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Ion-Pair Recognition by a Heteroditopic Triazole-Containing Receptor

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Abstract: A new heteroditopic calix[4]-diquinone triazole containing receptor capable of recognising both cations and anions through Lewis base and C–H hydrogen-bonding modes, respectively, of the triazole motif has been prepared. This ion-pair receptor cooperatively binds halide/monovalent-cation combinations in an aqueous mixture, with selectivity trends being established by ^{1}H NMR and UV/Vis spectroscopy. Cation binding by the calix[4]diquinone oxygen and triazole nitrogen donors enhances the strength of the halide complexation at the isophthalamide recognition site of the receptor. Conversely, anions bound in the receptor's isophthalamide cavity enhance cation recognition. ^{1}H NMR investigations in solution suggest that the receptor's triazole motifs are capable of coordinating simultaneously to both cation and anion guest species. Solid-state X-ray crystallographic structural analysis of a variety of receptor ion-pair adducts further demonstrates the dual cation–anion binding role of the triazole group.

Keywords: anions · calixarenes · cations · host–guest systems · ion pairs · receptors · triazoles

Introduction

The design and construction of heteroditopic receptor molecules for ion-pair recognition is currently an area of intense research activity.[1] This has been stimulated in part by compelling evidence that the cation and anion binding affinities and selectivity of monotopic receptor systems have been demonstrated to be critically influenced by the nature of counterions. Through favourable cooperative electrostatic interactions, ion-pair receptors have the potential to significantly enhance the efficacy of charged guest recognition and also to act as superior extraction and membrane transport agents.[1,2]

The 1,2,3-triazole motif is being used extensively as a covalent linkage in the facile copper(I)-catalysed azide–alkyne coupling synthesis of an ever increasing range of organic and biological molecules.[3] Importantly, the heterocycle is also proving to be a versatile ion recognising unit for both cations and anions. As a nitrogen-containing Lewis base, triazole-based ligands have been shown to coordinate transition-metal cations.[4] In contrast, aryl macrocyclic and acyclic triazole oligomers recognise halide anions through cooperative triazole C–H···anion hydrogen bonds.[5] Hence, the integration of the triazole motif into the design of heteroditopic receptors for ion-pair recognition is an attractive proposition. Surprisingly, to the best of our knowledge, only two examples of triazole-containing ditopic receptors have been reported.[6] Herein, we describe a novel heteroditopic calix[4]-diquinone triazole containing receptor, which recognises alkali metal cation/halide anion ion-pair species. ^{1}H NMR spectroscopic investigations in solution and solid-state X-ray crystallographic structural analysis suggest that the triazole motifs are capable of coordinating simultaneously to both cation and anion guest species.

Results and Discussion

Receptor design and synthesis: We have described previously a series of heteroditopic calix[4]diquinone polyether isophthalamide receptors that exhibit unprecedented cooperative AND ion-pair recognition, displaying little affinity for 'free' ions but enhanced binding of contact ion-pairs, such as NaCl.[7,8]

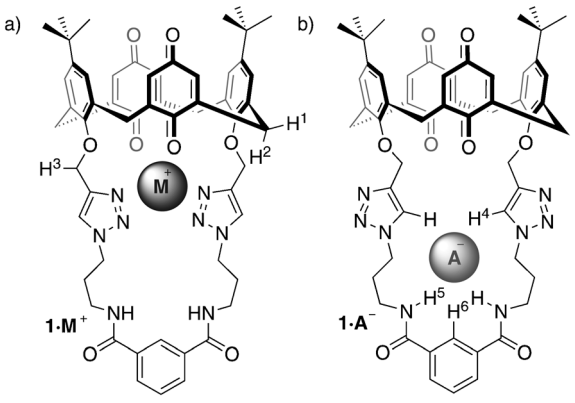

Figure 1. Target heteroditopic ion-pair receptor **1**: the triazole groups act as a) Lewis bases to coordinate a metal cation, and b) hydrogen-bond donors to bind an anion.

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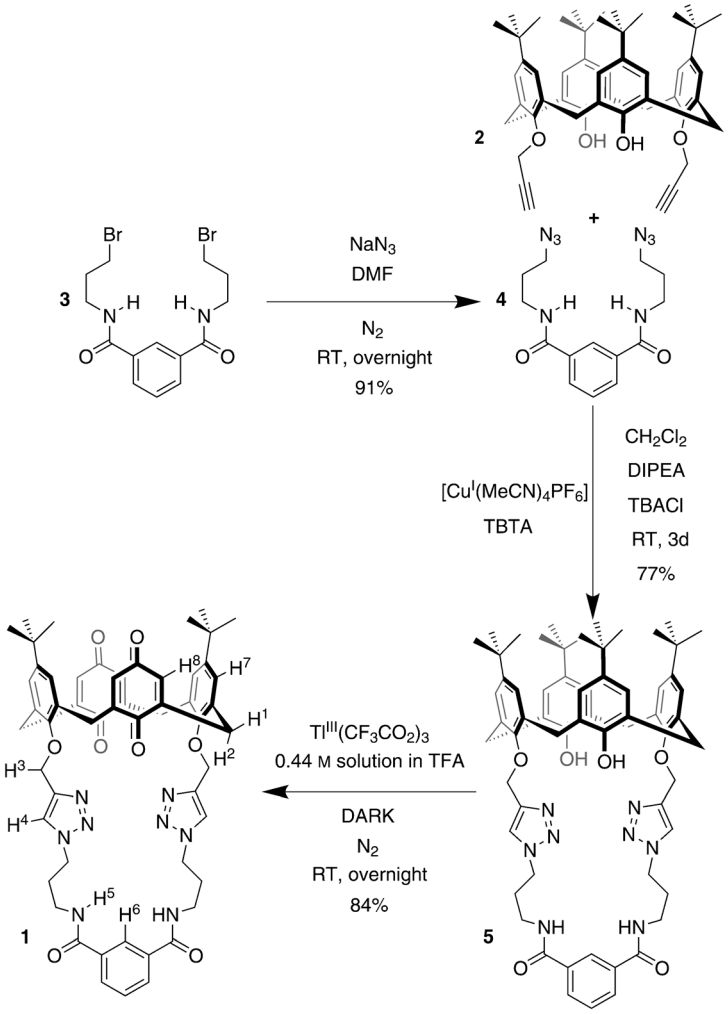
By replacing the polyether chain linkers with triazole groups, the target heteroditopic receptor **1**, shown in Figure 1, has the potential capability of recognising cations (Figure 1a), anions (Figure 1b) and ion-pairs through triazole-group participation.

The synthesis of receptor **1** is shown in Scheme 1. The copper(I)-catalysed azide–alkyne click (CuAAC) reaction of 1,3-bisalkyne lower-rim-functionalised calix[4]arene derivative **2**[9] with bisazide-functionalised isophthalamide compound **4**, prepared from reacting the corresponding bisbromide **3**[10] with sodium azide, afforded the bistriazole-containing macrocycle **5** in 49% yield. It is noteworthy that when the cyclisation reaction was carried out in the presence of one equivalent of tetrabutylammonium chloride, the yield increased significantly to 77%. This observation indicates that the chloride anion is acting as a template, through coordination to the isophthalamide motif in **4**, which preorganises the azide groups in a *syn*/*syn* conformation, favouring the cyclisation process. The target calix[4]diquinone triazole receptor **1** was then prepared in good yield (84%) by oxidation of macrocycle **5** with thallium(III) trifluoroacetate in trifluoroacetic acid (TFA; Scheme 1).



Scheme 1. Synthetic route to target macrocycle **1**.

The ditopic receptor was characterised by ^{1}H and ^{13}C NMR spectroscopy and electrospray mass spectrometry. Crystals of **1** suitable for X-ray single-crystal structural analysis were grown by slow evaporation of a solution of **1** in CD_3CN. The structure (Figure 2) shows the calix[4]diquinone unit adopting a partial cone conformation, with the two *tert*-butylphenyl rings almost parallel (14°) and the quinone rings are antiparallel but converge on the cavity, with an interplanar angle of 40°. The rest of the macrocycle lies in a nearly flat conformation, with the isophthalamide and triazoles adopting *syn*/*anti* conformations.

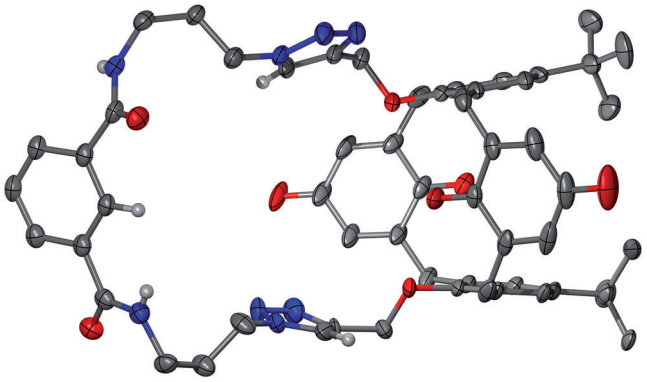


Figure 2. Single-crystal X-ray structure of **1** grown from CD_3CN. Non-donating hydrogen atoms and solvent molecules are omitted for clarity. Thermal ellipsoids are displayed at the 30% probability level.

Cation and anion binding studies: The cation and anion binding properties of **1** were investigated by using ^{1}H NMR and UV/Vis spectroscopic analysis. The addition of MPF_6 salts (M = K, Na and NH_4), in which hexafluorophosphate is used as a non-coordinating anion for ^{1}H NMR spectroscopic solutions of **1** in 2% D_2O/CD_3CN induced, in all cases, downfield shifts in the triazole protons (H^4): with potassium $\Delta\delta = +0.08$ and sodium $\Delta\delta = +0.09$ ppm, causing relatively larger perturbations than ammonium, $\Delta\delta = +0.04$ ppm (Figure 3).

It is noteworthy that the CH_2 protons (H^3) between the triazole and calix[4]diquinone motif are also shifted downfield upon cation addition, whilst the aromatic protons of the calix[4]diquinone (H^7, H^8) converge and the AB quartet of the calix CH_2 protons (H^1, H^2) diverge. This suggests that the calix[4]diquinone undergoes a conformational change in order for the lower-rim oxygen and triazole nitrogen donors to complex with the cation, as depicted in Figure 1a.

UV/Vis spectroscopic titrations were performed in 2% H_2O/CH_3CN, monitoring the n–π* quinone absorption of **1** upon addition of cations.[11] Typically, a significant enhancement of the n–π* quinone absorption was observed with K^+ and Na^+ (Figure 4). However, addition of NH_4^+ caused little alteration in the spectrum, suggesting very weak binding. Specfit[12] analysis of the UV/Vis titration

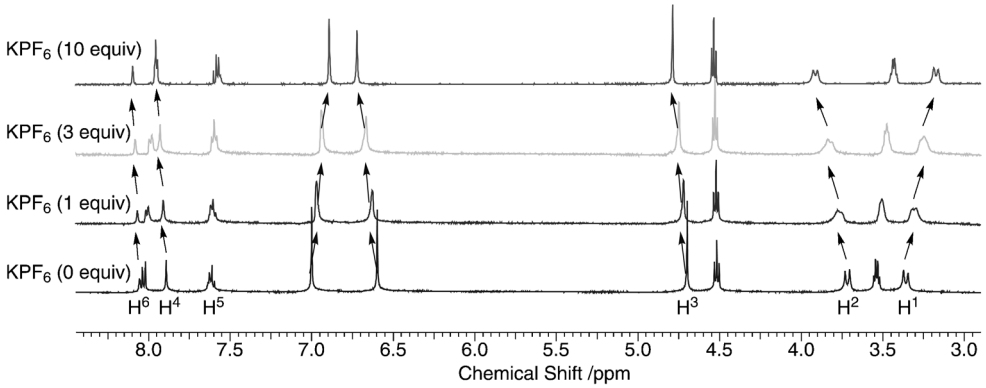


Figure 3. ^{1}H NMR (500 MHz) spectra of receptor **1** upon addition of equivalents of KPF_6 in 2% D_2O/CD_3CN; temperature: 293 K; $[\mathbf{1}]_i = 1.5\times10^{-3}$ mol dm^{-3}; titrant $[KPF_6] = 0.075$ mol dm^{-3}.

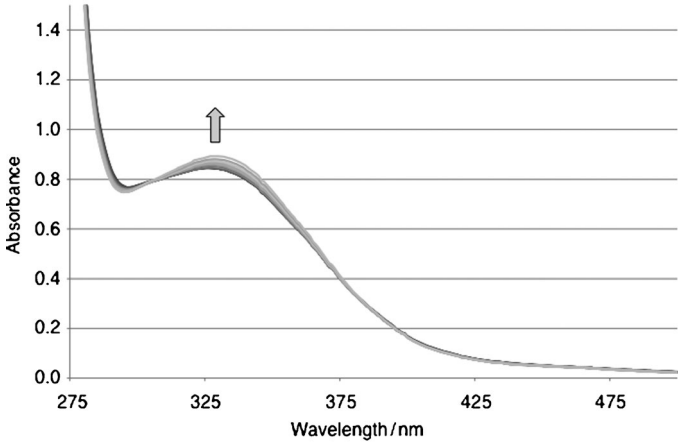


Figure 4. Enhancement of the n–π* quinone absorbance in response to addition of KPF_6. Solvent: 2% H_2O/CH_3CN; temperature: 298 K; $[\mathbf{1}]_i = 3\times10^{-4}$ mol dm^{-3}; titrant $[KPF_6] = 0.09$ mol dm^{-3}.

data gave 1:1 stoichiometric association constants (Table 1) that reveal that Na^+ forms the strongest cation complex, followed by K^+, and NH_4^+ is very weakly bound.

Table 1. UV/Vis spectroscopy K_{11} values for interactions of **1** with various cations[a]

Cation	Association K_{11} [M^{-1}][b]
K^+	155
Na^+	460
NH_4^+[c]	–[d]

[a] Solvent: 2% H_2O/CH_3CN; temperature: 298 K; $[\mathbf{1}]_i = 3\times10^{-4}$ mol dm^{-3}; titrant $[MPF_6] = 0.09$ mol dm^{-3}. [b] Errors <10%. [c] Titrant as a solution in 5% H_2O/CH_3CN for solubility. [d] Binding too weak to be determined.

Anion binding studies were undertaken by ^{1}H NMR spectroscopy, focusing on the triazole C*H* protons and the isophthalamide motif. Anions were added as their TBAX salts (X = Cl, Br and I), in which tetrabutylammonium (TBA) is a bulky non-coordinating cation. For each of the halide anions added, the isophthalamide (H^5), internal phenyl (H^6) and triazole (H^4) protons were all found to shift downfield (Figure 5). For the phenyl proton H^6, the halide-induced shifts $\Delta\delta$ were largest for chloride (+0.64 ppm), then bromide (+0.14 ppm), with iodide causing only a modest perturbation (+0.06 ppm). These results suggest that the halide anion is bound in the receptor cavity by cooperative hydrogen bonding by the triazole and isophthalamide groups, as shown in Figure 1b.

Job-plot analysis revealed a 1:1 binding mode for each halide and association constants were determined by using WinEQNMR2 analysis of the ^{1}H NMR titration data, monitoring the isophthalamide internal proton (H^6).[13] Table 2 reveals that receptor **1** exhibits a preference for the smaller, more charge-dense chloride anion,[14] which suggests that the bistriazole-isophthalamide cavity is of complementary size for Cl^-.

Crystals of a chloride complex of **1** suitable for X-ray single-crystal structural analysis were grown by slow evaporation of a solution of **1** in 2% D_2O/CD_3CN with an excess of TBACl. The structure (Figure 6) shows that a chloride anion is bound in an intermolecular manner between triazoles from different macrocycles, with triazole C–H···Cl hydrogen-bond lengths of 3.486(9) Å, supporting the ^{1}H NMR spectroscopy solution-state evidence for triazole CH–anion interactions.

The calix[4]diquinone unit is found to adopt a partial cone conformation, with the two *tert*-butylphenyl rings almost parallel and the quinone rings orientated convergently, with an interplanar angle of 48°. Another chloride is bound within the macrocycle cavity by hydrogen bonding to the isophthalamide protons (amide N–H···Cl 3.286(6), 3.238(6) Å and internal C–H···Cl 3.415(6) Å). The bulky TBA resides outside the macrocycle cavity but proximate to its chloride counteranion. Hence, the solid-state structure of the chloride-anion complex of **1** highlights the dominance of intermolecular triazole and amide halide anion interactions, whereas ^{1}H NMR spectroscopy anion-binding investigations in solution indicate halide recognition by cooperative intramolecular triazole and amide hydrogen bonds.

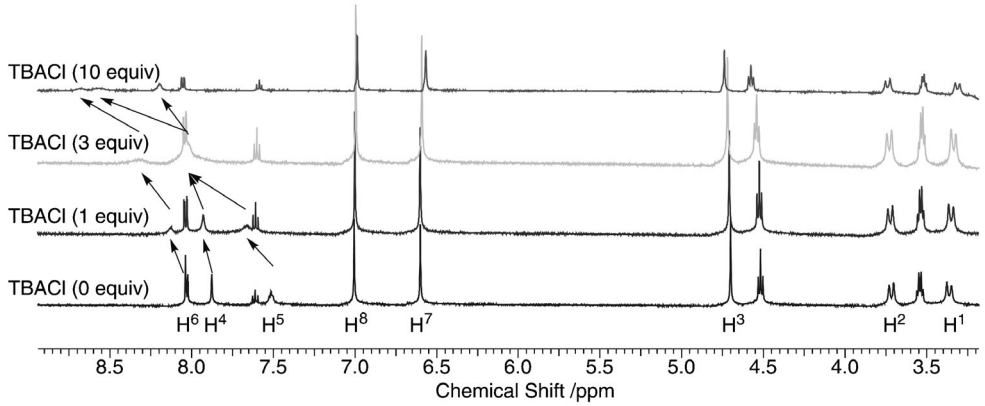


Figure 5. ^{1}H NMR (500 MHz) spectra of receptor **1** upon addition of equivalents of TBACl. In response, cavity triazole (H^4), isophthalamide (H^5) and internal CH (H^6) protons shift downfield. Solvent: 2% D_2O/CD_3CN; temperature: 293 K; $[\mathbf{1}]_i = 1.5\times10^{-3}$ mol dm^{-3}; titrant [TBACl] = 0.075 mol dm^{-3}.

Table 2. ^{1}H NMR spectroscopy K_{11} values for interactions of **1** with various anions[a]

Anion	Association K_{11} [M^{-1}][b]
Cl^-	178 (16)
Br^-	67 (5)
I^-	31 (3)

[a] ^{1}H NMR (500 MHz); solvent: 2% D_2O/CD_3CN; temperature: 293 K; $[\mathbf{1}]_i = 1.5\times10^{-3}$ mol dm^{-3}; titrant [TBAX] = 0.075 mol dm^{-3}. [b] Errors < 10%.

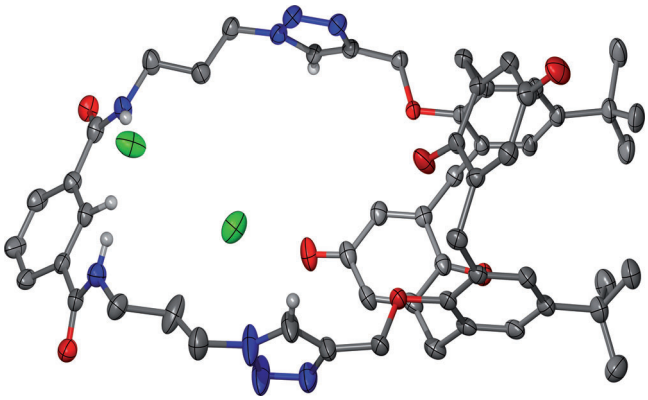


Figure 6. Single-crystal X-ray structure of **1**·2TBACl. Note the chloride bound intermolecularly by the triazole H^4. Hydrogen atoms not involved in hydrogen bonding and non-coordinating tetrabutylammonium cations are omitted for clarity. Thermal ellipsoids are displayed at the 30% probability level.

Ion-pair binding studies: ^{1}H NMR spectroscopy was used initially to monitor titration of halide anions (as TBAX salts) with solutions of macrocycle **1** in 2% D_2O/CD_3CN containing one equivalent of cation (MPF_6). The addition of up to one equivalent of chloride to **1**·KPF_6 (Figure 7) induced significant downfield shifts in the key bistriazole-isophthalamide protons, with the triazole proton (H^4) undergoing a larger magnitude of perturbation, $\Delta\delta = +0.19$ ppm for **1**·KPF_6 compared with $\Delta\delta = +0.09$ ppm for **1**. The isophthalamide (H^5) and phenyl (H^6) protons similarly exhibited greater downfield shifts by at least 0.1 ppm for addition of chloride to **1**·KPF_6 as compared to its addition to **1**.

Furthermore, chloride binding to **1**·KPF_6 concomitantly caused the calix[4]diquinone aryl protons (H^7, H^8) to converge, the calix CH_2 protons (H^1, H^2) to diverge and the α-CH_2 triazole proton (H^3) to shift downfield. Interestingly, further addition of chloride after one equivalent induced no more perturbations in these receptor proton signals, whereas the isophthalamide protons shifted progressively downfield.

A possible K^+Cl^- ion-pair binding mode is the S-shaped conformation depicted in Figure 8, in which the triazole motifs function simultaneously as a Lewis base to coordinate the cation and as C–H hydrogen-bond donors to bind the halide anion.

The association constants shown in Table 3 were determined by monitoring the isophthalamide phenyl proton H^6. In all cases, it was found that halide-anion binding was enhanced significantly in the presence of coordinating cations. Overall, K_{obs} for halide binding to **1**·MPF_6 was typically 3–11 times greater than the halide association constants determined for receptor **1** alone. Chloride appears to be the best size match for the isophthalamide and triazole cavity, forming the optimal ion-pair with Na^+Cl^-, and relatively weaker cooperative ion-pair associations are observed with the larger halides, bromide and iodide.

UV/Vis spectroscopic analysis was utilised to monitor the titration of cations into a solution of receptor **1** with one equivalent of halide anion in 2% H_2O/CH_3CN (Table 4). The n–π* quinone absorption was monitored and showed enhancement of the band centred at 325 nm in all instances (Figure 9). For all three cations studied, the presence of bound halides resulted in enhanced cation binding (Table 4), with optimal ion-pair cooperativity being observed with Na^+Cl^-, in agreement with the NMR spectroscopic titration results. Furthermore, the ammonium association, which was very weak in the absence of coordinating halide anions, is effectively "switched on" by chloride or bromide binding.

Further evidence for ion-pair binding was then sought in the solid state.

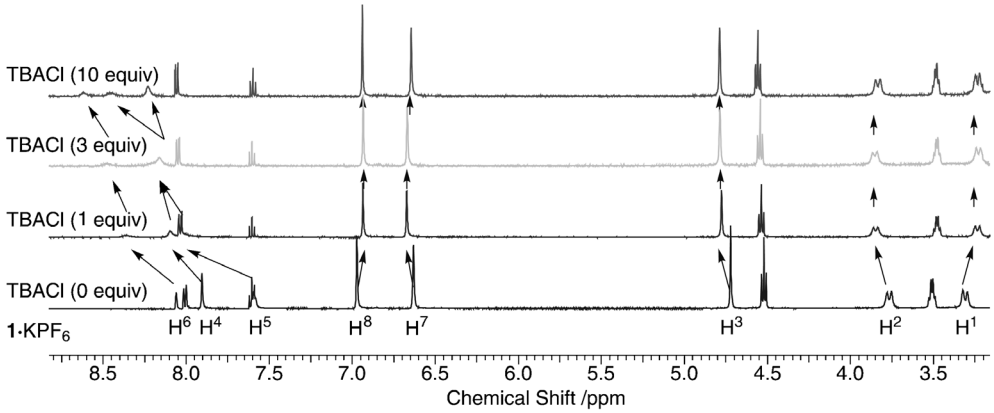


Figure 7. ^{1}H NMR spectra of receptor **1**·KPF_6 upon addition of equivalents of TBACl in 2% D_2O/CD_3CN with corresponding KCl ion-pair formation in the cavity; temperature: 293 K; $[\mathbf{1}\cdot KPF_6]_i = 1.5\times10^{-3}$ mol dm^{-3}; titrant [TBACl] = 0.075 mol dm^{-3}.

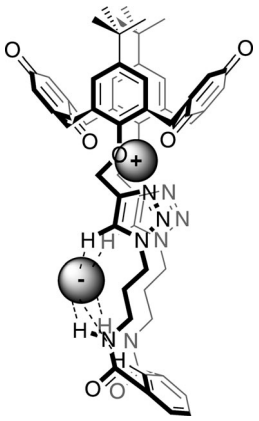


Figure 8. Possible solution-state ion-pair binding by heteroditopic receptor **1**.

Table 4. UV/Vis spectroscopy K_{obs} values for interactions of **1** with various ion-pair combinations[a]

Cation salt titrated	Anion salt in solution	Association K_{obs} [M^{-1}][b]	Cooperativity factor[c]
K^+	none	155	n/a
K^+	TBACl	330	2.1
K^+	TBABr	250	1.6
K^+	TBAI	220	1.4
Na^+	none	460	n/a
Na^+	TBACl	1000	2.2
Na^+	TBABr	640	1.4
NH_4^+[d]	none	–[e]	n/a
NH_4^+[d]	TBACl	370	n/a
NH_4^+[d]	TBABr	300	n/a

[a] Solvent: 2% H_2O/CH_3CN; temperature: 298 K; $[\mathbf{1}\cdot TBAX]_i = 3\times10^{-4}$ mol dm^{-3}; titrant $[MPF_6] = 0.09$ mol dm^{-3}. [b] Errors < 10%. [c] Cooperativity factor is calculated by $K_{obs(anion,ion\,pair)}/K_{obs(anion,free)}$. [d] Titrant as a solution in 5% H_2O/CH_3CN for solubility. [e] Binding too weak to be determined.

Table 3. ^{1}H NMR spectroscopy K_{obs} values for interactions of **1** with various ion-pair combinations[a]

Anion salt titrated	Cation salt in solution	Association K_{obs} [M^{-1}][b]	Cooperativity factor[c]
Cl^-	none	178 (16)	n/a
Cl^-	KPF_6	1711 (65)	9.6
Cl^-	$NaPF_6$	1950 (129)	10.9
Cl^-	NH_4PF_6	747 (28)	4.2
Br^-	none	67 (5)	n/a
Br^-	KPF_6	414 (36)	6.2
Br^-	$NaPF_6$	479 (42)	7.2
Br^-	NH_4PF_6	307 (22)	4.6
I^-	none	31 (3)	n/a
I^-	KPF_6	96 (5)	3.1

[a] ^{1}H NMR (500 MHz); solvent: 2% D_2O/CD_3CN; temperature: 293 K; $[\mathbf{1}\cdot MPF_6]_i = 1.5\times10^{-3}$ mol dm^{-3}; titrant $[TBAX] = 0.075$ mol dm^{-3}. [b] Errors < 10%. [c] Cooperativity factor is calculated by $K_{obs(cation,ion\,pair)}/K_{obs(cation,free)}$; n/a = not applicable.

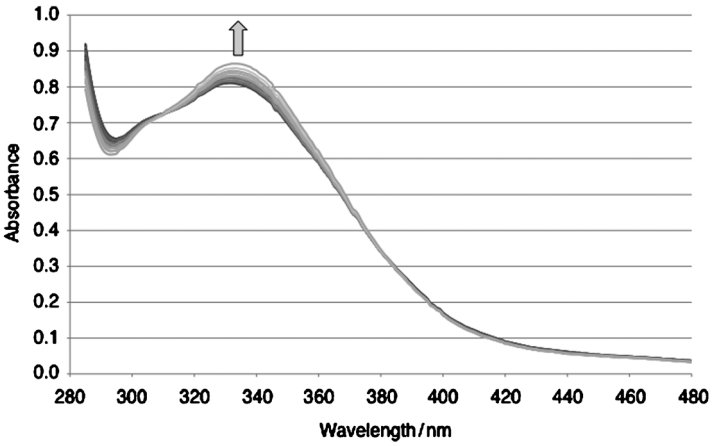


Figure 9. Enhancement of the n–π* quinone absorbance of **1**·TBACl in response to addition of KPF_6; solvent: 2% H_2O/CH_3CN; temperature: 298 K; $[\mathbf{1}]_i = 3\times10^{-4}$ mol dm^{-3}; titrant $[KPF_6] = 0.09$ mol dm^{-3}.

Ion-pair binding in the solid state: Crystals of macrocycle **1** with various ion pairs were grown by slow evaporation of a solution of **1**·MPF_6 (in which M is the desired coordinating cation) in 2% D_2O/CD_3CN in the presence of excess TBAX (in which X is the desired coordinating anion). In all cases for which crystals were successfully grown, neither TBA^+

nor PF_6^- were found in the crystal structure. In each of the cases in which coordinating cations were bound in the cavity, the calix[4]diquinone unit was observed to adopt a pinched-cone conformation; the two *tert*-butylphenyl rings were almost parallel and the quinone rings orientated convergently, with an interplanar angle of 68°, facilitating oxygen coordination to the cation.

***1**·KCl*: The K^+ and Cl^- ions are bound in the crystal structure in an unusual contact ion-pair manner, with intermolecular contacts. Importantly, the triazole motif acts as a Lewis base metal-cation binder and as a C–H···halide-anion hydrogen-bond donor (Figure 10), corroborating the evidence from the solution-state ^{1}H NMR spectroscopy ion-pair binding studies. In one position in the crystal, the triazole Lewis base nitrogen atom binds to the potassium, N···K 3.102(5) Å; in another position in the crystal the triazole CH hydrogen-bonds intermolecularly to chloride, C–H···Cl 3.546(6) Å.

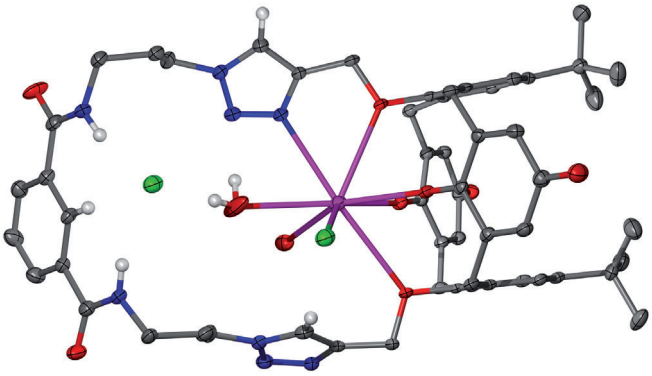


Figure 10. Single-crystal X-ray structure of **1**·KCl with the intermolecular K^+Cl^- contact ion-pair shown. Additionally, the triazole lone pair is shown to interact with K^+ and the triazole CH is shown to bind to Cl^-. Only hydrogen atoms involved in hydrogen bonding are shown for clarity. Thermal ellipsoids are displayed at the 30% probability level.

Oxygen interactions with the potassium cation (quinone O···K 2.643(4), 2.798(4) Å, phenyl O···K 2.949(3), 3.085(3) Å and an intermolecular quinone O···K 2.747(4) Å) are supplemented by the triazole nitrogen lone-pair coordination to potassium and also a contact ion-pair between the K^+ of one molecule and the Cl^- (centre-to-centre 3.304(2) Å) of an adjacent molecule in a pseudo-dimer configuration (Figure 11).[8] Chloride is held in position intramolecularly by the isophthalamide motif (amide N–H···Cl 3.291(5), 3.296(5) Å and an internal C–H···Cl 3.512(6) Å).

***1**·NaCl*: The Na^+ and Cl^- ions are separated by a water molecule in the macrocycle cavity (Figure 12). A triazole CH forms an intramolecular hydrogen-bonding cavity for chloride (triazole C–H···Cl 3.585(6) Å) together with the isophthalamide motif.

Calix[4]diquinone oxygen atoms interact with the sodium cation (quinone O···Na 2.357(5), 2.292(4) Å and phenyl

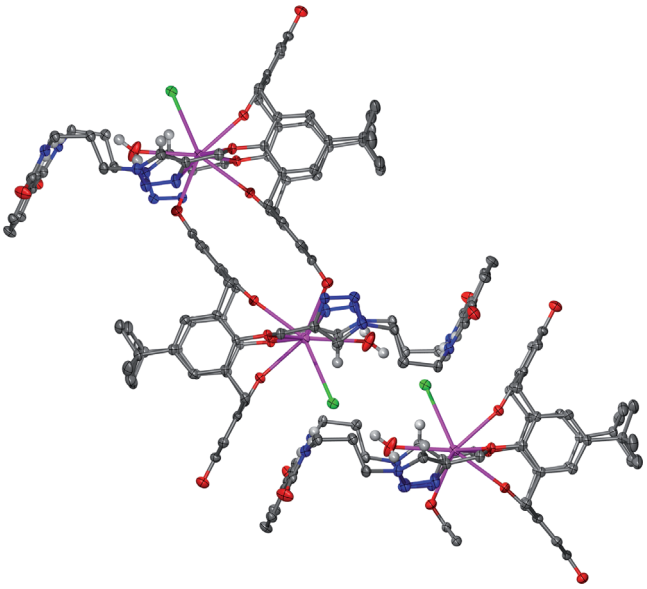


Figure 11. Single-crystal X-ray structure of $(\mathbf{1}\cdot KCl)_n$, demonstrating intermolecular packing and the key K^+Cl^- contact ion-pair. Only hydrogen atoms involved in hydrogen bonding are shown for clarity. Thermal ellipsoids are displayed at the 30% probability level.

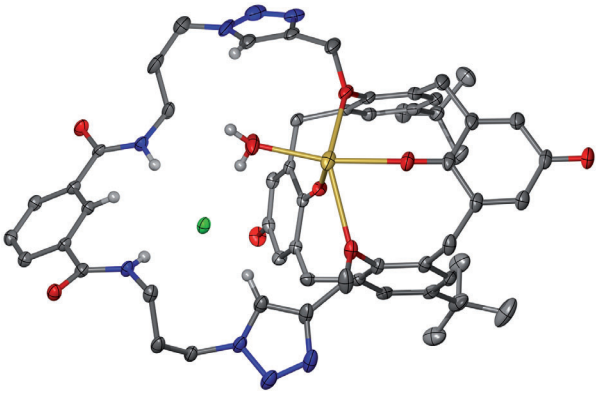


Figure 12. Single-crystal X-ray structure of **1**·NaCl with a water molecule separating the ion pair in the cavity. The Cl^- is bound by an array of intramolecular hydrogen bonds from the triazole and isophthalamide. Only hydrogen atoms involved in hydrogen bonding are shown for clarity. Thermal ellipsoids are displayed at the 30% probability level.

O···Na 2.740(5), 2.530(5) Å). In addition, the sodium ion is coordinated by a water molecule (Na···O 2.297(5) Å), which also hydrogen bonds to the chloride in the cavity (O–H···Cl 3.131(5) Å). The chloride is bound intramolecularly by the isophthalamide motif (amide N–H···Cl 3.310(5), 3.419(5) Å and internal C–H···Cl 3.515(6) Å) and also by the triazole hydrogen bond.

***1**·NH$_4$Cl*: The NH_4^+ and Cl^- ions are separated in the cavity by >6 Å and exhibit no apparent direct, nor even a solvent-mediated, interaction (Figure 13). In this case, the triazole motif binds chloride in an intermolecular fashion by a C–H···Cl bond.

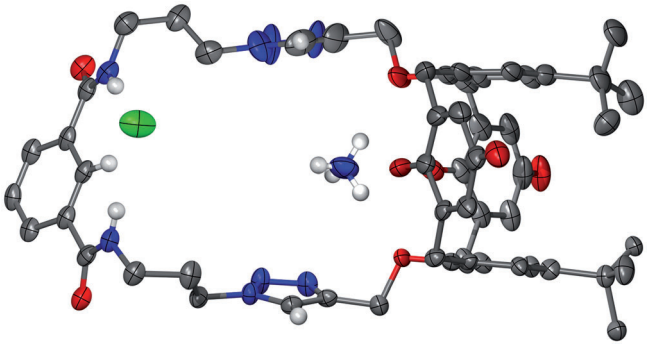


Figure 13. Single-crystal X-ray structure of **1**·NH_4Cl with the guest ions widely separated in the cavity. The triazole forms hydrogen bonds to Cl^- in an intermolecular fashion. Only hydrogen atoms involved in hydrogen bonding are shown for clarity. Thermal ellipsoids are displayed at the 30% probability level.

The oxygen interactions with the ammonium cation appear to be electrostatic rather than directed by hydrogen bonding (quinone O···NH_4 2.701(17), 2.758(16) Å and phenyl O···NH_4 2.930(14), 3.074(14) Å). The chloride is bound intramolecularly by the isophthalamide motif (amide N–H···Cl 3.453(10), 3.364(10) Å and internal C–H···Cl 3.628(12) Å) and also by the intermolecular triazole hydrogen bond.

1·KBr: The crystal structure of the **1**·KBr complex can be found in the Supporting Information.

Conclusion

A new heteroditopic calix[4]diquinone triazole containing receptor capable of recognising both cations and anions through respective Lewis base and C–H hydrogen-bonding modes of the triazole motif has been prepared. ^{1}H NMR and UV/Vis spectroscopic titration studies determined that the ion-pair receptor cooperatively binds halide–monovalent cation combinations in a polar solvent mixture of 2% water/acetonitrile. Cation binding by the calix[4]diquinone oxygen and triazole nitrogen donor groups enhances the strength of halide complexation in the receptor's isophthalamide site by up to 11 times in the case of the Na^+Cl^- ion pair. Conversely, halide-anion binding in the receptor's isophthalamide motif enhances cation complexation.

A number of receptor/ion-pair adduct solid-state structures have been determined by X-ray crystallography. These structures further corroborate the findings from the ^{1}H NMR spectroscopy ion-binding investigations in solution, that the receptor's triazole motifs are capable of coordinating simultaneously to both cation and anion guest species.

Experimental Section

All commercial-grade chemicals were used without further purification. TBAX and MPF_6 salts were stored under vacuum prior to use, in a desiccator containing phosphorus pentoxide and self-indicating silica. Mass spectra were obtained on a Bruker MicroTof (ESMS) instrument. NMR spectra were recorded on a Varian Mercury 300 (^{13}C) or Varian Unity Plus 500 (^{1}H) spectrometer with the solvent serving as the lock and internal reference. UV/Vis spectra were recorded on a PG Instruments T60U Spectrophotometer. Melting points were recorded on a Gallenkamp capillary melting-point apparatus and are uncorrected.

Dialkyne **2** and dibromide **3** have previously been synthesised.[9,10] A fresh solution of oxidising thallium(III) trifluoroacetate (0.44 mol dm^{-3}) in trifluoroacetic acid was prepared as reported by McKillop et al.[15]

N^1,N^3-bis(3-azidopropyl)isophthalamide (4): Dibromide **3** (2.00 g, 4.92 mmol) was dissolved in dry, degassed dimethylformamide (50 mL) and sodium azide (3.20 g, 10 equiv) was then added. The reaction mixture was stirred under a N_2 atmosphere at room temperature overnight and then added to H_2O (250 mL). A white precipitate formed and this was extracted from the aqueous layer with CH_2Cl_2 (6×100 mL). The combined organic fractions were dried over $MgSO_4$ and the solvents carefully removed in vacuo with no heating to give the desired product as a white solid (1.47 g, 4.45 mmol, 91%). M.p. 75–77 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ = 8.17 (t, ^4J(H,H) = 1.8 Hz, 1H; phenylH), 7.90 (dd, ^3J(H,H) = 7.8, ^4J(H,H) = 1.8 Hz, 2H; phenylH), 7.49 (t, ^3J(H,H) = 7.8 Hz, 1H; phenylH), 6.74 (br s, 2H; CONH), 3.54 (dt, ^3J(H,H) = 6.6, 6.0 Hz, 2H; NHCH_2R), 3.43 (t, ^3J(H,H) = 6.3 Hz, 2H; N_3CH_2R), 1.90 ppm (q, ^3J(H,H) = 6.6 Hz, 2H; RCH_2R); ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ = 167.2, 134.7, 130.0, 128.8, 125.3, 49.3, 37.7, 28.7 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{18}N_8O_2Na$: 353.1445 $[M+Na]^+$; found: 353.1443.

Macrocycle 5: N^1,N^3-bis(3-azidopropyl)isophthalamide **4** (100 mg, 0.303 mmol) and dialkyne **2** (220 mg, 0.303 mmol) were dissolved in dry dichloromethane (100 mL). To this were added tetrabutylammonium chloride (84 mg, 1 equiv), tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA; 2 mg, 1 mol%), $[Cu^I(MeCN)_4PF_6]$ (57 mg, 0.5 equiv) and diisopropylethylamine (158 μL, 3 equiv). The reaction mixture was stirred at room temperature under a N_2 atmosphere for 3 days. Crude TLC in 4% EtOH/CH_2Cl_2 showed full consumption of the starting materials. The reaction mixture was then washed with aqueous HCl (1 M; 100 mL), saturated aqueous $NaHCO_3$ (100 mL) and then H_2O (100 mL). The organic component was dried over $MgSO_4$ and the solvent removed in vacuo to give a pale yellow solid. This was then purified by column chromatography, first by removing a fast-running yellow fraction (CH_2Cl_2, 1 column volume (CV); 4% EtOH/CH_2Cl_2, 2.5 CV; 5% EtOH/CH_2Cl_2, 5 CV; 10% EtOH/CH_2Cl_2, 5 CV), isolating the pure macrocycle as a white glassy solid (247 mg, 77%). M.p. 200 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ = 8.02 (d, ^3J(H,H) = 6.6 Hz, 2H; phenylH), 7.82 (br s, 2H; CONH), 7.68 (br s, 1H; phenylH), 7.60 (s, 2H; triazoleH), 7.47 (t, ^3J(H,H) = 7.8 Hz, 1H; phenylH), 6.99 (s, 4H; calixH), 6.89 (s, 4H; calixH), 4.98 (s, 4H; OCH_2R), 4.73 (br t, ^3J(H,H) = 6.0 Hz, 4H; triazoleCH_2R), 4.08 (d, ^2J(H,H) = 12.9 Hz, 4H; calixCH_2calix), 3.70 (m, 4H; NHCH_2R), 3.24 (d, ^2J(H,H) = 12.9 Hz, 4H; calixCH_2calix), 2.35 (br s, 4H; RCH_2R), 1.93 (br s, 2H; OH), 1.23 (s, 18H; CCH_3), 1.04 ppm (s, 18H; CCH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ = 166.6, 150.2, 149.3, 147.7, 144.3, 141.9, 133.9, 132.8, 131.4, 129.5, 127.4, 125.8, 125.2, 124.4, 123.2, 69.1, 58.7, 49.2, 37.6, 34.1, 33.8, 32.1, 31.6, 31.0 ppm; HRMS (ESI): *m/z* calcd for $C_{64}H_{78}N_8O_6Na$: 1077.5937 $[M+Na]^+$; found: 1077.5914.

Receptor 1: Macrocycle **5** (500 mg, 0.474 mmol) was added to a solution of $Tl(CF_3CO_2)_3$ in TFA (0.44 M, 6.45 mL, 6 equiv). The reaction mixture was stirred under a N_2 atmosphere in the dark at room temperature for 2 days. CH_2Cl_2 (15 mL) was added to the orange reaction mixture, which was then washed with H_2O (3×15 mL), dried over $MgSO_4$ and the solvent removed in vacuo to give the impure product as a yellow solid (485 mg). This was then purified by recrystallisation from CH_2Cl_2/Et_2O and the desired product was collected and dried in vacuo to give a yellow solid (385 mg, 84%). M.p. 175 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ = 8.44 (s, 1H; phenylH), 8.11 (d, ^3J(H,H) = 7.8 Hz, 2H; phenylH), 7.95 (s, 2H; triazoleH), 7.58 (br s, 2H; CONH), 7.58 (t, ^3J(H,H) =

7.8 Hz, 1H; phenylH), 6.94 (s, 4H; quinoneH), 6.39 (s, 4H; calixH), 4.86 (s, 4H; OCH_2R), 4.58 (t, $^3J(H,H)=6.0$ Hz, 4H; triazoleCH_2R), 3.60 (m, 8H; quinoneCH_2calix, $NHCH_2R$), 3.36 (d, $^2J(H,H)=13.2$ Hz, 4H; quinoneCH_2calix), 2.40 (m, 4H; RCH_2R), 1.17 ppm (s, 18H; CCH_3); ^{13}C NMR (75 MHz, CD_3CN, 298 K): $\delta=188.9$, 185.6, 167.1, 154.3, 147.5, 146.7, 144.1, 134.2, 132.5, 130.8, 129.1, 128.9, 127.6, 124.6, 123.9, 66.9, 47.8, 36.9, 34.1, 33.7, 31.4, 29.8 ppm; HRMS (ESI): *m/z* calcd for $C_{56}H_{58}N_8O_8Na$: 993.4270 $[M+Na]^+$; found: 993.4269.

Crystals: Single-crystal diffraction data were collected at low temperature with $Cu_{K\alpha}$ radiation ($\lambda=1.5418$ Å) on an Oxford Diffraction/Agilent Technologies SuperNova diffractometer (for **1** and **1**·TBACl) or with synchrotron radiation ($\lambda=0.68890$ Å) by using beamline I19 (EH1) at the Diamond Light Source (for **1**·KCl, **1**·NaCl, **1**·NH_4Cl and **1**·KBr). The data were collected and reduced by using CrysAlisPro,[16] or CrystalClear.[17] The structures were solved with SuperFlip,[18] or SIR92,[19] and refined by using full-matrix least-squares fitting within CRYSTALS,[20] as described in the Supporting Information (CIF). In the case of compound **1** and adduct **1**·NH_4Cl, the Fourier difference map indicated the presence of diffuse electron density believed to be disordered solvent so PLATON/SQUEEZE was used and the discrete Fourier transform of the void regions were treated as contributions to the A and B parts of calculated structure factors.[21] Molecular graphics were produced by using X-Seed,[22] and POV-RAY.[23] CCDC-863826 (**1**), CCDC-863827 (**1**·2TBACl), CCDC-863828 (**1**·KCl), CCDC-863829 (**1**·NaCl), CCDC-863830 (**1**·NH_4Cl) and CCDC-863831 (**1**·KBr) contain the supplementary crystallographic data (excluding structure factors) for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

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