

Determination of all pK_a values of some di- and tricarboxylic unsaturated and epoxy acids, and their polylinear correlation with the carboxylic group atomic charges

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Abstract

For a series of seven unsaturated and seven epoxy di- and tricarboxylic acids, pK_a^a values were determined potentiometrically in aqueous media at 25 °C and an ionic strength of 0.1 M (NaCl). The thermodynamic pK_a^a values were correlated with the "composite" charge of the carboxylic group. The PM3 parametrization, with simulation of a dielectric solvent, was used in our work as a reliable method for atomic charges. The effect of water as a solvent was simulated as a dielectric continuum with corresponding dielectric constant, using the COSMO model implemented in MOPAC.

Correlation involves all pK_a^a values of epoxy di- and tri-carboxylic acids, i.e., including first, second and, when appropriate, third dissociation. As a result of the polylinear fit the composite charge for the carboxylic group is calculated as a weighted sum of atomic charges, according to the formula: $Q = q_H + A \cdot q_{O^-} + B \cdot q_C + C \cdot q_{O=}$ + D. These charges show good linear fit, and statistical weights of q_C and $q_{O=}$ are negligible.

Introduction

The fast growing number of organic protolytes demanded a more rational approach to the study of their reactivity. The huge advancement in computational technique added a considerable incentive for computational modelling to become an important complement to experimental research. Finding quantitative structure-reactivity relationships for chemically

analogous protolytes is a widely accepted approach for the estimation of acidity constants, particularly for the cases when experimental determination is not practicable.

The aim of this work was to find out the correlation between the pK_a values of some carboxylic acids and the calculated atomic charges on that functional group.

There are reports on the use of calculated electrostatic charges on carboxylic hydrogen for the estimation of pK_a values of carboxylic acids. Various approaches may be found in the literature. Correlations have been made with charges on carboxylic hydrogen as well as with the overall charge on -COOH group. Most of the mentioned reports comprise AM1 and PM3 semiempirical MO methods¹⁻³. Generally, these correlations were not good enough to attract wider interest for their systematic use. In one recent work⁴ it was shown that polylinear correlation with atomic charges on all four atoms in the carboxylic group offers very good model for the prediction of the reactivity of the compounds, bringing relevant mechanistic information, too.

We have tested the same approach on two series of organic acids: the simplest unsaturated and epoxy di- and tricarboxylic acids. Atomic charges in the carboxyl group have been obtained by semiempirical MNDO-PM3 method, including the COSMO model for the simulation of solvent medium (SCRF).

Materials and Methods

Apparatus and reagents. A PHM-240 pH-meter (Radiometer) with a GK 2401B combined electrode (Radiometer) was used for the pH measurements. Potentiometric titrations were performed using a TTT60 titrator with autoburette ABU 12 (Radiometer). The burette size was 2.5 ml, least significant volume 0.001ml. For the conversions of the measured pH values into p_{cH} values ($p_{cH} = -\log [H_3O^+]$) the relationship⁵: $p_{cH} = pH - A$ was used. The correction factor $A=0.13$ was obtained by potentiometric titration of a standard HCl solution with a standard NaOH solution at 25°C and constant ionic strength 0.1 M (NaCl).

All unsaturated acids were analytical grade (Aldrich, Fluka).

A corresponding group of α , β -epoxy di- and tri-carboxylic acids was synthesized by an improved⁶ method of Payne^{7,8}: In a 100 ml three-necked flask equipped with magnetic stirrer, thermometer and pH-electrode, unsaturated acid (1.25 mmol) was dissolved in water (40 ml). The pH was adjusted to 6.5 by the addition of 5% NaOH and/or 5% HCl. Then, sodium tungstate (0.25 mmol, 20 mol % of catalyst) and H_2O_2 (30 mmol, aqueous, 30%) was

added; the mixture was warmed to 65 °C and stirred magnetically. After 1.5 - 2 hours no further reaction could be detected by TLC (C₆H₆ : AcOEt = 7:3). The reaction mixture was left to cool down to room temperature and then 10 beads of a Platal catalyst (0.2% Pt on alumina beads, having 2-3 mm diameter) were added to destroy the excess of H₂O₂. Subsequently, the catalyst was removed by filtration, and the filtrate mixed with molar equivalent of aqueous barium chloride, acidified with 5% H₂SO₄ to pH 1.4. Precipitated barium sulphate was removed by filtration. The filtrate was extracted in a continuous extractor with 80 ml of Et₂O. The ethereal extract was dried over anhydrous magnesium sulphate and evaporated. The crude product was crystallized from 95% EtOH and left at -20 °C overnight, then filtered and dried in vacuum. Yields were 30-45%. All synthesized epoxy acids [*cis*-epoxysuccinic⁷ (epoxymaleic) acid, *trans*-epoxysuccinic⁷ (epoxyfumaric) acid, *cis*-epoxymethylsuccinic⁹ (epoxycitraconic) acid, *trans*-epoxymethylsuccinic¹⁰ (epoxymesaconic) acid, epoxyitaconic⁸, *cis*- and *trans*-epoxyaconitic¹¹ acid] were described previously. Melting points are given in Table 1. For all these compounds the high purity was confirmed by ¹H- and ¹³C-NMR spectra.

Table 1. Melting points of synthesized epoxy acids.

| Epoxy acid | m.p. EC | literature m.p. EC |
|--|---------|---|
| <i>cis</i> -Epoxy succinic acid | 148-149 | 148-149 ^{7a)} , 149 ^{7b)} |
| <i>trans</i> -Epoxy succinic acid | 208-209 | 207!209 ^{7a)} , 209 ^{7b)} |
| Epoxyitaconic acid | 133-134 | not reported ⁸⁾ |
| <i>cis</i> -Epoxy methyl succinic acid | 82-84 | oil ⁹⁾ |
| <i>trans</i> -Epoxy methyl succinic acid | 155-157 | not reported ^{10a)} , 156!157 ^{10b)} |
| <i>cis</i> -Epoxyaconitic acid | 176-178 | 173!178 ¹¹⁾ |
| <i>trans</i> -Epoxyaconitic acid | 168-170 | 168!170 ¹¹⁾ |

Determination of acidity constants. The acidity constants were determined potentiometrically in aqueous media at 25 °C and an ionic strength of 0.1 M (NaCl). For each investigated acid a solution (20.00 ml, 4.877·10⁻³ – 5.155·10⁻³ M), was titrated with standard NaOH solution (0.1029 - 0.1052 M). The titration was done in duplicate for each acid. From

obtained experimental data the average number of bound protons in the acid (\bar{n}_H), known as the formation function, was calculated using the following equation:

$$\bar{n}_H = \frac{n c_{\text{tot}} - [\text{Na}^+] - [\text{H}_3\text{O}^+] + [\text{OH}^-]}{c_{\text{tot}}} \quad (1)$$

where c_{tot} is the total concentration of the investigated acid, n is the number of carboxylic groups; $[\text{Na}^+]$ is the concentration of the added NaOH; $[\text{H}_3\text{O}^+]$ is the concentration of free hydronium ions originating from the dissociation of acid and of water, determined by pH-measurement; $[\text{OH}^-]$ is the concentration of hydroxide ions originating from the dissociation of water, which can be neglected in acidic media.

Method of calculation. The polycarboxylic acids were investigated using semiempirical molecular-orbital methods included in the program package MOPAC 7.0.¹² We used the PM3 method^{13,14} for optimizing all the structures in the neutral form and all possible ionic forms of acids, their anions, dianions and, when appropriate, trianions. The reaction centre, *i.e.* the carboxylic group whose atomic charges have to be used for the correlation with pK_a^a constants, is chosen as one which upon dissociation produces most stable corresponding anion. In the case of fumaric and epoxyfumaric acids, having two equivalent COOH groups, their pK_a values are corrected with 0.3 ($\approx \log 2$) for the correlation.

All molecular structures were optimized according the PM3 force field in vacuum. For the geometry optimisation in a polar medium, we have modelled the solvent as a dielectric continuum (COSMO model^{15,16}) with the dielectric constant for water, 78.4. (The solvent is treated as a perturbation on the gas phase system.) Significant difference between optimised structures in the gas phase and in solution has been confirmed.

Results and Discussion

Acidity constants were determined for acids shown in Scheme 1. They are as follows: maleic **1a**, fumaric **2a**, citraconic **3a**, mesaconic **4a**, itaconic **5a**, *cis*- and *trans*-aconitic **6a** and

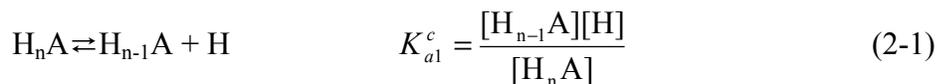
7a, next epoxy maleic **1b**, epoxy fumaric **2b**, epoxy citraconic **3b**, epoxy mesaconic **4b**, epoxy itaconic **5b**, *cis*- and *trans*-epoxyaconitic acid, respectively.



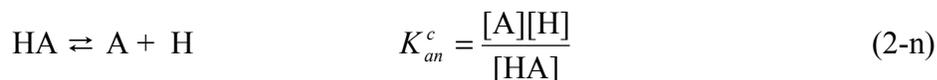
1. $R_1 = H$; $R_2 = H$; $R_3 = COOH$; $R_4 = COOH$
2. $R_1 = H$; $R_2 = COOH$; $R_3 = COOH$; $R_4 = H$
3. $R_1 = CH_3$; $R_2 = H$; $R_3 = COOH$; $R_4 = COOH$
4. $R_1 = CH_3$; $R_2 = COOH$; $R_3 = COOH$; $R_4 = H$
5. $R_1 = H$; $R_2 = H$; $R_3 = COOH$; $R_4 = CH_2COOH$
6. $R_1 = H$; $R_2 = CH_2COOH$; $R_3 = COOH$; $R_4 = COOH$
7. $R_1 = COOH$; $R_2 = CH_2COOH$; $R_3 = H$; $R_4 = COOH$

Scheme 1.

For the determination of acidity constants the potentiometric method, based on the relationship between formation function and the solution acidity, was applied¹⁷. For the acid H_nA for which the following equilibria are possible:



...



Formation function is defined as:

$$\bar{n}_H = \frac{\sum_0^n n[H_nA]}{\sum_0^n [H_nA]} \quad (3)$$

(For the sake of readability and generality, charges on ions are omitted)

In the case of dicarboxylic acids where the acido-basic processes overlap (close pK_a values) the determination was done in the pH range where all three species (H_2A , HA^- , A^{2-}) are present. From the expression for the formation function and acidity constants :

$$\bar{n}_H = \frac{2[H_2A] + [HA]}{[H_2A] + [HA] + [A]} \quad (4)$$

$$K_{a1}^c = \frac{[A][HA]}{[H_2A]} \quad (5)$$

$$K_{a2}^c = \frac{[A][H]}{[HA]} \quad (6)$$

the following linear relationship was obtained:

$$\underbrace{\frac{\bar{n}_H - 1}{\bar{n}_H}}_y [H_3O^+] = -K_{a2}^c + \frac{1}{K_{a1}^c} \underbrace{[H_3O^+]^2 \frac{2 - \bar{n}_H}{\bar{n}_H}}_x \quad (7)$$

In this way the acidity constants of fumaric, mesaconic, itaconic and all epoxy dicarboxylic acids have been determined.

For dicarboxylic acids (H_2A) having well separated acid-base processes (maleic and citraconic acid) the determination was done in two distinct pH ranges, as in the case of monocarboxylic acid. In the pH range where an acid-base pair H_2A-HA^- is dominant ($A^{2-} \rightarrow 0$):

$$\bar{n}_H = \frac{2[H_2A] + [HA]}{[H_2A] + [HA]} \quad (8)$$

The combination of equations (8) and (5) gives relationship (9):

$$\underbrace{\frac{2 - \bar{n}_H}{\bar{n}_H - 1}}_y = K_{a1}^c \underbrace{\frac{1}{[H_3O^+]}}_x \quad (9)$$

In pH range where the pair $HA^- - A^{2-}$ ($H_2A \rightarrow 0$) is dominant:

$$\bar{n}_H = \frac{[HA]}{[HA] + [A]} \quad (10)$$

The combination of the two equations with Eq. (6) gives:

$$\underbrace{\frac{1 - \bar{n}_H}{\bar{n}_H}}_y = K_{a2}^c \underbrace{\frac{1}{H_3O^+}}_x \quad (11)$$

For tricarboxylic acids the formation function and acidity constants are expressed as follows:

$$\bar{n}_H = \frac{3[H_3A] + 2[H_2A] + [HA]}{[H_3A] + [H_2A] + [HA] + [A]} \quad (12)$$

$$K_{a1}^c = \frac{[H][H_2A]}{[H_3A]} \quad (13)$$

$$K_{a2}^c = \frac{[H][HA]}{[H_2A]} \quad (14)$$

$$K_{a3}^c = \frac{[A][H]}{[HA]} \quad (15)$$

Combination of equations (12)-(15) gives:

$$\frac{\bar{n}_H - 1}{\bar{n}_H} [H] = -K_{a3}^c + \frac{1}{K_{a2}^c} [H]^2 \frac{2 - \bar{n}_H}{\bar{n}_H} + \frac{1}{K_{a1}^c K_{a2}^c} [H]^3 \frac{3 - \bar{n}_H}{\bar{n}_H} \quad (16)$$

In order to avoid complicated approaches (*e.g.* solving a set of equations or successive extrapolations) in equation (16), the determination of acidity constants was performed in two distinct pH ranges with the dominance of one, *i.e.* two acid-base pairs. For the studied tricarboxylic acids (except for *trans*-epoxyaconitic) the acidity constants were determined in the pH region containing H_3A , H_2A^- and HA^{2-} species:

$$\bar{n}_H = \frac{3[H_3A] + 2[H_2A] + [HA]}{[H_3A] + [H_2A] + [HA]} \quad (17)$$

Substituting equations (13) and (14) in (17), a linear relationship is obtained:

$$\underbrace{\frac{\bar{n}_H - 2}{\bar{n}_H - 1} [H_3O^+]}_y = -K_{a2}^c + \frac{1}{K_{a1}^c} \underbrace{[H_3O^+]^2 \frac{3 - \bar{n}_H}{\bar{n}_H - 1}}_x \quad (18)$$

In a second pH region the species H_2A^- , HA^{2-} and A^{3-} are dominant:

$$\bar{n}_H = \frac{2[H_2A] + [HA]}{[H_2A] + [HA] + [A]} \quad (19)$$

Combination of (14), (15) i (19) gives the relationship:

$$\underbrace{\frac{\bar{n}_H - 1}{\bar{n}_H} [H_3O^+]}_y = -K_{a3}^c + \frac{1}{K_{a2}^c} \underbrace{[H_3O^+]^2 \frac{2 - \bar{n}_H}{\bar{n}_H}}_x \quad (20)$$

Acidity constants K_{a1} and K_{a2} for *trans*-epoxyaconitic acid were determined using equation (18), in the pH region with dominant H_3A , H_2A^- and HA^{2-} molecular species.

Constant K_{a3} was determined in the pH region where only one acid-base pair $HA^{2-} - A^{3-}$ is present:

$$\bar{n}_H = \frac{[HA]}{[HA] + [A]} \quad (21)$$

Insertion of Eq. (15) in this equation gives:

$$\frac{1 - \bar{n}_H}{\bar{n}_H} = K_{a3}^c \frac{1}{H_3O^+} \quad (22)$$

As representative examples of linear relationships used in the determination of acidity constants, diagrams used for the determination of acidity constants of citraconic acid, in Fig. 1, *cis*-aconitic acid, in Fig 2, and *trans*-epoxyaconitic acid, in Fig 3, are presented.

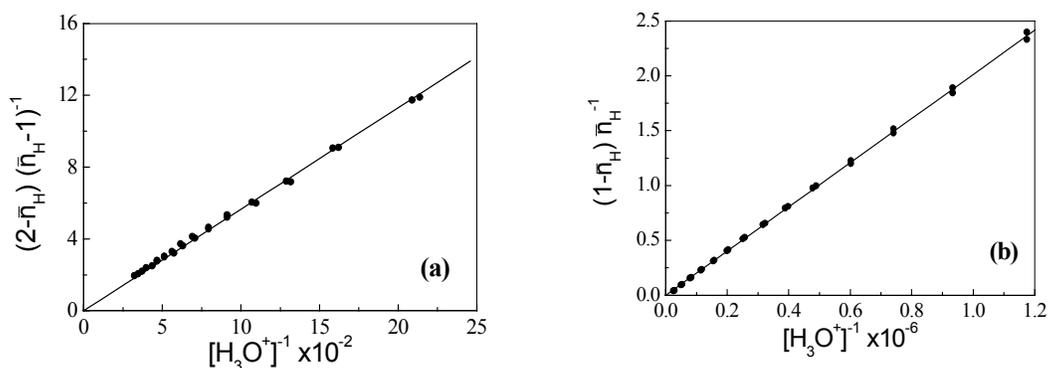


Figure 1 Potentiometric determination of acidity constants for citraconic acid
a) K_{a1}^c using eqn. (9); **b)** K_{a2}^c using eqn. (11).

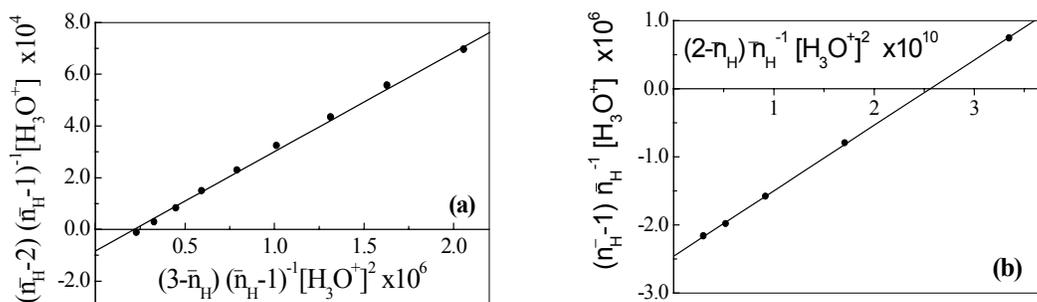


Figure 2. Potentiometric determination of acidity constants of *cis*-aconitic acid:
a) K_{a1}^c and K_{a2}^c using eqn. (18); **b)** K_{a2}^c and K_{a3}^c using eqn. (20).

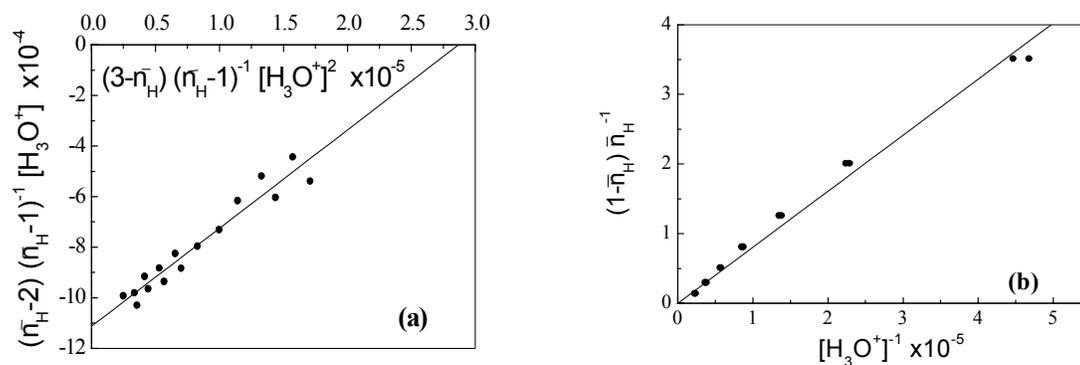


Figure 3. Potentiometric determination of acidity constants of *trans*-epoxyaconitic acid: **a)** K_{a1}^c and K_{a2}^c using eqn. (18); **b)** K_{a3}^c using eqn. (22).

Determined pK_a^c values for polycarboxylic acids are given in Table 2. Constants K_{a2} for *cis* and *trans*-aconitic acids and for *cis*-epoxyaconitic acid were determined through two linear relationships (ordinate intercept from equation (18) and slope from equation (20)). The values obtained are mutually consistent. In Table 2, both stoichiometric and thermodynamic values of constants are given. Conversion of stoichiometric (pK_a^c) into thermodynamic (pK_a^a) constants was done by use of activity coefficients obtained from the extended Debye-Hückel equation¹⁸.

Table 2. Stoichiometric ($pK_a^c \pm s$) and thermodynamic acidity constants (pK_a^a) of unsaturated and epoxy polycarboxylic acids. $I=0.1$ M (NaCl) ; $t=25$ °C

| <i>Acid</i> | pK_{a1}^c | pK_{a1}^a | pK_{a2}^c | pK_{a2}^a | pK_{a3}^c | pK_{a3}^a |
|---------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Maleic | 1.68±0.01 | 1.88 | 5.85±0.01 | 6.23 | | |
| Fumaric | 2.77±0.01 | 2.97 | 4.08±0.01 | 4.46 | | |
| Citraconic | 2.25±0.01 | 2.45 | 5.70±0.01 | 6.08 | | |
| Mesaconic | 2.84±0.01 | 3.04 | 4.47±0.01 | 4.85 | | |
| Itaconic | 3.70±0.01 | 3.90 | 5.18±0.01 | 5.56 | | |
| <i>cis</i> -Aconitic | 2.58±0.01 | 2.78 | 3.98±0.01 | 4.36 | | |
| | | | 4.08±0.05 | 4.46 | 5.61±0.01 | 6.21 |
| <i>trans</i> -Aconitic | 2.71±0.01 | 2.91 | 3.93±0.02 | 4.31 | | |
| | | | 3.97±0.01 | 4.35 | 5.56±0.01 | 6.16 |
| Epoxy maleic | 1.89±0.01 | 2.09 | 3.67±0.05 | 4.05 | | |
| Epoxy fumaric | 1.86±0.01 | 2.06 | 2.98±0.01 | 3.36 | | |
| Epoxy citraconic | 2.18±0.01 | 2.38 | 3.76±0.01 | 4.14 | | |
| Epoxy mesaconic | 1.90±0.01 | 2.10 | 3.25±0.02 | 3.63 | | |
| Epoxy itaconic | 3.00±0.01 | 3.20 | 4.91±0.03 | 5.29 | | |
| <i>cis</i> -Epoxyaconitic | 2.39±0.01 | 2.59 | 3.71±0.01 | 4.09 | | |
| | | | 3.72±0.02 | 4.10 | 5.38±0.01 | 5.98 |

| <i>Acid</i> | pK_{a1}^c | pK_{a1}^a | pK_{a2}^c | pK_{a2}^a | pK_{a3}^c | pK_{a3}^a |
|-----------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| <i>trans</i> -Epoxyaconitic | 1.60±0.03 | 1.80 | 2.95±0.01 | 3.33 | 5.10±0.01 | 5.70 |

pK_a Values for some of acids studied are given in the literature. Dependent on experimental conditions applied the values vary in the ranges: for: maleic acid¹⁹⁻²¹ pK_{a1} 1.65-2.00 and pK_{a2} 5.61-6.31; for fumaric acid^{24,25,28,29} pK_{a1} 3.02-3.04 and pK_{a2} 4.38-4.51; for citraconic acid²⁷ pK_{a2} 6.16; for mesaconic acid²⁷ pK_{a1} 3.07 and pK_{a2} 4.82; for itaconic acid^{19,27,30} pK_{a1} 3.01-3.68 and pK_{a2} 5.08-5.53; for epoxy maleic acid³¹ pK_{a1} 1.92 and pK_{a2} 3.92; for epoxy fumaric acid³² pK_{a1} 1.92 and pK_{a2} 3.25. Evidently, they are consistent with the values reported in this paper.

Semiempirical MO Calculations

Comparison of atomic charges of the carboxylic group (calculated by the semiempirical MO method) has been successfully done with gas-phase acidities of substituted benzoic acids.³³ The simulation of the dielectric medium has made possible the comparison of the properties of molecular species bearing various charges. Using the MNDO-PM3 semiempirical MO method we have calculated atomic charges for molecules and ions in a simulated water environment using dielectric constant 78.4. These calculated charges were correlated with pK_a^a values. Fumaric and epoxy fumaric acids have two equivalent carboxylic groups. For correlations the first pK_a^a values were augmented by $\log 2$, *i.e.* approx. 0.3.

The estimation of pK_a^a values of polycarboxylic acids by the correlation with carboxylic hydrogen charges was proven unsuccessful ($r = 0.4125$). The correlation with total charge of carboxylic group (sum of atomic charges for all atoms in -COOH group) was rather poor, having $r = 0.8610$.

The charges on all (four) atoms in -COOH were correlated (simultaneously) with the measured pK_a^a values. The regression analysis produces weighting factors (coefficients) of particular atomic charge. In this way one could deduce how important is electric charge on a certain atom in -COOH for the acidity of carboxylic acids. The negative sign of the coefficient for q_H is easy to understand, because the more positive hydrogen will more easily dissociate, making the acid stronger and lowering the pK_a^a value. This weighting factor is normalised to 1 (and other weights were accordingly renormalized) just to make it easier to compare the weights. The correlation involves all pK_a^a values of unsaturated and epoxy di-

and tri-carboxylic acids, *i.e.*, including first, second and, when appropriate, third dissociation, as shown in Table 3.

Table 3. pK_a^a Values of polycarboxylic acids, calculated atomic charges on carboxyl groups, and "composite" charge Q and Q' calculated according the equations (23) and (24), respectively. (pK_a^a values for fumaric and epoxyfumaric acids were corrected with 0.3)

| ACID | pK_a^a | q_H | q_{O-} | q_C | $q_{O=}$ | Q | Q' |
|--|----------|--------|----------|--------|----------|---------|---------|
| Maleic acid (1a) | 1.88 | 0.2794 | -0.3000 | 0.5227 | -0.5237 | 0.01779 | 0.02216 |
| Fumaric acid (2a) | 3.27 | 0.2762 | -0.3143 | 0.5226 | -0.5409 | 0.02868 | 0.03320 |
| Citraconic acid (3a) | 2.45 | 0.2752 | -0.2962 | 0.5228 | -0.5409 | 0.02074 | 0.02428 |
| Mesaconic acid (4a) | 3.04 | 0.2800 | -0.3077 | 0.5111 | -0.5267 | 0.02205 | 0.02578 |
| Itaconic acid (5a) | 3.90 | 0.2784 | -0.3025 | 0.4904 | -0.5295 | 0.02288 | 0.02453 |
| <i>cis</i> -Aconitic acid (6a) | 2.78 | 0.2794 | -0.2960 | 0.4951 | -0.5260 | 0.01816 | 0.01997 |
| <i>trans</i> -Aconitic acid (7a) | 2.91 | 0.2809 | -0.3029 | 0.5064 | -0.5166 | 0.01879 | 0.02225 |
| Maleic acid anion | 6.23 | 0.2885 | -0.3564 | 0.5238 | -0.5698 | 0.03811 | 0.04397 |
| Fumaric acid anion | 4.46 | 0.2729 | -0.3191 | 0.5257 | -0.5528 | 0.03453 | 0.03913 |
| Citraconic acid anion | 6.08 | 0.2862 | -0.3552 | 0.5299 | -0.5725 | 0.03941 | 0.04561 |
| Mesaconic acid anion | 4.85 | 0.2754 | -0.3150 | 0.5286 | -0.5425 | 0.02939 | 0.03438 |
| Itaconic acid anion | 5.56 | 0.2891 | -0.3623 | 0.4940 | -0.5743 | 0.04303 | 0.04660 |
| <i>cis</i> -Aconitic acid anion | 4.41 | 0.2783 | -0.3079 | 0.5071 | -0.5232 | 0.02404 | 0.02759 |
| <i>trans</i> -Aconitic acid anion | 4.33 | 0.2775 | -0.3089 | 0.5072 | -0.5223 | 0.02530 | 0.02894 |
| <i>cis</i> -Aconitic acid dianion | 6.21 | 0.2887 | -0.3590 | 0.4891 | -0.5642 | 0.04183 | 0.04519 |
| <i>trans</i> -Aconitic acid dianion | 6.16 | 0.2883 | -0.3587 | 0.4802 | -0.5501 | 0.04229 | 0.04543 |
| Epoxy maleic acid (1b) | 2.09 | 0.2897 | -0.3081 | 0.4798 | -0.5239 | 0.01501 | 0.01630 |
| Epoxy fumaric acid (2b) | 2.36 | 0.2791 | -0.2982 | 0.4967 | -0.5210 | 0.01923 | 0.02147 |
| Epoxy citraconic acid (3b) | 2.38 | 0.2813 | -0.2946 | 0.4662 | -0.5022 | 0.01707 | 0.01730 |
| Epoxy mesaconic acid (4b) | 2.10 | 0.2769 | -0.2875 | 0.4848 | -0.4995 | 0.01634 | 0.01781 |
| Epoxy itaconic acid (5b) | 3.20 | 0.2690 | -0.2877 | 0.4823 | -0.4945 | 0.02436 | 0.02582 |
| <i>cis</i> -Epoxyaconitic acid (6b) | 2.59 | 0.2718 | -0.2775 | 0.4588 | -0.4651 | 0.01738 | 0.01743 |
| <i>trans</i> -Epoxyaconitic acid (7b) | 1.80 | 0.2912 | -0.3064 | 0.4813 | -0.5134 | 0.01216 | 0.01387 |
| Epoxy maleic acid anion | 4.05 | 0.2900 | -0.3407 | 0.4930 | -0.5362 | 0.03326 | 0.03731 |
| Epoxy fumaric acid anion | 3.36 | 0.2747 | -0.2938 | 0.4881 | -0.5253 | 0.02233 | 0.02346 |
| Epoxy citraconic acid anion | 4.14 | 0.2927 | -0.3416 | 0.4864 | -0.5128 | 0.02758 | 0.03166 |
| Epoxy mesaconic acid anion | 3.63 | 0.2755 | -0.2951 | 0.4748 | -0.5154 | 0.02289 | 0.02337 |
| Epoxy itaconic acid anion | 5.29 | 0.2887 | -0.3540 | 0.4850 | -0.5538 | 0.03932 | 0.04245 |
| <i>cis</i> -Epoxyaconitic acid anion | 4.09 | 0.2887 | -0.3416 | 0.4932 | -0.5260 | 0.03151 | 0.03566 |
| <i>trans</i> -Epoxyaconitic acid anion | 3.33 | 0.2838 | -0.3142 | 0.4755 | -0.4864 | 0.02289 | 0.02554 |
| <i>cis</i> -Epoxyaconitic acid dianion | 5.98 | 0.2887 | -0.3540 | 0.4826 | -0.5497 | 0.03936 | 0.04245 |
| <i>trans</i> -Epoxyaconitic acid dianion | 5.70 | 0.2865 | -0.3528 | 0.4799 | -0.5418 | 0.04090 | 0.04399 |

q_H is the charge on carboxylic hydrogen

q_{O-} is the charge on hydroxylic oxygen in carboxyl group

q_C is the charge on carboxylic carbon

$q_{O=}$ is the charge on carboxylic oxygen in carboxyl group

As a result of the polylinear fit the "composite" charge, Q , for the carboxylic group is calculated as a weighted sum of atomic charges, according to the formula (23):

$$Q = q_H + A \cdot q_{O-} + B \cdot q_C + C \cdot q_{O=} + D \quad (23)$$

The values of the parameters (after the renormalization) are: -1 ± 0.0940 (for q_H); $A = -0.4931 \pm 0.0235$; $B = -0.0820 \pm 0.0321$; $C = -0.0368 \pm 0.0249$; $D = 0.1728 \pm 0.0344$; ($r = 0.9456, n = 32$).

The magnitude of parameters A-D could give insight into the mechanistic details of reactions involving carboxylic group. The major weight of charges on hydrogen and on hydroxylic oxygen, supports the well established concept of the polarity of O-H bond as a dominant factor determining the efficiency of carboxylic acid dissociation. This is directly confirmed by polylinear correlation including only charges on hydrogen and hydroxylic oxygen. The correlation with charges calculated by the equation:

$$Q' = q_H + A \cdot q_{O-} + B \quad (24)$$

is only slightly inferior to that from Eqn. (23) [-1 ± 0.1070 (for q_H); $A = -0.5480 \pm 0.0267$; $B = 0.1372 \pm 0.0314$; $r = 0.9384, n = 32$].

These charges are presented in Figure 4, showing a very good linear fit.

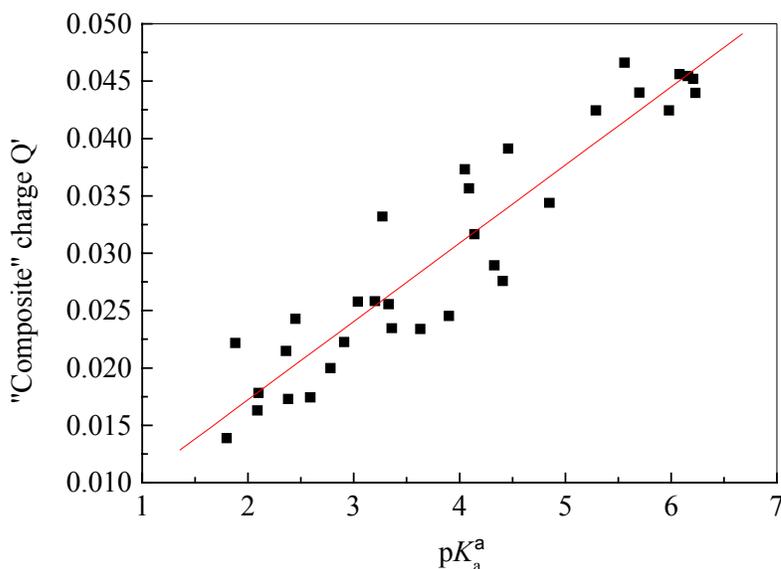


Figure 4. Correlation of measured pK_a^a values with the "composite" charge Q' calculated according the Eqn. (24); ($r = 0.9384$).

It should be noted that correlation involving only epoxy acids is much better ($r=0.9818$) than the correlation that involves only unsaturated acids ($r=0.9309$). This could be explained by a much greater change in entropy of solvation upon the ionisation of unsaturated acids. In our model, this change of entropy could not be directly taken into account.

***Acknowledgements.** This work was supported by the Ministry for Science, Technology and Development of Serbia.*

References

1. C. Sella, A. Hocquet and D. Bauer, *J. Chem. Research (S)*, 1996, 480.
2. A.G. Cook, L.R. Weasner and S.L. Folk, *J. Org. Chem.*, 1997, **62**, 7205.
3. A. Ponti and A. Gamba, *Gazetta Chimica Italiana*, 1997, **127**, 151.
4. B. Jovanović, I. Juranić, M. Mišić-Vuković, D. Brkić and Ž. Vitnik, *J. Chem. Research (S)*, 2000, 506; *J. Chem. Research (M)*, 2000, 1257.
5. L.B. Pfindt, D.M. Sladić, T.J. Janjić and G.V. Popović, *Analyst*, 1990, **115**, 383.
6. Lj.S. Stevović and I.O. Juranić, 37th Symposium of the Serbian Chemical Society, Novi Sad, *Book of Abstracts*, 1995, p.90.
7. a) G.B. Payne and P.H. Williams, *J. Org. Chem.*, 1959, **24**, 54; b) Kuhn R. and Ebel F., *Ber.* 1925 **58B**, 919.
8. K.S. Kirschenbaum and K.B. Sharpless, *J. Org. Chem.*, 1985, **50**, 1979.
9. M. Brock, D. Darley, S. Textor and W. Buckel, *Eur. J. Biochem.*, 2001, **268**, 3577.
10. a) G.W. Plaut, R.L. Beach and T. Aogaichi, *J. Biol. Chem.*, 1975, **250**, 6351; b) Y. Liwschitz, Y. Rabinsohn and D. Perera, *J. Amer. Chem. Soc.*, 1962, **85**, 1116.
11. R.W. Gutrie, J.G. Hamilton, R.W. Kierstead and O.N. Miller, 1974, US Pat. 3810931.
12. J.J.P. Stewart, *J. Comp. Aid. Molec. Design.*, 1990, **4**, 1.
13. J.J.P. Stewart, *J. Comput.Chem.*, 1989, **10**, 109.
14. J.J.P. Stewart, *J. Comput.Chem.*, 1989, **10**, 221.
15. A. Klamt and G. Schüürmann, *J. Chem. Soc. Perkin Trans. 2.* 1993, 799.
16. C.J. Cramer and D.G. Truhlan, *Chem. Rev.*, 1999, **90**, 2161.
17. H. Rossotti, *The Study of Ionic Equilibria*, Longman, London, New York, 1978, p.19.
18. J.M. Butler, *Ionic Equilibria and Mathematical Approach*, Addison-Wesley Publishing Company, California, 1964, pp. 432-435.

19. M. Yasada, K. Yamasaki and H. Ohtaki, *Bull. Chem. Soc. Jpn*, 1960, **33**, 1067.
20. H. J. de Brain, D. Kaitis and R. B. Temple, *Austral. J. Chem.* 1962, **15**, 457.
21. T. Nozaki, T. Mise and K. Higaki, *Nippon Kagaku Zasshi*, 1967, **88**, 1168.
22. K. S. Rajan and A. E. Martell, *J. Inorg. Nuclear Chem*, 1967, **29**, 523.
23. T. Tomita, E. Kyuno and R. Tsuchiya, *Bull. Chem. Soc. Jpn*, 1968, **41**, 1130.
24. V. Sihvonen, *Z. Elektrochem.*, 1930, **36**, 165.
25. B. Adell, *Z. Physik. Chem.*, 1940, **A186**, 27.
26. W. L. German and A. I. Vogel, *J. Am. Chem. Soc.* 1936, **58**, 1546.
27. E. Larison, *Z. Anorg. Chem.*, 1924, **140**, 292.
28. N. G. Topp and C. W. Davies, *J. Chem. Soc.*, 1940, **87**, **1538**.
29. W. L. German, A. I. Vogel and G. H. Jeffery, *Phil. Mag. Ser. 7*, 1936, **22**, 790.
30. S. Ramamoorthy and M. Santappa, *Bull. Chem. Soc. Jpn*, 1968, **41**, 1330.
31. A. Wassermann, *Helv. Chim. Acta* 1930, **13**, 207.
32. A. Wassermann, *Helv. Chim. Acta* 1930, **13**, 223.
33. T. B. McMahon and P. Kebarle, *J. Am. Chem. Soc.*, 1977, **99**, 2222.