Improved Yukawa–Tsuno equation and the substituent effect on pyridine basicity

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ABSTRACT: An improved Yukawa–Tsuno equation was obtained by inserting the resonance demand parameter r in the tetralinear extension of the Hammett equation constrained by a hyperbolic relation between *meta* and *para* substituent effects. The new equation with five adjustable parameters and other Yukawa–Tsuno models were applied to selected literature data for the ionization equilibria of 21 *meta*- and 20 *para*-substituted pyridinium ions in water at 25 °C. The data are best described by the new equation using either the sigma-benzoic acid scale with $r = 1.35 \pm 0.16$ or a truncated sigma-plus scale (in which sigma-zero constants are assigned to 4-alkyl substituents) with $r = 0.29 \pm 0.04$. Standard errors were estimated by Monte Carlo simulation. The results for the pyridinium ion demonstrate that the hyperconjugative effect by alkyl groups is inoperative and that through-resonance effects by electron-donating substituents are considerably hindered. The origin of this hindrance is ascribed to the particularities of nitrogen orbitals in heteroaromatic compounds. It is concluded that the pyridine reactivity lies between those of benzoic acid and benzylic cation, being much closer to the former. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: substituent effect; Yukawa–Tsuno equation; resonance demand; pyridine basicity

INTRODUCTION

The Yukawa–Tsuno equation[1,2] is the first modified Hammett equation in which *meta* and *para* derivatives are treated at different levels of complexity.[3] These equations require scales of position-dependent substituent constants and are most appropriate for the analysis of substituent effects in benzene derivatives, including heteroaromatic derivatives. On the other hand, Exner[4] and Shorter[5] have reviewed different multiparametric extensions of the Hammett equation in which *meta* and *para* derivatives are treated separately.[3] A recent addition to this field is Pytela's alternative interpretation of substituent effects[6–8] by means of a single constant per substituent.

Recently, we proposed[9] a hyperbolic model to interrelate *meta* and *para* substituent constants of the unified sigma-zero scale.[10] On the basis of this model, a constrained tetralinear version of the Hammett equation was developed[11] which yielded values for the *para*/*meta* ratio of the field or inductive effect in excellent agreement[11] with Dewar *et al.*'s model.[12] Then we referred to difficulties encountered while fitting data for the pyridinium ion series with sigma-plus constants, and

to Sawada *et al.*'s contribution[13] to the controversy on the proper scale to describe the pyridine reactivity.

The aims of the present paper are twofold. The first is to obtain an improved Yukawa–Tsuno equation from our previous plurilinear extension[11] of the Hammett equation. This leads to a constrained tetralinear equation with five adjustable parameters that allows for the higher complexity of the *para* derivatives while treating *meta* and *para* derivatives interrelately. The second is to compare the resonance demand in pyridine derivatives with that in benzoic acid and benzyl cation systems. With the help of the improved Yukawa–Tsuno equation, it is shown that, except for the 4-alkyl derivatives, the pyridine basicity can be described by the sigma-plus scale almost as accurately as by the benzoic acid scale, provided that allowance is made for the difference in resonance demand in these scales. Finally, we use a Monte Carlo method[14] to estimate standard errors in the resonance demand parameter, and present revised values and associate errors for the parameters of our hyperbolic model.[9]

THEORY

Yukawa–Tsuno equations

The Yukawa–Tsuno equation has been presented in

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different forms.[5] Using the symbol Δ to represent the experimental substituent effect on the parent compound,[15,16] we write it as[17]

$$\Delta = \delta + \rho[\sigma^\circ + r(\sigma - \sigma^\circ)] \qquad (1)$$

where the intercept δ is a statistical term, ρ is the reaction constant and r is the resonance demand measured with respect to a standard process. This is specified when the σ scale is chosen. We note that, for $r = 1$, Eqn (1) takes the form of the Hammett equation expressed on the σ scale.

If, as suggested by some workers,[3,18,19] *meta* and *para* derivatives are treated separately, then Eqn (1) should be decomposed into

$$\Delta_3 = \delta_3 + \rho_3\sigma_3^\circ \qquad (2)$$

$$\Delta_4 = \delta_4 + \rho_4[\sigma_4^\circ + r(\sigma_4 - \sigma_4^\circ)] \qquad (3)$$

since the difference $\sigma_3 - \sigma_3^\circ$ is zero.

The existence of a general link between the effect of a substituent from the *meta* and *para* positions should permit us to introduce constraints relating the fitting parameters for these two series. We addressed this problem in terms of a model[9,11] which uses the hyperbolic relationship in the form it is encountered in chemistry.[20] The incorporation of the Yukawa–Tsuno analysis into this model is straightforward, leading to

$$\Delta_{3n} = \delta_{3n} + \rho_{3n}\sigma_{3n}^\circ \qquad (4)$$

$$\Delta_{4n} = \delta_{4n} + \rho_{4n}[\sigma_{4n}^\circ + r(\sigma_{4n} - \sigma_{4n}^\circ)] \qquad (5)$$

$$\Delta_{3s} = \delta_{3s} + \rho_{3s}\sigma_{3s}^\circ \qquad (6)$$

$$\Delta_{4s} = \delta_{4s} + \rho_{4s}[\sigma_{4s}^\circ + r(\sigma_{4s} - \sigma_{4s}^\circ)] \qquad (7)$$

and to four additional relations [Eqns (26)–(28) and (61) in Ref. 11] constraining parameters in Eqns (4)–(7). Hence this tetralinear extension of the Yukawa–Tsuno equation consists of four equations with five independent parameters. The quantity r in Eqns (5) and (7) retains its original meaning[1,2,17] as the through-conjugation or direct-resonance demand relative to a standard system. In the above equations, subscripts n and s stand for normal and special substituents, respectively. The latter are distinguished from the former by the presence of a lone electron pair in the atom next to the aromatic ring.

After deducting direct resonance effects, *meta* and *para* substituent effects become related[11] by the following pair of conjugate rectangular hyperbolae with asymptotes defined by $\Delta_4/\Delta_3 = \lambda$ and $\Delta_4 = \gamma$:

$$\Delta_{4n} = \frac{\gamma\Delta_{4n}/\Delta_{3n} + \varepsilon_n}{\Delta_{4n}/\Delta_{3n} - \lambda} \qquad (8)$$

$$\Delta_{4s} = \frac{\gamma\Delta_{4s}/\Delta_{3s} + \varepsilon_s}{\Delta_{4s}/\Delta_{3s} - \lambda} \qquad (9)$$

We have shown[11] that the parameter λ gives the *para/meta* ratio for the non-mesomeric or field/inductive

effects. Because λ is an asymptotic quantity, it does not correspond to the value of Δ_4/Δ_3 for any real substituent.

RESULTS

Data used

Sigma constants and ΔpK_a data used in this work are given in Table 1. Their selection has been explained elsewhere.[11] Recently, Shorter[21] published new IUPAC recommended values for σ^{BA} constants. However, we have not revised our selected values because the number of substituents covered by Shorter[21] is not yet as extensive as in Table 1, and the differences in values are relatively minute.

Fitting experiments

A detailed description of the least-squares non-linear fitting procedure based on the Luus–Jaakola method[22] has been given previously.[11] Revised values for the numerical constants pertaining to our hyperbolic model[9] for the unified sigma-zero scale[10] have been used (see Appendix). Standard errors for the parameter r and the main model quantities λ and γ were calculated by a Monte Carlo method[14] briefly described in the Appendix.

Three versions of the Yukawa–Tsuno equation, namely our constrained tetralinear improvement based on Eqns (4)–(7), the bilinear model with separate equations for *meta* and *para* derivatives [Eqns (2) and (3)] and the unilinear original[17] Eqn (1) with non-zero intercept, were applied to the ionization constants in Table 1 for 21 *meta*- and 20 *para*-substituted pyridinium ions in water at 298 K. Data for the unsubstituted pyridinium ion were included once with the unilinear model and twice (one as a 3n substituent and the other as a 4n substituent) with the plurilinear models. For each model, correlation analysis was performed using the σ^{BA} and σ^+ scales.

Additionally, for reasons discussed below, a truncated σ^+ scale was also tested. This is obtained from the usual σ^+ scale by setting $\sigma^+ - \sigma^\circ = 0$ for the 4-alkyl groups (substituents *11–15* in Table 1). It can be said that this truncated σ^+ scale is designed for the cases where the hyperconjugative effect by 4-alkyl substituents is considered inoperative. The results of these correlation analyses are reported in Table 2, together with the relevant statistics. We appraise the goodness of fit by Exner's statistic[4,23,24] ψ, since our previous experience[11] showed it as a very strict criterion. Lastly, the statistical significance of introducing a variable r over a similar model with fixed $r = 1$ is measured by Ehrenson's statistic[25] $\mathfrak{R}_1$.

It follows from Table 2 that the description of pyridine basicities in water by the new constrained tetralinear

version of the Yukawa–Tsuno equation, depicted in Fig. 1 is superior to either the bilinear or the unilinear models. It also follows that a sliding scale of σ^{BA} and σ^+ values is statistically validated at a confidence level higher than 95%, and that the performance with the σ^{BA} and truncated σ^+ scales is better than that with the full σ^+ scale.

DISCUSSION

Substituent effects on the pyridine reactivity are remarkable in several aspects. They represent a case for which *meta* and *para* derivatives were found to be better correlated by lines of different reaction constants.[26] Bryson[27] suggested further that one can describe the *meta* series by two regression lines. Lastly, the controversy as to whether the pyridine system follows the benzoic acid or the sigma-plus reactivity cannot be considered satisfactorily settled. We now turn to the detailed

discussion of these aspects in the light of the present results.

Analysis of the *meta* series

In the analysis of pyridine basicities, the correlation of the *meta* substituents by two regression lines was first proposed by Bryson.[27] Interestingly, his separation matches exactly with our 3n and 3s groups. As noted before,[11] our hyperbolic model is consistent with error-free data for which ρ_{3n} and ρ_{3s} are different, this difference being related to δ_{3s} [see Eqn (41) in Ref. 11]. A value of 0.91 for $\rho_{3s} - \rho_{3n}$ (Table 2) compares well with the value of 0.82 obtained by Bryson.[27]

The behaviour of 3s substituents in the pyridine reactivity has been qualified as unexpected[28] and its origin ascribed[28,29] to the field-induced resonance effect.[30] This effect, which cannot be accounted for separately from pure field effects, should therefore explain the increased reaction constant for 3s substituents

Table 1. Sigma constants and data for ΔpK_a at 298 K used in this work

| No. | Substituent | Sigma constants[a] | | | | Pyridinium[b] | |
		σ_3°	σ_4°	$\sigma_4^{BA}-\sigma_4^\circ$	$\sigma_4^+-\sigma_4^\circ$	Δ_3	Δ_4
Special							
1	$N(CH_3)_2$	−0.095	−0.317	−0.313	−1.383	−1.25	−4.40
2	NH_2	−0.087	−0.295	−0.275	−1.005	−0.795	−3.925
3	OH	0.023	−0.221	−0.159	—	0.40	—
4	OCH_3	0.102	−0.120	−0.160	−0.660	0.43	−1.38
5	NHAc	0.144	0.002	−0.092	−0.602	0.86	−0.55
6	SCH_3	0.142	0.063	−0.063	−0.663	0.78	−0.74
7	F	0.335	0.151	−0.091	−0.221	2.20	—
8	Cl	0.365	0.242	−0.022	−0.132	2.365	1.38
9	Br	0.369	0.265	−0.045	−0.115	2.345	1.46
10	I	0.343	0.277	−0.067	−0.147	1.92	—
Normal							
11	$C(CH_3)_3$	−0.087	−0.150	0	−0.110	−0.65	−0.82
12	CH_3	−0.062	−0.135	0	−0.175	−0.50	−0.83
13	$CH(CH_3)_2$	−0.082	−0.132	0	−0.148	−0.55	−0.84
14	C_2H_5	−0.077	−0.127	0	−0.173	−0.53	−0.835
15	CH_2Ph	−0.047	−0.058	0	−0.212	—	−0.38
0	H	0	0	0	0	0	0
16	Ph	0.041	0.051	−0.031	−0.231	0.61	−0.14
17	CO_2H	0.356	0.440	0	0	—	—
18	CO_2R	0.349	0.441	0	0	2.12	1.72
19	COPh	0.362	0.456	0	0	2.03	1.86
20	$COCH_3$	0.360	0.469	0	0	1.95	1.70
21	CHO	0.410	0.473	0	0	—	—
22	CF_3	0.464	0.538	0	0	2.75	2.58
23	SO_2NH_2	0.578	0.582	0	0	—	—
24	CN	0.622	0.714	0	0	3.85	3.35
25	SO_2CH_3	0.685	0.728	0	0	—	3.61
26	NO_2	0.713	0.814	0	0	4.03	3.82

[a] σ° constants from Ref. 10; σ_4^{BA} and σ_4^+ constants from Ref. 4, pp. 61–62.
[b] Inonization of substituted pyridinium ions is water. See Ref. 11 for data selection and original references.

Table 2. Correlation analysis of the ionization of 3- and 4-monosubstituted pyridinium ions in water at 298 K[a]

	Yukawa–Tsuno model								
	Constrained tetralinear[b]			Bilinear[c]			Unilinear[d]		
Quantity	σ^{BA}	σ^+	Truncated σ^{+e}	σ^{BA}	σ^+	Truncated σ^{+e}	σ^{BA}	σ^+	Truncated σ^{+e}
Model parameters									
ρ_{3n}	6.069	6.083	6.070	6.167	6.167	6.167	5.341	5.195	5.349
ρ_{3s}	6.975	6.975	7.022	—	—	—	—	—	—
ρ_4/ρ_3	0.793	0.793	0.803	0.787	0.728	0.789	1	1	1
δ_{4n}	−0.098	−0.096	−0.105	−0.098	0.144	−0.068	−0.053	0.336	−0.039
δ_{3s}	−0.280	−0.275	−0.299	−0.082	−0.082	−0.082	—	—	—
ε_n	1.382	1.383	1.424	1.382	1.020	1.368	1.882	1.748	1.871
ε_s	0.471	0.469	0.491	0.419	0.195	0.398	0.533	0.437	0.521
λ	0.762 ±0.033[f]	0.761 ±0.031[f]	0.772 ±0.031[f]	0.756	0.700	0.758	0.961	0.961	0.961
γ	−1.223 ±0.087[f]	−1.222 ±0.079[f]	−1.247 ±0.077[f]	−1.227	−0.667	−1.171	−1.259	−1.136	−1.246
r	1.352 ±0.155[f]	0.299 ±0.35[f]	0.293 ±0.035[f]	1.656 ±0.195[f]	0.471 ±0.059[f]	0.374 ±0.044[f]	1.468 ±0.136[f]	0.356 ±0.035[f]	0.332 ±0.031[f]
Correlation statistics[g]									
n	43	43	43	43	43	43	42	42	42
p	5	5	5	5	5	5	3	3	3
s	0.243	0.254	0.246	0.271	0.278	0.284	0.356	0.364	0.358
ψ	0.127	0.133	0.129	0.142	0.146	0.149	0.184	0.188	0.186
$\mathfrak{R}_{1,n-p}$	1.068	1.987	2.069	1.153	1.383	1.721	1.076	1.735	1.927
$\mathfrak{R}_{1,n-p,95\%}$	1.052	1.052	1.052	1.052	1.052	1.052	1.051	1.051	1.051

[a] Data from Table 1.
[b] Equations (4)–(7) constrained by the hyperbolic model.
[c] Equations (2) and (3) treated as a single correlation.
[d] Equation (1).
[e] Assuming $\sigma^+ - \sigma^\circ = 0$ for the 4-alkyl groups.
[f] Standard errors calculated by Monte Carlo simulation (see Appendix).
[g] n, Number of data points; p, number of independent parameters; s, standard deviation of the fit; ψ, Exner's goodness-of-fit statistic defined by[4,23,24] $\psi = s/s_0$ where s_0 is the standard deviation of the data; $\mathfrak{R}_{1,n-p} = f_{p-1}/f_p$ is the f ratio in relation to the same fitting model with $r = 1$; $\mathfrak{R}_{1,n-p,95\%}$ is the $\mathfrak{R}$ statistic at the 95% confidence level (values taken from Ref. 25).

relative to 3n substituents, a feature precluded by the bilinear and unilinear models.

Sigma scale for pyridine reactivity

Pyridine basicities were initially correlated[31] by Hammett sigma-benzoic acid constants. Later, analysis by the dual substituent parameter treatment[32] assigned σ_R^+ constants to the pyridinium ion system, and from a remark by Ellam and Johnson[33] a long controversy ensued.[13,29,34–38]

Basically, Johnson and co-workers[33,36,38] consider the pyridine reactivity to be closer to the benzoic acid reactivity rather than to the sigma-plus reactivities. Their contention was then supported only by Sawada *et al.*[13] More recently, Reynolds *et al.*[39] suggested that σ_R^{BA} and σ_R^+ scales could be replaced by a new σ_R^+ scale such that σ_R^{BA} values would be generated by linear interpolation between σ_R° and the new σ_R^+ values. This suggests that the controversy could be settled by resorting to the Yukawa–Tsuno analysis, insomuch that different r values

associated with a single scale for resonance contributions would embrace the reactivities of benzoic acid, pyridinium ion, benzyl cation and α,α-dimethylbenzyl (or *tert*-cumyl) cation derivatives. However, the present results on the effect of the 4-alkyl groups indicate that the σ^{BA} and σ^+ scales cannot be unified so straightforwardly. We shall argue that the conditions for the operation of hyperconjugation in pyridinium ion and benzoic acid systems are alike, and different from those in benzylic cations. First some evidence is gathered from the literature.

For the pyridine system, Brown and Mihm[40] were the first to notice that the decrease in hyperconjugation in the *para* series from methyl to *tert*-butyl is relatively small. Notwithstanding this, hyperconjugation (which should be more aptly termed σ–π conjugation[41]) contributes to the stabilization of phenyl compounds, as demonstrated by thermochemical data by Luo and Holmes.[42] The stabilization energy, E_c, calculated by them for some alkylbenzenes, is plotted in Fig. 2 against the difference $\sigma_4^+ - \sigma_4^\circ$. An approximate linear relationship results, showing that the σ–π conjugation is effectively related to
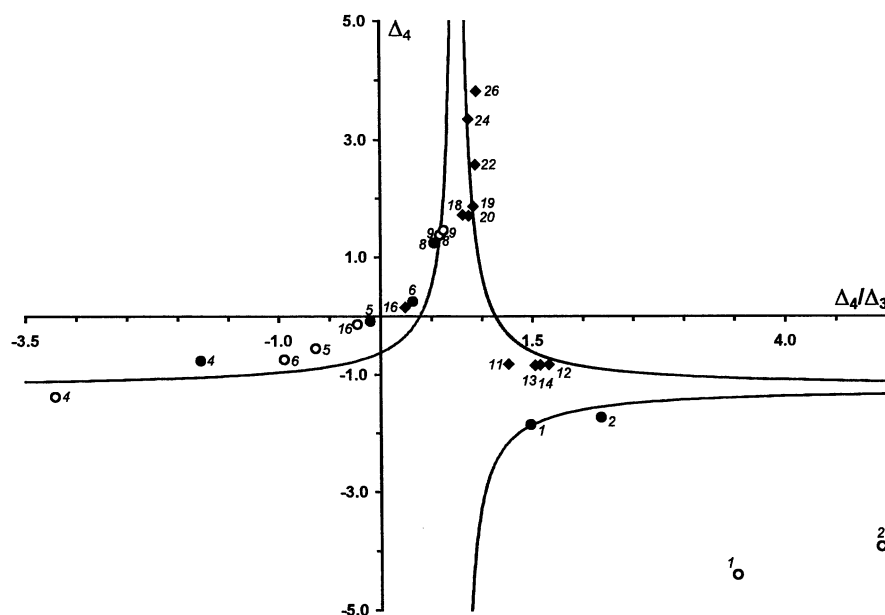
Figure 1. Interrelationship between Δ_4 and Δ_4/Δ_3 for the ionization of pyridinium ions in water at 25 °C. Diamonds are for normal substituents and circles for special substituents. Filled symbols are for experimental or estimated values without through-resonance contributions and empty symbols are for experimental values that include through-resonance contributions. The lines drawn are for the three-parameter hyperbolae [Eqns (8) and (9)] with parameters given by the constrained tetralinear Yukawa–Tsuno equation with σ^{BA} constants (Table 2). Experimental data and substituent numbering as in Table 1.

the sigma-plus scale. The fact that the difference $\sigma^{BA} - \sigma^\circ$ is generally considered to be zero for the 4-alkyl groups does not mean that there is no hyperconjugation but that this effect is about the same in the species forming an acid–base pair. In principle, theoretical calculations using an *ab initio* molecular orbital basis could clarify this problem. Unfortunately, only the methyl group is usually considered for these calculations
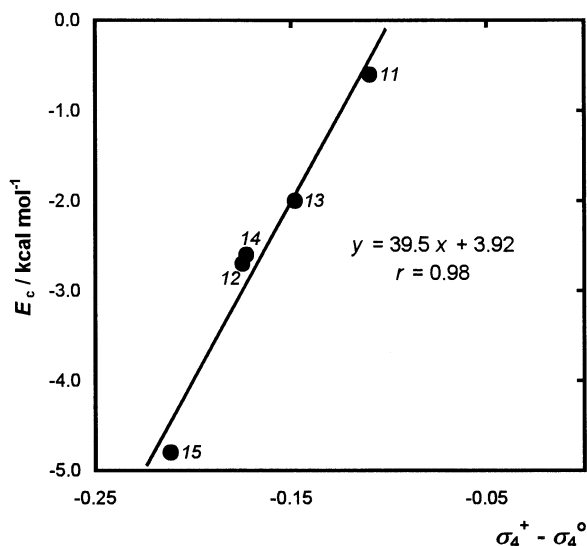

Figure 2. Stabilization energy, E_c, of alkylbenzenes[42] as a function of $\sigma_4^+ - \sigma_4^\circ$. Numbering as in Table 1. The data are correlated by E_c (kcal mol^{-1}) = 3.92 + 39.5 ($\sigma_4^+ - \sigma_4^\circ$) and a correlation coefficient of 0.981.

so that it is difficult to ascertain collective trends for the alkyl groups. Thus, Reynolds *et al.*[39] obtained π-electron transfer parameters for some substituted pyridinium ions and pyridines. The change in this parameter is[39] -0.016 for 4-CH$_3$, -0.013 for 4-CF$_3$, and -0.041 for 4-F. Although these molecular orbital calculations are for gas-phase conditions, Abboud *et al.*[43] and Aue *et al.*[44] demonstrated that 4-CH$_3$ and 4-CF$_3$ are among a large number of substituents for which the corresponding pyridines show an attenuation factor of *ca* 2.4 in their gas- to aqueous-phase Gibbs energy of protonation. Consequently, theoretical calculations for the methyl group appear to indicate a negligible hyperconjugative effect for the alkyl groups from the *para* position in the pyridine ring. Also, very recently Exner and Böhm[45] have concluded that hyperconjugation does not contribute significantly to the stability of 4-alkylbenzyl cations as isolated species, even though they propose a reappraisal of this effect.

Next we use the results reported in Table 2. Close inspection of the deviations showed a marked difference between alkyl (*11–15* in Table 1) and non-alkyl (*1, 2, 4–6, 8, 9* and *16* in Table 1) electron-donating *para*-substituents. The root mean square error for the latter is about the same when σ^{BA} or σ^+ scales are used with a given Yukawa–Tsuno model. This indicates that for the non-alkyl groups either sigma scale would be appropriate. In contrast, the situation is very different for the alkyl groups, as evidenced in Table 3. It is remarkable that these groups are best described by a truncated σ^+ scale in which $\sigma^+ - \sigma^\circ = 0$ for the 4-alkyl groups. Even

Table 3. Root mean square error (RMSE) for the 4-alkylpyridinium ions and resonance demand, *r*, in the fits of different Yukawa–Tsuno models using σ^{BA} and σ^+ scales

	Yukawa–Tsuno model					
	Constrained tetralinear[a]		Bilinear[b]		Unilinear[c]	
Scale	RMSE	*r*	RMSE	*r*	RMSE	*r*
σ^{BA}	0.08	1.35	0.08	1.66	0.07	1.47
σ^+	0.18	0.30	0.10	0.47	0.17	0.37
Truncated σ^{+d}	0.07	0.29	0.10	0.37	0.08	0.33

[a] Equations (4)–(7) constrained by the hyperbolic model.
[b] Equations (2) and (3).
[c] Equation (1).
[d] Assuming $\sigma^+ - \sigma^\circ = 0$ for the 4-alkyl groups.

the apparently indifferent case for the bilinear model can be ascribed to a numerical artificiality, as suggested by a marked variation in the corresponding *r* value (Table 3). This demonstrates a difference of kind: negligible hyperconjugative effect in pyridine and benzoic acid systems and stabilization through hyperconjugation or an equivalent effect[45] in benzylic cation systems. It remains to seek the origin of this dichotomy.

Pyridinium ions and benzylic cations bear a positive charge in the reaction centre that is supposed to be delocalized by electron-supplying substituents in the *para* position. However, through-resonance effects can be sterically hindered, as observed in aromatic amines by Hoefnagel *et al.*[46] More recently, Fujio, and co-workers[47,48] found a simple relationship between the resonance demand parameter *r* and the dihedral angle ϕ formed by the benzylic 2p π-orbital and the ring π-system. They observed that *r* goes from zero at $\phi = 90°$ to a maximum value at $\phi = 0°$. On the other hand, long ago Jones and Katritzky[49] emphasized the importance of the steric requirements of resonance to explain the stabilities of some pyridine derivatives. More specifically, Ellam and Johnson[33] considered that 'the fact that electron deficiency in the pyridine ion arises in the nitrogen sp^2 orbital which is orthogonal to the p-orbital aromatic system' could explain why the basic strength of pyridines correlate better with σ^{BA} than with σ^+ constants. Although accepting these basic explanations, we note that the resonance demand does not vanish completely as an angle $\phi = 90°$ would indicate. Since[47,48] $\cos^2 \phi = r/r_{max}$, if pyridinium ions are compared with secondary benzyl cations for which $r_{max} = 1.15$,[48] then from $r^+ = 0.293 \pm 0.035$ (Table 2) one obtains $\phi = 60 \pm 2°$, which is only two-thirds of the actual angle. Our interpretation of these seemingly contradictory arguments is as follows.
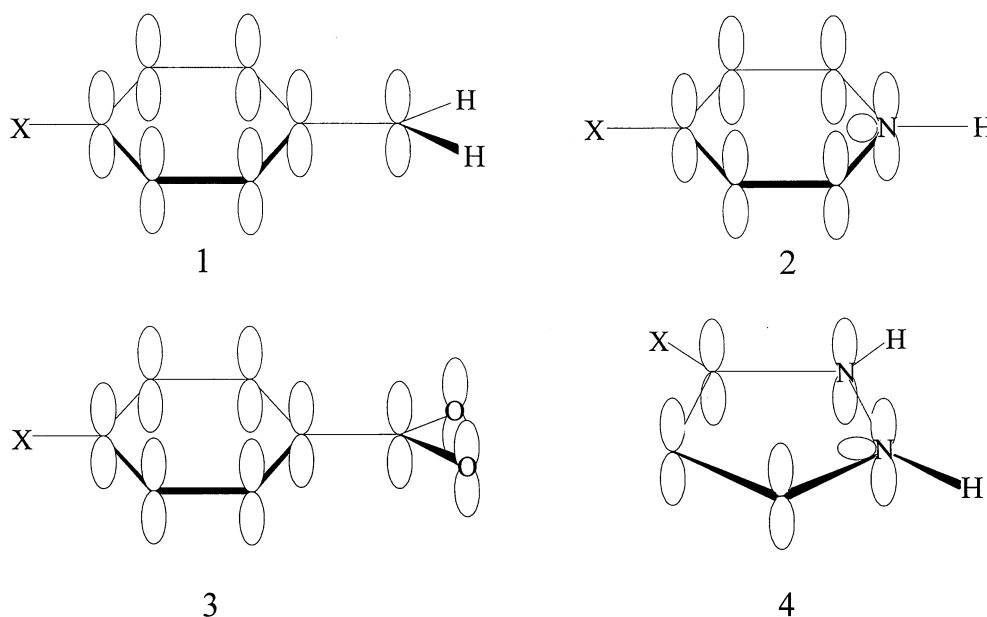
Figure 3. Structures showing the π-system of 4-substituted benzyl cation (**1**), pyridinium ion (**2**) and benzoate ion (**3**) and of 5-substituted pyrazolium ion (**4**).

Fujio and co-workers'[47,48,50,51] reasoning should apply to compounds in which the electron deficiency occurs in an orbital overlapping with the aromatic ring. In these systems a positive charge can be delocalized by hyperconjugation or by the alternative mechanism advanced by Exner and Böhm,[45] and steric inhibition of resonance, in the strict sense of Decouzon *et al.*,[52] may operate (see structure **1** in Fig. 3). On the other hand, as noted by Ellam and Johnson,[33] the positive charge borne by the pyridine ring originates in a sp^2 orbital belonging to the nitrogen atom which also contributes with a p-orbital to the aromatic π-system (Figure 3 structure **2**). An important insight into this situation is provided by modern valence bond theory calculations,[53] showing that some spin pairing can occur between orthogonal orbitals of an atom. If spin-coupled orbitals hinder hyperconjugative interactions while allowing a low degree of through-resonance effects, then our observations for the pyridine reactivity would be rationalized. A similar situation should arise in the pyrazole system[54] (Fig. 3 structure **4**). Finally, the absence of a positive charge would explain why there is no differential hyperconjugative effect in benzoic acid systems (Fig. 3 structure **3**).

Resonance demand parameter

The usefulness of Yukawa–Tsuno analyses depends on the precision with which the parameter r is obtained. In the absence of error estimates, Shorter (Ref. 5, p. 42) indicates that not much confidence should be placed on r values less than 0.3 or in the range 0.7–1.3. Since the values we obtained were mostly in these unclear regions, Monte Carlo experiments for error evaluation were performed as reported in the Appendix. It follows from the results in Table 2 that the relative error in r can amount to up to 12%, an error much larger that in the parameters λ and γ also given by the improved Yukawa–Tsuno equation. In spite of this, they are sufficiently low to allow meaningful conclusions to be drawn from the calculated r values.

Fujio and co-workers[48,51,55] refer to a value of $r^+ = 0.26$ for the σ^{BA} scale. Application of the constrained tetralinear model to the data in Table 1 for the benzoic acid reactivity yields $r^+ = 0.215$ with either the full or the truncated σ^+ scale. These estimates are in fair agreement because our approach tends to yield smaller r values, as seen in Table 2.

Now, using the truncated σ^+ scale, one obtains r^+ (pyridine reactivity)/r^+ (benzoic acid reactivity) = 1.36, a ratio in excellent accord with the value r^{BA} (pyridine reactivity) = 1.35. This demonstrates that the resonance demand in the ionization of pyridinium ions in water is undoubtedly higher than that in the benzoic acid system. Additionally, the equivalence between the σ^{BA} and the truncated σ^+ scales mediated by a certain r value is evidenced.

Parameter λ

The parameter λ is designed[9,11] to yield the *para/meta* ratio of field substituent effects. It was shown[11] to be best modelled by the through-space approach of Dewar *et al.*[12] This leads to a value[11] of 0.84 for the pyridinium ion series, whereas $\lambda = 0.80$ was obtained assuming $r^{BA} = 1$. Now an even lower value of 0.76 ± 0.03 results from the Yukawa–Tsuno analysis (Table 2), which, however, is very close to the value of 0.75 obtained[11] when the *para* special substituents are excluded from the correlation analysis. This lowering of the λ value can be ascribed to indirect *meta* resonance or field-induced resonance effects (FIRE).[28–30] Since[11] $\lambda = \lambda^\circ \, \rho_{4s}/\rho_{3s}$, where λ° refers to the reference system,[9] an increase in ρ_{3s} due to FIRE should result in a decrease in λ. In other words, λ values are theoretically calculated assuming that substituents bear equal electrical charges in the *meta* and in the *para* positions, whereas the operation of FIRE is experimentally equivalent to enhanced charges in 3s substituents and hence the observed λ value should be lower than the theoretically predicted value.

On the other hand, previous approaches have led to higher estimates for λ. Thus, in terms of the linear substituent free energy (LSFE) treatment,[56] Sawada *et al.*[13] found the ratio ρ_i^p/ρ_i^m for the pyridinium ion system to be 'virtually identical' with the corresponding ratio for the benzoic acid system. We note that the LSFE correlation[13,56] treats *meta* and *para* derivatives separately at the cost of eight adjustable parameters and yields[13] $\rho_i^p/\rho_i^m = 0.85$ for the reference system, against our value of 0.961 ± 0.005 (see the Appendix). In turn, on the basis of the Taft–Topsom treatment of substituent effects,[57] Abboud *et al.*[43] have demonstrated that polarizability effects are practically absent in aqueous solution where they found the *para/meta* ratio for the field effect in the pyridinium ion system to be 0.90. Therefore, only our improved Yukawa–Tsuno analysis has the ability to yield a realistic estimate of λ for the aqueous solution acidity of substituted pyridinium ions that takes into account the lowering of the contribution from FIRE.

CONCLUSIONS

An improved Yukawa–Tsuno equation with five adjustable parameters was derived from our previous constrained tetralinear extension[11] of the Hammett equation. The characteristic parameters of the new equation are λ, the *para/meta* ratio of field or inductive substituent effects, γ, an absolute measure of the Hammett reaction constant in the absence of through-resonance effects, and the Yukawa–Tsuno parameter r, the through-resonance demand relative to the sigma scale used.

By performing a non-linear correlation analysis of a large set of literature data for the ionization equilibria of 3- and 4-monosubstituted pyridinium ions in water at

25 °C, we found the following. In the *meta* series, our constrained tetralinear approach accommodates well the increased effect by electron-donating substituents, in relation to the other substituents,[27] originated in the field-induced resonance effect.[28–30] This effect is considered to be responsible for an observed λ value below theoretical calculations. In the *para* series, no significant differential hyperconjugative effect is observed for the alkyl groups,[40] and the resonance demand is equivalently described by the sigma-benzoic acid scale with $r^{BA} = 1.35 \pm 0.16$ or with a truncated sigma-plus scale by leaving out the alkyl groups with $r^+ = 0.29 \pm 0.04$, these standard errors being estimated by a Monte Carlo method.[14]

Although strong resonance interactions are expected for electron-donating substituents in reactions with an electron-deficient centre, the present results for the parameter *r* add evidence for the inhibition of resonance in the pyridinium ion due to the location of the electron-deficient centre in a nitrogen orbital orthogonal to the ring aromatic system.[33]

Acknowledgement

APPENDIX

Monte Carlo estimates of standard errors

We have been using the optimization method of Luus and Jaakola[22] for fitting data to linear and non-linear models.[9,11] However, this direct search procedure is not amenable to the assessment of uncertainties in the adjustable parameters. On the other hand, both Shorter[5] and Exner[4] have referred to the problems of a statistical nature associated with the determination of confidence intervals for the resonance demand parameter in Yukawa–Tsuno analyses.

A convenient way to overcome these difficulties is to employ a Monte Carlo simulation method.[14,58,59] Essentially, sets of pseudo-experimental data with a Gaussian standard error are randomly generated and then fitted to a model. By statistically treating a large number of values so obtained for the adjustable parameters, standard errors in these parameters are evaluated. Although Alper and Gelb[14] recommend obtaining confidence intervals from an ordered list of values for each of the fitting parameters, we simply assumed that these values are normally distributed. Hence, the reported standard errors should mean that there is a 68.3% probability that the 'true' value for a given parameter lies in the interval defined by adding and subtracting the standard error, respectively, to and from the best value for that parameter. A constant standard error of 0.25 was associated with each ΔpK_a value in Table 1. This choice was suggested by the standard deviation of the best fit in Table 2. In the preliminary experiments with the constrained tetralinear model, a few runs did not converge. This inconvenience was avoided by increasing the initial searching interval[11,22] for the adjustable parameters. At least 1000 Monte Carlo experiments were performed for a given fitting model in order to obtain the standard errors reported in Table 2. The best values and Monte Carlo average values were generally very close, the largest difference being less than 0.7%.

Revised parameters for the hyperbolic model

In our paper on the hyperbolic model[9] for the unified sigma-zero scale,[10] an annoying change of subscripts occurred in the expression for the standard errors in $\sigma_4^\circ / \sigma_3^\circ$. The expression given in footnote b to Table 1 in Ref. 99 should read

$$h_{4/3} = (h_3^2 \, \sigma_4^{\circ 2} + h_4^2 \, \sigma_3^{\circ 2})^{1/2} / \sigma_3^{\circ 2}$$

and the values in the last column of that table amended accordingly. New fits were performed and supplemented with Monte Carlo-calculated standard errors. The previously described[9] constrained non-linear least-rectangles weighted fitting procedure was used in these calculations. Monte Carlo error estimates[14] are based on 1000 simulations, of which only 15 did not converge on account of leading to a negative rectangle area. We observe further that an individual standard error[9,10] was assigned to each sigma-zero constant. Although this may introduce a double weighting in Monte Carlo experiments, it is an accepted procedure.[59] The following revised parameter values were obtained: $\lambda^\circ = 0.961 \pm 0.005$, $\gamma^\circ = -0.225 \pm 0.008$ and $\varepsilon_n^\circ = 0.343 \pm 0.001$. Since they are very close to the superseded values,[9] the consequences for the numerical results presented in Table A1 in Ref. 99 and Tables 3–9 in Ref.[11] are minimal. Finally, we highlight the very good precision associated with the parameters for our hyperbolic model.

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