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Physicochemical Properties and Complex Formation of Ethyl 2-Aryl(methyl)sulfonylamino-4,5,6,7tetrahydrobenzothiophene-3-carboxylates

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Abstract—Acid-base properties, solubility, and chemical stability of ethyl 2-aryl(methyl)sulfonylamino-4,5,6,7-tetrahydrobenzothiophene-3-carboxylates have been studied. Complexes of Cu(II), Co(II), and Ni(II) with one of the ligands have been prepared and isolated; their solubility products were determined.

Keywords: Gewald thiophene, physicochemical properties, complex formation, nonferrous metal

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The interest in chemistry of substituted thiophenes is to a great extent due to the possibility of formation of their oligo- and polymeric derivatives that possess unusual properties and can therefore be used as molecular switches, organic semiconductors, dyes, and biologically active compounds [1, 2]. The composition and structure of coordination compounds of thiophene derivatives with metal ions have been studied [3, 4]; the application of thiophene derivatives for metals concentration has been as well discussed, for instance, for gold leaching in hydrometallurgy [5].

In this work we prepared ethyl 2-aryl(methyl)sulfonylamino-4,5,6,7-tetrahydrobenzothiophene-3carboxylates **Ia–If** and studied their physicochemical properties and complex formation with Cu(II), Co(II), and Ni(II) to estimate the potential of their application in flotation technology.

The N-substituted sulfonyl thiophene derivatives **Ia–If** were chosen due to the presence of two functional fragments: substituted amine and carboxy groups that were anticipated to form chelates with non-ferrous metals and thus extend possible applications of the ligands. To the best of our knowledge, the application of sulfonyl derivatives of the Gewald-type thiophenes for concentration and separation of

nonferrous metals has not been discussed in the literature.



 $\begin{aligned} \mathbf{R} &= \mathbf{CH}_3 \ (\mathbf{a}); \ \mathbf{C}_6\mathbf{H}_5 \ (\mathbf{b}); \ \mathbf{C}_6\mathbf{H}_4(\mathbf{CH}_3\textbf{-}p) \ (\mathbf{c}); \ \mathbf{C}_6\mathbf{H}_4\mathbf{Cl}\textbf{-}p \ (\mathbf{d}); \\ \mathbf{C}_6\mathbf{H}_4(\mathbf{NO}_2\textbf{-}p) \ (\mathbf{e}); \ \mathbf{C}_6\mathbf{H}_4(\mathbf{NHCOCH}_3\textbf{-}p) \ (\mathbf{f}). \end{aligned}$

The prepared compounds **Ia–If** were white crystalline solids. Their yields and melting points are collected in Table 1. The composition and the structure of the products were confirmed by elemental analysis, IR, and ¹H NMR spectroscopy.

The following characteristic absorption bands were observed in IR spectra of the studied compounds: stretching vibrations of secondary amino group at $3170-3340 \text{ cm}^{-1}$, ester C=O stretching vibrations at $1655-1670 \text{ cm}^{-1}$ (two bands were observed in the case of compound **If**: at 1695, amide I band, and at 1660 cm^{-1}), and SO₂ stretching vibrations (symmetric at $1160-1180 \text{ cm}^{-1}$ and asymmetric at $1320-1340 \text{ cm}^{-1}$); the presence of NO₂ group in compound **Ie** was

confirmed by the absorption band of the asymmetric stretching vibrations at 1540 cm^{-1} .

Singlet signal of the NH group proton was observed in ¹H NMR spectra of the products at 10.35– 10.54 ppm (the spectrum of compounds **If** contained two singlets at 10.30 and 10.32 ppm). Aromatic ring protons resonated at 7.32–8.20 ppm, and multiplet signals of methylene protons were found at 1.67– 1.70 ppm (the groups in positions 5 and 6) or at 2.54– 2.57 ppm (the groups in positions 4 and 7). Ethoxy group signals appeared as quartets at 4.17–4.20 ppm (CH₂O) and triplets at 1.24–1.30 ppm (CH₃). The spectrum of compound **If** contained additionally a singlet at 2.11 ppm assigned to acetyl CH₃.

The industrial application of compounds is often determined by their solubility. For instance, the solubility of flotation and extraction agents to be used in hydrometallurgy processes should be reasonably high (above 0.03–0.1 mol/L in the corresponding solvents [6]). Experimental data collected in Table 2 show that compounds **Ia–If** can be applied as precipitants or collectors for ionic flotation in the form of solutions in ethanol or in 0.1 mol/L KOH; and they should be extracted with chloroform or xylene.

Table 1. Selected parameters of compounds Ia–If

Comp. no.	R	mp, °C	Yield, %	$R_{ m f}^{~ m a}$
Ia	CH ₃	76–78	68	0.67
Ib	C_6H_5	113–115	75	0.31
Ic	$p-C_6H_4(CH_3)$	125–127	78	0.31
Id	p-C ₆ H ₄ Cl	109–110	65	0.46
Ie	$p-C_6H_4NO_2$	133–135	75	0.39
If	<i>p</i> -C ₆ H ₄ NHCOCH ₃	149–151	69	0.33

Mobile phases: benzene–diethyl ether 1 : 2 (**Ia–Ic**); benzene (**Id**, **If**); benzene–diethyl ether–acetone 9 : 8 : 2 (**Ie**).

The compounds structure suggested that they should be acidic. Electron absorption spectra of the studied compounds confirmed the existence of different ionization states at different pH (see example in the figure). In particular, the spectra of their neutral aqueous-ethanolic solutions contained absorption bands at 208–210 nm (ester group), at 250 nm ($p-\pi^*$ conjugated thiophene ring), and at 300 nm (due to the electron density transfer from donor to acceptor). In the alkaline medium, the band at 300 nm shifted to longer wavelength by 25–30 nm and grew stronger.



Table 2. Solubility of compounds Ia–If, mmol/L (g/L)

Comp. no.	Ethanol 1 mol/L	1 mol/L KOH	Water	Hexane	Xylene	Isoamyl alcohol	Chloroform
Ia	>65 (>19)	40.0 (12.50)	0.3 (0.10)	13.0 (4.0)	>40 (>14)	21 (6.3)	>40 (>13)
Ib	18.0 (6.4)	8.0 (3.07)	1.4 (0.50)	6.8 (2.5)	360 (132.0)	12 (4.4)	1260 (459.7)
Ic	25.0 (9.6)	0.9 (0.33)	0.4 (0.16)	7.0 (2.6)	680 (258.6)	21 (7.8)	1950 (741.5)
Id	18.0 (7.0)	0.15 (0.06)	1.1 (0.43)	6.0 (2.4)	460 (184.8)	20 (7.9)	1590 (637.7)
Ie	3.4 (1.4)	1.8 (0.74)	0.73 (0.30)	1.2 (0.5)	515 (211.3)	3 (1.1)	1190 (489.4)
If	37.0 (15.6)	1.1 (0.47)	0.2 (0.10)	0.2 (0.1)	4 (1.6)	20 (8.3)	66 (27.7)

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Electron absorption spectra of solutions of ethyl-2-mesylamino-4,5,6,7-tetrahydrobenzothiophene-3-carboxylate (Ia, 10^{-5} mol/L) in aqueous ethanol at different pH: 6.6 (*1*), 9.0 (*2*), and 10.7 (*3*).

The ionization of compounds **Ia–If** in alkaline medium occurred as deprotonation of the sulfonamide group (Scheme 1).

In order to determine the compounds acidity constants, we studied the solutions absorbance at 320 nm as a function of pH. However, the absorbance change in the course of ionization was sufficiently high only in the case of compound **Ia**; therefore, the acidity constants of the rest of the products were determined by means of potentiometric titration.

As the studied compounds were poorly soluble in water, their ionization was studied in aqueous-

ethanolic solutions with varied ratio of water to ethanol. The determined acidity constants were then extrapolated to zero concentration of ethanol (linear fit of pK_a with mass fraction of ethanol) to get pK_a value in aqueous solution [7].

The so determined pK_a values of compounds **Ia–If** are given in Scheme 2.

The studied compounds were weak acids; the acidity constants of compounds **Ib–If** was linear with the Hammett constant σ :

$$pK_a = 7.55 - 1.41\sigma_{\text{para}} (r = 0.978)$$

The determined acidity constants suggested that the studied compounds should form complexes with nonferrous metals in neutral and alkaline media. It was therefore important to check the ligands stability in the alkaline medium. It was found that they were stable over 4 h at 60°C and over 24 h at 20°C (0.1 mol/L KOH).

Following the procedure described elsewhere [8] we prepared several complexes with compound **Ic** in the form of precipitates (Table 3). The complexes were insoluble in water, but soluble in ethanol, chloroform, and hexane. The IR spectroscopy (Table 4) and elemental analysis data suggested the complexes composition to be $[ML_2]$ (Scheme 3).

One of the requirements for a reagent to be used as collector in ionic flotation is a low solubility of its metal complex [9]. We calculated the solubility products SP of the prepared complexes as described in [8] (taking into account the metal ion and the ligand ionization states above the precipitate). The elec-

Scheme 2.						
Compound	Ia	Ib	Ic	Id	Ie	If
pK _a	7.57±0.05	7.64 ± 0.04	7.77±0.05	7.10±0.06	6.45 ± 0.04	7.58 ± 0.05
	7.69±0.03 (SP)					

 Table 3. Selected properties of metal complexes with ethyl 2-tosylamino-4,5,6,7-tetrahydrobenzothiophene-3-carboxylate Ic

 (HL)

Compound, color	pH range of formation	-log SP	Solubility, mol/L	$c_{\mathrm{M}}^{\mathrm{free}\ \mathrm{a}}$
[CuL ₂], dark-blue	7.0–10.8	17.08	$1.28 imes 10^{-6}$	$2.5 imes 10^{-4}$
[CoL ₂], light-brown	8.5–11	13.86	1.51×10^{-5}	$3.3 imes 10^{-2}$
[NiL ₂], green	7.4–10.8	16.02	$2.87 imes 10^{-6}$	$1.0 imes 10^{-2}$

^a As calculated from the dissociation constants of $[M(NH_3)_4]^{2+}$ complexes.



M = Cu, Co, Ni.

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were recorded on a MERCURY plus 300 spectrometer (Varian, USA). Melting points were determined using the PTP instrument in standard capillaries. Elemental analysis was performed with the CHNS-932 instrument (LECO Corporation, USA). Thin layer chromatography was run with the Silufol UV-254 plates using iodine vapor as developer.

Compounds Ia-If were prepared via interaction of ethyl 2-amino-4,5,6,7-tetrahydrobenzothiophene-3carboxylate with the corresponding sulfonyl chlorides at room temperature in pyridine; the products were crystallized from 2-propanol [11]. The parent ester was prepared in a single stage from cyclohexanone, cyanoacetic ester in alcoholic solution, and sulfur, using diethanolamine as catalyst [12]. The products purity was confirmed by IR and ¹H spectroscopy, TLC, and elemental analysis.

The fraction of the major component in the product was determined by potentiometric titration [13] of 0.1 g of the product in 30 mL of ethanol with 0.1 mol/L ethanolic KOH. The major component fraction was in all cases above 97%

$$W, \% = (V_{\text{KOH}}c_{\text{KOH}}M_{\text{I}})/m \times 10.$$

The products solubility was determined as described elsewhere, by gravimetry [14], spectro-photometry [14], and refractometry [15]. UV spectra were registered with the SF-2000 spectrophotometer; refractive index was measured using the IRF-22 refractometer. Acid dissociation constants were determined either by means of spectrophotometry or by potentiometry. pH and E of the solutions were measured with the I-160M ionomer (ANTEKh, Belarus) equipped with glass and silver chloride electrodes. The measured pH values were corrected for the ethanol presence as described elsewhere [16].

The pK_a values were calculated from potentiometry results as follows.

trolytes concentration was below 10⁻³ mol/L, and their activity coefficients were therefore taken equal to unity.

The complexes solubility products were calculated as follows:

$$SP = [M^{2+}][L^{-}]^{2},$$

where the equilibrium ligand concentration $[L^-]$ determined as

$$[L^{-}] = \{K[c_{\rm HL} - 2c_{\rm M}(S_{\rm i}/100)]\}/[{\rm H}^{+}],$$

where K, dissociation constant of the ligand HL; $c_{\rm M}$ and $c_{\rm HL}$, initial concentrations of the metal ion and the ligand, respectively, mol/L; S_i , degree of the metal ion precipitation at the observation point, %.

The calculated SP values are collected in Table 3. The most efficient precipitation with compound Ic was attained in the case of copper ions. Low solubility of the complexes in water suggested that the studied compounds were promising collectors to be used in ionic flotation of nonferrous metals. Comparison of the complexes solubility with concentration of the free metal ion in equilibrium with ammonia complexes $c_{\rm M}^{\rm free}$ [10] suggested that the complex formation reaction should be efficient for the precipitation of the metal ions from their ammonia solutions.

EXPERIMENTAL

IR spectra (mineral oil suspension) were recorded on a IFS-66/S Fourier spectrometer (Bruker, Germany), ¹H NMR spectra (DMSO- d_6 solutions)

Table 4. Position of stretching vibrations bands (cm⁻¹) in IR spectra of ethyl 2-tosylamino-4,5,6,7-tetrahydrobenzothiophene-3-carboxylate Ic (HL) and its metal complexes

Compound	v(N–H)	ν(C=O)	$\nu(SO_2)$
HL (Ic)	3117	1657	1160, 1323
[CuL ₂]	_	1595	1148, 1316
[CoL ₂]	_	1587	1145, 1317
[NiL ₂]	_	1563	1165, 1323

$$pK_{a} = \log \frac{(1-\alpha)c_{I} - [H^{+}] + [OH^{-}]}{\alpha c_{I} + [H^{+}] - [OH^{-}]} + pH$$

where α , degree of neutralization of the studied compound; c_{I} , the total compound concentration, mol/L; [H⁺] and [OH⁻], concentrations of the respective ions, mol/L.

Hydrolytic stability of the compounds was studied by spectrophotometry as described elsewhere [14].

The content of the metal ions in the solutions was determined using the iCE 3500 atomic absorption spectrometer with flame atomization (Thermo Fisher Scientific, USA).

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