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Fluorescent and colorimetric chemosensors for cations based on 1,8-naphthalimide derivatives: design principles and optical signalling mechanisms

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The application of 1,8-naphthalimide derivatives as the photoactive units for the design of optical chemosensors for metal cations and protons with different mechanisms of analyte binding signal transduction and different receptors is discussed. Examples are given of fluorescent and colorimetric cation chemosensors in which the change of the spectral characteristics of the naphthalimide chromophore upon complex formation is due to switching of photophysical processes of charge transfer, electron transfer, energy transfer or excimer formation. The problems of detection of heavy and transition metal cations as well as development of ratiometric optical probes are discussed.
The bibliography includes 170 references.

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I. Introduction

Determination of the contents of metal cations and hydrogen atoms in environmental objects and biological systems is an important practical task for industry, medicine and ecology and for chemical and biochemical studies. Among the extensive inventory of modern physicochemical methods of analysis, great popularity was gained by optical electron spectroscopy techniques,[1] which is due first of all to relative simplicity of experimental procedure in combination with high sensitivity towards analytes. In the last two decades, considerable progress along this line was achieved owing to the design of optical chemosensors, *i.e.*, molecules that contain a receptor that selectively binds the analyte and a signalling group that changes its spectral characteristics upon this interaction.[2–6]

A highly popular platform for the development of optical molecular devices of sensor type is the chromophore system of the naphthalic acid imide (1,8-naphthalimide). 1,8- Naphthalimide derivatives represent an important class of organic luminophores, which also find wide use as optical brighteners,[7] laser dyes,[8] solar cells,[9] fluorescence markers in biology,[10] electroluminescence materials,[11] antitumour agents[12] or reagents for luminescence craok detection.[13] The considerable interest in 1,8-naphthalimide derivatives as the photoactive component of optical chemosensors is caused, on the one hand, by relative simplicity of their synthesis and, on the other hand, by the great diversity of their photophysical properties. For example, the electron-withdrawing nature of the naphthalimide ring in the excited state accounts for the ability to form excimers and exciplexes with π-donor aromatic substrates[14,15] and for the photoinduced electron transfer.[16,17] Naphthalimide was used to prepare systems that were studied for electron excitation energy transfer.[18,19] The spectral properties of luminophores of this class are sensitive to the environment: in the vast majority of cases, they exhibit solvatochromic and solvatofluorochromic effects.[20–22] Interesting spectral behaviour was identified in the studies of optical properties

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of 1,8-naphthalimides in microheterogeneous environment (micelles, cyclodextrins).[23] Fine tuning of photophysical characteristics of the naphthalimide ring can also be achieved by introducing photochromic groups into the molecule.[24,25]

This review is devoted to the use of 1,8-naphthalimide derivatives as chromophores in the design of optical chemosensors for cations. Since the mid-1990s and up to now, a great number of original papers on this topic were published; however, almost no contemporary reviews systematically considering naphthalimide-based sensors for cations are available. Among the reviews devoted to 1,8-naphthalimide derivatives, noteworthy is the publication [26] discussing recent achievements in the design of optical sensors for anions, the review on the synthetic photochemistry of naphthalimides and related compounds,[27] and reviews devoted to the application of naphthalimide derivatives as antitumour drugs.[28–30] Some examples of the cation optical sensors containing a naphthalimide residue were reported in other publications.[31,32] It should be noted that the mentioned reviews [31,32] are more general and include also data on optical sensors based on other organic luminophores.

The present review consists of several sections. First, general approaches to the development of optical chemosensors for cations are considered, and then brief analysis of photophysical properties of 1,8-naphthalimide derivatives needed for the understanding of subsequent sections is presented. This is followed by particular examples of naphthalimide-based ionophores, which differ both in the mechanism of the change of spectral characteristics upon complexation and in the type of receptor used. We chose the most spectacular examples of naphthalimide fluoroionophore systems reflecting the key approaches to their design and the most important achievements in this area, so that the reasonable size of the review is not exceeded.

II. General approaches to the design of optical sensors for cations

Currently, there are two principal approaches to the development of fluorescent and colorimetric sensors for cations.[2,3,5,33–35] The first one is to link the fluorophore and the receptor by a spacer (Fig. 1), thus ensuring separation of these components in the ground state. This approach is used in the design of fluorescent PET (photoinduced electron transfer) sensors.[33–35] The spacer is most often a polymethylene chain. In this sensor, the receptor is electron donor (D, ED) and the fluorophore is electron acceptor (A, EA). As the fluorophore is excited, an electron from the HOMO moves to the LUMO; this enables electron transfer (PET) from the HOMO of the receptor (donor) to the singly occupied HOMO of the fluorophore (acceptor), and this quenches fluorescence of the latter (see Fig. 1). After the addition of a cation to the receptor, the HOMO energy level of the receptor becomes lower than the fluorophore HOMO level. As a consequence, the PET effect does not occur and the sensor starts to fluoresce. Most of the PET sensors operate according to this mechanism; however, in the case of transition metal cations, a different mechanism of the change of spectral properties is possible, namely, the electron transfer is directed from the fluorophore to the bound metal ion,[36] or fluorescence quenching occurs as a result of increase in the rate of the intersystem crossing in the fluorophore (in the case of paramagnetic ions).[32]

The second approach is to combine the sensor elements in such a way that one or several atoms of the receptor that are involved in cation binding are parts of the π-system of the photoactive moiety.[2,3,5] This model, which does not imply the presence of a spacer, uses most often chromophores with electron-donating and electron-withdrawing groups in conjugated positions. The absorption of light by these molecules is accompanied by electron density shift from the donor to the acceptor and, most often, results in an increase in the dipole moment on going to the excited state. Depending on the mode of receptor attachment, binding of the cation would induce either bathochromic or hypsochromic shift of the absorption maximum with a simultaneous change in the intensity (Fig. 2). Since the dipole moment increases in the excited state, binding of the cation in the case shown in Fig. 2 *a* results in more pronounced stabilization of the ground state and a hypsochromic shift of the spectral bands. In the case presented in Fig. 2 *b*, the increase in the partial negative charge on the EA substituent upon

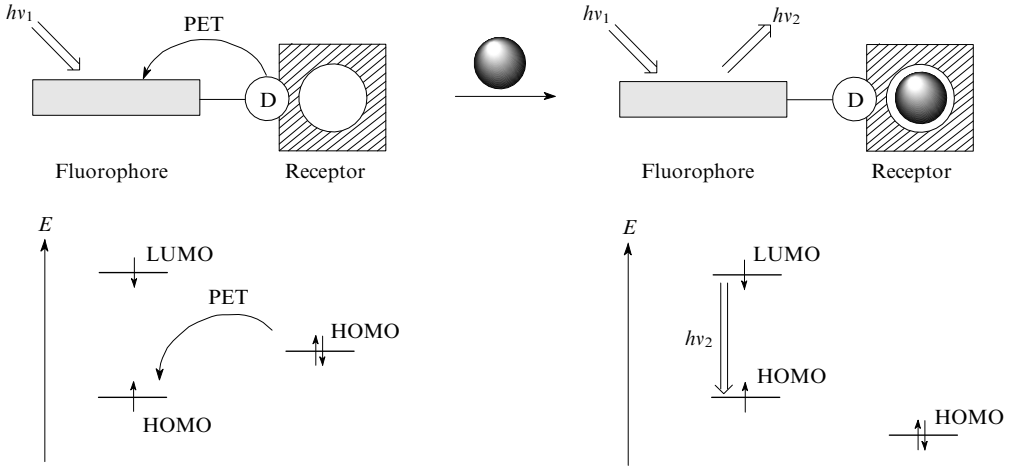


Figure 1. Schematics of the PET sensor for cation recognition.[2] The cation is shown as a bead.

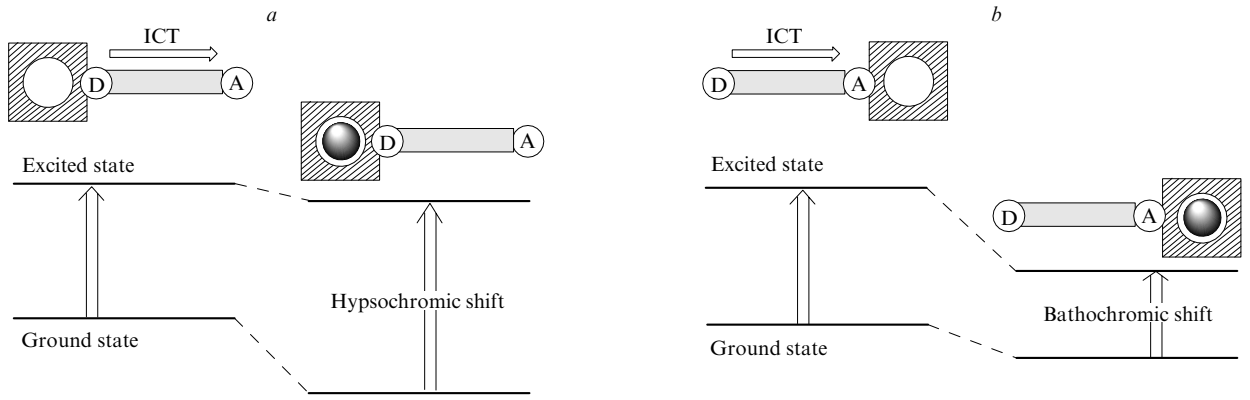


Figure 2. Energy diagram explaining the spectral shifts upon cation binding by the ICT sensor: ED substituent in the fluorophore structure is a part of the receptor (*a*); EA substituent in the fluorophore structure is a part of the receptor (*b*).[2]
The diagram corresponds to the case where the dipole moment in the excited state is greater than in the ground state.

charge transfer decreases the energy level of the excited state to a higher extent, which is manifested as a bathochromic shift of bands in the absorption spectrum. If the photoactive element is a fluorophore, a change in the band position and intensity is also observed in the fluorescence spectrum. Since the observed spectral effects are related to the increase (decrease) in the energy required to transfer the electron density between the donor and acceptor groups in the fluorophore conjugated system, this type of sensors is called ICT (intramolecular charge transfer) sensors.

Apart from the use of PET and ICT processes, there are also other approaches to the design of ion-sensitive optical devices. As shown in the recent years, additional opportunities for modulation of sensing properties are provided by the use of the chromophore ability to form exciplexes and to transfer the electron excitation energy.[5,32] The advantage of systems that employ these processes for switching of optical characteristics is creating conditions for the implementation of the ratiometric method for determination of the analyte concentration. According to the ratiometric procedure of measurements,[2,37] fluorescence intensity can be measured at different excitation or emission wavelengths and the intensity ratio would vary as a function of the analyte concentration. In this case, the calculation of the equilibrium concentration of the analyte does not require the knowledge of concentration of fluoroionophore molecules in the system or calibration of the detected signal.† For this reason, systems that exhibit a ratiometric optical response are of considerable practical interest for biosensors functioning *in vivo* and for the manufacture of microchips suitable for multi-ion analysis.[37]

Widely used are chemodosimeters — sensors the operation of which is based on a fast irreversible chemical reaction with the analyte. Most often, chemodosimeters exhibit fluorescence enhancement and represent an alternative to usual fluorescent PET and ICT sensors in those cases where complexation with a d-metal ion decreases the fluorescence intensity of the chromophore.

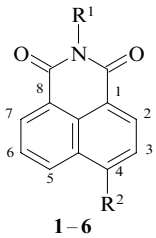
Among the whole diversity of chemosensors based on 1,8-naphthalimide derivatives, one can find examples of ion-sensitive compounds constructed using all approaches listed in this Section. The information presented in Sections IV to VII is classified according to the mechanism of the change in the spectral characteristics of the naphthalimide moiety upon the interaction of the sensor molecule with the cation.

III. Brief characteristics of spectral properties of 1,8-naphthalimide derivatives

The long-wavelength bands in the electronic absorption spectra of 1,8-naphthalimide (**1a**) and its derivative **1b** unsubstituted in the naphthalene ring occur at 330–360 nm and are due to $\pi-\pi^*$ type transitions.[38–41] Compounds of this type exhibit weak fluorescence with maxima at 340–460 nm. The quantum yield of fluorescence of *N*-methyl-1,8-naphthalimide (**1b**) is 0.005 in hexane and 0.22 in ethanol.[39] As it was shown,[38,41–44] the lower emitting state of compounds of this type has mainly the π,π^* nature and the low fluorescence quantum yield can be attributed to the relatively small energy difference between the $S_1^{\pi\pi^*}$ and $T_1^{n\pi^*}$ excited levels, resulting in the $S_1^{\pi\pi^*} \rightarrow T_1^{n\pi^*}$ intersystem crossing followed by non-radiative deactivation of the triplet state.

The introduction of $+M$ substituents into position 4 of the naphthalimide ring conjugated with the carbonyl groups

Structures 1–6



1–6

Compound	R^1	R^2	Compound	R^1	R^2
1a	H	H	**3a**	H	NMe_2
1b	Me	H	**3b**	Me	NMe_2
2a	H	Cl	**3c**	Bu^n	NH_2
2b	Me	Br	**4**	H	NO_2
			5	Bu^n	NHAc
			6	H	SMe

† Ratiometric technique can also be used for ICT sensors, because analyte binding results in a change in the positions of absorption and fluorescence maxima. In the case of classical PET systems, ratiometric measurements are impossible.

gives rise to strong long-wavelength charge transfer bands sensitive to the solvent polarity and caused by the electronic interaction of the ED substituent with the *peri*-carboximide group.[45,46] This is accompanied by a decrease in the energy of the $S_1^{\pi\pi^*}$ state[47] accompanied by an increase in the probability of the long-wavelength $S_0 \rightarrow S_1^{\pi\pi^*}$ transition and a decrease in the rate of intersystem crossing to the nearby triplet state, which is reflected also in a substantial increase in the fluorescence quantum yield.

If a chlorine atom exhibiting weak $+M$ effect serves as the electron-donating mesomeric substituent, the bathochromic shift on going from unsubstituted naphthalimide (**1a**) to 4-chloro-1,8-naphthalimide (**2a**) is relatively small being 9 nm in the absorption spectrum and 13 nm in the fluorescence spectrum (Fig. 3).[48] A similar picture is observed when a bromine atom is introduced in position 4 (compound **2b**).[39] The presence of the dimethylamino group in compounds **3a**,**b** induces much more pronounced bathochromic and bathofluoric shifts of the spectral bands with respect to 4-halo-substituted naphthalimides **2a**,**b** (see Fig. 3). Simultaneously the fluorescence intensity increases. Thus the quantum yield of fluorescence of derivative **3b** reaches 0.84 when hexane is used as the solvent.[39]

When a nitro group is introduced in position 4 of the unsubstituted naphthalimide ring (compound **4**), the absorption and fluorescence maxima exhibit a marked bathochromic shift and simultaneously the fine structure of the corresponding bands disappears (see Fig. 3). The long-wavelength absorption of 4-nitro derivatives, like that of 1,8-naphthalimides containing an ED substituent in position 4 of the naphthalene ring, is due to charge transfer; however, in this case, the electron density in the naphthalimide moiety shifts towards the NO_2 substituent possessing strong $-M$ effect.[48] The fluorescence quantum yield considerably decreases upon the introduction of the nitro group, which is due to low energy position of the $T_1^{n\pi^*}$ triplet level.[47]

The replacement of the amino group by the acetylamino group in position 4 of the naphthalene ring is accompanied by a hypsochromic shift of the absorption and fluorescence maxima and a decrease in the Stokes shift, which is due to the less pronounced ED character of the NHC(O)R substituent.[21,45,49,50] Indeed, acylation of amino derivative **3c** to give 4-acetamidonaphthalimide **5** entails a shift of the charge transfer band to the UV region (λ_{max}^{abs} = 363 nm in ethanol) and gives rise to blue fluorescence with λ_{max}^{fl} = 465 nm in ethanol.[45] 4-Alkoxy- and 4-aryloxynaphthalic acid imides show intense blue fluorescence.[20,51] The spectral properties of these derivatives are largely similar to the properties of 4-(acylamino)naphthalimides.[7,52]

A considerable red shift of the absorption and fluorescence maxima in the series of 1,8-naphthalimides can also be achieved by introducing a heterocyclic moiety into the molecule. Orange-coloured fluorescence is displayed by 4-pyrazolinyl derivatives **7**.[53] The long-wavelength absorption of compounds **7** is due to the pyrazoline moiety, which is highly polarized under the action of the electron-withdrawing naphthalimide residue: the electron density is shifted from the N(1) atom to the C(3) atom of the heterocycle. The introduction of a pyrazolinyl ring into a naphthalimide derivative molecule in such a way that the pyrrole nitrogen atom is linked to the naphthalene C(4) atom does not induce so great long-wavelength shift of spectral bands as observed in compounds **7**. For example, naphthalimides **8** prepared and characterized by Bian *et al.*[54] show green fluorescence at 520–540 nm.

The substituents at the imide nitrogen atom influence only slightly the absorption spectra but in some cases, they considerably affect the fluorescence spectra. The absorption and fluorescence maxima of *N*-alkyl naphthalimide derivatives are shifted by 10–20 nm to shorter wavelengths with

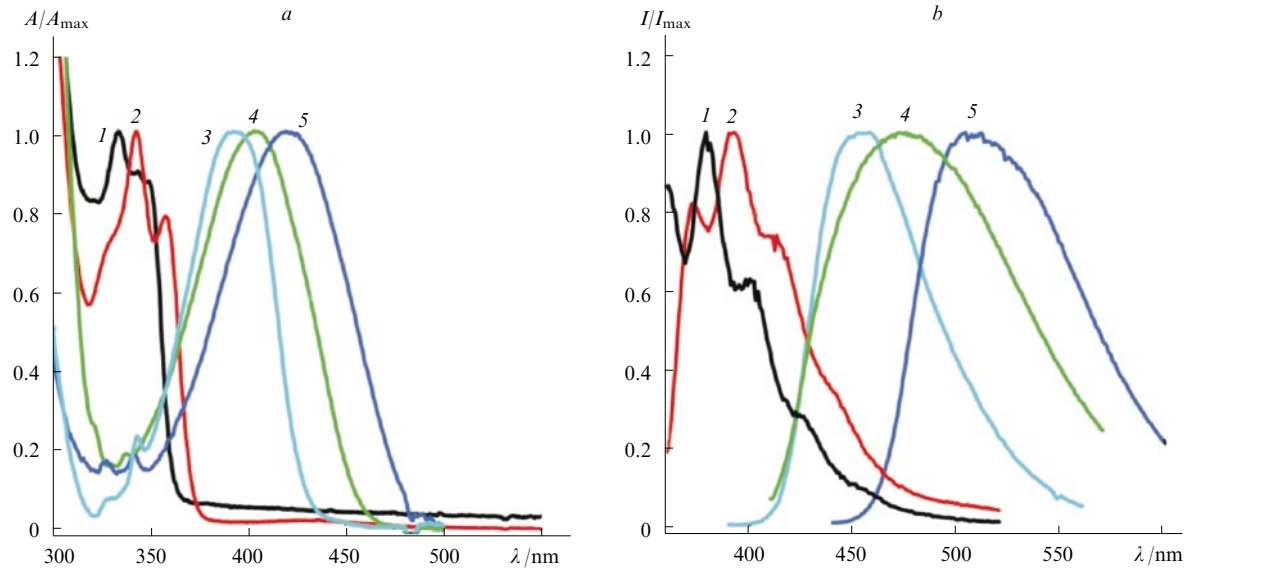
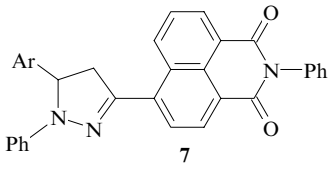


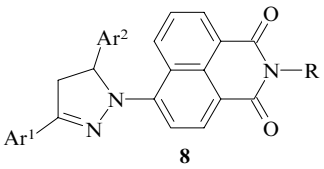
Figure 3. Absorption (*a*) and fluorescence (*b*) spectra of compounds **1a** (*1*), **2a** (*2*), **6** (*3*), **4** (*4*) and **3a** (*5*) in dichloromethane.[48] The absorption spectra were recorded for solutions of ~0.3 mmol litre^{-1} concentration. The fluorescence spectra were recorded for solutions of compounds **1a**, **2a**, **3a**, **4** and **6** with such a concentration that the optical density at the absorption maximum was in the 0.1–0.15 range.

Structures 7, 8



7

Ar = Ph, 4-$Me_2NC_6H_4$, *etc.*



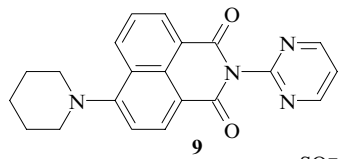
8

R = Bu^n, Bn; Ar^1 = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 2-thienyl; Ar^2 = Ph, 4-MeC_6H_4, 3-thienyl, 3,4-$(OCH_2O)C_6H_3$

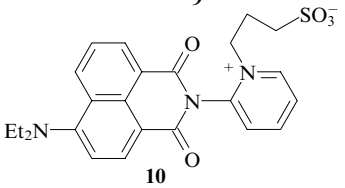
respect to those for *N*-phenylimide.[45] In the case of naphthalimides unsubstituted in the naphthalene ring, transition from the *N*-alkyl to *N*-phenyl derivative is accompanied by a considerable decrease in the lifetime and in the fluorescence quantum yield, which is related to an increase in the efficiency of internal conversion.[43] For some *N*-aryl 1,8-naphthalimide derivatives, dual fluorescence was observed,[43, 55–58] due to the presence of two emitting states with different energy. In one of these states, the *N*-aryl substituent and the naphthalimide moiety lie in one plane and in the other state, they are rotated through a definite angle relative to each other.

The presence of electron-withdrawing heterocyclic groups (pyridinyl, pyrimidinyl, thiazolyl) as substituents at imide nitrogen in 4-(dialkylamino)naphthalimide derivatives enhances the electron-withdrawing properties of the carboximide group.[59, 60] As a result, the change in the dipole moment on going to the excited state is greater for these derivatives than for analogous *N*-phenyl- and *N*-alkyl-substituted compounds, and, hence, their photophysical properties are more sensitive to the change in the solvent nature. It was proposed [59] to use compound **9** as a fluorescent indicator to determine the content of water in organic solvents. Quaternization of the pyridine nitrogen atom in the *N*-heteroaryl moiety leads to pronounced shift of fluorescence bands to longer wavelengths. For example, the fluorescence maxima of compound **10** in acetonitrile and in water are at 584 and 604 nm, respectively.[60]

Structures 9, 10



9



10

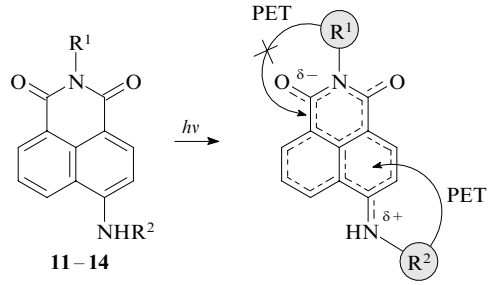
The electron-donating groups as parts of the substituent at the imide nitrogen atom can quench the fluorescence of the naphthalimide chromophore due to the electron transfer from the HOMO of these groups to the photoexcited naphthalimide residue. The ability of the naphthalimide ring to serve as an electron acceptor in the excited state is an important feature determining the possibility to use this type of luminophores for the design of fluorescent sensors. This feature of the photophysical properties of naphthalimide derivatives is considered in more detail in Section IV.

It can be seen from the above data that the photophysical characteristics of 1,8-naphthalimides are highly diverse and can vary over broad ranges depending on the structural features of their molecules. For this reason, 1,8-naphthalimides find wide use in the design of optical molecular sensor devices. The derivatives that have electron-donating substituents in position 4 of the naphthalene nucleus are of most interest from this standpoint, because they show pronounced absorption and fluorescence in the visible region and also have high thermo- and photostability.

IV. PET Sensors

Naphthalimide derivatives in which the donor group involved in PET interaction is covalently bonded *via* a spacer to the naphthalimide residue offer good prospects for the design of fluorescent sensors. As noted in Section II, the spacer is most often an oligomethylene chain, which ensures separation of the system components in the ground state. De Silva *et al.*[61,62] and Gao and Marcus [63] investigated directed electron transfer in 4-aminonaphthalimide derivatives **11**–**14** (Scheme 1) containing electron-donating tertiary amino groups in 4-substituents in the naphthalene nucleus (NHR^2) and at the imide nitrogen atom (R^1). The electronic absorption and fluorescence spectra of these compounds in aqueous methanol were measured as a function of the pH of the medium. It was assumed that protonation of the trialkylamino group would inhibit the PET process and, hence, bring about fluorescence enhancement.

Scheme 1



11–**14**

Compound	R^1	R^2
11	$CH_2CH_2NEt_2$	Bu^n
12	Bu^n	$CH_2CH_2NEt_2$
13	CH_2CH_2N(O)	$CH_2CH_2NEt_2$
14	$CH_2CH_2NEt_2$	CH_2CH_2N(O)

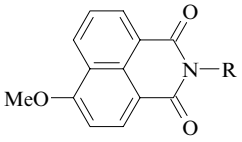
The clear-cut dependence of the fluorescence quantum yield on the pH was noted for compounds **12** [61] and **13**, **14**,[62] but was not observed for **11**.[61] In the pH range from 4 to 11, the quantum yield for **11** was ~0.1 and almost did not

change. Meanwhile, in the case of derivatives **13** and **14**, the quantum yield was fairly low ($\varphi^{fl} < 0.1$) in a basic medium but sharply increased as the solution was acidified ($\varphi^{fl} > 0.5$). The fluorescence was enhanced at pH values corresponding to the pK_a of the tertiary nitrogen atom contained in the 4-substituent of the naphthalene ring (at pH 8.7 and 5.7 for compounds **13** and **14**, respectively).‡ Hence, higher basicity of the diethylamino group compared to the morpholine group in isomers **13** and **14** accounts for the intense fluorescence of compound **13** at higher pH than in the case of compound **14**.[62]

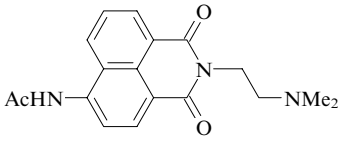
It was suggested[61,62] that the charge-separated state resulting from photoexcitation creates an intramolecular electrostatic field, which results in different heights of the activation barrier to the PET process (depending on the position of the donor group).[61,62] It can be seen from Scheme 1 that the electron transfer would be more probable on the side of the 4-substituent in the naphthalene moiety, because in this case, the positive end of the photoinduced dipole, which acts as the 'hole', is located more closely to this substituent. It is noteworthy that the thermodynamic driving force for both directions of the PET interaction is the same. More in-depth theoretical substantiation of the directed electron transfer in compounds **13** and **14** using the extended Hückel method was reported.[63]

The presence of the trialkylamino group in the substituent at the imide nitrogen atom in 4-methoxy derivative **15b**, unlike the above 4-amino-substituted **11**, **13** and **14**, resulted in efficient fluorescence quenching.[8] On going from **15a** to naphthalimide **15b**, the quantum yield in ethanol decreases from 0.35 to 0.02. In the presence of 5 vol.% of acetic acid, the intensity of fluorescence of a solution of naphthalimide **15b** increases 20-fold. A similar low level of fluorescence was found for 4-acetylamino naphthalimide **16**, which also contains an ED substituent in the *N*-alkyl moiety.

Structures 15, 16



15a,**b**

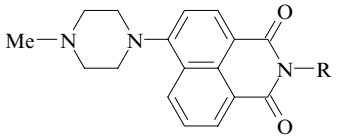


16

R = Et (**a**), CH_2CH_2N (**b**)

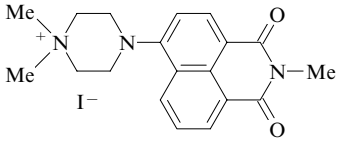
An example of fluorescent pH sensors is provided by naphthalimide derivatives **17a**,**b** containing a piperazine residue in position 4 of the naphthalene ring. In aqueous methanol at pH 11.0, compound **17a** shows only weak fluorescence (quantum yield $\varphi^{fl} = 0.0086$),[64] which is associated with electron transfer from the HOMO of the trialkylamino group to the photoexcited naphthalimide moiety. As the acidity increases, the nitrogen atom of the receptor that is not conjugated with the aromatic ring, is protonated and, as a consequence, the donor properties of the receptor disappear. Thus, the electron transfer becomes impossible and the fluorescence intensity increases ($\varphi^{fl} = 0.66$ at pH 2.3). Quaternization of the donor nitrogen atom in the receptor on going from compound **17a** to **18** also precludes the PET process. For this reason, compound **18** has a high fluorescence quantum yield comparable with that observed for derivative **17a** in acidic medium. The intensity of fluorescence of compound **18** is virtually independent of the pH.[64] Similarly to **17a**, pH-dependent fluorescence was found for compound **17b**.[65]

Structures 17, 18



17a,**b**

R = Me (**a**), All (**b**)



18

The piperazine substituent in position 4 of naphthalene in derivatives **17a** ,**b** can be coordinated to metal cations as a bidentate ligand. This coordination also hampers the electron transfer. It was shown[65] that binding of copper(II), iron(III) and zinc cations by compound **17b** in acetonitrile was accompanied by fluorescence enhancement, the most pronounced effect being observed for Cu^{2+} ions. Note that the complexation was accompanied by a hypsochromic shift of the fluorescence maximum of compound **17b**, which is indicative of participation of the tertiary nitrogen atom linked to the naphthalimide ring in the cation coordination.

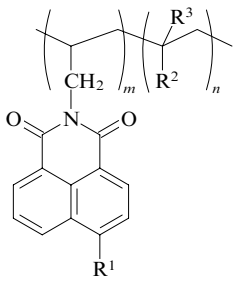
Owing to the presence of a double bond in the substituent at the imide nitrogen atom, naphthalimide derivative **17b** can be used as a monomer for the preparation of polymeric heterogeneous sensors in which the naphthalimide moiety is linked to the polymeric chain by a covalent bond. Systems of this type arouse considerable interest in researchers who develop optical chemosensors for cations. The introduction of fluoroionophoric groups into the polymer matrix appears promising from the practical standpoint because this allows one to repeatedly use the sensor material and to avoid contamination of the test solution with toxic chemicals,[66] provides conditions for analysis of aqueous solutions without special chemical modification of the structure of the ion-sensitive compound needed to make it soluble and complies with modern requirements to miniaturization and automation of analysis.[67]

Grabchev *et al.*[65] compared the sensing properties of monomeric dye **17b** and films prepared using copolymer **19a**, which has been obtained by radical polymerization of styrene with **17b**. Experiments identified considerable differences in the properties. Since binding to the metal cation was not accompanied by a shift of the fluorescence maximum, the researchers suggested that the piperazine receptor does not interact with the cation. An increase in the concentration of the metal cation in the solution into which the film has been immersed resulted in fluorescence quench-

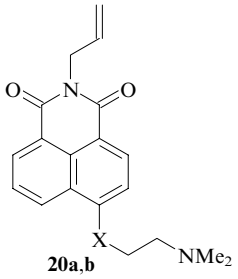
‡ It is known that the pK_a value of the conjugate acid BH^+ is numerically equal to the pH at which the concentration of the protonated (BH^+) and deprotonated (B) forms of base B are equal. For this reason, the pH range corresponding to most pronounced changes in the fluorescence intensity of the PET sensor for H^+ ions containing an amino group NR_2 that can be protonated as the receptor is usually in the range of pK_a ($^+NHR_2$) ± 1.5.

ing, the most pronounced changes being observed upon addition of Fe^{3+}. The decay of luminescence intensity was attributed to coordination of the metal cation to the carbonyl groups of the naphthalimide residue.

Structures 19–21



19a–c, 21



20a,b

X = NH (**a**), O (**b**)

R^2 = Ph, R^3 = H:

R^1 =  Me (**19a**), $NH(CH_2)_2NMe_2$ (**19b**),

$O(CH_2)_2NMe_2$ (**19c**); R^1 = $NH(CH_2)_2NMe_2$,

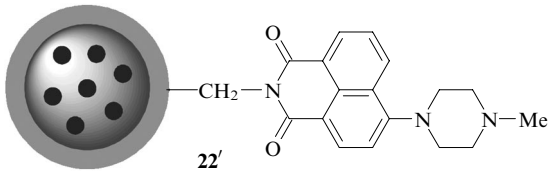
R^2 = CO_2Me, R^3 = Me (**21**)

Analogous changes in the sensing properties were observed on going from monomers **20a**,**b** to copolymers **19b**,**c**.[68,69] The addition of metal cations (Cu^{2+}, Zn^{2+}, Ni^{2+}, Mn^{2+}, Co^{2+}, Pb^{2+} and Fe^{3+}) to solutions of naphthalimides **20a**,**b** in acetonitrile was accompanied by enhancement of emission intensity, and simultaneously the fluorescence band shifted to shorter wavelengths. The most pronounced changes induced by binding of cations to compounds **20a**,**b** were observed in the case of Zn^{2+} (for sensor **20a**) and Fe^{3+} (for sensor **20b**). The addition of Fe^{3+} to an aqueous solution in which films of copolymers **19b**,**c** had been immersed resulted in fluorescence quenching. Note that the opposite situation was observed on acidification of the aqueous solution: protonation of the receptor amino groups resulted in enhancement of the fluorescence of films based on copolymers **19b**,**c**. The researchers[68,69] noted that polymeric heterogeneous sensors **19b**,**c** can be used to determine the degree of contamination of waste water by Fe^{3+} and H^+ ions.

Grabchev *et al.*[70] studied the effect of the structure of the polymer matrix on the sensor characteristics of copolymers **19b** and **21**. As shown by the studies, in the presence of Cu^{2+} cations in aqueous solution, copolymer **21** demonstrated enhancement of the fluorescence, which is not observed in the case of copolymer **19b**. The authors explained this difference in the sensing properties as being due to the fact that higher conformational mobility of the macromolecules of the poly(methyl methacrylate) matrix, together with lower packing density as compared with the polystyrene matrix create conditions for coordination of the cooper(II) cation to two nitrogen atoms of the substituent in position 4 of the naphthalene ring. Meanwhile, the increase in the fluorescence intensity of the film upon acidification of an aqueous solution is more pronounced in the case of copolymer **19b**, because the formation of hydrogen bonds between the protonated NMe_2 groups of the receptor and the carbonyl oxygen atoms of the methacrylate in copolymer **21** decreases the efficiency of inhibition of the PET process.

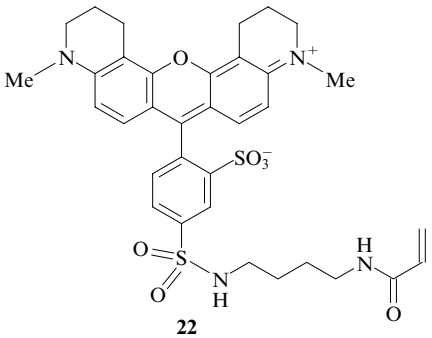
Great advantages for the design of ratiometric sensors able to detect cations in living cells and tissues are opened by immobilization of fluorescent chelating agents on the surface of nanoparticles. Nano-sized sensors have all of the above-listed advantages of heterogeneous fluorescent sensors. However, functionalization of nanoparticles in different ways allows them to be transported through cell membranes. Schulz *et al.*[71] proposed a preparation method and studied the sensing characteristics of nanoparticles **22′** based on polyacrylamide containing fragments of pH-sensitive 4-piperazinonaphthalimide **17b** immobilized by covalent bonding. Nanoparticles **22′** comprise a polymeric core containing indicator fluorophore **22**, which is enclosed in a shell made of the acrylamide–**17b** copolymer. As the pH decreased, the fluorescence intensity at 520 nm increased due to protonation of the tertiary nitrogen atom of the piperazine receptor. Since the change in the acidity almost did not affect the fluorescence spectrum of the encapsulated rhodamine dye **22** with a maximum at 600 nm, it was possible to use the intensity ratio of the 520 and 604 nm fluorescence for ratiometric pH determination. The presence in the polymeric core of dimethylamino groups, which can be protonated under physiological conditions, may give rise to a positive charge of the particles; as a result, the particles penetrated the cell membrane. The possibility of designing ratiometric sensors based on 4-piperazinonaphthalimide and indicator rhodamine dye was also demonstrated using silica gel nanoparticles.[72]

Structures 22, 22′



22′

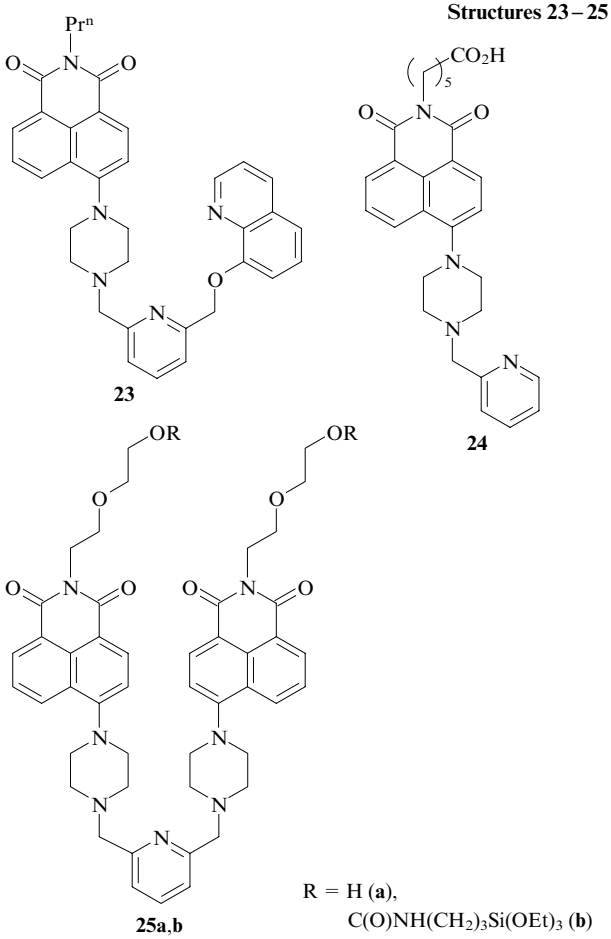
● is indicator fluorophore **22**



22

The introduction of pyridine and quinoline groups into the piperazine receptor in position 4 of the naphthalene ring produces selective fluorescent sensors for silver (compound **23**)[73] and mercury (**24** and **25a**) cations,[74,75] which operate in solutions in water or aqueous ethanol. Binding of cations by these derivatives was accompanied by the formation of 1 : 1 complexes in which the metal cation coordinates two nitrogen atoms of the piperazine ring, the pyridine (quinoline) nitrogen atom and the oxygen atom located in position 8 of the quinoline ring (in the case of complexation of compound **23**). In all cases, fluorescence enhancement was noted associated with suppression of the photoinduced electron transfer. On binding of Hg^{2+} ions by bis(naphtha-

Structures 23–25



23 **24** **25a,b**

limide) **25a**, an intramolecular excimer was formed as a result of interaction of two naphthalimide groups in the complex; this was manifested as a shift of the fluorescence maximum by 8 nm to longer wavelengths.[75]

Owing to the high sensitivity to Hg^{2+} cations related to the presence of two fluorophore moieties in one molecule, compound **25a** was used to prepare a heterogeneous sensor material based on silica gel.[76] Immobilization of the sensor on SiO_2 particles was attained through the formation of the Si–O covalent bond upon the reaction of the triethoxysilyl group in derivative **25b** obtained from **25a** with free OH groups on the silica surface. The limit of detection of mercury ions in aqueous solutions using this composite was 6.8×10^{-9} mol litre^{-1}. Furthermore, the produced material was proposed as an easily regenerable adsorbent for the purification of contaminated water from mercury(II). The possibility of regeneration is due to destruction of the mercury complex in 0.1 M HCl.

4-Amino-1,8-naphthalimide derivatives used most often in the design of fluorescent PET sensors are not always suitable for this purpose when considering the detection of transition metal cations. In view of the ability of these cations to decrease the efficiency of radiative deactivation of the fluorophore by the participation in electron (or energy) transfer or by enhancing the spin–orbit coupling in the complex, the expected increase in the emission intensity can be slight if any.[77] In some cases, fluorescence quenching may take place.[78] It is noteworthy that the use of fluorescence quenching as an analytical signal is inferior to the use of fluorescence enhancement, because this results in greater relative error of analysis.

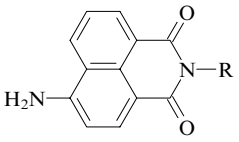
The research aimed at discovery of efficient PET sensors for transition metal cations gave rise to two approaches. The first is modification of the receptor in such a way as to minimize the undesirable fluorophore–metal cation interactions. For example, cryptands were proposed as receptors.[79,80] Despite the achieved good results, this method is not always suitable for solving the problem because the synthesis is faced with substantial difficulties. The second approach is to use the possibly most electron-deficient fluorophores. The decrease in the ED properties of the π-system, on the one hand, increases the driving force of the PET process, resulting in more pronounced fluorescence enhancement upon complexation, and, on the other hand, it deteriorates the fluorophore interaction with the quencher cation, which is a donor–acceptor interaction. This approach was implemented for naphthalimide derivatives.[77,81–87]

Derivatives containing a chlorine atom in position 4 of the naphthalene ring have a clear-cut electron-deficient nature as compared with 4-aminonaphthalimides. Indeed, whereas the oxidation potential of 4-aminonaphthalimide **26a** in acetonitrile was 1.27 V, 4-chloro derivative **27a** was not oxidized in the 0–2 V range under similar conditions.[81] The introduction of a dimethylamino group, which acts as the receptor, into the molecules of **26a** ($\varphi^{fl} = 0.63$) and **27a** ($\varphi^{fl} = 0.06$) to give compounds **26b** and **27b** was accompanied by quenching of fluorescence in MeCN by the PET effect by factors of 27 and 110, respectively,[77,81] which suggested sensing properties for both compounds. Nevertheless, considerable fluorescence enhancement following the addition of Cr^{III}, Fe^{III}, Co^{II}, Ni^{II} and Zn^{II} salts was noted only for compound **27b**,[77,81] which demonstrates the advantages of using the electron-deficient fluorophore. Interestingly, the degree of fluorescence enhancement§ of 4-chloro derivative **27b** proved to be 2–4 times higher than it would be expected upon complete suppression of the PET effect, *i.e.*, it was higher than 110. This was attributed[81] to an increase in the polarity and the proton-donor ability of the medium near the fluorophore caused by the presence of hydrated metal cations because the d-element salts used in experiments were mainly available as crystal hydrates. As it was found in a study of the photophysical properties of naphthalimide derivatives with the unsubstituted naphthalene ring,[20] which are similar to 4-halo derivatives in the orbital nature and the positions of excited levels, the increase in the solvent polarity and hydrogen bonding capacity induces a substantial increase in the fluorescence quantum yield. In the researchers' opinion, the abnormally high optical response of compound **27b** is attributable to this solvent effect, which facilitate the enhancement of fluorophore fluorescence upon suppression of the PET process.

Naphthalimide derivatives served for the design of selective sensors for the zinc cation,[75,86,88–92] which is a component of metalloenzymes and is significant for gene transcription processes. The interest in the sensors for zinc cations is related to the keen research into its neurobiological functions, which have been little studied to date. Compounds **28a**[88] and **29**[89] contain the *N*,*N*-bis(2-picolyl)-

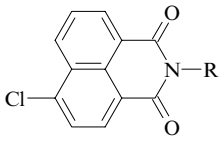
§ The degree of fluorescence enhancement is the ratio of fluorescence intensities of the solution after and before the addition of the metal cation.

Structures 26, 27



26a,b

R = H (**a**), $CH_2CH_2NMe_2$ (**b**)

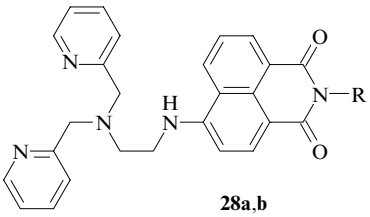


27a,b

R = Bu^n (**a**), $CH_2CH_2NMe_2$ (**b**)

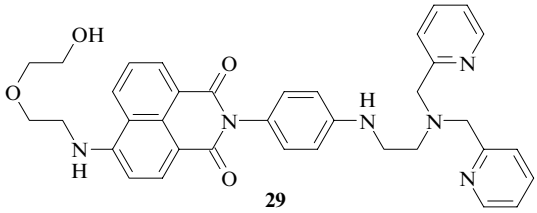
ethylenediamine receptor with high Zn^{2+} affinity in different positions of the naphthalene ring. The 4-aminonaphthalimide chromophore was chosen for its relatively long-wavelength fluorescence and low sensitivity to the pH of the medium; this is important when sensors are used to analyze biological objects. The presence of the 2-(2-aminoethoxy)-ethanol moiety in derivative **29** increases water solubility of the sensor.

Structures 28, 29



28a,b

R = Me (**a**), Bu^n (**b**)

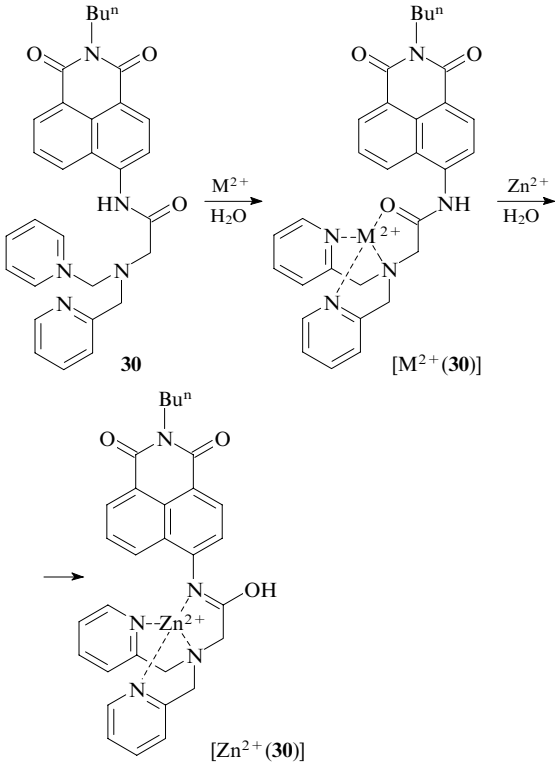


29

When zinc cations are added to aqueous solutions of compounds **28a** and **29**, the fluorescence intensity linearly increased up to the metal to ligand molar ratio of 1 : 1, and then remained constant. A pH-independent degree of fluorescence enhancement for sensors **28a** and **29** was observed at pH >7.0 and >3.6, respectively. This corresponded to the formation of stable complexes {stability constant of $[Zn^{2+}(\mathbf{28a})] \approx 10^9$},[88] the higher fluorescence level of which is related to inhibition of the PET interaction between the chromophore and the nitrogen atom of the receptor trialkylamino group. In the case of compound **28a**, binding of a zinc cation involves the nitrogen atom of the NHR group located in position 4 of the naphthalene ring; as a result, the absorption and fluorescence maxima shifted by 10 nm to shorter wavelength upon complex formation. The enhancement of fluorescence of compound **29** took place at constant λ_{max}^{fl} value. A study of the complexation selectivity demonstrated that among the cations Na^+, K^+, Mg^{2+}, Ca^{2+}, Mn^{2+}, Fe^{2+}, Fe^{3+}, Ni^{2+}, Cr^{3+}, Ag^+, Cd^{2+}, Cu^{2+} and Zn^{2+}, fluorescence enhancement is also induced by the addition of a cadmium cation, as is also the case for other sensors for Zn^{2+}. In the presence of Cu^{2+}, fluorescence quenching is observed, which is apparently, associated with electron (energy) transfer between the fluorophore and the coordinated metal cation. Biological cell assays were performed[89] and demonstrated that the sensor properties of compound **29** are retained in cells.

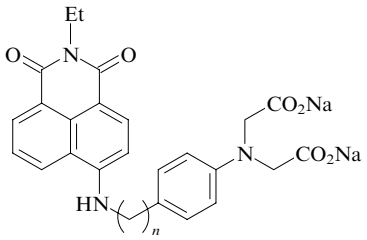
By introducing a carbonyl group into the spacer connecting the 4-aminonaphthalimide moiety with the bis(2-picolyl)amino group in compound **28b** to give compound **30** (Scheme 2), the fluorescence response observed upon binding of Zn^{2+} and Cd^{2+} cations by sensor **30** was differentiated.[85,86] Similarly to **28a,b**, complexation of compound **30** with these cations in aqueous solution was accompanied by fluorescence enhancement; however, the spectral peaks shifted to different directions: in the case of a Zn^{2+} cation, a bathochromic shift of λ_{max}^{fl} from 483 to 514 nm was observed, while in the presence of Cd^{2+}, the fluorescence band shifted by 37 nm to shorter wavelengths. This difference in the spectral behaviour is attributable to the fact that chelating agent **30** has the highest affinity to the zinc cation when exists as the hydroxy imide tautomer. Other transition metal cations, including cadmium, are complexed by the amide tautomer (see Scheme 2).[86]

Scheme 2



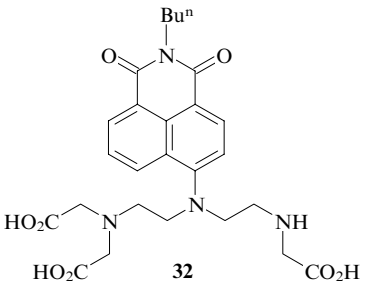
The high selectivity to the zinc cation among Group I and II metals in neutral aqueous solutions was found for 4-aminonaphthalimide derivatives **31a,b** and **32** containing an aminocarboxylate chelating receptor.[90–92] Compounds **31a,b** demonstrated a behaviour typical of classical PET sensors: fluorescence enhancement took place without significant changes in the positions and intensities of the long-wavelength bands in the absorption spectra. The elongation of the methylene spacer on going from **31a** to **31b** somewhat decreased the efficiency of the PET process in the free ligand and decreased the degree of fluorescence enhancement upon complexation (the ratios of the fluorescence quantum yields of the complex and the ligand were 56 and 20 for compounds **31a** and **31b**, respectively); however, the authors noted that the photostability of sensor **31b** was higher; in

Structures 31, 32



31a,**b**

n = 1 (**a**), 2 (**b**)



32

addition, it is also expected to be more stable against cell metabolites in *in vivo* assays.

In the case of compound **32**, the formation of 1 : 1 chelate with a zinc cation involved the central nitrogen atom bound to the naphthalimide ring and three carboxy groups.[92] As shown by quantum chemical density functional theory (DFT) calculations with the 6-31G* basis set using the B3LYP functional, the Zn–O(3) (2.02 Å), Zn–O(1) (2.08 Å), Zn–O(2) (2.09 Å) and Zn–N(1) (2.10 Å) bond lengths in the complex [Zn^{2+}(**32**)] are much shorter than the distances between the zinc cation and the N(3) (4.02 Å) and N(2) (2.27 Å) atoms (Fig. 4). Considering the geometry of the complex, the fluorescence enhancement upon complex formation was explained by not only suppression of the PET interaction in the ligand between the terminal amino groups and the fluorophore but also by the

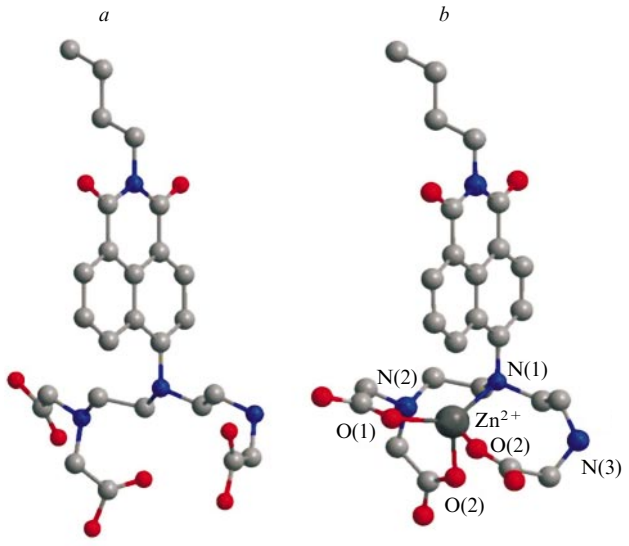


Figure 4. DFT-optimized geometry the molecule of **32** (*a*) and its complex with Zn^{2+} cation (*b*).[92]
For the sake of simplicity, hydrogen atoms are omitted.

influence of coordination on the charge transfer in the naphthalimide moiety.

Considerable attention is drawn by macromolecular fluorescent sensors based on dendrimers. Dendrimers (from Greek *dendros* meaning a tree) are three-dimensional highly branched macromolecules having a globular shape.[93] Poly(amidoamines) (PAMAM) are commercially available dendrimers. Their molecules are hydrophilic and comprise an ethylenediamine core with polyamidoamine chains running from the core in all directions. Thus, a PAMAM dendrimer contains tertiary amino groups and amide groups.

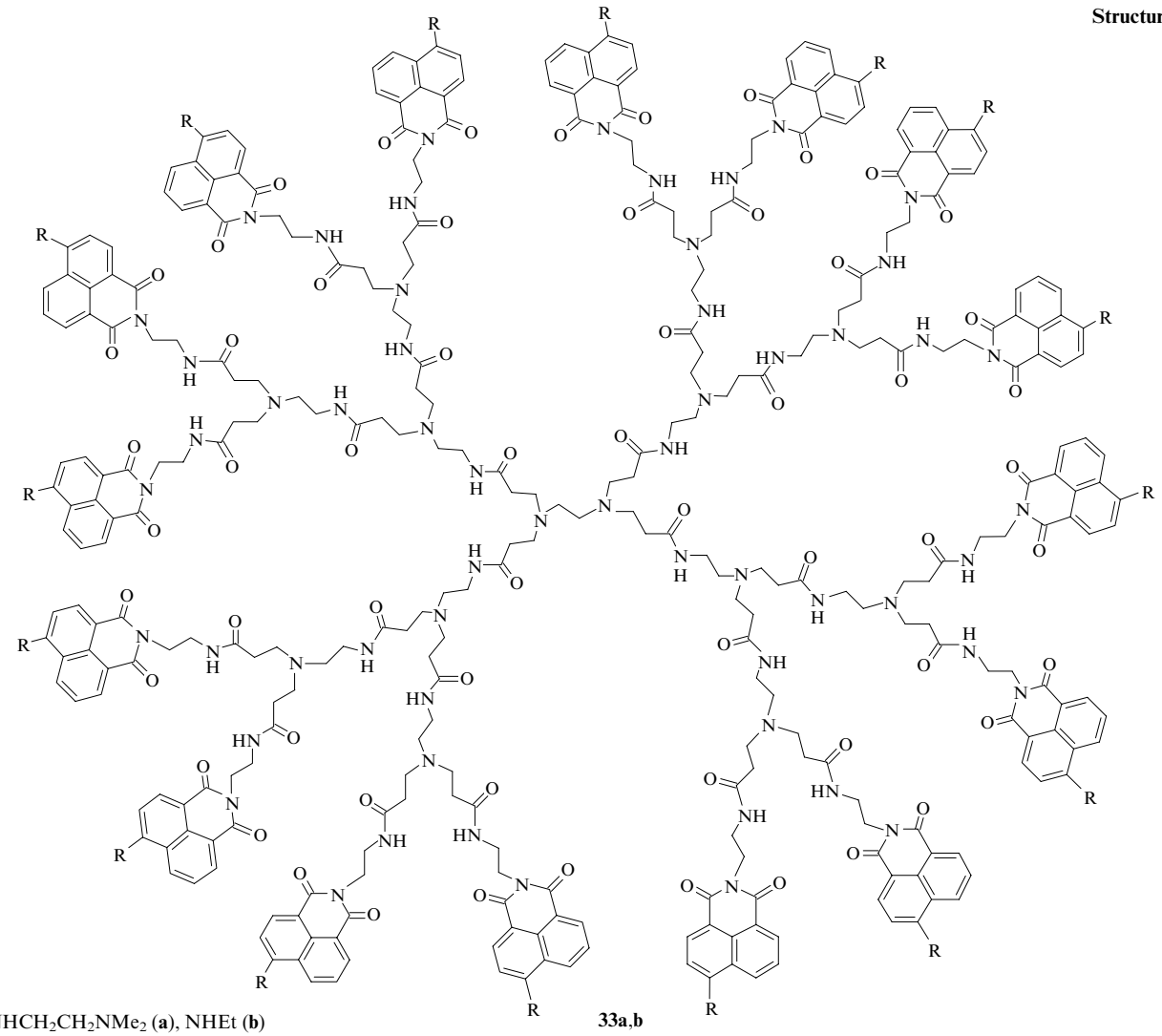
By attaching naphthalimide groups to the ends of the polyamidoamine chains, highly sensitive fluorescent sensors for cations are produced,[94–99] which is exemplified by structures **33a**,**b**. Binding of cations by these macromolecules may be accomplished by complex formation *via* interaction both with the inner donor atoms and with the terminal receptors (if present); this may give complexes containing more than one cation per dendrimer molecule.

In compound **33a**, the electron transfer to the photoexcited naphthalimide moiety can occur from either internal tertiary nitrogen atoms or the terminal amine receptor (R). As noted in the beginning of this Section, the latter process is preferred, because in this case, electron transfer occurs through the positively polarized end of the naphthalimide moiety. The change in the fluorescence characteristics of compound **33a** upon the addition of metal cations was studied in an aqueous solution.[94] Dendrimer **33a** was preliminarily attached to the polyamide matrix (where it was held by van der Waals interactions and hydrogen bonds), *i.e.*, it was used as a heterogeneous sensor. The addition of metal cations (Co^{2+}, Fe^{2+}, Fe^{3+} and Ni^{2+}) caused fluorescence to enhance, the enhancement being most pronounced in the case of the Ni^{2+} cation. Simultaneously, binding of cations induced a hypsochromic shift of the fluorescence maximum, which attested to the interaction of cations with the bidentate receptor located at the periphery of the macromolecule.

The addition of cations to a solution of dendrimer **33b** in DMF resulted in fluorescence quenching.[95] The fact that the absorption and fluorescence spectra did not shift upon complexation of dendrimer **33b** with metal cations indicates that this binding has been due to the coordination sites inside the globule. Fluorescence quenching in this case is apparently caused by energy transfer (or electron transfer) processes between the naphthalimide chromophore and metal complexes situated inside the macromolecule.

Fluoroionophore systems based on naphthalimide derivatives containing a macrocyclic receptor were reported. Panchenko *et al.*[100] investigated the sensing properties of 4-amino- and 4-(acetylamino)-1,8-naphthalimides **34a**,**b** with respect to calcium cations in acetonitrile. It was found that complexing of Ca^{2+} with the crown ether moiety gives 1 : 1 complexes, which show a higher fluorescence quantum yield than free ligands **34a**,**b**. Fluorescence enhancement was attributed to the decrease in the probability of the photoinduced electron transfer between the naphthalimide moiety and the *N*-phenylaza-15-crown-5 ether receptor upon the coordination with the cation, which was supported by PM6 semiempirical quantum chemical calculations. The sensing properties of compound **34a** with respect to the Ca^{2+} ions were retained upon inclusion of this compound into a hybrid organic-inorganic

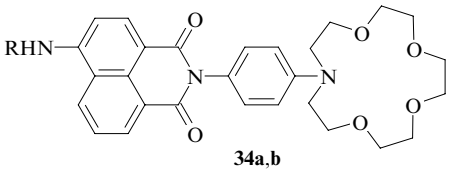
Structures 33



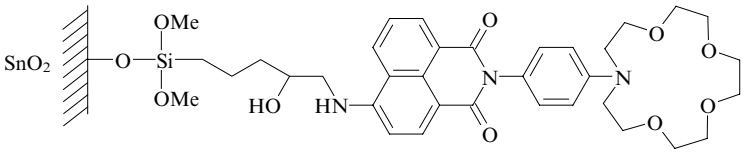
R = $NHCH_2CH_2NMe_2$ (**a**), NHEt (**b**)

33a,**b**

Structures 34, 35



34a,**b**



35

R = H (**a**), Ac (**b**)

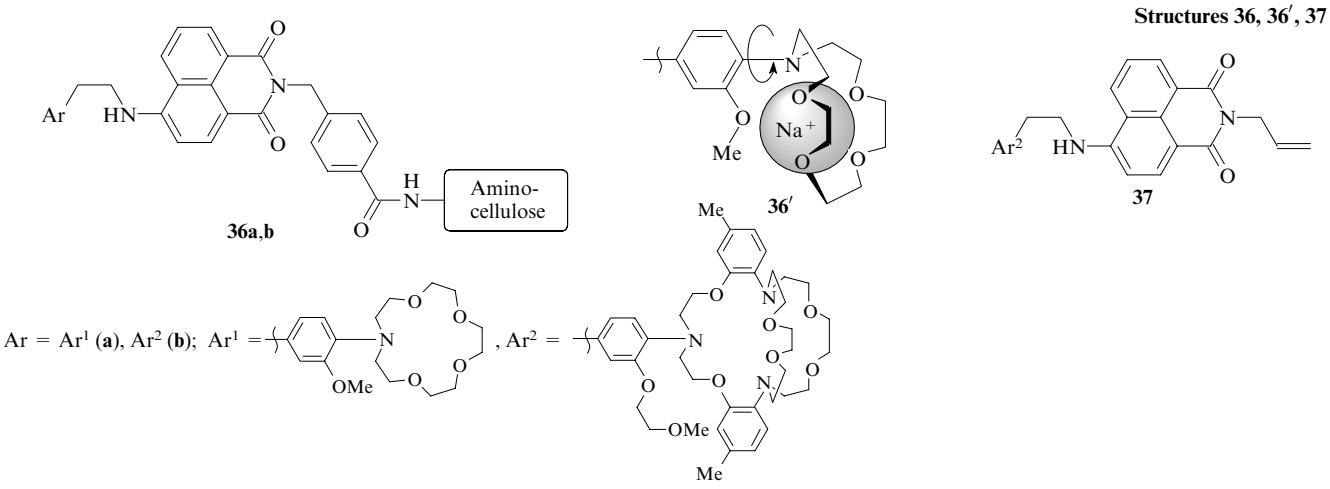
material **35** based on tin(IV) oxide.[101] The composite comprised microcrystalline SnO_2 threads with surface covalently bonded groups of fluorophore **34a**. Surface modification of the inorganic oxide was performed using organosilicon linkers.

Heterogeneous sensor **36a** was proposed for determination of the Na^+ content in blood.[102] The increase in the sodium chloride concentration in an aqueous buffer solution (pH 7.4, HEPES-buffer)¶ which was pumped through a cell with a sensor plate from 0 to 200 mmol litre^{-1} was accompanied by enhancement of fluorescence of the plates, the position of the maximum λ_{max}^{fl} remaining the same, which is due to suppression of the PET interaction between the *o*-anisidine group of the arylazacrown ether receptor and the 4-aminonaphthalimide ring upon complexation with the cation. It should be emphasized that the spectral changes were observed under conditions corresponding to clinically important ranges of Na^+ concentrations (100–180 mmol litre^{-1}) and pH (6.6–7.8).

The behaviour of sensor **36a** at extremely high concentrations of sodium and hydrogen ions was investigated.[102] The experiments demonstrated that the fluorescence intensity of compound **36a** is the same in a 6 M aqueous NaCl solution and in a 0.01 M HCl solution (pH 2). This result is unexpected if one takes into account the fact that the positive charge in the Na^+ complex with 15-azacrown-5 ether is distributed among six atoms, while in the proto-

¶ HEPES is 2-[4-(2-hydroxyethyl)piperazino]ethanesulfonic acid.

Structures 36, 36′, 37

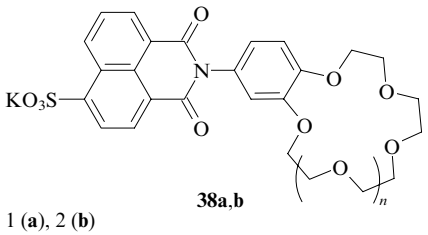


nated form of the receptor it is fully concentrated on the nitrogen atom. This suggests that fluorescence enhancement induced by binding of H^+ should be at least six times higher than the effect caused by complexing Na^+ ions. In practice, a 18-fold increase in the intensity of the emission signal was observed in both cases. The researchers cited [102] deem that the equal levels of fluorescence observed at high sodium and hydrogen ion concentrations can be due to the difference between the physical properties of the 6 M NaCl solution and the 0.01 M HCl solution, resulting in occasional coincidence of the naphthalimide fluorophore responses in the protonated and Na^+-saturated samples. An alternative interpretation is that the sodium cation, being located in the crown ether cavity, can form an additional coordination bond with the oxygen atom of the methoxy group. The formation of this bond is probably accompanied by the rotation of the crown ether moiety around the C–N bond (structure **36′**) and complete disruption of the conjugation between the lone pair of the macrorocycle nitrogen atom and the π-system of the benzene ring.

The replacement of the azacrown ether receptor in compound **36a** by the cryptand residue afforded heterogeneous PET sensor **36b** suitable for determination of potassium cations in aqueous solutions.[103] The mechanism of the change of the spectral characteristics of sensor **36b** upon complex formation is similar to that for compound **36a**. Sensor **36b** demonstrated fast and reversible fluorescence enhancement as the K^+ concentration increased from 2 to 10 mmol litre^{-1} in the presence of 160 mmol litre^{-1} of Na^+. Owing to this fact, sensor **36b** was used in the clinical analysis of whole blood. An analogous triazacryptand-containing chemosensor for the potassium cation was obtained by copolymerization of 2-hydroxyethyl methacrylate with monomer **37**.[104]

Water-soluble chemosensors **38a**,**b** for sodium and potassium cations based on 4-sulfonaphthalimide containing the benzocrown ether receptor were prepared.[105] Cation binding was accompanied by an increase in the dual fluorescence intensity due to suppression of the electron transfer between the benzocrown ether and naphthalimide moieties and by changes in the absorption spectra. Due to the smaller size of the crown ether cavity, compound **38a** selectively trapped Na^+ cations in the presence of K^+, which was confirmed by the absence of fluorescence enhancement upon the addition of KCl to an aqueous solution of compound **38a**. These molecules are examples of fluorescent sensors with dual fluorescence caused by the presence of two excited states between which dynamic equilibrium is established and maintained in the radiative deactivation process. These systems are suitable for ratiometric determination of the analyte ion concentration, which does not require calibration of the signal being detected using indicator fluorophores.

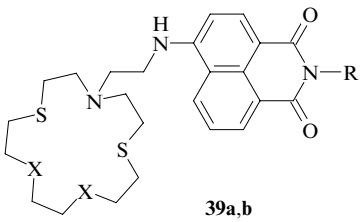
Structures 38



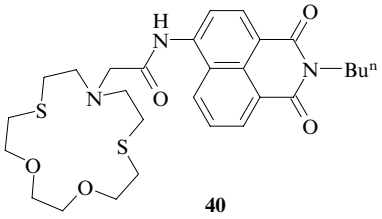
n = 1 (**a**), 2 (**b**)

An advantage of fluorescent sensors with crown ether receptors is the possibility to control the selectivity of cation binding by varying the size of the macrocycle and the nature of the heteroatoms present. The introduction of sulfur atoms into the receptor gives rise to selective sensors for 'soft' transition metal cations. 4-Aminonaphthalimide derivative **39a** containing an azatetrathia-15-crown-5 ether moiety was proposed as a fluorescent chemosensor for mercury(II) cations in aqueous ethanol solutions.[106] When the Hg^{2+} concentration increased, the fluorescence intensity increased linearly, resulting in a 5-fold growth of the

Structures 39, 40



X = S, R = Pr^n (**a**);
X = O, R = Bu^n (**b**)



quantum yield, which may be interpreted in terms of the PET mechanism of sensing. Whereas the presence of alkali metal, alkaline earth metal, lead and some d-metal (Cr^{3+}, Fe^{2+}, Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}) cations in solution did not induce significant spectral changes, the addition of Ag^+ caused fluorescence quenching of both free ligand **39a** and the complex [Hg^{2+}(**39a**)]. The low level of fluorescence of the complex [Ag^+(**39a**)] is probably associated with the d–π interaction between the fluorophore and the silver cation.

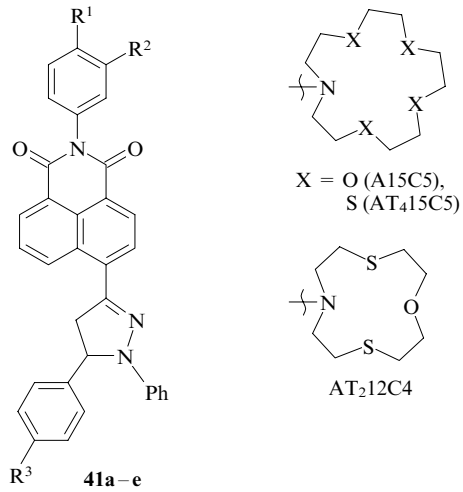
Lower stability of mercury complexes compared to silver complexes was confirmed by azadithia-15-crown-5 ether naphthalimide derivatives **39b** and **40** while investigating the complexation in a water–acetonitrile mixture by calorimetry.[87] Compound **39b** similarly to compound **39a** demonstrated considerable fluorescence enhancement only in the presence of Hg^{2+}, while the addition of Ag^+ increased the intensity only slightly. By comparing the results obtained for 4-amino derivatives of naphthalimide **39a**,**b**,[87, 106] one can conclude that the considered fluoroionophores are not 'perfect' sensors for the mercury(II) cation, because the highest selectivity of optical response (observed for Hg^{2+}) does not correspond to the highest complexation selectivity (observed for Ag^+).

In order to improve the sensing characteristics of compound **39b**, it was proposed to replace the secondary amino group linked to the naphthalimide ring by an amide group (derivative **40**). The presence of a more electron-deficient 4-(acylamino)naphthalimide fluorophore in sensor **40** structure made it possible to overcome the fluorescence quenching effect upon the complexation with the silver cation and to achieve an approximately 14-fold increase in the emission intensity.[87] The limit of detection of Ag^+ in a water–acetonitrile solution by sensor **40** was 1.0×10^{-8} mol litre^{-1}.

Colouring of some transition metal compounds may cause certain difficulties in the practical application of optical sensors because the absorption bands of d-metal complexes can fall in the range of absorption of the chosen fluorophore. From this standpoint, the use of a longer-wavelength fluorophore can in some cases be preferred. Indeed, crown-containing 4-pyrazolinyl-1,8-naphthalimide derivative **41a** exhibiting orange fluorescence (λ_{max}^{fl} = 677 nm, λ_{max}^{abs} = 493 nm in MeCN) was proposed as a PET sensor for Fe^{3+} cations (intense absorption of $FeCl_3$ in MeCN is observed at 350–400 nm).[107] As Fe^{3+} was complexed with ligand **41a** in acetonitrile, a 30-fold increase in the fluorescence intensity took place due to the decrease in the electron-donating properties of the *N*-phenylazacrown ether receptor. Analogous spectral effects were observed for derivatives **41b**,**c** [53] and **41d**.[108] Compound **41b** selectively trapped 'hard' alkali and alkaline earth metal cations (the latter were preferred), while compound **41c** bound Ag^+ and Hg^{2+} cations. It is noteworthy that the replacement of the *N*-phenylaza-15-crown-5 ether moiety in compound **41d** by the less electron-excessive benzo-15-crown-5 ether moiety almost eliminated the PET interaction in the free ligand **41e**. As a consequence, complexation of ligand **41e**, unlike that of compound **41d**, induces fluorescence quenching, which in all probability can be attributed to an increase in the electron-withdrawing character of carbonyl groups of the fluorophore upon coordination of the cation to the crown ether macrocycle.[108]

Effective binding of transition metal cations may be achieved by means of azamacrocyclic ligands. Using the 1,3-dipolar cycloaddition click reaction of aryl azide with the triple carbon–carbon bond, fluorescent PET sensors **42a** [109] and **42b** [110] based on 1,8-naphthalimide derivatives and containing a cyclam moiety as the receptor were prepared. The fluorescence enhancement upon complexation of ligands **42a**,**b** was due to suppression of the PET process between the naphthalimide fragment and nitrogen atoms of the macrocycle. Compound **42a** selectively trapped the zinc cation in an aqueous solution in the presence of Na^+, Ca^{2+}, Mg^{2+} and Fe^{3+} ions; however, the presence of excess Hg^{2+} or Cu^{2+} in the solution interfered with the determination. The authors noted that the N(3) atom of the triazole ring linked to the naphthalimide group is involved in cation binding by sensor **42a** apart from the azamacrocycle.[109] The presence of two naphthalimide moieties in derivative **42b** increased twofold the fluorescence response induced by complexation with Zn^{2+}. Nevertheless, no significant increase in the selectivity towards the zinc cation with respect to Cu^{2+} and Hg^{2+} was achieved.[110]

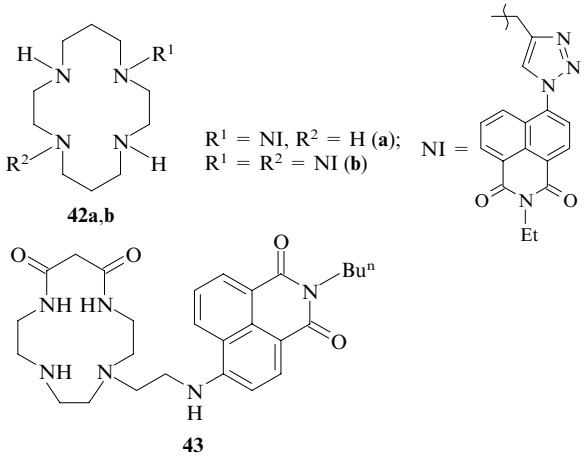
Structures 41



41a–e

$R^1 = R^2 = H$: R^3 = $AT_2$12C4 (**a**), A15C5 (**b**), $AT_4$15C5 (**c**);
$R^2 = R^3 = H$, R^1 = A15C5 (**d**); $R^1–R^2 = O(CH_2CH_2O)_4$, R^3 = H (**e**)

Structures 42, 43



42a,**b**

43

Certain interest has been aroused in recent years by cyclic dioxotetraamines, which are suitable as receptors for selective optical sensors for Cu^{2+}, Co^{2+} and Ni^{2+}.

Mu *et al.*[111] considered the influence of complexation with metal cations on the spectral properties of 4-aminonaphthalimide derivative **43** containing a dioxotetraamino macrocycle. In the presence of Cu^{2+} and Hg^{2+} ions, the solution turned from yellow-green to nearly colourless and to orange-coloured, respectively. The addition of other metal cations (Fe^{2+}, Co^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, Mg^{2+}, Mn^{2+} and Ag^{+}) did not change the solution colour. The colour change upon complexation with Cu^{2+} can be attributed to the participation of the nitrogen lone pair (LP) of the 4-amino group in the naphthalimide ring in the additional coordination with the copper cation located within the cavity of the macrocyclic receptor. The bathochromic shift that follows binding of the Hg^{2+} ion was interpreted[111] as being due to the $d-\pi$ interaction between the fluorophore and the cation having easily polarizable electron shell. Due to the larger radius, the Hg^{2+} ion does not fit in the macrocyclic cavity. Therefore, Hg^{2+} is bound by both the receptor and the 4-aminonaphthalimide moiety. Yet another explanation is that the interaction with Hg^{2+} is accompanied by deprotonation of the nitrogen atom attached to the naphthalimide ring; this increases its donor properties and, hence, facilitates the electron density shift to the CO groups of the imide moiety on exposure to light. It should also be noted that the complex of the copper ion with ligand **43** is more stable: the addition of Hg^{2+} into a solution containing [Cu^{2+}(**43**)] did not induce changes in the absorption spectrum of the complex.

Binding of Cu^{2+} and Hg^{2+} by compound **43** brought about a decrease in the fluorescence intensity caused by the possibility of electron (energy) transfer between the photoexcited naphthalimide ring and the coordinated metal cation (in the case of Cu^{2+}) and by the presence of strong spin – orbit coupling (in the case of Hg^{2+}). The presence of other cations (Ag^{+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Co^{2+}) had a much less pronounced spectral effect. A comparison of the sensing properties of compounds **39a**,**b**, **40** and **43** to mercury cations shows that a change in the nature of the receptor not only brings about different selectivities of complexation but can also dramatically influence the observed spectral changes. Indeed, compounds **39a**,**b** and **40** are typical PET sensors. In the case of ligand **43**, suppression of the PET process by complexation does not have a significant effect on the spectral response because the Cu^{2+} and Hg^{2+} cations interact with the π-system of the naphthalimide ring. Despite the fact that the structure of naphthalimide derivative **43** is typical of a PET sensor, *i.e.*, includes a fluorophore, a spacer and a receptor, the changes in photophysical characteristics induced by coordination of cations attest that this compound is an ICT type sensor.

V. ICT Sensors

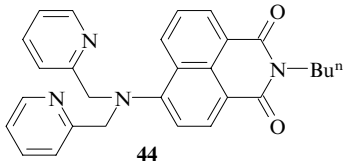
Examples of optical sensor systems in which complex formation influences the charge transfer process in the naphthalimide chromophore have been repeatedly come across in consideration of the fluorescent PET sensors. Apart from fluoroionophore **43**, this refers to naphthalimide derivatives **17a**,**b**, **20a**,**b**, **23**, **24**, **25a**,**b**, **28a**,**b**, **30**, **32** and **33a**. In these compounds, the interaction of the cation with the oxygen and nitrogen atoms incorporated in the conjugated system of the photoactive moiety led to some shift of the peaks in the absorption and fluorescence spectra to shorter wavelengths; however, the spectral response was mainly due to the PET effect. In this Section, we discuss the fluorescent and colorimetric sensors in which the ICT interaction plays the crucial role for transmitting the information about binding of the analyte ion.

As noted in Section II, an ICT chemosensor can be designed by introducing a receptor group into the chromophore molecule D–A on the side of either the electron-donating or electron-withdrawing substituent (see Fig. 2). In the series of naphthalimide derivatives, most of ion-sensitive ICT systems are constructed using the former approach. Ionophores in which the cation is coordinated to the carbonyl groups of the carboxymide moiety are encountered much more rarely. First, we shall consider ICT sensors containing the receptor in position 4 of the naphthalimide ring.

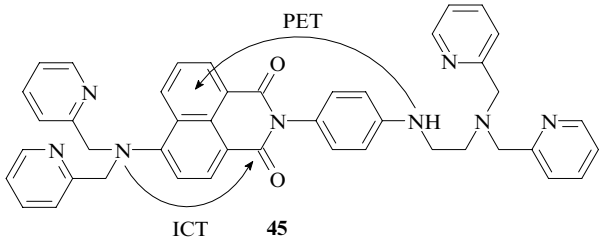
1. ICT sensors containing the receptor in position 4 of the naphthalimide ring

Compound **44** is a selective sensor for the copper(II) cation in aqueous acetonitrile solutions.[112] The receptor in derivative **44** is *N*,*N*-bis(2- picolyl)amino group (BPA). Since the LP of the central nitrogen atom of the receptor participates in the ICT interaction, binding of cations is expected to decrease the degree of charge transfer in the fluorophore and to be accompanied by a hypsochromic shift of the absorption and fluorescence maxima. Indeed, the addition of Cu^{2+} resulted in elimination of the absorption band with a 403 nm maximum corresponding to free ligand **44** and gave rise to a new band for the complex [Cu^{2+}(**44**)], which had a fine structure with maxima at 330 and 346 nm. The change in the solution colour from yellow to colourless was visible with the naked eye. In the fluorescence spectrum, the intensity was noted to decrease more than 70-fold, due to the paramagnetic nature of Cu^{2+}. The presence of other metal cations (Cr^{3+}, Mn^{2+}, Fe^{3+} , Co^{2+}, Ni^{2+}, Ag^{+}, Zn^{2+}, Cd^{2+} and Hg^{2+}) did not induce significant spectral changes. The structure of the complex formed by compound **44** with copper(II) chloride was studied[112] by X-ray diffraction analysis. As shown by single-crystal X-ray diffraction analysis, the copper atom has a coordination number of 5 and is linked to two pyridine nitrogen atoms, the nitrogen atom in position 4 of the naphthalimide ring and two chlorine atoms.

Structures 44, 45



44



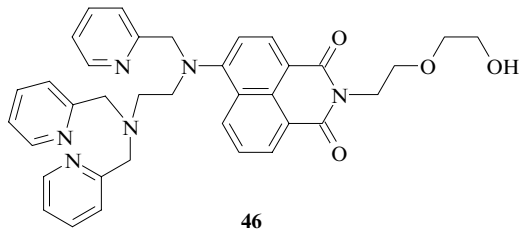
45

Interesting sensing properties were discovered for compound **45**, which differs from **44** by the presence of an *N*,*N*-bis(2-picolyl)-*N*′-phenylethylenediamine (BPPED) moiety functioning as the second receptor and ensuring the fluorescence quenching of the naphthalimide chromophore by

means of the PET effect.[113] Compound **45** selectively binds the Cu^{2+} and Zn^{2+} cations in MeCN; in both cases, the interaction of the cation with the BPPED receptor is observed initially (0–1 equiv. of M^{2+} in the solution) and after that (>1 equiv. of M^{2+}), coordination to the 4-BPA group takes place. In the absorption spectra, the optical effect appears after the addition of more than 1 equiv. of Cu^{2+} or Zn^{2+} and is manifested as a hypsochromic shift of the long-wavelength band by 48 nm (for Zn^{2+}) and 82 nm (for Cu^{2+}). The fluorescence intensity greatly increases when Zn^{2+} is linked to the BPPED group, due to suppression of the PET process. Further increase in the Zn^{2+} concentration (>1 equiv.) is accompanied by a minor decrease in the luminescence intensity and a hypsochromic shift of the maximum. The complex formation with the copper(II) cation involving both receptors induces fluorescence quenching. The authors cited note that owing to a combination of PET and ICT sensing properties in the same molecule, compound **45** can be regarded as a molecular logic gate in which the presence of Cu^{2+} and/or Zn^{2+} cations in the medium acts as the input signal and the changes in the absorption or fluorescence spectrum serve as the output signal.

Compound **46** is an example of an ICT sensor for the zinc cation in an aqueous solution, which exhibits fluorescence enhancement upon complex formation.[114] Binding of Zn^{2+} is accompanied by an increase in the quantum yield for ligand **46** from 0.039 to 0.942 and by a considerable hypsochromic shift of the absorption and fluorescence maxima (by 57 and 16 nm, respectively). A study of the selectivity towards alkali, alkaline earth and transition metal cations demonstrated that a comparable fluorescence response is also observed for cadmium(II) cations. The authors cited ascertained that enhancement of the fluorescence of compound **46** does not result from suppression of the PET process between the tertiary nitrogen atom bound to two 2-picolyl substituents, as it has been observed for PET sensors **28a**,**b** with a structurally related receptor, but is caused by the change in the photophysical characteristics of the naphthalimide fluorophore itself due to mitigation of the ICT interaction.

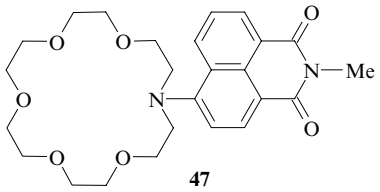
Structure 46



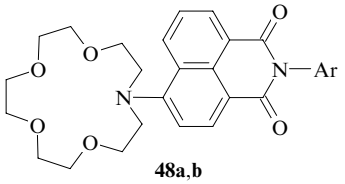
46

Compounds **47** and **48a**,**b** are known as ICT sensors based on naphthalimide derivatives containing an azacrown ether moiety as the 4-substituent in the naphthalimide ring.[100, 115, 116] The spectral luminescence properties of compound **47** in the presence of Group I and II metal cations (Li^+, Na^+, K^+, Cs^+, Mg^{2+}, Ca^{2+} and Ba^{2+}) were studied.[115] The formation of 1 : 1 complexes by ligand **47** brings about a hypsochromic shift $\Delta\lambda_{max}^{abs}$ in the absorption spectrum in acetonitrile, the magnitude of the shift increasing on going to cations with larger radii. In the case of Cs^+ and Ba^{2+}, the $\Delta\lambda_{max}^{abs}$ value reached 70 and 54 nm, respectively, which is indicative of strong interaction of the cation with the LP of nitrogen in position 4 of the naphthalimide ring. Meanwhile, the complexation with Li^+ did not change the position of λ_{max}^{abs}. Since the calculated stability constants of the complexes formed did not correlate with the observed spectral shifts, the authors cited [115] suggested that the binding ability of the receptor is determined by its oxygen-containing moiety, while the involvement of the nitrogen lone pair in the cation coordination determines the magnitude of the hypsochromic shift of λ_{max}^{abs}.

Structures 47, 48



47



48a,**b**

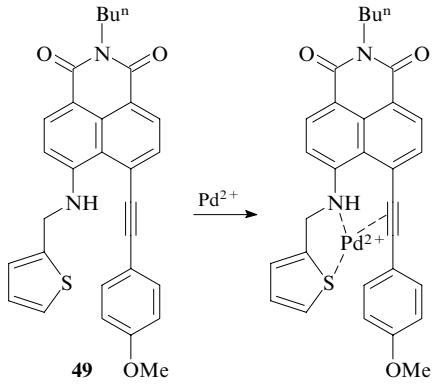
Ar = Ph (**a**), 4-$MeOC_6H_4$ (**b**)

In the fluorescence spectra of compound **47** in MeCN, the presence of cations brought about an intensity increase [115] and hampered transition to the non-fluorescent excited state with intramolecular charge transfer from the amino group to the carboximide group the formation of which accounts for the low level of fluorescence of free ligand **47** (quantum yield $\varphi^{fl} = 0.069$ in MeCN). This is accompanied by a hypsochromic shift (6–43 nm) of the fluorescence band. The most pronounced shift to shorter wavelengths took place in the case of doubly charged alkaline earth metal cations. Since the fluorescence quantum yields of the complexes [Ca^{2+}(**47**)] and [Ba^{2+}(**47**)] were similar to φ^{fl} of 4-amino-*N*-methyl-1,8-naphthalimide ($\varphi^{fl} = 0.64$ in MeCN), it was suggested that photoexcitation is followed by cleavage of the coordination bond between the macrocyclic nitrogen atom and the cation. It is noteworthy that the metal cation does not leave the crown ether cavity during the emission of light by the chromophore, as the fluorescence characteristics of the complex and the ligand are different. A similar re-coordination of the cation in the excited state occurred during the complex formation of Ca^{2+} with ligand **48a**.[100]

A shift of absorption and fluorescence maxima to shorter wavelengths upon binding of mercury(II) cations in aqueous methanol was detected for derivative **48b**.[116] The authors noted that the formation of the complex [Hg^{2+}(**48b**)] disturbs the ICT interactions between the nitrogen atom of the azacrown ether group and the naphthalimide ring, and this leads to fluorescence quenching. In the case of Na^+, K^+ and Mg^{2+}, the complex formation induced a minor increase in the emission band intensity.

The introduction of a thiophene group and a (*p*-methoxyphenyl)ethynyl group into the naphthalimide ring afforded chemosensor **49** (Scheme 3) for palladium(II) cations.[117] According to the results of ^1H NMR study of the complex formation, the cation coordination involved the carbon–carbon triple bond, the sulfur atom and the nitrogen atom of the secondary amino group. The absorption

Scheme 3



49

spectrum of ligand **49** in a neutral solution in aqueous ethanol exhibited two bands with maxima at 340 and 458 nm. The addition of 5 equivs of Pd^{2+} over a period of 1 min resulted in an increase in the extinction coefficient of the band with $\lambda_{max}^{abs} = 340$ nm band and broadening of the long-wavelength band with $\lambda_{max}^{abs} = 458$ nm, and also gave rise to a new absorption band at 270 nm, which was accompanied by a change of the solution colour from yellow to dark-red. Simultaneously, the fluorescence intensity at 536 nm greatly decreased. Sensor **49** demonstrated high selectivity with respect to Pd^{2+} in the presence of other d-metal cations that tend to coordinate π-bonds (Hg^{2+}, Pt^{2+}, Ag^{+}, Co^{2+}).

Certain advantages for the design of fluorescent and colorimetric sensors are provided by using 1,8-naphthalimide derivatives containing two amino groups in the naphthalene nucleus (compounds **50**–**54**).[118–125] As compared with monoaminonaphthalimides, the 4,5- and 3,4-disubstituted derivatives possess a cationophilic intramolecular cavity, which comprises two nitrogen atoms rigidly fixed in space, which belong to the amino groups attached to the naphthalene ring, and ionophoric regions of side chains. Most of compounds **50**–**54** are selective sensors for the copper(II) cation, which is due to the high stability of Cu^{2+} complexes with tetradentate receptors containing amide and pyridine nitrogen donor atoms.[126, 127] A specific feature of the properties of such chelating agents is that the amino groups of the naphthalimide ring tend to be deprotonated upon coordination to a metal cation. Since deprotonation appreciably increases the electron density on the nitrogen atom, the maxima in the absorption and fluorescence spectra undergo a pronounced bathochromic shift. This circumstance, first, enables the ratiometric determination of the metal cation and, second, creates favourable conditions for performing analysis in cells and tissues, as the long-wavelength fluorescence of the complex slightly overlaps with the short-wavelength fluorescence background of a biological medium. Note that proton elimination by no means always occurs, the possibility for this to happen being determined by the structure of the ionophoric moiety of the molecule.

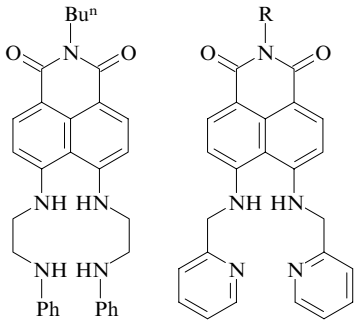
On binding of Cu^{2+} cations by compound **50**, the colour of the solution in aqueous ethanol changed from pale yellow ($\lambda_{max\,1} = 419$ nm, $\lambda_{max\,2} = 458$ nm) to pink, which was accompanied by the appearance of a new absorption band with the maximum at 509 nm corresponding to the complex $[Cu^{2+}(\mathbf{50}-2\,H)^{2-}]$.[118] Investigations showed that an excess of Cu^{2+} first results in the complex $[(Cu^{2+})_2(\mathbf{50})]$ in which each of the 2-(phenylamino)ethylamino groups holds one cation. Then both nitrogen atoms are deprotonated to give $[Cu^{2+}(\mathbf{50}-2\,H)^{2-}]$. In the presence of less than 1 equiv. of Cu^{2+}, the complex $[Cu^{2+}(\mathbf{50})]$ with a similar bidentate coordination was formed, and it was also able to be converted to $[Cu^{2+}(\mathbf{50}-2\,H)^{2-}]$. In the latter case, elimination of two protons required longer time (48 h). In the fluorescence spectrum, the long-wavelength shift of the maximum due to formation of the complex $[Cu^{2+}(\mathbf{50}-2\,H)^{2-}]$ was 74 nm.

The replacement of 2-(phenylamino)ethyl groups in compound **50** by 2-picolyl groups to give derivative **51a** does not disturb the selectivity to Cu^{2+} but markedly affects the spectral response to complexation. Higher electron-donating ability of the LP of pyridine nitrogen relative to the aniline nitrogen weakens the interaction between the copper cation and amino groups linked to the naphthalimide ring; as a result, the amino groups are not deprotonated and the absorption and fluorescence maxima shift to shorter wavelengths.[119]

The copolymer of compound **51b** and methyl methacrylate was employed to produce a heterogeneous sensor material able to adsorb copper(II) cations from a solution in aqueous acetonitrile.[120] The composite comprised nanosized polymeric fibres and had a high sensitivity to Cu^{2+}, which is due to its large specific surface area. As in the case of ligand **51a**, binding of Cu^{2+} resulted in a hypsochromic shift of the fluorescence maximum.

An undisputable advantage of derivatives **50** and **51a** over other ratiometric sensors for Cu^{2+} is the fact that fluorescence quenching due to electron (energy) transfer between the bound metal cation and fluorophore, which

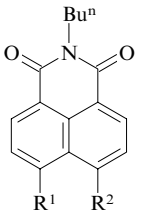
Structures 50–54



50

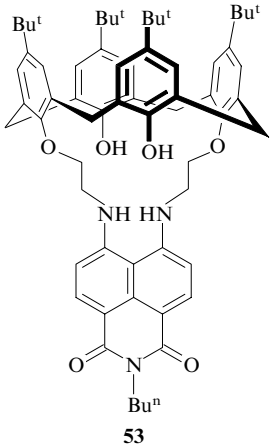
51a,b

R = Bu^n (**a**), All (**b**)

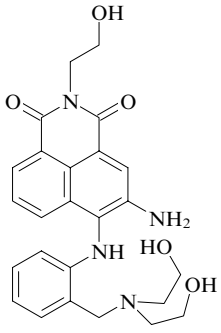


52a–d

R^1 = $NH(CH_2CH_2O)_6H$:
R^2 = NHPic (**a**), $NPic_2$ (**b**);
R^1 = $N(CH_2CH_2OH)_2$,
R^2 = NHPic (**c**);
R^1 = NHPic,
R^2 = $NPic_2$ (**d**)
(Pic is 2-picolyl)



53



54

accompanies the spectral changes, is almost missing. Thus the fluorescence quantum yields φ^{fl} for ligand **50** and the complex $[Cu^{2+}(\mathbf{50}-2\,H)^{2-}]$ were 0.0054 and 0.0046, respectively.[118] The authors cited [118, 119] deem that the formation of strong coordination bonds between Cu^{2+} and tetradentate receptors in molecules **50** and **51a** suppresses the undesirable metal–fluorophore interactions.

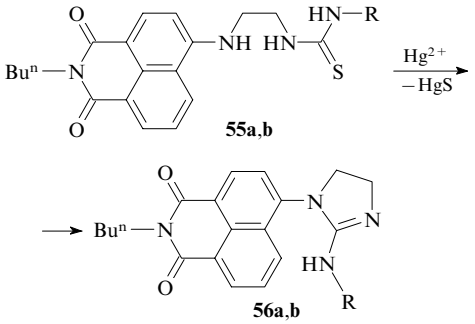
A specific structural feature of compounds **52a–c** is the presence of hexa(ethylene glycol) and diethanolamine residues in the receptor part of the molecule. These residues not only participate in metal cation binding but also provide good solubility of compounds **52a–c** in aqueous solutions.[121, 122] As in the case of derivative **50**, complex formation between ligand **52a** and Cu^{2+} was accompanied by a decrease in the fluorescence intensity band of the free ligand at 534 nm with a simultaneous increase in the intensity of the band of $[Cu^{2+}(\mathbf{52a})]$ with maximum at 478 nm. In the case of dipicolyl derivative **52b**, the coordination to Cu^{2+} induced a bathochromic shift of the absorption band, which attested to deprotonation of the secondary amino group of the naphthalimide ring. In the authors' opinion, the ease of proton elimination in compound **52b** is caused by intramolecular hydrogen bonding with the nitrogen atom bearing two picolyl substituents.[121] A similar tendency for deprotonation upon binding with Cu^{2+} was observed for **52c** [122] and **52d** [123] in which one amino group of the naphthalimide residue is also dialkylated. It is of interest that the bathochromic shift in the absorption spectrum of ligand **52d** was induced by the presence of Zn^{2+}, Co^{2+} and Ni^{2+} cations in solutions in aqueous acetonitrile; however, only in the case of the Zn^{2+} complex, no significant fluorescence quenching took place.[123]

Compound **53** is the first example of a calixarene derivative of naphthalimide.[124] A study of the sensing properties of ligand **53** with respect to various metal cations in acetonitrile demonstrated that the intramolecular cavity formed by the oxygen atoms of the calix[4]arene moieties and amine nitrogen atoms is capable of selective accommodation of copper(II) cations, resulting in a decrease in the absorption and fluorescence intensity. The ability of ligand **53** to detect Cu^{2+} is retained on going to solutions in water–acetonitrile mixtures. The bathochromic shift of the fluorescence maximum following the complexation with Cu^{2+} can be explained as being due to deprotonation of secondary nitrogen atoms bound to the naphthalimide ring. The presence in the intramolecular cavity of OH and NH groups capable of hydrogen bonding determines the ability of chemosensor **53** to selectively bind fluoride anions in the presence of $H_2PO_4^-$, HSO_4^-, AcO^-, I^-, Cl^- and Br^-. The coordination to F^- confirmed by ^1H NMR data was also accompanied by deprotonation of the NH groups, and this was manifested as fluorescence quenching and bathochromic shift of λ_{max}^{abs} and λ_{max}^{fl}.

Deprotonation of the amino groups of the naphthalimide residue is also possible for 3,4-diamino derivatives of naphthalimide. Compound **54** selectively bound the copper(II) cation in aqueous ethanol to give a 1 : 1 complex the absorption maximum of which was shifted bathochromically by 51 nm relative to the maximum of the free ligand.[125] According to a study, the coordination of Cu^{2+} involves two nitrogen atoms linked to the naphthalimide ring and the nitrogen and oxygen atoms of the diethanolamine group; the proton is eliminated from the secondary diarylamino group.

Chemodosimeters **55a,b** based on 4-aminonaphthalimide derivatives were prepared (Scheme 4); switching of the spectral characteristics of the 4-aminonaphthalimide fluorophore in these compounds occurs by the ICT mechanism.[128, 129] Mercury(II) cations induce irreversible intramolecular cyclization to give 4-imidazolyl naphthalimides **56a,b** . Since the electron-donating properties of the naphthalimide-linked nitrogen atoms in compounds **55a,b** decrease on going to cyclization products **56a,b**, the latter have absorption and fluorescence maxima in a shorter-wavelength region.

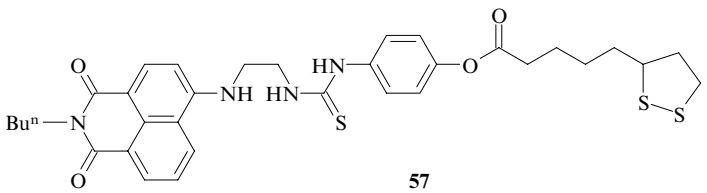
Scheme 4



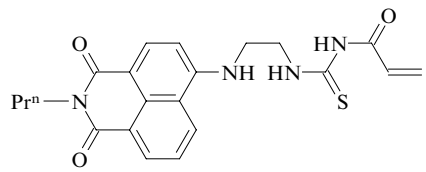
R = Bz (**a**), Ph (**b**)

Liu and Tian [128] studied the sensing properties of naphthalimide derivative **55a** in a water–acetonitrile solution. Studies of the selectivities to the Ag^+, Co^{2+}, Cu^{2+}, Hg^{2+}, Ni^{2+}, Pb^{2+} and Zn^{2+} cations showed that after 1 h only the solution containing Hg^{2+} changed the colour of fluorescence from yellow-green (λ_{max}^{fl} = 530 nm) to light-blue (λ_{max}^{fl} = 475 nm), the fluorescence intensity being increased 1.37-fold. The cyclization was also induced by the presence of silver cations; however, in this case, the time needed for complete conversion was 20 h. It is noteworthy that in the case of compound **55b**, which contains phenyl rather than benzoyl (as in **55a**) substituent R, desulfurization was accompanied by quenching of the fluorescence of the naphthalimide moiety.[129] The authors [128, 129] attributed this difference in the properties to the possibility of the photoinduced electron transfer in compound **55b** between the PhNH group bearing high electron density and the fluorophore.

Structures 57, 58

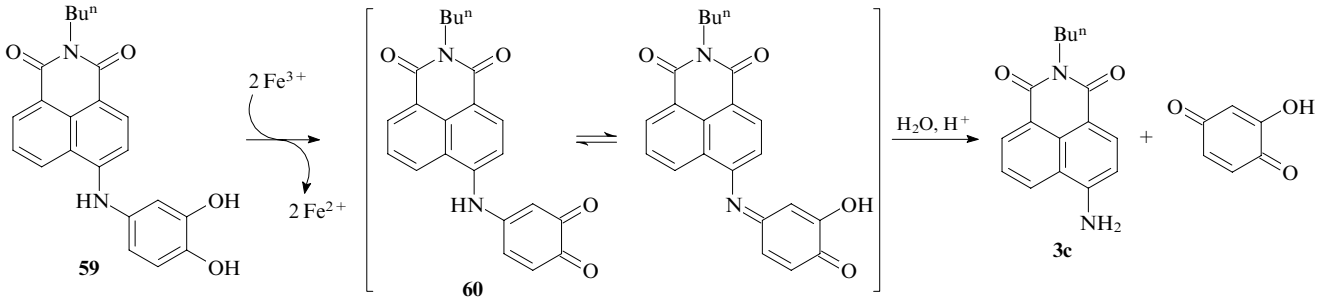


57



58

Scheme 5



As noted by Leng *et al.*,[129] a drawback of compounds **55a**,**b** as dosimeters is their low solubility in water, which markedly restricts their practical application. To overcome this drawback, nano-sized sensors were obtained from derivatives **57** and **58**. In the case of compound **57**, immobilization on the surface of gold nanoparticles was used.[129] The bonding to the metal surface was through the disulfide group in molecule **57**. Compound **58** was subjected to emulsion radical copolymerization with *N*-isopropylacrylamide, which gave a thermosensitive nanogel in which the particle size varied as a function of temperature.[130] At 25 °C, the nanogel was suitable for ratiometric determination of Hg^{2+} at the nanomolar level. Heating of the suspension above the phase transition temperature increased the sensitivity to mercury(II) cations.

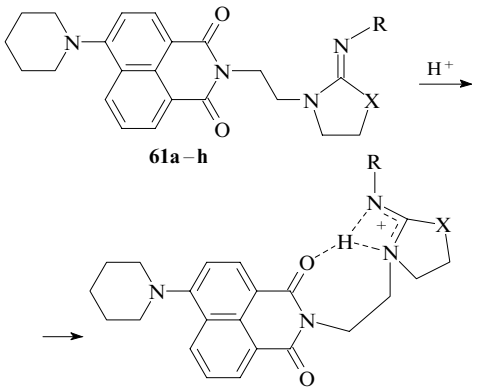
A great advantage of chemodosimeters over PET and ICT sensors considered above is the possibility to create systems that exhibit fluorescence enhancement upon the interaction with those transition metal cations that, when bound to the receptor of the ion-sensitive molecule, are often able to reduce the efficiency of the radiative deactivation of the fluorophore. An example of such chemodosimeter is compound **59** (Scheme 5).[131] The addition of 2 equivs of iron(III) nitrate to an anhydrous acetonitrile solution of compound **59** entailed a hypsochromic shift of the long-wavelength absorption band from 441 to 368 nm in the absorption spectrum; this was due to the decrease in the π-donor properties of the LP of nitrogen in position 4 of the naphthalimide ring as a result of oxidation of the catechol fragment with the Fe^{3+} cation. Gradual increase in the fluorescence intensity at 520 nm took place after the addition of water (1 vol.%) into the acetonitrile solution containing the oxidation product **60**. As shown by Jackson *et al.*,[131] the changes in the fluorescence spectrum were due to hydrolysis of aminoquinone **60**, which proceeded *via* the formation of the quinone–imine tautomer. It can be seen from Scheme 5 that hydrolysis gives, in particular, 4-amino-*N*-n-butyl-1,8-naphthalimide (**3c**), which possesses more intense fluorescence than compound **59**. The presence of an acid accelerated the hydrolysis. Analogous spectral changes also occurred in the case where oxidation was performed by a copper(II) cation, which, like Fe^{3+}, is a typical fluorescence quencher. The presence of other metal cations that either do not act as strong oxidants relative to the catechol group or do act as oxidants but cannot be complexed with this group had only a minor influence on the absorption and fluorescence spectra of compound **59**. As drawbacks of dosimeter **59**, one should mention low rate of hydrolysis of aminoquinone **60** and inapplicability of this compound in aqueous solutions because the fluorescence quantum yield of 4-aminonaphthalimide (**3c**) substantially decreases on going to protic solvents.

2. ICT sensors with receptors involving carbonyl groups of the carboximide residue of the naphthalimide ring

The presence of LP at the carbonyl oxygen atoms of the naphthalimide ring able to be coordinated to metal cations and H^+ ions can be used to design cationic optical ICT sensors in which binding of the substrate to be determined entails an increase in the extent of charge transfer in the chromophore and a bathochromic shift of the absorption and fluorescence spectral bands.

The formation of hydrogen bonds involving the C=O group of the naphthalimide moiety can be used to develop fluorescent pH indicators. This idea was implemented by Cui *et al.*,[132] who proceeded from the observation made by de Silva *et al.*[61,62] that intramolecular hydrogen bonding in 4-amino naphthalimide derivatives is accompanied by a decrease in the fluorescence quantum yield. Compounds **61a**–**h** containing 2-iminooxazolidine (**61a**–**g**) and 2-iminothiazolidine (**61h**) moieties were proposed as optical sensors for hydrogen ions (Scheme 6).[132] The presence of two closely spaced nitrogen atoms in the receptor creates conditions for effective coordination of the H^+ ion involving the oxygen LPs of the fluorophore CO groups. The pK_a values of the presented compounds **61** in ethanol buffer solutions varied in the 6.4–7.5 range.

Scheme 6



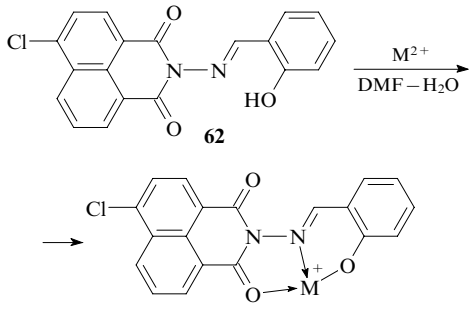
X = O: R = Ph (**a**), 2-MeC_6H_4 (**b**), 2-FC_6H_4 (**c**), 4-FC_6H_4 (**d**), 4-$O_2NC_6H_4$ (**e**), Me (**f**), naphthyl (**g**); X = S, R = Ph (**h**)

A study of the optical properties of derivatives **61a**–**h** revealed pH-sensitive fluorescence characteristics only for compounds **61a**,**b**,**h** containing either a phenyl or *o*-tolyl group R. As the acidity of the medium increased (in the pH range of 10.34–4.60), considerable fluorescence quenching of compounds **61a**,**b**,**h** (by factors of 4.9, 31.7 and 32.1,

respectively) and also a bathochromic shift of the maxima λ_{max}^{abs} and λ_{max}^{fl} took place. The replacement of the oxygen atom in the oxazolidine moiety by the less electronegative sulfur atom was beneficial for the sensing properties. Much less pronounced spectral changes observed in other cases may be due to destabilization of the hydrogen-bonded structure (see Scheme 6) following the decrease in the electron-donating power of the group R.

Azomethine derivative **62** of *N*-amino-4-chloro-1,8-naphthalimide (Scheme 7) was proposed as an optical sensor for cobalt(II) and copper(II) cations.[133]

Scheme 7



M = Co, Cu

The long-wavelength absorption of compound **62** in a DMF–water mixture with a maximum at 342 nm was attributed to charge transfer in the salicylideneimine group. The presence of alkali and alkaline earth metal cations and Fe^{3+}, Ni^{2+} and Zn^{2+} resulted in minor changes in the absorption spectrum. Upon the addition of Co^{2+} into the solution, the intensity of the ligand absorption maximum (342 nm) decreased with a simultaneous increase in the intensity of the 273 and 400 nm bands. In the case of Cu^{2+}, the initial ligand band (342 nm) was split into two intense bands with maxima at 314 and 390 nm. The authors did not discuss whether the electron transition bands in the complexes belong to the naphthalimide moiety of molecule **62** or to the salicylideneimine group. Using the data of IR spectroscopy and quantum chemical calculations, it was shown that binding of the cation involves the oxygen atom of one carbonyl group, the hydroxy group and the LP of the imino-group nitrogen (see Scheme 7). The composition of complexes (1 : 1) was confirmed by the data of mass spectrometry, spectrophotometric titration and elemental analysis.

The observed differences between the spectra of [Co^{2+}(**62**)] and [Cu^{2+}(**62**)] were attributed[133] to different geometries of these complexes. As shown by DFT calculations, in [Co^{2+}(**62**)], the five- and six-membered chelate metal rings lie in one plane, whereas the geometry of this fragment in [Cu^{2+}(**62**)] is non-planar, which is due to a smaller radius of the copper(II) cation compared to Co^{2+}.

VI. FRET Sensors

The non-radiative Förster resonance energy transfer (FRET) between two chromophores is one of the most important photophysical processes used (apart from the photoinduced electron transfer) to design optical molecular devices. This process is a unique tool for generating a fluorescence signal the intensity of which depends on the distance between the chromophores and their mutual orientation in space.[2,134] Since the FRET process occurs at distances comparable with the size of biomolecules (10–100 Å), recent practical applications of this process have been related, most often, to studies of biological phenomena caused by changes in the distances at the macromolecular level.[135–137] Meanwhile, application of FRET for the design of fluorescent sensors appears promising, because this provides the possibility of ratiometric determination of the analyte concentration[138,139] and of enhancement of the optical response upon complexation.[140] Nevertheless, relatively few papers (including those devoted to 1,8-naphthalimide derivatives) describe utilization of this mechanism for the design of optical chemosensors.

An obligatory structural unit of a fluorescent FRET chemosensor is the presence of two chromophores proximate in space, one being the donor (D) and the other being the acceptor (A) of the absorbed light energy. Effective non-radiative energy transfer requires the resonance tuning of moieties D and A, in particular, the fluorescence spectrum of the donor chromophore should overlap to one or another extent with the absorption spectrum of the acceptor.[2,134] In the general case, the mechanism of operation of a FRET sensor system is that binding of the receptor to the analyte provides modulation of the efficiency of energy transfer due to the change in the degree of overlap of the absorption and emission spectra of two chromophores, the distance between them and also due to enhancement or inhibition of other processes that compete with the FRET interaction in the photoexcited state. The perturbation of the photophysical parameters of the system that occurs upon complexation affects, in turn, the pattern of steady-state fluorescence spectra, and this is used as the analytical signal.

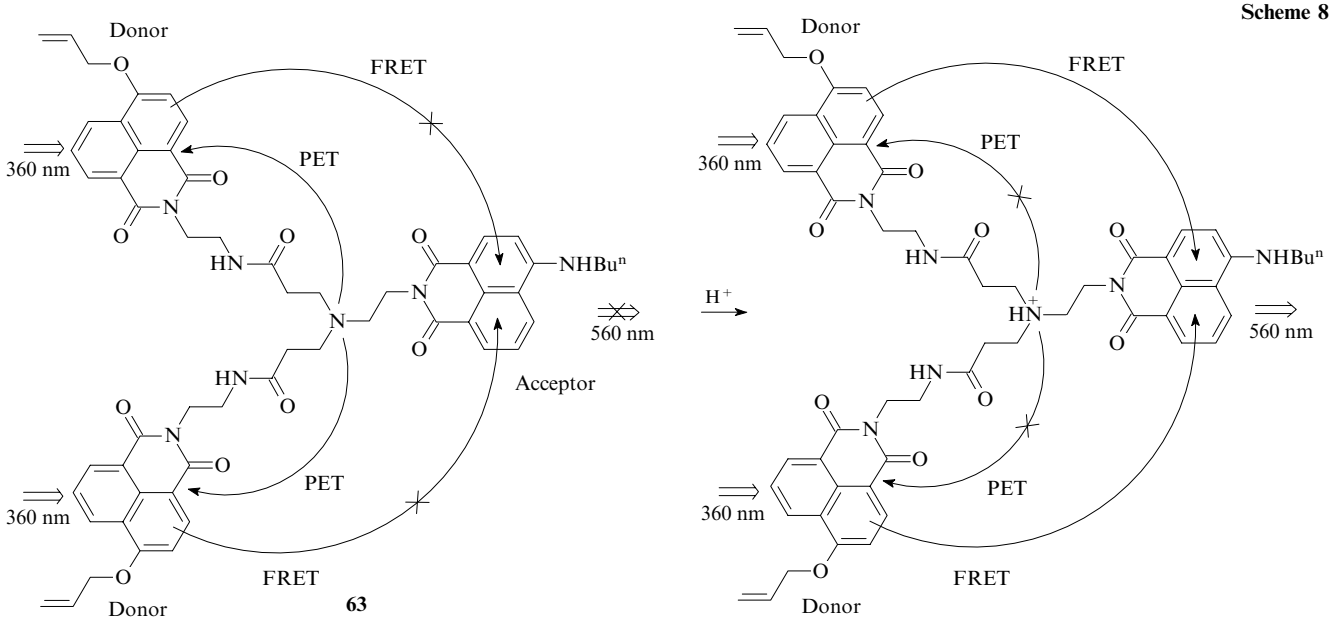
In order to obtain ion-sensitive FRET systems, the possibility of excitation energy transfer is often combined with the possibility of photoinduced electron transfer. In some cases, the FRET sensor can be designed in such a way that its interaction with the analyte would result in the isomerization of one of the photoactive moieties, which markedly affects the spectral characteristics of this moiety, or would be accompanied by the mutual approach of two chromophores.[32]

1,8-Naphthalimide derivatives possess a high potential for the design of fluorescent FRET chemosensors. Although systems with resonance energy transfer containing a naphthalimide fluorophore have been known for a rather long time,[13,141,142] most of sensor-related publications have appeared only during the last 5 years. Below examples are given and advantages are considered of using naphthalimide-containing fluoroionophores in which the mechanism of cation-induced changes in the optical properties includes the energy transfer process.

1. Cationic sensors combining energy transfer and electron transfer

Compound **63** (Scheme 8) was proposed as a fluorescent pH-sensor for a solution in aqueous ethanol.[143] The energy donors in derivative **63** are 4-alkoxynaphthalimide residues that show the fluorescence maximum at 465 nm. The absorption of the electron-withdrawing 4-aminonaphthalimide group occurs at 450 nm, which ensures the resonance energy transfer condition. Nevertheless, the FRET process in the non-protonated form of compound **63** is hampered due to the photoinduced electron transfer from the tertiary amino group located at the centre of the molecule to the

Scheme 8

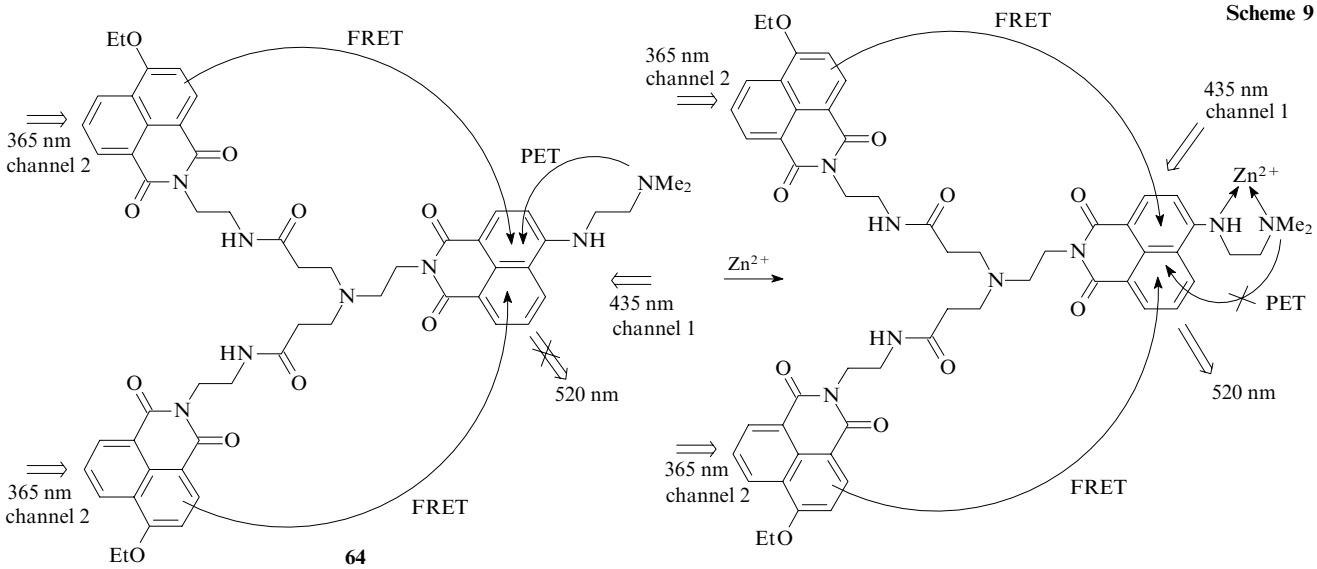


photoexcited donor chromophore. As a result, on excitation at the 360 nm wavelength corresponding to absorption of the 4-alkoxynaphthalimide residue, compound **63** demonstrated low intensity of yellow-green fluorescence at 560 nm typical of the acceptor chromophore. Protonation of the tertiary nitrogen atom in the pH range of 6.9–3.3 resulted in suppression of the PET process, and the efficiency of energy transfer increased by 29% (to 92%), which was accompanied by 2.2-fold enhancement of fluorescence with a maximum at 560 nm. Note that at the excitation wavelength of 460 nm, the fluorescence intensity almost did not change upon a decrease in the pH level, because the electron transfer from the receptor moiety is thermodynamically more favourable to more electron-deficient 4-alkoxynaphthalimide chromophore rather than to the 4-aminonaphthalimide residue.

The considered compound **63** demonstrates an advantage of FRET systems over the classical PET sensors consisting in the possibility to achieve enhancement of the fluorescence of the long-wavelength chromophore (in this particular case, 4-aminonaphthalimide), which is unable to ensure effective electron transfer and, hence, optical response upon complexation when combined with a receptor in a monochromophore PET system. As has already been noted for compound **11** (see Section IV, Scheme 1), protonation of the diethylamino group in the *N*-aryl fragment almost did not change the fluorescence quantum yield.

The use of resonance energy transfer for the design of a sensor system makes it possible to increase the optical response upon complexation. The presence of two electron-donating chromophores in compounds **63** (see Scheme 8) and **64** (Scheme 9) results in effective absorption of the exciting radiation, which finally promotes an increase in the generated fluorescence signal and increases the sensitivity of analysis. For example, in the detection of zinc ions in acetonitrile solution by compound **64** in which the *N*,*N*-dimethylethylenediamine group serves as the receptor, switching of the excitation wavelength from 435 nm (channel 1) to 365 nm (channel 2) allows one to achieve a higher degree of fluorescence enhancement at 520 nm, all

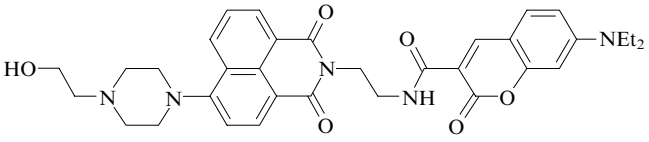
Scheme 9



other factors being the same. The limits of detection of Zn^{2+} were 1.66×10^{-6} mol litre^{-1} (λ_{ex} = 435 nm) and 1×10^{-7} mol litre^{-1} (λ_{ex} = 365 nm).[140]

The most significant advantage of the fluorescent FRET sensors is the possibility of ratiometric quantification of the analyte ions. An example of this system is water-soluble derivative **65** containing covalently attached pH-sensitive 4-piperazino-1,8-naphthalimide and coumarin residues.[144] Under basic conditions, the fluorescence spectrum measured at excitation wavelength of 405 nm exhibited a strong peak at 467 nm corresponding to emission of the coumarin residue. Acidification of the aqueous solution induced an increase in the intensity of yellow-green fluorescence with a maximum at 525 nm resulting from energy transfer to the naphthalimide chromophore and from suppression of the PET process upon protonation of nitrogen of the piperazine receptor. The fluorescence intensity ratio at wavelengths of 525 and 467 nm (I_{525}/I_{467}) varied from 2.62 to 0.22 as pH varied in the 3.0–10.0 range. Compound **65** proved to be suitable for determination of the medium acidity in the cells.

Structure 65

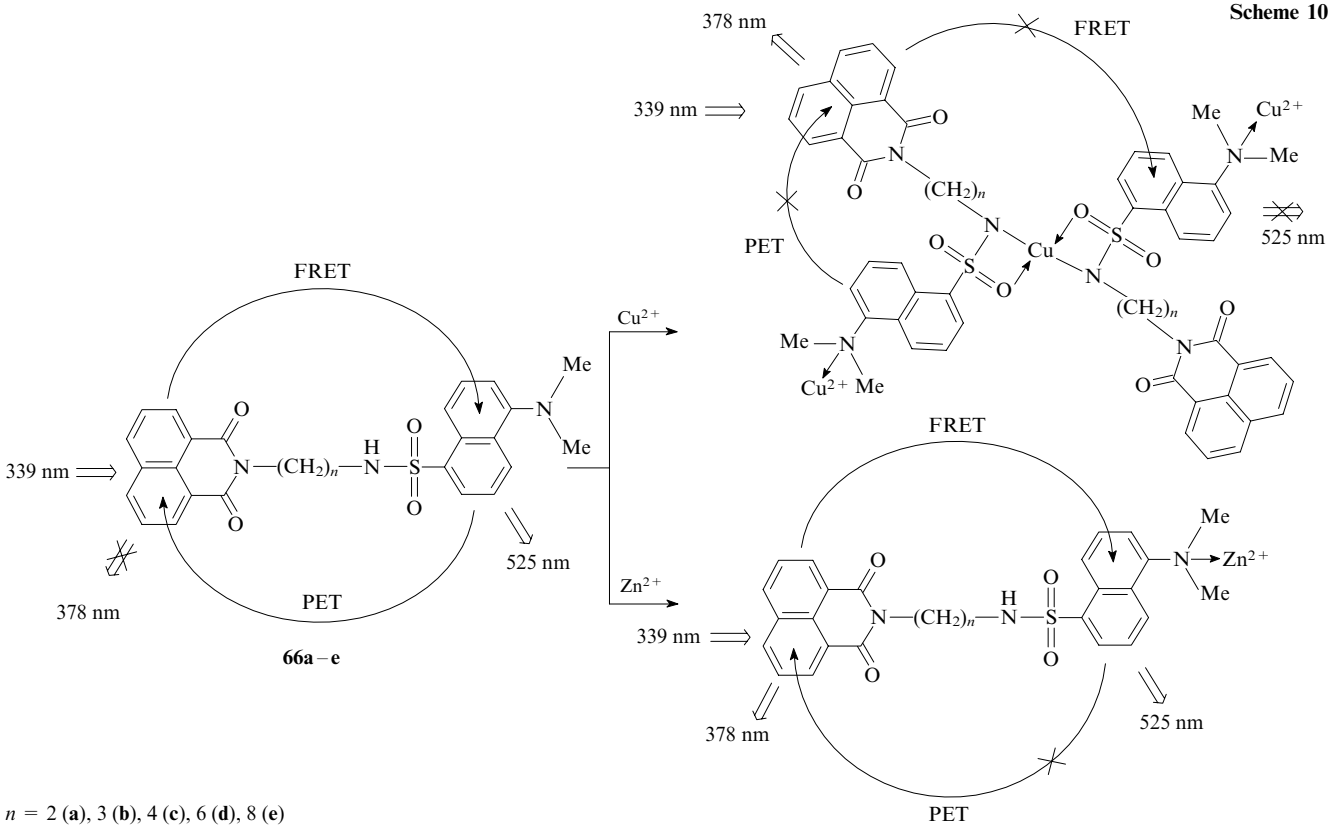


65

Cation-dependent spectral properties of bis-chromophore derivatives **66a–e** (Scheme 10) in which the 1,8-naphthalimide moiety unsubstituted in the naphthalene ring and the dansylamide moiety are linked by the oligomethylene chain were studied.[145–147] The interaction of compounds **66a–e** with a number of metal cations (Na^+, Li^+, K^+, Pb^{2+}, Hg^{2+}, Co^{2+}, Fe^{2+}, Cd^{2+}, Mg^{2+}, Ba^{2+}, Zn^{2+}, Cu^{2+}) in acetonitrile was studied using fluorescence and electronic absorption spectroscopy, NMR spectroscopy, isothermal calorimetry and laser flash photolysis.[145] It was found that optical response was induced by the presence of only copper and zinc cations; in the case of Cu^{2+}, the sulfonamide groups were deprotonated to give 2:3 complexes, whereas the Zn^{2+} coordination involves the dimethylamino groups of the dansyl moiety (see Scheme 10). In the case of Cu^{2+} complex formation, the intensity of the dansylamide chromophore fluorescence at 525 nm caused by energy transfer from the naphthalimide residue decreased; simultaneously fluorescence enhancement at 378 nm was observed. The authors interpreted these spectral changes as being due to the fact that binding of Cu^{2+} suppresses both the FRET process and the competing PET interaction between the chromophores (see Scheme 10). The decrease in the energy transfer efficiency is probably related to the hypsochromic shift of the absorption band of the dansylamide moiety (and, hence, to the extent of its overlap with the fluorescence band of the energy donor) caused by deprotonation of sulfonamide groups. Inhibition of the electron transfer process is due to the cation coordination to the dimethylamino group.

The formation of a 1:1 complex with zinc cations did not decrease the efficiency of energy transfer in compounds **66a–e** but hampered the electron transfer. The change in the fluorescence spectrum consisted in an increase in the naphthalimide band intensity (λ_{max} = 378 nm), while the intensity of the 525 nm band remained constant. As the length of the oligomethylene spacer increased, the degree of

Scheme 10



fluorescence enhancement on binding Zn^{2+} decreased due to weakening of the PET interaction.

On going from acetonitrile solutions to a water–acetonitrile mixture, the ability of Cu^{2+} and Zn^{2+} cations to form the coordination bond with nitrogen of the dimethylamino group of the dansyl moiety considerably decreased. It was shown[146] that under these conditions, compounds **66d** and **66e** form complexes with copper(II) cations having the composition ligand : cation = 2 : 1. In these complexes, the cation was bound to two sulfonamide groups of two ligands, which was also suitable for ratiometric quantification of Cu^{2+}. In the presence of Zn^{2+}, no spectral changes were observed.

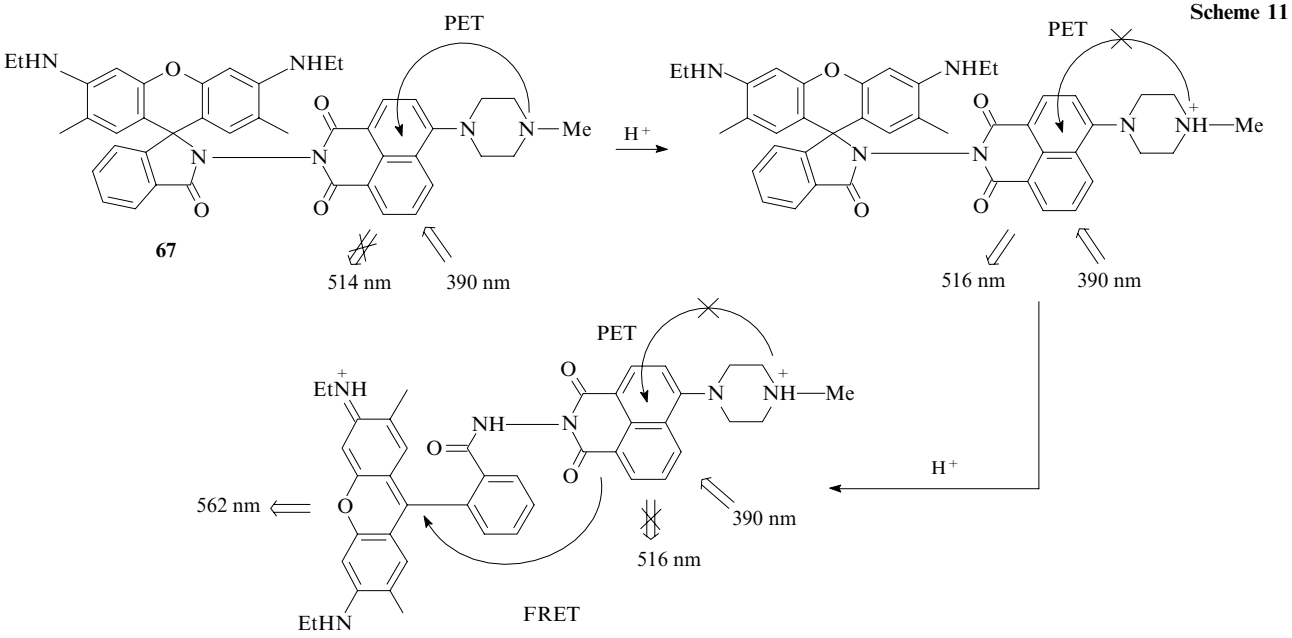
2. FRET systems using cation-induced opening of the spirolactam ring of rhodamine dyes

Ample opportunities for the design of ratiometric fluorescent sensors are opened by combinination in the same molecule of the naphthalimide chromophore with a rhodamine dye moiety able to switch to a coloured form in an acidic medium (or in the presence of metal cations). Bojnov *et al.*[148] studied pH-dependent fluorescence properties of bis-chromophore derivative **67** in a water–DMF mixture. In this compound, the aminonaphthalimide moiety acts as a donor, while the rhodamine 6G acts as an acceptor of the absorbed light energy (Scheme 11).

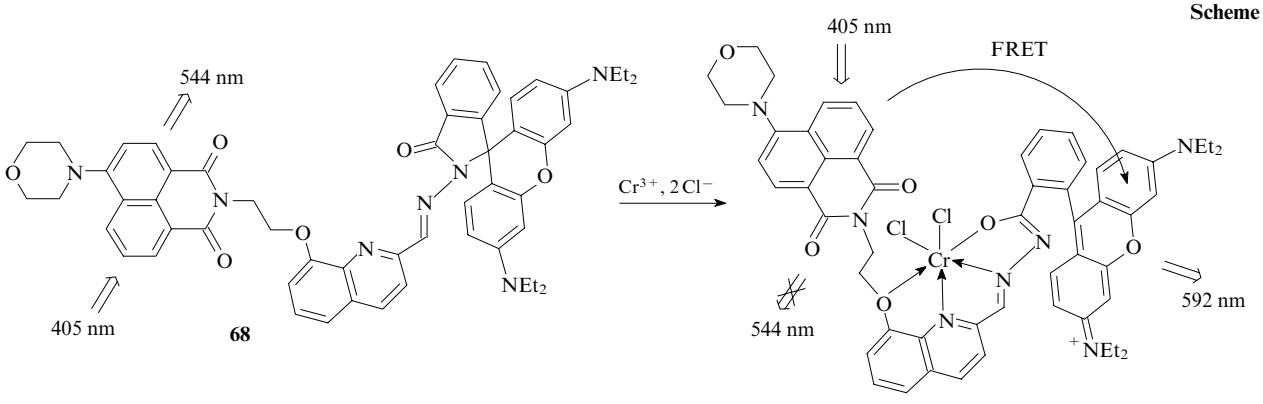
As the pH of the medium decreases from 8.22 to 5.89, the piperazine receptor in molecule **67** is protonated, which is accompanied by fluorescence enhancement at 516 nm due to suppression of the PET interaction, the rhodamine moiety being in non-fluorescent spirolactam form. The further acidification of the solution to pH 2.45 is accompanied by almost complete quenching of the fluorescence of the naphthalimide residue and the appearance of a new long-wavelength band corresponding to the emission of the open form of the rhodamine dye at 562 nm, which is due to energy transfer between two chromophores. Owing to the pronounced overlap between the absorption spectrum of the acceptor and the emission spectrum of the donor fluorophore (more than 90%), the efficiency of energy transfer in this system was 97%.

The cation-induced opening of the spirolactam ring of rhodamine dyes was used to design the selective FRET sensor **68** (Scheme 12) for trivalent chromium ions in aqueous ethanol solutions; as the donor chromophore this compound contained a 4-morpholinonaphthalimide residue.[149] Binding of Cr^{3+} by the multichelating receptor moiety of sensor **68** was accompanied by the formation of a quinoneimine form of rhodamine and switching of the

Scheme 11

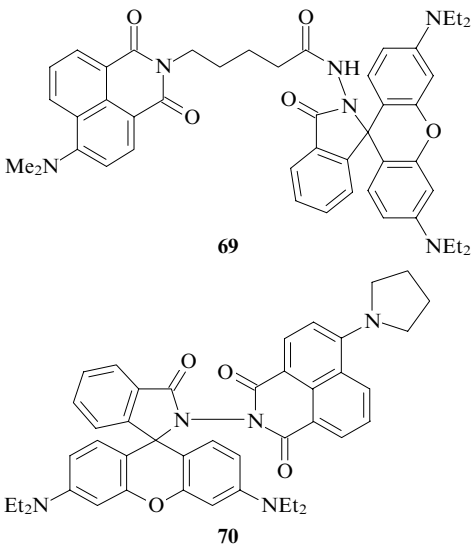


Scheme 12



fluorescence channel from 544 nm to 592 nm wavelength; simultaneously, the emission intensity ratio I_{592}/I_{544} increased from 0.77 to 5.63. Using fluorescence microscopy, it was demonstrated [149] that compound **68** can be used to determine the level of Cr^{3+} in living cells. Variation of the structure of the group connecting the naphthalimide and rhodamine fluorophores in **68** resulted in the ratiometric FRET sensors for Sn^{4+} (compound **69**) [150] and Hg^{2+}/Cr^{3+} (compound **70**) [151] that operate according to the same principle as compound **68**.

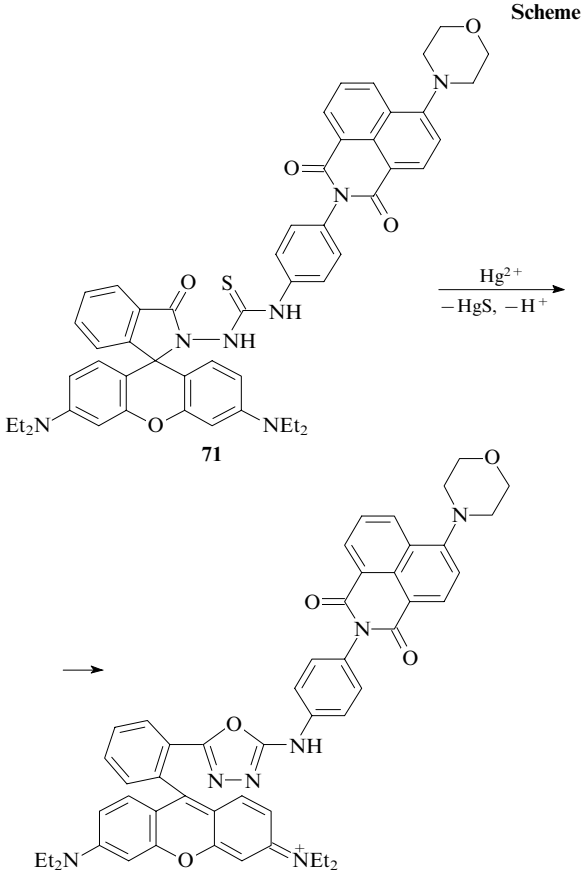
Structures 69, 70



69

70

Scheme 13



71

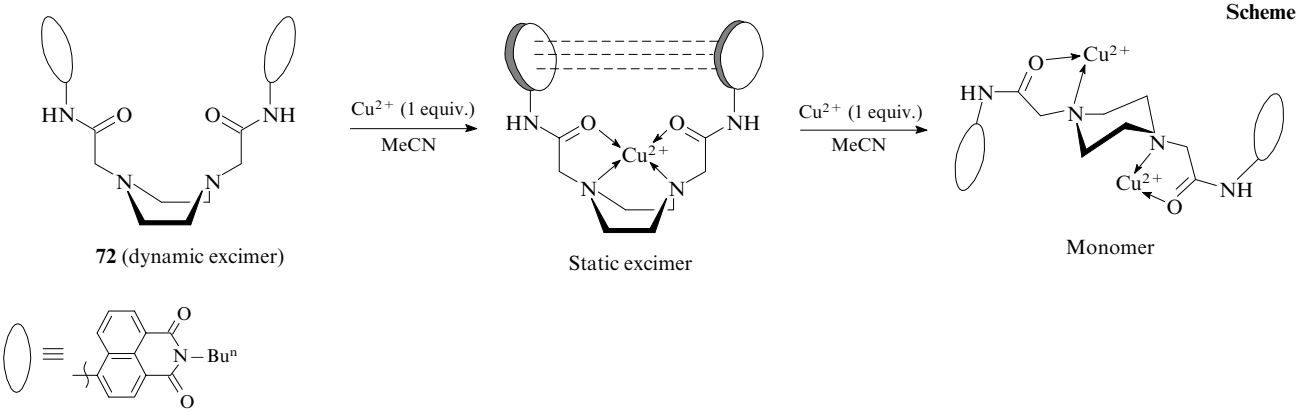
Chemodosimeter **71** based on 4-morpholinonaphthalimide and rhodamine (Scheme 13) suitable for ratiometric determination of mercury(II) in solutions in aqueous methanol was proposed.[152] The selectivity to Hg^{2+} is due to the specific feature of this cation to cause desulfurization of the thiocarbonyl group, which in the case of compound **71** resulted in irreversible opening of the spirolactam ring of the rhodamine moiety. The formation of the coloured form of the energy acceptor chromophore increased the intensity of the FRET-induced emission with a maximum at 585 nm.

VII. Sensors based on other signalling mechanisms

Employment of the ability of chromophores to form excimers upon photoexcitation is one more method for internal calibration of the sensor system, which creates conditions for ratiometric measurements. It is known that upon the excimer formation, the excitation energy is uniformly distributed between two interacting π-systems, which results in energy benefit and is accompanied by a bathochromic shift of the maximum in the fluorescence spectrum.[2]

There are very few known fluorescent sensors based on naphthalimide derivatives in which the spectral response generation involves the formation or destruction of excimers. Xu *et al.*[153] proposed fluoroionophore **72** containing two acylaminonaphthalimide residues; when complexed with copper(II), compound **72** switches the fluorescence channel from excimer emission to the monomer emission (Scheme 14). In the absence of a cation in polar solvents, compound **72** shows two fluorescence maxima (450 and 550 nm). The long-wavelength maximum corresponds to the dynamic excimer, which is formed upon intramolecular

Scheme 14



72 (dynamic excimer)

Static excimer

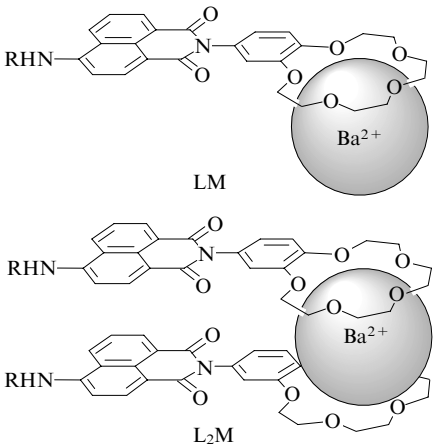
Monomer

interaction between the excited and non-excited naphthalimide chromophores provided that the piperazine ring in **72** is in the boat conformation. The addition of Cu^{2+} to a solution in amount of < 1 equiv. resulted in a 1 : 1 complex; simultaneously, the absorption spectrum showed broadening of the long-wavelength band, indicating aggregation of two chromophore groups in the ground state. Considerable fluorescence enhancement of the monomer at 450 nm with a simultaneous decrease in the intensity of luminescence of the static excimer took place following further increase in the Cu^{2+} concentration accompanied by the formation of the complex $[(Cu^{2+})_2(\mathbf{72})]$.

High selectivity with respect to copper(II) was manifested on going from acetonitrile solutions of compound **72** to aqueous solutions. In the presence of Li^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Cd^{2+}, Fe^{2+}, Fe^{3+}, Cr^{3+}, Ag^+, Hg^{2+} and Pb^{2+}, almost no fluorescence enhancement was observed. The increase in the intensity ratio at 461 and 558 nm wavelengths (I_{461}/I_{558}) during spectrofluorimetric titration allows using the ratiometric method for determination of Cu^{2+} in aqueous solution.

The formation of intramolecular excimer complexes was detected upon the reaction of 4-amino- and 4-amidonaphthalimide crown derivatives **73a**,**b** with barium cations in acetonitrile solution.[154] Since the radius of the barium cation exceeds the size of the benzo-15-crown-5 ether cavity, in the presence of Ba^{2+}, sandwich complexes L_2M stabilized by π-stacking interaction were formed. In the presence of a large excess of barium in solution, these complexes were destroyed to give complexes LM. Since molecules in the sandwich complexes have a stacked arrangement typical of *H*-aggregates, absorption of light induced the formation of intramolecular excimers having longer-wavelength fluorescence maximum and lower φ^{fl} values than the complexes LM. Note that the formation of L_2M was accompanied by quenching of fluorescence of free ligand **73a**, whereas in the case of ligand **73b**, the fluorescence intensity increased. As noted in the cited study,[154] the differences in the spectral behaviour are due to suppression of the photoinduced electron transfer from the benzocrown ether moiety to the fluorophore on going from compound **73a** to *N*-acetyl derivative **73b**; as a result, the ligand loses the ability to exhibit properties typical of fluorescent PET sensors.

Structures of complexes with ligands 73a,b

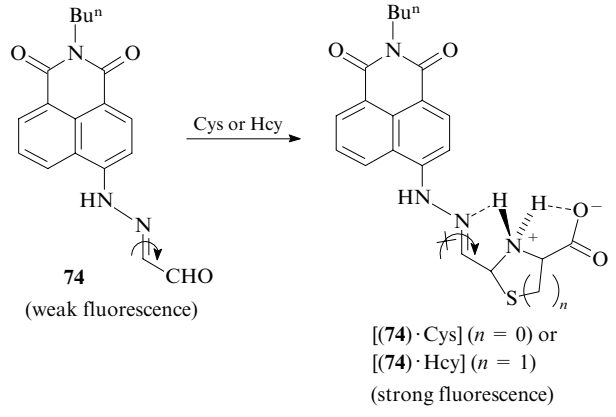


L = **73a**,**b** [R = H (**a**), Ac (**b**)]; M = Ba

All the above-considered optical sensors for cations based on 1,8-naphthalimide derivatives are designed according to a principle that implies involvement of photoinduced electron transfer (PET), intramolecular charge transfer (ICT), resonance energy transfer (FRET) or excimer formation in the generation of spectral response upon interaction of the sensor with the analyte. During the last 20 years, a great number of papers were published devoted to comprehensive studies of these processes and applications for the development of sensor systems. Meanwhile, intensive research of supramolecular chemistry in recent years resulted in original publications describing chemosensors based on new mechanisms of switching of optical characteristics. These mechanisms include: aggregation-induced emission (AIE);[155, 156] excited state intramolecular proton transfer (ESIPT);[157, 158] and isomerization around the C=N bond.[159–161] The research carried out along this line allows the design of optical devices with a more intricate set of sensing properties than those resulting from only traditional signalling mechanisms, which, beyond doubt, creates a huge potential for solving a broad range of analytical problems.[162]

Our analysis of the literature demonstrated that naphthalimide-based optical sensors utilizing AIE and ESIPT mechanisms have not yet been produced. However, we found two examples of naphthalimide sensors in which the optical properties are switched by means of isomerization around the C=N bond.[163, 164] Wang *et al.*[163] reported naphthalimide derivatives **74** (Scheme 15) able to detect cysteine (Cys) and homocysteine (Hcy) in aprotic solvent (DMSO). Although sensors for neutral molecules are beyond the scope of this review, we considered it pertinent to invoke this example in order to describe the use of photoinduced isomerization around the C=N bond. In the molecule of **74**, *E*,*Z* -isomerization in the excited state competes with the radiative relaxation channel; as a result, compound **74** demonstrates a low level of fluorescence. The reaction of Cys or Hcy with the carbonyl group of compound **74** afforded products in which the conformation of the C=N double bond is fixed by an intramolecular hydrogen bond (see Scheme 15). Hence, isomerization is hampered and fluorescence enhancement takes place.

Scheme 15

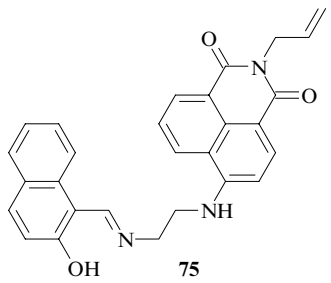


74
(weak fluorescence)

[(**74**)·Cys] (*n* = 0) or
[(**74**)·Hcy] (*n* = 1)
(strong fluorescence)

Naphthalimide derivative **75** is a fluorescent ratiometric sensor for copper(II).[164] On excitation at 360 nm, this compound showed dual fluorescence related to the presence of two chromophores. The complexation with Cu^{2+} at the

Structure 75



75

azomethine group suppressed isomerization in the naphthalene chromophore and thus enhanced the fluorescence intensity at 435 nm, similarly to the case of compound **74**. The intensity of the long-wavelength band at 510 nm corresponding to emission of the naphthalimide moiety decreased due to the fluorescence quenching effect induced by the paramagnetic ion. As noted by the authors, this could also affect the emission of light by the naphthalene ring, resulting in a low degree of fluorescence enhancement.

VIII. Conclusion

This review is an attempt to integrate the information about the use of 1,8-naphthalimide derivatives as the photoactive components of fluorescent and colorimetric chemosensors for analysis of cations. The considered examples of sensor systems demonstrate that a receptor can be connected to the 1,8-naphthalimide residue either on the side of an electron-donating substituent in position 4 of the naphthalene ring or by being introduced into the molecule as a part of the moiety bound to the imide nitrogen. In both cases, this may give both ICT sensors and sensors with the PET mechanism of switching of spectral characteristics upon complex formation. The nature of the receptor group may not only influence the selectivity of cation binding by ion-active naphthalimide derivatives but can also dramatically affect the character of the spectral changes observed. The ability of the naphthalimide ring to function as an electron excitation energy donor or acceptor and also to exhibit dual fluorescence and to form excimers extends the scope of applicability of naphthalimides for the design of optical sensors, which is illustrated by the presented examples of ratiometric fluoroionophore systems.

Development of the optical chemical sensors for cations is an actively progressing area of supramolecular chemistry. Despite the considerable advances in the sensor-related research achieved during the last several decades, the search for new selective chelating agents suitable to monitor hazardous chemicals in the environment or to analyze biological objects is still topical. 1,8-Naphthalimide derivatives represent an important class of luminophores as regards applicability for the design of optical chemosensors, first, due to the relative ease of synthetic operations for targeted modification of the molecular structure and, second, due to the diversity of photophysical properties of the naphthalimide fluorophore. Currently, a large number of chemosensors based on 1,8-naphthalimide have been prepared. Nevertheless, there are few systems combining high selectivity of complex formation, the absence of undesirable interactions between the bound metal cation and the fluorophore and high spectral response in an aqueous medium together with the possibility of performing ratiometric measurements. The deficiency of such compounds is indicated by the fact that the amount of patent information on optical sensors for cations based on 1,8-naphthalimide derivatives is quite limited. Examples of patented compounds are crown and cryptand PET sensors **36a**,**b** (see Section IV),[165, 166] 4-amino-substituted 1,8-naphthalimides suitable for determination of paramagnetic metal ions in nonaqueous media,[167, 168] pH level in lubricating oils [169] and in blood plasma.[170]

Analysis of the literature demonstrated that most of optical naphthalimide-based chemosensors for cations contain the 4-aminonaphthalimide residue as the photoactive component. Meanwhile, for living cell measurements, it is better to use fluorophores with longer-wavelength fluorescence maxima. In our opinion, the further progress in the design of optical cation sensors would be stimulated first of all by the necessity to fabricate systems suitable for *in vivo* analysis and may involve (i) search for new naphthalimide-based fluorophores exhibiting strong fluorescence near the boundary of visible and IR ranges of the electromagnetic spectrum; (ii) the use of new signalling mechanisms providing switching of the spectral characteristics upon complexation;[162] and (iii) development of heterogeneous fluorescent sensors and sensor nanomaterials.

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