168. Polar Effects. X. Polar Substituent Effects in the Solvolysis of 3-Substituted 1-Adamantyl Bromides and Toluenesulfonates

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Summary

The rate constants for 3-substituted adamantyl p-toluenesulfonates **3a–3k** in ethanol/water 80:20 correlate well with the respective inductive substituent constants σ_I^q. The reaction constant ρ for the toluenesulfonates **3** is 10% larger than for the corresponding bromides **2**, indicating somewhat more charge separation in the activation of the toluenesulfonates. Evidence is presented that stabilization of the resultant 1-adamantyl cations by induction involves graded 1,3-bridging, which is favored when the substituent is an electrofugal group, and that stabilization by n-electron donors involves C,C-hyperconjugation. Rate ratios for the toluenesulfonates **3** and the bromides **1** exceed 10^3 and are almost independent of the 3-substituents. The implications of this are discussed in the light of current hypotheses.

Introduction. – As shown in recent studies [1–5] reaction constants ρ, as derived from the *Hammett-Taft* equation $\log(k/k_0) = \rho \cdot \sigma_I^q$, are a sensitive probe for charge development in the transition state for the solvolyses of saturated compounds. In general the logarithms of the rate constants ($\log k$) correlate well with inductive substituent constants σ_I^q except when an anchimeric, frangomeric, C,C-hyperconjugative or a hitherto unrecognized polar effect of electrofugal groups [1] is superposed on the inductive (I) effect.

The reaction constant ρ was small, namely -0.12, for solvolysis of the primary bromides **1** in ethanol/water 80:20 [2], a typical k_s-process [6] involving strong nucleophilic solvent participation. The ρ-value was much larger, namely -1.14, for solvolysis of the 3-substituted bromoadamantanes **2** [1], a typical k_c-process [6] in which nucleophilic solvent participation is sterically excluded. For the tertiary chlorides **4** [4] the ρ-value was intermediate, namely -0.71, indicating a borderline k_s, k_c-process. But ρ-values are undoubtably influenced by further factors, since a much higher value of -2.0 [5] was observed for the 6*exo*-substituted 2*exo*-norbornyl toluenesulfonates **5** which possess the same conformation of the R–C–C–C–X chain as the bromoadamantanes **2** and also react by a k_c-process. However, since the leaving groups in **5** and **2** are different conclusions as to mechanism should not be drawn until the influence of the nucleofuge X on the ρ-value is established.

The main purpose of this work was, therefore, to compare the reaction constant p for the 3-substituted adamantyl p-toluenesulfonates **3a-3k** with the p-value for the corresponding bromides **2**. Furthermore, the exalted substituent effects of the n-electron donors OH, OCH_3 and SCH_3 and the electrofugal groups CH_2NH_2, $CONH_2$, CH_2OH, COO^- and $Sn(CH_3)_3$ [1] on the rates of the bromides **2** warranted an examination of the corresponding toluenesulfonates **3**, which should lead to the same intermediate 1-adamantyl cations. However, it soon became apparent that some of these substituents increase reactivity and, hence, decrease the stability of the toluenesulfonates to such an extent that the study had to be confined to the more tractable toluenesulfonates **3a-3n**.

A final question pertains to the controversy concerning the interpretation of the relative rates of tertiary toluenesulfonates and bromides, such as **3** and **2**, respectively, *i.e.* the so-called k_{OTs}/k_{Br} ratio. According to *DePuy & Bishop* [7] and *Hoffmann* [8] these rate ratios depend largely on the degree of charge separation between the cationic center and the nucleofuge in the transition state, high ratios, as observed for tertiary substrates [9], indicating large charge separation, low ratios, as observed for secondary and primary substrates [8], indicating small or negligible charge separation[1]). On the other hand *Schleyer et al.* [10] have reasoned that the observed increase of the k_{OTs}/k_{Br} ratio in the order primary < secondary << tertiary is due to a steric effect, namely ground state repulsion between the bulky OTs-group and the substituents at the cationic center which increases in the same order. It was hoped that these plausible but conflicting views could be tested by determining the rate ratio for **3** and **2** as a function of the substituent R.

Results. – The preparation of the 3-substituted adamantyl p-toluenesulfonates **3a-3n** and their hydrolyses to the corresponding adamantanols **6** in dioxane/water 70:30 are described in the accompanying paper [11]. The toluenesulfonates **3** yielded the alcohols **6** only, except for **3h** and **3i** which also yielded the diol **6a** by further hydrolysis of the haloalcohols **6b** and **6c**. Furthermore, the bromoalcohol **6c** and the methoxyadamantyl toluenesulfonate **3n** led to small amounts of the fragmentation product **7**. The hydroxymethyladamantyl toluenesulfonate **3l** was extremely unstable and decomposed upon recrystallization. A crude sample was therefore used for the product and rate studies. Rate constants were measured in ethanol/water 80:20 (v/v) by the conductometric method [1]. Rate constants, determined at three temperatures, are listed in *Table 1*, relative rates (k_{rel}) at 70° in *Table 2*.

Discussion. – The k_{rel}-values *(Table 2)* show that the ionization rates of the toluenesulfonates **3a-3n** are strongly influenced by the substituents, **3c** (R = i-C_3H_7) reacting 52,000 times faster than **3k** (R = NO_2). Furthermore, a plot of $\log k$ for the toluenesulfonates **3a-3k** against the respective inductive constants σ_I^q [12] leads to an excellent correlation (r = 0.998, *Fig. 1*). Hence, as in the case of the bromides **2** [1] the substituents control the rates of the toluenesulfonates **3a-3k** by their I-effects only. The reaction constant p for the toluenesulfonates **3** of -1.26 is 10% larger than for the bromides **2** (-1.14). This establishes that the rates of the toluenesulfonates **3** are somewhat more sensitive to polar substituents, a point that is discussed below.
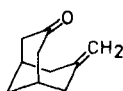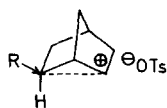
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[1])   *Hoffmann* proposed the use of k_{OTs}/k_{Br} ratios as a mechanistic criterion [8].

$R-CH_2CH_2CH_2Br$
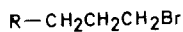
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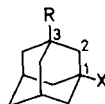
2 X = Br
3 X = OTs

R = a) H   h) Cl
    b) CH_3 i) Br
    c) $i\text{-}C_3H_7$ j) CN
    d) CH_2OCOCH_3 k) NO_2
    e) CH_2OTs l) CH_2OH
    f) $COOCH_3$ m) COONa
    g) $OCOCH_3$ n) OCH_3
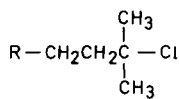
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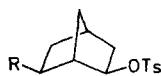
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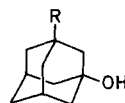
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R = a) OH , b) Cl ,
    c) Br , d) H , e) OCH_3

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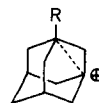
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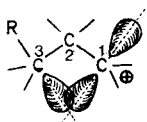
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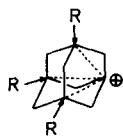
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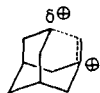
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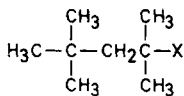
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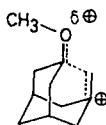
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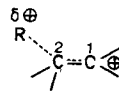
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17 a) X = OTs
       b) X = Br

Table 1. *First-order solvolysis rate constants for* 10^{-3}M *3-R-1-adamantyl* p-*toluenesulfonates* **3** *in ethanol/water 80:20 with 1.1 mol-equiv. of triethylamine*

R	T [°]	k [s⁻¹]	H$^{\neq}$ [kcal/mol]	S$^{\neq}$ [cal/mol · degree]
a) H	9.45	$6.30 \cdot 10^{-4}$	20.01	-2.29
	20.00	$2.32 \cdot 10^{-3}$		
	30.00	$7.56 \cdot 10^{-3}$		
	70.00	$4.09 \cdot 10^{-1\,a}$)		
b) CH₃	9.50	$5.03 \cdot 10^{-4}$	19.90	-3.10
	19.95	$1.87 \cdot 10^{-3}$		
	30.00	$5.92 \cdot 10^{-3}$		
	70.00	$3.17 \cdot 10^{-1\,a}$)		
c) i-C₃H₇	0.00	$2.74 \cdot 10^{-4}$	20.44	0.17
	9.98	$1.09 \cdot 10^{-3}$		
	20.05	$3.86 \cdot 10^{-3}$		
	70.00	$7.50 \cdot 10^{-1\,a}$)		
d) CH₂OCOCH₃	30.06	$3.66 \cdot 10^{-4}$	20.53	-6.56
	40.05	$1.16 \cdot 10^{-3}$		
	50.13	$3.23 \cdot 10^{-3}$		
	70.00	$2.21 \cdot 10^{-2\,a}$)		
e) CH₂OTs	40.07	$2.99 \cdot 10^{-4}$	21.68	-5.57
	50.12	$9.19 \cdot 10^{-4}$		
	60.00	$2.55 \cdot 10^{-3}$		
	70.00	$6.88 \cdot 10^{-3\,a}$)		
f) COOCH₃	50.00	$3.12 \cdot 10^{-4}$	22.70	-4.49
	59.85	$9.21 \cdot 10^{-4}$		
	70.00	$2.60 \cdot 10^{-3}$		
g) OCOCH₃	60.03	$3.53 \cdot 10^{-4}$	22.72	-6.34
	70.00	$9.94 \cdot 10^{-4}$		
	80.00	$2.61 \cdot 10^{-3}$		
h) Cl	70.00	$2.30 \cdot 10^{-4\,a}$)	22.27	-10.57
	80.13	$6.04 \cdot 10^{-4}$		
	90.27	$1.51 \cdot 10^{-3}$		
	99.60	$3.34 \cdot 10^{-3}$		
i) Br	70.00	$1.60 \cdot 10^{-4}$		
j) CN	70.00	$6.95 \cdot 10^{-5\,a}$)	22.25	-13.01
	89.95	$4.42 \cdot 10^{-4}$		
	100.00	$1.04 \cdot 10^{-3}$		
	109.72	$2.29 \cdot 10^{-3}$		
k) NO₂	70.00	$1.44 \cdot 10^{-5\,a}$)	23.30	-13.06
	100.05	$2.47 \cdot 10^{-4}$		
	110.13	$5.72 \cdot 10^{-4}$		
	120.28	$1.31 \cdot 10^{-3}$		
l) CH₂OH^{b})	10.00	$2.90 \cdot 10^{-4}$	21.27	0.50
	20.00	$1.09 \cdot 10^{-3}$		
	30.00	$3.76 \cdot 10^{-3}$		
	70.00	$2.61 \cdot 10^{-1\,a}$)		
m) COONa^{b})^{c})	10.00	$6.40 \cdot 10^{-4}$	22.59	6.72
	20.00	$2.63 \cdot 10^{-3}$		
	30.00	$9.65 \cdot 10^{-3}$		
	70.00	$8.68 \cdot 10^{-1\,a}$)		
n) OCH₃^{b})	20.00	$2.36 \cdot 10^{-4}$	21.75	-0.90
	30.00	$8.45 \cdot 10^{-4}$		
	40.00	$2.76 \cdot 10^{-3}$		
	70.00	$6.43 \cdot 10^{-2\,a}$)		

[a]) Extrapolated. [b]) These rate measurements were carried out by Mr. *Rolf Bielmann*. [c]) The sodium salt was reacted in the presence of 3 mol-equiv. NEt₃.

Table 2. *Relative rate constants for 3-R-1-adamantyl* p-*toluenesulfonates* **3** *in ethanol/water 80:20 at 70.0°* (inductive substituent constants σ_I^q, accelerations calculated from the plot in the *Figure* and k_{OTs}/k_{Br} ratios)

R	k_{rel}	σ_I^q	Accelerations	k_{OTs}/k_{Br}
a) H	1	0		5710
b) CH_3	$7.8 \cdot 10^{-1}$	0.11		5970
c) i-C_3H_7	1.83	-0.10		6880
d) CH_2OCOCH_3	$5.4 \cdot 10^{-2}$	0.90		
e) CH_2OTs	$1.7 \cdot 10^{-2}$	1.28		
f) $COOCH_3$	$6.4 \cdot 10^{-3}$	1.69		3440
g) $OCOCH_3$	$2.4 \cdot 10^{-3}$	2.16		
h) Cl	$5.6 \cdot 10^{-4}$	2.51		
i) Br	$3.9 \cdot 10^{-4}$	2.69		1900
j) CN	$1.7 \cdot 10^{-4}$	3.06		2270
k) NO_2	$3.5 \cdot 10^{-5}$	3.54		2920
l) CH_2OH	$6.4 \cdot 10^{-1}$	0.62	4	6127
m) COONa	2.1	0.72	18	5391
b) OCH_3	$1.6 \cdot 10^{-1}$	1.89	39	6602

On the other hand ρ for the adamantyl toluenesulfonates **3** is 37% smaller than for the corresponding norbornyl toluenesulfonates **5** (-2.0 [5]), a noteworthy result in view of the aforementioned conformational similarity. The large ρ-value for **5** indicated an unusually strong inductive interaction between C(6) and the incipient cationic center at C(2) and led to the conclusion that induction involves graded C-participation, *i.e.* 1,3-bridging, as illustrated in **8** [5] [13]. On this basis bridging appears to be less favorable in the adamantyl cation **9** than in the norbornyl cation **8**.

The difference between the inductive interactions in **8** and **9** are explicable if differential bridging strains [13] [14] are taken into account. For 1,3-bridging to be effective the back lobe of the dsp^3-orbital of the quasi-pentacoordinate C-atom should overlap well with the developing p-orbital of the cationic center as illustrated in **10** [15]. However, the resultant bonding generates more additional strain in the 1-adamantyl cation **9** than in the 2-norbornyl cation **8** because the cyclohexane chair conformations in the former are strongly deformed by incorporation of quasi-pentacoordinate C-atoms[2]).

1,3-Bridging in **9** should be enhanced by electrofugal substituents, for these are σ-electron donors $a-b$ in fragmentation of the type $a-b-c-d-X \rightarrow a-b+c=d+X$: [16]. In fact **31** (R = CH_2OH) and **3m** (R = COO^-) gave rise to accelerations of 4 and 18, respectively *(Table 2)* based on the inductive regression line in the *Figure*. Accelerations due to a large variety of electrofugal groups were observed in the solvolysis of the bromides **2** [1], the chlorides **4** [4] and the toluenesulfonates **5** [5]. It is therefore concluded that the exalted effects of electrofugal substituents are caused by enhanced bridging in the transition state of k_c-processes.

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[2])   The reaction constant ρ is a measure of the sensitivity of the rate to R. In the 1-adamantyl cation **9** the two unsubstituted bridgehead C-atoms can also bridge and thereby increase strain.
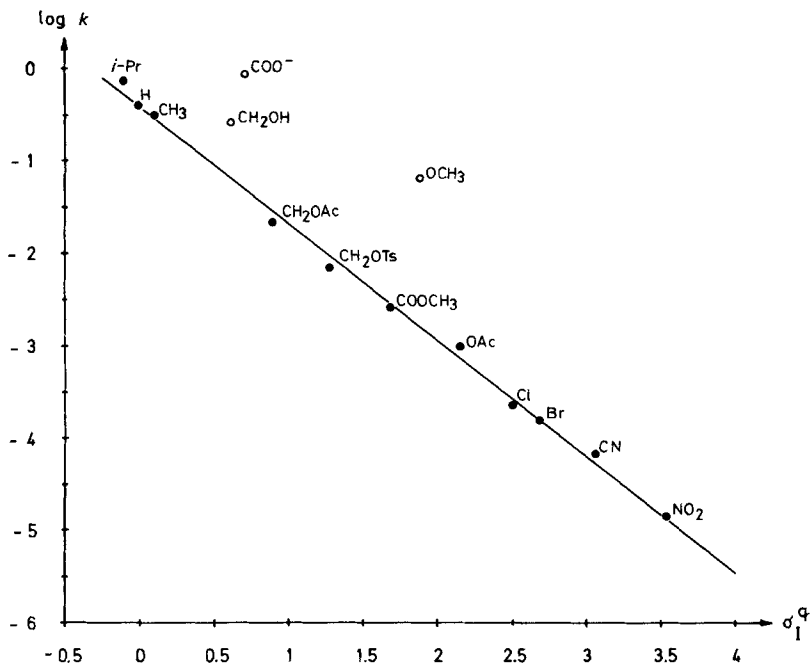
Figure. *Plot of log k for 3-substituted 1-adamantyl toluenesulfonates* **1** *vs. inductive substituent constants* σ_I^q (open circles not included in the regression)

This hypothesis is supported by the ^{1}H-NMR.-spectrum of the 1-adamantyl cation **11** (R = H) under stable ion conditions. *Schleyer et al.* [17] observed that the three H-atoms in 3-position are more deshielded (by 0.90 ppm) than the six H-atoms adjacent to the cationic center. They attributed this 'anomalous' deshielding effect to the overlap of the p-orbital at C(1) with the back lobes of the β-C, H-bonds, thereby favoring selective withdrawal of electron density from these three H-atoms. As illustrated in **11** (R = H) this amounts to triple 1,3-bridging.

This view is also supported by the formation of 1,3-dehydroadamantane **12** when 1,3-dibromoadamantane **2i** is treated with lithium in ether [11]. The highly deformed and therefore strained[3] tetracyclic hydrocarbon **12** was first obtained by *Pincock* upon treatment of **2i** with sodium-potassium dispersion or with butyllithium [19]. In the presence of water **12** is readily hydrolyzed to 1-adamantanol (**6d**). It is significant that in a derivative of **12** the 1,3-bond was shown to be remarkably long, namely 1.64 Å [20] and that the bridgehead C-atoms C(1) and C(3) have an 'inverted' propellane structure similar to the one proposed above for the 1,3-bridged cation **9**. Lithium is a highly electrofugal metal and would therefore be expected to undergo 1,3-elimination very readily *via* a 1,3-bridged transition state.

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[3]   The calculated strain energy for **12** is 64 kcal/mol [18].

On the other hand it appears unlikely that charge delocalization in *unsubstituted* 1-adamantyl cations is due to C, C-hyperconjugation as illustrated in **13** (for one σ-bond only). In fact this was practically ruled out in earlier work [21] [22] which showed that the solvolysis of 1-bromoadamantane (**2a**) is retarded when the H-atom in 3-position is replaced by methyl groups[4]). When branching in 3-position did produce a rate increase, as in **14**, it was traced to a steric effect [21]. On the other hand the failure of a methyl group at C(3) in **2b** and **3b**, or at all three 3-positions of **2** [21], to increase the rate of ionization indicates that 1,3-bridging is favored in unsubstituted 1-adamantyl cations, for alkyl groups are not as electrofugal and hence as effective σ-electron donors[5]) as H-atoms.

It now appears that C, C-hyperconjugation is a stabilizing factor in k_c-processes only when a p- or a π-electron donor is attached to the C-atom in the 3-position. This follows from the rates of the adamantyl bromides **2** in which R = OH, OCH$_3$, SCH$_3$ and C$_6$H$_5$ [1] and is now confirmed by the rate of the 3-methoxyadamantyl toluenesulfonate **3n** which is 39 times higher than calculated from the σ_I^q value of the methoxy group (*Table 2* and *Figure*). The fact that small amounts of the fragmentation product **7** are obtained beside the alcohol **6e** supports formula **15** which illustrates the incipient fragmentation of the intermediate cation[6]).

It is noteworthy that C, C- and C, H-hyperconjugation are related, as illustrated in **16**, where R is an electrofugal group [16] or an H-atom, respectively. In the former case breaking of the R, C(2)-bond leads to olefin-forming fragmentation, in the latter case to 1,2-elimination. C, H-Hyperconjugation is probably unimportant in the 1-adamantyl cation **11** because the orientation of the six H, C(2)-bonds is *gauche* with respect to the axis of the p-orbital at C(1). This conclusion is supported by the aforementioned ¹H-NMR. spectrum of the 1-adamantyl cation [17].

Table 2 shows that the k_{OTs}/k_{Br} ratios for **3** and **2** are large, namely > 10³, and that they remain relatively constant as the substituent R is varied. As already mentioned the reaction constant for the toluenesulfonates **3** ($\rho = -1.26$) is 10% larger than for the bromides **2** ($\rho = -1.14$ [1]). Although moderate this difference ($\Delta\rho$) indicates more charge separation in the transition state for the toluenesulfonates **3** than for the bromides **2**. However, a larger ρ-value would have been expected if high k_{OTs}/k_{Br} ratios indicated large charge separation as claimed by *Hoffmann* [8].

On the other hand the k_{OTs}/k_{Br} ratios of the toluenesulfonates **3** are relatively constant and show only a small tendency to decrease with k_{rel} *(Table 2)*. This points to a steric origin of high k_{OTs}/k_{Br} ratios for tertiary substrates, as proposed by *Schleyer* [10], namely constant ground state repulsion between the bulky OTs-group and the cationic center. This view is supported by the almost identical k_{OTs}/k_{Br} ratios for the bicyclo[2.2.2]octyl derivatives **17a** and **17b** ($k_{OTs}/k_{Br} = 2.5 \cdot 10^3$ (70°)) [9] in which the nucleofugal OTs and Br have the same steric environment as in **3a** and **2a**, respectively, but react *ca.* 10⁴ times more slowly. *Hoffmann* and *Schleyer's*

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4)   This also applies to the corresponding chlorides and iodides [23].
5)   With the possible exception of *t*-butyl.
6)   C, C-Hyperconjugation as in **15** permits electron density to be transferred from the n-electron donor at C(3) to the cationic center without exceeding the octett around C(3).

apparently conflicting explanations for the high k_{OTs}/k_{Br} ratios of tertiary substrates can, however, be reconciled if it is assumed that the strained C, OTs-bond is already stretched and hence more polar in the ground state and that it therefore undergoes heterolysis more readily.

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