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Fluorescent Photoinduced Electron Transfer (PET) Sensing Molecules with *p*-Phenylenediamine as Electron Donor

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Fluorescent photoinduced electron-transfer sensors were made from *p*-phenylenediamine-substituted azacrown ethers attached with a dansyl group, in which the *p*-phenylenediamine moiety serves as electron donor and the dansyl group acts as the acceptor. Chelation-enhanced fluorescence was observed upon addition of metal salts. Selective fluorescence response was observed for Mg^{2+} and/or Ca^{2+} versus Na^{+} and K^{+} due to size match and charge density sensitivity of the *p*-phenylenediamine moiety.

Introduction

Crown ethers are well-known for their excellent affinity toward alkali and alkaline earth metal cations.[1] Various fluorescent PET (photoinduced electron transfer) sensors have been made through the combination of a crown ether and a fluorophore.[2] In most cases the crown ether acts as the receptor and the crown ether nitrogen acts as the electron donor. TMPD (tetramethyl-*p*-phenylenediamine) is a very good electron donor, and is easily oxidized to a stable radical cation, the characteristic blue color of which is the so-called Würster's Blue.[3] Due to their unique electronic properties, TMPD and TAPD (tetraalkyl-*p*-phenylenediamine) derivatives have long been a subject for electrochemical and spectroscopic studies involving electron-transfer or charge-transfer processes.[4] Molecular devices, such as donor−acceptor systems, can be developed based on the electron-rich property of TAPD. We have recently made a number of TAPD-substituted monoazacrown and diazacrown ether derivatives through our new synthetic methodology.[5] Previous studies in our laboratory showed that a *p*-phenylenediamine moiety can be used as an electron donor, which efficiently quenches the fluorescence of an acceptor within the same molecule.[6] Fluorescence and electrochemical studies of our new crown ether derivatives indicate that *p*-phenylenediamine selectively responds to divalent metal cations versus monovalent metal cations.[7] Herein we report development and binding studies of new fluorescent PET molecules using TAPD as the electron donor and the dansyl group as the fluorescent probe. The purpose of this study was to establish proof of principle that a TAPD would indeed be a suitable donor for such systems, and for this reason we have used a well-known receptor/analyte combination (crown ether/metal cation).

Fluorescence Studies. Chart 1 summarizes all the dansyl derivatives we have studied. The dansyl group was chosen as the fluorophore because it has been widely used for fluorescent labeling of amines.[8] Attachment of the dansyl group to the corresponding amine was carried out through standard procedures.[9] Except for the control compound **1**, all other compounds bear a TAPD moiety as the electron donor on the structures. The arrows indicate the possible PET pathways. Compound **1** has no electron donor so no PET occurs; **2**−**5** are similar where the dansyl group and the TAPD moiety are on the same side of the crown ether; **3** and **4** are similar in that the second crown amine is modified as amide; **5** is different from **4** having a benzyl instead of a benzoyl

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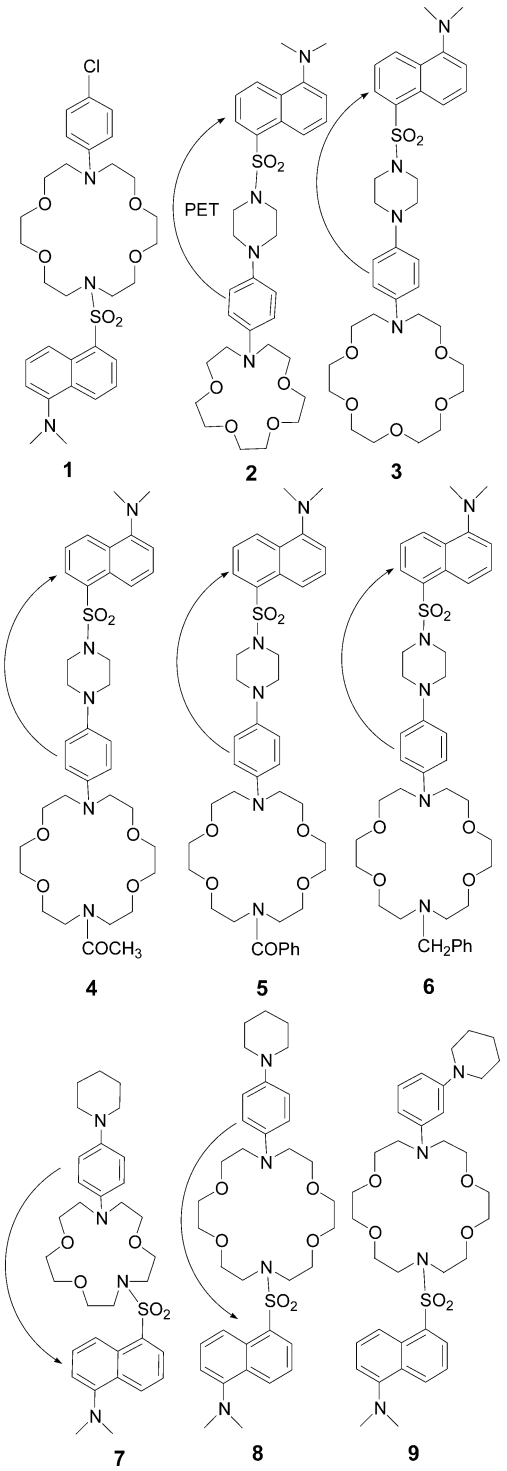
CHART 1



group, which is expected to significantly change the azacrown binding properties; **7** and **8** are arranged with the dansyl group and the TAPD on opposite sides of the crown ether; and **9** is similar to **8** with *m*-phenylenediamine instead of *p*-phenylenediamine as the potential electron donor.

However, in all these compounds, the arrangement (at either the same or opposite sites of the crown ether) of the donor and the fluorophore is not ideal. The piperazine ring is small but relatively rigid, therefore the TAPD moiety and the fluorophore are spatially close, but they cannot align perfectly parallel to each other. The crown ether ring is much larger than the piperazine ring, but it is very flexible so that the TAPD moiety and the fluorophore could come close enough to allow the PET to occur.

Compounds **2**−**8** (containing the TAPD moiety) turn blue on exposure to UV light, indicating they form the Würster's Blue radical cation by PET.[3] UV absorption and fluorescence emission spectra of all these compounds were obtained in acetonitrile. As expected, they all behave as PET systems in which the TAPD moiety is the electron donor and the excited dansyl group is the electron acceptor, and CHEF (chelation-enhanced fluorescence) was observed upon addition of various metal perchlorates.

All compounds show spectral characteristics typical of dansyl derivatives.[10] The absorption spectra indicate a major peak with λ_{max} at around 263 nm and a broad lower intensity peak with λ_{max} at around 330 nm. The *m*-phenylenediamine derivative **9** shows two peaks with λ_{max} at 243 and 313 nm (overlapping the lower intensity peak). In the presence of metal perchlorates, four types of change were observed for the absorption (Figure 1a). The major peak of **2**, **3**, and **6** undergoes a blue shift (maximum 8 nm). The major peak of **4** and **5** has a smaller blue shift (around 3 nm). The major peak of **7** and **8** shows increased intensity and no shift (Figure 1c), while the major peak of **9** shows decreased intensity and no shift (Figure 1d). The fluorescence spectra are relatively simple. The emission shows one broad peak with λ_{max} at around 540 nm for all compounds (Figure 1b). Only the intensity changes upon addition of metal perchlorates. The magnitude of change in the presence of different metal salts depends greatly on the structure of the compound.

Figure 2 illustrates the ratio change of the emission intensity with and without metal salts (note the expanded ordinate scale in the lower chart). Up to 10 equiv, the fluorescence of **1** decreases slightly with added metal salts. At 50 equiv, $Mg(ClO_4)_2$ and $Ca(ClO_4)_2$ quench about 3% and 10% of the fluorescence intensity, respectively. The changes for **2** and **3** are the largest. The fluorescence of **2** responded very selectively to $Mg(ClO_4)_2$ and $Ca(ClO_4)_2$ versus $NaClO_4$ and $KClO_4$. The fluorescence of **3** responded to all four metal perchlorates: the order of selectivity is $Ca(ClO_4)_2 > KClO_4 > Mg(ClO_4)_2 > NaClO_4$. The fluorescence response of **8** is more selective to $Mg(ClO_4)_2$, and $Ca(ClO_4)_2$ induces a smaller increase, while $NaClO_4$ and $KClO_4$ cause no appreciable change. The intensity changes of **4**, **5**, **7**, and **9** are very similar to that of **8**, for which $Mg(ClO_4)_2$ causes the largest increase. A very small increase was observed for the *m*-phenylenediamine derivative **9**. The emission change of compound **6** is very unique, being switched on only by $Ca(ClO_4)_2$.

Fluorescence binding studies of *N*-dansyl-monoaza-15-crown-5 (**10**) and *N*-dansyl-monoaza-18-crown-6 (**11**) have been investigated by Ossowski et al. (Chart 2).[11] In CH_3CN, at 50 equiv, $NaClO_4$, $KClO_4$, and $Mg(ClO_4)_2$ slightly

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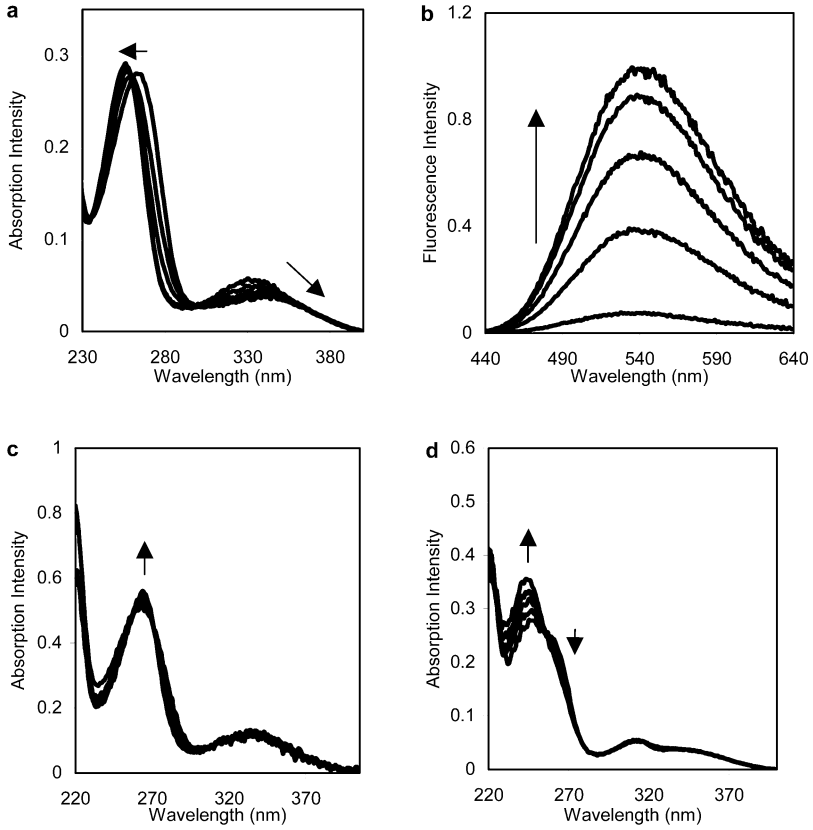
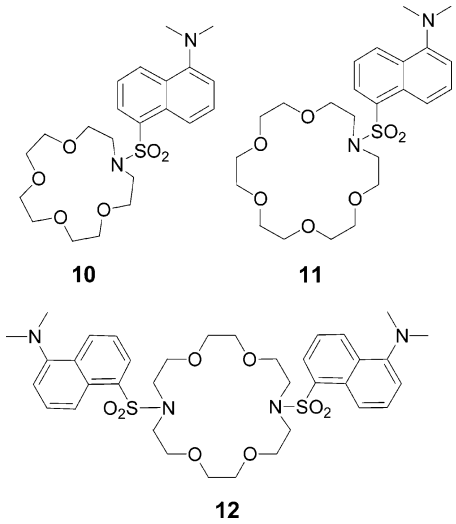


FIGURE 1. UV absorption (a) and fluorescence emission (b) spectra of **2** upon addition of $Ca(ClO_4)_2$ and UV absorption of **8** (c) and **9** (d) upon addition of $Mg(ClO_4)_2$ (molar equivalent of $M(ClO_4)_2$: 0, 0.5, 1, 5, 10 (along the arrowed direction); $\lambda_{Ex.} = 354$ nm, $\lambda_{Em.} = 540$ nm).

CHART 2



quench the fluorescence of both compounds, while $Ca(ClO_4)_2$ *quenches* 50% fluorescence of **10** and 80% of **11**, respectively. Very poor binding for Na^+ was reported for *N*,*N*′-bisdansyl-diaza-18-crown-6 (**12**), for which the crystal structure indicates that the sulfonate oxygen atoms do not coordinate to Na^+.[12] Apparently, a simple combination of azacrown ether and dansyl group does not lead to selective recognition, so the arylated diaza crown ethers described here offer some considerable potential advantages.

The emission change of the control compound **1** is similar to that of the known dansyl armed monoazacrown ethers **10** and **11**, but the quenching by metal salts is less effective, which is probably due to the attraction of metal cation by the *N*-phenyl moiety, leading to less effective contact of the metal cation with the dansyl group. The lack of change in the fluorescence of **1** is consistent with the *m*-phenylenediamine moiety being a poorer electron donor. The relatively high quantum yield of **1** and **9** also indicates that no PET occurs in those two molecules. There are two electron donors in **6** (though the tertiary benzylamine is rather distant), but the quantum yield is not lower than the quantum yield of those containing only one electron donor (Table 1). One could assume that only one set of PET occurs in **6** and that it is from the TAPD moiety to the dansyl group. The somewhat higher quantum yield for **7** and **8** than for **1** and **2** is likely due to the greater separation of the TAPD moiety from the dansyl group, leading to less efficient PET. The stability constants were calculated from the absorption spectra based on the Lambert−Beer law, but the data do not completely parallel the fluorescence responses.

NMR Studies. NMR spectroscopy has been widely used for studying the binding between crown ethers and metal cations.[13] Coordination of the metal cation to the crown ether induces conformational reorganization of the

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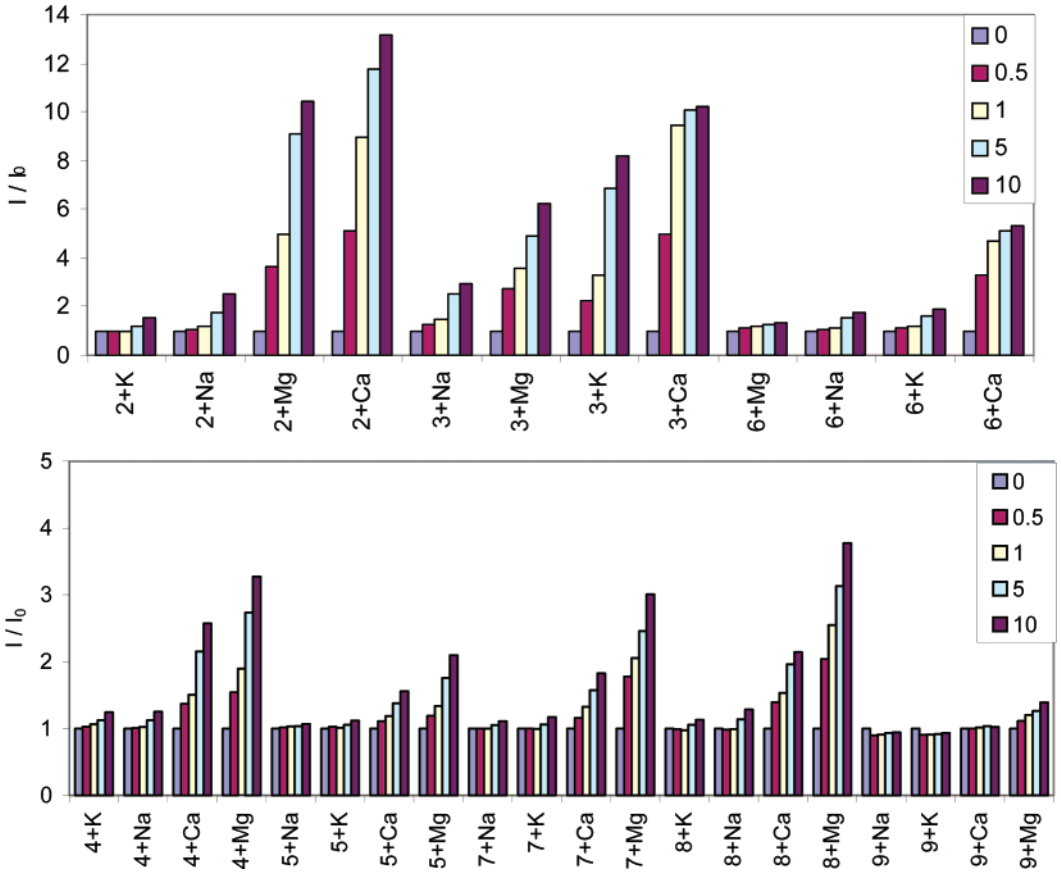

FIGURE 2. Change of fluorescence intensity upon addition of metal perchlorates (I/I_0: intensity in the presence/absence of metal perchlorates; molar equilavents of metal perchlorates: 0, 0.5, 1, 5, 10 shown in the legend; $\lambda_{Ex.} = 354$ nm, $\lambda_{Em.} = 540$ nm).

TABLE 1. Quantum Yields (Φ) and Stability Constants (*K*: L/mol) of 1−9 in CH_3CN

		Na^+		K^+		Mg^{2+}		Ca^{2+}	
	Φ_0	Φ	log *K*	Φ	log *K*	Φ	log *K*	Φ	log *K*
1	0.25								
2	0.02	0.06	3.6	0.03	3.8	0.24	5.3	0.25	6.1
3	0.03	0.07	4.4	0.2	4.7	0.16	4.7	0.22	7.5
4	0.03	0.04	5.0	0.04	4.8	0.09	4.7	0.07	4.2
5	0.05	0.05	4.1	0.05	3.9	0.1	5.3	0.08	4.0
6	0.04	0.07	5.6	0.08	3.3	0.06	3.9	0.22	3.2
7	0.06	0.07	2.1	0.06	3.5	0.2	5.1	0.18	4.3
8	0.04	0.07	3.6	0.06	3.0	0.16	5.6	0.09	4.9
9	0.15	0.14	2.6	0.15	6.0	0.21	5.3	0.16	4.5

ligand, and as a result, the chemical shifts and splitting patterns of the protons from the crown ether and the groups nearby undergo certain changes.

Addition of $Mg(ClO_4)_2$ to a solution of **2** in CD_3CN causes shifting and broadening of several peaks (Figure 3): the phenyl doublet at 6.9 ppm shifts downfield by 0.52 ppm and overlaps with the dansyl doublet at 7.4 ppm; the phenyl doublet at 6.7 ppm shifts downfield by 0.33 ppm and becomes broad; the crown ether multiplet moves downfield by about 0.3 ppm and becomes broad; the two piperazine triplets also become broad, and one of them shifts downfield by about 0.2 ppm; and the peaks for the dansyl moiety have almost no change. Addition of $Mg(ClO_4)_2$ to a solution of **8** in CD_3CN causes severe broadening of the two phenyl doublets (almost invisible), broadening of the crown ether multiplet, the piperidine triplet at 3.0 ppm and multiplet at 1.6−1.7 ppm, and the dansyl H(8) doublet. The majority of the dansyl peaks remain unchanged (Figure 4). Addition of $Mg(ClO_4)_2$ to a solution of **4** in CD_3CN causes broadening of several peaks (Figure 5): the two phenyl doublets (almost invisible), the crown ether multiplet, and the two piperazine triplets. The acetyl CH_3 singlet shifts downfield by 0.2 ppm. The dansyl peaks remain unchanged.

Apparently Mg^{2+} interacts with the TAPD moiety and the crown ether in all three compounds. Molecular orbital calculations suggest that aromatic amides coordinate with alkaline earth metal cations through both the carbonyl oxygen of the amide group and π-electrons of the aromatic ring.[14] The downfield shift of the CH_3 singlet indicates that the acetyl amide of **4** is interacting with Mg^{2+}, which weakens the effect of Mg^{2+} on the PET, leading to a smaller increase of the quantum yield compared with **2**, **3**, **6**, **7**, and **8**. The small quantum yield increase from **5** is likely due to the same effect. The

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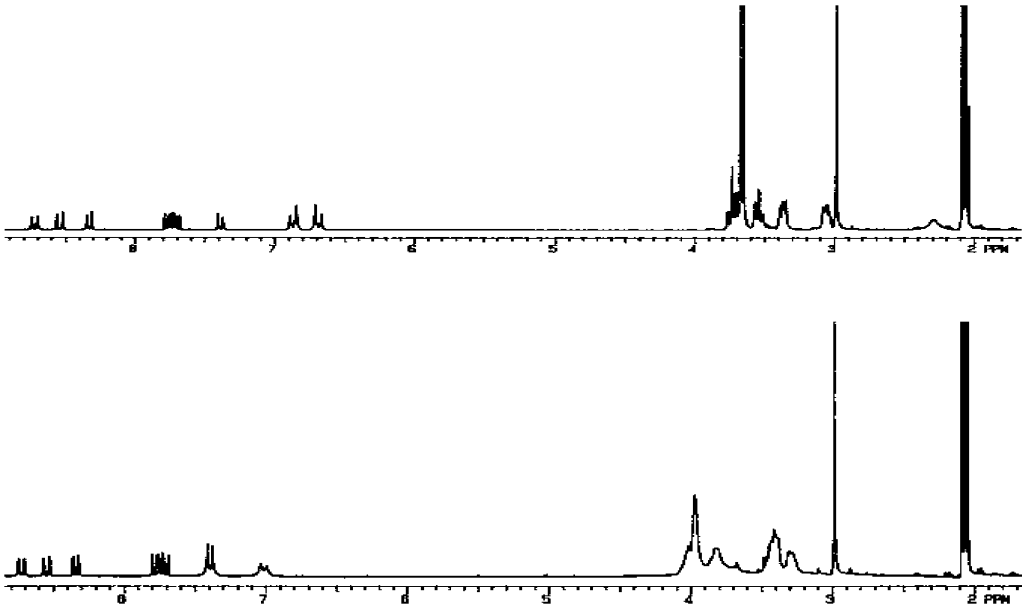

FIGURE 3. ^{1}H NMR spectra of **2** in the absence (top) and presence (bottom) of 1 molar equiv of $Mg(ClO_4)_2$ in CD_3CN (200 MHz).

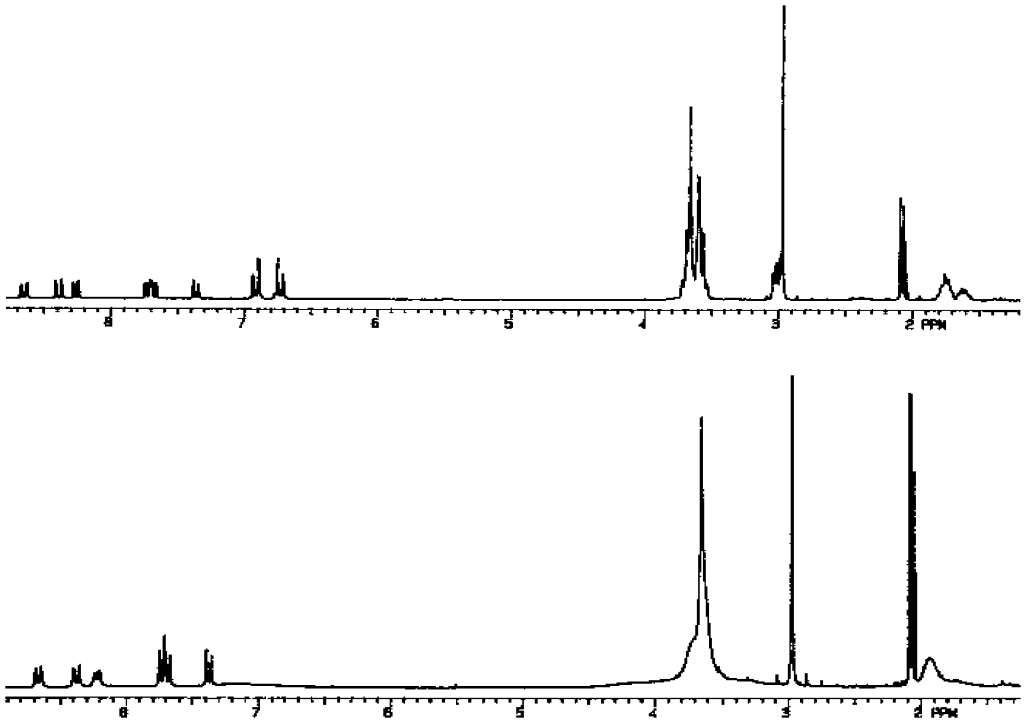

FIGURE 4. ^{1}H NMR spectra of **8** in the absence (top) and presence (bottom) of 1 molar equiv of $Mg(ClO_4)_2$ in CD_3CN (200 MHz).

dansyl group of **8** is only slightly affected by Mg^{2+}, which suggests that the sulfonate oxygen is not interacting with Mg^{2+}, which is similar as reported for **12**.

Discussion

A number of factors affect the binding of a crown ether ligand and a metal cation. Besides the size match effect and charge density of the metal cation, structural modification of the azacrown ether nitrogen is also very important for selective binding. Three types of PET molecule were studied here (Figure 6). Compounds **2** and **3** are RD-σ-A type (receptor−donor−σ bond acceptor), **4** and **5** are CoRD-σ-A type (co-binding receptor−donor−σ bond acceptor), and **7** to **9** are DRA type (donor−receptor−acceptor). From the standpoint of the receptor, **4** and **5** are similar to **8** in which the second crown ether nitrogen is modified as amide, therefore similar binding properties can be expected.

The very selective response of **2** toward Ca^{2+} and Mg^{2+} is probably due to greater sensitivity of the TAPD moiety toward higher charge density, and the small size of the

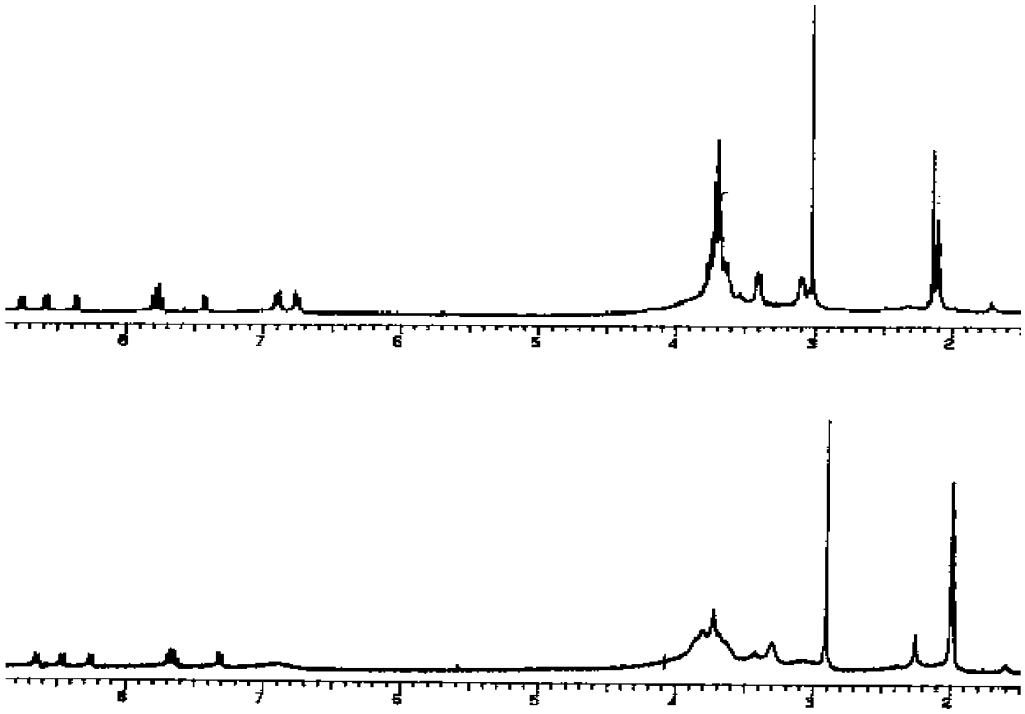

FIGURE 5. ^{1}H NMR spectra of **4** in the absence (top) and presence (bottom) of 1 molar equiv of $Mg(ClO_4)_2$ in CD_3CN (300 MHz).

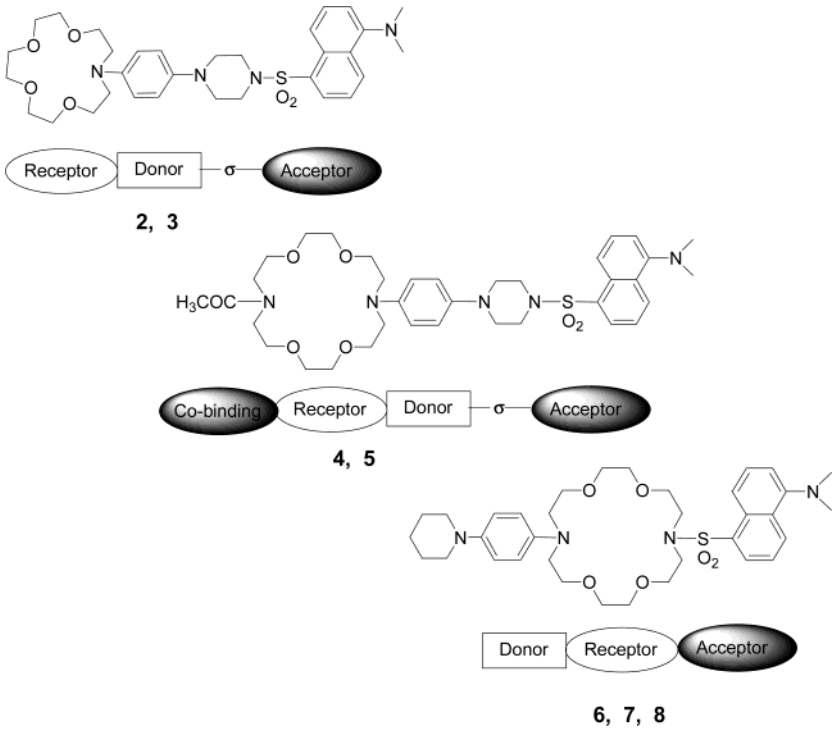

FIGURE 6. Graphical illustration of the different structures of PET molecules.

crown ether, for which both Ca^{2+} and Mg^{2+} fit well; **3** bears a larger crown ether for which Na^+ and Mg^{2+} are too small but Ca^{2+} and K^+ fit better, therefore better response was observed for the latter two ions. Compound **6** has donor−acceptor structure similar to **2** and **3** and a slightly different receptor—a diazacrown ether; the fluorescence response is very unique, only responds to Ca^{2+}, which is likely due to the large available binding cavity and the sensitivity of the TAPD moiety toward the high charge density of Ca^{2+}.

The larger increase in quantum yields for **2**, **3**, and **6** than for **4**, **5**, **7**, and **8** suggests a more efficient interruption of the PET process upon cation binding through a stronger interaction between the TAPD moiety and metal cation in **2**, **3**, and **6**. This is consistent with the corresponding structural features. For **2**, **3**, and **6**,

metal cations mainly contact the crown ether and the TAPD moiety, while for **4**, **5**, **7**, and **8**, metal cations sit between the TAPD and the amide moiety. In the case of **4** and **5**, the amide carbonyl co-coordinates with metal cations, while in **7** and **8**, the crown ether is relatively crowded and therefore less accessible. Both situations lead to weaker interaction between the TAPD moiety and metal cation, hence less efficient inhibition of the PET process.

Conclusions

In conclusion, we have investigated the binding properties of a number of TAPD crown ether derivatives. The results indicate that TAPD can be used as an electron donor for PET fluorescence sensing. The very selective response of these TAPD molecules toward divalent metal cations over monovalent metal cations can be further manipulated to design new molecules with better selectivity. While this work has used well-established principles for receptor/analyte recognition, it is likely that any nitrogen-bound receptor can be employed, thereby allowing a broad range of analytes to be detected selectively, as long as receptor/analyte binding leads to a significant change in the redox potential of the TAPD. This underlying concept will form the basis of future studies in our laboratory.

Experimental Section

General Procedure for Dansyl Attachment. The previously prepared amine[5] and dansyl chloride (2 equiv) were dissolved in CH_2Cl_2, and Cs_2CO_3 (2 equiv) was added to the solution. The mixture was stirred at room temperature, and the reaction was monitored by TLC. After the reaction was complete, the solution was filtered through Celite, the solvent was removed by rotary evaporation, and the residue was purified by flash chromatography.

{5-[16-(4-Chlorophenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-sulfonyl]naphthalen-1-yl}dimethylamine (1). Flash chromatography (CH_2Cl_2/hexanes/Et_3N 10/10/1, R_f 0.4) afforded the product as a yellow-green waxy solid in 82% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.54 (1H, d, J = 8.6 Hz), 8.31 (1H, d, J = 8.7 Hz), 8.15 (1H, d, J = 8.6 Hz), 7.54 (1H, dd, J = 8.6 Hz), 7.50 (1H, dd, J = 8.6 Hz), 7.18 (1H, d, J = 6.8 Hz), 7.12 (2H, d, J = 9.2 Hz), 6.58 (2H, d, J = 9.2 Hz), 3.4−3.7 (24H), 2.88 (6H, s). ^{13}C NMR (50 MHz, CD_3Cl_3) δ 151.8, 146.6, 135.6, 130.2, 129.1, 128.7, 128.1, 123.2, 120.8, 119.6, 115.3, 112.9, 70.8, 70.7, 70.6, 69.0, 51.5, 48.3, 45.5. HRMS-FAB calcd for $C_{30}H_{40}O_6N_3SCl$ 605.2326, found 605.2336.

Dimethyl-(5-{4-[4-(1,4,7,10-tetraoxa-13-azacyclopentadec-13-yl)phenyl]piperidine-1-sulfonyl}naphthalen-1-yl)amine (2). Flash chromatography (CH_2Cl_2/petroleum ether/Et_3N 1/1/0.01, R_f 0.26) afforded the product as a yellow-green waxy solid in 68% yield. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.67 (1H, d, J = 8.5 Hz), 8.56 (1H, d, J = 8.7 Hz), 8.27 (1H, dd, J = 7.3, 1.2 Hz), 7.72 (1H, dd, J = 8.5, 7.3 Hz), 7.65(1H, dd, J = 8.7, 7.7 Hz), 7.33 (1H, d, J = 7.7 Hz), 6.82 (2H, d, J = 9.1 Hz), 6.62 (2H, d, J = 9.1 Hz), 3.70 (4H, t, J = 6.05 Hz), 3.5−3.6 (12H), 3.50 (4H, t, J = 6.0 Hz), 3.30 (4H, t, J = 5.0 Hz), 3.03 (4H, t, J = 5.0 Hz), 2.9 (6H, s). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 151.7, 143.3, 132.6, 130.7, 13130.6, 130.1, 128.0, 123.2, 119.9, 119.8, 115.3, 112.3, 77.7, 77.3, 77.2, 77.1, 76.5, 71.4, 70.3, 68.8, 52.6, 51.2, 46.0, 45.5. HRMS-FAB calcd for $C_{32}H_{44}O_6N_4S$ 612.2982, found 612.2952.

Dimethyl-(5-{4-[4-(1,4,7,10,13-pentaoxa-16-azacyclopentaocta-16-yl)phenyl]piperidine-1-sulfonyl}naphthalen-1-yl)amine (3). Flash chromatography (CH_2Cl_2/hexanes/Et_3N 1/1/0.2, R_f 0.34) afforded the product as a yellow-green waxy solid in 80% yield. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.63 (1H, dt, J = 8.6, 1.1 Hz), 8.52 (1H, dt, J = 8.7, 0.9 Hz), 8.19 (1H, dd, J = 7.4, 1.3 Hz), 7.68 (1H, dd, J = 8.6, 7.4 Hz), 7.62(1H, dd, J = 8.7, 7.6 Hz), 7.29 (1H, dd, J = 7.6, 0.9 Hz), 6.80 (2H, d, J = 9.2 Hz), 6.62 (2H, d, J = 9.2 Hz), 3.4−3.7 (24H), 3.28 (4H), 3.00 (4H), 2.88 (6H, s), 2.00 (3H, s). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 170.5, 152.9, 144.3, 142.9, 134.2, 131.5, 131.0, 129.0, 124.4, 120.8, 120.2, 116.3, 113.8, 71.7, 71.6, 71.0, 70.6, 70.1, 70.0, 52.4, 51.7, 50.4, 47.5, 47.0, 45.8, 21.9. HRMS-FAB calcd for $C_{34}H_{48}O_7N_4S$ 656.3244, found 657.3311.

(5-{4-[4-(16-Benzyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl)phenyl]piperazine-1-sulfonyl}naphthalen-1-yl)dimethylamine (4). Flash chromatography (CH_2Cl_2/hexanes/Et_3N:1/1/0.03, R_f 0.1) afforded the product as a yellow-green waxy solid in 64% yield. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.63 (1H, d, J = 8.6 Hz), 8.52 (1H, d, J = 8.7 Hz), 8.27 (1H, dd, J = 7.4, 1.3 Hz), 7.68 (1H, dd, J = 8.6, 7.4 Hz), 7.61 (1H, dd, J = 8.7, 7.5 Hz), 7.30 (1H, d, J = 7.6, 0.9 Hz), 6.79 (2H, d, J = 9.2 Hz), 6.63 (2H, d, J = 9.2 Hz), 3.5−3.7 (24H), 3.27 (4H), 3.00 (4H), 2.88 (6H, s), 2.00 (3H, s). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 170.5, 152.9, 144.3, 142.9, 134.2, 131.5, 131.0, 129.0, 124.4, 120.8, 120.2, 116.3, 113.8, 71.7, 71.6, 71.0, 70.6, 70.1, 70.0, 52.4, 51.7, 50.4, 47.5, 47.0, 45.8, 21.9. HRMS-FAB calcd for $C_{36}H_{51}O_7N_5S$ 697.3509, found 697.3465.

(16-{4-[4-(5-(Dimethylamino)naphthalene-1-sulfonyl)-piperazin-1-yl]phenyl}-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl)phenylmethanone (5). Flash chromatography (CH_2Cl_2/hexanes/Et_3N 1/2/0.1, R_f 0.1) afforded the product as a yellow-green waxy solid in 80% yield. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.67 (1H, d, J = 8.5 Hz), 8.56 (1H, d, J = 8.7 Hz), 7.43 (5H, s), 8.27 (1H, dd, J = 7.3, 1.2 Hz), 7.72 (1H, dd, J = 8.5, 7.4 Hz), 7.65 (1H, dd, J = 8.7, 7.5 Hz), 7.32 (1H, d, J = 7.5 Hz), 6.83 (2H, d, J = 9.1 Hz), 6.65 (2H, d, J = 9.1 Hz), 3.5−3.8 (24H), 3.30 (4H, t, J = 4.9 Hz), 3.03 (4H, t, J = 4.9 Hz), 2.92 (6H, s). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 172.0, 152.9, 144.4, 143.0, 138.7, 134.2, 131.4, 131.0, 129.8, 129.2, 128.9, 127.6, 124.4, 120.9, 120.2, 116.3, 113.8, 71.6, 70.1, 52.4, 51.8, 47.0, 45.7. HRMS-FAB calcd for $C_{41}H_{53}O_7N_5S$ 759.3666, found 759.3616.

(5-{4-[4-(16-Benzyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl)phenyl]piperazine-1-sulfonyl}naphthalen-1-yl)dimethylamine (6). Flash chromatography (CH_2Cl_2/hexanes/Et_3N 1/2/0.1, R_f 0.2) afforded the product as a yellow waxy solid in 60% yield. ^{1}H NMR (300 MHz, CD_3COCD_3) δ 8.67 (1H, d, J = 8.5 Hz), 8.56 (1H, d, J = 8.7 Hz), 8.27 (1H, dd, J = 7.3, 1.2 Hz), 7.72 (1H, dd, J = 8.5, 7.3 Hz), 7.65 (1H, dd, J = 8.7, 7.5 Hz), 7.2−7.4 (6H), 6.83 (2H, d, J = 9.1 Hz), 6.67 (2H, d, J = 9.1 Hz), 3.5−3.7 (22H), 3.31 (4H, t, J = 4.9 Hz), 3.04 (4H, t, J = 4.9 Hz), 2.92 (6H, s), 2.80 (4H). ^{13}C NMR (75 MHz, CD_3COCD_3) δ 152.7, 144.2, 142.8, 141.2, 141.0, 140.9, 134.1, 131.3, 130.9, 129.5, 128.8, 127.4, 124.2, 120.7, 120.1, 116.2, 113.6, 711.6, 71.3, 70.8, 69.8, 60.5, 54.7, 52.2, 51.6, 46.8, 45.6. HRMS-FAB calcd for $C_{41}H_{55}O_6N_5S$ 745.3873, found 745.3881.

Dimethyl-{5-[13-(4-piperidin-1-ylphenyl)-1,4,10-trioxa-7,13-diazacyclopentadecane-7-sulfonyl]naphthalen-1-yl}amine (7). Flash chromatography (CH_2Cl_2/hexanes/Et_3N 1/2/0.1, R_f 0.4) afforded the product as a yellow solid in 90% yield: mp 50−52 °C; ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.56 (1H, d, J = 8.5 Hz), 8.36 (1H, d, J = 8.7 Hz), 7.62 (1H, dd, J = 8.5, 7.3 Hz), 7.60 (1H, dd, J = 8.7, 7.6 Hz), 8.19 (1H, dd, J = 7.3, 1.3 Hz), 7.27 (1H, dd, J = 7.6, 0.9 Hz), 6.70 (4H, two br s), 3.4−3.7 (20H), 2.87 (6H, s), 1.4−1.7 (6H). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 152.8, 145.1, 143.7, 137.2, 131.1, 130.7, 129.3, 128.8, 124.4, 120.8, 119.9, 116.2, 114.4, 72.3, 71.8, 71.4, 70.5, 53.0, 49.9, 49.4, 45.8, 25.2. HRMS-FAB calcd for $C_{33}H_{46}O_5N_4S$ 610.3189, found 610.3178.

Dimethyl-{5-[16-(4-piperidin-1-ylphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-sulfonyl]naphthalen-1-yl}amine (8). Flash chromatography (CH_2Cl_2/hexanes/CH_3OH (NH_3) 1/1/0.1, R_f 0.4) afforded the product as a yellow-green waxy solid in 68% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ

8.52 (1H, d, J = 8.5 Hz), 8.32 (1H, d, J = 8.7 Hz), 8.16 (1H, dd, J = 7.3, 1.2 Hz), 7.55 (1H, dd, J = 8.7, 7.3 Hz), 7.50 (1H, dd, J = 8.5, 7.5 Hz), 7.18 (1H, d, J = 7.5 Hz), 6.88 (2H, d, J = 9.1 Hz), 6.63 (2H, d, J = 9.1 Hz), 3.5−3.7 (24H), 3.00 (4H, t, J = 5.5 Hz), 2.88 (6H, s), 1.4−1.8 (6H). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 152.8, 144.7, 143.6, 137.7, 131.1, 131.0, 130.0, 128.9, 128.8, 124.4, 120.8, 120.0, 116.2, 114.4, 71.6, 71.5, 71.2, 70.3, 53.3, 52.5, 49.2, 45.7, 27.2, 25.2. HRMS-FAB calcd for $C_{35}H_{50}O_6N_4S$ 654.3451, found 654.3445.

Dimethyl-{5-[16-(3-piperidin-1-ylphenyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-sulfonyl]naphthale-1-yl}amine (9). Flash chromatography (CH_2Cl_2/hexanes/CH_3OH/Et_3N 1/1/0.05/0.05, R_f 0.5) afforded the product as a yellow-green waxy solid in 73% yield. ^{1}H NMR (200 MHz, CD_3COCD_3) δ 8.56 (1H, d, J = 8.4 Hz), 8.36 (1H, d, J = 8.7 Hz), 8.18 (1H, dd, J = 7.3, 1.3 Hz), 7.62 (1H, dd, J = 8.7, 7.7 Hz), 7.60 (1H, dd, J = 8.4, 7.3 Hz), 7.28 (1H, d, J = 7.7 Hz), 6.96 (1H, t, J = 8.2 Hz), 6.28 (1H, d, J = 1.3 Hz), 6.22 (1H, ddd, J = 8.2, 1.3, 0.9 Hz), 6.22 (1H, ddd, J = 8.2, 1.3 Hz, 0.7), 3.5−3.7 (24H), 3.09(4H, t, J = 5.2 Hz), 2.88 (6H, t, J = 5.5 Hz), 1.64 (6H). ^{13}C NMR (50 MHz, CD_3COCD_3) δ 154.7, 152.8, 149.9, 137.6, 131.1, 130.8, 130.3, 128.9, 128.8, 124.4, 120.8, 116.2, 106.1, 104.5, 101.7, 71.6, 71.5, 71.2, 70.1, 52.3, 51.7, 49.2, 45.7, 26.9, 25.4. HRMS-FAB calcd for $C_{35}H_{50}O_6N_4S$ 654.3451, found 654.3430.

Fluorescence Binding Studies. The procedure for fluorescence titration has been described in ref 7a.

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Supporting Information Available: Titration spectra of UV absorption and fluorescence emission and ^{1}H and ^{13}C NMR spectra of **1**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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