The Analyst

# Prediction of electrophoretic mobilities.

## Part 2.† Effect of acid dissociation constant on the intrinsic mobilities of aliphatic carboxylates and amines

**Shilin Fu, Dongmei Li and Charles A. Lucy***

*Department of Chemistry, The University of Calgary, 2500 University Drive NW, Calgary, Alberta, Canada T2N 1N4. E-mail: Lucy@chem.ucalgary.ca*

**Electrophoretic mobility is the most important parameter governing the separation of solutes in capillary zone electrophoresis (CZE). Classical theoretical models for the prediction of absolute mobilities consider only the effect of hydrodynamic friction. Application of these models to literature mobility data demonstrates that they are not appropriate for small organic solutes. Accurate prediction of absolute mobilities of small ions requires an additional frictional term, the dielectric friction. Dielectric friction results from the work necessary to orientate the solvent dipoles in response to the solute charge. This study investigates whether the p*K* value of a charged functional group can be used as a relative measure for the dielectric friction. Using the p$K_a$ as a measure of dielectric friction of weak acids, the absolute mobility of aliphatic carboxylates is given by:**

$$\mu_0 = \frac{10^{-3}(6.8 \pm 1.2)}{V^{(0.620 \pm 0.036)} + (0.6 \pm 0.24)\mathrm{p}K_a}$$

**where *V* is the van der Waals molecular volume (Å$^3$) determined by molecular modeling. The uncertainties are the standard deviations of the parameters. The average error between the predicted absolute mobility and literature values for 15 aliphatic carboxylates was 3.7%. Similarly, use of the p$K_b$ as a proxy for the dielectric friction for weak bases yields the following expression for the absolute mobilities of aliphatic monoamines:**

$$\mu_0 = \frac{10^{-3}(7.8 \pm 1.3)}{V^{(0.62 \pm 0.03)} + (0.66 \pm 0.23)\mathrm{p}K_b}$$

**The average prediction error for 34 aliphatic monoamines was 4.5%.**

***Keywords:*** *Absolute mobility; aliphatic carboxylates; dielectric friction; electrophoretic mobilities; hydrodynamic friction; molecular modeling*

Inarguably, the most important parameter governing electrophoretic separations is mobility. Excellent discussions have been made as to the effect of numerous experimental variables such as pH[1] and complexant concentration[2] on the apparent mobility of an ion. These models discuss how these parameters modify the intrinsic mobility of the fully charged ion ($\mu_{A-}$ or $\mu_{B+}$). Yet, discussion of actual intrinsic mobility of an ion is generally limited to the simplistic statement that mobility is related to the charge-to-size ratio of the solute. However, the intrinsic mobility behaviour of ions is much more complex. For instance, $CCl_3COO^-$ and n-$C_4H_9COO^-$ have about the same molecular volume (104.3 Å$^3$ and 105.3 Å$^3$ respectively). However the absolute mobility of $CCl_3COO^-$ ($3.62 \times 10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$) is much higher than that of n-$C_4H_9COO^-$ ($2.98 \times 10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$). If the alternative statement that mobility is related to the charge-to-mass ratio is used, the relative mobilities of $CCl_3COO^-$ and n-$C_4H_9COO^-$ are even more perplexing. $CCl_3COO^-$ possesses a much greater mass (162.4 g mol$^{-1}$), and yet has a much greater mobility than the lighter n-$C_4H_9COO^{-1}$ (101.1 g mol$^{-1}$)!

This paper investigates the factors that govern the intrinsic mobility of aliphatic carboxylates and amines. Two fundamental frictional factors are found to be important: the hydrodynamic friction which is related to the molecular volume or mass of the solute, and the dielectric friction which is related to the charge distribution within the solute. The dissociation constant of the ionized functionality is used as a convenient measure of the charge distribution.

### Background

This work deals with modeling of the intrinsic mobility of the aliphatic carboxylates and monoamines. The intrinsic mobility of an ion refers to the mobility of the fully ionized form of a molecule ($\mu_{A-}$ and $\mu_{B+}$). In this paper, discussion is restricted to the prediction of intrinsic mobilities at infinite dilution (absolute mobilities). This eliminates complications arising from solution conditions such as ionic strength and ion association which would convolute the present discussion. The effect of ionic strength is addressed elsewhere.[3]

#### *Hydrodynamic models*

Numerous models have been proposed for predicting electrophoretic mobility.[4] By and large, these possess the general form:

$$\mu_0 = \frac{q}{f_h} \quad (1)$$

where $\mu_0$ is the mobility at infinite dilution, $q$ is the charge of the solute and $f_h$ is the hydrodynamic friction factor associated with moving the solute through a continuum solvent of finite viscosity. There are many commonalities between models for electrophoretic mobility and diffusion coefficients as the frictional term appears in the denominator of each.[5,6]

The most common hydrodynamic model for mobility is related to the Stokes–Einstein diffusion model, and is known as the Hückel equation.[7,8] In this model, the solute of charge $q$ is assumed to be a sphere of radius $r$ moving through a continuum medium of viscosity $\eta$:

$$\mu_0 = \frac{q}{6\pi\eta r} \quad (2)$$

The Hückel equation was originally derived for large spherical analytes only. Not surprisingly, this model fails to accurately predict mobilities when the solute approaches the size of the

† For Part 1, see *Anal Chem.*, 1998, 70, 173.

solvent molecules,[4,9–13] as is commonly the case in CZE. Other theoretical models have been derived to account for additional factors such as the shape of the molecule.[14,15] However these are equally unsuccessful at modeling absolute mobilities of small solutes.[4,16,17]

Numerous empirical models have been developed for prediction of electrophoretic mobilities[4,8,18,19] and diffusion coefficients[20,21] of small solutes. These models have consistently found that the power dependence on solute radius is much greater than that predicted by eqn. (2). Typically the observed dependence on radius was in the order of $r^{-2}$. This dependence is more commonly expressed in terms of molecular volume ($V^{-0.6}$) or molecular weight ($W^{-0.6}$). To date no fundamental explanation has been given for this surprising power dependence, although it has been suggested that it may be related to the radius of gyration of the solutes.[22]

### *Dielectric friction*

However while hydrodynamic models have been reasonably successful for large neutral molecules and ions, they break down when the size of the ion approaches that of the solvent. This breakdown is apparent in the relative mobilities of the alkali metal ions ($Li^+ < Na^+ < K^+$). The classical explanation for this has been termed the solvent-berg model.[23] In this model the solvent molecules adjacent to the ion are considered to be rigidly bound to the ion. These solvent molecules add to the effective diameter of the ion, resulting in the inverse relationship between crystallographic radii and hydrated radii for the alkali metals. However, such a model is difficult to quantify as evidenced by the wide discrepancies in reported hydration numbers for simple ions.[24] Further, the model is unrealistic as solvation is truly a dynamic process.

In 1920 Max Born proposed an alternative model to explain the mobilities of the alkali metal ions. He postulated that an additional dielectric friction is caused by the orientation of the solvent dipoles in response to the ionic charge. After the ion passes, energy is dissipated during the relaxation of the solvent to its equilibrium polarization. This additional energy dissipation enhances the overall friction experienced by the ion. That is, the mobility of an ion is governed by both the hydrodynamic friction ($f_h$) and a dielectric friction ($f_{dl}$):

$$\mu_0 = \frac{q}{f_h + f_{dl}} \tag{3}$$

Born's idea has been further developed by numerous workers using the assumption of point charges within a continuum medium.[25] One of the most advanced formulations of this approach is the Hubbard–Onsager expression which describes the dielectric friction coefficient:[26,27]

$$f_{dl} = \left(\frac{17}{280}\right)\frac{\tau_D e^2}{r^3}\left(\frac{\varepsilon_0 - \varepsilon_\infty}{{\varepsilon_0}^2}\right) \tag{4}$$

where $\tau_D$ is the Debye dielectric relaxation time of the pure solvent, $e$ is the ion charge, $r$ is the ionic radius, and $\varepsilon_0$ and $\varepsilon_\infty$ are the low and high frequency dielectric constants of the solvent. The most striking feature of eqn. (4) is the strong inverse dependence of dielectric friction upon the radius of the ion. As the ionic radius increases, the dielectric friction decreases dramatically.

However, molecular dynamic simulations of ion mobility[23] and experimental measurements of rotational diffusion[28] demonstrate that it is the extended charge distribution for the solute that governs the dielectric friction.

### *Charge distribution*

The goal of this work is to develop expressions for prediction of intrinsic mobility of small organic solutes that incorporate the effect of dielectric friction. It is thus desirable to have a convenient measure of the charge distribution for a solute. However, how does one define the charge distribution of an organic molecule such as $CCl_3COO^-$ or n-$C_4H_9COO^-$?

Fortunately, for aliphatic and substituted aliphatic acids, the charge distribution of a carboxylate anion significantly influences the acid dissociation constant (p$K_a$) of the corresponding carboxylic acid.[29] The primary factor that influences the dissociation constants of aliphatic carboxylates is electron-delocalization. Electrical work must be done to move a proton from the neutral acid to the solvent molecules (water).[29] The amount of work depends on the location and distribution of the dipoles and electrical charges within the acid. For aliphatic carboxylates, electron-delocalization results mainly from inductive and/or electrostatic effects. The inductive effect changes the distribution of the charge directly through the bonds in the acid molecules. The electrostatic effect, on the other hand, modifies the charge distribution indirectly, *e.g.*, through the solvent molecules. The inductive and electrostatic effects usually occur simultaneously and in the same direction. It is therefore difficult to separate them. Therefore, in the discussion below the term 'inductive effect' is used to describe both the inductive and electrostatic effects.

A substituent has an acid-strengthening effect if its insertion decreases the electron density on the carboxyl group.[29] For example, in monochloroacetic acid, the electronegative substituent (-Cl) withdraws charge from the -$COO^-$ group, thereby increasing the charge distribution within the molecule. As a result of the electron withdrawing character of chlorine, the p$K_a$ of monochloroacetic acid (p$K_a$ = 2.87) is much lower than that of acetic acid (p$K_a$ = 4.76).

Inductive effects are approximately additive. As a result, the p$K_a$ decreases from mono- to di- to tri-chloro acetic acid (Table 1). The magnitude of the inductive effect increases significantly as the distance separating the substituent from the charge center decreases. This is reflected in the increasing acidity (decreasing p$K_a$) from $ClCH_2CH_2CH_2COOH$ to $ClCH_2CH_2COOH$ to $ClCH_2COOH$.

Steric effects also influence acid dissociation constants. Bulky aliphatic chains around the carboxyl group make solvation of the carboxylate ion more difficult, resulting in an

**Table 1** Literature absolute mobilities and physicochemical parameters for carboxylates

| Molecule | Absolute mobility/ $10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$ | p$K_a$ (25 °C;[a] $I$ = 0) | Molecular weight ($W$)/ g mol$^{-1}$ | Molecular volume ($V$)/ Å$^3$ |
|---|---|---|---|---|
| $HCOO^-$ | 5.71[b] | 3.75 | 45.02 | 39.75 |
| $CH_3COO^-$ | 4.24[c] | 4.76 | 59.04 | 55.95 |
| $CH_2ClCOO^-$ | 4.19[b], 4.37[c] | 2.87 | 93.49 | 70.12 |
| $CH_3CH_2COO^-$ | 3.69[b], 3.71[d] | 4.87 | 73.07 | 72.73 |
| $CH_2ClCH_2COO^-$ | 3.68[b] | 4.11 | 107.5 | 86.75 |
| $CHCl_2COO^-$ | 3.94[b] | 1.30 | 127.9 | 88.27 |
| $CH_3CH_2CH_2COO^-$ | 3.37[b] | 4.82 | 87.10 | 89.07 |
| $CCl_3COO^-$ | 3.62[b] | 0.90[f] | 162.4 | 104.3 |
| n-$C_4H_9COO^-$ | 2.98[e] | 4.84 | 101.1 | 105.3 |
| $(CH_3)_3CCOO^-$ | 3.16[b] | 5.03 | 101.1 | 110.1 |
| n-$C_5H_{11}COO^-$ | 3.05[b] | 4.86 | 115.2 | 122.0 |
| n-$C_6H_{13}COO^-$ | 2.87[b] | 4.86 | 129.2 | 138.4 |
| n-$C_7H_{15}COO^-$ | 2.74[b] | 4.89 | 143.2 | 154.6 |
| n-$C_8H_{17}COO^-$ | 2.67[b] | 4.96[f] | 157.2 | 171.1 |
| n-$C_9H_{19}COO^-$ | 2.21[b] | 4.96[g] | 171.3 | 187.6 |

[a] Data from ref. 37. [b] Data from ref. 33. [c] Data from ref. 34. [d] Data from ref. 10. [e] Data from ref. 35. [f] p$K_a$ values were calculated using eqn. 1.16 in ref. 29. For $CCl_3COOH$, its p$K_a'$ is 0.77 at ionic strength 0.1 M; the p$K_a'$ of n-$C_8H_{17}COOH$ is equal to 4.95 at ionic strength 0.0004 M. [g] p$K_a$ value is estimated from the p$K_a$ values of n-$C_5$ to n-$C_{10}$ carboxylates.

increase in the p$K_a$. However, even for extreme differences in stereochemistry [pivalic acid, $(CH_3)_3CCOOH$ and pentanoic acid, n-$C_4H_9COOH$], the acid dissociation constants do not differ significantly (p$K_a$ = 5.03 and 4.84, respectively).

Thus the p$K_a$ is an effective measure of the charge distribution within a fully deprotonated carboxylate ion. Acid dissociation constants (p$K_a$) at infinite dilution for the carboxylic acids studied are given in Table 1.

## Experimental

### *Determination of molecular volume*

Molecular volumes of 15 aliphatic carboxylates were calculated using Molecular Modeling Pro (Window Chem Software, Version 1.44), as described previously.[4] Molecular Modeling Pro calculates molecular volume by summing the van der Waals increments of Bondi,[30] which allow for atomic volume variation due to the functionality of the atom. The van der Waals increments of some common atoms and groups are given in refs. 30 and 31. Volumes calculated using Molecular Modeling Pro and manually using Bondi's increments[30,31] yielded comparable results for nine neutral molecules (mean difference = −0.6%, standard deviation = 4%).

It should be noted that molecular volumes calculated using other molecular modeling programs such as Insight II (Version 95.0.2, Biosym Technologies, San Diego, CA, USA) yielded significantly different molecular volumes. Use of volumes generated with Insight II yield comparable equations to those reported herein.[32]

### *Numerical fitting of data*

The optimum constants used in the expressions were obtained using both the Solver function of Microsoft Excel (version 5.0) and the Curve Fitter function of SlideWrite *Plus* (Version 2.0 for Windows, Advanced Graphics Software, Inc., Carlsbad, CA, USA). Solver iteratively alters the parameters to minimize the sum of the squares of the residuals. Curve Fitter uses the iterative Levenberg–Marquardt algorithm which yields parameters based on the minimization of the sum of the squared deviations. Both methods yielded the same fit constants. The uncertainties quoted in the equations below are the standard deviations of the fit constants determined using Curve Fitter.

## Results and discussion

Literature absolute mobilities were used to investigate whether the acid dissociation constants of carboxylates influence the intrinsic mobility of the solute. These literature values were compiled from a number of sources[10,33–35] and are tabulated in Table 1. Some solutes are reported in more than one source. Based on the discrepancy between the duplicate values it is estimated that there is a 3.8% error associated with the literature values. A literature absolute mobility for iodoacetate ($1.21 \times 10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$) was also found.[10] However, it was not included in this study as the molecular modeling programs were not parameterized for iodine. For monochloroacetate, its absolute mobilities from different sources were significantly different ($4.19 \times 10^{-4}$ and $4.37 \times 10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$). In this case, they were treated as independent data to generate the best fit equations. The molecular weight, volume and acid dissociation constants for the carboxylates are also given in Table 1.

The agreement between the literature absolute mobilities and those predicted using the Hückel model [eqn. (2)] were poor. The average relative error is 7.5%. The failure of the Hückel equation for predicting the mobility of the carboxylates is consistent with its lack of success with other small solutes.[4,9–11]

As discussed above, mobility seems to correlate with volume to a power greater than that predicted by the Hückel equation. A nonlinear regression of the absolute mobilities of the carboxylates in Table 1 was performed in which the power on the volume term was an adjustable parameter. The resultant best fit expression was:

$$\mu_0 = \frac{10^{-3}(4.05 \pm 0.69)}{V^{(0.539 \pm 0.039)}} \quad (5)$$

where $\mu_0$ is the absolute mobility in cm$^2$ V$^{-1}$ s$^{-1}$ and $V$ is the molecular volume in Å$^3$ as determined using Molecular Modeling Pro. The uncertainties in eqn. (5) are the standard deviations of the parameters determined by nonlinear regression using SlideWrite's Curve Fitter function. The correlation between the predicted absolute mobilities using eqn. (5) and the literature mobilities is shown in Fig. 1. It can be seen from Fig. 1 that the correlation between the predicted and literature absolute mobilities is fair (correlation coefficient $r$ = 0.9641). The slope and intercept of the linear regression line in Fig. 1 are 0.9309 and 0.2437, respectively. (Ideally the slope of this correlation plot should be 1.00 and the intercept should be 0.00). Using only this one physicochemical parameter (molecular volume), the average relative error between the predicted absolute mobilities and the literature mobilities is 5.2%. The chlorinated solutes are given different symbols in Fig. 1 for reasons discussed in the next section.

### *Carboxylates by weight based model*

In our previous study of mobilities of monoamines it was found that the absolute mobility could be related to the molecular weight of the solute.[4] The data in Table 1 was fit to an expression comparable to eqn. (5) except that molecular weight replaced molecular volume. However the resultant equation did not accurately predict the absolute mobility of carboxylates. An average error of 12.7% was observed between the predicted and literature mobilities. Particularly noteworthy was the 15.9% error observed for the chlorinated carboxylates. If the halogenated aliphatic carboxylates are not included in the data set used to generate the expression, the resultant expression is:

$$\mu_0 = \frac{10^{-3}(6.1 \pm 1.2)}{W^{(0.639 \pm 0.046)}} \quad (6)$$

The correlation between the absolute mobilities predicted using this equation and the literature mobilities is shown in Fig. 2. Excluding the chlorinated carboxylates, the average relative error between the predicted and literature mobilities is 5.4%.

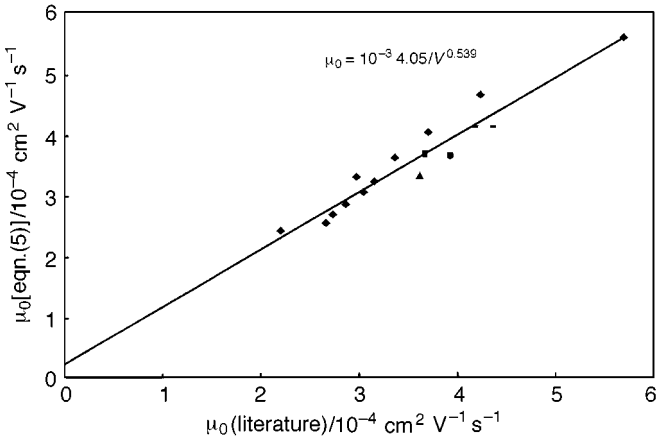


**Fig. 1** Correlation between absolute mobilities ($\mu_0$) estimated using molecular volume to a power [eqn. (5)] with the literature absolute mobilities for the 15 aliphatic carboxylates in Table 1. The symbol ◆ indicates an aliphatic carboxylate while ▲ = $CCl_3COO^-$, ■ = $CH_2ClCH_2COO^-$, ● = $CHCl_2COO^-$ and ■ = $CH_2ClCOO^-$. The line is the linear regression between the predicted and literature mobilities.

The correlation coefficient ($r$), slope and intercept of the linear regression line in Fig. 2 (excluding halogenated carboxylates) are 0.9752, 0.9691, and 0.0986, respectively. As can be seen in Fig. 2, the chlorinated carboxylates deviate significantly from the absolute mobilities predicted by eqn. (6). Thus, while weight based models of mobility are extremely convenient, they must be used with caution.

### *Effect of p$K_a$ on intrinsic mobility of carboxylates*

As discussed above, both hydrodynamic and dielectric frictions should to be considered in modeling electrophoretic mobilities. Above, we proposed to use the p$K_a$ as a convenient measure of the charge distribution within a carboxylate. Nonlinear curve fitting of the absolute mobilities in Table 1 to the molecular volume and p$K_a$ yielded:

$$\mu_0 = \frac{10^{-3}(6.8 \pm 1.2)}{V^{(0.620 \pm 0.036)} + (0.66 \pm 0.24)\mathrm{p}K_a} \qquad (7)$$

Fig. 3 shows that there is excellent agreement between the mobilities predicted using eqn. (7) and the literature absolute mobilities. The average relative error between the predicted and literature absolute mobilities is only 3.7%. This is approximately the error associated with the literature absolute mobilities. The correlation coefficient ($r$) of the linear regression line of Fig. 3 is 0.9865, and the slope (0.9819) and intercept (0.062) of the linear regression line in Fig. 3 are very close to the ideal behaviour (ideal slope 1.00, ideal intercept 0.00).

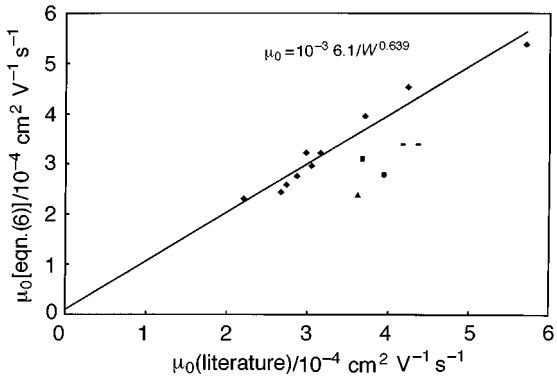


**Fig. 2** Correlation between absolute mobilities ($\mu_0$) estimated using molecular weight to a power [eqn. (6)] with the literature absolute mobilities for the 15 aliphatic carboxylates in Table 1. Symbols as in Fig. 1. The line is the linear regression between the predicted and literature mobilities for nonchlorinated carboxylates.

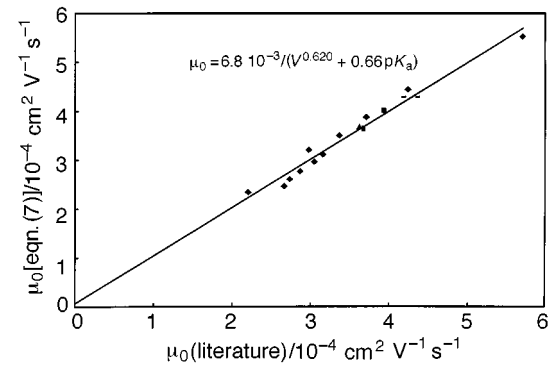


**Fig. 3** Correlation between absolute mobilities ($\mu_0$) estimated using molecular volume to a power and p$K_a$ [eqn. (7)] with the literature absolute mobilities for the 15 aliphatic carboxylates in Table 1. Symbols as in Fig. 1. The line is the linear regression between the predicted and literature mobilities.

The significant improvement in the predicted mobility upon inclusion of p$K_a$ to reflect the dielectric friction validates the incorporation of this term into our model for mobility. The error associated with the literature values precludes any further investigation of other factors such as shape that may affect electrophoretic mobilities. In studies of structurally rigid aromatic molecules the hydrodynamic friction term was observed to have a different form, and one that was dependent upon shape.[36] Despite the change in the hydrodynamic friction term, the p$K_a$ was still an effective term in describing the charge-dependent friction of aromatic carboxylates. Thus, while the applicability of eqn. (7) is limited to aliphatic carboxylates, it is believed that the p$K_a$ is an effective descriptor of charge density, and thus the dielectric friction, for organic acids.

### *Monoamines revisited*

Recently we reported expressions which related the mobility of aliphatic monoamines to molecular weight and hydration number.[4] These expressions yielded an average prediction error of only 4.1% for a data set of 34 aliphatic monoamines possessing no other functional groups. However when this expression was applied to a data set of seven monoamines possessing hydroxyl, ketone and carboxylic acid functionalities, the error between predicted and literature mobilities increased to 7.2%. Investigations of the origin of the hydration numbers used in our previous predictions indicated that they were semi-quantitative at best. Therefore, it was of great interest to determine if a dissociation constant could be used as a more reliable measure of the dielectric friction for monoamines.

In an anlogy to carboxylates, p$K_b$ is used as the descriptor of charge distribution in monoamines. Table 2 lists the 34 monoamines (possessing no other functional group) and their associated physicochemical parameters that are used to generate the expressions for predicting absolute mobility. Note that the p$K_b$ values for quaternary amines (permanently charged) were arbitrarily defined as zero. For any permanently charged species, its p$K_b$ value has no physical meaning. However, the stronger the protonation ability of a monoamine, the smaller its p$K_b$. Since quaternary amines are permanently charged, in analogy to permanently protonated, we assume its p$K_b$ to be zero.

Performing nonlinear regression between the absolute mobilities in Table 2 and the molecular volume and p$K_b$ of the monoamines yielded the best fit expression:

$$\mu_0 = \frac{10^{-3}(7.8 \pm 1.3)}{V^{(0.62 \pm 0.03)} + (0.66 \pm 0.23) \times \mathrm{p}K_b} \qquad (8)$$

The average relative error between the absolute mobilties predicted using eqn. (8) and the literature values in Table 2 was 4.5%. The correlation coefficient, slope and intercept of the linear regression line for the predicted mobilities plotted *versus* the literature mobilities (Fig. 4) are 0.9887, 0.9766 and 0.079, respectively.

Alternatively if molecular weight and p$K_b$ are used as the parameters to predict the absolute mobilities of monoamines, the best fit equation is:

$$\mu_0 = \frac{10^{-3}(5.5 \pm 0.8)}{W^{(0.58 \pm 0.03)} + (0.39 \pm 0.14) \times \mathrm{p}K_b} \qquad (9)$$

The average error between the predicted absolute mobilities and the literature values is 4.3%. The correlation coefficient, slope and intercept of the linear regression line in the predicted mobilities *versus* literature mobilities (plot not shown) are 0.9894, 0.9767 and 0.080, respectively. These fit parameters are comparable to those achieved when molecular weight and

hydration number were used to predict the mobility of these same monoamines.[4]

**Table 2** Physicochemical parameters and electrophoretic mobilities of monovalent amines possessing no other functional groups

| Molecule | $\mu_0$ (literature)/ $10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$ | p$K_b$ (25 °C; $I$ = 0) | Molecular weight ($W$) | Molecular volume ($V$)/Å$^3$ |
|---|---|---|---|---|
| Ammonium | 7.62[a] | 4.75[f] | 18.04 | 23.28 |
| Methylammonium | 6.20[b] | 3.36[g] | 32.06 | 42.02 |
| Dimethylammonium | 5.46[b] | 3.226[g] | 46.09 | 61.3 |
| Ethylammonium | 4.85[a] | 3.364[g] | 46.09 | 58.4 |
| Trimethylammonium | 5.03[b] | 4.200[g] | 60.12 | 80.4 |
| Tetramethylammonium | 4.43[c] | 0 | 74.15 | 99.7 |
| i-Butylammonium | 3.94[d] | 3.52[g] | 74.15 | 91.6 |
| Propylammonium | 4.30[a] | 3.434[g] | 60.11 | 74.8 |
| Diethylammonium | 3.89[a] | 3.067[g] | 74.15 | 94.1 |
| Piperidinium | 3.86[d] | 2.877[g] | 86.16 | 99.3 |
| Pentylammonium | 3.83[d] | 3.403[g] | 88.17 | 107.6 |
| Ethyltrimethylammonium | 4.20[d] | 0 | 88.17 | 116.1 |
| Dipropylammonium | 3.31[b] | 3.00[g] | 102.20 | 126.9 |
| Propyltrimethylammonium | 3.80[a] | 0 | 102.20 | 132.4 |
| Triethylammonium | 3.52[a] | 3.285[g] | 102.20 | 129.6 |
| Butyltrimethylammonium | 3.48[d] | 0 | 116.23 | 149.3 |
| Tetraethylammonium | 3.39[a] | 0 | 130.25 | 163.8 |
| Tripropylammonium | 2.79[b] | 3.34[g] | 144.28 | 177.3 |
| Hexyltrimethylammonium | 3.07[d] | 0 | 144.28 | 182.2 |
| Benzyltrimethylammonium | 3.59[d] | 0 | 150.24 | 171.9 |
| Octyltrimethylammonium | 2.75[d] | 0 | 172.33 | 215.3 |
| Tetra-n-propylammonium | 2.43[d] | 0 | 186.36 | 232.4 |
| n-Dodecylammonium | 2.47[a] | 3.37[h] | 186.36 | 222.5 |
| Decyltrimethylammonium | 2.53[d] | 0 | 200.39 | 247.6 |
| Dodecyltrimethylammonium | 2.34[d] | 0 | 228.44 | 281.0 |
| Tetra-n-butylammonium | 2.02[d] | 0 | 242.47 | 297.9 |
| Tetradecyltrimethylammonium | 2.23[d] | 0 | 256.49 | 314.5 |
| Hexadecyltrimethylammonium | 2.17[d] | 0 | 284.55 | 347.8 |
| Tetra-i-pentylammonium | 1.86[d] | 0 | 298.57 | 362.2 |
| Tetra-n-pentylammonium | 1.81[d] | 0 | 298.57 | 363.5 |
| Octadecyltrimethylammonium | 2.08[e] | 0 | 312.60 | 378.2 |
| Octadecyltriethylammonium | 1.86[d] | 0 | 354.68 | 428.7 |
| Octadecyltripropylammonium | 1.78[d] | 0 | 396.76 | 479.6 |
| Octadecyltributylammonium | 1.72[d] | 0 | 438.84 | 528.0 |

[a] Data obtained from ref. 38. [b] Data obtained from ref. 39. [c] Data obtained from ref. 34. [d] Data obtained from ref. 40. [e] Data obtained from ref. 41. [f] Data obtained from ref. 40. [g] Data obtained from ref. 42. [h] Data obtained from ref. 29.

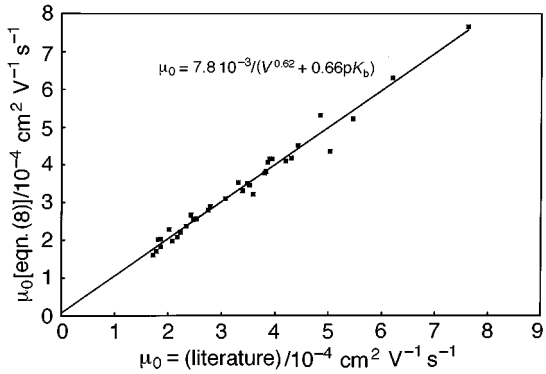


**Fig. 4** Correlation between absolute mobilities ($\mu_0$) estimated using molecular volume to a power and p$K_b$ [eqn. (8)] with the literature absolute mobilities for the 34 aliphatic amines in Table 2. The line is the linear regression between the predicted and literature mobilities.

However, the real test of a model is to apply it to solutes not included in the data set used to generate the model. Table 3 shows seven amines possessing additional functional groups for which literature absolute mobility values were available.[4] Using eqn. (9) the average error between the predicted absolute mobilities and the literature values was 5.0%. This is substantially lower than that achieved using molecular weight and hydration number (7.2%).[4] Similarly the prediction error for these monoamines decreased from 8.2% using molecular volume and hydration to 6.7% using eqn. (8).[4,32]

### *Commonalities*

The primary objective of this work was to generate expressions that account for the influence of both hydrodynamic and dielectric friction on the absolute mobility of small organic ions. The success with which this has been achieved is reflected in the commonalities between eqn. (7), which describes the mobility of carboxylates, and eqn. (8) for monoamines. Despite these expressions being derived for different types of solutes, the three fit parameters (numerator, power on volume and dielectric friction constant) are statistically equivalent between the two equations. This indicates that these terms are reflecting similar phenomena in the two cases.

Further, the power on the molecular volume [0.62 in eqns. (7) and (8)] is very similar to that arising in empirical expressions for diffusion, such as the Wilke–Chang ($V^{-0.6}$) and Hayduk–Laudie ($V^{-0.589}$). The Wilke–Chang and Hayduk–Laudie expressions are based on data sets containing only uncharged molecules. Thus these expressions reflect only hydrodynamic friction effects. The similarity in the power dependence of eqns. (7) and (8) with these diffusion equations indicates that the volume term reflects solely the influence of hydrodynamic friction. Thus, the p$K$ terms have successfully devolved the dielectric friction from the overall frictional behaviour.

However, on-going studies of aromatic acids have demonstrated that the hydrodynamic friction of these structurally rigid molecules differs from that observed for aliphatic acids and bases. That is, hydrodynamic friction term in eqns. (7) and (8) would be different for aromatic compounds. Thus, the applicability of these equations is limited to aliphatic compounds.

## Conclusion

Expressions for electrophoretic mobility based solely on molecular weight or volume failed to accurately reflect the behaviour of the aliphatic carboxylates and amines studied. Molecular weight was particularly inappropriate for halogenated carboxylates. It was necessary to account for the influence of dielectric friction to accurately predict mobilities. The p$K_a$

**Table 3** Physicochemical parameters and absolute mobilities of amines with other functional groups

| Molecule | $\mu_0$ (literature)/ $10^{-4}$ cm$^2$ V$^{-1}$ s$^{-1}$ | p$K_b$ (25 °C; $I$ = 0) | Molecular weight ($W$)/g mol$^{-1}$ | Molecular volume ($V$)/Å$^3$ |
|---|---|---|---|---|
| $^+NH_3CH_2CH_2OH$ | 4.37[a] | 4.502[d] | 62.09 | 67.33 |
| $HOCH_2CH_2N^+(CH_3)_3$ | 3.96[b] | 0 | 104.17 | 125.03 |
| $(HOCH_2)_3CNH_3^+$ | 2.95[c] | 5.925[d] | 122.14 | 118.00 |
| $CH_3NHCOCH_2N^+(CH_3)_3$ | 3.46[b] | 0 | 131.20 | 148.50 |
| $^+NH_3(CH_2)_5CO$ OH | 2.88[c] | 3.196[d] | 132.18 | 136.17 |
| $(HOCH_2CH_2)_2(CH_3)_2N^+$ | 3.48[b] | 0 | 134.20 | 149.69 |
| His$^+$ | 2.96[c] | 4.92[d] | 156.16 | 139.20 |

[a] Data obtained from ref. 40. [b] Data obtained from ref. 38. [c] Data obtained from ref. 43. [d] Data obtained from reference 42.

for carboxylates and p$K_b$ for amines was a convenient means of incorporating such effects. Thus, absolute electrophoretic mobility can be estimated using molecular volume and the acid or base dissociation constant.

This work was supported by the Natural Science and Engineering Research Council of Canada and by The University of Calgary.

## References


1 Smith, S. C., and Khaledi, M. G., *Anal. Chem.*, 1993, **65**, 193.
2 Rawjee, Y. Y., Williams, R. L., and Vigh, Gy., *J. Chromatogr. A*, 1993, **625**, 233.
3 Li, D., Fu, S., and Lucy, C. A., *Anal. Chem.*, submitted for publication.
4 Fu, S., and Lucy, C. A., *Anal. Chem.*, 1998, **70**, 173.
5 Cussler, E. L., *Diffusion: Mass Transfer in Fluid Systems*, Cambridge University Press, New York, 2nd edn., 1997, section 6.1.4.
6 Bockris, J. O'M., and Reddy, A. K. N., *Modern Electrochemistry*, Plenum Press, New York, 1970, vol. 1, section 4.4.6.
7 Hiemenz, P. C., *Principles of Colloid and Surface Chemistry*, Marcel Dekker, New York, 2nd edn., 1986, p. 747.
8 Grossman, P. D., Colburn, J. C., and Lauer, H. H., *Anal. Biochem.*, 1989, **179**, 28.
9 Edward, J. T., *Sci. Proc., R.D.S.*, 1957, **27**, 273.
10 Robinson, R. A., and Stokes, R. H., *Electrolyte Solutions*, Butterworth Scientific Publications, London, 2nd edn., 1959, pp. 118–132.
11 Spernol, A., *J. Phys. Chem.*, 1956, **60**, 703.
12 Cussler, E. L., *Diffusion: Mass Transfer in Fluid Systems*, Cambridge University Press, New York, 2nd edn., 1997, section 5.2.1.
13 Cheng, P. V., and Schachman, H. K., *J. Polym. Sci.*, 1955, **16**, 19.
14 Perrin, F., *J. Phys. Radium*, 1934, **5**, 497.
15 Perrin, F., *J. Phys. Radium*, 1936, **7**, 1.
16 Edward, J. T., *Sci. Proc., R.D.S.*, 1957, **27**, 287.
17 Ihnat, M., and Goring, D. I. A., *Can. J. Chem.*, 1967, **45**, 2353.
18 Offord, R. E., *Nature* (*London*), 1966, **211**, 591.
19 Compton, B. J., *J. Chromatogr.*, 1991, **559**, 357.
20 Wilke, C. R., and Chang, P., *AIChE J.*, 1955, **1**, 264.
21 Hayduk, W., and Laudie, H., *AIChE J.*, 1974, **20**, 611.
22 Hayduk, W., and Minhas, B. S., *Can. J. Chem. Eng.*, 1982, **60**, 295.
23 Biswas, R., and Bagchi, B., *J. Chem. Phys.*, 1997, **106**, 5587.
24 Bockris, J. O'M., and Reddy, A. K. N., *Modern Electrochemistry*, Plenum Press, New York, 1970, vol. 1, section 2.4.1.
25 Kay, R., *Pure Appl. Chem.*, 1991, **63**, 1393.
26 Evans, D. F., Tominaga, T., Hubbard, J. B., and Wolynes, P. G., *J. Phys. Chem.*, 1979, **83**, 2669.
27 Hubbard, J., and Onsager, L., *J. Chem. Phys.*, 1977, **67**, 4850.
28 Hartman, R. S., Alavi, D. S., and Waldeck, D. H., *J. Phys. Chem.*, 1991, **95**, 7872.
29 Perrin, D. D., Dempsey, B., and Serjeant, E. P., *p*$K_a$ *Prediction for Organic Acids and Bases*, Chapman and Hall, New York, 1981, pp. 1–20.
30 Bondi, A., *J. Phys. Chem.*, 1964, **68**, 441.
31 Edward, J. T., *J. Chem. Educ.*, 1970, **47**, 261.
32 Fu, S., MSc Thesis, University of Calgary, Canada, 1998.
33 Hirokawa, T., Nishino, M., and Kiso, Y., *J. Chromatogr.*, 1982, **252**, 49.
34 Beckers, J. L., and Everaerts, F. M., *J. Chromatogr.*, 1989, **470**, 277.
35 Landolt-Börnstein, *Zahlenwerte und Funktionen*, 6 Aufl. Bd. II, Teil 7, Springers, Berlin, 1960, p. 264.
36 Li, D., and Lucy, C. A., manuscript in preparation.
37 Martell, A. E., and Smith, R. M., *Critical Stability Constants*, Plenum Press, New York, 1977, vol. 3, pp. 1–19.
38 Edward, J. T., in *Advances in Chromatography*, ed. Giddings, J. C., and Keller, R. A., Marcel Dekker, New York, 1966, vol. 2, pp. 63–98.
39 Moor, T. S., and Winmill, T. F., *J. Chem. Soc.*, 1912, **101**, 1635.
40 *Handbook of Chemistry and Physics*, 1st Student Edition, ed. Weast, R. C., CRC Press, Boca Raton, FL, 1991, pp. D102–106.
41 Kuhn, D. W., and Kraus, C. A., *J. Am. Chem. Soc.*, 1950, **72**, 3676.
42 Martell, A. E., and Smith, R. M., *Critical Stability Constants*, Plenum Press, New York, 1975, vol. 2.
43 Hirokawa, T., and Kiso, Y., *J. Chromatogr.*, 1982, **252**, 33.


*Paper 8/00624E*
*Received January 22, 1998*
*Accepted May 18, 1998*