Propylene Carbonate as a Nonaqueous Solvent for Capillary Electrophoresis: Mobility and Ionization Constant of Aliphatic Amines

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The two properties of aliphatic amines were investigated in propylene carbonate as solvent that are decisive for capillary electrophoretic migration: the actual mobilities and the pKₐ* values. Solutes were eight primary, secondary, and tertiary amines. Roughly, the actual ionic mobilities of the ammonium ions are inversely proportional to the solvent viscosity, fairly obeying Walden’s rule. The pKₐ* values of the cation acids, HB⁺ (the corresponding acids of the amines, B⁻), were related to the conventional pH* scale of the buffers. Determined from the effective mobilities as a function of the pH*, they are increased by ~7 units compared to water. This increase was interpreted based on the concept of the standard free energy of transfer of the individual species in the acid–base equilibrium. The corresponding medium effect on the proton, log m⁺/H⁺ (the logarithm of the transfer activity coefficient m⁺/H⁺) is ~4, which could take place in these solvents although their dielectric constants are higher than 30. Although ion association might enhance selectivity in some cases, its unpredictable magnitude (connected to the lack on data about association constants) makes such organic solvent systems not easily suited for optimization. In practice, many solvents of potential interest have the limitation that they possess a restricted compatibility with the most common detector in capillary zone electrophoresis (CZE), the UV absorbance detector, because they have an optical cutoff in the range of 230–260 nm. Thus, few organic solvents have been used in CZE (for a review, see, for example, ref 1). One interesting example is propylene carbonate (PC, 4-methyl-1,3-dioxolan-2-one), a medium for acid–base titrations used for a long time. We demonstrated in a previous paper that it is well suited for CZE of organic solutes using conductivity detection. Its optical properties (cutoff at 200–230 nm²) allow nevertheless the application of the UV absorbance detector at least for analytes with sufficiently high extinction coefficients at an appropriate wavelength. Tjernlund and Hansen⁴ applied it to microcolumn separations with UV detection for a kind of electrokinetic chromatography to resolve neutral solutes by the aid of “solvophobic” interactions with alkylammonium ions. The same detection was used in one of our previous papers for CZE.⁵

A remarkable property of PC⁶ is its high relative permittivity (εᵣ = 66.1) compared to other organic solvents (N-methylamides are exceptions). PC enables working at normal or elevated temperature (freezing point −54.5 °C, boiling point 242 °C). Its density (d = 1.198 g cm⁻³) is larger than that of many organic solvents, and its viscosity (η = 2.513 × 10⁻³ Pa·s) is comparably higher than water, the alcohols, and ACN but lower than DMSO. Its viscosity results in relatively low ionic mobilities, compared to water and many other organic solvents. Interestingly for CZE, it might selectively influence the acid–base properties of solutes; in this respect, it is similar to ACN. However, only few data on pKₐ* values are available for PC.

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There are several other potential advantages of PC as a solvent in CZE. Most remarkable are two: the high relative permittivity (see above), and the low dependence of the ratio $\mu / D$ on the ionic strength of the BGE ($\mu$ is the mobility, and $D$ is the diffusion coefficient of the analyte). (i) The high relative permittivity suppresses ion association, which allows a more straightforward prediction of the optimal separation conditions, because in this case the separation parameters are better defined (the extent of ion pair formation is hard to predict, and corresponding association constants are nearly not available from the literature). In this respect, PC resembles water as solvent and is in contrast to acetonitrile and methanol (where surprisingly high ion pair formation was found). (ii) The ratio $\mu / D$ is decisive for the maximum achievable plate number in CZE (when longitudinal diffusion is the only cause of peak broadening). Note that the mobility is always more strongly reduced by increasing ionic strength than the diffusion coefficient, and thus, the ratio $\mu / D$ decreases with ionic strength. Consequently the maximum plate number decreases as well. The magnitude of this reduction depends on the relative permittivity and the viscosity of the solvent. In comparison with other organic solvents, PC seems to be as favorable as water in this respect and much more favorable than commonly used methanol and acetonitrile.

In previous work, we observed changes in the migration sequence of amines in PC, compared to water and a number of other organic solvents. To get insight into the cause of such effects, we systematically investigate in the present paper in PC the two parameters decisive for the electrophoretic migration: the actual ionic mobilities (that of the fully charged ions) and the $pK_a$ values in comparison to water. The aliphanic amines shown in Figure 1 are selected as analytes. All compounds are strong bases in water, with $pK_a$ values around 10. The $pK_a*$ values in the organic solvent were determined by measurement of the effective mobilities in BGEs with different $pH^*$. The $pH^*$ scale established here is based on the conventional $pK_a*$ values of certain acids and bases as pointed out in a previous publication. Conventional $pH^*$ values of the BGEs are adjusted by mixing these acids or bases with their respective salts, according to the Henderson–Hasselbalch equation. In this way, systematic errors (due to liquid junction potentials and aqueous reference buffers) that take place in measuring the buffering $pH^*$ by the use of a glass electrode are excluded.

As the majority of the analytes are non-UV absorbing (and because of the optical cutoff of PC at 230 nm), the electrical conductivity detector was used in connection with the UV absorbance detector. The conductivity detector has the further advantage that there is no restriction concerning the light absorbance of the buffering electrolytes used for the BGEs.

**EXPERIMENTAL SECTION**

**Instrumentation.** All experiments were carried out with a 30 CE instrument (Agilent Technologies, Palo Alto, CA) with fused-silica capillaries of i.d. 50 $\mu$m, o.d. 375 $\mu$m, total length 30.5 cm,
3DCE instrument and has a compact construction. Output signal frequency CCD was laboratory-made; its construction was described previously (see, for example, refs 2 and 12). The detector cell together with the electronics is built into the cassette of the CE instrument and has a compact construction. The distance between the two detector cells is 5.5 cm. The employed configuration easily enables one to use both detection techniques simultaneously.

Chemicals. Propylene carbonate (99%), tetraethylammonium acetate, tetrahydramionium acetate, butyramine (99.5%), dipropylamine (99%), N-dodecylamine (98%), N-methylcyclohexylamine (98%), and tetraphenylphosphonium tetraphenylborate (p.a.) were obtained from Fluka (Buchs, Switzerland). Acetic acid, glacial (99.7%), N,N-dimethyldodecyleine (97%), and propylamine hydrochloride were obtained from Aldrich (Steinheim, Germany). Anthracene and perchloric acid (70–72% both analytical grade) were obtained from Merck (Darmstadt, Germany). Amitriptyline hydrochloride, nortriptyline hydrochloride, and doxepin hydrochloride were obtained from Sigma (Steinheim, Germany).

Procedures. The background electrolytes used are specified in Table 1. The pH* values of the buffers are those calculated according to the Henderson–Hasselbalch equation. The pH* values of 19.04 for butyramine and 16.95 for propylamine in PC are taken from the literature. According to the literature, perchloric acid is a strong acid in the nonaqueous solvent (pK* of HClO4 is 1.3). However, a small amount of water leads to the presence of H2ClO4 which is fully dissociated in propylene carbonate. Due to the presence of water traces in the BGEs (see Table 1), full dissociation of perchloric acid can be assumed under the present conditions.

The actual and the effective mobilities of the analytes were measured in duplicate by CZE in the usual way from their velocity and the electric field strength. The span was typically within 0.05 × 10−9 m2 V−1 s−1. We further use the term mobility units for 10−9 m2 V−1 s−1. The mobilities were corrected for the EOF.

The mobility of the EOF was determined with a pressure-mediated dual-ion technique as described in our previous paper. The precision of the values measured in duplicate, expressed by the span, is typically 0.02 mobility unit.

The solubility of free bases in water and PC, respectively, at saturation was measured by CZE as follows: to 100 μL of solvent in an Eppendorf vial, an excess of amine (sufficient to ensure formation of two phases) was added. The closed vial was placed in an ultrasonic bath for 10 min at 25.0 °C. After phase separation, the solvent phase was diluted (10 or 100 times for water or PC, respectively) and an aliquot injected into the CZE column with conductivity detection. The BGE for determination of the concentration of the amine in the solvent at saturation contained 0.02 mol L−1 perchloric acid in N,N-dimethylacetamide as nonaqueous solvent. Separation voltage was 10 kV, with typical current ~9 μA. All samples were run in duplicate, and the solubility was calculated from the sample peak area by the aid of a calibration curve in the usual way.

Curve fitting was carried out by Origin 6.1 software (OriginLab Corp., Northampton, MA).

RESULTS AND DISCUSSION

Mobilities. In Table 2, the actual mobilities of the analytes in solutions of perchloric acid in PC as solvent at the ionic strength of 25 mmol L−1 are presented. It can be assumed that all analytes are present as fully protonated ammonium ions in this acidic solution. In the same table, the absolute ionic mobilities (at zero ionic strength) in water are given (for the drugs Amitriptylin, Nortryptylin, and Doxepin, no such values were found in the literature). For a comparison of the mobilities in both solvents, one must take into account that the presence of the counterions lowers the mobilities. The dependence of the mobility of ion, i, on ionic strength is expressed by the limiting equation according to Debye, Hückel, and Onsager (see, for example ref 16) extended by Falkenhagen and Pitts, which is for uni-univalent electrolytes given by

$$\mu_i = \mu_0 - \left[ \frac{8.204 \times 10^5}{(\varepsilon r T)^{3/2}} \mu_0 \right] + \frac{4.275}{\eta (\varepsilon r T)^{1/2}} \sqrt{1 + 50.29a (\varepsilon r T)^{-1/2}}$$

where the suffix 0 indicates zero ionic strength; the mobility is in units of 10−9 m2 V−1 s−1; \(\varepsilon_r\) and \(\eta\) are dielectric constant (the relative permittivity) and the viscosity (in Pa s), of the solvent, respectively; \(T\) is the absolute temperature; and \(I\) is the ionic strength in mol L−1, a is the distance of closest approach between ion and counterion. When the ions are considered as point charges (a = 0), the denominator of the term outside the brackets in eq 1 is unit, and the mobility decreases linearly with the square root of \(I\) by the so-called Onsager limiting slope of the

<table>
<thead>
<tr>
<th>Table 1. Conventional pH* and Composition of the BGEs Used for the Determination of the Mobilities of the Analytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>conventional pH*</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>1.6</td>
</tr>
<tr>
<td>16.95</td>
</tr>
<tr>
<td>18.04</td>
</tr>
<tr>
<td>20.04</td>
</tr>
</tbody>
</table>


line (see, for example, the discussion given in refs 7, 8, 20, and 21).

Insertion of the appropriate physical constants of water at T = 298 K enables the calculation of the mobilities of the analytes at 0.025 mol L\(^{-1}\) ionic strength from the absolute mobilities (which are known from the literature). The resulting actual mobilities are given in Table 2. They were obtained taking a factor of 2.4 as the value for 50.29\(^\circ\)C in the denominator of eq 2, as described by Li and co-workers\(^\text{[22]}\) for similar ammonium ions.

The actual mobilities in PC are significantly lower than in water. For a particular ion, they differ by a factor of \(~3\). In a first approach, this reduction can be interpreted by the different frictional resistance acting on the moving ions. This extension of Walden’s rule leads to a surprisingly good accordance of the normalized mobility (that corrected by the solvent viscosity) in water and PC (see Table 2). The extended Walden products for a particular ion vary only between 3 and 17% (note for comparison that the mobilities vary by up to 330%). This accordance is not obvious, because Walden’s rule is based on the oversimplification that the mobilities depend on the actual mobility and the dielectric friction\(^\text{[23]}\) are not regarded in this model.

According to the Henderson—Hasselbalch relation the effective mobility depends on the actual mobility and the \(pK_a\) of the analyte, and the pH of the BGE by

\[
\mu_{\text{eff}} = \frac{\mu_{\text{act}}}{1 + 10^{pH - pK_a^*}}
\]

The typical titration curves for mobility versus pH* are indeed followed by the experimental data, as shown for two examples in Figure 2. It allows derivation of the \(pK_a^*\) value: it is the pH at the inflection point of the curve. The resulting \(pK_a^*\) values of the solutes are given in Table 3.

![Figure 2. Typical plot of mobility as a function of the conventional pH* of the BGE. The BGE composition is given in Table 1. The curves are fitted according to the Henderson—Hasselbalch relation (see, for example, eq 2): \(\square\), propylamine; \(\circ\), methylcyclohexylamine; \(\triangle\), EOF.](image)

**Table 2. Actual Mobilities, \(\mu_{\text{act}}\), at 25 mmol L\(^{-1}\) Ionic Strength, and Their Products with Solvent Viscosity, \(\eta\), in PC and Water. Temperature 25 \(^\circ\)C**

<table>
<thead>
<tr>
<th>analytes</th>
<th>PC</th>
<th>(\mu_{\text{act}})</th>
<th>(\mu_{\text{act}}/\eta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>propylaminonium</td>
<td>11.25</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>dipropylaminonium</td>
<td>11.03</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>methylcyclohexylammonium</td>
<td>10.66</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>dodecylammonium</td>
<td>7.46</td>
<td>18.8</td>
<td></td>
</tr>
<tr>
<td>dimethyl/dodecylammonium</td>
<td>8.39</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td>dimethyldodecylammonium</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(\mu_{\text{act}}\) and \(\mu_{\text{act}}/\eta\) in water were taken from the literature.\(^\text{34}\) The actual mobilities in water at ionic strength of 0.025 mol/L were calculated according to ref 22 (see text for details). Viscosity of water is 0.8904 \(\times 10^{-3}\) Pa s and of PC 2.513 \(\times 10^{-3}\) Pa s.\(^\text{30}\)

\(K\) values. The change of the \(pK_a\) values when transferring the protolysis equilibrium of a cation acid and its conjugated base from water to an organic solvent reflects the particular stabilization of all three particles involved in the reaction: the proton, the cation acid \(HB^+\), and the uncharged particle, the molecular base, B. This change can be interpreted by the concept of the transfer activity coefficient and the medium effect (see, for example, refs 24–28).

The concept is based on the standard free energy, \(\Delta G^o\), of transferring 1 mol of individual species, \(k\), from water, \(W\), to

\[
HB^+ = H^+ + B
\]

**Table 3. \(pK_a^*\) Values of the Analytes (as Cation Acid) in PC Obtained by Fitting the Measured Mobilities to Eq 2**

<table>
<thead>
<tr>
<th>analyte</th>
<th>(pK_a^*)</th>
<th>analyte</th>
<th>(pK_a^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>17, 42</td>
<td>DA</td>
<td>17, 51</td>
</tr>
<tr>
<td>DPA</td>
<td>17, 65</td>
<td>AMI</td>
<td>17, 67</td>
</tr>
<tr>
<td>MCHA</td>
<td>17, 64</td>
<td>NOR</td>
<td>17, 58</td>
</tr>
<tr>
<td>DMCHA</td>
<td>17, 71</td>
<td>DOX</td>
<td>17, 62</td>
</tr>
</tbody>
</table>

\(\Delta G^o\) values are based on the conventional pH* scale (for details, see text). The abbreviations are according to Figure 1.

\(\Delta G^o\) values of the analyte polarizability and the medium effect (see, for example, refs 24–28). The concept is based on the standard free energy, \(\Delta G^o\), of transferring 1 mol of individual species, \(k\), from water, \(W\), to

\[
HB^+ = H^+ + B
\]

**Figure 2. Typical plot of mobility as a function of the conventional pH* of the BGE. The BGE composition is given in Table 1. The curves are fitted according to the Henderson—Hasselbalch relation (see, for example, eq 2): \(\square\), propylamine; \(\circ\), methylcyclohexylamine; \(\triangle\), EOF.**

\(\Delta G^o\) values are based on the conventional pH* scale (for details, see text). The abbreviations are according to Figure 1.

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solvent. It is negative when the particle is more stable in S, and positive when it is better stabilized in W. The total standard free energy of transfer is composed from the contributions of the individual species involved in equilibrium. The equilibrium constant is connected to $\Delta G^\circ_2$ in the usual way as

$$\Delta G^\circ_2 = -RT \ln K_a$$

(4)

Based on this concept, the change of the $pK_a$ values of the cation acid can be related to the transfer activity coefficients, $m_B$ or the medium effects (the logarithm, $\log m_B$) of the individual species according to

$$\Delta pK_a = pK_a^S - pK_a^W = \log \left( \frac{m_{HB}^S}{m_{HB}^W} \right) = \log m_{HB}^+ + \log m_B^S - \log m_B^W$$

(5)

It can be seen that the change in $pK_a$ depends on (i) the basicity of the solvent compared to water, reflected by $\log m_{HB}^+$; (ii) the stabilization of the protonated base, the cation $HB^+$, expressed by $\log m_{HB}^+$; (iii) the stabilization of the free, molecular base, expressed by $\log m_B$.

**1. The Total Medium Effect.** The $pK_a^+$ values (Table 3) are derived from the mobilities measured in the BGEs at different pH by a curve fit to eq 2. The error for the determination of the $pK_a^+$ values was in the range of 0.04 pK unit (expressed as $\sqrt{C_2/C_1}$, where $C_2$ is the diagonal element of the variance–covariance matrix). All analytes have similar $pK_a^+$ values, between 17.4 and 17.7, irrespective of their degree of substitution on the nitrogen group. This is in some contrast to water, where the tertiary aliphatic amines with dimethyl substitution are slightly less basic than primary and secondary amines (see below). It should be noted that the range of $pK_a$'s even in water is quite narrow; it lays within 1.5 pK units only. However, PC seemingly levels this small difference in basicity between amines (see also ref 29).

Comparison of the $pK_a^+$ values in Table 3 with the $pK_a$ values in water shows that the cation acids are significantly less acidic in PC. For primary and secondary amines ($pK_a$ in water for DA is 10.63,30 for PA 10.69,31 for DPA 11.0) the corresponding $\Delta pK_a$ values for DA, PA, and PC are 6.9, 6.7, and 6.7 pK units, respectively. For the tertiary DMDA, $\Delta pK_a$ is $\sim$8 units, taking a value of 9.5 for a tertiary, aliphatic, dimethyl-substituted amine in water.20 These $\Delta pK_a$ values are in good accordance with values found for cation acids derived from ring-substituted pyridines29 and pyridine N-oxides.32

Table 4. Solubilities, $\Phi$, at Saturation of Free Bases in Water (W) and PC, Respectively

<table>
<thead>
<tr>
<th>analyte</th>
<th>$\Phi^W$</th>
<th>$\Phi^PC$</th>
<th>$\log \Phi^W/ \Phi^PC$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPA</td>
<td>$3.47 \times 10^{-1}$</td>
<td>$3.26 \times 10^2$</td>
<td>$\sim$ -1</td>
</tr>
<tr>
<td>MCHA</td>
<td>$1.65 \times 10^{-1}$</td>
<td>$1.10 \times 10^2$</td>
<td>$\sim$ -2</td>
</tr>
<tr>
<td>DA</td>
<td>$2.22 \times 10^{-1}$</td>
<td>$1.62 \times 10^{-3}$</td>
<td>$\sim$ -0.9</td>
</tr>
<tr>
<td>DMDA</td>
<td>$7.40 \times 10^{-3}$</td>
<td>$8.86 \times 10^{-2}$</td>
<td>$\sim$ -1</td>
</tr>
</tbody>
</table>

2 The solubilities are given in mol L$^{-1}$. The differences of $\log \Phi^W/ \Phi^PC$ for determinations in duplicate was $\lt$0.1. From ref 36. Full miscibility was observed at a 100-fold excess of the analyte over PC. Due to practical reasons, a possible miscibility gap was not determined.

According to eq 5, the $\Delta pK_a$ for the amines is composed from the individual contributions of the medium effect on the proton, the molecular base, and the ammonium ion. These contributions are discussed in the following.

**2. Medium Effect on the Proton, $\log m_{HS}$.** We found two values for the standard free energy of transfer, $\Delta G^\circ_2$, for the proton (50 kJ mol$^{-1}$, 45.7 kJ mol$^{-1}$) from water to PC in the literature. Accordingly, PC is a much less basic solvent than water. The corresponding medium effect, $\log m_{HS}^+$, has the high value of +8.8 and +8, respectively (the value was calculated according to eq 4). It reflects the much lower stabilization of the proton in PC. It is in the same order as the $pK_a$ shift of the cation acids under consideration; however, it is not the only effect that determines the position of the acid–base equilibrium.

**3. Medium Effect on the Molecular Species, $\log m_B$.** A value for the medium effect on the molecular species, B, can be derived from its solubility, $\Phi_B$, at saturation in the different solvents,33 according to

$$\log m_B^S = \log m_B^W + \log (\Phi_B^W/ \Phi_B^S)$$

(6)

Intuitively one accepts the assumption that the molecular species is better stabilized in the organic solvent, which would result in a larger solubility of the organic amines in PC. Unfortunately, only few quantitative data about solubilities of the present analytes in water are available, and for PC, the situation is even worse. Thus, we determined the solubilities experimentally by CZE for those analytes that are available as free bases (Table 4). As the $\Delta G^\circ_2$ values were given on the molar scale, we express the solubility on this scale as well.

In PC, the solubility is larger by 1 order of magnitude or more, compared to water. Thus, the medium effect on B is $\sim$1; the molecular species contributes to the $pK_a$ with a decrease by the same values (see eq 5). The medium effect on the molecular base (taking a value $\sim$2 for $\log m_B$) together with that on the proton ($\log m_{HS}^+$~ +8) reaches $\sim$6. The difference to the total medium effect ($\Delta pK_a^+$ is $\sim$7–8) is thus about 1 to 2. This difference should stem from the remaining contribution brought by the cationic species, HB$^+$.
(4) Medium Effect on the Ammonium Cation, \( \log m^{+}/HB^{+} \).

No direct values are available from the literature for the medium effect on the present ammonium cations. However, we can get an estimate for the magnitude of the effect by comparison with tetraalkylammonium ions, for which data are known. \( \Delta G^0 \) from water to PC for tetramethylammonium, tetraethylammonium, tetrapropylammonium, and tetrabutylammonium is \(-11\), \(-13\), \(-22\), and \(-31\) kJ mol\(^{-1}\), respectively.\(^6\) The negative sign of all values indicates that these ions are more stable in PC than in water, a finding that is in contrast to the proton. It follows that the common assumption that a solvent stabilizing the proton stabilizes the cation acid as well (often taken to explain the lower shift of the \( pK_a \) values of cation acids compared to neutral acids) is too simplifying. However, the negative value of \( \Delta G^0 \) on HB\(^+\) contributes to a reduction of the acidity of the cation acids.

We assume that the analytes behave similar to tetraalkylammonium with short alkyl chains, because for both types of ions the positive charge is not such strongly shielded as it is in long-chained symmetrical quaternary ammonium ions. Due to the larger charge density on N\(^+\) for the present protonated analytes, \( \Delta G^0 \) could be expected in the lower range of the values given above. Thus, we take a value of \(-10\) kJ mol\(^{-1}\) and a medium effect of \(-2\) or lower for the HB\(^+\) species of the analytes. Indeed, it can be seen that this value reasonably completes the sum of the contributions of the single species to the \( pK_a \) shift of \( 7-8 \) units.

CONCLUSIONS

(i) The actual ionic mobilities of the ammonium ions in PC are strongly reduced compared to water. This reduction correlates fairly with the viscosity of the solvents. This is not usual, because especially ionic migration in water is often determined by structural effects of the solvent in the vicinity of the ion (solvation, microviscosity, orientation of the solvent molecules in the field of the ion, etc.) rather than by bulk phase properties (e.g., macroviscosity).

(ii) The \( pK_a \) values of the analytes increase in PC by about \( 7-8 \) units compared to water. This increase can be assessed to the contributions stemming from (a) the destabilization of the proton in PC. The corresponding contribution to \( \Delta pK_a \) is \(+8\) units. (b) The stabilization of the cation acid HB\(^+\) in PC, contributing with \(-2\) \( pK_a \) units or less. (c) The stabilization of the molecular base, B, in PC, reflected by the better solubility in the organic solvent, contributing with \(-2\) \( pK_a \) units and more. These individual effects together result in a \( \Delta pK_a \) of \(-8\) units, which is close to the experimentally determined shift. The difference of these two values might be caused by the overestimated high literature value for the medium effect on the proton.

(iii) The most pronounced contribution to the shift of the \( pK_a^* \) values of the cation acids is caused by the significantly lower basicity of PC compared to water. The effects on the \( pK_a^* \) shift due to the higher solubility of B in the organic solvent and the better stabilization of HB\(^+\) seem to compensate each other.

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