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B-Strain and Solvolytic Reactivity Revisited. Nucleophilic Solvent Participation and Abnormal Rate Ratios for Tertiary Chloroalkanes

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More than half a century elapsed since the concept of steric strain was first advanced to offer reasonable interpretations of several chemical behaviors taking place in highly branched aliphatic systems.[1] Its quantitative evaluation has been developed to become one of the major themes in physical organic chemistry.[2,3] In 1949, Brown and Fletcher gave the first detailed report on the B(back)-strain effects in the solvolysis of tertiary chloroalkanes in 80% ethanol.[4] It was proposed that as the tetrahedral chloride ionized to a trigonal carbocation, strain would be relieved with bulkier systems showing greater reactivity. For examples, 2-chloro-2-methylpropane (*tert*-butyl chloride **1a**) was less reactive than 2-chloro-2-methylbutane (**1b**), and 3-chloro-3-methylpentane (**2a**) was less reactive than 3-chloro-3-ethylpentane (**2b**). However, the introduction of an isopropyl group in place of the ethyl group in **1b** or **2b** resulted in a decrease of reaction rate, whereas a further replacement of the isopropyl group by *tert*-butyl group made a small rate-enhancement for 2-*tert*-butyl-2-chloropropane (**1d**) but a large one for 3-*tert*-butyl-3-chloropentane (**2d**) (Scheme 1).[4]

Several possibilities, such as electronic effects of the alkyl substituent and steric hindrance to the solvation of ions had been suggested to rationalize the irregularity,[4] but to our knowledge no conclusion was ever reached. On the other hand, 2-bromo- and 2-chloro-2-methylpropanes have been considered to solvolyze via a nonlimiting mechanism from the observation of the nonlinear log k vs mY plot,[5] and a similar phenomenon has been observed in the solvolysis of **1d**.[6] From our study on the solvolysis of chlorides **1b**, **1d**, **2a**−**2d**, we demonstrate that the *abnormal* trend of inverse isopropyl/ethyl and *tert*-butyl/ethyl reactivity ratios is due to the swamping of the relief of B-strain by nucleophilic solvent participation.

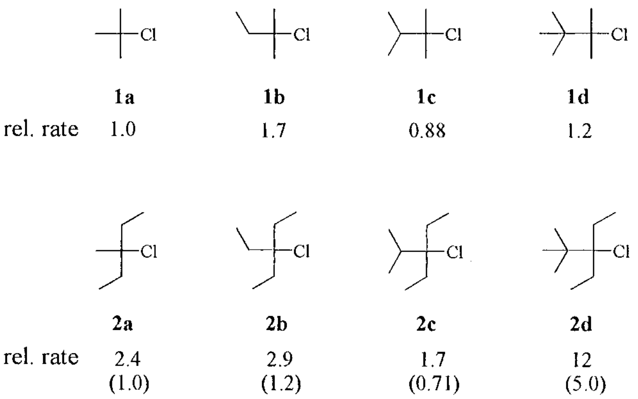
Results and Discussion

Chlorides **1b**, **1d**, **2a**−**2d** were prepared from the controlled chlorination[7] of corresponding alcohols and were solvolyzed in a variety of solvents. Pertinent data of first-order conductometrical rate constants are listed in Table 1. Correlation analyses of log k against Y_{Cl}[8−10] using the single-parameter Grunwald−Winstein equation (eq 1)[11] revealed excellent linear relationships for **2c** and **2d** (Table 2), but downward deviation of data points obtained in 97% hexafluoro-2-propanol (by weight, 97H*w*), 70% trifluoroethanol (70T*w*), and in trifluoroethanol−ethanol (TE) for other substrates. Representative examples are illustrated in Figure 1. For the dual-parameter equation (eq 2),[12] despite the claim of N_{T} as a general choice among various scales of solvent nucleophilicities,[13] we found the use of N_{OTs} by Fujio *et al.*[14] was more appropriate than the use of N_{T} for certain benzylic chlorides.[15] It is likely due to the importance of the electrophilic pull of anionic leaving group in solvolysis,[16] which is absent in the substrate to define N_{T} scale. The results are given in Table 2.[17] In the case of **2c**, the k(97H*w*) from linear log k vs mY plots, 0.435/s, is in good agreement with that obtained from Arrhenius plots (Table 1). Thus, the extrapolated rate constant for **2d** in 97H*w*, 4.33/s, could be obtained from eq 1. Recent work by Takeuchi and co-workers indicated a unique solvent effect in a Grunwald−Winstein relationship for highly congested systems.[18] But no such a phenomenon was found in the present study.

$$\log k = mY \qquad \text{(eq 1)}$$

$$\log k = mY + lN \qquad \text{(eq 2)}$$

Scheme 1



It is interesting to note that the inverse isopropyl/ethyl rate ratio for **2** and the inverse *tert*-butyl/ethyl rate ratio

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Table 1. Pertinent Rate Constants for Solvolysis of Tertiary Alkyl Chlorides

	k (s^{-1}, 25 °C)					
solvent[a]	**1b**	**1d**	**2a**	**2b**	**2c**	**2d**
90E	2.86×10^{-6} [b]					2.15×10^{-5}
80E	1.57×10^{-5} [b]	1.10×10^{-5} [c]	2.26×10^{-5}	2.78×10^{-5}	1.37×10^{-5}	1.05×10^{-4}
70E	5.74×10^{-5} [b]	4.45×10^{-5} [c]	1.01×10^{-4}	1.20×10^{-4}	5.15×10^{-5}	4.94×10^{-4}
60E	2.09×10^{-4}	1.38×10^{-4} [c]	2.96×10^{-4}	3.84×10^{-4}	1.95×10^{-4}	1.62×10^{-3}
50E	7.54×10^{-4}	5.88×10^{-4}	1.12×10^{-3}	1.34×10^{-3}	7.56×10^{-4}	5.82×10^{-3}
80A	3.20×10^{-6} [b]		3.80×10^{-6} [d]			2.11×10^{-5}
70A	1.89×10^{-5} [b]	1.56×10^{-5}	2.87×10^{-5}	4.10×10^{-5}	1.75×10^{-5}	1.39×10^{-4}
60A	7.87×10^{-5}	7.04×10^{-5} [c]	1.41×10^{-4}	2.08×10^{-4}	1.08×10^{-4}	7.90×10^{-4}
50A	4.49×10^{-4}	3.29×10^{-4} [c]	5.56×10^{-4}	9.68×10^{-4}	4.59×10^{-4}	3.68×10^{-3}
40A	1.61×10^{-3}	1.47×10^{-3} [c]	2.36×10^{-3}	3.72×10^{-3}	2.10×10^{-3}	1.59×10^{-2}
100M	1.81×10^{-6} [b]	2.06×10^{-6} [c]				
90M			1.64×10^{-5}			
80M	4.40×10^{-5}	4.10×10^{-5}	8.45×10^{-5}	1.34×10^{-4}	6.95×10^{-5}	5.94×10^{-4}
70M	1.85×10^{-4}	1.80×10^{-4}	3.69×10^{-4}	5.31×10^{-4}	2.75×10^{-4}	2.71×10^{-3}
60M	7.17×10^{-4}	6.80×10^{-4} [c]	1.36×10^{-3}	1.80×10^{-3}	1.19×10^{-3}	8.50×10^{-3}
100T	3.82×10^{-4}	1.11×10^{-3}	9.59×10^{-4}	1.83×10^{-3}	3.78×10^{-3}	3.82×10^{-2}
80T20E	7.92×10^{-5}	2.03×10^{-4}	1.73×10^{-4}	3.19×10^{-4}	5.17×10^{-4}	5.21×10^{-3}
60T40E	1.10×10^{-5} [d]	2.13×10^{-5}	2.45×10^{-5}	4.42×10^{-5}	5.57×10^{-5}	3.87×10^{-4}
40T60E	2.90×10^{-6} [d]					
70T*w*	8.60×10^{-4}	1.99×10^{-3}			4.77×10^{-3}	5.42×10^{-2}
97H*w*	1.32×10^{-2}	6.10×10^{-2}	4.71×10^{-2}	1.21×10^{-1}	4.32×10^{-1} [d]	4.33[e]

[a] A, E, H, M, and T denote acetone, ethanol, hexafluoro-2-propanol, methanol, and trifluoroethanol, respectively. The number indicates the volume percent of the specific solvent in the mixture, except those followed by *w* refer to weight percent. [b] From T.-R. Wu, Ph. D. Thesis, National Taiwan University, August, 1989. [c] Reference 6. [d] Extrapolated from data obtained at other temperatures, see Experimental Section. [e] Extrapolated from eq 1, see: Results and Discussion.

Table 2. Correlation Analyses Using Single- and Dual-Parameter Grunwald–Winstein Equations

substrate	parameter	n	R	m	SD[a]	l	SD[a]
1b	Y_{Cl}	20	0.957	0.655	0.047		
	Y_{Cl}, N_{OTs}	19	0.991	0.835	0.033	0.351	0.046
1d	Y_{Cl}	17	0.990	0.733	0.025		
	Y_{Cl}, N_{OTs}	16	0.997	0.820	0.029	0.138	0.031
2a	Y_{Cl}	17	0.967	0.686	0.047		
	Y_{Cl}, N_{OTs}	15	0.996	0.881	0.029	0.298	0.033
2b	Y_{Cl}	15	0.972	0.697	0.047		
	Y_{Cl}, N_{OTs}	14	0.995	0.901	0.035	0.249	0.036
2c	Y_{Cl}	15	0.998	0.869	0.015		
2d	Y_{Cl}	17	0.998	0.887	0.014		

[a] Standard deviation.

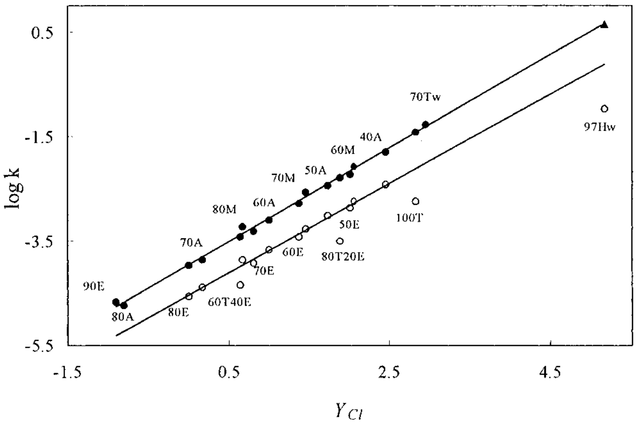

Figure 1. Plots of log k values for **2b** (○) and **2d** (●) against Y_{Cl} (▲ for extrapolated value).

for **1** were observed only in strongly and moderately nucleophilic solvents (aqueous acetone, ethanol, and methanol), but not in weakly nucleophilic solvents (97H, 70T*w*, and TE). The solvolysis of 2-chloro-2-methylpropane (**1a**) has been considered to proceed via a nonlimiting mechanism based on the observation of the deviation of log ks in weakly nucleophilic solvents from linear plots against log k for 1-chloroadamantane (i.e., Y_{Cl}),[5,19] and also from an appreciable l value obtained from eq 2.[9] Similar phenomenon of nonlinear log k vs Y_{Cl} plots was also observed in the solvolysis of **1d**.[6] In other words, even a *tert*-butyl group in **1** is not large enough to block the backside completely for nucleophilic solvent participation.[20] More remarkably, the rate-enhancement due to solvent intervention is so effective in the case of **1b** that it overshadows the relief of B-strain for *tert*-butyl group and solvent participation in **1d**, giving $k(\mathbf{1b}) > k(\mathbf{1d})$ in aqueous acetone, ethanol, and methanol. On the contrary, the normal order of $k(\mathbf{1d}) < k(\mathbf{1b})$, as predicted from the relief of B-strain, was observed in TE, 70T*w*, and 97H*w*.

Consequently, the solvolysis rate ratio of 4.6 for **1d**/**1b** in 97H*w*[21,22] might be then regarded as the relative B-strain for *tert*-butyl/ethyl in 2-alkyl-2-chloropropanes (**1**). Moreover, we found $k(\mathbf{1a})$ in 97H*w* as 2.26×10^{-3}/s (lit.[23,24] 2.00 to 2.69×10^{-3}/s), so the relative B-strain for *tert*-butyl/methyl could be assigned as 27, and ethyl/methyl as 5.8. The former value, 27, is considerably larger than the previously observed *tert*-butyl/methyl reactivity ratios for 2-alkyl-2-propyl chlorides (1.2)[4] and *p*-nitrobenzoates (4.36)[25] in nucleophilic solvents and may be considered as the *normal* factor responsible for the relief of B-strain for *tert*-butyl vs methyl in this system.

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(21) Although trifluoroacetic acid was considered to be the least nucleophilic solvent,[22] in our experience it was difficult to obtain reproducible rate constants for halides in this solvent. Moreover, the solvolysis in 97HFIP was considered closer to limiting than in trifluoroacetic acid.[5] Consequently, 97HFIP was the choice of solvent for limiting solvolysis.

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Table 1 shows that for **2a** to **2d** in nucleophilic solvents, the trend of rate constants is invariably **2d**>**2b**>**2a**>**2c**. Obviously, nucleophilic solvent participation in the 3-alkyl-3-pentyl system is not so strong that the relief of B-strain for *tert*-butyl group becomes dominant, although inverse isopropyl/ethyl and isopropyl/methyl orders of reactivities can still be observed. In weakly nucleophilic solvents, however, a *normal* trend of **2d**>**2c**>**2b**>**2a** was found as predicted from the relief of B-strain. Again, nucleophilic solvent participation is no more overwhelming. Rate ratios in 97H*w* are 92:9.2:2.6: 1 for **2d**:**2c**:**2b**:**2a**. The ratio of 92:1 for **2d**/**2a** and 36:1 for **2d**/**2b** in 97H*w* indicate larger B-strain relief for *tert*-butyl vs methyl and for *tert*-butyl vs ethyl in the 3-alkyl-3-pentyl than the 3-alkyl-2-propyl system. However, the rate ratio for **2b**/**2a** in 97H*w*, 2.6, was smaller than that found for **1b**/**1a** (5.8, vide supra). It is likely due to the different ground-state energy difference in those two systems.[26] In addition, the present results suggest the necessity of reexamination about previous work on the correlation between calculated strain energies and the solvolytic reactivity of tertiary alkyl substrates observed in nucleophilic solvents.[25,27] Further studies are in progress.

Experimental Section

General Remarks. Boiling points and melting points are uncorrected. Proton NMR spectra (200 or 300 MHz) were used for characterization of chlorides.

Materials. The controlled chlorination[7] of alcohols were employed to prepare chlorides **1b**, **1d**, and **2a**–**2d**.[4] The products were purified by distillation at atmosphere pressure or under vacuum. In every case, the proton NMR spectrum indicated a single isomer compatible with the assigned structure. Solvents for kinetic studies were commercially available spectral or reagent grade ones which, except for hexafluoro-2-propanol, had been purified according to conventional methods.[28]

Kinetic Measurements. Conductometric rate constants were obtained as described in the previous work.[16] Rate constants determined in 80% ethanol are in good agreement with literature data.[4] Most of the rate constants were measured directly at 25 °C (±0.02 °C), whereas a few were obtained from Arrhenius plots. For **1b**, k(25 °C) in 60T40E was calculated from $k(70\ °\text{C}) = 1.68 \times 10^{-3}$/s, $k(60\ °\text{C}) = 6.09 \times 10^{-4}$/s and $k(50\ °\text{C}) = 2.14 \times 10^{-4}$/s; k(25 °C) in 40T60E was calculated from $k(70\ °\text{C}) = 4.13 \times 10^{-4}$/s and $k(55\ °\text{C}) = 9.20 \times 10^{-5}$/s. For **2a**, k(25 °C) in 80A was calculated from $k(75\ °\text{C}) = 1.02 \times 10^{-3}$/s, $k(65\ °\text{C}) = 3.87 \times 10^{-4}$/s and $k(50\ °\text{C}) = 7.72 \times 10^{-5}$/s. For **2c**, k(25 °C) in 97H*w* was calculated from $k(5\ °\text{C}) = 6.50 \times 10^{-2}$/s, and $k(10\ °\text{C}) = 1.07 \times 10^{-2}$/s. Due to the viscosity of 97H*w*, no reliable k could be measured at temperature lower than 5 °C. The results are given in Table 1.

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[26] MM2 studies on the carbenium ions from the solvolysis of alkyl bromides suggested larger difference between ΔH ($R^+ - RBr$) for *tert*-butyl and 2-methyl-2-butyl than that between 2-methyl-2-butyl and 2-methyl-2-pentyl.[27] In ongoing research we obtain similar results from MM3 calculations on a series of tertiary alkyl chlorides.

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