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New conjugate of bis(*o*-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetate with naphthalimide as a fluorescent sensor for calcium cations

Marina A. Zakharko,*[a] Pavel A. Panchenko,[a,b] Pavel A. Ignatov,[b] Yurii V. Fedorov[a] and Olga A. Fedorova[a,b]

[a] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: Marina_Zr@mail.ru*

[b] *D. I. Mendeleev University of Chemical Technology of Russia, 125047 Moscow, Russian Federation*

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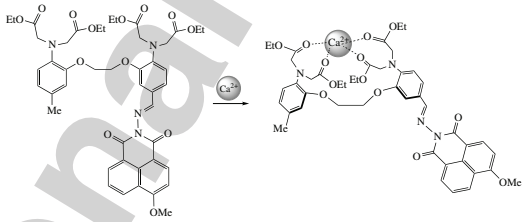
New 4-methoxy-1,8-naphthalimide derivative equipped with bis(*o*-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetate receptor moiety at the imide nitrogen atom showed a fluorescent response to Ca^{2+} cations due to the formation of complexes of 1 : 1 ligand–metal composition.



Keywords: sensor, calcium cation, fluorescence, 1,8-naphthalimide, photoinduced electron transfer.

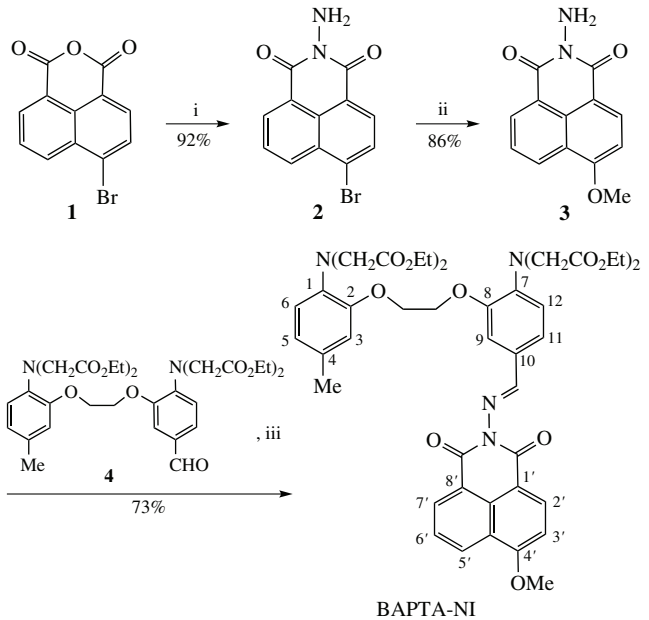
The development of highly selective and sensitive sensors for Ca^{2+} cations is an urgent goal in supramolecular chemistry because they are in high demand in medical and biological chemistry. Calcium cations are involved in blood coagulation processes and regulate muscle contractions and transmission of nerve impulses. Therefore, a disturbance of calcium metabolism can serve as an indicator of serious diseases.[1–3] Fast and highly accurate determination of ion concentration under physiological conditions can be achieved by fluorescence spectroscopy.[4]

Luminophores based on 1,8-naphthalimide are widely used as optical platforms in the development of fluorescent chemosensors for *in vitro* detection of metal cations,[5–9] anions[10,11] and small molecules.[13–15] The optical sensors based on the intramolecular photoinduced electron transfer (PET) from a donor group in the receptor moiety of the sensor to the naphthalimide core are of great practical interest. The PET process after the photoexcitation significantly decreases the fluorescence quantum yield of the system. Binding of an electron-rich functional group involved in the PET process with a metal cation reduces the electron transfer efficiency and produces an optical signal resulting in fluorescence buildup ('turn-on' signal). This type of response is preferable to 'turn-off' (quenching the sensor fluorescence upon binding with the analyte) because 'turn-on' sensors are usually characterized by high optical response and signal-to-noise ratios.

A derivative of 1,2-bis(*o*-aminophenoxy)ethane-*N*,*N*,*N*′,*N*′-tetraacetic acid (BAPTA), one of the best-known chelators for Ca^{2+} ions, was used as the receptor moiety of the sensor. BAPTA binds calcium ions in aqueous solutions with high efficiency, it is insensitive to the medium acidity in the physiological pH range[16–24] and has high selectivity for the binding of Ca^{2+} ions in comparison with Mg^{2+}: the $\lg K_{(L)\cdot Ca^{2+}}/\lg K_{(L)\cdot Mg^{2+}}$ value is 5.2.[16] The presence of biologically active ions such as Zn^{2+}, Mg^{2+} as well as Mn^{2+} does not interfere with the detection of calcium.[19] 4-Methoxy substituted naphthalimide was selected as a fluorophore. It has a relatively strong electron-deficient nature in excited state, which makes fluorescence switching by the PET mechanism more contrast in comparison with 4-amino derivatives often used in the development of sensor devices.[5,6]

The synthesis of compound BAPTA-NI (Scheme 1) included the preparation of Schiff base from 1-amino-4-methoxy-1,8-naphthalimide **3** and formyl derivative **4** at the key step. Compounds **2**–**4** were obtained as reported[19,25–27] from 4-bromonaphthalic anhydride **1** and 5-methyl-2-nitrophenol, respectively (for details, see Online Supplementary Materials).

Comparison of the fluorescence quantum yields of BAPTA-NI ($\varphi^{fl} = 0.0022$) and *N*-ethyl-4-methoxynaphthalimide ($\varphi^{fl} = 0.64$[28]) in water allows us to assume that the fluorescence



Scheme 1 *Reagents and conditions*: i, N_2H_4, EtOH, Δ; ii, MeONa, MeOH, Δ; iii, AcOH, EtOH, Δ.