228. Polar Effects

Part 14

Inductive Charge Dispersal in Bicyclo[2.2.2]oct-1-yl Cations

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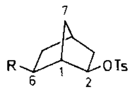
The rate constants (log k) for solvolysis of 2-, 3-, and 4-substituted bicyclo[2.2.2]octyl p-nitrobenzenesulfonates **10**, **11**, and **12**, respectively, correlate linearly with the corresponding inductive substituent constants σ_I^q. The formation of the ion pairs **9** is, therefore, controlled by the *I* effect of neighboring substituents. It follows from the corresponding reaction constants ρ_I of -1.54, -1.12, and -1.22 that inductivity is highest at the positions α to C(1). It is lower and practically equal at the β- and γ-positions. Therefore, charge dispersal is similar to that previously observed in the quinuclidinium ion **7**.

The observation that the solvolysis rates of many bi- and tricyclic arenesulfonates are controlled by the inductive (*I*) effect of neighboring substituents has led to a new method to gauge charge dispersal in carbocations [1].

This method makes use of the *Hammett*-type equation $\log k/k_0 = \rho_I \sigma_I^q$, where k and k_0 are the rate constants for the substituted and unsubstituted compounds, respectively. σ_I^q are the inductive constants [2] for the substituents used as probes for charge dispersal, and ρ_I are the derived reaction constants that gauge the inductivity of the C-atoms to which the substituents are attached.

For instance, the ρ_I values for the substituted C-atoms in the solvolysis of the 2-norbornyl, 2-bicyclo[2.2.2]octyl and 2-adamantyl p-toluenesulfonates (tosylates) **1**, **2**, and **3** are -2.00 [3], -1.50 [4], and -0.80 [5], respectively. Inductivity thus differs widely, although these tosylates possess the common partial structure **4**[1]. It was, therefore, concluded that ρ_I values reflect directional electron mobility, a property which is evidently subject to constraints imposed by the entire molecule [1].



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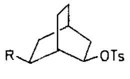

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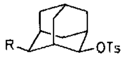

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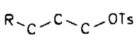

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In the solvolysis of substituted 2-*exo*- and 2-*endo*-norbornyl tosylates **5** and **6**, respectively, in 80% (v/v) EtOH positive charge is mainly dispersed to C(6); but substantial charge is transmitted to other neighboring C-atoms [6][2]. The same applies to the

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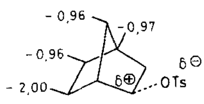
[1] It was ascertained in each case that solvolysis proceeds by the unimolecular S_N1 mechanism, *i.e.* without appreciable nucleophilic solvent participation.

[2] The strong participation of the dorsal C(6) in the ionization of **5** and the lesser involvement of the dorsal C(7) in **6** are considered to be the reason for the high *exo/endo* rate ratio for unsubstituted **5** and **6**, respectively [1].



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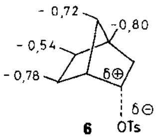

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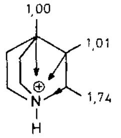

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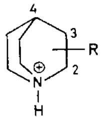

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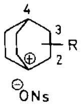
quinuclidinium ion **7**, as shown by the pK_a values of 2-, 3-, and 4-substituted quinuclidinium perchlorates **8**. Charge is dispersed mostly to the three equivalent positions α to N, but less to the three β- and the γ-positions [7].

Using the same method, charge dispersal has now been determined in the bicyclo[2.2.2]oct-1-yl (BO) cation **9** (R=H). Solvolysis rate constants for series of 2-, 3-, and 4-substituted bicyclo[2.2.2]octyl *p*-nitrobenzenesulfonates (nisylates) **10**, **11**, and **12**, respectively, were measured in 80% EtOH, the strength of the substituent effects again serving as probes for inductivity.



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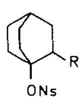

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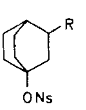

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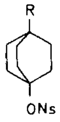

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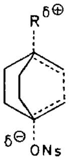
Despite their close structural similarity, the quinuclidinium and the cation **9** differ in two important respects. Thus, pK_a values are determined with free solvated cations **8**, while rate constants for solvolysis of BO-nisylates reflect the transition states for the formation of contact ion pairs **9**[3]), in which the anion is expected to affect electron mobility in the incipient cation. Also, cationic C-atoms are strongly electrophilic and should attract electrons from neighboring C-atoms more strongly than the ammonio N-atom in **8**. How these factors would balance could not be foreseen.

The rate constants in 80% EtOH for twenty 4-substituted nisylates **12** were reported previously [9]. Whereas most of them correlated well with the respective σ_I^q values, those obtained with nisylates containing a potentially electrofugal substituent[4]) at C(4), such as CH_2OH, CH_2NH_2, $CONH_2$, COO^- as well as hydrogen, gave rise to rate enhancements by factors of 2 to 8 based on σ_I^q values. These weakly exalted substituent effects were tentatively ascribed to twofold hyperconjugation involving the R–C(4) and the three ethano bonds as illustrated in **13** (for one bridge only). This proposal was rejected by *Wenke* and *Lenoir* on theoretical grounds [11]. Recently, however, *Adcock et al.* have apparently revived this concept as σ,σ hyperconjugation [12] to rationalize ^{19}F chemical shifts in 4-substituted BO-fluorides.



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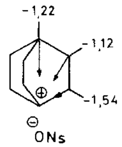

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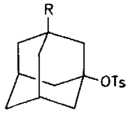

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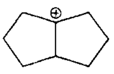

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[3]) It is generally accepted that ionization transition states are satisfactory models for the resultant ion pair [8].

[4]) These are strong electron donors in heterolytic fragmentation [10].

A few electrofugal substituents (CH_2OH, $CONH_2$) were included in the present study in order to determine their effect in the 2- and 3-position of **10** and **11**, respectively. The preparation of the nisylates by standard methods and their hydrolyses are [9] [13] or will be published [14] elsewhere.

Results and Discussion. – The rate constants for the series of nisylates **10a–k**, **11b–l**, and **12b–l** are listed in *Tables 1, 2,* and *3,* respectively. When $5 \cdot 10^{-2}$M solutions of the nisylates were hydrolyzed in 70% dioxane, the corresponding bicyclo[2.2.2]octan-1-ols were formed exclusively [9] [13] [14], *i.e.* no rearrangements or hydride shifts were observed.

A plot of log *k* for the 2-substituted nisylates **10** *vs.* the corresponding σ_I^q values *(Fig. 1)* led to a ρ_I value of −1.54 (r = 0.994). The points for the electrofugal substituents

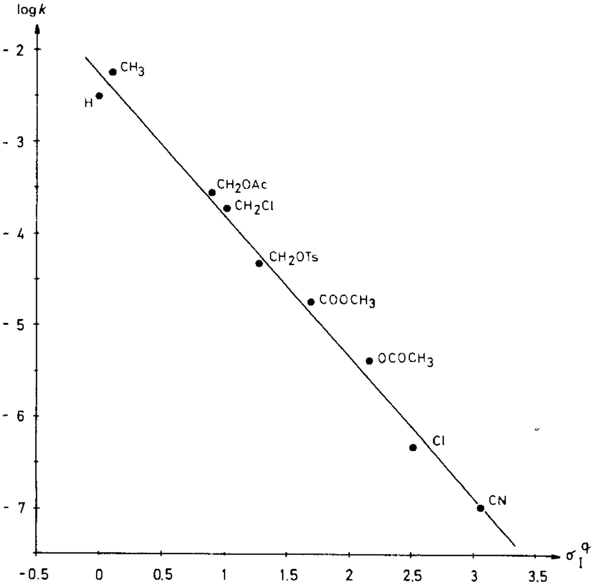

Fig. 1. *Plot of log* k *for* 10^{-3}M *solutions of 2-substituted bicyclo[2.2.2]octyl nisylates* **10** *in 80% (v/v) EtOH* vs. *inductive substituent constants* σ_I^q (determined conductometrically)

CH_2OH and CH_2OCH_3 correspond to accelerations of 6.0 and 3.4, respectively, based on the regression line[5])[6]). When log *k* for the 3-substituted nisylates **11** were plotted likewise (*Fig. 2,* upper line), a ρ_I of −1.12 with a somewhat smaller correlation coefficient of 0.987 was obtained. Finally, a plot of log *k* for the 4-substituted nisylates **12** against σ_I^q *(Fig. 2,* lower line) led to a ρ_I of −1.22 (r = 0.987). The electrofugal substituents CH_2OH and $CONH_2$ both gave rise to rate enhancements based on the regression lines in *Fig. 2,* namely 2.4 and 4.2 in the series **11** and 2.2 and 4.1 in the series **12**, respectively.

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[5]) The exalted effect of electrofugal groups is probably due to the fact that σ_I^q values are based on the pK_a of 4-substituted quinuclidinium perchlorates [2] in which ammonio $N^{\oplus}$ is less electron-attracting than electrophilic $C^{\oplus}$.

[6]) These points were omitted from the regression in all cases.

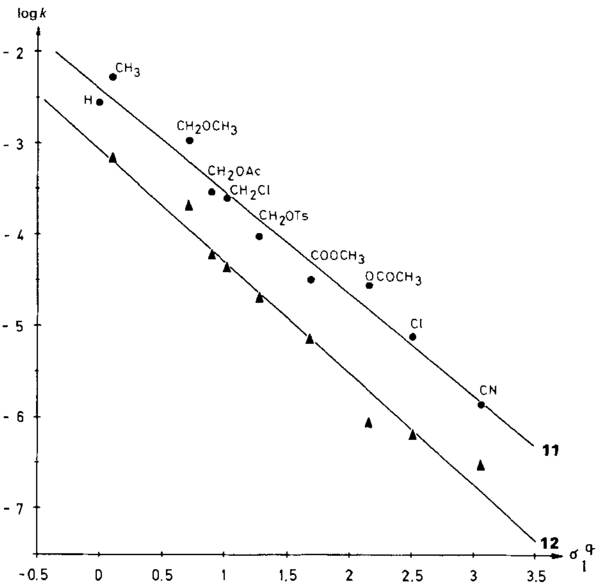

Fig. 2. *Plots of log* k *for* 10^{-3}M *solutions of 3- and 4-substituted bicyclo[2.2.2]octyl nisylates* **11** *and* **12**, *respectively, in 80% (v/v) EtOH* vs. *inductive substituent constants* σ_I^q (determined conductometrically)

In contrast to the series **10** and **11**, where the points for hydrogen lie close to the regression line, the point for H–C(4) in the series **12** lies significantly above the line and corresponds to an acceleration of 3.6. Also, due to the absence of hydrogen at C(4), rates of the 4-substituted nisylates **12** are all somewhat lower than the rates of the series **11** (*Fig. 2*). Since this unusual stabilizing effect of hydrogen at C(4) in the BO cation is not observed in other structures, such as 2-norbornane **1** [3] [6], 2-bicyclo[2.2.2]octane **2** [4] and 2-adamantane **3** [5], it is tempting to ascribe it to the location of the H-atom on the threefold symmetry axis of **12**, as discussed below.[7])

The ρ_I values for the BO-ion pair **9** are summarized in **14**. They illustrate the inductivity of the C-atoms α,β, and γ to the cationic center at C(1). As expected, it is highest at the three equivalent α-C-atoms, where the direct *I* effect coincides with the σ bonds. In this case, inductivity is *ca.* 14% lower than at the α-positions of the quinuclidinium ion **7**. But rate measurements, as mentioned above, gauge the activation free enthalpy of the transition state, where the positive charge of the cation is not fully formed and where the incipient anion should reduce its dispersal. On the other hand, inductivity at the β- and γ-C-atoms in the BO-ion pair **14** are 10 to 20% higher than in **7**, in agreement with the electrophilic nature of the carbenium ion center and its greater distance to the β- and γ-C-atoms.

Inductivity at the γ-C-atom of the BO-ion pair **9** is slightly higher (*ca.* 9%) than at the β-C-atoms. This difference, however, is barely within the limits of the accuracy of the

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[7]) *Schleyer* and *Woodworth* [15], who were the first to study the effect of substituents at C(4) on solvolysis rates of BO arenesulfonates, attributed the abnormal behavior of hydrogen compared with other substituents to a structural change upon replacing it by bulkier groups.

Table 1. *First-Order Rate Constants for 10^{-3}*M *Solutions of 2-R-Bicyclo[2.2.2]-octyl* p-*Nitrobenzenesulfonates* **10** (in 80% (v/v) EtOH; mean deviation ±1.5%)

R	T [°]	k [s^{-1}]	$H^{\neq}$ [kcal/mol]	$S^{\neq}$ [cal/mol·degree]
10a H	50.29	$3.94 \cdot 10^{-4}$	22.3	−5.2
	60.07	$1.15 \cdot 10^{-3}$		
	70.00a)	$3.10 \cdot 10^{-3}$		
	70.04	$3.08 \cdot 10^{-3}$		
b CH_3	40.25	$2.03 \cdot 10^{-4}$	23.1	−1.9
	50.26	$6.73 \cdot 10^{-4}$		
	60.06	$1.96 \cdot 10^{-3}$		
	70.00a)	$5.57 \cdot 10^{-3}$		
c CH_2OH	49.86	$4.21 \cdot 10^{-4}$	23.2	−2.3
	59.84	$1.29 \cdot 10^{-3}$		
	70.00a)	$3.74 \cdot 10^{-3}$		
	70.01	$3.74 \cdot 10^{-3}$		
d CH_2OCH_3	70.00a)	$2.74 \cdot 10^{-4}$	23.8	−5.8
	70.33	$2.84 \cdot 10^{-4}$		
	80.37	$7.82 \cdot 10^{-4}$		
	90.27	$2.04 \cdot 10^{-3}$		
e CH_2OAc	70.00a)	$2.74 \cdot 10^{-4}$	23.8	−5.75
	70.33	$2.84 \cdot 10^{-4}$		
	80.37	$7.82 \cdot 10^{-4}$		
	90.27	$2.04 \cdot 10^{-3}$		
f CH_2Cl	70.00a)	$1.86 \cdot 10^{-4}$	24.3	−5.1
	70.06	$1.85 \cdot 10^{-4}$		
	80.12	$5.39 \cdot 10^{-4}$		
	90.24	$1.42 \cdot 10^{-3}$		
g CH_2OTs	70.00a)	$4.64 \cdot 10^{-5}$	24.6	−7.0
	80.10	$1.33 \cdot 10^{-4}$		
	90.24	$3.70 \cdot 10^{-4}$		
	99.83	$8.95 \cdot 10^{-4}$		
h $COOCH_3$	70.00a)	$1.84 \cdot 10^{-5}$	25.7	−5.6
	90.01	$1.55 \cdot 10^{-4}$		
	99.99	$4.14 \cdot 10^{-4}$		
	110.03	$1.05 \cdot 10^{-3}$		
i $OCOCH_3$	70.00a)	$4.16 \cdot 10^{-6}$	25.8	−8.25
	109.68	$2.28 \cdot 10^{-4}$		
	119.76	$5.50 \cdot 10^{-4}$		
	129.86	$1.32 \cdot 10^{-3}$		

Table 2. *First-Order Rate Constants for 10^{-3}*M *Solutions of 3-R-Bicyclo[2.2.2]-octyl* p-*Nitrobenzenesulfonates* **11** (in 80% (v/v) EtOH, mean deviation ±1.5%)

R	T [°]	k [s^{-1}]	$H^{\neq}$ [kcal/mol]	$S^{\neq}$ [cal/mol·degree]
11b CH_3	49.83	$6.26 \cdot 10^{-4}$	22.6	−3.5
	59.83	$1.89 \cdot 10^{-3}$		
	69.87	$5.17 \cdot 10^{-3}$		
	70.00a)	$5.28 \cdot 10^{-3}$		
c CH_2OH	59.73	$6.80 \cdot 10^{-4}$	22.8	−4.6
	69.80	$1.99 \cdot 10^{-3}$		
	70.00a)	$1.99 \cdot 10^{-3}$		
	79.89	$5.17 \cdot 10^{-3}$		
d CH_2OCH_3	59.92	$3.48 \cdot 10^{-4}$	23.9	−2.9
	69.98	$1.04 \cdot 10^{-3}$		
	70.00a)	$1.04 \cdot 10^{-3}$		
	80.02	$2.87 \cdot 10^{-3}$		
e CH_2OAc	69.82	$2.84 \cdot 10^{-4}$	23.9	−5.4
	70.00a)	$2.90 \cdot 10^{-4}$		
	79.89	$8.03 \cdot 10^{-4}$		
	89.95	$2.10 \cdot 10^{-3}$		
f CH_2Cl	69.82	$2.39 \cdot 10^{-4}$	23.8	−5.9
	70.00a)	$2.43 \cdot 10^{-4}$		
	79.89	$6.64 \cdot 10^{-4}$		
	89.95	$1.76 \cdot 10^{-3}$		
g CH_2OTs	70.00a)	$9.66 \cdot 10^{-5}$	23.0	−10.3
	89.95	$6.46 \cdot 10^{-4}$		
	99.92	$1.58 \cdot 10^{-3}$		
	109.99	$3.60 \cdot 10^{-3}$		
h $COOCH_3$	70.00a)	$3.16 \cdot 10^{-5}$	24.4	−8.3
	89.95	$2.36 \cdot 10^{-4}$		
	99.92	$6.18 \cdot 10^{-4}$		
	109.94	$1.45 \cdot 10^{-3}$		
i $OCOCH_3$	70.00a)	$2.84 \cdot 10^{-5}$	22.4	−8.4
	90.10	$2.18 \cdot 10^{-4}$		
	100.57	$5.80 \cdot 10^{-4}$		
	110.20	$1.36 \cdot 10^{-3}$		
j Cl	70.00a)	$7.77 \cdot 10^{-6}$	24.6	−10.5
	99.22	$1.43 \cdot 10^{-4}$		
	109.51	$3.61 \cdot 10^{-4}$		
	119.58	$8.46 \cdot 10^{-4}$		

j Cl	70.00[a])	$4.65\cdot10^{-7}$	28.2	−5.7
	109.99	$3.90\cdot10^{-5}$		
	120.03	$1.01\cdot10^{-4}$		
	130.06	$2.59\cdot10^{-4}$		
k CN	70.00[a])	$1.05\cdot10^{-7}$	27.3	−11.2
	120.22	$2.00\cdot10^{-5}$		
	130.01	$4.79\cdot10^{-5}$		
	135.09	$7.41\cdot10^{-5}$		

[a]) Extrapolated.

k CN	70.00[a])	$1.39\cdot10^{-6}$	25.8	−10.4
	110.11	$8.11\cdot10^{-5}$		
	120.16	$2.03\cdot10^{-4}$		
	130.19	$4.61\cdot10^{-4}$		
l $CONH_2$	70.00[a])	$1.55\cdot10^{-4}$	23.9	−6.65
	79.85	$4.22\cdot10^{-4}$		
	89.99	$1.14\cdot10^{-3}$		
	99.92	$2.78\cdot10^{-3}$		

[a]) Extrapolated.

Table 3. *First-Order Rate Constants for* 10^{-3}*M Solutions of 4-R-Bicyclo[2.2.2]octyl* p-*Nitrobenzenesulfonates* **12** (in 80% (v/v) EtOH; mean deviation ±1.5%)

R	T[°]	k[s^{-1}]	$H^{\neq}$ [kcal/mol]	$S^{\neq}$ [cal/mol·degree]
12b CH_3[a])	65.00	$4.10\cdot10^{-4}$	23.3	−5.4
	70.00[b])	$6.89\cdot10^{-4}$		
	75.00	$1.14\cdot10^{-3}$		
	90.00	$4.79\cdot10^{-3}$		
c CH_2OH[a])	65.00	$1.91\cdot10^{-4}$	24.6	−3.1
	70.00[b])	$3.29\cdot10^{-4}$		
	75.00	$5.58\cdot10^{-4}$		
	85.00	$1.56\cdot10^{-3}$		
d CH_2OCH_3	69.81	$2.07\cdot10^{-4}$	24.5	−4.1
	70.00[b])	$2.11\cdot10^{-4}$		
	79.91	$5.95\cdot10^{-4}$		
	89.99	$1.61\cdot10^{-3}$		
e CH_2OAc	70.00[b])	$6.07\cdot10^{-5}$	24.7	−6.1
	79.93	$1.73\cdot10^{-4}$		
	90.24	$4.84\cdot10^{-4}$		
	99.87	$1.20\cdot10^{-3}$		
f CH_2Cl	70.00[b])	$4.34\cdot10^{-5}$	24.9	−6.3
	80.05	$1.26\cdot10^{-4}$		
	89.99	$3.42\cdot10^{-4}$		
	100.06	$8.90\cdot10^{-4}$		
g CH_2OTs	70.00[b])	$2.04\cdot10^{-5}$	25.2	−6.9
	90.59	$1.75\cdot10^{-4}$		
	100.13	$4.37\cdot10^{-4}$		
	110.02	$1.08\cdot10^{-3}$		
h $COOCH_3$[a])	70.00[b])	$7.07\cdot10^{-6}$	26.6	−4.9
	100.00	$1.79\cdot10^{-4}$		
	110.00	$4.52\cdot10^{-4}$		
	120.00	$1.17\cdot10^{-3}$		
i $OCOCH_3$	70.00[b])	$9.08\cdot10^{-7}$	27.4	−6.5
	109.90	$6.65\cdot10^{-5}$		
	119.99	$1.75\cdot10^{-4}$		
	130.09	$4.25\cdot10^{-4}$		
j Cl	70.00[b])	$6.54\cdot10^{-7}$	26.8	−9.0
	115.03	$7.12\cdot10^{-5}$		
	125.11	$1.74\cdot10^{-4}$		
	135.22	$4.18\cdot10^{-4}$		
k CN[a])	70.00[b])	$3.12\cdot10^{-7}$	26.7	−10.8
	110.00	$2.07\cdot10^{-5}$		
	120.00	$5.19\cdot10^{-5}$		
	130.00	$1.24\cdot10^{-4}$		
l $CONH_2$[a])	70.00[b])	$2.10\cdot10^{-5}$	24.4	−9.2
	100.00[a])	$4.02\cdot10^{-4}$		
	109.98	$9.88\cdot10^{-4}$		
	119.99	$2.25\cdot10^{-3}$		

[a]) Known values [9]. [b]) Extrapolated.

method[8]). It is clear, however, that the inductivities, as well as the corresponding C(1)–C(3) and C(1)–C(4) distances of 2.53 and 2.59 Å, respectively, [16] are almost the same in the series **11** and **12**. This is to be expected if induction involves a direct shift of electron density towards the cationic center, as illustrated in **14** and as postulated for **7** [7].

It is noteworthy that the log k values for the series **11** and **12** correlate well with log k for 3-substituted adamantyl tosylates **15** [17]. In the latter case, however, ρ_I is somewhat larger, namely -1.26, which indicates that C(1)–C(3) electron mobility is higher in **15** than in **14**. As reported in [7], the chemical shifts in the ^{1}H- and ^{13}C-NMR spectra of the quinuclidinium ion **9** (R=H) agree well with the observed inductivities[9]). Unfortunately, such data is not obtainable for the free BO cation due to its rapid rearrangement to the bicyclo[3.3.0]oct-1-yl cation **16** under long-lived conditions [18].

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[8]) Standard deviations of the pK_a, upon which σ_I^q values are based, and of the conductometric rate measurements, as well uncertainties regarding the orientation of dipolar substituents, contribute to this limitation, as in most *Hammett* treatments.

[9]) The ^{13}C-NMR signals for the α-, β-, and γ-C-atoms in the quinuclidinium ion in CF_3COOH were reported as 48.10, 22.90, and 19.30, respectively [19].