282. Polar Effects in the Solvolysis of 4-Substituted Bicyclo[2.2.2]octyl *p*-Nitrobenzenesulfonates. Polar Effects. VII.

by **Cyril A. Grob** and **Roland Rich**

Institute of Organic Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel

(28.IX.79)

Summary

Hydrolysis of bicyclo[2.2.2]octyl *p*-nitrobenzenesulfonate (**14a**, X = *p*-$NO_2C_6H_4SO_3$), and nineteen 4-R-substituted derivatives **14b–14t** in 70% aqueous dioxane yield the corresponding bicyclo[2.2.2]octanols **14** (X = OH), exclusively. The 7-center fragmentation to 1,4-dimethylidene-cyclohexane (**15**) is not observed. The logarithms of most of the rate constants, measured in 80% ethanol, correlate well with the corresponding inductive substituent constants σ_I^q of R. Hence, in these cases ionization rate is controlled by the inductive effect of R only. Poor correlations result when the substituents are potentially electrofugal groups, such as COO^-, CH_2OH, CH_2NH_2, $CONH_2$ and H, the deviations from the inductive regression line corresponding to rate enhancements of 1.6 to 8. These exalted substituent effects are tentatively ascribed to extended hyperconjugation involving two σ-bonds. This study corroborates previous evidence that the inductive effect alone does not fully account for the polar effect of some substituents in reactions involving carbocations.

In a recent paper in this series [1] a new experimental method for the determination of inductive substituent constants σ_I^q was introduced. This method, which is based on the measurement of the pK_a of quinuclidinium perchlorate (**1**, R = H), and of numerous 4-substituted derivatives[1]), avoids the disadvantages inherent in previous ones [1].

When applied to studies of substituent effects in nucleophilic substitution reactions σ_I^q values correlated well with the logarithms of observed rate constants for bimolecular substitution (S_N2) [3] but not for some solvolysis reactions proceeding by way of carbeniumions [4] [5], as in the solvolysis of 1-R-substituted 3-bromo-adamantanes (**2a**) in 80% ethanol. In fact, in the latter case three kinds of substituent effects were discerned:

a) When R was hydrogen and alkyl or an electron-withdrawing (– I) substituent, such as $BrCH_2$, COOH, Br or CN, the logarithms of the first order rate constants (log *k*) correlated very well with the respective σ_I^q values. In these cases, then, ionization to adamantyl cations **3**, the precursors of adamantanols **2b** and ethyl ethers **2c**, is controlled by the inductive effect of R alone;

---

[1]) In a further paper these σ_I^q values are reexamined and revised where necessary [2].

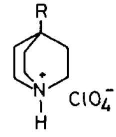
0018-019X/79/8/2793-09$01.00/0

b) When R was a n-electron donor, such as OH, OCH_3 and SCH_3, or a π-electron donor, such as C_6H_5 or $CH_3C{=}CH_2$, and therefore also exerted a potential mesomeric effect, reactions were faster than anticipated on the basis of the respective σ_I^q values. These accelerations were ascribed to C,C-hyperconjugative relay of positive charge from the cationic center at C(3) to the substituent at C(1), as illustrated in **4**. However accelerations were also observed when R was an electrofugal group [6], such as $(CH_3)_3Sn$, H_2NCO, $HOCH_2$, H_2NCH_2 or COO^-, *i.e.* groups *a–b* which are split off without the bonding electron pair in heterolytic fragmentation of the type [6]:

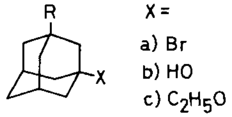
$$a{-}b{-}c{-}d{-}X \rightarrow a{-}b + c{=}d + X{:}$$

Since these groups release electrons in fragmentation they were considered capable of augmenting hyperconjugation of the C(1),C(2)-bond in the incipient cation **5**²), *i.e.* by acting as σ-electron donors at C(1);

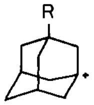
c) The largest rate increases were observed when R was a powerful n-electron donor, such as O^-, S^- and $(CH_3)_2N$. In these cases, however, fragmentation to the bicyclic olefins **6** (R = O, S and $(CH_3)_2N^+$, respectively) occurred. The large accelerations were therefore ascribed to the frangomeric effect [8] of these substituents. As shown in the preceeding paper [5] γ-substituents R exert similar polar effects in the solvolysis of acyclic tertiary chlorides **7**. However, these effects were not as strongly transmitted as in the adamantane series.



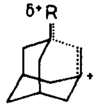
1



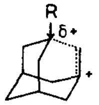
2



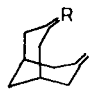
3



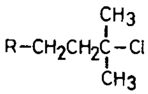
4



5

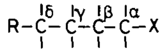


6



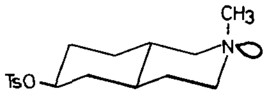
$$R{-}CH_2CH_2\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}Cl$$

7

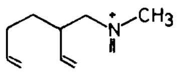


$$R{-}\overset{\delta}{C}{-}\overset{\gamma}{C}{-}\overset{\beta}{C}{-}\overset{\alpha}{C}{-}X$$

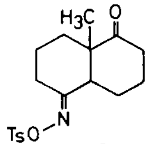
8



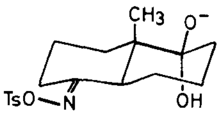
9



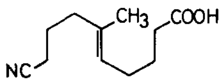
10



11



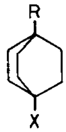
12



13

---

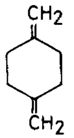
²) Another mechanism by which electrofugal groups could assist ionization is by exerting an inductomeric effect [7].



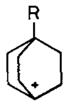
14

R =
a) H
b) COO^-
c) $t\text{-}C_4H_9$
d) $iso\text{-}C_3H_7$
e) C_2H_5
f) CH_3
g) CH_2OH

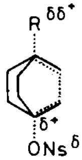
R =
h) CH_2NH_2
i) $CH_3C{=}CH_2$
j) C_6H_5
k) $(CH_3)_2N$
l) $CONH_2$
m) COOH
n) OH
o) $NHCOOC_2H_5$
p) $COOC_2H_5$
q) $COOCH_3$
r) OCH_3
s) Br
t) CN



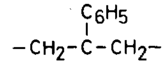
15



16

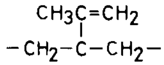


17



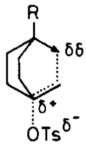
$$\overset{C_6H_5}{-CH_2-\overset{|}{C}-CH_2-}$$

18



$$\overset{CH_3C=CH_2}{-CH_2-\overset{|}{C}-CH_2-}$$

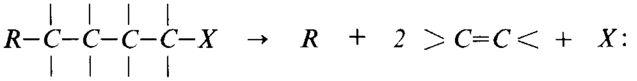
19



R = C_6H_5, $CH_3C{=}CH_2$

20

These findings raised the question whether the same effects would be observed when the substituent R is separated from the nucleofuge X by an additional carbon atom as in **8**, *i.e.* whether the substituents listed above under a) would still exert only a −I-effect. Clearly, the +*M*-substituents of b) and c) can no longer stabilize a positive charge at C_γ by delocalization of n- and π-electrons, *i.e.* by C,C-hyperconjugation or fragmentation unless they constitute an electrofugal group *a-b* in conjunction with C_γ. On the other hand when R in **8** itself is an electrofugal group, such as H_2NCH_2, $HOCH_2$, H_2NCO or COO^-, fragmentation, as formulated below, becomes a possible though doubtful alternative:



$$R-\underset{|}{\overset{|}{C}}-\underset{|}{\overset{|}{C}}-\underset{|}{\overset{|}{C}}-\underset{|}{\overset{|}{C}}-X \rightarrow R + 2 >C{=}C< + X:$$

For example, the ε-amino-tosylate **9**, which conforms to type **8** ($R{=}R_2NCH_2$), does not fragment to the olefinic immoniumsalt **10** in spite of the favorable alignment of bonds [9], the reason probably being that the process is thermochemically unfavorable. On the other hand the diketomonoxime **11** readily undergoes quantitative 7-center fragmentation to the nitriloacid **13** with hydroxide ion, presumably *via* the adduct **12**³). In view of these results it seemed desirable to examine whether other compounds of type **8** are capable of undergoing 7-center fragmentation.

Sulfonates of 4-substituted bicyclo[2.2.2]octanols (**14**, X = OH), such as the *p*-nitrobenzenesulfonates (nisylates **14**, $X{=}p\text{-}NO_2C_6H_4SO_3$) proved to be excellent models with which to study the questions outlined above⁴). Consequently, a detailed

---

³) Formation of carboxyl and cyano groups as in **13** is associated with a large negative enthalpy change.

⁴) Due to their spherical shape and the antiperiplanar orientation of the bonds involved polar effects should be strongly transmitted in these molecules [5]. Furthermore, location of the nucleofuge ONs and the substituent R at the bridgehead positions precludes the incursion of steric and neighboring group effects.

Table 1. *First order rate constants* k[a]) *for* 10^{-3}M *4-substituted bicyclo[2.2.2]-octyl* p-*nitrobenzenesulfonates in 80 vol.-% ethanol*

No.	R	T [°]	*k* [s^{-1}]	$\Delta H^{\ddagger}$ [kcal/mol]	$\Delta S^{\ddagger}$ [cal/mol · degree]
a	H	49.96	$3.64 \cdot 10^{-4}$	21.97	−6.44
		60.01	$1.07 \cdot 10^{-3}$		
		70.00	$2.85 \cdot 10^{-3}$		
		75.00	$4.62 \cdot 10^{-3}$[b])		
b	COO^-	60.07	$3.67 \cdot 10^{-4}$	26.96	6.42
		70.00	$1.21 \cdot 10^{-3}$		
		75.00	$2.19 \cdot 10^{-3}$[b])		
		80.02	$3.88 \cdot 10^{-3}$		
c	*t*-C_4H_9	55.00	$2.22 \cdot 10^{-4}$	23.37	−4.23
		65.00	$6.67 \cdot 10^{-4}$		
		75.00	$1.85 \cdot 10^{-3}$		
d	*iso*-C_3H_7	55.04	$1.80 \cdot 10^{-4}$	23.76	−3.48
		65.00	$5.34 \cdot 10^{-4}$		
		75.00	$1.53 \cdot 10^{-3}$		
e	C_2H_5	54.99	$1.51 \cdot 10^{-4}$	23.77	−3.78
		65.00	$4.58 \cdot 10^{-4}$		
		75.00	$1.30 \cdot 10^{-3}$		
f	CH_3	65.00	$4.10 \cdot 10^{-4}$	23.30	−5.39
		75.00	$1.14 \cdot 10^{-3}$		
		90.00	$4.79 \cdot 10^{-3}$		
g	CH_2OH	65.00	$1.91 \cdot 10^{-4}$	24.58	−3.11
		75.00	$5.58 \cdot 10^{-4}$		
		85.00	$1.56 \cdot 10^{-3}$		
h	CH_2NH_2	65.00	$1.84 \cdot 10^{-4}$	24.76	−2.66
		75.00	$5.44 \cdot 10^{-4}$		
		85.00	$1.53 \cdot 10^{-3}$		
i	$CH_3C{=}CH_2$	64.99	$1.68 \cdot 10^{-4}$	24.42	−3.86
		75.00	$4.87 \cdot 10^{-4}$		
		85.00	$1.35 \cdot 10^{-3}$		
j	C_6H_5	70.00	$1.62 \cdot 10^{-4}$	24.48	−4.81
		75.00	$2.77 \cdot 10^{-4}$[b])		
		80.00	$4.69 \cdot 10^{-4}$		
		90.00	$1.24 \cdot 10^{-3}$		
k	$(CH_3)_2N$	75.00	$7.40 \cdot 10^{-5}$[b])	26.43	−1.85
		80.00	$1.29 \cdot 10^{-4}$		
		90.00	$3.76 \cdot 10^{-4}$		
		99.69	$9.91 \cdot 10^{-4}$		
l	$CONH_2$	75.00	$3.56 \cdot 10^{-5}$[b])	24.37	−9.19
		100.00	$4.02 \cdot 10^{-4}$		
		109.98	$9.88 \cdot 10^{-4}$		
		119.99	$2.25 \cdot 10^{-3}$		
m	COOH	75.00	$2.32 \cdot 10^{-5}$[b])	25.16	−7.77
		99.99	$2.83 \cdot 10^{-4}$		
		110.00	$7.15 \cdot 10^{-4}$		
		120.00	$1.68 \cdot 10^{-3}$		
n	OH	75.00	$2.12 \cdot 10^{-5}$[b])	25.73	−6.31
		100.00	$2.74 \cdot 10^{-4}$		
		110.00	$7.02 \cdot 10^{-4}$		
		120.01	$1.69 \cdot 10^{-3}$		
o	NHCOOEt	75.00	$1.80 \cdot 10^{-5}$[b])	25.98	−5.92
		100.03	$2.39 \cdot 10^{-4}$		
		109.99	$6.15 \cdot 10^{-4}$		
		119.99	$1.49 \cdot 10^{-3}$		
p	COOEt	75.00	$1.37 \cdot 10^{-5}$[b])	26.30	−5.56
		100.00	$1.87 \cdot 10^{-4}$		
		110.00	$4.86 \cdot 10^{-4}$		
		120.00	$1.20 \cdot 10^{-3}$		
q	$COOCH_3$	75.00	$1.26 \cdot 10^{-5}$[b])	26.61	−4.85
		100.00	$1.79 \cdot 10^{-4}$		
		110.00	$4.52 \cdot 10^{-4}$		
		120.00	$1.17 \cdot 10^{-3}$		
r	OCH_3	75.00	$1.02 \cdot 10^{-5}$[b])	26.01	−6.99
		100.00	$1.35 \cdot 10^{-4}$		
		110.00	$3.51 \cdot 10^{-4}$		
		120.06	$8.51 \cdot 10^{-4}$		
s	Br	75.00	$2.18 \cdot 10^{-6}$[b])	26.06	−9.90
		110.00	$7.51 \cdot 10^{-5}$		
		120.00	$1.83 \cdot 10^{-4}$		
		130.00	$4.32 \cdot 10^{-4}$		
t	CN	75.00	$5.47 \cdot 10^{-7}$[b])	26.78	−10.59
		110.00	$2.07 \cdot 10^{-5}$		
		120.00	$5.19 \cdot 10^{-5}$		
		130.00	$1.24 \cdot 10^{-4}$		

[a]) Average of 3-5 runs. [b]) Extrapolated.

study of the solvolysis rates and products of the nisylates **14a-14t** (X = ONs), was undertaken. The main objective was to determine whether the logarithms of the rate constants (log *k*) correlate with the inductive substituent constants σ_I^q of R or whether additional polar effects are involved. Prior to this study only bicyclo[2.2.2]-octyl-*p*-bromobenzenesulfonate (**14a**) and its 4-alkyl derivatives **14c-14f** (X = *p*-$BrC_6H_4SO_3$) had been studied in detail [11]. Reference to this work and to a recent theoretical paper in this field [12] will be made in the Discussion.

The preparation of the nisylates **14a-15t** is described in an accompanying paper [13]. Their first order rate constants in 80 vol.-% ethanol and the corresponding activation parameters ΔH^{+} and ΔS^{+} are listed in *Table 1*[5]). Preparative hydrolyses of the nisylates were carried out in 70% dioxane which has approximately the same ionizing power as 80% ethanol. Careful scrutiny of the reaction products revealed that 4-substituted bicyclo[2.2.2]octanols (**14**, X = OH) were the only substances present and that no 7-center fragmentation to 1,4-dimethylidene-cyclohexane (**15**) had occurred.

Discussion. - The nisylates **14a-14t** (X = ONs) yield the corresponding alcohols in a first order reaction. A mechanism involving intermediate bicyclo[2.2.2]octyl cations (**16**) is therefore indicated. Their rate of formation is strongly influenced by the substituents R, the most reactive nisylate **14a** (R = H), reacting 8446 times as fast as the least reactive **14t** (R = CN) *(Table 2)*.

Table 2. *Relative rate constants for* **14a-14t** *in 80 vol.-% ethanol, inductive substituent constants* σ_I^q *and accelerations derived from the plot in Figure 1*

No.	R	$k_{rel}^{75°}$	σ_I^q a)	Acceleration
a	H	8446	0	3.6
b	COO^-	4003	0.61	8.1
c	*t*-C_4H_9	3382	−0.18	
d	*iso*-C_3H_7	2797	−0.08	
e	C_2H_5	2377	0.03	
f	CH_3	2084	0.11	
g	CH_2OH	1020	0.66	2.3
h	CH_2NH_2	995	0.52	1.6
i	$CH_3C{=}CH_2$	890	0.60	1.8
j	C_6H_5	506	0.85	1.9
k	$(CH_3)_2N$	135	1.05	
l	$CONH_2$	65	1.82	2.8
m	COOH	42	1.70b)	
n	OH	39	1.74	
o	NHCOOEt	33	1.56	
p	COOEt	25	1.70	
q	$COOCH_3$	23	1.70	
r	OCH_3	19	1.86	
s	Br	4	2.65	
t	CN	1	3.04	

a) Revised values [2]. b) σ_I^q value for the ethyl ester.

---

[5]) For a preliminary report see [14].

Surprisingly, the unsubstituted nisylate **14a** is more reactive than the 4-alkyl derivatives **14c–14f**. The latter, however, follow the usual inductive order, the sequence being $H > t\text{-}C_4H_9 > iso\text{-}C_3H_7 > C_2H_5 > CH_3$. In their earlier study of the acetolysis of the corresponding *p*-bromobenzenesulfonates *Schleyer & Woodworth* [11] observed the anomalous position of hydrogen, which they ascribed to an increase in the C(1),C(4)-distance as hydrogen is replaced by the bulkier alkyl groups. Steric hindrance to solvation has also been put forward to explain the above sequence [12]; however, in the solvolysis of the corresponding adamantyl bromides **2** (X = Br) the observed sequence $t\text{-}C_4H_9 > iso\text{-}C_3H_7 > C_2H_5 > H > CH_3$ is again almost normal [4]. Whatever the reason for these differences the explanation given below should also be considered.

When log *k* for **14a–14t** (X = ONs) are plotted against the corresponding σ_I^q values the points show considerable scattering *(Fig. 1)* and the calculated regression line (not shown in the *Figure*) corresponds to a correlation coefficient r of 0,9734. However, when the seven points which deviate most (*Fig. 1*, open circles) are omitted a good correlation and the regression line shown in the plot result (r = 0.9962; maximum deviation = 14%). The ionization rates for these nisylates, then, is controlled only by the inductive effect of the substituent R. The reaction constant ρ is -1.09, *i.e.* only a little less than the ρ value found for the adamantyl bromides (**2a**), *i.e.* -1.14.

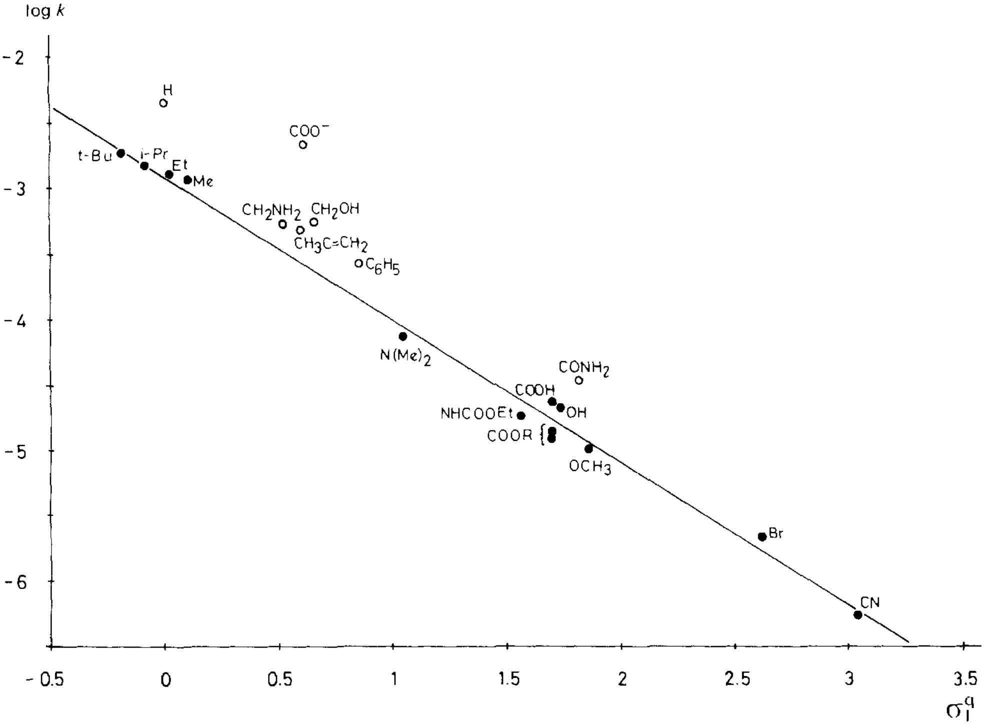


Fig. 1. *Relationship between log* k *for 4-substituted bicyclo[2.2.2]octyl nisylates in 80% ethanol and inductive substituent constants* σ_I^q

The points omitted in the correlation correspond to the nisylates in which R=H, COO^-, $HOCH_2$, H_2NCH_2, H_2NCO, $CH_3C=CH_2$ and C_6H_5, the deviations corresponding to reaction rates which are 1.6 to 8 times higher than anticipated on the basis of the respective σ_I^q values *(Table 2)*. This distinction between two kinds of substituents, *i.e.* the ones which exert an inductive effect only and those which exert an exalted effect, is justified when the common nature of the latter is taken into account. Thus, the groups COO^-, $HOCH_2$, H_2NCH_2 and H_2NCO are potentially electrofugal in fragmentation [6], whereas hydrogen is a common electrofuge in elimination[6]. Since these groups act as σ-electron donors in these reactions it is not unreasonable to assume that they also act as weak donors in the transition state for the ionization of the respective nisylates.

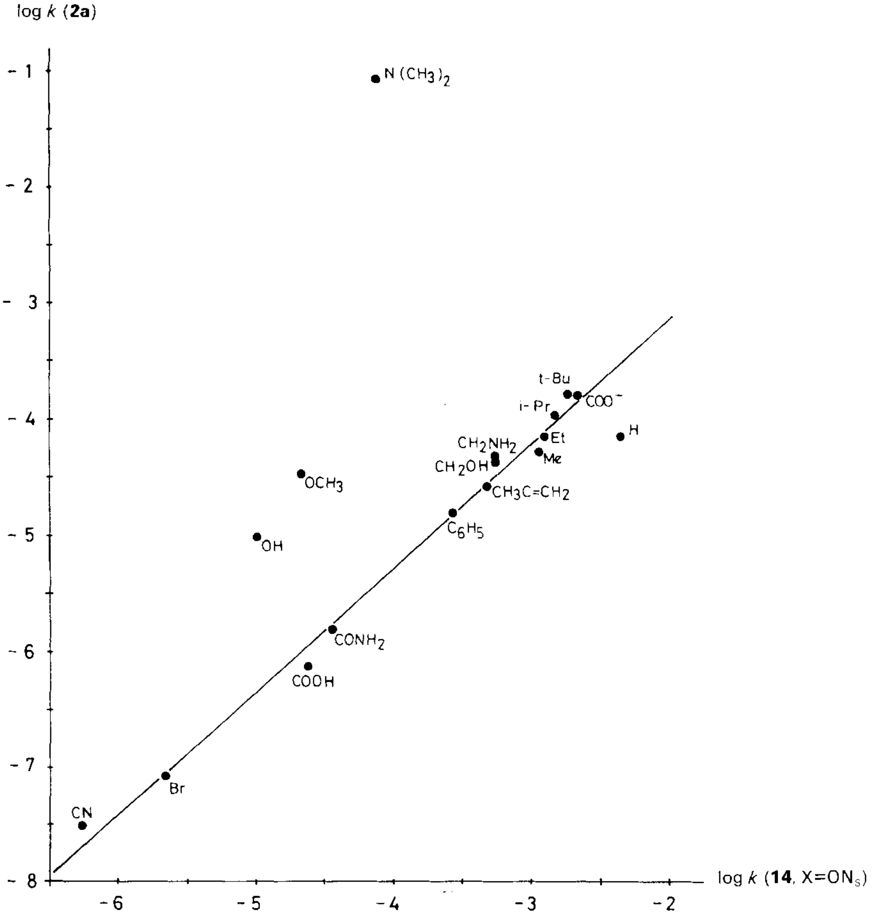


Fig. 2. *Relationship between log* k *for 1-substituted 3-bromoadamantanes* (**2a**) *and log* k *for 4-substituted bicyclo[2.2.2]octyl nisylates* (**14**, X=ONs) *in 80% ethanol*

---

[6] These groups are split off as CO_2, $O=CH_2$, $H_2\overset{+}{N}=CH_2$, HNCO and H^+, respectively.

It is tempting to describe this effect as twofold hyperconjugation5) involving the C(2),C(3) and the C(4)-R bonds, as illustrated in **17**7). A small part of the positive charge generated at C(1) is thereby transferred to the substituent R. Formula **17** also depicts the transition state for a hypothetical 7-center fragmentation leading to an electrofugal fragment R and the diolefin **15**. Instead, bond delocalization does not progress to the point where cleavage occurs and an energetically more favorable reaction, *i.e.* substitution takes place8).

Wenke & Lenoir [12] have recently contended that theory does not support twofold hyperconjugation [14] as a stabilizing mechanism for the bicyclo[2.2.2]-octyl-1 cation (**16**, R=H). However, they do not offer an alternative explanation for the accelerating effect of electrofugal substituents at C(4), which were unfortunately not included in their calculations.

As shown in *Figure 1* and *Table 2* the nisylates **14i** and **14j** with R=$CH_3C{=}CH_2$ and C_6H_5, respectively, react almost twice as fast as expected on the basis of the substituent σ_I^q values. An explanation is provided by the fact that, in conjunction with C(4), these substituents form the strongly electrofugal allylic and benzylic groups **18** and **19**9). As σ-electron donors they should enhance hyperconjugation of the C(2),C(3)-bond7) by stabilizing the partial positive charge generated at C(3) in the transition state **20**.

It is instructive to compare the effect of substituents R on the rates of the adamantyl bromides **2a** [4] and the bicyclooctyl nisylates **14**. When log *k* values for the two series are plotted against each other (see *Fig. 2*) a good correlation results (r=0.9961) with four notable exceptions: the points for $(CH_3)_2N$, OH and OCH_3 lie well above the regression line, the point for hydrogen below it. This is not surprising because the $(CH_3)_2N$ group leads to concerted fragmentation of the adamantyl bromide **2a** (R=$(CH_3)_2N$) [4] but can exert only its inductive effect in the nisylate **14k**. Likewise the OH- and OCH_3-groups hyperconjugate in the former case [4] but not in the latter. In view of these additional effects the higher reactivity of these adamantyl as compared to the bicyclooctyl derivatives is to be expected. On the other hand the unsubstituted bicyclooctyl nisylate **14a** is relatively more reactive than adamantyl bromide **2a** (R=H), which confirms that a special effect, such as the extended hyperconjugation depicted in **17** (R=H) assists its ionization.

Financial support by the *Swiss National Science Foundation* is gratefully acknowledged.

---

7) For clarity σ-bond delocalization is indicated by dotted lines in only one of the three equivalent ethano-bridges.

8) As pointed out [4] [7] hyperconjugation merges with fragmentation when the electron donor is a sufficiently active electrofuge.

9) In fragmentation these groups are converted to stable tertiary allylic and benzylic cations.

Experimental Part

Solvolyses. 0.2M solutions of the nisylates **14a-14t** in 70% W/W aqueous dioxane were reacted for ten half lives in the presence of 3 equiv. of triethylamine except for the nisylate **15b** (R = COO$^-$), which was solvolyzed with 3 equiv. of KOH. Dioxane was then removed by distillation through a short column. The residue was extracted three times with ether, the extracts were washed with water, dried over Na_2SO_4 and evaporated to dryness. The residues, which in all cases consisted only of the corresponding bicyclo[2.2.2]octan-1-ols (**14**, X = OH) were purified by crystallization and identified by comparison with authentic samples [13].

Rate measurements. The rates of the nisylates in 80 vol.-% ethanol were followed conductometrically by the method described [15]. Measurements were made at three temperatures, constant to ±0.03°, as listed in *Table 1* and repeated two to five times.

REFERENCES

[1] *C.A. Grob & M.G. Schlageter*, Helv. *59*, 264 (1976).
[2] *C.A. Grob, B. Schaub & M.G. Schlageter*, in preparation.
[3] *C.A. Grob & M.G. Schlageter*, Helv. *60*, 1884 (1977).
[4] *W. Fischer & C.A. Grob*, Helv. *61*, 1588 (1978).
[5] *C.A. Grob & A. Waldner*, Helv. *62*, 1736 (1979).
[6] *C.A. Grob & P.W. Schiess*, Angew. Chemie *79*, 1 (1967); intern. edit. *6*, 1 (1967).
[7] *C.A. Grob*, Angew. Chemie *88*, 621 (1976); intern. edit. *10*, 569 (1976).
[8] *C.A. Grob*, Angew. Chemie *81*, 543 (1969); intern. edit. *8*, 535 (1969).
[9] *Klaus Günther Artz*, Dissertation, University of Basel 1963.
[10] *C.A. Grob & H. von Tschammer*, Helv. *51*, 1082 (1968).
[11] *P. von R. Schleyer & C.W. Woodworth*, J. Amer. chem. Soc. *90*, 6528 (1968).
[12] *G. Wenke & D. Lenoir*, Tetrahedron Letters *1979*, 2823.
[13] *C.A. Grob & R. Rich*, Helv. *62*, 2802 (1979).
[14] *C.A. Grob & R. Rich*, Tetrahedron Letters *1978*, 663.
[15] *C.A. Grob, F.M. Unger, E.D. Weiler & A. Weiss*, Helv. *55*, 501 (1972).