Letters to the Editor

1-Amino-3-(4-methoxybenzylamino)-1-phenylpropane as a new water-soluble fluorescent reagent to zinc ion

*M. M. Vorob´ev,[a] L. A. Sviridova,[b] N. I. Vorozhtsov,[b] A. A. Ambartsumyan,[a] and K. A. Kochetkov[a]**

[a]A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (499) 135 5085. E-mail: const@ineos.ac.ru
[b]Department of Chemistry, M. V. Lomonosov Moscow State University, 1 Leninskie gory, 119899 Moscow, Russian Federation. Fax: +7 (495) 932 8846. E-mail: svirid@org.chem.msu.ru

Zinc(II) plays an important role in biology and medicine being involved in many physiological and pathological processes in the human organism.[1] Rapt attention is given to search for fluorescent labels to Zn^{2+} ions, since the fluorescence analysis method[2] makes it possible to rapidly and quantitatively determine the content of these ions. However, the value of many reagents related mainly to heterocyclic compounds[2] decreases because their low solubility in water[3] and the non-stoichiometric amount of the reagent required for determination of Zn^{2+} ions. The number of known water-soluble reagents is rather restricted.[4]

We studied the fluorescence properties of new water-soluble linear diamine, *viz.*, 1-amino-3-(4-methoxybenzylamino)-1-phenylpropane (**L**). Compound **L** was synthesized from the corresponding pyrazolidine derivative[5] by the cleavage at the N—N bond with borane in THF using our earlier developed procedure.[6] The fluorescence excitation spectrum of diamine ligand **L** in an aqueous medium contains a band with a maximum at 228 nm (Fig. 1, curve *1*). The excitation of a solution of compound **L** with a wavelength of 228 nm results in the appearance of a fluorescence band with a maximum at

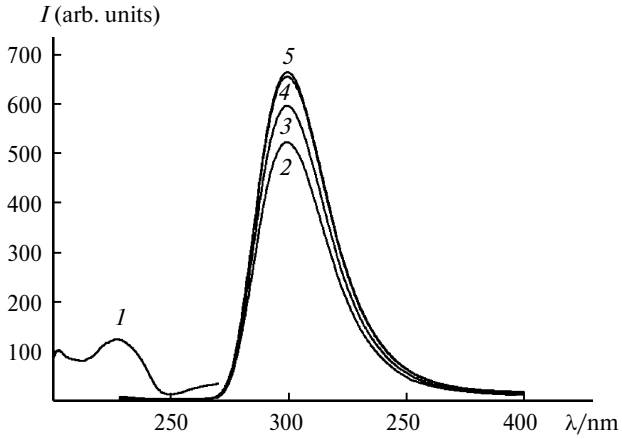

Fig. 1. Excitation (*1*) and fluorescence spectra of initial diamine **L** (*2*) in a phosphate buffer (pH 7.8) and after introduction of $ZnCl_2$ into the solution in the ratio Zn^{2+}/**L**: 0.5 (*3*), 1 (*4*), and 3 (*5*).

* Dedicated to the Academician of the Russian Academy of Sciences S. M. Aldoshin on the occasion of his 60th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 0573—0574, February, 2013.

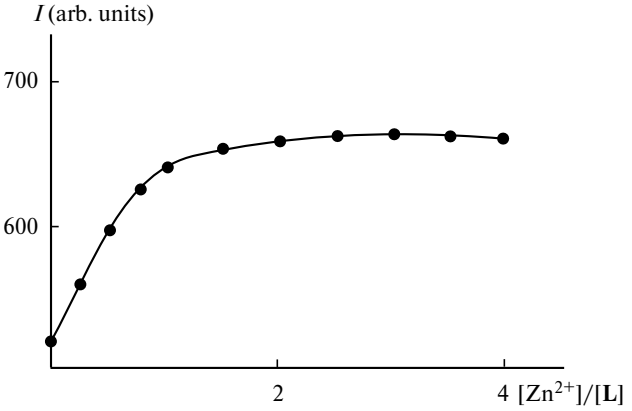

Fig. 2. Change in the fluorescence intensity (λ_d = 300 nm) upon coordination of diamine **L** with zinc ion.

300 nm (see Fig. 1, curve *2*). The introduction of $ZnCl_2$ into the solution increased the fluorescence intensity of the ligand due to coordination with zinc ion (see Fig. 1, curves *3—5*; Fig. 2). Thus, diamine ligand **L** can be used for zinc determination in an aqueous solution.

We used the analytical procedure of zinc determination by fluorescence spectroscopy.[7]

Fluorescence spectra were obtained on a Perkin-Elmer LS 55 luminescence spectrometer (USA). IR spectra were recorded on an UR-20 instrument. ^{1}H NMR spectra were measured on a Bruker Avance 300 instrument using $CDCl_3$ as a solvent. Elemental analysis was carried out on an EA1108 CHNS-O automated CHN microanalyzer (Carlo Erba). The melting point was measured with an Electrothermal IA 9000 melting point indicator in a sealed capillary.

1-Amino-3-(4-methoxybenzylamino)-1-phenylpropane (L). A solution of borane in THF (7 mL, 6.0 mmol) was added by portions in an argon flow to 1-(4-methoxybenzyl)-3-phenylpyrazolidine.[5] The reaction mixture was refluxed for 8 h, and concentrated HCl was added to pH 1. The solvent was evaporated. The mixture was extracted with ether (2×15 mL). The aqueous fraction was alkalized to pH 9 and extracted with ether (5×15 mL). The extract was dried over Na_2SO_4, and the solvent was evaporated. The oily product was obtained in a yield of 0.43 g (80%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.89 (m, 2 H, $C(2)H_2$); 2.67 (m, 2 H, $N—CH_2$); 3.69 (s, 2 H, CH_2Ph); 3.80 (s, 3 H, CH_3O); 4.02 (m, 1 H, H(1)); 6.88 (d, 2 H, Ar, J = 8 Hz); 7.21—7.28 (m, 11 H, Ph + 2 H_{Ar} + NH + NH_2). IR, ν/cm^{-1}: 3200, 3300 (NH_2, NHR). To refine the elementary composition of compound **L**, its dihydrochloride was obtained by the addition of an excess of an alcohol solution of HCl to free base **L**. The mixture was kept for 2 days, the solvent was evaporated, and the residue was recrystallized from alcohol. M.p. 135 °C. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.49 (m, 2 H, $C(2)H_2$); 2.74 (m, 2 H, $N—CH_2$); 3.04 (s, 3 H, OCH_3); 3.37 (s, 1 H, NH); 3.98 (dd, 2 H, CH_2Ph); 4.49 (m, 1 H, H(3)); 6.91, 7.48 (4H, AA´BB´, Ar); 7.36 (m, 3 H, Ph); 7.63 (m, 2 H, Ph); 9.41 (s, 3 H, NH_3^+). Found (%): C, 57.02; H, 6.62; Cl, 19.86; N, 7.61. $C_{17}H_{22}N_2O \cdot 2HCl$. Calculated (%): C, 56.82; H, 6.68; Cl, 19.51; N, 7.79.

This work was financially supported by the Presidium of the Russian Academy of Sciences (Program R5 "Fundamental Sciences to Medicine"), the Division of Chemistry and Materials Science of the Russian Academy of Sciences (Program No. 09 "Biomolecular and Medicine Chemistry"), and the Russian Foundation for Basic Research (Project No. 11-04-01245).

References

1. B. L. Vallie, K. H. Falchuk, *Physiol. Rev.*, 1993, **73**, 79.
2. (a) N. Onozawa-Komatsuzaki, Y. Himeda, H. Sugihara, *Tetrahedron Lett.*, 2001, **42**, 9199; (b) C. Ichimura, Y. Shiraishi, T. Hirai, *Tetrahedron*, 2010, **66**, 5594; (c) S. Atilgar, T. Ozdemir, E. U. Akkaya, *Organic Lett.*, 2008, **10**, 4065; (d) K. Komatsu, Y. Urano, H. Kojima, T. Nagano, *J. Am. Chem. Soc.*, 2007, **129**, 13447.
3. (a) N. C. Lim, H. C. Freake, C. Bruckner, *Chem. Eur. J.*, 2005, **11**, 384; (b) Q. Yin, Z. Zhang, Y.-F. Zhao, *J. Chem. Res.*, 2006, 160.
4. S. Aoki, K. Sakurama, N. Matsuo, Y. Yamada, R. Takasaka, S.-I. Tanuma, M. Shiro, K. Takeda, E. Kymura, *Chem. Eur. J.*, 2006, **12**, 9066.
5. N. I. Vorozhtsov, M. V. Gerasimov, G. A. Golubeva, L. A. Sviridova, *Vestn. Mos. Gos. Univ., Ser. 2. Khim.*, 2004, **45**, 399 [*Vestn. Mosk. Univ., Ser. Khim.* (*Engl. Transl.*), 2004].
6. K. A. Kochetkov, A. N. Tavtorkin, N. I. Vorozhtsov, L. A. Sviridova, A. M. Moroz, I. R. Dorozhkova, *Russ. Chem. Bull.* (*Int. Ed.*), 2011, **60**, 702 [*Izv. Akad. Nauk*, *Ser. Khim.*, 2011, 688].
7. C. Ichimura, Y. Shiraishi, T. Hirai, *Tetrahedron*, 2010, **66**, 5594.

Received October 29, 2012;
in revised form January 23, 2013