163. Polar Effects

Part 15

Twin γ-Substituent Effects in the Formation of Adamantyl-1-cations

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Solvolysis rates of several adamant-1-yl (= tricyclo[3.3.1.1^{3,7}]dec-1-yl) *p*-toluenesulfonates and bromides **2** identically substituted at C(3) and C(5) (twin substitution) have been determined and compared with the rates of the corresponding 3-monosubstituted compounds **1**. As expected, the rate factors for twin substitution are much larger, but less than the square of the rate factors for single substitution. Also the rate factors per substitutent in **2** are considerably smaller than those for one substituent in **1**. This attenuation is attributed to electron repulsion which limits the convergence of electron density to the cationic center. On the other hand, the inductivity for twin substitution ($\rho_I = -2.55$) is *ca.* twice as high as for mono-substitution ($\rho_I = -1.26$).

Four kinds of polar substituent effects are discernible in solvolysis reactions of 3-substituted adamant-1-yl (= tricyclo[3.3.1.1^{3,7}]dec-1-yl) bromides and tosylates *(= p-toluenesulfonates)* **1** (X = Br and OTs, resp.), namely inductive, hyperconjugative, frangomeric, and homohyperconjugative effects [1][2]. This follows from the reaction products and from the relationship between the rate constants *k* (in 80% EtOH) and the inductive constants σ_I^q [3] of the substituents. Alkyl groups and common electron-attracting substituents like $COOCH_3$, OAc, Br, CN, and NO_2 as well as *H*–C(3) control rates of formation of the adamant-1-yl cations **5** by their inductive (*I*) effects only, as shown by the linear correlation of log *k* with the corresponding σ_I^q values [1]. The latter were derived from the pK_a values of 4-substituted quinuclidinium perchlorates **4** [3] which are also controlled by *I* effects.

On the other hand, rates were 3 to 44 times higher than calculated from the regression line for log *k vs.* σ_I^q, when R was a $+M$ substituent or *n* electron donor such as OH, OCH_3, or SCH_3. These exalted polar substituent effects were attributed to C,C hyperconjugative relay of positive charge from the cationic center C(1) to the substituents in the incipient cations **6** (the dotted lines imply weak bonding interactions).

However, if the $+M$ effect of the substituents were stronger, as in **1** (R = NH_2, O^-, or S^-), C,C hyperconjugation merged with concerted fragmentation [4] and led to accelerated formation of the corresponding bicyclic compounds **8** (R = NH_2^+, O, or S, resp.). In these cases, formula **6** represents the transition state for fragmentation to **8**.

Finally, the rates of 3-substituted adamant-1-yl bromides and tosylates **1** were 4 to 26 times higher than predicted by their σ_I^q values for R = CH_2OH, $COO^\ominus$, or $(CH_3)_3Sn$ [1][2].

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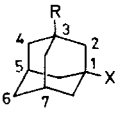
[1] According to the equation $\log k = \rho_I \cdot \sigma_I^q + \log k_0$.



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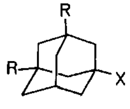

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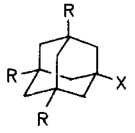

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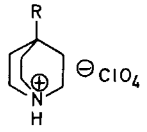

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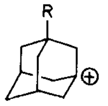
R =

a H
b CH_2OH
c CH_2OAc
d CH_2OTs
e $COOCH_3$
f $(CH_3)_3Si$



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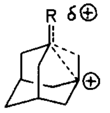

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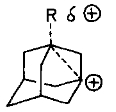

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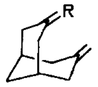

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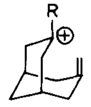

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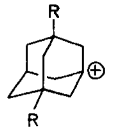

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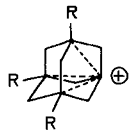

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These substituents are electrofugal and, hence, donate a σ electron pair in heterolytic fragmentation [4]. It was, therefore, concluded that they exert a homohyperconjugative effect, as illustrated in **7**[2])[3]).

A question that has apparently not been clearly answered pertains to the polar effects of two identical substituents located at the same distance and equally oriented with respect to the reaction center. Such 'twin substituents' are present in 3,5-disubstituted adamantanes **2**, where X is a nucleofuge such as Br or OTs[4]).

It has been known for some time that the successive introduction of CH_3 groups at the bridgehead positions 3, 5, and 7 of adamant-1-yl bromide, as in **1**, **2**, and **3** ($R = CH_3$, $X = Br$), respectively, reduces solvolysis rates by a factor of *ca.* 1.47 per CH_3 group [7]. This is contrary to what would be expected, if the corresponding adamant-1-yl cations were stabilized by hyperconjugation involving the β,γ-bonds, as illustrated (for one bond only) in **9**. On the other hand, the small $-I$ effect of a CH_3 group at sp^3-C-atom ($\sigma_I^q = 0.11$

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[2]) The same distinction between inductive, hyperconjugative, frangomeric, and homohyperconjugative effects can be made in solvolyses of 6-*exo*-substituted 2-*exo*-norbornyl tosylates [5].

[3]) Hyperconjugative and homohyperconjugative effects have recently been discussed by *Adcock* and *Kok* [6] in connection with substituent chemical shifts in the ^{19}F-NMR spectra of 3-substituted adamant-1-yl fluorides.

[4]) The structure **2** has a plane of symmetry through C(1), C(4), and C(7).

[3]) or steric hindrance to solvation at the bridgehead C-atoms could also account for the small rate decrease.

A stronger response of rate to multiple substitution is to be expected, when the substituents exert a larger *I* effect than CH_3. This is now shown to be the case for the 3,5-disubstituted adamant-1-yl tosylates **2b–e** (X = OTs). In 80% EtOH, these compounds reacted in a convenient temperature range. However, **1f** and **2f** (X = OTs) which contain electron-donating γ-Me_3Si substituents ($\sigma_I^q = -0.16$)[5]) were unstable and had to be replaced by less reactive bromides **1f** and **2f** (X = Br). In fact, *Shiner* and coworkers [8] have recently shown that γ-trimethylsilyl groups promote solvolysis by stabilizing the incipient carbenium ions.

The preparation and rate constants of the known 3-substituted adamant-1-yl tosylates **1b–e** (X = OTs) have already been reported [2]. The disubstituted analogs **2b–e** (X = OTs), however, were unknown and are described elsewhere [9]. On the other hand, the synthesis of the 3-mono- and 3,5-bis(trimethylsilyl)adamant-1-yl bromides, **1f** and **2f** (X = Br), respectively, presented insuperable difficulties, until a very mild method for the bromination of adamantane and its trimethylsilyl derivatives **1f** and **2f** (X = H) was found[6]).

The hydrolysis of all tosylates and bromides **1** and **2** (X = OTs and Br), respectively, in 70% dioxane afforded the corresponding adamantanols **1** and **2** (X = OH), respectively, in quantitative yield. The first-order rate constants (*Table 1*) were determined conductometrically [11]. Relative rates *k*(rel) and rate ratios **k2**/**k1** are listed in *Table 2*.

Table 1. *First-Order Rate Constants for 10^{-3}* M *Solutions of 3-Mono- and 3,5-Disubstituted Adamant-1-yl* (p-*Toluenesulfonates and Bromides,* **1** *and* **2**, *Respectively, in 80%* (v/v) *EtOH*[a])

	R	X	T[°]	*k***1**[s^{-1}]	*k***2**[s^{-1}]
a	H	OTs	70.00	$4.09 \cdot 10^{-1}$ [b])	$4.09 \cdot 10^{-1}$
b	CH_2OH	OTs	70.00	$2.61 \cdot 10^{-1}$ [b])	$1.12 \cdot 10^{-1}$
c	CH_2OAc	OTs	70.00	$2.21 \cdot 10^{-2}$ [b])	$1.68 \cdot 10^{-3}$
d	CH_2OTs	OTs	70.00	$6.88 \cdot 10^{-3}$ [b])	$1.51 \cdot 10^{-4}$
e	$COOCH_3$	OTs	70.00	$2.60 \cdot 10^{-3}$ [b])	$2.28 \cdot 10^{-5}$ [c])
			100.00		$4.39 \cdot 10^{-4}$
			110.00		$1.08 \cdot 10^{-3}$
			120.00		$2.47 \cdot 10^{-3}$
a	H	Br	70.00	$7.16 \cdot 10^{-5}$ [d])	
f	Me_3Si	Br	70.00	$6.15 \cdot 10^{-4}$ [b])	$2.36 \cdot 10^{-3}$ [c])
			70.05	$6.18 \cdot 10^{-4}$	
			80.04	$1.58 \cdot 10^{-3}$	
			89.94	$3.80 \cdot 10^{-3}$	
			50.37		$2.76 \cdot 10^{-4}$
			60.19		$8.44 \cdot 10^{-4}$

[a]) Average of at least two independent measurements; mean deviation ± 1.15%.
[b]) [2].
[c]) Extrapolated.
[d]) [7b].

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[5]) See *Exper. Part.*

[6]) See [10].

Table 2. *Relative Rate Constants* (k(rel)), *Rate Ratios* ($k\mathbf{2}/k\mathbf{1}$), *and Inductive Substituent Constants* (σ_I^q)

	R	X	$k\mathbf{1}$(rel)	$k\mathbf{2}$(rel)	$k\mathbf{2}/k\mathbf{1}$	$\sqrt{k\mathbf{2}(\text{rel})}$	σ_I^q
a	H	OTs	1	1	1	1	0
b	CH_2OH	OTs	1/1.6	1/3.7	1/2.3	1/1.91	0.62
c	CH_2OAc	OTs	1/19	1/243	1/13	1/15.6	0.90
d	CH_2OTs	OTs	1/59	1/2708	1/46	1/52	1.28
e	$COOCH_3$	OTs	1/157	1/17940	1/114	1/134	1.69
a	H	Br	1	1	1	1	0
f	$(CH_3)_3Si$	Br	8.6	33	3.8	5.7	– 0.16[a])

[a]) See *Exper. Part.*

Discussion. – As the $k\mathbf{1}$(rel) values in *Table 2* show, the substituents **b**–**e** reduce the rate of the parent tosylate **1a** (X = OTs) by factors of 1.6 to 157. In contrast, the Me_3Si group in **1f** (X = Br) increases the rate by a factor of 8.6, in accordance with its $+I$ effect. The upper plot in the *Figure* is the reported regression line for log k *vs.* σ_I^q for several 3-mono-substituted adamant-1-yl tosylates [2], but shows only the points for **1c**–**e** (X = OTs)[7]). Inclusion of the point for **1f** (X = Br) in the reported plot for 3-substituted adamant-1-yl bromides **1** (X = Br) [1] reveals that the Me_3Si group exerts an exalted polar effect leading to an acceleration of 5.2 based on the regression line. This finding suggests that the electrofugal γ-Me_3Si group[8]) promotes homohyperconjugation in carbenium ions, as illustrated in the cation **7** (R = Me_3Si). This cation and its precursor **1f** (R = Br) possess the rigid W conformation conductive to 1,3 bridging [5][14] involving in this case the back lobe of the C–Si bond, *i.e.* a 'percaudal' interaction, according to *Shiner* and coworkers [8].

The $k\mathbf{2}$(rel) values in *Table 2* show that the rate constants for the twin-substituted tosylates **2** (X = OTs) decrease by factors of 3.7 to 17940 relative to the parent tosylate **1a** (X = OTs), *i.e.* as the $-I$ effect of the substituents increases *(Table 2, Column 7)*. On the other hand, the twin-substituted bromide **2f** (X = Br) reacts 33 times faster than the parent bromide **2a** (X = Br), in keeping with the $+I$ effect of the Me_3Si group[9]). However, the $k\mathbf{2}$(rel) values are less than the square of the corresponding k**1**(rel) values. This would not be the case, if the substituents contributed the same rate factor.

This is also borne out by the $k\mathbf{2}/k\mathbf{1}$ ratios in *Table 2*. These show that the rate effects of the second substituents are smaller than those of the first substituent. Thus, the rate decrease caused by the second substituents in the tosylates **2c**, **2d**, and **2e** is *ca.* 70% of the decrease due to the first. On the other hand, the rate increase due to both Me_3Si groups in the bromide **2f** (X = Br) is only 45% of the increase caused by the first group. Since ionization of the twin-substituted compounds presumably leads directly to the symmetrical adamantyl cation **10**, the rate factor per substituent should equal the square root of $k\mathbf{2}$(rel) *(Table 2, Column 6)*. However, with the exception of **2b** (X = OTs) which contains the electrofugal CH_2OH group[10]), the rate factor per substituent is actually smaller than

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[7]) The point for the electrofugal substituent R = CH_2OH corresponds to an acceleration of 4 [2] and was omitted in *Fig. 1*.

[8]) A β-Me_3Si group can lead to olefin-forming fragmentation of the type $R_3Si{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X \rightarrow R_3Si^+ + C{=}C + X$ [12].

[9]) See the preliminary communication [13].

[10]) The $-I$ effect of CH_2OH in **1b** and **2b** (X = OTs) is smaller than calculated on the basis of its σ_I^q value.

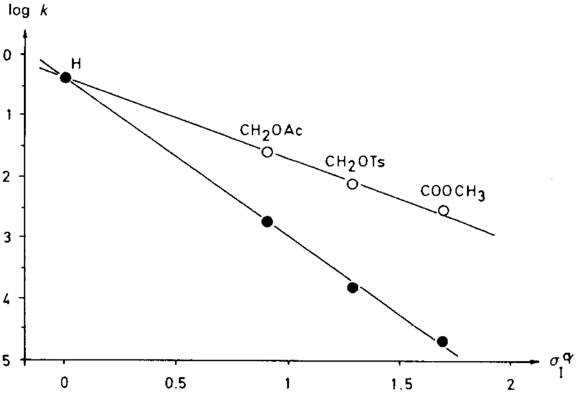

Figure. *Plot of log* k *for 3-substituted adamant-1-yl* p-*toluenesulfonates* **1** (X = OTs; upper line) *and for 3,5-disubstituted adamant-1-yl* p-*toluenesulfonates* **2** (X = OTs; lower line) vs. *inductive substituent constants* σ_I^q

that due to a single substituent (see k **1**(rel)), *i.e.* the second substituent reduces the effect of the first.

A possible rationale for this is based on the hypothesis that through-space induction in carbenium ions involves graded bridging [5][14], as illustrated for all three bridgehead C-atoms in the parent adamant-1-yl cation **11** (R=H). In fact, the ^{1}H- and ^{13}C-NMR spectra of the stable adamant-1-yl cation reported by *Olah* and coworkers [15] show that electron density is withdrawn mainly from the three bridgehead C- and H-atoms[11]). This convergence of electrons toward C(1) should increase their mutual repulsion and thereby reduce the polar effect per substituent, especially when the latter is an electron donor, as in the case of the Me_3Si group.

A further point of interest is that log k values for the twin-substituted tosylates **2** (X = OTs) also correlate linearly with σ_I^q (*Figure*, lower line) with a ρ_I of −2.55. This is *ca.* twice the ρ_I of −1.26 reported for the mono-substituted tosylates **1** (X = OTs) [2] (*Figure*, upper line)[12]). Hence, the inductivity, *i.e.* the sensitivity of rate to the substituents, appears to be doubled by twin substitution. This raises the question, whether solvolysis of 3,5,7-trisubstituted adamantanes **3** would lead to threefold inductivity, *i.e.* a ρ_I of *ca.* −3.8. However, a substituent sensitivity of this order would render rate comparisons in the easily accessible temperature range almost impracticable.

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[11]) These authors rationalize their findings in terms of a C,C-hyperconjugative effect, as in **9** (R=H). On the other hand, the X-ray data of *Laube* [16] show that the C(1)–C(3) distance in the stable 3,5,7-trimethyladamant-1-yl cation is *ca.* 8% shorter than normal. This suggests weak 1,3-bridging as in **11** ($R=CH_3$).

[12]) The points for the electrofugal CH_2OH in **1** and **2** (X=OTs) which correspond to accelerations of 4 and 10, respectively, have been omitted from these plots.

Experimental Part

4-(Trimethylsilyl)quinuclidine Hydroperchlorate (R = Me_3Si; **4**). Me_3SiLi was prepared from 3 ml (15 mmol) of hexamethyldisilane according to [17] and cooled to −78°. A soln. of 800 mg (4.2 mmol) of 4-bromoquinuclidine **4** (R = Br) [18] in 4 ml of THF was then added dropwise. Workup as described in [17] gave 5 ml of a concentrated soln. of the product in pentane. This was cooled to 0°, and a calculated amount of $HClO_4$ (4.2 mmol) in 5 ml of acetone was added slowly. Evaporation *in vacuo* and crystallization from i-PrOH yielded 720 mg (60%) of the hydroperchlorate. M.p. 295–305° (with dec.). IR (KBr): 2780, 2640, 1430, 1250, 837. ^1H-NMR ($CDCl_3$): −0.05 (*s*, Me_3Si); 1.89 (*m*, 3 CH_2); 3.42 (*m*, 3 CH_2). MS of free base: 183 (M^+). Anal. calc. for $C_{10}H_{22}ClNO_4Si$ (283.83): C 42.32, H 7.81, N 4.93; found: C 42.17, H 8.01, N 5.05. p*Ka* in 0.1M KCl at 25° [3]: for **4** (R = H) 11.31 ([3]: 11.29); for **4** (R = Me_3Si) 11.47; $\sigma_I^q = -0.16$[13].

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[13] Measured by Mr. *R. Bielmann*.