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Strapped Calix[2]furan[4]pyrroles, Novel Examples of Ditopic Molecular Receptors

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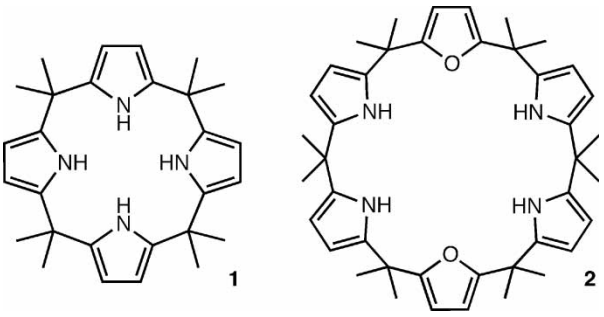
The cyclocondensation of polyether chains functionalised with dipyrromethane units at both ends with 2,5-bis[(α-hydroxy-α,α-dimethyl)methyl]furan yield novel strapped calix[2]furan[4]pyrroles. These receptors were studied for their ability to act as ion-pair ligands towards fluoride salts.

Keywords: Strapped heterocalixarenes; Calixpyrroles; Ditopic receptors; Cesium fluoride

INTRODUCTION

Since the discovery that calix[4]pyrrole **1** is capable of binding anions and neutral molecules [1–3] by means of multiple hydrogen bonds, macrocyclic anion-binding receptors containing pyrrole units have been a topic of intense research [4–6]. A number of hybrid systems containing both pyrrole and other aromatic units (including furan, thiophene, pyridil, and benzo rings) are described in the literature [7–13]. Some of these structures contain more than four pyrroles and/or other heterocyclic units and are often referred to as 'expanded' calixpyrroles [10,12,14–16].

The anion-binding properties of calixpyrroles can be modulated considerably by the nature of the substituents at the aliphatic bridging carbon atoms (meso positions) [17–23], by the nature of the substituents at the β-positions of the pyrrole rings [16,24–27], and as a function of the macroring size [9]. One additional means to modulate the anion-binding properties of calixpyrroles is to link two (or more) *meso* positions with a suitable bridge, and a number of examples of such molecules based on the calix[4]pyrrole have been described [28–30].



In recent years there has also been growing interest in ditopic receptors capable of binding tight ion-pairs. These contain substructures, each of which is capable of binding a specific anion and cation respectively [31–37]. However, examples of such receptors based on hybrid and expanded calixpyrroles have not been reported.

A few years ago, a synthesis of calix[2]furan[4]pyrrole **2** was reported, and this was found to complex fluoride strongly and selectively [9] compared to a number of other anions, including chloride, bromide, dihydrogen phosphate, hydrogen sulphate, and nitrate. Macrocycle **2** was originally obtained by the selective homologation to pyrrole of four furan units of the corresponding calix[6]furan. However, we realised that this structure can also be obtained by the 2 + 2 cyclocondensation of dipyrrilmethanes with 2,5-bis[(α-hydroxy-α,α-dimethyl)methyl]furan **8** (Scheme 1) [11]. Since the dipyrromethane units can

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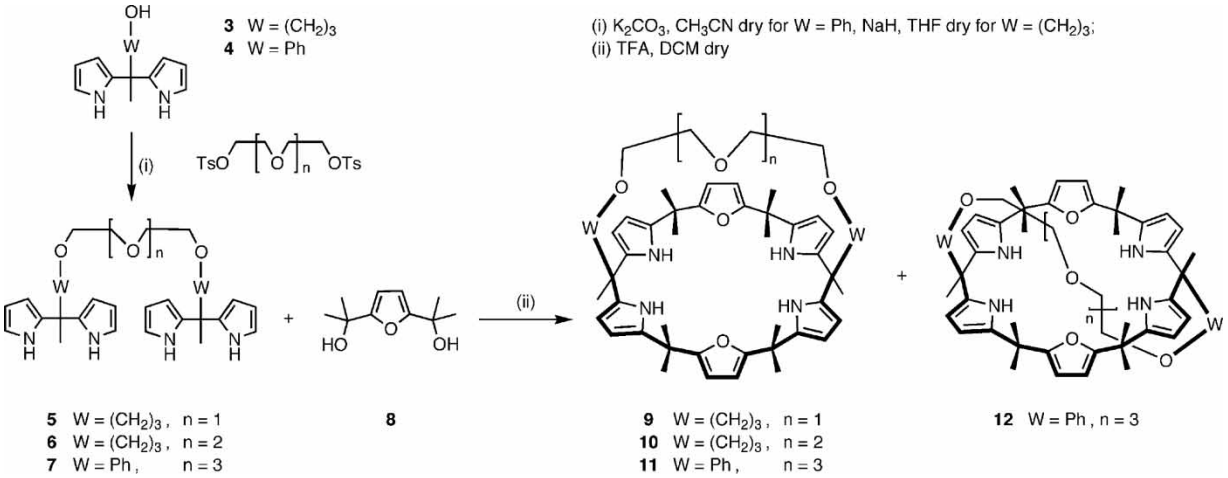

SCHEME 1 .

be assembled at the termini of a 'strapping' chain that may contain binding sites suitable to complex cations, the strategy outlined in Scheme 1 (*vide infra*) is a convenient method for the construction of strapped calix[2]furan[4]pyrroles that have the potential to behave as ditopic receptors for fluoride salts.

Here we report the first syntheses of the novel *meso* strapped calix[2]furan[4]pyrroles **9**–**12** in which the strap contains polyether chains with our initial findings on their host-guest chemistry towards a number of fluoride salts.

RESULTS AND DISCUSSION

The dipyrromethane **3** is a known compound [28,30], and **4** was prepared by the acid-promoted condensation of *p*-hydroxyacetophenone and pyrrole. Condensation of **3** or **4** with the appropriate polyethylene glycol bistosylate gave the bis-dipyrrilmethanes **5**–**7** which were subjected to cyclization with diol **8** to give the strapped calix[2]furan[4]-pyrroles **9**–**12**. When this reaction was conducted with **7**, two isomeric compounds (**11** and **12**) having significantly different chromatographic mobility (SiO_2, DCM:EtOAc, 95:5) were isolated from the reaction mixture, (5% yield each): these being the *syn* and *anti meso* strapped isomers. Although the macrocyclic structures were evident from ^1H and ^{13}C NMR spectra, these could not provide a means to assign their stereochemistry because the time-averaged symmetries of **11** and **12** generate two analogous patterns of resonances. Nevertheless, indirect evidence of their stereochemistry was given by complexation experiments (*vide infra*). The same cyclization involving bis-dipyrrilmethanes **5** and **6** with **8** gave the cryptand-like structures **9** and **10** (10% and 22% respectively) as single isomers, which according to their host-guest chemistry (*vide infra*), were assigned the *syn* strapped stereochemistry. The higher yield of **10** compared to those of **9**, **11**, and **12** seems consistent with an optimal length of the strap, which probably templates the macrocyclization process. All of the new compounds gave MALDI-TOF and positive ESI mass spectra which were consistent with the proposed structures.

The complexation properties of **9**–**12** were explored in DCM and acetonitrile by means of ^1H NMR titrations and solid/organic solvent extraction experiments using fluoride salts with various counterions (Table I). Although in numerous cases the measurement of the association constants (Ka) by means of NMR titrations was hampered by the disappearance of the NH resonances upon addition

TABLE I Complexation properties of structures **2**, **9**–**12.**

	Salt	9	10	11	12	2
1	*n*-Bu_4NF	$D^{\dagger}$	$588 \pm 164^{(\dagger,\S)}$	$74 \pm 6^{(\dagger,\S)}$	$43 \pm 6^{(\dagger,\S)}$	$<5x10^{4(\dagger,\S,\P)}$
2	*n*-Bu_2NH_2F	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{\dagger}$	$X^{\dagger}$	$X^{\dagger}$,$324 \pm 48^{\ddagger}$
3	$(PhCH_2)_2NH_2F$	$X^{\dagger}$	$X^{(\dagger,\ddagger)}$	$X^{\dagger}$	$X^{\dagger}$	$X^{\dagger}$,$D^{\ddagger}$
4	*n*-$BuNH_3F$	$V^{(\dagger,\ddagger)}$	$V^{(\dagger,\ddagger)}$	X^{a}	$X^{\ddagger}$	$V^{(\dagger,\ddagger)}$
5	Na^+F^-	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$
6	KF	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{\dagger}$,$V^{\ddagger}$
7	CsF	$X^{\dagger}$,$V^{\ddagger}$	$V^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$X^{(\dagger,\ddagger)}$	$V^{(\dagger,\ddagger)}$

† DCM. ‡ Acetonitrile. ¶ See reference [9]. § Ka (M^{-1}); V: a CIS was observed; X: No CIS was observed; D: the NH resonance disappeared upon addition of the salt.

of the salt, qualitative assessments were often possible by means of competition experiments between different receptors for a given salt.

Since the *n*-Bu_4N^+ is expected to interact negligibly with the straps, its fluoride salt offers a means to assess the effect of the straps on the binding ability of the calix portion of receptors **9**–**12** with respect to **2**. Entry 1, Table I, shows that the straps used here generally reduce fluoride binding, with the presence of the electron-rich aromatic ring at the meso positions being the most effective. The Ka of **12** for fluoride is smaller than that of **11**. This difference suggests that the threaded structure should be assigned to **12**, which cannot bind the anion by inclusion because the calix cavity is already filled by the strap [38]. Unfortunately, to date we have been unable to obtain crystals of either **11** or **12** nor of any of their complexes to confirm this stereochemical assignment by means of X-ray analysis.

The salts *n*-Bu_2NH_2F and $(PhCH_2)_2NH_2F$ were not complexed by **2** in DCM. The complex **2**·*n*-Bu_2NH_2F was formed in acetonitrile (kinetically slow behavior on the ^{1}H NMR time scale, Ka, $324 \pm 48\,M^{-1}$); in this solvent $(PhCH_2)_2NH_2F$ also formed a complex with **2**, but the disappearance of the NH resonances prevented the measurement of a Ka value. The salts *n*-Bu_2NH_2F and $(PhCH_2)_2NH_2F$ were not complexed by **9**–**12** in either DCM or acetonitrile. However, *n*-$BuNH_3F$ was complexed by **9**, **10** and **2**. The Ka values for these complexes could not be measured by NMR titration in either DCM or acetonitrile because the pyrrole NH resonances disappeared with the initial additions of salt, and became visible only in the presence of a slight excess (ca. two or more equivalents) of salt. In DCM the addition of a slight excess of *n*-$BuNH_3F$ to either **9** or **10** caused substantial complexation induced shifts (CIS) of the NH resonances as well as of the β-pyrrole CH and *also* of the -OCH_2–CH_2O- protons. In acetonitrile **9** and **10** with the same concentrations of *n*-$BuNH_3F$ complexed fluoride less effectively: the CISs for the pyrrole NH were smaller, while the other resonances were only marginally perturbed. Since the ion-pair of *n*-$BuNH_3F$ is more dissociated in acetonitrile than in DCM, the stronger binding in DCM suggests that in this solvent the complexation involves mostly the ion-paired salt rather than fluoride. This conclusion is also supported by the fact that **2**, which lacks the polyether chain that can interact with the cation, binds *n*-$BuNH_3F$ better in acetonitrile than in DCM, thus showing a behavior which is reversed with respect to **10** [39].

A competition experiment for the binding of *n*-$BuNH_3F$ involving **10** and **2** in acetonitrile shows that **2** is a stronger fluoride ligand than **10** since the NH signal of **10** is not affected at all when the mixture has the composition **10**/**2**/salt = 1/1/2. The same experiment in DCM was hampered by the disappearance of all of the NH signals upon addition of the salt.

We then tested the complexation of **9**–**12** with NaF, KF, and CsF. In a typical experiment, a solution of the receptor in either DCM or acetonitrile was mixed with the solid salt and subjected to sonication (allowing sufficient time for complete equilibration as confirmed by the lack of any additional changes in the ^{1}H NMR spectra of the solutions). Receptors **9**–**12** were ineffective as complexing agents for NaF and KF in DCM. In this solvent only **10** gave a complex with CsF that was kinetically slow on the NMR time-scale: the two sets of resonances for the free and bound receptor equilibrated at a 4:6 ratio after two days (21°C, 3.0 mM solution of the receptor). In acetonitrile under identical conditions both **9** and **10** were fully complexed with CsF; **10**·CsF was formed faster than **9**·CsF (30 min and 3 h respectively) and both complexes were kinetically slow on the NMR time-scale. Macrocycles **11** and **12** did not show any affinity for CsF in either DCM or acetonitrile.

Similar experiments with macrocycle **2** led to almost quantitative formation of a 1:1 complex with either KF and CsF in acetonitrile. In DCM the **2**·CsF complex was insoluble, and the formation of **2**·KF was not detected. In a competition experiment **2** and **10** (1:1) in acetonitrile were sonicated with CsF. The **2**·CsF complex was rapidly formed before any **10**·CsF complex could be detected by ^{1}H NMR. The solution was rapidly filtered, concentrated, dried and suspended in DCM. The ^{1}H NMR spectrum of this mixture contained only the resonances of the free receptor **10** and did not change over time. Conversely, when a mixture of **2** and **10** (1:1) was sonicated with CsF in DCM it was evident that the amount of **2** in solution decreased over time due to the formation of insoluble **2**·CsF, while no **10**·CsF complex was observed.

Although **2** and **9**–**12** could bind CsF, adopting features similar to those observed by Sessler *et al.* [40] for calix[4]pyrrole **1**, in the case of the strapped receptors described here the different behaviors towards CsF must arise from the participation of the different straps in the binding process. Thus we believe that receptor **10** is more effective than **9**, **11** and **12** in DCM because it can better bind the CsF as an ion-pair. Fig. 1 shows that in DCM **10** undergoes *simultaneous* significant CISs of both the calix and the polyether protons with *n*-$BuNH_3F$ (c) and with CsF (d), but *n*-Bu_4NF (b) mostly affects the pyrrole protons.

Although binding of fluoride by the calix portion receptor **10** is reduced with respect to **2**, selectivity towards fluoride appears to be maintained because no CISs could be detected when **10** was treated with various *n*-Bu_4N^+ salts (carbonate, nitrate, chloride, hydrogenphosphate) in either DCM or acetonitrile.

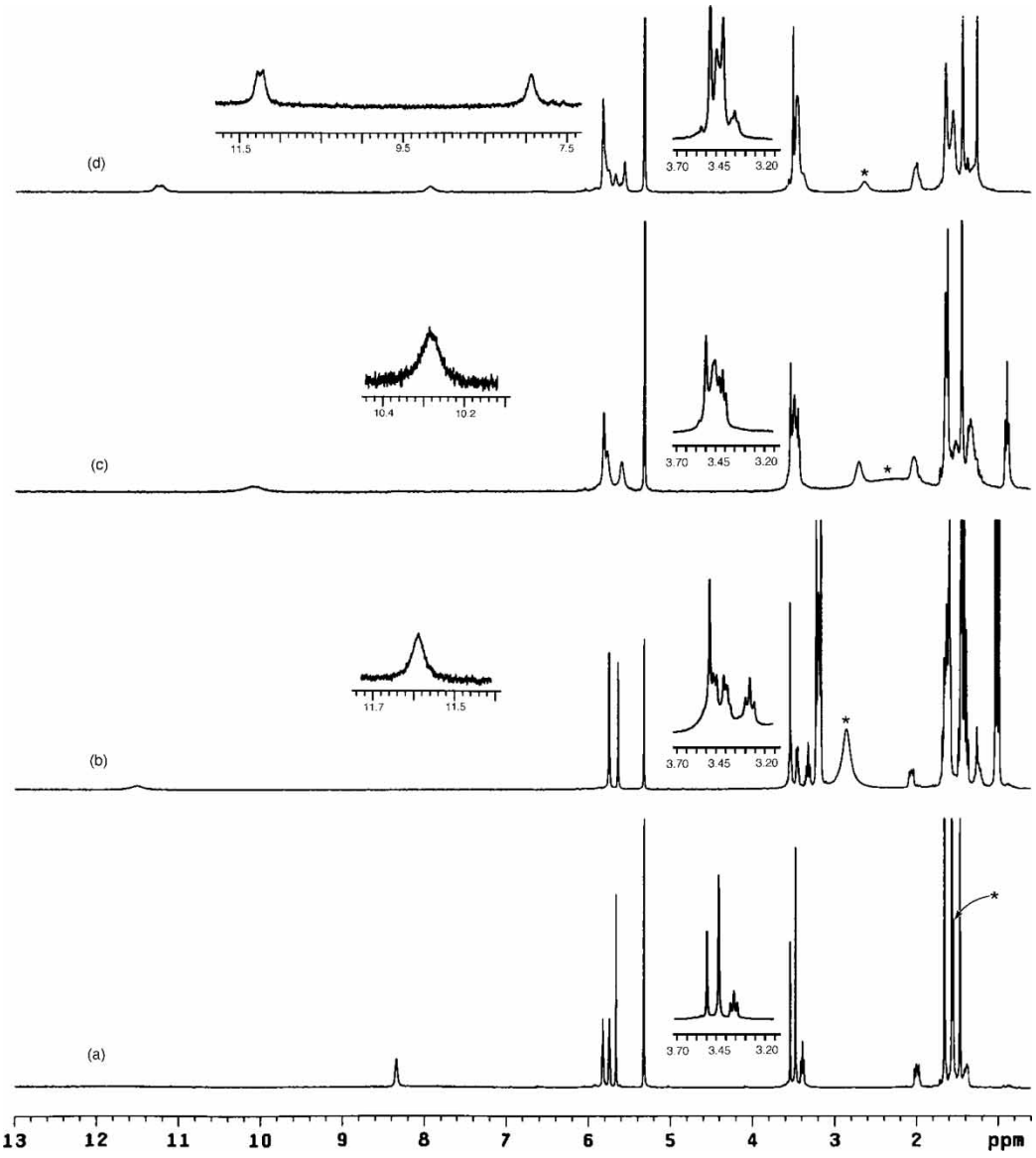

FIGURE 1 ^{1}H NMR Spectra (in CD_2Cl_2) of: (a) free **10**; (b) **10** + *n*-Bu_4NF; (c) **10** + *n*-$BuNH_3F$; (d) **10** + CSF. (*) Adventitious water.

The potential interaction between Cs^+ and the polyether moiety of receptor **10** was explored using cesioum picrate. In DCM, even in the presence of **10**, this salt was found to be extremely insoluble. In acetonitrile the ^{1}H-NMR spectrum of a 1:1 solution of this salt with receptor **10** (ca. 10^{-3} M), shows no CISs. Therefore we believe that Cs^+ is not appreciably complexed by receptor **10** unless a suitable anion (*i.e.* fluoride) is also present.

CONCLUSIONS

This work demonstrates that strapped hybrid expanded calixpyrroles can be conveniently obtained using the synthetic strategy outlined in Scheme 1. The macrocyclization yield may become acceptable (see **10**) depending on the length/nature of the strap. We are currently investigating a number of such syntheses using the thiophene analogue of **8** and other aromatic and heteroaromatic bis-electrophiles as well as different straps.

Although in the cryptand-like structures **9**, **10** and **11**, self-complexation driven by dipole–dipole NH···O interaction is potentially a major obstacle to the effective binding of ion-pairs, this appears to be overwhelmed by the stronger ion-dipole interactions when the cryptand is exposed to a ion-pair with the appropriate stereoelectronic match.

X-ray evidence for the inclusion of the CsF as an ion-pair within **10** is currently not available, but the qualitative data discussed above including the kinetically slow behaviour **10**·CsF compared with **10**·*n*-Bu_4NF strongly suggest the inclusion of this salt.

EXPERIMENTAL

General

All chemicals were standard reagent grade and were used without further purification. All air-sensitive and/or moisture sensitive reactions were conducted under a dry argon atmosphere. Thin layer chromatography (TLC) was conducted on Merck SiO_2 60 F254 plastic plates. Compounds were visualised with iodine, vanillin, or by examination under UV light. Column chromatography was conducted on Aldrich Silica gel 230–400 mesh, 60 Å. Melting points were determined on a Kofler hot stage apparatus, and are not corrected. ^1H and ^{13}C NMR spectra were recorded at 21 ± 1°C on a Varian Gemini-300 at 300 and 75 MHz, respectively, using the residual proton resonances of the solvents ($CDCl_3$, CD_3CN and CD_2Cl_2) as δ reference. MALDI-TOF mass spectra were acquired in reflector mode (resolution > 10,000) on a Voyager STR instrument (Applied Biosystems, Framingham, MA, USA) equipped with a nitrogen laser (λ 337 nm) and provided with delayed extraction technology. Ions formed by the pulsed laser beam were accelerated through 24 kV. ESI mass spectra were acquired on a Mariner ESI-TOF instrument (resolution > 7,000) (Applied Biosystems, Framingham, MA, USA) using CH_3CN (positive ions mode). Accurate mass measurements were performed by ESI. In all cases differences between measured and calculated masses were below 10 ppm. Comparisons between measured and calculated isotopic patterns were also performed.

For the NMR titrations, the ^1HNMR spectrum of the receptor under investigation (ca. 5 mM in either CD_2Cl_2 or CD_3CN) was recorded after the addition of known amounts of salt as concentrated solution in the same solvent, and the total volume was kept constant by evaporation with dry nitrogen. The observed CISs were used in the EQNMR programme [41] and fitted to the 1:1 binding model. Solvents were used as supplied from sealed ampules and care was taken to minimise exposure to moisture. All salts were dried before use. However, trace amounts of water could not be removed due to the extremely hydrophilic nature of the salts. Since water has been demonstrated to lower the values of the observed binding constants, figures given in Table I should be considered as the minimum observable value when operating under strictly unhydrous conditions.

5-Methyl,5-(4-hydroxyphenyl)dipyrromethane (4)

p-Hydroxyacetophenone (5.0 g, 0.036 mol) was dissolved in pyrrole (26 mL), and the mixture was cooled at 0°C under an Ar atmosphere under vigorous stirring before adding TFA (2.82 mL, 0.036 mol). The mixture was allowed to reach room temperature. After 3 days the mixture was treated with $NaHCO_3$ solution (excess, saturated) and extracted with DCM. The organic phase was dried, concentrated and excess pyrrole was removed by short path distillation under reduced pressure. The residue was subjected to flash chromatography (SiO_2, DCM) to give **3** as the first eluted fraction which was crystallised from EtOAc/light petroleum: 1.64 g, 29%, m.p. 167–168°C from EtOAc/light petroleum; ^1H NMR ($CDCl_3$): δ 2.03 (s, 3H, CH_3), 4.90 (sb, 1H, OH), 5.98 and 6.18 (2 × m, 2 × 2H, pyrrole-β-H), 6.67 (m, 2H, pyrrole-α-H), 6.68 and 6.97 (2 × d, 2 × 2H, AA'BB' system, Ar-H), 7.81 (sb, 2H, NH); ^{13}C NMR ($CDCl_3$): δ 29.0 (CH_3), 44.1 (Cq), 106.1, 108.2, 114.8, 116.8, 128.7 (CH), 137.7, 139.5, 154.2 (Cq).

Diethylene Glycol bis[4,4-bis(1H-pyrrol-2-yl)pentyl] (5) and Triethylene Glycol bis[4,4-bis(1H-pyrrol-2-yl)pentyl] (6)

Dipyrromethane **3** (1.0 g, 4.57 mmol) was dissolved in dry THF (50 ml) and NaH (164 mg, 83 mmol) was added under Ar atmosphere at room temperature. After 10 min, the appropriate tosylate (2.29 mmol in 5 ml of THF) was added with a syringe. The mixture was refluxed for 24 h, cooled to room-temperature before adding water (1 ml), and concentrated to *ca* 5 ml under reduced pressure and extracted with DCM/water (25 ml each). The organic phase was dried ($MgSO_4$) and concentrated. The crude products were purified by column chromatography (SiO_2, DCM/EtOAc 95/5) to give **5** or **6**.

5: (238 mg, 22%, colorless oil): ^1H NMR ($CDCl_3$): δ 1.38 (m, 4H, CH_2), 1.55 (s, 6H, CH_3), 2.01 (m, 4H, CH_2), 3.33 (t, 4H, OCH_2), 3.47 and 3.64 (2 × m, 4H and 4H, OCH_2CH_2O), 6.05 and 6.10 (2 × m, 4H × 4H, pyrrole-β-H), 6.57 (m, 4H, pyrrole-α-H), 7.99 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 24.3, 26.6, 36.6, 38.8, 69.4, 70.7, 70.8, 104.5, 107.5, 116.9, 138.1.

6: (300 mg, 25%, colorless oil): ^1H NMR ($CDCl_3$): δ 1.48 (m, 4H, CH_2), 1.57 (s, 6H, CH_3), 2.06 (m, 4H, CH_2), 3.37 (t, 4H, OCH_2), 3.45 and 3.56 (2 × m, 4H and 4H, OCH_2CH_2O), 3.65 (s, 4H, OCH_2CH_2O), 6.05 and 6.11 (2 × m, 4H and 4H, pyrrole-β-H), 6.60 (m, 4H, pyrrole-α-H), 8.15 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 24.5, 26.6, 36.9, 38.9, 69.5, 70.6, 70.6, 70.9, 104.4, 107.6, 116.8, 138.0.

Tetraethylene Glycol bis[5-methyl, 5-(1,4-phenylene)dipyrromethane] (7)

Dipyrrylmethane **4** (1.0 g, 3.98 mmol) was dissolved in dry CH_3CN (40 ml) and K_2CO_3 (5.5 g 39.8 mmol) was added under Ar atmosphere. The mixture was refluxed for 30 min, before adding a solution of tetraethylene glycol ditosylate (1.0 g, 1.99 mmol) in

CH_3CN (1 ml), and maintained at reflux for 10 h. After cooling to room temperature, the mixture was filtered, concentrated and extracted with DCM/H_2O. The organic phase was dried, and concentrated to give **7** as a pale yellow oil (1.0 g, 76%) which was sufficiently pure to be used in the subsequent synthetic step. A small sample was purified by column chromatography (SiO_2, DCM/EtOAc 9:1). ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 6H, CH_3), 3.70, 3.84 and 4.10 (3 × m, 8H, 4H and 4H, OCH_2), 5.96 and 6.17 (2 × m, 4H and 4H, pyrrole-β-H), 6.66 (m, 4H, pyrrole-α-H), 6.82 and 7.02 (2 × m, 4H and 4H, AA'BB' system, Ar-H), 7.77 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 29.0, 44.1, 67.4, 69.7, 70.7, 70.8, 106.1, 108.2, 114.1, 116.8, 128.4, 137.7, 139.5, 157.4.

General Procedure for the Synthesis of Macropolycycles 9–12

A solution of the appropriate bis-dipyrryl derivative (**5**, **6**, or **7**; 3.0 mM) and **8** (6.0 mM) in dry DCM was cooled to −18°C under Ar atmosphere before adding (dropwise, with vigorous stirring) a 1:20 mixture of TFA in DCM, sufficient to obtain a final concentration of 1.5 mM of TFA in the reaction mixture. These reactions were conducted on 1.0–0.3 g of **5**, **6**, or **7**. After 1 h the mixture was treated with solid powdered K_2CO_3, filtered, and extracted with H_2O. The organic phase was dried, concentrated and subjected to column chromatography (SiO_2, DCM/EtOAc 95/5).

9: (colorless oil, 10%, the most chromatographically mobile component of the crude mixture); ^{1}H NMR (CD_3CN): δ 1.53 (m, 4H, CH_2), 1.40, 1.50, 1.51 (3 × s, 12H, 6H, and 12H, CH_3), 2.11 (m, 4H, CH_2), 3.32 (t, 4H, OCH_2), 3.42 and 3.50 (2 × m, 4H and 4H, OCH_2CH_2O), 5.59 and 5.70 (2 × m, 4H and 4H, pyrrole-H), 5.82 (s, 4H, furan-CH), 8.05 (sb, 4H, NH); ^{1}H NMR (CD_2Cl_2): δ 1.41, 1.53, 1.62 (3 × s and overlapping m, 34H, CH_3 and CH_2), 1.95 (m, 4H, CH_2), 3.36 (t, 4H, OCH_2), 3.45 and 3.50 (2 × m, 4H and 4H, OCH_2CH_2O), 5.66 (s, 4H, furan-CH), 5.76 and 5.84 (2 × m, 4H and 4H, pyrrole-H), 7.98 (sb, 4H, NH); ^{1}H NMR ($CDCl_3$): δ 1.42, 1.55, 1.64 (3 × s and overlapping m, 34H, CH_3 and CH_2), 1.96 (m, 4H, CH_2), 3.40 (t, 4H, OCH_2), 3.47 and 3.54 (2 × m, 4H and 4H, OCH_2CH_2O), 5.65 (s, 4H, furan-CH), 5.80 and 5.89 (2 × m, 4H and 4H, pyrrole-H), 7.99 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 24.8, 27.4, 27.4, 36.3, 37.8, 39.0, 70.1, 70.4, 71.0, 103.4, 103.8, 103.9, 136.8, 137.2, 159.9.

10: (colorless oil, 22%, the most chromatographically mobile component of the crude mixture); ^{1}H NMR (CD_3CN): δ 1.32 (m, 4H, CH_2), 1.42, 1.51, 1.54 (3 × s, 12H, 6H, and 12H, CH_3), 2.12 (m, 4H, CH_2), 3.33 (t, 4H, OCH_2), 3.43 and 3.48 (2 × m, 4H and 4H, OCH_2CH_2O), 3.51 (s, 4H, OCH_2CH_2O), 5.62 and 5.69 (2 × m, 4H and 4H, pyrrole-H), 5.81 (s, 4H, furan-CH), 8.25 (sb, 4H, NH); ^{1}H NMR (CD_2Cl_2): δ 1.38 (m, 4H, CH_2), 1.46, 1.55, 1.57 (3 × s, 30H, CH_3), 1.99 (m, 4H, CH_2), 3.39 (t, 4H, OCH_2), 3.48 and 3.54 (2 × s, 8H and 4H, OCH_2CH_2O), 5.66 (s, 4H, furan-CH), 5.74 and 5.82 (2 × m, 4H and 4H, pyrrole-H), 8.34 (sb, 4H, NH); ^{1}H NMR ($CDCl_3$): δ 1.27, 1.60 (2 × s and overlapping m, 34H, CH_3 and CH_2), 2.02 (m, 4H, CH_2), 3.42 (t, 4H, OCH_2), 3.50 and 3.58 (bs and s, 8H and 4H, OCH_2CH_2O), 5.64 (s, 4H, furan-CH), 5.80 and 5.89 (2 × m, 4H and 4H, pyrrole-H), 8.24 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 25.0, 26.3, 26.3, 27.7, 36.3, 37.3, 38.9, 69.7, 70.5, 70.5, 71.0, 103.3, 103.7, 103.7, 136.8, 137.3, 159.9.

11: (colorless oil, 5%, the most chromatographically mobile component of the crude mixture); ^{1}H NMR (CD_3CN): δ 1.35 (s, 12H, CH_3), 1.39 (s, 12H, CH_3), 1.84 (s, 6H, CH_3), 3.56, 3.72 and 4.01 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.61 and 5.76 (2 × m, 4x4H, pyrrole-H), 5.87 (s, 4H, furan-H), 6.72 and 6.80 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 8.05 (sb, 4H, NH); ^{1}H NMR (CD_2Cl_2): δ 1.38 (s, 12H, CH_3), 1.41 (s, 12H, CH_3), 1.90 (s, 6H, CH_3), 3.65, 3.77 and 4.02 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.67 (s, 4H, furan-H), 5.80 and 5.86 (2 × m, 4 × 4H, pyrrole-H), 6.73 and 6.91 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 7.42 (sb, 4H, NH); ^{1}H NMR ($CDCl_3$): δ 1.43 (s, 12H, CH_3), 1.45 (s, 12H, CH_3), 1.94 (s, 6H, CH_3), 3.71, 3.84 and 4.03 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.55 (s, 4H, furan-H), 5.88 and 5.81 (2 × m, 4 × 4H, pyrrole-H), 6.74 and 6.96 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 7.44 (sb, 4H, NH);^{13}C NMR ($CDCl_3$): δ 27.7, 27.7, 29.4, 36.3, 44.3, 67.5, 69.7, 70.8, 70.9, 103.8, 104.2, 114.1, 128.4, 136.6, 139.9, 157.4, 159.7.

12: (colorless oil, 5%, the second most chromatographically mobile component of the crude mixture); ^{1}H NMR (CD_3CN): δ 1.44 (s, 12H, CH_3), 1.52 (s, 12H, CH_3), 1.72 (s, 6H, CH_3), 3.49, 3.68 and 4.07 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.23 and 5.49 (2 × m, 4 × 4H, pyrrole-H), 6.01 (s, 4H, furan-H), 6.75 and 6.86 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 8.16 (sb, 4H, NH); ^{1}H NMR (CD_2Cl_2): δ 1.45 (s, 12H, CH_3), 1.52 (s, 12H, CH_3), 1.70 (s, 6H, CH_3), 3.53, 3.74 and 4.09 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.39 and 5.62 (2 × m, 4 × 4H, pyrrole-H), 5.96 (s, 4H, furan-H), 6.76 and 6.93 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 7.63 (sb, 4H, NH); ^{1}H NMR ($CDCl_3$): δ 1.48 (s, 12H, CH_3), 1.54 (s, 12H, CH_3), 1.75 (s, 6H, CH_3), 3.51, 3.78 and 4.14 (3 × m, 8H, 4H and 4H, OCH_2CH_2O), 5.52 and 5.69 (2 × m, 4 × 4H, pyrrole-H), 5.90 (s, 4H, furan-H), 6.80 and 6.94 (2 × m, 2 × 4H, AA'BB' system, Ar-H), 7.75 (sb, 4H, NH); ^{13}C NMR ($CDCl_3$): δ 27.4, 28.1, 29.5, 36.3, 44.2, 67.3, 69.8, 70.7, 70.8, 103.3, 104.1, 105.8, 114.2, 128.4, 136.3, 137.4, 140.3, 159.7.

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[38] The *anti* strapped receptor **12** could adopt a non threaded conformation with a twisted arrangement of the calix[2]furan[4]pyrrole part (as in the figure '8'). This may possess more conformational rigidity and thus still show no binding. We thank one of the referees for highlighting this possibility.
[39] With *n*-$BuNH_3F$ (3 equivalents) the δ value of the NH resonance in acetonitrile is that of the fully complexed receptor (δ 12.47). However the same mixture in DCM shows the NH resonances at δ corresponding to ca. 38% complexation. The NH δ values observed for the complex 2·F- obtained by saturation of the binding with fluoride salts is almost the same in both DCM and acetonitrile, irrespective of the counterions used.
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