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

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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 atomic charges of carboxylic group calculated by the MNDO-PM3 semiempirical MO method.

Keywords: dicarboxylic epoxy acid, tricarboxylic epoxy acid, polylinear correlation

The fast growing number of organic protolytes demand a more rational approach to the study of their reactivity. The huge advancement in computational techniques has enabled a complementary study method. Finding a 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 thermodynamic values of some carboxylic acids (Scheme 1) and the calculated charges on the atoms in carboxyl groups.

a b

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.

The formulae of the unsaturated and epoxy acids studied in this work are given in Scheme 1: maleic **1a**, fumaric **2a**, citraconic **3a**, mesaconic **4a**, itaconic **5a**, *cis*- and *trans*-aconitic **6a** and **7a**, next, epoxymaleic **1b**, epoxyfumaric **2b**, epoxycitraconic **3b**, epoxymesaconic **4b**, epoxyitaconic **5b**, *cis*- *trans*-epoxyaconitic acid **6b** and **7b**, respectively.

The acidity constants for these acids were determined potentiometrically[17] in aqueous media at 25 °C and an ionic strength of 0.1 M (NaCl).

Atomic charges of polycarboxylic acids were calculated using a semiempirical molecular-orbital method included in the program package MOPAC 7.0.[12] We used the PM3 method[13,14] for optimising all the structures in the neutral form and all possible ionic forms of acids, their anions, dianions and, when appropriate, trianions.

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All molecular structures were optimised 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 simulation of dielectric medium has made it possible to compare the properties of molecular species bearing various charges. Significant difference between the optimised structures in the gas phase and in solution has been confirmed. These calculated charges were correlated with thermodynamic values. Fumaric and epoxyfumaric acids have two equivalent carboxylic groups. For correlations the first the pK^a_a values were augmented by log2, *i.e.* approx. 0.3. Correlation involves all the pK^a_a values of the unsaturated and epoxy di- and tri-carboxylic acids, *i.e.*, including first, second and ,when appropriate, third dissociation, as shown in Table 3. It is worth noting that use of a solvation model in the calculation enabled simultaneous correlation of neutral and and ionic molecular species.

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 formula (23):

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

The values of the parameters are: –1±0.0940 (for q_H); A = –0.4931±0.0235; B = –0.0820±0.0321; C = –0.0368±0.0249; D = 0.1728±0.0344; (r = 0.9456, n = 32). The values of coefficients, obtained by polylinear regression, were scaled to normalize the weight of q_H to unity

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

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

is only slightly inferior to that from Eqn (23) [(r = 0.9384, n = 32); –1±0.1070 (for q_H); A = –0.5480±0.0267; B = 0.1372±0,0314;]. These charges are presented in Fig. 4, showing a very good linear fit.

It should be noted that correlation involving only epoxy acids is much better (r=0.9818, n = 16) than the correlation that involves only unsaturated acids (r=0.9309, n = 16). This could

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 correct to ± 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
cis-Aconitic acid (**6a**)	2.78	0.2794	–0.2960	0.4951	–0.5260	0.01816	0.01997
trans-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
cis-Aconitoc acid anion	4.41	0.2783	–0.3079	0.5071	–0.5232	0.02404	0.02759
trans-Aconitic acid anion	4.33	0.2775	–0.3089	0.5072	–0.5223	0.02530	0.02894
cis-Aconitic acid dianion	6.21	0.2887	–0.3590	0.4891	–0.5642	0.04183	0.04519
trans-Aconitic acid dianion	6.16	0.2883	–0.3587	0.4802	–0.5501	0.04229	0.04543
Epoxymaleic acid (**1b**)	2.09	0.2897	–0.3081	0.4798	–0.5239	0.01501	0.01630
Epoxyfumaric acid (**2b**)	2.36	0.2791	–0.2982	0.4967	–0.5210	0.01923	0.02147
Epoxycitraconic acid (**3b**)	2.38	0.2813	–0.2946	0.4662	–0.5022	0.01707	0.01730
Epoxymesaconic acid (**4b**)	2.10	0.2769	–0.2875	0.4848	–0.4995	0.01634	0.01781
Epoxyitaconic acid (**5b**)	3.20	0.2690	–0.2877	0.4823	–0.4945	0.02436	0.02582
cis-Epoxyaconitic acid (**6b**)	2.59	0.2718	–0.2775	0.4588	–0.4651	0.01738	0.01743
trans-Epoxyaconitic acid (**7b**)	1.80	0.2912	–0.3064	0.4813	–0.5134	0.01216	0.01387
Epoxymaleic acid anion	4.05	0.2900	–0.3407	0.4930	–0.5362	0.03326	0.03731
Epoxyfumaric acid anion	3.36	0.2747	–0.2938	0.4881	–0.5253	0.02233	0.02346
Epoxycitraconic acid anion	4.14	0.2927	–0.3416	0.4864	–0.5128	0.02758	0.03166
Epoxymesaconic acid anion	3.63	0.2755	–0.2951	0.4748	–0.5154	0.02289	0.02337
Epoxyitaconic acid anion	5.29	0.2887	–0.3540	0.4850	–0.5538	0.03932	0.04245
cis-Epoxyaconitic acid anion	4.09	0.2887	–0.3416	0.4932	–0.5260	0.03151	0.03566
trans-Epoxyaconitic acid anion	3.33	0.2838	–0.3142	0.4755	–0.4864	0.02289	0.02554
cis-Epoxyaconitic acid dianion	5.98	0.2887	–0.3540	0.4826	–0.5497	0.03936	0.04245
trans-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.

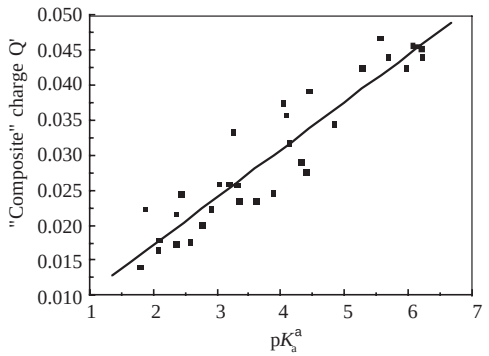

Fig. 4 Correlation of measured pK^a_a values with the "composite" charge Q′ calculated according the Eqn (24); (r = 0.9384, n = 32).

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.

Techniques used: Potentiometry, semiempirical MO calculations (MNDO-PM3)

References: 33

Table 1: Melting points of synthesized epoxy acids.

Table 2: A survey of the stoichiometric ($pK^c_a \pm s$) and thermodynamic acidity constants (pK^a_a) of unsaturated and epoxy polycarboxylic acids.

Figure 1: Potentiometric determination of acidity constants for citraconic acid.

Figure 2: Potentiometric determination of acidity constants of cis-aconitic acid.

Figure 3: Potentiometric determination of acidity constants of trans-epoxyaconitic acid.

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