from cyclohexane to colourless prisms (168 mg; 68.5%), m.p. 90–91° (Lit. for unlabeled compound: 90.8–91.5° [15]). The compound sublimed at 60°/0.1 Torr.

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31. The Derivation of Inductive Substituent Constants from pK_a Values of 4-Substituted Quinuclidines. Polar Effects. Part I

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(29. X. 75)

Summary. Thermodynamic pK_a-values have been determined for 38 4-substituted quinuclidinium perchlorates. They are remarkably sensitive to the polar effect of the substituent and cover a range of 3.63 pK_a units. Furthermore, they vary linearly and almost equally with temperature since the contribution of the $T\Delta S°$ term to the free energy of ionization is relatively small and constant. The magnitude of the polar effect of the 4-cyano group varies with the solvent and appears to depend on its ability to form hydrogen bonds to the substituent rather than its dielectric constant.

New inductive substituent constants σ_I^q are derived from the pK_a values. Their correlation with known inductive constants is only fair or unsatisfactory, especially as regards the relative order of hydrogen and the alkyl groups. The discrepancies can be ascribed mainly to the different models used to derive the substituent constants.

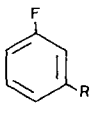
Several methods have been developed for the quantitative determination of polar substituent effects on the reactivity (rates and equilibria) at a non-conjugating reaction center.

Of these methods one due to *Taft* [1] has been most widely used. It is based on measurements of differences of hydrolysis rates of substituted and unsubstituted esters under acidic and alkaline conditions. The polar substituent constants σ^* obtained in this way are proportional to *Taft's* inductive constants σ_I[1]) and are assumed to be devoid of contributions from steric and conjugative effects, a view which has been questioned by *Shorter* [2] and, more recently, by *Charton* [3].

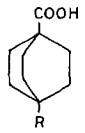
A second method, also due to *Taft* [4], is based on the chemical shifts of ^{19}F in the NMR.-spectra of meta-substituted fluorobenzenes (I). These shifts correlate well with *Taft's* σ_I constants and are practically independent of the solvent.

$$RCH_2COOH + H_2O \rightleftarrows RCH_2COO^- + H_3O^+ \qquad \text{(reaction 1)}$$

Using a more direct approach *Charton* has derived 'inductive' substituent constants σ_I from pK_a values of substituted acetic acids in water (reaction 1) [5]. Although satisfactory for small substituents, the method is considered to be unreliable when bulky groups hinder the solvation of the carboxylate ion [2]. Furthermore, the relative acidities of carboxylic acids are frequently temperature dependent because of the large contribution of the entropy term to the free energy of ionization [6].



I



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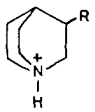
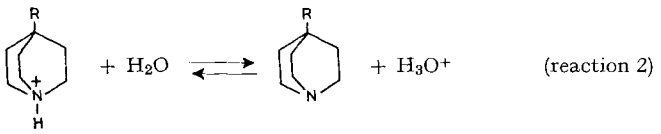


III

Some of these defects are absent in rigid highly symmetrical acids, such as the 4-substituted bicyclo[2.2.2]octane carboxylic acids (II) of *Roberts* [7]. However, in these compounds substituent effects tend to be attenuated due to the large number of intervening bonds. Thus, the pK_a of II, where R = H and $COOC_2H_5$, respectively, differ by less than 0.5 units and those of the 4-alkyl derivatives are practically indistinguishable [8].

Much stronger responses to substituents are observed in the pK_a of 3-substituted quinuclidinium salts (III) which were measured in this laboratory [9]. However, free rotation of unsymmetrical substituents R, such as $COCH_3$ and $CONH_2$, leads to varying dipole orientations and, therefore, no definite conclusions concerning the magnitude of polar substituent effects can be drawn from these measurements.



(reaction 2)

IV

Most of the shortcomings of present methods for determining polar or inductive substituent effects are absent in 4-substituted quinuclidines (IV) (reaction 2) and it has been recognized for some time that these highly symmetrical and sufficiently

[1]) $\sigma_I = 0.45\,\sigma^*$

Table 1. *Thermodynamic pK_a-values for 4-R-quinuclidinium-perchlorates in water at 25.0 °C*

Nr.	R	pK_a^T	$\pm s$ [a]	N [b]	σ_I^q [c]
1	H	11.12	0.017	8	–
2	CH_3	11.01	0.002	2	0.11
3	C_2H_5	11.09	0.004	2	0.03
4	i-C_3H_7	11.20	0.004	2	−0.08
5	t-C_4H_9	11.27	0.004	3	−0.15
6	CH_2OH	10.46	0.003	2	0.66
7	CH_2OCH_3	10.46	0.014	2	0.66
8	CH_2OCOCH_3	10.24	0.012	2	0.88
9	$CH_2OSO_2C_6H_4CH_3$-p	9.84	0.003	2	1.28
10	CH_2Cl	10.15	0.003	2	0.97
11	CH_2Br	10.10	0.016	2	1.02
12	CH_2J	10.08	0.008	2	1.04
13	$CH(OH)_2$	9.89	0.011	2	1.23
14	$CH=CH_2$	10.56	0.008	2	0.56
15	$C(CH_3)=CH_2$	10.52	0.007	5	0.60
16	$C\equiv CH$	9.48	0.015	2	1.64
17	C_6H_5	10.18	0.015	2	0.94
18	COO^- [d]	10.54	0.016	3	0.58
19	$COOCH_3$	9.42	0.007	2	1.70
20	$COOC_2H_5$	9.42	0.003	2	1.70
21	$COCH_3$	9.43	0.005	3	1.69
22	$CONH_2$	9.34	0.002	2	1.78
23	CN	8.08	0.015	5	3.04
24	NH_2 [e]	10.14	0.013	2	0.98
25	$NHCH_3$ [e]	10.32	0.017	2	0.80
26	$N(CH_3)_2$ [e]	10.15	0.030	2	0.97
27	$NHCOCH_3$	9.54	0.005	2	1.58
28	$NHCOOC_2H_5$	9.56	0.015	2	1.56
29	NO_2	7.64	0.013	2	3.48
30	OH	9.44	0.013	2	1.68
31	OCH_3	9.31	0.011	2	1.81
32	$OCOCH_3$	9.00	0.014	2	2.12
33	SCH_3 [f]	9.46	0.005	2	1.66
34	SO_2CH_3	7.89	0.035	2	3.23
35	F	8.55	0.008	3	2.57 [g]
36	Cl	8.61	0.001	2	2.51
37	Br	8.47	0.011	4	2.65
38	J	8.78	0.001	2	2.34

a) Standard deviation.

b) Number of titrations.

c) $\sigma_I^q = pK_a^H - pK_a^R$.

d) The pK_a of the COOH group in the hydroperchlorate is 3.54 ± 0.021.

e) The pK_a^1-values of the three di-hydroperchlorates are 6.79 (± 0.001), 6.91 (± 0.001) and 6.41 (± 0.004), respectively.

f) The pK_a of quinuclidine-4-thiol [12f] could not be determined accurately because of overlapping of pK_a^1 and pK_a^2.

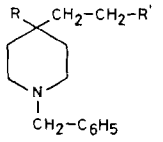
g) The constants for the halogens are possibly composite numbers (see text).

water soluble compounds should be particularly suitable for the derivation of polar substituent constants [10] [11]. Thus, although the 4-substituent is close to the reaction center (ca. 2.55 Å) it cannot interfere with solvation by a steric effect. Furthermore, its net polar effect is orientated in the axis of the molecule and is transmitted through three ethano-bridges, *i.e.* a region of low dielectric constant. The resultant effect should therefore be strong and relatively independent of the surrounding medium. Finally, reactants and products carry a single positive charge (reaction 2) and less differential solvation occurs than in the ionization of neutral acids (reaction 1). But despite the merits of 4-substituted quinuclidines their inaccessibility has presented a severe obstacle to systematic studies. Recently, a large number of new representatives has become available in this laboratory and preliminary pK_a values have been obtained [12a–f].

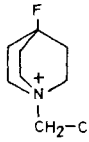
In this study thermodynamic, *i.e.* concentration-independent pK_a^T values for quinuclidinium perchlorate and 38 4-derivatives, including the hitherto unknown 4-fluoro-derivative, have been measured and the derived inductive substituent constants correlated with published data. Also, the effect of temperature on the pK_a^T of a selected group of quinuclidinium salts has been measured and the contribution of the enthalpy and entropy terms to the free energy of reaction (2) calculated.

Furthermore, pK_a measurements of quinuclidine and its 4-cyano-derivative in solvents of different dielectric constant have lead to an evaluation of the influence of the solvent on the magnitude of the polar substituent effect. Finally, reference is made to a recent paper of *Palecek & Hlavaty* [13] who measured and discussed the pK_a of some known 4-substituted quinuclidines in mixed solvents.

Results. – The 4-substituted quinuclidines selected for this study are listed in Table 1 and are numbered **1–38**. The hitherto unknown 4-fluoroquinuclidine (**35**) was prepared from 1-benzyl-4-hydroxy-4(β-hydroxyethyl)-piperidine (V). The latter was converted to the tertiary fluoride VI with 100% hydrofluoric acid. Treatment of VI with thionyl bromide furnished the fluorobromide VII which cyclized to the quaternary salt VIII upon heating in benzene. Hydrogenation over palladium yielded the hydrobromide of **35** which was converted to the hydroperchlorate in the usual way.



V R = R' = OH
VI R = F, R' = OH
VII R = F, R' = Br



Br^- VIII

The thermodynamic pK_a values (pK_a^T) for the hydroperchlorates **1–38** were obtained by potentiometric titration of aqueous solutions of the salts with NaOH at 25.0 °C. From the volume of added titrator and the resulting pH the pK_a^T values were calculated with equation (1) [14]

$$pK_a^T = pH + \log \frac{C_T - C_A + [HO^-] - [H^+]}{C_A - [HO^-] + [H^+]} \cdot f_{HQ^+} \qquad (1)$$

where f_{HQ^+} is the activity coefficient of the quinuclidinium ion HQ^+ and C_T is the sum of $[HQ^+]$ and $[Q]$, C_A is the concentration of NaOH. Equation (1) includes a

correction for dilution by the titrator and furnishes a pK_a^T value for every titration point. The activity coefficients f_{HQ^+} were calculated with the *Debye-Hückel* formula (2) [14].

$$-\log f_{HQ^+} = \frac{0.5115\sqrt{I} \cdot z^2}{1 + 0.3291 \cdot \mathring{a} \cdot \sqrt{I}} \tag{2}$$

where z is the ionic charge, $\mathring{a}$ is the mean interionic distance (5 Å) and I the ionic strength, *i.e.* $0.5 \cdot \sum_i c_i \cdot z_i^2$. For the monocationic acids HQ^+ I follows from equation (3):

$$I = 0.5\,([Na^+] + [HQ^+] + [H^+] + [ClO_4^-] + [HO^-]) = C_T + [HO^-] \tag{3}$$

since $[HQ^+]$ equals $[ClO_4^-] + [HO^-] - [Na^+] - [H^+]$ due to the balance of charges.

Since equation (1) requires concentration instead of activity terms, as obtained from pH measurements, $[H^+]$ and $HO^-]$ were calculated with equation (2) by the method of successive approximations [14]. The f_{H^+} values so obtained furnish $[H^+]$ according to (4).

$$[H^+] = \frac{10^{-pH}}{f_{H^+}}. \tag{4}$$

The dicationic acids **24**, **25** and **26** have two dissociable protons and therefore two pK_a values. pK_a^1 corresponds to reaction at the 4-amino group, pK_a^2 to the reaction at the 1-aza position. This follows from the signal for the $N(CH_3)_2$ group (*s*, 6H) at 2.92 ppm in the NMR.-spectra of **26**-dihydroperchlorate in D_2O which undergoes a large shift of 0.63 ppm upfield upon formation of the mono-hydroperchlorate (δ = 2.29 ppm). A smaller shift upfield results upon formation of the free base **26** (δ = 2.11). The pK_a^T values in Table 1 pertain to pK_a^2 values. pK_a^1 values are included as footnotes. The latter were calculated from equation (1) by replacing f_{QH^+} with $f_{QH_2^{++}}/f_{QH^+} = 4$. pK_a^2 is calculated with equation (5), the ionic strength I being given by (6).

$$pK_a^2 = pH + \log \frac{2\,C_T - C_A + [HO^-] - [H^+]}{C_A - C_T - [HO^-] + [H^+]} \cdot f_{QH^+} \tag{5}$$

$$I = 2\,C_T + [HO^-]. \tag{6}$$

The pK_a^T values were derived from 15 to 20 titration points and submitted to a *Nalimov* test [15] in order to eliminate random deviations. The results are listed in Table 1 together with the standard deviations *s* and the number of titrations *N*[2]). The agreement between the pK_a^T values and the uncorrected pK_a values reported earlier [12 c–f] is satisfactory with the exception of the values for the strongest bases **1–5**. The pK_a values measured by *Palecek* & *Hlavaty* [13] in 5% aqueous ethanol deviate more, *i.e.* on the average by 0.07 units.

The *temperature dependence* of the pK_a^T values for five compounds, namely **1**, **2**, **4**, **23** and **33**, was determined by measurements at 15.0°, 25.0° and 35.0° (Table 2). As shown in Fig. 1 the pK_a^T values decrease linearly with temperature. The thermodynamic functions ΔG^0, ΔH^0 and $T\Delta S^0$ for reaction (2) were calculated in the usual

[2]) The computer programs developed for these measurements are contained in [16].

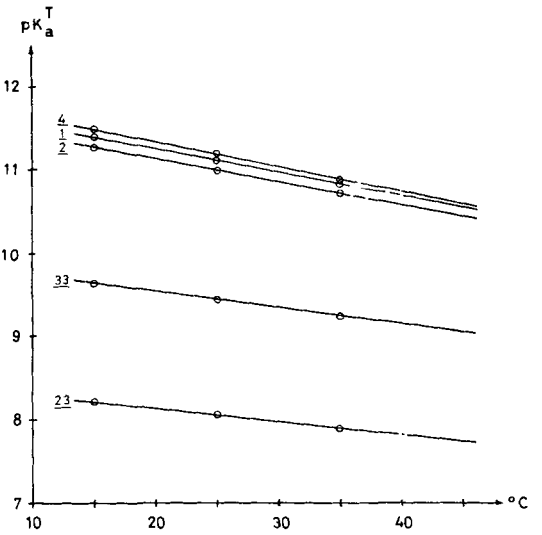


Fig. 1. *Plot of* pK_a^T *against temperature* (°C)

Table 2. *Temperature dependence of the* pK_a^T*-values for 4-R-quinuclidinium perchlorates in water*

Nr.	R	15.0°	25.0°	35.0°
1	H	11.40	11.12	10.85
2	CH_3	11.28	11.01	10.73
4	i-C_3H_7	11.49	11.20	10.90
23	CN	8.20	8.08	7.89
33	SCH_3	9.64	9.46	9.25

way from the relationship $\Delta G^0 = \Delta H^0 - T\Delta S^0 = 2.303\ RT\ pK_a^T$ and are listed in Table 3.

Table 3. *Thermodynamic functions for the protonation equilibrium of 4-R-quinuclidinium perchlorates at 298° K in kcal/mol*

Nr.	R	$\Delta G°$	$\Delta H°$	$T\Delta S°$
1	H	15.16	11.17	– 3.99
2	CH_3	15.01	11.17	– 3.85
4	i-C_3H_7	15.78	11.98	– 3.87
23	CN	11.02	6.28	– 4.74
33	SCH_3	12.90	7.91	– 4.99

In order to determine the *dependence of substituent effect upon solvent* pK_a values (uncorrected) for **1** and **23** were measured in three additional solvents of widely different dielectric constant ε, *i.e.* 50% ethanol, 80% ethanol and 80% methyl cellosolve, according to equation (7) (Table 4).

$$pK_a^C = pH + \log [QH^+]/[Q]. \tag{7}$$

Table 4. *pK_a^C-values of quinuclidine* (**1**) *and 4-cyanoquinuclidine* (**23**) *in various solvents at 25.0°C*

Solvent	ε	pK_a^C [a]		ΔpK_a^C
		1	**23**	
Water [b]	78	11.12	8.08	3.04
50% (*w*/*w*) ethanol	49	10.15	7.29	2.86
80% (*v*/*v*) ethanol	35	9.53	6.88	2.65
50% (*w*/*w*) methylcellosolve	33	9.52	6.93	2.59

[a] Concentration constant (see eq. (7)).
[b] Thermodynamic pK_a-values were used.

The ε values for the last two solvents are not reported in the literature and were therefore determined in the usual way [17] with the aid of a calibration curve obtained with solvents of known ε [18]. The values of Δ pK_a in Table 4 measure the effect of the cyano group as a function of the solvent.

Discussion. – The *pK_a^T values* listed in Table 1 cover a wide range, *i.e.* from 11.27 for the weakest acid **5** to 7.64 for the strongest **29**. Polar substituent effects are therefore strongly transmitted through the quinuclidine molecule, in fact more so than in the case of substituted acetic acids, although one more σ-bond intervenes between substituent and dissociable proton in the former models. Thus, the difference between the pK_a for acetic acid and its nitro-derivative is 3.08 [19], in the case of quinuclidine (**1**) and its 4-nitro-derivative it is 3.48.

The pK_a^T values for 4-substituted quinuclidines show a remarkably similar temperature dependence, as illustrated with compounds **1**, **2**, **4**, **23** and **33** in Table 2. Thus, pK_a^T values decrease linearly and in almost the same degree as the temperature is increased from 15° to 35° (Fig. 1). This is due to the fact that the enthalpy term ΔH^0 contributes mainly to the free energy ΔG^0 of ionization and hence to the polar substitutent effect (Table 3). On the other hand the contribution of the entropy term $T\Delta S^0$ is relatively small and constant. By contrast the pK_a values for substituted acetic acids are mainly determined by the entropy term [6].

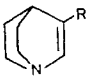
As for the pK_a^T values of compounds **1**–**38** (Table 1) the alkyl groups (**2**–**5**) are base-strengthening (or acid-weakening) in the accepted inductive order for reactions in solution [20][3]), however, with hydrogen occupying a medium position, namely $CH_3 < C_2H_5 \sim H < i\text{-}C_3H_7 < t\text{-}C_4H_9$. The differences between the alkyl groups are small, albeit significant and follow the order observed with the 3-alkyl-quinuclidines III [12c].

The relative polar effects of alkyl groups are still somewhat controversial and evidence at hand indicates that they can release or withdraw electrons in accordance with the requirements of the reaction [22] [23]. Since the quinuclidine molecule assumes a positive charge upon salt formation, its electron-releasing properties are elicited. Furthermore, large groups are better electron donors because they are more polarizable [20] [23].

The electron withdrawing role of methyl relative to hydrogen in 3- and 4-methylquinuclidine deserves special comment. It has been shown before that this order can be

[3]) This distinction is of prime importance since the order can be reversed in the gasphase [21].

observed when methyl is attached to saturated sp^3 carbon atom, the evidence including solvolysis rates [24–26] and dipole moments of alkanes [27]. Now pK_a measurements support these findings. In contrast, methyl at unsaturated (sp^2 and sp) carbon atom is strongly electron releasing as shown earlier [28] by the comparison of the pK_a values for dehydroquinuclidine (IX, R = H) (9.88) and the 3-methyl-derivative (IX, R = CH_3) (10.11).



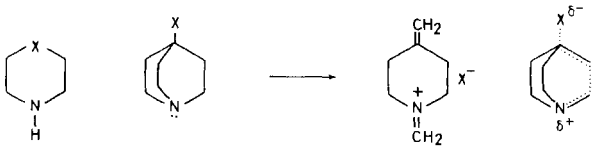
IX

Substitution of a hydrogen atom in the 4-methyl group by an electronegative atom, such as oxygen or halogen, lowers the pK_a^T values substancially (**6–13** in Table 1). The effect is especially pronounced in the 4-carbaldehyde **13**. A similar electron-withdrawing effect is exerted by unsaturated groups, such as alkenyl (**14** and **15**), alkinyl (**16**) and phenyl (**17**). It is noteworthy that substitution of the α-hydrogen atom in the vinyl group of **14** by methyl, as in **15**, increases the electronegativity of the group as a whole significantly.

A stronger lowering of the pK_a^T values occurs when the sp^2 or sp carbon atom bound to C(4) is attached to oxygen or nitrogen atom, as in the esters **19** and **20**, the ketone **21**, the amide **22** and the nitrile **23**. The carboxylate group in **18** is weakly electron-*attracting* despite its negative charge.

Of the substituents attached to C(4) by a hetero atom the amino groups in **24**, **25** and **26** are electron-attracting in the order $NH_2 \sim N(CH_3)_2 < NHCH_3$. Presumably, this is because the secondary amino group is most basic and therefore forms the strongest hydrogen bonds to water. The introduction of carbonyl groups, as in the amide **27** and the carbamate **28**, and of oxygen atoms, as in the nitro compound **29**, lowers pK_a^T appreciably.

The electron withdrawing effect of oxygen at C(4) in compounds **30**, **31** and **32** falls in the order $HO < CH_3O < CH_3COO$. The weaker effect of the hydroxy group is presumably due to its hydrogen bonding to oxygen in water, which should increase electron density at the C(4) oxygen atom. The pK_a^T values for the methoxy- and methylthio-derivatives (**31** and **33** resp.) confirm the results of *Hall* [30] who found morpholine (X, X = O) to be a weaker base than thiomorpholine (X, X = S). As expected the methyl-sulfone group in **34** is strongly electron attracting.

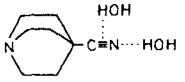


X XI XII XIII

The pK_a^T values for the 4-haloquinuclidines **35–38** follow the electron attracting order Br > F > Cl > I instead of the usual inductive order F > Cl > Br > I, as observed in halo acetic acids. In addition, Δ pK_a between the strongest and weakest acid is 0.59 units in the latter case but only 0.31 for the former compounds **35–38**.

These unexpected results are apparently connected to the well known ability of 4-haloquinuclidines (XI) to undergo solvolytic fragmentation to the immonium salts XII. The observed rate order[4], *i.e.* I > Br > Cl > F [31] is the reverse of the inductive order. Although practically no fragmentation occurs under the conditions of the pK_a measurements at 25.0 °C[5]) it is conceivable that electrons are partly transmitted from nitrogen to halogen by *hyperconjugation* involving one or all three C–C σ-bonds of the ethano-bridges, as illustrated in XIII. This *incipient fragmentation* should be favored in a ionizing solvent, such as water, and tend to decrease the basicity of the nitrogen atom in the above fragmentation order. Although both inductive and hyperconjugative electron withdrawal are base-weakening, the order in which the halogens exert these effects will be reversed. It is at present not possible to assess the contributions of these effects to the total polar effect of the halogens and further studies are undoubtedly required. However, due to the decreasing inductive contributions in the order F > Cl > Br > I and the increasing hyperconjugative contribution in the reverse order the effect of the halogens will tend to become more equal and bromine might well show the strongest net effect.

The *solvent dependence* of the polar effect of the cyano group is illustrated by the pK_a values for quinuclidine (**1**) and its 4-cyano-derivative (**23**) in water and the three other solvents of varying dielectric constant ε listed in Table 4, *i.e.* 50% ethanol, 80% ethanol and 80% methyl cellosolve. The ΔpK_a values, which are included in the Table, are a measure of the substituent effect as a function of the solvent and they decrease from 3.04 in water ($\varepsilon = 78$) to 2.59 in 80% methyl cellosolve ($\varepsilon = 33$), *i.e.* by 15%[6]). This is the reverse of what should be expected on the basis of the field and chain models for the transmission of polar effects because the latter should be strongest in the solvent of lowest dielectric constant[7]). Clearly then, another effect is responsible, such as the interaction of the solvent with the cyano group itself. Thus, hydrogen bonding of its electron pairs to water molecules, as in XIV, should enhance the electronegativity of the group as a whole. Furthermore, the effect should become less pronounced as the ability to form hydrogen bonds is decreased. This result casts doubt on the constancy of 'substituent constants' regardless of solvent, as is tacitly assumed in many linear free energy relationships; however further studies of substituent-solvent interactions are needed.



XIV

4) The rate of fragmentation of 4-fluoroquinuclidine has not yet been measured. The stability of the base in water, however, indicates a very low reaction rate in keeping with the low nucleofugal activity of fluorine.

5) This applies also to the highly reactive 4-iodo-derivative **38** as evidenced by the constant pK_a values obtained throughout the titration.

6) *Palecek* [13] reports an 18% difference beetween the pK_a of **1** and **23** in 5% ethanol/water and 80% methyl cellosolve/water. Nevertheless, he states that the substituent effect is insensitive to the solvent.

7) For a recent review of the origin of the inductive effect see [32].

A new set of *inductive substituent constants* can be derived from the pK_a^T values of 4-substituted quinuclidines in water at 25.0° using hydrogen as the standard of reference, according to equation (8). σ_I^q is the inductive substituent constant[8])

$$pK_a^H - pK_a^R = \varrho\, \sigma_I^q \tag{8}$$

and ϱ the reaction constant which is arbitrarily taken to be unity. The σ_I^q values so derived are listed in Table 1 and are correlated with published sets of substituent constants in Fig. 2 and 3.

The plot of σ_I^q against *Taft*'s σ_I constants (Fig. 2) shows only a fair correlation (coefficient r = 0.906)[9]). The point for hydrogen lies far off the regression line as do

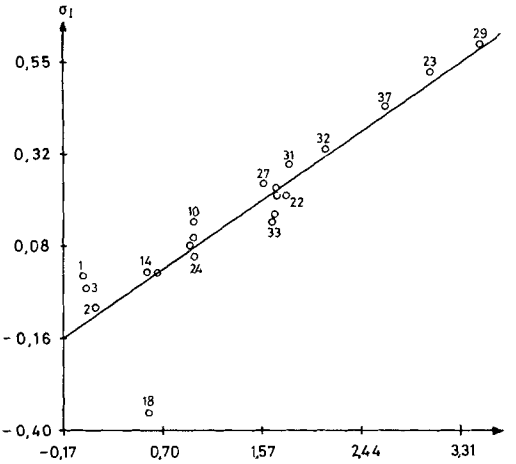


Fig. 2. *Plot of* σ_I^q *against* Taft's σ_I *constants* [4]

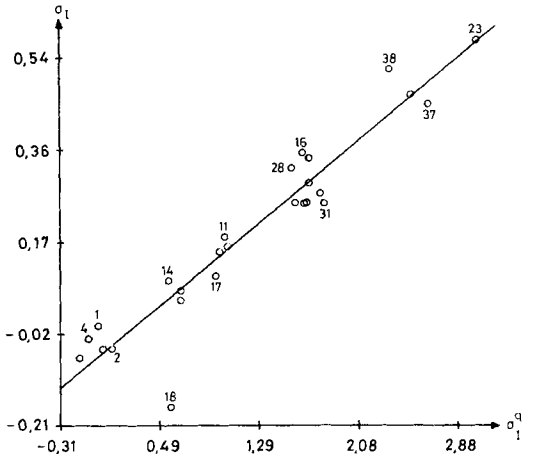


Fig. 3. *Plot of* σ_I^q *against* Charton's σ_I *constants* [5]

8) The superscript q indicates that quinuclidines are the standards of reference.

9) According to *Palecek* [13] excellent correlations are obtained.

those for the substituents C_2H_5 (**3**), COO^- (**18**) and CH_3S (**33**). The correlation with *Charton*'s σ_I constants ($r = 0.949$) (Fig. 3) is also unsatisfactory[9]), especially for hydrogen, the alkyl groups and for COO^-, where even the order of the substituent constants is reversed. This fact points clearly to one of the main reasons for the discrepancies, namely the use of different standards. As mentioned, the inductive order for the alkyl groups at unsaturated sp^2 and sp carbon atom is $H < CH_3 < C_2H_5 < i\text{-Pr} < t\text{-Bu}$, whereas at saturated sp^3 carbon atom it is $CH_3 < H \sim Et < i\text{-Pr} < t\text{-Bu}$. Since the standards used by *Taft* and *Charton* are unsaturated compounds, *i.e.* substituted acetic acids and esters and fluorobenzenes, and those in the present study are saturated, poor correlation would be expected in some cases. Furthermore, when the inductive order is clearly disturbed by the incursion of an additional polar effect, as seems the case with the 4-haloquinuclidines, it is better to gauge the composite effect in terms of a polar substituent constant.

In *conclusion*, 4-substituted quinuclidines are excellent models for the determination of inductive substituent effects since the latter are strongly transmitted and easily determined by pK_a measurements. Furthermore, the pK_a values vary linearly and almost equally with temperature because the substituent effect is determined predominantly by the reaction enthalpy. However, the effect of a substituent can vary somewhat due to its interaction with the solvent. Obviously, solvent independent, intrinsic inductive constants can only result from measurements in the gas phase, *e.g.* by ion cyclotron resonance. However, most organic reactions are carried out in solution and therefore the standards by which rates and equilibria are compared should also be derived from reactions in solution.

We thank PD Dr. *H. G. Seiler* for assistance and advice with the pK_a measurements and the «*Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung*» (grants Nr. 2.617.72 and 2.164.74) for financial support.

Experimental Part

Melting points (m.p.) were determined on a *Kofler*-Block and are corrected. IR. spectra in cm^{-1}, NMR. spectra in δ-values (ppm).

1-Benzyl-4-fluoro-4-(β-hydroxymethyl)-piperidine (*VI*). To 1.5 g (6.4 mmol) of 1-benzyl-4-hydroxy-4-(β-hydroxyethyl)-piperidine (V) [31] in a teflone flask, which was cooled with ice in a *Dewar* flask, 30 g of hydrofluoric acid were added from a pressure bottle. The clear reaction mixture was kept at 0° for 4 days and the excess HF distilled *in vacuo* at 20° into a gas absorber. The residue was taken up in saturated aqueous K_2CO_3 and the mixture extracted 4 times with ether. The ether extracts were dried over Na_2SO_4 and evaporated through a *Vigreux* column. The residue, 1.72 g of a yellow oil, was flash-distilled in a bulb tube at 100–110°/0.01 Torr to give a pure, slightly yellow wax of m.p. 42–43°. – IR. (KBr): 1075 (C—F), 1022 (C—O). – NMR. ($CDCl_3$/D_2O): 1.71 (t, 2H); 1.89–2.20 (m, 4H); 2.20–2.75 (*m*, 4H); 3.54 (*s*, 2H) NCH_2 Aryl.

$C_{14}H_{20}FNO$ (237.32) Calc. C 70.86 H 8.49 N 5.90% Found C 70.96 H 8.26 N 6.17%

Hydroperchlorate: from ethanol, m.p. 103–104°.

$C_{14}H_{21}ClFNO_5$ (337.78) Calc. C 49.78 H 6.27 N 4.15% Found C 49.85 H 6.26 N 4.42%

1-Benzyl-4-fluoroquinuclidinium bromide (*VIII*). To 3.0 g (12.6 mmol) of the above compound in 200 ml abs. benzene were added dropwise with stirring under N_2 3.45 g (19 mmol) of distilled thionyl bromide. After 12 h at 25° and 3 h warming to 45° the mixture was cooled and slowly hydrolyzed with saturated aqueous K_2CO_3 and extracted twice with 100 ml of benzene. The benzene extracts were dried over Na_2SO_4, filtered and boiled under reflux for 2 h, when 3.5 g

(92%) of the salt VIII had crystallized out. Recrystallization from 2-propanol yielded 2.90 g (77%), decomposition > 300°. – IR. (KBr): 1090 (C–F).

$C_{14}H_{19}BrFN$ (300.22) Calc. C 56.01 H 6.38 N 4.67% Found C 55.81 H 6.36 N 4.78%

4-Fluoroquinuclidinium bromide and perchlorate. 2.9 g (9.6 mmol) of the above salt VIII were hydrogenated in 50 ml methanol over 300 mg of 10% Pd/C at normal pressure and temperature. Filtration and evaporation yielded the hydrobromide of **35** which was recrystallized twice from ethanol. 1.83 g (90%) needles, decomposition > 285°. – IR. (KBr): 1090 (C–F).

$C_7H_{13}BrFN$ (210.10) Calc. C 40.02 H 6.24 N 6.67% Found C 39.90 H 6.05 N 6.53%

Hydroperchlorate: from ethanol, decomposition > 275°.

$C_7H_{13}O_4ClFN$ (229.64) Calc. C 36.61 H 5.71 N 6.10% Found C 36.89 H 5.74 N 6.04%

The free base of **35** was liberated from the salts with saturated aqueous K_2CO_3 and extracted with ether. After drying the ether was evaporated through a *Vigreux* column. Sublimation of the residue at 25°/10^{-2} Torr yielded pure 4-fluoroquinuclidine (**35**), m.p. (cap.) 61–62°. – MS. (*m/e*): 129 (M^+, 100), 128 (43), 110 (9), 69 (43), 44 (69), 43 (62).

Elemental analysis by Mr. *E. Thommen*, NMR.-spectra by Mr. *K. Aegerter*.

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32. Ein Tricarbonyleisen-π-Komplex mit einem Silacyclohexadienyl-Liganden

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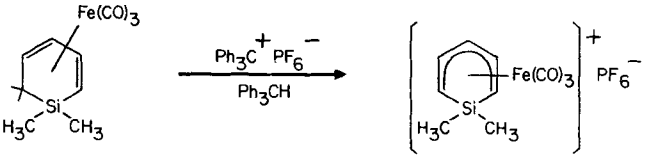
(18. XI. 75)

A Tricarbonyl Iron-π-Complex with a Silacyclohexadienyl-Ligand. – *Summary.* The triphenylmethyl cation abstracts a hydride ion from 1,1-dimethyl-1-silacyclohexa-2,4-diene-tricarbonyl iron to give the 1,1-dimethyl-1-silacyclohexadienyl-tricarbonyl iron cation.

Für die Existenz von Metall-π-Komplexen mit einem Silacyclohexadienyl-Liganden wurde kürzlich ein erster Hinweis erhalten. 1,1-Dimethyl-1-silacyclohexa-2,4-dien-tricarbonyleisen (**1**) [1] wird im Massenspektrometer z.T. zu Bis(1,1-dimethyl-1-silacyclohexadienyl)eisen(II) pyrolysiert[2]). Dessen Molekel-Ion tritt im Massenspektrum von **1** bei *m/e* 302 ($C_{14}H_{22}FeSi_2$; Mol. Gew.: Ber. 302,0609, Gef. 302,0608) auf [1].

Die direkte Herstellung eines Silacyclohexadienyl-Metall-π-Komplexes gelang nun durch die Abspaltung eines Hydrid-Anions aus **1** mittels Triphenylmethyl-hexafluorophosphat in Methylenchlorid bei 0–10°.



1 **2**

1,1-Dimethyl-1-silacyclohexadienyl-tricarbonyleisen-hexafluorophosphat (**2**), luftbeständige, hellgelbe Nadeln (aus Aceton) vom Smp. 175–177° (Ausbeute 80%), löslich in Wasser, Äthanol und Aceton, unlöslich in weniger polaren Solventien, ist der erste Übergangsmetall-Komplex mit einem durch das Metall stabilisierten pseudo-aromatischen Silicium-Ringsystem (6π-Elektronensystem) als Liganden.

[1]) Experimentell mitbearbeitet von *H. U. Kellenberger*.
[2]) Pyrolyse-Experimente ausserhalb des Massenspektrometers zur Gewinnung dieser Verbindung sind im Gange.