Acid-base and complexation properties of *gem*-diphosphonic and *gem*-diphosphinic acids in aqueous solutions and micellar media of surfactants

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Acid-base and complexation properties of *gem*-disubstituted phosphorus acids, *viz.*, methylenediphosphonic, 1-hydroxyethylidene-1,1-diphosphonic, *P*,*P*´-diphenylmethylenediphosphinic, and *P*,*P*´-diphenyl-1-hydroxyethylidene-1,1-diphosphinic acids, were studied in aqueous solutions and in the presence of biomimetics (micelles of ionic surfactants). The dissociation constants of the acids and stability constants of complexes with magnesium(II) and copper(II) ions were determined in aqueous solutions and microheterogeneous media containing sodium dodecyl sulfate, cetylpyridinium chloride, or cetylpyridinium nitrate (ionic strength 0.1 mol L^{-1}, temperature 25 °C).

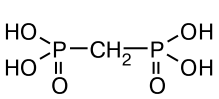
Key words: *gem*-diphosphonic acids, *gem*-diphosphinic acids, dissociation constants, complexation, micelles, surfactants, potentiometry.

Diphosphonates containing P—C—P bonds, which are structural analogs of pyrophosphates, possess pronounced biological activity and find use in therapeutics.[1] Among the most studied substances of this class are 1-hydroxyethylidene-1,1-diphosphonic acid (HEDP) and its salts. They are used as medicines (regulators of calcium metabolism, stabilizers of cell membranes, for the treatment of tumor and rheumatoid diseases); an antisclerotic effect of diphosphonates and their positive influence on the immune system and genetic apparatus of cells were observed.[1,2] An interest in studying the acid-base and complexation properties of HEDP and its analogs is caused by important practical applications.

Published data on chemical equilibria obtained mainly for aqueous or mixed solutions do not reflect the specificity of behavior of a reagent in biological systems, being microheterogeneous media. In the presence of biological microaggregates, quantitative characteristics of chemical equilibria can change compared to those of aqueous solutions. More adequate models of biological systems (biomimetics) are considered to be organized solutions containing diphilic microaggregates of surfactants, such as micelles, vesicles, and bilayers.[3] That is the reason why micellar solutions of surfactants were chosen as media for studying equilibria of biologically active *gem*-diphosphonic acids. In addition, surfactants themselves act sometimes as components of pharmaceutical preparations. The use of micellar solutions of surfactants is known, for example, for controlling the hydrolytic stability of organophosphorus medicines.[4]

To establish specific features of the behavior of *gem*-diphosphonic acids, it seemed of interest to compare their equilibria with those of their phosphinic prototypes, namely, *gem*-diphosphinic acids in which one OH group at each phosphorus atom is replaced by an alkyl or aryl group.

We chose four acids for the study: two *gem*-diphosphonic acids, *viz.*, methylenediphosphonic (**1**) and 1-hydroxyethylidene-1,1-diphosphonic (**2**) acids, and two *gem*-diphosphinic acids with phenyl substituents at the phosphorus atom, *viz.*, *P*,*P*´-diphenylmethylenediphos-



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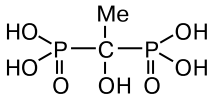

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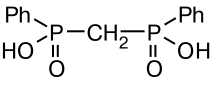

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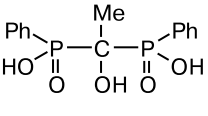

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phinic (**3**) and *P*,*P*′-diphenylhydroxyethylidene-1,1-diphosphinic (**4**) acids, the latter being synthesized from acetyl chloride and $PhPCl_2$.

$$MeC(O)Cl + 2\ PhPCl_2 \xrightarrow{H_2O} \mathbf{4}$$

The purpose of this work is to characterize the acid-base properties of diphosphonic acids and their phosphinic analogs and the equilibria of their complexation with copper(II) and magnesium(II) ions in aqueous solutions and in organized solutions of an anionic surfactant (sodium dodecyl sulfate (SDS)) and cationic surfactants (cetylpyridinium chloride (CPC) or cetylpyridinium nitrate (CPN)).

Experimental

Objects of study were methylenediphosphonic acid (**1**) (Aldrich) (m.p. 197—199 °C, neutralization equivalent (found/calculated) 176.00/176.00) and 1-hydroxyethylidene-1,1-diphosphonic acid (**2**) (monohydrate, m.p. 104—105 °C, neutralization equivalent (found/calculated) 224.04/224.04). Both substances were purified by recrystallization. The characteristics of the samples used corresponded to the published data.

P,*P*′-Diphenylmethylenediphosphinic acid (**3**) was synthesized and purified as described previously.[5]

***P*,*P*′-Diphenyl-1-hydroxyethylidene-1,1-diphosphinic acid (4).** A mixture of acetyl chloride (6 g, 0.076 mol) and $PhPCl_2$ (3.8 g, 0.019 mol) was stored for 15 min at 50 °C and cooled to ~20 °C, and water (0.7 mL, 0.04 mol) was added. The resulting mixture was heated for 1 h at 50 °C. Excess acetyl chloride was distilled off at 110 °C. Water (0.2 mL) was added to the residue, and the mixture was stored for 0.5 h at 110 °C. After cooling, a glassy mixture was extracted with water, and a precipitate (2 g), formed on staying from an aqueous extract, was doubly recrystallized from ethanol. Acid **4** (0.9 g) was obtained in 29% yield, m.p. 195—197 °C. Found (%): C, 51.32; H, 4.84; P, 19.17. $C_{14}H_{16}O_5P_2$. Calculated (%): C, 51.53; H, 4.90; P, 19.02. ^{31}P-{^1H} NMR (ethanol), δ: 32.9 (s). Neutralization equivalent (found/calculated): 326.00/326.00.

Materials and reagents. Carbonate-free doubly distilled water and $Mg(NO_3)_2 \cdot 6H_2O$, $MgCl_2 \cdot 6H_2O$, $Cu(NO_3)_2 \cdot 3H_2O$, NaOH, $NaNO_3$, KNO_3, and NaCl (reagent grade or analytical purity grade) were used to prepare solutions. Commercial preparations of sodium dodecyl sulfate (Sigma) with the weight fraction of the main substance at least 99% and cetylpyridinium chloride (Acros) with the weight fraction of the main substance at least 99% were used as received. To exclude a negative influence of chloride on a Cu^{2+}-selective electrode, cetylpyridinium nitrate (CPN) synthesized by a previously described procedure[6] was used in measurements with this electrode. The content of the main substance in CPN was determined by the iodometric titration of excess potassium bichromate unreacted with a cationic surfactant.[7] The concentrations of the starting solutions of Mg^{II} and Cu^{II} were determined complexonometrically. Carbonate-free solutions of NaOH were prepared from a saturated solution of NaOH and standardized by weighed samples of adipic acid with phenolphthalein as indicator.

Potentiometric studies were performed at 25.0±0.1 °C in a cell with a liquid bridge of the capillary—ground joint type filled with a 2 *M* aqueous solution of KNO_3. Acid-base equilibria of *gem*-disubstituted phosphorus acids were studied by pH-metric titration with an ESL-63-07 glass electrode. Complexation was studied by competitive pH-metry and direct potentiometry with a Cu^{2+}-selective chalcogenide solid-phase electrode, and an EVL-1M3 electrode was used as a reference electrode. The emf values were measured using a compensation scheme (R-307 potentiometer, a pH-121 pH-meter as a null-instrument) with an error of at most ±0.2 mV. A pH-metric cell was calibrated by standard buffer solutions with pH 3.56 and 9.18. A cell with a Cu^{2+}-selective electrode was calibrated by solutions containing $1 \cdot 10^{-4}$ and $1 \cdot 10^{-3}$ mol L^{-1} $Cu(NO_3)_2$ at a constant ionic strength (*I*) of 0.1 mol L^{-1} ($NaNO_3$). Calibrating solutions for a Cu^{2+}-selective electrode, which contained the same amount of a surfactant as the solutions under study, were used for measurements in a surfactant medium. It has previously[8] been found with metal-containing buffer solutions that the potential of a Cu^{2+}-selective electrode in aqueous and micellar solutions obeys the Nernst equation in a region of low concentrations of unbound Cu^{2+} ions up to pCu values of 11.

The concentration of the acids under study in titrated solutions was $1.0 \cdot 10^{-3}$ mol L^{-1} (in the presence of CPN, $1.0 \cdot 10^{-4}$ mol L^{-1}), and the volume of a titrated solution was 20 mL. For studying acid-base equilibria, titration curves contained 20—40 points in a region of pH 2.5—10.5. A supporting electrolyte for the creation of a ionic strength (0.1 mol L^{-1}) was $NaNO_3$ or NaCl. Complexation was studied at a metal : ligand ratio of 1 : 1. In CPC-based media (supporting electrolyte NaCl), $MgCl_2$ was used as magnesium salt, and in other cases (supporting electrolyte $NaNO_3$) magnesium and copper nitrates were used.

When studying acid-base equilibria and complexation, the surfactant concentration (0.05 mol L^{-1} SDS, 0.1 mol L^{-1} CPC, and 0.0125 mol L^{-1} CPN) was chosen in such a way that the concentration of micelles calculated from the aggregation numbers and critical micelle concentration (CMC) achieved a concentration of *gem*-disubstituted phosphorus acids. Under the experimental conditions, the CMC for SDS is $2 \cdot 10^{-3}$ mol L^{-1} and that for CPC is $6 \cdot 10^{-4}$ mol L^{-1}.

A slow equilibration during the titration of **1** in the presence of cations has previously[9] been reported. We did not reveal these specific features in experiments. In similar experiments on the titration of acid **1**, as well as on the titration of other *gem*-disubstituted phosphorus acids, the pH values were established during 10—20 min and remained unchanged within ±0.003 pH units.

Potentiometric titration data were processed according to the CLINP program,[10] which makes it possible to refine models of interactions simultaneously with the calculation of equilibrium constants.

The complexation of Na^+ ions with anions of acids **1** and **2** were taken into account when pK_{a3} and pK_{a4} were determined and stability constants of the complexes in aqueous solutions were calculated using the published data.[11,12] For acid **1** (I = 0.1 mol L^{-1}),[11] $\log K(HL^{3-}+Na^+)$ = 0.84, $\log K$ ($L^{4-}+2Na^+$) = 2.64. For acid **2**,[12] the data concerning I = 0.5 mol L^{-1} were reduced to I = 0.1 mol L^{-1} by the estimation of the activity coefficients using the Davis equa-

tion. The obtained values of $\log K(HL^{3-}+Na^+) = 0.55$ and $\log K(L^{4-}+Na^+) = 1.35$ were used in further calculations.

No correction to the complexation of acids **3** and **4** with the Na^+ ion was introduced, assuming that these acids do not form complexes (or form very weak complexes) with the Na^+ ion (published data are lacking).

^{31}P NMR spectra were recorded on a Bruker AMX-400 instrument using 85% H_3PO_4 as external standard.

Results and Discussion

Acid-base properties of *gem*-disubstituted phosphorus acids in aqueous solutions and micellar solutions of surfactants. Published data on the dissociation constants of *gem*-disubstituted phosphorus acids in aqueous solutions relate to different supporting electrolytes: Me_4NCl (**1** [13,14] and **2** [11,13,15]), KCl (**1** [9] and **2** [9,16,17]), NaCl (**2** [15,18]), $NaClO_4$ (**2** [19]), Et_4NClO_4 (**2** [20]), and KNO_3 (**2** [21] and **3** [5]). We used sodium salts as supporting electrolytes, because the anionic surfactant itself (SDS) contains Na^+ ions. In aqueous and micellar solutions of SDS and CPN, a ionic strength in solutions of 0.1 mol L^{-1} was maintained by $NaNO_3$ additives, and in CPC solutions it was provided by NaCl additives.

Since a contribution, made by charged surfactant microaggregates to the ionic strength, cannot be estimated unambiguously,[22,23] the ionic strengths of micellar solutions were calculated ignoring self-aggregation when a ionic surfactant can formally be considered as a strong electrolyte. The true ionic strength of micellar solutions, at least SDS solutions, is somewhat lower than this estimate.[22] To evaluate a correctness of this assumption, in some experiments in micellar solutions we created higher formal ionic strengths than those in aqueous solutions: 0.12 and 0.15 mol L^{-1}. However, it turned out that the variation of the ionic strength in this region exerts an insignificant effect on the equilibrium constants. When the ionic strength changed from 0.1 to 0.15 mol L^{-1}, the maximum change in $\log K$ was observed for the reactions involving the tetracharged anions of acid **2** and amounted to 0.1 log. units (protonation reactions) and 0.2 log. units (complexation).

At a chosen level of concentrations of the acids under study, it seems impossible to determine some dissociation constants of *gem*-disubstituted phosphorus acids (Table 1), because the method of potentiometric titration makes it possible to determine (with a sufficient accuracy) only constants K_{ai}, whose values range in the interval[24,25]

$$C > K_{ai} > K_W/C,$$

where C is the concentration of the protolyte under study.

The dissociation of the aliphatic hydroxy group (pK_{a3} for **4**, pK_{a5} for **2**) was not considered for both acids containing this group. According to the NMR data, for acid **2** $pK_{a5} > 14.5$.[26] As known, in the most cases of complexation, the aliphatic group of acid **2** is not coordinated and is not dissociated or is coordinated without dissociation.[1] Thus, acids **2** and **4** were considered in the framework of this study as tetra- (H_4L) and dibasic (H_2L) acids.

Table 1. Parameters of the mixed dissociation constants (pK_a) of *gem*-disubstituted phosphorus acids **1**—**4** (25 °C; $I = 0.1$ mol L^{-1})

Acid	pK_a[a]	Medium (supporting electrolyte)		
		H_2O ($NaNO_3$)	SDS ($NaNO_3$)	CPC (NaCl)
1	pK_{a1}	—	—	—
	pK_{a2}	2.64±0.11	2.96±0.03	—
	pK_{a3}	6.67±0.04	6.88±0.05	5.53±0.05
	pK_{a4}	9.80±0.07	9.75±0.06	7.21±0.10
2	pK_{a1}	—	—	—
	pK_{a2}	2.82±0.04	3.16±0.06, 3.11±0.04[b]	2.45±0.12, 2.40±0.16[c]
	pK_{a3}	7.05±0.05	7.24±0.07, 7.17±0.04[b]	6.15±0.06, 6.08±0.03[c]
	pK_{a4}	9.98±0.03	10.02±0.04, 9.92±0.05[b]	8.12±0.06, 8.02±0.05[c]
3	pK_{a1}	2.79±0.10	3.07±0.07, 3.06±0.07[b]	2.52±0.19, 2.50±0.20[c]
	pK_{a2}	3.47±0.04	3.54±0.05, 3.46±0.04[b]	3.44±0.03, 3.39±0.06[c]
4	pK_{a1}	3.05±0.14	2.80±0.20, 2.80±0.19[b]	2.37±0.19, 2.35±0.17[c]
	pK_{a2}	6.06±0.06	6.02±0.04, 5.99±0.07[b]	5.99±0.05, 5.94±0.04[c]

[a] The half-width of the confidence interval was calculated from the mean square error (root-mean-square deviation) with a confidence probability of 0.95.
[b] $I = 0.12$ mol L^{-1}.
[c] $I = 0.15$ mol L^{-1}.

The values obtained for the mixed dissociation constants (pK_{ai}) for the acids under study are presented in Table 1. The dissociation constants (K_{ai}) correspond to the following equations (charges are not indicated)

$$H_{n-i+1}L \rightleftharpoons H_{n-i}L + H,$$

$$K_{ai} = [H_{n-i}L](H)[H_{n-i+1}L]^{-1}.$$

The $pK_{ai}(H_2O)$ values found for acid **2** agree rather well with the most reliable values recommended by IUPAC.[1,27] Some discrepancy in pK_{a4} is due, most likely, to a low accuracy of the complexation constants with Na^+ used[11,12] in the calculations and, in addition, the latter were corrected (see Experimental).

Probably, pK_{a4} for acid **1** is markedly lower than the published[9,12,13] value for the same reason. The other $pK_{ai}(H_2O)$ values for acid **1** differ insignificantly from the published data. This can be explained by the use of different supporting electrolytes and/or different ionic strengths.

The data for aqueous solutions of acid **3** somewhat differ from the earlier published values[5] ($pK_{a1} < 1$, $pK_{a2} = 3.71\pm0.02$, 0.1 mol L^{-1} KNO_3). An estimate of $pK_{a1} < 1$ seems to be underestimated, because the studies[5] were carried out at the acid concentration of 0.005 mol L^{-1}, which does not allow one to determine $pK_{a1} < 2$. Minor differences in pK_{a2} are likely caused by the use of different supporting electrolytes.

gem-Diphosphonic acids **1** and **2** are almost completely dissociated by the first step ($pK_{a1} < 2$) in both aqueous solutions and organized solutions of surfactants. *gem*-Diphosphinic acids having a Ph group at each phosphorus atom (**3** and **4**) dissociate by the first step as acids of moderate strength in all solutions (see Table 1).

The pK_{ai} values of all *gem*-disubstituted phosphorus acids increase in the presence of anionic microaggregates (SDS) and decrease compared to aqueous solutions in the presence of cationic (CPC) surfactants. In particular, acid **1** in a medium of cationic CPC micelles dissociated as a strong acid by both the first and second steps (see Table 1).

Such character of changing pK_{ai} in a medium of ionic surfactants is observed for protolytes solubilized by surfactant microaggregates.[7,28] The main body of data kind was obtained for acid-base indicators.[7,28] Similar effects were observed for reagents of other classes,[29—32] in particular, phosphorus-containing compounds.[29—31] The influence of anionic (SDS) and cationic (cetyltrimethylammonium bromide and cetyltrimethylammonium chloride) surfactants on the dissociation of aminoalkyl phosphonates, 2-dimethylaminomethylphenol, and bis(chloromethyl)phosphinic *p*-nitroanilide was explained by the electrostatic interaction of the acidic and basic species of the protolyte with the surface of charged micelles and was described using binding constants for each species.[29,30,32]

gem-Diphosphonic (**1** and **2**) and *gem*-diphosphinic (**3** and **4**) acids belong to different types according to Izmailov´s classification.[33]

The influence of a microheterogeneous medium on the properties of protolytes can be caused by the binding of particular protolytic species by surfactant microaggregates due to hydrophobic and electrostatic interactions. The contribution of these effects to the measured dissociation constant will differ for acids of different chemical types. It can be expected that electrostatic interactions will be more significant for tetrabasic *gem*-diphosphonic acids, while hydrophobic interactions will have almost the same significance for dibasic *gem*-di(phenylphosphinic) acids.

The role of the electrostatic component increases with the elimination of each subsequent proton and an increase in the negative charge of the dissociation product. In the case of cationic surfactants, the electrostatic interaction favors binding of the dissociation products. Therefore, the completeness of the binding of the dissociation products of *gem*-disubstituted phosphorus acids by the micellar pseudo-phase of cationic surfactants should increase with the elimination of protons and, hence, the influence of cationic surfactants on pK_{ai} should enhance on going to higher dissociation steps.

This is the same character of the CPC influence that is observed for *gem*-diphosphonic acids **1** and **2** (see Table 1). The $\Delta pK_{ai}(H_2O—CPC)$ values increase on going from one dissociation step to another from 0.37 ± 0.13 to 1.86 ± 0.07 for acid **2** and from 1.14 ± 0.06 to 2.59 ± 0.12 for acid **1**.

In the case of anionic surfactants, the electrostatic interaction prevents the dissociation products to bind. Micelles of anionic surfactants should most strongly bind the neutral species $(H_nL)^0$; therefore, the effect of a micellar medium is more pronounced in the initial dissociation steps. The $\Delta pK_{ai}(SDS—H_2O)$ values decrease on going from one dissociation step to another from 0.32 ± 0.11 to -0.05 ± 0.09 for acid **1** and from 0.34 ± 0.07 to 0.04 ± 0.05 for acid **2** (see Table 1). It is most likely that tri- and tetracharged anions, which are the products of the last dissociation steps (HL^{3-} and L^{4-}), exist completely in the aqueous phase bulk, because the corresponding dissociation constants in the presence of SDS are virtually the same as those in aqueous solutions.

As a whole, the influence of the cationic surfactants on the acidic properties of *gem*-diphosponic acids is more significant than that of the anionic surfactants. Unlike solutions of SDS, solutions of CPC have a differentiating effect on the strength of these acids. As known, a medium is considered to be differentiating if the difference between the dissociation constants of two electrolytes is higher than that in water. The values $\Delta pK_{ai}(\mathbf{2} - \mathbf{1}) = pK_{ai}(\mathbf{2}) - pK_{ai}(\mathbf{1})$ in aqueous solutions and SDS-based solutions are almost the same (Table 2), whereas $\Delta pK_{ai}(\mathbf{2} - \mathbf{1})$ in CPC-based solutions are several times higher than those in aqueous solutions.

Table 2. Values of ΔpK_{ai} for pairs of *gem*-diphosphonic (**1**, **2**) and *gem*-diphosphinic (**3**, **4**) acids (25 °C; $I = 0.1$ mol L^{-1})

Pairs of acids	ΔpK_a*	Medium (supporting electrolyte)		
		H_2O ($NaNO_3$)	SDS ($NaNO_3$)	CPC (NaCl)
2—1	pK_{a1}	—	—	—
	pK_{a2}	0.18±0.12	0.20±0.07	—
	pK_{a3}	0.38±0.06	0.36±0.09	0.62±0.08
	pK_{a4}	0.18±0.08	0.27±0.07	0.91±0.12
4—3	pK_{a1}	0.26±0.17	−0.27±0.21	−0.15±0.27
	pK_{a2}	2.59±0.07	2.46±0.06	2.55±0.06

* The half-width of the confidence interval was calculated from the mean square error (root-mean-square deviation) with a confidence probability of 0.95.

Dibasic *gem*-di(phenyl-substituted) phosphinic acids are electrolytes of moderate strength by the first dissociation step. The presence of hydrophobic Ph groups at each phosphorus atom should unambiguously affect the binding of particular species by surfactant microaggregates, and contributions from the electrostatic and hydrophobic components can be compensated.

Solutions of the anionic surfactant (SDS) have approximately the same effect on the acidic properties of **3** as on the acidic properties of phosphonic analogs **1** and **2**. However, in the case of acid **4**, the effect is almost absent even in the first dissociation step. An enhancement of the acidic properties in a medium of the cationic surfactants is reliably detected only in the first dissociation steps of *gem*-di(phenyl-substituted) phosphinic acids (or, more rigidly, only for **4**). Unlike phosphonic prototypes, for which the dissociation enhances (pK_{ai} decreases) in CPC solutions with an increase in the negative charge of participants of the corresponding equilibrium, the dissociation constants by the second steps of *gem*-di(phenyl-substituted) phosphinic acids in the presence of CPC remain almost unchanged and the differentiating effect of micellar solutions on the acids of this group is absent (see Table 2). This situation indicates that the molecules of *gem*-di(phenyl-substituted) phosphinic acids are weakly bound by surfactant microaggregates and the products of their dissociation are not virtually bound.

Complexation of magnesium(II) and copper(II) ions with anions of *gem*-disubstituted phosphorus acids. According to published data, in aqueous solutions the anions of acid **1** interact with Mg^{2+} to form the complexes[9,14,34] MgL^{2-} and $MgHL^{-}$, whereas with Cu^{2+} they form the complexes[9] CuL^{2-}, $CuHL^{-}$, CuL_2^{6-}, $CuHL_2^{5-}$, Cu_2L, and Cu_2HL^{+}. Data on the composition of metal complexes with acid **2** presented by independent authors are rather contradictory, because they were obtained at different metal to ligand ratios and in different acidity intervals.[9,11,20,21,35–39] Both anions of acid **2** with the nondissociated aliphatic hydroxy group[11,20] (L^{4-} or HL^{4-})[35,36] and the $H_{-1}L$ species, whose aliphatic hydroxy group is dissociated,[9,21,37–39] were considered as ligands. However, in the last case, almost all complexes found contain one or several protons.[9,37–39] The exceptions are binuclear complexes[9,37] $Mg_2H_{-1}L^{-}$ and $Cu_2H_{-1}L^{-}$ and a complex $Cu(H_{-1}L)_2^{8-}$ formed in strongly alkaline solutions in excess ligand.[39] It is assumed[37] that in binuclear complexes the oxygen atom of the deprotonated hydroxy group in the anion of acid **2** acts as a bridging moiety.

The complexation of Mg^{II} and Cu^{II} with ligands **3** and **4** were not studied earlier.

When processing the experimental data, we verified the hypotheses about the formation of the following complexes: ML^{2-}, MHL^{-}, MH_2L, MH_3L^{+}, $MOHL^{3-}$, $M(HL)_2^{4-}$, $M(H_2L)_2^{2-}$, M_2L, ML_2^{6-} for acids **1** and **2**; ML, MHL^{+}, MH_2L^{2+}, $MOHL^{-}$, $M(HL)_2$, M_2L^{2+}, and ML_2^{2-} for acids **3** and **4**.

Table 3. Logarithms of the concentration stability constants ($\log K$)[a] of the complexes of *gem*-disubstituted phosphorus acids **1—4** with Mg^{2+} and Cu^{2+} (25 °C; I = 0.1 mol L^{-1})

Complex	Medium (supporting electrolyte)		
	H_2O ($NaNO_3$)	SDS ($NaNO_3$)	CPC (NaCl)[b] CPN ($NaNO_3$)[c]
	1 (H_4L)		
MgL^{2-}	5.71±0.05	4.83±0.04	—
$MgHL^{-}$	2.78±0.19	2.52±0.09	2.86±0.08
$MgOHL^{3-}$	10.66±0.15	9.46±0.14	7.28±0.18
CuL^{2-}	9.82±0.03	9.22±0.08	—
$CuHL^{-}$	8.04±0.06	7.5±0.3	6.06±0.03
	2 (H_4L)		
MgL^{2-}	6.87±0.06	5.75±0.06	5.15±0.02
$MgHL^{-}$	4.01±0.06	3.52±0.19	3.17±0.03
CuL^{2-}	11.28±0.06	10.99±0.05	7.71±0.11
$CuHL^{-}$	8.45±0.11	7.64±0.08	—
	3 (H_2L)		
MgL	4.15±0.10	3.93±0.08	3.52±0.04
CuL	4.14±0.02	4.73±0.02	4.37±0.02
CuL_2^{2-}	7.09±0.09	—	—
	4 (H_2L)		
MgL	4.78±0.19	4.29±0.10	3.68±0.06
CuL	4.94±0.06	5.75±0.04	—
CuL_2^{2-}	9.71±0.08	—	9.60±0.04

[a] The half-width of the confidence interval was calculated from the mean square error (root-mean-square deviation) with a confidence probability of 0.95.
[b] For studying complexation with Mg^{II}.
[c] For studying complexation with Cu^{II}.

The final models of complexation and logarithms of the overall concentration stability constants of the ML and ML_2 complexes and the formation constants of the hydroxo- and proton-containing complexes according to the reactions shown below (hereinafter the charges are not presented) are given in Table 3.

$$M + L \rightleftharpoons ML,\ K = [ML][M]^{-1}[L]^{-1},$$

$$M + HL \rightleftharpoons MHL,\ K = [MHL][M]^{-1}[HL]^{-1},$$

$$M + L + OH \rightleftharpoons MOHL,\ K = [MOHL][M]^{-1}[L]^{-1}[OH]^{-1},$$

$$M + 2\,L \rightleftharpoons ML_2,\ K = [ML_2][M]^{-1}[L]^{-2}.$$

The study of complexes with complexone **2** could not either confirm or reject an assumption about the displacement of a proton of the aliphatic hydroxy group by the complex-forming agent according to the reaction

$$M^{2+} + L^{4-} - H^{+} \rightleftharpoons (MH_{-1}L)^{3-}.$$

Taking into account this reaction in the case of Mg^{2+} somewhat improved the description of the experimental potentiometric data at pH > 7.5, although the maximum yield of the complex did not reach 10%. It is also known[1] that for the most part of cations, including alkaline-earth and 3d metals (M^{2+}), the formation of these species can be neglected. Therefore, this reaction was not included into the final models.

Under the experimental conditions (concentration of *gem*-disubstituted phosphorus acids $1 \cdot 10^{-3}$ mol L^{-1}, ratio M : L = 1 : 1), polynuclear complexes and complexes with $\log K_i < 3$, where K_i is the stepwise stability constant equal to $[ML_2][ML]^{-1}[L]^{-1}$, are not virtually formed.

A comparison of the stability constants of the complexes of acids **3** and **4** confirmed the earlier found[34,37] regularity for the complexes of acids **1** and **2**, namely, the presence of an aliphatic hydroxy group in the ligand increases the stability of the complex. Phosphinic acids form less stable complexes than their phosphonic analogs do (*cf.*, the values for acids **1** and **3**, **2** and **4** in Table 3), which is due to a decrease in the electrostatic interaction with a complex-forming cation with a decrease in the charge of coordinating groups. The effects of the aliphatic hydroxy group and Ph groups observed for complexation in aqueous solutions are retained on going to micellar solutions.

The influence of a micellar surfactant medium on the stability of complexes is caused by differences in binding of a complex-forming cation, a ligand, and a complex by microaggregates of the medium or monomers of a surfactant.[7,40] The binding of complex-forming cations by anionic SDS micelles can be described using binding constants[6] K_b corresponding to the equilibrium

$$M^{2+} + m \rightleftharpoons (M^{2+})_m,$$
$$K_b = [M^{2+}]_m/\{[M^{2+}](C - CMC)\},$$

where M^{2+} is the metal ion in the solution bulk, $(M^{2+})_m$ is the micellarly bound metal ion, $[M^{2+}]$ and $[M^{2+}]_m$ are the concentrations referred to the overall volume of the solution, and C is the overall concentration of an anionic surfactant.

For Cu^{2+} ions in a solution with a SDS concentration of 0.05 mol L^{-1}, $\log K_b = 2.34 \pm 0.03$ was found.[6] Since the binding of inorganic cations by SDS micelles is caused by the electrostatic interaction and is not specific,[41] it can be assumed that $\log K_b$ for the Mg^{II} ions is close to the value obtained for Cu^{II}.

Cationic micelles of CPC bind anionic ligands, which is indicated by the results of studying the dissociation of *gem*-disubstituted phosphorus acids. Anionic complexes should be bound by the same micelles to a less extent, because the charges of the complexes are lower than those of the corresponding ligands.

Taking into account processes of binding of reactants by the micellar pseudo-phase, we can understand why the stability of the complexes decreases on going from aqueous solutions to micellar media. The stability of the Mg^{II} complexes with all *gem*-disubstituted phosphorus acids decreases in the series: aqueous solution > SDS > CPC. The stability constants of the Cu^{II} complexes with the anions of acids **1** and **2** decrease in the same sequence (see Table 3). An analogous decrease in the stability in micellar solutions of SDS was observed[40] for the Cu^{II} complexes with iminodiacetate, which effect was explained by the competitive action of anionic heads of surfactants.

The influence of the micellar medium on the stability of the Cu^{II} complexes with the anions of acids **3** and **4** has somewhat different character. The pK_{a2} values of these acids remain almost unchanged on going from aqueous solutions to micellar media (see Table 1). It follows from this that the anions of these acids (L^{2-}) are not bound to a noticeable extent by either cationic or, the more so, anionic micelles. The stability of the uncharged CuL complexes of acid **4** in a medium of anionic SDS micelles increases, whereas the stability of the anionic CuL_2^{2-} complexes decreases to such an extent that they are not virtually detected at a copper(II) concentration of $1 \cdot 10^{-3}$ mol L^{-1}. In a medium of cationic CPC and CPN micelles, on the contrary, the anionic complex of acid **4** CuL_2^{2-} that formed is stabilized, most likely, by the electrostatic interaction with cationic micelles or monomers of CPC and CPN. However, the complexes of acid **3**, which are less stable than the complexes of acid **4**, behave in a different manner: on going to micellar media, the stability of the CuL complex somewhat decreases and the complex CuL_2^{2-}, whose $\log K_i < 3$ even in aqueous solutions, is not virtually formed.

Thus, in both aqueous solutions and organized solutions of surfactants, phosphinic acids are weaker than their phosphonic analogs. The presence of substituents in the methylene bridge in both groups of compounds lowers, as a rule, the acidity of the reagent in all media studied.*

The acidic properties of *gem*-disubstituted phosphorus acids change in a characteristic manner in the presence of biomimetics (micelles of surfactants). In the presence of cationic microaggregates, the acidic properties of the compounds under study enhance and, in the presence of anionic surfactants, weaken in comparison with aqueous solutions (except for acid **4**, whose acidity remains unchanged within the experimental error). The binding of the more highly charged anions by cationic micro-

* Acid **4** is an exception: its acidity by the first step in micellar media within the experimental error is almost equal to the acidity of unsubstituted analog **3**.

aggregates enhances and the binding by anionic microaggregates weakens as dissociation of the acids occurs. Correspondingly, the effect of the cationic micellar phase enhances, and the effect of the anionic phase weakens with dissociation.

As a whole, the strength of *gem*-diphosphonic acids decreases in the series: cationic surfactants (CPC) > aqueous solutions > solutions of anionic surfactants (SDS). The same tendency is observed for the dissociation of *gem*-diphosphinic acids by the first step. The dissociation constants of these acids by the second step remain unchanged in the presence of surfactants.

The influence of substituents on the stability of the complexes is the same for aqueous solutions and micellar media of surfactants. The presence of substituents in the methylene bridge of the ligand enhances the stability of the complexes with magnesium(II) and copper(II) ions. *gem*-Di(phenyl-substituted) phosphinic acids form less stable complexes than their phosphonic analogs.

On going from aqueous solutions to microheterogeneous surfactant media, the stability of the Mg^{II} complexes with all ligands and the Cu^{II} complexes with the anions of *gem*-diphosphonic acids decrease in the series: aqueous solutions > SDS > CPC. The common feature of the complexation of Cu^{II} with *gem*-diphosphinic ligands, which are not virtually bound by surfactant micelles, is an increase in the stability of the uncharged CuL complexes in a medium of anionic SDS micelles. In some cases, the model of complexation changes on going from water to micellar media.

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