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Extraction of Copper(II) Carboxylates with Chloroform under Substoichiometric Conditions

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Abstract—The features are considered of binding carboxylic acids (HR) as dimeric solvated copper(II) complexes at the copper(II) extraction with chloroform under substoichiometric conditions, with excess of the metal ion in the aqueous phase. The fundamental difference in the optimization of the quantitative extraction of copper(II) in the form of any carboxylate with a maximum ratio of Cu:R and the total binding with carboxylic acids to form the copper complex of the minimum stoichiometry was noted. It was found that quantitative binding of HR occurred at the extraction of mixed-ligand acetate–carboxylate copper(II) complexes without control over the aqueous phase acidity when acetic acid medium or copper(II) acetate was used, but not copper chloride, nitrate, perchlorate, or sulfate. The possibility of determination by extraction–photometric method by the color of the Cu(II) complex was shown that was suitable only to those carboxylic acids, whose logarithm of the partition coefficient in the water–chloroform mixture was higher than three.

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The copper(II) ions are known to be extractable with organic solvents containing dissolved carboxylic acid. This is used both for separation of Cu(II) from other heavy metals, and for its concentration with subsequent determination [1, 2]. According to the existing concepts [3, 4], the process of formation of the extractable form can be described by the equation:

$$2Cu^{2+} + 4\,HR + 2S = Cu_2R_4{\cdot}2S + 4H^+, \qquad (1)$$

where S is the solvating component, which increases the hydrophobicity of the Cu_2R_4 complex, where two copper(II) ions are linked by the bridging carboxy groups of four molecules of deprotonated carboxylic acid (R^-). At the extraction by polar solvents (higher alcohols), each dimer fragment is solvated by two molecules of organic solvent S [5]. In the case of extraction of a copper(II) carboxylate by a non-polar solvent (benzene, chloroform, CCl_4) the role of the donor additive S plays a molecule of undissociated carboxylic acid HR [6]. The complex composition becomes $Cu_2R_4{\cdot}2HR$, and its stoichiometry, that is, the metal:carboxylic acid ratio, increases to 1:3. In such systems, to create optimal conditions for extraction and to provide quantitative extraction of copper(II) to the organic phase, it is necessary to create excessive concentration of the carboxylic acid.

There are some problems when their solution requires such optimization of the extraction process that the maximum possible binding of HR as a $Cu_2R_4{\cdot}2HR$ complex should be achieved. Such dimers were suggested, in particular, as analytical forms for the selective extraction–photometric determination of some carboxylic acids, popular non-steroidal anti-inflammatory drugs: ibuprofen [7], diclofenac [8], and tolmetin [9]. It is essential that the conditions of formation and extraction of such analytical forms [7–9] have been found purely empirically and have not been not optimized in terms of theory, ionic equilibria, although the dimeric structure of the series of copper carboxylates was confirmed by XRD for aspirin [10], ibuprofen [11, 12] flurbiprofen [13, 14], naproxen [11], suprofen [15], tolmetin [11], diclofenac [11, 16], indomethacin [17], mefenamic acid [18], nifluminic acid [19, 20], flufenaminic acid [21, 22], and tolfenaminic acid [23, 24].

The purpose of this study was to substantiate the optimal conditions (pH of the aqueous phase and its ionic composition, the ratio of the concentrations of copper(II) and HR, the HR distribution in the water–chloroform system) necessary for complete binding the carboxylic acid as the copper complex and its quantitative transfer into the organic phase in substoichiometric conditions [at low concentrations of HR in the organic phase and a high content of copper(II) in the aqueous phase].

Typically, the efficiency of the extraction process is characterized by the degree of extraction (P, %) that is, by a percentage of the whole matter passed into the organic phase. During extraction of complex compounds, such determination is valid for the direct problem, that is, for the extraction of metal ions from aqueous phase into the organic. In the case of inverse problems, the completeness of transfer of the ligand into the organic phase as a metal complex it is more correct to estimate the degree of binding (P_{HR}, %), because often the carboxylic acid HR is present in the organic phase already before the extraction. The difference between these characteristics follows from the expressions (2) for the basic process of extraction of copper(II) carboxylates.

$$\begin{gathered} 2\mathrm{Cu}^{2+} + 6\mathrm{HR} = \mathrm{Cu_2R_4{\cdot}2HR} + 4\mathrm{H}^+, \qquad (2) \\ P_{\mathrm{Cu}}, \% = \{2\,[\mathrm{Cu_2R_4{\cdot}2\,HR}]/c_{\mathrm{Cu}}\}\times 100, \\ P_{\mathrm{HR}}, \% = \{6\,[\mathrm{Cu_2R_4{\cdot}2\,HR}]/c_{\mathrm{HR}}\}\times 100. \end{gathered}$$

where $[\mathrm{Cu_2R_4{\cdot}2HR}]$ is the equilibrium concentration of the extracted complex in the organic phase, M, c_{Cu} is the initial concentration of copper(II) in aqueous phase, M, c_{HR} is the initial concentration of carboxylic acid in the organic phase, M.

In this paper we consider some features of the formation and extraction of the complexes of some acids listed in Table 1. Table 1 comprises the well-known literature data on their ionization constant (pK) [25], the calculated values of distribution coefficients of HR in the water–chloroform system (log P_{HR}), and the extraction constants of the corresponding copper(II) carboxylates experimentally determined in this work. While Table 1 shows the data for some well-known non-steroidal anti-inflammatory preparations, the main conclusions of this study are made on the basis of data obtained with benzoic and with isomeric toluic acids.

Determination of the concentration of copper(II) in organic phase. The carboxylic acids listed in Table 1 interact with copper(II) salt in the pH range 4–7 to form colored complexes extractable by chloroform. They absorb light in the range 500–800 nm (Fig. 1). The absorption maximum is at λ = 670 nm and virtually does not depend on the nature of the carboxylic acid. This absorption is due to *d–d* electronic transitions of the copper(II) ion, hence, the optical density is proportional to the concentration of Cu(II) in the extract under the photometry.

In respect to the concentration of copper(II), the extraction equilibrium is logically represented in a simplified form (3):

$$\mathrm{Cu}^{2+} + 3\,\mathrm{HR} = \mathrm{CuR_2{\cdot}HR} + 2\mathrm{H}^+. \qquad (3)$$

The optical density of the chloroform extract at 670 nm is defined as $A = \varepsilon^{*}_{\mathrm{Cu}} l c^{\mathrm{w}}_{\mathrm{Cu}}$, where $\varepsilon^{*}_{\mathrm{Cu}}$ is a conventional molar absorption coefficient of the analytical form $\mathrm{CuR_2{\cdot}HR}$, l is thickness of the absorbing layer, cm, $c^{\mathrm{w}}_{\mathrm{Cu}}$ is the total concentration of copper(II), M. As seen from the equations of calibration graphs (4)–(7) obtained under the conditions of the overwhelming excess of various carboxylic acids, the values of $\varepsilon^{*}_{\mathrm{Cu}}$ (the coefficients at c_{Cu}) for various carboxylic acids are approximately equal and amounted to ~320 l cm^{-1} mol^{-1}. This means that to solve the direct problem (photometric determination of copper concentration by extraction of its carboxylates) the carboxylic acid nature is not important.

$$\begin{gathered} A = 322.36\, c_{\mathrm{Cu}} - 0.0043, \qquad (4) \\ R^2 = 0.9983; \text{ benzoic acid,} \end{gathered}$$

$$\begin{gathered} A = 324.60\, c_{\mathrm{Cu}} + 0.0057, \qquad (5) \\ R^2 = 0.9992; \textit{o}\text{-toluic acid,} \end{gathered}$$

$$\begin{gathered} A = 323.52\, c_{\mathrm{Cu}} + 0.0030, \qquad (6) \\ R^2 = 0.9990; \textit{m}\text{-toluic acid,} \end{gathered}$$

$$\begin{gathered} A = 321.25\, c_{\mathrm{Cu}} - 0.0225, \qquad (7) \\ R^2 = 0.999; \text{ ibuprofen.} \end{gathered}$$

Effect of the component ratio. To reveal the features of extraction of copper(II) with an excess or at a shortage of a carboxylic acid, a method of isomolar series is useful. All the extraction experiments were carried out at pH 5.0 created by adding appropriate amount of 0.1 M solution of NaOH. It was found that the color of chloroform phase is observed only at an excess of benzoic acid over the copper(II) ions. If the concentration in the aqueous phase c_{Cu} is greater than the concentration of benzoic acid in chloroform, then at the extraction a stable emulsion is formed. In the case of more hydrophobic toluic acids the separation of phases is possible, and optical density of the chloroform extract can be measured in the entire range of the Cu:HR ratio. Despite these differences in extractability of copper complexes by benzoic and toluic acids, the ratio of components in a light-absorbing forms in both cases is 1:3.

Based on these data, we can conclude that under the conditions of excess of copper(II) ions the higher the

Table 1. Selected physicochemical constants of carboxylic acids

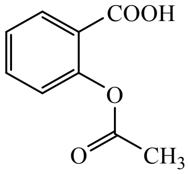
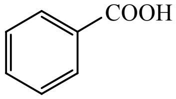
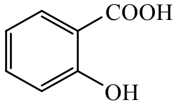
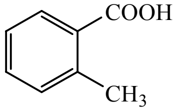
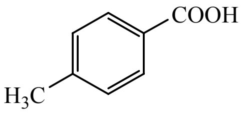
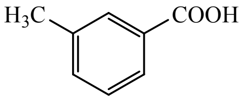
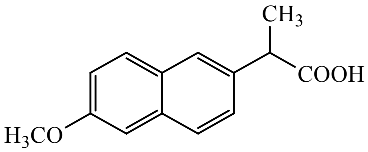
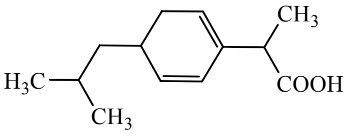
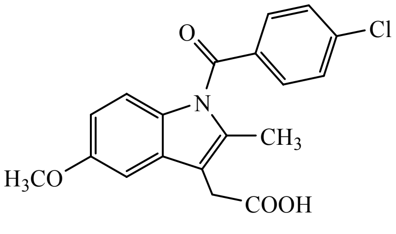
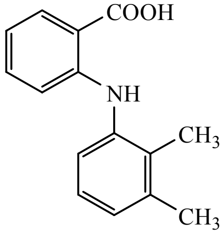
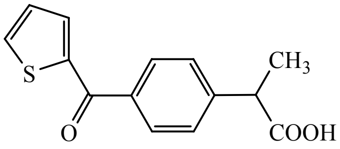
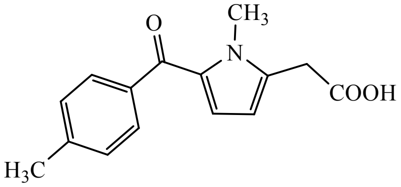
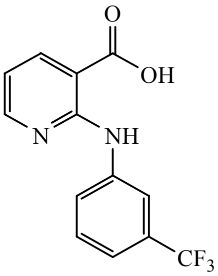
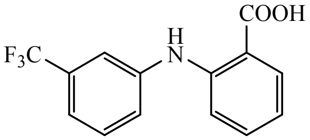
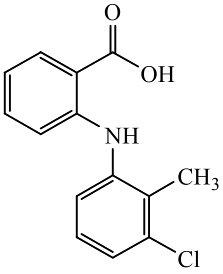
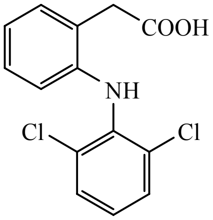
Run no.	Carboxylic acid	Structural formula	pK [25]	log P_{HR}[a]	log K_e[b]	Estimated efficiency of binding as a $Cu_2OAc_4 \cdot 2HR$
1	Aspirin		3.49	0.5	–5.65	Low
2	Benzoic acid		4.02	0.97	–5.36	Low
3	Salycilic acid		3.08	1.27	–4.80	Low
4	*m*-Toluic acid		4.10	1.56	–4.68	Low
5	*p*-Toluic acid		4.20	1.57	–4.62	Low
6	*o*-Toluic acid		3.98	1.76	–4.51	Low
7	Naproxen		4.50	2.23	–4.40	Medium
8	Ibuprofen		4.50	3.01	–4.33	Medium [7]
9	Indomethacin		4.66	3.61	–4.25	High
10	Mefenamic acid		4.20	4.85	–4.21	High

Table 1. (Contd.)

Run no.	Carboxylic acid	Structural formula	p*K* [25]	log P_{HR}[a]	log K_e[b]	Estimated efficiency of binding as a $Cu_2OAc_4 \cdot 2HR$
11	Suprofen		4.26	2.14		Medium
12	Tolmetin		4.22	2.57		Medium [9]
13	Nifluminic acid		4.44	2.81		Medium
14	Flufenaminic acid		4.51	3.86		High
15	Tolfenaminic acid		4.50	4.74		High
16	Diclofenac		4.60	4.95		High [8]

[a] Calculated with the SPARC software [26]. [b] Our data.

hydrophobicity of carboxylic acid, the greater the extent of its copper complex(II) transfer into the chloroform phase. This conclusion is consistent with the data on the distribution coefficient log P_{HR} of individual carboxylic acids in the water–chloroform system shown in Table 1.

Effect of pH of the aqueous phase. In studying the effect of pH significant differences in the curves of extraction for the different Cu:HR ratios were revealed. A large excess of ligand enhances the extraction degree c_{Cu} to 100% and remains constant in a certain range of pH values. This plateau is larger if

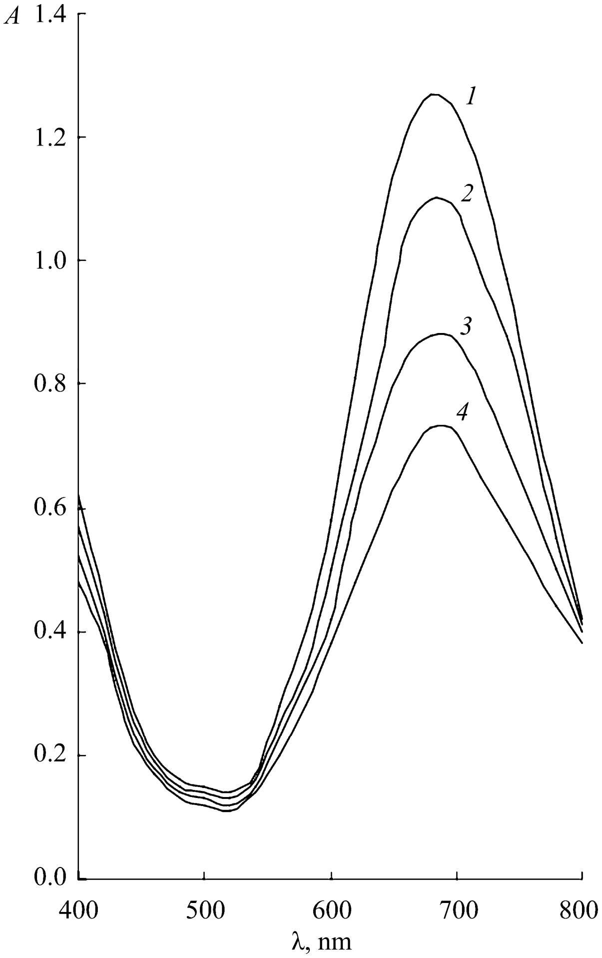


Fig. 1. Absorption spectra of chloroform extracts obtained by extraction of Cu(II) with (*1*) ibuprofen, (*2*) *m*-toluic acid, (*3*) *o*-toluic acid, and (*4*) benzoic acid at pH 5. c_{Cu} = 0.01 M, c_{HR} = 0.02 M.

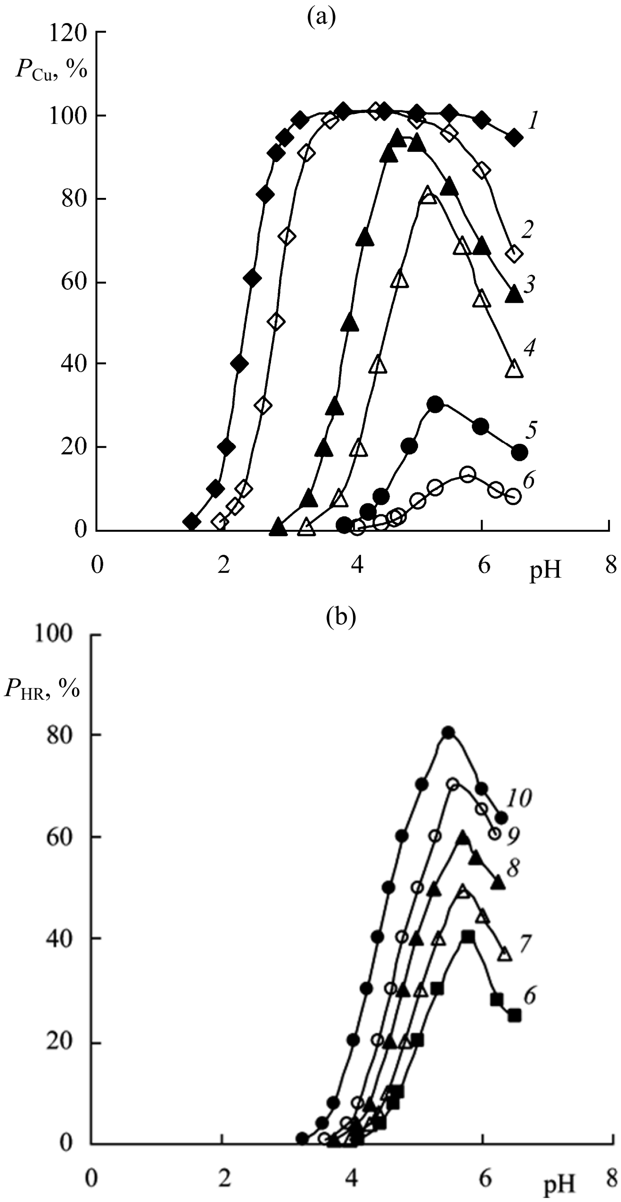


Fig. 2. (a) The degree of extraction of copper(II) (P_{Cu},%) and (b) the degree of binding of *m*-toluic acid (P_{HR},%) in a complex vs. pH at the different Cu:HR ratios. c_{HR}, M: (*1*) 1, (*2*) 0.5, (*3*) 0.1, (*4*) 0,05, (*5*) 0.02, and (*6*–*10*) 0.01. $V(H_2O) = V(CHCl_3)$ = 10 ml; l = 1 cm.

the excess of ligand relative to copper(II) ion is greater (Fig. 2, curves *1*–*6*). A decrease in the excess of the ligand (up to the ratio Cu:HR = 1:1) transforms the plateau into a point and simultaneously decreases the copper(II) extraction. If then the excess of copper(II) in aqueous phase is increasd at constant c_{HR}, the optical density of the chloroform extract rises again, but the nature of the optical density dependence on pH remains the same: the absorption maximum occurs at a single point. The position of this peak is shifted slightly, but steadily, to acidic region with increasing the Cu:HR ratio. The results presented in Fig. 2b show that even at a large excess of c_{Cu} in the aqueous phase the 100% binding of *m*-toluic acid is not reached.

Thus, in the substoichiometric conditions ($c_{Cu} \geq c_{HR}$), to achieve maximum optical density of the extract (complete binding of HR in the copper complex) it is necessary to create various optimal pH values of the environment depending on the Cu:HR ratio. This difference in behavior of the extraction system with an excess of ligand or metal can be understood by considering the structure of the product of reaction (2). It is evident that the formation of the solvated complex requires the presence of ligand in two forms: deprotonated (R^-) and molecular (HR). The concentration ratio of these forms depends on the pH of the solution. The complete binding of the carboxylic acid in a complex is possible only if $2c_R = c_{HR}$. Under the conditions of excess of the ligand, only a part of its molecules are linked into the complex, so changing the pH of the system does not affect the complex yield, but only changes the HR:R$^-$ ratio. With an excess of complexing metal all the molecules of a carboxylic acid are consumed for the complex formation, and the ratio of HR:R$^-$ must be strictly 1:2, which is possible only at a fixed pH. This limitation is extremely unfavorable to ensure complete binding and extraction of carboxylic acids in the form of copper complex.

Determination of extraction constants. The equilibrium (3) can be characterized by the conventional extraction constant (8). This allows a comparison of the data in a series of similar ligands (carboxylic acids) as well as evaluation of efficiency of the copper(II) carboxylates extraction at the different metal–ligand ratios.

$$K_e = [CuR_2{\cdot}HR][H^+]^2/[Cu^{2+}][HR]^3. \tag{8}$$

Given the dissociation of carboxylic acid in the aqueous phase [Eq. (9)] and its partition constant between chloroform and water [Eq. (10)], we write the material balance Eqs. (11) and (12).

$$HR_w = H^+ + R^-, \tag{9}$$

$$K = [H^+][R^-]/[HR]_w,$$
$$P_{HR} = [HR_o]/[HR_w], \tag{10}$$

$$c_{Cu} = [Cu^{2+}] + [CuR_2{\cdot}HR], \tag{11}$$

$$\begin{aligned} c_{HR} &= [R^-] + [HR_0] + [HR_w] + 3\,[CuR_2{\cdot}HR] \\ &= K[HR_o]/[H^+]P_{HR} + [HR_0] + [HR_0]/P_{HR} \\ &\quad + 3\,[CuR_2{\cdot}HR]. \end{aligned} \tag{12}$$

Substituting Eqs. (11) and (12) into [Eq. (8)], we obtain:

$$K_e = \frac{[CuR_2{\cdot}HR]([H^+] + [H^+]/P_{HR} + K/P_{HR})^3}{(c_{Cu} - [CuR_2{\cdot}HR])(c_{HR} - 3\,[CuR_2{\cdot}HR])^3[H^+]} \tag{13}$$

and after taking the logarithm:

$$\log \frac{[CuR_2{\cdot}HR]}{c_{Cu} - [CuR_2{\cdot}HR]}$$

$$= 3\log \frac{(c_{HR} - 3\,[CuR_2{\cdot}HR])P_{HR}}{[H^+]P + [H^+] + K} - \text{pH} + \log K_e. \tag{14}$$

When constructing a plot in the coordinates $y = \log [CuR_2{\cdot}HR]/(c_{Cu} - [CuR_2{\cdot}HR])$, $x = 3\log \{(c_{HR} - 3[CuR_2{\cdot}HR])P_{HR}/([H^+] + [H^+]P_{HR} + K)\} - \text{pH}$ we should obtain a straight line intersecting the ordinate axis at $y = \log K_e$.

Relations of the form (14) are widely used for experimental determination of extraction constants of copper(II) carboxylates under the conditions of carboxylic acid excess [3–5]. It was of interest to determine the suitability and possible limitations of the use of Eq. (14) for the substoichiometric conditions, where the extraction constant is essentially the binding constant. For the calculations the ascending portions of the curves in Fig. 2 were used for the ratios Cu(II):HR = 50:1, 1:1, and 1:100. The results are shown in Table 2 and in Fig. 3 as the contour markers. All groups of points fall well to the common dotted line. These data show that for the calculation of extraction (binding) constants the results obtained under the conditions of excess of either ligand, or metal can be used. A shift of individual groups of points relative to each other is explained by the fact that the extraction at different Cu:L ratios is carried out at different pH values.

To determine the extraction constants,in practice simplified equations are often used that do not take into account, for example, the dissociation of carboxylic acid or its distribution constant between aqueous and organic phases. It is believed that in the presence of a large excess of carboxylic acid its concentration in the organic phase little depends on the P_{HR}, and the HR:R$^-$ ratio remains optimal in a wide range of pH values. Without taking into account the pK (HR ionization), the Eq. (14) is transformed into Eq. (15), and without considering the HR partition in the water–chloroform system (P_{HR}) we have Eq. (16).

$$\log \frac{[CuR_2{\cdot}HR]}{c_{Cu} - [CuR_2{\cdot}HR]}$$

$$= 3\log \frac{c_R - 3\,[CuR_2{\cdot}HR]}{1 + P_{HR}} + 2\,\text{pH} + \log K_e, \tag{15}$$

$$y = \log \frac{[CuR_2{\cdot}HR]}{c_{Cu} - [CuR_2{\cdot}HR]},$$

$$x_1 = 3\log \frac{c_R - 3\,[CuR_2{\cdot}HR]}{1 + P_{HR}} + 2\,\text{pH},$$

$$\log \frac{[CuR_2{\cdot}HR]}{c_{Cu} - [CuR_2{\cdot}HR]}$$

$$= 3\log \frac{c_R - 3\,[CuR_2{\cdot}HR]}{[H^+] + K_\alpha} - \text{pH} + \log K_e, \tag{16}$$

Table 2. Data for the calculation of the extraction (binding) constants in the system of copper(II) perchlorate–*m*-toluic acid with various c_{Cu}:c_{HR} ratios

pH	$[CuR_2HR]$, M	y	x [Eq. (6)]	x_1 [Eq. (7)]	X_2 [Eq. (8)]
c_{Cu} 0.01 M, c_{HR} 1 M					
1.47	0.000203	–1.683	2.904	–1.776	2.936
1.84	0.001009	–0.950	3.640	–1.039	3.669
2.02	0.002019	–0.597	3.996	–0.683	4.021
2.24	0.004038	–0.169	4.428	–0.251	4.446
2.42	0.006056	0.186	4.780	–0.101	4.789
2.64	0.008075	0.623	5.211	–0.533	5.204
2.81	0.009084	0.997	5.547	–0.868	5.519
2.94	0.009788	1.267	5.805	–0.127	5.755
3.18	0.009891	1.956	6.281	–0.606	6.173
c_{Cu} 0.01 M, c_{HR} 0.01 M					
4.10	3.44E-05	–2.462	2.117	–2.529	1.283
4.45	0.000134	–1.866	2.735	–1.869	1.315
4.65	0.000269	–1559	3.037	–1.525	1.217
4.72	0.000338	–1.457	3.127	–1.414	1.161
5.02	0.000672	–1.143	3.449	–0.968	0.839
5.31	0.001009	–0.950	3.644	–0.565	0.442
5.80	0.001347	–0.808	3.781	0.211	–0.200
c_{Cu} 0.5 M, c_{HR} 0.01 M					
3.24	3.44E-05	–4.163	0.426	–4.249	0.298
3.56	0.000134	–3.571	1.021	–3.649	0.736
3.74	0.000269	–3.269	1.320	–3.345	0.899
4.04	0.000672	–2.871	1.721	–2.929	0.971
4.23	0.001009	–2.694	1.908	–2.725	0.877
4.39	0.001347	–2.568	2.004	–2.610	0.696
4.58	0.001681	–2.472	2.109	–2.470	0.433
4.79	0.002019	–2.392	2.172	–2.134	0.056
5.09	0.002356	–2.325	2.243	–1.860	–0.516
5.50	0.002691	–2.267	2.149	–1.623	–1.395

$$y = \log \frac{[CuR_2{\cdot}HR]}{c_{Cu} - [CuR_2{\cdot}HR]},$$

$$x_2 = 3\log \frac{c_R - 3\,[CuR_2{\cdot}HR]}{[H^+] + K} - \mathrm{pH}.$$

The presentation of results in the coordinates $x_1 - y$ (Fig. 3, curves *2a*, *3a*) shows that at ignoring the dissociation of the ligand the intersection of the $y = f(x_1)$ plot with the ordinate axis leads to an unrealistic value of the extraction constant. In the absence of the data on the ligand partition constant, the simplified Eq. (16) gives the same result as the full Eq. (14) under the conditions of the ligand excess, however, at the equimolar ratio or the metal ions excess, the corresponding graphs (Fig. 3, curves *2b*, *3b*) are bent so the determination of the extraction constant becomes impossible. This means that at determining K_e (extraction constant) of copper(II) carboxylates under substoichiometric conditions it is necessary to use the full Eq. (14) that takes into account the equilibria associated with both the dissociation of HR in the aqueous phase and its interfacial partition. The corresponding results are listed in Table 2, which show that the efficiency of binding carboxylic acids into the copper complexes (the constants of extraction) are satisfactorily correlated with the constants of distribution of individual acids between the aqueous and organic phases (Fig. 4).

Effect of acetate ions. We found experimentally that the curves of extraction of copper(II) carboxylates do not depend on the nature of the inorganic anion (Cl^-, NO_3^-, ClO_4^-, SO_4^{3-}) of the initial copper salt and appear as shows Fig. 2. An exception is the acetate ion. When using $Cu(CH_3COO)_2$, the extraction of the copper(II) carboxylate (any in the Table 1) is effective without the control of the pH of aqueous phase. As can be seen from Fig. 5, adding sodium acetate (NaAc) to any copper(II) inorganic salts leads to a sharp increase in the optical density of the extracts (increase in the degree of extraction of the copper carboxylate), with the maximum c_{Ac} = 0.15–0.25 M. However, the addition of CH_3COONa to a system that contains the original copper(II) acetate reduces the light absorption of the chloroform extract.

The observed effects can be attributed to the formation of a mixed form of extractable binuclear complex according to Eq. (17).

$$2Cu^{2+} + 4\,AcO^- + 2\,HR = Cu_2OAc_4{\cdot}2\,HR. \qquad (17)$$

Due to a significant excess of AcO^- compared to HR, in the aqueous solution a significant amount of copper(II) acetate is formed as a dimeric structure Cu_2OAc_4, and the presence of HR molecule in chloroform now plays only the role of a solvating component. It is essential that this process is carried out without adjusting the pH of the aqueous phase, as follows from the Eq. (17).

Reducing the optical density of extracts at a very large excess of AcO^- is due, most likely, to the competition for proton between the acetate and R^- anions:

$$AcO^- + HR = HOAc + R^-.$$

This equilibrium decreases the concentration of molecular form of HR, and, consequently, spoils the condition of formation of $Cu_2OAc_4{\cdot}2HR$ structure.

Thus, at the extraction of copper(II) carboxylates with chloroform, the role of acidity of the aqueous phase is to create conditions for a definite ratio of equilibrium concentrations [HR] and [R^-]. At the excess of the ligand this ratio can vary in a wide range, and in the substoichiometric conditions the pH value is strictly defined by the total concentration of HR. In both cases, the R^- anion acts as a component responsible for the creation of the dimeric unit Cu_2R_4, and HR acts as a solvating component contributing to the transport of the dimeric complex into the organic phase.

At the overwhelming (in relation to HR) concentration of sodium acetate, the dimeric fragment is formed with the participation of the Ac^- rather than

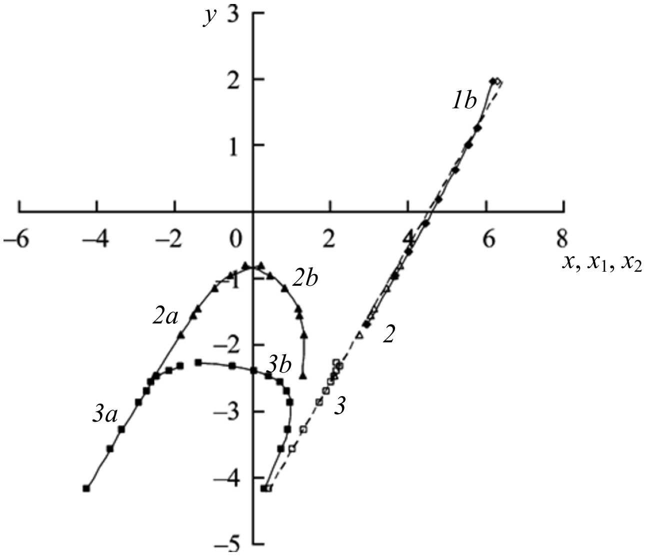


Fig. 3. Determination of extraction (binding) constants in the system of copper(II) perchlorate–*m*-toluic acid at a ratio of c_{Cu}:c_{HR} = (*1*) 1:100, (*2*) 1:1, and (*3*) 50:1. (*1–3*) calculated with Eq. (5), (*2a–3a*) calculated with Eq. (6), (*1b–3b*) calculated with Eq. (7).

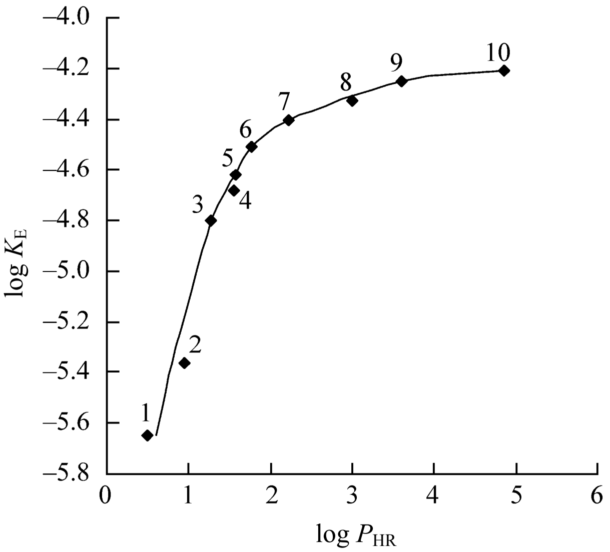


Fig. 4. Extraction constant vs. the acid partition constant. The numbers at the points correspond to the numbers in Table 1.

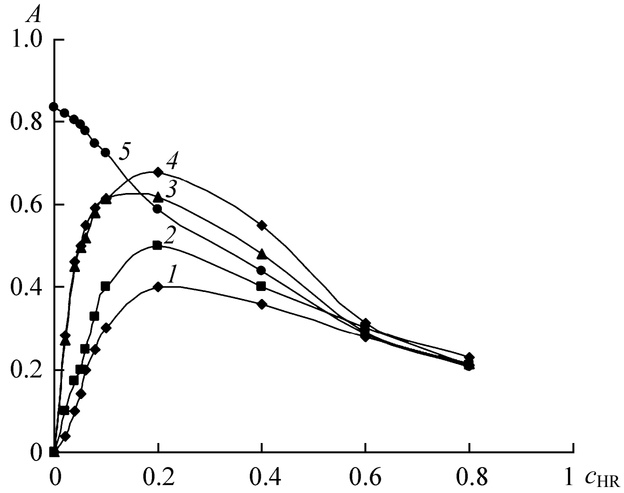


Fig. 5. The dependence of the optical density of the extracts in the presence of CH_3COONa additives at the extraction of copper(II) from (*1*) nitrate, (*2*) chloride, (*3*) sulfate, (*4*) perchlorate, and (*5*) acetate media. c_{Cu} = 0.01 M, c_{HR} = 0.01 M.

R^- anion. In this case, the whole amount of HR existing in the organic phase in the molecular form serves only as the solvation component. Thus, when sodium acetate is added, the required ratio of anionic and molecular forms in the total amount of carboxylic acids is produced not by control over the pH of the aqueous phase, but by the choice of an appropriate ratio of AcO^- and HR, which can vary quite widely. This creates conditions for the formation of an analytical form in which the ratio of the component to be determined (HR) and chromophore [Cu(II) ions] is 1:1. The same result is achieved when copper(II) acetate is used as a source copper salt. Due to the high concentration of copper(II) acetate in aqueous phase the system becomes a buffer and self-controlling that is optimal for maximal binding HR.

The data in Table 1 allow a forecast of efficiency of HR binding in the analytical form $Cu_2OAc_4{\cdot}2HR$ and feasibility of developing an extraction–photometric method for determining it. Obviously, a probability of the positive prediction is high for the highly hydrophobic acids as mefenamic, flufenaminic, and tolfenaminic. At the same time, some of non-steroidal anti-inflammatory preparations (ibuprofen, tolmetin) are not optimal objects for the extraction–photometric determination as the copper complexes [7, 9] due to insufficiently high values of their distribution constants in the chloroform–water system. It is significant that in the cited works the copper salt serving as a reagent is taken in the form of acetate, although the reasons for this choice are not discussed or commented.

The important role of hydrophobicity of the acid under study in the development of technique of their extraction–photometric determination is confirmed by the published data on their extraction in the form of ion associates with cationic dyes. Such techniques are unknown for determining benzoic, salicylic acids, aspirin ($\log P_{HR} < 2$), while methylene blue is bound effectively in the organic phase with diclofenac [27], mefenamic and flufenaminic acids [28]. Methyl violet can be used for extraction–photometric determination of ibuprofen, ketoprofen, and mefenamic acid [29], and astrafloksin to determine diclofenac [30].

EXPERIMENTAL

We used the copper(II) salts of chemically pure grade. Organic acids, benzoic and toluic acids, were preliminary recrystallized from ethanol; ibuprofen, naproxen, indomethacin and mefenamic acid were used as the pharmaceutical substances. Chloroform pure grade was additionally purified by distillation. The calibration graphs for determination of copper(II) in the organic phase were built as follows. To the aqueous phase (10 ml) containing various amounts (0.2–3 mg) of copper ion(II) was added 10 ml of chloroform pre-saturated with the corresponding carboxylic acid. The aqueous phase was adjusted to pH 6.5 by adding 0.1 M NaOH, and extracted. After phase separation, chloroform layer was filtered through a paper filter, exposed to photometry, and then the graph was built in the coordinates: the initial concentration of copper(II) (M) in the aqueous phase (c^{w}_{Cu}) vs. optical density (*A*). In the extracts with c^{0}_{Cu} > 0.02 M the copper(II) concentration was determined additionally by complexometric titration.

The pH of the aqueous phase was measured using ionomer EV-74 equipped with a measuring glass electrode and silver chloride reference electrode. The absorption spectra of chloroform extracts were recorded on a Lambda-9 Perkin-Elmer spectrophotometer. Computer processing of data and calculation of the constants of extraction was performed using the shell of the Excel software.

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