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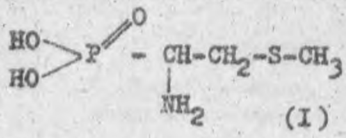
PROTONATION CONSTANTS AND COMPLEX FORMATION CONSTANTS OF α-AMINO-ω-ALKYLTHIO-1-ALKANEPHOSPHONIC ACIDS WITH Cu(II) IONS

Potentiometric method was used to determine the protonation constants of α-amino-ω-alkylthio-1-alkanephosphonic acids. Determination of complex formation constants of these acids with Cu(II)ions was made with the help of the method of Irving and Rossotti.

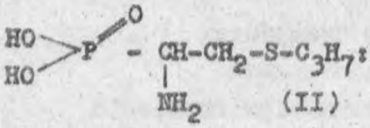
The synthesis of phosphonic analogues of natural amino acids [1] being in its rapid development which may be observed in recent years is very useful in obtaining phosphonic peptides having antimetabolic properties [2-3]. The discovery of antibacterial properties of phosphocysteine and L-alanylo-L-1-aminoethylphosphonic acid [3-5] has led to the synthesis of new S - substituted derivatives of phosphocysteine and phosphohomocysteine [6-7]. These compounds and its complexes with heavy metal ions may possess better and sometimes specific antibacterial activity.

The aim of our paper was to investigate acidic - basic properties of aminoalkylthioalkanephosphonic acids and its complex forming power with Cu(II)ions. We took upon our investigations five acids being obtained lately, Its explicit forms are listed below:



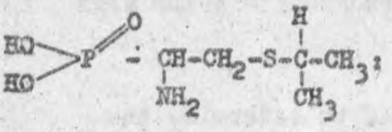
: 1-amino-2-methylthioethylphosphonic acid

(I)



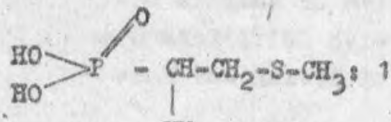
: 1-amino-2-propylthioethylphosphonic acid

(II)



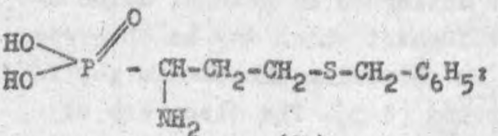
: 1-amino-2-isopropylthioethylphosphonic acid

(III)



: 1-amino-3-methylthiopropylphosphonic acid

(IV)



: 1-amino-3-benzylthiopropylphosphonic acid

(V)

REAGENTS AND APPARATUS

Investigated acids have been obtained firstly by dr Z.Kudzin and vere analytically pure.

Its molar masses were as follows:
I - M=171,158 II-M=185,176 III,IV - M=199,212 V - M=261, 283. 10^{-2}M solutions of acids I, II, III and IV were prepared by dissolving 10^{-3}M of a substance in 10 cm^3 of 10^{-1}M solution of HNO_3 and filled up to the volume of 100 cm^3 with a triply distilled water.

The V acid was insoluble in 10^{-1}M solution of HNO_3, so its solutions with approximate concentrations about 10^{-2}M were obtained by dissolving a weighted sample of a substance in 10^{-2}M solution of NaOH and then filled up with adequate volume of water. Appropriate solutions of HNO_3 and NaOH were obtained from standard analytically pure weighted samples made in POCh Gliwice. NaCl and $CuCl_2 - 2H_2O$ were also analytically pure and made in POCh Gliwice.

Determination of protonation constants of aminoalkylthioalkanephosphonic acids and its complex formation constants has been made with the help of M - 517 pH-meter. Its indications have been calibrated by the use of analytically pure buffers made in POCh Gliwice with pH =3.7 and 10.

MEASUREMENTS AND RESULTS

Protonation constants of acids I, II, III and IV were determined from titration curves, where 10^{-1}M solution of NaOH was standing for a titrant.

In the case of acid V the titration was performed with the help of 10^{-1}M solution of HNO_3.

Titrations were carried out in solutions of the following composition: 20 cm^3 of the stock solution / about 10^{-2}M of a given acid/, 5 cm^3 of 1M solution of NaCl and 25 cm^3 of water. Titrations needed for the determination of complex formation constants of acids with Cu(II) ions have been performed in solutions of the composition: 20 cm^3 of the initial solution (about 10^{-2}M of acid), 5 cm^3 of 1M solution of NaCl, 5 cm^3 of 10^{-2}M solution of $CuCl_2$ and 20 cm^3 of water. Each titration was triply repeated and average was taken as a final result.

Use of 1M solution of NaCl in each measurement was permiting to keep ionic strength constant $\mu = 0.1$.

The titration curves have been obtained by making graph dependence of SEM(pH)versus the volume of titrant added.

An example is given on figure 1.

Titration curve of acid V - line I and titration curve of acid V in the presence of Cu(II)ions - line II

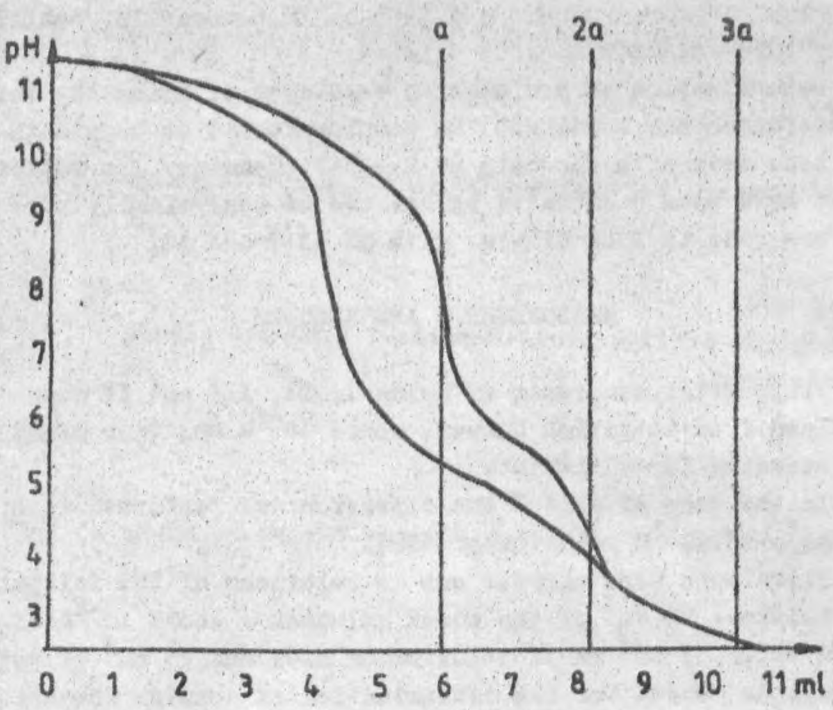


Fig. 1. Titration curves: I - 50 cm^3 of $4,6 \cdot 10^{-3}$M solution of 1-amino-3-benzylthiopropanephosphonic acid II - the same solution in a presence of 10^{-3}M of $CuCl_2$. Titrations have been performed by the use of 0,1M solution of HNO_3.

DETERMINATION OF PROTONATION CONSTANTS OF ACIDS

Protonation constants of acids I-V have been determined by the method described precisely in the monography of I n c z e d y [8]. The curves of I titrations indicate that the differences between logarithmes of stepwise protonation constants are greater then 2.8, so it was not necessary to determine these constants by the method of S c h w a r t z e n b a c h [9].

We made use of the equation describing values of the constants K_i in the form:

$$\log K_i = \lg \frac{(1-a+n-i)\, C_{H_nL} - [H^+] + [OH^-]}{(a-n+i)\, C_{H_nL} + [H^+] - [OH^-]} + pH$$

In the case of our compounds n = 3, a-stands the degree of neutralization and i - is the number of successive constant (e.g. i = 1,2 or 3) . In each case calculations have been performed for 7 values of a: 0,2+i-1, 0,3+i-1, 0,4+i-1, 0,5+i-1, 0,6+i-1, 0,7+i-1 and 0,8+i-1.

Results are presented in tables I-V

Table 1. Values of protonation constants $-K_i$ and dissociation constants K_i' of 1-amino-2-methylthioethanephosphonic acid.

a	K_3	K_1'	a	$K_2 \cdot 10^{-5}$	$K_2' \cdot 10^{6}$	a	$K_1 \cdot 10^{-9}$	$K_3' \cdot 10^{10}$
0,2	0	-	1,2	1,53	6,54	2,2	3,27	3,05
0,3	0	-	1,3	1,58	6,34	2,3	3,32	3,01
0,4	0	-	1,4	1,54	6,50	2,4	3,31	3,02
0,5	0	-	1,5	1,55	6,45	2,5	3,38	2,96
0,6	0	-	1,6	1,54	6,50	2,6	3,32	3,01
0,7	0	-	1,7	1,57	6,37	2,7	3,35	2,98
0,8	0	-	1,8	1,53	6,54	2,8	3,23	3,09

$K_3 = 0$ $K_2 = (1,55 \pm 0,05) \cdot 10^{5}$ $K_1 = (3,31 \pm 0,1) \cdot 10^{9}$

$K_1' = \infty$ $K_2' = (6,45 \pm 0,1) \cdot 10^{-6}$ $K_3' = (3,02 \pm 0,1) \cdot 10^{-10}$

Table 2. Values of protonation constants - K_i and dissociation constants K_i' of 1-amino-2-propylthioethanephosphonic acid.

a	K_3	$K_1' \cdot 10^2$	a	$K_2 \cdot 10^{-5}$	$K_2' \cdot 10^6$	a	$K_1 \cdot 10^{-9}$	$K_3' \cdot 10^{10}$
0,2	49,51	2,02	1,2	3,29	3,04	2,2	5,29	1,93
0,3	48,82	2,05	1,3	3,45	2,90	2,3	4,98	2,01
0,4	50,01	2,00	1,4	3,37	2,98	2,4	5,15	1,95
0,5	51,50	1,94	1,5	3,53	2,83	2,5	5,27	1,90
0,6	50,23	1,99	1,6	3,41	2,93	2,6	5,17	1,94
0,7	48,62	2,05	1,7	3,29	3,04	2.7	5.08	1,97
0,8	50,99	1,96	1,8	3,39	2,95	2,8	5,13	1,95

$K_3 = 49,9 \pm 2$ $K_2 = (3,39 \pm 0,2) \cdot 10^5$ $K_1 = (5,15 \pm 0,2) \cdot 10^9$

$K_1' = (2,0 \pm 0,1) \cdot 10^{-2}$ $K_2' = (2,95 \pm 0,1) \cdot 10^{-6}$

$K_3' = (1,95 \pm 0,1) \cdot 10^{-10}$

Table 3. Values of protonation constants - K_i and dissociation constants K_i' of 1-amino-2-isopropylthioethanephosphonic acid.

a	K_3	$K_1' \cdot 10^2$	a	$K_2 \cdot 10^{-5}$	$K_2' \cdot 10^6$	a	$K_1 \cdot 10^{-9}$	$K_3' \cdot 10^{10}$
0,2	28,2	3,55	1,2	2,12	4,72	2,2	3,73	2,69
0,3	26,89	3,71	1,3	2,02	4,95	2,3	3,80	2.63
0,4	28,45	3,53	1,4	2,11	4,74	2,4	3,78	2,64
0,5	29,19	3,42	1,5	2,18	4,59	2,5	3,71	2,65
0,6	27,65	3,62	1,6	2,09	4,79	2,6	3,85	2,60
0,7	27,86	3,59	1,7	2,07	4,83	2,7	3,83	2,61
0,8	27,76	3,60	1,8	2,06	4,85	2,8	3,93	2,54

$K_3 = 28,0 \pm 1,5$ $K_2 = (2,09 \pm 0,1) \cdot 10^5$ $K_1 = (3,80 \pm 0,2) \cdot 10^9$

$K_1' = (3,57 \pm 0,2) \cdot 10^{-2}$ $K_2' = (4,78 \pm 0,2) \cdot 10^{-6}$ $K_3' = (2,62 \pm 0,1) \cdot 10^{-10}$

Table 4. Values of protonation constants - K_i and dissociation constants - K_i' of 1-amino-3-methylthiopropanephosphonic acid.

a	K_3	K_1'	a	$K_2 \cdot 10^{-5}$	$K_2' \cdot 10^6$	a	$K_1 \cdot 10^{-9}$	$K_3' \cdot 10^{10}$
0,2	0	-	1,2	1,66	6,03	2,2	2,49	4,01
0,3	0	-	1,3	1,69	5,92	2,3	2,63	3,80
0,4	0	-	1,4	1,74	5,75	2,4	2,51	3,98
0,5	0	-	1,5	1,88	5,32	2,5	2,71	3,69
0,6	0	-	1,6	1,73	5,77	2,6	2,51	3,98
0,7	0	-	1,7	1,78	5,51	2,7	2,57	3,89
0,8	0	-	1,8	1,70	5,88	2,8	2,58	3,88

$K_3 = 0$ $K_2 = (1,74 \pm 0,15) \cdot 10^5$ $K_1 = (2,57 \pm 0,15) \cdot 10^9$

$K_1' = \infty$ $K_2' = (5,75 \pm 0,3) \cdot 10^{-6}$ $K_3' = (3,89 \pm 0,2) \cdot 10^{-10}$

Table 5. Values of protonation constants - K_i and dissociation constants - K_i' of 1-amino-3-benzylthiopropanephosphonic acid.

a	K_3	K_1'	a	$K_2 \cdot 10^{-5}$	$K_2' \cdot 10^6$	a	$K_1 \cdot 10^{-9}$	$K_3' \cdot 10^{10}$
0,2	0	-	1,2	3,39	2,94	2,2	4,09	2,44
0,3	0	-	1,3	3,51	2,85	2,3	4,09	2,44
0,4	0	-	1,4	3,50	2,86	2,4	4,27	2,32
0,5	0	-	1,5	3,45	2,90	2,5	4,16	2,40
0,6	0	-	1,6	3,50	2,86	2,6	4,24	2,36
0,7	0	-	1,7	3,47	2,88	2,7	4,18	2,39
0,8	0	-	1,8	3,48	2,87	2,8	4,16	2,40

$K_3 = 0$ $K_2 = (3,47 \pm 0,1) \cdot 10^5$ $K_1 = (4,17 \pm 0,1) \cdot 10^9$

$K_1' = \infty$ $K_2' = (2,88 \pm 0,1) \cdot 10^{-6}$ $K_3' = (2,40 \pm 0,1) \cdot 10^{-10}$

DETERMINATION OF THE COMPLEX FORMATION CONSTANTS

pH - metric determination of the complex formation constants is displayed in the fact, that in formation of the complex MeL_m one deals with a following equilibrium:

$$Me^{+z} + m\,H_nL \rightleftharpoons MeL_m^{+z-nm} + nmH^+$$

change of hydrogen ions concentration may be regarded as a measure of a ligand "linking".

Simple equations arising from both mass and charge balances in a titrated solution (with $C_{H_nL} > N.C_{Me}$, where N stands for the highest coordination number) lead to the equations describing the concentration of the free ligand. In the case of compounds being upon our investigation the concentration of the free ligand is described by the equation:

$$[L] = \frac{(3-a)C_{H_3L} - [H^+] + [OH^-]}{[H^+]K_1 + 2[H^+]^2 K_1K_2 + 3[H^+]^3 K_1K_2K_3}$$

with an assumption that L may occur in the form of H_3L a - - stands the degree of neutralization of the ligand in the presence of Cu(II)ions being determined from the curve II. Knowing the entire concentration of both Cu(II) ions and the ligand one may final the mean number of ligands n around Cu(II) ion for a given value of pH using the equation.

$$\bar{n} = \frac{C_{H_3L} - [L]\,\alpha_{L(H)}}{C_{Cu(II)}}$$

$\alpha L(H)$ is a function of protonation of acid H_3L in the form:

$$\alpha L(H) = 1 + [H^+]K_1 + [H^+]^2 K_1K_2 + [H^+]^3 K_1K_2K_3$$

The knowledge of $\bar{n}$ values and corresponding concentrations of the free ligand allowes to construct the complex formation curves. These curves of complex formation for acid

I - V are presented on fig. 2-6

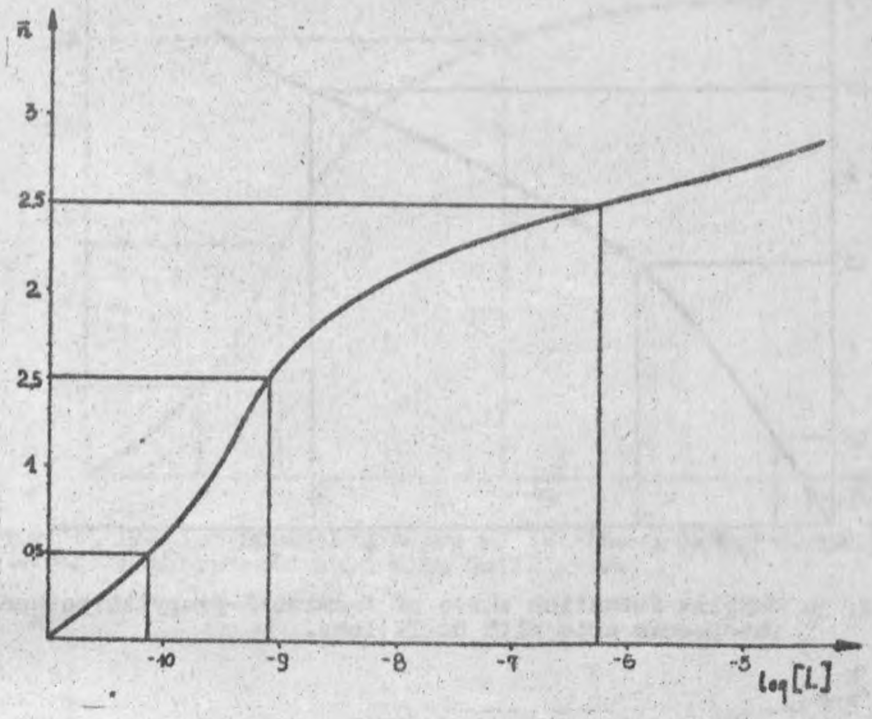


Fig. 2. Complex formation curve of 1-amino-2-methylthioethanephosphonic acid with Cu(II)ions.

The run of these curves shows that lg β_i - lg β_{i+1} < 2.8, so it follows that the method of graphical determination proposed by B j e r r u m [10] will give, in this case, only approximate values of β_i.

Therefore, the correct values of the complex formation constants have been determined by the linear equations method of I r v i n g and R o s s o t t i [11] with the help of the function:

$$\sum^{N}(\bar{n} - n)\beta_n [L]^n = 0$$

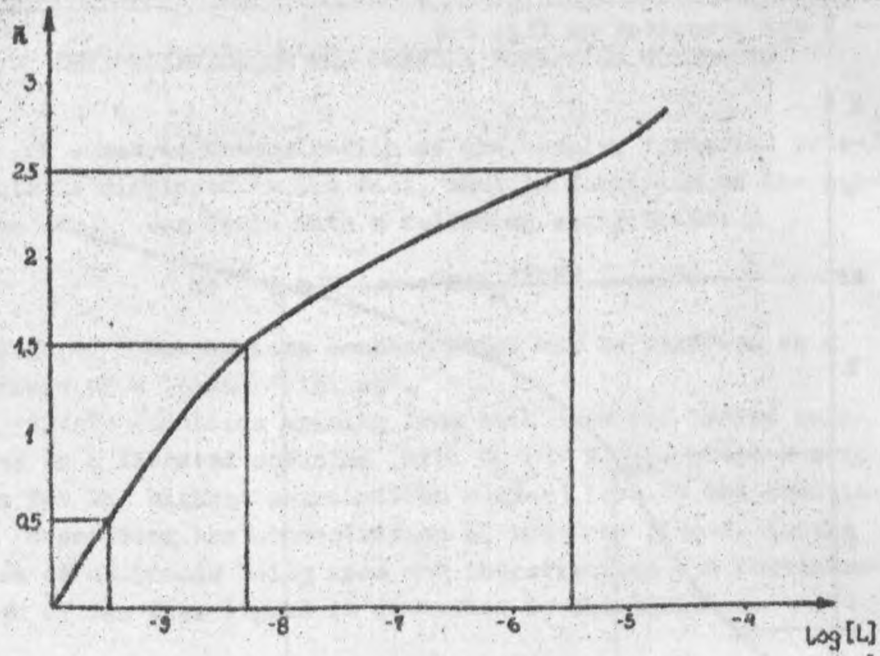


Fig. 3. Complex formation curve of 1-amino-2-propylthioethanephosphonic acid with Cu(II)ions.

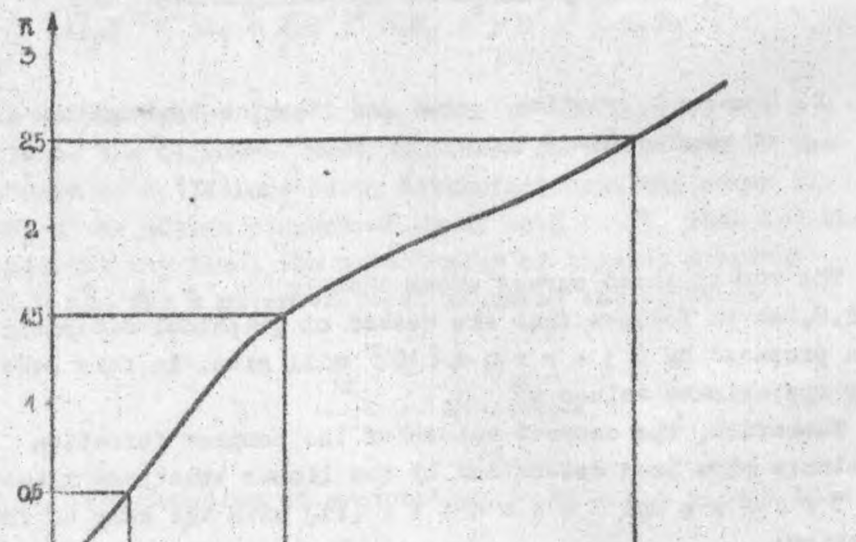


Fig. 4. Complex formation curve of 1-amino-2-isopropylthioethanephosphonic acid with Cu(II)ions.

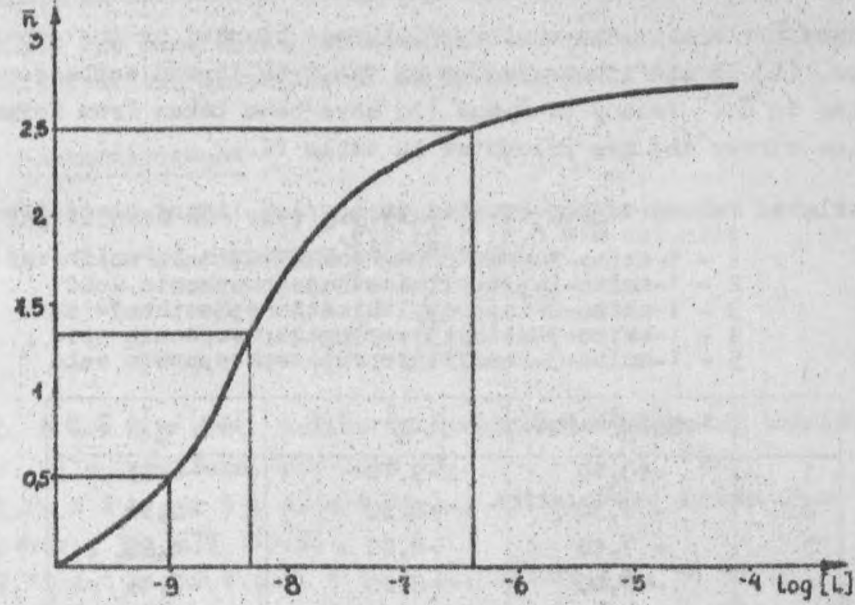


Fig. 5. Complex formation curve of 1-amino-3-methylthiopropanephosphonic acid with Cu(II)ions.

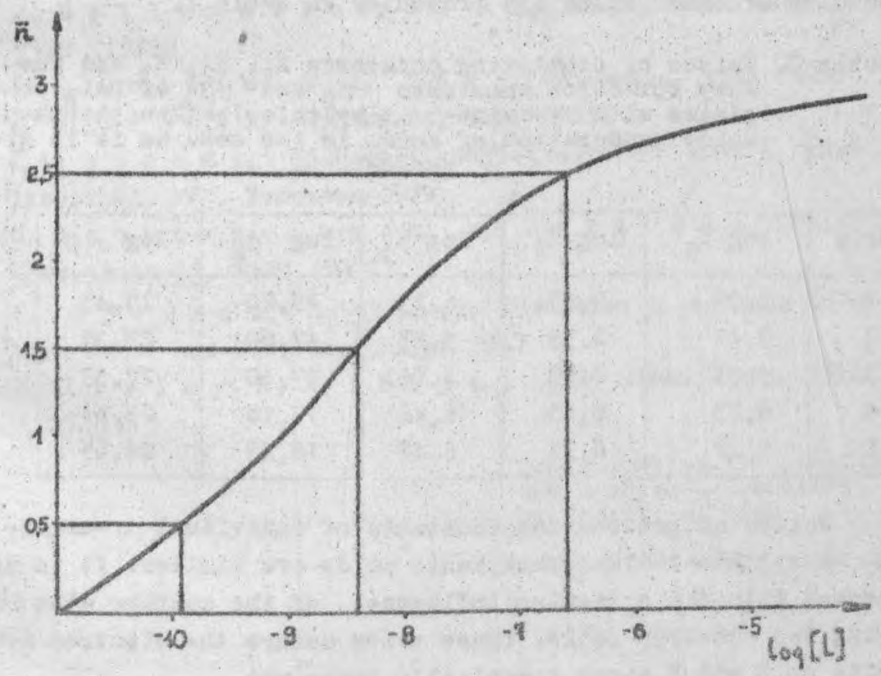


Fig. 6. Complex formation curve of 1-amino-3-benzylthiopropanephosphonic acid with Cu(II)ions.

where $\bar{n}$ is the mean number of ligands bounded by the central ion, [L] is the concentration of the free ligand corresponding to $\bar{n}$. Values of $\bar{n}$ and [L] have been taken from formation curves and are presented in table VI.

Table 6. Values of non-bounded in complex ligand concentration for $\bar{n}$ = 0,5; 1,5; 2,5.
1 - 1-amino-2-methylthioethanephosphonic acid
2 - 1-amino-2-propylthioethanephosphonic acid
3 - 1-amino-2-isopropylthioethanephosphonic acid
4 - 1-amino-3-methylthiopropanephosphonic acid
5 - 1-amino-3-benzylthiopropanephosphonic acid

Acid	$\log[L_{\bar{n}}]$ = 0,5	$\log[L_{\bar{n}}]$ = 1,5	$\log[L_{\bar{n}}]$ = 2,5
1	-10,10	-9,10	-6,25
2	- 9,50	-8,30	-5,55
3	- 9,40	-8,00	-4,99
4	- 9,00	-8,20	-6,45
5	- 9,95	-8,30	-6.40

Results of calculation are presented en table 7.

Table 7. Values of complexing constants K_1, K_2, K_3 and summary formation constants β_2 and β_3 of CuL_n complexes with α-amino-ω-alkylthio-1-alkanephosphonic acids enumeration of acids is the same as it is given tab. 6.

Acid	$\log K_1$	$\log K_2$	$\log K_3$	$\log \beta_2$	$\log \beta_3$
1	9,95	9,25	6,25	19,20	25,45
2	9,41	8,39	5,55	17,80	23,35
3	9,35	8,05	4,99	17,40	22,39
4	8,73	8,45	6,46	17,18	23,64
5	9,92	8,31	6,42	18,23	24,65

Values of protonation constants of individual α-amino-ω-alkylthio-1-alkanephosphonic acids are similar. It is connected with the screening influence of the sulphur atom having two electron pairs. These pairs assure the electron density on O and N atoms practically invariant.

In practise, the spatial surroundings of ligand atoms in molecules of all investigated acids is also invariant, so one obtaines the same values of coordination numbers and similar stability of the complexes of acids with Cu(II) ions.

Acknowledgment

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References

1. D. R e d m o r e, Topics in Phosphorous Chemistry, vol. 8, J. Wiley and Sons, New York 1976
2. F.R. A t h e r t o n, e t a l., Antimicrob. Agents Chemother., 15, 677 (1979)
3. F.R. A t h e r t o n, e t a l., Nature 272, 56 (1978)
4. P. M a s t a l e r z, J. Z y g m u n t, Pol. J. Chem., 52, 2271 (1978)
5. J. S p i t z m e l l e r, e t a l., Tetrahedron Lett., 4929 (1979)
6. Z. H. K u d z i n, W. J. S t e c, Synthesis, 1032 (1980)
7. Z. H. K u d z i n, Synthesis, 643 (1981)
8. J. I n c z e d y, Równowagi kompleksowania w chemii analitycznej, PWN, Warszawa 1979
9. G. S c h w a r z e n b a c h, H. A c k e r m a n, Helv. Chim. Acta 31, 1029 (1948)
10. J. B j e r r u m, Metal ammine formation in aqueous solution Haase and Son, Kopenhagen 1957
11. H. I r v i n g, H. S. R o s s o t i, J. Chem. Soc., 3397 (1953)

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STAŁE PROTONOWANIA ORAZ STAŁE TWORZENIA KOMPLEKSÓW KWASÓW α-AMINO-ω-ALKILOTIO-1-ALKANOFOSFONOWYCH Z JONAMI Cu(II)

Przy pomocy metody potencjometrycznej wyznaczono stałe protonowania kwasów α-amino-ω-alkilotio-1-alkanofosfonowych. Stałe tworzenia kompleksów tych kwasów z jonami Cu(II) wyznaczono z krzywych tworzenia metodą Irvinga i Rossottiego.