JOC *Article*

Spectroscopic Correlations between Supermolecules and Molecules. Anatomy of the Ion-Modulated Electronic Properties of the Nitrogen Donor in Monoazacrown-Derived Intrinsic Fluoroionophores†

Jye-Shane Yang,* Chung-Yu Hwang, Chia-Chun Hsieh, and Shih-Yi Chiou

Department of Chemistry, National Central University, Chung-Li, Taiwan 32054

jsyang@cc.ncu.edu.tw

Received October 6, 2003

The synthesis, absorption and emission spectra, fluorescence quantum yields, and fluorescence lifetimes of three compound series of *trans*-4,4′-disubstituted aminostilbenes (**1**−**3**) are reported. The chromo-/fluoroionophoric behavior of the monoaza-15-crown-5- (A15C5) and monoaza-18-crown-6 (A18C6)-derived species ($\mathbf{1A_5}$−$\mathbf{3A_5}$ and $\mathbf{1A_6}$−$\mathbf{3A_6}$) in acetonitrile and dichloromethane are also investigated. Great similarities in electronic spectroscopic properties (chemical shifts, wavelength, intensity, and lifetime) between the metal ion-complexed supermolecules and the corresponding chloro-substituted molecules have been observed: namely, $\mathbf{1A_5}/Ca^{2+}$−$\mathbf{3A_5}/Ca^{2+}$ ∼ $\mathbf{1A_6}/Ba^{2+}$−$\mathbf{3A_6}/Ba^{2+}$ ∼ **1C**−**3C** in acetonitrile and $\mathbf{1A_5}/Na^{+}$−$\mathbf{2A_5}/Na^{+}$ ∼ $\mathbf{1A_6}/K^{+}$−$\mathbf{2A_6}/K^{+}$ ∼ **1C**−**2C** in dichloromethane. Such spectroscopic correlations allow us to define the metal ion-modulated electronic character of the azacrown nitrogen atom in the ground and excited states and, in turn, to gain insights into the observed fluoroionophoric behavior of these probes in terms of the size and direction of fluorescence shifts and intensity variations.

Introduction

The cation−coronand interaction is well documented[1−3] and constitutes one of the features for many important areas of chemical investigation such as ion recognition and separation,[3,4] ion sensing and detection,[4,5] and construction of molecular devices.[4,6] The stability of a cation−coronand complex (a coronate)[3] is determined by the collective and cooperative interactions between the cation and each donor atom of the coronand, which competes with the cation−solvent interaction (solvation). Parameters that affect the value of the coronate stability constant (K) include the relative cation and coronand cavity sizes, number and stereochemical arrangement of coronand donor atoms, substitution on the macrocycle ring, charge number of cation, counterion electrostatic interactions, and solvent donicity.[1−3] For a specific type of coronands such as *N*-aryl-substituted monoaza-15-crown-5 (A15C5), more coronate stability-correlated parameters have been derived, including the sum of bond angles about the amino nitrogen,[7] the NMR chemical shifts of the *N*-phenyl and crown protons,[8] and the calculated charge density on the dimethylamino group.[9]

Understanding of the difference in electronic nature of the donor atoms in coronands vs coronates is particularly important in understanding how the cation−coronand interactions govern the spectral changes of coronand-based intrinsic chromo-/fluoroionophores. For example, in many monoazacrown-derived systems (e.g., compound $\mathbf{1A_5}$) the azacrown nitrogen donor is directly integrated with the aromatic chromo-/fluorophore. As a result, the spectroscopic behavior is expected to be affected more by the nitrogen than the oxygen donors of the azacrown moiety. The event of cation binding modulates the electronic nature of the nitrogen donor and concomitantly the electronic structure of the chromo-/fluorophore. The intrinsic difference in absorption/emission properties between the ion-free (a molecule) and the ion-bound (a supermolecule) species thus dictates the chromo-/fluoroionophoric behavior, namely the size and direction of

---

† This paper is dedicated to Professor Kwang-Ting Liu on the occasion of his 65th birthday.

(1) Izatt, R. M.; Bradshaw, J. S.; Nielsen, S. A.; Lamb, J. D.; Christensen, J. J. *Chem. Rev.* **1985**, *85*, 271−339 and references therein.

(2) Vögtle, F.; Weber, E. *Crown Ethers and Analogues*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Avon, UK, 1989; Chapter 4.

(3) Gokel, G. W. *Crown Ethers and Cryptands*; Royal Society of Chemistry: Letchworth, UK, 1991.

(4) *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vogtle, F., Lehn, J.-M., Eds.; Pergamon: Oxford, UK, 1996; Vols. 1 and 10.

(5) (a) De Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515−1566. (b) Valeur, B.; Leray, I. *Coord. Chem. Rev.* **2000**, *205*, 3−40. (c) Bricks, J. L.; Slominskii, J. L.; Kudinova, M. A.; Tolmachev, A. I.; Rurack, K.; Resch-Genger, U.; Rettig, W. *J. Photochem. Photobiol. A*: *Chem.* **2000**, *132*, 193−208.

(6) Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res.* **1998**, *31*, 405−414.

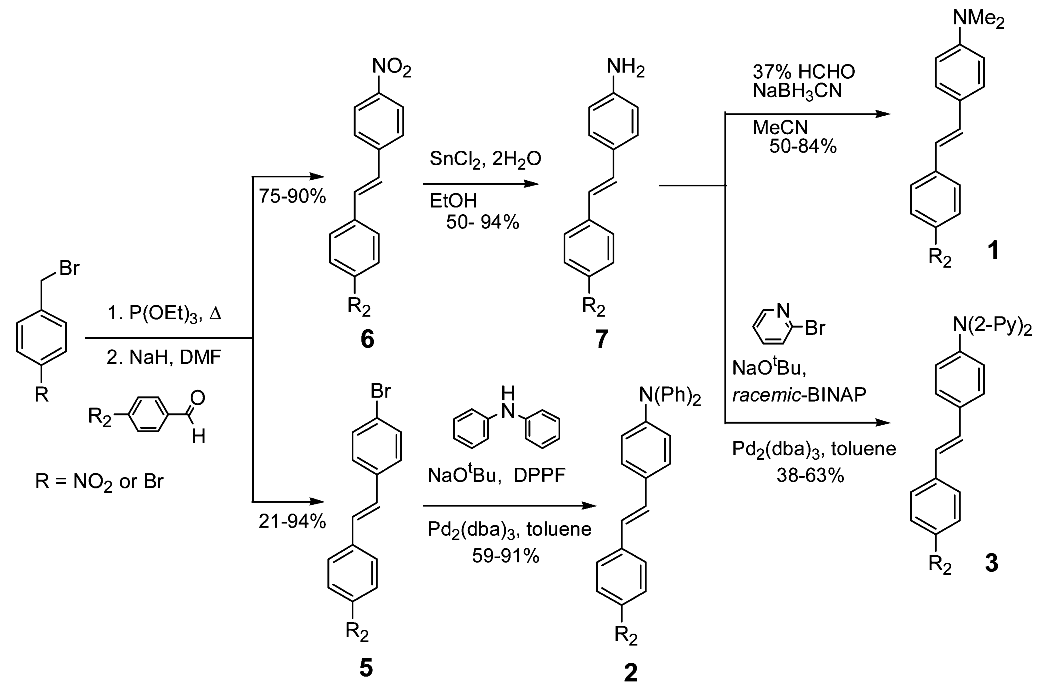
(7) Jonker, S. A.; Van Dijk, S. I.; Goubitz, K.; Reiss, C. A.; Schuddeboom, W.; Verhoeven, J. W. *Mol. Cryst. Liq. Cryst.* **1990**, *183*, 273−282.

(8) Fery-Forgues, S.; Bourson, J.; Dallery, L.; Valeur, B. *New J. Chem.* **1990**, *14*, 617−623.

(9) Rurack, K.; Sczepan, M.; Spieles, M.; Resch-Genger, U.; Rettig, W. *Chem. Phys. Lett.* **2000**, *320*, 87−94.

10.1021/jo035462k CCC: $27.50

SCHEME 1



both wavelength shifts and intensity variations. Although a correlation between the *K* values or related parameters and the size of cation-induced spectral shifts has been successful and meaningful for a particular probe that interacts with different cations,[7,8,10] such a correlation could not apply to the situation of a group of different probes. For one reason, the *K* value is a measure of the collective cation−coronand interactions and does not necessarily reflect the relative extent of electronic perturbation on the particular donor atom(s) that is also a part of the chromo-/fluorophore (e.g, the azacrown N atom in $\mathbf{1A_5}$). In addition, the cation−coronand interactions could be affected upon electronic excitation of the fluorophore with an extent depending on the nature of the fluorophore. For instance, a weakening of the cation−nitrogen interactions has been noticed for donor (azacrown)− or donor−acceptor-type systems (e.g., $\mathbf{4A_5}$) in the excited state on the basis of a much less binding-induced shift in emission vs absorption bands.[11−13] In contrast, the fluorescence response is significant in donor (azacrown)−donor-type systems (e.g., $\mathbf{1A_5}$), presumably due to the difference in the photoinduced internal charge transfer (ICT) process, where the ion-bound azacrown nitrogen no longer behaves as an electron donor.[14] In this context, it is desired to have a direct definition of the electronic character of the coronate donor atoms in both the ground and the excited states in order to gain insight into the observed chromo-/fluoroionophoric behavior among different systems.

As demonstrated by the donor−donor stilbenes $\mathbf{1A_5}$−$\mathbf{3A_5}$ and $\mathbf{1A_6}$−$\mathbf{3A_6}$, we report herein an approach toward an anatomy of the cation-modulated electronic properties of the nitrogen donor in A15C5- and monoaza-18-crown-6 (A18C6)-derived intrinsic probes by electronic spectroscopic correlations of the ion-bound supermolecules with structurally related but “uncrowned” molecules. We have observed that both the absorption and fluorescence properties of supermolecules $\mathbf{1A_5}$/Ca^{2+}−$\mathbf{3A_5}$/Ca^{2+} and $\mathbf{1A_6}$/Ba^{2+}−$\mathbf{3A_6}$/Ba^{2+} closely resemble those of the corresponding Cl-substituted molecules (**1C**−**3C**) in acetonitrile despite the distinct fluoroionophoric behavior displayed by each probe. The similarity in electronic properties for $\mathbf{1A_5}$/Ca^{2+}−$\mathbf{3A_5}$/Ca^{2+} and **1C**−**3C** in acetonitrile-d_6 is further supported by the similar ^{1}H NMR chemical shifts of the stilbene protons. Spectroscopic correlations between $\mathbf{1A_5}$/Na$^+$−$\mathbf{2A_5}$/Na$^+$ and $\mathbf{1A_6}$/K$^+$−$\mathbf{2A_6}$/K$^+$ and **1C**−**2C** in dichloromethane are also observed. Implications of such correlations in metal ion−azacrown interactions and the fluoroionophoric behavior of A15C5- and A18C6-derived intrinsic probes will be discussed.

Results and Discussion:

Synthesis. As shown in Scheme 1, the synthesis of compound series **1**−**3** started with the conventional Wittig[15] or Horner−Wadsworth−Emmons[16] reactions for the construction of the 4,4′-disubstituted *trans*-stilbene backbone bearing a bromo or nitro group along with the desired R$_2$ substituents **A**−**I** (**5** and **6**). The starting

---

[10] Rurack, K.; Bricks, J. L.; Reck, G.; Radeglia, R.; Resch-Genger, U. *J. Phys. Chem. A* **2000**, *104*, 3087−3109.

[11] (a) Létard, J.-F.; Lapouyade, R.; Rettig, W. *Pure Appl. Chem.* **1993**, *65*, 1705−1712. (b) Dumon, P.; Jonusauskas, G.; Dupuy, F.; Pée, P.; Rullière, C.; Létard, J.-F.; Lapouyade, R. *J. Phys. Chem.* **1994**, *98*, 10391−10396. (c) Mathevet, R.; Jonusauskas, G.; Rullière, C.; Létard, J.-F.; Lapouyade, R. *J. Phys. Chem.* **1995**, *99*, 15709−15713.

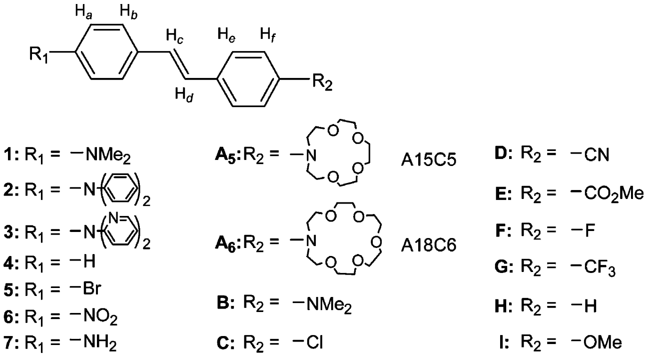
[12] (a) Crochet, P.; Malval, J.-P.; Lapouyade, R. *Chem. Commun.* **2000**, 289−290. (b) Rurack, K.; Rettig, W.; Resch-Genger, U. *Chem. Commun.* **2000**, 407−408.

[13] (a) Rurack, K.; Koval’chuck, A.; Bricks, J. L.; Slominskii, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 6205−6206. (b) Malval, J.-P.; Gosse, I.; Morand, J.-P.; Lapouyade, R. *J. Am. Chem. Soc.* **2002**, *124*, 904−905.

[14] Delmond, S.; Létard, J.-F.; Lapouyade, R.; Mathevet, R.; Jonusauskas, G.; Rullière, C. *New J. Chem.* **1996**, *20*, 861−869.

[15] Maercker, A. *Org. React.* **1965**, *14*, 270−490.

[16] Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73−253.



materials of A15C5- and A18C6-substituted benzaldehyde were prepared according to the method of Dix and Vögtle.[17] A reduction of the nitro group in **6** by tin(II) chloride produced compound **7**,[18] which was followed by *N*-methylation[19] with formaldehyde and sodium cyanoborohydride and by *N*-arylation[20] with palladium catalyst and phosphine ligands to form compounds **1** and **3**, respectively. The corresponding Pd-catalyzed amination reaction between **5** and diphenylamine afforded compound **2**. Typical synthetic procedures and related discussion have been previously reported for the preparation of **2H**[21] and **3H**.[22]

Photophysical Properties of Aminostilbenes. The spectroscopy and excited-state behavior of diaminostilbenes **1A$_5$** and **1B** in acetonitrile have been previously investigated.[14,23,24] Despite the structural symmetry, **1B** exhibits a fairly large excited-state dipole moment (6−9 D),[23] indicating the presence of strong ICT upon electronic excitation. Both the absorption and emission spectra of **1A$_5$** are similar to those of **1B**, which suggests that the A15C5 oxygen donors in **1A$_5$** have little electronic effect on the diaminostilbene fluorophore. Likewise, the electronic spectra of **2A$_5$** and **3A$_5$** are similar to those of **2B** and **3B**, respectively (Table 1). The fluorescence quantum yields (Φ_f) and lifetimes (τ_f) of compounds **1A$_5$**−**3A$_5$** are also similar to those of **1B**−**3B**, although the corresponding values are slightly larger in the former compounds. A larger value of Φ_f or τ_f for the A15C5- vs the dimethylamino (DMA)-substituted compounds has been observed in other systems and attributed to a reduced mobility of the bulkier A15C5 vs DMA donor group.[10,25]

TABLE 1. Maxima of UV−Vis Absorption (λ_{Abs}) and Fluorescence (λ_f), Stokes Shifts ($\Delta\nu_{st}$), Fluorescence Decay Times (τ_f), and Fluorescence Quantum Yields (Φ_f) for 1−4 and Some of Their Metal Ion Complexes in Acetonitrile at Room Temperature (ca. 298 K)^a

compd	λ_{abs} (nm)	λ_f (nm)	$\Delta\nu_{st}$ (cm^{-1})^b	Φ_f (%)	τ_f (ns)
1A$_5$	367^c	416, 434^c	3438	59^d	1.01^d
1A$_5$/Ca^{2+}	360^c	452^c	5654	8^c	0.28
1A$_6$	367	420	3438	52	1.25
1A$_6$/Ba^{2+}	358	455	5955	8	0.35
1B	366^e	422^e	3626	57^e	1.07^d
1C	357	455	6033	5	0.25
2A$_5$	378	440	3728	25	0.75
2A$_5$/Ca^{2+}	367	466	5789	42	2.78
2A$_5$/Ba^{2+}	370	457	5145		
2A$_5$/Mg^{2+}	375	449	4395		
2A$_6$	374	444	4215	26	0.73
2A$_6$/Ca^{2+}	365	463	5799		
2A$_6$/Ba^{2+}	366	465	5669	50	2.61
2A$_6$/Mg^{2+}	371	463	5356		
2A$_6$/K$^+$	373	453	4735		
2B	375	442	4042	21	0.68
2C	368	469	5852	43	2.86
2D	388	521	6579	17	2.78
2E	383	516	6730	18	2.83
2F	361	456	5771	53	2.81
2G	373	494	6567	30	2.88
2H	362	455	5646	51	2.55
2I	361	439	4922	62	2.44
3A$_5$	371	447	4583	12	0.47
3A$_5$/Ca^{2+}	342	424	5655	42	1.24
3A$_6$	370	447	4656	11	0.58
3A$_6$/Ba^{2+}	343	426	5680	40	1.32
3B	368	449	4902	10	0.44
3C	343	423	5514	45	1.26
4A$_5$	356^f	437^f	5207	1^f	
4A$_5$/Ca^{2+}	308^f	424^f	8883	1^f	
4C	298,311	339,353	3896		

^{a} Data were collected from sample solutions prepared under atmosphere without degassing or inert gas bubbling. ^{b} $\Delta\nu_{st} = \nu_{abs} - \nu_{fl}$ of spectral maxima or weighted maxima. ^{c} Data from ref 14. ^{d} Data from this work. ^{e} Data from ref 23a. ^{f} Data from ref 11b.

An increase of the ring size on going from A15C5 to A18C6 (i.e., **1A$_5$**−**3A$_5$** vs **1A$_6$**−**3A$_6$**) only slightly affects the photophysical properties of diaminostilbenes (Table 1). This could be attributed to a small increase in the C−N twist angle between the phenyl and the azacrown CNC planes as a result of the increased steric hindrance between the ortho hydrogens on the stilbene (H$_f$) and the methylene groups in the azacrown.[26] An increase in the twist angle is expected to cause a reduction in the electron-donating ability of the azacrown nitrogen and in the π-conjugation length of the fluorophore. This is consistent with the observation of a slightly blue-shifted absorption but red-shifted fluorescence for **1A$_6$**−**3A$_6$** vs **1A$_5$**−**3A$_5$**.

As shown in Table 1, a replacement of one of the two DMA groups in **1B** by a diphenylamino (**2B**) or a dipyridylamino (**3B**) group results in a dramatic change in spectroscopic behavior. In comparison to those of **1B**, both the absorption and emission spectra of **2B** and **3B** are red-shifted due to the increase in π-conjugation length of the chromophores.[21] On the basis of the size of the Stokes shift, the relative extent of photoinduced ICT character is **3B** > **2B** > **1B**. The reverse trend is observed for their fluorescence quantum yield and lifetimes (i.e., **1B** > **2B** > **3B**). Since intersystem crossing has been shown to be efficient for **1B**[24] and **2H**[21] in both polar and nonpolar solvents, the reduced fluorescence efficiency of **2B** and **3B** vs **1B** could be in part attributed to an increased rate in intersystem crossing as a result of a decreased singlet−triplet energy gap.

---

(17) Dix, J. P.; Vögtle, F. *Chem. Ber.* **1980**, *113*, 457−470.

(18) Bellamy, F. D.; Ou, K. *Tetrahedron Lett.* **1984**, *25*, 839−842.

(19) Borch, R. F.; Hassid A. I. *J. Org. Chem.* **1972**, *37*, 1673−1674.

(20) (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805−818. (b) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046−2067.

(21) Yang, J.-S.; Chiou, S.-Y.; Liau, K.-L. *J. Am. Chem. Soc.* **2002**, *124*, 2518−2527.

(22) Yang, J.-S.; Lin, Y.-H.; Yang, C.-S. *Org. Lett.* **2002**, *4*, 777−780.

(23) (a) Létard, J.-F.; Lapouyade, R.; Rettig, W. *J. Am. Chem. Soc.* **1993**, *115*, 2441−2447. (b) Létard, J.-F.; Lapouyade, R.; Rettig, W. *Chem. Phys. Lett.* **1994**, *222*, 209−216.

(24) Lewis, F. D.; Weigel, W.; Zuo, X. *J. Phys. Chem. A* **2001**, *105*, 4691−4696.

(25) Lednev, I. K.; Ye, T.-Q.; Hester, R. E.; Moore, J. N. *J. Phys. Chem. A* **1997**, *101*, 4966−4972.

(26) Létard, J.-F.; Delmond, S.; Lapouyade, R.; Braun, D.; Rettig, W.; Kreissler, M. *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 517−527.

It has been shown that the photophysical behavior of *trans*-4,4′-disubstituted stilbenes containing a DMA group such as **1C**, **1D**, **1E**, and **1I** is strongly dependent on the other substituent.[27] A nice correlation between the fluorescence quantum yield and the Hammett σ-constants has been observed: the stronger the "push−pull" character of the stilbene is, as defined by the electronic difference between the two substituents, the smaller the fluorescence quantum yield becomes.[26] Such a feature is essentially retained for the diphenylamino-substituted analogues, i.e., compounds **2B**−**2I**. It should be noted that the one having the largest fluorescence quantum yield in the compounds **1** series is **1B** but it is **2I** in the compounds **2** series (Table 1). In addition, the fluorescence quantum yield is generally larger for **2C**−**2I** than **1C**−**1I**, which could be attributed to the "amino conjugation effect".[21] A more detailed discussion of such an effect for **1H** and **2H** has been recently reported.[21] Since this effect is associated with the double bond torsion in the singlet state, the singlet-state mechanism for trans → cis photoisomerization appears to be important in these aminostilbenes, consistent with the previous conclusion based on **1C** and **1I**.[27] It also should be noted that the fluorescence lifetimes are much less sensitive to substitution than the fluorescence quantum yields in both systems **1** and **2**.

The spectroscopic data for compounds **1** and **2** determined in less polar dichloromethane solvent are shown in Table 2. When compared with the corresponding data in acetonitrile, the position of the absorption is slightly red shifted by 3−6 nm (negative solvatochromism), but the shift for the fluorescence is relatively larger and hypsochromic (positive solvatofluorochromism). A similar solvent effect has been observed for **1A**$_5$ and *trans*-4,4′-diaminostilbene.[14,28] The solvent effect on the fluorescence position is consistent with the significantly larger ICT character of these aminostilbenes in the excited vs ground state. As for the fluorescence quantum yields and lifetimes, the values are decreased for **1A**$_5$, **1A**$_6$, and **1B** but increased for **2A**$_5$−**2I** on going from acetonitrile to dichloromethane. A strongly fluorescent twisted ICT state (TICT) has been proposed to participate in the excited states of **1A**$_5$ and **1B**.[14,23] The difference in solvent effect between compounds **1** and **2** might result from a different role of such a TICT state. More investigation of this issue is required to reach a pertinent conclusion.

Complexation Behavior of 1A$_5$−3A$_5$ and 1A$_6$−3A$_6$. The effect of the alkali and alkaline earth metal ions Li$^+$, Na$^+$, K$^+$, Mg^{2+}, Ca^{2+}, and Ba^{2+} in perchlorate salts on the electronic absorption and emission spectra of **1A**$_5$−**3A**$_5$ and **1A**$_6$−**3A**$_6$ in acetonitrile has been investigated. The spectra are slightly or not at all affected by the monovalent alkali metal ions, and the largest spectral shifts for **1A**$_5$−**3A**$_5$ and **1A**$_6$−**3A**$_6$ are induced by Ca^{2+} and Ba^{2+}, respectively, in accord with the selectivity previously observed for other azacrown-derived systems.[17,26,29,30] Figure 1 shows the absorption and fluorescence spectra of **1A**$_5$−**3A**$_5$ in acetonitrile in the absence and the presence of excess Ca^{2+} (~100 equiv). In agreement with the previous report,[11] the absorption spectrum of **1A**$_5$ is blue shifted in the presence of Ca^{2+}, due to the azacrown nitrogen−Ca^{2+} interactions that reduce the chromophoric π-system, and the corresponding fluorescence spectrum is red shifted, due to the increased ICT character in the excited state. While the absorption spectra of **2A**$_5$ and **3A**$_5$ are also blue-shifted upon the addition of Ca^{2+}, the fluorescence shifts to the red for **2A**$_5$ but to the blue for **3A**$_5$. Furthermore, unlike the Ca^{2+}-induced fluorescence intensity weakening and fluorescence lifetime shortening in **1A**$_5$, the Ca^{2+}-binding of **2A**$_5$ and **3A**$_5$ leads to fluorescence enhancement by a factor of 1.7−3.5 and lifetime increase by a factor of 2.6−3.7. It is interesting to note that the chromo-/fluoroionophoric behavior of **1A**$_6$−**3A**$_6$ to Ba^{2+} closely resembles that of **1A**$_5$−**3A**$_5$ to Ca^{2+} (Table 1). In other words, the electronic effect exerted by A15C5/Ca^{2+} is similar to that exerted by A18C6/Ba^{2+} for the fluorophores **1**−**3**.

TABLE 2. Maxima of UV−Vis Absorption (λ_{abs}) and Fluorescence (λ_f), Stokes Shifts ($\Delta\nu_{st}$), Fluorescence Decay Times (τ_f), and Fluorescence Quantum Yields (Φ_f) for 1−4 and Some of Their Metal Ion Complexes in Dichloromethane at Room Temperature (ca. 298 K)[a]

compd	λ_{abs} (nm)	λ_f (nm)	$\Delta\nu_{st}$ (cm^{-1})[b]	Φ_f (%)	τ_f (ns)
1A$_5$	370	414	2872	28	0.85
1A$_5$/Ca^{2+}	363	445	5076	8	0.29
1A$_5$/Na$^+$	362	433	4530	6	0.34
1A$_6$	369	417	3119	29	0.90
1A$_6$/Ba^{2+}	361	441	5025	10	0.33
1A$_6$/K$^+$	363	435	4560	9	0.66
1B	369	415	3004	29	0.91
1C	362	436	4689	6	0.23
2A$_5$	382	428	2814	46	1.02
2A$_5$/Ca^{2+}	374	464	5186	55	2.47
2A$_5$/Ba^{2+}	375	464	5115	73	2.38
2A$_5$/Mg^{2+}	380	465	4810		
2A$_5$/Na$^+$	374	449	4466	54	2.30
2A$_5$/K$^+$	381	432	3099		
2A$_6$	381	429	2937	52	0.88
2A$_6$/Ca^{2+}	373	457	4928	70	1.85
2A$_6$/Ba^{2+}	374	458	4904	74	2.63
2A$_6$/Na$^+$	375	443	4094		
2A$_6$/K$^+$	373	450	4587	62	2.13
2B	380	428	2951	40	0.91
2C	373	452	4686	58	2.46
2D	395	503	5436	31	2.40
2E	388	501	5813	30	2.08
2F	366	445	4850	62	2.60
2G	379	477	5421	42	2.46
2H	366	442	4698	58	2.53
2I	367	434	4206	63	2.37

[a] Data were collected from sample solutions prepared under atmosphere without degassing or inert gas bubbling. [b] $\Delta\nu_{st} = \nu_{abs} - \nu_{fl}$ of spectral maxima.

The complex stability constants, expressed as log*K*, determined by absorption titration spectra[31] for **1A**$_5$−**3A**$_5$ and **1A**$_6$−**3A**$_6$ with Na$^+$, K$^+$, Ca^{2+}, and Ba^{2+} in acetonitrile are shown in Table 3. Despite the distinct fluorescence responses (position, intensity, and lifetime) of **1A**$_5$−**3A**$_5$ to Ca^{2+}, the log*K* values of **1A**$_5$/Ca^{2+}−**3A**$_5$/Ca^{2+} are only

---

(27) Papper, V.; Pines, D.; Likhtenshtein, G.; Pines, E. *J. Photochem. Photobiol. A: Chem.* **1997**, *111*, 87−96.

(28) Zhao, Y.; Khodorkovsky, V.; Cohen, J.; Priel, Z. *J. Photochem. Photobiol. A: Chem.* **1996**, *99*, 23−28.

(29) Rurack, K. *Spectrochim. Acta A* **2001**, *57*, 2161−2195.

(30) (a) Löhr, H.-G.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65−72. (b) Fery-Forgues, S.; Le Bris, M.-T.; Guetté, J.-P.; Valeur, B. *J. Phys. Chem.* **1988**, *92*, 6233−6237. (c) Cazaux, L.; Faher, M.; Lopez, A.; Picard, C.; Tisnes, P. *J. Photochem. Photobiol. A: Chem.* **1994**, *77*, 217−225.

(31) Connors, K. A. *Binding Constants—The Measurement of Molecular Complex Stability*; John Wiley & Sons: New York, 1987; Chapter 4.

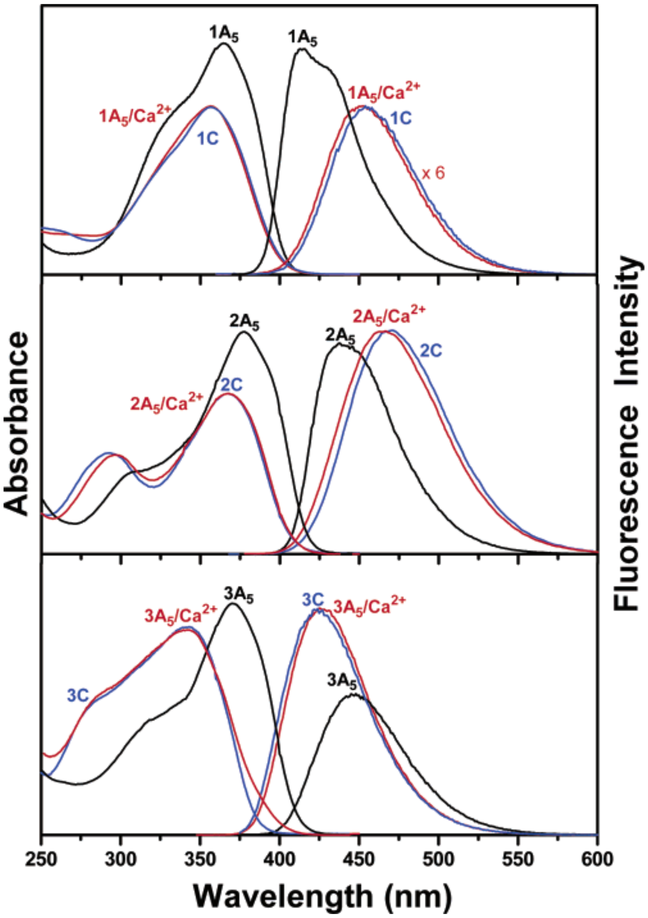


FIGURE 1. Absorption and fluorescence (λ_{ex} = 365 nm) spectra of (A) **$1A_5$**, **$1A_5$**/Ca^{2+}, and **1C**, (B) **$2A_5$**, **$2A_5$**/Ca^{2+}, and **2C**, and (C) **$3A_5$**, **$3A_5$**/Ca^{2+}, and **3C** in acetonitrile.

TABLE 3. Complex Stability Constants (log *K*) of $1A_5$–$3A_5$ and $1A_6$–$3A_6$ in Acetonitrile[a]

compd	Na^+	K^+	Ca^{2+}	Ba^{2+}
$1A_5$	3.4 (5.2)	n.d.	4.9[b] (5.7)	4.5
$2A_5$	3.6 (5.1)	n.d	4.8 (5.4)	4.4
$3A_5$	3.9	n.d	4.7	4.7
$1A_6$	n.d.	4.5 (5.0)	5.4	5.4
$2A_6$	n.d.	4.2 (4.8)	5.1	5.1
$3A_6$	n.d.	4.5	4.9	5.0

[a] The values given in parentheses were determined in dichloromethane. [b] Data from ref 14.

TABLE 4. Chemical Shifts[a] **of Stilbene Protons (H_a–H_f) from the ^1H NMR Spectra (500 MHz) of 1–3 (2 mM)**[b] **in Acetonitrile-d_3**

compd	δH_a	δH_b	δH_c	δH_d	δH_e	δH_f
$1A_5$	6.72	7.35	6.85	6.85	7.32	6.66
1B	6.72	7.35	6.86	6.86	7.35	6.72
1C	6.74	7.41	6.93	7.10	7.48	7.33
$1A_5$/Ca^{2+}	6.73	7.40	6.95	7.08	7.54	7.27
$2A_5$	6.98	7.41	6.99	6.90	7.36	6.68
2B	6.98	7.40	6.99	6.92	7.39	6.73
2C	6.99	7.45	7.06	7.15	7.51	7.36
$2A_5$/Ca^{2+}	6.98	7.45	7.07	7.14	7.57	7.29
$3A_5$	7.00	7.49	7.06	6.94	7.38	6.70
3B	7.00	7.49	7.07	6.97	7.41	6.74
3C	7.00	7.53	7.13	7.20	7.54	7.37
$3A_5$/Ca^{2+}	6.98	7.55	7.15	7.18	7.59	7.30

[a] Data were recorded with respect to the solvent peak at δ 1.93 ppm. [b] The mole ratio of **$1A_5$–$3A_5$**:Ca^{2+} is 1:100.

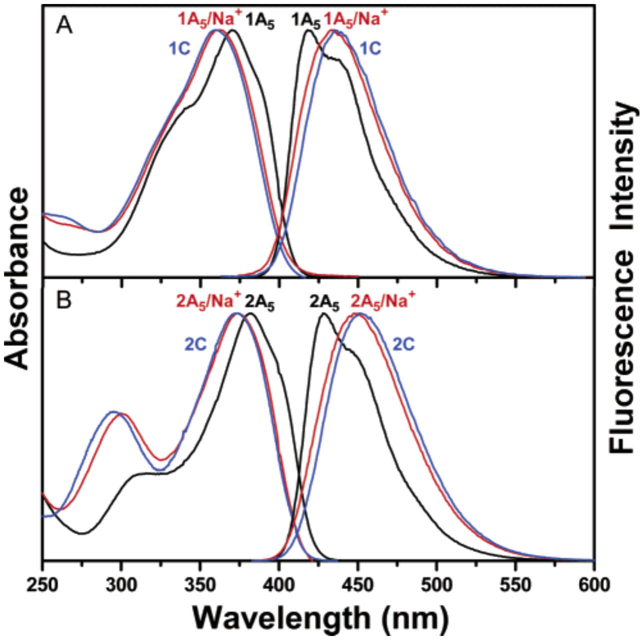


FIGURE 2. Normalized absorption and fluorescence spectra of (A) **$1A_5$**, **$1A_5$**/Na^+, and **1C** and (B) **$2A_5$**, **$2A_5$**/Na^+, and **2C** in dichloromethane.

slightly different from one another. The similarity in log*K* value for **$1A_5$**/Ca^{2+}–**$3A_5$**/Ca^{2+} is also consistent with the similar Ca^{2+}-induced shifts in their ^1H NMR spectra. According to Fery-Forgues et al. on the studies of 4-substituted Ph-A15C5 derivatives,[8] the difference between the Ca^{2+}-induced change in the chemical shift of the ortho and that of meta protons, i.e., $[\Delta\delta(H_{ortho}) - \Delta\delta(H_{meta})]$, is proportional to their log*K* values. As shown in Table 4, the values of $[\Delta\delta(H_f) - \Delta\delta(H_e)]$ are nearly the same (0.39–0.40 ppm) in all three cases. Apparently, the N-substituents in the R_1 group merely cause a small influence on the A15C5–Ca^{2+} interactions. Therefore, the observed difference in fluoroionophoric behavior among **$1A_5$–$3A_5$** should simply result from the intrinsic difference in the fluorophores (vide infra). In comparison, complexes **$1A_6$**/Ba^{2+}–**$3A_6$**/Ba^{2+} possess larger log*K* values, which could be attributed to the larger number of donor atoms in A18C6 vs A15C5. It is also noted that **$1A_5$–$3A_5$** show a larger selectivity than **$1A_6$–$3A_6$** toward Ca^{2+} and Ba^{2+}.

The chromo-/fluoroionophoric behavior of **$1A_5$**, **$2A_5$**, **$1A_6$**, and **$2A_6$** in less polar dichloromethane solvent has also been investigated (Figure 2). The corresponding studies on **$3A_5$** and **$3A_6$** were not performed, because in dichloromethane the interaction between the bis(2-pyridyl)amino (R_1) group and metal ions seems not negligible and might complicate the spectral analysis. As indicated by the larger log*K* values for the same complexes (Table 3), the cation–azacrown interactions are stronger in dichloromethane vs acetonitrile, due to the poorer cation solvation interactions. While this is accompanied by a larger spectral shift in the cases of the monovalent Na^+ and K^+, the spectral shifts induced by the divalent ions Ca^{2+} and Ba^{2+} are decreased (Table 2). As a result, the cation selectivity by these fluoroionophores is decreased. For example, the spectra of both **$2A_5$** and **$2A_6$** could not differentiate Ca^{2+} from Ba^{2+}, and the absorption shifts induced by Na^+, K^+, Ca^{2+}, and Ba^{2+} are essentially the same for **$2A_6$** in dichloromethane. Like the cases between **$1A_5$**/Ca^{2+}−**$3A_5$**/Ca^{2+} and **$1A_6$**/Ba^{2+}−**$3A_6$**/Ba^{2+} in acetonitrile, the spectroscopic properties of **$1A_5$**/Na^+ and **$2A_5$**/Na^+ closely resemble those of **$1A_6$**/K^+ and **$2A_6$**/K^+, respectively, in dichloromethane.

Supermolecule−Molecule Correlation and Its Implications. In addition to the above-mentioned correlations between different complexes, spectroscopic correlations between complexes (supermolecules) and molecules are also observed. As demonstrated by complexes **$1A_5$**/Ca^{2+}−**$3A_5$**/Ca^{2+} in acetonitrile, their spectroscopic data are in great similarity, with a difference within the experimental uncertainties (i.e., ±2 nm in λ_{abs} and λ_{fl}, ±10% in Φ_f, and ±0.10 ns in τ_f) to those for the corresponding Cl-derivatives **1C**−**3C** (Table 1 and Figure 1). Such results suggest that the interactions between Ca^{2+} and the A15C5 nitrogen atom in acetonitrile are all similar in **$1A_5$**/Ca^{2+}−**$3A_5$**/Ca^{2+}, consistent with their similar log$K$ values (Table 3), and that the Ca^{2+}-modulated nitrogen atom in A15C5/Ca^{2+} has an electronic nature corresponding to a chlorine atom. In particular, such a correlation exists in the excited state as well as in the ground state, indicating that electronic excitation of the fluorophores has a negligible effect on the interactions between A15C5 and Ca^{2+}, and the complexes are essentially stable during their excited-state lifetimes (0.28−2.78 ns). On the basis of the Hammett substituent constants,[32] the electronic character of a p-Cl substituent ($\sigma = 0.23$) is electron withdrawing with a strength between that of a p-F ($\sigma = 0.06$) and a p-carbonyl ester group ($\sigma = 0.50$) and is very different from that of an electron-donating p-amino group ($\sigma = -0.66$). The dependence of the spectroscopic properties of 4,4′-disubstituted aminostilbenes on the R_2 substituent could be illustrated by the comparison of compounds **2A**−**2I** (Table 1). Thus, it is such a difference between **$1A_5$**−**$3A_5$** and the corresponding **1C**−**3C** that determines the observed chromo-/fluoroionophoric behavior for **$1A_5$**−**$3A_5$** upon interacting with Ca^{2+} in acetonitrile. Likewise, a spectroscopic correlation of **$1A_6$**/Ba^{2+}−**$3A_6$**/Ba^{2+} ∼ **1C**−**3C** in acetonitrile also exists. In dichloromethane, the azacrown nitrogen in A15C5/Ca^{2+} and A18C6/Ca^{2+} has an induction strength larger than that of Cl but lower than that of CF_3 based on the relative fluorescence position of the complexes **$2A_5$**/Ca^{2+} and **$2A_6$**/Ba^{2+} and compounds **2A**−**2I** (Table 2). However, the substituent effect of A15C5/Na^+ and A18C6/K^+ reaches a level similar to that of Cl in dichloromethane, i.e., **$1A_5$**/Na^+−**$2A_5$**/Na^+ ∼ **$1A_6$**/K^+−**$2A_6$**/K^+ ∼ **1C**−**2C** (Figure 2).

The ground-state electronic correlation between **$1A_5$**/Ca^{2+}−**$3A_5$**/Ca^{2+} and **1C**−**3C** in acetonitrile-d_3 is further supported by ^1H NMR spectroscopy. As is depicted by the case of **$3A_5$** (Figure 3), the introduction of Ca^{2+} leads to a significant downfield shifting ($\Delta\delta = 0.60$ ppm) of the stilbene protons (H_f) localized in the ortho position to the A15C5. The extent of downfield shifting decreases for those (H_b−H_e) at farther distances than H_f to the A15C5 and becomes negligible for the protons (H_a) near the dipyridylamino group (Table 4). The chemical shifts of the pyridyl protons are either unchanged or slightly shifted, which supports our previous conclusion based on **3H** that interactions between the dipyridylamino group and Ca^{2+} in acetonitrile are negligible.[22] In accord with the electronic spectra, the ^1H NMR spectrum of **3C** resembles that of **$3A_5$**/Ca^{2+} with a small deviation (0.02−0.07 ppm) comparable to that (0−0.04 ppm) between the spectra of **$3A_5$** and **3B**. It should be noted that a chemical shift can be affected not only by the electronic inductive and resonance properties but also by the size and anisotropy of substituents. Thus, the observed ^1H NMR correlation between **1C**−**3C** and **$1A_5$**/Ca^{2+}−**$3A_5$**/Ca^{2+} is remarkable in view of their dramatic differences in size and anisotropy (sphere vs bulky nonsphere shape).

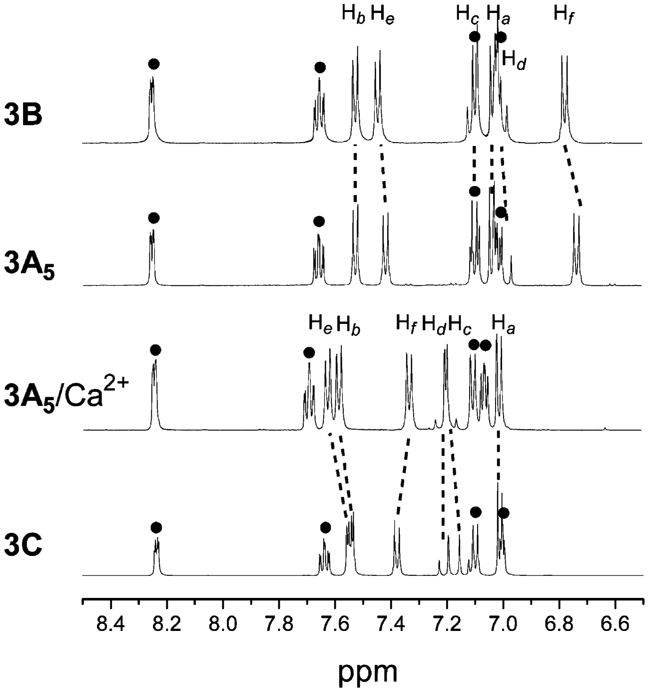


FIGURE 3. ^1H NMR spectra (500 MHz) of **$3A_5$**, **3B**, **3C**, and **$3A_5$**/Ca^{2+} in acetonitrile-d_3. The substrate concentration is ca. 2 mM. The solid circles denote peaks due to the N-pyridyl protons, and the dashed lines are to correlate the stilbene protons.

In principle, the interactions of cations with azacrown ether will reduce the electron-donating strength of the nitrogen atom, and the maximum effect will occur when the nitrogen atom becomes a fully charged ammonium ion. A continued spectrum of electronic character ranging from the unperturbed amino group to the fully charged ammonium ion should exist for the cation-modulated nitrogen atom, depending on the extent of interactions, and, in turn, on those parameters that affect the complex stability constant. Thus, the spectroscopic properties of a complex could not always correlate with those of a molecule, because the number of molecular substituents with well-defined electronic effects is limited. Even worse, the substituent effect on the photophysical behavior of an aromatic system depends not only on the electron "push−pull" character but also on the size, bonding, and geometry of the substituent. For example, some molecular substituents such as Br, I, carbonyl, and nitro groups are know to facilitate intersystem crossing of the excited fluorophore (e.g., stilbene), leading to lower fluorescence

---

[32] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Happer & Row: New York, 1987; p 144.

quantum yields.[33] For substituents that possess π-conjugated bonding such as CN and carbonyl groups, the π-conjugation effect on the spectra often surpasses the induction effect (e.g., the fluorescence maximum **2D** (521 nm) > **2A$_5$**/H$^+$ (492 nm) in acetonitrile). Moreover, some cations, particularly the paramagnetic cations (e.g., Ni^{2+} and Cu^{2+}), could interact with the excited fluorophore not only by electrostatic coordination but also by energy or electron transfer, leading to fluorescence quenching.[34] With these in mind, the nice supermolecule−molecule correlation in both positions of spectra and the yields and lifetimes of fluorescence for systems **1**−**3** appear to be novel and unique, and it is anticipated that changes in any one of the parameters (e.g., solvent and counterion) will remove the observed correlations: namely, A15C5/Ca^{2+}(ClO$_4^-$)$_2$ ∼ A18C6/Ba^{2+}(ClO$_4^-$)$_2$ ∼ Cl in acetonitrile and A15C5/Na$^+$(ClO$_4^-$) ∼ A18C6/K$^+$(ClO$_4^-$) ∼ Cl in dichloromethane.

Nonetheless, implications of these correlations deserve our attention. An electronic correlation of a nitrogen atom with a chlorine atom is reminiscent of their similarity in electronegativity (3.04 vs 3.16).[35] The main factor that differentiates the electronic effect of an amino group from that of a chloro substituent in aromatic compounds is the resonance effect of the lone pair electrons. A good overlap between the carbon and nitrogen 2p orbitals makes the amino group an excellent electron donor, whereas the poor overlap between the carbon 2p and chlorine 3p (or sp^3) orbitals keeps the chlorine atom as an electron-withdrawing substituent. In this context, a reduction in C−N orbital overlap will reduce the amino group resonance effect and meanwhile the difference in electronic effect between the amino nitrogen and the chlorine atom. This could be achieved by pyramidalizing (sp^3 hybridization) the nitrogen atom and/or by twisting the C−N bond. Indeed, an increase of the degree of pyramidalization of the azacrown nitrogen upon metal ion complexation has been observed in many other systems,[7−10,36] and the degree of pyramidalization in some cases correlates well with the chromoionophoric shift.[7] Azacrown-derived probes that undergo complexation-induced C−N twisting have also been reported.[37] Since the alkali and alkaline-earth metal ions that provide the strongest interactions for A15C5 and A18C6 are Ca^{2+} and Ba^{2+}, respectively, it appears that the maximum electrostatic perturbation of metal ions on the azacrown nitrogen in acetonitrile is to localize the nitrogen lone-pair electrons. Our results also suggest that a decrease in cation solvation on going from acetonitrile to dichloromethane strengthens the electrostatic interaction between the azacrown and the metal ions in such a way that Ca^{2+} and Ba^{2+} can further polarize the N−M^{2+} coordination bond and results in a partially positive-charged nitrogen, and that Na$^+$ and K$^+$ become capable of localizing the nitrogen lone pair electrons. Regarding the distinct size of azacrown vs Cl, the nice spectroscopic correlations observed herein indicate that the excited-state behavior of the cation-bound fluorophores **1**−**3** is insensitive to the motion of the cation-bound azacrown moiety.

For comparison, the spectroscopic properties of donor-substituted stilbene **4A$_5$**, its complex **4A$_5$**/Ca^{2+}, and **4C** in acetonitrile were also examined (Table 1). While the absorption maximum of **4A$_5$**/Ca^{2+} is approximately the same as that of **4C**, their fluorescence positions are rather different (Table 1).[38] The slightly lower value of log$K$ (4.4)[11] for **4A$_5$**/Ca^{2+} in comparison to that for **1A$_5$**/Ca^{2+}−**3A$_5$**/Ca^{2+} might indicate a slightly weaker interaction between Ca^{2+} and the azacrown nitrogen, but this appears not sufficient to account for the large discrepancies in fluorescence maximum (4744 cm^{-1}) between **4A$_5$**/Ca^{2+} and **4C**. Instead, a weakening of the Ca^{2+}−N bonding, resulting in a weaker electronic influence of Ca^{2+} on the azacrown nitrogen, on going from the ground state to the excited state is implicated. This is in accord with the previous studies on donor−donor- vs donor−(acceptor)-type ICT systems, where the latter systems, including **4A$_5$**/Ca^{2+}, are destined to undergo the excited-state Ca^{2+} decoordination reaction.[11−13]

Concluding Remarks

Novel spectroscopic correlations between metal ion-complexed supermolecules and structurally related molecules have been observed, including **1A$_5$**/Ca^{2+}−**3A$_5$**/Ca^{2+} ∼ **1A$_6$**/Ba^{2+}−**3A$_6$**/Ba^{2+} ∼ **1C**−**3C** in acetonitrile and **1A$_5$**/Na$^+$−**2A$_5$**/Na$^+$ ∼ **1A$_6$**/K$^+$−**2A$_6$**/K$^+$ ∼ **1C**−**2C** in dichloromethane. While comparisons between complexes and molecules in the ground state by ^{1}H NMR or UV−vis absorption spectroscopy have been previously performed for some azacrown-derived intrinsic fluoroionophores,[8,29] the correlations reported herein have for the first time allowed a more accurate description of the metal ion-modulated electronic character of the azacrown nitrogen in the excited state as well as in the ground state. A persistent correlation in both the absorption (ground state) and emission (excited state) spectra suggests that the cation−azacrown interactions in these donor−donor stilbenes are little affected by electronic excitation and the subsequent relaxation of the fluorophores. The similar complex stability constants but distinct fluoroionophoric behavior observed for systems **1**−**3** show that the N-substituents can strongly affect the intrinsic properties of the aminostilbene fluorophore but not the azacrown−metal ion interactions. With such correlations, the electronic nature of the metal ion-perturbed fluorophores could be further investigated based on the electronically correlated molecules, since both experimental and theoretical studies on a molecule vs supermolecule are more feasible. A modulation of the azacrown nitrogen with a character from strongly electron donating (free probe) to moderately electron withdrawing resembling a chlorine atom (complexed probe) appears to be sufficient for

---

(33) (a) Saltiel, J.; Sun, Y.-P. *Photochromism, Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, The Netherlands, 1990; pp 64−164. (b) Saltiel, J.; Charlton, J. L. *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, pp 25−89.

(34) Varnes, A. W.; Dodson, R. B.; Wehry, E. L. *J. Am. Chem. Soc.* **1972**, *94*, 946−950.

(35) *Handbook of Chemistry and Physics*; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1997.

(36) Alfimov, M. V.; Churakov, A. V.; Fedorov, Y. V.; Fedorova, O. A.; Gromov, S. P.; Hester, R. E.; Howard, J. A. K.; Kuz'mina, L. G.; Lednev, I. K.; Moore, J. N. *J. Chem. Soc., Perkin Trans. 2* **1997**, 2249−2256.

(37) Witulski, B.; Weber, M.; Bergsträsser, U.; Desvergne, J.-P.; Bassani, D. M.; Bouas-Laurent, H. *Org. Lett.* **2001**, *3*, 1467−1470.

(38) Compound **4C** shows vibronic structures in the electronic spectra. For the purpose of comparison with **4A$_5$**/Ca^{2+}, the weighted spectral maxima for the absorption and emission of **4C** were estimated to be ca. 308 and 350 nm, respectively.

creating a sensitive ICT-based probe in acetonitrile. However, the stability constant and thus the extent of electronic perturbation of metal ions on the azacrown nitrogen is expected to be substantially lower in aqueous solutions. A cooperative binding of the azacrown with other ligands in the probe molecule might be a solution for retaining or improving the metal ion−azacrown interactions in aqueous conditions. Azacrown ethers are also employed in forming fluoroionophores that signal the complexation event by the mechanism of photoinduced electron transfer (PET).[5] Since the energetics of PET from the azacrown nitrogen (donor) to the excited fluorophore (acceptor) depend on the electronic character of the nitrogen donor, our results also should be informative for the PET- and azacrown-based probes. Finally, it is interesting to point out that the knowledge of cation−coronand interactions in terms of selectivity and stability has offered a basis for the development of chromo-/fluoroionophores, and now our results show the feedback of these probes, providing a better understanding of the cation−coronand interactions in terms of the binding character between the cation and the donor atoms.

Experimental Section

Methods. The degassed solution of anthracene in hexane ($\Phi_f = 0.27$)[39] was used as standard for the fluorescence quantum yield determinations of systems **1**−**3** in normal atmosphere with solvent refractive index correction. All fluorescence spectra are uncorrected and an error of ±10% is estimated for the fluorescence quantum yields. The lifetime data were determined with excitation and emission wavelengths at the absorption and fluorescence maxima of the corresponding substrates. All the fluorescence decay curves can be fit with a single exponential. The goodness of nonlinear least-squares fit was judged by the reduced χ^2 value (<1.3 in all cases), the randomness of the residuals, and the autocorrelation function. Fluorescence and absorption titration spectra were recorded with 1×10^{-5} M acetonitrile or dichloromethane solutions for all cases. The fluorescence four-wall cuvette was charged with 3 mL of fluoroionophores and a magnetic stir bar. The acetonitrile solution of perchlorate salts used for complexation studies is at a concentration of 0.005 M. Aliquots of salt solution were added at the prescribed increments. Solutions were allowed to equilibrate for 15 min before the measurementwas taken. Experimentation with longer equilibration times did not produce noticeable differences. The spectroscopic properties of complexes were determined in the presence of excess metal ions (~100 equiv), which is beyond the ending of titration (<50 equiv), where no further shifts were observed in both the absorption and fluorescence spectra. Complex stability constants were determined based on the absorption titration curves.[31]

Materials. Solvents for organic synthesis were reagent grade or HPLC grade but all were HPLC grade for spectra and quantum yield measurements. Compounds **1A₅**,[8] **1B**,[40] **1C**,[27] **2D**,[41] **2H**,[22] **2I**,[41] **5B**,[27] **5C**,[42] **5D**,[43] **5E**,[44] **5F**,[45] **5H**,[22] **5I**,[46] **6B**,[27] **6C**,[27] **7B**,[27] and **7C**[27] have been previously reported, and our melting points and/or ^{1}H NMR spectra conform to the literature values. The characterization data for the other compounds are provided in the Supporting Information.

Acknowledgment. Financial support for this research was provided by the National Science Council (NSC 91-2113-M-008-011 and NSC 92-2113-M-008-006).

Supporting Information Available: Detailed characterization data and ^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035462K

---

(39) Dawson, W. R.; Windsor, M. W. *J. Phys. Chem.* **1968**, *72*, 3251−3260.

(40) Stewart, F. H. C. *J. Org. Chem.* **1961**, *26*, 3604−3605.

(41) Yang, J.-S.; Wang, C.-M.; Hwang, C.-Y.; Liau, K.-L.; Chiou, S.-Y. *Photochem. Photobiol. Sci.* **2003**, *2*, 1225−1231.

(42) Tewari, R. S.; Kumari, N.; Kendurkar, P. S. *J. Chem. Eng. Data* **1976**, *21*, 125−131.

(43) Bance, S.; Barber, H. J.; Woolman, A. M. *J. Chem. Soc.* **1943**, 1−4.

(44) Fuson, R. C.; Cooke, H. G., Jr. *J. Am. Chem. Soc.* **1940**, *62*, 1180−1183.

(45) Gascoyne, J. M.; Mitchell, P. J.; Phillips, L. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1051−1057.

(46) Diana, G. D.; Carabateas, P. M.; Johnson, R. E.; Williams, G. L.; Pancic, F.; Collins, J. C. *J. Med. Chem.* **1978**, *21*, 889−894.