Communication

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Redox-Responsive H-Bonding: Amplifying the Effect of Electron Transfer Using Proton-Coupled Electron Transfer

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ABSTRACT: A new strategy to create highly redox-responsive H-bond dimers based on proton-coupled electron transfer is proposed that capitalizes on the importance of secondary H-bonds in determining overall binding strength in H-bond dimers. Electron transfer induced proton transfer across a H-bond can be used to significantly strengthen the overall binding by both creating strong ionic H-bonds and by changing the secondary H-bonds from unfavorable to favorable. The viability and potency of this approach is demonstrated with an electroactive DAD (A = H-acceptor, D = H-donor) array, $H(MQ^+)H$, paired with an electroinactive ADA array, O(NH)O. NMR titration of $H(MQ^+)H$ with O(NH)O in 0.1 M NBu_4PF_6/CD_2Cl_2 gives a K_{assoc} of 500 M^{-1}, typical of DAD-ADA dimers. However, upon two electron reduction in 0.1 M NBu_4PF_6/CH_2Cl_2, cyclic voltammetry studies indicate a 1.8×10^5 increase in binding strength, corresponding to a very large K_{assoc} of 9×10^7 M^{-1}. The latter value is typical of DDD-AAA H-bond dimers, consistent with proton transfer across the central H-bond upon reduction.

This paper introduces a new method to achieve highly redox-responsive H-bonding by utilizing electron transfer, ET, to initiate proton transfer, PT, across a H-bond in a linear H-bond array. Creation of stimuli-responsive systems in which application of an external signal causes a desired change in the structure and properties of a supramolecular assembly is a current focus in supramolecular chemistry.[1-5] ET is one possible signal,[6-10] which, if done electrochemically, offers several unique attributes, including no chemical waste generation, high selectivity and surface sensitivity, and the possibility of a straightforward interface with current electronic devices.[11]

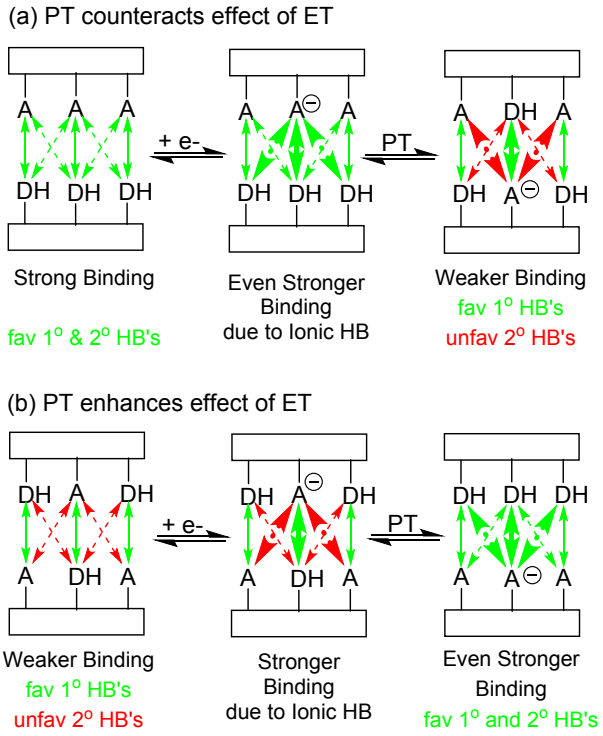
As with other stimuli, the key is that ET perturbs the strength of the weak interactions controlling the supramolecular structure. Due to their strength and directionality, H-bonds are one of the most important of these interactions. As a result, H-bond complexes have played[12-21] and continue to play a very significant role in the development of supramolecular chemistry.[22-31] Because of their substantial electrostatic character, it is also straightforward to perturb the strength of H-bonds using ET. This trait has found particular application in the design of anion receptors,[32] however, redox-responsive H-bonding is not commonly used in other supramolecular applications. There are some notable exceptions, such as Leigh's H-bond based molecular shuttle,[33-34] Zimmerman's demonstration of controlled gelation using a redox-active 4 H-bond array,[35-36] and Diederich's molecular grippers.[37] However, ET is more commonly used to perturb other types of weak interactions, particularly electrostatic, solvation, pi donor-acceptor and metal-ligand coordination. The amazing things that can be accomplished using these strategies are epitomized by the Nobel prize winning work of Stoddart[38] and Sauvage[39] on molecular switches and machines. However, given the unique attributes of H-bonding, greater use of redox-responsive H-bonding in supramolecular chemistry could be highly advantageous, leading to new design possibilities for stimuli-responsive devices and materials. To that end, there is a need for innovative strategies that produce redox-responsive H-bonding systems with greater selectivity and greater differences in binding strength between oxidation states, coupled with good electrochemical reversibility.

For a number of years now, our group[40-45] and others[46-52] have worked on the development of electroactive H-bond systems in which ET changes the charge on the atoms involved in the H-bonds and by doing so either strengthens or weakens the primary H-bond interactions. However, it is well-known that in linear H-bond arrays with multiple, closely-spaced H-bonds, it is not only the number and strength of the H-bonds that affect the overall binding strength, but also the H-bond pattern.[53-54] The strongest binding is always observed when all the H-donors (D) are on one side and all the H-acceptors (A) are on the other. The standard explanation for this involves the secondary H-bonds.[53-57] In the above case, not only are the primary (linear) H-bonds favorable, but also all the secondary (diagonal) H-bonds are favorable. In contrast, if D's and A's alternate, then, even though the primary H-bonds are favorable, all the secondary H-bonds are unfavorable. Recently it has been suggested that the real reason for this phenomenon is that grouping D's and A's together leads to a larger build-up of charge, which strengthens both the electrostatic and covalent components of the H-bonds.[58] Whatever the cause, the effect is real, and as a result, K_{assoc} values for DDD-AAA H-bond complexes[59-60] are typically $>10^5$ times larger than DAD-ADA complexes.[56, 61]

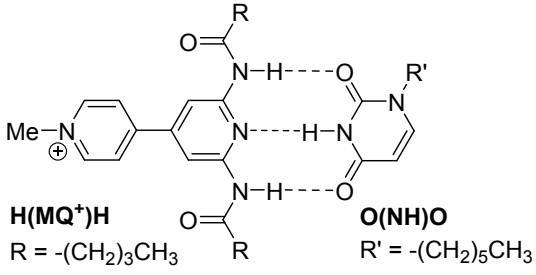
Given the above, we hypothesized that ET that leads to PT across the H-bond could lead to a much larger change in binding strength than ET alone. The basic concept is illustrated in Scheme 1 for a reduction that increases the

negative charge on A. This will create a stronger primary H-bond. However, if the increase in charge also leads to PT, then a change in the H-bond pattern will also result. As illustrated in Scheme 1(a), if the secondary interactions are favorable to begin with, they will become unfavorable after PT. So, if the objective of the ET was to strengthen the H-bond, the PT in this case will undermine that goal. However, if the secondary interactions are unfavorable to begin with, Scheme 1(b), then the PT will switch the secondary interactions to favorable, thus further strengthening the H-bonding.

Scheme 1. Effect of PCET on H-Bond Dimer Strength

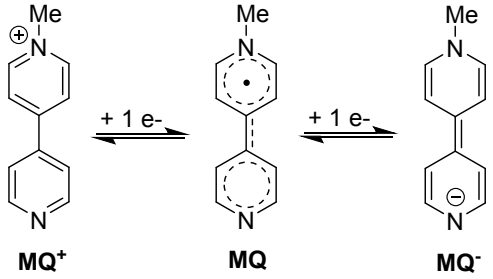


To test this idea, an electroactive derivative of the well-studied 2,6-diamidopyridine DAD-type H-bond array was formed by attaching a pyridinium group to the 4-position of the pyridine via a Suzuki coupling reaction. Complete details on the synthesis and characterization of this compound, H(MQ$^+$)H, are provided in the Supporting Information (SI). For this study, the uracil derivative, O(NH)O, was chosen as an electroinactive ADA-type binding partner for H(MQ$^+$)H.



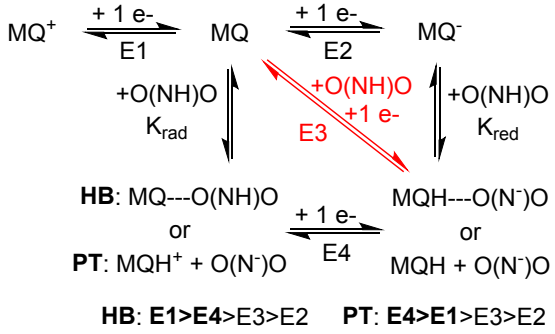
Dimerization of O(NH)O and H(MQ$^+$)H was first confirmed by ^{1}H NMR titration. As shown in Figure S6 in the SI, ^{1}H NMR titration of H(MQ$^+$)H with O(NH)O under electrochemical conditions (0.1 M NBu_4PF_6/CD_2Cl_2) results in a significant downfield shift of the amide NH's as expected if they are H-bonding to the carbonyl O's of the added O(NH)O. The observed shifts fit well to a 1:1 binding isotherm, Figure S7, giving a K_{assoc} of 505 M^{-1}. This is a typical value for a DAD-ADA array, in which the unfavorable secondary H-bonds offset the three strong primary H-bonds.

Scheme 2. Monoquat Redox Reactions



The electroactive motif in H(MQ$^+$)H is the central N-methyl-4,4'-bipyridinum, which is commonly called "monoquat", MQ$^+$. As shown in Scheme 2, MQ$^+$ undergoes two sequential one electron reductions in aprotic solvents forming first the uncharged radical and then the quinoidal anion. A small increase in the basicity of the pyridine N would be expected upon reduction to the radical, followed by a much larger increase in basicity upon formation of the quinoidal anion.

Scheme 3. General Scheme for Reduction of MQ$^+$ in the Presence of O(NH)O



Possible redox reactions that could occur upon addition of O(NH)O to MQ$^+$ (or H(MQ$^+$)H) are outlined in Scheme 3. Given the large increase in basicity upon reduction of MQ to MQ$^-$, the strongest interaction between O(NH)O and either MQ$^+$ or H(MQ$^+$)H will be in the fully reduced anion state. This interaction could either be formation of a H-bond, HB, complex (with or without PT) or full PT resulting in the formation of the solvent-separated conjugate acid and base. In either case, with one equivalent of O(NH)O added, the second reduction will occur at potential E3, corresponding to the red diagonal in Scheme 3. E3 will be positive of E2 due to stabilization of the fully reduced MQ$^-$ by HB or PT. However, since the overall reaction has O(NH)O as a reactant, from the Nernst equation, addition of more O(NH)O will shift the observed E of the second reduction further positive until it reaches E4. At this point, the observed E quits changing, since the overall reaction (bottom row in Scheme 3) no longer involves O(NH)O

directly, being either reduction of the already formed HB complex or reduction of the already protonated radical, MQH^+.

The difference between HB and full PT is where E4 falls relative to E1. If it is PT, E4 will be positive of E1, since it will be easier to reduce the radical cation than the original cation; if it is HB, E4 will be negative of E1, because it will be harder to reduce the overall zero charge H-bond complex than the original cation. This means full PT will lead to the second reduction shifting into the first, eventually resulting in a single two electron transfer, but HB will not. With HB, the maximum potential shift of the second reduction will stop short of the first reduction.

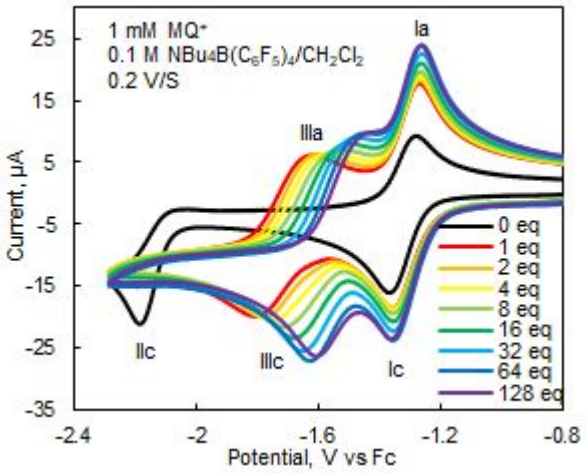


Figure 1. Background-subtracted CV's of MQ^+ with added O(NH)O in 0.1 M $NBu_4B(C_6F_5)_4/CH_2Cl_2$.

Since MQ^+ just has one strong H-bonding group (the pyridyl N), full PT leading to the solvent separated conjugate acid and conjugate base is much more likely than formation of a strong H-bond complex. This hypothesis was tested by recording cyclic voltammograms (CV's) of MQ^+ with increasing concentrations of O(NH)O in CH_2Cl_2, Figure 1. In the absence of O(NH)O, two sequential reductions, Ic and IIc, are observed, black trace. The first reduction is completely reversible if the scan direction is reversed before the second reduction, but the second reduction is irreversible as indicated by the absence of the corresponding oxidation peak. Similar behavior is observed with $H(MQ^+)H$ in CH_2Cl_2, Figure 2. However, in acetonitrile, both reductions of MQ are completely reversible, Figure S8, so we attribute the irreversibility of the second reduction to reaction of the anion with CH_2Cl_2.[62]

As expected, addition of O(NH)O to MQ^+ has a significant effect on the voltammetry. With addition of just 1 equivalent there is a +380 mV shift in the $E_{1/2}$ of the second reduction (now labeled wave III) accompanied by a switch from irreversible to reversible behavior, indicating reaction of the anion with the solvent has been prevented. There is little change in $E_{1/2}$ of the first reduction but there is a small increase in current. As more O(NH)O is added, wave III continues to shift positive while wave I continues to increase in current. Additions were stopped at 128 equivalents due to the onset of electrode fouling, but clearly there is no indication that wave III has reached its maximum shift As discussed above, this is exactly the behavior expected if full PT occurs between MQ^- and O(NH)O leading to the solvent-separated MQH and $O(N^-)O$.[63]

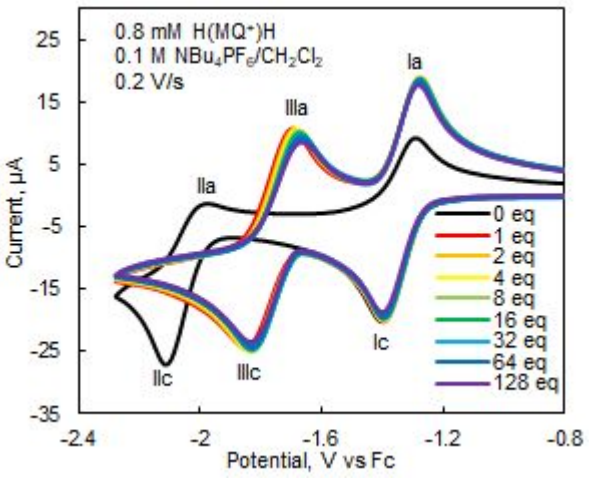


Figure 2. Background-subtracted CV's of $H(MQ^+)H$ with added O(NH)O in 0.1 M NBu_4PF_6/CH_2Cl_2.

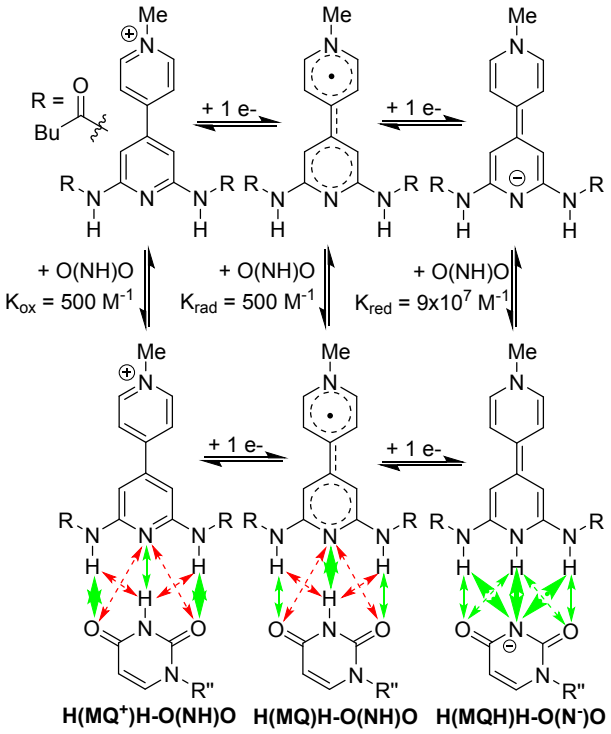
For comparison, Figure 2 shows CV's resulting from addition of O(NH)O to $H(MQ^+)H$ under similar conditions.[64] As with MQ^+, addition of only one equivalent of O(NH)O, red trace, causes little change in $E_{1/2}$ of the first reduction, but the second reduction shifts positive by a substantial amount and becomes fully reversible. However, unlike MQ^+, further additions of 2, 4 and 8 equivalents of O(NH)O, only lead to a slight further positive shift in $E_{1/2}$ of the second reduction. Beyond that, there is no significant further shift, indicating that the maximum $E_{1/2}$ shift has been reached long before the second CV wave merges with the first. In contrast to the behavior observed with MQ^+ and O(NH)O, this behavior is consistent with the formation of a very strong 1:1 H-bond complex between the fully reduced $H(MQ^-)H$ and O(NH)O rather than formation of the solvent separated conjugate acid and conjugate base.

$$\frac{K_{red}}{K_{ox}} = 10^{\frac{\Delta E_{max}}{0.0592\ V}} \quad (1)$$

The simplest reaction scheme that can account for the observed voltammetry of $H(MQ^+)H$ in the presence of O(NH)O in CH_2Cl_2 is given in Scheme 4. Estimates of the K_{assoc} values in the different oxidation states can be made using the relationship between the maximum $\Delta E_{1/2}$ and the ratio of the equilibrium constants for a square scheme, eq 1. From the NMR titration, K_{ox} = 505 M^{-1}. Since there is no significant $E_{1/2}$ shift in the first reduction upon addition of O(NH)O, K_{rad} must also be close to 505 M^{-1}. However, K_{red} shows a significant positive shift with $\Delta E_{1/2,\ max}$ = 0.311 V (average of 5 independent runs). From eq 1, this corresponds to a 1.8×10^5-fold increase in binding constant, making $K_{red} = 9\times10^7$ M^{-1}. This very large value is consistent with those reported for DDD-AAA H-bond dimers,[59-60] suggesting that, as predicted, PT across the H-bond occurs upon addition of the second electron to give the $H(MQH)H–O(N^-)O$ dimer. That PT should occur is also consistent with the observed voltammetry of MQ^+ and O(NH)O, which indicates that the fully reduced MQ^- is a strong enough base to deprotonate O(NH)O. Finally, UV-vis spectroelectrochemical studies described in the SI strongly

support the hypothesis that the fully reduced complex involves H(MQH)H and O(N⁻)O, rather than H(MQ⁻)H and O(NH)O.

Scheme 4. Reduction of H(MQ⁺)H in the Presence of O(NH)O in CH_2Cl_2



In conclusion, this study demonstrates a powerful new PCET-based strategy for creating highly redox-responsive H-bond dimers through cooperation between electron transfer and proton transfer. Strong, selective stimuli-responsive bonding, such as that demonstrated with H(MQ⁺)H-O(NH)O, is key to many supramolecular applications under current investigation, e.g., those involving the controlled release/uptake of chemicals, as well as future applications involving molecular machines. Whether H(MQ⁺)-O(NH)O has the long-term stability for practical application remains to be seen, but the principles are not unique to this system, and undoubtably there are even better PCET-based redox-responsive H-bonding systems out there awaiting discovery.

ASSOCIATED CONTENT

Supporting Information. Synthetic procedures, structural characterization of H(MQ⁺)H, NMR titration data with fits to 1:1 binding isotherm, voltammetry procedures, results of UV-vis spectroelectrochemical studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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REFERENCES

1. Zhang, Y.-M.; Liu, Y.-H.; Liu, Y., Cyclodextrin-Based Multistimuli-Responsive Supramolecular Assemblies and Their Biological Functions. *Adv. Mater.* **2020**, *32*, 1806158.
2. Isaacs, L., Stimuli Responsive Systems Constructed Using Cucurbit n uril-Type Molecular Containers. *Acc. Chem. Res.* **2014**, *47*, 2052-2062.
3. Kakuta, T.; Yamagishi, T.; Ogoshi, T., Stimuli-Responsive Supramolecular Assemblies Constructed from Pillar n arenes. *Acc. Chem. Res.* **2018**, *51*, 1656-1666.
4. Yan, X.; Wang, F.; Zheng, B.; Huang, F., Stimuli-responsive supramolecular polymeric materials. *Chem. Soc. Rev.* **2012**, *41*, 6042-6065.
5. Hoque, J.; Sangaj, N.; Varghese, S., Stimuli-Responsive Supramolecular Hydrogels and Their Applications in Regenerative Medicine. *Macromol. Biosci.* **2019**, *19*, 1800259.
6. Nijhuis, C. A.; Ravoo, B. J.; Huskens, J.; Reinhoudt, D. N., Electrochemically controlled supramolecular systems. *Coord. Chem. Rev.* **2007**, *251*, 1761-1780.
7. Gu, H. B.; Mu, S. D.; Qiu, G. R.; Liu, X.; Zhang, L.; Yuan, Y. F.; Astruc, D., Redox-stimuli-responsive drug delivery systems with supramolecular ferrocenyl-containing polymers for controlled release. *Coord. Chem. Rev.* **2018**, *364*, 51-85.
8. Liu, X.; Zhao, L.; Liu, F.; Astruc, D.; Gu, H., Supramolecular redox-responsive ferrocene hydrogels and microgels. *Coord. Chem. Rev.* **2020**, *419*, 213406.
9. Schröder, Hendrik V.; Schalley, C. A., Electrochemically switchable rotaxanes: recent strides in new directions. *Chem. Sci.* **2019**, *10*, 9626-9639.
10. Baroncini, M.; Silvi, S.; Credi, A., Photo- and Redox-Driven Artificial Molecular Motors. *Chem. Rev.* **2020**, *120*, 200-268.
11. Coskun, A.; Spruell, J. M.; Barin, G.; Dichtel, W. R.; Flood, A. H.; Botros, Y. Y.; Stoddart, J. F., High hopes: can molecular electronics realise its potential? *Chem. Soc. Rev.* **2012**, *41*, 4827-4859.
12. Cram, D. J., The Design of Molecular Hosts, Guests, and Their Complexes (Nobel Lecture). *Angew. Chem.-Int. Edit. Engl.* **1988**, *27*, 1009-1020.
13. Lehn, J.-M., Supramolecular Chemistry—Scope and Perspectives Molecules, Supermolecules, and Molecular Devices (Nobel Lecture). *Angew. Chem.-Int. Edit. Engl.* **1988**, *27*, 89-112.
14. Chang, S. K.; Hamilton, A. D., Molecular recognition of biologically-interesting substrates: synthesis of an artifical receptor for barbiturates employing six hydrogen bonds. *J. Am. Chem. Soc.* **1988**, *110*, 1318-1319.
15. Simard, M.; Su, D.; Wuest, J. D., Use of hydrogen bonds to control molecular aggregation. Self-assembly of three-dimensional networks with large chambers. *J. Am. Chem. Soc.* **1991**, *113*, 4696-4698.
16. Wyler, R.; de Mendoza, J.; Rebek Jr., J., A Synthetic Cavity Assembles Through Self-Complementary Hydrogen Bonds. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1699-1701.
17. Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D.; Mammen, M.; Gordon, D. M., Noncovalent Synthesis: Using Physical-Organic Chemistry To Make Aggregates. *Acc. Chem. Res.* **1995**, *28*, 37-44.

18. MacGillivray, L. R.; Atwood, J. L., A chiral spherical molecular assembly held together by 60 hydrogen bonds. *Nature* **1997**, *389*, 469-472.

19. Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W., Reversible polymers formed from self-complementary monomers using quadruple hydrogen bonding. *Science* **1997**, *278*, 1601-1604.

20. Gatti, F. G.; Leigh, D. A.; Nepogodiev, S. A.; Slawin, A. M. Z.; Teat, S. J.; Wong, J. K. Y., Stiff, and Sticky in the Right Places: The Dramatic Influence of Preorganizing Guest Binding Sites on the Hydrogen Bond-Directed Assembly of Rotaxanes. *J. Am. Chem. Soc.* **2001**, *123*, 5983-5989.

21. Park, T.; Todd, E. M.; Nakashima, S.; Zimmerman, S. C., A quadruply hydrogen bonded heterocomplex displaying high-fidelity recognition. *J. Am. Chem. Soc.* **2005**, *127*, 18133-18142.

22. Liu, Y.; Zhao, W.; Chen, C.-H.; Flood, A. H., Chloride capture using a C–H hydrogen-bonding cage. *Science* **2019**, *365*, 159-161.

23. Sun, Y. R.; Gu, J.; Wang, H. Y.; Sessler, J. L.; Thordarson, P.; Lin, Y. J.; Gong, H. G., AAAA-DDDD Quadruple H-Bond-Assisted Ionic Interactions: Robust Bis(guanidinium)/Dicarboxylate Heteroduplexes in Water. *J. Am. Chem. Soc.* **2019**, *141*, 20146-20154.

24. Coubrough, H. M.; van der Lubbe, S. C. C.; Hetherington, K.; Minard, A.; Pask, C.; Howard, M. J.; Fonseca Guerra, C.; Wilson, A. J., Supramolecular Self-Sorting Networks using Hydrogen-Bonding Motifs. *Chemistry – A European Journal* **2019**, *25*, 785-795.

25. Shi, Q.; Zhou, X.; Yuan, W.; Su, X.; Neniškis, A.; Wei, X.; Taujenis, L.; Snarskis, G.; Ward, J. S.; Rissanen, K.; de Mendoza, J.; Orentas, E., Selective Formation of S4- and T-Symmetric Supramolecular Tetrahedral Cages and Helicates in Polar Media Assembled via Cooperative Action of Coordination and Hydrogen Bonds. *J. Am. Chem. Soc.* **2020**, *142*, 3658-3670.

26. Merget, S.; Catti, L.; Piccini, G.; Tiefenbacher, K., Requirements for Terpene Cyclizations inside the Supramolecular Resorcinarene Capsule: Bound Water and Its Protonation Determine the Catalytic Activity. *J. Am. Chem. Soc.* **2020**, *142*, 4400-4410.

27. Zhang, Q.; Li, T.; Duan, A.; Dong, S. Y.; Zhao, W. X.; Stang, P. J., Formation of a Supramolecular Polymeric Adhesive via Water-Participant Hydrogen Bond Formation. *J. Am. Chem. Soc.* **2019**, *141*, 8058-8063.

28. Meng, P.; Brock, A.; Xu, Y.; Han, C.; Chen, S.; Yan, C.; McMurtrie, J.; Xu, J., Crystal Transformation from the Incorporation of Coordinate Bonds into a Hydrogen-Bonded Network Yields Robust Free-Standing Supramolecular Membranes. *J. Am. Chem. Soc.* **2020**, *142*, 479-486.

29. Hisaki, I.; Xin, C.; Takahashi, K.; Nakamura, T., Designing Hydrogen-Bonded Organic Frameworks (HOFs) with Permanent Porosity. *Angew. Chem.-Int. Edit.* **2019**, *58*, 11160-11170.

30. Evans, N. H., Recent Advances in the Synthesis and Application of Hydrogen Bond Templated Rotaxanes and Catenanes. *Eur. J. Org. Chem.* **2019**, *2019*, 3320-3343.

31. Biagini, C.; Fielden, S. D. P.; Leigh, D. A.; Schaufelberger, F.; Di Stefano, S.; Thomas, D., Dissipative Catalysis with a Molecular Machine. *Angew. Chem.-Int. Edit.* **2019**, *58*, 9876-9880.

32. Hein, R.; Beer, P. D.; Davis, J. J., Electrochemical Anion Sensing: Supramolecular Approaches. *Chem. Rev.* **2020**, *120*, 1888-1935.

33. Altieri, A.; Gatti, F. G.; Kay, E. R.; Leigh, D. A.; Martel, D.; Paolucci, F.; Slawin, A. M. Z.; Wong, J. K. Y., Electrochemically Switchable Hydrogen-Bonded Molecular Shuttles. *J. Am. Chem. Soc.* **2003**, *125*, 8644-8654.

34. Fioravanti, G.; Haraszkiewicz, N.; Kay, E. R.; Mendoza, S. M.; Bruno, C.; Marcaccio, M.; Wiering, P. G.; Paolucci, F.; Rudolf, P.; Brouwer, A. M.; Leigh, D. A., Three State Redox-Active Molecular Shuttle That Switches in Solution and on a Surface. *J. Am. Chem. Soc.* **2008**, *130*, 2593-2601.

35. Li, Y.; Park, T.; Quansah, J. K.; Zimmerman, S. C., Synthesis of a Redox-Responsive Quadruple Hydrogen-Bonding Unit for Applications in Supramolecular Chemistry. *J. Am. Chem. Soc.* **2011**, *133*, 17118-17121.

36. Ji, X.; Jie, K.; Zimmerman, S. C.; Huang, F., A double supramolecular crosslinked polymer gel exhibiting macroscale expansion and contraction behavior and multistimuli responsiveness. *Polym. Chem.* **2015**, *6*, 1912-1917.

37. Milić, J. V.; Diederich, F., The Quest for Molecular Grippers: Photo-Electric Control of Molecular Gripping Machinery. *Chem.-Eur. J.* **2019**, *25*, 8440-8452.

38. Stoddart, J. F., Mechanically Interlocked Molecules (MIMs)-Molecular Shuttles, Switches, and Machines (Nobel Lecture). *Angew. Chem.-Int. Edit.* **2017**, *56*, 11094-11125.

39. Sauvage, J. P., From Chemical Topology to Molecular Machines (Nobel Lecture). *Angew. Chem.-Int. Edit.* **2017**, *56*, 11080-11093.

40. Ge, Y.; Lilienthal, R. R.; Smith, D. K., Electrochemically-Controlled Hydrogen Bonding. Selective Recognition of Urea and Amide Derivatives by Simple Redox-Dependent Receptors. *J. Am. Chem. Soc.* **1996**, *118*, 3976-7.

41. Ge, Y.; Miller, L.; Ouimet, T.; Smith, D. K., Electrochemically Controlled Hydrogen Bonding. o-Quinones as Simple Redox-Dependent Receptors for Arylureas. *J. Org. Chem.* **2000**, *65*, 8831-8838.

42. Bu, J.; Lilienthal, N. D.; Woods, J. E.; Nohrden, C. E.; Hoang, K. T.; Truong, D.; Smith, D. K., Electrochemically Controlled Hydrogen Bonding. Nitrobenzenes as Simple Redox-Dependent Receptors for Arylureas. *J. Am. Chem. Soc.* **2005**, *127*, 6423-6429.

43. Woods, J. E.; Ge, Y.; Smith, D. K., Electrochemically Controlled Hydrogen Bonding. Electrolyte Effects in an Oxidation-Based Arylurea-Amide System. *J. Am. Chem. Soc.* **2008**, *130*, 10070-10071.

44. Clare, L. A.; Smith, D. K., Use of an electrochemically-induced proton-coupled electron transfer reaction to control dimerization in a ureidopyrimidone 4 H-bond array. *Chem. Commun.* **2016**, *52*, 7253-7256.

45. Cedano, M. R.; Smith, D. K., Redox-Responsive Dimerization in a Ferrocene-Ureidopyrimidone Supramolecular Assembly. *J. Org. Chem.* **2018**, *83*, 11595-11603.

46. Kajiki, T.; Moriya, H.; Hoshino, K.; Kuroi, T.; Kondo, S. i.; Nabeshima, T.; Yano, Y., Functionalized Flavin Receptors. Regulation of Redox Properties of 6-Azaflavin via Hydrogen Bondings with Melamine Derivatives Bearing Guanidinium Ion(s) in Organic Solvents. *J. Org. Chem.* **1999**, *64*, 9679-9689.

47. Carr, J. D.; Coles, S. J.; Hursthouse, M. B.; Light, M. E.; Tucker, J. H. R.; Westwood, J., Redox-switched control of binding strength in hydrogen-bonded metallocene complexes. *Angew. Chem., Int. Ed.* **2000**, *39*, 3296-3299.

48. Gray, M.; Cuello, A. O.; Cooke, G.; Rotello, V. M., Hydrogen Bonding in Redox-Modulated Molecular Recognition. An Experimental and Theoretical Investigation. *J. Am. Chem. Soc.* **2003**, *125*, 7882-7888.

49. Cheng, H.-C.; Chiu, K. Y.; Tu, Y.-J.; Yang, T.-F.; Su, Y. O., Electrochemically Controlled Multiple Hydrogen Bonding between Triarylamines and Imidazoles. *Org. Lett.* **2013**, *15*, 3868-3871.

50. Martinez-Gonzalez, E.; Armendariz-Vidales, G.; Ascenso, J. R.; Marcos, P. M.; Frontana, C., Site-Specific Description of the Enhanced Recognition Between Electrogenerated Nitrobenzene Anions and Dihomooxacalix[4]arene Bidentate Ureas. *J. Org. Chem.* **2015**, *80*, 4581-4589.

51. Benson, C. R.; Fatila, E. M.; Lee, S.; Marzo, M. G.; Pink, M.; Mills, M. B.; Preuss, K. E.; Flood, A. H., Extreme Stabilization and Redox Switching of Organic Anions and Radical Anions by Large-Cavity, CH Hydrogen-Bonding Cyanostar Macrocycles. *J. Am. Chem. Soc.* **2016**, *138*, 15057-15065.

52. Turek, A. K.; Hardee, D. J.; Ullman, A. M.; Nocera, D. G.; Jacobsen, E. N., Activation of Electron-Deficient Quinones through

Hydrogen-Bond-Donor-Coupled Electron Transfer. *Angew. Chem.-Int. Edit.* **2016**, *55*, 539-544.

53. Jorgensen, W. L.; Pranata, J., Importance of secondary interactions in triply hydrogen bonded complexes: guanine-cytosine vs uracil-2,6-diaminopyridine. *J. Am. Chem. Soc.* **1990**, *112*, 2008-2010.

54. Pranata, J.; Wierschke, S. G.; Jorgensen, W. L., OPLS potential functions for nucleotide bases. Relative association constants of hydrogen-bonded base pairs in chloroform. *J. Am. Chem. Soc.* **1991**, *113*, 2810-2819.

55. Sartorius, J.; Schneider, H. J., A general scheme based on empirical increments for the prediction of hydrogen-bond associations of nucleobases and of synthetic host-guest complexes. *Chem. - Eur. J.* **1996**, *2*, 1446-1452.

56. Murray, T. J.; Zimmerman, S. C., New Triply Hydrogen-Bonded Complexes with HIghly Variable Stabilities. *J. Am. Chem. Soc.* **1992**, *114*, 4010-4011.

57. Blight, B. A.; Hunter, C. A.; Leigh, D. A.; McNab, H.; Thomson, P. I. T., An AAAA-DDDD quadruple hydrogen-bond array. *Nat. Chem.* **2011**, *3*, 244-248.

58. van der Lubbe, S. C. C.; Zaccaria, F.; Sun, X. B.; Guerra, C. F., Secondary Electrostatic Interaction Model Revised: Prediction Comes Mainly from Measuring Charge Accumulation in Hydrogen-Bonded Monomers. *J. Am. Chem. Soc.* **2019**, *141*, 4878-4885.

59. Blight, B. A.; Camara-Campos, A.; Djurdjevic, S.; Kaller, M.; Leigh, D. A.; McMillan, F. M.; McNab, H.; Slawin, A. M. Z., AAA-DDD Triple Hydrogen Bond Complexes. *J. Am. Chem. Soc.* **2009**, *131*, 14116-14122.

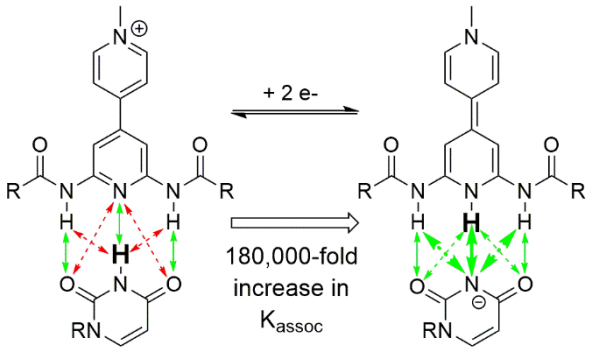
60. Han, Y.-F.; Chen, W.-Q.; Wang, H.-B.; Yuan, Y.-X.; Wu, N.-N.; Song, X.-Z.; Yang, L., An AAA-DDD Triply Hydrogen-Bonded Complex Easily Accessible for Supramolecular Polymers. *Chem.-Eur. J.* **2015**, *20*, 16980-16986.

61. Beijer, F. H.; Sijbesma, R. P.; Vekemans, J.; Meijer, E. W.; Kooijman, H.; Spek, A. L., Hydrogen-bonded complexes of diaminopyridines and diaminotriazines: Opposite effect of acylation on complex stabilities. *J. Org. Chem.* **1996**, *61*, 6371-6380.

62. Staley, P. A.; Lopez, E. M.; Clare, L. A.; Smith, D. K., Kinetic Stabilization of Quinone Dianions via Hydrogen Bonding by Water in Aprotic Solvents. *J. Phys. Chem. C* **2015**, *119*, 20319-20327.

63. Although the final product is not the HB complex, it is highly likely that a HB intermediate is involved in the overall reaction occurring in wave III. See Clare, L. A.; Pham, T. D.; Rafou, L. A.; Buenaventura, A. G.; Scott, T. R.; Mikhaylova, V.; Smith, D. K., The Role of H-Bonding in Nonconcerted Proton-Coupled Electron Transfer: Explaining the Voltammetry of Phenylenediamines in the Presence of Weak Bases in Acetonitrile. *J. Phys. Chem. C* **2019**, *123*, 23390-23402.

64. Due to solubility issues, $NBu_4B(C_6F_5)_4$ was used as the electrolyte with MQ^+ in CH_2Cl_2, whereas the more common (and much less expensive) electrolyte, NBu_4PF_6, was used with $H(MQ^+)H$. If anything use of $NBu_4B(C_6F_5)_4$ with MQ^+ would have promoted H-bonding over proton transfer.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