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Effect of Solvents on the Selectivity of Free-Radical Chlorination of Functionalized Ethanes, Propanes, and Tetrachloroethene

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Abstract—Free radical reactions of hydrogen abstraction from methane, ethane, propane, and isobutane by radicals X (X = $Cl^{\bullet}$, $Br^{\bullet}$, $I^{\bullet}$, and $CH_3^{\bullet}$) are used as an example to study the applicability of the molecular mechanics (MM) method and the modified intermediate neglect of differential overlap method (PM3) to describing the trends in activation energies. The activation energies of only some, but not all, reaction series are adequately described by the MM (if special parameterization is used) and PM3 methods. All of the four reaction series follow the same correlation within the framework of the parabolic model of a transition state. The correlation of activation energies with the energies of highest occupied molecular orbitals (HOMO) of substrates and solvents is explained. For the correct description of trends in the HOMO energies in the series of studied molecules, the PM3 method was parameterized. The MM and PM3 methods are used to reveal the effect of a solvent on the activation energies of the regioselective and substrate-selective free-radical chlorination of substituted ethanes and propanes. The calculations of the structure and strength of complexes formed by solvent molecules, chloroethane, its radical, and the chlorine radical made it possible to propose a mechanism for the solvent effect on regioselectivity. This mechanism consists in the stabilization of the transition state formed by the α-abstraction of a carbon atom from the C–Cl bond in the aromatic solvent. Different trends exist for aromatic and nonaromatic solvents for changes in the activation energies of the competitive chlorination of tetrachloroethene and 1,2-dichloroethane depending on the solvent concentration. These trends can be reduced to one trend if one considers the HOMO energies of solvents and the substrate and takes into account reactant concentrations.

INTRODUCTION

Factors determining the selectivity of free-radical abstraction reactions of hydrocarbons are commonly believed to be related to the high electrophilicity of the chlorine radical [1]. Therefore, hydrogen abstraction reactions by this radical are characterized by a certain degree of charge separation [2], which makes them sensitive to the polarity effect. On the other hand, chlorine radicals can coordinate to electron-donor molecules and form complexes, which can abstract hydrogen [3]. The electron-donor ability of the reaction medium components is believed to determine the strength of these complexes and the respective selectivity in hydrogen abstraction reactions. The important role of the electron-donor ability of a solvent in the liquid-phase free-radical chlorination of hydrocarbons is supported by correlations between the activation parameters of the regioselective chlorination of substituted ethanes and propanes and the energies of the highest occupied molecular orbitals (HOMO) of solvents [4]. A feature that distinguishes these correlations from others that use various parameters of substituents is that the solvent and the substrate are considered in a similar way. Reactions occurring in the presence of a solvent are viewed as a reaction in the medium of a solvent/substrate. The correspondence of the activation parameters and the HOMO energies of the solvent can be evidence for the intensity of the effect of universal molecular forces on the reaction selectivity. The effect of specific solvation on regioselectivity remains unclear. There are contradictory data in the literature on the structure of a complex between a chlorine radical and a solvent. The role of the substrate is not even mentioned. However, earlier we have considered correlations that were characterized by different slopes of lines for different substrates on the corresponding plots [4]. In connection with this, it is necessary to study the mechanism of changing the process selectivity depending on the electronic structures of the components and intermediates in the reaction medium. In this work, we interpret experimental data for two reaction series—the regioselective chlorination of substituted ethanes and propanes and the competitive chlorination of 1,2-dichloroethane and tetrachloroethene—based on the quantum-chemical calculations of substrates, their radicals, solvents, and their complexes with chlorine.

CALCULATION METHODS

Potential energy surface calculations were carried out using the empirical quantum-chemical method of molecular mechanics (MM). To check the capabilities of this method, we calculated the structures of transition states for the hydrogen atom abstraction by radi-

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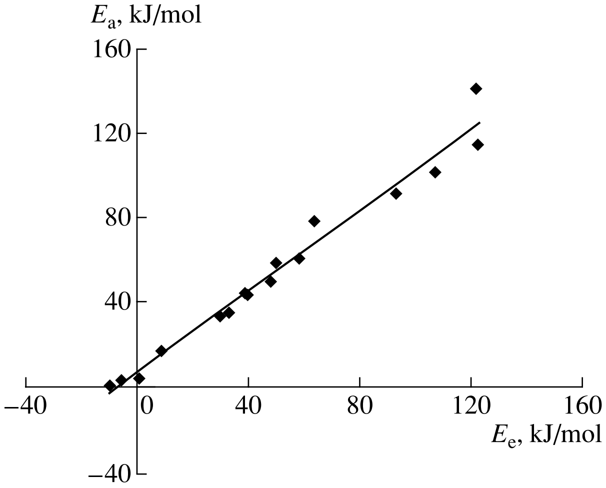

Fig. 1. A plot of experimental activation energies for hydrogen atom abstraction from methane, ethane, propane, and isobutane [9–13] by radicals (X = Cl, Br, I, CH_3) versus the calculated activation energies according to the parabolic model of the transition state [14]; R^2 = 0.98.

cals $Cl^\bullet$, $Br^\bullet$, $I^\bullet$, and $C^\bullet H_3$ from methane, ethane, propane (from the secondary carbon atom), and isobutane (from the tertiary carbon atom). By analogy with [5], we assumed that the attacking atom approaches the hydrogen atom in the direction of the axis of a breaking C–H bond. The beginning of the interaction corresponded to the H---X distance equal to the sum of the van der Waals radii of a hydrogen atom and atom X of the reactant. Then, at a fixed distance between C and X, the hydrogen atom in the ≡C–H---X group moved from C to X. For each change in the position of the hydrogen atom, we optimized the geometry of other parts of reacting molecules. On the potential energy surface, the transition state corresponded to the substrate–reactant system (Sbt---H---X), where the potential energy curves intersected. One of the potential energy curves corresponded to the cleavage of the C–H bond and the other corresponded to the cleavage of the H–X bond in the Sbt---H---X system. Here, Sbt stands for the substrate radical. The activation energy (E_a) was calculated as a value proportional to the difference between the energy of the transition state and the energy ΔE_{in} of the system of initial reactants when they do not interact. The use of standard parameters of the MM method led to the contradictions of experimental and calculated data. The standard parameters of the method did not take into account fine differences between the C–H bonds at a primary, secondary, and tertiary carbon atoms, and in the $–CH_2Cl$ group. Therefore, we obtained modified parameters based on the literature data [6–8] (Table 1).

Table 1. Modified parameters of the MM method

Molecule	Bond	*l*, Å	*k*, mdyne/Å
CH_4	C–H	1.091	5.34
C_2H_6	C–H	1.091	5.14
C_3H_8	C_{sec}–H	1.096	4.98
	C–H	1.091	5.14
iso-C_4H_{10}	C_{tetr}–H	1.108	4.81
	C–H	1.091	5.14
CH_3Cl	C–H	1.103	4.70
HCl	H–Cl	1.275	5.12
HBr	H–Br	1.414	4.08
HI	H–I	1.609	3.14

Changes in the activation energies calculated using modified parameters correlated with experimental data [9–13] with high correlation reliability coefficients for two reaction series ($X=Cl^\bullet$ and $C^\bullet H_3$). However, the points for the reaction series with $X=Br^\bullet$ and $I^\bullet$ form separate correlations. The calculated values of activation energies were higher than the experimental ones in all cases, and the proportionality coefficient ranged from 0.44 to 1.18.

A better result followed from the empirical consideration of kinetic data in the framework of the parabolic model of the transition state [14]. The activation energy can be calculated by the formula [15]

$$E_a = \left\{\frac{b_i r_e}{1-\alpha^2}\left[1-\alpha\left(1-\frac{1-\alpha^2}{(b_i r_e)}\Delta H_e\right)^{1/2}\right]\right\}^2 - \frac{1}{2}(hcN_A\nu_i - RT), \qquad (1)$$

where $\Delta H_e = D_i - D_f + \frac{1}{2}hcN_A(\nu_i - \nu_f)$; D_i and D_f are the energies of breaking and forming chemical bonds; $\alpha = \frac{b_i}{b_f}$; b_i and b_f are the coefficients that characterize the dynamic properties of the bonds ($b = \sqrt{2\mu}\,\pi\nu$); ν_i and ν_f are the wavenumbers of zero-point vibrations of bonds; *h* is the Planck constant; N_A is the Avogadro constant; *c* is the velocity of light; *R* is the universal gas constant; *T* is the absolute temperature; r_e is the distance to which the abstracted hydrogen atom moves during the elementary act; and μ is the reduced weight of the bond. The second term on the right-hand side of the formula includes the correction for the zero-point vibration in addition to the zero-point energy of the transition state.

Figure 1 shows a plot of experimental activation energies (E_a) of hydrogen atom abstraction by radicals X (X = $Cl^\bullet$, $Br^\bullet$, $I^\bullet$, and $C^\bullet H_3$) from the simplest alkanes versus the calculated activated energy. In the calculation, we used the C–H bond energies for methane, for primary, secondary, and tertiary C–H bonds, and for the bonds in the molecules HCl, HBr, and HI equal to 427, 410, 393, 377, 431, 366, and 294 kJ/mol, respectively [1, 16]. Other values were borrowed from [15]. Specifically, the values of r_e are 2.67 (for X=$Cl^\bullet$), 4.61 ($C^\bullet H_3$), 3.54 ($Br^\bullet$), and 3.58×10^{-11} m ($I^\bullet$). It is seen that the activation energies of four different types of reactions approach the same correlation with the parameter E_e. Although the value of correlation reliability is rather high ($R^2 = 0.98$), two of the sixteen values of E_e are negative due to the correction for the zero vibration of the breaking bond. At the same time, the use of the value $r_e = 4.3 \times 10^{-11}$ m obtained by us for X=$Cl^\bullet$ (see below) removes the negative values of E_e. However, the quality of correlation decreased ($R^2 = 0.85$). It is important that, according to the refined definition of the Hammond postulate in the framework of the parabolic model of the transition state [15], the transition from the early to the late transition state takes place in the series of reactants X=$Cl^\bullet$, $C^\bullet H_3$, $Br^\bullet$, and $I^\bullet$. Thus, a parameter like E_e can be used as a test parameter for the description of several reaction series. This is important for the study of the role of a solvent because radical X forms more or less stable complexes in the solvent and its activity changes. From the formal standpoint, the replacement of a solvent can be considered as a change in the reaction series or the reaction type.

In qualitative molecular orbital theory, the proportionality of the full energy of a molecule to the sum of the orbital energies of valence electrons [17] is reliably established. Therefore, it is possible to replace the bond energies by the corresponding energies of molecular orbitals. In addition to the results obtained in [4], this is further evidence for the possibility of considering the activation parameters of reactions based on the quantum-chemical index of an isolated molecule (the HOMO energy). For the reaction series considered in this work, the energies of CH and HX bonds in hydrocarbon and chlorinated hydrocarbon molecules correlate well with the corresponding energies of molecular orbitals. Therefore, it is reasonable to use MO energies (ε) instead of bond energies in formula (1). Moreover, their application can provide information on the nature of the transition state. As a rule, an elementary act occurs due to the most mobile electrons responsible for a chemical bond. Therefore, the values of D_i and D_f, which involve the contributions from other electrons of the bond, may give somewhat different values than ε_i and ε_f when calculating E_e. Therefore, using the experimental values $\varepsilon_A = \varepsilon_{CH}$ and $\varepsilon_B = \varepsilon_{HX}$ for HOMO of CH and HX bonds [18, 19] and expression (1), we obtained the values of $E_e(\varepsilon)$ for four cited reactions. The resulting data correlate linearly with experimental ones and $R^2 = 0.97$. The values r_e are 4.3 (X=$Cl^\bullet$), 4.61 ($C^\bullet H_3$), 4.8($Br^\bullet$), and 5.4×10^{-11} m ($I^\bullet$). They agree well with the known relation between the bond energy and length.

Table 2. Experimental (E_i^{exp}) [16, 17] and PM3-calculated ($-\varepsilon_{HOMO}$) values of photoionization energies for a number of studied hydrocarbons

Molecule	E_i^{exp}, eV	$-\varepsilon_{HOMO}$, eV	$-\varepsilon^{*1}_{HOMO}$, eV
CH_4	12.51	13.64	14.25
C_2H_6	11.57	11.98	12.85
C_3H_8	10.90	11.51	12.44
iso-C_4H_{10}	10.40	11.59	12.32
C_6H_6	9.24	9.75	9.87
C_6H_5F	9.11	9.81	9.84
C_6H_5Cl	9.07	9.39	9.72
C_6H_5CN	9.71	10.10	10.19
$C_6H_5CF_3$	9.70	10.19	10.40
C_2H_5Cl	11.02	10.41	10.69

Note: [1] Changed values of the exponents of valence orbitals of hydrogen, chlorine, and fluorine are used.

In connection with this, the use of calculated values of MO energies can be useful when interpreting the reactivity of the systems under consideration. However, we found that, along with the others, the PM3 method with standard parameterization poorly describes changes in the experimental values of the first energies of photoionization (ε_{HOMO}) in the series of studied molecules (Table 2). Therefore, in order to use the MP3 method for the calculation of HOMO energies ε^{*}_{HOMO}, we measured the values of exponents for some orbitals: $\zeta_{1s}(H) = 1.2$, $\zeta_{2s}(F) = 4.71$, $\zeta_{2p}(F) = 2.39$, $\zeta_{3s}(Cl) = 2.25$, and $\zeta_{3p}(Cl) = 2.55$.

Another method for estimating the activation parameters of reactions consists in direct calculation of the activation energy by the PM3 method. Using procedures described in [5], we first optimized geometries of initial reactants and reaction products and then calculated the standard enthalpies of the substrate (ΔH_f^0(SbtH)) and radical (ΔH_f^0(X)) formation. Then, we modeled and optimized the geometries of complexes formed by initial reactants and those formed by the products. We searched for the transition state so that the position of a hydrogen atom to be abstracted and a radical that approaches this atom corresponded to the energy minimum in the transition of atoms from the state in the first complex to the state in the second complex. We considered only transition states with linear geometries of the Sbt—H—X group. After calculating the standard enthalpy of formation of the transition state (ΔH_f^0(TS)), we found the activation energy of the reaction using the expression

$$E_a = \Delta H_f^0(\text{TS}) - \Delta H_f^0(\text{SbtH}) - \Delta H_f^0(\text{X}) + RT.$$

The results of calculation are presented in Table 3.

It is seen that only in one case (when $X=C^{\bullet}H_3$) is there a qualitative agreement between calculated and experimental data. Without considering possible reasons for this failure, we would like to note only that this problem calls for the study of the potential energy surfaces of specific reactions. This problem becomes still more complicated if we include solvent molecules. Therefore, we gave up estimating the activation energies of the reactions under study by semiempirical methods at this stage. At the same time, the calculated energies of formation of complexes between substrates and the same radical correlate well with the activation energies of reactions with early transition states ($X=Cl^{\bullet}$) and do not correlate in the case of late transition states ($X=I^{\bullet}$). Analogously, the calculated energies of formation of complexes between substrate radicals and HX molecules correlate well with the activation energies of reactions with early transition states and do not correlate in the case of late transition states. We also found that the calculated effective charges of hydrogen atoms and covalences of carbon atoms in substrates agree well with the apparent reactivity series: methane < ethane < isobutane. These reactivity indices allow the qualitative analysis of the effect of structural and polarity factors on the activation parameters of reactions.

RESULTS AND DISCUSSION

It is commonly believed that the main contribution to an increase in the selectivity of free-radical chlorination is determined by chlorine radical interaction with a solvent. However, changes in process regioselectivity forces us to give special attention to solvent–substrate interactions.

The above methods were used in the studies of solvent effects on the selectivities of two types of reactions: the regioselective chlorination of substituted ethanes and propanes [4] and the competitive chlorination of tetrachloroethene and 1,2-dichloroethane [20]. The relative HOMO energies allow us to expect that the formation of donor–acceptor complexes of chlorine radical and solvent molecules is energetically more favorable than the formation of its complexes with substrate molecules. This was confirmed by the calculations of benzene–chlorine and chloroethane-chlorine complexes (Table 4). The use of calculations for estimating the transfer of electron density from the solvent molecule to the chlorine radical does not lead to unequivocal conclusions. The nonempirical SCF MO LCAO Hartree–Fock method predicts a much smaller excessive negative charge on the chlorine radical than semiempirical methods do. The *ab initio* method gives the values of charges which agree better with the relative energies of complex formation.

Because the chlorine radical acquires an excessive negative charge, the value and sign of charges at hydrogen atoms of the substrate can determine the direction of the attack of each complex onto the hydrocarbon substrate. In this connection, Table 5 lists the calculated values of effective charges of hydrogen atoms in substrate molecules. The effective charges of hydrogen atoms attached to α-carbon atoms are always higher than the charges of atoms attached to β- and γ-carbon atoms. The relative values of effective charges qualitatively correspond to an increase (the electrostatic component) in the activation energy of the chlorination reaction in the series of hydrogen atom positions: $\alpha < \beta < \gamma$.

The covalences of carbon atoms also predict a higher reactivity of the α-position compared to β- and γ-positions (Table 5). The lower the value of covalence in a specific molecule, the higher the free covalence as a reactivity measure in radical reactions. Therefore, we do not exclude the role of the intramolecular environment of a carbon atom from which a hydrogen atom is abstracted in the transition state. This was confirmed when considering the structure and energy of complexes formed by a substrate molecule (or its radical) and a solvent molecule. Thus, chloroethane self-solvation is more energetically favorable than solvation by a series of aromatic solvents discussed in [4]. Structures where the molecules are coordinated to each other via the α-carbon atoms with attached chlorine atoms are more stable than others. The most stable complexes of

Table 3. PM3-method and experimental activation energies (kJ/mol) in the reactions of hydrogen atom abstraction by radicals ($X = Cl^{\bullet}, Br^{\bullet}, I^{\bullet}, C^{\bullet}H_3$) from simplest alkanes

Alkane	$X = Cl^{\bullet}$		$X = Br^{\bullet}$		$X = I^{\bullet}$		$X = C^{\bullet}H_3$	
	calculation	experiment [9]	calculation	experiment [11, 12]	calculation	experiment [13]	calculation	experiment [9]
$H_3C–H$	–34.3	16	–3.2	78.1	305.3	141	44.9	60.9
$C_2H_5–H$	–76.0	4.2	0.1	58.8	2.5	115	33.0	50.0
$(CH_3)_2CH–H$	–105.3	2.9	–0.7	43.7	2.5	102	24.8	43.3
$(CH_3)_3C–H$	128.1	0.4	–1.2	32.8	2.5	92	19.1	34.4

chloroethane with aromatic solvents also have structures where the substrate is coordinated to the π-electron system of the benzene ring by the α-carbon atom. The energies of complex formation are low: between 4 (benzene) and 8 (self-solvation) kJ/mol. Conversely, radicals formed when hydrogen atoms are abstracted from the substrate are more stable in aromatic solvents. The chloromethyl group of chloroethane is more stabilized than the methyl group (Table 6). The stabilization of the substrate and its radicals is about the same in self-solvation. At the same time, the stabilization of the radical is an order of magnitude greater than the stabilization of the substrate in aromatic solvents. We found that the best qualitative correspondence between the difference of the experimental activation energies $\Delta E_a(\alpha - \beta)$ for substrates in α- and β-positions and the calculated energies of complex formation is observed for the substrate radical–solvent complexes (Table 6). This result assumes a better stabilization of the transition state with the participation of an α-carbon atom in aromatic solvents.

This conclusion was supported by the calculations of the potential energy surface of chloroethane chlorination in the medium of benzene or chloroethane by MM calculations, which showed that the transition state is more stabilized in the medium of benzene (Fig. 2). In these calculations, we found transition states with a structure where the chlorine radical and substrate in the composition of the transition state are coordinated to a larger degree to the same benzene molecule. Because the chlorine radical is a stronger acceptor of electron density and forms a stronger complex with benzene than chloroethane, the reason for the participation of two HOMOs in correlations cited above becomes clear [4]. The highest HOMO of the solvent participates in the formation of a bond with the chlorine radical, whereas the other, lower HOMO is responsible for the formation of a bond between benzene and the second acceptor (substrate). The simultaneous coordi-

Table 4. Coordination, complex-formation energies (E_{compl}), and charges at the chlorine radical in the formation of its complex with chloroethane according to quantum-chemical calculations

Method	Coordination		$-E_{compl}$, kJ/mol		$-\delta$, at. units	
	benzene	chloroethane	benzene	chloroethane	benzene	chloroethane
MM	π-complex	–Cl···Cl	13	3	0	0.08
CNDO	σ–	–H···Cl	110	30	0.16	0.41
INDO	σ–	–Cl···Cl	280	130	0.48	0.23
MINDO3	σ–	–Cl···Cl	140	100	0.27	0.19
MNDO	σ–	–Cl···Cl	150	70	0.22	0.11
MNDO/d	σ–	–Cl···Cl	140	60	0.17	0.11
AM1	σ–	–Cl···Cl	120	30	0.13	0.29
PM3	σ–	–Cl···Cl	110	50	0.07	0.32
3G	σ–	–Cl···Cl	110	~3	0.21	0
3-21	σ–	–Cl···Cl	~15	~7	0.02	0.01
6-31*	σ–	–Cl···Cl	~12	~0	0.03	0
6-31**	σ–	–Cl···Cl	~9	~3	0.13	0

Table 5. Effective charges of the hydrogen atoms (q_H) and covalences of carbon atoms ($V_c(C)$) for the cleaved C–H bond in substrates calculated by the PM3 method (in atomic units)

Molecule	q_H			$V_c(C)$		
	α	β	γ	α	β	γ
CH_3CH_2Cl	0.06	0.05	–	3.95	3.98	–
$CH_3CH_2Cl_2$	0.09	0.06	–	3.92	3.95	–
$CH_2ClCHCl_2$	0.10	0.08	–	3.92	3.95	–
$CH_3CHClCH_3$	0.07	0.05	–	3.94	3.97	–
$CH_3CH_2CH_2Cl$	0.06	0.06	0.04	3.94	3.97	3.98
$CH_3CH(CN)CH_3$	0.08	0.05	–	3.93	3.97	–
$CH_3CH(OCOCH_3)CH_3$	0.07	0.05	–	3.91	3.98	–

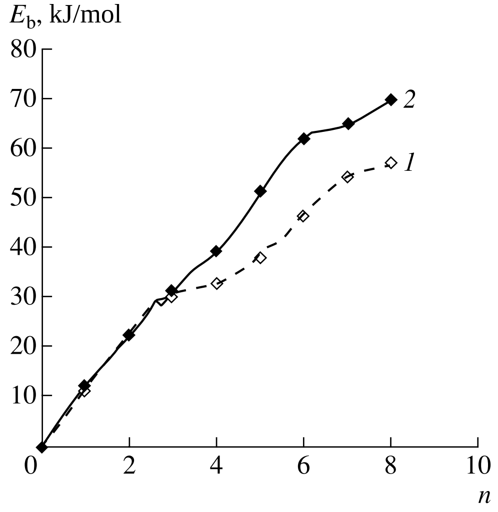

Fig. 2. A plot of the binding energy (E_b) calculated by the MM method for the transition state in $C_\alpha H$ bond cleavage in the chloroethane–chlorine system versus the number (*n*) of surrounding solvent molecules: (*1*) chloroethane and (*2*) benzene.

nation of the substrate and chlorine radical with another substrate molecule in self-solvation was not found.

Because the ΔE_a–ε_{solv} dependences for different substrates described in graphical form have different slopes [4], it is necessary to consider substrate characteristics corresponding to donor–acceptor interaction. The lowest unoccupied molecular orbitals (LUMO) of substrates involving noticeable contributions of hydrogen atoms attached to α- and β-carbons of the substrate have energies that differ by only 0.3–1 eV. LUMO corresponding to the β-position is higher in energy. Therefore, we conjecture the following mechanism for the solvent effect on the process selectivity. A solvent supplies its antibonding electrons to LUMOs of a substrate corresponding to CCl and CH bonds and makes these bonds weaker. Due to the difference in LUMO energies, the solvent more strongly affects the C_α–H bonds than C_β–H (especially in the formation of a transition state). Thus, the formation of a complex with the substrate leads to a decrease in the activation energy of the reaction in the α-position, and the formation of a complex with chlorine leads to a general increase in the activation energies for α- and β-positions. As a result, the regioselectivity of chlorination increases, although the rate of this process decreases.

Table 6. Differences in the energies of complex formation for β- and α-chloroethyl radicals and solvent molecules (ΔE_1), the energies of complex formation for radical–chlorine–solvent complexes (ΔE_2) calculated by the PM3 method, and the experimental values for the difference between the activation energies of hydrogen atom abstraction from α- and β-positions in the reaction of free radical chlorination of chloroethane

Solvent	ΔE_1, kJ/mol	ΔE_2, kJ/mol	ΔE_a(α–β) [4], ±0.50 kJ/mol
C_6H_6	6.69	10.33	3.98
C_6H_5F	6.23	9.71	3.89
C_6H_5Cl	6.90	9.96	4.05
$C_6H_5CF_3$	5.56	8.08	2.80
$C_6H_5CCl_3$	6.07	8.79	3.70
1,2-$C_6H_4Cl_2$	6.07	10.00	2.60
1,2,4-$C_6H_3Cl_3$	5.56	9.75	2.10
CH_3CH_2Cl	1.20	8.03	1.33

For the regioselective chlorination of substituted ethanes and propanes [4], experimental data on the energies of intramolecular solvent–substrate interactions are not available. The parabolic model of the transition state (formula (1)) suggests that the calculated difference in the activation energies of chlorination at α- and β-positions is not determined directly by the energy of complex formation in the chlorine–solvent system when a solvent is changed. However, the stabilization of the transition state in hydrogen atom abstraction from the α-position is stronger than in the case of abstraction from the β-position. If we subtract the correction for the stabilization energy from the activation energy calculated by formula (1), then for two positions of the substrate we have

$$\Delta E_a(\alpha - \beta) \approx A - \Delta E_{stab}(\alpha - \beta), \qquad (2)$$

where *A* is a constant equal to the difference of formulas (1) for α- and β-positions, and $\Delta E_{stab}(\alpha - \beta)$ is the difference in the stabilization energies of the transition states for α- and β-positions. To estimate the interaction energy between a solvent and the transition state, we used the semiempirical Wolfsberg–Helmoholtz relation

$$\beta = KS(\varepsilon_i + \varepsilon_{Sol}), \qquad (3)$$

where *K* is a constant, *S* is the overlap integral of the transition state and the solvent, and ε_i and ε_{Sol} are the energies of MO of the transition state and the solvent, respectively. The value of integral β should depend on the position of the substrate reaction center. Therefore, for instance, for chloroethane chlorination at α- and β-positions, we introduce factor λ that corresponds to the relation $K_\beta S_\beta = \lambda K_\alpha S_\alpha$, where $0 < \lambda < 1$. Upon substituting λ into expression (2), we have

$$\Delta E_a(\alpha - \beta) \approx A + K_\alpha S_\alpha (1 - \lambda)(\varepsilon_{Sol} + \varepsilon_i).$$

Thus, by analogy with [4], we have linear relationships between the activation parameters of regioselective chlorination and solvent HOMO energies when the MO energies are calculated by the PM3 method with modified parameters.

According to the mechanism of free-radical chlorination in solvating media [20] and proceeding from the above speculation on the process of complex formation, the main step that determined the product composition is the abstraction of a hydrogen atom from the substrate via the following scheme:

$$(\mathrm{Cl}^\bullet)\mathrm{Sol} + (\mathrm{H{-}R})\mathrm{Sol} \rightleftharpoons [\mathrm{Sol{-}{-}{-}Cl{-}{-}{-}H{-}{-}{-}R{-}{-}{-}Sol}]^\bullet \longrightarrow (\mathrm{HCl})\mathrm{Sol} + (\mathrm{R}^\bullet)\mathrm{Sol}.$$

In this scheme, the transition state involves the substrate, chlorine radical, and solvent. It cannot be excluded that the molecule of an aromatic solvent can simultaneously participate in the interaction with the substrate and the chlorine radical.

According to [21], for regioselective chlorination, a change in the interaction energy $\Delta E_{\mathrm{s-r}}$ of the solvated reactant (r), which is the chlorine radical, with the abstracted hydrogen atom is expressed by the following formula depending on the hydrogen atom position (α- and β-positions in the same substrate S)

$$\Delta E_{\mathrm{s-r}} = c_{\mathrm{r}}^2\Sigma(c_{\alpha j}^2\beta_\alpha^2 - c_{\beta j}^2\beta_\beta^2)/(\varepsilon_j - \varepsilon_{\mathrm{Sol}}), \qquad (4)$$

where c_{r} is the contribution of atomic orbitals (AO) of the reactant (chlorine radical) to MO of its complex with the solvent, $c_{\alpha j}$ and $c_{\beta j}$ are the contributions of AOs of hydrogen to the jth MO of the substrate, and β_α and β_β are the integrals of the interaction of reaction centers in α- and β-positions of the substrate with the reactant. Here, we neglect changes in the electrostatic component of the interaction when the substrate and the solvent are changed. Taking into account formula (3) and after substitutions into formula (2), we obtain that the energy change is proportional to a change in the parameter b' determined by the formula

$$b' = \Sigma(\varepsilon_i + \varepsilon_j)(c_{\alpha j}^2 - \lambda c_{\beta j}^2)/(\varepsilon_j - \varepsilon_{\mathrm{Sol}}).$$

By changing λ and $\varepsilon_{\mathrm{Sol}}$, we can construct a plot of b determined from the regression formulas $\Delta E_{\mathrm{a}} = a + b\varepsilon_{\mathrm{Sol}}$ [4] versus b' (Fig. 3).

We found that the value of correlation reliability is almost independent of λ. This fact suggests that the

Table 7. The difference in the activation energies of the regioselective chlorination of tetrachloroethene and 1,2-dichloroethane (ΔE_{a}) at different molar concentration ratios solvent/1,2-dichloroethane C_{sol}/C_2

Solvent	C_{sol}/C_2	$\Delta E_{\mathrm{a}} \pm 0.4$, kJ/mol	Solvent	C_{sol}/C_2	$\Delta E_{\mathrm{a}} \pm 0.4$, kJ/mol
1,2-dichloroethane	1.000	17.9	hexachloroacetone	0.210	20.5
tetrachloromethane	0.234	16.9		0.560	19.0
	0.624	16.0		1.260	17.3
	1.405	14.5		3.351	13.8
	3.732	13.9	benzene	0.254	21.7
dichloromethane	0.354	15.6		0.678	25.6
	0.946	14.5		1.524	29.2
	2.128	13.5		4.057	30.7
	5.662	12.2	chlorobenzene	0.222	23.7
1,1,1-trichloroethane	0.224	16.1		0.592	28.3
	0.597	15.3		1.332	28.9
	1.345	15.0		3.544	28.3
	3.579	14.3	fluorobenzene	0.241	21.6
Freon-113	0.188	18.5		0.642	25.9
	0.503	15.9		1.443	26.3
	1.131	13.6		3.842	26.6
	3.004	12.9			

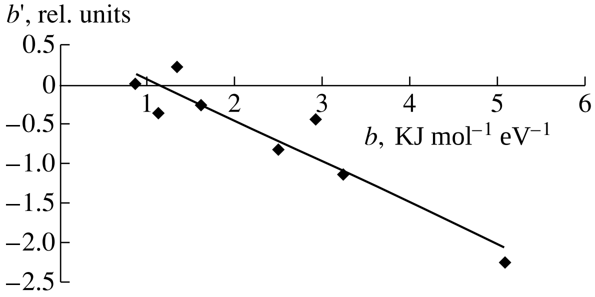

Fig. 3. A plot of parameter b determined from regression dependences $\Delta E(\alpha-\beta)$ and $\Delta E(\gamma-\beta) = a + b\varepsilon_{Sol}$ [4] versus theoretical parameter b' at $\lambda = 1$ and $\varepsilon_{Sol} = 11.8$ eV; $R^2 = 0.87$.

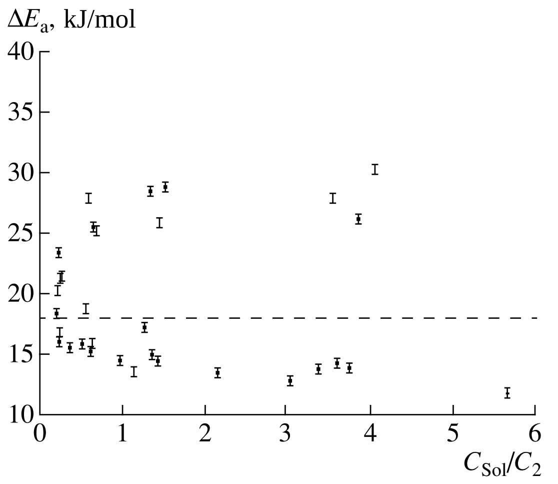

Fig. 4. A plot of the difference between the activation energies (ΔE_a) versus relative molar concentration of a solvent C_{Sol}/C_2. The dashed line shows the activation energy for 1,2-dichloroethane solvent. The values are shown with the confidence interval of ±0.4 kJ/mol, which is maximal for the experimental values of activation energy differences.

contribution from hydrogen atoms in the β-position (H_β) is small. That is, the slopes of dependences are only determined by the sensitivity of α-hydrogen atoms (H_α). Indeed, the contributions of orbitals H_β to HOMO are usually small compared to the contributions of H_α. Thus, the sensitivity of substrates to the solvent nature is due to the energy and contributions from the orbitals of abstracted hydrogen atoms to their HOMOs.

This conclusion was checked using other reaction systems. Let us consider the reaction of competitive free-radical chlorination of tetrachloroethene and 1,2-dichloroethane in the medium of nine different solvents [22]. Experimental data from [22] were processed using the dependence of the activation energy of competitive reactions on the solvent concentration. The results are summarized in Table 7, where the activation energies are compared to the ratio C_{Sol}/C_2 of the molar concentrations of a solvent C_{Sol} and 1,2-dichlorethane C_2, which is an aliphatic substrate taken in excess over tetrachloroethene C_1. In connection with this, we assumed that 1,2-dichloroethane and tetrachloroethene play the role of a solvent responsible for the solvation of each of the competitors. Table 7 shows that an increase in the concentration of the nonaromatic solvent leads to a smoothening of the difference in the activation energies of the competitive reactions, and an increase in the concentration of the aromatic solvent leads to a sharpening of this difference. Figure 4 shows the resulting data together with a point for the solvent concentration equal to zero, and we can see two branches in different directions. For nonaromatic solvents, the main factor that affects a change in the difference between the activation energies is the relative concentration of a solvent. This curve becomes almost horizontal and shows some oscillation, when the relative molar fraction is equal to 2. For aromatic solvents, whose concentration is also an important factor for the energy difference between the competitive reactions, a sharper dependence on the solvent nature is observed.

The effect of the concentration of an aromatic solvent can be related to the HOMO energy. By analogy with the cited correlations, the correlation of the differences between the activation energies of the competitive reactions with HOMO energies of solvents is observed for the 1,2-dichloroethane–tetrachloroethene system. In the case of chlorination of this system without an additional solvent, 1,2-dichloroethane was chosen as a medium because it was in tenfold excess compared to tetrachloroethene.

We found that the point corresponding to the chlorination in the medium of one of the substrates shown with a dashed line in Fig. 4 belong to the middle portion of data along the ordinate axis. This led us to assume that the difference in the HOMO energies of the solvent and substrate Δε(Sol–SbtH) determines the direction and the value of the solvent effect on the selectivity of the chlorination of the 1,2-dichloroethane–tetrachloroethene system. Then, we can expect the correspondence of the difference between the activation energies and the product of the relative concentration of the solvent and Δε(Sol–SbtH). Using data from Table 7 excluding the results that refer to the region $C_{Sol}/C_2 > 2$, the dependence shown in Fig. 4 can be transformed into the dependence shown in Fig. 5.

In the linear dependence shown in Fig. 5, aromatic and nonaromatic solvents have peer points. Therefore, we conclude that the selectivity of chlorination is determined by similar effects of a solvent on the transition state of a reaction through the interaction of its HOMO. This effect largely depends on the relative energy of HOMO and the relative concentrations of a substrate and a solvent. In the interval of concentrations where this dependence is explicit (in our case, <2 relative units), the dependence of the selectivity on the solvent concentration is linear. The same dependence is also seen when other data are processed. Thus, data from [23, 24] on the chlorination of 2,3-dimethylbutane in

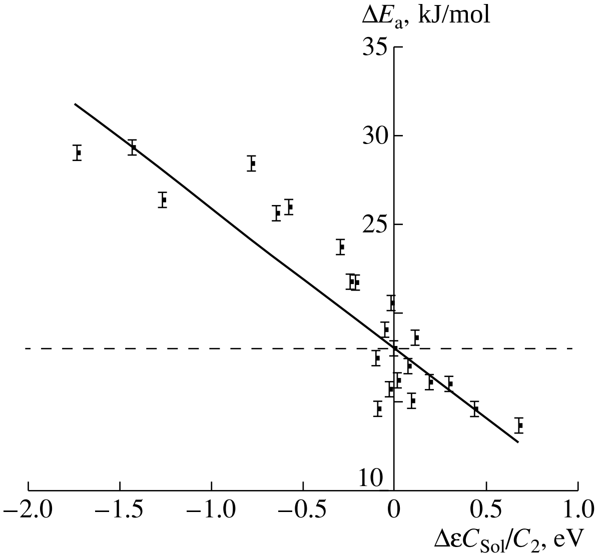

Fig. 5. A plot of the difference between the activation energies of substrates (ΔE_a) versus the weighted (with respect to the solvent concentration) difference of the HOMO energies of solvent and substrate ($\Delta\varepsilon_{Sol}/C_2$). The dashed line shows the activation energy for the case when one of the substrates is a solvent. Correlation parameters: $y = -7.95x + 18.11$ and $R^2 = 0.81$. The values are shown with the confidence interval of ±0.4 kJ/mol, which is maximal for the experimental values of activation energy differences.

the mixture of benzene shown in the coordinates of the logarithm of the relative selectivity versus relative molar concentration of benzene give dependences analogous to the upper branch in Fig. 4. If we exclude the experimental points with the relative concentrations equal or higher than 2, we obtain linear correlations with $R^2 = 0.85$ for [23] and 0.99 for [24].

For the reactions of competitive chlorination, we observed the qualitative correspondence between the process selectivity and the calculated energies of complex formation in the solvent–chlorine radical system. We did not find such a correlation in the first reaction series for the regioselective chlorination of substituted ethanes and propanes, but we found the correlation with the formation energies of complexes between the solvent molecules and hydrocarbon radicals formed from the substrates. Unlike the first series, the second series of reactions does not show the correlation of the difference between the stabilization energies of hydrocarbon radicals by a solvent molecule and the experimental values of the difference between activation energies. Thus, the reaction system of competitive chlorination can be categorized as a system with an early transition state, which makes it different from the systems of regioselective chlorination with late transition states. Indeed, in the first reaction series, we considered chlorination reactions in aromatic solvents, whereas most data from the second series refer to noncomplex-forming nonaromatic solvents. As can be seen from Table 4, the energy of formation of complexes between aromatic solvents and chlorine radicals is several times higher than the energy of the interaction of a nonaromatic solvent. Therefore, according to the Hammond postulate [25], for a less exothermic reaction we can expect a late transition state. As a consequence, in the free-radical chlorination of hydrocarbons, a late transition state is probable in an aromatic solvent, and an early transition state is probable in a nonaromatic solvent.

Thus, aromatic and nonaromatic solvents affect the process selectivity via the same mechanism. The difference is only in the structure and relative strengths of their complexes with a substrate, its radical, or the chlorine radical.

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