

A brief history of p(H,D) results

The practice of making corrections for changing between H₂O and D₂O was mentioned in a 1945 paper by Fischer and Potter¹—prior to the Covington et al.² and the Mikkelsen and Nielsen³ publications. They noted that commonly we are “... setting the instrument with normal water and applying a correction to the 'apparent pH'.” The correction they suggested for a glass/calomel system is +0.25 pD units at room temperature. In fact, only a year later in a paper from the same group recommending the 0.41 pH-unit correction,⁴ critically evaluated the values of ΔpK_a for 15 different weak acids. They were interested in checking an observation that ΔpK_a changed nearly linearly with pK_a^H , but found the relationship did not hold. In addition, the values of ΔpK_a were not described by adding a single value as suggested by Covington, et al.²

Many early papers dating back to the 1930s described the effects of D₂O on p(H,D) values for measurements on buffers using glass electrodes with H₂O internal filling solutions; the experimental values of ΔpK_a for the various acids and buffer systems that were used for testing were reported. As introduced above, the measurements covered in those papers did not show a consistent difference of 0.41 between D₂O and H₂O.

In a 1936 paper, Korman and La Mer⁵ reported ΔpK_a values for salicylic acid of 0.60 and for acetic acid of 0.48. (Other, later measurements of acetic acid found $\Delta pK_a = 0.509 \pm 0.006^6$ and $0.5132.^7$) In 1936, Schwarzenbach et al.,⁸ using a half cell consisting of the buffers in D₂O with a Pt|D₂ electrode measured versus a calomel electrode in H₂O connected by a capillary, reported *inter alia* for phosphoric acid $\Delta pK_{a1} = 0.206$ and $\Delta pK_{a2} = 0.461$ and for acetic acid $\Delta pK_a = 0.457$. In 1939, Martin and Butler⁹ reported dissociation constants obtained spectrophotometrically for a number of acids and also collected data from other publications to show that ΔpK_a exhibited a not quite monotonic increase as a function of the measured pK_a^H . But the ΔpK_a values ranged from 0.44 for chloroacetic acid to 0.57 for *o*-nitrophenol and 0.61 for 3,5-dinitrophenol.

Later papers confirmed the variations in ΔpK_a s. In 1941, Kingerley and La Mer¹⁰ found that at 25 °C for the H₂O dissociation, $pK_a^H = 13.97$, and for that of D₂O, $pK_a^D = 14.81$. That is, $\Delta pK_a = 0.838$. In 1960 Glasoe and Long¹¹ published a note showing that for a 0.01 M DCl pH ~2 solution, the value of pD measured was *lower* by 0.39 to 0.40 units with the same result for four different commercial glass pH electrodes. They also noted the ΔpK_a values for eight different acids, and their measured ΔpK_a values at

comparable ionic strengths varied between +0.20 and +0.63. But other than acetate, the buffers were not those that are now commonly used especially in biological *in vitro* solutions. Also, in approximate agreement with Covington et al.,² the earlier 1960 paper from Mikkelsen and Nielsen³ reported results from measuring the potential of a glass electrode against a calomel electrode in pure H₂O compared to the glass electrode against a calomel electrode with D₂O for both inside and outside solutions. They found that $pD = pH + 0.44$ at 22 °C. In 1964, Salomaa et al.¹² used a glass electrode filled with H₂O to measure the first ionization constants of phosphoric acid, arsenic acid, and acetic acid as they changed with D₂O content and ionic strength. The acetate buffer was also measured with conductivity, which produced the same result. Together, these measurements showed that the liquid junction potential did not contribute significantly to the p(H,D) measurement. In addition, the dependence on the D₂O content was slightly nonlinear, and the values of ΔpK_a were 0.20, 0.29, and 0.52 respectively. Then in 1966, Wehry and Rogers¹³ measured the ΔpK_a s for a number of substituted phenols spectrophotometrically. The ΔpK_a s do tend to increase with increasing pK_a^H ,^{5, 6, 9, 11, 14, 15} but the measured ΔpK_a varied over a range of 0.48 to 0.62 with the pK_a^H values ranging from 4.06 to 10.24. Even though there is a tendency to have a ΔpK_a increase with pK_a^H , it is not a hard and fast rule. For example Gold and Lowe⁶ found that acetic acid and borate with pK_a s of 4.8 and 9.2 have similar ΔpK_a values near 0.5. Later results confirmed the variations. In 1975, Lowe and Smith¹⁶ measured the dissociation constant of benzoic acid as a function of D₂O volume fraction both with conductance and with a glass electrode. They found the dissociation constants in H₂O and D₂O to be 4.201 ± 0.004 and 4.693 ± 0.004 , respectively; $\Delta pK_a = 0.492$ and essentially the same by both techniques. As noted in the descriptions above, a number of other groups have also seen a nearly linear dependence with the volume fraction of D₂O.^{5, 6, 11, 12, 17} And finally, in 1985 ΔpK_a s for glycine, alanine, and ethylenediamine—three buffers with pK_a values near 10—were measured.¹⁸ They have ΔpK_a values of 0.64, 0.67, and 0.57, respectively.

Supplement References

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