95. Inductive Charge Dispersal in Quinuclidinium Ions

Polar Effects, Part 13

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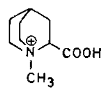
Inductive charge dispersal to the α-, β- and γ-positions of the solvated quinuclidinium ion has been examined by comparing the pK_a and the derived inductivities ρ_I of several 2-, 3- and 4-substituted quinuclidinium perchlorates **4**, **5**, and **6**, respectively. The same inductivity is observed at the practically equidistant β- and γ-positions. It, therefore, appears that polar substituent effects are transmitted directly through the molecule. As expected, inductivity is considerably higher at the α-positions where through-bond and direct induction coincide. The fact that the pK_a of all three series of salts correlate linearly with each other points to the common nature of these inductive electron displacements.

Previous studies [1] have shown that the pK_a of α-, β- and γ-ammonio acids, such as the 2-, 3- and 4-carboxyquinuclidinium perchlorates **1**, **2**, and **3**, respectively, correlate well with the reciprocal distances ($1/r$) between the positive N-atom and the carboxy proton according to the *Bjerrum*-type equation: Δ p$K_a = -e^2/2.3\,k\,T\,r\,D_E$ [2]. Δ pK_a refers to the difference between the pK_a of the ammonio acid and the pK_a of the corresponding uncharged acid. D_E is the so-called effective dielectric constant in the *Kirkwood-Westheimer* modification [3] of the *Bjerrum* equation. It was, therefore, concluded that polar substituent effects are transmitted directly through the molecule in agreement with the field model, rather than by successive polarization of the connecting σ-bonds (σ inductive effect)[1]). On the other hand, the above correlation led to unrealistic pK_a values for the uncharged acids[2]), as also noted by *Wepster* and coworkers [6]. This fact indicated that D_E does not remain constant as r is varied and detracts from the value of the above equation.



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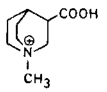

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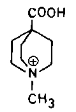

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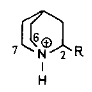

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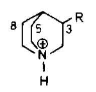

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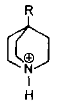

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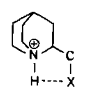

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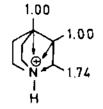

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[1]) Reviews: [4] [5].

[2]) The calculated pK_a values were more than 1.5 pK_a units too high for $r = \infty$.

Subsequently, the pK_a of a large number of 4-substituted quinuclidinium perchlorates **6** were measured in which the source of the polar effect varied while the distances to the reaction center remained constant [7]. From these pK_a values, a new set of inductive substituent constants σ_I^q were derived according to the equation pK_a^H – pK_a^R = $\rho_I\sigma_I^q$, where pK_a^H and pK_a^R refer to the unsubstituted and substituted quinuclidinium salts **6**, respectively, and ρ_I is a reaction constant arbitrarily defined as unity. Since steric, conjugative, and hyperconjugative effects do not play a significant role in these models, the σ_I^q constants are useful in correlating reaction rates and equilibria with the inductive (*I*) effect of substituents³). The reaction constants ρ_I are a measure of the sensitivity of the reaction to the *I* effect of substituents. This parameter, the so-called inductivity of the system, has been determined as a function of structure for several S_N1 reactions [8].

The present study is concerned with the inductivities of 2-, 3- and 4-substituted quinuclidinium perchlorates **4**, **5**, and **6**, respectively, as measured by their pK_a values⁴). A comparison of the pK_a of these three series of salts should reveal how the positive charge is dispersed in the quinuclidinium cation as a function of distance and chain length. The average interatomic distances in quinuclidinium salts, namely C(2)–N$^+$, C(3)–N$^+$, and C(4)–N$^+$ are reported to be 1.51 Å, 2.45 Å, and 2.53 Å, respectively [10]; *i.e.* the C(4)–N$^+$ distance is only 3% greater than the C(3)–N$^+$ distance, so that the comparison of the pK_a values is of special interest. Thus, if direct distance were the dominant factor, the inductivities of the two series **5** and **6** should be practically the same. If, on the other hand, a strong σ inductive effect were superposed on the direct effect, as claimed by *Wepster* and coworkers [6], transmission of the polar effects of substituents at C(3) should be stronger than those of substituents at C(4). In the series **4**, however, where the direct mode of transmission is shorter and practically coincides with the through-bond mode, a still larger effect was expected.

Certain structural features could, however, detract from the value of comparing substituent effects on pK_a in the series **4**, **5**, and **6**. Thus, in the symmetrical case **6**, the net dipole interaction of rotating substituents with the N-atom is constant, whereas in the asymmetrical series **4** and **5** it varies with rotation and is conformation-dependent.

A further difficulty, illustrated by space-filling models, arises in the series **4** where intramolecular H-bonding of certain substituents, such as CH_2OH and $CONH_2$ to the N$^+$–H atom could be envisaged. Such acid-weakening bonding would oppose the -*I* effect of these substituents. In addition, steric hindrance to solvation in the series **4** could affect the correlation of pK_a with σ_I^q.

The preparation of several 2- and 3-substituted quinuclidinium perchlorates **4** und **5**, respectively, and their pK_a are reported in [11]. In this article, the pK_a of the series **4** and **5** are compared and correlated with the known pK_a of their 4-substituted isomers **6** [7]. All three series of pK_a values are summarized in the *Table*.

Discussion. – In *Fig. 1*, the pK_a values for the 2-substituted salts **4** are plotted against the pK_a values for the corresponding 4-substituted salts **6**. The slope of the regression line corresponds to a ρ_I of 1.74 (r = 0.977) and indicates that inductivity is indeed much stronger in the series **4** than in the series **6**, where ρ_I = 1 by definition. The deviations of some of the points from the regression line could well be due to different dipole orien-

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³) For a recent review, see [8].

⁴) For a preliminary communication, see [9].

Table. *pK_a Values of 2-, 3- and 4-Substituted Quinuclidinium Perchlorates* (25.0 °C in 0.1M aq. KCl soln.; maximum deviation ±0.015 pK_a units)a))

R	2-R	3-R	4-R
H	11.29	11.29	11.29
CH_3	11.33	11.29	11.18
CH_2OH	10.85	10.56	10.67
CH_2OAc	9.88	10.29	10.39
CH_2Cl	9.68	10.15	10.27
CH_2OTs	9.09	9.78	10.01
COOEt	8.80	9.64	9.59
OH		9.91	9.53
$CONH_2$	9.04	9.82	9.47
OCH_3	8.87		9.40
OAc		9.27	9.13
Cl	6.98	8.85	8.78
CN	5.85	7.89	8.23

a) Of at least two independent measurements.

tations of substituents in **4** and **6**. On the other hand, there is no clear indication that they are caused by differencial H-bonding. In fact, the latter could be negligible due to the unfavorable X···H–N$^+$ angle of *ca.* 90° (X = O, N, or Cl) in these cations, as illustrated in formula **7**.

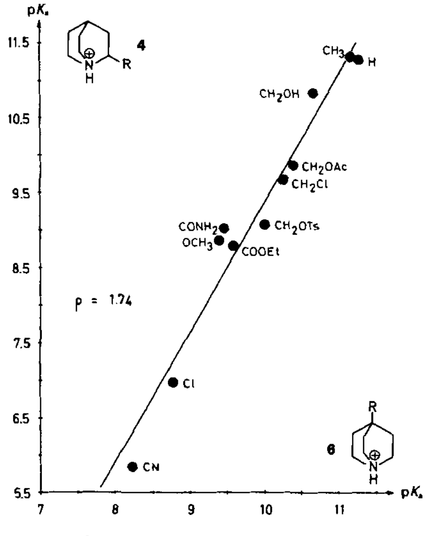

Fig. 1. *Plot of pK_a for the series* **4** vs. *pK_a for the series* **6**

When the pK_a values for the 3-substituted salts **5** are plotted against the pK_a values for the 4-substituted salts **6** *(Fig. 2)*, the slope ρ_I of the regression line (r = 0.975) is unity. This means that inductivity in the two structures is the same within the limit of error. This result would only be expected if the direct mode alone accounted for the transmission of polar substituent effects, since the C(3)–N and C(4)–N distances are practically the same. If a σ-inductive effect were superposed on the direct effect, inductivity should be higher in the series **5**.

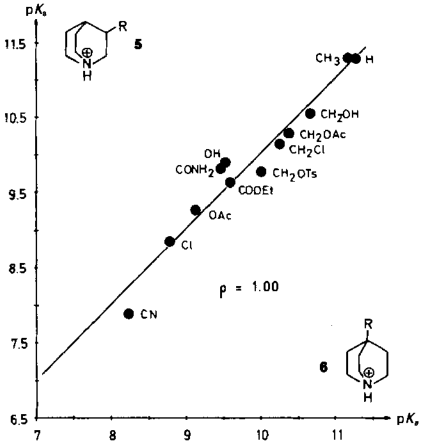

Fig. 2. *Plot of p*K_a *for the series* **5** vs. *p*K_a *for the series* **6**

The points in the plot of *Fig. 2* show apparently random scattering. As indicated in the *Table,* the pK_a values for **5** are in some cases higher and, in other cases, lower than those for the series **6**. This scattering could again be due to different dipole orientations of the substituents at C(3) and C(4). In view of this possibility, it is surprising that the deviations from the regression line in *Fig. 2* are not larger. As expected, the pK_a for the series **4** and **5** correlate well (r = 0.989), with a regression line of slope 1.70.

The pK_a values indicate that the polar effects of substituents at C(3) and, for symmetry reasons, at C(5) and C(8), are transmitted with equal intensity to the N-atom as those of substituents at C(4). In other words, charge is dispersed equally to the β- and γ-positions of the quinuclidinium ion. As expected, charge dispersal is strongest to the α-positions C(2), C(6), and C(7), where through-bond transmission coincides with direct transmission. This conclusion is supported by the ^{1}H-NMR spectrum of quinuclidinium hydrochloride in D_2O, in which the α-, β-, and γ-protons appear at 3.3, 2.0, and 2.0, respectively, relative to sodium 3-(trimethylsilyl)propanesulfonate [12].

The fact that the pK_a of all three series **4**, **5**, and **6** correlate with each other points to the common nature of induction in these structures. It can be described as a shift of electron density toward or away from the reaction center, either directly through the cage or along the lines to adjacent atoms, according to the electron mobility of the structure. This is illustrated by the arrows and the ρ_I values in **8** (drawn in only one of the three ethano bridges). Since the space within the confines of a molecule is a region of high electron density, this model offers a more explicit description of the way polar effects are transmitted than the *Bjerrum* [2] and later field models [3] [5], in which the medium, vaguely defined as space, is assigned a 'microscopic' dielectric constant D_E. Furthermore, the above results again raise the question [1] whether it is meaningful to uphold the traditional distinction between two intrinsically different effects referred to as the field and the σ inductive effect [5].

REFERENCES

[1] C. A. Grob, A. Kaiser, T. Schweizer, *Helv. Chim. Acta* **1977,** *60,* 391.
[2] N. Bjerrum, *Z. Phys. Chem.* **1923,** *106,* 219.
[3] F. H. Westheimer, J. G. Kirkwood, *J. Chem. Phys.* **1938,** *6,* 513.
[4] L. M. Stock, *J. Chem. Educ.* **1972,** *49,* 400.
[5] W. F. Reynolds, in 'Progress in Phys. org. Chem.', John Wiley and Sons, New York, 1983, Vol. 14, p. 165; W. F. Reynolds, *J. Chem. Soc., Perkin Trans. 2* **1980,** 985.
[6] A. J. Hoefnagel, M. A. Hoefnagel, B. M. Wepster, *J. Org. Chem.* **1978,** *43,* 4720.
[7] C. A. Grob, B. Schaub, M. G. Schlageter, *Helv. Chim. Acta* **1980,** *63,* 57; C. A. Grob, M. G. Schlageter, *ibid.* **1976,** *59,* 264.
[8] C. A. Grob, *Acc. Chem. Res.* **1983,** *16,* 426.
[9] R. Bielmann, C. A. Grob, D. Küry, G. W. Yao, *Tetrahedron Lett.* **1985,** *26,* 315.
[10] M. Zehnder, *Helv. Chim. Acta* **1980,** *63,* 750; M. Kurahashi, P. Engel, W. Nowacki, *Z. Kristallogr.* **1980,** *152,* 135, 147.
[11] R. Bielmann, C. A. Grob, H. Seiler, *Helv. Chim. Acta,* in preparation.
[12] *'Aldrich'*-NMR-Spectra, Vol. II, 87C, **1974.**