A new class of functionalized calix[4]arenes as neutral receptors for colorimetric detection of fluoride ions†

Har Mohindra Chawla,* Rahul Shrivastava and Satya Narayan Sahu

Received (in Montpellier, France) 21st January 2008, Accepted 23rd April 2008
First published as an Advance Article on the web 15th July 2008
DOI: 10.1039/b800502h

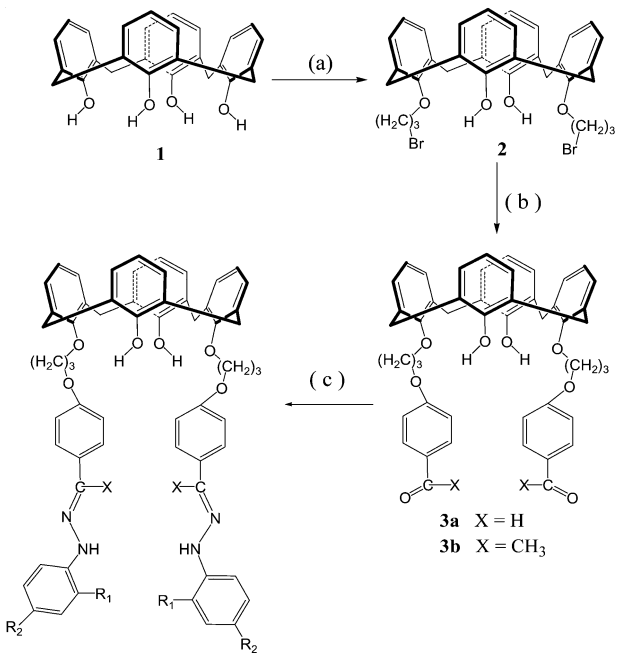
A new class of functionalized calix[4]arenes have been synthesized and evaluated for colorimetric detection of fluoride ions. The molecular receptor **4b** selectively recognizes fluoride ions *via* H-bonds and subsequent deprotonation to elicit a distinct colour change from yellow to dark purple.

Introduction

Recognition of fluoride ions is an important target for diverse applications in chemical and biological processes.[1] Real-time monitoring and accurate detection of fluoride ions using convenient colorimetric assay are important aims for practical field applications. Amongst several approaches adopted[2] for the development of fluoride ion receptors, the recognition of fluoride through neutral receptors[3] seems to be of utmost significance. Previous work on colorimetric sensing of fluoride ions concerns with molecular hosts employing different combinations of amide, urea, thiourea and pyrrole units[4] which coordinate and bind the anionic species through N–H–X hydrogen bonds. The anion interaction triggers a change in the photophysical response of the chromogen present in the host molecule to allow fluoride ion sensing through a colour change.[5–7] Due to its small size and high electronegativity, fluoride ion represents a special case where an ion can form strong hydrogen bonds at lower concentrations and can act as a sufficiently strong base at higher concentrations to promote deprotonation through typical Brønsted acid–base reactions.[8] Distinction between these two processes has often been blurred in the case of fluoride recognition experiments.[9] Since calix[*n*]arenes[10] possess a preorganised molecular architecture for ionic and molecular recognition,[11] we envisaged the use of these scaffolds for sensing of fluoride ions through host–guest interactions. The choice of calix[4]arene scaffold was prompted by our previous work[12] on anion recognition as well as possible use of calixarene cavity for supporting fluoride entrapment through proper functionalization. Though examples of calix[4]arene based fluoride receptors utilizing photoinduced electron transfer (PET) or photoinduced charge transfer (PCT) have been reported,[13] there is a paucity of colorimetric sensors for selective detection and estimation of fluoride ions at low concentrations.[14] We report herein the synthesis and evaluation of five new calix[4]arene derivatives (**4a–e**) with hydrazone functionalities in distal 1,3-positions at their lower rim for the target purpose. Amongst the synthesized compounds, **4b** was found to exhibit selective binding with fluoride ions *via* H-bond interactions and elicit a distinct 'naked eye' colour change from yellow to dark purple through efficient deprotonation.

Results and discussion

The synthesis of **4a–e** could be achieved through facile synthetic protocols (Scheme 1). The required starting materials calix[4]arene **1**, bis(bromopropyl)calix[4]arene **2** and



Comp. No	X	R_1	R_2
4a	H	H	H
4b	H	H	NO_2
4c	H	NO_2	NO_2
4d	CH_3	H	NO_2
4e	CH_3	NO_2	NO_2

Scheme 1 Synthesis of receptors **4a–e**. *Reagents and conditions*: (a) $Br–(CH_2)_3–Br$, K_2CO_3, CH_3CN, reflux, 15 h;[12a] (b) *p*-hydroxybenzaldehyde or *p*-hydroxyacetophenone, K_2CO_3, CH_3CN, reflux, 12 h;[12a] (c) phenyl hydrazine derivatives, ethanol.

Department of Chemistry, Indian Institute of Technology, Hauz Khas, New Delhi-110016, India. E-mail: hmchawla@chemistry.iitd.ernet.in; Fax: +91 11-26591502; Tel: +91 11-26591517

† Electronic supplementary information (ESI) available: UV-visible spectra, titration plots and binding curves of **4b** and **4c** upon addition of TBA-anions, ^1H NMR spectra for **4b** and **4c** and COSY spectra for **4b**, and **4b** + F^- and ^{19}F NMR spectra. See DOI: 10.1039/b800502h

calix[4]arene derivatives **3a,b** in cone conformation were prepared according to previous literature procedures.[12a] Reaction of **3a** and **3b** with phenylhydrazine reagents gave **4a–e** in 88–94% yields. The elemental and spectroscopic analysis of **4a–e** were consistent with their indicated structures. For instance **4b** showed a pair of doublets at δ 3.48 and 4.17 for axial and equatorial protons, respectively in the ^{1}H NMR spectrum and a distinct signal at δ 30.2 for the methylene carbons in its ^{13}C NMR spectrum indicated its symmetrical conformation.[15] The singlets of –NH and –OH protons appeared at δ 11.15 and 8.46, respectively which disappeared on deuteration with D_2O. The FT-IR spectrum exhibited a sharp peak at 1598 cm^{-1} for the >C=N– absorptions.

The binding of **4a–e** with various anions (such as F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, ClO_4^- and PF_6^-, in the form of their tetrabutylammonium salts) was first monitored through visual and colorimetric observations in DMSO–CH_3CN (0.5 : 9.5 v/v). It was found that the receptor **4b** exhibited a prominent and instant colour change from light yellow to dark purple only with fluoride ions while **4c** gave a marked colour change on interaction with fluoride as well as with dihydrogen phosphate and acetate anions (Fig. 1). Receptor **4a** did not give any visual response while **4d** and **4e** gave similar colour changes as observed in the case of **4b** and **4c**, respectively on treatment with the tested anions under similar conditions.

When investigated spectrophotometrically, the interaction of **4b** with fluoride ions exhibited a bathochromic shift ($\Delta\lambda_{max}$) of 143 nm in its UV-visible spectrum at 5×10^{-5} M concentration with the appearance of a new absorption peak at 549 nm whereas no shift in the absorption maxima was observed with other anionic species (Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, ClO_4^- and PF_6^-) as depicted in Fig. 2(a). It was observed that gradual addition of a standard solution of tetrabutylammonium fluoride (TBAF), progressively decreased the intensity of the absorption peak at 406 nm with concurrent increase in the absorption peak centred at 549 nm in the UV-visible spectrum (Fig. 2). A colour change from yellow to light purple was observed when the concentration of fluoride ion approached one equivalent with respect to **4b**.

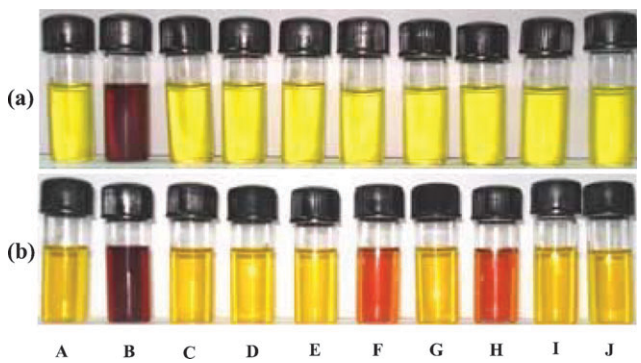


Fig. 1 Selectivity of **4b** for fluoride over other anions. Colour changes of **4b** (a) and **4c** (b) (50 μM) in DMSO–CH_3CN (0.5 : 9.5 v/v) with the addition of TBA anions (5×10^{-4} M): A = free receptor, B = F^-, C = Cl^-, D = Br^-, E = I^-, F = $H_2PO_4^-$, G = HSO_4^-, H = AcO^-, I = ClO_4^-, J = PF_6^-.

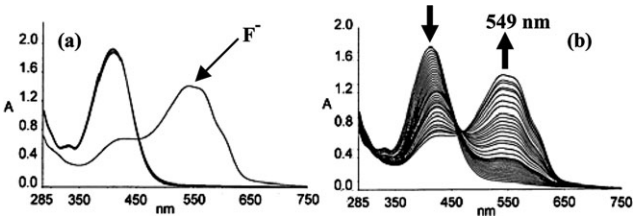


Fig. 2 (a) Absorption spectra of **4b** (5×10^{-5} M) upon addition of F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, ClO_4^- and PF_6^- ions (as tetrabutylammonium salts) (1×10^{-4} M) in DMSO–CH_3CN (0.5 : 9.5 v/v). (b) UV-visible titrations of **4b** with 0–8 equiv. of F^-.

Further addition of fluoride ions to **4b** increased the intensity of the absorption band centered at 549 nm with concurrent deepening of the purple colour that reached its limiting value on addition of four equivalents of fluoride ions. Given the fact that fluoride ion can deprotonate one or more NH protons of the receptor beyond two equivalents,[16] the observed spectrophotometric titration profile of **4b** with fluoride was quite surprising. Detailed analysis of the UV-visible titration results indicated that the limiting value in the absorption maxima centered at 549 nm was attained at four equivalents of F^- instead of two equivalents. This can be accounted for by hypothesizing that the initial addition of one equivalent of F^- establishes a hydrogen bond interaction with NH protons of the receptor (1 : 1 complex) followed by formation of 2 : 1 (F^- : **4b**) hydrogen-bond adduct on addition of a second equivalent of F^- ions.[14a,17] Further addition of F^- ions beyond two equivalents seems to result in the deprotonation of the NH protons. Experimental observations indicate that the bathochromic shift observed during the **4b**–F^- interaction is either due to the formation of hydrogen bonds with the hydrazone –NH or its deprotonation by fluoride ions which results in a visual colour change possibly through efficient charge transfer.[18] It was interesting to note that addition of a few drops of protic solvents (water or methanol) triggered the disappearance of the observed colour of the **4b**–fluoride complex with immediate regeneration of the original receptor colour. This suggested that the fluoride–calix[4]arene interaction did not involve any plausible bond formation and that the complexation of fluoride ion and **4b** was reversible in nature.

The binding mode of fluoride ions with receptor **4b** was further investigated by ^{1}H NMR titration experiments in DMSO-d_6. The NMR spectrum of **4b** in the presence of increasing equivalents of tetrabutylammonium fluoride (Fig. 3) demonstrated that addition of fluoride ions leads to the broadening of hydrazone –NH signal at δ 11.15 which completely disappears on addition of excess of fluoride. No effect on the chemical shift of CH and OH protons during this process indicates that these functions do not participate in the anion binding process. Detailed analysis of the ^{1}H NMR titration spectra revealed some interesting aspects about the mode of fluoride binding with receptor **4b**. Gradual addition of fluoride ion to **4b** was found to result in an upfield chemical shift in the aromatic C–H_a protons of the *p*-nitrophenyl unit which continues up to the addition of four equivalents of F^- while C–H_b protons are insensitive up to the addition of two equivalents. Addition of fluoride beyond two equivalents was found to

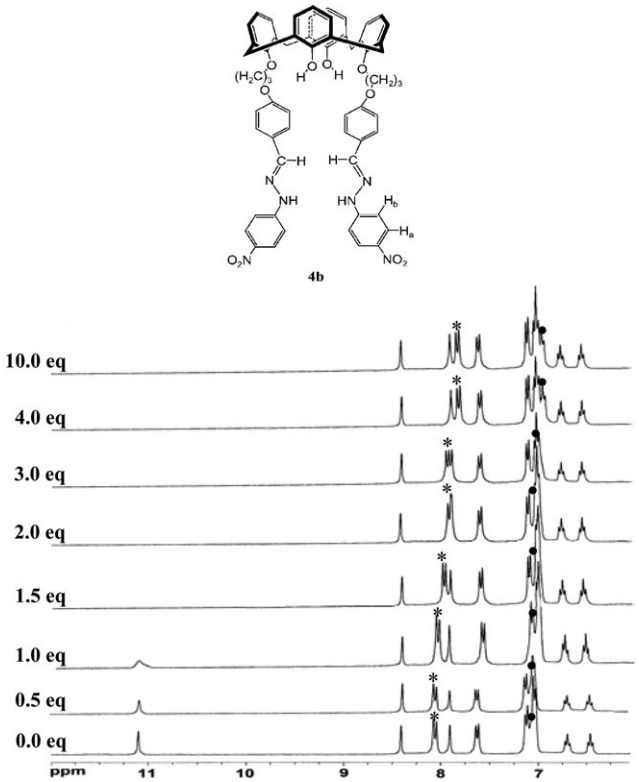


Fig. 3 Partial ^{1}H NMR (300 MHz and 298 K) spectra of **4b** (10 mM) upon addition of various equiv. of TBAF (40 mM) in DMSO-d_6. Numbers at the left side indicate the equivalent amounts of F^- added (* = ArH_a, • = ArH_b).

exhibit an upfield shift in the H_b nuclei which reached its limiting value on addition of four equivalents of F^- ions. This was marked by the appearance of an additional broad signal at about 16 ppm in the ^{1}H NMR spectrum that could be ascribed to the formation of a more stable bifluoride $[HF_2]^-$ species[19] with highest calculated hydrogen bond energy (39 kcal mol^{-1}).[20] These observations indicate that the first two equivalents of F^- ions are used up to interact through hydrogen bonds with the NH protons of hydrazone subunits of receptor **4b** while addition beyond two equivalents of fluoride results in the deprotonation of the NH protons to induce an upfield shift of the H_b proton due to *through-bond* propagation of electron density.

In order to confirm the deprotonation process during the fluoride complexation with **4b**, the UV-visible and ^{1}H NMR experiments were performed with tetrabutylammonium hydroxide (TBAOH). The UV-visible titration experiments of **4b** with a standard solution of TBAOH, revealed a similar spectral pattern as observed in Fig. 2(b) with the difference that the absorption band centered at 549 nm reached its limiting value on addition of two equivalents of hydroxide ions (see ESI†). This can possibly be ascribed to the highly basic nature of hydroxide ion which instantly deprotonates the acidic hydrazone NH protons through Brønsted acid–base type reactions. This was confirmed by the ^{1}H NMR experiments with gradual addition of hydroxide ions to a 10 mM solution of **4b** in DMSO-d_6 (see ESI†). A similar pattern of upfield chemical shifts in H_a and H_b protons (as observed in Fig. 3) were observed and the saturation point could be reached on addition of two equivalents of hydroxide ions.

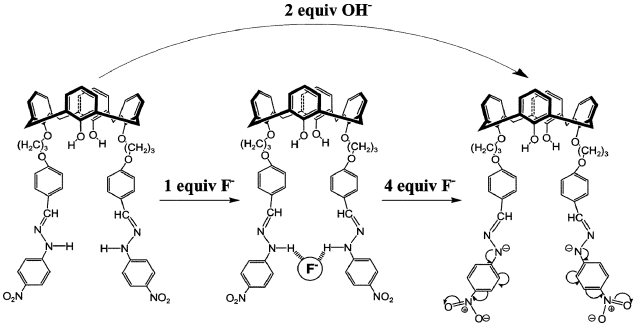
These observations suggested that the deprotonation of **4b** can take place in the presence of two equivalents of hydroxide ions while the fluoride ion interacts with **4b** *via* hydrogen bonds up to the addition of two equivalents after which it leads to deprotonation of NH fragments like that in a typical base[8] and the process gets completed by the addition of four equivalents of fluoride ion as evidenced by the appearance of a broad signal at 16 ppm for bifluoride species (HF_2^-). The proposed mode of fluoride binding with **4b** through sequential hydrogen bond formation and deprotonation was established by ^{19}F NMR spectroscopy. When one equivalent of fluoride ion was added to **4b** the fluoride signal shifted from δ −106.4 to −143.5 ppm indicating the formation of hydrogen-bonded fluoride (HF) species. Further addition of fluoride in excess (8 equiv.) shifted the fluoride signal to δ −140.3 ppm which could be assigned to bifluoride (HF_2^-) species (see ESI†). These findings were further confirmed by 2D COSY spectrum of **4b** in the presence of excess fluoride ion and its absence. Deprotonation of NH fragments was established through correlation of *p*-nitrophenyl protons H_a and H_b in the COSY spectrum (see ESI†). The deprotonated **4b** seems to be stabilized by the delocalization of negative charge on the nitrogen atom over the nitrophenyl group as illustrated in Scheme 2.

Similar experiments with **4c**, **4d** and **4e** gave bathochromic shifts in the UV-visible spectrum with fluoride ions (Table 1) while receptors **4c** and **4e** exhibited shifts of lesser magnitude in their λ_{max} values on addition of tetrabutylammonium dihydrogen phosphate and acetate ions (Fig. 4).

The additional binding ability of receptors **4c** and **4e** for dihydrogen phosphate and acetate ions can possibly be ascribed to the comparatively less basic nature of the NH protons due to the presence of two electron withdrawing nitro substituents.

The UV-visible titration profile of **4c** with F^- ion have revealed a progressive decrease of absorption maxima centered at 389 nm and gradual appearance of a new peak at 485 nm with a colour change from yellow to purple which reached a saturation point on addition of four equivalents of fluoride ions (see ESI†).

The titration profiles with AcO^- and $H_2PO_4^-$ ions reached their limiting values on addition of one equivalent of the respective anions (Fig. 5). These observations suggest that



Scheme 2 A proposed binding mode and deprotonation of **4b** with fluoride and hydroxide ions.

Table 1 Shift in absorption peak (λ_{max}) for receptors **4a–e** in the presence of fluoride ion

Receptors (L)	λ_{max}/nm (L)[a]	λ_{max}/nm (L + F^-)[b]	$\Delta\lambda_{max}$/nm
4a	342	351	09
4b	406	549	143
4c[c]	389	485	96
4d	407	548	141
4e[c]	387	484	97

[a] Absorption spectra were taken at a concentration of 50 μM in DMSO–CH_3CN (0.5 : 9.5 v/v) solution. [b] Tetrabutylammonium fluoride (1×10^{-4} M) was added. [c] Concentration was 20 μM.

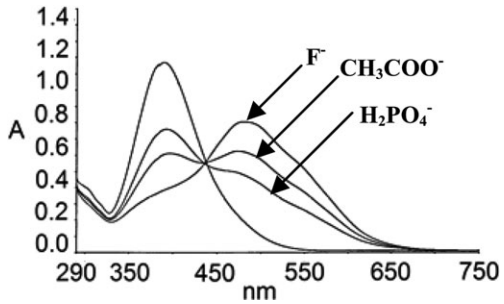


Fig. 4 Absorption spectra of **4c** (2×10^{-5} M) upon addition of F^-, Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, ClO_4^- and PF_6^- ions (as tetrabutylammonium salts) (1×10^{-4} M) in DMSO–CH_3CN (0.5 : 9.5 v/v).

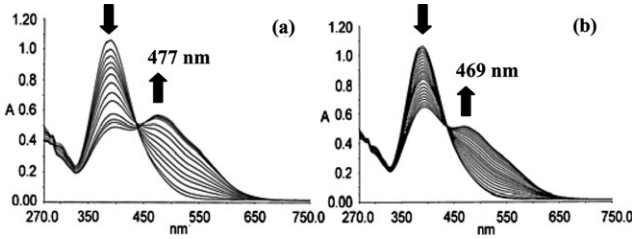
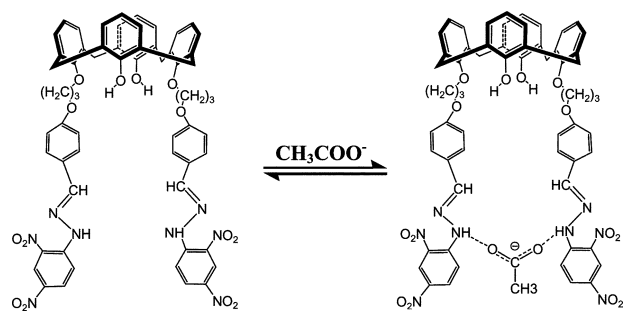


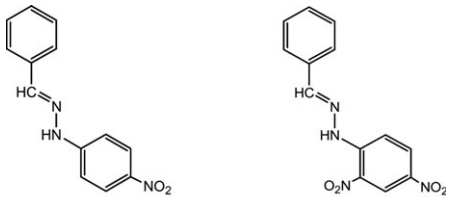
Fig. 5 UV-visible titrations of **4c** with 0–5 equiv. of (a) AcO^- (b) $H_2PO_4^-$.

the binding of F^- ions with **4c** proceeds in a similar manner as that of **4b** while the AcO^- and $H_2PO_4^-$ ions interact with **4c** exclusively through hydrogen bonding (Scheme 3).

To investigate the role of the preorganized structure of calix[4]-arene, we designed other compounds **5** and **6** (Scheme 4), which resemble the single binding pod of receptors **4b** and **4c**. Anion



Scheme 3 A proposed binding mode of **4c** with acetate ion.



Scheme 4

Table 2 Association constants from UV-visible titrations for complexes of receptors **4b–e** with anionic guests in DMSO–CH_3CN (0.5 : 9.5 v/v)[a]

	K_a/M^{-1}		
Receptor	F^-	CH_3COO^-	$H_2PO_4^-$
4b	9.9×10^6	—	—
4c	1.7×10^6	6.3×10^5	4.7×10^5
4d	7.3×10^6	—	—
4e	3.5×10^6	6.7×10^5	5.1×10^5

[a] The anions were added in the form of their TBA salts.

recognition experiments with **5** and **6** at 100 μM concentration revealed no change in their absorption spectra upon addition of either tetrabutylammonium salt of acetate or dihydrogen phosphate while small changes were observed in the absorption spectra of **5** and **6** upon addition of TBAF. However, it was noticed that the spectral changes were not as significant as observed with receptors **4b** and **4c** within the studied fluoride concentration range. These observations proved that although **4b**, **5** and **4c**, **6** have the same type of binding sites, only an appropriate size of the pseudocavity of **4b** and **4c** can bind the anions more effectively.

The receptors **4d** and **4e** exhibited a similar behavior in the UV-visible and colorimetric experiments as that of **4b** and **4c**, respectively thereby suggesting that the azomethine CH protons (in **4b** and **4c**) when replaced by a methyl group (in **4d** and **4e**) do not affect the binding mode of anions. The binding constants[21] (K_a) for **4b–e** with fluoride, acetate and dihydrogen phosphate ions are summarized in Table 2. The higher binding constant obtained for fluoride ion is possibly due to its more basic nature that leads to a stronger hydrogen bond interaction with the receptor molecules in comparison to the case of acetate and dihydrogen phosphate anions.

Conclusion

We conclude that the synthesized new class of neutral calix[4]-arene receptors with hydrazone functions at their lower rim (**4b–e**) exhibit a prominent 'naked-eye' colour change and significant bathochromic shifts when interacted with fluoride ions. Receptor **4b** exhibits a selective binding with fluoride ions *via* H-bond interactions in preference to Cl^-, Br^-, I^-, $H_2PO_4^-$, HSO_4^-, AcO^-, ClO_4^- and PF_6^- ions and elicits a distinct colour change from yellow to dark purple through efficient

deprotonation. These observations pave a way for the development of selective colorimetric sensors for fluoride ions. Further work on this subject is in progress.

Experimental

Synthesis of starting materials

Compounds **1**, **2**, **3a** and **3b** were synthesized by the methods reported earlier.[12a]

Synthesis of calix[4]arene-bis(phenylhydrazone) derivative 4a. A solution of **3a** (0.97 g, 1.3 mmol) in 35 ml of acetonitrile–ethanol (1 : 1 v/v) was treated with 17.0 ml of phenylhydrazine solution.[22] The mixture was heated on a water bath (50 °C) until crystallization began. Further crystallization was allowed to continue at room temperature and the product obtained was filtered off and dried under vacuum to give calix[4]arene-bis(phenylhydrazone) derivative **4a** as an off-white solid, yield (88%, 1.089 g); mp 185 °C; IR (KBr) ν_{max}/cm^{-1}: 3289, 1605; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.49 (s, 2H, N*H*), 8.05 (s, 2H, O*H*), 7.43 (d, 4H, Ar*H*, J = 7.8 Hz), 7.36 (s, 2H, –N=C*H*), 7.18 (br s, 4H, Ar*H*), 6.97 (m, 10H, Ar*H*), 6.84 (br s, 8H, Ar*H*), 6.68 (t, J = 7.2 Hz, 2H, Ar*H*), 6.58 (t, J = 7.2 Hz, 2H, Ar*H*), 4.29 (br s, 4H, OCH_2CH$_2$CH$_2$), 4.19 (d, J = 13.2 Hz, 4H, ArCH_2Ar), 4.08 (br s, 4H, CH$_2$CH$_2$CH_2O), 3.30 (d, J = 13.2 Hz, 4H, ArCH_2Ar), 2.33 (br s, 4H, CH$_2$CH_2CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.9, 154.2, 150.2, 147.2, 141.3, 138.2, 133.2, 128.3, 128.2, 127.3, 126.1, 125.4, 124.2, 117.5, 114.2, 111.0, 72.13 63.47 30.4, 28.5. FAB MS m/z 929 (M + 1, calc. 928). Anal. calc. for $C_{60}H_{56}N_4O_6$: C, 77.56; H, 6.08; N, 6.03. Found C, 77.11; H, 5.98; N, 6.21%.

General procedure for the synthesis of calix[4]arene-bis-(4-nitrophenylhydrazone) derivatives (4b and 4d). A solution of **3a** (0.97 g, 1.3 mmol) and **3b** (1.01 g, 1.3 mmol) in 35 ml of chloroform–ethanol mixture (1 : 2 v/v), 4-nitrophenylhydrazine (0.50 g, 3.2 mmol) and 2 ml of glacial acetic acid was added. The mixture was refluxed for 6 h and then cooled to room temperature. The whole reaction mixture was evaporated and distilled water was added to it. The precipitate obtained was filtered off, washed with water (3 × 25 ml) and then dried under vacuum to give calix[4]arene-bis(4-nitrophenylhydrazone) derivatives **4b** and **4d** as yellow solids.

Compound 4b. Yield (91%, 1.20 g); mp 165 °C; IR (KBr) ν_{max}/cm^{-1}: 3294, 1598, 1501; ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.15 (s, 2H, N*H*), 8.46 (s, 2H, O*H*), 8.11 (d, J = 8.9 Hz, 4H, ArH_{NO_2}), 7.98 (s, 2H, –N=C*H*), 7.68 (d, J = 8.3 Hz, 4H, Ar*H*), 7.09–7.20 (m, 16H, ArH_{NO_2} + Ar*H* + ArH_{calix}), 6.82 (t, J = 7.2 Hz, 2H, ArH_{calix}), 6.61 (t, J = 7.2 Hz, 2H, ArH_{calix}), 4.52 (br s, 4H, OCH_2CH$_2$CH$_2$), 4.17 (m, 8H, ArCH_2Ar + CH$_2$CH$_2$CH_2O), 3.48 (d, J = 12.7 Hz, 4H, ArCH_2Ar), 2.41 (br s, 4H, CH$_2$CH_2CH$_2$). ^{13}C NMR (75 MHz, DMSO-d_6): δ 158.7, 152.0, 150.6, 149.8, 140.5, 137.6, 132.8, 128.1, 127.6, 127.0, 126.8, 125.1, 124.8, 118.5, 113.7, 110.1, 72.1, 63.4, 30.2, 28.8. FAB MS m/z 1019 (M + 1, calc. 1018). Anal. calc. for $C_{60}H_{54}N_6O_{10}$: C, 70.71; H, 5.34; N, 8.25. Found C, 70.65; H, 5.25; N, 8.05%.

Compound 4d. Yield (89%, 1.21 g); mp 167 °C; IR (KBr) ν_{max}/cm^{-1}: 3298, 1596, 1508; ^{1}H NMR (DMSO-d_6) δ 10.94 (s, 2H, N*H*), 8.30 (s, 2H, O*H*), 8.07 (d, J = 8.7 Hz, 4H, ArH_{NO_2}), 7.78 (d, J = 8.4 Hz, 4H, Ar*H*), 7.00–7.06 (m, 16H, ArH_{NO_2} + Ar*H* + ArH_{calix}), 6.84 (t, J = 7.2 Hz, 2H, ArH_{calix}), 6.63 (t, J = 7.2 Hz, 2H, ArH_{calix}), 4.53 (br s, 4H, OCH_2CH$_2$CH$_2$), 4.21 (d, J = 12.8 Hz, 4H, ArCH_2Ar), 4.17 (br s, 4H, CH$_2$CH$_2$CH_2O), 3.38 (d, J = 12.8 Hz, 4H, ArCH_2Ar), 2.45 (br s, 4H, CH$_2$CH_2CH$_2$), 2.29 (s, 6H, CCH_3). ^{13}C NMR (75 MHz, DMSO-d_6): δ 161.3, 152.1, 151.5, 144.5, 134.4, 129.4, 128.9 128.5, 128.0, 127.71 126.4, 123.1, 119.6, 115.8, 114.6, 73.4, 64.8, 30.42 29.5, 12.3. FAB MS m/z 1047 (M + 1, calc. 1046). Anal. calc. for $C_{62}H_{58}N_6O_{10}$: C, 71.11; H, 5.58; N, 8.03. Found C, 70.85; H, 5.31; N, 8.15%.

General procedure for the synthesis of calix[4]arene-bis(2,4-dinitrophenylhydrazone) derivatives (4c and 4e). A solution of **3a** (0.97 g, 1.3 mmol) and **3b** (1.01 g, 1.3 mmol) in 35 ml of chloroform–ethanol (1 : 2 v/v), 2,4-dinitrophenylhydrazine (0.63 g, 3.2 mmol) and 2 ml of concentrated sulfuric acid was added. The mixture was stirred at room temperature for 5 h. After completion of the reaction (monitored through TLC) the precipitate obtained was filtered off, washed with ethanol (3 × 20 ml) and dried under vacuum to give calix[4]arene-bis(2,4-dinitrophenylhydrazone) derivatives **4c** and **4e** as red solids.

Compound 4c. Yield (93%, 1.33 g); mp >280 °C (charred); IR (KBr) ν_{max}/cm^{-1}: 3287, 1613, 1507; ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.43 (s, 2H, N*H*), 8.76 (s, 2H, O*H*), 8.47 (s, 2H, ArH_{NO_2}), 8.46 (s, 2H, –N=C*H*), 8.26 (d, J = 9.3 Hz, 2H, ArH_{NO_2}), 7.88 (d, J = 9.3 Hz, 2H, ArH_{NO_2}), 7.63 (d, J = 8.0 Hz, 4H, Ar*H*), 7.19 (d, J = 7.2 Hz, 4H, ArH_{calix}), 7.10 (d, J = 7.2 Hz, 4H, ArH_{calix}), 7.00 (d, J = 8.04 Hz, 4H, Ar*H*), 6.83 (t, J = 7.5 Hz, 2H, ArH_{calix}), 6.63 (t, J = 7.5, 2H, ArH_{calix}), 4.46 (br s, 4H, OCH_2CH$_2$CH$_2$), 4.23 (d, J = 12.8 Hz, 4H, ArCH_2Ar), 4.16 (br s, 4H, CH$_2$CH$_2$CH_2O), 3.49 (d, J = 12.8 Hz, 4H, ArCH_2Ar), 2.43 (br s, 4H, CH$_2$C-H_2CH$_2$). ^{13}C NMR (75 MHz, DMSO-d_6): δ 160.2, 152.3, 151.3, 148.9, 144.0, 136.5, 133.3, 129.1, 128.7, 128.2, 127.5, 126.1, 125.0, 122.3, 118.8, 116.2, 114.6, 72.6, 64.3, 30.2, 29.2. FAB MS m/z 1109 (M + 1, calc. 1108). Anal. calc. for $C_{60}H_{52}N_8O_{14}$: C, 64.98; H, 4.73; N, 10.10. Found C, 64.91; H, 4.69; N, 10.05%.

Compound 4e. Yield (94%, 1.38 g); mp >282 °C (charred); IR (KBr) ν_{max}/cm^{-1}: 3307, 1610, 1505; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.89 (s, 2H, N*H*), 8.69 (s, 2H, O*H*), 8.44 (s, 2H, ArH_{NO_2}), 8.24 (d, J = 9.3 Hz, 2H, ArH_{NO_2}), 7.82 (d, J = 9.3 Hz, 2H, Ar*H*), 7.76 (d, J = 8.1 Hz, 4H, Ar*H*), 7.13 (d, J = 6.9 Hz, 4H, ArH_{calix}), 7.05 (d, J = 7.2 Hz, 4H, ArH_{calix}), 6.96 (d, J = 8.1 Hz, 4H, Ar*H*), 6.80 (t, J = 7.2 Hz, 2H, Ar*H*), 6.59 (t, J = 7.2 Hz, 2H, Ar*H*), 4.35 (br s, 4H, OCH_2CH$_2$CH$_2$), 4.16 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 4.10 (br s, 4H, CH$_2$CH$_2$CH_2O), 3.51 (d, J = 12.6 Hz, 4H, ArCH_2Ar), 2.38 (br s, 4H, CH$_2$CH_2CH$_2$), 2.21 (s, 6H, CCH_3), ^{13}C NMR (75 MHz, DMSO-d_6): δ 160.2, 152.3, 151.3, 144.1, 133.7, 129.9, 128.9, 128.5, 128.0, 127.7, 125.4, 122.7, 119.2, 116.3, 114.2, 73.0, 64.3, 30.4, 29.4, 12.7. FAB MS m/z 1137 (M + 1, calc. 1136). Anal. calc. for $C_{62}H_{56}N_8O_{14}$: C, 65.48; H, 4.96; N, 9.85. Found C, 65.21; H, 4.79; N, 10.05%.

Synthesis of compound 5. To a solution of benzaldehyde (1.0 g, 9.3 mmol) in 35 ml of ethanol, 4-nitrophenylhydrazine (1.73 g, 0.01 mol) and 2 ml of glacial acetic acid was added. The mixture was refluxed for 3 h and then cooled to room temperature. The whole reaction mixture was evaporated and distilled water was added to it. The precipitate obtained was filtered off, washed with water (3 × 25 ml) and then dried under vacuum to give **5** (yield 97%, 2.20 g) as a light yellow solid; mp 137 °C; IR (KBr) ν_{max}/cm^{-1}: 1593, 1501; ^1H NMR (300 MHz, DMSO-d_6): δ 11.26 (s, 1H, N*H*), 8.17 (d, J = 8.4 Hz, 2H, ArH_{NO_2}), 7.89 (s, 1H, –N=C*H*), 7.59 (d, J = 7.9 Hz, 2H, Ar*H*), 7.16 (d, J = 8.4 Hz, 2H, ArH_{NO_2}), 7.04–7.13 (m, 3H, Ar*H*). ^{13}C NMR (75 MHz, DMSO-d_6): δ 153.4, 149.2, 147.7, 145.8, 145.2, 139.8, 129.4, 128.4, 127.5, 124.3, 123.1, 122.7, 110.1. FAB MS m/z 242 (M + 1, calc. 241). Anal. calc. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found C, 64.23; H, 4.20; N, 17.63%.

Synthesis of compound 6. A solution of benzaldehyde (1.0 g, 9.3 mmol) in 35 ml of ethanol, 2,4-dinitrophenylhydrazine (2.20 g, 0.01 mol) and 2 ml of concentrated sulfuric acid was added. The mixture was stirred at room temperature for 2 h. After completion of the reaction (monitored through TLC) the precipitate obtained was filtered, washed with ethanol (3 × 20 ml) and dried under vacuum to give **6** (yield 95%, 1.30 g) as a red solid; mp 149 °C; IR (KBr) ν_{max}/cm^{-1}: 1620, 1502; ^1H NMR (300 MHz, DMSO-d_6): δ 11.49 (s, 1H, N*H*), 8.39 (s, 1H, ArH_{NO_2}), 8.33 (s, 1H, –N=C*H*), 8.25 (d, J = 8.9 Hz, 1H, ArH_{NO_2}), 7.83 (d, J = 8.9 Hz, 1H, ArH_{NO_2}), 7.42 (d, J = 7.8 Hz, 2H, Ar*H*), 7.19–7.24 (m, 3H, Ar*H*). ^{13}C NMR (75 MHz, DMSO-d_6): δ 161.2, 158.4, 157.1, 153.9, 150.4, 148.4, 132.4, 129.4, 128.1, 127.2, 126.5, 124.6, 118.2. FAB MS m/z 287 (M + 1, calc. 286). Anal. calc. for $C_{13}H_{10}N_4O_4$: C, 54.55; H, 3.52; N, 19.57. Found C, 54.83; H, 3.69; N, 19.84%.

General method for UV-visible titrations and colorimetric experiments. The solvents for the UV-visible measurements and colorimetric experiments were all of spectroscopic grade. Stock solutions of the receptors **4b** and **4d** of 5×10^{-5} M and **4c** and **4e** of 2×10^{-5} M were prepared by dissolution in DMSO–CH_3CN (0.5 : 9.5 v/v). Anions used in this experiments were all in the form of their tetrabutylammonium salts and a stock solution of 1×10^{-3} M for each anion was prepared in acetonitrile. UV-visible titrations were performed with a series of solutions of every receptor molecules and standard solution of anions were added by a microsyringe in desired equivalent ratios. In colorimetric experiments, the appropriate equivalents of the anions were added according to those used in the corresponding UV-visible titration experiments.

General method for ^1H NMR titrations and ^{19}F NMR experiments. A 10 mM solution of receptors **4b** and **4c** were prepared in DMSO-d_6. To 0.5 ml of receptor solutions, various equivalents of tetrabutylammonium fluoride (40 mM) and tetrabutylammonium hydroxide (40 mM) were added to an NMR tube and the spectra were recorded. ^{19}F NMR spectra were recorded on a 300 MHz Bruker DPX 300 instrument at 298 K using $CFCl_3$ as an internal standard.

Acknowledgements

The authors gratefully acknowledge the assistance received from the Sophisticated Analytical Instrument Facility, CDRI, Lucknow for FAB-MS spectra, DST, DBT, MOEF, MFPI and MRD, Govt. of India for financial assistance and the Council of Scientific and Industrial Research, India for senior research fellowships to S. N. S and R. S.

References

1 (*a*) K. L. Kirk, *Biochemistry of the Halogens and Inorganic Halides*, Plenum Press, New York, 1991, pp. 58; (*b*) M. Kleerekoper, *Endocrinol. Metab. Clin. North Am.*, 1998, **27**, 441; (*c*) J. A. Weatherall, *Pharmacology of Fluorides*, in *Handbook of Experimental Pharmacology XX/1*, Springer-Verlag, Berlin, 1969, Part 1, pp. 141–172.
2 (*a*) P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 1; (*b*) P. A. Gale, *Coord. Chem. Rev.*, 2001, **213**, 79; (*c*) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486; (*d*) P. A. Gale, *Coord. Chem. Rev.*, 2000, **199**, 181; (*e*) J. L. Sessler and J. M. Davis, *Acc. Chem. Res.*, 2001, **34**, 989.
3 (*a*) M. J. Chmielewski and J. Jurczak, *Chem.–Eur. J.*, 2005, **11**, 6080; (*b*) P. A. Gale, *Acc. Chem. Res.*, 2006, **39**, 465.
4 (*a*) T. Gunnlaugsson, M. Glynn, G. M. Hussey, P. E. Kruger and F. M. Pfeffer, *Coord. Chem. Rev.*, 2006, **250**, 3094; (*b*) C. R. Bondy and S. J. Loeb, *Coord. Chem. Rev.*, 2003, **240**, 77; (*c*) K. Choi and A. D. Hamilton, *Coord. Chem. Rev.*, 2003, **240**, 101; (*d*) C. Suksai and T. Tuntulani, *Chem. Soc. Rev.*, 2003, **32**, 192.
5 (*a*) C. Lee, D. H. Lee and J.-I. Hong, *Tetrahedron Lett.*, 2001, **42**, 8665; (*b*) K. H. Lee, H.-Y. Lee, D. H. Lee and J.-I. Hong, *Tetrahedron Lett.*, 2001, **42**, 5447; (*c*) D. H. Lee, K. H. Lee and J.-I. Hong, *Org. Lett.*, 2001, **3**, 5; (*d*) D. H. Lee, H. Y. Lee, K. H. Lee and J.-I. Hong, *Chem. Commun.*, 2001, 1188; (*e*) P. Anzenbacher, Jr, A. C. Try, H. Miyaji, K. Jursikova, V. M. Lynch, M. Marquez and J. L. Sessler, *J. Am. Chem. Soc.*, 2000, **122**, 10232.
6 (*a*) P. A. Gale, L. J. Twyman, C. I. Handlin and J. L. Sessler, *Chem. Commun.*, 1999, 1851; (*b*) K. Niikura, A. P. Bisson and E. V. Anslyn, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1111.
7 (*a*) R. Martinez-Manez and F. Sancenon, *Chem. Rev.*, 2003, **103**, 4419; (*b*) D. E. Gomez, L. Fabbrizzi and M. Licchelli, *J. Org. Chem.*, 2005, **70**, 5717, and references therein; (*c*) D. A. Jose, D. K. Kumar, B. Ganguly and A. Das, *Org. Lett.*, 2004, **6**, 3445; (*d*) E. J. Cho, B. J. Ryu, Y. J. Lee and K. C. Nam, *Org. Lett.*, 2005, **7**, 2607; (*e*) S. Y. Kim and J.-I. Hong, *Org. Lett.*, 2007, **9**, 3109; (*f*) Z. Lin, S. Ou, C. Duan, B. Zhang and Z. Bai, *Chem. Commun.*, 2006, 624.
8 (*a*) T. Ghosh, B. G. Maiya and M. W. Wong, *J. Phys. Chem. A*, 2004, **108**, 11249; (*b*) X. Peng, Y. Wu, J. Fan, M. Tian and K. Han, *J. Org. Chem.*, 2005, **70**, 10524; (*c*) D. E. Gomez, L. Fabbrizzi and M. Licchelli, *J. Org. Chem.*, 2005, **70**, 5717; (*d*) V. Amendola, D. Boiocchi, B. Colasson and L. Fabbrizzi, *Inorg. Chem.*, 2006, **45**, 6138; (*e*) M. Boiocche, L. D. Boca, D. E. Gomez, L. Fabbrizzi, M. Licchelli and E. Monzani, *Chem.–Eur. J.*, 2005, **11**, 5648; (*f*) T. Gunnlaugsson, P. E. Kruger, P. Jensen, J. Tierney, H. D. P. Ali and G. M. Hussey, *J. Org. Chem.*, 2005, **70**, 10875.
9 (*a*) M. Boiocchi, L. Del Boca, D. E. Gomez, L. Fabbrizzi, M. Licchelli and E. Monzani, *J. Am. Chem. Soc.*, 2004, **126**, 16507; (*b*) D. E. Gomez, L. Fabbrizzi, M. Licchelli and E. Monzani, *Org. Biomol. Chem.*, 2005, **3**, 1495; (*c*) V. Amendola, D. E. Gomez, L. Fabbrizzi and M. Licchelli, *Acc. Chem. Res.*, 2006, **39**, 343.
10 (*a*) C. D. Gutsche, in *Calixarenes Revisited: Monographs in Supramolecular Chemistry*, ed. J. F. Stoddart, The Royal Society of Chemistry, Cambridge, UK, 1998; (*b*) In *Calixarenes 2001*, ed. Z. Asfari, V. Bohmer, J. Harrowfield and J. Vicens, Kluwer Academic Publishers, Dordrecht, 2001.
11 (*a*) S. Ben Sdira, C. Felix, M.-B. Giudicelli, F. Vocanson, M. Perrin and R. Lamartine, *Tetrahedron Lett.*, 2005, **46**, 5659; (*b*) S.-Y. Liu, Y.-B. He, J.-L. Wu, L.-H. Wei, H.-J. Qin, L.-Z. Meng and L. Hu, *Org. Biomol. Chem.*, 2004, **2**, 1582; (*c*) H. M. Chawla, S. P. Singh, S. N. Sahu and S. Upreti, *Tetrahedron*, 2006, **62**, 7854; (*d*) H. M. Chawla, S. P. Singh and S. Upreti, *Tetrahedron*, 2006, **62**, 2901; (*e*) H. M. Chawla, S. P. Singh and S. Upreti, *Tetrahedron*, 2006, **62**,

9758; (*f*) H. M. Chawla, S. P. Singh and S. Upreti, *Tetrahedron*, 2007, **63**, 5636; (*g*) H. M. Chawla, N. Pant, B. Srivastava and S. Upreti, *Org. Lett*., 2006, **8**, 2237; (*h*) S. Kumar, H. M. Chawla and R. Varadarajan, *Tetrahedron*, 2003, **59**, 7481.
12 (*a*) H. M. Chawla, S. N. Sahu and R. Shrivastava, *Tetrahedron Lett*., 2007, **48**, 6054; (*b*) H. M. Chawla and S. P. Singh, *Tetrahedron*, 2008, **64**, 741.
13 (*a*) S. H. Lee, H. J. Kim, Y. O. Lee, J. Vicens and J. S. Kim, *Tetrahedron Lett*., 2006, **47**, 4373; (*b*) S. K. Kim, J. H. Bok, R. A. Bartsch, J. Y. Lee and J. S. Kim, *Org. Lett*., 2005, **7**, 4839.
14 (*a*) E. Quinlan, S. E. Matthews and T. Gunnlaugsson, *Tetrahedron Lett*., 2006, **47**, 9333; (*b*) C.-F. Chen and Q.-Y. Chen, *New J. Chem*., 2006, **30**, 143; (*c*) M. H. Lee, D. T. Quang, H. S. Jung, J. Yoon, C. H. Lee and J. S. Kim, *J. Org. Chem*., 2007, **72**, 4242; (*d*) E. Quinlan, S. E. Matthews and T. Gunnlaugsson, *J. Org. Chem*., 2007, **72**, 7497.
15 C. Jaime, J. de Mendoza, P. Prados, P. M. Nieto and C. Sanchez, *J. Org. Chem*., 1991, **56**, 3372.
16 (*a*) T. Gunnlaugsson, P. E. Kruger, T. C. Lee, R. Parkesh, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett*., 2003, **44**, 6575; (*b*) T. Gunnlaugsson, P. E. Kruger, P. Jensen, F. M. Pfeffer and G. M. Hussey, *Tetrahedron Lett*., 2003, **44**, 8909; (*c*) S. Camiolo, P. A. Gale, M. B. Hursthouse and M. E. Light, *Org. Biomol. Chem*., 2003, **1**, 741.
17 D. H. Lee, J. H. Im, J.-H. Lee and J.-I. Hong, *Tetrahedron Lett*., 2002, **43**, 9637.
18 (*a*) M. Vazquez, L. Fabbrizzi, A. Taglietti, R. M. Pedrido, A. M. G. Noya and M. R. Bermejo, *Angew. Chem., Int. Ed*., 2004, **43**, 1962; (*b*) H. Miyaji, W. Sato and J. L. Sessler, *Angew. Chem., Int. Ed*., 2001, **40**, 154; (*c*) C. B. Black, B. Andrioletti, A. C. Try, C. Ruiperez and J. L. Sessler, *J. Am. Chem. Soc*., 1999, **121**, 10438; (*d*) H. H. Hammud, A. Ghannoum and M. S. Masoud, *Spectrochim. Acta, Part A*, 2006, **63**, 255.
19 (*a*) S. O. Kang, D. Powell, V. W. Day and K. Bowman-James, *Angew. Chem., Int. Ed*., 2006, **45**, 1921; (*b*) J. M. Linares, D. Powell and K. Bowman-James, *Coord. Chem. Rev*., 2003, **240**, 57.
20 S. Gronert, *J. Am. Chem. Soc*., 1993, **115**, 10258.
21 In *Binding Constants*, ed. K. A. Conners, Wiley, New York, 1987, pp. 21–101 and 141–187.
22 B. S. Furniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, Longman, UK, 1996, pp. 1258.