Cation-triggered ‘switching on’ of the red/near infra-red (NIR) fluorescence of rigid fluorophore–spacer–receptor ionophores

Knut Rurack,*[a] Ute Resch-Genger,[a] Julia L. Bricks[b] and Monika Spieles[a]

[a] *Dept. I.3902, Federal Institute for Materials Research and Testing (BAM), Richard-Willstaetter Str. 11, D-12489 Berlin, Germany. E-mail: knut.rurack@bam.de*

[b] *Institute of Organic Chemistry, National Academy of Sciences of the Ukraine, Murmanskaya 5, 253660, Kiev-94, Ukraine*

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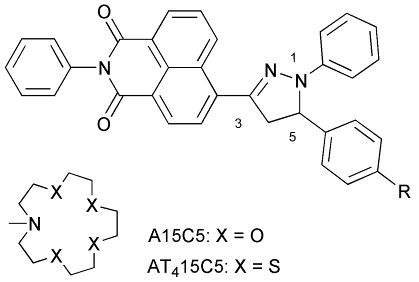
Fluorophore–spacer–receptor ionophores 1 and 2 show a strong cation-induced enhancement of the fluorescence at λ > 650 nm in the presence of Hg^{II} and Ag^{I} (1) or Pb^{II}, alkaline-earth and alkali metal ions (2).

Molecular signaling systems relying on drastic changes in fluorescence intensity and/or band position upon binding to an inorganic/organic substance have lately received much attention as photonic molecular devices.[1] As functionalized hosts for inorganic guests such as main group, heavy, and transition metal ions or anions, ionophores that consist of an ion-responsive receptor and a (potentially, *i.e.* in the ‘switched on’ state) highly emissive chromophore, separated by a short alkyl spacer thus preventing pronounced electronic interaction in the ground state, are of particular interest.[2] This molecular constitution allows to combine an electron-donating receptor with a reducable chromophore to invoke fast signaling processes such as intramolecular electron transfer (ET).[3] Among composite ET fluoroionophores, dyes containing a small and rigid spacer are especially advantageous in terms of minimally separated molecular subunits with efficient transduction capability. Recently, such probe molecules based on the Δ^2-pyrazoline chromophore were introduced, showing a cation-induced ‘switching on’ of the fluorescence upon binding to main group[4] and/or heavy metal ions.[4b] In these substituted 1,3,5-triaryl-Δ^2-pyrazolines, not only does the spacer-separated receptor at the 5-position acts as an electron donor but the main chromophore itself (including the ring fragment C(3)=N(2)–N(1)) consists of a donor (D: N(1) and 1-substituent) and an acceptor (A: C(3) = N(2) and 3-substituent) subunit, and thus the intramolecular ET reaction from the 5-donor does not quench a chromophore-localized state (as, for instance in donor–alkyl-substituted anthracenes or pyrenes)[5] but rather a highly emissive charge transfer (CT) excited state.[4b] This constitution harbors two important advantages for rational probe design: (i) rigidized D–A-fluorophores with allowed CT transtitions (*e.g.* the basic 1,3-diaryl-Δ^2-pyrazoline chromophore)[4b] usually show broad and largely Stokes-shifted absorption and emission bands often accompanied by high fluorescence quantum yields and (ii) the tuning of composite D–A-chromophores by combining specific D and A units is synthetically well feasible. Here, we extended this design concept to the red/near infra-red (NIR) region by the introduction of the strong *N*-phenyl-1,8-naphthalimide (PhNI) acceptor to the 3-position of the Δ^2-pyrazoline ring yielding **1**–**4**. **1** and **2** are equipped with cation-sensitive anilino crown units showing strongly different ion binding preferences and **3** and **4** act as model compounds.



1: R = AT$_4$15C5
2: R = A15C5
3: R = H
4: R = NMe$_2$

A15C5: X = O
AT$_4$15C5: X = S

The efficient separation of the electron donating 5-*p*-receptor unit and the main 1,3-diaryl-Δ^2-pyrazoline chromophore by the rigid spacer is suggested from the nearly identical positions of the absorption and emission bands of **1**–**4** in acetonitrile, the solvent we used for the complexation studies (Table 1). The broad, structureless and largely Stokes-shifted absorption and emission bands underline the CT character of the optical transitions in the 1,3-chromophore. In accordance with results obtained for their 3-benzothiazol-2-yl-substituted analogues,[4b] both, the intensive low energy absorption band ($\varepsilon \approx 2 \times 10^4$ M^{-1} cm^{-1} for all the dyes) and the considerably high fluorescence quantum yield of the reference compound **3** reveal that allowed CT transitions determine the spectroscopic properties of the 3-PhNI-Δ^2-pyrazolines. When comparing the fluorescence quantum yield and lifetime data of **3** with those of **1**, **2** and **4**, the quenching electron transfer interaction (virtually no changes in spectral band position, see above) of a 5-*p*-anilino donor is evident. Since the radiative rate constants $k_f = \phi_f/\tau_f$ of **1**–**4** are very similar ($k_f \approx 0.9 \times 10^8$ s^{-1}), the rate constant of the ET quenching process in **1**, **2** and **4** can be calculated from

Table 1 Spectroscopic data of **1** and its Hg^{II} and Ag^{I} complexes, **2** and its Li^{I}, Na^{I}, K^{I}, Mg^{II}, Ca^{II}, Sr^{II}, Ba^{II} and Pb^{II} complexes, **3** and **4** in acetonitrile at room temperature[a]

	λ_{abs}/nm	λ_{em}/nm	ϕ_f	τ_f/ns	log K_S
1	488	680	0.007[b]	0.076	—
1$\subset$Hg^{II}	483	667	20[c]	1.57	> 5.2[d]
1$\subset$Ag^{I}	484	673	15[c]	1.22	4.95
2	493	679	0.003[b]	0.029	—
2$\subset$Li^{I}	489	675	11[c]	0.35	2.92
2$\subset$Na^{I}	487	673	17[c]	0.65	2.47
2$\subset$Mg^{II}	484	669	40[c]	1.14	2.99
2$\subset$Ca^{II}	484	668	43[c]	1.08	4.40
2$\subset$Sr^{II}	484	668	39[c]	1.23	3.74
2$\subset$Ba^{II}	485	670	37[c]	0.99	3.68
2$\subset$Pb^{II}	483	667	47[c]	1.53	> 5.2[d]
3	490	682	0.18[b]	1.32	—
4	484	670	0.002[b]	0.017	—

[a] *Experimental conditions*: c (dye) = 5×10^{-6} M, $\lambda_{exc} \approx 480$ nm (at the respective isosbestic points) for steady-state, 480 nm for time-resolved fluorescence measurements. The cation selectivity is identical to that of related pairs of aza-oxa and aza-thia crowns.[4b,9] [b] Fluorescence quantum yield determined relative to fluorescein 27 in 0.1 M NaOH ($\phi_f = 0.90 \pm 0.03$).[12] [c] Relative fluorescence enhancement with respect to ϕ_f of the corresponding free dye. [d] Too high to be determined with acceptable accuracy with the method employed.

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† Electronic supplementary information (ESI) available: experimental details including synthesis of **1**–**4** and optical spectroscopy. See http://www.rsc.org/suppdata/cc/b0/b006430k/

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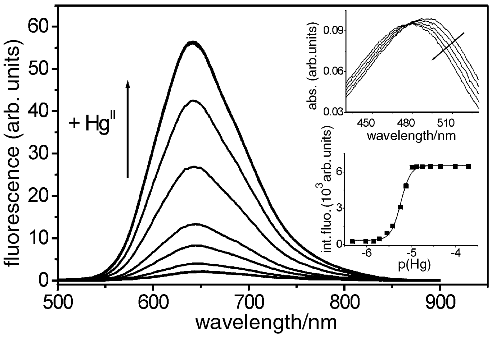

Fig. 1 Fluorescence titration spectra ($\lambda_{\mathrm{exc}} = 478$ nm) of **1** (5×10^{-6} M) with $Hg(ClO_4)_2$ (concentration range: 5×10^{-7} to 2×10^{-3} M) in acetonitrile. Upper inset: selected absorption titration spectra (isosbestic point: 478 nm; arrow indicates the direction of change upon Hg^{II} addition). Lower inset: fit (——) of the integrated intensity (■) of the fluoroescence titration.

the measured fluorescence lifetime according to $k_{\mathrm{ET}} = \tau_f^{(\mathbf{X})-1} - \tau_f^{(\mathbf{3})-1}$ with X = **1**, **2**, **4** by using that of **3** as a reference (Table 1). This yields k_{ET} of 12, 34 and 58 ns^{-1} for **1**, **2** and **4**, respectively. These rate constants are rather small and are thus not related to the solvent relaxation time (the longitudinal solvent relaxation time in acetonitrile was determined to 0.2 ps)[6] suggesting a nonadiabatic electron transfer process.

Upon cation addition to **1** and **2**, the changes in spectral band position are comparatively small (Table 1 and, as an example, the titration of **1** with $Hg(ClO_4)_2$ shown in Fig. 1) as is expected for an ET signaling mechanism. Accordingly, binding of a cation to the electron donating 5-*p*-receptor strongly alters its redox potential and weakens its donor strength thus decelerting the ET quenching process. As is evident from Table 1, the cation-induced changes in fluorescence quantum yield and lifetime are drastic and are directly related to the charge density of the metal ion, *i.e.* the inhibition of the ET reaction being stronger for Hg^{II} than for Ag^{I} (for **1**) and for alkaline-earth metal ions relative to alkali metal ions (for **2**). For the complexes with divalent Hg^{II}, Ca^{II} and Pb^{II}, all of them tightly binding to the fluorescent sensor molecules, even a complete 'switching off' of the ET process is manifested by rate constants of radiative and non-radiative deactivation which are nearly identical to those of the reference compound **3**, lacking a 5-*p*-anilino donor. In all the cases, the fit of the spectrofluorometric titration data[4*b*,7] yielded a 1:1 complex stoichiometry.

Besides the favorable fluorescence enhancement characteristics, the cation selectivity can easily be directed by tuning of the 5-*p*-receptor. Whereas **1**, containing four 'soft'[8] sulfur donor atoms in the 15-crown-5 receptor, only binds to the thiophilic heavy and transition metal ions Hg^{II} and Ag^{I} (for a detailed discussion of ion selectivities and preferences, see refs 4(*b*) and 9), **2** with a monoaza-tetraoxa-15-crown-5 unit shows changes in its spectroscopic properties in the presence of the 'hard'[8] group I and II metal ions as well as Pb^{II}. The power of the present design concept, especially for Hg^{II} (**1**) and Pb^{II} (**2**) commonly known as fluorescence quenchers[10] and for sensing applications in the red/NIR, is apparent.[11]

In summary, we have shown that upon combining intramolecular charge and electron transfer processes in a simple fluorophore–spacer–receptor ionophore with a small but rigid spacer, an efficient cation-triggered 'switching on' of the intramolecular charge transfer fluorescence can selectively be achieved even with advantageous emission features such as broad and largely Stokes shifted bands and considerably high fluorescence quantum yields in the red/NIR spectral region.

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11 It is interesting that the corresponding substituted chalcone-type dyes ($PhNI–CO–CH{=}CH–C_6H_4R$ with R = H, NMe_2 or crowns), which were obtained as intermediates within the Δ^2-pyrazoline synthesis (see ESI†), do not fluoresce ($\phi_f < 1 \times 10^{-5}$) and thus cannot be exploited for sensing purposes as, for instance their benzothiazole derivatives.[9] This is most probably due to the close neighborhood of the carbonyl and the PhNI group, since electron acceptors at the 4-position of the naphthalimide chromophore are known to quench its fluorescence.[13]

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