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Studies on the Solvolytic Reactivity of Tertiary Chloroalkanes in Hexafluoro-2-propanol by ab Initio and Force Field Calculations

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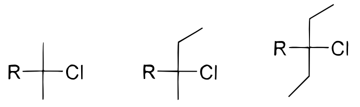
B-strain (back strain) has long been considered to make an important contribution to the reactivity of highly branched aliphatic substrates, in which ionization is facilitated by the relief of steric crowding in going from the tetrahedral ground state to the trigonal carbenium ion transition state.[1,2] The enhancement of rate becomes larger in bulkier systems. In the solvolysis of tertiary chloroalkanes **1**−**5** and **8**−**10** in 80% aqueous ethanol (80E), however, irregular trends of reactivity were observed.[3] Moreover, in the study of the solvolytic reactivity in 80% ethanol and MM2 force field calculation of strain energies Müller and co-workers found a good strain−reactivity correlation for bridgehead bicyclic and polycyclic systems but a poor one for acyclic tertiary derivatives.[4] On the other hand, in a recent study of solvent effects on the solvolytic reactivity for chlorides **1**, **2**, **4**, **5**, and **8**−**10**, we demonstrated that the irregularity was likely due to the swamping of the relief of B-strain by nucleophilic solvent assistance, and normal trends of reactivity could be found in the solvolysis of poorly nucleophilic solvent system, such as trifluoroethanol and 97% (w/w) aqueous hexafluoro-2-propanol (97H*w*).[5] Now we would like to corroborate this point by ab initio and force field calculations.



1 R = Me **2** R = Me **5** R = Me
2 R = Et **5** R = Et **8** R = Et
3 R = *i*-Pr **6** R = *i*-Pr **9** R = *i*-Pr
4 R = *t*-Bu **7** R = *t*-Bu **10** R = *t*-Bu

Results and Discussion

Solvolytic rate constants for 2-chloro-2-methylpropane (**1**), 2-chloro-2-methylbutane (**2**), 2-*tert*-butyl-2-chloropropane (**4**), 3-chloro-3-methylpentane (**5**), 3-chloro-3-ethylpentane (**8**), 3-chloro-3-isopropylpentane (**9**), and 3-*tert*-butyl-3-chloropentane (**10**) in 97H*w* have been observed.[5] 2-Chloro-2-isopropylpropane (**3**), 2-chloro-2-isopropylbutane (**6**), and 2-*tert*-butyl-2-chlorobutane (**7**) were prepared from the controlled chlorination[6] of corresponding alcohols. The rate constants in 97H*w* were obtained directly at 25 °C by conductometric methods (for **3** and **6**) or by extrapolation from linear Grunwald−Winstein plots[7] of log k against Y_{Cl}[8] with $m = 0.812$ ($R = 0.997$, for **7**).[9] First-order rate constants in 80% ethanol[5,9] and in 97H*w* (±2%) and relative rate ratios are shown in Table 1. Obviously, normal trends of reactivity accompanied with the changing of B-strain could be found in the solvolysis in 97H*w*, a solvent of very low nucleophilicity.[10]

Table 1. Solvolytic Rate Constants in 80E and 97H*w* for 1−10

	k (25 °C, 1/s)		relative reactivity in 97H*w*		
substrate	80E[a]	97H*w*[b]	k/k_1	k/k_2	k/k_5
1	9.26×10^{-6}	2.26×10^{-3}	1.0		
2	1.57×10^{-5}	1.32×10^{-2} [a]	5.8	1.0	
3	7.31×10^{-6} [c]	2.96×10^{-2}	13.1		
4	1.10×10^{-5}	6.10×10^{-2} [a]	27.0		
5	2.26×10^{-5}	4.71×10^{-2} [a]	20.8	3.6	1.0
6	1.34×10^{-5} [b]	1.38×10^{-1}	61.1	10.5	
7	7.07×10^{-5} [c]	1.08[d]	47.8	81.8	
8	2.78×10^{-5}	1.21×10^{-1} [a]	53.5		2.6
9	1.37×10^{-5}	4.32×10^{-1} [a]	191		9.2
10	1.05×10^{-4}	4.33[a]	1.92×10^{3}		91.9

[a] Reference 5 unless otherwise mentioned, 80E denotes 80% ethanol. [b] This work unless otherwise mentioned; 97H*w* denotes 97% (*w*/*w*) hexafluoro-2-propanol. [c] Reference 9. [d] Extrapolated from single-parameter Grunwald−Winstein equation (ref 7).

Both MM3 force field and ab initio calculations with the RHF/6-31G* basis set indicated good agreement with experimental data for chlorides **1**−**3**.[11,12] Therefore, similar calculations for chlorides **1**−**10** and corresponding carbenium ions were carried out. The strain energies were calculated by using the MM3(94) program. The necessary parameters related to carbenium ion were estimated by the automatic MM3 parameter estimation program provided by the MM3(94) program. Ab initio calculations were carried out with the Hartree−Fock approximation using the 6-31G* basis set by SPARTAN version 4.1 program.[13] The energies at different conformational minima for chloroalkanes and carbenium ions were calculated,[14,15] and the average energies derived from Boltzmann distribution are recorded in Table 2. If the calculation was performed only with the conformer of the lowest energy, the maximum deviation would be 0.22 kcal/mol for force field study and 0.0043 hartrees for ab initio study. The calculated strain energy differ-

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(2) Peters, E. N.; Brown, H. C. *J. Am. Chem. Soc.* **1975**, *97*, 2892.

(3) Brown, H. C.; Fletcher, R. S. *J. Am. Chem. Soc.* **1949**, *71*, 1845.

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(12) Shim, J.-Y.; Allinger, N. L.; Bowen, J. P. *J. Phys. Org. Chem.* **1997**, *10*, 3.

(13) SPARTAN Version 4.1, Wavefunction, Inc., 18401 Von Karman Ave., #370, Irvine, CA 92715.

(14) Our calculations for various conformations of chlorides **2** and **3** are consistent with those reported (ref 11). For the cation derived from **2**, our result is also in harmony with the literature data (ref 15).

(15) Farcasiu, D.; Norton, S. H. *J. Org. Chem.* **1997**, *62*, 5374.

10.1021/jo981089i CCC: $15.00

Table 2. Calculated Strain Energies and ab Initio Energies for 1−10

substrate	strain energy (kcal/mol) E_{st}(RCl)	strain energy (kcal/mol) E_{st}(R^+)	ΔE_{st}(R^+−RCl) (kcal/mol)	total energy (hartrees) E(RCl)	total energy (hartrees) E(R^+)	ΔE_{iso}[a] (kcal/mol)
1	0.98	3.22	2.24	−616.205 88	−156.442 55	0
2	2.54	3.45	0.91	−655.237 86	−195.480 18	−3.55
3	4.97	4.31	−0.66	−694.267 91	−234.516 51	−7.49
4	7.81	6.13	−1.68	−733.295 60	−273.548 68	−10.29
5	4.26	3.55	−0.71	−694.269 47	−234.517 29	−7.00
6	6.89	4.35	−2.54	−733.299 12	−273.553 21	−10.93
7	10.22	6.49	−3.73	−772.325 73	−312.584 35	−13.78
8	6.06	3.88	−2.18	−733.300 90	−273.553 23	−9.83
9	8.87	4.79	−4.08	−772.329 87	−312.588 40	−13.72
10	15.50	7.39	−8.11	−811.351 05	−351.618 27	−19.17

[a] Derived from eq 1, where 1 hartree = 627.5 kcal/mol.

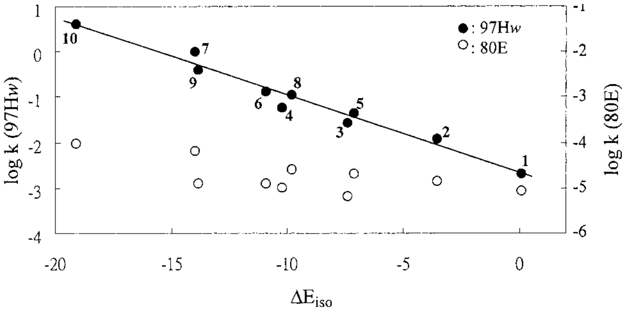

Figure 1. Plots of log k for the solvolysis in 97Hw and 80E vs ΔE_{iso}.

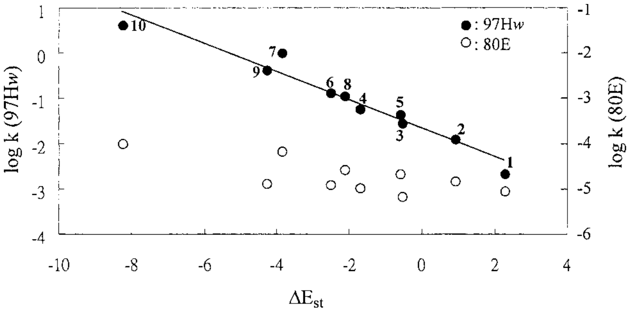

Figure 2. Plots of log k for the solvolysis in 97Hw and 80E vs ΔE_{st}.

ence, ΔE_{st}, and heat of isodesmic reaction (eq 1),[16] ΔE_{iso}, are also listed in Table 2.

$$RCl + (CH_3)_3C^+ \xrightarrow{\Delta E_{iso}} R^+ + (CH_3)_3CCl \qquad (1)$$

The plots of log k for **1**−**10** against the heat of isodesmic reaction, ΔE_{iso}, revealed a good linear relationship for those measured in 97Hw (R = 0.982; slope = −0.170) but only a scattered relationship for those measured in 80E (R = 0.690; slope = −0.048) (Figure 1). MM3 force field calculations also gave similar results. Figure 2 shows a good linear correlation between log k (97Hw) against strain energy difference ΔE_{st} (R = 0.972; slope = −0.319) and a very poor correlation in the case of log k (80E) (R = 0.743; slope = −0.097). The agreement between the two approaches and the larger variation in the calculated energy difference (ca. 10−20 kcal/mol) than that estimated from rate data (ca. 2−4 kcal/mol) are in line with those found in bridgehead solvolyses at similar level of calculation.[4,17]

Although the necessity of using hexafluoro-2-propanol as the solvent for studying the reactivity of secondary substrates has been noted,[10,18] the present results clearly demonstrate its advantage of avoiding nucleophilic solvent participation even in the solvolysis of tertiary substrates. Moreover, despite the claim of insignificant participation by nucleophilic solvent in the solvolysis of tertiary chlorides was made,[19] other studies showed evidence for the importance of nucleophilic solvent intervention,[20,21] especially for the solvolysis in the solvent of low ionizing power.[22] The trend of increasing *tert*-butyl/methyl rate ratios, from 27 (**4**/**1**) to 82 (**7**/**2**) and to 92 (**10**/**5**), is in line with the increasing size of α-alkyl substituents in the substrate. The considerably large ratio for chloride in 97Hw (27) than in 80% ethanol (1.2) and than in p-nitrobenzoate in 80% acetone (4.36)[23] indicates the effect of the relief of B-strain is overshadowed by the intervention of nucleophilic solvent. Therefore, theoretical calculations would be useful to the study of solvolytic reactivities only if no significant solvent participation is involved. Indeed, our study on the regression analysis using limited data available for the calculated $D°$ (R^+Br^-) (by MM2) of corresponding bromides of **1**, **2**, **4**, and **5**[4] against log ks of solvolysis in 97Hw resulted in a linear relationship (R = 0.996),[24] although a random dispersion of data points was also found in the case of using log k's in 80E.

In conclusion, nucleophilic solvent participation is likely to be present in the solvolysis of tertiary chloro-

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[16] Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986; pp 298−308.

[17] A more recent work (Abboud, J.-L. M.; Castano, O.; Della, E. W.; Herreros, M.; Müller, P.; Notario, R.; Rossier, J.-C. *J. Am. Chem. Soc.* **1997**, *119*, 2262.) employing an elaborate method of gas-phase stability measurement and calculations at MP2/6-311G** level resulted in a larger slope (−0.492) and an excellent linear correlation between log k (solvolysis) against $\Delta G°$ for halide exchange in bridgehead carbocations.

[18] For example, see: Schneider, H.-J.; Becker, N.; Schmidt, G.; Thomas, F. *J. Org. Chem.* **1986**, *51*, 3602.

[19] For examples, see: (a) Richard, J. P.; Amyes, T. L.; Ventor, T. *J. Am. Chem. Soc.* **1991**, *113*, 5871. (b) Richard, J. P.; Jagannadham, V.; Amyes, T. L.; Mishima, M.; Tsuno, Y. *J. Am. Chem. Soc.* **1994**, *116*, 6706.

[20] For examples, see: (a) Liu, K.-T.; Chang, L.-W.; Chen, P.-S. *J. Org. Chem.* **1992**, *57*, 5741. (b) Kevill, D. N.; D'Souza, M. J. *J. Chem. Res., Synop.* **1993**, 174. (c) Takeuchi, K.; Ohga, Y.; Ushino, T.; Takasuka, M. *J. Phys. Org. Chem.* **1997**, *10*, 717.

[21] It was also supported by recent observations[5,9] of excellent linear relationships in the correlation analysis using the dual-parameter equation (Winstein, S.; Grunwald, E.; Jones, H. W. *J. Am. Chem. Soc.* **1951**, *73*, 2700), log $k = mY_{Cl} + lN_{OTs}$, for the solvolysis of **1**−**6** and **8**.

[22] For example, an azide salt effect was observed for the solvolysis of *tert*-cumyl chloride in 90% acetone (Liu, K.-T.; Chen, P.-S.; Hu, C.-R.; Sheu, H.-C. *J. Phys. Org. Chem.* **1993**, *6*, 122) but not in 50% aqueous trifluoroethanol (ref 19a).

[23] Lomas, J. S.; Luong, P. K.; Dubois, J.-E. *J. Org. Chem.* **1979**, *44*, 1647.

[24] Unpublished results from this laboratory.

alkanes, and it is advisable that experimental rate data obtained in solvent of very low nucleophilicity should be used for the study of correlation with calculated energy.

Experimental Section

Materials. Chlorides **3**, **6**, and **7** were obtained from the controlled chlorination[6] of the commercial available alcohol. The proton NMR spectrum (300 MHz) indicated a single isomer in harmony with the assigned structure in every case. Spectral grade ethanol was purified by using the conventional method.[25] Reagent-grade hexafluoro-2-propanol was used without further purification.[26]

Kinetic Measurements. Conductometric rate constants were measured as described previously.[27]

Calculations. The Spartan version 4.1 program on a Dec Alpha 3000/700 system was used for the ab initio calculations. MM3(94) calculations including conformational searches were carried out on a Risc 6000/3BT workstation.

Acknowledgment. We are indebted to the National Science Council for financial support of this research.

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(25) Perrin, D. D.; Armarogo, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.

(26) It was found in a preliminary study that the same result was obtained by using purified and unpurified hexafluoro-2-propanol, respectively.

(27) Liu, K.-T.; Tang, C.-S. *J. Org. Chem.* **1996**, *61*, 1523.