# Critical Evaluation of Stability Constants of Phosphonic Acids

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A. Popov, and A. Vendilo
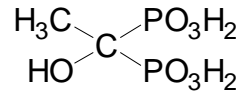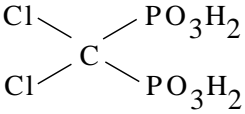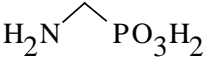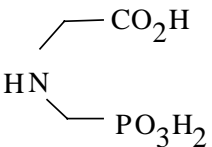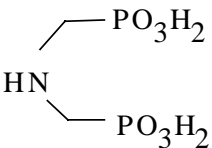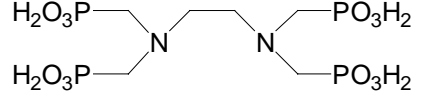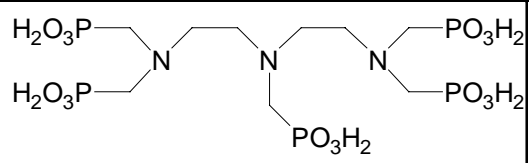
# Framework

Stability constants for aqueous equilibria are of extreme importance for a broad variety of technologies, agriculture, and medicine. Unfortunately, the data published usually reveal a drastic diversity, which sometimes exceeds several orders of magnitude. In this project, ten organophosphonates (Table 1) have been selected for evaluation and critically reviewed.

**Initial Observation**: <u>All</u> the data published on IDPH, NTPH, and EDTPH for the protonation equilibrium H+L=HL ($\log K_1$) seemed to be unreliable and could not be endorsed. The corresponding $K_{ML}$ values based on the erroneous $\log K_1$ also could not be accepted.
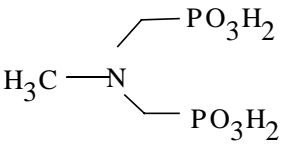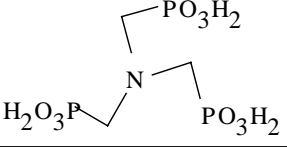    The cause seems to be that the removal of the last proton in this case, takes place at a very high pH, *e.g.,* 12-14, and determination by glass electrode is not adequate, while an alternative use of NMR in one run of experiments also appeared to be unreliable. This finding was reported in our critical review [1].

# Table 1.  Organophosphonates considered in this project

| Ligand common name | IUPAC recommended name | Ligand structure | Short Name |
|---|---|---|---|
| Methylphosphonic acid | Methylphosphonic acid | | MPA, $H_2$mpa |
| 1-Hydroxyethane-1,1-bis(phosphonic acid) | (1-Hydroxyethane-1,1-diyl)bis(phosphonic acid) |  | HEDPA, $H_4$hedpa |
| Dichlormethylenebis(phosphonic acid) | (Dichloromethylene)bis(phosphonic acid) |  | CMDPA, $H_4$cmdpa |
| Aminomethanephosphonic acid | (Aminomethyl)phosphonic acid |  | AMPH, $H_2$amph |
| N-(Phosphonomethyl)glycine | [(phosphonomethyl)amino]ethanoic acid |  | PMG, $H_3$pmg |
| Imino-N,N-bis(methylenephosphonic acid) | (iminodimethylene)bis(phosphonic acid) |  | IDPH, $H_4$idph |
| N-Methylamino-N,N-bis(methylenephosphonic acid) | [(methylimino)dimethylene]bis(phosphonic acid) |  | MIDPH, $H_4$midph |
| Nitrilotris(methylenephosphonic acid) | [Nitrilotris(methylene)]tris(phosphonic acid) |  | NTPH, $H_6$ntph |
| 1,2-Diaminoethane-N,N,N',N'-tetrakis(methylenephosphonic acid) | [Ethylenebis(nitrilodimethylene)]tetrakis(phosphonic acid) |  | EDTPH, $H_8$edtph |
| 1,4,7-Triazaheptane-N,N,N',N",N"-pentakis(methylenephosphonic acid) | {[(phosphonomethyl)imino]bis(ethylenenitrilodimethylene)}tetrakis(phosphonic acid) |  | DTPPH, $H_{10}$dtpph |

# Determination of a high protonation constant

Determination of a high protonation constant (p$K$~13-15) at the commonly used ionic strength $I$=0.1 mol·dm$^{-3}$ is a challenge for researchers. When the natural p$K$ value of a ligand at $I$= 0.1 mol·dm$^{-3}$ is higher than 12.5-12.8, its correct measurement by a single NMR titration procedure for $I$=0.1 mol·dm$^{-3}$ becomes physically impossible.

To overcome this problem, the following stepwise approach is proposed in the present study.

# Overcoming the measurement problem

As the first step, a set of NMR data for high ionic strength, *e.g.,* $I$=1.0 mol·dm$^{-3}$ , must be obtained at different pH values. This operation has  two advantages: (*i*) the p$K$ limit shifts from 12.5 to 13.5 - 13.7; and (*ii*) because K$^+$ (Na$^+$) ions form complexes with organophosphonates, the natural p$K$ becomes lower. These factors could make the "plateau" for chemical shift $\delta_L$ observable at pH<13. Generally, at a high [K$^+$]:[L] ratio, $\delta_L$ is a linear function of ionic strength.
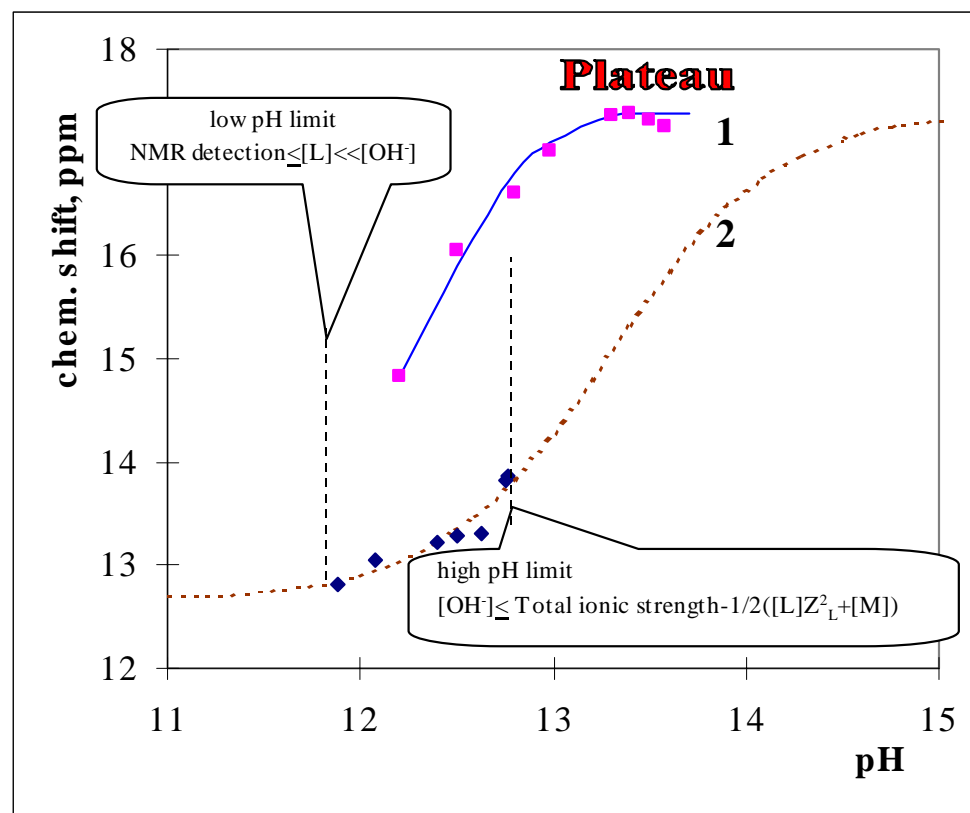


**Fig. 1.** pH dependence of the $^{31}$P NMR chemical shift $\delta$ of  EDTPH for $I$=1.0 (1)  and 0.1 (2) mol·dm$^{-3}$ (KOH/KNO$_3$) at 25 $^o$C

The second step includes a set of $\delta_L$ points at different ionic strengths, *e.g.* 1- 3 mol·dm$^{-3}$ , within the pH range, where $\delta_L$ is independent of pH.

An extrapolation of the resulting straight line to $I$=0.1 mol·dm$^{-3}$ gives a missing value of $\delta_L$* (*indicates the hypothetical numerical value of $\delta_L$, which is independent of pH and corresponds to $I$=0.1 mol·dm$^{-3}$).
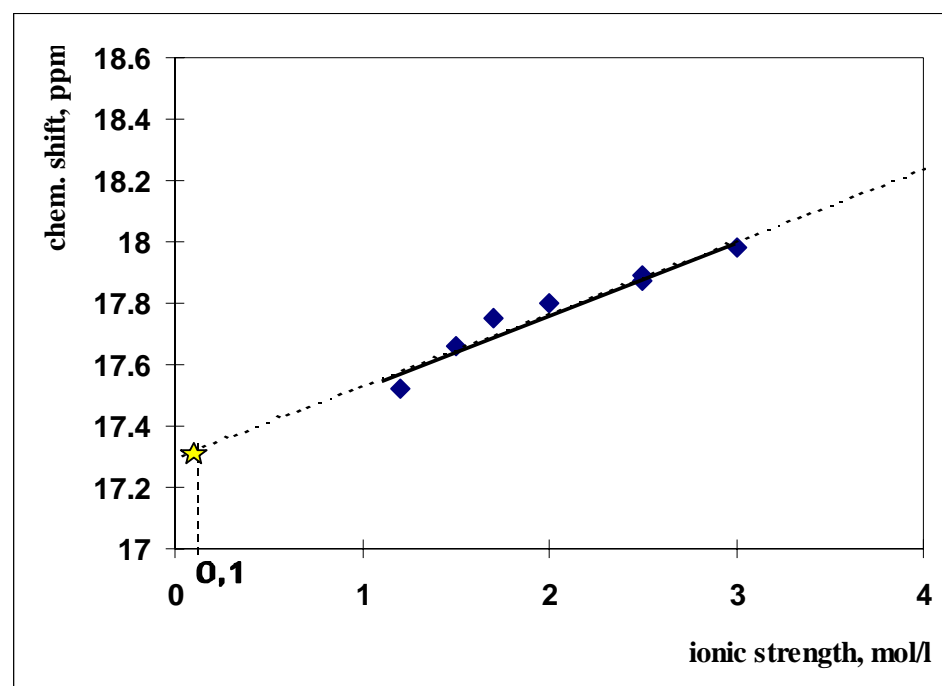


**Fig. 2.** Plot of $^{31}$P NMR chemical shift of EDTPH versus ionic strength $I$ mol·dm$^{-3}$ (KOH/KNO$_3$) at 25 $^o$C and pH 13.6 - 13.8

The third and the last step includes the measurement of d versus pH at $I$=0.1 mol·dm$^{-3}$ below the half-neutralization point and a subsequent treatment of the titration curve using experimental $\delta_{HL}$ and $\delta_L$* values.

The corresponding data for EDTPH are presented in Figures 1 - 3.
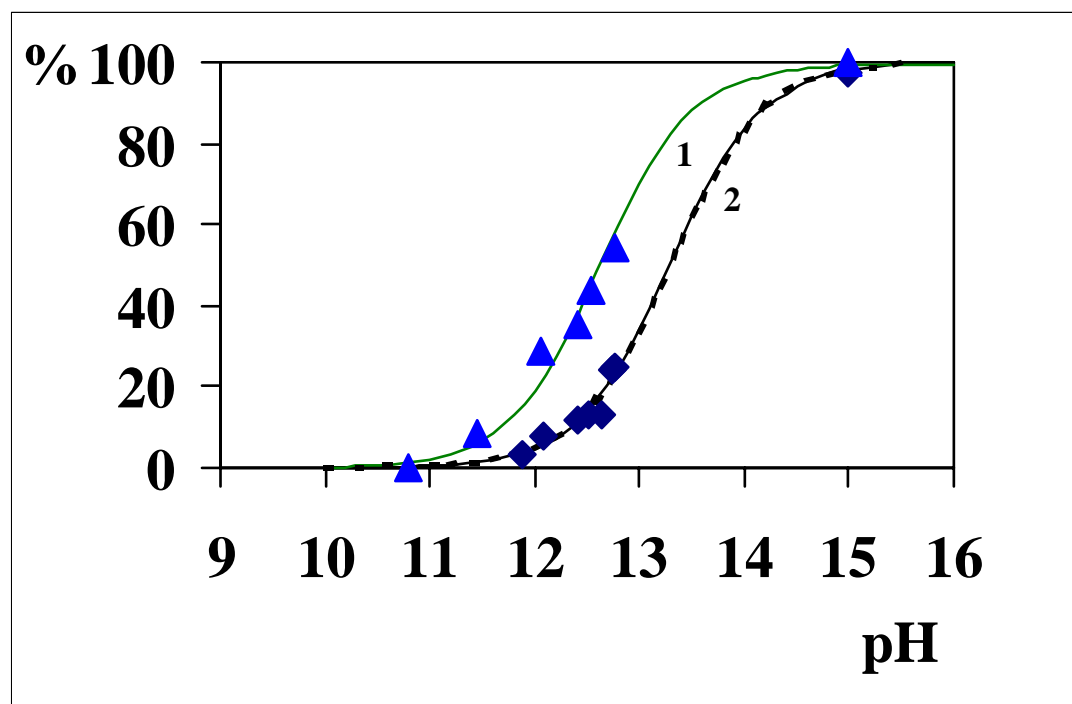


**Fig. 3.** Normalized NMR titration curves of EDTPH for $I$=0.15 mol·dm$^{-3}$ (NaOH/NaCl) at 37 $^o$C (1); and $I$=0.1 mol·dm$^{-3}$ (KOH/KNO$_3$) at 25 $^o$C (2)

- It should also be stressed that <u>all</u> experimental data obtained <u>are not based</u> on pH measurements. The concentration of ligand $C_L$ should meet the requirement $C_L \ll [OH^-]$, and the initial $[OH^-]$ is therefore taken as an equilibrium value of one. Then the pH is calculated using an appropriate $pK_w$ value.

- Our data are presented in Table 2, along with those obtained with a glass electrode and via a single run NMR titration, which could not provide the ionic strength constancy. The results reveal a general, sometimes very large, underestimation of the $\log K_1$ values for organophosphonates ranging from 0.1 up to 2.7 log units.

**Table 2.** Equilibrium Constants $K_1$ of IDPH, NTPH, and EDTPH

| Ligand | Method | I, mol dm$^{-3}$ | T, $^{\circ}$C | log$K_1$ | $\Delta$ log$K_1$ | Reference |
|---|---|---|---|---|---|---|
| IDPH | NMR $^{31}$P | 0.1 M KNO$_3$ | 25 | 11.2 | | this work |
| | glass electrode | 0.2 M KCl | 25 | 10.97 | 0.23 | 2 |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 10.79 | 0.41 | 3 |
| | glass electrode | 0.2 M KCl | 25 | 10.60 | 0.6 | 4 |
| NTPH | NMR $^{31}$P | 0.1 M KNO$_3$ | 25 | 12.9 | | this work |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 12.8 | 0.1 | 7 |
| | glass electrode | 0.2 M KCl | 25 | 12.30 | 0.6 | 2 |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 12.5 | 0.4 | 5 |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 12.1 | 0.8 | 6 |
| | NMR $^{31}$P | 0.1 M KNO$_3$ | 25 | 12.7 | 0.2 | 7 |
| | glass electrode | 0.2 M KCl | 25 | 12.27 | 0.63 | 8 |
| EDTPH | NMR $^{31}$P | 0.1 M KNO$_3$ | 25 | 13.3 | | this work |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 12.9 | 0.4 | 9 |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 13.07 | 0.23 | 10 |
| | glass electrode | $\rightarrow$0.1 M KNO$_3$ | 25 | 13.1 | 0.2 | 11 |
| | glass electrode | 0.1 M KNO$_3$ | 25 | 10.60 | 2.7 | 12 |
| | NMR $^{31}$P | 0.15 M NaCl | 37 | 12.6 | | this work |
| | glass electrode | 0.15 M NaCl | 37 | 10.67 | 1.93 | 13 |

# References

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