

Chalcogen Bonding Ion-Pair Cryptand Host Discrimination of Potassium Halide Salts

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Abstract: A series of chalcogen, halogen and hydrogen bonding heteroditopic macrobicyclic cryptands are reported and their potassium halide ion-pair recognition properties investigated. Saliently, the co-bound potassium cation was determined to be crucial in switching on the bromide and iodide recognition properties of the respective cryptand receptor. Importantly, the nature of the sigmahole mediated interaction employed in the anion recognition component is demonstrated to significantly augment the ion-pair binding behaviour, markedly so for the halogen bonding analogue. Most notably the incorporation of a chelating chalcogen bonding donor motif significantly improves the selectivity towards KBr over KI, relative to halogen and hydrogen bonding analogues.

Introduction

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The plethora of roles that charged species play in biological, environmental and technological spheres has resulted in the burgeoning field of supramolecular host-guest chemistry, which focuses on the construction of synthetic receptors for the selective recognition and sensing of a vast array of cationic and anionic species.^[1-3] However, necessarily implicated in the recognition of a given charged species is the presence of its counterion(s), which has been demonstrated to dramatically affect the binding behaviour of monotopic host systems. Heteroditopic receptors, incorporating both cation and anion binding sites, are capable of exploiting this interplay between co-bound ion-pairs, enhancing the efficacy of charged guest

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recognition via favourable intramolecular electrostatic interactions and conformational allosteric cooperativity, relative to monotopic analogues.^[4-9] Although recent years have seen a diversification in strategies to affect cation complexation, such as cation- π interactions^[10-12] or the employment of interlocked receptor topologies,^[13-15] to elicit highly specific interaction modes, the commensurate anion binding motif variation in ionpair receptor design has been largely restricted to hydrogen bond donors.^[7-9] The sigma-hole non-covalent interactions, halogen bonding (XB) and chalcogen bonding (ChB), have been shown to exhibit potent anion binding strength and selectivities, which includes superior enantioselectivity^[17] and sensory response output, in comparison to analogous hydrogen bonding (HB) receptor analogues.^[18-21] Despite this, their incorporation into heteroditopic structural host frameworks is rare, with only a handful of examples of XB and one ChB ion-pair receptor reported to date.^[13,22-25]

Herein, we report the first sigma-hole heteroditopic cryptands, which feature a dibenzo-30-crown-10 (DB30C10) motif for potassium cation binding, bridged by bidentate ChB, and XB donors for anion recognition. (Figure 1). Ion-pair binding investigations notably demonstrate DB30 C10-potassium cation encapsulation switches on bromide and iodide halide recognition. Importantly, the nature of the sigma-hole mediated anion binding interaction dramatically influences both halide affinity and selectivity, with the chalcogen bonding heteroditopic cryptand exhibiting significant discrimination between the two potassium halide salts.



Figure 1. Target heteroditopic ChB, XB and HB cryptands for potassium halide ion-pair recognition.

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Results and Discussion

Synthesis of heteroditopic cryptands

The target XB, ChB and HB heteroditopic cryptands were prepared via a CuAAC 'click' macrocyclisation strategy between cis-functionalised DB30C10 bis-azide precursor $5^{[26]}$ and the appropriately functionalised alkynes. The requisite iodo- and tellurium-functionalised alkyne precursors, **2** and **4** were synthesized according to Scheme 1, from commercially available 1,3-diethynylbenzene **1**. Treatment of **1** with 2.2 equivalents *n*-BuLi at -78°C in anhydrous THF and subsequent reaction of the lithiated bis-alkyne with a solution of I₂ afforded bis-iodoalkyne **2** in 80% yield after purification by silica gel column chromatography.

Reaction of 1 with finely ground $AgNO_3$ in a basic methanol solution facilitated precipitation and isolation of bis-Ag(I)acetylide 3, as an air stable solid, which demonstrated no deterioration in quality over the course of 6 months. Methyl tellurium(II) bromide, generated in-situ via treatment of a dimethyl ditelluride solution with 1 M Br₂ in CH₂Cl₂, was reacted with a THF suspension of 3, affording the bis-telluromethyl functionalized alkyne 4 in 65% yield, after chromatographic purification. With the alkyne precursors in hand, the target XB, ChB and HB heteroditopic cryptands were prepared via CuAAC cyclisation reactions between cis-functionalised DB30 C10 bisazide 5 and an equimolar amount of the appropriately



Scheme 1. Synthesis of the iodo- and tellurium- functionalised alkyne precursors.

functionalized alkyne in the presence of Cu(MeCN)₄PF₆ and Cu(I) stabilising ligand, tris(benzyltriazolylmethyl) amine (TBTA) (Scheme 2). Subsequent purification by column chromatography afforded the cryptand-like receptors in yields ranging from 27%-35%. (See Supporting Information for further synthetic details and characterisation data).

¹H NMR Binding studies

In order to assess the ability of the receptors to function as ionpair receptors, preliminary qualitative ¹H NMR potassium halide salt complexation experiments were undertaken in 1:1 CD₃CN: CDCl₃. In a typical experiment the ¹H NMR spectrum of the appropriate free cryptand was compared with 1:1 stoichiometric solutions of the cryptand + KPF₆ and cryptand + KI (representative example for 1-XB shown in Figure 2a). Importantly, in the cases of 1-XB and 1-ChB upon the addition of KPF₆, a perturbation to the chemical shifts of the crown ether methylene protons was observed, indicative of potassium metal cation complexation at the respective cryptand's DB30C10 recognition site. An upfield shift of the internal benzene proton (c) was attributed to K⁺ induced conformational changes. Upon addition of KI, the same aryl proton c shifted downfield, suggesting iodide complexation in the vicinity of the respective XB/ChB anion binding cavity. In addition, for 1.ChB dramatic perturbations were also observed in the TeMe signal (h) upon varying the counteranion of the K⁺ salt, further indicating ChB's participation in the complexation event of the ion-pair (Figures S14 and S15).

Similar observations were observed in an analogous experiment with HB cryptand **1-HB** (Figure S17). Downfield shifts of the proto-triazole and internal benzene proton signals, upon the addition of KPF_6 were attributed to the K⁺ recognition mediated conformational changes. Addition of KI induced a downfield shift in the triazole signal, concomitant with HB mediated anion binding, whilst a similar shift of internal benzene proton resonance *c* was not observed.

Attention then turned to quantifying the halide anion recognition properties of the cryptands 1-ChB, 1-XB, 1-HB, wherein ¹H NMR anion binding titration experiments were



Scheme 2. CuAAC Mediated macrocyclization reactions between DB30 C10 bis-azide and alkyne components.

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Figure 2. Truncated ¹H NMR spectra of a) 1·XB, 1·XB + KPF₆ and 1·XB + KI b) 1·XB + KPF₆ with increasing equivalents of TBABr (1:1 CDCl₃/ CD₃CN, 298 K, 500 MHz).



Figure 3. Anion binding isotherms generated from monitoring perturbations of the internal phenyl proton signal of respective heteroditopic receptor **1·XB**, **1·ChB**, **1·HB** + 1 equivalent KPF₆ upon addition of TBA bromide and iodide (1:1 CDCl₃/ CD₃CN, 298 K, 500 MHz).

conducted in 1:1 CD₃CN:CDCl₃ solvent mixtures. Notably, upon the addition of tetrabutylammonium (TBA) halide salts, negligible chemical shift perturbations were observed in all cases. In contrast however, addition of aliquots of TBA anion solutions to the heteroditopic receptors pre-complexed with one equivalent of potassium hexafluorophosphate exhibited significant downfield perturbations of the internal benzene resonance (*c*) of the respective cryptand (representative example for 1-XB shown in crucial for bromide and iodide anion binding, in effect switching on halide recognition via favourable electrostatic interactions. Bindfit analysis^[27] of the titration binding isotherm data (Figure 3) determined 1:1 stoichiometric association constants displayed in Table 1.

Comparison of the halide anion affinities for the heteroditopic cryptand structures reveals $1 \cdot XB \cdot KPF_6$ possesses significantly enhanced anion affinity for both bromide and iodide relative to the hydrogen and chalcogen bonding analogues. An impressive three orders of magnitude switch on of binding for

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Table 1. Anion association constants	$(K_a/M^{-1})^{[a]}$ for 1·XB, 1·ChB and 1·HB in
the presence of 1 equivalent KPF ₆ .	

the presence of requivalent RT ₆ .						
Anion	1∙XB	1•ChB	1∙HB			
Br [−] I [−]	2170 2980	126 16	75 99			

[a] K_a values calculated using Bindfit[®] software using a 1:1 host-guest binding model. Errors (±) less than 10%. All anions added as their TBA salts. Solvent = 1:1 CDCl₃:CD₃CN. T = 298 K. Analogous experiments conducted with TBACl resulted in KCl salt precipitation.

both heavy halide guest species. It is noteworthy that close inspection of the bromide and iodide association constants reveals that whilst **1·XB** demonstrates a considerable 30-fold enhancement in terms of affinity relative to **1·ChB** and **1·HB**, the ability of the XB- cryptand to discriminate between KI and KBr ion-pairs is modest, $K_a(I^-)/K_a(Br^-) = 1.3$ and almost identical to that of **1·HB** $K_a(I^-)/K_a(Br^-) = 1.4$. In contrast however, notwith-



standing the attenuated ion-pair binding affinity of 1·ChB, the incorporation of the bidentate telluromethyl-triazole donors endows the ChB cryptand with notable selectivity towards KBr over KI, $K_a(Br^-)/K_a(I^-)=8$. This may be attributed to a relatively superior 1·ChB·KPF host-bromide halide guest anion size match complementarity, whereas iodide is too large to gain the full electrostatic benefit of a proximal co-bound potassium cation.

Solid state characterisation of potassium iodide ion-pair cryptand complex

Solid state evidence for the postulated heteroditopic cryptand ion-pair complexation mode was obtained from single crystal Xray diffraction structural analysis of crystals from a chloroform sample of $1 \cdot XB \cdot KI$. Figure 4 illustrates KI complexation by the XB cryptand in the solid state. The structure reveals a coordinatively saturated, 10-coordinate K⁺ cation encapsulated in a



Figure 4. Solid state structure of the **1-XB** Kl complex as a wire frame (top) and space filling representations (bottom), showing 10-cordinate potassium (cyan) complexation and bidentate XB-iodide (purple) formation. For clarity hydrogen atoms are omitted and a selected configuration of disorderded polyether chain is displayed.

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'tennis ball seam-like' manner by the DB30 C10 crown ether, consistent with previously reported structures.^[28,29] The bidentate XB formation between two iodotriazoles and iodide is evidenced by inspection of the C–I···I⁻ distances, which are significantly shorter than the sum of the van der Waals radii (see Supporting Information for details). Owing to the large size of the iodotriazole donor groups and iodide guest, XB iodide coordination is in a non-planar fashion with respect to the rigid bridged benzene spacer unit.

Conclusions

In conclusion, a series of novel sigma-hole heteroditopic macrobicyclic cryptand-like receptors were synthesised, consisting of a cis-bis-functionalised dibenzo-30-crown-10 cation binding moiety strapped with chelating ChB bis-telluromethyl, XB iodo and proto-triazole-based anion binding motifs. ¹H NMR ion-pair binding titration experiments in 1:1 CD₃CN:CDCl₃ reveal that co-complexation with K⁺ switches on the bromide and iodide halide recognition properties of the receptors, markedly augmented with the XB cryptand receptor. Furthermore, the incorporation of ChB and XB donors in the heteroditopic host architecture profoundly influences the potassium halide ionpair recognition properties. Importantly, the ChB receptor demonstrates selectivity towards KBr over KI and serves to highlight the possibility of subtly modulating ion-pair recognition behaviour by judicious exploitation of the unique geometric and electronic properties of sigma-hole mediated anion recognition, presenting an exciting future avenue in ion-pair host design.

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Conflict of Interest

The authors declare no conflict of interest.

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COMMUNICATION



Chalcogen bonding (ChB) and halogen bonding (XB) ion-pair heteroditopic cryptands exhibit cooperative recognition of potassium halide salts. Incorporation of bidentate triazolebased ChB or XB donor motifs into a dibenzo-30-crown-10-based macrobicyclic receptor framework is demonstrated to profoundly influence selectivity and affinity behaviour towards the recognition of KBr and KI ion-pairs relative to hydrogen bonding analogues. A. Docker, Dr. T. Bunchuay, M. Ahrens, Dr. A. J. Martinez-Martinez, Prof. P. D. Beer*

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