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Thiosemicarbazones as Effective Fluorescent Sensors for Cations and Anions

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Abstract— Series of anthracene-containing chemosensors was synthesized by the reaction of 4-R-thiosemicarbazides with aromatic aldehydes. Spectral studies showed their high sensory activity with respect to a group of cations and anions like Hg^{2+}, F^-, CN^-, AcO^- etc.

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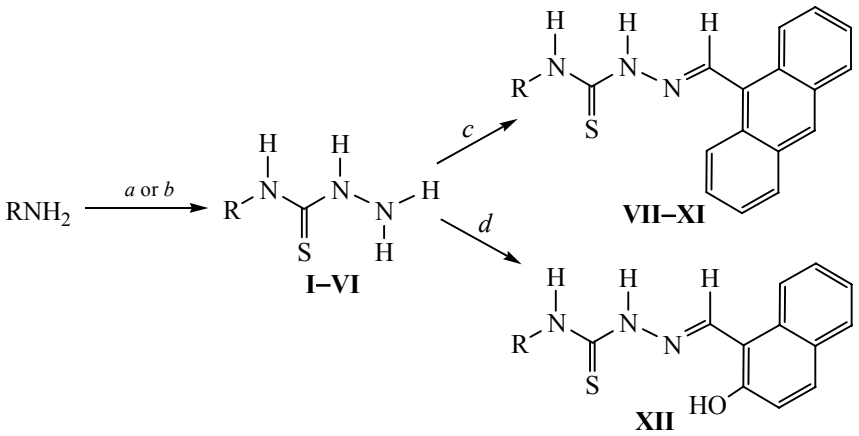
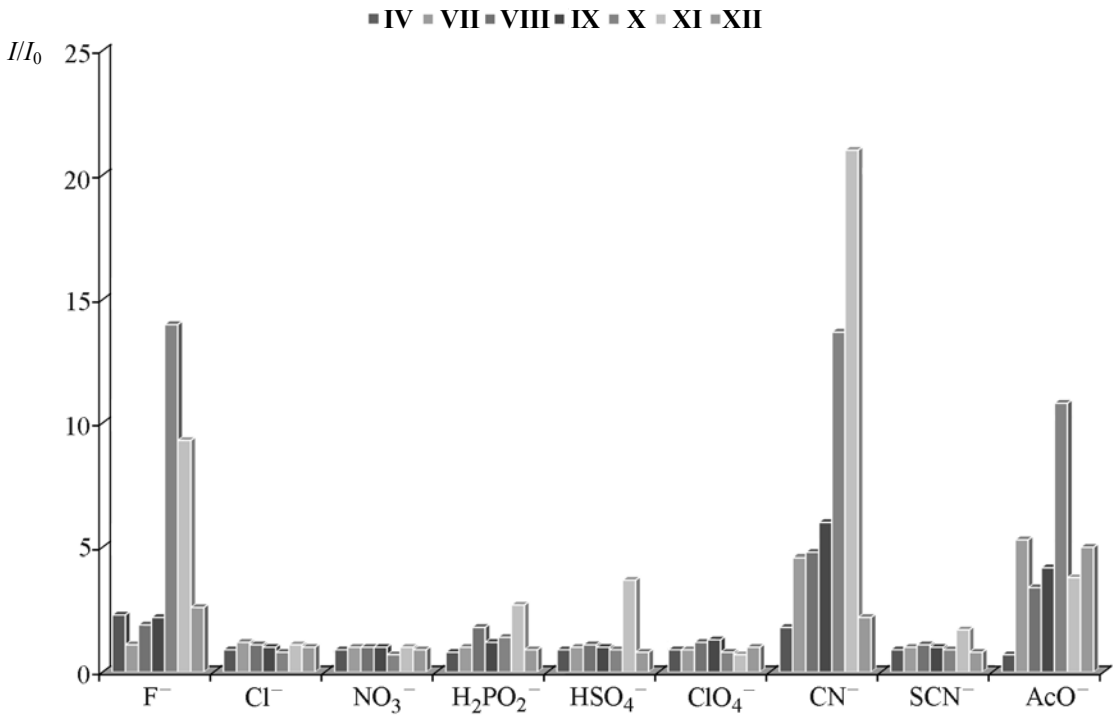
Recently a significant progress was reached in the development of fluorescent chemosensors capable to recognize selectively different analytes of ionic nature, which is primarily associated with the development of research of the sensory processes [1–4]. The basis of the most effects observed in the ionochromic molecules consists in two principal types of interactions: electrostatic and hydrogen bonds formation [1, 2].

Thus, the effect of anion sensors is based on their ability to form hydrogen bonds between their receptor part and a negatively charged pollutant. Depending on the structure of the receptor, such sensors are able to selectively recognize anions of different nature, geometry, and the charge [5–7]. Most effective in this case are sensors of neutral nature containing amide or thioamide tautomeric fragments capable of forming stable hydrogen bonds [8–10]. Several derivatives of thiosemicarbazide exhibit sensory properties with respect to both cations and anions. In these compounds the receptor often acts also as a signal fragment [11–14]. The presence of a fluorescent substituent in the sensor molecule increases its sensitivity and creates advantages in accuracy and mobility at performing analyses.

We have previously developed mono- and dithiourea derivatives containing 9-anthrylmethyl fragment as highly effective sensors to Hg^{2+} cations [15, 16]. To obtain new sensitive sulfur-containing cation and anion sensors, we synthesized a number of thiosemicarbazides **I–VI**.



a, (1) CS_2, NH_4OH, (2) $ClCH_2CO_2Na$, (3) NH_2NH_2; *b*, $NH_2NHC(S)SMe$; *c*, 9-acarbaldehyde, H^+, 1-BuOH; *d*, 2-hydroxynaphthalene-1-carbaldehyde, H^+; R = H (**I, VII**), CH_2Ph (**II, VIII**), CH_2CH_2Ph (**III, IX**), 9-$C_{14}H_9CH_2$ (**IV, XII**), 2-$MeOC_6H_4$ (**V, X**), 4-$Et_2NC_6H_4$ (**VI, XI**).



The relative change in fluorescence intensity of compounds **IV, VII–XII** ($c = 5.0\times10^{-6}$ M) in MeCN with additives of NBu_4^+ A^- salts ($c = 2.5 \times 10^{-5}$ M).

Thioamides **II** and **III** were synthesized by successive interaction of the corresponding amines with carbon disulfide, sodium chloroacetate, and hydrazine hydrate (method *a*) [17], and derivatives **IV–VI**, by the reaction of aromatic amines and (anthracen-9-ylmethyl)amine with methylhydrazine carbodithioate (method *b*) [18]. The ^{1}H NMR spectrum of compound **IV** contains characteristic signals of protons of the thiosemicarbazide group (both NH_2 and NH), and of the CH_2 fragment (a doublet, δ 5.63 ppm, *J* 7.2 Hz).

The thiosemicarbazides obtained were then brought into the condensathion reacthion with anthracene-9-carbaldehyde to form compounds **VII–XI** and 2-hydroxynaphthalene-1-carbaldehyde to obtain the derivative **XII**. The formation of thiosemicarbazone fragment is indicated by the disappearance in the ^{1}H NMR spectra of the signal of NH_2 protons and downfield shift of the signals of two NH protons.

According to the data of electron absorption spectroscopy, compounds **IV** and **XII** possess only the fluorescence of the "classic" anthracene type with λ_{max} = 412–414 nm. In the case of derivatives **VII–XI** the maximum suffers a red shift by ~15–85 nm relative to the ordinary values, and the structure of the spectrum is unusual for the anthracene derivatives: the spectrum contains one broad band. On the basis of fluorescence spectra we studied the chemosensory activity of the obtained thioamides **I–XII** with respect to the group of cathions: H^+, Zn^{2+}, Cd^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Pb^{2+}, and Hg^{2+}. As was the case of the previously described derivative **I** [11], the most selective is the response to the ions Cu^{2+} and Hg^{2+}. This is primarily due to the presence of *soft* nucleophilic center, the sulfur atom, and the possibility of prototropic tautomerism in the thioamide fragment. The maximum sensitivity with respect to the mercury(II) ions in a series of derivatives is exhibited by thiosemicarbazone **VI**: at the interaction 16-fold increase in the fluorescence burn occurs. Other cations did not cause any significant changes in the fluorescence intensity (I/I_0 in the range of 0.7–2.3). At adding trifluoroacetic acid to a soluthion of sensor **IV** a red shift of fluorescence maximum by 40 nm occurs with a slight increase in its intensity.

We investigated also the interaction of the derivatives **IV**, **VII–XII** with tetrabutylammonium salts containing anions F^- , Cl^-, CN^-, SCN^-, NO_3^-, $H_2PO_2^-$, ClO_4^-, HSO_4^-, and AcO^- (see the figure).

Significant changes in the fluorescence intensity were noted only at the interaction with fluoride,

cyanide, and acetate anions. The maximum fluorescence burn occurred at adding these anions to the derivatives **X/XI**, 14.0/9.0, 14.0/21.0, and 11.0/4.0 times, respectively. With the other derivatives no high sensitivity and selectivity in the detecthion of anions was observed.

In going from thiosemicarbazide **X** to **XI** a sharp increase occurs in the selectivity with respect to the cyanide anion. In addithion, the ions CN^- and F^- cause blue shift of the fluorescence maximum of thioamides **X** by ~25 nm. The most significant shift of fluorescence maxima occurs at adding $NBu_4^+F^-$ to a soluthion of imine **VIII**: a blue shift by 84 nm, and at adding $NBu_4^+CN^-$ to a soluthion of imine **XII**: a red shift by 49 nm.

Thus, the study of 3-[(anthracen-9-ylmethylidene)-amino]-1-R-thioureas as potential chemosensors for various cations and anions showed their high selectivity towards Hg^{2+} cations and F^- and CN^- anions.

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Varian Unity-300 spectrometer (300 MHz). As internal references residual signals of $CHCl_3$, δ 7.25 ppm, and $(CH_3)_2SO$, δ 2.50 ppm, were used. The electron absorption spectra were recorded on a Varian Cary 100 spectrophotometer, the luminescence spectra were measured on a Hitachi 650-60 and a Varian Eclipse spectrofluorimeters. The IR spectra were recorded on a Specord 75IR instrument from the samples in mineral oil. Melting points were determined in glass capillaries on a PMP (M) device. Completeness of the reactions and individuality of the compounds obtained were monitored by TLC (plates Silufol U254, eluent chloroform, development by the iodine vapor in a humid chamber).

General procedure for the preparathion of 1-R-3-aminothioureas (II–VI). Derivatives **II** and **III** were synthesized by the method of [17], **IV**–**VI**, according to [18].

3-Amino-1-benzylthiourea (II). Yield 82%, mp 132–133ºC (MeCN). Found, %: C 52.95; H 6.05; N 23.23; S 17.77. $C_8H_{11}N_3S$. Calculated, %: C 53.01; H 6.12; N 23.18; S 17.69.

3-**Amino-1-[2-phenylethyl]thiourea (III).** Yield 82%, mp 118–119ºC (MeCN). Found, %: C 55.41; H 6.65; N 21.44; S 16.50. Calculated, %: C 55.35; H 6.71; N 21.52; S 16.42.

3-Amino-1-(anthracen-9-ylmethyl)thiourea (IV). Yield 73%, mp 254–255ºC (1-butanol). IR spectrum, ν, cm^{-1}: 3300, 3100, 1520, 1450. ^{1}H NMR spectrum, δ, ppm (DMSO-d_6): 4.20 br.s (2H, NH_2), 5.63 d (2H, *J* 7.2 Hz, CH_2), 7.40–8.56 m (10H, H_{Ar}, NH); 8.69 br.s (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5\times10^{-5}$ M): 415. Found, %: C 68.38, H 5.30; N 14.84; S 11.48. Calculated, %: C 68.30; H 5.37; N 14.93; S 11.40.

3-Amino-1-(2-methoxyphenyl)thiourea (V). Yield 80%, mp 166–167ºC (EtOH). Found, %: C 48.80; H 5.54; N 21.22; S 16.33. Calculated, %: C 48.71; H 5.62; N 21.30; S 16.25.

3-Amino-1-[4-(diethylamino)phenyl]thiourea (VI). Yield 87%, mp 137–138ºC (MeCN). Found, %: C 55.50; H 7.55; N 23.43; S 13.52. $C_{11}H_{18}N_4S$. Calculated, %: C 55.43; H 7.61; N 23.51; S 13.45.

General procedure for obtaining compounds (VII–XII, **XIII).** A soluthion of 2 mmol of an appropriate aminothiourea **I–VI** and 2 mmol of anthracene-9-carbaldehyde (synthesis of compounds **VII–XII**) or 2-hydroxynaphtalene-1-carbaldehyde (synthesis of imine **XIII**) in 20 ml of 1-butanol was heated for 2 h. The solvent was evaporated in a vacuum and the residue was crystallized.

3-[(Anthracen-9-ylmethylidene)amino]thiourea (VII). Yield 85%, mp 225–226ºC (193–194ºC [11]). IR spectrum, ν, cm^{-1}: 3300, 3100, 1595, 1530, 1460, 1235. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.35 br.s (1H, NH); 7.42–7.60 m (4H, H_{Ar}, NH_2), 5.8 d (4H, *J* 8.6 Hz , H_{Ar}); 8.12 br.s (1H, NH); 8.50–8.58 m (3H, H_{Ar}); 9.28 s (1H, CH) 11.65 s (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5\times10^{-5}$ M): 497. Found, %: C 68.85; H 4.75; N 14.96; S 11.44. $C_{16}H_{13}N_3S$. Calculated, %: C 68.79; H 4.69; N 15.04; S 11.48.

3-[(Anthracen-9-ylmethylidene)amino]-1-benzylthiourea (VIII). Yield 88%, mp 232–233ºC. IR spectrum, ν, cm^{-1}: 3290, 3100, 1600, 1535, 1460. ^{1} H NMR spectrum (DMSO-d_6), δ, ppm: 4.86 d (2H, *J* 7.0 Hz, CH_2), 7.12–7.60 m (9H, H_{Ar}); 8.04 d (4H, *J* 8.6 Hz, H_{Ar}); 8.42–8.60 m (4H, H_{Ar}, NH); 9.30 s (1H, CH), 11.80 s (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5\times10^{-5}$ M): 497. Found, %: C 74.85; H 5.25; N 11.29; S 8.61. $C_{23}H_{19}N_3S$. Calculated, %: C 74.77; H 5.18; N 11.37; S 8.68.

3-[(Anthracen-9-ylmethylidene)amino]-1-(2-phenylethyl)thiourea (IX). Yield 81%, mp 165–

166ºC. IR spectrum, ν, cm^{-1}: 3300, 3100, 1590, 1530, 1455. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.00 m (2H, *J* 7.4 Hz, CH_2) 4.00 to (2H, *J* 7.2 Hz, CH_2), 7.08–7.33 m (5H , H_{Ar}); 7.43–7.68 m (5H, H_{Ar}, NH); 7.96–8.12 m (2H, H_{Ar}); 8.30–8.42 m (2H, H_{Ar}); 8.52 s (1H, H_{Ar}); 9.00 s (1H, CH), 10.07 s (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5\times10^{-5}$ M): 455. Found, %: C 75.21; H 5.45; N 11.04; S 8.30. $C_{24}H_{21}N_3S$. Calculated, %: C 75.16; H 5.52; N 10.96; S 8.36.

3-[(Anthracen-9-ylmethylidene)amino]-1-(2-methoxyphenyl)thiourea (X). Yield 78%, mp 212–212–213ºC. IR spectrum, ν, cm^{-1}: 3280, 3080, 1520, 1465. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.78 s (3H, CH_3), 6.90–7.20 m (3H, H_{Ar}); 7.50–7.75 m (4H, H_{Ar}); 8.18 d (2H, *J* 8.4 Hz, H_{Ar}); 8.57–8.82 m (4H , H_{Ar}); 9.48 a (1H, CH), 9.96 s (1H, NH), 12.16 s (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5 \times 10^{-5}$ M): 475. Found, %: C 71.71; H 5.05; N 10.85; S 8.24. $C_{23}H_{19}N_3OS$. Calculated, %: C 71.66; H 4.97; N 10.90; S 8.32.

3-[(Anthracen-9-ylmethylidene)amino]-1-[2-(diethylamino)phenyl]thiourea (XI). Yield 92%, mp 186–187ºC. IR spectrum, ν, cm^{-1}: 3300, 3080, 1510, 1460. ^{1} H NMR spectrum (DMSO-d_6), δ, ppm: 1.15 t (6H, *J* 7.2 Hz, $2CH_3$) 3.32 to (4H, *J* 7.0 Hz, $2CH_2$), 6.65 d (2H, *J* 8.2 Hz, H_{Ar}); 7.38 d (2H, *J* 8.2 Hz, H_{Ar}); 7.42–7.70 m (4H, H_{Ar}); 8.07 d (2H, *J* 8.6 Hz, H_{Ar}); 8.40–8.60 m (3H , H_{Ar}); 9.06 s (2H, CH); 9.08 s (2H, NH); 10.06 from (1H, NH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5 \times 10^{-5}$ M): 432. Found, %: C 73.30; H 6.08; N 13.04; S 7.58. $C_{26}H_{26}N_4S$. Calculated, %: C 73.21; H 6.14; N 13.13; S 7.52.

3-[(2-Hydroxynaphthalen-1-ylmethylidene)amino]-1-(anthracen-9-ylmethyl)thiourea (XII). Yield 82% yield, 293–294ºC (1-butanol-DMF). IR spectrum, ν, cm^{-1}: 3330, 3100, 1610, 1515, 1460. ^1H NMR spectrum, δ, ppm (DMSO-d_6): 5.77 d (2H, *J* 7.4 Hz, CH_2), 6.88–7.23 m (3H, H_{Ar}), 7.42–7.73 m (6H, H_{Ar}); 8.00–8.20 m (4H, H_{Ar}, NH); 8.40–8.60 m (3H, H_{Ar}); 8.95 s (1H, CH), 10.29 br.s (1H, NH); 11.50 br.s (1H, OH). The fluorescence spectrum in acetonitrile, λ_{max}, nm ($c = 5 \times 10^{-5}$ M): 415. Found, %: C 74.38, H 4.92; N 9.73; S 7.30. $C_{27}H_{21}N_3SO$. Calculated, %: C74.46; H 4.86; N 9.65; S 7.36.

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