

The Grunwald–Winstein relationship in the solvolysis of crowded tertiary alkyl chlorides. Hindered hydration and hydrophobic effect

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ABSTRACT: Various highly crowded tertiary alkyl chlorides having a neopentyl or a (1-adamantyl)methyl substituent on the reaction center were subjected to solvolysis rate studies, and the Grunwald–Winstein (GW) type relationship with respect to the Y_{Cl} scale was examined. Analyses of the plots showed that these bulky substituents efficiently preclude the nucleophilic solvent participation from the rear side and that the data points for non-aqueous protic solvents give linear GW type plots. On the other hand, increased crowding causes considerable downward dispersions of the data points in aqueous mixtures of ethanol, acetone and 1-propanol. The magnitude of the downward dispersion increases in this order, giving a curvature with a downward bulge in the GW type relationship. Aqueous mixtures of the smallest alcohol, methanol, on the other hand, give only slight downward dispersions of the data points, which constitute a linear GW type plot. These results can be explained in terms of two causes. First, structural crowding makes the transition state of ionization less susceptible to the Brønsted base-type hydration to the β -hydrogens than 1-chloroadamantane as the standard of the Y_{Cl} scale. Second, with highly hydrophobic substrates the first solvation shell in aqueous ethanol is expected to become more ethanol rich than the bulk phase, causing less easy ionization of the substrate. The rate data can be semiquantitatively analyzed by using Hansch's hydrophobicity parameters. The present anomalies found in solvolysis reactions are regarded as a kinetic version of Wepster's observations of the solvent effects on the magnitude of Hammett σ constants of bulky alkyl groups. Copyright © 2001 John Wiley & Sons, Ltd.

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KEYWORDS: solvolysis rate; tertiary alkyl chloride; steric congestion; solvent effect; Grunwald–Winstein relationship; solvation; hydrophobic effect

INTRODUCTION

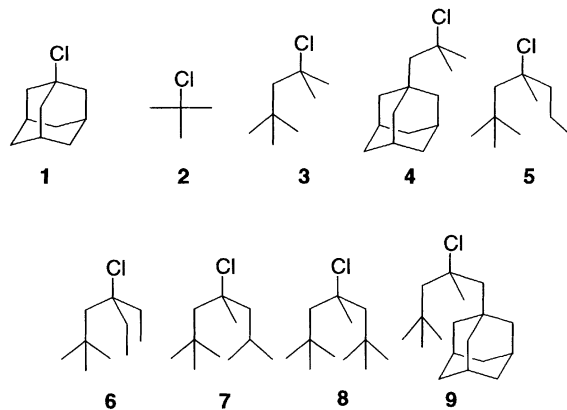
Tertiary chloroalkanes constitute a family of popular substrates in solvolysis studies.¹ However, systematic work related to the solvent effects on their solvolytic reactivities, in particular on the Grunwald–Winstein (GW) relationship, has been started only recently by the Liu's² and our³ groups. This paper presents a full account of the solvent effects in the solvolysis of various crowded tertiary chloroalkanes **3–9** in comparison with 2-chloro-2-methylpropane (**2**).

The GW relationship was originally proposed as a linear free energy relationship in solvolytic reactions as

represented by the equation

$$\log k/k_o = mY \quad 1$$

where k and k_o are the first-order rate constants of solvolysis of a given compound in a given solvent and in



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80% EtOH–20% H₂O (v/v) at 25.0 °C, respectively.⁴ As the reference compound **2** was selected, and the ionizing power of a solvent, *Y*, was defined by placing *m* = 1.00 for **2** in eqn (1).⁴

In 1970, Schleyer and co-workers noted that even **2** would be subject to nucleophilic solvent participation (NSP),^{5a} and in 1982, Bentley and co-workers redefined *Y*_{Cl} by using 1-chloroadamantane (**1**)^{5b,c} as the standard chloride whose rear side is geometrically precluded from NSP [Eqn. (2)]:

$$\log k/k_0 = mY_{\text{Cl}} \quad 2$$

They examined the GW type relationship of **2** against *Y*_{Cl} and found that the data points for water and aqueous mixtures of organic solvents fall upward with respect to those for fluorinated solvents, such as 2,2,2-trifluoroethanol (TFE), 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) and trifluoroacetic acid (TFA).^{5b} Recently, we reported that all the data points in many solvents examined for 2-chloro-2,4,4-trimethylpentane (**3**) are well accommodated by a single *mY*_{Cl} plot because the rear side of **3** is effectively shielded by the *tert*-butyl group.^{3a,c,d} We extended the study to the highly crowded 4-chloro-2,2,4,6,6-pentamethylheptane (**8**) and found that the data points of aqueous organic solvents come below those of non-aqueous solvents.^{3b} The result was interpreted as suggesting that the bulky *tert*-butyl groups inhibit not only the NSP toward the cationic center, but also the Brønsted base-type hydration toward the β-hydrogens in the transition state of ionization.^{3b} Further studies on the solvolysis of **8** revealed that a downward bulge was evident for the aqueous ethanol data points.^{3d} This phenomenon was ascribed to hydrophobic effects.^{3d}

This paper summarizes the accumulated rate data for the solvolysis of **3–9** and some additional rate data for **1** and **2**, and again emphasizes the important factors of the Brønsted base-type hydration and hydrophobic effects as the cause of dispersions of data points in the GW type relationship with respect to *Y*_{Cl}.

RESULTS

Substrates

The chlorides except for **5**, **7** and **9** were reported recently.⁶ The chlorides **5**, **7** and **9** were prepared from the corresponding known alcohols by hydrochlorination with HCl gas. The new precursor alcohol corresponding to **9** was obtained by treating 1-(1-adamantyl)-4,4-dimethyl-2-pentanone with methyllithium.

Solvolysis rates

1-Chloroadamantane (1). New *Y*_{Cl} values for some

Table 1. Rate constants of solvolysis for 1-chloroadamantane (**1**) in TFE–MeOH, TFE–DMSO, and 1-propanol–H₂O at 25.0 °C, and the corresponding *Y*_{Cl} values

Solvent ^a	<i>k</i> × 10 ⁵ (s ^{−1})	<i>Y</i> _{Cl} ^b
80T20M	0.0357 ^{c,d}	1.65
60T40M	0.0041 ^{e,f}	0.71
90T10D	0.0413 ^{c,g}	1.71
80T20D	0.00385 ^{c,h}	0.68
70P30W	0.0026 ^{e,i}	0.51
60P40W	0.0073 ^{e,j}	0.96

^a M, T, D, P and W denote methanol, 2,2,2-trifluoroethanol, dimethyl sulfoxide, 1-propanol, and water, respectively. The numbers mean volume-% of each component at 25.0 °C. The concentration of substrate was 0.020 mol dm^{−3}.

^b The *Y*_{Cl} values were calculated by using *k*₀ = 8 × 10^{−9} s^{−1} for 80E20W^{5b} and Eqn. (2) with *m* = 1.

^c Determined titrimetrically in a single run in the presence of 0.025 mol dm^{−3} 2,6-lutidine within an experimental error ±2%.

^d *k* = 7.54 × 10^{−6} s^{−1} (50.0 °C), 9.15 × 10^{−5} s^{−1} (75.0 °C); Δ*H*‡ = 22.3 kcal mol^{−1}; Δ*S*‡ = −13.2 cal mol^{−1} K^{−1}.

^e Extrapolated from data determined titrimetrically in the presence of 0.025 mol dm^{−3} 2,6-lutidine at other temperatures.

^f *k* = 1.05 × 10^{−6} s^{−1} (50.0 °C), 1.69 × 10^{−5} s^{−1} (75.0 °C); Δ*H*‡ = 24.3 kcal mol^{−1}; Δ*S*‡ = −11.0 cal mol^{−1} K^{−1}.

^g *k* = 1.05 × 10^{−5} s^{−1} (50.0 °C), 1.34 × 10^{−4} s^{−1} (75.0 °C); Δ*H*‡ = 23.3 kcal mol^{−1}; Δ*S*‡ = −9.6 cal mol^{−1} K^{−1}.

^h *k* = 9.63 × 10^{−7} s^{−1} (50.0 °C), 1.61 × 10^{−5} s^{−1} (75.0 °C); Δ*H*‡ = 24.3 kcal mol^{−1}; Δ*S*‡ = −11.0 cal mol^{−1} K^{−1}.

ⁱ *k* = 7.19 × 10^{−7} s^{−1} (50.0 °C), 1.33 × 10^{−5} s^{−1} (75.0 °C), 1.50 × 10^{−4} s^{−1} (100.0 °C); Δ*H*‡ = 25.0 kcal mol^{−1}; Δ*S*‡ = −9.4 cal mol^{−1} K^{−1}.

^j *k* = 2.08 × 10^{−6} s^{−1} (50.0 °C), 3.71 × 10^{−5} s^{−1} (75.0 °C), 4.38 × 10^{−4} s^{−1} (100.0 °C); Δ*H*‡ = 25.0 kcal mol^{−1}; Δ*S*‡ = −7.2 cal mol^{−1} K^{−1}.

binary solvent systems containing TFE and MeOH, TFE and DMSO, and 1-propanol and water were obtained by determining the solvolysis rates of **1** in these solvents. The results are summarized in Table 1.

2-Chloro-2-methylpropane (2) and 2-chloro-2,4,4-trimethylpentane (3). New rate constants of solvolysis of **2** were obtained in some binary solvent systems containing TFE and MeOH, TFE and DMSO, and 60% TFE–40% EtOH (60T40E), and are summarized in Table 2. Table 2 also gives some newly determined rate constants for **3** in 50% MeOH–50% water (50M50W) and three TFE–EtOH mixtures.

Other congested tertiaryl chloroalkanes (4–9). The rates of solvolysis for **4–9** were determined in various solvent systems and are summarized in Table 3. The rate of **8** in 80E20W has also been reported in the literature.⁷ Eleven out of 25 rate constants for the solvolysis of **8** in Table 3 were reported previously.^{3b}

Solvolysis products

Previously, we reported that the methanolysis of **3** at 50 °C gave the corresponding methyl ether and alkenes in

Table 2. Newly determined rate constants of solvolysis for 2-chloro-2-methylpropane (**2**) and 2-chloro-2,4,4-trimethylpentane (**3**) in TFE–MeOH, TFE–DMSO, 50% MeOH or TFE–EtOH at 25.0 °C

Solvent ^a	$k \times 10^5 \text{ (s}^{-1}\text{)}$	
	2	3
80T20M	2.11 ^{b,c}	—
60T40M	0.595 ^{b,d}	—
90T10D	2.12 ^{b,e}	—
80T20D	0.391 ^{b,f}	—
50M50W	^g	3520 ^h
60T40E	0.408 ^b	52.1 ^b
50T50E	^g	19.9 ^b
40T60E	—	7.45 ^b

^a E, M, T, D and W denote ethanol, methanol, 2,2,2-trifluoroethanol, dimethyl sulfoxide and water, respectively. The numbers mean volume % of each component at 25.0 °C. The concentration of substrate was 0.020 mol dm⁻³ in titrimetric runs or $(2\text{--}3) \times 10^{-4}$ mol dm⁻³ in conductimetric runs.

^b Determined titrimetrically in a single run in the presence of 0.025 mol dm⁻³ 2,6-lutidine within an experimental error $\pm 2\%$.

^c $k = 3.92 \times 10^{-4} \text{ s}^{-1}$ (50.0 °C); $\Delta H^\ddagger = 21.8 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -6.9 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^d $k = 1.18 \times 10^{-4} \text{ s}^{-1}$ (50.0 °C); $\Delta H^\ddagger = 22.3 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -7.7 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^e $k = 4.16 \times 10^{-4} \text{ s}^{-1}$ (50.0 °C); $\Delta H^\ddagger = 22.2 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -5.5 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^f $k = 8.90 \times 10^{-5} \text{ s}^{-1}$ (50.0 °C); $\Delta H^\ddagger = 23.3 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -5.0 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^g See Table S1 in Supplementary Material.

^h Determined conductimetrically in the absence of a buffer within an experimental error of $\pm 1\%$.

26 and 74% yields, respectively.^{3c} In the methanolysis of **4** the yields of the methyl ether and alkenes were 30 and 70%, respectively, at 25 °C (Scheme 1). With increase in crowding, the yield of methyl ether decreased; **6** (at 50 °C) and **8** (at 25 °C) gave the corresponding methyl ether in 12 and 6% yields, respectively. In the less nucleophilic solvent TFE the substitution product was formed in 1% or less yield from **6** and **8**.

DISCUSSION

The Grunwald–Winstein (GW) type relationship

As mentioned above, Bentley and Carter found that the GW type plot for 2-chloro-2-methylpropane (**2**) against Y_{Cl} showed dispersions of the data points for fluorinated solvents below the aqueous ethanol, aqueous methanol and aqueous acetone data points.^{5b} The faster rates of solvolysis of **2** in aqueous organic solvents such as EtOH–H₂O, MeOH–H₂O, TFE–H₂O and acetone–H₂O than expected from fluorinated solvent data points were ascribed to nucleophilic assistance to ionization in aqueous solvent mixtures.^{5b}

We carefully examined the data points for fluorinated solvents and further added some data points for the solvents as shown in Table 2. In consequence, it turned

out that all the data points for non-aqueous solvents with the exception of formic acid are well accommodated by a single straight line with $m = 0.58$ ($r = 0.9967$) (Fig. 1).^{3d} The magnitude of this value is considerably smaller than the m values (0.73–0.77) for the other crowded compounds **3–9** employed in this work. This can be ascribed to the greater NSP of ethanol and methanol than the fluorinated solvents. It should also be noted that the methanol data point deviates slightly upwards (Fig. 1). The non-aqueous solvent systems, which we concluded could be accommodated by the single linear relation, include 97HFIP, TFA, TFE, TFE–EtOH, TFE–MeOH, TFE–DMSO, AcOH, MeOH and EtOH. In this respect, the marked upward deviation of the formic acid data point suggests a significant contribution to cation stabilization, which deserves careful examination

The upward deviations of the data points for aqueous solvent mixtures are obviously caused by the very fast rate of **2** in water ($Y_{\text{Cl}} = 4.57^{5b,c}$). Clearly, the problem is focused on the question of why water accelerates dramatically the solvolysis of **2** as compared with **1** (see below). It should also be pointed out that the aqueous methanol data points are linear whereas the aqueous ethanol and aqueous acetone lines show a slight upward bulge.

In contrast, all the data points for the solvolysis of **3** in both aqueous and non-aqueous solvents are well accommodated by a single straight line (Fig. 1). Liu and co-workers reported that 3-chloro-3-isopropylpentane and 3-*tert*-butyl-3-chloropentane behave similarly to **3** in the GW relationship.² Phenomenologically, this would have been caused by the close approach of the water data point to the non-aqueous line. Most of the solvolysis rates used for the plots in Fig. 1 are reported ones; all the data are summarized in Table S1 in the Supplementary Material.

The linear behavior of the GW relationship for **3** suggested that compounds **4–9** having greater congestion would also behave similarly. Figures 2 and 3 show the GW plots for **4–6** and **7–9**, respectively. There are a few new phenomena that have not been noted before in this field, as follows.

(1) In the GW plots of **4**, **5**, **6** (Fig. 2) and **7** (Fig. 3), the aqueous methanol data points are nearly accommodated by the linear correlation for non-aqueous solvents. Since the aqueous methanol lines are essentially linear, the water data point would fall on the non-aqueous line. On the other hand, the aqueous ethanol and aqueous acetone data points fall below the non-aqueous line. Obviously, these aqueous solvent mixtures show a curvature with a downward bulge.

(2) In the highly crowded compounds **8** and **9**, the deviation of the aqueous ethanol, aqueous acetone and two aqueous 1-propanol data points becomes enormous. In these compounds, the hypothetical water data points are supposed to fall below the non-aqueous line, since the aqueous methanol lines are almost linear. This is also

Table 3. Rate constants of solvolysis of congested tertiary chloroalkanes

Solvent ^a	Y_{Cl}^b	$10^5 k \text{ (s}^{-1}\text{) at 25.0}^\circ\text{C}$					
		4	5	6	7	8	9
100E	-2.5	0.800 ^{c,d}	1.17 ^c	1.26 ^c	3.92 ^c	21.7 ^c	37.7 ^c
90E10W	-0.9	7.78 ^c	10.1 ^c	11.4 ^c	31.8 ^c	156 ^e	233 ^e
80E20W	0.00	32.0 ^c	40.0 ^c	46.5 ^c	113 ^e	527 ^{e,f}	708 ^e
70E30W	0.8	93.7 ^e	124 ^e	144 ^e	318 ^e	1500 ^e	1760 ^e
60E40W	1.38	245 ^e	349 ^e	481 ^e	1070 ^e	4280 ^e	4190 ^e
50E50W	2.02			1600 ^e			
40E60W	2.75			9170 ^g			
100M	-1.2	7.64 ^c	11.9 ^c	13.9 ^c	39.3 ^c	202 ^e	370 ^e
90M10W	-0.2	39.6 ^e	61.3 ^e	70.7 ^e	174 ^e	955 ^e	1560 ^e
80M20W	0.67	164 ^e	207 ^e	319 ^e	703 ^e	3910 ^e	5280 ^e
70M30W	1.46	568 ^e	879 ^e	1130 ^e	2830 ^e	13900 ^{e,h}	21200 ^e
60M40W	2.07		2180 ^e		10500 ^e		
70A30W	0.17	34.7 ^e	51.0 ^c	55.4 ^e	135 ^e	596 ^e	684 ^e
50A50W	1.73	632 ^e	1040 ^e	1210 ^e	1910 ^e	6140 ^e	8280 ^e
40A60W	2.46			5130 ^g			
AcOH	-1.6					134 ⁱ	
100T	(2.83) ^j	7390 ^k	18800 ^k	15100 ^{k,l}		283000 ^{k,m,n}	
97T3W	2.83	8010 ^k					
70T30W	2.96	9800 ^k	13300 ^k	18700 ^{k,o}		227000 ^{k,m,p}	
50T50W	3.16	11100 ^k		19600 ^{k,m,q}			
80T20E	1.89 ^r	922 ^k	1630 ^k	2220 ^k	6750 ^k	43000 ^{k,m,s}	
60T40E	0.63 ^r	130 ^k	209 ^k	285 ^k	779 ^k	5100 ^k	10100 ^k
50T50E	0.16 ^r	46.9 ^k	81.9 ^k		299 ^k	1900 ^k	3540 ^k
40T60E	-0.48 ^r	22.0 ^k				691 ^k	1410 ^k
20T80E	-1.42 ^r					112 ^k	
80T20M	1.65 ^t					36600 ^{k,m,u}	
60T40M	0.71 ^t					5920 ^{k,v}	
90T10D	1.71 ^t					42800 ^{k,w}	
80T20D	0.68 ^t					5100 ^{k,x}	
70P30W	0.51 ^t					431 ^g	
60P40W	0.96 ^t					855 ^g	

^a E, M, A, T, D, P, and W denote ethanol, methanol, acetone, 2,2,2-trifluoroethanol, dimethyl sulfoxide, 1-propanol and water, respectively. The numbers mean volume % of each component at 25.0 °C, except for the T–W system, which is based on weight %. The concentration of substrate was 0.020 mol dm⁻³ in titrimetric runs or (2–3) × 10⁻⁴ mol dm⁻³ in conductimetric runs.

^b Quoted from Ref. 5c unless noted otherwise.

^c Determined titrimetrically in a single run in the presence of 0.025 mol dm⁻³ 2,6-lutidine within an experimental error ±2% unless noted otherwise.

^d $k = 2.05 \times 10^{-4} \text{ s}^{-1}$ (50.0 °C); $\Delta H^\ddagger = 24.2 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -0.5 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^e Determined conductimetrically in duplicate in the presence of 0.025 mol dm⁻³ 2,6-lutidine within an experimental error of ±1%.

^f A reported value is $5.25 \times 10^{-3} \text{ s}^{-1}$.

^g Determined conductimetrically in duplicate in the absence of 2,6-lutidine within an experimental error of ±1%.

^h $k = 0.0734 \text{ s}^{-1}$ (18.38 °C), 0.109 s^{-1} (22.5 °C), 0.136 s^{-1} (24.7 °C); $\Delta H^\ddagger = 16.2 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -8.1 \text{ cal mol}^{-1} \text{ K}^{-1}$.

ⁱ Determined in the presence of 0.025 mol dm⁻³ NaOAc.

^j The value of 97T3W was assumed.

^k Determined conductimetrically in duplicate in the presence of 0.00125 mol dm⁻³ 2,6-lutidine within an experimental error of ±1%.

^l $k = 0.0481 \text{ s}^{-1}$ (9.7 °C), 0.111 s^{-1} (20.5 °C); $\Delta H^\ddagger = 12.0 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -22.1 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^m Extrapolated from data at other temperatures.

ⁿ $k = 0.0547 \text{ s}^{-1}$ (-20.0 °C), 0.124 s^{-1} (-12.0 °C), 0.351 s^{-1} (-0.6 °C); $\Delta H^\ddagger = 12.5 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -14.4 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^o $k = 0.0459 \text{ s}^{-1}$ (12.1 °C), 0.111 s^{-1} (20.0 °C); $\Delta H^\ddagger = 17.8 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -2.3 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^p $k = 0.0575 \text{ s}^{-1}$ (-10.5 °C), 0.108 s^{-1} (-5.0 °C), 0.180 s^{-1} (-0.6 °C); $\Delta H^\ddagger = 15.5 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -4.8 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^q $k = 0.0454 \text{ s}^{-1}$ (9.0 °C), 0.0753 s^{-1} (14.0 °C), 0.120 s^{-1} (19.5 °C); $\Delta H^\ddagger = 14.6 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -12.9 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^r Ref.13a.

^s $k = 0.0537 \text{ s}^{-1}$ (5.0 °C), 0.0919 s^{-1} (10.0 °C), 0.204 s^{-1} (17.5 °C); $\Delta H^\ddagger = 16.6 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -4.6 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^t See Table 1.

^u $k = 0.0790 \text{ s}^{-1}$ (9.5 °C), 0.130 s^{-1} (14.3 °C), 0.216 s^{-1} (19.5 °C); $\Delta H^\ddagger = 15.9 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -7.1 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^v $k = 0.0288 \text{ s}^{-1}$ (18.3 °C), 0.0334 s^{-1} (19.7 °C), 0.0423 s^{-1} (22.0 °C); $\Delta H^\ddagger = 17.9 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -4.0 \text{ cal mol}^{-1} \text{ K}^{-1}$.

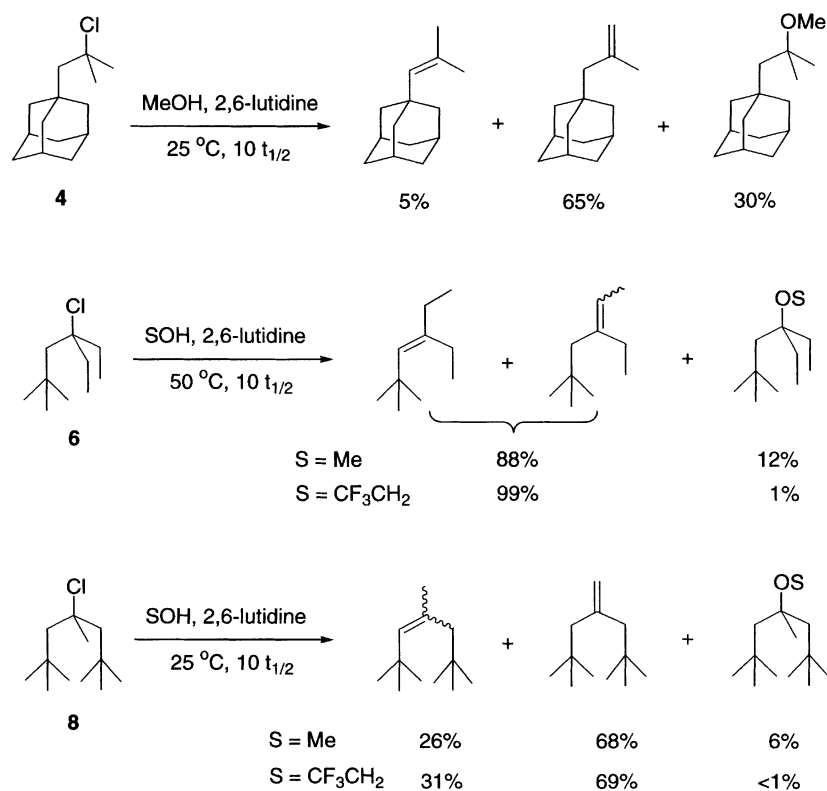
^w $k = 0.0973 \text{ s}^{-1}$ (10.5 °C), 0.215 s^{-1} (18.1 °C); $\Delta H^\ddagger = 16.6 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -4.6 \text{ cal mol}^{-1} \text{ K}^{-1}$.

^x $k = 0.0272 \text{ s}^{-1}$ (19.32 °C), 0.0328 s^{-1} (20.95 °C), 0.0406 s^{-1} (22.91 °C), 0.0594 s^{-1} (26.40 °C), 0.255 s^{-1} (40.00 °C); $\Delta H^\ddagger = 19.1 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger = -0.3 \text{ cal mol}^{-1} \text{ K}^{-1}$.

supported by the slower rate of **8** in 70T than in 100T despite the greater Y_{Cl} value of the former (2.96)^{5b,c} than the latter (2.83).^{5b,c}

The above two features appear to be characteristic of

highly alkyl-substituted substrates. It is suggested that **8** and **9** may be less nucleophilically assisted than the standard 1-chloroadamantane (**1**). We have found that 1-bromo-3,5,7-triisopropyladamantane (**10**) also shows



Scheme 1

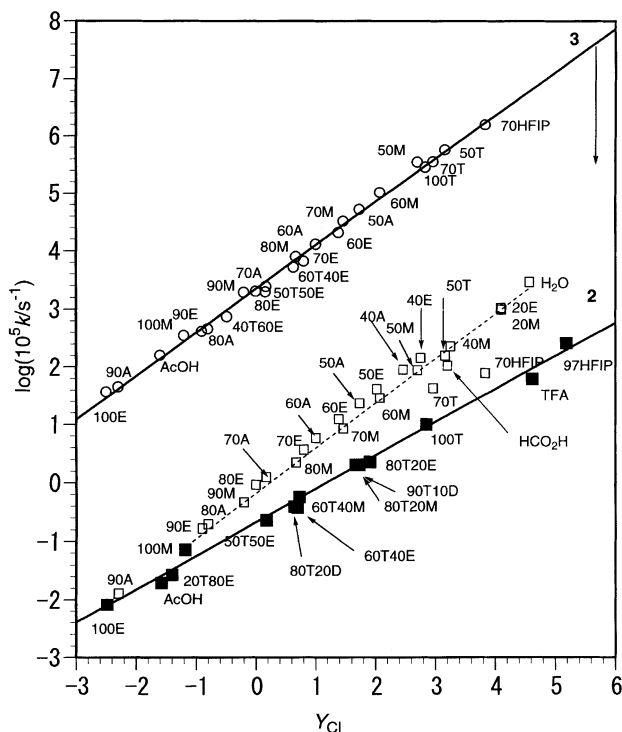
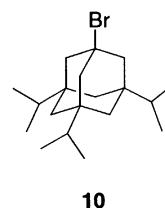


Figure 1. Grunwald–Winstein plots with respect to Y_{Cl} for the solvolysis of **2** and **3** at 25 °C. The points for **3** are shifted upward by 2 units for clarity. The m value for **2** in non-aqueous solvents is 0.58 ($r=0.9967$) and that for **3** in all solvents is 0.75 ($r=0.9977$)

very similar behavior in the GW plot.^{3d} We ascribe the downward positioning of the water data point below the non-aqueous solvent line and the bulge found for aqueous ethanol and aqueous acetone data points to different causes as discussed below.

Steric hindrance to Brønsted-base type hydration

1-Chloroadamantane (**1**) cannot be attacked by a nucleophile from the rear side. Therefore, the result that **1** is more susceptible to solvent nucleophilicity than **8** or **9** may be interpreted as a sign that **1** is more strongly solvated than **8** or **9** on the cation side in the transition state of ionization. In the early work by Bentley, and co-workers, they postulated that the NSP as indicated by using Eqn. (2) is considered to involve the interactions with both the reacting carbon atom and the hydrogen atoms, in particular the β -hydrogens.⁸ Recently, Richard *et al.* pointed out that Brønsted base-type solvation to β -



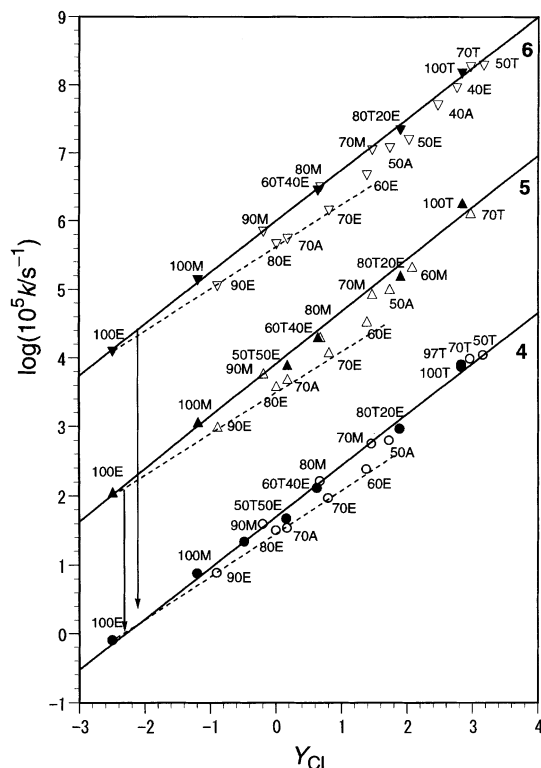


Figure 2. Grunwald-Winstein plots with respect to Y_{Cl} for the solvolysis of **4**, **5** and **6** at 25°C. The points for **5** and **6** are shifted upward by 2 and 4 units, respectively, for clarity. The m values for **4**, **5** and **6** in non-aqueous solvents are 0.74 ($r = 0.9976$), 0.76 ($r = 0.9959$) and 0.75 ($r = 0.9995$), respectively

hydrogens would be more important than nucleophilic assistance toward carbenium carbon in the ionization step of cumyl substrates.⁹ According to Monte Carlo and RISM calculations on the hydration of a $t\text{-Bu}^+\text{Cl}^-$ ion pair, the average primary hydration number is about 1 for carbenium carbon, but it amounts to 3 for each methyl group.¹⁰ The latter type of solvation to β -hydrogens in the transition state of ionization of **8** or **9** should be severely blocked owing to the presence of bulky *tert*-butyl or adamantyl groups. The downward positioning of the water points below the non-aqueous line may be ascribed to greater steric hindrance of hydration toward β -hydrogens in **8** or **9** than in **1**.

Dependence of curvature on substrate and solvent

Marked deviations with a curved shape in the GW type plot, which are observed for the solvolysis of crowded substrates in aqueous ethanol, aqueous acetone and aqueous 1-propanol (Figs. 2 and 3), call for caution and place a limitation on the use of these solvent systems. Aqueous methanol is a good solvent system in this respect, but poor solubilities of substrates restrict its wide

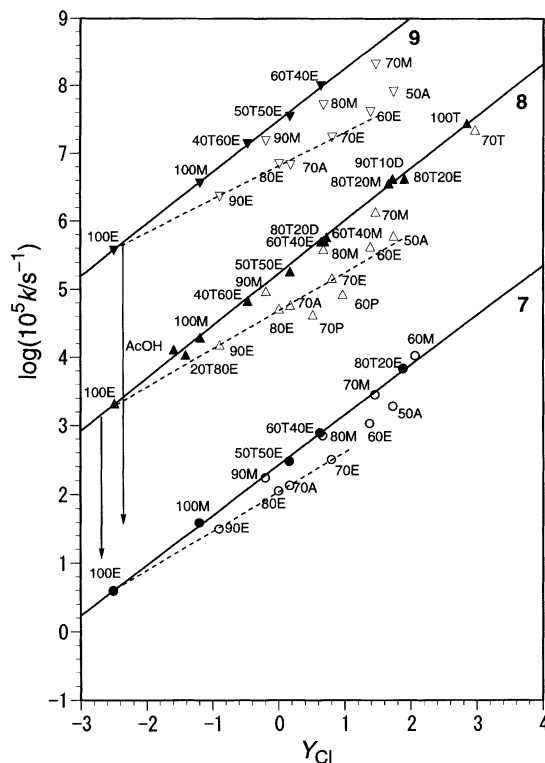


Figure 3. Grunwald-Winstein plots with respect to Y_{Cl} for the solvolysis of **7**, **8** and **9** at 25°C. The points for **8** and **9** are shifted upward by 2 and 4 units, respectively, for clarity. The m values for **7**, **8** and **9** in non-aqueous solvents are 0.73 ($r = 0.9994$), 0.77 ($r = 0.9987$) and 0.76 ($r = 0.9992$), respectively

use. Several factors could be behind the behavior of the solvents to give curvatures, including hydrophobic effects, changing cluster structure, possibility of solvent sorting or formation of water pools, difference in ground-state solvation between substrates, and even mechanistic differences between the crowded alkyl systems and standard 1-chloroadamantane (**1**). Among these possibilities, we prefer the hydrophobic effect (see below).

The marked curvatures of the plots of aqueous ethanol data (Figs. 2 and 3) stem from significant deviations from linearity in the $\log k$ vs water mole fraction ($f_{\text{H}_2\text{O}}$) plots [Fig. 4(a)]. More comprehensible plots are given in Fig. 4(b), where the deviations ($\Delta \log k$) in Fig. 4(a) are plotted against $f_{\text{H}_2\text{O}}$. The deviation increases in the order $2 < 1 \leq 3 < 6 < 8 < 9$.

We examined similar plots for aqueous methanol and TFE-EtOH systems, but the former showed only slight deviations of $< 0.2 \log k$ unit, and the latter gave an essentially linear plot of $\log k$ vs. TFE mole fraction as shown in Fig. 5 for **1**, **2**, **3** and **8**.

Hydrophobic effects

The deviation in the linear free energy relationship

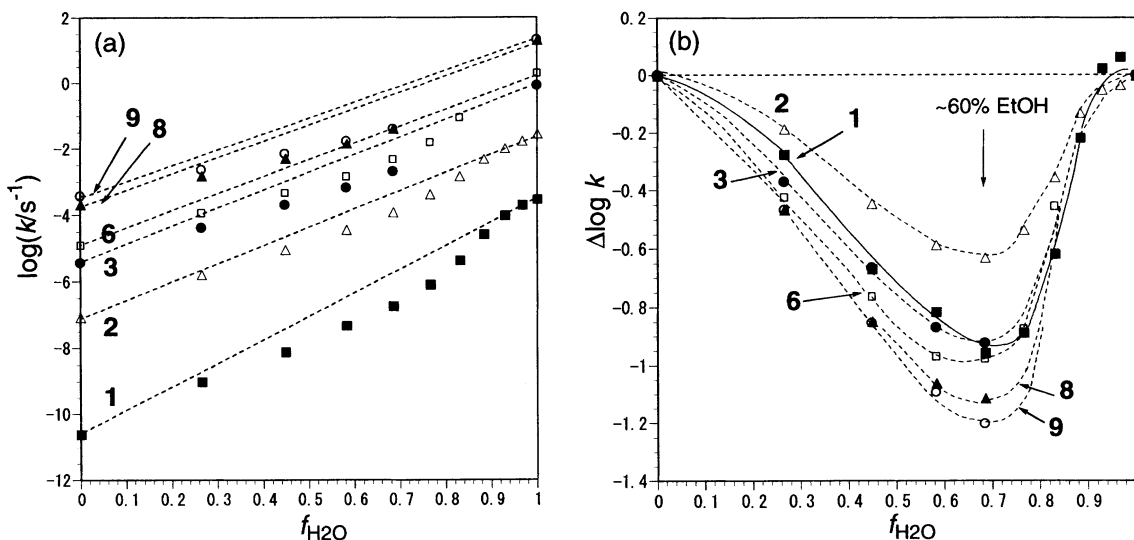


Figure 4. (a) Plots of $\log k$ against mole fraction of water in the solvolysis of **1**, **2**, **3**, **6**, **8** and **9** in EtOH–H₂O at 25 °C. The rate constants in water for **1** and **2** were taken from Refs 5b and 4, respectively, and those for **3**, **6**, **8** and **9** were estimated by extrapolation of the MeOH–H₂O data points to Y_{Cl} of water (4.57) in Figs 1–3. (b) Plots of deviations of $\log k$ from a straight line in Fig. 4(a) against mole fraction of water

caused by solvent effects has been reported in the Hammett rule. Hoefnagel and Wepster found that the Hammett σ constants of bulky alkyl groups, such as *tert*-butyl and 1,1-diethylpropyl (Et₃C), become significantly more negative (less ionizing) in aqueous ethanol or aqueous *tert*-butyl alcohol than in water, and the results were ascribed to the hydrophobic effect.¹¹ They applied Hansch's hydrophobic constant (π)¹² for substituents to improve the Hammett relationship in aqueous organic solvents.¹¹ The present results in solvolysis reactions constitute a kinetic version of Hoefnagel and Wepster's observations. We assume that the more alkylated the substrate, the more water molecules are expelled from the solvation shell. Presumably, the first solvation shell becomes more ethanol-rich than the bulk phase. This would lead to less easy ionization of the substrate.

We wished to examine semiquantitatively the sensitivity of hydrophobic effect in aqueous methanol and aqueous ethanol. Since the extent of downward deviation from the non-aqueous line indicates the magnitude of the hydrophobic effect, we examined the rates in 70E30W and 80M20W relative to that in 60T40E as a standard for each substrate. These solvent systems have similar respective Y_{Cl} values, 0.8,^{5b,c} 0.67^{5b,c} and 0.63^{13a} (Table 3). Therefore, the quantities defined by $\log(k_{70E}/k_{60T40E})$ and $\log(k_{80M}/k_{60T40E})$ may be regarded as a parameter of the hydrophobic effect exerted by 70E and 80M at a Y_{Cl} value of approximately 0.7. The magnitude of the hydrophobic effect with respect to the substrate structure may be evaluated by making a plot of $\log(k_{70E}/k_{60T40E})$ and $\log(k_{80M}/k_{60T40E})$ vs relative Hansch's hydrophobic constants ($\sum\pi$). We selected 2-chloro-2-methylpropane (**2**) as a standard ($\sum\pi = 0$), and the $\sum\pi$ values of other compounds were calculated by assuming the additivity of

π . For example, $\sum\pi$ of **6** was evaluated as 3.10 by considering that the three hydrogens of **2** were replaced by a *tert*-butyl ($\pi = 1.98$)¹² and two methyl ($\pi = 0.56$)¹² groups. Table 4 summarizes the $\sum\pi$, $\log(k_{70E}/k_{60T40E})$, and $\log(k_{80M}/k_{60T40E})$ values, and Fig. 6 shows the relationships between the two logarithmic rate ratios and $\sum\pi$.

A comparison of the slopes, -0.25 for 70E and -0.09 for 80M, indicates that the former solvent system is about 2–3 times more sensitive to the hydrophobicity of the substrate. The upward deviations of the values for **2** from the correlation lines in Fig. 6 would be ascribed to NSP

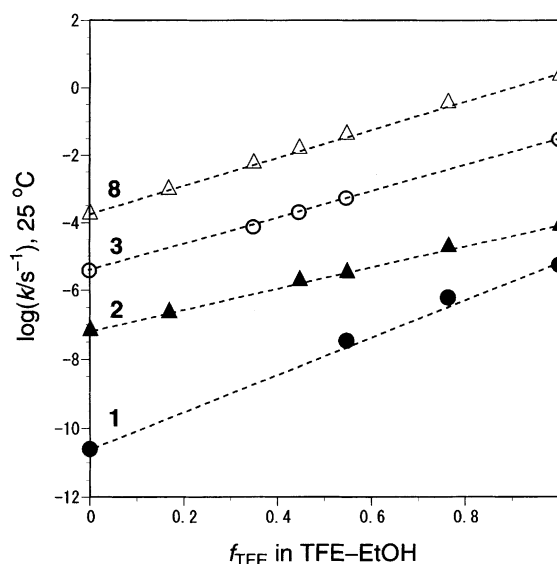


Figure 5. Plots of $\log k$ against mole fraction of TFE in the solvolysis of **1**, **2**, **3** and **8** in TFE–EtOH at 25 °C

Table 4. Total π ($\sum\pi$) relative to **2** and logarithmic rate ratios between the rate in 70% EtOH or 80% MeOH and that in 60% TFE–40% EtOH

Compound	$\sum\pi^a$	$\text{Log}(k_{70\text{E}}/k_{60\text{T40E}})^b$	$\text{Log}(k_{80\text{M}}/k_{60\text{T40E}})^b$
2	0	0.94	0.74
3	1.98	0.10	0.18
4	3.30	−0.14	0.10
5	3.00	−0.23	0.00
6	3.10	−0.30	0.05
7	3.51	−0.39	−0.05
8	3.96	−0.54	−0.12
9	5.28	−0.76	−0.28

^a Relative to **2**. For π , see Ref. 12.

^b For rate data, see Tables 2, 3 and S1.

including the Brønsted base-type solvation. Recently, Tada *et al.* reported the hydrophobic effects on the solvatochromism (E_T) in various aqueous organic solvents.¹⁴

Possibilities of differential ion-pair return or mechanistic change

Recently, Kevill and D'Souza^{13b} applied Eqn. (3) to a limited number of rate data^{3b} for **8** that we reported in 1997:

$$\log k/k_0 = mY_{\text{Cl}} + hI \quad 3$$

Equation (3) was originally developed to correct the charge delocalization to an aromatic ring,¹⁵ but it was also shown to be usable for correction of ion-pair return.¹⁶ Compounds **8** and **9** mainly give alkenes as solvolysis product. This means that the leaving group, once ionized, mainly attacks one of the neighboring hydrogen atoms, and the fraction of ion-pair return would be very small. On the basis of the fairly good fit of the plot, they suggested a possibility of reduced ion-pair return.^{13b} However, the behavior of **10** in the GW plot against $Y_{\text{Br}}^{5b,c}$ parameters, which is very similar to that of **8** and **9**,^{3d} lessens the possibility of reduced ion-pair return as a cause of deviations in the GW relationship in Figs 2 and 3.

It was also suggested by Bentley *et al.* that the unexpectedly slow rates of solvolysis of congested alkyl compounds in aqueous ethanol might be caused by mechanistic changes to concerted elimination.¹⁷ However, this possibility would be low since **10**, which cannot undergo the elimination reaction, also shows marked deviations in the GW relationship similarly to the congested substrates used in the present study.^{3d}

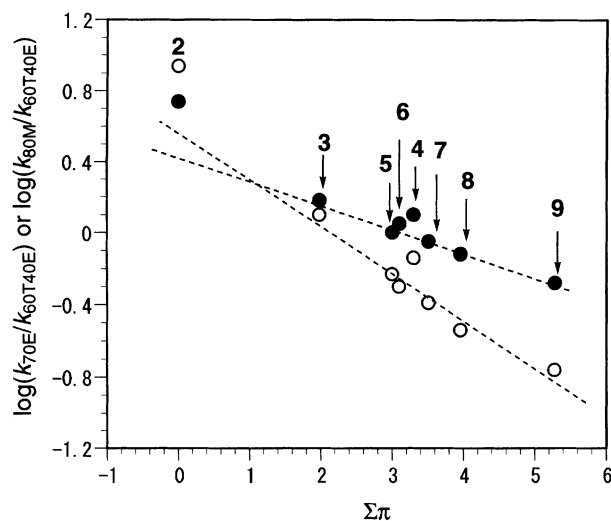


Figure 6. Plots of $\log(k_{70\text{E}}/k_{60\text{T40E}})$ (○) and $\log(k_{80\text{M}}/k_{60\text{T40E}})$ (●) values against $\sum\pi$ for the solvolysis of **2–9** at 25 °C

EXPERIMENTAL

Boiling and melting points are uncorrected. ¹H and ¹³C NMR spectra were recorded in CDCl₃ at 270 and 68 MHz, respectively. Medium-pressure liquid chromatography (MPLC) was conducted on Merck silica gel 60 (230–400 mesh). The known alcohols corresponding to **5** and **7** were prepared by treating 4,4-dimethyl-2-pentanone (Aldrich) with propylmagnesium bromide and isobutyllithium, respectively. Most of the solvolysis solvents were purified as described previously.¹⁸ 1-Propanol was distilled over CaH₂. DMSO was distilled over CaH₂ under reduced pressure. HFIP was dried over molecular sieves 3A and distilled. Solvent mixtures based on volume-% were prepared by mixing weighed components by using the following densities¹⁹ at 25 °C; water (0.99705), acetone (0.78440), ethanol (0.78493), methanol (0.78637), TFE (1.3686, an extrapolated value from 1.4106 and 1.3736 at 0 and 22 °C, respectively) and DMSO (1.09537).

1-(1-Adamantyl)-2,4,4-trimethyl-2-pentanol. 1-(1-Adamantyl)-4,4-dimethyl-2-pentanone²⁰ (1.59 g, 6.39 mmol) was treated with methylolithium (9.54 mmol) in diethyl ether. Usual work-up of the reaction mixture followed by MPLC [SiO₂, hexane–diethyl ether (97:3)] afforded the alcohol (1.63 g) in 96% yield. Colorless crystals, m.p. 55.5–56.5 °C. Found: C, 81.63; H, 12.41. C₁₈H₃₂O requires C, 81.75; H, 12.20%. δ_{H} , 1.03 (9H, s), 1.21 (1H, s), 1.36 (3H, s), 1.34 (1H, d, J 14.8 Hz), 1.39 (1H, d, J 14.8 Hz), 1.49 (1H, d, J 14.8 Hz), 1.53 (1H, d, J 14.8 Hz), 1.67–1.70 (12H, m), 1.89–1.98 (3H, m); δ_{C} , 28.9 (CH), 29.7 (CH₃), 31.6 (C), 31.8 (CH₃), 34.0 (C), 37.1 (CH₂), 44.2 (CH₂), 57.1 (CH₂), 58.7 (CH₂), 76.4 (C).

General procedure for the preparation of **5 and **7**.** The corresponding known alcohols (ca 1.5 g) were treated

with dry HCl gas in pentane at -40°C for 5–10 min. The solution was dried with a small amount of CaCl_2 , flushed with N_2 and filtered. Pentane was evaporated and the chloride was distilled under reduced pressure. The chlorides were used for rate studies without being subjected to microanalysis because of their instability.

4-Chloro-2,2,4-trimethylheptane (5). B.p. $42.0\text{--}42.5^{\circ}\text{C}$ at 6 mmHg. δH , 0.93 (3H, t, J 7.3 Hz), 1.05 (9H, s), 1.45–1.60 (2H, m), 1.63 (3H, s), 1.74–1.82 (2H, m), 1.85 (1H, d, J 15.2 Hz), 1.89 (1H, d, J 15.2 Hz); δC , 14.2 (CH_3), 18.2 (CH_2), 31.5 ($4 \times \text{CH}_3$), 32.3 (C), 48.8 (CH_2), 55.7 (CH_2), 75.8 (C).

4-Chloro-2,2,4,6-tetramethylheptane (7). B.p. 43.0°C at 4 mmHg. δH , 1.00 (6H, d, J 6.6 Hz), 1.06 (9H, s), 1.65 (3H, s), 1.68 (1H, dd, J 5.6, 14.8 Hz), 1.78 (1H, d, J 15.2 Hz), 1.79 (1H, dd, J 5.6, 14.8 Hz), 1.91 (1H, d, J 15.2 Hz), 1.89–2.00 (1H, m); δC , 25.0 (CH), 25.1 (CH_3), 31.4 (CH_3), 31.7 (CH_3), 32.3 (C), 55.4 (CH_2), 56.7 (CH_2), 75.8 (C).

1-(2-Chloro-2,4,4-trimethylpentyl)adamantane (9). The precursor alcohol (414 mg, 1.57 mmol) in CH_2Cl_2 was treated with dry HCl gas at -40°C for 2 min. The reaction mixture was treated with a small amount of CaCl_2 , flushed with N_2 , and filtered. Evaporation of the solvent afforded a yellow liquid, which was found by ^1H and ^{13}C NMR to contain three kinds of alkenes and **9** showing the chlorinated carbon at 76.0 ppm. The NMR spectra showed that **9** was present in about 40%, and no indication was found for the formation of other chloride isomers. All of the four *tert*-butyl signals and all the olefinic protons in ^1H NMR spectra were unambiguously assigned (see Supplementary Material). The mixture was used for rate studies without further purification.

General procedures for product studies. The solvolysis was conducted for a solution of 0.04 mol dm^{-3} substrate in the presence of 0.05 mol dm^{-3} 2,6-lutidine for 10 half-lives at appropriate temperatures. The reaction solution was mixed with saturated aqueous NaCl and successively extracted with pentane. The combined pentane layer was washed with saturated aqueous NaCl three times and dried (MgSO_4). The product distributions were determined by GLC (PEG 20M, $2\text{m} \times 3 \text{ mm}\phi$ id) for the extract, or by ^1H NMR for the crude product after distillation of pentane on a 30 cm Vigreux column.

Methanolysis of 1-(2-chloromethylpropyl)adamantane (4). GLC analyses showed the ratio between alkenes and the methyl ether to be 70:30. ^1H NMR analysis showed the formation of the *endo*-alkene [δH 4.84 (br s)] and the *exo*-alkene [δH 4.50 (m), 4.76 (m)] in a ratio of 5:65.

Methanolysis and trifluoroethanolysis of 4-chloro-4-ethyl-2,2-dimethylhexane (6). The product ratio be-

tween alkenes and substitution product was determined by GLC. The methoxyl ^1H signal appeared at δH 3.12. Detailed analysis of alkenes was not carried out.

Methanolysis and trifluoroethanolysis of 4-chloro-2,2,4,6,6-pentamethylheptane (8). The product ratios were determined by ^1H NMR. The methyl ether showed the methoxyl signal at δH 3.12. No indication for the formation of the trifluoroethyl ether was found. The ratio between the *endo*- (presumably a mixture of *Z*- and *E*-forms) and *exo*-alkenes was determined based on the respective signals at δH 5.11 (br s) and 4.79 (s).

Kinetic Methods. The titrimetric and conductimetric rate constants were determined as described previously.¹⁸

Supplementary Material

A table of the rate constants for **2** and **3** used for the plots in Fig. 1 and ^1H NMR spectra for **9** are available at the epoc website at <http://www.wiley.com/epoc>.

Acknowledgements

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