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Quantitative Treatment of Rate Enhancement Due to F-strain in the Solvolysis of (Z)-2-Ethylidene-1-adamantyl Mesylate and Halides[†]

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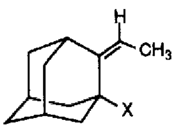
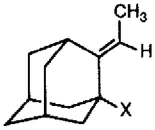
Abstract: *The Z:E rate ratios for the trifluoroethanolysis at 25 °C of the title mesylate, chloride, bromide, and iodide are 126, 1020, 2230, and 9680, respectively, whose logarithms are linearly correlated with MM2 steric energies and Hansch's Es values.*

Establishment of quantitative relations between reactivity and steric effects is one of important goals in physical organic chemistry.[1] Recent progress in molecular mechanics calculations achieved a great success in explaining various rate data of solvolysis on the steric basis.[2] However, the effect of leaving group strain (F-strain) in enhancing solvolytic reactivity has not necessarily been well studied. Most of the studies have emphasized marked F-strain in sulfonates or p-nitrobenzoates and its unimportance in halides or alcohols;[3] the F-strain effect of a leaving group atom directly attached to the reaction center has been taken as unimportant. Only the work reported by Brown and Stern in 1950 is relevant to the F-strain effect in halides.[4] They found that the rate ratio (R = t-Bu) : (R = Me) in the solvolysis of RMe_2C-X increases with the bulkiness of X in the manner 1.21 (X = Cl), 1.68 (X = Br), and 2.84 (X = I) in 80% ethanol at 25 °C.[4] These results show a small but definite trend supporting the leaving group strain effect.

Recently, we suggested that (*Z*)-2-ethylidenebicyclo[2.2.2]oct-1-yl[5] and (*Z*)-2-ethylidene-1-adamantyl[6] derivatives are good models to test the F-strain effect of a leaving group atom which is directly attached to the reaction center.[7] We now report a quantitative treatment of marked increases in F-strain effect for the trifluoroethanolysis of (*Z*)-2-ethylidene-1-adamantyl system as the leaving group is varied OMs, Cl, Br, and I.





X = OMs	(*Z*)-**1**-OMs	(*E*)-**1**-OMs
X = Cl	(*Z*)-**1**-Cl	(*E*)-**1**-Cl
X = Br	(*Z*)-**1**-Br	(*E*)-**1**-Br
X = I	(*Z*)-**1**-I	(*E*)-**1**-I

The synthesis and solvolysis of the mesylates and chlorides were reported previously.[6] The bromides were prepared by treating the corresponding alcohols with thionyl bromide.[8] Attempts to iodinate the alcohols with

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[†] This work is respectfully dedicated to Professor Emeritus Herbert C. Brown on the occasion of his 80th birthday.

P_2I_4[9] or Me_3SiI[10] failed; therefore, a new route was developed.[11] Acylative ring-expansion of noradamantane-3-carbaldehyde (**2**) with benzoyl triflate[12] followed by the addition of n-$Bu_4N^+I^-$ to the reaction mixture gave 1-iodo-2-adamantyl benzoate (**3**). Reduction of **3** with $LiAlH_4$ followed by oxidation of **4** with pyridinium chlorochromate afforded 1-iodo-2-adamantanone (**5**). The Wittig ethylidenation of **5** gave (*Z*)-2-ethylidene-1-adamantyl iodide [**(Z)-1-I**].[13] The hydrochlorination of **(Z)-1-I** with HCl gas gave **6**, which was then dehydrochlorinated with DBU to give **(*E*)-1-I**.[14] The rates of trifluoroethanolysis of the bromides and iodides were determined in the presence of 2,6-lutidine. The results are summarized in Table 1, together with previously reported data for the mesylates and chlorides. Each substrate gave only the corresponding bridgehead trifluoroethyl ether.

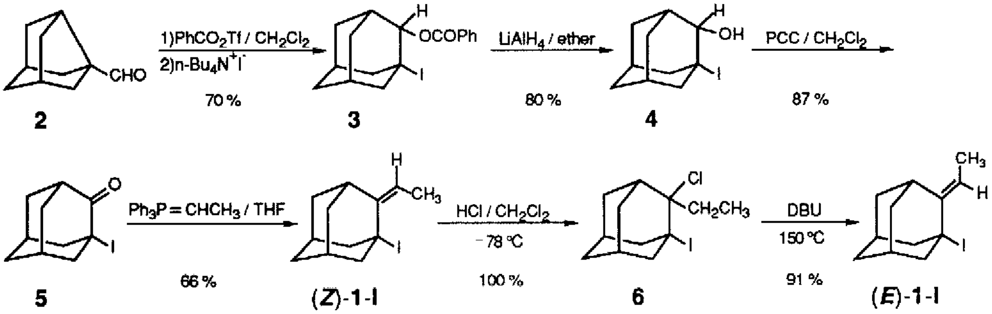


Table 1. The Rates, *Z*: *E* Rate Ratios, and Activation Parameters for the Solvolysis of 2-Ethylidene-1-adamantyl Derivatives in 2,2,2-Trifluoroethanol at 25 °C [a]

compound	temp (°C)	k (s^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal $mol^{-1}deg^{-1}$)	*Z*: *E* rate ratio at 25 °C
(Z)-1-OMs	25	4.41×10^{-2} [b,c]	18.2	-3.7	126±3
(*E*)-1-OMs	25	3.51×10^{-4} [b,c]	20.9	-4.4	1
(Z)-1-Cl	25	3.95×10^{-6} [c,d]	19.5	-17.8	1020±160
(*E*)-1-Cl	25	3.86×10^{-9} [c,d]	23.4	-18.5	1
(Z)-1-Br	25	2.50×10^{-4} [b,e,f]	18.5	-13.0	2230±90
(*E*)-1-Br	25	1.12×10^{-7} [d,g]	22.4	-15.1	1
(Z)-1-I	25	9.78×10^{-4} [b,h]	20.2	-4.5	9680±400
(*E*)-1-I	25	1.01×10^{-7} [d,i]	24.1	-9.7	1

a) The rates were determined for 2×10^{-4} or 2×10^{-2}M substrate in the presence of 1.2×10^{-3} or 2.5×10^{-2}M 2,6-lutidine in conductimetric or titrimetric measurement, respectively. b) Determined conductimetrically within an experimental error ±1.0%. c) See ref. 6. d) Extrapolated from data at other temperatures which were determined titrimetrically within an experimental error ±1.5%. e) 1.17×10^{-3} s^{-1} at 40 °C. f) A titrimetric measurement gave 2.55×10^{-4} s^{-1}. g) 2.25×10^{-6} s^{-1} at 50 °C; 2.99×10^{-5} s^{-1} at 75 °C; 2.75×10^{-4} s^{-1} at 100 °C. h) 5.26×10^{-3} s^{-1} at 40 °C. i) 2.48×10^{-6} s^{-1} at 50 °C; 4.19×10^{-5} s^{-1} at 75 °C; 4.27×10^{-4} s^{-1} at 100 °C.

First, a plot of log k values for **(*E*)-1-X**'s against those for the corresponding 1-adamantyl compounds in 97% TFE[15] gives a good linear correlation with a slope 1.0 (Fig. 1), indicating essential absence of extra F-strain effect in **(*E*)-1-X**'s. In contrast, the points for **(Z)-1-X**'s scatter, supporting the development of F-strain.

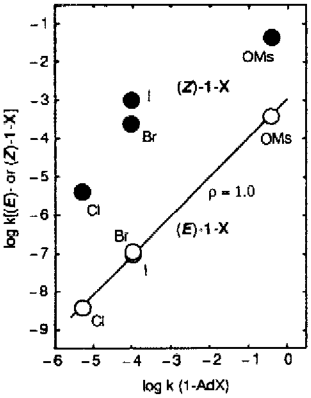


Fig. 1. Plot of log k for **1-X** in TFE vs. log k for 1-AdX in 97% TFE at 25 °C.

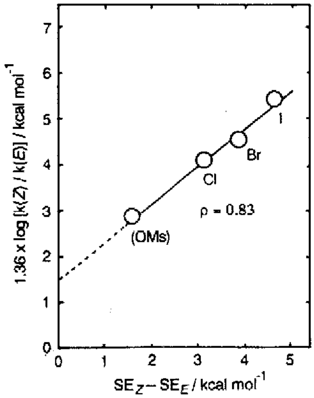


Fig. 2. Plot of 1.36 x log[k(*Z*)/k(*E*)] vs. steric energy difference (SE_Z - SE_E).

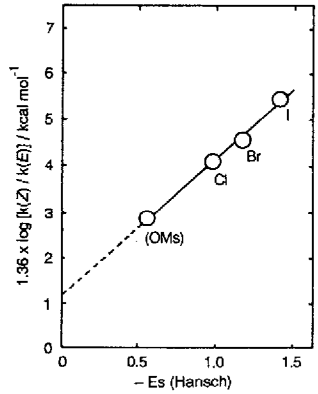
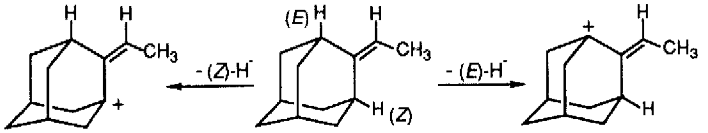


Fig. 3. Plot of 1.36 x log[k(*Z*)/k(*E*)] vs. Hansch's Es.

Secondly, 1.36 x log[k(*Z*)/k(*E*)] values are linearly correlated with the MM2 steric energy differences between the *Z* and *E* isomers (SE_Z - SE_E) with a slope 0.83 (Fig. 2).[16] This indicates that a change in the SE_Z - SE_E value on changing the leaving group is very close to the change in the $\Delta G^{\ddagger}$ difference between the two isomers.[17] Close inspections of steric energies have revealed that the greater steric energies of the *Z* isomers are primarily ascribed to the van der Waals repulsions between the (*Z*)-methyl and the leaving group atom directly attached to the reaction center and thereby induced deformation of the skeleton. The intercept value of 1.5 kcal mol^{-1}, or 1.2 kcal mol^{-1} when only the halides data are employed, should be taken as meaningful and not due to inherent errors in MM2 calculations. The values suggest that the hypothetical heterolysis of 2-ethylideneadamantane (Scheme 1) would be more favorable by 1.2 ~ 1.5 kcal mol^{-1} for the bridgehead hydrogen at the *Z* position than that at the *E* position.[18] MM2 calculations on 2-ethylideneadamantane have indicated that the van der Waals repulsion between the methyl group and the (*Z*)-hydrogen is greater than that between the vinylic hydrogen and the (*E*)-hydrogen by 0.6 kcal mol^{-1}. This energy difference can account for 40 - 50% of the intercept value.



Scheme 1

Thirdly, a plot of 1.36 x log[k(*Z*)/k(*E*)] values against Hansch's Es values[19] is also nicely linear (Fig. 3). Since Hansch's Es scale is a function of the average radius of substituent, the linear correlation in Fig. 3 reinforces the notion that the major origin of the large *Z*:*E* rate ratios is F-strain. Moreover, the intercept value corresponding to the hydride leaving group (Es = 0) is 1.2 kcal mol^{-1}, or 1.0 kcal mol^{-1} when only the halides data are employed, in good agreement with that obtained in Fig. 2.

In conclusion, marked F-strain effects in halides solvolysis were realized for the first time by using (*Z*)-2-ethylidene-1-adamantyl derivatives, and the rate data were satisfactorily interpreted in terms of MM2 calculations and Hansch's Es values. However, there remains a possibility that the transition state for the *Z* isomers might be more stable than that of the *E* isomers by 1 ~ 1.5 kcal mol^{-1} .

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8. **(Z)-1-Br**: mp 58.5-59.0 °C; ^{13}C NMR ($CDCl_3$) δ 14.0, 32.3, 35.2, 38.4, 47.1, 52.6, 67.4, 116.1, 143.7. **(*E*)-1-Br**: mp 27.0-27.5 °C; ^{13}C NMR ($CDCl_3$) δ 12.4, 32.4, 34.6, 35.2, 37.3, 51.8, 72.8, 115.7, 144.9.
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11. All the intermediate compounds **3-6** gave satisfactory microanalytical and spectral data. **3**: mp 118.5-119.0 °C; **4**: mp 58.5-59.0 °C; **5**: mp 116.0-117.0 °C; **6**: mp 67.0-68.0 °C.
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13. The *Z*: *E* ratio in the Wittig ethylidenation was 95 : 5. **(Z)-1-I**: mp 25.0-26.0 °C; ^{13}C NMR ($CDCl_3$) δ 14.1, 33.2, 35.4, 38.6, 47.7, 48.7, 56.7, 116.5, 144.7.
14. The *E*: *Z* ratio in the dehydrochlorination was $\geq$99 : $\leq$1. **(*E*)-1-I**: mp 24.0-25.0 °C; ^{13}C NMR ($CDCl_3$) δ 12.9, 33.3, 34.4, 35.3, 37.5, 55.3, 61.8, 120.4, 146.3.
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16. The MM2(87) program was obtained from QCPE. For obtaining the steric energy difference between **(Z)-1-OMs** and **(*E*)-1-OMs**, the corresponding alcohols were used as surrogates by assuming *anti* conformation of the hydroxyl group. Calculations on the ethyl ethers also gave similar results. The details will be reported in a full paper.
17. The less negative $\Delta S^{\ddagger}$ values for the *Z* isomers than those for the *E* ones indicate less solvation in the more congested *Z* isomers. By the compensation effect this should result in greater $\Delta H^{\ddagger}$ than expected when $\Delta S^{\ddagger}$ values are identical. Therefore, we used $\Delta G^{\ddagger}$ values for evaluation of the F-strain effect.
18. In other words, it is suggested that the transition state from the *Z* isomers is more stable than that from the *E* isomers by 1.2 ~ 1.5 kcal mol^{-1}. Calculations on the cations are in progress in this laboratory.
19. Kutter, E., Hansch, C. *J. Med. Chem.* **1969**, *12*, 647-652; Unger, S. H., Hansch, C: Quantitative Models of Steric Effects. In *Progress in Physical Organic Chemistry*; Taft, R. W. Ed.; Wiley-Interscience: New York, 1976; *12*, pp. 91-118. As an Es value for the methanesulfonyloxy group was employed that of the ethoxy group.

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