Extremely Large Acceleration of the Solvolysis of 1-Adamantyl Chloride upon Incorporation of a Spiro Adamantane Substituent: Solvolysis of 1-Chlorospiro[adamantane-2,2′-adamantane]

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Front strain (F-strain),[1,2] involving the (*Z*)-methyl group and the leaving atom directly attached to the reaction center, has been proposed to significantly accelerate the solvolysis of (*Z*)-2-ethylidene-1-adamantyl derivatives.[3,4] The (*Z*)-isomer of the chloride was shown[4] to solvolyze in 2,2,2-trifluoroethanol (TFE) at 25 °C about 10^3 times faster than the corresponding (*E*)-isomer, which solvolyzed only about 6 times faster than 2-methylene-1-adamantyl chloride.

In a consideration of candidates which might show further increases in the amount of F-strain for a 2-substituted-1-adamantyl halide, MM2 calculations indicate that 1-substituted derivatives of spiro[adamantane-2,2′-adamantane], simplified to [1]diadamantane in terminology developed by Schleyer,[5] will demonstrate an appreciable interaction between the 1-substituent and the closest methylene hydrogens of the nonsubstituted adamantyl unit. Qualitative support for this proposal comes from the report[6] that the 1-bromo derivative undergoes hydrolysis on standing in air, to give the corresponding 1-hydroxy derivative, indicating a considerable increase in reactivity relative to the rather unreactive[7,8] 1-adamantyl bromide.[9]

We report a study of the specific rates of solvolysis of 1-chloro[1]diadamantane (**1**), prepared by the reaction of 1-hydroxy[1]diadamantane[6,10] with thionyl chloride.[11] Compound **1** is so reactive that the specific rates, as obtained by titration of the extent of developed acid,[12] could be determined, even at 0 °C, only in solvents less ionizing than 80% ethanol. Indeed, the specific rates of solvolysis are extremely similar to those for 1-bicyclo[3,3.3]undecyl (1-manxyl) chloride (**2**), a bridgehead chloride whose unusually high reactivity was explained on the basis of a relief of angle strain during carbocation formation.[13] The ratio of the specific rates of solvolysis of **1** relative to **2** in 80% acetone at 0.0 °C is 0.62, with the *k*(**2**) value estimated from the reported[13] specific rate and enthalpy of activation data, and the corresponding *k*(**1**)/*k*(**2**) values for solvolyses in 80% ethanol are 0.67 at 0.0 °C and 1.12 at 25.0 °C. The specific rates obtained are reported in Table 1, together with Grunwald−Winstein Y_{Cl} values.[8,14,15]

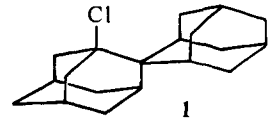

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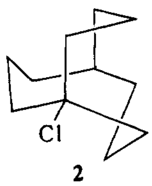
Table 1. First-Order Rate Coefficients for the Solvolysis of 1-Chloro[1]diadamantane (**1**) in Pure and Binary Solvents at 0.0 °C and Y_{Cl} Values

solvent[a]	10^4k, s^{-1}	Y_{Cl}[b]
100% EtOH[c,d]	2.10 ± 0.05	−2.52
95% EtOH[c]	10.5 ± 0.3	−1.61
90% EtOH[c]	35.9 ± 2.0	−0.94
20T−80E[c]	18.8 ± 0.7	−1.42
100% MeOH[c]	68.7 ± 1.5	−1.17
95% acetone	0.236 ± 0.004	−3.19
90% acetone[e]	2.32 ± 0.05	−2.22
80% acetone	34.1 ± 1.8	−0.83

[a] Mixed solvents on a volume−volume basis at 25.0 °C and with water as the other component, except for the TFE−EtOH (T−E) mixture; all runs performed at least in duplicate. [b] Estimated as described in footnote 15. [c] Reactant solution obtained by addition at 0.0 °C of 1.0 mL of a *ca*, 0.08 M stock solution of **1** in acetone to 20.0 mL of the listed solvent. [d] Also 10^4k (s^{-1}) values (with standard deviation) of 1.14 ± 0.04 at −6.3 °C, 15.5 ± 0.5 at 15.0 °C, and 46.1 ± 1.5 at 25.0 °C; $\Delta H^{\ddagger}_{298}$ = 18,6 ± 0.7 kcal mol^{-1}, $\Delta S^{\ddagger}_{298}$ = −7.0 ± 2.5 eu. [e] Also 10^4k (s^{-1}) values (with standard deviation) of 0.85 ± 0.02 at −8.6 °C, 13.4 ± 0.3 at 15.0 °C, and 39.8 ± 1.5 at 25.0 °C; $\Delta H^{\ddagger}_{298}$ = 17.5 ± 0.2 kcal mol^{-1}, $\Delta S^{\ddagger}_{298}$ = −11.0 ± 0.8 eu.



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A Grunwald-Winstein correlation in the eight solvents (Figure 1) leads to a sensitivity toward changes in solvent ionizing power (*m* value) of 0.95 ± 0.10 [correlation coefficient (*r*) of 0.971]; neglect of the data for 100% methanol leads to values for *m* of 0,89 ± 0.06 and for *r* of 0.988. The specific rates can be compared to those for solvolysis of 1-adamantyl chloride, the large difference in rates requiring temperature and/or ionizing power extrapolations. Comparisons of this type are reported in Table 2. The specific rates of solvolysis are about 10^8 times larger for **1** than for 1-adamantyl chloride, with the fairly small variations in the ratio observed with changes in solvent ionizing power and temperature being consistent with the lower *m* value

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(11) 1-Chloro[1]diadamantane was synthesized by stirring 1-hydroxy-[1]diadamantane for 15 min with excess freshly distilled thionyl chloride at room temperature and then removing the residual thionyl chloride under vacuum: mp 141−142 °C; ^{13}C NMR δ 78.4 (CCl), 48.3 (C_q), 46.3 (2 CH_2), 41.1 (CH_2), 37.1 (CH_2), 35.8 (CH), 33.8 (2 CH_2), 33.5 (2 CH_2), 31.7 (2 CH), 31.5 (2 CH), 30.3 (2 CH_2), 27.7 (CH), 27.0 (CH). Anal. Calcd for $C_{19}H_{27}Cl$: C, 78.45; H, 9.36; Cl, 12.19. Found: C, 78.45; H, 9.37; Cl, 12.29.

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(15) The required negative Y_{Cl} values have been estimated from the equation $Y = 0.38N_T + 0.86\,Y_{Cl} + c$, where *c* is the residual value applicable to the appropriate aqueous−organic system (Kevill, D. N.; D'Souza, M. J. *J. Chem. Res., Synop.* **1993**, 174). Where the Y_{Cl} values have also been obtained by extrapolation of a plot against *Y* values (refs 8 and 14), there is excellent agreement.

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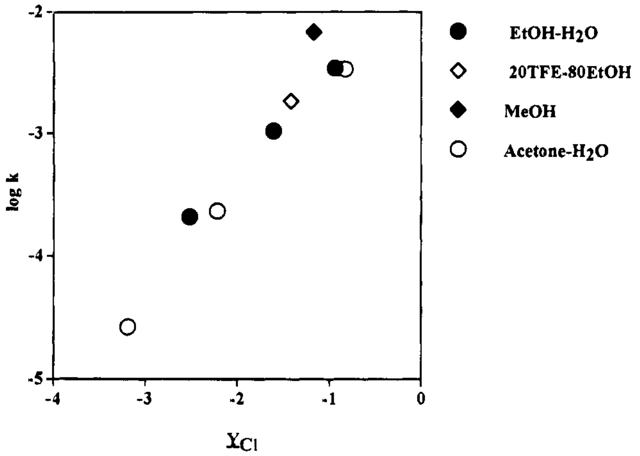

Figure 1. Grunwald–Winstein correlation of the specific rates of solvolysis of **1** at 0.0 °C against Y_{Cl} values.

Table 2. Comparisons of the Specific Rates of Solvolysis of 1-Chloro[1]diadamantane, *k*(**1**), and 1-Chloroadamantane, *k*(1-AdCl)

solvent	*T*, °C	10^4k(**1**), s^{-1}	$10^{12}k$(1-AdCl), s^{-1}	*k*(**1**)/*k*(1-AdCl)
100% EtOH	25.0	46^a	27^b	1.7×10^8
90% acetone	25.0	40^a	54^b	0.74×10^8
80% EtOH	25.0	4500^c	9100^d	0.54×10^8
80% EtOH	0.0	210^e	170^d	1.2×10^8

[a] Experimental value from footnotes to Table 1. [b] Calculated from Y_{Cl} value and k_0 value (80% ethanol) of 9.1×10^{-9} s^{-1} (refs 8 and 14). [c] From the value for 100% ethanol and assuming that the *m* value of 0.79 at 0.0 °C also applies at 25.0 °C. [d] From an Arrhenius plot extrapolation of data at higher temperatures (ref 8). [e] From intercept of Grunwald–Winstein plot of the four ethanol-containing solvents (Table 1) against Y_{Cl} values ($m = 0.79 \pm 0.06$, $r = 0.996$).

and enthalpy of activation (ethanolysis: 18.6 kcal mol^{-1} for **1** and 25.1 kcal mol^{-1} for 1-adamantyl chloride[8]) for solvolyses of **1** relative to solvolyses of 1-adamantyl chloride. The lower *m* value is consistent with the considerably reduced enthalpy of activation being reflected in an earlier transition state and, therefore, a reduced sensitivity toward changes in solvent ionizing power.

The range of solvolytic reactivities of bridgehead derivatives spans about 23 orders of magnitude,[16] from 1-manxyl[13] to 4-tricyclo[2.2.1.0^{2,6}]heptyl (4-nortricyclyl).[17] From the late 1960s onward,[18–20] attempts have been made to apply structure–reactivity relationships to the available data by means of molecular mechanics calculations on a suitable surrogate for the ground state and an ad hoc model of the carbocation intermediate. A unified data set was proposed[16] in which rate constants for a common leaving group, tosylate, under standard conditions (80% EtOH at 70 °C) were calculated from data for other leaving groups and conditions. This data set forms the basis of Müller's development of a carbocation force field;[20,21] for simplicity, the leaving group has been modeled not by OTs but by H, OH, Cl, Br,[22] and occasionally other groups.[20]

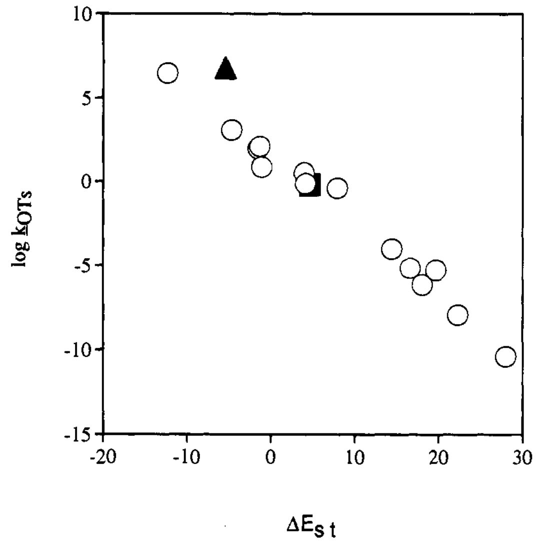

Figure 2. Plot of log k_{OTs} for solvolysis of bridgehead *p*-toluenesulfonate esters (70 °C, 80% EtOH) against ΔE_{st} (R^+–RCl); circles represent compounds 1, 2, 4, 6–8, 10–15, 17, and 18 of ref 16, the square represents compound 35 of ref 21 (1-homoadamantyl), and the triangle is the point for the 1-[1]diadamantyl tosylate.

To estimate the reactivity of 1-chloro[1]diadamantane by this procedure, we took 15 bridgehead structures covering the range from 1-norbornyl to 1-manxyl and plotted their log k_{OTs} values against the difference in the MMP2(85)[23] steric energies of the chloride and the cation (modeled by the UNICAT4 force field):[21] $\log k_{OTs} = 1.51 - 0.40\Delta E_{st}$ ($r = 0.991$). A k_{OTs} value of 5.8×10^6 s^{-1} (twice the value for 1-manxyl) was calculated for 1-[1]diadamantyl tosylate by extrapolation of the chloride rate constants in 80% EtOH (Table 2) to 70 °C and multiplying by 1.6×10^5, the generally accepted value for the OTs/Cl ratio.[16] Steric energies are 54.7 and 49.3 kcal mol^{-1} for the chloride and the cation, respectively, making ΔE_{st} −5.4 kcal mol^{-1}. The datum for the 1-[1]diadamantyl system therefore lies 3.1 log units above the regression line (Figure 2). Compared to the 1-adamantyl system (which is not very well correlated either) the 1-[1]diadamantyl tosylate is still $10^{1.8}$ times more reactive than predicted by the MM correlation.

The reason for this discrepancy cannot be the OTs/Cl factor, since the plot in the vicinity of [1]diadamantane is defined by chlorides. A more likely explanation is that the degree of F-strain present in 1-chloro[1]diadamantane is much greater than in any of the defining structures (note that *trans,trans,trans*-13-tricyclo[7.3.1.0^{5,13}]tridecanyl *p*-nitrobenzoate shows F-strain, but not the chloride[24]) and its reactivity is poorly modeled, with the force field for either the chloride or the cation (or both) being inadequate. Molecular mechanics ignores the hyperconjugative stabilization in carbocations and the associated geometrical changes,[20] but, paradoxically, this does not appear to have hindered its application to bridgehead reactivity correlation. Nevertheless, in this highly atypical structure it is conceivable that factors other than strain are involved.

To summarize, molecular mechanics calculations suggest that the extremely high solvolysis rate of 1-chloro[1]diadamantane, approximately 10^8 times that for 1-adamantyl chloride, is due very largely, but not entirely, to steric interactions between the chloride leaving group and the closest methylene hydrogens on the nonsubstituted adamantyl moiety. Studies involving extension to other leaving groups are underway and will be reported in due course.

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