of these complexes and the transition states for the studied reactions are given in Table 1.

Scheme 2



1—6

1: $R^1 = R^2 = H$, X = Cl
2: $R^1 = R^2 = H$, X = Br
3: $R^1 = R^2 = Me$, X = Cl
4: $R^1 = R^2 = Me$, X = Br
5a: $R^1 = Me$, $R^2 = CN$, X = Cl
5b: $R^1 = CN$, $R^2 = Me$, X = Cl
6a: $R^1 = Me$, $R^2 = CN$, X = Br
6b: $R^1 = CN$, $R^2 = Me$, X = Br

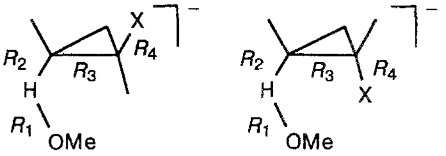
In all of the cases, two minima were localized on the potential energy surface. These correspond to ion-dipole complexes formed by *trans* and *cis* routes. The selected geometric parameters of complexes are given in Table 2. The $MeO{-}H^\beta$ distances in the complexes are rather large (~2 Å) and in all cases, the geometry of the initial reagents changes only slightly. The $C{-}H^\beta$ and C—X bonds change most substantially as a result of the formation of the complex (on the average, these bonds lengthen

Table 1. Heats of formation (kcal mol^{-1}) of the ion—dipole complexes ($\Delta_f H_c$) and transition states ($\Delta_f H_{TS}$) of the E2 reactions of compounds **1—6** calculated by the AM1 method

Compound	$\Delta_f H_c$		$\Delta_f H_{TS}$	
	trans	*cis*	*trans*	*cis*
1	−37.3 (−9.1)	−34.5 (−6.2)	−30.5 (−2.1)	−27.1 (1.3)
2	−25.6 (−9.6)	−22.8 (−6.8)	−19.4 (−3.4)	−15.9 (0.1)
3	−50.6 (−11.0)	−46.3 (−6.4)	−42.4 (−2.8)	−38.5 (1.1)
4	−38.7 (−11.4)	−34.6 (−7.3)	−31.2 (−3.9)	−27.2 (0.1)
5a	−18.2 (−18.5)	−10.2 (−10.3)	−12.5 (−12.8)	−5.5 (−5.8)
6a	−6.1 (−18.7)	1.6 (−11.0)	−0.9 (−13.5)	5.7 (−7.2)
5b	−12.0 (−12.1)	−14.0 (−14.1)	−9.2 (−9.3)	−9.6 (−9.7)
6b	0.1 (−12.3)	−2.1 (−14.5)	2.5 (−9.9)	2.2 (−10.2)

Note. The values relative to the initial reactants are given in parentheses.

Table 2. Selected geometric parameters of the ion—dipole complexes and transition states of the E2 reactions of compounds **1—6**



Compound	R_1	R_2	R_3	R_4	α*	φ**
			Ion—dipole complexes			
1 *trans*	1.940	1.132	1.499	1.740	149	67
cis	1.967	1.129	1.501	1.728	157	−167
2 *trans*	1.933	1.134	1.501	1.905	169	−49
cis	1.960	1.129	1.503	1.894	162	179
3 *trans*	2.047	1.125	1.497	1.740	168	−149
cis	1.961	1.130	1.497	1.726	155	−171
4 *trans*	2.034	1.127	1.498	1.905	149	−42
cis	1.955	1.131	1.499	1.893	162	173
5a *trans*	2.141	1.139	1.495	1.733	125	−12
cis	2.044	1.120	1.493	1.724	124	147
5b *trans*	2.095	1.123	1.495	1.899	127	−14
cis	2.000	1.123	1.495	1.899	125	145
6a *trans*	1.861	1.140	1.492	1.733	125	−12
cis	1.949	1.133	1.496	1.719	156	−81
6b *trans*	1.853	1.142	1.493	1.900	167	107
cis	1.946	1.134	1.497	1.889	154	−87
			Transition states			
1 *trans*	1.257	1.341	1.478	1.765	179	133
cis	1.242	1.355	1.483	1.745	174	−168
2 *trans*	1.287	1.922	1.481	1.929	179	131
cis	1.273	1.330	1.497	1.910	171	178
3 *trans*	1.263	1.340	1.480	1.762	179	154
cis	1.258	1.343	1.479	1.743	175	−168
4 *trans*	1.290	1.321	1.476	1.928	179	143
cis	1.283	1.326	1.481	1.910	175	−169
5a *trans*	1.370	1.276	1.479	1.746	172	−37
cis	1.375	1.274	1.482	1.730	169	122
5b *trans*	1.379	1.272	1.481	1.914	172	−39
cis	1.397	1.262	1.485	1.898	169	146
6a *trans*	1.404	1.258	1.480	1.747	174	84
cis	1.374	1.274	1.483	1.731	176	−109
6b *trans*	1.421	1.250	1.481	1.916	175	101
cis	1.383	1.271	1.485	1.900	175	−114

* α is the $OC^{\beta}H$ bond angle.

** φ is the $OHC^{\beta}C^{\alpha}$ dihedral angle.

by 2 and 1 %, respectively). The energies of formation of the complexes are small (see Table 1) and are typical of complexes of this kind.[20]

According to the calculations, the energy profile of the E2 elimination reaction of cyclic compounds is identical to that observed for alkanes. The ion-dipole complex formed in the gas phase through the transition state (TS) isomerizes to a second complex, which dissociates to the corresponding cyclopropene, the halogen ion, and MeOH. We localized the transition states for both *trans* and *cis* E2 elimination (see Table 1).

For the *trans* pathway, a H^{β}—C^{β}—C^{α}—X angle of 137—140° is typical, while for the *cis* pathway, an approximately periplanar orientation of the H^{β}—C^{β} and C^{α}—X bonds is observed (the dihedral angles change from 0 to 20°). The C—H^{β}—O fragment is linear; the C—H^{β} bonds are elongated. The C—H^{β} bond length (1.341 Å), which we determined in the transition state for *trans* interaction between MeO^- and PrCl (**1**), is comparable to the values of the C—H^{β} bonds (1.34 and 1.35 Å) calculated[8] by the *ab initio* method in the 6-31+G* basis for the reaction of F^- and PH^- with EtOMe. The hydrogen atom is roughly halfway between the nucleophile and the C^{β} atom, but it is located closer to the nucleophile in compounds **1—4** and closer to the C^{β} atom when the nucleophile reacts with cyano-substituted halocyclopropanes **5** and **6**.

In the transition states, the C—Cl and C—Br bonds are elongated, but to a lesser extent than those obtained by *ab initio* calculations; the C—C bonds are shortened and their lengths vary in the range 1.478—1.485 Å (−1.3 %). According to *ab initio* calculations,[8,9] the lengths of analogous bonds vary in the range 1.39—1.50 Å depending on the approach (entering) and leaving groups. Therefore, the obtained structural data as well as the energies of formation of the complexes are in good agreement with the experimental values and the results of *ab initio* calculations.[8,9,20]

The replacement of hydrogen atoms with methyl groups in the initial cyclopropane has no substantial effect on the geometric characteristics of the transition states, while the replacement of one methyl group with a cyano group substantially affects the transition state geometry. In the latter case, the proton is located closer to the β-carbon atom than to the attacking group, the carbon—halogen bond is less elongated, and the C—C bond is essentially unchanged.

In the cyclic systems discussed above, the *trans* route is more favorable than the *cis* route except for systems **5b** and **6b**, that is, the retention of the periplanar structure is not a sufficient condition for the occurrence of the transition state. Our calculations demonstrated that the difference in energy between the *trans* and *cis* approaches of the MeO^- group in going from PrCl to the cyclic analog actually decreases by 2.6 kcal mol^{-1}, primarily because of the insufficient planarity of the transition state of the *trans* pathway, as was suggested previously. However, this geometric factor is insufficient for predominance of the *cis* pathway. When calculations were performed for *cis* elimination of PrCl, *gauche* elimination was found to be more favorable as was determined previously.[8] Note that in the works by Dewar[6,7] for analogous systems, only the *trans* pathway was considered.

It has been noted repeatedly that conformational features of bimolecular elimination reactions are determined by orbital and steric factors and the *cis* pathway is unstable mainly because of steric interactions. In a planar cyclic system such as cyclopropane, the *trans* route is less stabilized by orbital interactions, and in the stereoisomers of **5b** and **6b**, this route is hindered because of unfavorable electrostatic interaction between the negatively charged C≡N substituent and the MeO^- nucleophile. This is reflected primarily in the fact that the sum of the $C-H^{\beta}$ and $H^{\beta}-O$ bond lengths is maximum in the latter cases (2.658 compared to 2.648 Å in **1—4**, **5a**, and **6a**). The analysis of the results of our calculations demonstrates that, for compounds **5b** and **6b**, for which the *trans* route is unstable due to steric and orbital factors, *cis* elimination predominates over *trans* elimination.

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