Synthesis and structures of 3-hydroxy-6-(R-phenylazo)-7,8-benzo-1,2,3,4-tetrahydroquinolines as products of analytical test reactions for nitrite and nitrate anions

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An improved procedure was proposed for the synthesis of 3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline, which is used as a reagent for the analytical test reaction for nitrate and nitrite anions based on azo coupling with diazo compounds. 3-Hydroxy-6-(R-phenylazo)-7,8-benzo-1,2,3,4-tetrahydroquinolines (R = 2-COOH, 4-COOH, or 4-SO_3H) were synthesized by azo coupling reactions in 65—70% yields. The structures of these compounds were confirmed by elemental analysis, ^1H NMR and IR spectroscopy, and X-ray diffraction. Based on the X-ray data, the bathochromic shift in the UV spectrum of the *o*-carboxy isomer compared to the *p*-carboxy isomer ($\Delta\lambda_{max}$ = 50 nm) is attributed to a strong intramolecular hydrogen bond.

Key words: 3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline; Griess reaction; azo compounds, synthesis, molecular structure, crystal structure; analytical test reactions for the nitrite ion.

A modification of known organic compounds and the synthesis of new organic compounds, which provide a deep color in reactions with analyte compounds and can be used for rapid tests, is a challenge to analytical chemistry. In some cases, these analytical reactions produce arylazo compounds intensely absorbing light in the visible region. Known methods for the determination of nitrates and nitrites by the Griess reaction often use cancerogenic dermatosic 1-naphthylamine and *N*-(1-naphthyl)ethylenediamine, which have an unpleasant odor and are unstable to light and in air, as azo components in the reactions with aryldiazo compounds. The latter are generated in the reactions of arylamines with nitrite ions or reduced nitrate ions. Azo coupling of 1-naphthylamine and *N*-(1-naphthyl)ethylenediamine with 4-diazobenzenesulfonic acid (sulfamic acid) affords orange-red compounds.[1] Earlier,[2—4] the noncancerogenic analytical reagent 3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline (**1**) has been proposed. The latter compound has no drawbacks stated above. Molecule **1** contains a nearly planar tricyclic system with restricted rotation about the C—N bond and bears the hydroxy group capable of forming intermolecular hydrogen bonds, for example, with the hydroxy group of cellulose due to which reagent **1** can be immobilized on a cellulose support. The conjugated bond system in molecule **1** provides a deep color of the products of azo coupling with diazo compounds. Reagent **1** and products of its test reactions are resistant to light and are stable at high temperatures and, consequently, they can be stored over a long time in containers or as samples immobilized on a paper.

In the present study, we synthesized compound **1** and products of its azo coupling with aryldiazo compounds and characterized these compounds by spectroscopic methods. The compositions and structures of these products were determined and the possibilities of their use as test indicators for the NO_2^- and NO_3^- anions (in the latter case, after preliminary reduction to NO_2^-) were examined.

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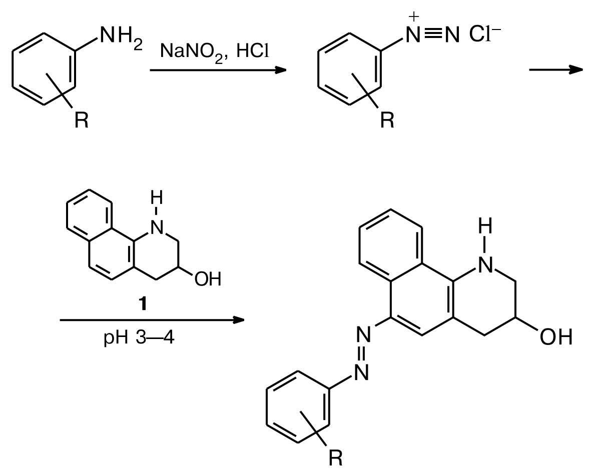
Results and Discussion

Earlier, 3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline hydrochloride (**1**) has been prepared by condensation of 1-naphthylamine with 3-chloro-1,2-epoxypropane (epichlorohydrin) in PhCl [5] or in aqueous EtOH.[6] The base was synthesized by reprecipitation of the hydrochloride with water from pyridine. The yield of the reaction product was not reported. We examined this procedure and found that an increase in the reaction temperature by using higher-boiling 1,2-dichlorobenzene instead of PhCl as the solvent enhances the yield of compound **1** from 34 to 60%. Besides, we developed a simpler and safe procedure for the transformation of hydrochloride **1** into the base with aqueous NH_3.

Compound **1** is a convenient reagent for Griess-type test reactions for NO_2^- and NO_3^- anions. To find the optimal reagents, we simulated these reactions, in particular, for the purpose of elucidating the effect of the nature of the substituent in the starting arylamines on the bathochromic shift.

3-Hydroxy-6-(R-phenylazo)-7,8-benzo-1,2,3,4-tetrahydroquinolines **2—4** (R = 4-COOH (**2**), 2-COOH (**3**), or 4-SO_3H (**4**)) were synthesized in 65—75% yields by diazotization of arylamines followed by azo coupling of the resulting diazo compounds with azo component **1** (Scheme 1).

Scheme 1



2—4

R = 4-COOH (**2**), 2-COOH (**3**), 4-SO_3H (**4**)

The IR spectra of compounds **1—4** show analogous intense C—O absorption bands at 1060 cm^{-1} assigned to the C—OH fragment of the ring. The IR spectrum of compound **1** has intense absorption bands of OH (3424 cm^{-1}), NH (3350 cm^{-1}), CH arom. (3045 cm^{-1}), and CH_2 (2916 (ν_s) and 2820 cm^{-1} (ν_{as})) groups. The IR spectra of azo compounds **2—4** show bands of the same groups, but these bands are substantially broadened. In the spectrum of compound **3**, these bands merge into a broad intense band at 3400—2400 cm^{-1} due, apparently, to hydrogen bonding with the solvent (Me_2CO, EtOH, or water depending on the purification procedure). The presence of solvate molecules in crystalline azo compounds **2—4** was confirmed by the change in solubility (for **2**), X-ray diffraction data (for **3**), and the weight change upon heating *in vacuo* (for **4**). Unlike the spectrum of compound **1**, the IR spectra of azo compounds **2—4** show also stretching bands of C—N groups at 1300—1200 cm^{-1} and $N{=}N_{trans}$ groups at 1550—1520, 1456, and 960 cm^{-1}. The IR spectra of carboxy compounds **2** and **3** have intense bands of C=O groups at 1692 and 1664 cm^{-1}, respectively. The IR spectrum of sulfo compound **4** shows bands of S—O (1028, 1004, and 1000 cm^{-1}), S=O (1360, 1316, and 1164 cm^{-1}), and C—S (664 and 620 cm^{-1}) groups.

The presence of intense signals at δ 2.71—3.81 assigned to the protons at the C(2)—C(4) atoms and a signal at δ 4.03—4.29 (OH) in the ^{1}H NMR spectra of compounds **1—4** (Table 1) confirms the retention of the hydrogenated 3-hydroxyquinoline ring in the azo derivatives. It should be noted that the electron-withdrawing effect of the arylazo group on this ring in azo compounds **2—4** (downfield shifts of the signals in the spectra of these compounds compared to compound **1**) is observed only for the protons at the C(2) atom at position 2 with respect

Table 1. ^{1}H NMR spectra of compounds **1—4** (δ)

Compound	C(2)H$_2$	C(3)H	C(4)H$_2$	OH (s)	NH	C(6)H	H heteroarom. (m, 5 H)	H arom.
1	3.27, 3.45 (both d)	3.04 (m)	2.71, 2.78 (both d)	4.03	4.84 (s)	6.08 (d)	7.05—7.96	—
2	3.59, 3.80 (both d)	3.14 (m)	2.88, 2.93 (both d)	4.29	4.74 (br.s)	—	7.63—7.68, 8.25—8.77	7.78 (d, 2 H, C(2´), C(6´)); 8.05 (d, 2 H, C(3´), C(5´))
3	3.61, 3.77 (both d)	3.29 (m)	2.77, 2.84 (both d)	4.29	5.10 (s)	—	7.32—7.45, 7.86—8.85	7.49—7.83 (m, 4 H)
4	2.74—3.81 (m)			4.29	—	—	7.32—7.74, 8.20, 8.77—8.80	7.80 (d, 2 H, C(2´), C(6´)); 8.30 (d, 2 H, C(3´), C(5´))

to the amino group, which, in turn, is at position 4 with respect to the arylazo group. In the spectra of azo compounds **2—4**, the signals for the aromatic protons of the heterocycle are substantially shifted downfield compared to those in the spectrum of compound **1**. In molecule **3**, the 2-carboxy group cannot interact with the amino group because of the presence of the intramolecular hydrogen bond. As a result, the proton of the amino group is observed as an intense sharp singlet at δ 5.10. In the spectrum of compound **2**, this signal (at δ 4.74) is substantially broadened due to an interaction of the amino group with the 4-carboxy group. This signal is absent from the spectrum of sulfonic acid **4** indicating the zwitterionic structure of this compound.

The character of the nucleophilic activity of compound **1** is clearly confirmed by the ^{1}H NMR spectrum. The signal for the proton at the C(6) atom is observed at higher field compared to the signals for the other aromatic protons, which is evidence for the highest electron density on the carbon atom at position 6 with respect to which the electron-donating NH group is in the *para* position. This signal is absent from the spectra of compounds **2—4**. The signals for the other aromatic protons are shifted downfield by 1—2 ppm (see Table 1). Therefore, we demonstrated that azo coupling can occur at the C(6) atom. The other positions in the aromatic moiety of compound **1** are inactive in azo coupling reactions.

Azo compounds **2—4** isolated in individual state have a deep color and high molar absorption coefficients (Fig. 1).

Azo compound **3** has a violet color. The bathochromic shift of the maximum in the electronic absorption spectrum with respect to the maximum in the spectrum of isomer **2** is 50 nm. Presumably, there is a strong inramolecular hydrogen bond between the nitrogen atom of the azo group and the carboxy group, which is in the *ortho* position with respect to the azo group, in azo compound **3**. This is responsible for the bathochromic shift of the maximum in the absorption spectrum of *ortho* isomer **3** compared to *para* isomer **2**.

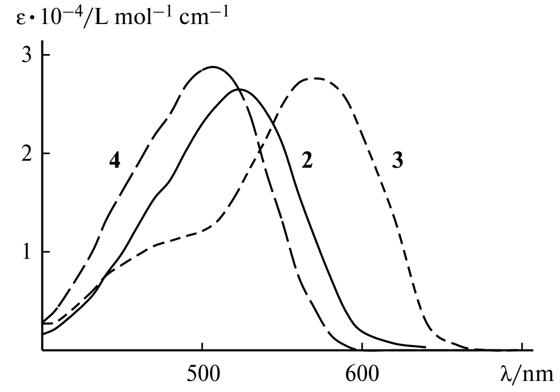


Fig. 1. Electronic absorption spectra of azo compounds **2—4**.

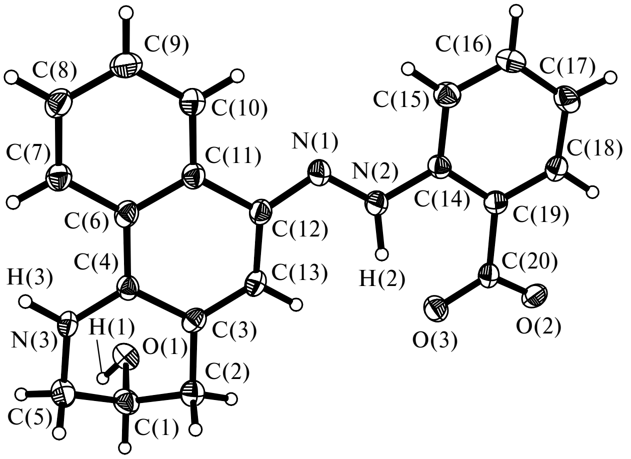


Fig. 2. Structure of compound **3** based on X-ray diffraction data. Selected bond lengths/Å: O(1)—C(1), 1.389(5); O(2)—C(20), 1.242(4); O(3)—C(20), 1.247(4); N(1)—N(2), 1.305(4); N(1)—C(12), 1.313(4); N(2)—C(14), 1.388(4); N(3)—C(4), 1.306(4); N(3)—C(5), 1.459(4).

Actually, X-ray diffraction study of compound **3** (Fig. 2) demonstrated that the hydrogen atom, which was found in difference electron density maps and refined isotropically, is located at a distance of 1.02 Å from the N(2) atom (N(1)—N(2), 1.314(5) Å). The O...H distance is 1.63 Å. Deprotonation of the carboxylate fragment gives rise to a short intermolecular hydrogen bond (1.86 Å) with the hydroxy group of the adjacent molecule **3**, resulting in the formation of an associate of two molecules coordinated in a head-to-tail fashion (Fig. 3). The C—C bond lengths in the aryl fragment are equalized and vary in the range of 1.385(5)—1.402(6) Å.

Therefore, we demonstrated that the carbon atom at position 6 of 3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline exhibits high nucleophilic activity in azo coupling reactions with 4- and 2-diazobenzoic acids and with 4-diazobenzenesulfonic acid giving rise to intensely colored azo dyes. Among these dyes, the largest bathochromic shift is observed in the electronic absorption spectrum of 6-[(2-carboxyphenyl)azo]-3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline. The latter compound may be of interest as a reagent for the determination of nitrates and nitrites in orange or red media.

Experimental

The IR spectra were recorded on a Specord M-80 instrument (KBr pellets). The ^{1}H NMR spectra in DMSO-d$_6$ were measured on a Varian VXR-300 spectrometer (300 MHz) with Me$_4$Si as the internal standard. The electronic absorption spectra in the 400—700 nm region were recorded on a TU-1800 spectrophotometer (Taiwan).

3-Hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline (1). A mixture of 1-naphthylamine (42.9 g, 0.3 mol), epichlorohydrin (27.9 g, 0.3 mol), and 1,2-dichlorobenzene (40 mL) was

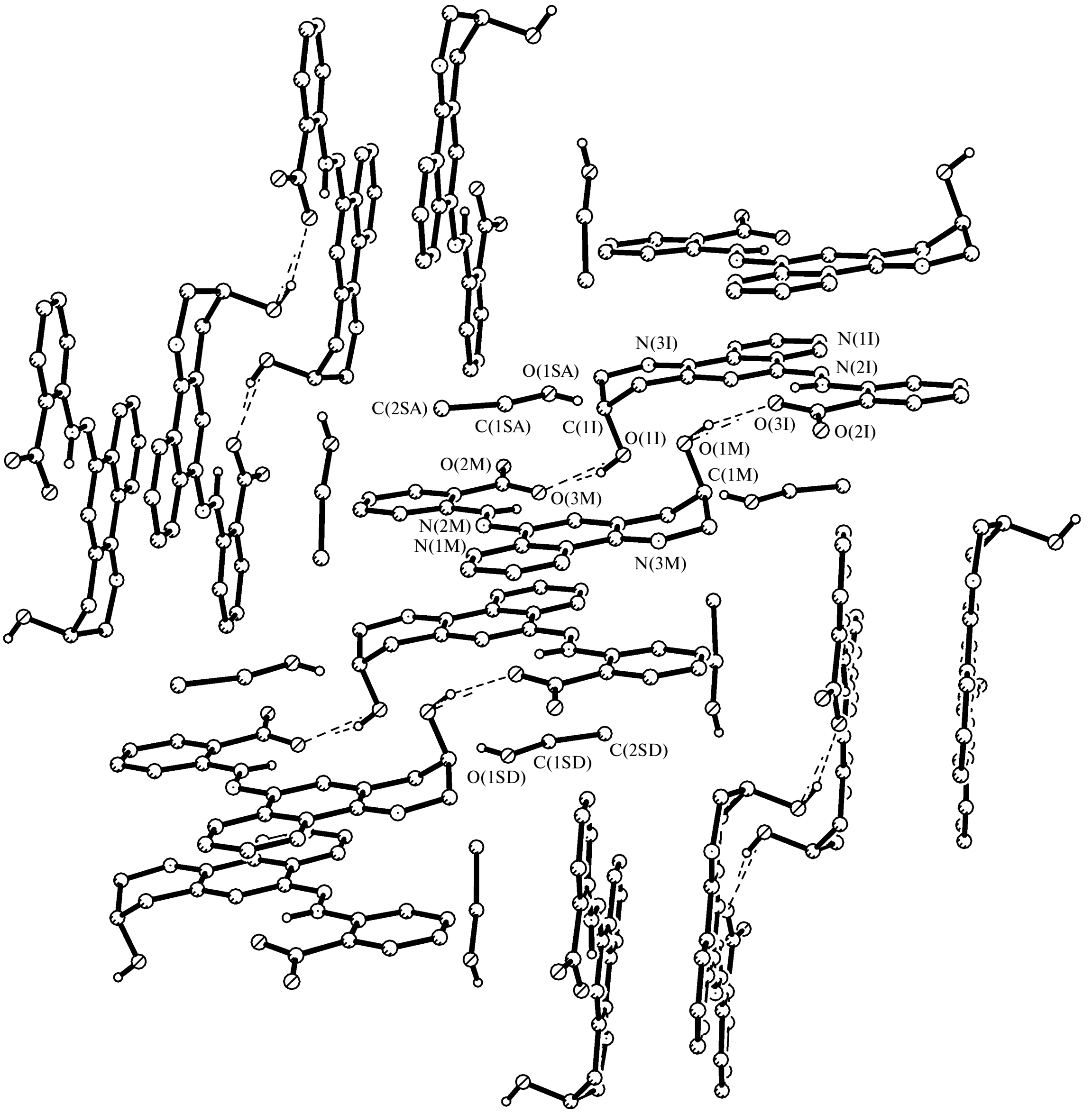


Fig. 3. Fragment of the molecular packing of **3** in the unit cell (co-crystallizate of molecule **3** with 1/2 of the EtOH molecule).

stirred at 160 °C for 7 h under airtight conditions on a sand bath equipped with a relay. The precipitate that formed was separated and successively washed with PhCl (10 mL) and hexane (10 mL). The product was stirred with 25% aqueous NH_3 (150 mL), separated, washed with water to neutral pH, and dried. A finely crystalline powder was obtained in a yield of 35 g (60%), R_f 0.82 ($CHCl_3$ as the eluent), m.p. 148—150 °C. Sublimation of the product afforded white fibrous crystals with m.p. 152 °C (*cf.* lit. data[5]: colorless needle-like crystals, m.p. 151.9—152.2 °C). IR, ν/cm^{-1}: 3424 (O—H); 3350 (N—H bond.); 3045 (C—H aliph.); 2916 ($\nu_s(CH_2)$); 2820 ($\nu_{as}(CH_2)$); 1576, 1528, 1488 (C=C arom.); 1352 (C arom.—N); 1320 (C aliph.—N, C—C, C—O); 1260, 1128 (C—C arom.); 1060 (C—O_{COH}); 1032 (C—C); 980 (C—N—C); 796, 744, 730, 656 (C—H arom.).

6-[(4-Carboxyphenyl)azo]-3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline (2). A 10% aqueous $NaNO_2$ solution (1.4 mL, 2 mmol) was added dropwise with stirring to a mixture of 4-aminobenzoic acid (0.28 g, 2 mmol), 10% AcOH (6 mL, 10 mmol), and a 1 *M* HCl solution (2 mL, 2 mmol) at 0—3 °C. The presence of $NaNO_2$ was monitored using a iodide-starch paper. The resulting solution was added with stirring to a solution of compound **1** (0.39 g, 2 mmol) in EtOH (43 mL), heating of the solution being prevented. After 1 h, water (30 mL) was added. The dark-red precipitate that formed was filtered off, successively washed with water (100 mL) and EtOH (20 mL), and dried *in vacuo* over an alkaline. Reprecipitation of the product from DMF with a 20-fold volume of a 1 : 1 Me_2CO—hexane mixture gave a crystalline black compound with a greenish-gold tint, t.decomp. 192—193 °C. A crimson-red solution in EtOH was obtained. UV (EtOH), λ_{max}/nm (ε_{max}): 522.0 (26600). The yield was 0.45 g (65%). Found (%): C, 60.02; H, 6.26; N, 12.52. $C_{20}H_{17}N_3O_3 \cdot Me_2NCOH \cdot 2H_2O$. Calculated (%): C, 60.52; H, 6.18; N, 12.27. Heating of a solution of compound **2** in

Pr^{i}OH afforded a precipitate as small dark aggregates insoluble in Me$_2$CO and Pr^{i}OH but soluble in DMF and DMSO with red coloration. Found (%): C, 69.02; H, 4.01; N, 11.65. $C_{20}H_{17}N_3O_3$. Calculated (%): C, 69.15; H, 4.93; N, 12.10. IR, ν/cm^{-1}: 3400 (O—H); 3270 (N—H bond.); 3070 (C—H aliph.); 2850—2950, 2300—2600 (C—H aliph., H—O bond.); 1692 (C=O); 1600, 1544, 1480 (C=C arom.); 1456, 1436 (N=N$_{trans}$); 1412 (C aliph.—N); 1364 (C arom.—N); 1308, 1264 (C—C); 1244 (C—O); 1164, 1128 (C—C arom.); 1112, 1060 (C—O$_{COH}$); 1040 (C—C, C—O); 1012 (C—O); 960 (C—N—C); 856, 816, 772, 688, 616 (C—H arom.).

6-[(2-Carboxyphenyl)azo]-3-hydroxy-7,8-benzo-1,2,3,4-tetrahydroquinoline (3). A diazo solution consisting of 2-aminobenzoic (anthranilic) acid (0.42 g, 3 mmol), 10% AcOH (7.5 mL, 12.5 mmol), a 1 *M* HCl solution (2.3 mL, 2.3 mmol), and a 10% NaNO$_2$ solution (2.1 mL, 3 mmol) was added dropwise with vigorous stirring to a mixture of compound **1** (0.585 g, 3 mmol) in water (40 mL), DMF (20 mL), and EtOH (20 mL) at 0—3 °C for 1 h. The reaction mixture was kept in a refrigerator for 48 h. The dark-violet precipitate that formed was filtered off, successively washed with water (150 mL) and EtOH (20 mL), and dried. The yield was 0.9 g (79%), t.decomp. 185 °C. A violet solution in EtOH was obtained. UV (EtOH), λ_{max}/nm (ε_{max}): 572.0 (27600). Found (%): C, 62.67; H, 5.70; N, 10.94. $C_{20}H_{17}N_3O_3 \cdot 2H_2O$. Calculated (%): C, 62.65; H, 5.53; N, 10.96. A portion of the product was dissolved in boiling EtOH. The hot solution was filtered through a glass sinter into a thermally insulated vessel and kept at ~20 °C for two weeks. The prismatic single crystals that formed were separated from the solution by decantation and dried in air at ~20 °C. X-ray diffraction data for the molecules of composition $C_{20}H_{17}N_3O_3 \cdot 0.5EtOH$ are presented in Figs 2 and 3. IR, ν/cm^{-1}: 2400—3400 br (O—H bond., N—H bond., O—H, C—H aliph.); 1672 (C=O); 1604, 1588, 1528, 1484 (C=C arom.); 1452 (N=N$_{trans}$); 1400—1200 br; 1160 (C—C); 1128 (C—C arom.); 1088, 1068, 1040 (C—O); 980 (C—N—C); 852, 752, 708, 684, 652 (C—H arom.).

3-Hydroxy-6-[(4-sulfophenyl)azo]-7,8-benzo-1,2,3,4-tetrahydroquinoline (4). A 10% NaNO$_2$ solution (1.4 mL, 2 mmol) was added with stirring to a mixture of sulfanilic acid (0.346 g, 2 mmol), 10% AcOH (6 mL, 10 mmol), and a 1 *M* HCl solution (2 mL, 2 mmol) at 0—1 °C. After 1 h, the resulting suspension was added dropwise to a solution of compound **1** (0.39 g, 2 mmol) in EtOH (43 mL), heating of the reaction mixture being prevented. Then the mixture was stirred for 1 h. The brown-violet precipitate that formed was filtered off, successively washed with water (100 mL), DMF (20 mL), and EtOH (20 mL), and dried. Reprecipitation was performed from DMF with an Me$_2$CO—hexane mixture (1 : 1, v/v), t.decomp. 158—164 °C. Then the reaction product was reprecipitated from a 10% NaOH solution with a fourfold volume of 5% AcOH, washed with a twofold volume of 1 *M* HCl, then with water to neutral pH, and, finally, with Me$_2$CO and hexane. The yield was 0.9 g (79%), t.decomp. 185 °C. A solution of compound **4** in a mixture of equal volumes of EtOH, DMF, water, and Me$_2$CO is orange-red. UV, λ_{max}/nm (ε_{max}): 506.2 (28800). Found (%): C, 55.51; H, 4.69; N, 10.03; S, 7.61. $C_{19}H_{17}N_3O_4S \cdot 2H_2O$. Calculated (%): C, 54.40; H, 5.01; N, 10.02; S, 7.61. IR, ν/cm^{-1}: 3400 (O—H); 3230 (N—H bond.); 3190—2980 (O—H of water, C—H aliph., C—H arom.); 1600, 1548, 1484 (C=C arom.); 1460 (N=N$_{trans}$); 1410 (C aliph.—N); 1360 (C arom.—N); 1316, 1280 (C—S); 1260, 1120 (C—C arom.); 1090 (C—C, C—O); 1028, 1004, 1000 (C—S); 980 (C—N—C); 836, 760 (C—H arom.); 724, 664, 620 (C—H). After drying at 100 °C (100 Torr), the weight loss was 8.01% (2 H$_2$O). T.decomp. 205—214 °C. Found (%): C, 58.91; H, 4.53; N, 10.70; S, 8.26. $C_{19}H_{17}N_3O_4S$. Calculated (%): C, 59.52; H, 4.49; N, 10.96; S, 8.36.

X-ray diffraction study of 3. X-ray diffraction study was carried out in the X-ray Structural Center (A. N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences) according to standard procedures[7] on a Bruker AXS SMART 1000 diffractometer equipped with a CCD detector (λ(Mo), graphite monochromator, ω scanning technique with a step of 0.3°, the exposure time per frame was 10 s, $2\theta_{max} = 52°$). For compound **3** · 0.5EtOH: $C_{21}H_{20}N_3O_{3.5}$, M = 370.4, space group *Pccn*, $a = 19.065(8)$ Å, $b = 21.619(8)$ Å, $c = 9.770(4)$ Å, $V = 4027(3)$ Å^3, 120 K, $Z = 8$, 10263 reflections were measured of which 3551 reflections were with $F^2 > 2\sigma(I)$, $d_{calc} = 1.222$ g cm^{-3}, $\mu = 0.085$ cm^{-1}, $R_1 = 0.0657$, $wR_2 = 0.1264$. The molecular structure of **3** is shown in Figs 2 and 3.

References

1. V. M. Ostrovskaya, O. A. Zaporozhets, G. K. Budnikov, and N. M. Chernavskaya, *Voda. Indikatornye sistemy* [*Water. Indicator Systems*], Izd-vo FGUP VTII, Moscow, 2004, 59 (in Russian).
2. V. M. Ostrovskaya, Pat. RF 2009486; *Byul. izobret.* [*Invention Bull.*], 1994, 5 (in Russian).
3. V. M. Ostrovskaya, *26th Int. Symp. on Environmental Anal. Chem. (Vienna, April 9—12, 1996), Book of Abstrs*, Vienna, 1996, FR 15.
4. V. M. Ostrovskaya, O. A. Prokopenko, S. E. Nefedov, and Yu. L. Shishkin, Pat. RF 2265828; *Byul. izobret.* [*Invention Bull.*], 2005, 34 (in Russian).
5. N. N. Vorozhtsov and S. I. Kutkevichus, *Zh. Obshch. Khim.*, 1957, **27**, 2521 [*J. Gen. Chem. USSR*, 1957, **27** (Engl. Transl.)].
6. J. R. Merchant and S. S. Salgar, *J. Ind. Chem. Soc.*, 1963, **40**, 23.
7. *SMART (Control) and SAINT (Integration) Software, Version 5.0*, Bruker AXS Inc., Madison, WI, 1997.

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