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Re-evaluated data of dissociation constants of alendronic, pamidronic and olpadronic acids

Invited Paper

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Abstract: The dissociation constants of (4-amino-1-hydroxybutylidene)bisphosphonic (alendronic) acid, (3-(dimethylamino)-1-hydroxypropylidene)bisphosphonic (olpadronic) acid and (3-amino-1-hydroxypropylidene)bisphosphonic (pamidronic) acid were obtained in aqueous solutions (0.10 M KCl) and micellar solutions of cetylpyridinium chloride (0.10 M CPC) at 25.0°C. With the exception of the third dissociation constant of alendronic acid, the dissociation constants of alendronic, olpadronic and pamidronic acids in aqueous solutions matched literature data. The possibility of sodium alendronate determination by acid-base titration by NaOH solution was theoretically grounded on the basis of re-evaluated data of alendronic acid dissociation constants.

Keywords: *Alendronate • Olpadronate, pamidronate, dissociation constant • Micellar media effect*

1. Introduction

Sodium salts of (4-amino-1-hydroxybutylidene) bisphosphonic (alendronic) acid, (3-(dimethylamino)-1-hydroxypropylidene)bisphosphonic (olpadronic) acid and (3-amino-1-hydroxypropylidene)bisphosphonic (pamidronic) acid are successfully used for the medical treatment of bone diseases, such as osteoporosis, Paget disease, metastatic bone diseases, *etc.* [1]. Thus, numerous pharmaceutical formulations that contain these active substances have been developed [2]. The analysis of aminobisphosphonic acids is an interesting problem. The use of chromatographic methods introduced several problems: 1) UV-Vis or fluorescent detection can not be used owing to lack of chromophores in the molecule; 2) conventional reversed-phase liquid chromatography (RP-HPLC) is not a good choice, because aminobisphosphonates are hydrophilic and ionized in the pH range used with reversed-phase silica based columns and strong metal chelating ability causes adsorption problems; 3) gas chromatography can not be used due to insufficient volatility of aminobisphosphonates.

Several high-performance liquid chromatographic methods based on post- or precolumn derivatization of bisphosphonates have been developed [3-11]. For example, Ion-pair chromatography with mass-spectrometric [12], refractive index [13] and conductometric [14] detection have been proposed. The anion-exchange chromatography with refractive index detection is recommended by British Pharmacopoeia for the determination of sodium alendronate [15]. Most chromatographic analysis of aminobisphosphonates have required extensive sample preparation, the use of a non-routine detector and a special column and/or apparatus.

In addition to chromatographic methods, the spectrophotometric method after derivatization of alendronate with o-phthalaldehyde [7] and titrimetric method [16] were proposed for alendronate determination. The acid-base titrimetric method will be quite useful for routine analysis of sodium alendronate due to its accuracy, simplicity and low cost. Therefore, most of pharmacopoeia methods of active substance quantification are titrimetric. However, the theoretical basis of determination of sodium alendronate by acid-base titration is complicated by very close third, fourth and fifth dissociation constant of alendronic acid [17] (Table 1). Moreover, alendronic acid is very weak by the third dissociation step (Table 1). As a result, the acid-base titration of sodium alendronate should be problematic (Fig. 2, curve 1).

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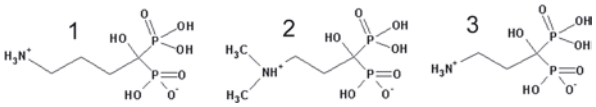

Figure 1. Zwitterionic structures of alendronic (1), olpadronic (2) and pamidronic (3) acids

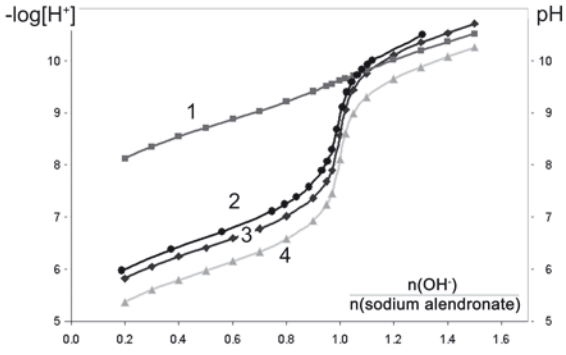

Figure 2. Calculated and experimental titration curves of 0.02 M sodium alendronate with 0.04 M alkali solution.

1 – Calculated curve by using pK_a values from ref. [17];
2 – Experimental curve obtained in aqueous solution;
3 – Calculated curve by using pK_a values obtained in this work in aqueous solution;
4 – Calculated curve by using pK_a values obtained in this work in micellar CPC solution.

Table 1. Indexes of dissociation constants of aminobisphosphonic acids

	Literature data			This work	This work
	0.1 M KCl [17][1]	0.2 M KCl [20][2]	0.1 M [21][3]	0.1 M KCl	0.1 M CPC
Alendronic acid					
pK_{a2}	2.72±0.05	2.16	2.22	2.24±0.01[4]	2.34±0.02[4]
pK_{a3}	8.73±0.05	6.21	6.39	6.38±0.03	5.97±0.02
pK_{a4}	10.5±0.1	10.77	10.96	10.68±0.06	10.25±0.03
pK_{a5}	11.6±0.1	12.04	11.82	11.4±0.2	10.5±0.1
Olpadronic acid					
pK_{a2}	2.55±0.05				
pK_{a3}	5.83±0.05			5.97±0.03[5]	5.39±0.03[5]
pK_{a4}	9.9±0.1			9.75±0.05	9.35±0.06
pK_{a5}	10.8±0.1			10.96±0.14	10.30±0.08
Pamidronic acid					
pK_{a2}	2.35±0.05		1.93		
pK_{a3}	5.89±0.05		6.04	6.01±0.01[5]	5.39±0.01[5]
pK_{a4}	9.7±0.1		10.18	9.97±0.02	9.46±0.02
pK_{a5}	10.8±0.1		12.14	10.74±0.05	10.40±0.04

[1]concentration of aminobisphosphonic acids 1.0 × 10^{-3} M; pH-potentiometric titration, calibrated by standard pH buffers; 25.0°C
[2]concentration of aminobisphosphonic acids 2.0 × 10^{-3} M; pH-potentiometric titration, calibrated in hydrogen ion concentration, 25.0°C
[3]concentration of aminobisphosphonic acids from 2.0 × 10^{-3} to 8.0 × 10^{-3} M; pH-potentiometric titration at 25.0°C and $^{31}P\{^1H\}$NMR pH titration at 22°C, calibrated by blank titration
[4]5.0 × 10^{-3} M sodium alendronate; 25.0°C; K_{a2} is stoichiometric constant; K_{a3} - K_{a5} are mixed constants; for other conditions see Experimental Procedures
[5]1.0 × 10^{-3} M olpadronic or pamidronic acid; 25.0°C; K_{a3} - K_{a5} are mixed constants; for other conditions see Experimental Procedures

The dissociation constants of alendronic acid have been obtained [17] and are widely cited by other authors and referral databases [18]. However, it is interesting that other authors [20,21] have determined different dissociation constants of alendronic acid and have not dissolved this discrepancy. On the other hand, the stability constants of copper complexes with alendronic acid have been determined [22] without observation of disagreement between dissociation constants obtained in the previous works [17] and [20]. Thus, the determination of reliable dissociation constants of alendronic acid and its analogs are of primary importance. They will be useful for modeling and prediction of the technological, environmental and pharmaco-kinetic equilibria, waste management *etc.*

In this work the dissociation constants of alendronic, olpadronic and pamidronic acids in aqueous solutions were re-evaluated. This should confirm or reject the possibility of sodium alendronate determination by acid-base titration in aqueous solutions. The dissociation constants of alendronic, olpadronic and pamidronic acid were also determined in micellar solutions of cationic surfactant cetylpyridinium chloride (CPC), because it is known that the strength of an acid increases in the presence of cationic micelles [23]. This observation allows the development of simple titrimetric methods of aminobisphosphonates determination in pharmaceutical formulations. Moreover, micelles of surfactants are often considered as adequate models of biological membranes and the data of dissociation constants of aminobisphosphonates in CPC media can be useful for modeling the behavior of drugs in biological systems [19].

2. Experimental Procedures

2.1 Reagents and standard solutions

Certified reference material (CRM) of sodium alendronate trihydrate tested by pharmacopoeia method [15] was kindly donated by Join-stock company «Stoma», Kharkov, Ukraine. The olpadronic and pamidronic acids were synthesized and purified in A.N. Nesmeyanov Institute of Organoelement Compounds, Russia. Tablets "Sodium alendronate" containing 10 mg of sodium alendronate were purchased in a Ukrainian pharmacy. The cetylpyridinium chloride was purchased from Merck. The 0.100 M HCl solution was prepared from analytically grade concentrated HCl and standardized by titration of weighted amounts of Na_2CO_3. Carbonate-free 0.100 M KOH solution was prepared by technique described in [24] and standardized by titration of weighted amounts of adipinic acid. Carbonate-free 0.100 M NaOH solution was prepared from saturated NaOH solution and standardized by titration of weighted amounts

of adipinic acid. Working solutions of HCl, NaOH and KOH were prepared by appropriate dilution of standard solutions before titrations. The working solution of tetraethylammonium hydroxide was prepared from 10% (w/w) analytical grade solution of tetraethylammonium hydroxide by appropriate dilution. Analytical grade KCl was used for preparation of supporting electrolyte. Acid-base indicators thymol blue and phenolphthalein were used as provided from Ukrainian suppliers.

2.2 Apparatus

The electromotive force was measured with using a compensation scheme (P-307 potentiometer, a pH-121 pH-meter as a null-instrument) with standard deviation of at most 0.2 mV. The glass electrode ESL-63-07 and silver/silver chloride electrode EVL-1M3 as a reference electrode were used. The titrations were performed at 25.0 ± 0.1°C in a cell with glass electrode, reference electrode and salt bridge. Calibrations of potentiometric cell were conducted using standard buffer solutions with pH 1.68, 3.56, 4.01, 6.86, and 9.18.

2.3 Procedure of dissociation constants determination

The dissociation constants of alendronic, olpadronic and pamidronic acids were determined based on the pH titrations. The concentration of sodium alendronate was 5.00×10^{-3} M, the concentrations of olpadronic and pamidronic acids were 1.00×10^{-3} M, and the volume of titrated solution was 20 mL. The first dissociation constant of alendronic acid, and first and second dissociation constants of olpadronic and pamidronic acids could not be calculated because values of dissociation constants are higher than concentration of acids in titrated solution. The second dissociation constant of alendronic acid was calculated from data of sodium alendronate titration with 5.00×10^{-3} M HCl. The third, fourth and fifth dissociation constants were calculated from data of sodium alendronate titration with 1.50×10^{-2} M KOH. The three dissociation constants of olpadronic and pamidronic acids were calculated by titration of their solutions with concentration 1.00×10^{-3} M with 4.00×10^{-3} M KOH. The potassium hydroxide was used as titrant to prevent the formation of complexes with Na^+ that was observed for some bisphosphonic acids [23, 25]. The concentration of KCl as supporting electrolyte was 0.10 M for titrations in aqueous solutions. When studying acid-base equilibria in micellar media the concentration of CPC was 0.10 M. The titration curves were generated based on the 20 data points for pK_{a2} calculation of alendronic acid and from the 40 data points for pK_{a3}, pK_{a4}, pK_{a5} calculation. The titration curves of olpadronic and pamidronic acids consisted of approximately 40 data points and these curves were used to calculate the dissociation constants. Since the aminobisphosphonates were titrated in a basic medium for determination of pK_{a3}-pK_{a5} the influence of carbon dioxide had to be prevented by using nitrogen. The nitrogen was purified according to known procedure [24] and used for excluding of carbon dioxide from titration vessel.

2.4 Software and processing

The data of potentiometric titrations for dissociation constants determination were treated by CLINP 2.1 program (http://www.bestnet.kharkov.ua/kholin/clinp.html). The titration curves of sodium alendronate were modeled by program EQUIL 1.1 developed by Prof. A. Bugaevsky on the basis of Cruise algorithm [26]. The dissociation constants calculated in replicate titrations were averaged by taking into account the variance for each constant and correlations between constants for each replicate titration [27]. This approach was realized by using MATLAB 7.0 (http://www.mathworks.com).

3. Results and discussion

Alendronic, olpadronic and pamidronic acids (Fig. 1) have six functional groups that could be ionized: five H^+ donors (four POH groups, geminate OH group) and one amino group as H^+ acceptor. The zwitterion is the most probable structure of the electroneutral forms of alendronic, olpadronic and pamidronic acids [28,29]. The dissociation of the geminate OH group of bisphosphosphonates in aqueous solutions was not observed up to pH 13 [22,30]. The pK_{a1} values of alendronic and olpadronic acids that corresponds to the dissociation of -POH group in cationic acid H_5L^+ with the formation of zwitterion were obtained [21] by using NMR-controlled titrations. These pK_{a1} were around 1 for alendronic and olpadronic acids. It is evident that application of the standard titrimetric procedure for pK_a determination does not allow calculating of pK_{a1} [31] due to minor presence of H_5L^+ form in the equilibrium state of alendronic, olpadronic and pamidronic acids solutions with concentration around 5.00×10^{-3} M. Thus, the protolytic properties of alendronic, olpadronic and pamidronic acids in pH range from 2 to 13 can be described in terms of four dissociation steps: pK_{a2}, pK_{a3}, pK_{a4} (related with dissociation of POH groups) and pK_{a5} (related with dissociation of NH_3^+ group) [32].

3.1 Dissociation constants of alendronic, olpadronic and pamidronic acids in aqueous solution

The alendronic, olpadronic and pamidronic are the middle-strong acids by the second step of dissociation [17]. Thus, the two points must be taken into account for pK_{a2} determination: the concentration of acids should be higher then the value of dissociation constant [31]; the concentration of hydrogen ions should be considered in mass-balance equations by estimation of their concentration from measured pH values. To calculate the concentration of hydrogen ions from pH values and correctly include them into the mass-balance equations the activity coefficient of hydrogen ions in aqueous solution was obtained by equation (1):

$$\lg \gamma_H = \frac{-0.5\sqrt{I}}{1+3.29a\sqrt{I}} - bI \qquad (1)$$

where I – ionic strength, *a* and *b* – coefficients that are changed for different supporting electrolytes (for KCl a = 6.1; b = 0.113 [33]). Thus, the calculated pK_{a2} of alendronic acid can be expressed in concentration units.

The obtained pK_{a2} of alendronic acid is 0.5 logarithmic units lower than the previously obtained values (Table 1). However, this value is more reliable, because the concentration of alendronic acid in solution was 5.00×10^{-3} M, which is five times more than in the previous report [17]. This allows increasing the yield of form $H_4L^{\pm}$ to 30% from the total concentration of alendronic acid. Moreover, pK_{a2} is equal to previously reported pK_{a2} values [20,21] if the uncertainty of their determination is taking into account. The lower concentration of olpadronic and pamidronic acids than sodium alendronate in titrated solutions did not allow for the reliable estimation of their pK_{a2} values.

The pK_{a3} – pK_{a5} values obtained in this work are mixed constants, because the activity of hydrogen ions was used for their calculations. The pK_a values for alendronic, olpadronic, pamidronic acids in aqueous solutions are close to mixed constants obtained previously [17] (the unknown method [17] of dissociation constants calculation and estimation of their uncertainties do not allow for the directly comparison of data). The one exception is pK_{a3} of alendronic acid, which in our work is lower [17], but well agreed with pK_{a3} from [21] and close to value from [20] (Table 1). The fact of overrated value of pK_{a3} in [17] can not be explained by differences in experimental conditions or method and must be assumed as mistaken.

pK_{a3} alendronic and pamidronic acids obtained in our work is agreed with data obtained in [21]. Other differences between constants determined by us and authors of works [20,21] could be explained by differences in experimental conditions (method, temperature, ionic strength, and nature of supporting electrolyte).

3.2 Effect of CPC micellar media on protolytic properties of aminobisphosphonic acids

In CPC micellar media, the acidity of alendronic, olpadronic and pamidronic acid is intensified based on Hartley's rule [34-38] for all dissociation steps except second step for alendronic acid (Table 1). This peculiarity can be explained by the effect of ionic strength on the value of concentration dissociation constant. The activity coefficient of hydrogen ions used for the calculation of pK_{a2} of alendronic acid in micellar solution of CPC was set equal to the activity coefficient for aqueous solution of KCl. This was done because the problem of ionic strength calculation for micellar solutions has not been resolved, although it is known that ionic strength in micellar solutions is somewhat lower than total concentration of ionic surfactant [40].

The micellar media effect on pK_{a3}, pK_{a4}, pK_{a5} of investigated acids agreed with obtained in work [23] for structurally related gem-diphosphonic acids. The shift of pK_{a3} is especially important for developing a method of titrimetric determination of alendronate by acid-base titration. However, increasing of strength of alendronic acid is not significant for practical use, because shift of pK_{a3} only slightly affects the characteristics of titration (Fig. 2, curves 3 and 4). Thus, the aqueous solutions were used for quantitative determination of sodium alendronate in tablets and pharmaceutical substance below.

3.3 Determination of sodium alendronate in pharmaceutical substance and tablets

Fig. 2 presents the experimental (curve 2) and calculated (curve 3) titration curves of sodium alendronate in aqueous solution by a strong aqueous base. The deviations between two curves can be explained by differences between pH values measured by glass electrode and $-\log[H^+]$ values used for calculated curve 3. It is clear that end-point of sodium alendronate titration can easily be determined by color changing of acid-base indicator added to titrated solution as well as by analyzing of potentiometric titration data.

The standard solutions of NaOH are often used for routine analysis in pharmaceutical laboratories because their carbonate-free solutions can be prepared more easily than KOH solution [24]. However, some bisphosphonic acids form complexes with sodium ions that influence on shape and localization of titration curve [22,23]. These effects were investigated by comparison

of titrations of sodium alendronate by 0.0100 M NaOH solution or $(C_2H_5)_4NOH$ solution, which cation can not form complexes with bisphosphonic acids [25]. The end-points of potentiometric titrations were determined by using the second derivative curve. The end-point of titrations with mixed thymol blue-phenolphthalein indicator with pT 9.0 was determined by yellow-violet color transition [39]. Table 2 demonstrates that the results of determining the mass fraction of sodium alendronate in a pharmaceutical substance are independent from titrant nature and agreed very well with certified value. Thus, NaOH solution can be applied as titrant for sodium alendronate determination.

The tablets of sodium alendronate were analyzed by acid-base titration with a NaOH solution using the following procedure. Tablets were triturated in a porcelain mortar. An amount of powder equivalent to 60 mg of sodium alendronate was dissolved in 20 mL of water and titrated with 2.00 × 10^{-3} M NaOH solution. The mass of sodium alendronate in pharmaceutical formulations was 11.29 ± 0.05 mg per tablet, which is comparable to the declared value of 10 mg.

Table 2. Determination of sodium alendronate in pharmaceutical substance by acid-base titration

Mass fraction of dried sodium alendronate (%) in CRM of sodium alendronate trihydrate		
Titrant		
NaOH	$(C_2H_5)_4NOH$	Certified value
83.4±0.5	83.6±0.6	83.3

4. Conclusions

Reliable data of dissociation constants of alendronic, olpadronic and pamidronic acids in aqueous solutions and micellar solutions of cetylpyridinium chloride were obtained. The method of sodium alendronate determination by acid-base titration proposed earlier [16] was theoretically grounded on the basis of re-evaluated data of third dissociation constant of alendronic acid. The increasing of aminobisphosphonic acids strength was observer in micellar solutions of CPC, but shifts of dissociation constants are not remarkable for improving of characteristics of acid-base titration. The absence of bias of sodium alendronate determination due to complexation with sodium ions were proved experimentally. Thus, the simple, rapid and inexpensive titrimetric method of sodium alendronate determination in pharmaceutical formulations can be useful alternative to known chromatographic methods.

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References

[1] J.-M. Rondeau, F. Bitsch, E. Bourgien, M. Geiser, R. Hemmig, M. Kroemer, S. Lehmann, P. Ramage, S. Rieffel, A. Strauss, J.R. Green, W. Jahnke, ChemMedChem 1, 267 (2006)

[2] K.D. Tripathi, Essentials of Medical Pharmacology (Jaypee Brothers Medical Publishers, New Delhi, 2001)

[3] R.W. Sparidans, J. den Hartigh, Pharmacy World and Science 21, 1 (1999)

[4] J.D. Marco, S.E. Biffar, D.G. Reed, M.A. Brooks, J. Pharm. Biomed. Anal. 7, 1719 (1989)

[5] W.F. Kline, B.K. Matuszewski, W.F. Bayne, J. Chromatogr. 534, 139 (1990)

[6] W.F. Kline, B.K. Matuszewski, J. Chromatogr. 583 183 (1992)

[7] S.K. Deeb, I.I. Hamdan, S.M. Najjar, Talanta 64, 695, (2004)

[8] C. Apostolou, Y. Dotsikas, C. Kousoulos, G. Tsatsou, F. Colocouri, G.-S. Soumelas, Y.L. Loukas, J. Pharm. Biomed. Anal. 43, 1151 (2007)

[9] M.J. Lovdahl, D.J. Pictrzyk, J. Chromatogr. A 850, 143, (1999)

[10] R.W. Sparidans, J. Hartigh, J.H. Beijnen, P. Vermeij, J. Chromatogr. A 782, 211 (1997)

[11] O. Quattrocchi, L. Frisardi, M. Iglesias, M. Noya, M. Caputto, D. Ferraris, D. Siliprandi, E. Piccinni, J. Pharm. Biomed. Anal. 24, 1011 (2001)

[12] X-Z. Qin, E.W. Tsai, T. Sakuma, D.P. Ip, J. Chromatogr. A 686, 205 (1994)

[13] Y.-H.R. Han, X.-Z. Qin, J. Chromatogr. A 719, 345, (1996)

[14] E.W. Tsai, D.P. Ip, M.A. Brooks, J. Chromatogr. 596, 217 (1992)

[15] British pharmacopoeia 2005 (electronic edition, www.pharmacopoeia.co.uk). Sodium Alendronate. The stationery office. British pharmacopoeia Volume I and II. Monographs: Medical and pharmaceutical substances.

[16] A.H. Moreno, H.R. Pezza, L. Pezza, Chem. Anal. 49, 1 (2004)
[17] M.N. Kabachnik, T.Ya. Medved, N.M. Dyatlova, Yu.M. Polikarpov, B.K. Shcherbakov, F.K. Bel'skiy, Izv. Akad. Nauk USSR, Ser. Khim. 433 (1978) (in Russian)
[18] The Merck Index, Monograph number: 00229, 14th edition (Merck & Co., Inc., Whitehouse Station, New Jersey, USA)
[19] C. Treiner, J. Coll. Inter. Sci. 93, 33 (1983)
[20] M. Dyba, M. Jezowska-Bojczuk, E. Kiss, T. Kiss, H. Kozlowski, Y. Leroux, D.E. Manouni, J. Chem. Soc. Dalton Trans. 1119 (1996)
[21] G. Hagele, Z. Szakacs, J. Ollig, S. Hermens, C. Pfaff, Heteroatom Chem. 11, 562 (2000)
[22] T.A. Matkovskaya, K.I. Popov, E.L. Yurr'eva, Bisfosfonaty. Svoistva, stroenie i primenenie v meditsine [Bisphosphonates. Properties, Structure, and Application in Medicine] (Khimiya, Moscow, 2001) (in Russian)
[23] L.P. Loginova, I.V. Levin, A.G. Matveeva, S.A. Pisareva, E.E. Nifant'ev, Russ. Chem. Bull. 53, 1919 (2004)
[24] A. Albert, E.P. Serjeant, Ionization constants of acids and bases: a laboratory manual (London, Methuen, 1962)
[25] H. Wada, Q. Fernando, Anal. Chem. 44, 1640 (1972)
[26] D.R. Cruise, J. Phys. Chem. 68, 3797 (1964)
[27] A.A. Bugaevskiy, L.E. Nikishina, A.V. Mutin, Yu.V. Kholin. E.A. Reshetnyak, M.I. Rubtsov, L.L. Lukackaya, Ukr. Khim. Zhurn. 56, 775 (1990) (In Russian)
[28] M.N. Rusina, T.M. Balashova, B.V. Zhadanov, A.Yu. Citrina, I.A. Polyakova, Zh. Obshchie Khimii USSR 47, 1721 (1997) (in Russian)
[29] M.I. Kabachnik, F.I. Bel'skiy, M.P. Komarova, B.K. Shcherbakov, E.I. Matrosov, Yu.M. Polikarpov, N.M. Dyatlova, T.Ya. Medved, Izv. Akad. Nauk USSR, Ser. Khim. 28, 1726 (1979) (in Russian)
[30] K. Popov, E. Niskanen, H. Ronkkomaki, L.H.J. Lajunen, New J. Chem. 23, 1209 (1999).
[31] I. Nagypal, A. Gergely, Magyar Kem. Fol. 78, 18 (1972)
[32] S.V. Matveev, F.I. Bel'skiy, A.G. Matveeva, A.Yu. Gukasova, Yu. M. Polikarpov, M.I. Kabachnik, Russ. Chem. Bull. 47, 1736 (1998)
[33] N.P. Komar, Khimicheskaya Metrologiya. Gomogennie ionnie ravnovesiya. [Chemical metrology. Homogeneous ionic equilibria] (Visha shkola, Kharkov, 1983) (in Russian)
[34] G.S. Hartley, J.W. Roe, Trans. Faraday Soc. 36, 101 (1940)
[35] P. Mukerjee, K.J. Banerjee, J. Phys. Chem. 68, 3567 (1964)
[36] M.S. Fernandez, P. Fromherz, J. Phys. Chem. 81, 1755 (1977)
[37] N.O. Mchedlov-Petrossyan, Pure Appl. Chem. 80, 7, iv (2008)
[38] G.S. Hartley, Trans. Faraday Soc. 30, 444 (1934)
[39] Yu.Yu. Lur'e, Spravochnic po analiticheskoy khimii [Handbook on analytical chemistry] (Khimiya, Moscow, 1989) (In Russian)
[40] N. Jalsenjak, J. Coll. Inter. Sci. 293, 230 (2006)