New evidence for through-space transmission of substituent effects in benzene derivatives†

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Electrostatic interaction energies between dipolar substituents and dipolar or charged reaction sites are re-examined. At short interaction distances and given orientations, the point-dipole approximation is shown to introduce important errors. Exact expressions are derived for correcting current equations for both interaction types, including the Kirkwood–Westheimer equation. The parameter λ for describing *para–meta* ratios of substituent inductive or Electra effects in benzene derivatives is modelled in terms of electrostatic interaction energy. Using the new equations it is shown that parameter λ can take values smaller or greater than unity, approaching a value of 2 at very large distances. Experimental λ values are calculated using reliable literature data for the ionisation equilibria of substituted phenylethanoic and 3-phenylpropanoic acids in ethanol–water mixtures. Theoretical λ values for these reactions are obtained taking into account rotational and conformational changes in the corresponding carboxylate anions. From the good agreement between experimental and theoretical λ values, it is concluded that there is through-space transmission of substituent effects in benzene derivatives.

Introduction

Current analyses of substituent effects on organic reactivity are based, to a large extent, on experimental values for transmission coefficients associated with different scales of substituent constants.[1] For reactions of benzene derivatives, we have claimed that a further important parameter is the *para–meta* ratio of the substituent inductive or Electra effect.[2] Despite prolonged controversy,[3] our theoretical treatment is committed to identifying the mode of transmission of the inductive or Electra[2a] effect as a through-space transmission.

In this work we develop a theoretical analysis of parameter λ defined as the ratio of electric field effects from *para* and *meta* positions in benzene derivatives. The analysis is focused on interactions between dipolar substituents and either dipolar or charged reaction sites at varying distance from the benzene ring. We exemplify the shortcomings of using point-dipole approximations at short distances and derive exact correcting factors for the calculation of dipole–charge and coplanar dipole–dipole interaction energies. For both types of interaction we show that parameter λ can be smaller or greater than unity, depending on the distance. Using literature data,[4] we apply the tetralinear approach of substituent effects[2b,c] to the ionisation equilibria of mono-substituted phenylethanoic and 3-phenylpropanoic acids in ethanol–water mixtures. We report new evidence supporting an electric field nature of substituent Electra effects.

Electrostatic theory background

In a medium of electric permittivity ε, a fixed electric point-charge Q creates an electrostatic field, the potential V of which at a distance r is given by eqn. (1).

$$V = \frac{Q}{4\pi\varepsilon r} \qquad (1)$$

The electric energy E_e acquired by a point charge Q' placed in this field is $E_e = VQ'$. Hence, at distance r from Q, the energy acquired by Q' is characterised by eqn. (2).

$$E_e = \frac{QQ'}{4\pi\varepsilon r} \qquad (2)$$

According to the law of superposition of potentials, in a given point the potential is the sum of the potentials originated separately by different charges. A simple electric dipole is composed of two equal charges of opposite sign, Q and $-Q$, separated by a fixed distance $l = 2a$. Therefore the interaction energy between this dipole and charge Q' is described by eqn. (3).[5]

$$E_e\,(\text{dipole–charge}) = \frac{QQ'}{4\pi\varepsilon}\left(\frac{1}{r_+} - \frac{1}{r_-}\right) \qquad (3)$$

A common approximation uses the vector electric dipole moment $\boldsymbol{\mu}$ the scalar value of which is $\mu = Ql$. We start out by rewriting eqn. (3) in the form of eqn. (4) and (5).

$$E_e\,(\text{dipole–charge}) = \frac{\mu Q'}{4\pi\varepsilon l}\left(\frac{1}{r_+} - \frac{1}{r_-}\right) \qquad (4)$$

For a short dipole at long interaction distances, r_+ and r_- may be measured from the middle of dipole length (point-

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† Electronic supplementary information (ESI) available: Table S1 containing literature data for substituent constants and pK_a values used in this work. See http://www.rsc.org/suppdata/p2/b1/b106418e/

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$$E_e\,(\text{dipole–charge}) = \frac{\mu Q'}{4\pi\varepsilon l}\,\frac{r_- - r_+}{r_+ r_-} \qquad (5)$$

dipole approximation). In this approximation the product r_+r_- can be equated to r^2 and the difference $r_- - r_+$ be approximated by $l\cos\theta$. Here θ is the angle formed by vector $\boldsymbol{\mu}$, whose direction is taken to be from the negative to the positive charge, and the line joining this point-dipole to point-charge Q'. The resulting interaction energy is expressed by eqn. (6).

$$E_e\,(\boldsymbol{\mu}\text{–charge}) = \frac{Q'\mu\cos\theta}{4\pi\varepsilon r^2} \qquad (6)$$

The latter (approximate) equation forms the basis of the historically important Kirkwood–Westheimer model[6] for expressing the influence of a dipolar substituent on the dissociation constant of carboxylic acids.

Generally eqn. (6) under- or overestimates dipole–charge interaction energies. We point out the consequences of the approximations made in obtaining eqn. (6). Thus its validity decreases as (i) interaction distances decrease, for fixed dipole length and interaction angle; and (ii) dipole lengths increase, for fixed interaction distance and angle. However, in modelling electric field chemical effects in terms of eqn. (6), only rarely has the latter source of approximation been pointed out.[7] Furthermore, at fixed dipole length and interaction distance, the error introduced by eqn. (6) depends on the interaction angle θ. In this respect Exner and co-workers[3a,e,j] have commented that the influence of the angle θ is overestimated by eqn. (6). Here we note that for a dipole having $l = 0.2$ nm, at $r = 0.2$ nm from a point charge, eqn. (6) underestimates E_e by 25% at $\theta = 0°$, gives the same value as eqn. (3)–(5) at $\theta = 36°$ and overestimates E_e by 38% at $\theta = 80°$. This problem is further complicated by the fact that the angle at which eqn. (6) gives the correct answer is a function of both l and r.

We turn our attention to dipole–dipole interactions. These are constituted by the interactions between charges Q and $-Q$, on the one hand, and charges Q' and $-Q'$, on the other. Eqn. (7), which is readily obtained from eqn. (2), expresses the corresponding interaction energy.[3j]

$$E_e(\text{dipole–dipole}) = \frac{QQ'}{4\pi\varepsilon}\left(\frac{1}{r_{++}} - \frac{1}{r_{+-}} + \frac{1}{r_{--}} - \frac{1}{r_{-+}}\right) \qquad (7)$$

This interaction energy can equivalently be expressed in terms of dipole moments μ and μ' together with their lengths l and l' leading to eqn. (8).

$$E_e(\text{dipole–dipole}) = \frac{\mu\mu'}{4\pi\varepsilon ll'}\left(\frac{1}{r_{++}} - \frac{1}{r_{+-}} + \frac{1}{r_{--}} - \frac{1}{r_{-+}}\right) \qquad (8)$$

However, in the chemical literature preference is often given to the approximation using point-dipole–point-dipole interactions. Under this approximation, interaction energies are given by eqn. (9).[8]

$$E_e(\boldsymbol{\mu} - \boldsymbol{\mu}') = -\frac{\mu\mu'}{4\pi\varepsilon r^3}[2\cos\theta\cos\theta' - \sin\theta\sin\theta'\cos(\varphi - \varphi')] \qquad (9)$$

In the latter equation, θ is the angle defined by vectors $\boldsymbol{r}$ and $\boldsymbol{\mu}$, and similarly for θ'. The vector $\boldsymbol{r}$ is oriented from $\boldsymbol{\mu}$ to $\boldsymbol{\mu}'$, and ϕ and ϕ' are dihedral angles referred to a common reference plane. The case of coplanar dipoles is of special interest. For $\phi - \phi' = 0°$ eqn. (10) is obtained.[3j,l,9]

$$E_e(\boldsymbol{\mu} - \boldsymbol{\mu}'; \varphi - \varphi' = 0°) = -\frac{\mu\mu'}{4\pi\varepsilon r^3}(2\cos\theta\cos\theta' - \sin\theta\sin\theta') \qquad (10)$$

In this case the angle Θ formed by vectors $\boldsymbol{\mu}$ and $\boldsymbol{\mu}'$ is given by the difference $\theta - \theta'$ if $\theta > \theta'$, or by $\theta' - \theta$ if $\theta < \theta'$.

At a fixed distance maximum attractive energy between coplanar dipoles is attained for $\phi - \phi' = 180°$. At this dihedral angle eqn. (9) leads to eqn. (11), and $\Theta = \theta + \theta'$ if $\theta + \theta' > 180°$, or $\Theta = 360° - (\theta + \theta')$ if $\theta + \theta' < 180°$.

$$E_e(\boldsymbol{\mu} - \boldsymbol{\mu}'; \varphi - \varphi' = 180°) = -\frac{\mu\mu'}{4\pi\varepsilon r^3}(2\cos\theta\cos\theta' + \sin\theta\sin\theta') \qquad (11)$$

Alternatively, from the trigonometric relation $\cos(\theta \pm \theta') = \cos\theta\cos\theta' \mp \sin\theta\sin\theta'$, eqn. (10) and (11) can be condensed into eqn. (12).

$$E_e(\boldsymbol{\mu} - \boldsymbol{\mu}'; \text{coplanar}) = \frac{\mu\mu'}{4\pi\varepsilon r^3}(\cos\Theta - 3\cos\theta\cos\theta') \qquad (12)$$

The point-dipole approximation generally leads to under- or overestimates of interaction energies between dipoles, the pattern of deviations being similar to the aforementioned case of dipole–charge interactions. Thus, for two coplanar dipoles having equal length ($l = l' = 0.15$ nm) at a short distance ($r = 0.25$ nm), fixing $\theta = 0°$ eqn. (12) underestimates E_e by 36% at $\theta' = 0°$, giving the same value as eqn. (7) and (8) at $\theta' = 56.3°$ and overestimating E_e by 14% at $\theta' = 80°$. A more detailed comparison is made by Hirschfelder *et al.*,[8b] who conclude that the deviations of the real dipoles from the point-dipole approximation is appreciable when $r/l < 2$.

Results and discussion

New equations for interactions with dipoles

Estimation of electrostatic interactions from dipolar substituents has been considered to be more conveniently done using known dipole moments rather than unknown point charges. The equations developed below are free from the errors due to the point-dipole approximation while retaining the use of dipole moments.

For dipole–charge interactions, distances r_+ and r_- can be expressed in terms of r, a ($= l/2$) and θ using the cosine rule for triangles; eqn. (13) and (14).

$$r_+^2 = r^2 + a^2 - 2ar\cos\theta \qquad (13)$$

$$r_-^2 = r^2 + a^2 + 2ar\cos\theta \qquad (14)$$

Hence the difference $1/r_+ - 1/r_-$ is given by eqn. (15).

$$1/r_+ - 1/r_- = (1/r)\{[1 + (a/r)^2 - 2(a/r)\cos\theta]^{-1/2} - [1 + (a/r)^2 + 2(a/r)\cos\theta]^{-1/2}\} \qquad (15)$$

Next eqn. (15) is inserted into eqn. (4). Since $l = 2a$, we obtain eqn. (16).

$$E_e(\text{dipole–charge}) = (Q'\mu/8\pi\varepsilon ar)\{[1 + (a/r)^2 - 2(a/r)\cos\theta]^{-1/2} - [1 + (a/r)^2 + 2(a/r)\cos\theta]^{-1/2}\} \qquad (16)$$

In relation to approximate eqn. (6), the extra parameter in eqn. (16) is the dipole half-length a. The latter quantity can usually be accurately calculated from structural data. Values obtained using eqn. (6) will be correct following multiplication by the factor f given in eqn. (17), where $x = a/r$.

$$f(\text{dipole–charge}) = \frac{(1+x^2-2x\cos\theta)^{-1/2}-(1+x^2+2x\cos\theta)^{-1/2}}{2x\cos\theta} \quad (17)$$

This equation clearly shows that the ratio a/r and θ are the significant parameters determining the correcting factor f to approximate eqn. (6). Therefore, the corrected Kirkwood–Westheimer equation for describing the effect of dipolar substituents on dissociation constants of carboxilic acids is expressed by eqn. (18).

$$\log(K/K_0) = \frac{fe\mu\cos\theta}{2.303k4\pi\varepsilon r^2} \quad (18)$$

Here K/K_0 is the ratio between ionisation equilibrium constants for substituted and unsubstituted acids, f is the correcting factor given by eqn. (17), e is the elementary charge, k is the Boltzmann constant and T is the temperature.

The case of interacting electric dipoles is more involved. We begin with two coplanar dipoles for which $\phi - \phi' = 180°$. We designate by d_+ the line joining the positive pole in dipole $\boldsymbol{\mu}$ to the centre of dipole $\boldsymbol{\mu}'$, the angle α_+ being formed by lines d_+ and r. From the cosine rule in triangles eqn. (19)–(21) follow.

$$(r_{++})^2 = (a')^2 + (d_+)^2 + 2a'd_+\cos(\theta' - \alpha_+) \quad (19)$$

$$(r_{+-})^2 = (a')^2 + (d_+)^2 - 2a'd_+\cos(\theta' - \alpha_+) \quad (20)$$

$$(d_+)^2 = r^2 + a^2 - 2ar\cos\theta \quad (21)$$

Similar equations are obtained for geometric parameters relating the negative pole in $\boldsymbol{\mu}$ to both poles in $\boldsymbol{\mu}'$; eqn. (22)–(24).

$$(r_{--})^2 = (a')^2 + (d_-)^2 - 2a'd_-\cos(\theta' + \alpha_-) \quad (22)$$

$$(r_{-+})^2 = (a')^2 + (d_-)^2 + 2a'd_-\cos(\theta' + \alpha_-) \quad (23)$$

$$(d_-)^2 = r^2 + a^2 + 2ar\cos\theta \quad (24)$$

At this point we observe that only the angles α_+ and α_- remain to be determined. To this end we apply the sine rule to the triangles $[a, d_+, r]$ and $[a, d_-, r]$, which leads to eqn. (25) and (26).

$$\alpha_+ = \arcsin(a\sin\theta/d_+) \quad (25)$$

$$\alpha_- = \arcsin(a\sin\theta/d_-) \quad (26)$$

Noting that $l = 2a$ and $l' = 2a'$, in the case $\phi - \phi' = 180°$ we have now the means for recasting eqn. (8) in terms of μ, μ', r, a, a', θ and θ'. Although involved, the expression thus obtained is simple to implement on a desk computer. Similarly, for coplanar dipoles we find that the correcting factor f to the values for $E_e(\boldsymbol{\mu} - \boldsymbol{\mu}')$ calculated in terms of the approximate eqn. (10)–(12) is expressed by eqn. (27), in which upper signs apply to the case $\phi - \phi' = 0°$ and lower signs to the case $\phi - \phi' = 180°$.

$$\begin{aligned} f(\text{coplanar dipole–dipole}) = {} & [1/4xx'(\cos\Theta - 3\cos\theta\cos\theta')] \times \{[1 + x^2 + x'^2 - 2x\cos\theta + 2x'(1 + x^2 - 2x\cos\theta)^{1/2}\cos(\theta' \pm \alpha_+)]^{-1/2} - \\ & [1 + x^2 + x'^2 - 2x\cos\theta - 2x'(1 + x^2 - 2x\cos\theta)^{1/2}\cos(\theta' \pm \alpha_+)]^{-1/2} + [1 + x^2 + x'^2 + 2x\cos\theta - 2x'(1 + x^2 + 2x\cos\theta)^{1/2}\cos(\theta' \mp \alpha_-)]^{-1/2} - \\ & [1 + x^2 + x'^2 + 2x\cos\theta + 2x'(1 + x^2 + 2x\cos\theta)^{1/2}\cos(\theta' \mp \alpha_-)]^{-1/2}\} \quad (27) \end{aligned}$$

The shorthand $x = a/r$ and $x' = a'/r$ is used in the above equation, where angles α_+ and α_- are respectively given by eqn. (28) and (29), which follow from eqn. (21) and (24)–(26).

$$\alpha_+ = \arcsin[x(1 + x^2 - 2x\cos\theta)^{-1/2}\sin\theta] \quad (28)$$

$$\alpha_- = \arcsin[x(1 + x^2 + 2x\cos\theta)^{-1/2}\sin\theta] \quad (29)$$

In the context of coplanar dipole–dipole interactions we find that x, x', θ and θ' are the only parameters required for correcting electrostatic energies estimated at short distances in terms of eqn. (10)–(12). Accurate values can thus be calculated using eqn. (30), in which f is given by eqn. (27).

$$E_e(\text{coplanar dipole–dipole}) = \frac{f\mu\mu'}{4\pi\varepsilon r^3}(\cos\Theta - 3\cos\theta\cos\theta') \quad (30)$$

Theoretical parameter λ for coplanar dipole–dipole interactions

Theoretical calculations of parameter λ are based on the electrostatic theory. A model for neutral activated complexes in reactions of benzene derivatives consists of a reaction centre R bearing electric dipole moment μ_R at distance d from the benzene ring along its 1,4 axis, and of a given substituent X (dipole moment, μ_X) in either *para* or *meta* position. Electrostatic interaction energies between coplanar dipoles are accurately described by either eqn. (8) or (30), where ε is now to be regarded as the effective permittivity across distance r joining the centres of dipoles X and R.

For the purpose of theoretical calculations, we identify parameter λ with the *para*/*meta* ratio of electrostatic interaction energies between substituents and reaction site. Assuming identical effective permittivities for field effects from *para* and *meta* positions, then parameter $\lambda(\mu_X, \mu_R$; coplanar) for dipole–dipole interactions is given by the algebraically equivalent eqn. (31) and (32).

$$\lambda(\mu_X, \mu_R) = \left(\frac{1}{r_{++}} - \frac{1}{r_{+-}} + \frac{1}{r_{--}} - \frac{1}{r_{-+}}\right)_{para} \Bigg/ \left(\frac{1}{r_{++}} - \frac{1}{r_{+-}} + \frac{1}{r_{--}} - \frac{1}{r_{-+}}\right)_{meta} \quad (31)$$

$$\lambda(\mu_X, \mu_R;\ \text{coplanar}) = \frac{f_p(\cos\Theta_p - 3\cos\theta_{p\text{-X}}\cos\theta_{p\text{-R}})}{f_m(\cos\Theta_m - 3\cos\theta_{m\text{-X}}\cos\theta_{m\text{-R}})}(r_m/r_p)^3 \quad (32)$$

In the present context it is important to note that we have arrived at two equivalent expressions for parameter λ that are free from the usual difficulties associated with the electrostatic field treatment.[3h,10] Indeed, only geometric quantities are required to calculate λ using eqn. (31) or (32). In our model we fix $\theta_{p\text{-R}} = 0°$, *i.e.* both poles of reaction centre R are situated on line d. Hence $\Theta_p = \theta_{p\text{-X}} = 0°$, $\Theta_m = 60°$ and $\theta_{m\text{-R}} = 60° - \theta_{m\text{-X}}$, and eqn. (33) is obtained from eqn. (32).

$$\lambda(\mu_X, \mu_R;\ \text{coplanar}) = \frac{2f_p}{f_m[3\cos\theta_{m\text{-X}}\cos(60° - \theta_{m\text{-X}}) - 0.5]}(r_m/r_p)^3 \quad (33)$$

As the interaction distance increases, both correcting factors f_p and f_m and distances r_m and r_p become very close to each other and $\theta_{m\text{-X}}$ tends to 60°. In this way we find from eqn. (33) that the *para*/*meta* ratio of field effects will approach a higher bounding value of two as the reaction site becomes increasingly far away from the benzene ring. It is therefore remarkable that parameter λ can take values considerably in excess of unity.

Following Dewar *et al.*,[11] the poles of a dipolar substituent are localised in its α-atom and nearest carbon atom belonging to the benzene ring. This convention implicitly accounts in part for polarisation effects across sigma bonds. From an average over 26 substituents,[2c] this dipole length is estimated to be $l_X = 0.153$ nm. This value, together with tabulated molecular parameters,[12] is then used in the geometric calculation of the variables f_p, f_m, $\theta_{m\text{-}X}$, r_m and r_p in eqn. (33), in the case of dipole length $l_R = 0.1$ nm. We chose the benzene 1,4 axis for measuring distances *d*. Curve *A* in Fig. 1 shows the variation of $\lambda(\mu_X, \mu_R)$ against *d*. However, an angular dependence of parameter λ should be observed for other geometries. Thus an interesting new tool has been designed for elucidating reaction mechanisms, provided that accurate values for parameter λ can be experimentally determined. That this is a promising tool will be shown in a subsequent paper,[13] where the oxidation reaction of benzyl alcohols in anhydrous media is discussed.

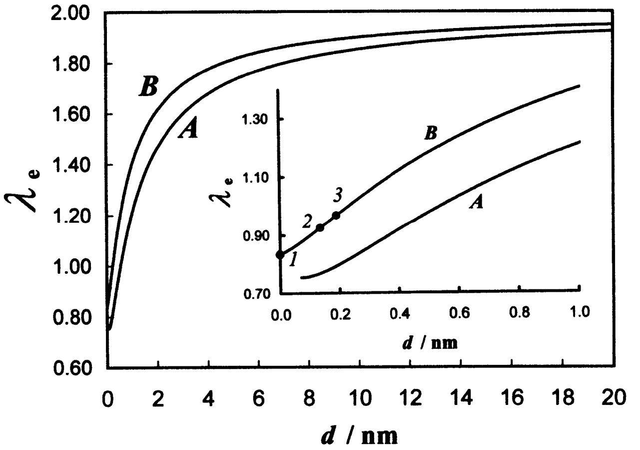


Fig. 1 The *para*/*meta* ratio of electrostatic field effects, λ_e, for a dipolar substituent as a function of distance *d* from the benzene ring for (*A*) a dipole having length $l = 0.1$ nm situated on the 1,4 axis, and (*B*) a charged reaction site on the 1,4 axis. In the inset the variation is magnified for short distances corresponding to the following molecular frameworks: (*1*), pyridinium cation; (*2*), anilinium cation and phenolate anion; (*3*), benzoate anion.

Theoretical parameter λ for dipole–charge interactions

We turn attention to the field effect of a polar substituent on a charged reaction site. In this case substituent electrostatic effects have been regarded as resulting from either electric dipole moments[14] or, more accurately, from two equal partial electric charges of opposite sign.[11] Both treatments take into account substituent dipole orientation. We have successfully used Dewar *et al.*'s approach[11] to model parameter λ for the dissociation equilibria of substituted pyridinium ions, phenols, anilinium ions and benzoic acids, obtaining values in the range 0.84–0.98.[2b,c] It is therefore of interest to extend these calculations to molecular frameworks in which there is a charged site farther from the benzene nucleus than in the above examples.

From eqn. (4) we find that parameter λ for dipole–charge interactions is given by eqn. (34),[2c] the alternative eqn. (35) following from eqn. (16) and (17).

$$\lambda(\mu_X, \text{charge}) = \left(\frac{1}{r_+} - \frac{1}{r_-}\right)_{para} \Bigg/ \left(\frac{1}{r_+} - \frac{1}{r_-}\right)_{meta} \qquad (34)$$

$$\lambda(\mu_X, \text{charge}) = \frac{f_p \cos\theta_p}{f_m \cos\theta_m}(r_m/r_p)^2 \qquad (35)$$

Similarly to dipole–dipole interactions, only geometric parameters are required for theoretical calculations of *para*/*meta* ratios of dipole–charge interactions.

Next we study the effect of charge distance on parameter λ. At very long distances *d* along the benzene 1,4 axis, in eqn. (35) both ratios f_p/f_m and r_m/r_p are approximately unity whereas cos θ_p/cos θ_m approaches 1/cos 60° = 2. Therefore parameter λ for dipole–charge interactions has a higher limiting value equal to two, which turns out to be the same as in the case of dipole–dipole interactions. The monotonic variation of λ with the position of a charged centre on the benzene 1,4 axis is given by curve *B* in Fig. 1.

For both types of interaction, our experience has shown that calculation procedures directly based on eqn. (31) and (34) are easier to implement on a spreadsheet than eqn. (32) and (35). Results of these calculations demonstrate that the *para*/*meta* ratio of substituent electric field effects depends noticeably on molecular frameworks. Thus from eqn. (34) we obtain values of about 0.84 at close distances, increasing to 1.12 at 0.4 nm, and a limiting upper value equal to 2 at an infinite distance. This finding contrasts with the early assumption[15] of an invariant λ = 1, as well as with Exner's empirically determined[1a,i,16] λ = 1.14.

Experimental and theoretical parameter λ for phenylethanoate and 3-phenylpropanoate anions

Phenylethanoic and 3-phenylpropranoic acids have interesting molecular frameworks for studying substituent effects. Since methylene groups efficiently block the transmission of direct resonance effects to the reaction site, sigma-zero constants are appropriate for describing substituent effects on the ionisation equilibria of these organic acids.

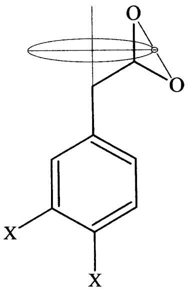
In the analysis developed below we use the unified σ^0 scale[1j] and reliable ΔpK_a data at 298 K from Wepster's laboratory[4] for mono-substituted phenylethanoic acids (comprising 12 *meta* and 15 *para* derivatives in 75% ethanol–water solvent, and 11 *meta* and 15 *para* derivatives in 50% ethanol–water solvent) and for mono-substituted 3-phenylpropranoic acids (comprising 6 *meta* and 3 *para* derivatives in 75% ethanol–water solvent, and 5 *meta* and 3 *para* derivatives in 50% ethanol–water solvent). These data (recorded in Table S1 †) are treated with our tetralinear method,[2c] which is designed to yield experimental values for parameter λ. Monte Carlo estimates of standard errors are calculated using a procedure previously described.[2b] The results thus obtained are summarised in Table 1. The four reaction series are correlated by the constrained tetralinear equation with small standard deviations. Derived λ values have accuracy of about 5% in 75% aqueous ethanol and 8% in 50% aqueous ethanol. No solvent dependence of parameter λ can be firmly inferred from values in Table 1. In fact, for both acids differences between λ values are well within their combined errors.

Numerical values in Table 1 for parameter λ deserve further discussion. At first sight it seems strange that almost identical experimental values are obtained for the molecular frameworks of phenylethanoate and 3-phenylpropranoate ions. This is because in the former there is a methylene group insulating benzene ring from the carboxylate anion, whereas in the latter there are two methylene groups. Interestingly this finding can be explained in terms of the electrostatic interpretation of parameter λ. Assuming free rotation about carbon–carbon single bonds, the centre of negative charges in phenylethanoate ions describes a circle with radius equal to 0.188 nm on a plane normal to the phenyl 1,4 axis, and 0.229 nm distant from the benzene nucleus (Scheme 1). In this case distances in eqn. (34) and (35) are not uniquely defined, parameter λ being a function of rotation ϕ about the phenyl 1,4 axis. We define an average $\bar{\lambda}_e(\phi)$ value using eqn. (36).

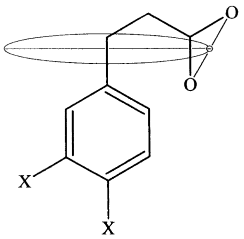
Table 1 Experimental and theoretical parameter λ for the ionisation of benzenoid acids in aqueous ethanol at 298 K

Acid	Solvent	SD[a]	λ[b]	λ_e[c]
Phenylethanoic	75% EtOH–H_2O	0.034	1.03 ± 0.05	1.067
	50% EtOH–H_2O	0.043	1.13 ± 0.09	
3-Phenylpropanoic	75% EtOH–H_2O	0.019	1.02 ± 0.06	1.019 (*syn*)
	50% EtOH–H_2O	0.023	1.08 ± 0.09	1.123 (*anti*)

[a] Standard deviation in units of ΔpK_a for the best fit of data in Table S1 to the constrained tetralinear equation. [b] Monte Carlo errors are averages over 1000 simulations. [c] Theoretically calculated values using electrostatic theory (see text).



Scheme 1



Scheme 2

$$\overline{\lambda_e}(\phi) = \int_0^{2\pi} \lambda_e(\phi)\mathrm{d}\phi/2\pi \qquad (36)$$

For conformations corresponding to one-degree intervals in rotation ϕ, distances in eqn. (34) were analytically calculated and the resulting individual λ_e values numerically integrated. Fixing $\phi = 0°$ for the conformation in which the *meta* substituent and carboxylate group are at their farthest, we calculated $\lambda_e(0°) = 1.002$, $\lambda_e(90°) = 1.039$ and $\lambda_e(180°) = 1.193$. From eqn. (36) we obtained $\overline{\lambda_e}(\phi) = 1.067$, which is in very good agreement with experimental values in the confidence intervals 0.98–1.08 and 1.04–1.22 (Table 1).

The case of 3-phenylpropanoate ion is not so straightforward. Inspection of its molecular framework indicates that important consequences for charge location arise from conformational changes due to rotation about the single bond linking their methylene groups. In the eclipsed at 0° (*syn*) conformation, the centre of negative charges describes a large circle around the phenyl 1,4 axis, being centred at $d = 0.047$ nm and having a radius equal to 0.239 nm (Scheme 2). The complex variation of $\lambda_e(syn)$ as a function of rotation ϕ is shown in Fig. 2. Following a 180° rotation about the C_2–C_3 bond, the centre of negative charges in the staggered (*anti*) conformation describes a small circle (radius, 0.112 nm) around the same axis as above, being centred at $d = 0.378$ nm. On the basis of eqn. (36), average $\overline{\lambda_e}(\phi)$ values were calculated for both extreme conformers. In this way we obtained $\overline{\lambda_e}(syn) = 1.019\lambda_e$ and $\overline{\lambda_e}(anti) = 1.123$. Predicting the actual theoretical parameter λ_e requires calculation of relative conformer populations. Although this has been done for related problems,[17] we simply observe that best experimental λ values of 1.02 and 1.08 reported in Table 1 for 3-phenylpropanoate ions are between calculated values for *syn* and *anti* conformers.

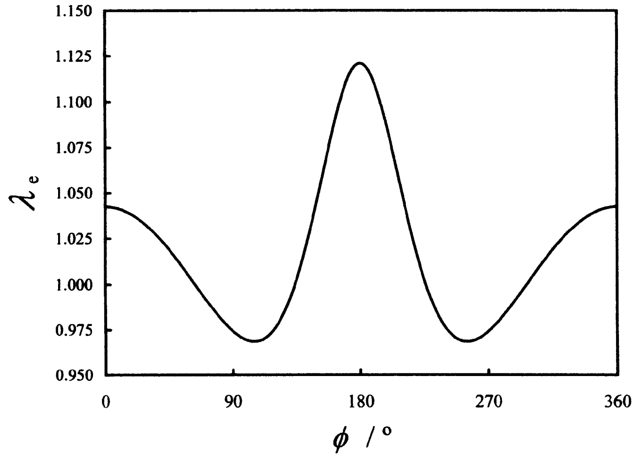


Fig. 2 The *para*/*meta* ratio of electrostatic field effects, $\lambda_e(syn)$, for a dipolar substituent in 3-phenylpropanoate ions (see Scheme 2) as a function of the rotation ϕ about the phenyl 1,4 axis.

Best experimental values for the *para*/*meta* ratio of the substituent Electra effect near to or greater than unity are also remarkable in that they cannot be explained using models for transmitting the Electra effect through sigma bonds.[18] Indeed, the latter models invariably predict λ values smaller than unity.[2c]

In summary, at short interaction distances we have refined the Kirkwood–Westheimer approach to substituent effects and calculated accurate values for the ratio of electrostatic field effects from *para* and *meta* positions in derivatives of phenylethanoic and 3-phenylpropanoic acids. These ratios, which are found to lie in the range 1.02–1.12, are taken as theoretical values for the parameter λ. Previous calculations[2b,c] for different molecular frameworks yielded ratios between 0.84 and 0.98. Therefore, from the good agreement between theory and experiment over an extended range of λ values we conclude that the Electra or inductive effect in benzene derivatives is of electrostatic origin and is transmitted through space from polar substituents to reaction sites in the *meta* or *para* positions.

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