$C_8H_{11}N_2O_5P$: C, 39.03; H, 4.50; N, 11.38. Found: C, 39,05; H, 4.45; N, 11.45.

All the crystal structures were determined from diffractometer intensity data. Structure solutions were carried out by direct methods and refined by full-matrix least-squares routines using the SHELX-76 program.

Acknowledgment. Financial assistance of the Council of the University of Cape Town and the Council for Scientific and Industrial Research is gratefully acknowledged.

Registry No. 1a, 7472-54-0; **1b**, 3393-96-2; **1c**, 51-66-1; **5a**, 58046-12-1; **5b**, 25627-05-8; **5c**, 78258-13-6.

Substituent Effects. 9. Two Charged Groups. Remarks on the Eucken/Kirkwood-Westheimer Model and the Reversed-Field Effect

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Received September 29, 1981

Thermodynamic dissociation constants are given for 3,5-$(NMe_3^+)_2$-, 3,5-$(SO_3^-)_2$-, and 3-NMe_3^+-5-$SO_3^-C_6H_3COOH$ in water and ethanol-water mixtures. These follow the extended Hammett equation $\Delta = \rho\sigma^L + \delta^B$ (δ^B is the electrostatic Bjerrum term). This equation also accounts for the phenolic dissociation of the zwitterionic form of tyrosine (VI) and *N,N,N*-trimethyltyrosine (VII). In the latter compound the "reversed field" is acid weakening; nevertheless, acid strengthening is observed. Some other reversed-field models are given. The data strongly favor the view that the electrostatic field is not the prevailing factor. Substituent effects in 0–4 M NaCl are also presented; the zwitterionic compounds (V and VII) conform to the behavior of dipole-substituted acids.

In previous papers[1,2] we have discussed and applied an extended Hammett equation which covers not only the effects of dipole substituents but also those of charged (pole) substituents:

$$\Delta = \rho\sigma^{Ln} + \delta^B \qquad (1)$$

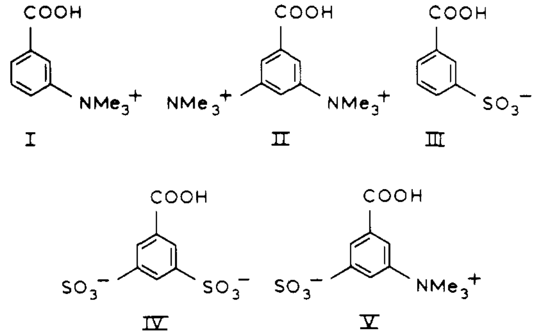
In this equation Δ is the substituent effect ($\log K - \log K^0$), $\rho = \rho_m$ is the reaction constant obtained with a set of standard meta σ values, σ^{Ln} is a "normal" σ value (for dipole substituents $\sigma^{Ln} = \sigma^n$ or σ^0; for pole substituents σ^{Ln} values were derived and tabulated),[1] and δ^B is the Bjerrum term. This last term is believed to account for, e.g., the work involved in bringing a dissociating proton to infinity against the electrostatic field of the pole or dipole of the substituent and is considered to be (almost) structure independent. The $\rho\sigma$ term, then, covers the ionization and is structure dependent.[3] For solvents with a high dielectric constant, D_s, δ^B is small for dipole substituents, so that eq 1 practically reduces to the Hammett equation; for charged substituents, δ^B cannot be neglected. For ionic reactions in the gas phase, δ^B is already large for dipole substituents[1,4] and should be taken into account when investigating structural correlations of the Hammett type.

For proton dissociation in water at 25 °C with $D_s = 78.5$ and a singly charged substituent, Bjerrum[5] obtained:

$$\delta^B = 3.1/r \qquad (2)$$

where δ^B is in p*K* units and *r* is the distance between substituent charge and proton (in angstroms). Generalizing for media with dielectric constant D_s, eq 3 can be written:

Chart I



$$\delta^B = 243/D_s r \qquad (3)$$

In what follows we shall also refer to ${}^eD_E$, the "empirical effective dielectric constant".[1] The concept was introduced by Eucken[6] (discussing dipole effects) and is simply defined as the dielectric constant number[7] required to obtain the observed substituent effect from an equation representing coulombic interactions like eq 3. Hence, ${}^eD_E$ for pole–pole interaction is defined by

$$\Delta = 243/{}^eD_E r \qquad (4)$$

Thus, for 3-$NMe_3^+C_6H_4COOH$ in water, with $\Delta = 1.03$ and $r = 6.3$ Å,[1] ${}^eD_E = 37$.

For dipoles δ^B can be obtained from eq 2 or 3 treating the effect of the dipole as the sum of the effects of two point charges with the appropriate (fractional) charges at the ends of the dipole vector. Often, the approximate eq 5 corresponding with eq 2 is used,

$$\delta^B = (0.65\mu \cos \theta)/r^2 \qquad (5)$$

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[1] Hoefnagel, A. J.; Hoefnagel, M. A.; Wepster, B. M. *J. Org. Chem.* **1978**, *43*, 4720.

[2] van de Graaf, B.; Hoefnagel, A. J.; Wepster, B. M. *J. Org. Chem.* **1981**, *46*, 653.

[3] For recent work treating protonic dissociation as a two-stage process see: Blandamer, M. J.; Scott, J. W. M.; Robertson, R. E. *J. Chem. Soc., Perkin Trans. 2* **1981**, 447.

[4] Cf.: Topsom, R. D. *Tetrahedron Lett.* **1980**, *21*, 403; *J. Am. Chem. Soc.* **1981**, *103*, 39. Hehre, W. J.; Taagepera, M.; Taft, R. W.; Topsom, R. D. *J. Am. Chem. Soc.* **1981**, *103*, 1344. Yoder, C. S.; Yoder, C. H. *Ibid.* **1980**, *102*, 1245.

[5] Bjerrum, N. *Z. Phys. Chem., Stoechiom. Verwandtschaftsl.* **1923**, *106*, 219.

[6] Eucken, A. *Angew. Chem.* **1932**, *45*, 203.

[7] King, E. J. "Acid-Base Equilibria"; Pergamon Press: Oxford, 1965; p 160: "... 'effective dielectric constant' constant"...is only a convenient locution to preserve the formalities of the Bjerrum and Eucken equations".

0022-3263/82/1947-2318$01.25/0

Table I.[a] Benzoic Acids Having One or Two Charged Substituents: Thermodynamic pK Values at 25 °C and Their Analysis

compd	solvent	pK_a	Δ	δ^B	$\Delta - \delta^B$	σ	σ^L	dev
H[b]	H_2O	4.21						
	10E	4.37						
	50E	5.48						
	75E	6.29						
$3\text{-}NMe_3^+\ I^-$ [b]	H_2O	3.18	1.03	0.49	0.54	1.03	0.54	−0.05
	10E	3.26	1.11	0.52	0.59	1.02	0.54	−0.05
	50E	3.77	1.71	0.73	0.98	1.13	0.65	0.09
	75E	4.23	2.06	1.00	1.06	1.23	0.63	0.07
$3,5\text{-}(NMe_3^+)_2(ClO_4^-)_2$	H_2O	2.25	1.96	0.99	0.97	1.96	0.97	−0.08
	10E	2.25	2.12	1.05	1.07	1.94	0.98	−0.08
	50E	2.32	3.16	1.45	1.71	2.08	1.13	0.12
	75E	2.43	3.86	2.01	1.85	2.31	1.11	0.09
$3\text{-}SO_3^-\ Na^+$ [b]	H_2O	4.11	0.10	−0.45	0.55	0.10	0.55	0.04
	10E	4.29	0.08	−0.48	0.56	0.07	0.51	0.00
	50E	5.41	0.07	−0.66	0.73	0.05	0.48	−0.04
	75E	6.38	−0.09	−0.92	0.83	−0.05	0.50	−0.02
$3,5\text{-}(SO_3^-)_2(K^+)_2$	H_2O	4.05	0.16	−0.90	1.06	0.16	1.06	0.09
	10E	4.27	0.10	−0.96	1.06	0.09	0.97	0.00
	50E	5.45	0.03	−1.32	1.35	0.02	0.89	−0.12
	75E	6.54	−0.25	−1.83	1.58	−0.15	0.94	−0.04
$3\text{-}NMe_3^+\text{-}5\text{-}SO_3^-$	H_2O	3.10	1.11	0.04	1.07	1.11	1.07	0.03
	10E	3.23	1.14	0.05	1.09	1.04	1.00	−0.05
	50E	3.80	1.68	0.06	1.62	1.11	1.07	0.03
	75E	4.50	1.79	0.09	1.70	1.07	1.02	−0.04

[a] Solvent, 10E stands for 10 volumes of absolute ethanol in 100 volumes of final solution, etc.; $\Delta = pK(PhCOOH) - pK(\text{substituted compound})$; δ^B, see eq 3 [D_s for: H_2O, 78.5; 10E, 73.9; 50E, 53.4; 75E, 38.6. For N^+, $r = 6.280$ Å, $\delta^B(H_2O) = 0.494$; for $3\text{-}SO_3^-$, $r = 6.895$ Å, $\delta^B(H_2O) = -0.450$]. $\sigma = \Delta/\rho$ (ρ^1 for: 10E, 1.092; 50E, 1.516; 75E, 1.672). $\sigma^L = (\Delta - \delta^B)/\rho$. Dev = deviation, i.e., $\Delta - \Delta(\text{calcd})$; $\Delta(\text{calcd})$ from eq 1, using average σ^L values (see text). [b] Reference 1.

where μ is the dipole moment (Debye units) and θ is the angle (degrees) between the dipole and the line of length r (angstroms) joining the center of the dipole and the dissociating proton. The generalized equation is

$$\delta^B = (51\mu \cos \theta)/D_s r^2 \qquad (6)$$

and the equation defining ${}^eD_E$ is

$$\Delta = (51\mu \cos \theta)/{}^eD_E r^2 \qquad (7)$$

Thus, for $4\text{-}NO_2C_6H_4COOH$ in water for which $\Delta = 0.78$, $\mu = 4.0$ D, $\theta = 180°$, and $r = 7.5$ Å,[1] ${}^eD_E = 4.6$.

In our earlier work[1] we provided and analyzed, inter alia, the data for $3\text{-}NMe_3^+$- and $3\text{-}SO_3^-C_6H_4COOH$, I and III, (Chart I) in water and in 10, 50, and 75 volume percent of ethanol (10E, 50E, and 75E). The present study is an extension to the benzoic acids II, IV, and V with two poles in the same solvents and in 0–4 M NaCl. Moreover, attention is paid to some of the microscopic dissociation constants relating to the α-amino acid tyrosine and its N-trimethylated derivative. Both types of compounds are relevant with respect to our discussion[1] of the Eucken/Kirkwood–Westheimer model and the theory of polar effects.

Results and Discussion

(A) Compounds I–V in Water and Aqueous Ethanol. Table I gives our data on I–V and an analysis of these in terms of eq 1, assuming δ^B to be additive. The most obvious result is that the σ^L values for 3,5-disubstitution are slightly less than twice those for 3-substitution; the average values for I–V are 0.59, 1.05, 0.51, 0.97, and 1.04, respectively. Such nonadditivity is not abnormal. For example, the ratio $\Delta(3,5\text{-}(NO_2)_2)/\Delta(3\text{-}NO_2)$ has been found by Dippy et al.[8] in water to be 1.94; our value[1] in 10E is 1.91, in 50E is 1.90, and in 75E is 1.91. This deviation from additivity for σ^L leads to a similar deviation for Δ as far as these are positive; negative Δ values are more than additive. It can be easily verified that this is in accordance with eq 1.

It will be observed that Δ is positive for III and IV in H_2O, 10E, and 50E but negative in 75E. According to eq 1 this is due to the fact that ρ follows $1/D_s$ up until 50E but lags behind in 75E.[1] For IV the figures are

$$H_2O\text{:} \quad \Delta = 1 \times 0.97 - 0.90 = 0.07$$

$$50E\text{:} \quad \Delta = 1.516 \times 0.97 - 1.47 \times 0.90 = 0.15$$

$$75E\text{:} \quad \Delta = 1.672 \times 0.97 - 2.03 \times 0.90 = -0.21$$

The above data extend and strengthen our earlier comments[1] on the Kirkwood–Westheimer (K-W) model.[9] Calculations with this model yield the same effective dielectric constants ${}^tD_E$ for positive and negative poles at corresponding locations in one and the same cavity. II, IV, and V form a set meeting this geometrical situation almost perfectly. Hence, when dealing with the charged substituents as poles, the relative substituent effects in these compounds are predicted as +2, −2, and 0; the observed values are roughly +2, 0, and +1. When Eucken's approach is used, the same inconsistency appears as an inconstancy of ${}^eD_E$: +39, −440, and +3.1, respectively.

The above observations can be taken to mean that other effects, in addition to those of the poles, play a role. One such effect has been suggested to be that of the electric dipole associated with the charged substituent. This idea has been worked out, within the framework of the cavity model, by Wilcox and McIntyre[10] for COO^- in a bicyclooctanecarboxylic acid. Working backward from the experimental result, these authors found 3.2 D to be satisfactory. Bell et al.[11] compared the effects of SO_3^- and

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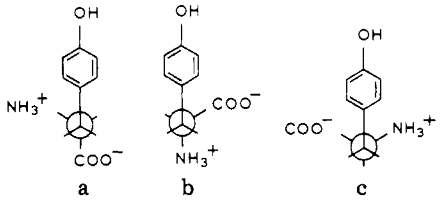
[8] Dippy, J. F. J.; Hughes, S. R. C. *Tetrahedron* **1963**, *19*, 1527.

[9] Kirkwood, J. G.; Westheimer, F. H. *J. Chem. Phys.* **1938**, *6*, 506. Westheimer, F. H.; Kirkwood, J. G. *Ibid.* **1938**, *6*, 513. Westheimer, F. H.; Shookhoff, M. W. *J. Am. Chem. Soc.* **1939**, *61*, 555. Westheimer, F. H. *Ibid.* **1939**, *61*, 1977. For further papers see ref 1, footnotes 20 and 52 (for ref 52f in the text on page 4738 column 2 read ref 52h); Ehrenson, S. *J. Phys. Chem.* **1977**, *81*, 1520; *Chem. Phys. Lett.* **1978**, *56*, 523. Orttung, W. H. *J. Am. Chem. Soc.* **1978**, *100*, 4369. Friedl, Z.; Hapala, J.; Exner, O. *Collect. Czech. Chem. Commun.* **1979**, *44*, 2928.

[10] Wilcox, C. F.; McIntyre, J. S. *J. Org. Chem.* **1965**, *30*, 777.

Table II.[a] Conformers of Tyrosine Zwitterion VI



	a	b	c
r N^+	6.522	8.111	6.522
COO^-	8.751	6.548	6.548
δ^B N^+	0.475	0.382	0.475
COO^-	−0.354	−0.473	−0.473
δ^B	+0.121	−0.091	+0.002
ratio	47	23	30
pK(calcd)	9.62	9.83	9.74

[a] The distances r are for the zwitterion charges to the phenolic proton in angstroms (in three decimals for arithmetic purposes); δ^B is the sum of the individual Bjerrum terms; pK(calcd) pertains to the individual conformers which, in the ratio given, yield the calculated observable pK = 9.70 (see text).

COO^- in a series of aliphatic acids and, assuming the negative charges to have the same influence, deduced 2.0 D as the *difference* between the dipoles involved. As for our benzoic acids III and IV, agreement with experiment can be obtained by assuming the structure $S^{2+}O_3^{3-}$ with C–S = 1.80 Å and C–S–O = 2.20 Å (linear), and, for example, the pair D_E = 78.5 and 47 or 40 and 25 for the negative and positive charges, respectively. Agreement can also be obtained by describing SO_3^- as having one negative charge and two SO dipoles.

As indicated in a previous paper[1] we consider the above pole/dipole approach as "hardly attractive". The dipole components cannot be measured directly, and their parametrization carries the burden of the preceding parametrization of (depths of) the poles in the cavity model.[12] Apart from this, we have observed that even the pole/dipole model is not able to cope with a number of data of different types.[13] We therefore believe that one or more other effects are of importance in addition to the direct coulombic interactions. From this point of view the success of the dichotomous eq 1 is satisfactory, even though it has little to say about the nature of the $\rho\sigma$ term.

(B) Tyrosine and *N,N,N*-Trimethyltyrosine. The 12 "microscopic" dissociation constants of tyrosine, derived by Edsall et al.,[14] offer other examples of interest. Our first concern is the phenolic dissociation of the zwitterionic molecule VI with one positive and one negative charge. The case is more complicated than that for V due to the presence of the three rotamers a–c, each with its own "submicroconstant" (Table II). Conformer a has a positive δ^B, conformer b has a negative δ^B, and δ^B of conformer c is virtually negligible. In dipole terms, the charges in a represent a dipole of 13.9 D[15] with r = 7.6 Å and θ = 40°; in b the same dipole is roughly in the opposite direction with r = 7.2 Å and θ = 122°; in c, θ = 89.5°.

The effective Bjerrum term, $\delta_E{}^B$, pertaining to the mixture can be calculated on the basis of the conformer ratio a/b/c of 47:23:30. This ratio follows from the ^1H NMR vicinal coupling constants in D_2O at pD 6.5 (J = 7.81 and 5.12 Hz) by application of Pachler's approximations[16] and by using Kainosho and Ajisaka's assignment[17] based on ^1H NMR spectra of a specifically monodeuterated sample. X-ray work presents examples of all three conformers[18] but is helpful in so far as these show good adherence to staggering around C(α)–C(β) and no abnormal distances or valency angles; accordingly, the calculated values of δ^B can be relied upon. These data yield $\delta_E{}^B$ = +0.045.[19]

The microconstant of VI, denoted pk_{12} by Edsall et al.,[14] can now be calculated from eq 1, with pK(phenol) = 10.00[1] and ρ(ArOH) = 2.205[1] and by estimating σ^L from published average values[1,20] as $\sigma^L[4\text{-}CH_2CH(NH_3^+)COO^-] = \sigma^L(4\text{-}CH_2CH_2COO^-) + [\sigma^L(4\text{-}CH_2CH_2NH_3^+) - \sigma^n(CH_2\,CH_3)] = -0.04 + 0.03 + 0.13 = 0.12$. The resulting p$k_{12}$ of 9.70 compares well with Edsall et al.'s value, 9.71.

In the context of this paper a small refinement is called for with respect to the σ^L values. For simplicity's sake and due to a lack of the required data, σ^L values were calculated[1] with δ^B values pertaining to the trans conformers. If the trans conformer is taken to be favored by 0.54 kcal/mol[21] in $PhCH_2CH_2COO^-$ and by 0.2 kcal/mol[22] in $PhCH_2CH_2NH_3^+$, the data for ArOH and ArCOOH in water[1] give $\sigma^L(4\text{-}CH_2CH_2COO^-) = -0.01$ and $\sigma^L(4\text{-}CH_2CH_2NH_3^+) = -0.03$. We now obtain p$k_{12}$ = 9.76, also in good agreement with Edsall et al.'s value. In fact, the agreements are better than can be hoped for in view of the uncertainties involved; in this connection we specifically mention the implicit assumption that σ^L values are the same in the several conformers.

It is possible to calculate the other microconstants of tyrosine from our extended Hammett or Hine equations.[1] We shall not persue this further with the exception of the

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[11] Bell, R. P. "The Proton in Chemistry", 2nd ed.; Chapman and Hall: London, 1973; p 98. Bell, R. P.; Wright, G. A. *Trans. Faraday Soc.* **1961**, *57*, 1377. Cf. also: Bell, R. P.; Rawlinson, D. J. *J. Chem. Soc.* **1958**, 4387.

[12] The pole/dipole approach has never been attempted for the NH_3^+ or NMe_3^+ group, probably because there are no sign problems. Hence, the claim that the pole approach is satisfactory for NMe_3^+ is inconsistent with the necessity to invoke both pole and dipole components for negatively charged substituents like SO_3^-, COO^-, and PO_3^{2-}.

[13] See ref 1, sections 10.1.a, 10.1.b, 10.2.a, 10.2.b, 10.3, 8.a, 8.b, 8.g.1, 8.g.2, and 8.g.5. Section 10.2.a is supported by data from: Edward, J. T.; Farrell, P. G.; Hallé, J. C.; Kirchnerova, J.; Schaal, R.; Terrier, F. *J. Org. Chem.* **1979**, *44*, 615. Section 10.3, dealing with the DDM reaction, has been criticized by W. F. Reynolds (*J. Chem. Soc., Perkin Trans. 2* **1980**, 985) on the argument that charged intermediates are formed so that substituent effects as large as those in acid dissociation would have to be expected. We note that neither the K-W model nor δ^B covers the charge reorganization during the reaction; this point has been discussed in ref 1 (p 4742) with regard to the much more extensive reorganization in aromatic substitution. By the same token, the observation by S. Acevedo and K. Bowden (*J. Chem. Soc., Chem. Commun.* **1977**, 608) that the substituent effects in their paracyclophane derivatives are similar in acid dissociation, alkaline ester hydrolysis, *and* the DDM reaction suggests that these cannot be explained by the K-W model. It would seem possible that steric hindrance to solvation is at play in the pseudo-gem and pseudo-ortho derivatives rather than a reversed-field effect.

[14] Martin, R. B.; Edsall, J. T.; Wetlaufer, D. B.; Hollingworth, B. R. *J. Biol. Chem.* **1958**, *233*, 1429.

[15] Based on our standard geometries.[1] Other estimations are similar. See: Buckingham, A. D. *Aust. J. Chem.* **1953**, *6*, 323. Chung, K.; Hedges, R. M.; Macfarlane, R. D. *J. Am. Chem. Soc.* **1976**, *98*, 7523.

[16] Pachler, K. G. R. *Spectrochim. Acta* **1963**, *19*, 2085; **1964**, *20*, 581.

[17] Kainosho, M.; Ajisaka, K. *J. Am. Chem. Soc.* **1975**, *97*, 5630.

[18] Examples are as follows. Conformation a in DL-2-(hydroxyphenyl)alanine hydrochloride: Mostad, A.; Rømming, C.; Tressum, L. *Acta Chem. Scand.* **1977**, *B31*, 119. Conformation b in L-tyrosine hydrochloride and conformation c in L-tyrosine: Frey, M. N.; Koetzle, T. F.; Lehmann, M. S.; Hamilton, W. C. *J. Chem. Phys.* **1973**, *58*, 2547.

[19] $\delta_E{}^B = \log(0.47 \times 10^{0.121} + 0.23 \times 10^{-0.091} + 0.30 \times 10^{0.002}) = 0.0449$.

[20] Hoefnagel, A. J.; Wepster, B. M. *J. Am. Chem. Soc.* **1973**, *95*, 5357.

[21] Taken to be equal to the value derived for $PhCH_2CH_2COOH$ in $CDCl_3$ by: Spassov, S. L.; Simova, S. D. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1113. Coupling constants at different pD values suggest that the values for COOH and COO^- do not differ strongly (ref 17 and Experimental Section).

[22] This value gives a ratio of a/b corresponding with that of tyrosine in acid medium. It is supported by preliminary work (J. M. A. Baas and H. Koudstaal) on (β-phenylethyl)ammonium ion in D_2O, showing vicinal coupling constants of 8.0 and 6.5 Hz, corresponding with 43% trans conformer. The estimation of 98.8% trans conformer by Weintraub and Hopfinger (Weintraub, H. J. R.; Hopfinger, A. J. *J. Theor. Biol.* **1973**, *41*, 53) must be in error.

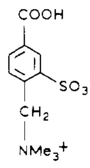
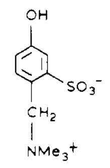
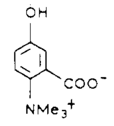
differences obtained by Edsall et al.[14] and denoted $pk_{23} - pk_3 = 0.60$ and $pk_{21} - pk_1 = 0.40$. The former relates to the difference of the substituent effects of 4-O^- and 4-OH on the NH_3^+ dissociation and the latter to that on the COOH dissociation. The required $\rho(ArCH_2CH_2NH_3^+)$ in water can be estimated as $0.5\ \rho(ArCH_2NH_3^+) = 0.5 \times 1.129^1 = 0.565$; $\rho(ArCH_2CH_2COOH) = 0.24$.[1] Further, $\rho^{Ln}(4\text{-}O^-) - \sigma^n(4\text{-}OH) = -0.45 + 0.17 = -0.28$.[1,20] When using the conformer ratio of tyrosine in acid medium, an a/b/c ratio of 44:27:29 from the vicinal coupling constants $J = 7.48$ and 5.55 Hz, and the appropriate δ^B values,[23] we obtain $pk_{23} - pk_3 = 0.565 \times 0.28 + 0.46 = 0.62$,[24] and $pk_{21} - pk_1 = 0.24 \times 0.28 + 0.41 = 0.48$.[24] These values are in satisfactory agreement with the literature, both absolute and differentially. This indicates that the difference between these differences is caused by differences in ρ as well as in electrostatic effects.

Turning our attention to *N,N,N*-trimethyltyrosine it is obvious that the conformer ratio of its zwitterionic form, VII, will be different from that of VI. Accepting trans $PhCH_2CH_2NMe_3^+$ to be favored over gauche by 1.4 kcal/mol,[25] and assuming additivity, we see that an a/b/c ratio of 18:75:7 follows. This ratio is in reasonable agreement with the ratio 10:85:5 that is obtained from the ^1H NMR vicinal coupling constants in D_2O at pD 6.5, $J = 12.00$ and 3.67 Hz.[26] The former ratio gives $\delta_E{}^B = -0.038$; the latter, to be accepted here, gives $\delta_E{}^B = -0.061$. The essential point is that the dominance of conformer b in VII causes the sign of $\delta_E{}^B$ to be opposite that of VI.

On application of the average $\sigma^L(4\text{-}CH_2CH_2NMe_3^+) = 0.03$,[1] a calculation as for VI gives $pk_{12} = 9.80$. The same value is obtained by using $\sigma^L(4\text{-}CH_2CH_2NMe_3^+) = 0.00$[27] obtained from $4\text{-}CH_2CH_2NMe_3^+C_6H_4COOH$ in water by taking account of the contributions by the gauche conformers, and the above-mentioned corrected $\sigma^L(4\text{-}CH_2CH_2COO^-) = -0.01$. Hence, VII is calculated to be a slightly weaker acid than VI for which the same procedures gave $pk_{12} = 9.70$ and 9.76. This is in semiquantitative agreement with the values $pk_{12} = 9.71$ for VI and $pk_{12} = 9.88$ for VII determined by Edsall et al.[14] and considered as a discrepancy by the authors since, usually, NMe_3^+ shows a stronger negative effect than NH_3^+.[28] The present analysis indicates that the reversal of the accepted order is due to the change in sign of $\delta_E{}^B$ resulting from the different conformer ratio.

The most important aspect of the pk_{12} values of VI and VII is that the substituent effects of the 4-$CH_2CH(N^+)$-COO^- moieties have the same positive sign although the electrostatic effects have opposite signs. In terms of empirical effective dielectric constants, the discrepancy can be expressed by noting that the calculated $^eD_E = +13$ for VI is of the usual order with dipole substitution explicable by the K-W model but that $^eD_E = -40$ for VII is not and lacks direct physical meaning. Alternatively, when $\Delta = 0.29$ for VI is accepted as entirely due to the electrostatic effects in question, the substituent effect in VII would have to be expected as $\Delta = 0.29\ \delta_E{}^B(VII)/\delta_E{}^B(VI) = 0.29\ (-0.061)/0.045 = -0.39$; i.e., $pk_{12}(VII) = 10.39$ instead of the observed 9.88. Hence, the equal sign of the effects observed for VI and VII once more emphasizes the inadequacy of coulombic field effects in covering the entire polar effect. In eq 1 the $\rho\sigma^L$ term represents the additional factor(s).

Table III.[a] Some Compounds with Negative δ^B and Predicted Positive Δ Values

	 VIII	 IX	 X
δ^{B+}	0.40	0.47	0.52
δ^{B-}	−0.45	−0.53	−0.54
δ^B	−0.05	−0.06	−0.02
Δ(calcd)	0.77	1.88	1.84

[a] Δ(calcd) is the sum of the substituent effects in the respective monosubstituted benzoic acids or phenols. The data used are as follows (ref 1, negative substituent first): VIII, 0.10, 0.67; IX, 0.59, 1.29; X, 0.04, 1.80.

(C) Other Model Compounds with a "Reversed Field Effect".[29] On application of charged substituents of opposite sign, it is not difficult to devise other models with a negative δ^B, i.e., with a reversed substituent field. Three examples of acids are given in Table III; they pose no conformational problems and avoid complications due to substituents ortho to the functional group. None of these compounds has been investigated yet, but the substituent effects of the respective monosubstituted compounds are known[1] so that the actual effects can be estimated by assuming additivity. In all three compounds the negative δ^B is accompanied by an estimated large positive Δ. As to detail, it will be noted that VIII and IX have similar negative δ^B values but largely different positive Δ values. Again, IX and X have approximately the same large positive Δ but different δ^B values. It is true that the exact location of the charges, and thus δ^B, is debatable and that the 3,4-disubstituted compounds might show deviations from additivity. It is hardly conceivable, however, that such factors would make the comparisons of Table III invalid.

(D) Substituent Effects in Aqueous NaCl. Substituent effects measured in 4 M NaCl should be almost free of Bjerrum effects since the work involved in bringing the proton to infinity is completely or largely compensated by the work involved in bringing the sodium ion to its position in the (assumed) ion pair. This is one of the rationales given[1] for the observation, first made by Palm and his associates,[30] that the difference between the sub-

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[23] NH_3^+ dissociation: conformations a and c, −0.495; b, −0.380. COOH dissociation: a, −0.333; b and c, −0.481.

[24] These calculations are not strictly correct since the actual conformer ratio of the anion will be slightly different. Judging from ref 17 and other work, one can see that the variations in population are not large, and they will not give appreciably different results. Thus, a ratio of 53:22:25 gives values of 0.63 and 0.46, respectively.

[25] In D_2O: Terui, Y.; Ueyama, M.; Satoh, S.; Tori, K. *Tetrahedron* **1974**, *30*, 1465. Cf. $PhCH_2CH_2\text{-}t\text{-}Bu$, 1.7 kcal/mol (in CCl_4): Whitesides, G. M.; Sevenair, J. P.; Goetz, R. W. *J. Am. Chem. Soc.* **1967**, *89*, 1135.

[26] The much larger conformational requirements of NMe_3^+ in VII than of NH_3^+ in VI exclude the ratio 85:10:5; this holds independent of the assignment in VI.[12,17]

[27] The revised $\sigma^L(4\text{-}CH_2CH_2NMe_3^+) = 0.00$, and $\sigma^L(4\text{-}CH_2CH_2NH_3^+) = -0.03$ are in the expected order since the usual order of polar effects is $NMe_3^+ > NH_3^+$ (see ref 28). Thus, the revision removes the apparent anomaly that, e.g., the corresponding benzoic acids have the same p*K*.[1] However, the revision introduces the anomaly that $\sigma^L(4\text{-}CH_2CH_2COO^-) > \sigma^L(4\text{-}CH_2CH_2NH_3^+)$ which is contrary to what $\sigma_I{}^L(COO^-) = 0.24^1$ and $\sigma_I{}^L(NH_3^+) = 0.45^1$ suggest. It should be appreciated that such small differences are doubtful as to their interpretation.

[28] The rule that NMe_3^+ has a stronger polar effect than NH_3^+ is very well documented and appears also in Edsall et al.'s k_1 of tyrosine and *N,N,N*-trimethyltyrosine. An extensive quantitative comparison is part of ref 2.

[29] The term was introduced by: Bennett, G. M.; Mosses, A. N. *J. Chem. Soc.* **1930**, 2364. Cf.: Ingold, C. K. *J. Chem. Soc.* **1933**, 1124, footnote.

[30] Palm, V. A.; Nummert, V. M.; Püssa, T. O.; Karelson, M. M.; Koppel, I. A. *Reakts. Sposobn. Org. Soedin.* **1973**, *10*, 223 (English summary, pp 239–42). For later papers see ref 1, footnote 29.

Table IV.[a] Substituent Effects, ΔpK_m, for Benzoic Acids in Aqueous NaCl at 25 °C

3-NMe_3^+		$3,5\text{-(NMe}_3^+)_2$		3-SO_3^-		$3,5\text{-(SO}_3^-)_2$		$3\text{-NMe}_3^+\text{-}5\text{-SO}_3^-$	
I	ΔpK_m	I	ΔpK_m	I	ΔpK_m	I	ΔpK_m	I	ΔpK_m
0	1.03	0	1.96	0	0.10	0	0.16	0	1.11
0.003	0.98	0.017	1.71	0.008	0.14	0.016	0.33	0.002	1.10
0.006	0.97	0.019	1.72	0.008	0.15	0.025	0.39	0.002	1.10
0.020	0.92	0.028	1.68	0.011	0.18	0.026	0.41	0.010	1.08
0.120	0.85	0.119	1.54	0.108	0.30	0.125	0.58	0.110	1.10
0.52	0.71	0.52	1.34	0.51	0.41	0.53	0.74	0.51	1.07
1.02	0.65	1.02	1.26	1.01	0.42	1.03	0.80	1.01	1.06
2.52	0.60	2.52	1.17	2.51	0.45	2.53	0.83	2.51	1.03
4.02	0.54	4.02	1.14	4.01	0.44	4.02	0.84	4.01	0.96
$\Delta - \Delta^\infty$	0.49		0.82		−0.34		−0.68		0.15
δ^B	0.49		0.99		−0.45		−0.90		0.04

[a] For the definition of the "mixed constant" K_m see ref 1. I is the ionic strength. pK_m of PhCOOH (I, pK_m): 0.1, 4.10; 0.5, 3.98; 1, 3.90; 2.5, 3.77; 4, 3.66. Values for I = 0–0.028 were calculated from pK = 4.21[1] by application of the Debye-Hückel theory[1]. $\Delta pK_m = pK_m(\text{PhCOOH}) - pK_m(\text{substituted compound})$. Δ^∞ is the substituent effect in 4 M NaCl. For δ^B, see Table I.

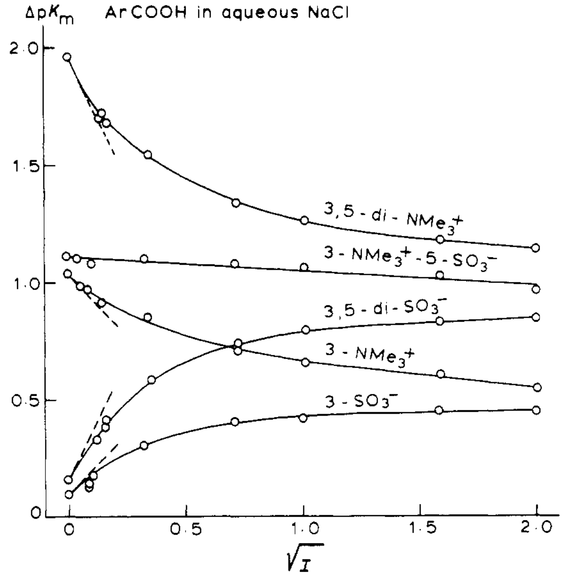

Figure 1. Dependence of the substituent effects, ΔpK_m, upon ionic strength for I–V. The broken lines represent the Debye–Hückel limiting slopes.

stituent effects in water and in 4 M NaCl (Δ^∞) is approximately equal to δ^B:

$$\Delta - \Delta^\infty = \delta^B \qquad (8)$$

Figure 1 shows the behavior found for I–V at various ionic strengths; the actual data are in Table IV. Little comment is needed. The most general point is that good additivity is shown also at intermediate ionic strengths. Equation 8 is followed better with NMe_3^+ than with SO_3^-, but the picture is certainly not unsatisfactory. The pK difference between 3-NMe_3^+- and $3\text{-SO}_3^-C_6H_4COOH$ decreases from 0.93 at I = 0 to 0.10 at I = 4; this change is 88% of the sum of the absolute values of the respective Bjerrum terms $\sum|\delta^B|$ = 0.94. The difference between the pK values of the disubstituted compounds II and IV decreases from 1.80 to 0.30; this change is 79% of $\sum|\delta^B|$ = 1.89.

As to the zwitterionic V, the small positive δ^B = 0.04 predicts a small decrease of the substituent effect when NaCl is added. This is found, although at concentrations above 1 M NaCl the decrease becomes somewhat larger than δ^B.[31] For the phenolic dissociation of VII the opposite trend should be expected since δ^B = −0.06 has the opposite sign; this is confirmed by the observation that Δ = 0.06 increases to Δ^∞ = 0.09. Admitting that such small differences are hardly outside experimental error and therefore of doubtful reliability, it remains satisfactory that these compounds essentially show the behavior of those with dipoles of the usual type.

Experimental Section

Materials. 3,5-Bis(trimethylammonio)benzoic Acid Diperchlorate (II). Repeated methylation of ethyl 3,5-diaminobenzoate in methanol with methyl iodide, while keeping the solution alkaline (phenolphthalein) by addition of concentrated potassium hydroxide solution,[32] yielded a mixture of the desired compound in the form of its diiodide, $3\text{-NMe}_2\text{-}5\text{-NMe}_3^+C_6H_4COOH\ I^-$, and their methyl esters. This mixture (5 g) was warmed with 4 mL of 2 M KOH to give a clear solution, from which, after addition of 0.3 mL of $HClO_4$ (70%), the desired compound was obtained as white crystals which, after recrystallization from water and drying in vacuo at 78 °C, had a melting point of 279 °C dec. C and H analysis was not possible (explosions); a correct N analysis and ^1H NMR spectrum were obtained.

In aqueous LiCl the following ΔpK_m values were observed ([LiCl], M, ΔpK_m): 3.35, 1.16; 5.03, 1.16; 6.71, 1.18. Hence, LiCl and NaCl have the same effects (although pK_m values for PhCOOH differ).

Dipotassium 3,5-Disulfonatobenzoic Acid (IV). Tripotassium 3,5-disulfonatobenzoate[33] (9 g) was treated with 11 mL of 2 M HCl, and the white solid was dissolved by addition of 4 mL of water and warming. Cooling yielded the desired compound which was recrystallized from water and dried in vacuo at 78 °C: correct C and H analysis; mp >360 °C.

3-(Trimethylammonio)-5-sulfonatobenzoic Acid (V). Catalytic hydrogenation of potassium 3-nitro-5-sulfonatobenzoic acid[34] in 65% methanol at room temperature and atmospheric pressure with Raney nickel as a catalyst was followed by repeated methylation in 50% methanol with methyl iodide while the solution was kept alkaline with concentrated KOH in 50% methanol.[32] Acidification with HI (d = 1.70) and recrystallization from 80% acetone gave the betaine which was dried in vacuo at 78 °C: correct equivalent weight, C, H, and N analyses, and ^1H NMR spectrum; mp 355 °C dec.

L-Tyrosine (Diamalt A. G., München) was recrystallized from water, mp 298 °C dec.

***N,N,N*-Trimethyltyrosine:**[14] mp 255 °C dec (after drying in vacuo at 110 °C) (lit.[14] mp ~260 °C); correct C, H, and N analyses and ^1H NMR spectrum. In aqueous NaCl the following ΔpK_m values were obtained ([NaCl], M, ΔpK_m): 0, 0.06; 0.1, 0.08;

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[31] The vicinal coupling constants in 4 M NaCl, J = 12.02 and 3.75 Hz, indicate that the electrolyte hardly affects the conformer ratio.

[32] Cf.: Adams, C. S. U.S. Patent 2 147 897, 1947; *Chem. Abstr.* **1947**, *41*, 7416.

[33] Arthur, H. R.; Ng, Y. L. *J. Chem. Soc.* **1959**, 3094.

[34] Limpricht, H.; v. Uslar, L. *Justus Liebigs Ann. Chem.* **1858**, *106*, 27.

0.5, 0.09; 1, 0.10; 2.5, 0.08; 4, 0.09.

p*K* Measurements. Our general procedures have been described extensively.[1] For some of the lower pK_a values higher concentrations were used, e.g., 0.01 M for II in water. We further note that the Debye–Hückel corrections for II, III, and in particular IV are large due to the higher charge numbers involved. Thus, with IV in 75E the corrections for the two concentrations are 0.727 and 0.858. Even in this extreme case the derived thermodynamic values, 6.544 and 6.537, respectively, come close together.

^{1}H NMR Spectra. Dilute solutions (1 mg of sample/mL of solvent) in D_2O were measured on a Nicolet NT-200 apparatus at 20 ± 2 °C. The following coupling constants (in hertz) were obtained by iterative analysis (LAOCOON-8). Tyrosine: pD = 0.1 (DCl), 7.48, 5.55, −14.65; pD = 6.5, 7.81, 5.12, −14.67; pD = 12.9 (NaOD), 7.53, 5.10, −13.71. The vicinal constants agree well with those from ref 17. *N,N,N*-Trimethyltyrosine: pD = 0.1, 12.02, 4.10, −12.77; pD = 6.5, 12.00, 3.67, −12.51; pD = 12.9, 11.62, 3.73, −12.71; in 4 M NaCl, 12.02, 3.75, −12.66.

Geometries. Distances were obtained by using the standard geometries of ref 1.

Acknowledgment. We thank Dr. J. A. Peters from this laboratory for taking the NMR spectra.

Registry No. I, 81158-75-0; II, 81158-76-1; II $2ClO_4^-$, 81158-77-2; III, 60728-23-6; IV, 81158-78-3; IV $2K^+$, 22038-37-5; V, 81158-79-4; VIII, 81158-80-7; IX, 81158-81-8; X, 81158-82-9; 3-NMe_2-5$NMe_3^+C_6H_4COOH$ I^-, 81158-83-0; 3-NMe_2-5$NMe_3^+C_6H_4COOMe$ I^-, 81158-84-1; ethyl 3,5-diaminobenzoate, 1949-51-5; tripotassium 3,5-disulfonatobenzoate, 81177-88-0; potassium 3-nitro-5-sulfonatobenzoic acid, 81177-80-2; L-tyrosine, 60-18-4; *N,N,N*-trimethyltyrosine, 81158-85-2.

Photochemistry of Vinyl Halides. Vinyl Cation from Photolysis of 1,1-Diaryl-2-halopropenes

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Received April 21, 1981

Irradiation of 1,1-diaryl-2-halopropenes in methanol gave 1,1-diarylpropenes, 1,1-diarylallenes, 1,2-diaryl-1-methoxypropenes, and 9-methoxy-10-methylphenanthrenes. The propenes are derived from vinyl radicals which are generated by homolytic fission of the carbon–halogen bonds. The allenes, the methoxypropenes, and the phenanthrenes are derived from ionic intermediates. When the aryl substituents are more electron rich and the halogen atoms had higher electron affinity, the amounts of products from the ionic intermediates increased. These results suggest that vinyl cations are generated by electron transfer in the radical pairs. The vinyl cations gave the allenes by deprotonation or changed to more stabilized vinyl cations by a 1,2-aryl shift. The phenanthrenes were formed from the methoxypropenes which were obtained by nucleophilic attack of the solvent, methanol, on the rearranged vinyl cations. When the photolysis was carried out in THF which is subject to hydrogen abstraction, the yield of the radical product, i.e., propene, increased. However, the photolysis in ethylene glycol or in methanol at −70 °C elicited a decrease in the yield of the radical products. Sensitized irradiation of 2-bromo-1,1-diarylpropenes with benzophenone or acetophenone resulted in no reaction, and this suggested that the photolysis occurred via the excited singlet state.

There are several examples of photolysis of organic halides which give ionic intermediates. In all these cases, e.g., benzyl,[1] norbornyl,[2] and adamantyl[2] halides, the halogen atom is bonded to an sp^3-hybridized carbon.

However, until recently there has never been any apparent evidence that photolysis of vinyl halides in which the halogen atom is bonded to an sp^2-hybridized carbon gives a vinyl cation. It is generally known that photolysis of vinyl halides leads to a cis–trans isomerization of the double bond or to homolytic fission of the carbon–halogen bond with a consequent formation of products from the derived radical intermediate.[3]

Recently we reported that photolysis of β,β-bis(methoxyphenyl)vinyl bromides in benzene gave bis(methoxyphenyl)acetylenes. We suggested that an intermediate vinyl cation was formed by an internal electron transfer in the radical pair which was formed in the homolytic fission of the carbon–halogen bond.[4] McNeely and Kropp found that photolysis of alicyclic vinyl halides gave solvent-incorporated products which were interpreted as resulting from intermediate vinyl cations.[5] Sket and Zupan also proposed a similar mechanism for the photolysis of 1,1-diphenyl-2-haloethylenes.[6]

The photolysis of 1,1-diaryl-2-halopropenes is a very suitable reaction for a detailed mechanistic study of vinyl cation formation for several reasons. (a) Both radical and ionic products are formed and their ratios have mechanistic significance. (b) The 1,1-diaryl-2-halopropenes do not give solvolysis products by initial heterolytic carbon–halogen bond cleavage under the conditions of the photolysis experiment. (c) Whereas, in the case of photolysis of 1,1-diaryl-2-haloethylenes,[4] a possible formation of vinylidene carbenes cannot be excluded, such intermediates cannot be formed with 1,1-diaryl-2-halopropenes. (d) Structural variation in the β substituent and the halogen atom (Cl, Br, and I) as well as change in the solvent and the temperature can be used as mechanistic tools.

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