

ELECTROSTATIC EFFECTS ON IONIZATION EQUILIBRIA. CARBOXYLIC ACIDS AND AMINES DERIVED FROM 1-INDANONE*

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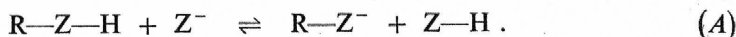
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Isomeric 4(6)-derivatives of 1-indanone (*Va*-*c*, *VIa*-*c*) were synthesized as model molecules in which the oxo substituent is differently oriented in space (angle Θ) with respect to the functional group in the 4- or 6-position. The relative dissociation constants of the carboxylic acids *Va* and *VIa* in two mixed aqueous solvents were compared with the prediction of the electrostatic theory based on a spherical or ellipsoidal cavity model. Even when the theory yields reasonable figures as to their order of magnitude, it generally underestimates the overall effect and overestimates the differences between isomers as given by $\cos \Theta$; in the case of amines *Vb* and *VIb* the relation of isomers is even reversed. It is concluded that such unsymmetrical molecules are not well accommodated by a regular-shaped cavity model; probably the substituent acts also by another mechanism in addition to the electrostatic effect. Therefore, molecules of this type cannot resolve the dichotomy between the through-space and through-bonds transmission of substituent effects.

In the approach called here simply the electrostatic theory, an equilibrium constant is theoretically predicted using only the framework of classical electrostatics. It means that the non-electrostatic contributions to the Gibbs energy are either neglected or eliminated by a proper choice of model molecules. As a further necessary approximation these molecules are treated as a system of discrete charges in a homogeneous medium characterized by an effective dielectric constant ϵ_{ef} . In the previous communications^{1,2} we dealt with the application to conformational equilibria, in this paper we proceed to ionization equilibria. The latter application has been much more elaborated^{3,4}; however, the problems are different in either case and have never been confronted.

In the present form⁵⁻⁸ the electrostatic theory is applied to an isodesmic reaction



Alternatively the species *Z* and *RZ* may be uncharged, *ZH* and *RZH* are then cations. In any case the number and type of bonds involved is equal on either side of the reaction, similarly as in conformational equilibria. Even so, the *Z*-*H* bond energy need not necessarily be exactly equal in the substituted (*RZH*) and unsubstituted (*ZH*)

acid; this may cause deviations from the electrostatic calculations. Another cause can be a too strong non-electrostatic interaction, *e.g.* mesomeric, between the substituent R and the anionic centre in RZ^- ; hence such molecules as 4-nitrophenol are clearly excluded. However, the most important difference as compared to conformational equilibria originates in the experimental conditions. Until recently, the equilibrium constants of reactions (A) have been only obtained as a ratio of two dissociation constants, determined mostly in water or in polar solvents. Then all the molecules and ions involved appear as solvated species and the solvation energies need not completely cancel. In addition, the effective dielectric constant ϵ_{ef} is to be calculated from the external (macroscopic) dielectric constant of the solvent (ϵ_e) and the internal constant (ϵ_i) attributed to the solute molecule (usually $\epsilon_i \approx 2$). In the calculation the solute molecule is represented as a cavity of simple geometrical form such as a sphere⁸, a prolate⁹ or oblate¹⁰ ellipsoid, the geometrical parameters being adjusted in different way¹¹⁻¹⁴. The calculation of ϵ_{ef} has become so important that many authors have focused their attention only to this point and the whole theory was often connected with the names of Kirkwood and Westheimer, who devised the first cavity model⁸.

Evidently the electrostatic theory is much more difficult to apply in the case of ionization than of conformational equilibria. On the other hand, there is an advantage of the former that the charges involved are larger and easier to estimate. In reaction (A) the dominant feature is the interaction of the substituent R with the negative charge in the anion RZ^- . If R is a dipolar substituent, its effect on the dissociation constant is expressed as⁷

$$\log(K/K^0) = \frac{e \mu \cos \Theta}{2 \cdot 3kT r^2 \epsilon_{ef}}, \quad (1)$$

where μ is the substituent dipole, r is the distance of its centre from the position of hydrogen in $R-Z-H$ (taken from H to R), Θ is the angle of the two vectors μ and r . Eq. (1) expresses the energy of proton transfer from the non-solvated molecule RZH to the non-solvated anion Z^- provided that the bond $Z-H$ has been already broken. To bring the reaction (A) to completion, still the new $Z-H$ bond is to be formed and the two species solvated again. As mentioned, these energies (solvation-desolvation, bond-breaking-bond-forming) are assumed to cancel but need not necessarily do so exactly.

A more sophisticated equation¹⁵ takes into account also the dipole of the $Z-H$ bond in the unsubstituted molecule:

$$\log(K/K^0) = \frac{e}{2 \cdot 3kT} \left(\frac{\mu_x \cos \Theta_x}{r_x^2 \epsilon_{ef,x}} - \frac{\mu_H \cos \Theta_H}{r_H^2 \epsilon_{ef,H}} \right) \quad (2)$$

The second term is much less important and the values r_x and r_H , or $\epsilon_{ef,x}$ and $\epsilon_{ef,H}$, respectively, do not differ dramatically. Hence, the results obtained with Eqs (1) and (2) are very similar. In this paper we use Eq. (1) and account for the dipole in the unsubstituted compound by substituting for μ the vector difference of C—X and C—H dipoles.

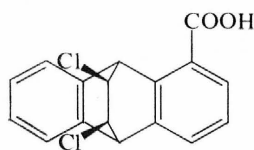
When Eq. (1) is to be verified experimentally, rigid molecules are most efficient as they allow exact determining of both r and θ . There are now the following possibilities:

a) The dissociation constant calculated according to Eq. (1) is simply compared with experiment for a particular molecule^{8-11,13-22}. In this manner not only the basic assumptions of the theory are tested but also the cavity model used to estimate ϵ_{ef} ; this model is usually of decisive importance.

b) One compound is investigated in different solvents and ϵ_{ef} calculated according to a uniform cavity model²³⁻²⁹. This model is very important even in this case but an absolute fit need not be required, only the correct pattern of the solvent dependence.

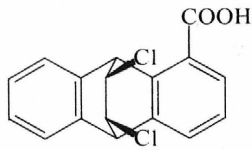
c) Within the series of compounds only the substituent is varied. Eq. (1) then expresses mainly the dependence on μ , small variations of r and θ may be accounted for. Provided the substituents are similar in size, ϵ_{ef} can be taken as constant and treated as an adjustable parameter^{15,16,22,30-32}, irrespective of any cavity model.

d) Two similar compounds are compared with the same substituent and in the same solvent, the difference being in the geometrical parameters r and/or θ . This approach is the most popular^{16,33-48} and has been used mainly to decide between the through-space and through-bonds transmission of substituent effects⁴, in other terms between the field effect and σ -inductive effect, respectively⁴. From this point of view the most effective model systems are those involving either two molecules with the same number of intervening bonds but rather different geometry (e.g.³⁵ I and II), or *vice versa* (e.g.¹⁶ III and IV). The effective dielectric constants are in the latter case less different and easier to calculate than in the former.



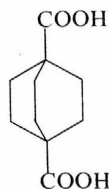
I

$r = 601$ pm
 $\theta = 46^\circ$



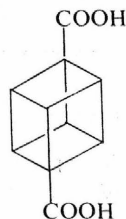
II

$r = 544$ pm
 $\theta = 89^\circ$



III

$r = 857$ pm
 $\theta = 0^\circ$

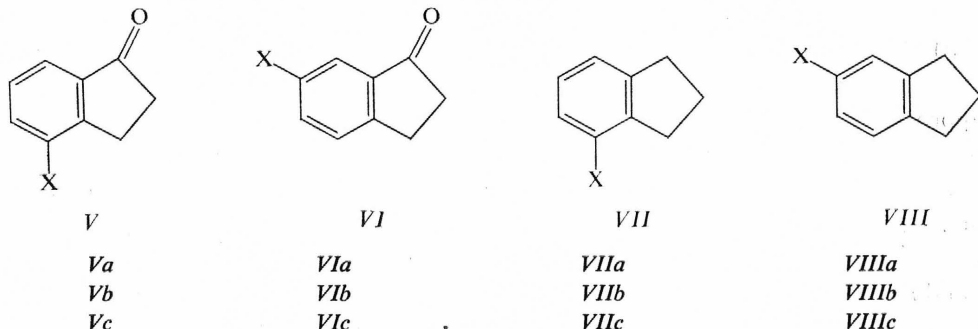


IV

$r = 867$ pm
 $\theta = 0^\circ$

In this paper we follow still the common approach under (d), of course, the simple test under (a) can be carried out, too. The model compounds we have chosen, the isomeric 1-oxoindane-4(6)-carboxylic acids (*Va* and *VIa*) and the respective amines *Vb*, and *VIb*, have no particular merits compared to the previous ones, they furnish merely a new simple example. In comparison with previous work we paid relatively much attention to calculation of ϵ_{ef} by means of various cavity models. In the literature the problem is presented incorrectly as an antagonism between the through-space and through-bond transmission^{3,4}. The transmission must take place in space; the problem should be worded whether this space is better approximated as a continuum with a uniform dielectric constant or as a system of channels (bonds) the orientation of which is not decisive. Furthermore the theory of through-bond transmission has been elaborated for polycyclic systems^{3,4,14} in an untenable manner^{4,9}. It follows that our experiments are not intended to resolve the mentioned antagonism; they should rather show inasmuch model compounds of the type *I–VI* can be helpful in verifying the basic assumptions of the electrostatic theory.

In the molecules *Va–c*, *VIa–c* only the carbonyl oxygen is considered as substituent; it means that their properties are always compared to the molecules *VIIa–c* and *VIIIa–c*, respectively, as the reference compounds. This is necessary in order to eliminate the steric effect of the aliphatic chain in *V*.



a; X = COOH, *b*; X = NH₂, *c*; X = CN,

EXPERIMENTAL AND RESULTS

Materials

Melting points were determined on a Kofler block and are uncorrected. Analytical samples were dried over phosphorus pentoxide at 25°C/10 Pa. The identity of samples was checked by melting point determination, by thin-layer (TLC) and gas-liquid (GLC) chromatography, by elemental analysis and by infrared, ¹H-NMR and mass spectra. The IR spectra were taken on a Zeiss UR-20 instrument and wavenumbers are given in cm⁻¹. The ¹H-NMR spectra were measured on a Varian HA-100 spectrometer and are given in the δ -scale with tetramethylsilane as an internal standard. The mass spectra were recorded on a AEI MS-907 spectrometer.

4-Aminoindan-1-one (Vb) was prepared⁵⁰ from the corresponding 4-nitro derivative⁵¹; yield 72%, m.p. 124°C (ethanol), literature reports⁵⁰ 123–124°C. ¹H-NMR spectrum (CDCl₃): 2.50–2.74 (m, 2 H, ArCH₂), 2.76–3.02 (m, 2 H, COCH₂), 4.19 (bs, 2 H, *W* 1/2 = 4 Hz, NH₂), 6.79–7.28 (m, 3 H, aromatic H). IR spectrum (CHCl₃): 3490, 3459 sh ($\nu_{\text{as}}(\text{NH}_2)$), 3403, 3379 sh ($\nu_{\text{s}}(\text{NH}_2)$).

6-Aminoindan-1-one (VIb) was prepared in the same way as Vb; yield 82%, m.p. 176°C (ethanol), literature reports⁵² 168–171°C. ¹H-NMR spectrum (CDCl₃ + 2% DMSO-d₆): 2.47–2.67 (m, 2 H, ArCH₂), 2.79–3.04 (m, 2 H, COCH₂), 4.22 (bs, 2 H, *W* 1/2 = 10 Hz, NH₂), 6.81 to 7.28 (m, 3 H, aromatic H). IR spectrum (CHCl₃): 3490, 3460 sh, ($\nu_{\text{as}}\text{NH}_2$), 3403, 3382 sh ($\nu_{\text{s}}\text{NH}_2$).

1-Oxoindane-4-carbonitrile (Vc) was prepared from Vb by the general method for aromatic nitriles and purified by sublimation; yield 41%, m.p. 117°C, literature⁵³ reports 116–117°C. ¹H-NMR spectrum (CDCl₃): 2.73–2.95 (m, 2 H, COCH₂), 3.25–3.46 (m, 2 H, ArCH₂), 7.53 (t, 1 H, *J*₀ = 8 Hz, H 6), 7.90 (dd, 1 H, *J*₀ = 8 Hz, *J*_m = 1.5 Hz, H5), 7.98 (d, 1 H, *J*₀ = 8 Hz, H7). IR spectrum (tetrachloroethylene): 2234 (C≡N).

1-Oxoindane-6-carbonitrile (VIc) was prepared in 49% yield as described for Vc; m.p. 107°C. ¹H-NMR spectrum (CDCl₃): 2.68–2.92 (m, 2 H, COCH₂), 3.12–3.37 (m, 2 H, ArCH₂), 7.63 (d, 1 H, *J*₀ = 8 Hz, H4), 7.84 (dd, 1 H, *J*₀ = 8 Hz, *J*_m = 2 Hz, H5), 8.04 (bs, 1 H, *W* 1/2 = 3 Hz, H7). IR spectrum (tetrachloroethylene): 2235 (C≡N). For C₁₀H₇NO (157.2) calculated: 76.42% C, 4.49% H, 8.91% N; found: 76.61% C, 4.67% H, 8.98% N.

1-Oxoindane-4-carboxylic acid (Va). Since we were unable to obtain this compound according to refs^{54,55}, the described procedure was modified in such a way that the reaction was carried out at 150°C for 15 min. The crude product was purified by taking up in 50% ethanol; yield 50%, m.p. 226°C (water), literature⁵⁴ reports 225–226°C. ¹H-NMR spectrum (CDCl₃): 2.50 to 2.93 (m, 2 H, COCH₂), 3.28–3.67 (m, 2 H, ArCH₂), 7.35–7.75 (m, 1 H, H6), 7.93 (dd, 1 H, *J*₀ = 7 Hz, *J*_m = 2 Hz, H7), 8.33 (dd, 1 H, *J*₀ = 7 Hz, *J*_m = 2 Hz, H5).

1-Oxoindane-6-carboxylic acid (VIa) was prepared from the nitrile VIc by alkaline hydrolysis to the amide (yield 71%) and subsequent acid hydrolysis (yield 74%); m.p. 255°C (water), literature⁵⁶ reports 256°C. ¹H-NMR spectrum (CDCl₃ + 2% hexadeuteriodimethyl sulphoxide): 2.64–2.87 (m, 2 H, COCH₂), 3.07–3.32 (m, 2 H, ArCH₂), 7.56 (d, 1 H, *J*₀ = 8 Hz, H4), 8.25 (dd, 1 H, *J*₀ = 8 Hz, *J*_m = 2 Hz, H5), 8.35 (d, 1 H, *J*_m = 2 Hz, H7).

4-Indanecarboxylic acid (VIIa) was prepared by Wolff-Kishner reduction of Va; yield 67%, m.p. 152°C (sublimated), literature⁵⁷ reports 155°C. ¹H-NMR spectrum (CDCl₃): 1.92–2.36 (m, 2 H, H2), 2.96 (t, 2 H, *J* = 7 Hz, H1), 3.35 (t, 2 H, *J* = 7 Hz, H3), 7.1–8.0 (m, 3 H, aromatic H).

5-Indanecarboxylic acid (VIIIa) was prepared in the same way as VIIa; yield 57%, m.p. 183°C (sublimated), literature⁵⁸ reports 179.5–181.5°C. ¹H-NMR spectrum (CDCl₃): 1.93–2.32 (m, 2 H, H2), 2.99 (t, 4 H, *J* = 7 Hz, H1, H3), 7.21–8.08 (m, 3 H, aromatic H).

4-Indanamine (VIIb) was prepared from VIIa by the general method for aromatic amines (heating with hydroxylamine hydrochloride and polyphosphoric acid to 165–170°C 5 min) and isolated as hydrochloride; yield 27%, m.p. 162–166°C (decompn., methanol-diethyl ether). Mass spectrum: 133 (M–HCl). For C₉H₁₂ClN (169.7) calculated: 63.71% C, 7.13% H, 20.90% Cl, 8.26% N; found: 63.67% C, 7.18% H, 21.10% Cl, 7.80% N.

5-Indanamine (VIIIb) was prepared in the same way as VIIb; yield 21%, m.p. 165° (decompn., methanol-diethyl ether). Mass spectrum: 133 (M–HCl). For C₉H₁₂ClN (169.7) calculated: 63.71% C, 7.13% H, 20.90% Cl, 8.26% N; found: 63.15% C, 6.96% H, 21.23% Cl, 8.36% N.

4-Indanecarbonitrile (VIIc) was prepared from VIIa via the amide (yield 54%) which was dehydrated with thionyl chloride in dimethylformamide to yield VIIc (42%); b.p. 80–85°C/650 Pa, literature⁵⁹ reports 139–141°C/1500 Pa. IR spectrum (tetrachloroethylene): 2232 (C≡N). Mass spectrum: 143 (M⁺).

5-Indanecarbonitrile (VIIIc) was prepared in the same way as VIIc; yield 44%, b.p. 83–85°C : 650 Pa, literature⁵⁷ reports m.p. 31°C. IR spectrum (tetrachloroethylene): 2232 (C≡N). Mass spectrum: 143 (M⁺).

Physical Measurements

The apparent dissociation constants in 50% (by volume) ethanol and 80% (by weight) 2-methoxyethanol (methyl cellosolve) were determined by potentiometric titration using a Beckman Research pH Meter, a glass indication electrode Beckman AS7LB and a saturated calomel reference electrode Beckman KLB. Solutions of the acids ($5 \cdot 10^{-3}$ M) were titrated with 0.1 M aqueous potassium hydroxide added in equal portions (0.05 ml) from a piston burette with a micrometric screw controlled by a stepping motor (precision ± 0.002 ml). The initial concentration of the solvent was chosen in such a way that the required concentration was reached at the half-neutralisation point. The solution was thermostated at $25 \pm 0.05^\circ\text{C}$ and magnetically stirred under an atmosphere of nitrogen saturated with the vapour of the respective solvent. Before each measurement the pH-meter was standardized with 0.02 M solution of potassium hydrogen phthalate in 50% (vol.) ethanol (pH 5.51, ref.¹⁹) or with 0.05 M aqueous potassium hydrogen phthalate (pH 4.008) according to the solvent to be used, 50% ethanol or 80% methyl cellosolve, respectively.

The pK values were read off automatically and stored on a recording tape together with the corresponding total volumes of the reagent. These data consisting of c. 25 points were processed⁶⁰ by fitting an empirical spline function of the third degree; its inflection point then represents the neutralization equivalent and the half-neutralization point gives the pK value. The whole procedure was checked by repeated determination of the dissociation constant of benzoic acid (pK 5.75 in 50% ethanol⁶¹, 6.63 in 80% methyl cellosolve⁶²). All the values given in Table I are related to these standards. In independent repeated experiments the pK values were reproducible to 0.05 pK in 50% ethanol and to 0.03 pK in 80% methyl cellosolve (range of extreme values), or usually better.

The IR absorption spectra were measured on a Perkin-Elmer model 621 spectrometer. In the case of the nitriles Vc–VIIIc they were recorded within the 2200–2290 cm^{-1} region at $40 \pm \pm 0.3^\circ\text{C}$ in 0.06 M tetrachloroethylene solution in 0.1 cm NaCl cells. The integrated absorption intensities were calculated on a HP 9830A calculator using a program written by Dr A. Vitek (Institute of Organic Chemistry and Biochemistry) and based on the Lorentz-type band shape. The results are listed in Table III. The IR spectra of the carboxylic acids Va–VIIIa were recorded in the 3400–3700 cm^{-1} region in 10^{-3} M tetrachloromethane solution at $39 \pm 1^\circ\text{C}$ in 4.0 cm Infrasil cells. The OH stretching frequencies are given in Table I.

Calculations

The relative dissociation constants K/K^0 predicted by the electrostatic theory were calculated from Eq. (1) substituting for μ the algebraic sum of the C=O and CH₂ bond moments⁶³ (i.e. $2.5 + 0.35$ D). The effective dielectric constant ϵ_{ef} was calculated using the cavity models of three types: a) the Kirkwood–Westheimer sphere⁸ in the Tanford modification¹¹, viz. with the proton and the point dipole in a depth of 150 pm under the cavity surface, b) the Kirkwood–Westheimer prolate ellipsoid⁹ in the same modification¹¹, c) the more sophisticated ellipsoidal cavity of Ehrenson¹³ with the proton 160 pm and the point dipole 260 pm under the surface and with the minor

axis estimated so as to encompass the whole molecule (Figs 1*a*, *b*). In any case the distance r and the angle θ were determined from the standard geometrical parameters⁶⁴: bond lengths (in pm) C—C in the aromatic ring 140, C_{ar}—C(O) 150, C_{ar}—C(O) in the five-membered ring 145, C_{ar}—C_{al} 152, C_{al}—C(O) 150, C_{al}—C_{al} 154, C_{ar}—H 108, C_{al}—H 109, C=O 124, C_{ar}—N 140; bond angles C_{ar}—C_{ar}—C(O) 110°, C_{ar}—C_{ar}—CH₂ 114°, C_{ar}—C=O 127°, C_{ar}—C(O)—CH₂ 105°, the benzene ring hexagonal. The proton of the COOH group was situated as usual⁸ 145 pm from the carboxyl carbon in the direction of the C_{ar}—C bond. Similarly the proton of the NH₃⁽⁺⁾ groups was situated 32 pm from nitrogen. The internal dielectric constant was put equal to 2, the external dielectric constant for 50% (vol) ethanol was ⁶⁵ 53.8 (at 25°C), that of 80% (weight) methyl cellosolve⁶⁶ 33.0. The calculated values are given in Table II.

DISCUSSION

The most important experimental data are the dissociation constants which were determined in two solvent systems. Table I confirms that the carboxylic acids are stronger in 50% ethanol while the ammonium ions are stronger acids in 80% methyl cellosolve, this means that the ionic species are more stabilized in the more polar solvent as expected. The relative dissociation constants, however, depend very little on the solvent (Table II, last column). In the case of the ammonium ions they are virtually equal, in the case of carboxylic acids they differ by some 10–18%, this

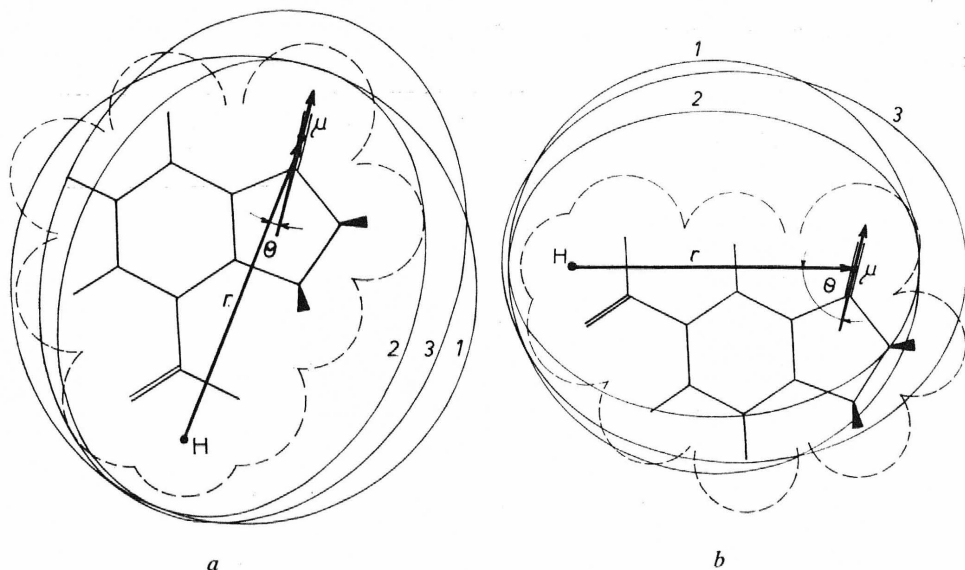


FIG. 1

Molecules of 1-Oxoindane-4-carboxylic Acid (*a*) and 1-Oxoindane-6-carboxylic Acid (*b*) and Their Representation by Various Cavity Models

1 Kirkwood–Westheimer sphere⁸, 2 Kirkwood–Westheimer ellipsoid⁹, 3 Ehrenson ellipsoid¹³.

ratio agrees satisfactorily with the ratio of Hammett ρ constants for the two solvents⁶² (c. 1.2). Hence the results may be discussed irrespective of the solvent.

The next problem is which of the three cavity models is most appropriate. None of the idealized cavities corresponds even approximately to the actual shape and volume of the molecules (Fig. 1). In particular the thickness of these flat molecules is overestimated badly by all three models, the spherical model being the least adequate. Hence one could be satisfied if the theory reproduced the experimental data in a qualitative sense. Such an agreement is achieved in the case of carboxylic acids *Va* and *VIa*: all the models predict correctly that the substitution in the 4-position is more effective than in the 6-position. For this result the difference in the angle θ is decisive whereas the cavity model itself is of less importance. It is further evident that all the models overestimate the difference between the two isomers while they underestimate the substituent effects in the whole. Since all the cavities are too large, one would expect the predicted values of ϵ_{ef} to be too low and the relative dissociation constants too large. Quite on the contrary the latter is invariably too low and the spherical model, geometrically least appropriate, gives still the best results.

TABLE I

Apparent Dissociation Constants and O—H Stretching Frequencies of 4(6)-Substituted 1-Indanones and 4(5)-Substituted Indanes

Compound	Substitution	pK_a 50% EtOH	pK_a 80% MCS	$\nu(\text{O—H})^a$ cm^{-1}
1-Indanones				
<i>Va</i>	4-COOH	5.34	6.12	3 534.5
<i>VIa</i>	6-COOH	5.29	6.14	3 538
<i>Vb</i>	4-NH ₃ +	3.16	2.36	—
<i>VIb</i>	6-NH ₃ +	3.57	2.78	—
Indanes				
<i>VIIa</i>	4-COOH	6.22	7.16	3 541.5
<i>VIIIa</i>	5-COOH +	6.06	6.98	3 544
<i>VIIb</i>	4-NH ₃ +	4.43	3.60	—
<i>VIIIb</i>	5-NH ₃	5.10	4.29	—

^a In tetrachloromethane solution.

Another cavity model which would yield still a lower effective dielectric constant is only possible with an enhanced parameter d , the depth of the dipole or the hydrogen atom under the cavity surface. In order to retain its accepted physical meaning^{11,13}, this depth cannot much exceed the chosen value of 150 pm. However, values larger than 200 pm would be necessary to match the experimental results in the case of Va,b while in the case of VIa,b any realistic value is insufficient.

As regards the difference between isomers, our data prove the general significance of angle Θ for substituent effects. However, the dependence on $\cos \Theta$ as required

TABLE II

Electrostatic Calculations of Dissociation Constants of Indanone Derivatives $Vab, VIab$

Compound	r pm $\Theta, ^\circ$	Sphere ^a $\log K/K^0$ ϵ_{ef}	Ellipsoid ^b $\log K/K^0$ ϵ_{ef}	Ellipsoid ^c $\log K/K^0$ ϵ_{ef}	Experimental $\log K/K^0$ ϵ_{ef}^d
50% (volume) ethanol					
Va	676	0.66	0.35	0.58	0.88
4-COOH	7	(4.72)	(9.03)	(5.39)	(3.56)
VIa	653	0.30	0.18	0.30	0.77
6-COOH	66	(4.61)	(7.66)	(4.55)	(1.79)
Vb	565	1.06	0.65	1.10	1.27
⁺ 4-NH ₃	12	(4.16)	(6.76)	(4.04)	(3.48)
VIb	545	0.41	0.26	0.42	1.53
⁺ 6-NH ₃	70	(4.06)	(6.41)	(3.98)	(1.09)
80% (weight) methyl cellosolve					
Va	676	0.69	0.38	0.62	1.04
4-COOH	7	(4.52)	(8.36)	(5.08)	(3.02)
VIa	653	0.31	0.17	0.32	0.84
6-COOH	66	(4.41)	(7.94)	(4.35)	(1.64)
Vb	565	1.10	0.69	1.14	1.24
⁺ 4-NH ₃	12	(4.02)	(6.44)	(3.89)	(3.57)
VIb	545	0.42	0.27	0.43	1.51
⁺ 6-NH ₃	70	(3.93)	(6.13)	(3.83)	(1.10)

^a Kirkwood–Westheimer sphere⁸; ^b Kirkwood–Westheimer ellipsoid⁹; ^c Ehrenson ellipsoid¹³; ^d calculated from the experimental pK 's and Eq. (1).

by Eq. (1) is either not followed or compensated by some other factor. Even here any reasonable change of the cavity model and hence of ϵ_{ef} does not help. Since the cavities are less adequate in the case of 6-isomers (Fig. 1), ϵ_{ef} of the latter should be actually larger; this would only sharpen the difference between isomers. Therefore the conclusion seems substantiated that the electrostatic theory does not describe the substituent effect correctly in this case.

A quite different picture is obtained when proceeding to the amines *Vb*, *VIb*. The calculated values $\log(K/K^0)$ are too low as above, but in addition even their ratio is given wrongly by the theory. In variance with the carboxylic acids the substituent effect on the 6-position is now stronger but this is not reflected in the calculated values which are still controlled by the angle θ . Any cavity model can hardly reverse their ratio. The less can any model yield an effective dielectric constant less than 2 as required by the experimental value for *VIb*. The theory clearly fails in this case. It is true that the electrostatic calculations have dealt hitherto with carboxylic acids almost exclusively; we do not see, however, any principal reason why it should fail for aromatic amines. Several such applications are known^{24,67} and specific deviations were noted only for directly conjugated substituents (4-nitroaniline). In the case of our compounds, one could think that the substituent effect on the sterically hindered NH_2 group in *Vb* is reduced, but the data of Table II would rather require that it were abnormally enhanced in *VIb*. This cannot be explained in any simple manner.

The IR spectral data are not immediately related to the electrostatic theory. We have measured them only to see inasmuch they parallel the results from dissociation constants. The O—H stretching frequencies of substituted benzoic acids are closely correlated with their pK values⁶⁸, stronger acids being connected with lower frequencies. This holds for our acids *Va*, *VIa* as far as they are compared to *VIIa* and *VIIIa*.

It does, however, not hold for small differences existing between *Va* and *VIa*, or between *VIIa* and *VIIIa*, due probably to steric effects. The substituents effects represented by the differences *Va*—*VIIa* and *VIa*—*VIIIa*, respectively, are transmitted more effectively to the 4-position. This conclusion is not so dependable as from the dissociation constants with respect to the experimental uncertainty.

The integrated absorption intensities of the $\text{C}\equiv\text{N}$ stretching band in substituted benzonitriles follow only roughly the pK values of the corresponding benzoic acids since they depend more on mesomeric effects⁶⁹; a similar dependence of the frequencies is more restricted⁶⁹. The $\text{C}\equiv\text{N}$ frequencies in Table III fit the general pattern (higher values correspond to stronger acids) while the intensities show a similar behaviour as the O—H frequencies of Table I. According to the intensities the substituent effects are transmitted with greater intensity to the 6-position, while according to the frequencies no difference is observed.

Summarizing our results, two facts are pertinent: a) The predicted substituents effects are generally too low, and b) the relation between isomers, differing in the angle θ , is either overestimated by the theory (carboxylic acids *Va*, *VI*) or even reversed (amines *Vb*, *VIb*). Of the two findings the former seems less important to us,

since it can be explained by several features neglected in deriving Eq. (1): bond energies or σ -inductive effect, π -inductive effect, solvation energies, or entropy contribution. In addition the theory can be accommodated, in particular by modifying the parameter d , to compensate for some of these effects if they are operative. We are of the opinion that these effects exist and are not negligible; they could be evidenced most probably by means of gas phase measurements.

On the other hand, the results obtained in this and previous work^{33,35,37,38,40,47} on the isomeric, sterically differing molecules revealed the significance of the substituent angle θ . Any concept neglecting this angle, e.g. the transmission through the sigma bonds⁴ must be thus incomplete at least. If, however, Eq. (1) overestimates the influence of θ , irrespective of the cavity model used, one can again refer to some of the named additional effects. Most popular in such cases was recourse to the σ -inductive effect^{34,70}. Since many of the molecules investigated were bicyclic,

TABLE III

The C \equiv N Frequencies (cm^{-1}) and Intensities ($\text{l mol}^{-1} \text{cm}^{-2}$) of Nitriles *Vc*–*VIIIc*

Compound	Substitution	$\nu(\text{C}\equiv\text{N})^a$	$\Delta\nu^{1/2}$	B^b	ΔB^c
I-Indanones					
<i>Vc</i>	4-CN	2 234.1	7.9	774	370
<i>Vic</i>	6-CN	2 235.0	7.5	872	513
Indanes					
<i>VIIc</i>	4-CN	2 231.6	9.3	1 144	—
<i>VIIIc</i>	5-CN	2 232.2	9.2	1 385	—

^a In tetrachloroethylene solution; ^b integrated absorption intensity; ^c difference $B_{\text{indane}} - B_{\text{indanone}}$.

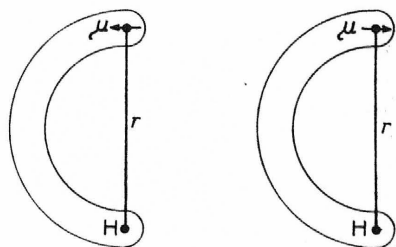


FIG. 2

Schematic Picture of an Extreme Case of Molecules which Cannot Be Approximated by a Cavity Model

the original concept of successive falling off with each bond⁴ was complemented by the assumption that the effect is simply additive with respect to all possible ways^{4,14}; this point is particularly open to criticism^{4,9}. If we accept this kind of reasoning, there are four ways of transmission in each molecule *Va* and *VIa* (or *Vb* and *VIb*, respectively). Taking into account the different transmission coefficients for sp^2 and sp^3 carbon atoms⁷⁰, we calculate a ratio 1.096: 1 representing relative I_σ effects. If we consider only the shortest way, this ratio is 1 : 1, of course. These figures cannot explain the observed dissociation constants either taken by themselves, or in combination with an electrostatic contribution. We use them only to show that discrepancies of the electrostatic approach cannot simply serve as argument in favour of the I_σ theory, or *vice versa*.

Another possible explanation of the observed discrepancies could be seen in the fundamental limitation of the cavity model. Molecules with large values of Θ are necessarily very unsymmetrical in shape and cannot be satisfactorily described by any model whatever value ϵ_{ef} it might give. Let us observe the simplified extreme cases in Fig. 2. Since $\Theta = 90$, the calculated electrostatic effect is zero irrespective of ϵ_{ef} . However, the actual dissociation constants must differ in the two cases and the substituent effect cannot equal zero exactly. The cavity models as well as the concept of an effective dielectric constant are strictly applicable only to symmetrical molecules with the vector r as a symmetry axis. Approximately this concept can be used to molecules which fill up the geometric cavity with a reasonable precision. We conclude that the effect of Θ should be studied on molecules with a relatively regular shape but with Θ sufficiently different from zero. In this way we hope the non-electrostatic contributions to the substituent effect can be disclosed.

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REFERENCES

1. Exner O., Friedl Z.: This Journal 42, 3030 (1977).
2. Friedl Z., Exner O.: This Journal 43, 2591 (1978).
3. Stock L. M.: J. Chem. Educ. 49, 400 (1972).
4. Ehrenson S.: Progr. Phys. Org. Chem. 2, 195 (1964).
5. Eucken A.: Angew. Chem. 45, 203 (1932).
6. Smallwood H. M.: J. Amer. Chem. Soc. 54, 3048 (1932).
7. Schwarzenbach G., Egli H.: Helv. Chim. Acta 17, 1183 (1934).
8. Kirkwood J. G., Westheimer F. H.: J. Chem. Phys. 6, 506 (1938).
9. Westheimer F. H., Kirkwood J. G.: J. Chem. Phys. 6, 513 (1938).
10. Sarmousakis J. N.: J. Chem. Phys. 12, 277 (1944).
11. Tanford C.: J. Amer. Chem. Soc. 79, 5348 (1957).
12. Edward J. T., Farrell P. G., Job J. L.: J. Chem. Phys. 57, 5251 (1972).

13. Ehrenson S.: *J. Amer. Chem. Soc.* *98*, 7510 (1976).
14. Roberts J. D., Moreland W. T., jr: *J. Amer. Chem. Soc.* *75*, 2167 (1953).
15. Holtz H. D., Stock L. M.: *J. Amer. Chem. Soc.* *86*, 5188 (1964).
16. Baker F. W., Parish R. C., Stock L. M.: *J. Amer. Chem. Soc.* *89*, 5677 (1967).
17. Westheimer F. H., Shookhoff M. W.: *J. Amer. Chem. Soc.* *61*, 555 (1939).
18. Siegel S., Komarmy J. H.: *J. Amer. Chem. Soc.* *82*, 2547 (1960).
19. Wilcox C. F., McIntyre J. S.: *J. Org. Chem.* *30*, 777 (1965).
20. Bowden K., Parkin D. C.: *Can. J. Chem.* *47*, 177 (1969).
21. Liotta C. L., Fisher W. F., Greene G. H.: *Chem. Commun.* *1969*, 1251.
22. Liotta C. L., Fisher W. F., Greene G. H., Joyner B. L.: *J. Amer. Chem. Soc.* *94*, 4891 (1972).
23. Kilpatrick M., Eanes R. D.: *J. Amer. Chem. Soc.* *65*, 589 (1943).
24. Willi A. V.: *Helv. Chim. Acta* *40*, 2019, 2032 (1957).
25. Ritchie C. D., Lewis E. S.: *J. Amer. Chem. Soc.* *84*, 591 (1962).
26. Kalfus K., Večeřa M., Exner O.: *This Journal* *35*, 1195 (1970).
27. Kilpatrick M., Morse J. G.: *J. Amer. Chem. Soc.* *75*, 1846 (1953).
28. Kirchnerova J., Farrell P. G., Edward J. T., Halle J. C., Schaal R.: *Can. J. Chem.* *56*, 1130 (1978).
29. Westheimer F. H., Jones W. A., Lad R. A.: *J. Chem. Phys.* *10*, 478 (1942).
30. Kilpatrick M., Mears W. H.: *J. Amer. Chem. Soc.* *62*, 3047, 3051 (1940).
31. Westheimer F. H.: *J. Amer. Chem. Soc.* *61*, 1977 (1939).
32. Winstein S., Grunwald E., Ingraham L. L.: *J. Amer. Chem. Soc.* *70*, 821 (1948).
33. Golden R., Stock L. M.: *J. Amer. Chem. Soc.* *94*, 3080 (1972).
34. Exner O., Jonáš J.: *This Journal* *27*, 2296 (1962).
35. Wang C. T., Grubbs E. J.: *J. Org. Chem.* *42*, 534 (1977).
36. Wilcox C. F., Leung C.: *J. Amer. Chem. Soc.* *90*, 336 (1968).
37. Acevedo S., Bowden K.: *J. Chem. Soc., Chem. Commun.* *1977*, 608.
38. Liotta C. L., Fisher W. F., Slightom E. L., Harris C. L.: *J. Amer. Chem. Soc.* *94*, 2129 (1972).
39. Cole T. W., jr, Mayers C. J., Stock L. M.: *J. Amer. Chem. Soc.* *96*, 4555 (1974).
40. Bowden K., Parkin D. C.: *Can. J. Chem.* *47*, 185 (1969).
41. Hojow M., Katsurakawa K., Yoshida Z.: *Tetrahedron Lett.* *1968*, 1497.
42. Newman M. S., Merrill S. H.: *J. Amer. Chem. Soc.* *77*, 5552 (1955).
43. Roberts J. D., Carboni R. A.: *J. Amer. Chem. Soc.* *77*, 5554 (1955).
44. Solomon I. J., Filler R.: *J. Amer. Chem. Soc.* *85*, 3492 (1963).
45. Wells P. R., Adcock W.: *Aust. J. Chem.* *18*, 1365 (1965).
46. Grubbs E. J., Fitzgerald R., Phillips R. E., Petty R.: *Tetrahedron* *27*, 935 (1971).
47. Liotta C. L., Fisher W. F., Harris C. L.: *Chem. Commun.* *1971*, 1312.
48. McLendon C. L., Dorn H. C., Crabtree P. N., Bellettini A. G., Grubbs E. J.: *J. Org. Chem.* *41*, 2387 (1976).
49. Exner O., Fiedler P.: Unpublished results.
50. Hach V., Protiva M.: *Chem. Listy* *51*, 2099 (1957).
51. Hasbun J. A., Barker K. K., Mertes M. P.: *J. Med. Chem.* *16*, 847 (1973).
52. Koelsch C. F., Scheiderbauer R. A.: *J. Amer. Chem. Soc.* *65*, 2311 (1943).
53. Hoyer H.: *J. Prakt. Chem.* *139*, 94 (1934).
54. Kubota T., Tomita Y., Suzuki K.: *Tetrahedron Lett.* *1961*, 223.
55. Tomita Y.: *Nippon Kagaku Zasshi* *82*, 505 (1961); *Chem. Abstr.* *57*, 16542.
56. Baddeley G., Williamson R.: *J. Chem. Soc.* *1956*, 4647.
57. Lindner J., Schmitt F., Zaunbauer B.: *Monatsh. Chem.* *72*, 216 (1939).
58. Fieser L. F., Hershberg E. B.: *J. Amer. Chem. Soc.* *62*, 49 (1940).

59. Fieser L. F., Hershberg E. B.: *J. Amer. Chem. Soc.* **59**, 394 (1937).
60. Vitek A.: Unpublished results.
61. Roberts J. D., McElhill E. A., Armstrong R.: *J. Amer. Chem. Soc.* **71**, 2923 (1949).
62. Kalfus K., Kroupa J., Večeřa M., Exner O.: *This Journal* **40**, 3009 (1975).
63. Exner O.: *Dipole Moments in Organic Chemistry*, p. 33. Thieme, Stuttgart 1975.
64. Pople J. A., Gordon M. S.: *J. Amer. Chem. Soc.* **89**, 4253 (1967).
65. LeHuérrou M.-L., Guérillot C. R.: *C. R. Acad. Sci.* **258**, 2549 (1964).
66. Grob C. A.: *Angew. Chem., Int. Ed. Engl.* **15**, 569 (1976).
67. Kilpatrick M., Arenberg C. A.: *J. Amer. Chem. Soc.* **75**, 3812 (1953).
68. Exner O., Svátek E.: *This Journal* **36**, 534 (1971).
69. Exner O., Boček K.: *This Journal* **38**, 50 (1973).
70. Bowden K.: *Can. J. Chem.* **41**, 2781 (1963).

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