

# Dynamic Covalent Self-Assembly of Chloride- and Ion-Pair-Templated Cryptates

Selina Hollstein, Oleksandr Shyshov, Marko Hanževački, Jie Zhao, Tamara Rudolf, Christof M. Jäger, and Max von Delius\*

**Abstract:** While supramolecular hosts capable of binding and transporting anions and ion pairs are now widely available, self-assembled architectures are still rare, even though they offer an inherent mechanism for the release of the guest ion(s). In this work, we report the dynamic covalent self-assembly of tripodal, urea-based anion cryptates that are held together by two orthoester bridgeheads. These hosts exhibit affinity for anions such as  $\text{Cl}^-$ ,  $\text{Br}^-$  or  $\text{I}^-$  in the moderate range that is typically advantageous for applications in membrane transport. In unprecedented experiments, we were able to dissociate the Cs-Cl ion pair by simultaneously assembling suitably sized orthoester hosts around the  $\text{Cs}^+$  and the  $\text{Cl}^-$  ion.

## Introduction

Half a century ago, pioneering reports by Park and Lehn<sup>[1]</sup> demonstrated that simple anions such as chloride could be encapsulated within artificial receptors. Over the past two decades, progress in synthesis<sup>[2]</sup> has been driven and accompanied by a growing body of research on applications of anion receptors,<sup>[3]</sup> most notably in sensing,<sup>[4]</sup> transport<sup>[5]</sup> and for environmental<sup>[6]</sup> as well as medicinal purposes.<sup>[7]</sup>

While a large number of conventionally synthesized anion receptors have been reported to date, with some macrobicyclic architectures featuring exceptionally high binding affinities,<sup>[8]</sup> self-assembled, purely organic<sup>[9]</sup> hosts for anions are still scarce. To the best of our knowledge, self-

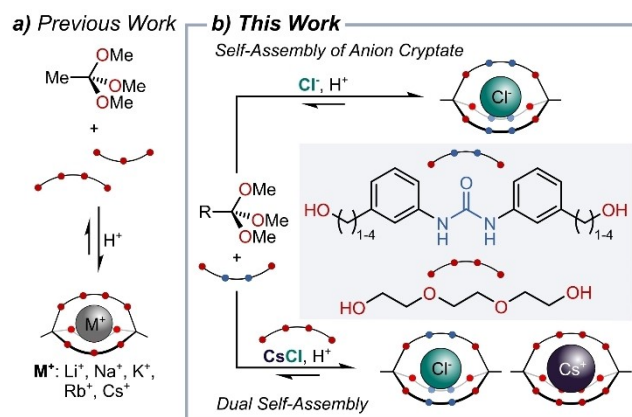
assembled, purely organic hosts for ion pairs are elusive. Examples for self-assembled, organic anion receptors include hydrogen-bonded cages (guest:  $\text{PO}_4^{3-}$  or  $\text{SO}_4^{2-}$ ),<sup>[10]</sup> disulfide-based dimers of cyclic peptides (guest:  $\text{SO}_4^{2-}$ )<sup>[11]</sup> and architectures based on imines or acyl hydrazones.<sup>[12]</sup> For applications where effective anion transport benefits from the stimuli-responsive dissociation of the guest,<sup>[13]</sup> it seems likely that self-assembled hosts could play a decisive role, because they offer an inherent release mechanism.

Given the fact that tripodal architectures are especially widespread in anion receptor chemistry,<sup>[14]</sup> we wondered whether we could make use of the dynamic covalent chemistry<sup>[15]</sup> of orthoesters,<sup>[16]</sup> which we had previously employed to self-assemble cryptates for simple cations (Figure 1a).<sup>[17]</sup> Such orthoester cryptands degrade in aqueous solvent with tunable rate constants and therefore offer a pH-driven release mechanism<sup>[18]</sup> that could be of use in the context of supramolecular medicinal chemistry.<sup>[7a,b,19]</sup> Herein, we report the dynamic covalent self-assembly of such hosts based on the chloride-templated reaction of simple orthoesters with urea-based diols (Figure 1b, top). While their poor solubility precluded membrane transport experiments with this first generation of cryptands, we were able to use Cs-Cl as a dual template and simultaneously self-assemble two different orthoester hosts to encapsulate the  $\text{Cs}^+$  cation and the  $\text{Cl}^-$  anion (Figure 1b, bottom).

[\*] S. Hollstein, Dr. O. Shyshov, Dr. J. Zhao, T. Rudolf, Prof. Dr. M. von Delius  
 Institute of Organic Chemistry, Ulm University  
 Albert-Einstein-Allee 11,  
 89081 Ulm (Germany)  
 E-mail: max.vondelius@uni-ulm.de

Dr. M. Hanževački, Dr. C. M. Jäger  
 Department of Chemical and Environmental Engineering,  
 University of Nottingham  
 University Park, Nottingham  
 NG7 2RD (UK)

© 2022 The Authors. Angewandte Chemie International Edition published by Wiley-VCH GmbH. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.



**Figure 1.** a) Previous work based on metal-templated orthoester cryptates. b) Chloride-templated self-assembly of orthoester cryptates and one-pot co-assembly of anion and cation cryptates ( $\text{R} = \text{CH}_3, \text{H}$ ).

## Results and Discussion

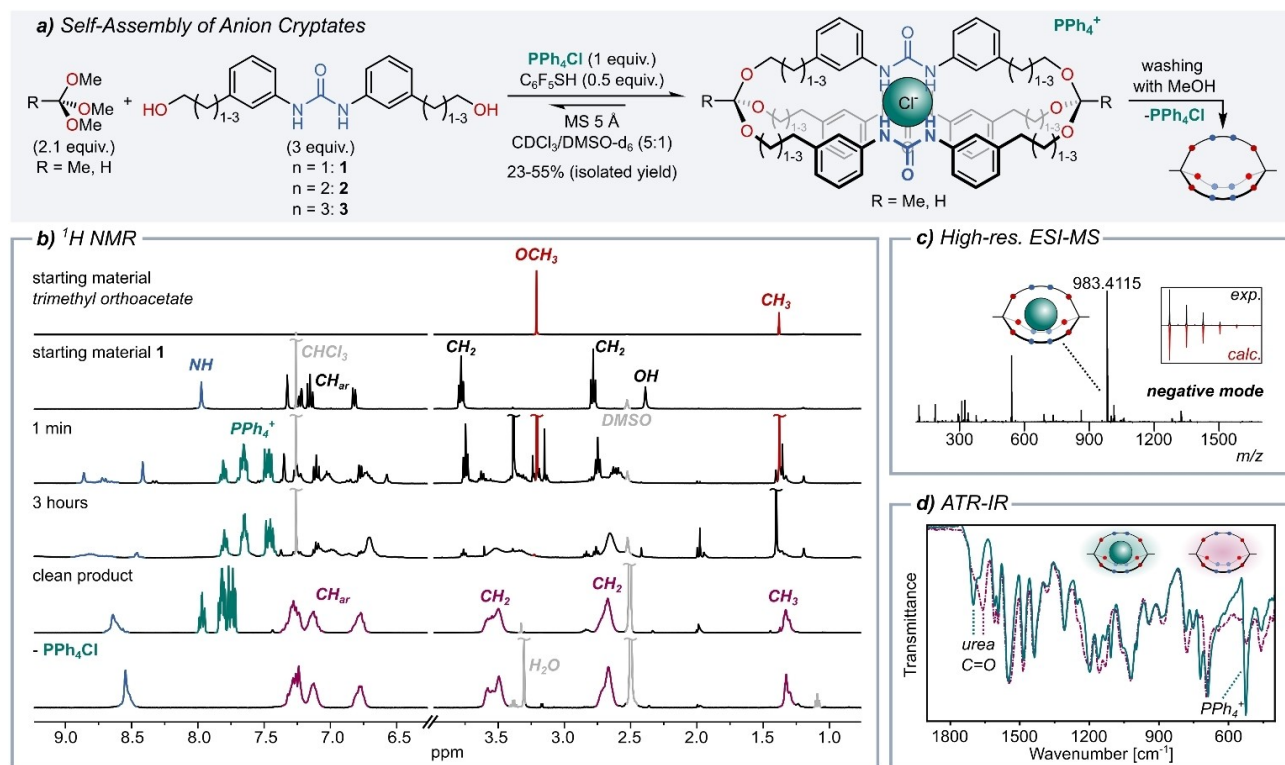
## Chloride-Templated Self-Assembly of Cryptates

When designing building blocks for self-assembled anion-binding architectures, the choice of anion-binding motif is of paramount importance. We chose (di)phenylurea, because an abundance of non-macrocylic, tripodal anion receptors of this type are reported.<sup>[14]</sup> We therefore synthesized bishydroxyalkylphenyl urea compounds with varying alkyl chain length (**1–3**) that should act as linkers between two orthoester bridgeheads in the envisaged cryptates. For orthoester-based self-assembly reactions, we chose an acid catalyst whose conjugate base would bind to urea only weakly, a mixed solvent system that represents a good compromise between solubility and (non)interference with hydrogen bonding and a chloride salt with a weakly binding counterion. Addition of molecular sieves (5 Å) helps keeping the reaction medium anhydrous and shifts the equilibrium to the product side by adsorption of methanol.<sup>[16a,17,18]</sup>

In a typical self-assembly experiment, we therefore treated a solution of diol **1** with trimethyl orthoacetate, a catalytic amount of acid 2,3,4,5,6-pentafluorothiophenol, and a stoichiometric amount of the template tetraphenylphosphonium chloride (Figure 2a). The reaction was moni-

tored by <sup>1</sup>H-NMR spectroscopy (Figure 2b), clearly indicating efficient orthoester exchange, because after only three hours the signal belonging to the methoxy groups of the orthoester had fully disappeared. Interestingly, the time required for complete methoxy group (and MeOH) displacement differed substantially between diols **1**, **2** and **3** (3 h, 18 h and 18 h, respectively), raising the question whether this could be due to a difference in Cl<sup>-</sup> binding affinity.

After quenching the self-assembly reactions by adding excess triethylamine, precipitation from diethyl ether furnished the pure products [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup>, [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C3]PPh<sub>4</sub><sup>+</sup>, [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C4]PPh<sub>4</sub><sup>+</sup> and [Cl<sup>-</sup>o-H<sub>2</sub>-ur-C4]PPh<sub>4</sub><sup>+</sup> in isolated yields of 55%, 48%, 23% and 44%, respectively. The formation of the chloride-binding cryptates was corroborated by <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectroscopy (Figure 2b and Figure S2), high-resolution mass spectrometry (Figure 2c) and attenuated total reflection-infrared spectroscopy (Figure 2d). The representative <sup>1</sup>H-NMR spectrum of [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup> is indicative of a pure compound, but exhibits significant peak broadening, which also has been found in a related thiourea host.<sup>[20]</sup>



**Figure 2.** a) Chloride-templated synthesis of orthoester/urea cryptates. Reaction conditions: 30 μmol tetraphenylphosphonium chloride, 63 μmol trimethyl orthoacetate or trimethyl orthoformate, 90 μmol diol **1**, **2** or **3** and 15 μmol 2,3,4,5,6-pentafluorothiophenol in CDCl<sub>3</sub>/deuterated dimethyl sulfoxide (DMSO-d<sub>6</sub>) mixture (5:1, 3.3 mL); MS: molecular sieves. Reaction time: 3 hours (n = 1), 18 hours (n = 2, 3). b) <sup>1</sup>H-NMR stacked plot for the synthesis and purification of o-Me<sub>2</sub>-ur-C2. Spectra of starting materials and reaction control were recorded in CDCl<sub>3</sub> and spectra of cryptate and cryptand were recorded in DMSO-d<sub>6</sub>. c) High-resolution electron spray mass spectrometry in negative mode of [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup>. Minor peaks originate from solvents or hydrolysis products. Inset: experimental and calculated isotopic distribution of product peak. d) Attenuated total reflection-infrared (ATR-IR) spectra of [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup> (teal) and o-Me<sub>2</sub>-ur-C2 (purple).

### Molecular Dynamics: Structure and H-Bonding

To gain insights into the dynamic structure of cryptands and cryptates, we carried out microsecond molecular-dynamics (MD) simulations. These confirm a very high flexibility of the cryptate systems that is significantly influenced by the solvent composition. Simulations were carried out for *o*-Me<sub>2</sub>-ur-C2 in the presence and absence of Cl<sup>-</sup> in pure chloroform or DMSO as well as in a 5:1 solvent mixture. In DMSO, the cryptand demonstrates high flexibility with the possibility for DMSO molecules to enter the cryptand and form hydrogen bonds with urea NH groups. In the apolar solvent chloroform on the other hand, *o*-Me<sub>2</sub>-ur-C2 demonstrates a slightly more compact structure, with hydrogen bonds frequently formed between the urea functionalities (Figure 3 and Figure S50).

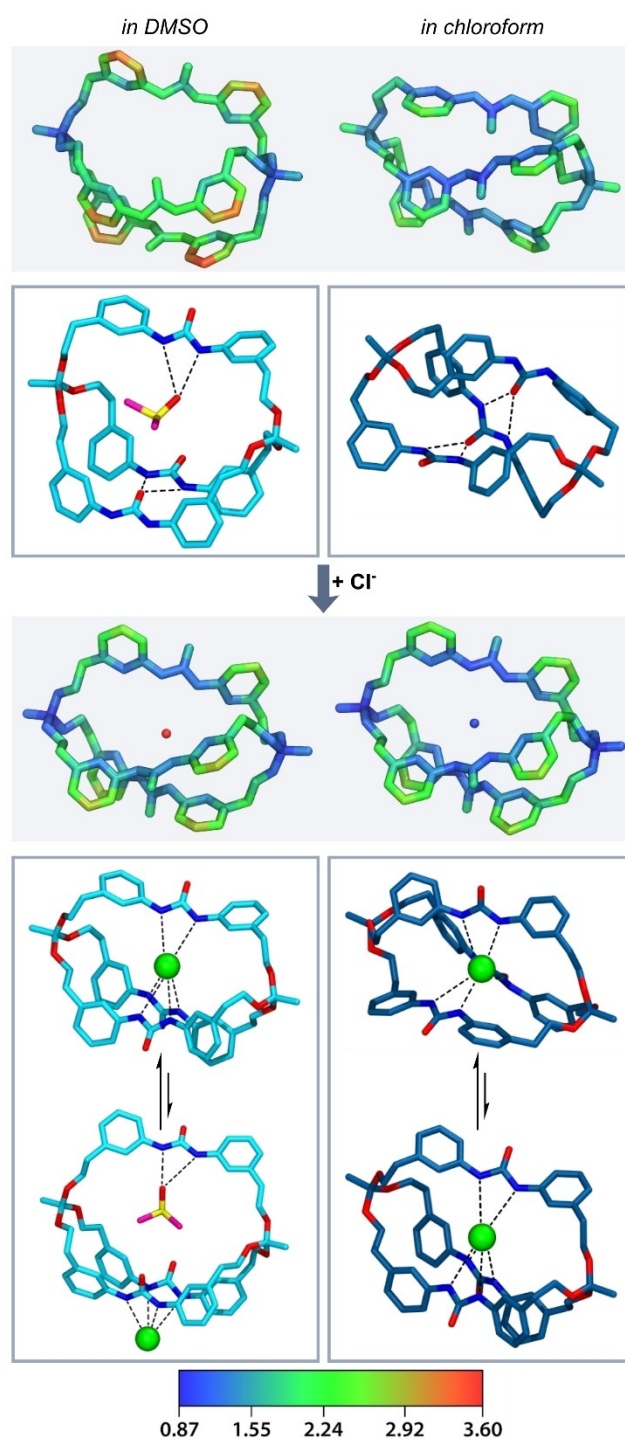
In complex with Cl<sup>-</sup>, the predominant structure is such that all three urea entities bind to the encapsulated anion. Still, the flexibility of the cryptate framework remains high, as shown in Figure 3 (and Figure S51). Higher fluctuations were observed in the phenyl containing linkers, while orthoester bridgeheads and urea groups remained more static. The phenyl linkers demonstrate varying interactions, including frequent but transient  $\pi$ -stacking interactions between linkers.

Importantly, an additional binding geometry can be found in longer simulations when DMSO is present. Here again, DMSO can enter the cavity, forming hydrogen bonds to urea, leaving the chloride ion only two further urea units to bind. This alternative binding mode, although less frequent, also demonstrated a lifetime of up to 500 ns in simulations in 5:1 (chloroform/DMSO) solvent (Figure S52c).

Thus, with DMSO present two different, slowly exchanging binding modes can exist (see Figure 3) where the Cl<sup>-</sup> ion either binds all three or only two urea units. A similar change in the complexation of Cl<sup>-</sup> by *o*-Me<sub>2</sub>-ur-C2 has not been observed in any of the performed simulations in chloroform underlining this important solvent effect. The combination of high conformational flexibility, with overall atomic fluctuations up to remarkable six times higher compared to the cation binding cryptate systems investigated before,<sup>[21]</sup> asymmetric Cl<sup>-</sup> coordination, and competitive DMSO inclusion could therefore explain the broadened peaks in the <sup>1</sup>H-NMR spectra as well as the moderate experimental binding affinities (see below). The dynamic binding mode may also be the reason why we were unable to obtain single crystals for X-ray crystallography, despite extensive efforts.

### Host–Guest Titrations and MS/MS Studies of Heteroleptic Cryptands

To achieve the removal of the chloride template, we treated the solid cryptate [Cl<sup>-</sup>⊂*o*-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup> with anhydrous methanol, in the hope that this would lead to the selective dissolution of the tetraphenylphosphonium chloride. After stirring the suspension for one day, the empty cryptand was



**Figure 3.** Dynamic structural analysis of *o*-Me<sub>2</sub>-ur-C2 from MD simulations. Flexibility of cages indicated by atomic root mean square fluctuations (rmsf) of heavy atoms applied as color scale on centroid structures. Color scale values presented in Å. Representative conformations in DMSO (left) and chloroform (right) without (top) and with (bottom) chloride ion binding demonstrate the possibility of DMSO molecules binding inside the cage with and without presence of the anion, whilst structures without chloride in chloroform demonstrate frequent intramolecular hydrogen bonding between urea units.



obtained as indicated by the missing  $\text{PPh}_4^+$  signals in the  $^1\text{H-NMR}$  spectrum (Figure 2b, bottom). As expected, the signal of the proton belonging to the urea moiety shifted upfield upon removal of the chloride ion, but not as much as in diol **1**, which could be an additional indication for a (dynamic) competition between chloride binding and intramolecular hydrogen bonding. Evidence for hydrogen bonding was obtained by ATR-IR measurements. When comparing the spectra of the cryptate and cryptand, the expected shift of the urea carbonyl band to lower wave number (from 1700 to  $1660\text{ cm}^{-1}$ )<sup>[22]</sup> is observed (Figure 2d, exemplary for  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C2}]\text{PPh}_4^+$ ).

With the empty cryptands in hand, we were able to determine the binding constants to different anions, namely chloride, bromide, iodide and nitrate (with counterion  $\text{PPh}_4^+$  or  $\text{NMe}_4^+$ ). The use of fluoride was ruled out as addition of fluoride would lead to deprotonation of the urea moieties.<sup>[23]</sup> We performed the titration of **o-Me<sub>2</sub>-ur-C2** with chloride in the solvent mixture chloroform/DMSO (5:1) to enable a direct comparison between association constants and self-assembly reactions. We obtained an association constant ( $K_a$ ) of  $286 \pm 23\text{ M}^{-1}$ . At the concentration used in the self-assembly reactions (9 mM) this binding constant implies that ca. 55% of the complex is formed (according to Bindsim on [supramolecular.org](http://supramolecular.org)<sup>[24]</sup>), which correlates with the observed isolated yield of 55% for  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C2}]\text{PPh}_4^+$ .

For solubility reasons, comparative titrations for all cryptands and different anions were performed in pure DMSO, even though this solvent is highly competitive due to its high dielectric constant ( $\epsilon = 47$ )<sup>[25]</sup>. This should be kept in mind, when comparing the  $K_a$  values reported here with related work in the field (often carried out in less competitive medium). When considering the binding constants observed for the different halide ions for host **o-Me<sub>2</sub>-ur-C2**, a moderate selectivity for chloride can be inferred (Table 1). The  $K_a$  values determined for **o-Me<sub>2</sub>-ur-C2** and its larger analogues **o-Me<sub>2</sub>-ur-C3** and **o-Me<sub>2</sub>-ur-C4** are decreasing with ascending number of methylene groups, which could reflect the best size fit for **o-Me<sub>2</sub>-ur-C2** and the chloride ion and/or the entropic cost derived from extending the aliphatic spacer towards the orthoester bridgehead.

To leverage the orthoester bridgehead for increasing the binding strength, we self-assembled cryptand **o-H<sub>2</sub>-ur-C4**, which is based on orthoformate ( $\text{R}=\text{H}$ ) in which additional hydrogen bonding could occur between the anion and an inverted bridgehead.<sup>[21b,26]</sup> The fact that we observed a moderately higher binding affinity for this host, yet no shift of the orthoformate  $^1\text{H-NMR}$  signal during titration with  $\text{TPPCL}$ , suggests that this small difference (factor 2) is due to structural differences between orthoacetate and orthoformate cages<sup>[18]</sup> rather than the *in/in* binding we had originally hoped for. In any case, competition with intramolecular hydrogen bonding<sup>[27]</sup> (and the competitive solvent) prevents even higher binding constants. In this context, it should be kept in mind that moderate binding constants are often sufficient or even beneficial for transmembrane anion transport.<sup>[27,28]</sup>

**Table 1:** Binding affinities of orthoester cryptand **o-Me<sub>2</sub>-ur-C2** to  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$  and  $\text{NO}_3^-$  salts and cryptands **o-Me<sub>2</sub>-ur-C3**, **o-Me<sub>2</sub>-ur-C4** and **o-H<sub>2</sub>-ur-C4** to  $\text{Cl}^-$  salt ( $K_a$  values in  $\text{CDCl}_3/\text{DMSO-d}_6$  (5:1) or  $\text{DMSO-d}_6$  containing up to 10% water at 298 K).

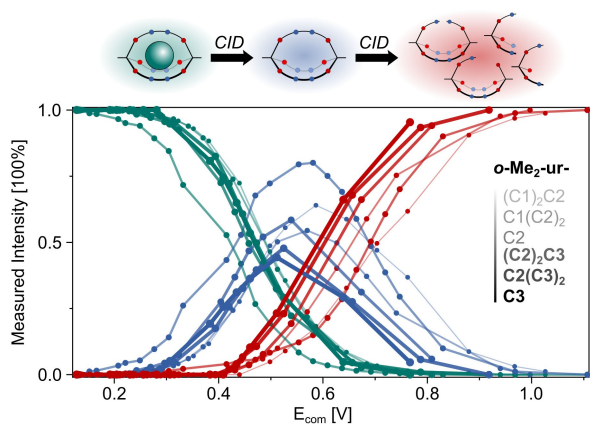
Host	$K_a$ [ $\text{M}^{-1}$ ] for Guests			
	$\text{Cl}^-$ <sup>[a]</sup>	$\text{Br}^-$ <sup>[a]</sup>	$\text{I}^-$ <sup>[a]</sup>	$\text{NO}_3^-$ <sup>[a]</sup>
<b>o-Me<sub>2</sub>-ur-C2</b> (in 5:1 $\text{CDCl}_3/\text{DMSO-d}_6$ )	$286 \pm 23$ <sup>[d]</sup>	n.d.	n.d.	n.d.
<b>o-Me<sub>2</sub>-ur-C2</b> (in $\text{DMSO-d}_6$ )	$37 \pm 9$ <sup>[c]</sup>	$16 \pm 1$ <sup>[d]</sup>	$10 \pm 1$ <sup>[d]</sup>	$8.6 \pm 0.3$ <sup>[d]</sup>
<b>o-Me<sub>2</sub>-ur-C3</b> (in $\text{DMSO-d}_6$ )	$27 \pm 1$ <sup>[d]</sup>	n.d.	n.d.	n.d.
<b>o-Me<sub>2</sub>-ur-C4</b> (in $\text{DMSO-d}_6$ )	$17 \pm 1$ <sup>[d]</sup>	n.d.	n.d.	n.d.
<b>o-H<sub>2</sub>-ur-C4</b> (in $\text{DMSO-d}_6$ )	$32.0 \pm 0.4$ <sup>[d]</sup>	n.d.	n.d.	n.d.

[a] Added as tetraphenylphosphonium salt. [b] Added as tetramethylammonium salt. [c]  $K_a$  determined in triplicate; this error corresponds to 95% confidence interval. [d] Error corresponds to goodness of fit produced by Bindfit on [supramolecular.org](http://supramolecular.org).<sup>[24]</sup> n.d. = not determined.

To identify the smallest possible size of cryptate for a chloride ion, we synthesized a diol containing a C1 chain (**S9**) in addition to diols **1**, **2** and **3**. Using our established self-assembly conditions and C1 diol **S9**, we were unable to observe the formation of the corresponding chloride cryptate. Interestingly, when using a mixture of **S9** and **1**, the formation of two cryptates with different sizes ( $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-(C1)}_2\text{C2}]\text{PPh}_4^+$ ,  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C1(C2)}_2]\text{PPh}_4^+$ ) was observed in high resolution ESI-MS measurements. We deduce that the smallest possible cryptate capable of strongly binding a chloride template incorporates two short C1 diols and one longer C2 diol ( $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-(C1)}_2\text{C2}]\text{PPh}_4^+$ ). When we used a mixture of **1** and **2**, all four possible cryptates ( $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C2}]\text{PPh}_4^+$ ,  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-(C2)}_2\text{C3}]\text{PPh}_4^+$ ,  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C2(C3)}_2]\text{PPh}_4^+$ ,  $[\text{Cl}^- \subset \text{o-Me}_2\text{-ur-C3}]\text{PPh}_4^+$ ) could be detected (Table S4). Tandem mass spectrometry (ESI-MS/MS)<sup>[29]</sup> allowed us to investigate the stability of such heteroleptic cryptands and their chloride complexes without having to isolate them from mixtures. In the gas-phase, each precursor ion of the six cryptates was therefore subjected to increasing collision energies which first results in the release of the chloride ion (decrease of cryptate, green curve in Figure 4) and increase of cryptand (blue curve in Figure 4), followed by cryptand degradation via bond breakage (red curve in Figure 4; first urea then orthoester).

### Dual Self-Assembly of Anion and Cation Cryptates

Having isolated and investigated these chloride-templated cryptands, we wondered whether  $\text{CsCl}$  could be used as an “ion pair template” in experiments aiming to self-assemble hosts for the cation and anion simultaneously using the same dynamic covalent exchange reaction. To this end, we treated a chloroform/dimethyl sulfoxide (5:1) solution of diol **1** and



**Figure 4.** Ratio of cryptate, cryptand and products of degradation depending of applied voltage obtained by electrospray-ionisation collision-induced dissociation mass spectroscopy (ESI-CID-MS) measurements. After isolation of the product peak, increasing the voltage leads to release of the chloride ion (decrease of cryptate, green curve), formation of cryptand (blue curve) and subsequently, cryptand degradation (red curve). Ratio determined by relative intensities of corresponding mass peaks. Collision energy is given as center-of-mass frame ( $E_{com}$ ) in dependence on masses of collision gas ( $N_2$ ) and precursor ion. The lines are shown to guide the eye.

triethylene glycol (TEG) with trimethyl orthoacetate, CsCl and 2,3,4,5,6-pentafluorothiophenol as mild acid catalyst (Figure 5a). After only 18 hours,  $^1H$ -NMR spectroscopy revealed the complete consumption of orthoesters, along with signals indicative of the expected orthoester cryptates. Similar to the aforementioned procedure, the pure product was obtained in good yield (59%) after quenching of the exchange reaction with triethylamine, followed by precipitation with diethyl ether. As expected, the  $^1H$ -NMR spectrum of this material resembles the sum of spectra for the individual cryptates  $[Cl^- \cdot o\text{-Me}_2\text{-ur-C2}]PPh_4^+$  and  $[Cs^+ \cdot o\text{-Me}_2\text{-2.2.2}]BARF^-$  (Figure 5b). The same “additive spectrum” is observed by ATR-IR (Figures S38 and S39).

To investigate the association of the hosts to the two guest ions, additional amounts of CsCl were added and both  $^1H$ - and  $^{133}Cs$ -NMR spectra were recorded. The  $^1H$ -NMR spectra show a pronounced shift of the signal corresponding to the urea moiety, whereas the other signals are not affected (Figure S40a). We explain this finding by DMSO competing more effectively for  $Cs^+$  than for  $Cl^-$  binding, which is in agreement with previous observations.<sup>[30]</sup> Nevertheless, a  $^{133}Cs$ -NMR<sup>[31]</sup> titration experiment clearly shows a shift of the signal towards the reference ( $CsCl$  as external standard in  $DMSO-d_6$ ), confirming that the  $Cs^+$  ion is bound, albeit weakly (Figure 5c). The identity of the sample was further confirmed by high resolution ESI-MS measurements. In the positive mode, only the positively charged part of the ion pair receptor  $[Cs^+ \cdot o\text{-Me}_2\text{-2.2.2}]$  was detected, while in the negative mode only  $[Cl^- \cdot o\text{-Me}_2\text{-ur-C2}]$  was observed. No larger complexes or mixed cryptates containing both kinds of diols were found (Figure 5d).

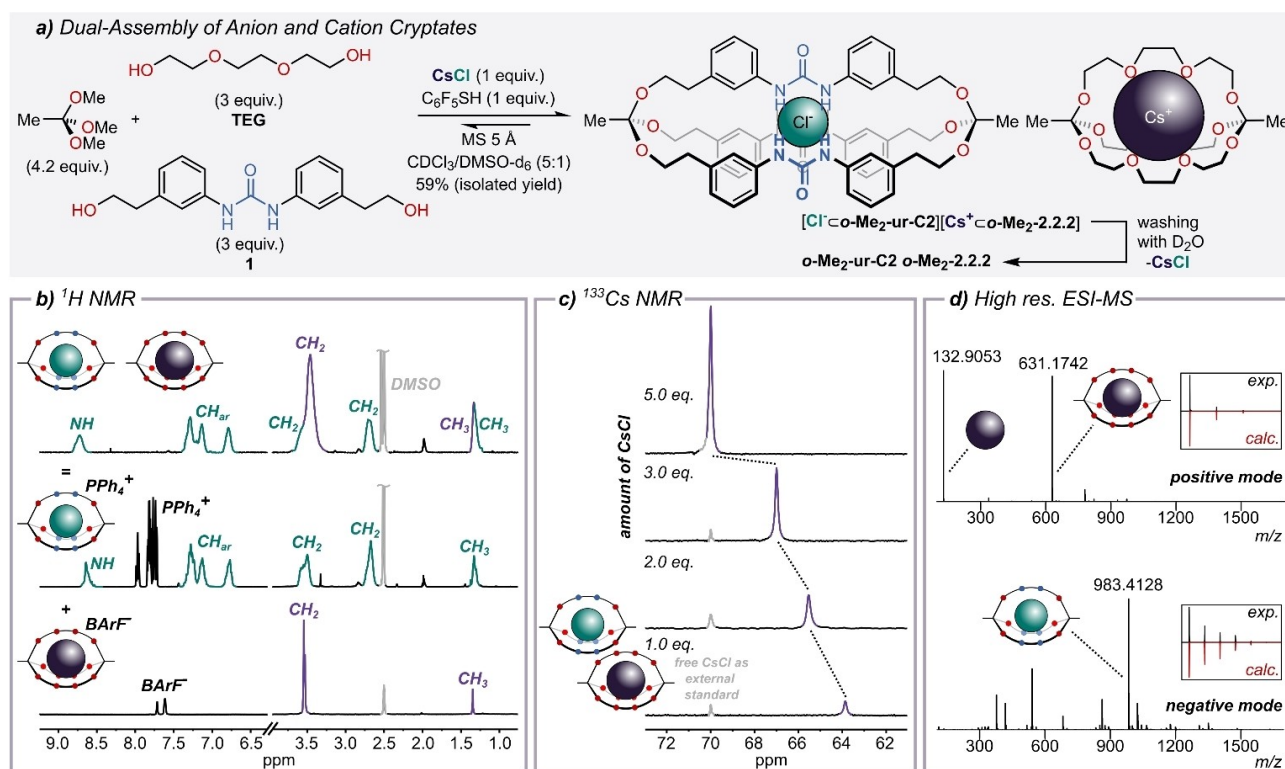
Next, we attempted to remove the  $CsCl$  from this unusual dual-host ion pair receptor.<sup>[32]</sup> Having failed with

other methods (e.g. washing with MeOH or a solution of NaOH in  $D_2O$ ), we found that repeated washing of the precipitate with  $D_2O$  decreased the amount of salt, such that only traces of  $Cs^+$  were detectable by  $^{133}Cs$ -NMR (Figure S33). To gain further insights into the process of cryptate formation, we decided to deliberately inhibit the template effect of  $CsCl$  by using only dimethyl sulfoxide as a highly competitive solvent (Figures S35 and S36). While  $^1H$ -NMR spectroscopy indicated that orthoester exchange proceeded successfully, no signals of the two expected cryptates could be detected by ESI-MS. We deduce from this finding that the  $Cs^+$  and  $Cl^-$  ions indeed act in concert to drive the self-assembly reaction forward.

To gain deeper insights into the driving force behind the formation of each cryptate, we performed the self-assembly reaction with under-stoichiometric amounts of trimethyl orthoacetate (2.1 equiv) such that diols **TEG** and **1** have to compete for the orthoester. In this experiment, we still observed the formation of both cryptates, but no longer in a 1:1 ratio. In the non-competitive experiment, cryptates  $[Cl^- \cdot o\text{-Me}_2\text{-ur-C2}]$  and  $[Cs^+ \cdot o\text{-Me}_2\text{-2.2.2}]$  are formed in ca. 1:1 ratio (as determined by quant.  $^{13}C$ -NMR spectroscopy). However, when using only half of the orthoester, the cryptates form in ca. 2:1 ratio, thus suggesting that the formation of the chloride cryptate is somewhat preferred. Additionally, we carried out the self-assemblies of each cryptate separately using  $CsCl$  as the source for the  $Cs^+$  or  $Cl^-$  ion (previously these two ions had been complemented with weakly coordinating counterions  $BARF^-$  and  $PPh_4^+$ , respectively). Interestingly, compound  $[Cl^- \cdot o\text{-Me}_2\text{-ur-C2}]Cs^+$  was obtained in 42% yield (Chapter 5.6 in the Supporting Information) in this way, whereas only traces of  $[Cs^+ \cdot o\text{-Me}_2\text{-2.2.2}]Cl^-$  could be detected in this attempt to prepare this compound from  $CsCl$  (Chapter 5.7 in the Supporting Information). We conclude from these three experiments that the formation of the chloride cryptate is thermodynamically highly preferred in this solvent mixture ( $CDCl_3/DMSO-d_6$  5:1) and provides most of the driving force in mixed experiments. In contrast, the cesium cryptate  $[Cs^+ \cdot o\text{-Me}_2\text{-2.2.2}]$  is only formed in the dual assembly experiment as a consequence of the formation of  $[Cl^- \cdot o\text{-Me}_2\text{-ur-C2}]$ , and the chloride cryptate can be seen as a large, weakly coordinating anion that enhances the  $Cs^+$  template effect. While the supramolecular binding of anions is generally seen as more difficult than the binding of cations, our  $CsCl$ -driven dual host self-assembly clearly represents a case where the opposite is true (at least in  $CDCl_3/DMSO-d_6$  5:1).

## Conclusion

We report the self-assembly of macrobicyclic hosts for simple anions based on the urea binding motif and orthoester bridgeheads. The cryptands and cryptates exhibit complex intramolecular hydrogen bonding equilibria that may be relevant in most multivalent anion receptors and transporters possessing a certain degree of flexibility. Our self-assembly approach allowed facile access to (mixtures of)



**Figure 5.** a) Cesium chloride-templated co-assembly of two orthoester cryptates. Reaction conditions: 45 μmol cesium chloride, 189 μmol trimethyl orthoacetate, 135 μmol triethylene glycol, 135 μmol diol **1** and 45 μmol 2,3,4,5,6-pentafluorothiophenol in CDCl<sub>3</sub>/DMSO-d<sub>6</sub> mixture (MS: molecular sieves). Reaction time: 18 hours. b) Stacked plot of product after precipitation with diethyl ether (top), [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]PPh<sub>4</sub><sup>+</sup> (middle) and [Cs<sup>+</sup>o-Me<sub>2</sub>-2.2.2]BArF<sup>-</sup> (bottom). c) <sup>133</sup>Cs-NMR spectra of [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2][Cs<sup>+</sup>o-Me<sub>2</sub>-2.2.2] and addition of up to five equivalents CsCl. d) High-resolution electron spray mass spectra. Top: positive mode. Main peaks belong to Cs<sup>+</sup> ion and [Cs<sup>+</sup>o-Me<sub>2</sub>-2.2.2]. Inset: top: experimental and bottom: calculated isotopic pattern of [Cs<sup>+</sup>o-Me<sub>2</sub>-2.2.2]. Bottom: negative mode. Main peak belongs to [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2]. Inset: top: experimental and bottom: calculated isotopic pattern of [Cl<sup>-</sup>o-Me<sub>2</sub>-ur-C2].

heteroleptic host–guest complexes, which, thanks to tandem mass spectrometry, could be studied in the gas-phase without need of isolation in bulk. Having established both anion- and cation-templated orthoester hosts, we attempted to combine the two chemistries in one pot and were indeed able to realize such a dual self-assembly with CsCl playing the role of an “ion pair template”. Future work will focus on more water-soluble building blocks for membrane transport and release studies.

## Acknowledgements

This work was supported by the European Union (ERCstg 802428 “SUPRANET”) and the Deutsche Forschungsgemeinschaft (Emmy-Noether grant DE1830/2-1). O.S. is grateful for a doctoral scholarship by the German Academic Exchange Service (DAAD). C.M.J. and M.H. acknowledge the access to the University of Nottingham High Performance Computing Facility. We thank the anonymous reviewers for suggesting valuable follow-up experiments, especially those that clarified the relative magnitude of the Cs<sup>+</sup>- and Cl<sup>-</sup>-based template effect. Open Access funding enabled and organized by Projekt DEAL.

## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are openly available in [supramolecular.org](http://supramolecular.org) at <http://app.supramolecular.org/bindfit/view/442e7e14-12ab-4beb-81fb-0c5b3837e0ef> and Figshare <https://doi.org/10.6084/m9.figshare.19086995>.

**Keywords:** Chloride Binding · Host–Guest Chemistry · Ion Pairs · Molecular Dynamics · Self-Assembly

- [1] a) H. E. Simmons, C. H. Park, *J. Am. Chem. Soc.* **1968**, *90*, 2428–2429; b) C. H. Park, H. E. Simmons, *J. Am. Chem. Soc.* **1968**, *90*, 2429–2431; c) C. H. Park, H. E. Simmons, *J. Am. Chem. Soc.* **1968**, *90*, 2431–2432; d) J. Lehn, E. Sonveaux, A. K. Willard, *J. Am. Chem. Soc.* **1978**, *100*, 4914–4916; e) F. P. Schmidtchen, M. Berger, *Chem. Rev.* **1997**, *97*, 1609–1646.  
[2] a) S. O. Kang, J. M. Llinares, V. W. Day, K. Bowman-James, *Chem. Soc. Rev.* **2010**, *39*, 3980–4003; b) P. Ballester, *Chem.*



- Soc. Rev.* **2010**, *39*, 3810–3830; c) U. Manna, G. Das, *Coord. Chem. Rev.* **2021**, *427*, 213547; d) J. Zhao, D. Yang, X. J. Yang, B. Wu, *Coord. Chem. Rev.* **2019**, *378*, 415–444; e) M. Delecluse, C. Colomban, B. Chatelet, S. Chevallier-Michaud, D. Moral-eda, J. P. Dutasta, A. Martinez, *J. Org. Chem.* **2020**, *85*, 4706–4711; f) H. A. Fargher, N. Lau, H. C. Richardson, P. H. Y. Cheong, M. M. Haley, M. D. Pluth, D. W. Johnson, *J. Am. Chem. Soc.* **2020**, *142*, 8243–8251; g) M. J. Langton, S. W. Robinson, I. Marques, V. Félix, P. D. Beer, *Nat. Chem.* **2014**, *6*, 1039–1043; h) C. J. Serpell, A. Y. Park, C. V. Robinson, P. D. Beer, *Chem. Commun.* **2021**, *57*, 101–104; i) C. L. Deng, J. P. Bard, J. A. Lohrman, J. E. Barker, L. N. Zakharov, D. W. Johnson, M. M. Haley, *Angew. Chem. Int. Ed.* **2019**, *58*, 3934–3938; *Angew. Chem.* **2019**, *131*, 3974–3978.
- [3] a) L. K. Macreadie, A. M. Gilchrist, D. A. McNaughton, W. G. Ryder, M. Fares, P. A. Gale, *Chem* **2022**, *8*, 46–118; b) L. Chen, S. N. Berry, X. Wu, E. N. W. Howe, P. A. Gale, *Chem* **2020**, *6*, 61–141; c) P. A. Gale, E. N. W. Howe, X. Wu, *Chem* **2016**, *1*, 351–422; d) N. Busschaert, C. Caltagirone, W. Van Rossom, P. A. Gale, *Chem. Rev.* **2015**, *115*, 8038–8155; e) N. H. Evans, P. D. Beer, *Angew. Chem. Int. Ed.* **2014**, *53*, 11716–11754; *Angew. Chem.* **2014**, *126*, 11908–11948.
- [4] a) R. Hein, P. D. Beer, J. J. Davis, *Chem. Rev.* **2020**, *120*, 1888–1935; b) P. A. Gale, C. Caltagirone, *Chem. Soc. Rev.* **2015**, *44*, 4212–4227; c) W. Chen, C. Guo, Q. He, X. Chi, V. M. Lynch, Z. Zhang, J. Su, H. Tian, J. L. Sessler, *J. Am. Chem. Soc.* **2019**, *141*, 14798–14806; d) A.-F. Li, J.-H. Wang, F. Wang, Y.-B. Jiang, *Chem. Soc. Rev.* **2010**, *39*, 3595–3596; e) P. D. Beer, P. A. Gale, *Angew. Chem. Int. Ed.* **2001**, *40*, 486–516; *Angew. Chem.* **2001**, *113*, 502–532; f) J. Bartl, L. Reinke, M. Koch, S. Kubik, *Chem. Commun.* **2020**, *56*, 10457–10460; g) D. P. Farrell, A. L. Sargent, W. E. Allen, *Supramol. Chem.* **2016**, *28*, 45–52; h) D. A. McNaughton, M. Fares, G. Picci, P. A. Gale, C. Caltagirone, *Coord. Chem. Rev.* **2021**, *427*, 213573; i) C. L. Vonnegut, A. M. Shonkwiler, L. N. Zakharov, M. M. Haley, D. W. Johnson, *Chem. Commun.* **2016**, *52*, 9506–9509; j) C. G. Collins, E. M. Peck, P. J. Kramer, B. D. Smith, *Chem. Sci.* **2013**, *4*, 2557–2563; k) C. F. Chow, P. Y. Ho, C.-B. Gong, *Analyst* **2014**, *139*, 4256–4263.
- [5] a) X. Wu, E. N. W. Howe, P. A. Gale, *Acc. Chem. Res.* **2018**, *51*, 1870–1879; b) X. Wu, A. M. Gilchrist, P. A. Gale, *Chem* **2020**, *6*, 1296–1309; c) A. Vargas Jentzsch, A. Hennig, J. Mareda, S. Matile, *Acc. Chem. Res.* **2013**, *46*, 2791–2800; d) M. J. Spooner, H. Li, I. Marques, P. M. R. Costa, X. Wu, E. N. W. Howe, N. Busschaert, S. J. Moore, M. E. Light, D. N. Sheppard, V. Félix, P. A. Gale, *Chem. Sci.* **2019**, *10*, 1976–1985; e) I. Carreira-Barral, M. Mielczarek, D. Alonso-Carrillo, V. Capurro, V. Soto-Cerrato, R. Pérez-Tomás, E. Caci, M. García-Valverde, R. Quesada, *Chem. Commun.* **2020**, *56*, 3218–3221; f) G. Picci, I. Carreira-Barral, D. Alonso-Carrillo, D. Sanz-González, P. Fernández-López, M. García-Valverde, C. Caltagirone, R. Quesada, *Supramol. Chem.* **2020**, *32*, 112–118; g) G. Grauwels, H. Valkenier, A. P. Davis, I. Jabin, K. Bartik, *Angew. Chem. Int. Ed.* **2019**, *58*, 6921–6925; *Angew. Chem.* **2019**, *131*, 6995–6999; h) C. M. Dias, H. Li, H. Valkenier, L. E. Karagiannidis, P. A. Gale, D. N. Sheppard, A. P. Davis, *Org. Biomol. Chem.* **2018**, *16*, 1083–1087; i) X. Wu, L. W. Judd, E. N. W. Howe, A. M. Withecombe, V. Soto-Cerrato, H. Li, N. Busschaert, H. Valkenier, R. Pérez-Tomás, D. N. Sheppard, Y. B. Jiang, A. P. Davis, P. A. Gale, *Chem* **2016**, *1*, 127–146; j) H. Valkenier, O. Akrawi, P. Jurček, K. Sleziačková, T. Lízal, K. Bartik, V. Šindelář, *Chem* **2019**, *5*, 429–444; k) L. Martínez-Crespo, L. Halgreen, M. Soares, I. Marques, V. Félix, H. Valkenier, *Org. Biomol. Chem.* **2021**, *19*, 8324–8337.
- [6] a) X. Ji, R. T. Wu, L. Long, C. Guo, N. M. Khashab, F. Huang, J. L. Sessler, *J. Am. Chem. Soc.* **2018**, *140*, 2777–2780; b) M. T. Albelda, J. C. Frías, E. García-España, H. J. Schneider, *Chem. Soc. Rev.* **2012**, *41*, 3859–3877; c) D. Zhang, T. K. Ronson, J. Mosquera, A. Martinez, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2018**, *57*, 3717–3721; *Angew. Chem.* **2018**, *130*, 3779–3783; d) W. Liu, A. G. Oliver, B. D. Smith, *J. Org. Chem.* **2019**, *84*, 4050–4057; e) R. B. P. Elmes, K. K. Y. Yuen, K. A. Jolliffe, *Chem. Eur. J.* **2014**, *20*, 7373–7380; f) A. Thevenet, A. Miljkovic, S. La Cognata, C. Marie, C. Tamin, N. Boubals, C. Mangano, V. Amendola, P. Guilbaud, *Dalton Trans.* **2021**, *50*, 1620–1630; g) C. Jia, B. Wu, S. Li, X. Huang, Q. Zhao, Q. S. Li, X. J. Yang, *Angew. Chem. Int. Ed.* **2011**, *50*, 486–490; *Angew. Chem.* **2011**, *123*, 506–510.
- [7] a) P. A. Gale, J. T. Davis, R. Quesada, *Chem. Soc. Rev.* **2017**, *46*, 2497–2519; b) J. T. Davis, P. A. Gale, R. Quesada, *Chem. Soc. Rev.* **2020**, *49*, 6056–6086; c) S. H. Park, S. H. Park, E. N. W. Howe, J. Y. Hyun, L. J. Chen, I. Hwang, G. Vargas-Zuñiga, N. Busschaert, P. A. Gale, J. L. Sessler, I. Shin, *Chem* **2019**, *5*, 2079–2098; d) H. Li, H. Valkenier, A. G. Thorne, C. M. Dias, J. A. Cooper, M. Kieffer, N. Busschaert, P. A. Gale, D. N. Sheppard, A. P. Davis, *Chem. Sci.* **2019**, *10*, 9663–9672; e) N. Busschaert, S. H. Park, K. H. Baek, Y. P. Choi, J. Park, E. N. W. Howe, J. R. Hiscock, L. E. Karagiannidis, I. Marques, V. Félix, W. Namkung, J. L. Sessler, P. A. Gale, I. Shin, *Nat. Chem.* **2017**, *9*, 667–675; f) S. K. Ko, S. K. Kim, A. Share, V. M. Lynch, J. Park, W. Namkung, W. Van Rossom, N. Busschaert, P. A. Gale, J. L. Sessler, I. Shin, *Nat. Chem.* **2014**, *6*, 885–892; g) N. Akhtar, O. Biswas, D. Manna, *Chem. Commun.* **2020**, *56*, 14137–14153; h) L. A. Marchetti, L. K. Kumawat, N. Mao, J. C. Stephens, R. B. P. Elmes, *Chem* **2019**, *5*, 1398–1485; i) L. Tapia, I. Alfonso, J. Solà, *Org. Biomol. Chem.* **2021**, *19*, 9527–9540; j) A. Roy, P. Talukdar, *ChemBioChem* **2021**, *22*, 2925–2940; k) J. Yang, G. Yu, J. L. Sessler, I. Shin, P. A. Gale, F. Huang, *Chem* **2021**, *7*, 3256–3291.
- [8] a) Y. Liu, W. Zhao, C.-H. Chen, A. H. Flood, *Science* **2019**, *365*, 159–161; b) F. C. Parks, E. G. Sheetz, S. R. Stutsman, A. Lutolli, S. Debnath, K. Raghavachari, A. H. Flood, *J. Am. Chem. Soc.* **2022**, *144*, 1274–1287.
- [9] a) C. T. McTernan, T. K. Ronson, J. R. Nitschke, *J. Am. Chem. Soc.* **2021**, *143*, 664–670; b) M. Kieffer, R. A. Bilbeisi, J. D. Thoburn, J. K. Clegg, J. R. Nitschke, *Angew. Chem. Int. Ed.* **2020**, *59*, 11369–11373; *Angew. Chem.* **2020**, *132*, 11465–11469; c) Z. Lu, T. K. Ronson, J. R. Nitschke, *Chem. Sci.* **2020**, *11*, 1097–1101; d) S. Wang, Z. Huang, A. Li, Y. Zhao, W. Zuo, Y. Li, H. Miao, J. Ma, W. Sun, X. Wang, L. Cao, B. Wu, C. Jia, *Angew. Chem. Int. Ed.* **2021**, *60*, 9573–9579; *Angew. Chem.* **2021**, *133*, 9659–9665; e) S. J. Allison, J. Bryk, C. J. Clemett, R. A. Faulkner, M. Ginger, H. B. S. Griffiths, J. Harmer, P. J. Owen-Lynch, E. Pinder, H. Wurdak, R. M. Phillips, C. R. Rice, *Nat. Commun.* **2021**, *12*, 3898; f) R. Andrews, S. Begum, C. J. Clemett, R. A. Faulkner, M. L. Ginger, J. Harmer, M. Molinari, G. M. B. Parkes, Z. M. H. Qureshi, C. R. Rice, M. D. Ward, H. M. Williams, P. B. Wilson, *Angew. Chem. Int. Ed.* **2020**, *59*, 20480–20484; *Angew. Chem.* **2020**, *132*, 20660–20664.
- [10] a) W. Zhang, Y. Feng, B. Li, D. Yang, L. Hou, W. Zhao, X. J. Yang, B. Wu, *Chem. Eur. J.* **2022**, *28*, e20210367; b) J. Fu, B. Zheng, H. Zhang, Y. Zhao, D. Zhang, W. Zhang, X. J. Yang, B. Wu, *Chem. Commun.* **2020**, *56*, 2475–2478; c) W. Zhang, D. Yang, J. Zhao, L. Hou, J. L. Sessler, X. J. Yang, B. Wu, *J. Am. Chem. Soc.* **2018**, *140*, 5248–5256; d) X. Bai, C. Jia, Y. Zhao, D. Yang, S. C. Wang, A. Li, Y. T. Chan, Y. Y. Wang, X. J. Yang, B. Wu, *Angew. Chem. Int. Ed.* **2018**, *57*, 1851–1855; *Angew. Chem.* **2018**, *130*, 1869–1873; e) D. Yang, J. Zhao, L. Yu, X. Lin, W. Zhang, H. Ma, A. Gogoll, Z. Zhang, Y. Wang, X. J. Yang, B. Wu, *J. Am. Chem. Soc.* **2017**, *139*, 5946–5951; f) D. Yang, J. Zhao, Y. Zhao, Y. Lei, L. Cao, X. J. Yang, M. Davi, N. De Sousa Amadeu, C. Janiak, Z. Zhang, Y. Y. Wang, B. Wu, *Angew. Chem. Int. Ed.* **2015**, *54*, 8658–8661; *Angew. Chem.*

- 2015, 127, 8782–8785; g) B. Wu, F. Cui, Y. Lei, S. Li, N. De Sousa Amadeu, C. Janiak, Y. J. Lin, L. H. Weng, Y. Y. Wang, X. J. Yang, *Angew. Chem. Int. Ed.* **2013**, 52, 5096–5100; *Angew. Chem.* **2013**, 125, 5200–5204.
- [11] a) Z. Rodriguez-Docampo, E. Eugenieva-Ilieva, C. Reyheller, A. M. Belenguer, S. Kubik, S. Otto, *Chem. Commun.* **2011**, 47, 9798–9800; b) S. Otto, S. Kubik, *J. Am. Chem. Soc.* **2003**, 125, 7804–7805.
- [12] a) H. Xie, T. J. Finnegan, V. W. Liyana Gunawardana, R. Z. Pavlović, C. E. Moore, J. D. Badjić, *J. Am. Chem. Soc.* **2021**, 143, 3874–3880; b) E. A. Katayev, G. D. Pantos, M. D. Reshetova, V. N. Khrustalev, V. M. Lynch, Y. A. Ustynyuk, J. L. Sessler, *Angew. Chem. Int. Ed.* **2005**, 44, 7386–7390; *Angew. Chem.* **2005**, 117, 7552–7556; c) S. R. Beeren, J. K. M. Sanders, *J. Am. Chem. Soc.* **2011**, 133, 3804–3807.
- [13] a) L. Tapia, Y. Pérez, M. Bolte, J. Casas, J. Solà, R. Quesada, I. Alfonso, *Angew. Chem. Int. Ed.* **2019**, 58, 12465–12468; *Angew. Chem.* **2019**, 131, 12595–12598; b) H. Fernández-Caro, I. Lostalé-Seijo, M. Martínez-Calvo, J. Mosquera, J. L. Mascarañas, J. Montenegro, *Chem. Sci.* **2019**, 10, 8930–8938; c) X. Chi, W. Cen, J. A. Queenan, L. Long, V. M. Lynch, N. M. Khashab, J. L. Sessler, *J. Am. Chem. Soc.* **2019**, 141, 6468–6472; d) M. Fares, X. Wu, D. Ramesh, W. Lewis, P. A. Keller, E. N. W. Howe, R. Pérez-Tomás, P. A. Gale, *Angew. Chem. Int. Ed.* **2020**, 59, 17614–17621; *Angew. Chem.* **2020**, 132, 17767–17774; e) A. Kerckhoffs, Z. Bo, S. E. Penty, F. Duarte, M. J. Langton, *Org. Biomol. Chem.* **2021**, 19, 9058–9067; f) S. J. Wezenberg, L.-J. Chen, J. E. Bos, B. L. Feringa, E. N. W. Howe, X. Wu, M. A. Siegler, P. A. Gale, *J. Am. Chem. Soc.* **2022**, 144, 331–338; g) Y. Eygeris, M. Gupta, J. Kim, G. Sahay, *Acc. Chem. Res.* **2022**, 55, 2–12.
- [14] a) C. Jia, W. Zuo, D. Zhang, X. J. Yang, B. Wu, *Chem. Commun.* **2016**, 52, 9614–9627; b) V. Blažek Bregović, N. Basarić, K. Mlinarić-Majerski, *Coord. Chem. Rev.* **2015**, 295, 80–124; c) J. Zhao, D. Yang, Y. Zhao, L. Cao, Z. Zhang, X. J. Yang, B. Wu, *Dalton Trans.* **2016**, 45, 7360–7365; d) N. Busschaert, P. A. Gale, C. J. E. Haynes, M. E. Light, S. J. Moore, C. C. Tong, T. Davis, W. A. Harrell, *Chem. Commun.* **2010**, 46, 6252–6254; e) A. Basu, G. Das, *J. Org. Chem.* **2014**, 79, 2647–2656.
- [15] a) A. Herrmann, *Chem. Soc. Rev.* **2014**, 43, 1899–1933; b) Y. Jin, C. Yu, R. J. Denman, W. Zhang, *Chem. Soc. Rev.* **2013**, 42, 6634–6654; c) Y. Jin, Q. Wang, P. Taynton, W. Zhang, *Acc. Chem. Res.* **2014**, 47, 1575–1586; d) J. Li, P. Nowak, S. Otto, *J. Am. Chem. Soc.* **2013**, 135, 9222–9239; e) P. T. Corbett, J. Leclair, L. Vial, K. R. West, J. Wietor, J. K. M. Sanders, S. Otto, *Chem. Rev.* **2006**, 106, 3652–3711; f) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders, J. F. Stoddart, *Angew. Chem. Int. Ed.* **2002**, 41, 898–952; *Angew. Chem.* **2002**, 114, 938–993; g) J. F. Reuther, S. D. Dahlhauser, E. V. Anslyn, *Angew. Chem. Int. Ed.* **2019**, 58, 74–85; *Angew. Chem.* **2019**, 131, 76–88; h) E. Moulin, G. Cormos, N. Giuseppone, *Chem. Soc. Rev.* **2012**, 41, 1031–1049; i) *Dynamic Covalent Chemistry: Principles, Reactions, and Applications* (Eds.: W. Zhang, Y. Jin), Wiley-VCH, Weinheim, **2018**.
- [16] a) R. C. Brachvogel, M. von Delius, *Chem. Sci.* **2015**, 6, 1399–1403; b) R. C. Brachvogel, M. von Delius, *Eur. J. Org. Chem.* **2016**, 3662–3670.
- [17] a) R. C. Brachvogel, F. Hampel, M. von Delius, *Nat. Commun.* **2015**, 6, 7129; b) O. Shyshov, R. C. Brachvogel, T. Bachmann, R. Srikantharajah, D. Segets, F. Hampel, R. Puchta, M. von Delius, *Angew. Chem. Int. Ed.* **2017**, 56, 776–781; *Angew. Chem.* **2017**, 129, 794–799.
- [18] H. Löw, E. Mena-Osteritz, M. von Delius, *Chem. Sci.* **2018**, 9, 4785–4793.
- [19] a) J. Zhou, L. Rao, G. Yu, T. R. Cook, X. Chen, F. Huang, *Chem. Soc. Rev.* **2021**, 50, 2839–2891; b) J. Zhou, G. Yu, F. Huang, *Chem. Soc. Rev.* **2017**, 46, 7021–7053; c) D. A. Uhlenheuer, K. Petkau, L. Brunsfeld, *Chem. Soc. Rev.* **2010**, 39, 2817–2826; d) G. Gasparini, E. K. Bang, J. Montenegro, S. Matile, *Chem. Commun.* **2015**, 51, 10389–10402.
- [20] L. H. Perruchoud, A. Hadzovic, X. Zhang, *Chem. Eur. J.* **2015**, 21, 8711–8715.
- [21] a) X. Wang, O. Shyshov, M. Hanževački, C. M. Jäger, M. von Delius, *J. Am. Chem. Soc.* **2019**, 141, 8868–8876; b) H. Löw, E. Mena-Osteritz, K. M. Mullen, C. M. Jäger, M. von Delius, *ChemPlusChem* **2020**, 85, 1008–1012.
- [22] A. M. Rijs, E. R. Kay, D. A. Leigh, W. J. Buma, *J. Phys. Chem. A* **2011**, 115, 9669–9675.
- [23] G. Jakab, C. Tancon, Z. Zhang, K. M. Lippert, P. R. Schreiner, *Org. Lett.* **2012**, 14, 1724–1727.
- [24] a) P. Thordarson, *Chem. Soc. Rev.* **2011**, 40, 1305–1323; b) D. Brynn Hibbert, P. Thordarson, *Chem. Commun.* **2016**, 52, 12792–12805.
- [25] R. A. Hovermale, P. G. Sears, *J. Phys. Chem.* **1956**, 60, 1579–1580.
- [26] H. Löw, E. Mena-Osteritz, M. von Delius, *Chem. Commun.* **2019**, 55, 11434–11437.
- [27] C. J. E. Haynes, N. Busschaert, I. L. Kirby, J. Herniman, M. E. Light, N. J. Wells, I. Marques, V. Félix, P. A. Gale, *Org. Biomol. Chem.* **2014**, 12, 62–72.
- [28] a) S. J. Moore, C. J. E. Haynes, J. González, J. L. Sutton, S. J. Brooks, M. E. Light, J. Herniman, G. J. Langley, V. Soto-Cerrato, R. Pérez-Tomás, I. Marques, P. J. Costa, V. Félix, P. A. Gale, *Chem. Sci.* **2013**, 4, 103–117; b) S. J. Edwards, H. Valkenier, N. Busschaert, P. A. Gale, A. P. Davis, *Angew. Chem. Int. Ed.* **2015**, 54, 4592–4596; *Angew. Chem.* **2015**, 127, 4675–4679.
- [29] a) M. B. Minameyer, Y. Xu, S. Frühwald, A. Görling, M. von Delius, T. Drewello, *Chem. Eur. J.* **2020**, 26, 8729–8741; b) Z. Qi, T. Heinrich, S. Moorthy, C. A. Schalley, *Chem. Soc. Rev.* **2015**, 44, 515–531.
- [30] R.-C. Brachvogel, H. Maid, M. von Delius, *Int. J. Mol. Sci.* **2015**, 16, 20641–20656.
- [31] D. Zhang, T. K. Ronson, J. L. Greenfield, T. Brotin, P. Berthault, E. Leónce, J. L. Zhu, L. Xu, J. R. Nitschke, *J. Am. Chem. Soc.* **2019**, 141, 8339–8345.
- [32] a) M. Cametti, M. Nissinen, A. Dalla Cort, L. Mandolini, K. Rissanen, *J. Am. Chem. Soc.* **2005**, 127, 3831–3837; b) Q. He, G. I. Vargas-Zúñiga, S. H. Kim, S. K. Kim, J. L. Sessler, *Chem. Rev.* **2019**, 119, 9753–9835; c) S. K. Kim, J. L. Sessler, *Chem. Soc. Rev.* **2010**, 39, 3784–3809; d) A. J. McConnell, P. D. Beer, *Angew. Chem. Int. Ed.* **2012**, 51, 5052–5061; *Angew. Chem.* **2012**, 124, 5138–5148; e) A. J. McConnell, A. Docker, P. D. Beer, *ChemPlusChem* **2020**, 85, 1824–1841; f) J. H. Yang, V. M. Lynch, J. L. Sessler, S. K. Kim, *Supramol. Chem.* **2019**, 31, 203–210; g) R. C. Knighton, P. D. Beer, *Org. Chem. Front.* **2021**, 8, 2468–2472; h) Y. C. Tse, A. Docker, Z. Zhang, P. D. Beer, *Chem. Commun.* **2021**, 57, 4950–4953; i) Z. Kokan, M. J. Chmielewski, *J. Am. Chem. Soc.* **2018**, 140, 16010–16014.

Manuscript received: February 2, 2022

Accepted manuscript online: April 5, 2022

Version of record online: May 12, 2022