

Supporting Information

The Chaotropic Effect as an Assembly Motif in Chemistry

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1. Two-dimensional illustration of the extended Hofmeister scale

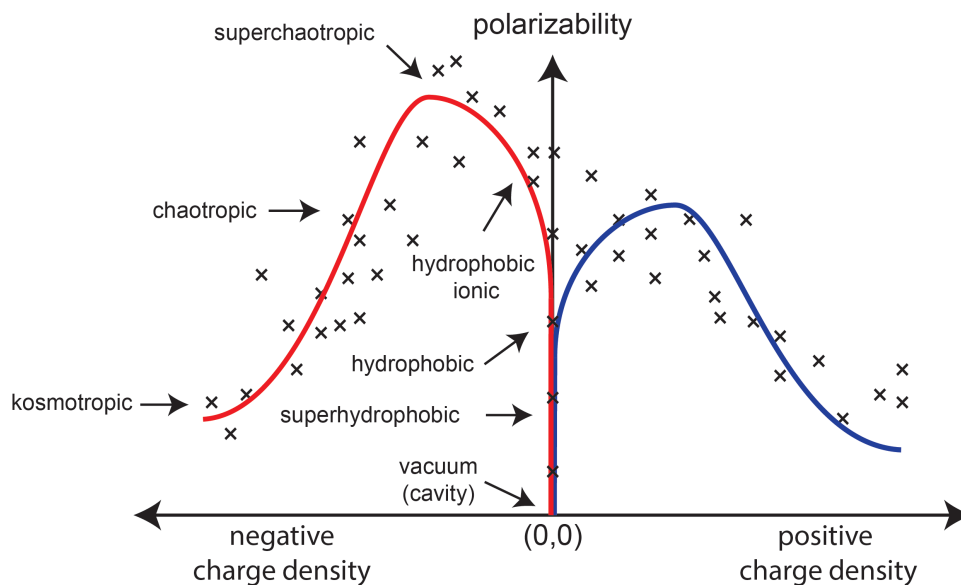


Figure S1: Two-dimensional, purely schematic illustration of the extended Hofmeister scale with specification of the superchaotropic, hydrophobic ionic, and superhydrophobic regions and reflecting the on average higher polarizability of anions (left) versus cations (right). The red line would correspond to the one-dimensional, linearized solvation scale depicted in Figure 1b of the main text.

2. Interplay and differentiation of the chaotropic effect from the non-classical hydrophobic effect and dispersion interactions

As outlined in the main text, the chaotropic effect and the hydrophobic effect are generally expected to have characteristic thermochemical signatures such that they can be differentiated on this basis. Strictly speaking, this differentiation is only possible when a *classical* hydrophobic effect is operative, that is, when desolvation leads to a favorable entropic component. In special cases, for example, when the binding involves the desolvation of a small hydrophobic cavity, for example of a macrocyclic host or a biological binding site, its desolvation may also result in a negative enthalpic contribution. This is referred to as the *non-classical* hydrophobic effect, which has recently been reviewed.^[1] This effect arises from limitations in hydrogen bonding of water molecules inside confined hydrophobic environments, such that the release of this “high-energy water” to the bulk leads to an increased, enthalpically favored hydrogen bonding upon displacement by another cavity binder (Figure S2).^[1,2] Therefore, when a chaotropic species binds to a macrocyclic cavity, the corresponding negative complexation enthalpy may constitute a composite effect arising from both the chaotropic effect and the non-classical hydrophobic effect. In these cases, the determination of the dominant driving force may be more intricate and the thermochemical data alone are inconclusive. For large macrocycles, such as γ -CD and larger CDs, the non-classical hydrophobic effect is known to be small^[1] such that the observed exceptionally strong binding of the dodecaborate cluster series must be predominantly due to the chaotropic effect.^[3] Contributions due to the non-classical hydrophobic effect should also remain constant when different species either displace all water molecules or the same number of water molecules from the cavity; this is expected to be the case for equally guests, such as adamantane and $B_{12}H_{12}^{2-}$, see Table S1. This allows the attribution to the chaotropic

effect to be made on the basis of systematic investigations (differently halogenated dodecaborate anions) or the comparison of the absolute affinity of chaotropic and hydrophobic species.^[3,4] The differentiation between the chaotropic effect and non-classical hydrophobic effect has been first emphasized by Matějček and coworkers for the micellization of classical surfactants and intrinsically amphiphilic metallacarboranes.^[5,6]

Table S1: Calculated polarizabilities (in \AA^3) of selected classical kosmotropic (F^-) and chaotropic anions (PF_6^-), superchaotropic anions (dodecaborate clusters and POMs), and a hydrophobic anion (BPh_4^-), as well as adamantane and diamantane as examples of hydrophobic neutral molecules; values are calculated in the gas phase by using the B3LYP/aug-cc-pvdz method; the ordering corresponds to that in Figure 1b, main text.

solute	$V/\text{\AA}^3$	$\alpha/\text{\AA}^3$ [a]
F^-	9.3	1.0
PF_6^-	56.0	5.2
$\text{B}_{12}\text{H}_{12}^{2-}$	152.4	25.7
$\text{B}_{12}\text{Cl}_{12}^{2-}$	333.1	46.7
$\text{B}_{12}\text{Br}_{12}^{2-}$	415.6	58.2
$\text{B}_{12}\text{I}_{12}^{2-}$ [a]	519.6	84.1
$\text{PW}_{12}\text{O}_{40}^{3-}$ [b]	494.2	82.8
BPh_4^-	326.9	46.2
diamantane	192.4	21.7
adamantane	147.3	16.2

[a] Calculated by employing pseudopotentials to describe the inner core orbitals of the iodine atoms. [b] Single-point calculations performed for the geometry obtained from XRD structures at the B3LYP/3-21G* and Def2-QZVP level of theory by employing pseudopotentials to describe the inner core orbitals of the tungsten atoms.

Another challenge is the dissection of dispersion interactions as a complementary driving force for association processes involving chaotropic ions. Because dispersion-driven binding events are also characterized by a negative enthalpy (due to the involved London dispersion forces) and a negative entropy (due the formation of highly ordered structures), their thermochemical fingerprint is the same as that of chaotrope desolvation. Additionally, chaotropic, in particular superchaotropic, ions exhibit high polarizabilities due to their large molecular size (see Figure S1 and Table S1), such that dispersion interactions are significant. This is particularly true for anions, which are intrinsically more polarizable than cations (Figure S1). Therefore, it is expected that dispersion interactions always contribute a share and act in concert with chaotrope desolvation. In fact, many effects caused by chaotropic ions have been empirically related to their polarizability and dispersion interactions (Table S1).^[3,7-10] This situation exactly parallels that for the hydrophobic effect which is also known to be always convoluted with dispersion interactions, leading to a debate which continues to date, since the dissection is experimentally challenging.^[11-14] Systematic studies with hosts of varying polarizability^[15,16] may be constructive to dissect the dispersive contributions. Ultimately, this opens a wide field for a combination of electronic-structure methods, such as dispersion-corrected DFT calculations, and molecular dynamics simulations or continuum solvation models to theoretically analyze and predict the relative importance of dispersion and desolvation related to the chaotropic effect. Studies in the gas phase, where only dispersion interactions remain, are also instructive.^[17,18]

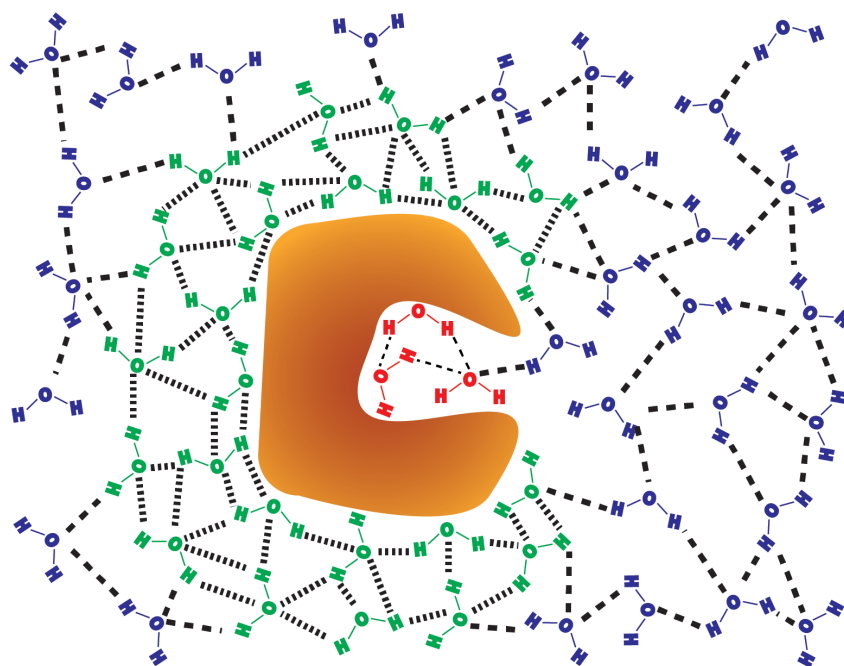


Figure S2: The displacement of highly structured and strongly hydrogen-bonded water molecules (shown in green) around a flat or convex surface is related to the classical hydrophobic effect ($\Delta S > 0$). The displacement of weakly hydrogen-bonded water (shown in red) inside concave binding sites is related to the non-classical hydrophobic effect ($\Delta H < 0$), see ref.^[1]. Bulk water is shown in blue.

3. Exploiting the orthogonality of hydrophobic and chaotropic binding

Most recently, the chaotropic effect has been established as an orthogonal assembly motif, which allows for the design of responsive supramolecular networks between CB_n and dodecaborate anions in water.^[19] Note that both, hydrophobic and chaotropic species, have an intrinsic affinity to hydrophobic surfaces. Accordingly, a competition for binding of hydrophobic and chaotropic species to nonpolar cavities can arise, which has been observed early for CDs^[20] and analyzed in more detail for the binding to the so-called octa-acid host.^[21-23] When the hydrophobic and chaotropic species and the cavity size of the receptor are carefully selected, e.g., when one component is too large to bind to the cavity, the different driving forces can be rationally used in the design of new supramolecular assemblies. For example, we have recently provided a new strategy for engineering multi-responsive supramolecular networks in water through the combination of the chaotropic and hydrophobic effect (Figure S3; identical to Figure 5b in the main text).^[19] In detail, we linked a dodecaborate cluster, as a superchaotropic unit, to an auxiliary photochromic hydrophobic unit (i.e., azobenzene), which allows for both effects to act as assembly motifs in water with cucurbiturils (CB_n) as a macrocyclic host. The dodecaborate residue binds to the exterior surface of CB_7 (chaotropic effect), while azobenzene moiety shows a preferential affinity for inclusion into CB_7 (hydrophobic effect).^[19] The hydrophobic effect can be switched off by UV irradiation (formation of the less tightly bound *cis* azobenzene), while the chaotropic effect can be switched off by the addition of strong acid or a stronger competitive binder (γ -CD).^[19] This interplay of the two effects could enable noncovalent chemistry into several directions, including materials science.

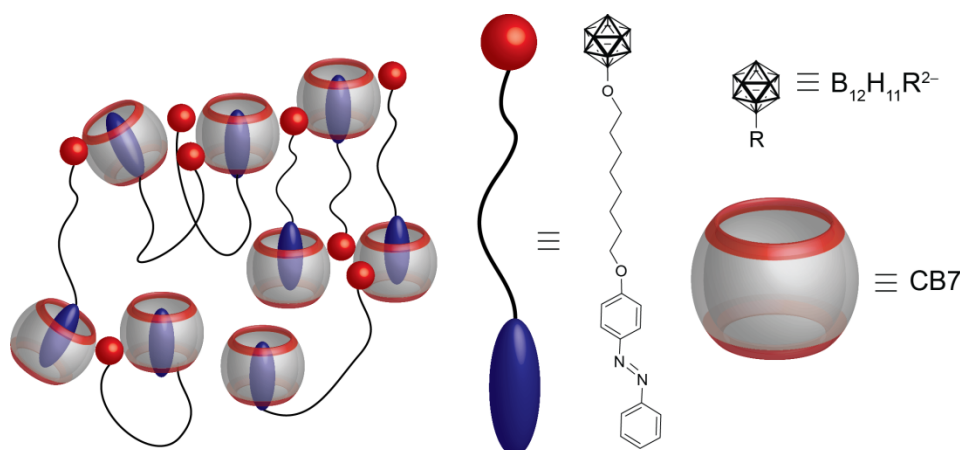


Figure S3: Assembly of cucurbiturils in the presence of an amphiphilic dodecaborate-functionalized azobenzene. The red residue illustrates a superchaotropic unit as recognition site to the exterior surface of CB7 and the blue unit represents an auxiliary hydrophobic unit which shows a preferential affinity for inclusion complexation with CB7. The Figure is identical to Figure 5b in the main text.

4. References

- [1] F. Biedermann, W. M. Nau, H.-J. Schneider, *Angew. Chem. Int. Ed.* **2014**, *53*, 11158-11171; *Angew. Chem.* **2014**, *126*, 11338-11352.
- [2] A. J. Metherell, W. Cullen, N. H. Williams, M. D. Ward, *Chem. - Eur. J.* **2018**, *24*, 1554-1560.
- [3] 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; *Angew. Chem.* **2015**, *127*, 6956-6960.
- [4] K. I. Assaf, D. Gabel, W. Zimmermann, W. M. Nau, *Org. Biomol. Chem.* **2016**, *14*, 7702-7706.
- [5] R. Fernandez-Alvarez, V. Ďorđovič, M. Uchman, P. Matějček, *Langmuir* **2018**, *34*, 3541-3554.
- [6] M. Uchman, A. I. Abrikosov, M. Lepšík, M. Lund, P. Matějček, *Adv. Theory Simul.* **2018**, *1*, 1700002.
- [7] W. Kunz, P. Lo Nostro, B. W. Ninham, *Curr. Opin. Colloid Interface Sci.* **2004**, *9*, 1-18.
- [8] P. Lo Nostro, B. W. Ninham, S. Milani, A. Lo Nostro, G. Pesavento, P. Baglioni, *Biophys. Chem.* **2006**, *124*, 208-213.
- [9] M. Hou, R. Lu, A. Yu, *RSC Adv.* **2014**, *4*, 23078-23083.
- [10] T. T. Duignan, D. F. Parsons, B. W. Ninham, *Chem. Phys. Lett.* **2014**, *608*, 55-59.
- [11] K. I. Assaf, M. Florea, J. Antony, N. M. Henriksen, J. Yin, A. Hansen, Z.-w. Qu, R. Sure, D. Klapstein, M. K. Gilson, S. Grimme, W. M. Nau, *J. Phys. Chem. B* **2017**, *121*, 11144-11162.
- [12] T. Liu, H. -J. Schneider, *Angew. Chem. Int. Ed.* **2002**, *41*, 1368-1370; *Angew. Chem.* **2002**, *114*, 1418-1420.
- [13] L. Yang, C. Adam, G. S. Nichol, S. L. Cockroft, *Nat. Chem.* **2013**, *5*, 1006-1010.
- [14] K. D. Shimizu, *Nat. Chem.* **2013**, *5*, 989-990.
- [15] C. Marquez, W. M. Nau, *Angew. Chem. Int. Ed.* **2001**, *40*, 4387-4390; *Angew. Chem.* **2001**, *113*, 4515-4518.
- [16] W. M. Nau, A. Hennig, A. L. Koner, in: *Fluorescence of Supramolecules, Polymers, and Nanosystems, Springer Ser. Fluoresc.*, Vol. 4 (Ed: M. N. Berberan-Santos), **2008**, pp. 185-211.
- [17] S. M. Eyrilmez, E. Bernhardt, J. Z. Dávalos, M. Lepšík, P. Hobza, K. I. Assaf, W. M. Nau, J. Holub, J. M. Oliva-Enrich, J. Fanfrlík, D. Hnyk, *Phys. Chem. Chem. Phys.* **2017**, *19*, 11748-11752.
- [18] J. Warneke, C. Jenne, J. Bernarding, V. A. Azov, M. Plaumann, *Chem. Commun.* **2016**, *52*, 6300-6303.
- [19] W. Wang, X. Wang, J. Cao, J. Liu, B. Qi, X. Zhou, S. Zhang, D. Gabel, W. M. Nau, K. I. Assaf, H. Zhang, *Chem. Commun.* **2018**, *54*, 2098-2101.
- [20] F. Cramer, W. Saenger, H. C. Spatz, *J. Am. Chem. Soc.* **1967**, *89*, 14-20.
- [21] C. L. D. Gibb, B. C. Gibb, *J. Am. Chem. Soc.* **2011**, *133*, 7344-7347.
- [22] C. L. D. Gibb, E. E. Oertling, S. Velaga, B. C. Gibb, *J. Phys. Chem. B* **2015**, *119*, 5624-5638.
- [23] R. S. Carnegie, C. L. D. Gibb, B. C. Gibb, *Angew. Chem. Int. Ed.* **2014**, *53*, 11498-11500; *Angew. Chem.* **2014**, *126*, 11682-11684.