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Dissociation Constants of Morpholino- and Piperidino-methylphosphonic Acids and Stability Constants of Their Copper, Nickel, and Zinc Complexes

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Dissociation constants (K_a) of morpholinomethylphosphonic acid, piperidinomethylphosphonic acid, and the well-known pH buffer morpholinopropylsulfonic acid were determined potentiometrically at $I = 0.1$ mol dm^{-3} NaCl ionic strength at (25 ± 0.5) °C. Stability constants for Cu^{2+}−, Ni^{2+}−, and Zn^{2+}−morpholinopropylsulfonate and −piperidinomethylphosphonate complexes were determined.

Introduction

Recently, investigations have been made of the NMR spectra of morpholinomethylphosphonic acid (MMPA) and piperidinomethylphosphonic acid (PMPA) in aqueous solution.[1,2] However, there are no investigations that have reported the dissociation constants of these aminophosphonic acids or the stability constants of their transition-metal complexes, but Lukes et al.[3] have investigated the dissociation constant of the related piperidinomethylphosphinic acid ($(CH_2)_4NH^+CH_2PHO_2^-$) and stability constants of complexes formed with Mg, Ca^{2+}, Pb^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, and Zn^{2+}. The aim of this work was to measure, by potentiometric titration, the dissociation constants of MMPA and PMPA and the stability constants of their complexes with Cu^{2+}, Ni^{2+}, and Zn^{2+}. The dissociation constants of the well-known pH buffer morpholinopropylsulfonic acid (MOPS) were determined for comparison.

Experimental Section

Chemicals. Samples of MMPA and PMPA (99% pure containing one molecule of crystal water) were provided by Dr. Lockhart.[1,2] Morpholinopropylsulfonic acid (MOPS, 98% pure) was a commercial sample (Sigma). Solutions (0.05 mol dm^{-3}) were made up of each. AnalaR NaOH/NaCl (BDH) or $(CH_3)_4NCl/(CH_3)_4NOH$ (Aldrich) was used as the titrant/background electrolyte. The titrants were calibrated against BDH ConvoL hydrochloric acid. Solutions (0.01 mol dm^{-3}) of $Cu(NO_3)_2\cdot 3H_2O$, $ZnCl_2$, and $Ni(NO_3)_2\cdot 6H_2O$ (BDH) were prepared. Potassium hydrogen phthalate (0.05 mol dm^{-3}) was prepared from a BDH AnalaR reagent.

Titration Procedure. The Molspin (Newcastle upon Tyne) automatic titration system,[4] interfaced to a PC, was used with a 10 cm^3 syringe, a glass electrode, and a calomel reference electrode (Russell pH (Auchtermuchty)). The filling solution of the ceramic junction reference electrode was 3.5 mol dm^{-3} KCl. Electrodes were calibrated with potassium hydrogen phthalate buffer at pH 4.008. The titration cell (100 cm^3) was controlled at 25 ± 0.5 °C, stirred by magnetic follower, and purged with nitrogen gas. Ten milliliters of 0.1 mol dm^{-3} alkali ($(CH_3)_4NOH$ or NaOH) was put into the motor-driven syringe (increment volume 0.03−0.05 mL.) The 360 titration data points collected were analyzed using SUPERQUAD.[5]

Results and Discussion

Titration reaction curves with NaOH showed three end points for MMPA. PMPA showed only two clear end points; the expected third could not be distinguished because of the high value of pK_{a3}.

pK_a values are shown in Table 1 for aminoalkylphosphonic acids and phosphonic acid. pK_a values of the latter were determined and found to be exactly the same as given by Martell and Smith.[6] Compared with methylphosphonic acid values, phosphonic acid values are smaller. As the number of methylene groups increases in the alkylphosphonic acids, pK_a values increase (Table 1), as is also true with the aminophosphonic acids. Literature values of pK_a values for aminomethylphosphonic acid (AMPA)[7] are 0.44, 5.39, and 10.05, those for MMPA are 1.09, 5.10, and 8.83, and those for PMPA are 2.39, 5.35, and 11.00. pK_{a1} and pK_{a2} values relate to the phosphonate group and pK_{a3} values relate to the imino of the morpholino group. For comparison, pK_{a1} of morpholine (without a phosphonate group) is 8.72, and pK_a of piperidine is 11.16. The pK_{a1} value of methylphosphonic acid (MPA),[8,9] without the imino group, is fairly close to the pK_{a1} value of PMPA. Differences between the values of pK_{a2} depend on the alkyl chain length of the compound. Lukes et al.[3] obtained 8.41 for pK_{a1} of PMP, which is close to pK_{a3} of MMPA. Thus, pK_{a1} and pK_{a2} values relate to the hydroxyls of the phosphonic group and the pK_{a3} value relates to the imino group of MMPA and PMPA. pK_{a3} of MMPA is 8.83, but for PMPA the value is 11.00 because of the oxygen in the morpholine ring in MMPA. A redetermined pK_a value of the imino group of 8.72 for morpholine compares well to the value of 8.70 reported by Bruchlman and Verhoek.[10] The pK_a of piperidine has been given as 11.12 by Bjerrum,[11] and this is in accord with the present pK_{a3} value of PMPA of 11.00. The pK_{a1} and p$K_{a2\ \text{values}}$ of MMPA and PMPA are in the same regions. Table 2 shows the effect of changing the background media to tetramethylammonium chloride on the protonation constants of MMPA, PMPA, and MOPS.

Some experiments were carried out with the morpholino group-containing pH buffer substance, MOPS (Table 1). For

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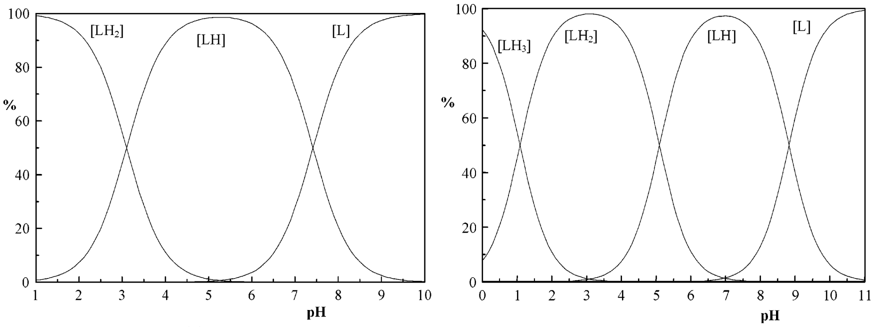
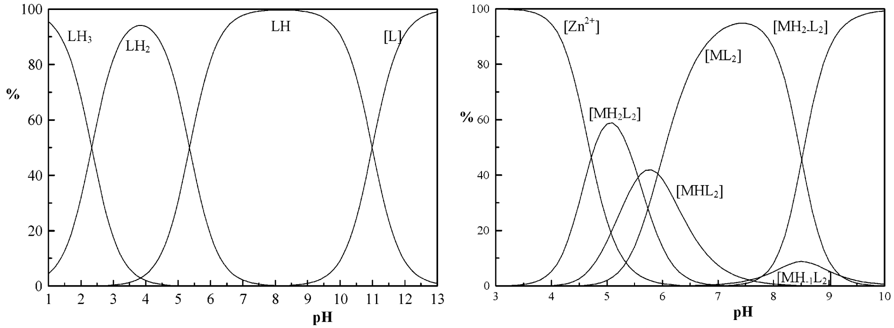
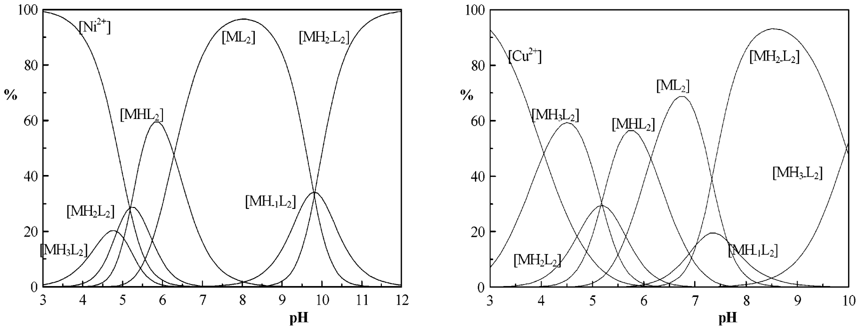


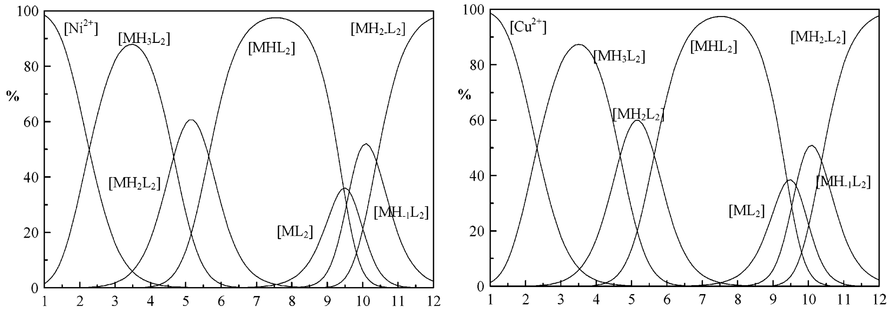
(a) MOPS (b) MMPA



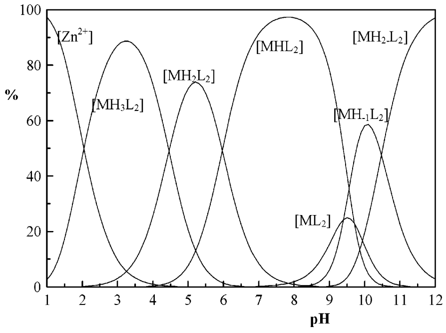
(c) PMPA (d) Zn-PMPA



(e) Ni-PMPA (f) Cu-PMPA



(g) Ni-MMPA (h) Cu-MMPA



(i) Zn-MMPA

Figure 1. Species distribution curves for (a) MOPS, (b) MMPA, (c) PMPA, (d) Zn−PMPA, (e) Ni−PMPA, (f) Cu−PMPA, (g) Ni−MMPA, (h) Cu−MMPA, and (i) Zn−MMPA in 0.1 mol dm^{-3} NaCl at 25 ± 0.5 °C.

Table 1. Acid Dissociation Constants in Aqueous Media at (25 ± 0.5) °C and I = 0.1 mol dm^{-3}

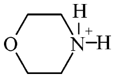
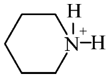
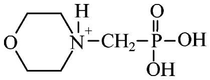
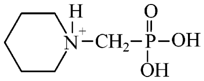
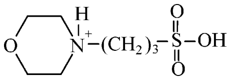
ligand	chemical structure (fully protonated form)	pK_{a1}	pK_{a2}	pK_{a3}	ref
morpholine		8.72			this work
		8.70			10
piperidine		11.12			11
morpholinomethylphosphonic acid (MMPA)		1.09	5.10	8.83	this work
piperidinomethylphosphonic acid (PMPA)		2.39	5.35	11.00	this work
morpholinopropylsulphonic acid (MOPS)		3.10	7.42		this work
			7.20		12
piperidinomethylphosphinic acid (PMP)	$(CH_2)_5NH^+CH_2PHO_2$		8.41		3
phosphonic acid (phosphorous acid) (PA)	H_3PO_3	1.50	6.79		6
		1.50	6.79		this work
methylphosphonic acid (MPA)	$CH_3PO_3H_2$	2.30	7.10		8
		2.12	7.29		9
aminomethylphosphonic acid (AMPA)	$^+NH_3CH_2PO(OH)_2$	0.44	5.39	10.05	7
		1.85	5.35	10.00	13
2-aminoethylphosphonic acid (AEPA)	$^+NH_3(CH_2)_2PO(OH)_2$	1.12	6.24	11.05	7
		2.45	7.00	10.8	13
3-aminopropylphosphonic acid (APPA)	$^+NH_3(CH_2)_3PO(OH)_2$	2.60	7.65	11.00	13

Table 2. Dissociation Constants for MMPA and PMPA for I = 0.1 mol dm^{-3} NaCl or $(CH_3)_4NCl$) at (25 ± 0.5) °C

dissociation constants	I = 0.1 mol dm^{-3} NaCl		I = 0.1 mol dm^{-3} $(CH_3)_4NCl$	
	MMPA	PMPA	MMPA	PMPA
pK_{a1}	1.09	2.39		2.17
pK_{a2}	5.10	5.35	5.16	5.39
pK_{a3}	8.83	11.00	8.93	10.99

this ligand, the pK_{a2} value is in agreement with the literature value[12] but slightly lower than those of MMPA and PMPA. The pK_{a1} value was obtained by the prior addition of HCl to protonate the sulfonate group of MOPS.

Similar experiments were conducted with tetramethylammonium hydroxide $(CH_3)_4NOH$) and tetramethylammonium chloride $(CH_3)_4NCl$) as the background at the same concentration. No significant differences were found (Table 2) except that the pK_{a2} value for PMPA is slightly lower with $(CH_3)_4NCl$. The pK_{a1} of MMPA could not be obtained because of the low concentration of ligand used.

Stability constants are given in Table 3 for M^{2+}−MMPA and −PMPA complexes. Their magnitude is in the order Ni > Cu > Zn for the complex ML_2. The values of other complexes are the same for Ni and Cu, but their Zn values are higher. For all M^{2+}−MMPA systems, ML_2, MHL_2, MH_2L_2, MH_3L_2, $M(OH)L_2$, and $M(OH)_2L_2$ complexes were found, and their stability constants are shown in Table 3. No values could be found in the literature for these species nor for M^{2+}−PMPA complexes shown in Table 3. The order of the stability constant values is Cu > Zn > Ni for all species, but all are much higher for M^{2+}−MMPA, which could be due to the piperidino ring in the PMPA molecule. No lgβ_{132} value was obtained with Zn−PMPA, which was found for Zn−MMPA. In contrast, an lgβ_{1-32} value has been found in the high-pH region of the Cu−PMPA system. Species distribution curves are shown in Figure 1a−i.

Table 3. Stability Constants of M^{2+}−MMPA and −PMPA Complexes (I = 0.1 mol dm^{-3} NaCl and 25 ± 0.5 °C)

species	[Ni^{2+}]	[Cu^{2+}]	[Zn^{2+}]
		MMPA	
ML_2	10.57 ± 0.02	10.57 ± 0.08	10.47 ± 0.04
MHL_2	20.04 ± 0.03	19.97 ± 0.10	20.18 ± 0.06
MH_2L_2	25.68 ± 0.04	25.60 ± 0.09	26.14 ± 0.10
MH_3L_2	30.33 ± 0.03	30.27 ± 0.07	30.59 ± 0.07
$MH_{-1}L_2$	0.95 ± 0.02	0.92 ± 0.08	1.07 ± 0.06
$MH_{-2}L_2$	−9.44 ± 0.02	−9.45 ± 0.06	−9.40 ± 0.02
		PMPA	
ML_2	17.57 ± 0.02	18.45 ± 0.03	18.21 ± 0.02
MHL_2	23.86 ± 0.03	24.58 ± 0.05	24.12 ± 0.05
MH_2L_2	29.05 ± 0.03	29.75 ± 0.05	29.68 ± 0.04
MH_3L_2	33.90 ± 0.1	34.94 ± 0.05	
$MH_{-1}L_2$	7.78 ± 0.03	10.81 ± 0.05	8.99 ± 0.04
$MH_{-2}L_2$	−2.05 ± 0.03	3.78 ± 0.03	1.19 ± 0.02
$MH_{-3}L_2$		−6.18 ± 0.03	

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Literature Cited

(1) Lowe, M. P.; Lockhart, J. C.; Matthews C. J.; Clegg, W.; Elsegood M. R. J.; Horsburgh, L. NMR, crystal structure and FAB mass

spectral studies of morpholinomethylphosphonic acid. *J. Chem. Soc., Perkin Trans. 2* **1994**, *9*, 1957−1963.

(2) Lowe, M. P.; Lockhart, J. C. Nuclear magnetic resonance studies of 4-hydroxypiperidinomethylphosphonic acid and its polyoxomolybdate conjugates *J. Chem. Soc., Dalton. Trans.* **1995**, *21*, 3511−3519.

(3) Lukes, I.; Bazakas, K.; Hermann, P.; Vojtisek, P. Aminomethylenephosphinic Acids and their Complexing Properties. *J. Chem. Soc., Dalton Trans*. **1992**, 939−944.

(4) Pettit, L. D. *Molspin Software for Molspin pH Meter*; Sourby Farm: Timble, Otley, U.K., 1992.

(5) Gans, P.; Sabatini A.; Vacca, A. SUPERQUAD: an improved general program for computation of formation constants from potentiometric data. *J. Chem. Soc., Dalton Trans.* **1985**, 1195−1200.

(6) Martell, A. E.; Smith, R. M. *Critical Stability Constants*; New York: Plenum Press, 1974.

(7) Wozniak, M.; Nowogrocky, G. Acidites et complexes des acides (alkyl- et aminoalkyl-) phosphoniques−II: Affinement multiparametrique applique aux complexations suivies par potentiometrie. *Talanta* **1978**, *25*, 633−641.

(8) Kluger, R.; Wasserstein, P.; Nakaota, K. Factors Controlling Association of Magnesium Ion and Acyl Phosphates. *J. Am. Chem. Soc.* **1975**, *97*, 4298−4303.

(9) Borisov, M. S.; Elesin, A. A.; Lebedev, I. A.; Piskunov, E. M.; Filimenev, V. T.; Yakovlev, G. N. Formation of complexes of trivalent Americium, Curium and Promethium with Methylphosphonic acids. *Radiokhimiya* **1967**, *9*, 166.

(10) Bruchlman, R. J.; Verhoek, F. H. The Basic Strengths of Amines as Measured by the Stabilities of Their Complexes with Silver Ions. *J. Am. Chem. Soc*. **1948**, *70*, 1401−1404.

(11) Bjerrum, J. On the Tendency of the Metal Ions toward Complex Formation. *Chem. Rev*. **1950**, *46*, 381−401.

(12) Sankar, M.; Bates, R. G. Buffers for the Physiological Range: Thermodynamic Constants of 3-(*N*-Morpholino)propanesulfonic Acid from 5 to 50 °C. *Anal. Chem*. **1978**, *50*, 1922.

(13) Chavane, V. Aminomethanephosphonic acid. *Ann. Chim. (Paris)* **1949**, *12*, 383.

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