Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

The Fluorescence Properties of Free and Cation-complexed Lariat Ethers having Sidearms Terminated by a Benzene Ring

Elizabeth K. Elliott[a]; Jiaxin Hu[b]; George W. Gokel[a]
[a] Department of Molecular Biology and Pharmacology, Washington University School of Medicine 660 South Euclid Avenue, St. Louis, MO, USA [b] Department of Chemistry, Washington University, St. Louis, MO, USA

To cite this Article Elliott, Elizabeth K. , Hu, Jiaxin and Gokel, George W.(2007) 'The Fluorescence Properties of Free and Cation-complexed Lariat Ethers having Sidearms Terminated by a Benzene Ring', Supramolecular Chemistry, 19: 3, 175 — 183
To link to this Article: DOI: 10.1080/10610270600954861
URL: http://dx.doi.org/10.1080/10610270600954861

Supramolecular Chemistry, April–May 2007 Vol. 19 (3), pp. 175–183

Taylor & Francis
Taylor & Francis Group

The Fluorescence Properties of Free and Cation-complexed Lariat Ethers having Sidearms Terminated by a Benzene Ring

ELIZABETH K. ELLIOTT[a], JIAXIN HU[b] and GEORGE W. GOKEL[a,b,*]

[a]*Department of Molecular Biology and Pharmacology, Washington University School of Medicine 660 South Euclid Avenue, Campus Box 8103, St. Louis, MO, USA;* [b]*Department of Chemistry, Washington University, 1 Brookings Drive, St. Louis, MO, USA*

(Received 11 July 2006; Accepted 31 July 2006)

Fluorescence and visible spectra of phenyl-sidearmed lariat ethers and of toluene, ethylbenzene, and propylbenzene were obtained in dichloromethane and acetonitrile solutions. Changes in their spectra were observed in the presence of KSCN or CF_3COOH in an effort to obtain solution confirmation of cation–pi interactions. The lariat ether receptor molecules, $Ph(CH_2)_{1-3}$ < N18N > $(CH_2)_{1-3}Ph$ gave quite different results even though they varied only in the sidearm chain length. In previous studies, solid state cation–pi complexes were obtained only with $Ph(CH_2)_2$ < N18N > $(CH_2)_2Ph$ and not with either $PhCH_2$ < N18N > CH_2Ph or $Ph(CH_2)_3$ < N18N > $(CH_2)_3Ph$. Variations in behavior in solution were noted among the three lariat ethers in the presence of different Lewis acids but definitive evidence for cation–pi interactions proved elusive.

Keywords: Fluorescence; Lariat ether; Receptor; Crown ether; Cation–pi; Cation–complexation

INTRODUCTION

We have reported extensive efforts [1] to characterize cation–pi interactions [2,3] involving the arenes benzene [4], phenol [5], and indole [6] with Na^+ and K^+. These three arenes are particularly important because they are the aromatic sidechains of phenylalanine, tyrosine, and tryptophan. Progress in understanding cation–pi interactions has been reviewed several times [7–9] but remains an issue of considerable contemporary interest.

The alkali metal cation–pi interactions involved in complexes of receptors **1**–**5** with various salts have largely been characterized by X-ray crystallography [10,11]. The ^{13}C-NMR studies we undertook have also proved to be informative, although limited thus far to unsaturated sidearms rather than arene-terminated ones [12]. Sodium and potassium were the predominant cations in the solid state studies but divalent calcium complexes were prepared as well. Efforts to observe the cation–pi interaction in Na^+ and K^+ complexes of dibenzyldiaza-18-crown-6 (**1**) had previously failed [13]. The solid state structure of **1** was reported and of **1**•KSCN, a complex in which K^+ was bound in the center of the macroring. The benzyl sidearms were extended from the macroring and the bound cation was solvated by axial SCN^- groups. In the same report, we showed that propargyl sidechains in *N*,*N*′-propargyl-4,13-diaza-18-crown-6 also turned away from the macroring, which included K^+ (from KSCN). The anion, rather than the sidearm pi-donors provided axial solvation to the ring-bound cation [13].

When the benzyl sidechain was elongated to 2-phenylethyl (i.e. **1** → **2**, see below), the solid state structures of **2**•KX complexes clearly showed axial solvation by the aromatic sidechain donor groups. In addition, when the sidechains of *N*,*N*′-*bis*(propargyl)-4,13-diaza-18-crown-6 were elongated from 2-propynyl to 3-butynyl, crystal structure data showed that the triple bond served as a pi-donor for the macroring-complexed cation [14]. Based on the successful solution NMR study noted above [12], and other recent work [15], we considered fluorescence as a method to detect cation–pi participation in solution.

The ability of crown ethers to complex alkali and alkaline earth metal cations [16] has been exploited in various analytical methodologies. An early example was the use of polymer-bound crown ethers in ion chromatography. Electrochemical sensing and switching was developed by merging redox-switchable groups with crown ethers and cryptands. Residues

*Corresponding author. E-mail: ggokel@wustl.edu

ISSN 1061-0278 print/ISSN 1029-0478 online © 2007 Taylor & Francis
DOI: 10.1080/10610270600954861

such as nitrobenzene [17], anthraquinone [18], and ferrocene [19] were linked to lariat ethers [20,21] to achieve cooperative binding. Optical reporters of complexation were also developed early in the history of macrocyclic chemistry. Applications of nitro-substituted phenols or azobenzenes as visible reporters of cation binding were developed in the laboratories of Misumi, Takagi, Shinkai, Pacey, and Kaneda. Takagi reviewed these efforts [22].

The greater sensitivity of fluorescence, compared to absorption spectroscopy, has led to numerous lariat ethers, cryptands, and crowned calixarenes that bear luminescent residues. Leray, Valeur, Vicens, and their coworkers reported ditopic calixarenes as fluorescent sensors for alkali metal cations [23,24]. Kubinyi *et al.* used dinitroazobenzene as the fluorescent reporter in a chiral, ditopic calix crown [25]. A K^+-selective fluorescent cryptand was reported by He and coworkers [26,27]. Ballardini *et al.* used a ditopic bis(naphthyl) cryptand as a receptor and sensor for protons and pentanediammonium ion [28]. Nakahara, Nakatsuji, and their coworkers recently reported the fluorescent detection of alkali metal cations by using a cryptand having attached a pyrenyl reporting group [29]. A fluorescent, bibracchial lariat ether having anthracene-terminated sidearms converted to a cryptand by virtue of an unanticipated 4 pi +4 pi cycloaddition reaction [30].

Most of the fluorescent sensors that have been studied use relatively simple macrocycles with pendant arms. These arms are typically terminated in residues that fluoresce more or less strongly depending on their structures. Minta and Tsien, in a pioneering paper, prepared a variety of fluorescent lariat ethers that were designed to function as indicators for cytosolic sodium cation [31]. Naphthalene was the fluorescent reporter in a compound designed to complex zinc and copper dications [32]. It was also a component in the ditopic receptor noted above [27]. The dansyl group, a substituted naphthalene residue, is highly fluorescent and has been incorporated in both one- and two-armed lariat ether receptors [33]. We had previously prepared *N*,*N*′-bis(dansyl)-4,13-diaza-18-crown-6 for use in fluorescent studies [34] of hydraphile channel compounds [35]. Anthracene has likewise proved to be a popular reporter group. The earliest example appears to be the report of Witulski *et al.*, who coupled the arene directly to aza-18-crown-6 [36]. The homolog, *N*-(9-anthracenylmethyl)aza-18-crown-6 was reported as a fluorescent sensor for the marine natural product saxitoxin [37]. Herrmann *et al.* incorporated 10-methylanthracene as a side-chain terminus to diaza-18-crown-6 and as a spacer unit in a corresponding ditopic cryptand [38].

Pyrene is highly fluorescent and also well known to form a dimeric excimer. Nakatsuji and coworkers have incorporated the pyrene residue as a sidearm terminus in several different lariat ether architectures [39–41]. β-Cyclodextrin was added to aqueous acetonitrile mixtures to augment excimer formation [42]. Benzocrown-cyclodextrin conjugates have also been reported recently by Liu *et al.* [43,44].

Numerous other dye-substituted crown ethers have been described that have been studied as sensors for alkali metal cations [45–50]. We note early work by Valeur and coworkers who attached coumarin derivatives to the sidearms of aza- and diazacrowns [51]. Valeur has reviewed his own work and the contributions made by others in his 2002 monograph titled *Molecular Fluorescence* [52]. Taken together, there is considerable literature on fluorescent reporters attached to macrocycles. For the most part, they have been used to detect alkali, alkaline earth, or inorganic cations. DeSilva and coworkers have exploited the photochemistry of fluorescent crown compounds to develop molecular switches and logic gates. This has led to an understanding of photoelectron transfer issues within these hybrid structures [53–55].

We now report our efforts to assess interactions between macrocycle-bound alkali metal cations and benzene, which serves as a pi-donor to Lewis acids. Our goal in the present study was to use sidearm fluorescence as a probe in solution of the cation–pi interaction that was apparent in numerous solid state structures.

RESULTS AND DISCUSSION

Compounds Studied

We anticipated that fluorescence would be weaker from benzene than from either phenol or indole. We began with phenyl-sidearmed compounds **1**, **2**, and **3**, along with models for their sidearms. Toluene, ethylbenzene, and propylbenzene were obtained from commercial sources. Syntheses of **1** [56], **2** [4], **3** [57], **4** [1], and **5** [1] have been previously reported.

Solid State Structures

We have used X-ray crystallographic methods to establish pi-sidearm participation in alkali metal complexes of **2**, **4**, and **5**. When the sidearm pi-systems were separated from the macroring by one carbon (benzyl, propargyl), typical crystalline crown complexes (crown·MX) were obtained but no evidence for any sidearm pi-interaction was apparent [58]. Similarly, when the sidearms were propylene rather than ethylene (i.e. **3** compared to **2**), solid complexes could be isolated but X-ray crystallography showed no evidence for cation–pi complexation. This apparent discontinuity in cation–pi donicity was surprising to us but it was observed consistently in the compounds studied.

Figure 1 shows the solid state structures of three complexes in four renderings. Sodium and potassium iodide complexes of dibenzyldiaza-18-crown-6 (**1**·NaI, panel a and **1**·KI panel b) are shown at the top of the figure [59]. The bottom of the figure (panels c and d) shows **2**·KI in two different views that illustrate the cation–pi interaction between benzene and K^+[60].

Crown ether complexes of MX salts usually have the cation (M^+) bound in the macroring and the anion (X^-) either in contact with the cation or hydrogen bonded by a water molecule to it. A ring-bound K^+ is in contact with I^- in panel b of Fig. 1. The K···I distance is 4.87 Å in this complex. Sodium cation (panel a) is not in contact with iodide, which is at a distance of 5.67 Å from the cation. A water molecule is visible below and to the right of Na^+ in the structure shown in panel a of Fig. 1. In this case, a network of water molecules solvates two essentially identical complexes from their exposed surfaces (not shown). The puckered macroring apparently prevents direct contact with the anion, but the water network provides Na^+ with additional solvation and the anion maintains the charge balance.

In neither the NaI or KI complex of **1** is there a cation–pi interaction. In **2**·KI, the benzene rings comprise axial donor groups for the ring bound cation. It is clear from panels c and d of Fig. 1 that the two benzene rings are organized directly above and below the K^+ ion. The distances from K^+ to the centroid are 3.43 Å and 3.44 Å. We have previously noted that the thickness of a benzene ring is about 3.5 Å and the diameter of octacoordinate K^+ is 3.02 Å. The minimum contact distance is therefore 3.26 Å, less than 0.2 Å shorter than the observed distance. Further, the arenes are offset from the straight line connecting them through the cation by only about 11° [61].

Absorption Spectra

The differences in complex structure noted above reflect an extensive study of these compounds in the solid state [62,63]. In previous work, cation–pi complexes were often, but not always, observed with **2** but never with either **1** or **3**. The arenes that correspond to these sidechains are toluene, ethylbenzene, and propylbenzene. Their absorption spectra are well known and were reported by Berlman [64]. When excited at 265 nm in cyclohexane, all three compounds absorb at $\lambda \approx 262$ nm. The molar extinction coefficients reported (in cyclohexane) for toluene, ethylbenzene, and propylbenzene are, respectively, ~280, ~250, and ~220. Table I records the values determined in this study for absorption and emission maxima as well as the extinction coefficients in both CH_2Cl_2 and CH_3CN resulting from the spectra.

The absorption maximum for toluene, ethylbenzene, and propylbenzene was ~262 nm when the irradiating wavelength was 265 nm. The extinction coefficients determined in this study do not differ significantly from those previously reported. Thus, for these three compounds, the absorption spectra are indifferent to the alkyl chain attached to benzene.

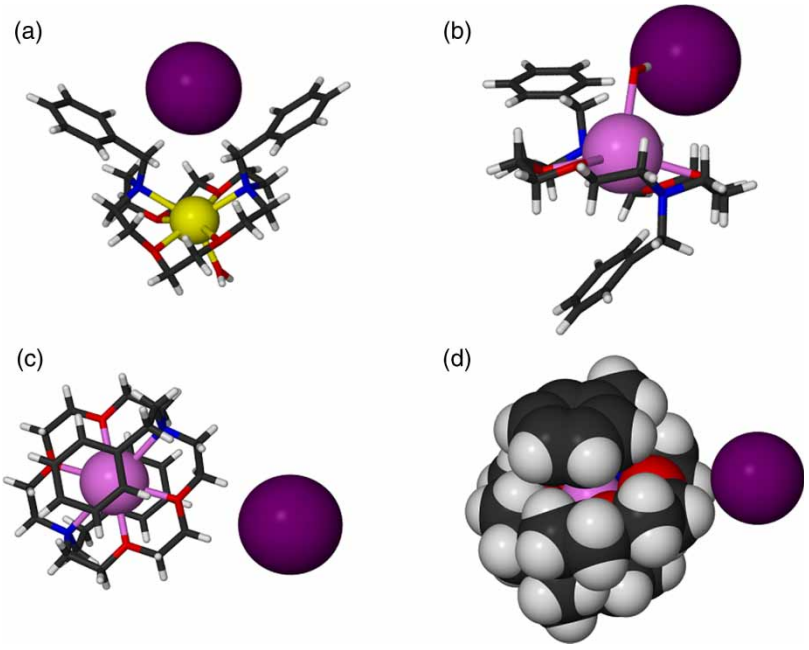

FIGURE 1 X-ray crystal structures of *N*,*N*′-dibenzyldiaza-18-crown-6 (**1**) complexing NaI (a) side view and (b) complexing KI. Panels c and d show *N*,*N*′-bis(2-phenylethyl)-4,13-diaza-18-crown-6, **2**, complexing KI (c, top view; d, side view in the space-filling format).

TABLE I Absorption and emission spectra for toluene, ethylbenzene, and propylbenzene

Compound	λ^a_{exc}	λ^a_{max} Abs[b]	λ^a_{max} Em[c]	ε[d]	Conc.[e]	Solvent
Toluene	265	263	288	256	3.50	CH_2Cl_2
	265	263	290	240	3.50	CH_3CN
Ethyl-benzene	265	262	289	228	5.09	CH_2Cl_2
	265	262	290	232	5.09	CH_3CN
Propyl-benzene	265	262	285	236	3.50	CH_2Cl_2
	265	262	284	224	3.50	CH_3CN

a) Recorded in nm; b) Absorption maximum; c) Emission maximum; d) In ($cm^{-1}M^{-1}$) Extinction coefficients determined at 2.5 mM, e) Concentration in mM for emission spectra.

UV-Visible Absorption Spectra of 1–3

The absorption spectra of toluene, ethylbenzene, and propylbenzene in CH_3CN correspond to results reported previously in less polar solvents. We obtained the absorption spectra of **1–3** in order to confirm that no unexpected effect ensued when the alkylbenzene was attached to 4,13-diaza-18-crown-6. These spectra are very similar to each other and have λ_{max} and molar extinction coefficient values that are comparable to *N*,*N*-dimethylbenzylamine. The similarity of the absorption spectra of **1–3** stands in contrast to the fluorescence spectra of the free receptor molecules as discussed below.This is shown in Fig. 3.

Fluorescence Spectra of 1–3

The fluorescence spectra of compounds **1–3** were determined in anhydrous, deoxygenated CH_3CN solution (see Fig. 2). The excitation wavelength in each case was 265 nm, the slit width was 5 nm, and the concentration was of each compound was 4.0 mM. Two differences are apparent when the absorption and fluorescence spectra are compared. First, the concentration required to obtain satisfactory fluorescence spectra was higher than required for the absorption spectra. Second, and of greater significance, is that **2** exhibits much stronger fluorescence than does either **1** or **3**.

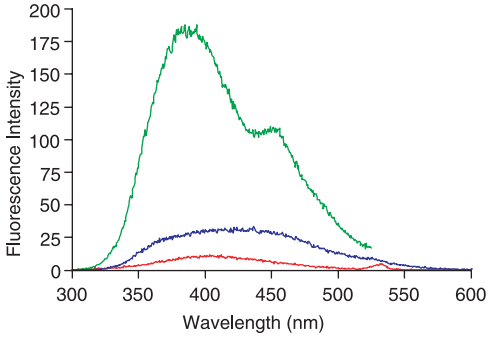

FIGURE 2 Fluorescence spectra of **1–3** determined in CH_3CN at 4.0 mM of receptor excited at $\lambda = 265$ nm (slit width 5 nm). The spectra are: **1**, red; **2**, green; and **3**, blue.

Titration of 1–3 With CF_3COOH

Compounds **1–3** (concentration = 4 mM) were titrated with CF_3COOH in CH_3CN solution (see Fig. 4). In principle, PET quenching would be eliminated by protonation of the macroring nitrogen atom. Photoelectron transfer presumably takes place between the macroring nitrogen, and to a lesser extent, oxygen atoms. A strong acid such as trifluoroacetic acid (CF_3COOH) should react rapidly and completely with the macroring amines.

In each of the three figure panels, the fluorescent response of the free receptor at a concentration of 4 mM in degassed CH_3CN is shown as a black trace. In all three cases, this is the trace closest to the baseline. The trace above it (red) represents the fluorescent response after addition of 1 equivalent of CF_3COOH. After addition of 2 equivalents of H^+, both nitrogens in diaza-18-crown-6 should be protonated and only the oxygen atom non-bonding and arene pi electrons will be available to photoquench the fluorescence signal. Figure 4, shows that after addition of 2 equivalents of protons, the fluorescence spectra of **1** and **3** are nearly unchanged even after addition of 20 equivalents of H^+. A significant difference is observed in the spectra of **2** after addition of two protons. The orange line (panel b, Fig. 4) shows that the fluorescence signal increases significantly after 2 equivalents of acid are present and a small amount even after 5 proton equivalents are present (green line). Thus, the behavior of **1** and **3** differs in this respect from that of **2**.

Compound **1** exhibits a new fluorescence band at $\lambda = 295$ nm while **2** and **3** do not. The spectral behavior observed for **1** suggests excimer formation [65]. We thus recorded the fluorescence spectra of **1** at concentrations from 0.11 mM to 8.7 mM in degassed acetonitrile solution. The results of these studies are shown in Fig. 5. At each concentration, 2 equivalents of CF_3COOH were added to protonate the macroring nitrogen atoms. Panel a of Fig. 4 (for **1**) shows that the fluorescence spectra are unchanged after 2 equivalents of acid are added. Thus, the possibility of nonbonding electron pair interactions involving nitrogen are not expected to affect the Fig. 5 spectra.

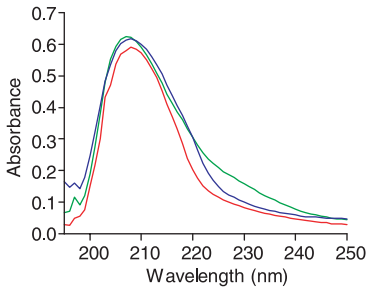

FIGURE 3 UV-visible spectra of **1–3** (concentration ~40 μM) in CH_3CN. The spectra are: **1**, red; **2**, green; and **3**, blue.

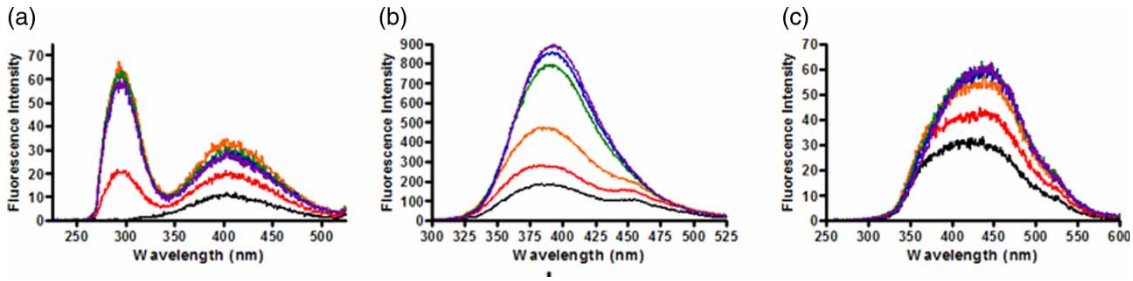

FIGURE 4 Fluorescence spectra of **1**–**3** (4 mM) in CH_3CN when titrated with CF_3COOH (λ_{Ex} = 265, slit width, 5 nm). (a) Titration of **1**; (b) titration of **2**; (c) titration of **3**. Color code: black, free receptor; red, 1 equiv.; orange, 2 equiv.; green, 5 equiv.; blue, 10 equiv.; and purple, 20 equiv. of trifluoroacetic acid (see colour online).

Spectra were recorded at 0.11, 0.22, 0.44, 0.87, 1.7, 4, and 8.7 mM. Data are shown only for 0.11 mM (black), 1.7 mM (blue), 4 mM (violet), and 8.7 mM (red) concentrations in Fig. 5, top panel. At the lowest concentration (0.11 mM, black line), the peak having a maximum near 295 nm is small and the peak at 404 nm is prominent. At a concentration 15-fold higher (blue line), the 295 nm peak has reached the highest fluorescence intensity observed in this series and the 404 nm peak has diminished some. When the concentration is approximately doubled from 1.7 mM to 4 mM, both peaks are less intense than at the lower concentration. At a final concentration of 8.7 mM, approximately 80-fold higher than the initial value, both peaks are again significantly reduced in intensity. The overall trend of these data can be seen in Fig. 5, lower panel, which shows a plot of fluorescence intensity ratios for the two peaks as a function of concentration. There is a gradual increase from 0–2 mM and then a leveling. This suggests that the excimer is formed intermolecularly. The peak at 295 nm is assigned to the monomer peak while the peak seen at 404 nm is the lower energy excimer peak. The spectra in Fig. 5 do not show a clear isoemissive point so more than one excited state species may be emitting.

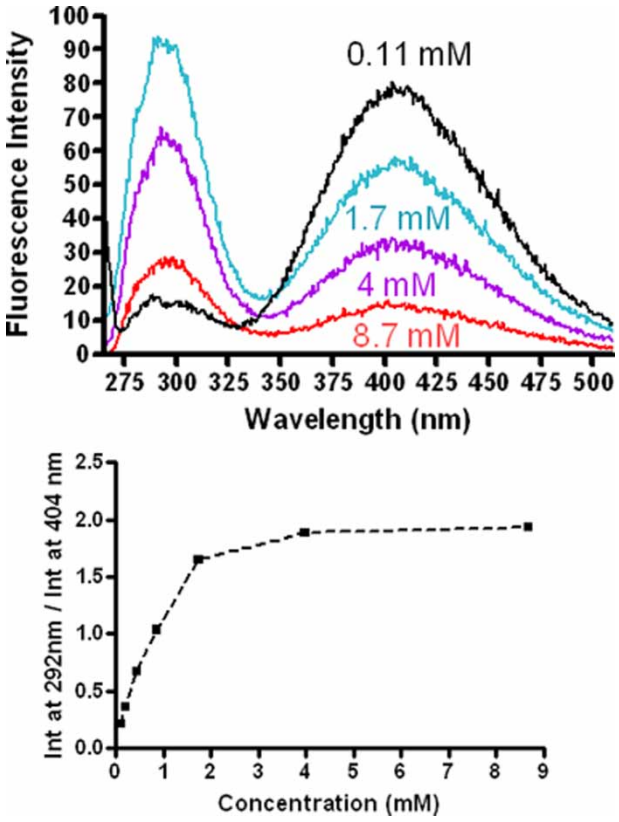

FIGURE 5 (Top) Fluorescence spectra of **1** in degassed CH_3CN. Acid concentration was 2 equivalents for the stated receptor concentration: black, 0.11 mM; blue, 1.7 mM; purple, 4 mM; and red, 8.7 mM. (Bottom) Plot of peak intensities as a function of concentration.

Conformations of Diazacrowns

It is clear that compounds **1**–**3** must exist in different conformations simply because the sidechains differ in structure. When either a protonic or Lewis acid is present, the lone pair electrons on nitrogen are involved as Lewis base donors and this further alters sidechain invertability and conformation. Some structural information is available for **1**–**3**. We reported the solid state structures of **1** and of its KSCN complex some years ago [66]. We have also reported the structure of **2** complexed by various salts [1]. Compound **2** is a low melting solid (mp 48–50 °C) but the extended sidechain conformations of *N*,*N*′-bis(2-(4-hydroxyphenyl)ethyl)-4,13-diaza-18-crown-6, **4** [1], and *N*,*N*′-bis(2-(pentafluorophenyl)ethyl)-4,13-diaza-18-crown-6, are similar and as expected for a phenylethyl residue. A visual comparison of expected sidearm conformations in **1**–**3** can be made by considering the calculated structures (Gaussian 03, gas phase) for the three dimethylamines that correspond to the sidechains, i.e., $(Ph(CH_2)_nN(CH_3)_2$ (n = 1–3). These are shown in Fig. 6 in panels a, b, and c, respectively.

The benzyl carbon in each structure is attached to the arene. It is obviously coplanar with the ring but the adjacent atom may not be. In both dimethylbenzylamine and dimethylphenylethylamine, the bond connected to the benzylic carbon is nearly perpendicular to the arene. In contrast, the aliphatic carbons and nitrogen in dimethylphenylpropylamine all lie in the same plane as the arene. The distances between the nitrogen and the *ipso*

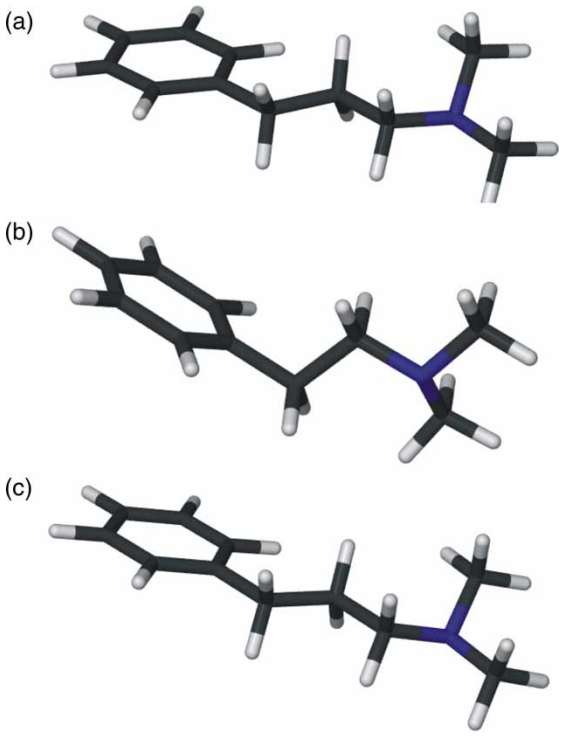

FIGURE 6 Computed structures for (a) *N,N*-dimethylbenzylamine; (b). *N,N*-dimethyl-2-phenylethylamine; (c) *N,N*-dimethyl-3-phenylpropylamine. (The structures were calculated by using Gaussian 03 for the gas phase.)

carbon are 2.47 Å, 3.83 Å, and 4.89 Å, for **1**–**3**, respectively. If the distance from nitrogen is measured to the benzene ring centroid, the corresponding distances are 3.72 Å, 5.15 Å, and 6.42 Å. Of course, the angle between the nitrogen lone-pair orbital and the arene's pi system also varies and this is expected to affect photoelectron transfer.

The conformation expected for a diprotonated diazacrown must differ from that of the free base. To our knowledge, three groups have reported structures of dibenzyldiaza-18-crown-6 proton complexes. Evans *et al.* [67] reported evidence for conformation-controlling C—H···pi interactions in HBr and HNO_3 complexes. These interactions were observed between a macroring ethyleneoxy C—H bond and the arene. The carbon-to-centroid distances were under 4 Å suggesting a significant interaction. The C—H···pi interaction was essentially confirmed for the **1**·$(HBF_4)_2$ complex in a recent study reported by Basok *et al.* [68] and Gaballa *et al.* [69] reported a significantly different conformation for $H_2\mathbf{1}^{2+}$ in the structure of **1**·H_2I_8. In this case, no C—H contact was apparent, but the ammonium proton on each macroring nitrogen was involved in a bifurcated hydrogen bond to the two nearest macroring oxygen atoms.

We are unaware of any structural information that is available for protonated forms of **2** and **3**. However, we have previously reported structures for the analog of **2** in which the sidechain benzene rings were replaced by indole residues (**5**) [1]. The free receptor molecule exhibits the sidearm-extended conformation typical of these macrocycles. Upon protonation, however, a conformation strongly reminiscent of that observed for cation–pi complexes is observed. Solid state structures of **5** (top panel) and **5**·$(HPF_6)_2$ (lower panel) receptors are shown in Fig. 7. Note that the hexafluorophosphate anion is disordered.

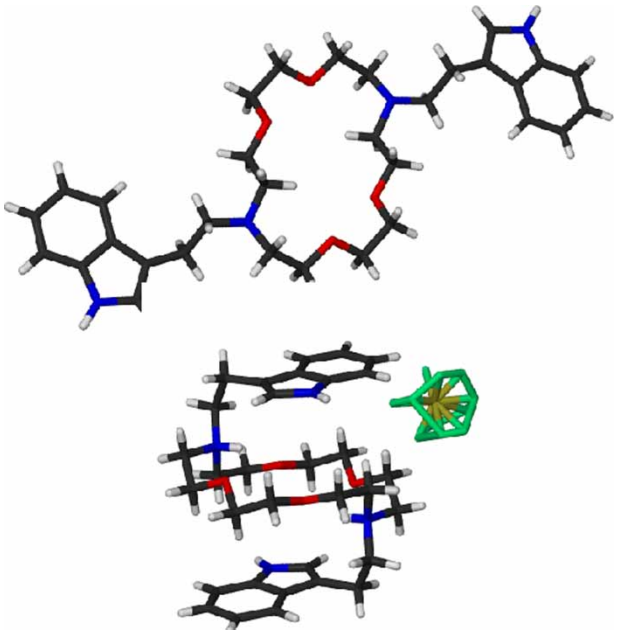

FIGURE 7 Solid state structures of **5** in the absence (top panel) and presence of HPF_6.

Taken together, the computational models and solid state structures show remarkable conformational variation in these compounds. It is therefore reasonable that the fluorescence spectra differ as much as they do. The different conformations alter both the orientation of electron-rich groups and the distances separating them. Both of these variables affect photoelectron transfer in fluorescent lariat ether compounds.

Titration of 1–3 with KSCN

Compounds **1**–**3** were titrated with KSCN in CH_3CN solution. Figure 8 shows fluorescence spectra for **1**–**3** (see Fig. 8 caption for concentrations) in the absence and in the presence of 5 equivalents of KSCN. Spectra were also obtained after addition of 10 and 20 equivalents of KSCN that were essentially identical to those shown for the lower salt concentration.

Complexation of **1**–**3** by KSCN involves the macroring heteroatoms in M^+-X interactions, where X is either O or N. Typically, a single cation is bound in the macroring by all six heteroatoms. Thus, a single equivalent of salt should prevent significant electron transfer from nitrogen during irradiation.

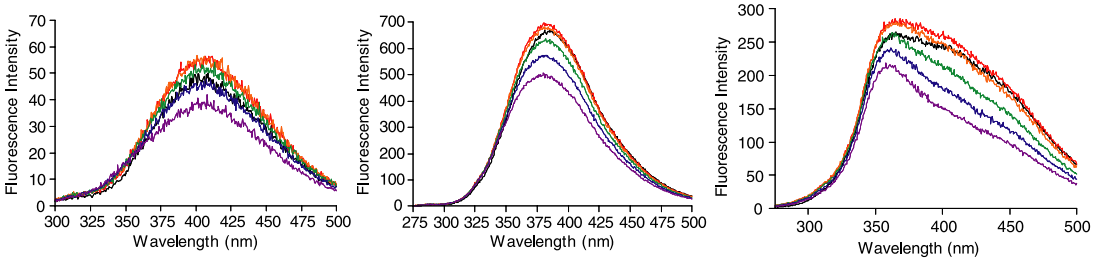

FIGURE 8 Titration of **1** (left, 0.796 mM), **2** (center, 0.145 mM), and **3** (right, 0.798 mM) in CH_3CN with KSCN. Excitation was at $\lambda = 265$ nm. Equivalents of KSCN added: black, 0; red, 1; orange, 2; green, 3; blue, 10; and purple, 20.

The fluorescence spectra differ some in peak position. Compounds **1** and **3** exhibit maxima near $\lambda = 360$ nm and 365 nm, respectively. At the same concentration (0.8 mM), the fluorescence intensity is under 60 for **1** and under 300 for **3**. This difference is significant but the maximal fluorescent intensity observed for **2** is nearly 700. Further, λ_{max} for **2** is near 370 nm in the absence of salt and close to 380 nm after 20 equivalents of KSCN have been added.

In all three cases, the fluorescence spectra of **1**–**3** increase in intensity after addition of a single equivalent of KSCN (black → red). Little difference is observed when a second equivalent is added; the orange and red lines shown in Fig. 8 are nearly superimposed in all three spectra. Addition of 5, 10, and 20 equivalents of salt progressively reduced the fluorescence intensity. Titration of toluene with KSCN in control experiments resulted in fluorescence quenching (data not shown). The change in intensity did not result from dilution as the volume change was ≤3%. The consistency of this effect suggests that it may reflect increased polarity in the medium. None of these observations translates clearly into evidence for cation–pi interactions between benzene and potassium in acetonitrile solution.

CONCLUSIONS

The fluorescence spectra of lariat ethers having sidearms terminated by benzene rings have been obtained in solution in the absence and presence of both protonic and Lewis acids. The fluorescence maxima observed for the arene in **1**–**3** varies in peak position and intensity. In the absence or presence of a cationic species, phenylethyl-sidearmed **2** invariably exhibits a more intense spectrum. In all previous studies, cation–pi complexes of either Na^+ or K^+ were obtained only with **2** and never with **1** or **3**. The spectral evidence comports with different solution behavior for **2** compared to either **1** or **3**.

Titrations of **1**–**3** with CF_3COOH resulted in varying degrees of fluorescence recovery by the diazacrowns. Shorter alkyl spacers in **1** and **2** showed a greater fluorescence increase. This may be due to H^+ induced conformational changes; such differences have certainly been observed in solid state structural studies. The fluorescence spectrum of **1** in the presence of H^+ shows a new peak near 295 nm in addition to the peak near 404 nm. The higher energy peak is observed at a wavelength similar to that of toluene, ethylbenzene, and propylbenzene. We conclude that both monomer and excimer are present in the acid titration spectrum of **1**. The intensity ratio of the higher and lower energy peaks varies with concentration. This observation is consistent with an intermolecular interaction.

Compared with H^+, the influence of K^+ on the fluorescence spectra of receptors **1**–**3** is less clear. The Lewis acid-lariat ether receptor interaction may be weaker and thus more difficult to observe than the protonic acid-receptor interaction. Compounds **1**–**3** experience a similar trend upon titration with K^+: a slight fluorescence increase followed by quenching. The decrease in fluorescence intensity could reflect an increase in solution polarity. Taken together, the optical spectra show significant differences in receptors **1**–**3** both alone and in the presence of Lewis acids. These differences, however, do not provide a reliable analytical method to assess cation–pi interaction under the experimental conditions studied.

EXPERIMENTAL SECTION

N,N′-Dibenzyl-4,13-diaza-18-crown-6, 1

Was prepared as previously described [53–55].

N,N′-bis(2-Phenylethyl)-4,13-diaza-18-crown-6, 2

Was prepared as previously described [4].

N,N′-bis(3-Phenylpropyl)-4,13-diaza-18-crown-6, 3

Was prepared as previously described [56].

N,N′-bis(2-(4-Hydroxyphenyl)ethyl)-4,13-diaza-18-crown-6, 4

Was prepared as previously described [1].

N,N′-bis(2-(3-Indolyl)ethyl)-4,13-diaza-18-crown-6, 5

Was prepared as previously described [1].

Toluene, ethylbenzene, propylbenzene, and CF_3COOH were obtained from Sigma-Aldrich and distilled prior to use. KSCN was dried under high vacuum overnight. CH_2Cl_2 and CH_3CN were distilled and degassed.

Absorbance Spectroscopy

Absorbance spectra were taken of **1**, **2**, **3**, toluene, ethylbenzene, and propylbenzene in CH_2Cl_2 and/or CH_3CN solution. Concentration of receptors **1**–**3** was 40 μM. Toluene, ethylbenzene, and propylbenzene were each measured at 2.5 mM. Data were recorded on a Beckman Coulter DU7400 spectrophotometer. The volume was 3.0 mL in a cell with a path length of 1.00 cm. Per sample reading, at least 5 absorbance scans were taken and averaged.

Fluorescence Spectroscopy

Spectra were recorded on a Perkin Elmer LS 50B fluorimeter. Compounds **1**–**3** were irradiated at $\lambda = 265$ nm. The emission slit width was 5.0 nm. The path length was 1.00 cm and each spectrum was obtained on 3.0 mL solution. For each spectrum, 5 repetitions were averaged to obtain a smooth curve. Fluorescence titrations of compounds **1**–**3** with KSCN and CF_3COOH were done in degassed CH_3CN solution. The concentrations of KSCN and CF_3COOH in CH_3CN solution were 96 mM and 130 mM, respectively. A maximum of 50 μL of each solution was required for H^+ or K^+ titration so the volume change from 3.0 mL in the cell was negligible. Pure CH_3CN was added up to 10% (v/v) and there was no change in any of the spectra (data not shown). Measurements were taken at room temperature. The absence of H_2O contaminant in the solvent was confirmed by a lack of fluorescence signal at 320 nm when excitation was set at $\lambda = 270$ nm. Concentration ranges were achieved by serial dilution of the original stock solution.

Calculations

The structures of the diamines shown in Fig. 6 were calculated for the gas phase using Gaussian 03. The structures were rendered as stick models by using POV-ray.

Acknowledgements

We thank the National Science Foundation for grant CHE-0415586, that supported this work.

References

[1] Meadows, E. S.; De Wall, S. L.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 3092.
[2] Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J. *Acc. Chem. Res.* **2002**, *35*, 878.
[3] Gokel, G. W. *Chem. Commun.* **2003**, 2847.
[4] De Wall, S. L.; Meadows, E. S.; Barbour, L. J.; Gokel, G. W. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 6271.
[5] De Wall, S. L.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 8405.
[6] De Wall, S. L.; Meadows, E. S.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 5613.
[7] Dougherty, D. *Science* **1996**, *271*, 1163.
[8] Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303.
[9] Gallivan, J. P.; Dougherty, D. A. *Proc. Natl. Acad. Sci. USA* **1999**, *96*, 9459.
[10] Gokel, G. W.; Wall, S. L. D.; Meadows, E. S. *Eur. J. Org. Chem.* **2000**, 2967.
[11] Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J. *Acc. Chem. Res.* **2002**, *35*, 878.
[12] Hu, J.; Gokel, G. W. *Chem. Commun.* **2003**, 2536.
[13] Arnold, K. A.; Viscariello, A. M.; Kim, M.; Gandour, R. D.; Fronczek, F. R.; Gokel, G. W. *Tetrahedron Lett.* **1988**, 3025.
[14] Hu, J.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 9486.
[15] Arya, P.; Channa, A.; Cragg, P. J.; Prince, P. D.; Steed, J. W. *New J. Chem.* **2002**, *26*, 440.
[16] *Cation Binding by Macrocycles*; Inoue, Y., Gokel, G. W., Eds.; Marcel Dekker: New York, 1990.
[17] Kaifer, A.; Echegoyen, L.; Gustowski, D.; Goli, D. M.; Gokel, G. W. *J. Am. Chem. Soc.* **1983**, *105*, 7168.
[18] Echegoyen, L.; Gustowski, D. A.; Gatto, V. J.; Gokel, G. W. *J. Chem. Soc. Chem. Commun.* **1986**, 220.
[19] Medina, J. C.; Goodnow, T. T.; Rojas, M. T.; Atwood, J. L.; Lynn, B. C.; Kaifer, A. E.; Gokel, G. W. *J. Am. Chem. Soc.* **1992**, *114*, 10583.
[20] Gokel, G. W.; Dishong, D. M.; Diamond, C. J. *J. C. S. Chem. Commun.* **1980**, 1053.
[21] Gokel, G. W. *Chem. Soc. Rev.* **1992**, *21*, 39.
[22] Takagi, M.; Ueno, K. *Top. Curr. Chem.* **1984**, *121*, 39.
[23] Leray, I.; Lefevre, J. P.; Delouis, J. F.; Delaire, J.; Valeur, B. *Chemistry* **2001**, *7*, 4590.
[24] Leray, I.; Asfari, Z.; Vicens, J.; Valeur, B. *J. Fluoresc.* **2004**, *14*, 451.
[25] Kubinyi, M.; Pal, K.; Baranyai, P.; Grofcsik, A.; Bitter, I.; Grun, A. *Chirality* **2004**, *16*, 174.
[26] He, H.; Mortellaro, M. A.; Leiner, M. J.; Fraatz, R. J.; Tusa, J. K. *J. Am. Chem. Soc.* **2003**, *125*, 1468.
[27] He, H.; Mortellaro, M. A.; Leiner, M. J.; Young, S. T.; Fraatz, R. J.; Tusa, J. K. *Anal. Chem.* **2003**, *75*, 549.
[28] Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Kotzyba-Hibert, F.; Lehn, J. -M.; Prodi, L. *J. Am. Chem. Soc.* **1994**, *116*, 5741.
[29] Nakahara, Y.; Kida, T.; Nakatsuji, Y.; Akashi, M. *Org. Biomol. Chem.* **2005**, *3*, 1787.
[30] McSkimming, G.; Tucker, J. H.; Bouas-Laurent, H.; Desvergne, J. P.; Coles, S. J.; Hursthouse, M. B.; Light, M. E. *Chem. Eur. J.* **2002**, *8*, 3331.
[31] Minta, A.; Tsien, R. Y. *J. Biol. Chem.* **1989**, *264*, 19449.
[32] Clares, M. P.; Aguilar, J.; Aucejo, R.; Lodeiro, C.; Albelda, M. T.; Pina, F.; Lima, J. C.; Parola, A. J.; Pina, J.; Seixas De Melo, J.; Soriano, C.; Garcia-Espana, E. *Inorg. Chem.* **2004**, *43*, 6114.
[33] Sulowska, H.; Wiczk, W.; Mlodzianowski, J.; Przyborowska, M.; Ossowski, T. *J. Photochem. Photobiol. A* **2002**, *150*, 249.
[34] Abel, E.; Maguire, G. E. M.; Murillo, O.; Suzuki, I.; Gokel, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 9043.
[35] Gokel, G. W. *Chem. Comm.* **2000**, 1.
[36] Witulski, B.; Zimmermann, Y.; Darcos, V.; Desvergne, J. -P.; Bassani, D. M.; Bouas-Laurent, H. *Tetrahedron Lett.* **1998**, *39*, 4807.
[37] Gawley, R. E.; Pinet, S.; Cardona, C. M.; Datta, P. K.; Ren, T.; Guida, W. C.; Nydick, J.; Leblanc, R. M. *J. Am. Chem. Soc.* **2002**, *124*, 13448.
[38] Herrmann, U.; Tummler, B.; Maass, G.; Koo Tze Mew, P.; Vogtle, F. *Biochemistry* **1984**, *23*, 4059.
[39] Nakahara, Y.; Matsumi, Y.; Zhang, W.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *Org. Lett.* **2002**, *4*, 2641.
[40] Nakahara, Y.; Kida, T.; Nakatsuji, Y.; Akashi, M. *J. Org. Chem.* **2004**, *69*, 4403.

[41] Nakahara, Y.; Kida, T.; Nakatsuji, Y.; Akashi, M. *Org. Biomol. Chem.* **2005**, *3*, 1787.
[42] Yamauchi, A.; Hayashita, T.; Kato, A.; Nishizawa, S.; Watanabe, M.; Teramae, N. *Anal. Chem.* **2000**, *72*, 5841.
[43] Liu, Y.; Yang, Y. W.; Li, L.; Chen, Y. *Org. Biomol. Chem.* **2004**, *2*, 1542.
[44] Liu, Y.; Duan, Z. Y.; Chen, Y.; Han, J. R.; Cui, L. *Org. Biomol. Chem.* **2004**, *2*, 2359.
[45] Patellis, A.-M.; Galy, J.-P.; Kister, J.; Chicheportiche, R.; Elguero, J. *J. Heterocyclic Chem.* **2001**, *38*, 1113.
[46] He, H.; Mortellaro, M. A.; Leiner, M. J.; Young, S. T.; Fraatz, R. J.; Tusa, J. K. *Anal. Chem.* **2003**, *75*, 549.
[47] Pond, S. J.; Tsutsumi, O.; Rumi, M.; Kwon, O.; Zojer, E.; Bredas, J. L.; Marder, S. R.; Perry, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 9291.
[48] Zhou, L. L.; Sun, H.; Li, H. P.; Wang, H.; Zhang, X. H.; Wu, S. K.; Lee, S. T. *Org. Lett.* **2004**, *6*, 1071.
[49] Martin, V. V.; Rothe, A.; Diwu, Z.; Gee, K. R. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5313.
[50] Martin, V. V.; Rothe, A.; Gee, K. R. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1851.
[51] Bourson, J.; Pouget, J.; Valeur, B. *J. Phys. Chem.* **1993**, *97*, 4552.
[52] Valeur, B. *Molecular Fluorescence: Principles and Applications*; Wiley-VCH: Weinheim, 2002; p 387.
[53] de Silva, A. P.; Gunaratne, H. Q.; Gunnlaugsson, T.; Huxley, A. J.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515.
[54] de Silva, A. P.; Eilers, J.; Zlokarnik, G. *Proc. Natl. Acad. Sci. U S A* **1999**, *96*, 8336.
[55] de Silva, A. P.; Fox, D. B.; Moody, T. S.; Weir, S. M. *Trends Biotechnol.* **2001**, *19*, 29.
[56] Gatto, V. J.; Miller, S. R.; Gokel, G. W. *Org. Syntheses* **1989**, *68*, 227.
[57] Hu, J.; Barbour, L. J.; Ferdani, R.; Gokel, G. W. *J. Supramol. Chem.* **2001**, *1*, 157.
[58] Gandour, R. D.; Fronczek, F. R.; Gatto, V. J.; Minganti, C.; Schultz, R. A.; White, B. D.; Arnold, K. A.; Mazzocchi, D.; Miller, S. R.; Gokel, G. W. *J. Am. Chem. Soc.* **1986**, *108*, 4078.
[59] Meadows, E. S.; DeWall, S. L.; Barbour, L. J.; Fronczek, F. R.; Kim, M.-S.; Gokel, G. W. *J. Am. Chem. Soc.* **2000**, *122*, 3325.
[60] De Wall, S. L.; Meadows, E. S.; Barbour, L. J.; Gokel, G. W. *Proc. Natl. Acad. Sci. USA* **2000**, *97*, 6271.
[61] Meadows, E. S.; De Wall, S. L.; Barbour, L. J.; Gokel, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 3092.
[62] Gokel, G. W.; Barbour, L. J.; Ferdani, R.; Hu, J *Acc. Chem. Res.* **2002**, *35*(10), 878.
[63] Hu, J.; Barbour, L. J.; Gokel, G. W. *Chem. Comm.* **2002**, 1808.
[64] Berlman, I. B. *Handbook of fluorescence spectra of aromatic molecules*; Academic Press: New York, 1971.
[65] Hirayama, F. *J. Chem. Phys.* **1965**, *42*, 3163.
[66] Arnold, K. A.; Viscariello, A. M.; Kim, M.; Gandour, R. D.; Fronczek, F. R.; Gokel, G. W. *Tetrahedron Lett.* **1988**, 3025.
[67] Evans, D. J.; Junk, P. C.; Smith, M. K. *New J. Chem.* **2002**, *26*, 1043.
[68] Basok, S. S.; Croitoru, L.; Fonari, M. S.; Ganin, E. V.; Gelmboldt, V. O.; Lipkowski, J.; Simonov, Y. A. *Acta Cryst.* **2005**, *C61*, o188.
[69] Gaballa, A. S.; Teleb, S. M.; Rusanov, E.; Steinborn, D. *Inorg. Chim. Acta* **2004**, *357*, 4144.