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Fluorescent Chemosensors for Mercury(II) Cations

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Abstract—The condensation of 4,5-dimethoxy-2-(morpholin-4-yl)aniline with anthracene-9-carbaldehyde gave *N*-(anthracen-9-ylmethyl)-4,5-dimethoxy-2-(morpholin-4-yl)aniline, a selective and efficient fluorescent chemosensor for mercury(II) cations.

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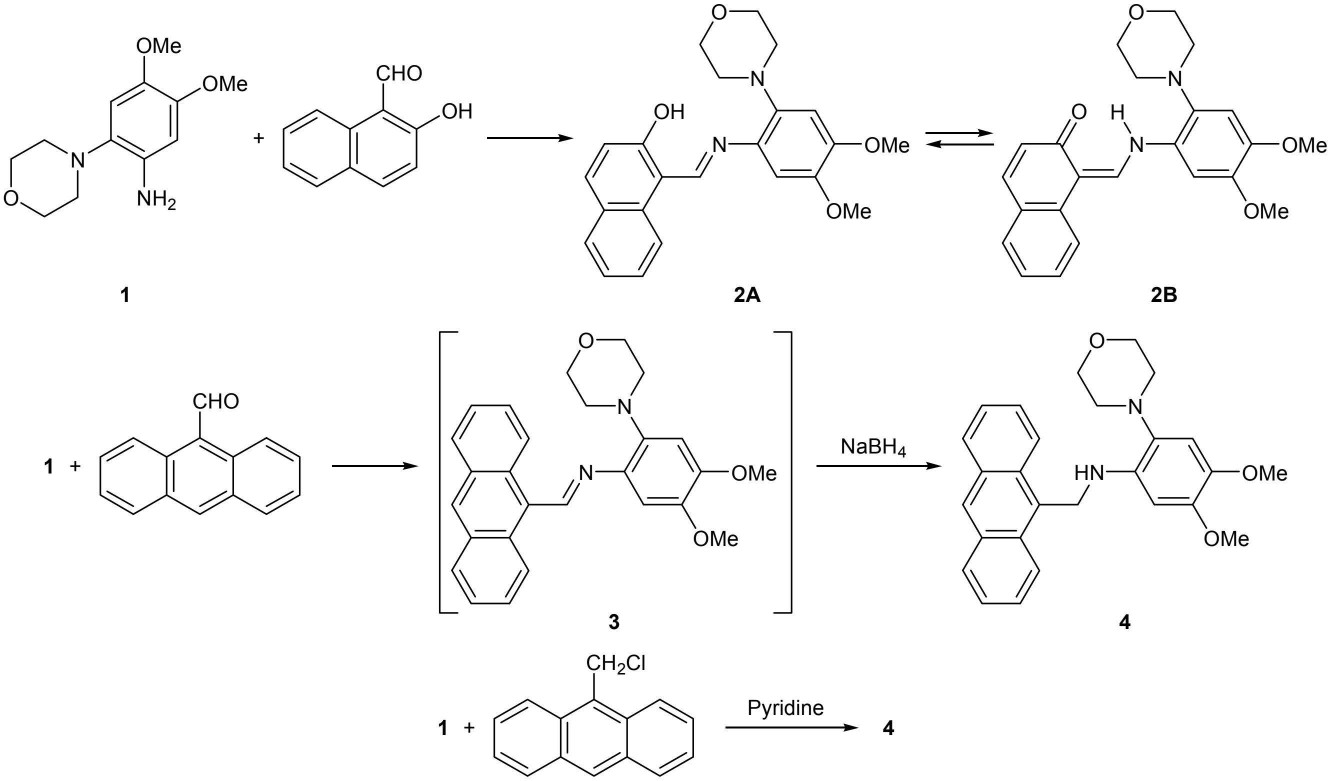
Various chemosensors are widely used in organic chemistry, biochemistry, and environmental studies to monitor cations, anions, and neutral molecules [1–6]. An important problem is the design of organic chemosensors for heavy metal ions [7–9]. Here, preference is given to fluorescent chemosensors characterized by high efficiency, sensitivity, and selectivity [10–12]. Our previous studies [13–16] showed that *N*-(2-aminophenyl)-*N*-(9-anthrylmethyl)amine derivatives can be used as efficient fluorescent chemosensors for mercury(II) ions. With the goal of obtaining new fluorogenic derivatives of this series we have modified the receptor entity.

By nitration of veratrole we synthesized 1,2-dimethoxy-4,5-dinitrobenzene. One nitro group in the latter was replaced by morpholine residue, and the other nitro group was then reduced to amino with hydrazine hydrate over Raney nickel. 4,5-Dimethoxy-2-(morpholin-4-yl)aniline (**1**) thus obtained was brought into condensation with 2-hydroxynaphthalene-1-carbaldehyde, which afforded Schiff base **2** (Scheme 1). The condensation product of amine **1** with anthracene-9-carbaldehyde, Schiff base **3**, turned out to be poorly soluble and was therefore unsuitable for use as chemosensor. By reaction of **1** with anthracene-9-carbaldehyde in the presence of sodium tetrahydridoborate we obtained amine **4**. Compound **4** can also be synthesized by direct alkylation of **1** with 9-(chloromethyl)anthracene in anhydrous pyridine.

In the ^{1}H NMR spectra of **2** and **4**, protons of the methoxy groups resonated as two singlets in the region δ 3.70–4.09 ppm. The spectrum of **2** characteristically showed doublet signals of the NH (OH) (δ 15.88 ppm) and N=CH protons (δ 9.40 ppm), and amine **4** displayed signals from the CH_2 and NH groups at δ 5.20 and 4.85 ppm, respectively. Schiff base **2** was found to exist in solution as two tautomers **A** and **B** (Scheme 1) at a ratio of 32 : 68, as followed from the coupling constant of the NH proton ($J = 8.9$ Hz) in the ^{1}H NMR spectrum [17].

Compound **4** in acetonitrile solution showed anthracene type fluorescence, in particular three emission maxima were observed in the region λ 390–460 nm (λ_{excit} 365 nm). Fluorophore-free compound **2** displayed a weak emission band with its maximum at λ 405 nm (λ_{excit} 340 nm). The chemosensing properties of **2** and **4** for H^+, Zn^{2+}, Cd^{2+}, Ni^{2+}, Co^{2+}, Cu^{2+}, Pb^{2+}, and Hg^{2+} ions were assessed in acetonitrile by fluorescence spectroscopy. For this purpose, 5 equiv of trifluoroacetic acid or the corresponding metal acetate was added to a solution of **2** or **4** in acetonitrile; the fluorescence spectra were recorded before and after addition of the test species. The addition of mercury(II) acetate to a solution of **4** induced increase of the fluorescence intensity by a factor of 72 (λ_{max} 422 nm). The fluorescence spectrum of **4** changed after addition of Cu^{2+}: a new long-wave emission band appeared at λ_{max} 512 nm. Compound **2**

Scheme 1.



showed response to mercury(II) ions and protons; the fluorescence intensity increased by factors of 35 and 8, respectively. The selectivity of sensor **4** was estimated by adding a mixture of Hg^{2+} and Cu^{2+} salts to a solution of **4**. As a result, 70-fold increase of the fluorescence intensity was observed at λ 422 nm, while no other bands appeared in the fluorescence spectrum. Other metal salts did not induce appreciable variations in the fluorescence spectrum. Chemosensor **2** showed no analogous efficiency or selectivity in the presence of other metal ions (see figure).

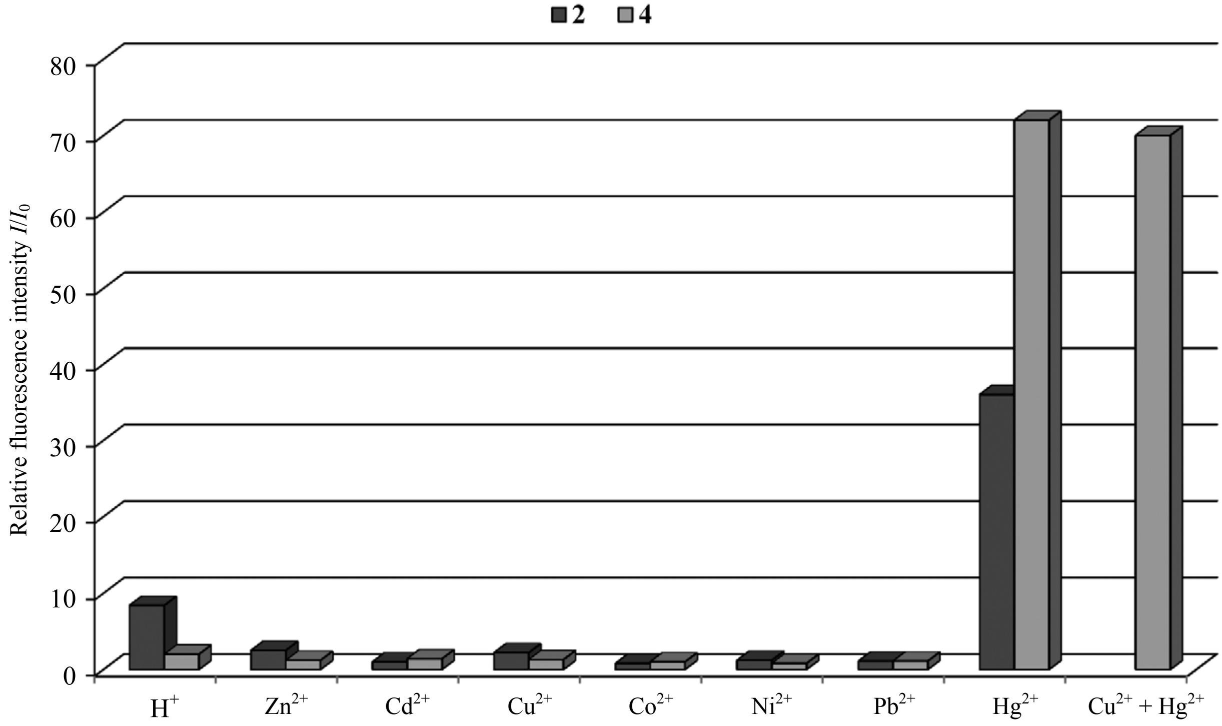
Thus, the new fluorescent chemosensors based on 4,5-dimethoxy-2-(morpholin-4-yl)aniline showed sensitivity to mercury(II) ions, and *N*-(anthracen-9-ylmethyl)-4,5-dimethoxy-2-(morpholin-4-yl)aniline turned out to be an efficient and selective fluorescent chemosensor for mercury(II) ions.

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Varian Unity 300 spectrometer (300 MHz) from solutions in DMSO-d_6; the chemical shifts were measured relative to residual proton signal of the solvent (δ 2.50 ppm). The electronic absorption spectra were taken on a Varian Cary 100 spectrophotometer, and the luminescence spectra were recorded on a Varian Cary Eclipse spectrofluorimeter. The IR spectra were measured on a Varian Excalibur 3100 FT-IR instrument equipped with an ATR accessory (ZnSe). The mass spectra (electron impact, 70 eV) were obtained on a Shimadzu GCMS-QP2010SE instrument with direct sample admission into the ion source. The melting points were measured in glass capillaries on a PTP (M) melting point apparatus. The progress of reactions and the purity of the isolated compounds were monitored by TLC on Silufol UV 254 plates using chloroform as eluent; spots were visualized by treatment with iodine vapor in a moist chamber.

1,2-Dimethoxy-4,5-dinitrobenzene was synthesized as described in [18]. Yield 82%, mp 123–124°C (from *i*-PrOH); published data [18]: mp 126–127°C.

4-(4,5-Dimethoxy-2-nitrophenyl)morpholine. A solution of 6.8 g (30 mmol) of 1,2-dimethoxy-4,5-dinitrobenzene in 10 mL of anhydrous morpholine was heated for 10 h. Excess morpholine was removed on a rotary evaporator under reduced pressure, the residue was dissolved in 50 mL of chloroform, and the solution was washed with water (5×50 mL) and dried over anhydrous sodium sulfate. The solvent was distilled off, and the residue was recrystallized from isopropyl



Relative changes of the fluorescence intensity of compounds **2** and **4** in acetonitrile ($c = 5.0 \times 10^{-6}$ M) on addition of various cations ($c = 2.5 \times 10^{-5}$ M).

alcohol. Yield 6.0 g (74%), mp 113–114°C (from *i*-PrOH); published data [19]: mp 115–117°C.

4,5-Dimethoxy-2-(morpholin-4-yl)aniline (**1**) was synthesized as described in [19]. Yield 85%, mp 106–107°C (from EtOH); published data [20]: mp 109°C.

1-{[4,5-Dimethoxy-2-(morpholin-4-yl)phenylimino]methyl}naphthalen-2-ol (2). 2-Hydroxynaphthalene-1-carbaldehyde, 0.52 g (3 mmol), was added to a solution of 0.71 g (3 mmol) of amine **1** in 10 mL of ethanol, and the mixture was refluxed for 2 h. The mixture was cooled, and the precipitate was filtered off, recrystallized from butan-1-ol–DMF (1:1), and dried in air. Yield 1.1 g (92%), mp 245–246°C. IR spectrum, ν, cm^{-1}: 3300 (OH), 1645 (C=N), 1465 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.80–2.93 m (4H, NCH_2), 3.70–3.98 m (10H, OCH_2, OMe), 6.65–6.86 m (2H, H_{arom}), 7.10–7.27 m (1H, H_{arom}), 7.32–7.74 m (4H, H_{arom}), 8.32 d (1H, H_{arom}, J = 7.5 Hz), 9.40 d (1H, CH=N, J = 8.9 Hz), 15.88 d (1H, NH or OH, J = 8.9 Hz). Fluorescence spectrum (acetonitrile, $c = 5 \times 10^{-5}$ M): λ_{max} 405 nm. Found, %: C 70.45; H 6.24; N 7.06. m/z 392 $[M]^+$. $C_{23}H_{24}N_2O_4$. Calculated, %: C 70.39; H 6.16; N 7.14. M 392.46.

***N*-(Anthracen-9-ylmethyl)-4,5-dimethoxy-2-(morpholin-4-yl)aniline (4).** *a*. Anthracene-9-carbaldehyde, 0.62 g (3 mmol), was added to a solution of 0.71 g (3 mmol) of amine **1** in 50 mL of ethanol–DMF (3:1), and the mixture was refluxed for 1 h. The mixture was cooled to 60–65°C, and 0.38 g (10 mmol) of finely powdered sodium tetrahydridoborate was added in portions with stirring. The mixture was cooled, 50 mL of water was added, and excess $NaBH_4$ was quenched with 10% acetic acid. After 1 h, the precipitate was filtered off, recrystallized from butan-1-ol, and dried in air. Yield 0.9 g (71%), mp 221–222°C. IR spectrum, ν, cm^{-1}: 1615 (C=N), 1470, 1380 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.60–2.74 m (4H, NCH_2), 3.29–3.52 m (4H, OCH_2), 3.86 s (3H, OMe), 4.00 s (3H, OMe), 4.85 br.s (1H, NH), 5.20 d (2H, CH_2, J = 4.5 Hz), 6.73 s (2H, H_{arom}), 7.45–7.57 m (4H, H_{arom}), 8.06 d (2H, H_{arom}, J = 9.2 Hz), 8.30 d (2H, H_{arom}, J = 9.2 Hz), 8.49 s (1H, H_{arom}). Fluorescence spectrum (acetonitrile, $c = 5 \times 10^{-5}$ M): λ_{max} 412 nm. Found, %: C 75.75; H 6.65; N 6.45. m/z 428 $[M]^+$. $C_{27}H_{28}N_2O_3$. Calculated, %: C 75.68; H 6.59; N 6.54. M 428.54.

b. 9-(Chloromethyl)anthracene, 0.91 g (4 mmol), was added to a solution of 0.71 g (3 mmol) of amine **1** in 10 mL of anhydrous pyridine, and the mixture was refluxed for 10 h. The mixture was diluted with 50 mL of water and cooled, and 2 h after the precipitate was filtered off and recrystallized from butan-1-ol. Yield

0.8 g (63%), mp 219–220°C. The spectral data and melting point of the product coincided with those of a sample prepared as described in *a*.

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REFERENCES

1. *Chemosensors: Principles, Strategies, and Applications*, Wang, B. and Anslyn, E.V., Eds., Hoboken, NJ: Wiley, 2011.
2. Bren, V.A., *Russ. Chem. Rev*., 2001, vol. 70, p. 1017.
3. Liu, Z., He, W., and Guo, Z., *Chem. Soc. Rev*., 2013, vol. 42, p. 1568.
4. Kim, H.N., Ren, W.X., Kim, J.S., and Yoon, J., *Chem. Soc. Rev*., 2012, vol. 41, p. 3210.
5. El-Safty, S.A. and Shenashen, M.A., *Trends Anal. Chem*., 2012, vol. 38, p. 98.
6. Carter, K.P., Young, A.M., and Palmer, A.E., *Chem. Rev*., 2014, vol. 114, p. 4564.
7. Saleem, M. and Lee, K.H., *RSC Adv*., 2015, vol. 5, p. 4926.
8. Formica, M., Fusi, V., Giorgi, L., and Micheloni, M., *Coord. Chem. Rev*., 2012, vol. 256, p. 170.
9. Kaur, N. and Kumar, S., *Tetrahedron*, 2011, vol. 67, p. 9233.
10. Valeur, B. and Berberan-Santos, M.N., *Molecular Fluorescence: Principles and Applications*, Weinheim: Wiley-VCH, 2012, 2nd ed.
11. Yu, L., Wang, S., Huang, K., Liu, Z., Gao, F., and Zeng, W., *Tetrahedron*, 2015, vol. 71, p. 4679.
12. Wu, J., Liu, W., Ge, J., Zhang, H., and Wang, P., *Chem. Soc. Rev*., 2011, vol. 40, p. 3483.
13. Tolpygin, I.E., Bren’, V.A., Dubonosov, A.D., Minkin, V.I., and Rybalkin, V.P., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1364.
14. Tolpygin, I.E., Rybalkin, V.P., Shepelenko, E.N., Popova, L.L., Revinskii, Yu.V., Tsukanov, A.V., Dmitrieva, O.I., Dubonosov, A.D., Bren’, V.A., and Minkin, V.I., *Russ. J. Org. Chem*., 2008, vol. 44, p. 557.
15. Tolpygin, I.E., Shepelenko, E.N., Revinskii, Yu.V., Tsukanov, A.V., Dubonosov, A.D., Bren’, V.A., and Minkin, V.I., *Russ. J. Org. Chem*., 2009, vol. 45, p. 161.
16. Tolpygin, I.E., Revinskii, Yu.V., Tsukanov, A.V., Dubonosov, A.D., Bren’, V.A., and Minkin, V.I., *Russ. J. Org. Chem*., 2011, vol. 47, p. 1305.
17. Brown, N.M.D. and Nonhebel, D.C., *Tetrahedron*, 1968, vol. 24, p. 5655.
18. Ehrlich, J. and Bogert, M.T., *J. Org. Chem*., 1947, vol. 12, p. 522.
19. Stogryn, E.L., *J. Med. Chem*., 1970, vol. 13, p. 1106.
20. Stogryn, E.L., *J. Med. Chem*., 1969, vol. 12, p. 185.