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On the Ion-Pair Recognition and Indication Features of a Fluorescent Heteroditopic Host Based on a BODIPY Core

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A fluorescent heteroditopic host for ion pairs and zwitterionic species has been synthesized. Its affinity towards a series of anions, cations and ion pairs in acetonitrile has been assessed, and the spectroscopic response has been evaluated. Solid–liquid extraction experiments of inorganic salts, α-amino acids and γ-aminobutyric acid (GABA) into acetonitrile solutions were performed, and the resulting complexes were analyzed by UV/Vis absorption, fluorescence and ^{1}H NMR spectroscopy. The discrimination patterns observed have been rationalized in terms of the molecular topologies of the host and guests.

Introduction

Supramolecular chemistry has significantly propelled advances in the field of chemical recognition for an almost limitless number of applications.[1] Over several decades, a multitude of receptors for cation recognition have been designed, synthesized and evaluated.[2] More recently, effective anion-binding hosts have also become a primary focus of research, which has resulted in the development of a sizeable library of compounds.[3] After the basic frameworks for the complexation of simple cationic and anionic species were rationalized and established, more sophisticated systems able to coordinate an anion and a cation simultaneously have been developed, and the increasing number of reports reflects this growing interest in ion-pair recognition.[4] Commonly, the simultaneous binding of cations and anions is achieved by employing combinations of hosts of a dedicated cation- or anion-recognition nature such as coronands, podands or calixarenes for cations and ureas, thioureas, calix[4]pyrroles, ammonium salts, metal complexes or guanidinium salts for anions.

Most of the reported ion-pair receptors are not selective but bind several salts, and the recognition patterns vary with the solvent employed. Thus, they are mainly used in separation applications such as solid–liquid extractions, the remobilization of insoluble salts into organic solution phases[5] or as carriers in membrane-based or liquid–liquid-type phase-transfer applications.[6] On the other hand, if the topology of the subunits of the host and of the host itself are adequately tailored, the selective recognition of zwitterionic species of biological interest (e.g., amino acids and neurotransmitters) becomes possible[7] and opens a route to the creation of new compounds with a potentially wide range of biomedical applications. However, although some of these systems already operate rather efficiently as binders, only very few examples of heteroditopic hosts as potent probe molecules have been devised. For optical probes, this is basically because the installation of two different signalling processes with a unique indication pattern for a cation, an anion and an ion pair in a single small molecule is not straightforward.[8]

Among the optical signalling units that can be incorporated into probes, the boron–dipyrromethene (BODIPY) core is a particularly versatile one as virtually all of the carbon positions on the central three-membered ring system are available for substitution and it guarantees pronounced spectroscopic responses in an advantageous wavelength range.[9] BODIPY-based probes with a single receptor have been studied extensively in recent years,[10] and the facile functionalization of BODIPYs has led to a sizeable library of fluorescent probes for the detection of diverse drugs.[11] Within the last five years, several BODIPY-type probes with two receptors have also been reported.[12] However, most of these molecules have been designed for a response toward two cationic metal ion species. Heteroditopic BODIPY hosts for ion-pair guests are very rare.[13]

We report here the synthesis, photophysical data and recognition properties towards ion pairs and zwitterionic spe-

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cies of the BODIPY-based heteroditopic receptor **1**.[14] Compound **1** (Figure 1) is composed of an 18-azacrown-6 moiety (A18C6) as a cation host and a *meso*-octamethylcalix[4]pyrrole (C[4]P) as anion host, both of which are electronically connected through the boron–dipyrromethene core, which, at the same time, acts as chromophore/fluorophore and electronic mediator/spacer between the two hosts.

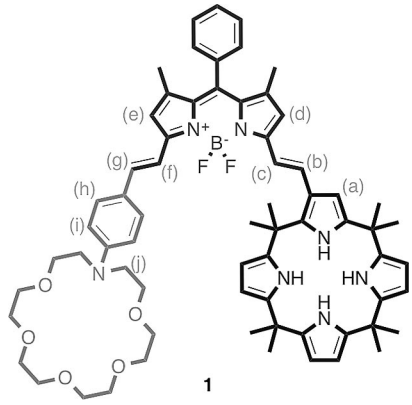
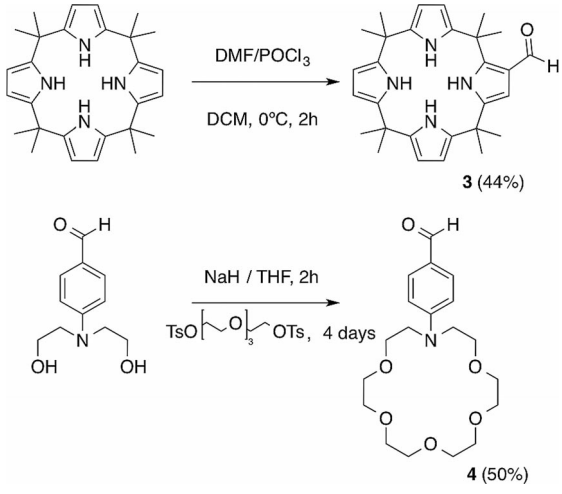


Figure 1. Heteroditopic receptor **1**.

Results and Discussion

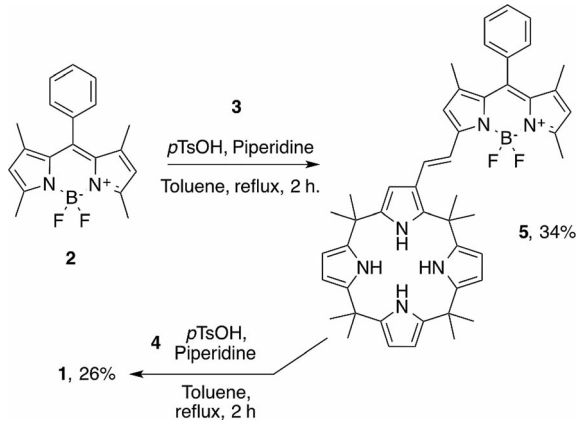
Synthetic Procedure

Compound **1** was synthesized by two consecutive Knoevenagel condensations between BODIPY **2** and the corresponding aldehyde derivative of the host moieties by using procedures described in the literature.[15] The synthesis of the aldehyde derivatives **3** and **4** is depicted in Scheme 1. The anion receptor **3** was obtained by the formylation of C[4]P with *N*,*N*-dimethylformamide (DMF) and phosphorus oxychloride. The cation receptor **4** was synthesized by the reaction of *p*-[bis(2-hydroxyethyl)amino]-benzaldehyde in the presence of NaH with the ditosylate derivative of tetraethylene glycol under high-dilution conditions.



Scheme 1. Synthesis of the anion and cation receptor moieties **3** and **4**.

Compound **2** was condensed with aldehyde **3** in the presence of piperidine and *p*-toluenesulfonic acid (TsOH) by using a Dean–Stark apparatus to afford **5** in 34% yield after purification by column chromatography. The resulting product was then condensed with aldehyde **4** under similar conditions to yield the final heteroditopic BODIPY receptor **1** as a green solid in 26% yield (Scheme 2). The new ligand was characterized by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry.



Scheme 2. Synthesis of the heteroditopic probe **1**.

Spectroscopic Properties

Compound **1** (1×10^{-5} M in MeCN) shows an absorption maximum at 685 nm with a molar absorption coefficient of 74600 $cm^{-1}M^{-1}$. This band corresponds to the $S_1 \leftarrow S_0$ ($\pi \rightarrow \pi^*$) (0→0) transition of the extended BODIPY dye and possesses a shoulder at 635 nm, which corresponds to the vibronic (0→1) transition of the same electronic transition. Weaker bands at 328 and 416 nm with ε = 27750 and 26630 $cm^{-1}M^{-1}$, respectively, are ascribed to $S_2 \leftarrow S_0$ and $S_3 \leftarrow S_0$ transitions in analogy to assignments by Qin et al. in related alkenyl–BODIPY derivatives.[16] The emission spectrum has a maximum at 743 nm, which appears broadened compared with the typically narrow BODIPY core emission, presumably because of an admixture of an intramolecular charge transfer (ICT) character involving the donor aniline and the acceptor BODIPY (Figure 2).[15a]

In addition, the significant Stokes shift observed between the absorption (λ_{abs}) and emission bands (λ_{em}) compared with that of the parent BODIPY **2** (λ_{abs} = 497 nm, λ_{em} = 505 nm) is consistent with the behaviour observed in other π-extended BODIPYs.[9a] The fluorescence quantum yield Φ_f of **1** in MeCN is 0.34, which is comparable to the values reported earlier by some of us for such red-absorbing BODIPY dyes.[17] The fluorescence decay is biexponential with an almost equal contribution of a short-lived (τ_1 = 0.28 ns, $a_{1,rel}$ = 0.49; $a_{x,rel}$ = relative amplitude of species *x*) and a long-lived component (τ_2 = 1.98 ns, $a_{2,rel}$ = 0.51). In

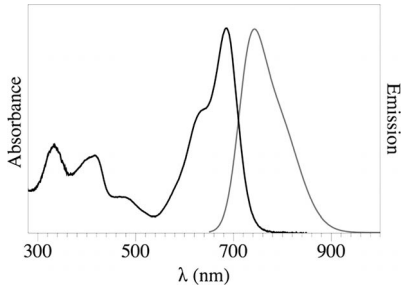


Figure 2. UV/Vis absorption and fluorescence spectrum (λ_{exc} = 685 nm) of **1** (1×10^{-5} M in CH_3CN).

contrast to dyes such as **6** (Figure 3), which show a single exponential decay (e.g., τ_f = 0.13 ns for **6** in MeCN),[15a] biexponential decays are often found for crown ether appended BODIPYs such as **7** and **8** (Figure 3).[15b,18] Such behaviour is related to the flexibility of the crown ether unit and its ability to adopt more than one preferential conformation in the ground and/or excited state. For instance, fluorescence lifetimes of 0.22 (a_{rel} = 0.54) and 1.42 ns (a_{rel} = 0.46) have been found for **7** in MeCN.[19]

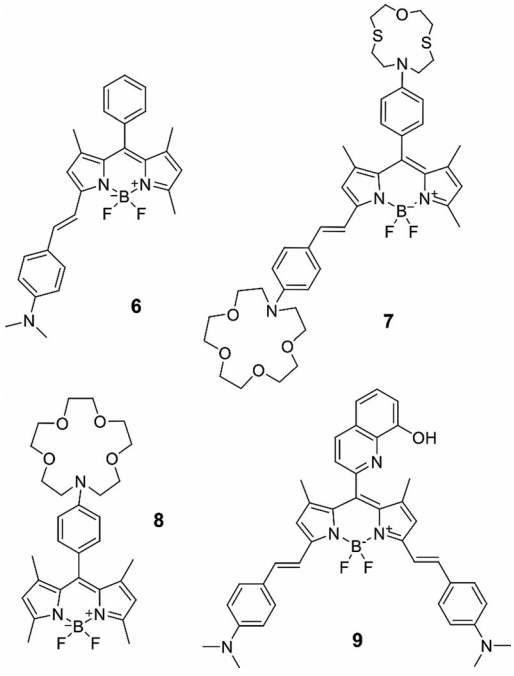


Figure 3. Previously reported BODIPY discussed in the text.

Complexation Studies

The affinity of **1** towards several ions in acetonitrile solution[20] was tested by UV/Vis spectroscopy. To examine the ion-binding properties of each coordination site independently, the noninterfering counterions ClO_4^- and NBu_4^+ (tetrabutylammonium, TBA) were employed for titrations with cations and anions, respectively. The interactions of these counterions with the hosts were negligible and neglected in the further studies. In this way, the affinity constants for Li^+, Na^+, K^+, and NH_4^+ cations and F^-, Cl^-, Br^- and AcO^- anions were obtained by UV/Vis titrations (Table 1). The values determined were consistent with the well-established complexation properties of both azacoronands and calixpyrroles.[21]

Table 1. Complexation constants ($\log K_a$) of **1** with various cations and anions in acetonitrile. Values were obtained after least-squares fits of UV/Vis titrations with the SpecFit© software[22] for a 1:1 binding model.

	1 + NH_4^+	**1** + K^+	**1** + Na^+	**1** + Li^+
$\log K_a$	3.2 ± 0.1	3.3 ± 0.1	3.0 ± 0.2	2.0 ± 0.3
	1 + F^-	**1** + AcO^-	**1** + Cl^-	**1** + Br^-
$\log K_a$	6.3 ± 0.2	5.0 ± 0.1	5.1 ± 0.1	<1

The optical properties of **1** in acetonitrile (1×10^{-5} M) in the presence of different cations and anions are listed in Table 2. To achieve full complexation, an excess of the mentioned salts was added.

Table 2. Optical properties of **1** (1×10^{-5} M in CH_3CN) in the presence of an excess of different ions. Cations and anions were added as ClO_4^- and TBA^+ salts, respectively (10 mg).

	λ_{abs} [nm]	$\Delta\lambda_{abs}$ [nm]	λ_{em} [nm]	$\Delta\lambda_{em}$ [nm]	Φ
1 + NH_4^+	653	–32	708	–35	0.53
1 + K^+	660	–25	717	–26	0.59
1 + Na^+	678	–7	728	–15	0.52
1 + Li^+	684	–1	729	–4	0.55
1	685	–	743	–	0.34
1 + F^-	696	+11	748	+5	0.006
1 + AcO^-	692	+7	746	+3	0.034
1 + Cl^-	688	+3	744	+1	0.18
1 + Br^-	687	+2	742	–1	0.23

As can be observed for the example of the F^- anion in Figure 4, the anionic guests produce bathochromic displacements of the main absorption as well as the emission band of up to ca. 5 nm accompanied by a quenching of the fluorescence. The bathochromic shift is consistent with an increase in the electron-donating strength of the C[4]P arm through coordination of the anion, and the absorption approximates that of bis-aminostyryl-substituted dyes such as **9** (Figure 3), which absorbs at 711 nm.[17] However, the comparatively strong reduction in the fluorescence quantum yield in **1**–F^-, cannot be explained within the simple framework of the colour rules of BODIPYs, that is, an enhanced internal conversion as the energy gap between the ground and excited states decreases (according to the energy-gap rule),[15a] but is tentatively attributed to the population of an only weakly emissive ICT state involving the complexed calix[4]pyrrole[23a–23d] and possibly possessing a certain charge-shift character.[23e] The involvement of the latter is known to result in nonfluorescent BODIPY dyes.[23f] The magnitude of these anion-induced shifts as well as the decrease in emission intensity is additionally related to the affinity of the C[4]P moiety towards the tested anion and reflects an order $F^- > AcO^- \approx Cl^- > Br^-$. Regarding the fluorescence decay behaviour, at a fixed anion–**1** ratio of 500:1, the quenching effect of the anions is ac-

companied by the appearance of a third fluorescence lifetime component, which decays even faster than the short-lived component of free **1**, for example, in 78 ps for F^- and 83 ps for Br^- (the uncertainty in the measurement is ±3 ps). Moreover, the relative amplitude of the shortest decay component for the F^- complex is more than twice that for the Br^- complex. This clearly indicates that once an anion is bound in the C[4]P unit its quenching ability is rather similar (at least for the monoatomic halides) and that the magnitude of the quenching in a titration series depends primarily on $\log K_a$. The latter is supported by the fact that the fluorescence lifetimes of **1**–F^- and **1**–Br^- are rather similar (78 vs. 83 ps).

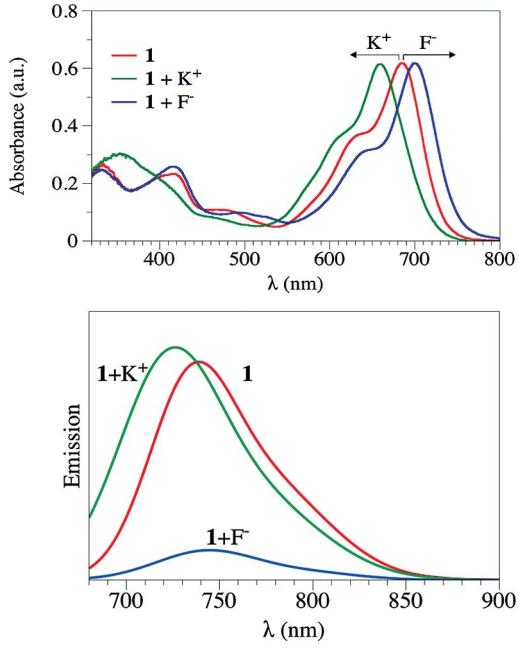


Figure 4. UV/Vis (top) and fluorescence emission (bottom) spectrum (λ_{exc} = 685 nm) of **1** (1×10^{-5} and 1×10^{-6} M in MeCN) in the absence (red) and presence of 500 equiv. of $KClO_4$ (green) and 500 equiv. of TBAF (blue). For a representative set of UV/Vis titration spectra, see Figures S14 and S15.

On the other hand, the addition of cations (as ClO_4^- salts) to MeCN solutions of **1** induced a hypsochromic shift of both the absorption and the emission band. This phenomenon is attributed to the coordination of the cation by the azacrown moiety.[12c,18,24] For instance, the binding of a Na^+ cation to the tetraoxa–monoaza crown of **7** leads to analogous hypsochromic shifts.[18] The positively charged cation monopolizes the lone electron pair of the crown ether nitrogen atom and weakens the electron donor strength of this unit and, hence, the ICT character, and there is a concomitant increase of the fluorescence emission. The magnitude of the observed shift follows the order $NH_4^+ \approx K^+ > Na^+ > Li^+$, which is in agreement with the coordination preference of A18C6.[2] In addition, Li^+ and Na^+ ions are also known to prefer oxygen over nitrogen coordination in such crowned dyes in acetonitrile, which leads to smaller spectral shifts that are frequently even accompanied by higher complexation constants.[25,26a] The spectroscopic changes upon saturation with several cations and anions are summarized in Table 2. The changes in fluorescence quantum yield upon the binding of **1** to the various cations are in line with other reports on BODIPYs carrying 3- or 5-styryl-appended amino crowns,[12,13] that is, excited-state decoordination[26a] does not play a role in such BODIPY-type ICT probes.

After proving the ability of **1** to bind discrete cations and anions, we tested its ability to coordinate and sense a cation and an anion at the same time and, thus, respond to an ion pair. For this purpose, the halide series (F^-, Cl^-, Br^-) of the first three alkali metal ions (Li^+, Na^+, K^+) was chosen. To overcome the problem of the low solubility of some of these salts in acetonitrile and even in water, [cf. LiF: 0.13 g in 100 mL at 25 °C], we opted for a modified phase-transfer protocol in the sense of solid–liquid extraction experiments, especially for the NMR experiments that required significantly higher concentrations.

For the NMR investigations in the solid–liquid extraction experiments, 5×10^{-3} M solutions of **1** in CD_3CN (1 mL) in a vial were saturated with the corresponding salt, and the mixture was mechanically stirred for 24 h. After that time, the solution was filtered, and the ^1H NMR spectrum was recorded. Simultaneous complexation of both cation and anion was clearly demonstrated because a shift of the NMR signals of both the azacrown and the calixpyrrole moieties was observed (Table 3).

Table 3. Change in ^1H NMR chemical shifts [ppm] of selected protons after complexation of **1** with different salts.

Salt	H_a	H_c	H_i	H_j
LiF	–0.01	–0.01	0.01	0
LiCl	–0.23	–0.16	0.08	0.01
LiBr	–0.25	–0.18	0.05	0.13
NaF	–0.02	–0.02	0.01	0.01
NaCl	–0.21	–0.14	0.10	0.05
NaBr	–0.26	–0.18	0.03	0.10
KF	–0.22	–0.11	0.26	–0.25
KCl	–0.20	–0.13	0.22	–0.19
KBr	–0.20	–0.13	0.28	–0.24

In general, anion coordination induced a shift in all of the proton signals related to the calixpyrrole moiety. Thus, the β-pyrrolic protons (H_a and others, Figure 1) and the vinylic proton H_c are shielded upon anion coordination (consistent with an electronic density injection of the anion to the conjugated system), whereas the N–H and *meso*-methyl groups and the H_b vinylic proton become deshielded.

On the other hand, cation coordination has a strong effect on the chemical shifts of the protons related to the A18C6 moiety. For instance, protons H_i and H_h (see Supporting Information) are deshielded upon cation coordination, along with the aliphatic protons of the coronand. This observation is consistent with the electronic demand of the cationic species.

Among all the salts studied, KF and KBr produced the largest shifts in the signals of H_c, H_i and H_j, indicating strong complexation. In contrast, the changes observed for

LiF and NaF were small, which indicates a low extent of complexation, presumably because of the high lattice energies of these salts (1036 and 923 kJ mol^{-1}, respectively). Notably, the complex with KBr shows sharp signals for the NH protons in contrast with the broad signals found for the other potassium salts (Figure 5). This behaviour can be related to the size of the bromide ion, which results in a perfect fit of the ion pair into the cavity and, thus, the rigidity of the ternary complex is enhanced. Another interesting observation was related to the signal of H_j when the Li^+, Na^+ and K^+ salts were compared. Whereas the Li^+ and Na^+ salts lead to a slight deshielding of H_j, the opposite behaviour was observed for K^+ salts regardless of the counteranion (Figure 5, cf. NaBr and KBr; see also Supporting Information). Thus, this behaviour seems to be related to the cation size. The small cations are preferably complexed by the oxygen atoms of the crown moiety and are most likely buried in the cavity. On the other hand, the larger K^+ cation completely fills the coronand cavity and induces a conformational change that inhibits the conjugation between the lone electron pair of the nitrogen atom and the styryl extension of the BODIPY core. This conformational modification puts H_j under the influence of the aromatic ring. The lack of conjugation is also supported by the larger shift of H_i in the potassium salts than in the other compounds studied.

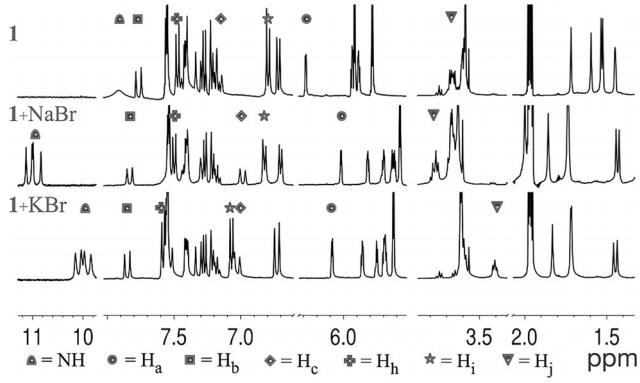


Figure 5. ^{1}H NMR spectra of **1** as free ligand (top) and in the presence of NaBr (middle) and KBr (bottom) in CD_3CN.

For the UV/Vis and fluorescence studies, an excess of the diverse salts (10 mg), previously dried, was added to 10^{-5} M CH_3CN solutions (3 mL) of **1**, and the mixtures were mechanically stirred for 24 h in the dark. After this time, the solutions were filtered and their spectroscopic properties were measured. The complexation of **1** with different inorganic salts generated different macroscopic responses in the two optical channels (absorption and emission).

All the alkali halides showed a hypochromic effect and a hypsochromic displacement of the main absorption band, which suggests that the electronic properties of the complexes are mainly governed by the interaction of the cation with the azacrown moiety and modulated by the presence of the anions (Figure 6). However, this is not the only effect to be taken into account, as the interaction of the anion with the C[4]P moiety could induce electrostatic and conformational changes in the ligand that would favour the cation complexation (see Supporting Information). Additionally, the ion-pair size and its association constant could play a role in the entire process.

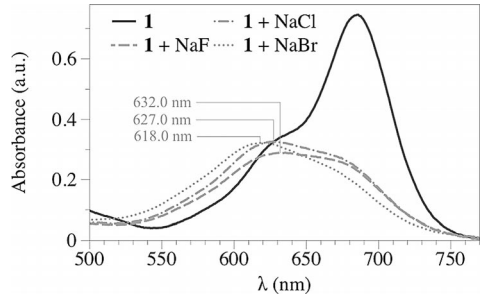


Figure 6. UV/Vis spectrum of **1** (1×10^{-5} M in CH_3CN) as a free ligand and after 24 h of mechanical agitation in the presence of 10 mg of NaF, NaCl and NaBr.

The fluorescence behaviour followed the same pattern as the absorption bands. All fluorescence emission spectra are slightly hypsochromically shifted, presumably because of the interaction of the cation with the azacrown moiety. Less-coordinating anions (Br^- or Cl^-) did not compensate the cation effect, whereas anions with a higher affinity for the C[4]P unit such as F^- reduced this blueshift. However, the distinct effect of anion binding, fluorescence quenching, was also found in all of the complexes formed (Figure 7).

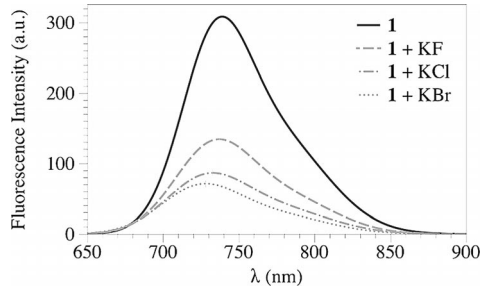


Figure 7. Fluorescence spectrum of **1** (1×10^{-5} M in CH_3CN) as a free ligand and after 24 h of mechanical agitation in the presence of 10 mg of KF, KCl and KBr.

The intensity of the quenching did not follow the trend observed with the corresponding anions as tetrabutylammonium salts, most likely because ion association is only considerably moderate for all of the TBA salts (e.g., K_a = 27.45 for TBABr and 24.71 for $TBAClO_4$).[26b,26c] However, the K^+ salts follow a comparable trend to that mentioned for Li^+ salts above (the only data available for K^+ salts is K_a = 32.68 for $KClO_4$).[26b,26c] The anion coordination of C[4]P seems to be modulated by the presence of the potassium ion. The strong interaction between K^+ and F^- ions displaces the anion to a certain degree from the C[4]P cavity; therefore, the extent of coordination is diminished compared with that of KBr, for example, because the Br^- ion is larger and undergoes weaker electrostatic interactions. These factors should allow the bromide ion to fit better into the C[4]P cavity and still fulfil the electrostatic needs of the K^+ cation. As a consequence, as compared to

the TBA salts, the bromide ion modulates the fluorescence intensity of **1** more efficiently in the presence of K^+.

However, the most dramatic effect besides spectral shifts and fluorescence quenching is the strong hypochromic change of the main BODIPY-centred absorption transitions. Such a pronounced reduction in oscillator strength cannot only be related to a decoupling of the nitrogen atom of the crown from the π system through cation complexation, for instance, protonated **6** (Figure 3) does not show such a behaviour,[15a] but is most probably related to a twisting of the appended pyrrole ring out of the BODIPY plane upon the formation of the ion-pair complex. The complexation of the ion pair, especially in the case of the larger and strongly electrostatically attracted ions such as K^+ and Br^-, can only occur if the crown unit adopts an "L" shape with the cavity pointing toward the void of the tweezers and if the entire C[4]P unit adopts an almost perpendicular conformation with regard to the π plane (see Figure 10).

Combining the observations obtained in the studies with different inorganic salts, we can span a matrix that allows the discrimination between different ion pairs on the basis of their absorption and fluorescence behaviour. In Figure 8, a 3D plot of the ratio between the absorption at 680 and 625 nm (*x* coordinate), the emission intensity (*z* coordinate) and the emission maximum wavelength (*y* coordinate) is presented. Upon closer inspection, it is evident that the different complexes show a particular clustering, which permits the identification of the different salts or ion pairs by comparatively simple means. The differences in effects for the weakly soluble salts (LiF, NaF, etc.) and the more soluble salts (e.g., KBr) in particular in the NMR and optical spectroscopic studies is presumably related to the effective ratios of the partners in the final measurement solutions. At NMR concentrations, too little of the weakly soluble salts are dissolved to achieve full complexation.

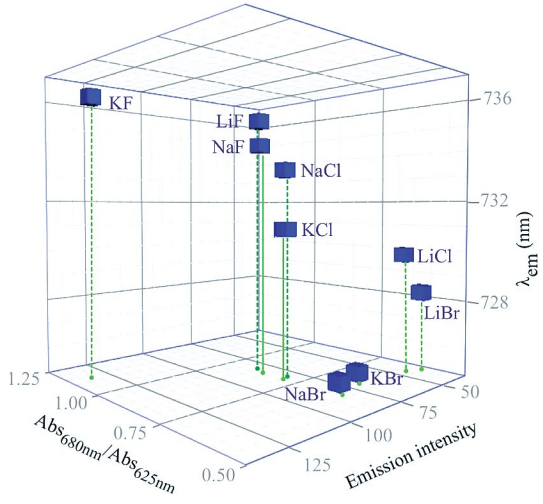


Figure 8. 3D representation of significant changes in the spectroscopic properties of **1** in the presence of different inorganic salts.

Considering other guests that express two differently charged entities, the tweezerlike architecture of **1** should also be suitable for the binding of zwitterionic guests of a certain topology, for instance, amino acids. For these experiments, glycine, tyrosine, arginine, cysteine, aspartic acid, glutamic acid and γ-aminobutyric acid (GABA) were considered. The amino acids were dried and added in an excess (10 mg) to 10^{-5} M CH_3CN solutions (3 mL) of **1** followed by mechanical stirring of the mixtures for 24 h in the dark. After filtration, the absorption and emission spectra of the solutions were recorded.

Glycine, tyrosine, cysteine and glutamic acid showed a very similar behaviour in absorption with a main band at ca. 677 nm and a shoulder at 631 nm (see the examples for Gly and GABA in Figure 9; for the other amino acids, see Supporting Information). These spectra are slightly hypsochromically shifted by ca. 10 nm compared with that of free **1**. This behaviour can be explained by the complexation of the ammonium group of the amino acid in analogy to the cation complexation features described above.

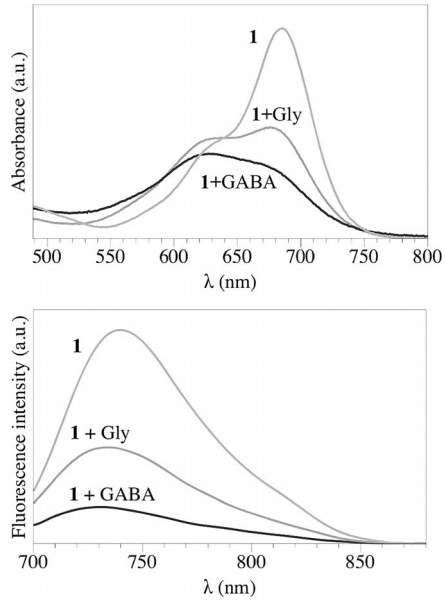


Figure 9. UV/Vis spectra of **1**, **1** + GABA and **1** + Gly (top) and emission spectra (λ_{exc} = 685 nm) of **1**, **1** + GABA and **1** + Gly (bottom).

However, when the UV/Vis spectra of **1** with sodium halides (Figure 6) are compared with the spectrum of **1** + Gly (Figure 9, top), it is clear that the interaction of the ammonium group with the azacrown ether is less pronounced for **1** + Gly. In addition, the binding of the ammonium group in the cavity of the crown seems to dominate over the binding of the carboxylate group to C[4]P. On the other hand, the UV/Vis spectra of the complexes of **1** with Arg and especially GABA show a shape that is very similar to that of the ion-pair complexes (Figure 6).

For GABA in particular, the distance between the anionic and cationic moieties seems to be much better suited to satisfy the coordination needs of **1**, presumably through 1:1 complexation by simultaneous binding of the guest in both the cation and the anion receptor.[27] Tentative structures for the possible complexes between **1** and GABA and

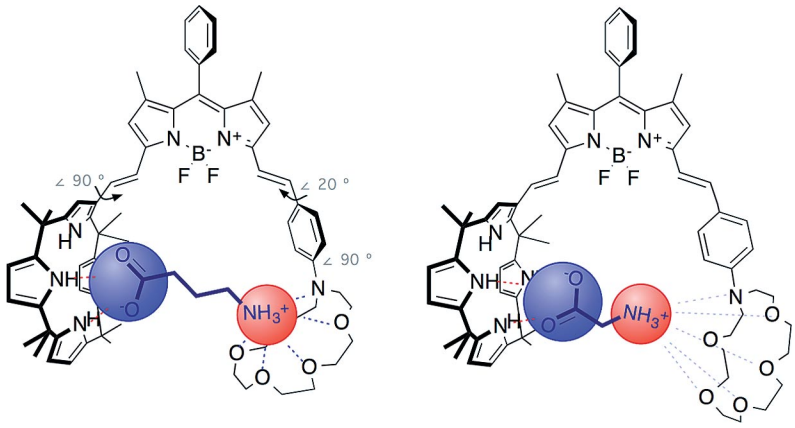


Figure 10. Schematic illustration of **1**–GABA (left) and **1**–Gly (right) complexes. The distance is adequate for the complexation of GABA with the two hosts, whereas glycine can only be complexed by either the azacrown or the calixpyrrole moiety. The angles shown are approximations based on results obtained after computation of a model compound.

Gly are shown in Figure 10. The truncation of the extended π system by twisting of the C[4]P moiety is also illustrated in Figure 10; this also leads to a reduction in oscillator strength and a hypochromic change in absorption in the case of the zwitterionic guests and supports the interpretation given above for the good fit of ion pairs such as K^+/Br^-.

The fluorescence spectra show a similar behaviour to those of the alkaline salts; the magnitude of fluorescence quenching seems to be related to the strength of the complexation. By following a similar approach to that previously described (using data from UV and fluorescence spectra), the studied amino acids can be discriminated (Figure 11).

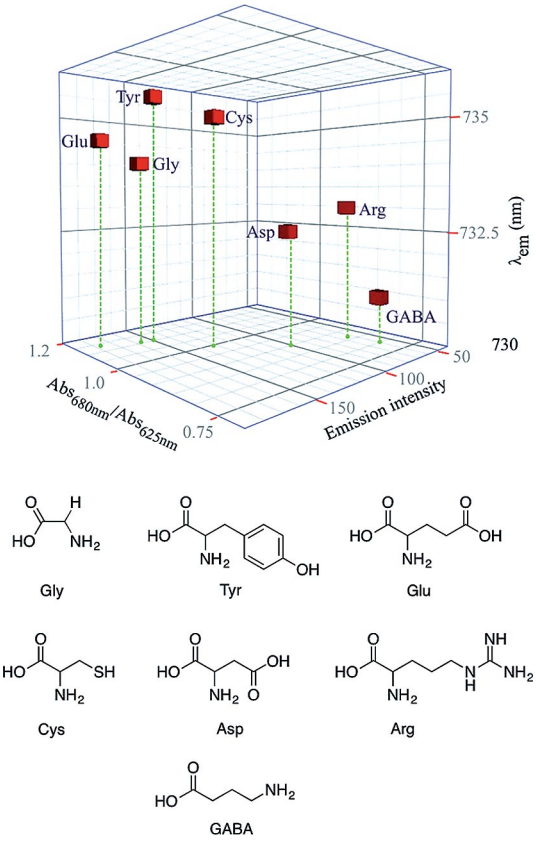


Figure 11. Top: 3D representation of significant changes in the optical properties of **1** in the presence of several amino acids. Bottom: structures of these amino acids.

Conclusions

We have synthesized a heteroditopic receptor for the simultaneous recognition of anions and cations. In the presence of cations with inactive counterions, hypsochromic shifts of both the absorption and emission bands were observed. By contrast, in the presence of anions with inactive counterions, bathochromic shifts of both the absorption and the emission bands along with fluorescence quenching were observed. In the presence of diverse alkali halides, clear changes in the UV/Vis, fluorescence and ^{1}H NMR spectra were observed. The combination of optical changes induced after complexation of different alkali halides is different in each case and can be used to discriminate between the salts. It is important to note that the single effects are retained in these cases and an additional hypochromic synergistic effect occurs, that is, the anion and cation do not annihilate each other like they do in various other reported systems. Finally, compound **1** also gives rise to different responses in the presence of zwitterionic amino acids. The distance between the ammonium and the carboxylate group is a crucial factor for the optical behaviour of the complexes.

Experimental Section

Materials and Methods: Tetrahydrofuran was distilled from Na prior to use. All other materials were purchased and used as received. The ^{1}H and ^{13}C NMR spectra were recorded by using Bruker DRX-500 and Bruker Avance 400 MHz spectrometers. HRMS spectra were recorded with an AB SCIEX QTOF mass spectrometer. UV/Vis measurements were performed by using 1 cm path length quartz cuvettes with a Shimadzu UV-2101PC spectrophotometer. Fluorescence spectra were recorded with Varian Cary

Eclipse and Horiba Jobin–Yvon FluoroMax-4P fluorescence spectrophotometers. Fluorescence experiments were performed with a 90° standard geometry with polarizers set at 54.7° for emission and 0° for excitation.

The fluorescence quantum yields (Φ_f) were determined relative to that of **3** in acetonitrile ($\Phi_f = 0.10 \pm 0.01$).[17]

The synthetic procedure for **2** can be found in ref.[15] The synthesis of **3** was performed as described in ref.[28]

The fluorescence lifetimes (τ_f) were determined by a unique customized laser impulse fluorometer with picosecond time resolution, which we described in an earlier publication.[29] The fluorescence was collected at a right angle (polarizer set at 54.7°), and the fluorescence decays were recorded with a modular single-photon timing unit.[17] Typical instrument response functions [full width at half-maximum (fwhm) ca. 40 ps] and a time division of 1.2 ps per channel allowed us to obtain an experimental accuracy of ±3 ps. Typical excitation energies were in the nanowatt to microwatt range (average laser power). The fluorescence lifetime profiles were analyzed with a PC by using the Global Unlimited V2.2 software package (Laboratory for Fluorescence Dynamics, University of Illinois), and the goodness of the fit was calculated from the reduced χ_R^2 and autocorrelation function $C(j)$ of the residuals.

UV/Vis quantitative analysis was performed by adding aliquots of different cations or anions (as ClO_4^- or TBA^+ salts) to 1×10^{-5} M CH_3CN solutions of **1**.

Solid–liquid phase extraction experiments were performed by adding the different salts (10 mg) to 1×10^{-5} M CH_3CN solutions (3 mL) of **1**. Mixtures were mechanically stirred for 24 h. After that time, the solutions were filtered, and the UV/Vis and fluorescence spectra were recorded.

Full complexation experiments of **1** with TBA^+ and ClO_4^- salts were achieved by adding an excess (ca. 10 mg) of the salts to 1×10^{-5} M CH_3CN solutions (3 mL) of **1**, which were then stirred for 24 h. The solutions were then filtered to remove the remaining solid (if any).

Compound 4: 4-[Bis(2-hydroxyethyl)amino]benzaldehyde (729 mg, 3.49 mmol) was dissolved in dry THF (220 mL) under an argon atmosphere. Then, 60% sodium hydride (860 mg, 21.11 mmol) was carefully added to the reaction mixture. The reaction was then heated to reflux for 2 h. After this time, tetraethylene glycol di-*p*-tosylate (1.83 g, 3.64 mmol) was added dropwise over 2 h with an automatic syringe. The macrocycle formation reaction was heated to reflux for 96 h. Then, water (10 mL) was added, and the mixture was stirred for 5 min. The organic solvent was evaporated, and the mixture was redissolved in EtOAc and washed three times with 10% $NaHCO_3$. The aqueous layer was reextracted with EtOAc, and the combined organic layers were washed with brine and dried with $MgSO_4$. The remnant oil was purified by flash chromatography with dichloromethane/MeOH (DCM/MeOH 95:5→80:20) as eluent to yield a yellowish oil (642 mg, 50%). *Rf* = 0.47 (DCM/MeOH, 95:5). IR: $\tilde{\nu}$ = 3330, 2971, 2927, 2887, 1656, 1452, 1385, 1098, 1049, 880 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 9.73 (s, 1 H), 7.72 (d, J = 8.8 Hz, 2 H), 6.75 (d, J = 8.8 Hz, 2 H), 3.79–3.57 (m, 24 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 190.10, 152.69, 132.13, 125.27, 111.05, 70.88, 70.84, 70.79, 70.77, 68.36, 51.47 ppm. HRMS (EI): calcd. for $C_{19}H_{30}NO_6$ $[M + H]^+$ 368.2068; found 368.2073.

Compound 5: BODIPY **2** (429 mg, 1.30 mmol) and aldehyde **3** (400 mg, 0.88 mmol) were dissolved in dry toluene (30 mL) in a two-neck round-bottomed flask connected to a Dean–Stark apparatus. Then, piperidine (2.8 mL), a small amount of 3 Å molecular sieves, and trace amounts of *p*TsOH were added to the mixture. The reaction was kept under argon at the reflux temperature of toluene for 2 h. After this time, the reaction mixture was allowed to reach room temperature, and then the solvent was evaporated. The residue was redissolved in EtOAc and washed with 10% NH_4Cl three times. The aqueous layer was reextracted with EtOAc, and the combined layers were dried with NaCl (satd.) and $MgSO_4$. The product was purified by column chromatography with neutralized silica (Et_3N) as the stationary phase and a hexane/EtOAc mixture (95:5→85:15) as eluent. A deep blue solid (225 mg, 34%) was obtained along with the disubstitution isomer (80 mg, 4%). *Rf* = 0.55 (EtOAc/Hex, 2:8). IR: $\tilde{\nu}$ = 3418, 2971, 2922, 2869, 1696, 1602, 1540, 1478, 1425, 1297, 1191, 1155, 1102, 1044, 982, 765 cm^{-1}. ^1H NMR (500 MHz, CD_2Cl_2): δ = 7.70 (d, J = 15.7 Hz, 1 H), 7.57–7.52 (m, 3 H), 7.40–7.36 (m, 2 H), 7.31 (s, 1 H), 7.29 (s, 1 H), 7.20 (dd, J = 15.9, 1.9 Hz, 1 H), 7.02 (s, 1 H), 6.95 (s, 1 H), 6.60 (s, 1 H), 6.39 (d, J = 2.9 Hz, 1 H), 6.04 (s, 1 H), 6.01–5.95 (m, 4 H), 5.91 (t, J = 3.0 Hz, 1 H), 5.87 (t, J = 3.0 Hz, 1 H), 2.58 (s, 3 H), 1.72 (s, 6 H), 1.57 (s, 6 H), 1.56 (s, 6 H), 1.55 (s, 6 H), 1.48 (s, 3 H), 1.44 (s, 3 H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2): δ = 155.26, 152.42, 143.26, 140.83, 139.38, 139.07, 138.92, 138.67, 138.63, 138.27, 137.50, 137.47, 137.44, 135.21, 132.93, 132.31, 130.97, 129.01, 128.77, 128.43, 120.25, 117.42, 117.32, 114.12, 103.68, 103.66, 103.52, 102.83, 102.78, 102.47, 101.85, 37.45, 35.15, 35.08, 35.01, 30.57, 29.50, 28.95, 28.41, 28.35, 14.38, 14.27, 13.94 ppm. HRMS (ESI): calcd. for $BC_{48}F_2H_{54}N_6$ $[M + H]^+$ 763.4466; found 763.4439.

Compound 1: Compound **5** (160 mg, 0.21 mmol) and aldehyde **4** (77 mg, 0.21 mmol) were dissolved in dry toluene (30 mL) in a two-neck round-bottomed flask connected to a Dean–Stark apparatus. Then, piperidine (0.2 mL), a small amount of 3 Å molecular sieves, and trace amounts of *p*TsOH were added to the mixture. The reaction mixture was heated to reflux under argon for 2 h. After this time, the mixture was allowed to reach room temperature, and then the solvent was evaporated. The residue was redissolved in EtOAc and washed with NH_4Cl 10% three times. The aqueous layer was reextracted with EtOAc, and the combined layers were dried with satd. NaCl and $MgSO_4$. The product was purified by column chromatography with neutralized silica (Et_3N) as the stationary phase and hexane/EtOAc (95:5→85:15) as the eluent. A dark green solid was obtained (62 mg, 27%). IR: $\tilde{\nu}$ = 3406, 3308, 3104, 3063, 2965, 2925, 2863, 1732, 1656, 1594, 1514, 1483, 1429, 1376, 1287, 1166, 1104, 1046, 984, 948, 770, 730 cm^{-1}. ^1H NMR (500 MHz, [D_2]dichloromethane): δ = 7.65 (d, J = 15.8 Hz, 1 H), 7.55–7.46 (m, 5 H), 7.48 (d, J = 16.8 Hz, 1 H), 7.39–7.33 (m, 3 H), 7.30 (s, 1 H), 7.21 (d, J = 15.8 Hz, 1 H), 7.20 (d, J = 16.8 Hz, 1 H), 6.99 (s, 1 H), 6.94 (s, 1 H), 6.72 (d, J = 8.9 Hz, 2 H), 6.63 (s, 1 H), 6.56 (s, 1 H), 6.42 (d, J = 2.8 Hz, 1 H), 5.99–5.91 (m, 4 H), 5.87 (t, J = 3.1 Hz, 1 H), 5.84 (t, J = 3.0 Hz, 1 H), 3.79–3.50 (m, 24 H), 1.70 (s, 6 H), 1.58 (s, 6 H), 1.53 (s, 6 H), 1.51 (s, 6 H), 1.45 (s, 3 H), 1.45 (s, 3 H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2): δ = 153.85, 152.95, 149.47, 141.94, 141.69, 139.91, 139.47, 139.12, 138.88, 138.82, 138.22, 138.16, 138.06, 137.10, 136.83, 136.04, 133.38, 133.33, 131.64, 129.62, 129.49, 129.42, 129.26, 125.05, 118.12, 117.57, 117.52, 115.14, 114.64, 112.31, 104.23, 104.18, 104.07, 103.42, 103.33, 103.09, 102.47, 71.30, 71.28, 71.19, 71.15, 69.07, 51.80, 38.04, 35.78, 35.68, 35.59, 30.09, 29.64, 29.02, 28.94, 14.88, 14.87 ppm. HRMS (ESI): calcd. for $BC_{67}F_2H_{80}N_7O_5$ 1112.6341; found 1112.6358.

Supporting Information (see footnote on the first page of this article): IR, NMR and HRMS spectra of **1**, NMR spectra of **1** in the

presence of different salts, emission and absorption spectra of **1** free and in the presence of different salts and amino acids, titration of **1** with TBAF and $KClO_4$ in acetonitrile.

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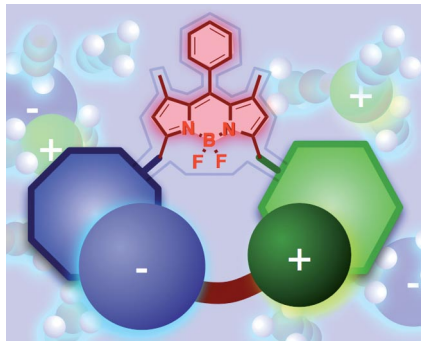
Sensors

Catching two balls: A BODIPY derivative bearing two independent yet complimentary hosts for anions and cations displays distinct absorption and fluorescence signalling patterns for different alkali metal halides. The compound also recognizes zwitterionic compounds such as amino acids and γ-aminobutyric acid (GABA).



Keywords: Sensors / Receptors / Ion-pair recognition / Zwitterion recognition / Fluorescence

