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Kinetics and Mechanism of Monomolecular Heterolysis of Cage-Like Compounds: XVIII. Solvent Effect on the Rate of Heterolysis of 3-Bromocyclohexene. Correlation Analysis of Solvation Effects

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Abstract—The kinetics of E1 dehydrobromination of 3-bromocyclohexene in 23 aprotic and 9 protic solvents were studied by the verdazyl technique. The reaction rate is described by the polarity, electrophilicity, and ionizing power parameters of the solvent. Nucleophilicity, polarizability, and cohesion parameters of the solvent do not affect the reaction rate. The effects of equilibrium and nonequilibrium solvation of the transition state are discussed.

Solvent effects on the rate of monomolecular heterolysis (S_N1, E1, solvolysis) are usually examined using tertiary substrates as models, most frequently *tert*-alkyl and cage-like derivatives [1–3]. Rear nucleophilic attack on such compounds is strongly hindered or impossible, which essentially affects solvation and complicates interpretation of solvation effects. Nucleophilic effect of solvents is a matter of continuous discussions. Some authors believe [1, 3–5] that heterolysis of *tert*-alkyl derivatives involves nucleophilic assistance by the solvent, while the others adhere to the opinion that such assistance is absent [2, 5–8]. Detailed studies of solvation effects in the heterolysis of *tert*-butyl halides [2, 9–11], adamantane derivatives substituted at the bridgehead position [12–14], cumyl chloride [15], 2-methyl-2-(*p*-methoxyphenyl)propyl *p*-toluenesulfonate [16], and 2-bromo-2-methyladamantane [17] showed that the rate of heterolysis of tertiary derivatives decreases as the solvent nucleophilicity rises [2, 18].

The negative effect of nucleophilic solvation indicates nonequilibrium solvation of the transition state [19, 20], i.e., the solvate shells of the initial and transition states have different structures. Equilibrium solvation of the transition state should increase the reaction rate [21]. Kim *et al.* [20, 22] showed that a satisfactory agreement (within an order of magnitude) between the experimental and calculated rate constants for heterolysis of *tert*-butyl halides in different solvents can be attained only with account taken of nonequilibrium solvation. However, the time necessary for formation of transition state ($\sim 10^{-13}$ s) [23] is insufficient for structural reorganization of the substrate solvate shell. This process takes 10^{-10} to 10^{-11} s [24, 25]. Therefore, nonequilibrium solvation was interpreted in terms of orientational polarization of the solvent [20, 22], which changes fairly quickly ($\sim 10^{-16}$ s) and may affect the formation of transition state. These data suggest the existence of nonequilibrium solvation of transition state, but they do not explain negative effect of nucleophilic solvation.

Reduction of the rate of heterolysis with rise in solvent nucleophilicity may be understood on the assumption that nucleophilic solvation involves an intermediate which is formed prior to the rate-determining stage [2]. Such intermediate may be a contact ion pair. Nucleophilic solvation stabilizes the intermediate and hampers nucleofuge departure according to the S_N1 mechanism [26, 27]. If this is the case, a question arises so as to which stage of the heterolysis process is rate-determining? It is known that product formation does not affect the reaction rate and that the latter is described by the first-order kinetic equation $v = k[\mathrm{RX}]$ [2, 28]. It is commonly assumed that the rate-determining stage is formation of solvent-separated ion pair from the substrate [29–31]. Therefore, the rate of heterolysis should increase with rise in solvent nucleophilicity (nucleophilic assistance by the solvent). However, detailed analysis of solvation effects using multiparameter equations based on the linear free energy relationship showed that heterolysis of tertiary substrates is not accompanied by nucleophilic solvent assistance [2, 6–18]. A conclusion was drawn that solvent-separated ion pair is formed after the rate-determining stage [2]. This means that the rate-determining stage should occupy an intermediate place between contact ion pair and solvent-separated ion pair on the reaction coordinate. The transformation of contact ion pair into solvent-separated ion pair is believed to occur in two steps: in the first step, ions in a contact ion pair move apart, and in the second step, solvent molecule occupies the interionic space [2, 18, 32]. Quantum-chemical analysis of ion separation in liquid showed that one more intermediate is present on the reaction coordinate between contact ion pair and solvent-separated ion pair. It was termed a contact ion pair which begins to divide [33, 34].

Taking into account the existence of voids in liquids [35, 36] (which occupy up to ~10% by volume [37]), monomolecular heterolytic dissociation of a covalent bond [2, 18] may be represented as successive formation of three types of ion pairs: contact (**A**), loose (**B**), and solvent-separated (**C**).

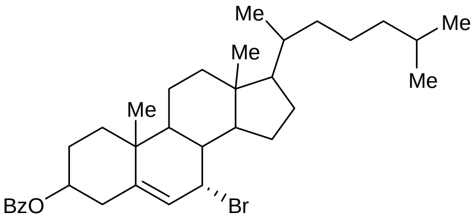
$$\mathrm{RX} \rightleftharpoons \underset{\mathbf{A}}{\mathrm{R^+X^-}} \rightleftharpoons \underset{\mathbf{B}}{\mathrm{R^+\cdots X^-}} \rightleftharpoons \underset{\mathbf{C}}{\mathrm{R^+|Solv|\,X^-}} \longrightarrow \text{Products}$$

The reaction begins with formation of contact ion pair which interacts with a solvent cavity in the rate-determining stage. As a result, loose ion pair is formed and is quickly converted into solvent-separated ion pair, and the latter is transformed (also quickly) into the products.

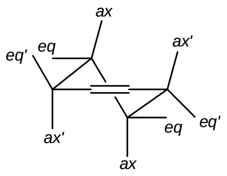
The above mechanistic considerations are based on the results of studies performed on tertiary substrates which cannot undergo substitution by the S_N2 mechanism, for rear nucleophilic attack on such substrates is impossible [1, 28]. The S_N1 (E1) mechanism implies that the initial molecule occur in equilibrium with the corresponding ion pair and that the lifetime of the latter be sufficient ($>10^{-10}$–10^{-11} s) to react with nucleophile. Therefore, not only tertiary but also activated secondary (Ph_2CHX [38]) and even primary (p-$MeOC_6H_4CH_2Cl$ [39]) derivatives can react according to the S_N1 pattern.

The nature of solvation effects in the heterolysis of tertiary substrates has been well documented [2, 9–18]. Here, the polarity and electrophilicity (or ionizing power) of a solvent, as well as cohesion, act to increase the reaction rate, whereas nucleophilicity and polarizability reduce it. The effects of polarizability and cohesion are related to the negative nucleophilic solvation effect: the greater the polarizability, the stronger the nucleophilic solvation of contact ion pair; the greater the energy of solvent self-association, the more difficult is to extract a solvent molecule for nucleophilic solvation of intermediate [2]. Negative nucleophilic solvation effects are seen most clearly in protic solvents, presumably due to formation of hydrogen bonds between molecules which are responsible for nucleophilic solvation of carbocation and electrophilic solvation of nucleofuge.

Solvation effects in the heterolysis of secondary substrates have been studied poorly; even less information is available for primary derivatives. There are detailed data on solvent effects on the rate of heterolysis of Ph_2CHBr [13] and limited data for the heterolysis of PhCHClMe [40] and 7α-bromocholesterol benzoate (**I**) [41].



I

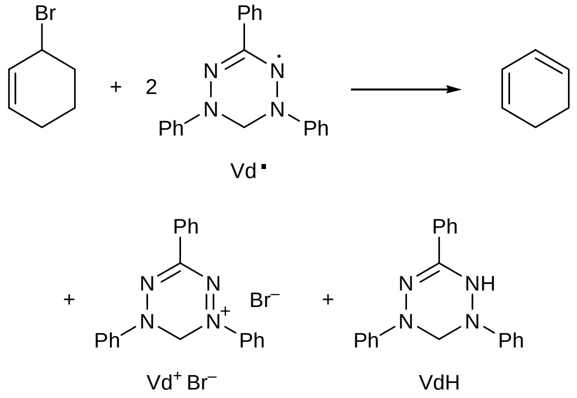


II

The rate of heterolysis of Ph_2CHBr depends on the solvent polarity and electrophilicity and is independent of the solvent nucleophilicity, which is typical of S_N1 reactions [13]. However, in keeping with published data, the substitution in benzhydryl halides [42, 43] and 1-phenylethyl halides [44, 45] can follow S_N2 mechanism. Hunziker and Mullner [46] presumed that dehydrobromination of compound **I** occurs according to the E2 mechanism. The rate of heterolysis of Ph_2CCl_2 [47] and p-methoxybenzotrichloride [48], for which rear nucleophilic solvation is possible, decreases as the solvent nucleophilicity rises.

The above stated prompted us to study in detail solvation effects in the heterolysis of compounds which are capable of reacting according to the S_N1 (E1) mechanism and are readily accessible for rear nucleophilic attack. An example of such substrates is 3-bromocyclohexene. It is known that the most stable cyclohexene conformer is *half-chair* (**II**), where the bonds in the allylic positions, pseudoaxial (*ax*') and pseudoequatorial (*eq*'), form a torsion angle of 59° [49]. Therefore, the corresponding carbon atoms are readily accessible for rear nucleophilic attack. Heterolysis of 3-bromocyclohexene can be regarded as a model of dehydrobromination of compound **I** [50], i.e., a reaction included in the large-scale synthesis of vitamin D_3 [51].

There are published data on the kinetics of heterolysis of 3-bromocyclohexene in acetonitrile [52] and nitrobenzene [53, 54] at 25°C. We performed kinetic experiments by the verdazyl technique [55] which employs 1,3,5-triphenylverdazyl ($Vd^\bullet$) as internal indicator. Verdazyl radical quickly and quantitatively reacts with the substrate solvent-separated ion pair to give cyclohexadiene, verdazylium bromide (Vd^+Br^-), and leuco verdazyl (VdH) according to scheme (1).



(1)

The reaction rate was monitored by spectrophotometry, following decrease in the concentration of $Vd^\bullet$ (λ_{max} ~720 nm). The reaction rate is satisfactorily described by first-order kinetic equation (2).

$$v = -\frac{\partial[\mathrm{Vd}]}{2\partial\tau} = k[\mathrm{C_6H_9Br}]. \tag{2}$$

Table contains our experimental and published rate constants measured at 25°C in 32 solvents and solvent parameters necessary for analysis of solvation effects. In the correlation analysis we used Koppel'–Pal'm equation (3) [6, 56] with the cohesion energy density δ^2 as an additional parameter, Kamlet–Taft equation (4) [7, 57], and Eq. (5).

$$\log k = a_0 + a_1\frac{\varepsilon - 1}{\varepsilon + 1} + a_2\frac{n^2 - 1}{n^2 + 1} + a_3E + a_4B + a_5\frac{\delta^2}{100}; \tag{3}$$

$$\log k = a_6 + a_1\pi^* + a_2\alpha + a_3\beta + a_4\frac{\delta^2}{100}; \tag{4}$$

$$\log k = a_0 + a_1E_\mathrm{T}\ (\text{or } Z) + a_2\frac{n^2 - 1}{n^2 + 1} + a_3B + a_4\frac{\delta^2}{100}. \tag{5}$$

Here, ε is the dielectric constant, n is the refractive index, E, α and V, β are, respectively, the empirical electrophilicity and nucleophilicity parameters, π^* is the dipolarity parameter (polarity + polarizability), E_T and Z are the solvatochromic parameters characterizing ionizing power, and $\delta^2 = (\Delta H_\mathrm{m} - RT)/V_\mathrm{m}$ is the parameter characterizing the energy of self-association [58] (where ΔH_m is the molar vaporization energy and V_m is the molar volume). The solvent parameters were taken from [56, 59, 60].

Application of Eqs. (3)–(5) to the whole set of solvents gave regression equations (6)–(9):

$$\log k = -(9.64 \pm 0.32) + (2.72 \pm 0.43)f(\varepsilon) + (0.0700 \pm 0.0040)E;$$
$$R = 0.972,\ S = 0.38,\ F = 246\ (1.85),\ n = 32; \tag{6}$$

$$\log k = -(9.84 \pm 0.37) + (2.70 \pm 0.34)\alpha + (0.572 \pm 0.082)\delta^2;$$
$$R = 0.970,\ S = 0.38,\ F = 482\ (1.87),\ n = 32; \tag{7}$$

$$\log k = -(17.7 \pm 0.5) + (0.0635 \pm 0.0030)E_\mathrm{T};$$
$$R = 0.970,\ S = 0.38,\ F = 482\ (1.87),\ n = 32; \tag{8}$$

$$\log k = -(19.5 \pm 0.4) + (0.0467 \pm 0.0020)Z;$$
$$R = 0.984,\ S = 0.28,\ F = 897\ (1.87),\ n = 32. \tag{9}$$

Hereinafter, $f(\varepsilon) = (\varepsilon - 1)/(\varepsilon + 1)$, and F is the apparent and critical (in parentheses) Fisher consistency [61] (a model is considered to be reliable when the former exceeds the latter).

The correlations drawn on the basis of Eqs. (3) and (5) show that the reaction rate depends on the ionizing power of the solvent or on its polarity and electrophilicity, which is the same (for the ionizing power is satisfactorily described by the polarity and electrophilicity parameters) [6, 59].

Solvent effect on the rate of heterolysis of 3-bromocyclohexene and solvent parameters

No.	Solvent	k_{25}, s^{-1} [a]	$-\log k_{25}$	ε_{20}	n_D^{20}	Z, kJ/mol	E_T, kJ/mol	E, kJ/mol	B, kJ/mol	$\delta^2/100$, kJ/l	π^*	α	β
1	MeOH	$(5.37 \pm 0.33) \times 10^{-4}$	3.27	32.7	1.329	350	232	62	2.61	8.58	0.60	0.98	0.66
2	EtOH	$(1.41 \pm 0.05) \times 10^{-4}$	3.85	24.3	1.361	333	217	49	2.81	6.78	0.54	0.86	0.75
3	PrOH	$(5.25 \pm 0.16) \times 10^{-5}$	4.28	20.2	1.385	328	212	44	2.67	5.99	0.52	0.84	0.90
4	*i*-PrOH	$(2.51 \pm 0.12) \times 10^{-5}$	4.60	18.3	1.377	319	206	39	2.82	5.56	0.48	0.76	0.84
5	BuOH	$(5.01 \pm 0.18) \times 10^{-5}$	4.30	17.1	1.399	325	210	43	2.76	5.41	0.47	0.84	0.84
6	*s*-BuOH	$(1.29 \pm 0.08) \times 10^{-5}$	4.89	16.6	1.398	316	197	30	2.82	5.19	0.40	0.69	0.80
7	*t*-BuOH	$(6.92 \pm 0.21) \times 10^{-6}$	5.16	10.9	1.385	298	183	21	2.95	4.60	0.41	0.42	0.93
8	Cyclohexanol	$(1.15 \pm 0.03) \times 10^{-5}$	4.94	15.0	1.467	314	196	29	2.89	5.15	0.45	0.66	0.84
9	*t*-AmOH	$(2.09 \pm 0.01) \times 10^{-6}$	5.68	5.80	1.386	296	172	19	3.03	4.60	0.40	0.28	0.93
10	DMSO	$(2.34 \pm 0.05) \times 10^{-6}$	5.63	46.7	1.479	294	189	14	4.33	7.08	1.00	0.00	0.76
11	Propylene carbonate	$(4.47 \pm 0.17) \times 10^{-6}$	5.35	62.9	1.421	303	195	21	2.18	7.40	0.83	0.00	0.40
12	γ-Butyrolactone	$(2.82 \pm 0.12) \times 10^{-6}$	5.55	41.0	1.437	290	185	12	2.48	6.95	0.87	0.00	0.49
13	Acetonitrile		5.59[b]	35.9	1.344	298	191	21	1.91	5.86	0.75	0.19	0.40
14	Nitrobenzene	$(1.02 \pm 0.02) \times 10^{-7}$ [c]	6.99	36.1	1.551	274	173	0.0	0.80	5.11	0.01	0.00	0.30
15	Benzonitrile	$(1.10 \pm 0.03) \times 10^{-7}$	6.96	25.2	1.528	272	173	0.0	1.85	5.15	0.90	0.00	0.37
16	Acetone	$(1.70 \pm 0.08) \times 10^{-7}$	6.77	21.4	1.359	275	176	8.5	2.68	3.88	0.71	0.08	0.43
17	Methyl ethyl ketone	$(4.37 \pm 0.06) \times 10^{-8}$	7.36	18.9	1.379	268	173	5.4	2.50	3.61	0.67	0.06	0.48
18	Acetophenone	$(5.13 \pm 0.02) \times 10^{-8}$	7.29	18.2	1.534	270	170	0.0	2.42	4.33	0.90	0.04	0.49
19	Cyclohexanone	$(3.80 \pm 0.04) \times 10^{-8}$	7.42	16.0	1.451	265	166	0.0	2.89	4.08	0.76	0.00	0.53
20	Ethyl acetate	$(6.03 \pm 0.10) \times 10^{-8}$	7.22	6.00	1.372	258	159	6.7	2.17	3.39	0.55	0.00	0.45
21	Tetrahydrofuran	$(1.62 \pm 0.03) \times 10^{-8}$	7.79	7.39	1.408	246	156	0.0	3.43	3.61	0.58	0.00	0.55
22	1,4-Dioxane	$(1.55 \pm 0.09) \times 10^{-8}$	7.81	2.27	1.422	270	150	0.0	2.84	4.20	0.55	0.00	0.37
23	Phenetole	$(4.37 \pm 0.12) \times 10^{-9}$	8.36	4.22	1.507	246	153	0.0	1.89	3.80	0.69	0.00	0.30
24	Diphenyl ether	$(3.72 \pm 0.04) \times 10^{-9}$	8.43	3.69	1.581	241	148	0.0	1.06	4.04	0.66	0.00	0.13
25	1,2-Dichloroethane	$(8.91 \pm 0.03) \times 10^{-8}$	7.05	10.4	1.551	265	173	9.6	0.48	4.12	0.81	0.00	0.10
26	Chlorobenzene	$(9.55 \pm 0.05) \times 10^{-9}$	8.02	5.74	1.524	249	154	0.0	0.45	3.76	0.71	0.00	0.07
27	1,2-Dichlorobenzene	$(1.95 \pm 0.04) \times 10^{-9}$	7.71	10.4	1.551	251	159	0.0	0.33	4.20	0.80	0.00	0.03
28	Chloroform	$(1.70 \pm 0.01) \times 10^{-7}$	6.77	4.89	1.446	264	163	14	0.17	3.57	0.58	0.20	0.10
29	Methylene chloride	$(1.74 \pm 0.03) \times 10^{-7}$	6.76	9.02	1.424	269	170	11	0.28	4.12	0.82	0.13	0.10
30	Benzene	$(2.01 \pm 0.22) \times 10^{-9}$	8.70	2.27	1.501	226	143	0.0	0.57	3.53	0.59	0.00	0.10
31	Toluene	$(5.01 \pm 0.22) \times 10^{-9}$	8.30	2.43	1.497	233	142	0.0	0.69	3.31	0.54	0.00	0.11
32	*p*-Xylene	$(9.55 \pm 0.40) \times 10^{-10}$	9.02	2.37	1.497	227	138	0.0	0.81	3.24	0.43	0.00	0.12

[a] Average value from 2–5 measurements.

[b] Data of [53].

[c] $k = (1.00 \pm 0.04) \times 10^{-7}$ s^{-1} [54].

For 32 solvents, we obtained Eq. (10):

$$E_T = (1118 \pm 3) + (0.988 \pm 0.039)E + (54.8 \pm 3.8)f(\varepsilon);$$
$$R = 0.991,\ S = 3.35,\ F = 763\ (1.85),\ n = 32. \qquad (10)$$

The polarizability, nucleophilicity, and cohesion energy density parameters are insignificant. The correlation factor R for five-parameter Eq. (3) is 0.979, while for four-parameter Eq. (5), $R = 0.975$ (0.986). Figure 1 shows the correlations between $\log k$ and E_T and between $\log k$ and Z. Using Eq. (4), we obtained a two-parameter correlation with the electrophilicity and cohesion energy density. This may be due to complex character of the parameter π^*, which sometimes leads to artefacts [10, 11].

Correlations like (6)–(9) are also typical of the heterolysis of tertiary substrates in aprotic solvents or in a set consisting of protic and aprotic solvents, the latter prevailing (as in our case). However, correlations for heterolysis of tertiary substrates in protic solvents usually include the nucleophilicity and polarizability parameters taken with the minus sign. Therefore, we performed correlation analysis of solvation effects separately for protic solvents. On the basis of Eqs. (3)–(5) we obtained correlations (11)–(14).

$$\log k = -(7.65 \pm 0.75) + (1.70 \pm 1.02)f(\varepsilon) + (0.0444 \pm 0.0050)E;$$
$$R = 0.990,\ S = 0.12,\ F = 142\ (4.15),\ n = 9; \qquad (11)$$

$$\log k = -(8.37 \pm 0.52) + (5.81 \pm 1.61)\pi^* + (1.51 \pm 0.49)\alpha;$$
$$R = 0.978,\ S = 0.18,\ F = 65\ (4.15),\ n = 9; \qquad (12)$$

$$\log k = -(12.5 \pm 0.6) + (0.0393 \pm 0.0030)E_T;$$
$$R = 0.983,\ S = 0.14,\ F = 202\ (3.73),\ n = 9; \qquad (13)$$

$$\log k = -(18.0 \pm 1.1) + (0.0419 \pm 0.0030)Z;$$
$$R = 0.977,\ S = 0.17,\ F = 146\ (3.73),\ n = 9. \qquad (14)$$

The rate of heterolysis of 3-bromocyclohexene in protic solvents is excellently or well described by the polarity (dipolarity) and electrophilicity parameters. Nucleophilicity of solvents does not affect the reaction rate. As applied to aprotic solvents, we obtained the same correlations [Eqs. (15)–(18)] as for the whole set of solvents:

$$\log k = -(9.63 \pm 0.29) + (2.53 \pm 0.41)f(\varepsilon) + (0.0870 \pm 0.0120)E;$$
$$R = 0.949,\ S = 0.34,\ F = 91.4\ (2.10),\ n = 23; \qquad (15)$$

$$\log k = -(10.8 \pm 0.3) + (7.50 \pm 1.07)\alpha + (0.662 \pm 0.63)\delta^2;$$
$$R = 0.954,\ S = 0.34,\ F = 90.1\ (2.28),\ n = 21; \qquad (16)$$

$$\log k = -(17.6 \pm 0.7) + (0.0612 \pm 0.0040)E_T;$$
$$R = 0.956,\ S = 0.31,\ F = 221\ (2.08),\ n = 23; \qquad (17)$$

$$\log k = -(19.4 \pm 0.7) + (0.0464 \pm 0.0030)Z;$$
$$R = 0.970,\ S = 0.26,\ F = 318\ (2.10),\ n = 22. \qquad (18)$$

The quality of correlations (15)–(18) is appreciably lower, presumably due to greater diversity of solvation effects including dipolar solvation. Satisfactory correlations (16) and (17) were obtained only when two (1,2-dichloroethane and ethyl acetate) and one (dioxane) solvents, respectively, were excluded.

A characteristic feature of heterolysis of tertiary substrates is that the correlations $\log k$—$E_T(Z)$ consist of two straight lines: one for protic solvents, and the other, for aprotic. This is explained by the fact that the negative nucleophilic solvation effect is most pronounced in protic solvents; therefore, the reaction rate is lower than might be expected from the linear dependence for aprotic solvents [2]. In the case of 3-bromocyclohexene, where solvent nucleophilicity does not affect the reaction rate, all points for protic and aprotic solvents satisfactorily fall onto a single straight line (Fig. 1). An analogous pattern was observed in the heterolysis of benzhydryl bromide [14].

Figure 2 illustrates the difference between secondary and tertiary substrates. The $\log k(C_6H_9Br)$ values

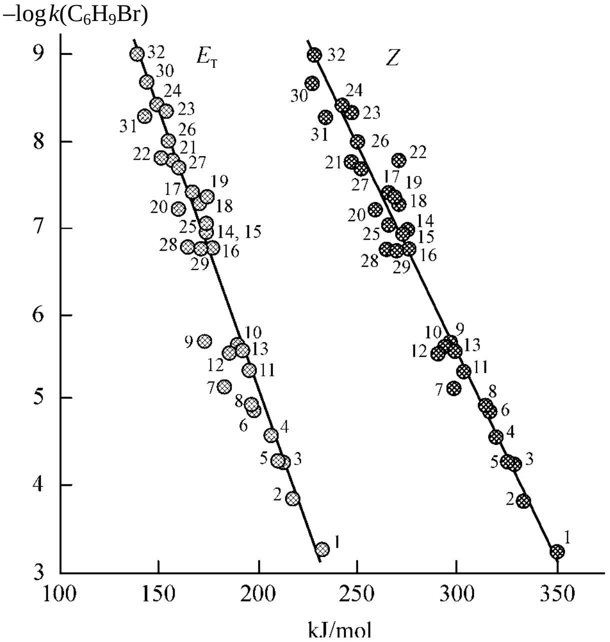


Fig. 1. Correlations between the ionizing power E_T (Z) of solvents and the rate of heterolysis of 3-bromocyclohexene at 25°C. For solvent numbering, see table.

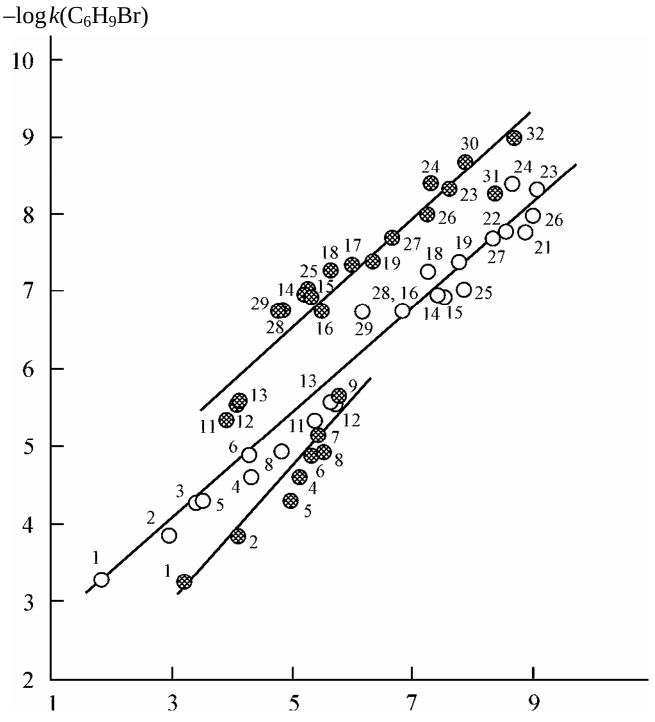


Fig. 2. Correlations $\log k(C_6H_9Br)$—$\log k(Ph_2CHBr)$ (light circles) and $\log k(C_6H_9Br)$—$\log k$(2-Br-2-MeAd) (dark circles). For solvent numbering, see table.

correlate well [Eq. (19)] with $\log k(Ph_2CHBr)$ values for protic and aprotic solvents.

$$\log k(C_6H_9Br) = (1.7 \pm 0.15) + (0.719 \pm 0.023) \log k(Ph_2CHBr);$$
$$R = 0.989,\ S = 0.24,\ F = 962\ (2.08),\ n = 23. \qquad (19)$$

By contrast, no correlation was found between $\log k(C_6H_9Br)$ and the corresponding data for 2-bromo-2-methyladamantane [17] for the whole set of solvents ($R = 0.83$); treatment of the data for protic and aprotic solvents separately gave satisfactory correlations (20) and (21), respectively.

$$\log k(C_6H_9Br) = (0.740 \pm 0.399)$$
$$+ (0.733 \pm 0.082) \log k(\text{2-Br-2-MeAd});$$
$$R = 0.973,\ S = 0.17,\ F = 87.9\ (4.95),\ n = 7; \qquad (20)$$

$$\log k(C_6H_9Br) = (3.18 \pm 0.29)$$
$$+ (0.685 \pm 0.047) \log k(\text{2-Br-2-MeAd});$$
$$R = 0.962,\ S = 0.30,\ F = 208\ (2.28),\ n = 19. \qquad (21)$$

Thus, in the heterolysis of tertiary substrates, increase in the solvent nucleophilicity reduces the reaction rate, while in the heterolysis of secondary substrates this parameter does not affect the rate of the process. The reason is that rear nucleophilic solvation of a covalent tertiary substrate is impossible because of steric factor; it appears at the stage of formation of contact ion pair, which stabilizes the intermediate and hampers departure of nucleofuge according to the S_N1 mechanism. This is clearly seen in protic solvents due to participation of hydrogen bonds. The negative effect of nucleophilic solvation may be regarded as a result of nonequilibrium solvation of transition state.

Secondary substrates, especially those like 3-bromocyclohexane, are readily accessible for nucleophilic solvation from the rear. There are stereochemical proofs for rear nucleophilic solvation of secondary substrates which react according to the S_N1 mechanism [44, 62, 63]. This sort of solvation hampers nucleophilic attack from the rear, and solvolysis of optically active compounds gives products with the same configuration. An example is the hydrolysis of 1-chloro-1-phenylethane in the presence of nitriles [44]. Due to nucleophilic solvation, phenolysis of optically active substrates occurs with partial or complete retention of configuration [44, 62].

The fact that the rate of heterolysis of secondary substrates does not depend on the solvent nucleophilicity is difficult to explain, though it is consistent with the up-to-date interpretation of the S_N1 (E1) mechanism [64, 65]. According to Ingold, the rate-determining stage of these reactions is formation of carbocation which quickly undergoes nucleophilic attack; here, the reaction rate should depend on the energy of solvation of ions thus formed [28]. Therefore, increase in the solvent nucleophilicity should favor the process. Our data indicate that increase in the solvent nucleophilicity either reduces the reaction rate or does not affect it.

It is reasonable to presume that nucleophilic solvation involves a covalent substrate (initial state) and that this solvation does not change upon formation of transition state [2], i.e., we have equilibrium solvation of transition state. Therefore, no solvent nucleophilicity effect is observed in cases when rear nucleophilic solvation is possible.

The importance of nucleophilic solvation is much more general than it may seem at first glance. One of the most widely used methods for quantitative estimation of solvent effects on the rate of heterolytic reactions (Grünwald–Winstein equations) utilizes *tert*-butyl chloride as reference substrate (later on, adamantyl derivatives were also used) [1, 4]. However, recent studies have shown that increase in the solvent nucleophilicity leads to decrease in the rate of heterolysis of tertiary substrates, which inevitably distorts comparative pattern of solvation effects. In fact, in many cases application of the Grünwald–Winstein equations gave unsatisfactory results [1, 66, 67]. More appropriate reference substrates are those for which solvent nucleophilicity does not affect the rate of heterolysis and the $\log k$—$E_T(Z)$ dependence is linear. Such compounds are, e.g., benzhydryl bromide and especially 3-bromocyclohexene which is more accessible for nucleophilic solvation from the rear.

The dependence of the rate of heterolysis of both secondary and tertiary substrates on the solvent electrophilicity indicates that in all cases electrophilic solvation of the transition state is nonequilibrium. The reaction rate increases as the solvent electrophilicity rises, for both electrophilic solvation of covalent substrate and additional electrophilic solvation of contact ion pair favor the reaction.

It should be emphasized that the concepts of equilibrium and nonequilibrium solvation of transition state are arbitrary. Assuming a contact ion pair as the initial state, all solvation effects become equilibrium, in keeping with the transition state theory [21].

EXPERIMENTAL

Kinetic experiments were performed in a spectrophotometric cell (SF-26 spectrophotometer) maintained at a constant temperature. The substrate concentration was 3.8×10^{-4} to 1.2×10^{-1} M, the concentration of the indicator was $(1–2.5) \times 10^{-4}$ M, and the substrate conversion was 0.017 to 8.6%. The rate constants were calculated as average values determined from 2–5 parallel runs. Equations (3)–(5) were treated by the least-squares procedure with the aid of SPSS software package; confidence probability 95%.

1,3,5-Triphenylverdazyl was synthesized and purified as described in [68]. The solvents were purified by standard methods [69].

3-Bromocyclohexene was synthesized by a modified procedure [68]. A suspension of 0.2 g of azobis(isobutyronitrile) in 100 ml of carbon tetrachloride was added to 32 g (0.18 mol) of finely powdered *N*-bromosuccinimide, 20 ml (15.2 g, 0.18 mol) of cyclohexene (distilled a month before) was then added under vigorous stirring, and the mixture was quickly heated to 82–84°C. It was stirred for 30 min at that temperature and cooled to 5°C. The precipitate of succinimide was filtered off and washed with 20 ml of cold carbon tetrachloride, the filtrate was evaporated under reduced pressure (18 mm), and the residue was twice distilled in a vacuum. Yield 18.6 g (62%), bp 37–38°C (4 mm), $n_D^{20} = 1.5292$; published data [70]: bp 51°C (10 mm), $n_D^{20} = 1.5290$.

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