CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Thermodynamics of Anion Binding by Chalcogen Bonding Receptors

Authors: Jason Y. C. Lim, Jane Y. Liew, and Paul D. Beer

To be cited as: *Chem. Eur. J.* 10.1002/chem.201803393

Link to VoR: http://dx.doi.org/10.1002/chem.201803393

Supported by
ACES

WILEY-VCH

10.1002/chem.201803393

FULL PAPER

WILEY-VCH

Thermodynamics of Anion Binding by Chalcogen Bonding Receptors

Jason Y. C. Lim[#],[a] Jane Y. Liew[# a] and Paul D. Beer*[b]

Abstract: The application of chalcogen bonding (ChB) to anion recognition is an underdeveloped area of host-guest supramolecular chemistry. The chemical instability of heavier chalcogen derivatives may in part be responsible for the lack of progress. Herein, we report the synthesis of a new structurally-simple, tellurium-based ChB binding motif whose robust stability has enabled the thermodynamic properties for ChB halide anion binding in polar aprotic and wet protic organic solvent media to be elucidated. The thermodynamic data reveals how the subtle interplay between ChB host, anion guest and solvent dictates halide binding selectivity and affinity trends. These findings help to provide a deeper insight into the nature of the ChB–anion interaction.

Introduction

Chalcogen bonding (ChB) is the attractive supramolecular interaction between an electron-deficient Group 16 element (S/Se/Te) and a Lewis base arising from electrophilic σ-holes on the chalcogen atom.[1] Like halogen bonding (XB), its more well-studied sister σ-hole interaction involving heavy Group 17 elements (Br/I),[2] ChB displays comparable binding strengths to the ubiquitous hydrogen bonding (HB) and more stringent directionality, allowing for greater precision in three dimensional spatial control of host-guest binding. Nonetheless, there are important differences between XB and ChB interactions. Most notably, while XB is restricted to an optimal R-X···B angle of 180°, the multivalent nature of chalcogen atoms allows more than one σ-hole to be present on the donor atom depending on its bonding character, resulting in a greater geometric diversity of interactions with Lewis bases.[3,4] Electronically, ChB differs from XB, being influenced not only by the intrinsic greater electropositivity of chalcogen donor atoms compared to halogens, but also by the cumulative effects of the number and spread of σ-holes, coupled with the nature and number of covalently bonded substituents. Although these unique attributes of ChB are exploited in recent applications in crystal engineering,[5,6] pharmaceutics,[7] catalysis,[8–10] self-assembly processes[11,12] and materials design,[13] solution-phase studies of ChB interactions remain extremely scarce.[14] In particular, only a handful of ChB receptor systems for anion binding, that include acyclic[3] and macrocyclic derivatives and rotaxanes[15] have been reported to date.

While several cationic Se-based ChB receptors are known,[3] the weakness of the C-Te bond (bond energy c.a. 200 kJ mol^{-1})[16] makes it susceptible to oxidation[17] and metal insertion reactions.[18-20] Thus, despite their potential for strong ChB interactions, cationic Te-based receptors are extremely rare,[21] with the few reported functional *neutral* Te-based anion binding receptors incorporated within aromatic heterocycles such as tellurophenes[22] or tellurodiazoles[23] for enhanced stability. With the objective of gaining a greater insight into the nature of the ChB receptor-anion interaction, we report herein the synthesis of a novel robust monocationic tellurium-based ChB donor motif **1.Te** comprised of exocyclic divalent Te donor atoms covalently linked to a strongly electron-withdrawing 3,5-bis(triazole) pyridinium group (Figure 1). The inherent stability of **1.Te** enabled the hitherto-unknown thermodynamic properties for ChB-halide anion binding in polar aprotic and wet protic organic solvent media to be determined. In comparison with acyclic and macrocyclic Se-based receptors **2.Se, 3.Se**, acyclic hydrogen bonding (**1.H**) and fluorine triazole functionalised (**2.F**) receptor analogues (Figure 1), the thermodynamic data helps to rationalize how the interplay between ChB receptor, anion guest and solvent medium affects halide binding selectivity and affinity trends.

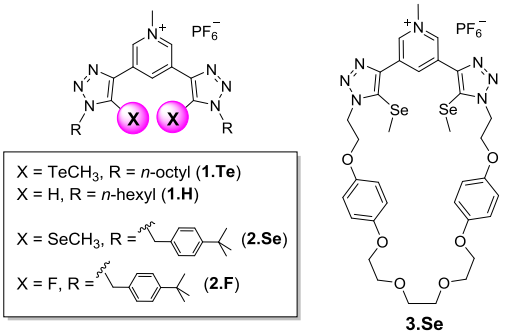


Figure 1. Structures of ChB hosts and structural analogues used in this study.

Results and Discussion

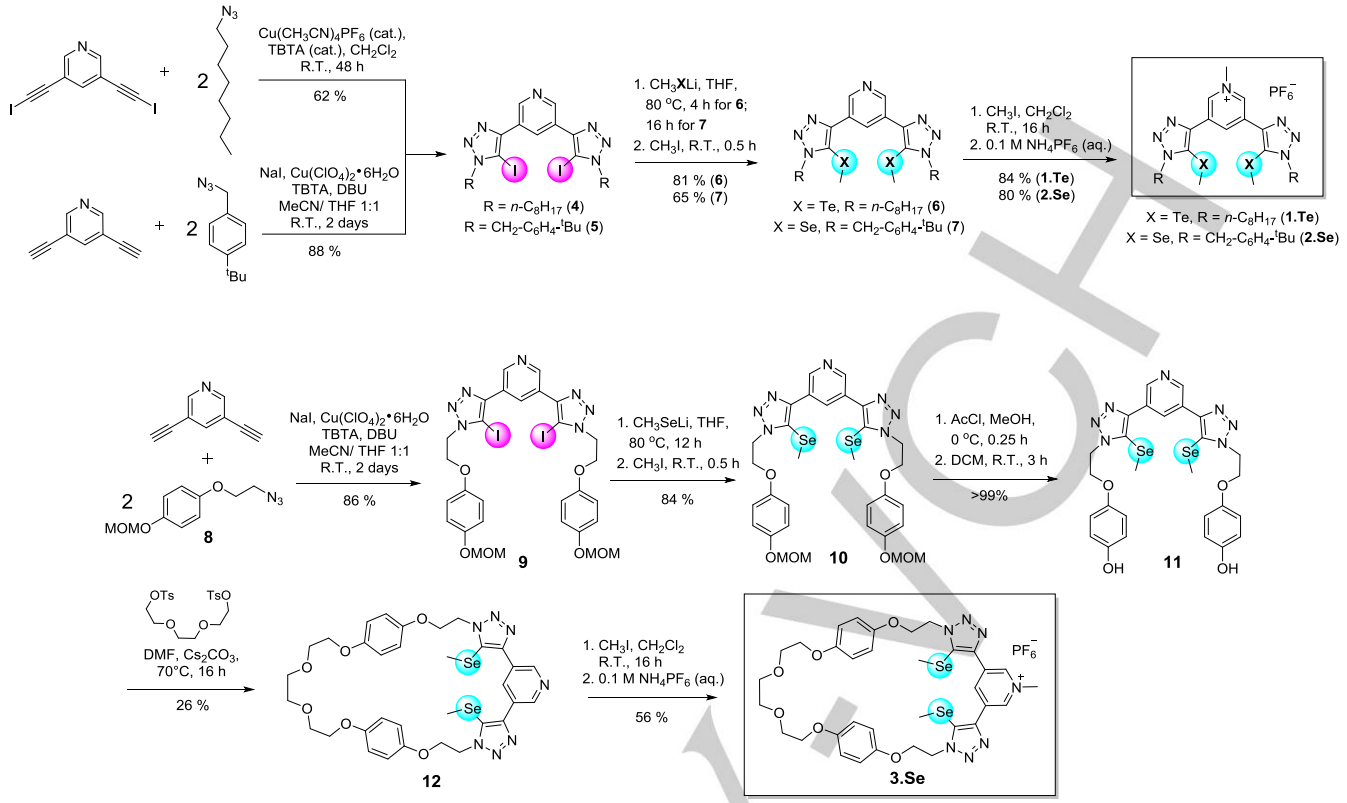
Synthesis of ChB Receptors

As shown in Scheme 1, the bis-triazole-containing structural framework of acyclic receptors **1.Te** and **2.Se** was constructed from the copper(I)-catalysed azide-alkyne cycloaddition (CuAAC) reactions either directly from 3,5-bis(ethynyl)pyridine[24] or from the corresponding iodoalkynes.[25] Following which, the methylchalcogeno-triazoles were generated by aromatic nucleophilic substitution (S_NAr) reactions of the iodotriazoles (**4**

[#] These authors contributed equally to the manuscript.

[a] Dr. J. Y. C. Lim; J. Y. Liew; Prof. P. D. Beer
Chemistry Research Laboratory, Department of Chemistry,
University of Oxford, 12 Mansfield Road, Oxford, OX1 3TA, UK.
E-mail: paul.beer@chem.ox.ac.uk

Supporting information for this article is given via a link at the end of the document.



Scheme 1. Synthesis of ChB receptors **1.Te**, **2.Se** and **3.Se**.

and **5**) by reactive methylchalcogenide anions generated *in-situ* from methyl lithium and the elemental chalcogen (Se/ Te). While methylseleno-triazoles were previously accessed[15] using a two-step procedure,[26] the use of THF as solvent allowed them to be directly formed in synthetically-viable yields in one step from iodotriazole precursors. Pyridine *N*-methylation of the neutral receptor precursors **6** and **7** using iodomethane, followed by anion exchange with aqueous NH_4PF_6 afforded **1.Te** and **2.Se** in good yields of 80 % and 84 % respectively.

This approach was then adopted to construct the structurally more elaborate macrocycle **3.Se.**[27] Using the methoxymethyl (MOM)-protected phenol **8**, a CuAAC 'Click' reaction afforded bis-iodotriazole **9**, which was converted to bis(methylseleno-triazole) **10** by reaction with in situ generated lithium methylselenide. MOM-deprotection under acidic conditions afforded the free bis-phenol **11**, and S_N2 ring-closing with triethylene glycol bis-tosylate afforded neutral macrocycle **12** in 26 % yield. The target cationic macrocycle **3.Se** was prepared using iodomethane prior to anion exchange. For all receptors, ^{1}H NMR characterisation confirmed the exclusive methylation of the central pyridine functionality, whilst ^{125}Te and ^{77}Se NMR spectroscopy ascertained the presence of the ChB donor atoms (see Section S2, Supporting Information).

Anion Binding Studies

The anion binding behaviour of receptors **1.Te**, **2.Se** and **3.Se** were first probed by ^{1}H NMR titration experiments in CD_3CN. The addition of tetrabutylammonium (TBA) chloride to **1.Te** ellicited large downfield shifts of the signals arising from the internal pyridinium aromatic proton (H_a) and the $TeCH_3$ moieties (Figure 2), whilst giving negligible perturbations of protons H_b and H_d even after 10 equivalents of Cl^-. Notably, significant downfield shifts of the $TeCH_3$ groups were also observed upon anion addition (see Fig. S3-1, ESI). In contrast, no perturbations of any of the proton signals arising from the octyl chains (e.g. H_c) were seen throughout the titrations. These observations strongly imply that the Cl^- guest is binding in the vicinity between the Te ChB donor groups. By monitoring the shifts of H_a, non-linear regression analysis of the titration data using the WinEQNMR2 software[28] determined anion association constants (K_a) shown in Table 1. For comparison, binding affinities were also determined for the HB receptor analogue (**1.H**)[29].

The ChB receptor **1.Te** exhibits appreciable affinities for a range of anions of differing charge densities and geometries (Table 1). It is noteworthy that by replacing the $TeCH_3$ units with hydrogen atoms in receptor **1.H**, all anion binding affinities are significantly reduced in magnitude. Contrasting anion affinity preferences between the ChB and HB receptors include **1.Te** binding all the halides more strongly than acetate, whereas **1.H** displays a higher affinity for acetate over the heavier halides bromide and iodide. While this may be a consequence of the contrasting directionalities of ChB and HB, these observations also suggest that ChB-mediated anion binding may be less sensitive to anion basicity than HB interactions. For the halides, while anion affinities for both **1.Te** and **1.H** decrease in order of charge density (Cl^- > Br^- > I^-), **1.Te** showed a larger enhancement in anion affinity relative to **1.H** with the softer and more lipophilic heavier halides (I^- and Br^-). This indicates that ChB interactions have an intrinsic preference for binding softer and more polarisable anions, which has been previously observed for XB[30]. However, a strong association was observed

between **1.Te** and $H_2PO_4^-$, showing an initial host-guest 2:1 binding (K_{21}) stoichiometry that became 1:1 (K_{11}) at higher anion concentrations. Contrastingly, $H_2PO_4^-$ addition to **1.H** resulted in precipitation of the host-guest complex. The significant differences in anion recognition properties between **1.Te** and **1.H** give a strong indication that ChB interactions dominate the binding of anions by **1.Te**. Further evidence of ChB's involvement in anion coordination was observed from the large upfield shifts of the tellurium receptor's ^{125}Te NMR signals ($\Delta\delta$ = -9.8 ppm) upon addition of 1.0 equivalent of Cl^- (see Figure S3-6, Supporting Information) which is consistent with the donation of electron density from Cl^- into the C-Te σ* orbital during ChB interactions.[15]

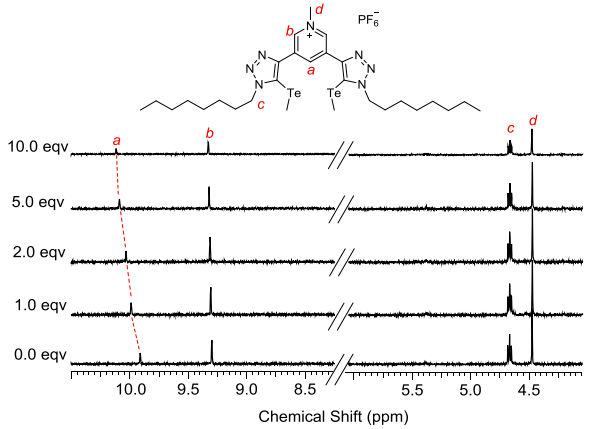


Figure 2. Partial ^{1}H NMR spectra of **1.Te** in the presence of increasing quantities of Cl^- ([**1.Te**]= 1.0 mM, CD_3CN, T = 298 K).[a]

Table 1. Association constants (K_a/ M^{-1}) of **1.Te** and **1.H** with different anions in CD_3CN at 298 K.[a]

Anion	K_a/ M^{-1}	
	1.Te	**1.H**
Cl^-	652 (13)	263 (8)
Br^-	503 (16)	106 (3) [b]
I^-	305 (11) [c]	59 (2) [b]
CH_3COO^-	269 (9)	198 (6)
N_3^-	330 (22)	92 (3)
$H_2PO_4^-$	K_{21} = 411 (40) [c] K_{11} = 1530 (138)	- [b,d]

[a] Values of K_a determined using the WinEQNMR2 software[28] by monitoring the internal proton H_a for **1.Te** and the triazole aromatic proton for **1.H** using a 1:1 host-guest binding model unless otherwise stated; Errors (±) in parentheses; [host] = 1.0 mM. CD_3CN, T = 298 K); [b] Values previously reported in ref. [29]; [c] $TeCH_3$ protons monitored instead of H_a; [d] precipitation of host during titration.

The significant anion affinities exhibited by **1.Te** in CD_3CN prompted us to determine the ChB receptor's anion binding properties in a range of solvent media of varying competitiveness. Analogous ^{1}H NMR titration experiments in d_6-acetone revealed large downfield perturbations of only the H_a and $TeCH_3$ proton signals of **1.Te**. This indicated that despite the weaker charge screening in acetone (dielectric constant ε = 20.7) compared with acetonitrile (ε = 37.5), which could favour electrostatically-driven binding in the vicinity of the cationic pyridinium nitrogen atom, Te-mediated ChB was still dominating the anion recognition. More than an order-of-magnitude enhancement in the K_a values were seen with Cl^- and I^- in acetone when compared to acetonitrile (Table 2). On the other hand, more competitive solvents such as d_6-DMSO resulted in considerably weaker Cl^- binding, whilst no detectable binding was observed in CD_3OD (see Section S3.2, Supporting Information). It is noteworthy that **1.Te** showed noticeably weaker Cl^- anion affinity compared to the XB pyridinium-3,5-bis(iodotriazole) receptor analogue (K_a = 387 M^{-1}) in d_6-DMSO.[29] Although tellurium is more electropositive than iodine, the significant discrepancy observed in this case may be due to a combination of the increased steric bulk of the larger $TeCH_3$ ChB-donor groups, the more diffuse σ-holes on the divalent Te atom compared to the monovalent XB-donor iodine atom,[31] and the potential electron-donating nature of the methyl group covalently bonded to Te reducing the electron-deficiency of its σ-hole.

Table 2. Anion association constants of **1.Te** and **1.H** in different solvents. [a]

Anion	**1.Te**			**1.H**
	d_6-acetone	d_6-DMSO	CD_3CN/ D_2O 99:1	CD_3CN/ D_2O 99:1
Cl^-	> 10^4 [b]	43 (3)	122 (1)	79 (3)
Br^-	- [c]	- [d]	183 (4)	62 (2)
I^-	3528 (54)	- [d]	139 (1)	44 (1)
$H_2PO_4^-$	- [d]	- [d]	100 (2)	- [c]

[a] Values of K_a determined using the WinEQNMR2 software[28] using a 1:1 host-guest binding model; Errors (±) in parentheses; [host] = 1.0 mM. CD_3CN, T = 298 K). [b] ^{1}H NMR titration of Cl^- with receptor **1.Te** in d_6-acetone were carried out at 298, 308 and 318 K, giving K_a >10^4 M^{-1} in each case. [c] precipitation of the host-guest complex observed during titration; [d] not performed.

The presence of water in an organic solvent has been shown to be detrimental to the anion affinities of HB[32] and XB[33] hosts, attributed to the increased energetic demands required to overcome anion hydration for binding to occur. To directly compare the effects of solvent hydration on ChB-mediated anion binding, ^{1}H NMR titration binding studies were also performed with **1.Te** in CD_3CN/ D_2O 99:1 v/v and the resulting host-guest 1:1 stoichiometric association constants are summarised in Table 2. Compared to the K_a values determined in dry CD_3CN (Table 1), the presence of just 1 % water by volume in the solvent resulted in a significant reduction of all anion affinities with the extent of magnitude decrease mirroring the anion's hydration energies ($H_2PO_4^-$ > Cl^- > Br^- > I^-).[34] As a consequence, **1.Te** exhibits comparable affinities for all anions studied, albeit with a slight preference for Br^-. The Hofmeister bias of binding the heavier, less-hydrated halides in wet solvent media closely mirrors the behaviour observed for XB host systems,[29,33,35] highlighting the similarity between both sister σ-hole interactions,

and contrasts with the binding preferences of HB donor hosts. This is clearly illustrated by the K_a values determined for **1.H** with the halides in CD_3CN/ D_2O 99:1 v/v (Table 2), which show a distinct anti-Hofmeister bias selectivity (K_a of $Cl^- > Br^- > I^-$).

Having ascertained the anion binding properties of **1.Te** in a variety of solvents, the effects of substituting the Te ChB-donor atom with Se was investigated using receptors **2.Se** and **3.Se**. As no evidence of binding with Cl^- was found using **3.Se**, in CD_3CN, halide binding studies were performed in the less competitive d_6-acetone. In this solvent, the addition of Cl^- to acyclic receptor **2.Se** elicited *downfield* perturbations of the signals arising from the external aromatic proton H_b and the pyridinium methyl group H_c, concomitantly giving an *upfield* shift of H_a (Figure 3), which is in stark contrast to Cl^- binding by **1.Te** shown in Figure 2.[36] Similar signal perturbations were also observed with the pyridinium-bis(methylseleno-triazole) moiety of macrocycle **3.Se**, whilst the rest of the macrocycle signals showed no appreciable shifts (see Figure S3-15, Supporting Information). These observations suggest that Cl^- is not binding in the cleft between both $SeCH_3$ units, but is predominantly interacting in the vicinity of the cationic pyridinium nitrogen atom of both receptors, possibly driven by Coulombic attraction and HB interactions with H_b and H_c. Indeed, the possibility of competing HB or to a much lesser extent, anion-π interactions, between anions and cationic aromatic receptor frameworks bearing XB donor groups has been recently demonstrated by Huber and co-workers,[37] providing support for this mode of interaction between Cl^- and **2.Se**/ **3.Se**. To provide further evidence, an analogous Cl^- titration experiment under identical conditions with the bis-fluorotriazole acyclic host analogue **2.F** was undertaken (see Figure 1 for structure). Significant downfield shifts were seen for only H_b and H_c immediately adjacent to the cationic pyridinium nitrogen atom (see Figure S3-18, Supporting Information). Furthermore, the similar Cl^- association constants determined for **3.Se** (K_a = 450 ± 23 M^{-1}) and **2.F** (K_a = 411 ± 21 M^{-1}), obtained by monitoring the downfield shifts of H_b, as well as the very small perturbations of the $SeCH_3$ ^{77}Se signals ($\Delta\delta_{Se}$ = +1.1 ppm over 10.0 equivalents of Cl^-) for **2.Se**, lends further support that Se-mediated ChB interactions play only a minor role in the halide anion association of **2.Se** and **3.Se**. Although one may expect that the ChB donor properties of Se-based receptors to be inferior to Te-containing analogues owing to the reduced polarizability of Se, the weakness of the ChB-anion interactions with **2.Se** and **3.Se** is surprising, considering that cationic methylseleno-triazolium (direct N^3-methylation on the triazole)[15] and divalent chalcogeno-benzimidazolium motifs[10] are potent ChB donors in both the solid state and in solution. Clearly, polarisation of neutral methylseleno-triazoles with a central cationic pydinium unit is insufficient to render the σ-holes on Se electron-deficient enough for strong anion interactions.

Summarising the anion binding results: (a) **1.Te** binds anions more strongly than its HB analogue **1.H** under identical solvent conditions, this is especially the case with the heavier halides bromide and iodide; (b) the nature of the solvent significantly influences the stability of the chalcogen-bonded host-anion guest complexes, where the strongest associations are observed in aprotic organic media of lower polarity (d_6-acetone > CD_3CN > d_6-DMSO > CD_3OD); (c) in wet solvent media (CD_3CN/D_2O 99:1) **1.Te** displays the Hofmeister bias of favouring the binding of the heavier halides.

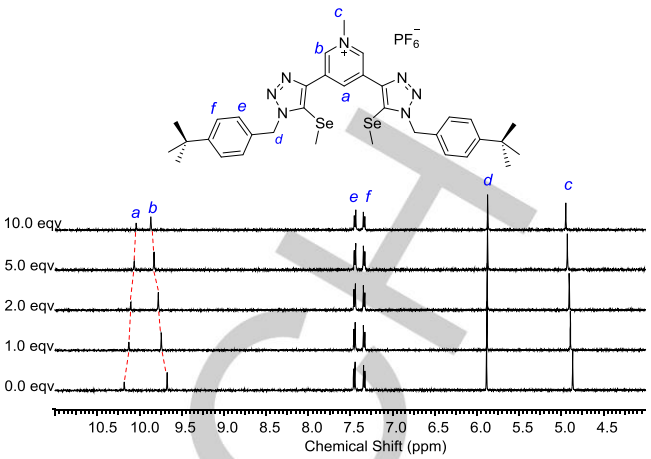


Figure 3. Partial ^1H NMR spectra of **2.Se** in the presence of increasing quantities of Cl^- ([**2.Se**]= 1.0 mM, CD_3CN, T = 298 K).

Thermodynamic Contributions to Binding

The thermodynamic enthalpic and entropic contributions behind the ChB halide anion binding trends determined in the previous section were elucidated using van't Hoff analysis (see Section S3.3, Supporting Information). Using this approach, variable-temperature (VT) ^1H NMR titration experiments were performed at temperatures spanning a range of at least 40 K to determine K_a values. Notably, **1.Te** did not show any evidence of thermal decomposition at temperatures as high as 338 K even in the presence of water, a testament to its thermal and chemical stability.[38] The thermodynamic halide binding data (ΔG, ΔH and $T\Delta S$) is collected in Table 3 and represented visually in Figure 4.

ChB-mediated binding of halides In CD_3CN, the ChB-mediated binding of halides to **1.Te** (Table 3, entries 1-3) was found to be strongly dominated by enthalpy in all cases. This is especially the case with bromide and iodide which exhibit significantly larger exothermic enthalpic magnitudes than chloride. Interestingly, whereas the binding of chloride is also entropically favourable, an almost negligible entropic contribution is observed for Br^- and entropy is dis-favoured for I^-. Clearly, the reduction in binding affinity observed with the heavier halides is driven *solely* by the increasingly unfavourable entropic contributions. It has been previously demonstrated computationally that interactions between ChB donors and the heavier, 'softer' and more polarisable halides possess greater covalency/ charge-transfer character,[15] which may partly account for the increasing exothermic contribution observed for Te-bromide and Te-iodide chalcogen bond formation. It is interesting to note that a similar trend of more exothermic binding compensated by greater loss in entropy (although ΔS was favourable in all cases) in the binding of Cl^-, Br^- and I^- was previously reported with iodoimidazolium XB hosts.[39] Nonetheless, the varying extents of halide desolvation during the anion binding process may also partly contribute towards the thermodynamic trends observed.

Influence of solvent As shown in Table 2, dramatic enhancements in the Cl^- and I^- affinities of **1.Te** was found in d_6-acetone compared with CD_3CN. Due to the very strong association of Cl^- (K_a > 10^4 M^{-1}), thermodynamic binding

parameters could not be determined accurately using ^{1}H NMR van't Hoff analysis. Nonetheless, **1.Te**-I$^-$ binding in d_6-acetone was observed to be driven by favourable enthalpic *and* entropic contributions (Table 3, entry 4), in contrast to binding in CD_3CN (Table 3, entry 3) which was exclusively enthalpically-driven. Surprisingly, the greater iodide affinity observed in d_6-acetone was not reflected in a larger exothermic enthalpy value; indeed the exothermic magnitude is significantly diminished. Instead, the augmented affinity results from a large favourable entropy increase. This unexpected result is difficult to rationalise, given that both solvents have similar Gutmann donor/acceptor numbers ($DN_{acetone}$ = 17.0 > $DN_{acetonitrile}$ = 14.1),[40] ($AN_{acetone}$ = 12.5 < $AN_{acetonitrile}$ = 19.3)[40] and free energies of iodide solvation.[41] Nonetheless, we tentatively suggest that these observations may be a consequence of changes in the solvent structure following host-guest binding. In the liquid phase, theoretical simulations have revealed that acetone[42] exhibits smaller degrees of short-range molecular ordering than acetonitrile,[41,43] with the latter adopting L-shaped and head-to-tail antiparallel configurations between neighbouring molecules. Upon binding between I$^-$ and **1.Te**, the released CD_3CN molecules undergo a greater extent of re-ordering compared with d_6-acetone, giving rise to a greater entropic penalty. A similar reasoning has been invoked to account for the exothermic, but entropically-disfavoured anion binding in solvents exhibiting a degree of structural-ordering such as water[44–46] and chloroform.[45]

Table 3. Thermodynamic parameters (ΔG, ΔH and $T\Delta S$) for halide binding by receptors **1.Te**, **1.H**, **2.Se** and **3.Se** in various solvent mixtures. [a]

S/N	Host	Solvent	Anion	ΔG/ kJ mol^{-1}	ΔH/ kJ mol^{-1}	$T\Delta S$/ kJ mol^{-1}
1	**1.Te**	CD_3CN	Cl$^-$	-16.1	-12.8	+3.2
2		CD_3CN	Br$^-$	-15.4	-15.2	+0.1
3		CD_3CN	I$^-$	-14.2	-16.6	-2.4
4		d_6-acetone	I$^-$	-20.2	-9.9	+10.3
5		CD_3CN/ D_2O 99:1	Br$^-$	-12.9	-12.5	+0.4
6	**1.H**	CD_3CN	Cl$^-$	-13.8	-2.9	+10.9
7	**2.Se**	d_6-acetone	Cl$^-$	-15.4	+3.6	+19.0
8	**3.Se**	d_6-acetone	Cl$^-$	-15.1	+6.2	+21.3

[a] Thermodynamic parameters were determined by van't Hoff analysis by plotting ln(K_a/ M^{-1}) against T^{-1}/ K^{-1} according to the equation: $R\ln K_a = -\Delta H/T + \Delta S$, where K_a represents the 1:1 host-guest stoichiometric association constants determined at temperature T using VT-NMR titrations; for each line of best fit, |Pearson's R| > 0.99 and errors for individual titrations <10 % (see Figs S3-29, S3-30, Supporting Information); [host] = 1.0 mM.

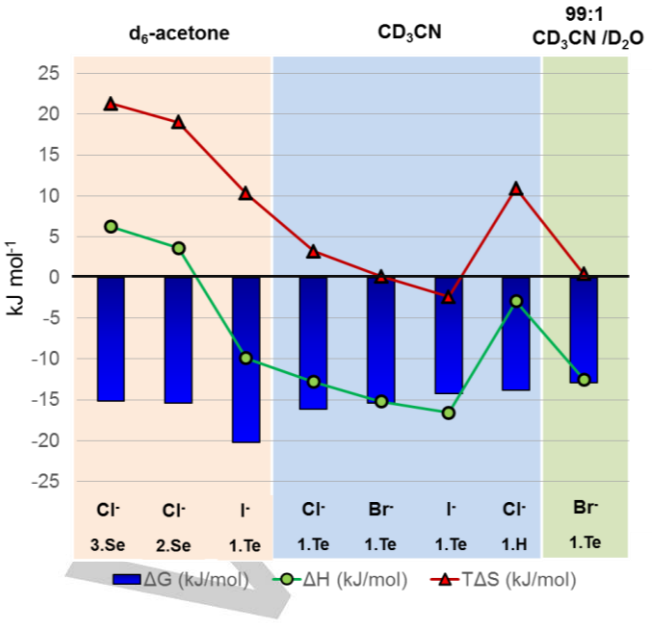


Figure 4. Thermodynamic parameters for binding of **1.Te**, **1.H**, **2.Se** and **3.Se** in various solvent mixtures to halide guests.

The van't Hoff analysis of Br$^-$ binding by **1.Te** in CD_3CN/ D_2O 99:1 *v/v* (Table 3, entry 5) proved insightful in elucidating the thermodynamic origins of the reduced anion affinities observed in the presence of water (Table 2). Compared to pure CD_3CN (Table 3, entry 2), Br$^-$ binding in the wet solvent retained the dominance of the enthalpic driving force over entropy, despite reducing the exothermic magnitude ($\Delta\Delta H$ = -2.7 kJ mol^{-1}). This observation is consistent with our previous computational findings on the effects of halide hydration on ChB binding:[15] the binding of hydrated halide anions brings the associated water molecules in its hydration shell into close proximity with the Te atoms, which disrupt the Te···Br$^-$ ChB interactions. At the same time, the stronger D_2O···Br$^-$ interactions compared with CD_3CN, reflected by the large acceptor number of D_2O (AN = 54.8),[40] during desolvation is enthalpically unfavourable. These factors in combination may manifest in the diminished exothermicity observed.

Differences between ChB- and HB-mediated anion binding

To understand the unique aspects of ChB-mediated anion binding, the thermodynamic parameters for the binding of Cl$^-$ to **1.H** were determined (Table 3, entry 6). Although Cl$^-$ binding was driven favourably by both enthalpy and entropy in CD_3CN, the entropic term dominates for **1.H**, accounting for nearly 80 % of the free energy of binding. In contrast, **1.Te**-Cl$^-$ binding was mostly dominated by enthalpy (Table 3, entry 1). A favourable entropic contribution to binding of anions to HB receptors in polar aprotic solvents with significant hydrogen bond basicity[47] such as acetonitrile[48–51] has been attributed to desolvation of the Lewis acidic host binding site during anion complexation.[32] The difference in thermodynamic signature with **1.Te** may suggest that its ChB-donor binding cavity is less extensively desolvated during anion binding. As the process of desolvation is inherently endothermic, this may also partly account for a much smaller exothermic binding contribution observed for **1.H** compared to **1.Te**.

Similarly, Cl^- binding by **2.Se** and **3.Se** in d_6-acetone was found to be driven exclusively by entropy (Table 3, entries 7 and 8), in stark contrast with that for I^- binding by **1.Te** in the same solvent (Table 3, entry 4). As mentioned previously, the Se atoms are insufficiently polarised by the cationic pyridinium-bis(triazole) receptor framework to allow strong ChB interactions with the halides, with the consequence that halide binding by **2.Se** and **3.Se** is predominantly electrostatically-driven, unlike the ChB interactions primarily responsible for I^- binding by **1.Te**. The large entropic driving force observed in each case is thus consistent with extensive host-guest desolvation upon anion association, whilst the absence of strong directional bonding interactions (e.g. HB) formed between **2.Se** and **3.Se** with Cl^- results in the lack of any favourable enthalpic contribution. Nonetheless, although the **3.Se**-Cl^- interaction is more favourable entropically, this is offset by a larger unfavourable endothermic enthalpy, resulting in almost identical Cl^- affinities for the Se receptors. Although this difference in thermodynamic signature is likely a consequence of the structural differences between **2.Se** and **3.Se**, no significant macrocyclic effect is observed which may be due to the exocyclic association of Cl^- on the periphery of the macrocycle **3.Se**.

Conclusions

In summary, we have prepared a new robust and stable cationic tellurium-based ChB-donor motif capable of binding a wide range of anions strongly in various solvent media even at elevated temperatures. These highly-desirable features have enabled the thermodynamic origins of ChB-mediated anion binding to be elucidated for the first time, giving an insight into the nature of this poorly understood σ-hole interaction. Compared with its HB analogue, the augmented anion affinities of ChB-donor **1.Te** in acetonitrile are characterised by a strong, dominant enthalpic driving force. Nonetheless, the importance of entropy is evident when it appears to dictate ChB-mediated anion binding trends in many instances, including the diminishing binding affinities of the heavier halides in acetonitrile and the stronger association observed in 'less competitive' aprotic solvents such as acetone. Preliminary studies in protic wet organic solvent media reveal bromide binding by **1.Te** to be again enthalpically favoured. Interestingly, replacement of the Te ChB-donor groups with Se in our present pyridinium host framework appeared to largely negate the ChB contributions. Our present findings thus serve to further emphasise the kinship between the sister σ-hole interactions ChB and XB for anion recognition. The integration of ChB and XB donor motifs into host structural frameworks for molecular recognition, sensing and related applications is continuing in our laboratories.

Acknowledgements

J.Y.C.L gratefully acknowledges the Agency for Science, Technology and Research (A*STAR), Singapore, for postgraduate research funding.

Keywords: chalcogen bonding • anion binding • thermodynamics • enthalpy • entropy

[1] C. Bleiholder, D. B. Werz, H. Köppel, R. Gleiter, *J. Am. Chem. Soc.* **2006**, *128*, 2666–2674.
[2] L. C. Gilday, S. W. Robinson, T. A. Barendt, M. J. Langton, B. R. Mullaney, P. D. Beer, *Chem. Rev.* **2015**, *115*, 7118–7195.
[3] J. Y. C. Lim, P. D. Beer, *Chem* **2018**, *4*, 731–783.
[4] M. H. Kolář, P. Hobza, *Chem. Rev.* **2016**, *116*, 5155–5187.
[5] J. Fanfrlík, A. Přáda, Z. Padělková, A. Pecina, J. Macháček, M. Lepšík, J. Holub, A. Růžička, D. Hnyk, P. Hobza, *Angew. Chem. Int. Ed.* **2014**, *53*, 10139–10142.
[6] Y. Zhang, W. Wang, *Crystals* **2018**, *8*, DOI 10.3390/cryst8040163.
[7] Y. Nagao, T. Hirata, S. Goto, S. Sano, A. Kakehi, K. Iizuka, M. Shiro, *J. Am. Chem. Soc.* **1998**, *120*, 3104–3110.
[8] S. Benz, J. López-Andarias, J. Mareda, N. Sakai, S. Matile, *Angew. Chem. Int. Ed.* **2016**, *56*, 812–815.
[9] S. Benz, J. Mareda, C. Besnard, N. Sakai, S. Matile, *Chem Sci* **2017**, *8*, 8164–8169.
[10] P. Wonner, L. Vogel, M. Düser, L. Gomes, F. Kniep, B. Mallick, D. B. Werz, S. M. Huber, *Angew. Chem. Int. Ed.* **2017**, *56*, 12009–12012.
[11] P. C. Ho, P. Szydlowski, J. Sinclair, P. J. W. Elder, J. Kübel, C. Gendy, L. M. Lee, H. Jenkins, J. F. Britten, D. R. Morim, et al., *Nat. Commun.* **2016**, *7*, 11299.
[12] L. Chen, J. Xiang, Y. Zhao, Q. Yan, *J. Am. Chem. Soc.* **2018**, *140*, 7079–7082.
[13] K. T. Mahmudov, M. N. Kopylovich, M. F. C. Guedes da Silva, A. J. L. Pombeiro, *Dalton Trans* **2017**, *46*, 10121–10138.
[14] D. J. Pascoe, K. B. Ling, S. L. Cockroft, *J. Am. Chem. Soc.* **2017**, *139*, 15160–15167.
[15] J. Y. C. Lim, I. Marques, A. L. Thompson, K. E. Christensen, V. Félix, P. D. Beer, *J. Am. Chem. Soc.* **2017**, *139*, 3122–3133.
[16] T. Chivers, R. S. Laitinen, *Chem Soc Rev* **2015**, *44*, 1725–1739.
[17] H. Park, L. J. Edgar, M. A. Lumba, L. M. Willis, M. Nitz, *Org Biomol Chem* **2015**, *13*, 7027–7033.
[18] H. A. Stefani, J. M. Pena, F. Manarin, R. A. Ando, D. M. Leal, N. Petragnani, *Tetrahedron Lett.* **2011**, *52*, 4398–4401.
[19] H. A. Stefani, N. C. S. Silva, S. N. S. Vasconcelos, F. Manarin, F. B. Souza, *Tetrahedron Lett.* **2013**, *54*, 2809–2812.
[20] H. A. Stefani, S. N. S. Vasconcelos, F. Manarin, D. M. Leal, F. B. Souza, L. S. Madureira, J. Zukerman-Schpector, M. N. Eberlin, M. N. Godoi, R. de Souza Galaverna, *Eur. J. Org. Chem.* **2013**, *2013*, 3780–3785.
[21] H. Zhao, F. P. Gabbaï, *Nat. Chem.* **2010**, *2*, 984–990.
[22] G. E. Garrett, E. I. Carrera, D. S. Seferos, M. S. Taylor, *Chem Commun* **2016**, *52*, 9881–9884.
[23] N. A. Semenov, N. A. Pushkarevsky, J. Beckmann, P. Finke, E. Lork, R. Mews, I. Y. Bagryanskaya, Y. V. Gatilov, S. N. Konchenko, V. G. Vasiliev, et al., *Eur. J. Inorg. Chem.* **2012**, *2012*, 3693–3703.
[24] W. S. Brotherton, R. J. Clark, L. Zhu, *J. Org. Chem.* **2012**, *77*, 6443–6455.
[25] J. E. Hein, J. C. Tripp, L. B. Krasnova, K. B. Sharpless, V. V. Fokin, *Angew. Chem. Int. Ed.* **2009**, *48*, 8018–8021.
[26] B. T. Worrell, J. E. Hein, V. V. Fokin, *Angew. Chem. Int. Ed.* **2012**, *51*, 11791–11794.
[27] Due to the lability of the C-Te bond, synthesis of the analogous Te-containing macrocycle proved challenging and could not be isolated in sufficient quantities for detailed anion binding studies.
[28] M. J. Hynes, *J. Chem. Soc. Dalton Trans.* **1993**, *2*, 311–312.
[29] S. W. Robinson, C. L. Mustoe, N. G. White, A. Brown, A. L. Thompson, P. Kennepohl, P. D. Beer, *J. Am. Chem. Soc.* **2015**, *137*, 499–507.
[30] M. G. Sarwar, B. Dragisic, S. Sagoo, M. S. Taylor, *Angew. Chem. Int. Ed.* **2010**, *49*, 1674–1677.
[31] A. Bauzá, A. Frontera, *Angew. Chem. Int. Ed.* **2015**, *54*, 7340–7343.
[32] A. Bianchi, E. García-España, in *Anion Coord. Chem.*, Wiley-VCH, Weinheim, **2012**, pp. 75–140.
[33] J. Y. C. Lim, T. Bunchuay, P. D. Beer, *Chem. – Eur. J.* **2017**, *23*, 4700–4707.
[34] Y. Marcus, *J Chem Soc Faraday Trans* **1991**, *87*, 2995–2999.
[35] M. J. Langton, S. W. Robinson, I. Marques, V. Félix, P. D. Beer, *Nat Chem* **2014**, *6*, 1039–1043.
[36] Lack of perturbations of signals arising from the ^{t}BuArCH$_2$- groups (i.e. H_d, H_e and H_f) show that they are not interacting with Cl^- nor involved in any significant desolvation processes accompanying anion binding. The possibility of the different terminal groups of **2.Se** and **1.Te** accounting for any differences in anion binding behaviour can thus be ruled out.
[37] N. Schulz, P. Sokkar, E. Engelage, S. Schindler, M. Erdelyi, E. Sanchez-Garcia, S. M. Huber, *Chem. – Eur. J.* **2018**, *24*, 3464–3473.
[38] For all host systems, halide guests and solvent conditions studied, plots of $\ln(K_a/\ M^{-1})$ against $T^{-1}/\ K^{-1}$ gave excellent linearity (|Pearson's R| > 0.99) indicating negligible changes in overall heat capacity of the system over the temperature range studied due to enthalpic invariance (C_p = dH/ dT).
[39] S. M. Walter, F. Kniep, L. Rout, F. P. Schmidtchen, E. Herdtweck, S. M. Huber, *J. Am. Chem. Soc.* **2012**, *134*, 8507–8512.
[40] V. Gutmann, *Electrochimica Acta* **1976**, *21*, 661–670.
[41] J. Richardi, P. H. Fries, H. Krienke, *J. Chem. Phys.* **1998**, *108*, 4079–4089.
[42] J. Richardi, P. H. Fries, R. Fischer, S. Rast, H. Krienke, *Mol. Phys.* **1998**, *93*, 925–938.

[43] J. Richardi, P. H. Fries, R. Fischer, S. Rast, H. Krienke, *J. Mol. Liq.* **1997**, *73–74*, 465–485.
[44] K. I. Assaf, M. S. Ural, F. Pan, T. Georgiev, S. Simova, K. Rissanen, D. Gabel, W. M. Nau, *Angew. Chem. Int. Ed.* **2015**, *54*, 6852–6856.
[45] T. Fiala, K. Sleziakova, K. Marsalek, K. Salvadori, V. Sindelar, *J. Org. Chem.* **2018**, *83*, 1903–1912.
[46] M. R. Sullivan, W. Yao, D. Tang, H. S. Ashbaugh, B. C. Gibb, *J. Phys. Chem. B* **2018**, *122*, 1702–1713.
[47] M. H. Abraham, *Chem Soc Rev* **1993**, *22*, 73–83.
[48] J. L. Sessler, L. R. Eller, W.-S. Cho, S. Nicolaou, A. Aguilar, J. T. Lee, V. M. Lynch, D. J. Magda, *Angew. Chem. Int. Ed.* **2005**, *44*, 5989–5992.
[49] V. D. Jadhav, E. Herdtweck, F. P. Schmidtchen, *Chem. – Eur. J.* **2008**, *14*, 6098–6107.
[50] M. Berger, F. P. Schmidtchen, *J. Am. Chem. Soc.* **1999**, *121*, 9986–9993.
[51] T. Zieliński, J. Jurczak, *Tetrahedron* **2005**, *61*, 4081–4089.

10.1002/chem.201803393

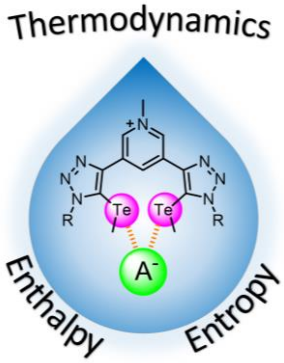
WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

A novel, stable cationic tellurium-containing motif enables the enthalpic and entropic origins of chalcogen bonding-mediated anion binding to be determined for the first time.



*Jason Y. C. Lim, Jane Y. Liew and Paul D. Beer**

Page No. – Page No.

Thermodynamics of Anion Binding by Chalcogen Bonding Receptors

Layout 2:

FULL PAPER

((Insert TOC Graphic here; max. width: 11.5 cm; max. height: 2.5 cm))

*Author(s), Corresponding Author(s)**

Page No. – Page No.

Title

Text for Table of Contents