Derivation of Molecular pK Values from pH-Dependences

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If the titration pK values of a dibasic acid are called $pK^* \pm \log p$, then its molecular pK values are $pK^* \pm \log(p+1/p)$. If the pH values at which the concentration of its mono-protonated form is half-maximal are called $pK^* \pm \log q$, then its molecular pK values are $pK^* \pm \log(q-4+1/q)$.

Simms (1926) pointed out that a dibasic acid with molecular dissociation constants K_1 and K_2 possessed the same titration curve as did an equimolar mixture of two monobasic acids of dissociation constants G_1 and G_2 , where $K_1 = G_1 + G_2$ and $1/K_2 = 1/G_1 + 1/G_2$. I remarked previously (Dixon, 1973, 1974, 1975) that this applies only in the absence of positively co-operative proton binding, i.e. only when $K_1 \geq 4K_2$, and that, if pK_2 and pK_1 are written as $pK^* \pm \log 2\alpha$, then pG_2 and pG_1 , the titration pK values, are given by $pK^* \pm \log(\alpha + \sqrt{\alpha^2 - 1})$. Thus pK^* is the mean of pK_1 and pK_2 , and also of pG_1 and pG_2 ; it is also the pH at which the concentration of the monoprotonated form of the dibasic acid is maximal. The quantity α , i.e. $\sqrt{K_1/4K_2}$, was also used as a parameter for expressing various concentrations and relationships; those given in the Appendix are examples.

In fact, however, there is seldom any need to discover pG values from pK values; it is the reverse that may be useful [see, e.g., Parsons & Raftery (1972)]. It follows from the above expressions that, if pG_2 and pG_1 are called $pK^* \pm \log p$, then pK_2 and pK_1 are given by $pK^* \pm \log(p+1/p)$.

The width at half its height is the easiest feature to measure from the bell-shaped curve that represents the dependence on pH of the concentration of the monoprotonated form of a dibasic acid. Variables such as the rates of enzyme-catalysed reactions that show a similar pH-dependence may do so by depend-

ing on the concentration of a monoprotonated form, because one protonation and one deprotonation deactivate the system. Despite dangers in such interpretations [see, e.g., Tipton & Dixon (1979)], derivation of the molecular pK values that correspond to a bell-shaped curve is often necessary. Alberty & Massey (1954) gave an expression for K_1 in terms of H_1 and H_2 , the values of $[H^+]$ that give half the maximum height, and of their geometric mean, i.e. the value of $[H^+]$ that gives the maximum height, which has been called K^* above. This expression was $K_1 = H_1 + H_2 - 4K^*$. Dixon (1973) gave an expression for H_1/K^* that may be rewritten in the terms defined above to give pH_2 and pH_1 equal to $pK^* \pm \log[\alpha + 2 + \sqrt{(\alpha + 2)^2 - 1}]$ (thus pK^* is the mean of pH_2 and pH_1 as well as of pK_2 and pK_1). Again, however, the more useful conversion is from pH_2 and pH_1 to pK_2 and pK_1 , not the reverse. If we let pH_2 and pH_1 be called $pK^* \pm \log q$, then pK_2 and pK_1 are given by $pK^* \pm \log(q-4+1/q)$, the plus sign applying to pK_2 (positively co-operative proton binding can lower pK_2 below pK_1).

This treatment is only a small rearrangement of the equation of Alberty & Massey (1954) because if:

$$\begin{aligned} K_1 &= H_1 + H_2 - 4K^* \\ K_1/K^* &= H_1/K^* + H_2/K^* - 4 \\ &= H_1/K^* + K^*/H_1 - 4 \quad (\text{because } H_1H_2 = K^{*2}) \end{aligned}$$

Table 1. Relationships between the molecular pK values of a dibasic acid and its other titration constants

Notes: (1) if $0 < \alpha < 1$ then proton binding is positively co-operative and no real titration pK values exist, because the titration curve is not then the sum of two one-site curves; (2) as positive co-operativity of proton binding becomes infinite, $\alpha \rightarrow 0$ and $q \rightarrow (2 + \sqrt{3})$; (3) a negative sign in front of either square-root sign has the same effect as one in front of the log term that contains it.

Molecular pK values	Values of pH at which the concentration of monoprotonated form is half maximal	Titration pK values
$pK^* \pm \log 2\alpha$	$pK^* \pm \log[\alpha + 2 + \sqrt{(\alpha + 2)^2 - 1}]$	$pK^* \pm \log[\alpha + \sqrt{\alpha^2 - 1}]$
$pK^* \pm \log(p+1/p)$		$pK^* \pm \log p$
$pK^* \pm \log(q-4+1/q)$	$pK^* \pm \log q$	

This justifies the expression given, since $\log(K_1/K^*)$ is half the difference between pK_1 and pK_2 , and H_1/K^* is q , so that $\log q$ is half the difference between pH_1 and pH_2 . Although the rearrangement is small, it may be useful, since it expresses the relationship explicitly in terms of pH and pK differences.

The above relationships are summarized in Table 1. They provide a simple way of deriving pK values from a bell-shaped curve of pH-dependence by reading the pH values, pH_1 and pH_2 , that make the dependent variable half-maximal, as well as their mean, pK^* , and letting $pH_2 - pH_1 = 2\log q$; the values of pK_2 and pK_1 are given by $pK^* \pm \log(q - 4 + 1/q)$. These can be used to plot a theoretical curve (see the Appendix) for comparison with the results.

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APPENDIX

The concentration of the monoprotonated form of a dibasic acid, expressed as a fraction of the sum of the concentrations of all forms of the acid, is $\alpha/(\alpha + \cosh x)$ where $x = 2.303(pH - pK^*)$. Hence the theoretical curve, expressed as a fraction of its own maximum, is $(\alpha + 1)/(\alpha + \cosh x)$ or $2(\alpha + 1)/(2\alpha + [H^+]/K^* + K^*/[H^+])$, so that determination

of α , i.e. $(q - 4 + 1/q)/2$ (which is equivalent to determining pK_1 and pK_2), allows this curve to be plotted. To find the value of the dependent variable that is characteristic of the monoprotonated form of a dibasic acid, allowance should be made for the fact that the maximal concentration of this form is a fraction $\alpha/(\alpha + 1)$ of the total concentration of the acid.