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Molecular recognition and switching via radical dimerization*

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Abstract: This article highlights the emerging use of the interactions of radical π-dimers to drive both molecular recognition and switching processes within supramolecular systems and mechanically interlocked molecular architectures. The enhanced stability experienced by dimers of radical cation species when encapsulated, as compared to when they are free in solution, is driving their useful incorporation into functional systems. The redox stimulation used in the production of radical cation species provides the ideal trigger for molecular switching events. Moreover, the nature and strength of the radical dimerization events introduces a completely novel recognition motif within supramolecular and mechanically interlocked molecular systems, complementing well-established techniques and enabling new research opportunities to blossom.

Keywords: π-dimerization; mechanical bonds; mechanostereochemistry; molecular machines; radical cations; supramolecular chemistry; tetrathiafulvalene; viologen.

INTRODUCTION

The nature of bonding within chemical architectures forms the cornerstone of chemical science. Whether atoms are held together through purely ionic interactions or share electrons equally within an ideal covalent bond, the joining of two atoms through chemical bonding is central to the fundamental understanding of chemical systems. Oftentimes, we become content with these two extreme cases (and classifications in between) to describe chemical bonding. However, of greater fascination are the more unusual types of bonding associated with (i) supramolecular interactions (i.e., hydrogen bonding, donor–acceptor π-stacking, etc.), (ii) mechanical bonding (i.e., catenation, rotaxanation, and knotting), and (iii) multi-atom-centered bonding (e.g., radical dimerization of planar π-systems). Each type of bonding offers unique characteristics that may be leveraged for different tasks. For example, the reversibility and dynamic nature of the bonding types (i), (ii), and (iii) provide the possibility to design switchable molecular systems, especially when robustness may be attained. A virtue of the mechanical bond is that it offers the robustness of a covalent bond, while maintaining much of the dynamic nature of the weaker supramolecular interactions. This short review focuses on what amounts to a renaissance in our understanding and practical use of one type of unusual bonding—the long multi-atom-centered radical dimerization of planar π-systems—within dynamic chemical systems to drive both molecular recognition and mechanical switching. I will begin by reviewing the earliest observations of multi-

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atom-centered radical dimerization and, thereafter, I will highlight the recent advances that have led to the use of this unusual class of bonding as a practical and fully orthogonal molecular recognition motif.

EARLY EXAMPLES OF RADICAL DIMERS

The π-dimerization of planar radical species was first observed in the middle of the last century [1–6] in both the solid state and in concentrated solutions at low temperatures. Under these conditions, equilibria are established between two paramagnetic free radical species and a diamagnetic dimer, most often with a particular equilibrium favoring the dissociated, non-dimer state. These types of dimeric associations have been observed for a whole range of different types of planar radical species, varying in both the size of the planar systems and the charges of the dimer components. Both radical anions and cations, as well as neutral free radicals, have been observed to associate with one another in this manner. Some of the most common radical π-dimeric species are illustrated in Fig. 1, including the associated radical anions of singly reduced tetracyanoethylene (TCNE) [7], and the neutral radical pairs of phenalenyl [8], as well as the radical cation π-dimers of singly oxidized tetrathiafulvalene (TTF) [9,10] and singly reduced bipyridium ($BIPY^{2+}$) units [11,12].

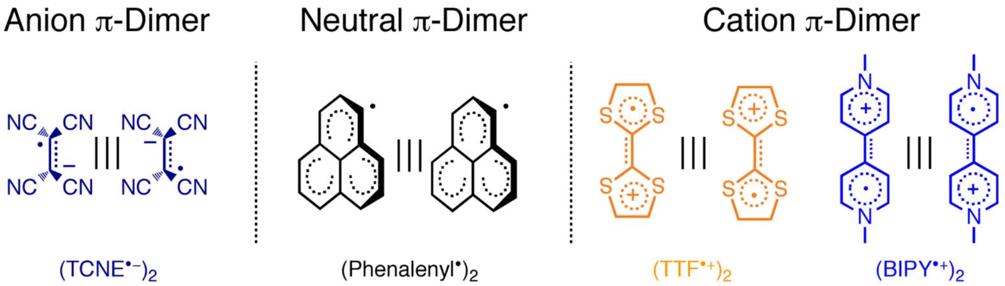

Fig. 1 Common π-dimers involving anionic tetracyanoethylene ($TCNE^{\bullet-}$) and neutral phenalenyl, as well as $TTF^{\bullet+}$ and $BIPY^{\bullet+}$ radical species. The cation π-dimers formed between $TTF^{\bullet+}$ and $BIPY^{\bullet+}$ appear to be the most useful for driving supramolecular recognition and switching processes. Redox activation provides a facile route to each of these radical π-dimers.

The π-association of phenalenyl has received much attention [8,13] as a model for the radical dimerization of large planar π-systems. The persistent (i.e., stable) neutral radical is readily generated during the oxidation of phenylene. Its stability can be attributed to the delocalization of the radical throughout the fused polycyclic structure, its character residing predominately on 6 of the 12 peripheral carbons [14,15]. When substituted with bulky side groups to prevent σ-binding (the radical–radical coupling to form a traditional covalent sigma (σ) bond), π-dimer formation is observed in concentrated deoxygenated solutions. Moreover, this π-dimer is comprised of two perfectly overlapping delocalized singly occupied molecular orbitals (SOMOs) on each phenalenyl unit in such a way that the two formal free radical electrons pair to form what has been described as a two-electron/12 atom-centered bond [15]. This reversible bonding has been studied both experimentally and computationally, leading to good agreement on the diamagnetic nature of the bond, the dissociation energy (~10–15 kcal/mol), and the antiparallel arrangement of the π-faces separated by an interplanar distance of ~3.2 Å.

Because of their stable redox chemistry and associated redox-driven property changes, π-electron-poor compounds, such as TCNE and methyl viologen, and π-electron-rich compounds, such as TTF, have laid the foundations for the development of electronic devices based upon organic molecules. Volumes have been written about each of these compounds [16,17], much more than I have room to discuss here. Suffice it to say that they have been well studied and are highly useful compounds, especially because they may either accept or donate electrons readily on demand—attributes that lend themselves well to applications, ranging from electron-mediated catalysis [18], photochromic displays [19], organic metals [16], and solar energy conversion [20]. Additionally, each of these species is well known [21,22] to self-assemble in donor–acceptor-based π-stacking motifs with planar compounds of the opposite polarity. Orthogonal to this "traditional" donor–acceptor π-stacking is the homodimerization of each in either their radical cation or radical anion forms. In contrast with the association of the neutral phenalenyl radical π-dimer, the dimerization of these charged radical species should result in the build-up of electrostatic repulsion within the complex. There has been some debate [23] in the literature as to whether solvent or counterion bridging may be present to help alleviate some of the Coloumbic repulsion experienced between the radical π-dimers. I will return to this subject later in the review. Regardless, weak association of these charged species has been observed, both in the solid state and in concentrated solutions. In each case, however, the radical π-dimers of the parent units have been only minor components of solution mixtures—i.e., formed with low association constants—or observed at low temperature in the solid state. Moreover, they exhibit air, temperature, and moisture sensitivity—all of which relegates the occurrence of such radical dimers to little more than chemical curiosities, rather than making them the basis for robust technologies.

SUPRAMOLECULAR ENCAPSULATION—STABILIZING RADICAL DIMERS

Whereas the parent compounds, TTF and methyl viologen, only form radical cation π-dimers under very specific conditions and can most readily be described as unstable and sensitive complexes, recent research has shown that supramolecular encapsulation greatly increases the association constant for these interesting dimeric species. In seminal work performed by Kim and co-workers [24], it was observed (Fig. 2a) that 1:1 complexes of $BIPY^{2+}$:cucurbit[8]uril (CB8) could be converted quantitatively to 2:1 complexes of $(BIPY^{\bullet+})_2$:CB8, following the single reduction of the included $BIPY^{2+}$ dication. CB8 is a highly symmetrical macropolycyclic cavitand, comprised of eight glycouril units. The molecule contains a large hydrophobic cavity fringed on the top and bottom with carbonyl functions [25]. These features make CB8 and its smaller homologues ideal hosts for hydrophobic planar guests in aqueous solution; moreover, the large cavity inside CB8 accommodates comfortably 2 equiv of the hydrophobic guest. The Korean team took advantage of these properties to form stabilized radical cation dimers of $(BIPY^{\bullet+})_2$ within the hydrophobic cavity of CB8. In the presence of the CB8 host, the association constant for the $(BIPY^{\bullet+})_2$ increases dramatically by over five orders of magnitude to $\sim 2 \times 10^7$ M^{-1} in aqueous solution. This significant enhancement in stability can be attributed to the apparent high local concentration of $BIPY^{\bullet+}$ dications within the cavity of CB8.

Utilizing these same design principles, Kim et al. [26] followed their initial studies on the radical π-dimerization of $(BIPY^{\bullet+})_2$ with an elegant study of the dimerization of $TTF^{\bullet+}$ radical cations, stabilized also through encapsulation within CB8. Because $BIPY^{\bullet+}$ is generated by the reduction of $BIPY^{2+}$, the resulting radical species is susceptible to re-oxidation in air back to $BIPY^{2+}$. Therefore, all experiments must be carried out in an inert atmosphere. By contrast, TTF may be oxidized singly or doubly to either the radical cation, $TTF^{\bullet+}$, or the dication, TTF^{2+}—both of which are persistent and stable species under atmospheric conditions in solution. These features enable $TTF^{\bullet+}$ radical cations to be generated and employed in a much wider variety of settings than the more sensitive $BIPY^{\bullet+}$ analogue. Indeed, Kim and co-workers [26] have found (Fig. 2b) that, not only is $TTF^{\bullet+}$ compatible with ambient conditions, but also CB8 acts as an effective oxidation catalyst for TTF in air. Essentially, the high stability of the radical cation $(TTF^{\bullet+})_2$ dimer within the CB8 cavity decreases the first oxidation potential of TTF to such an extent that O_2 in the air acts as an effective oxidant. The quantitative formation of diamagnetic $(TTF^{\bullet+})_2$ radical cation π-dimers within the CB8 cavity was also verified utilizing ^1H NMR, UV–vis–NIR, and electron paramagnetic resonance (EPR) spectroscopies.

These key studies—especially the findings of highly associated complexes for both types of radical-cation dimers based around $BIPY^{2+}$ and TTF—have enabled effective supramolecular switching to

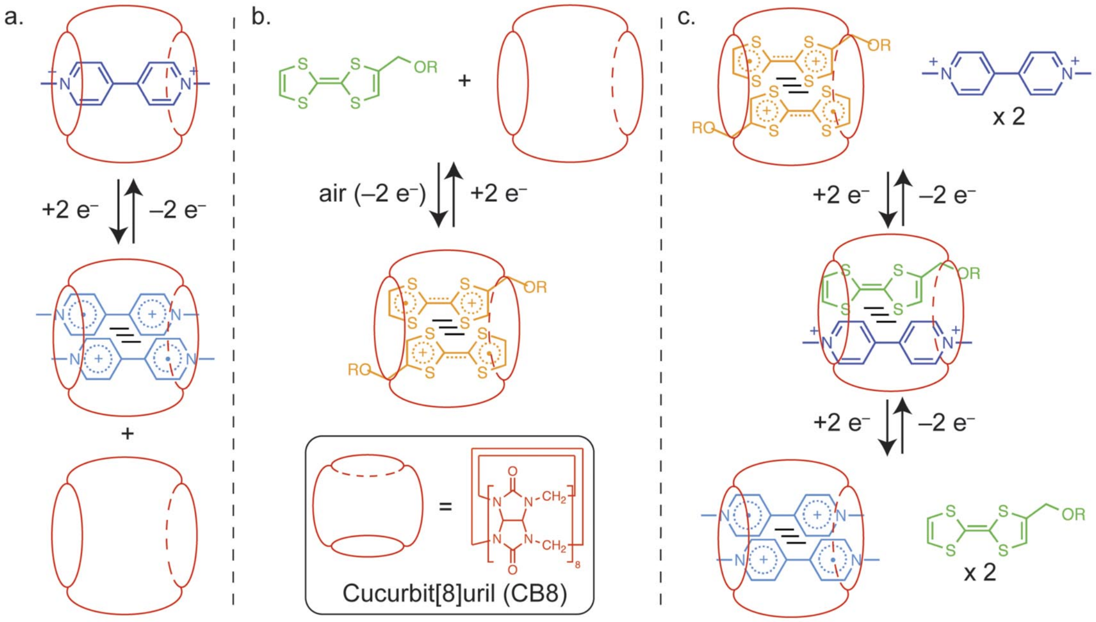

Fig. 2 The valuable role of encapsulation for the stabilization of radical π-dimers. CB8 significantly enhances the formation of both (a) $(BIPY^{\bullet +})_2$ [24] and (b) $(TTF^{\bullet +})_2$ dimers [26]. The clever combination of these two redox systems results in a three-state supramolecular switch (c) in which three inputs can be given, resulting in three separate outcomes [27].

be driven by radical π-dimerization. By mixing various equivalents of a TTF derivative, $BIPY^{2+}$, and CB8 under inert atmosphere, Kim et al. [27] have employed the CB8 as a host for three discrete dimeric pairs within its large cavity, the selection of which may be made through the redox state of the solution (Fig. 2c). Under zero electrochemical bias, the donor–acceptor heterodimer of TTF and $BIPY^{2+}$ is the predominant species formed within the cavity. However, this situation changes with the application of either positive or negative potentials—where oxidation results in the formation of encapsulated highly stabilized $(TTF^{\bullet +})_2$ radical cation dimers, while reduction results in the similarly encapsulated $(BIPY^{\bullet +})_2$ radical pair and the subsequent ejection of the other species.

A similar multistable supramolecular switching system, based upon CB8 pseudorotaxanes, was demonstrated by Stoddart and co-workers [28] who have shown that long molecules, incorporating both the electron-poor $BIPY^{2+}$ and electron-rich dioxynaphthalene (DNP) units joined through flexible tetraethylene glycol linkers, associate within the large CB8 macrocycle. Under zero electrochemical bias, a single thread is associated with the CB8 macrocycle and bent to allow double encapsulation of both the DNP and $BIPY^{2+}$ units in a donor–acceptor type of heterodimer structure. Upon the application of a reducing potential, however, the system rearranges to form the stabilized $(BIPY^{\bullet +})_2$ radical π-dimers within the CB8 cavity. Depending on the choice of the specific thread employed in the complex formation, either a single thread or two threads per CB8 ring are incorporated within the complex in the reduced $(BIPY^{\bullet +})_2$ dimerized state. Moreover, this supramolecular switching is fully reversible and operative under redox control.

By using a related encapsulation approach, Fujita and co-workers [29] have observed stabilized dimer pairs of TTF. In their system, however, it is the so-called mixed-valence dimer that is stabilized within the cavity of a self-assembled molecular cage. This cage structure forms spontaneously upon mixing Pd ions with 2 equiv of tris(4-pyridyl)triazine ligands and 3 bipyridine derivatives to form a highly symmetrical 11-component structure; the 2 tris(4-pyridyl)triazine ligands, moreover, are situated in parallel and separated by ~10 Å—providing ample room for the inclusion of 2 guests within the cavity. TTF is one of the few organic compounds in which mixed-valence species occur. It is composed of an associated pair of TTF units in which one unit is formally oxidized to the radical cation state ($TTF^{•+}$) while the other one remains neutral (Fig. 3). Within the dimer pair, however, the radical nature (i.e., the SOMO) is shared equally between the two units. We will denote this mixed-valence state as $(TTF)_2^{•+}$. These species exhibit very distinctive absorption characteristics with peaks occurring far into the near-IR region. By analogy with the radical cation dimer $(TTF^{•+})_2$, the mixed-valence dimeric state of the parent units alone only exists at low temperatures in the solid state. However, as a result of molecular encapsulation within the electron-poor, self-assembled molecular cage described above, Fujita and co-workers [29] have formed stabilized mixed-valence pairs within the large cavity, following the electrochemical oxidation of one of the TTF units.

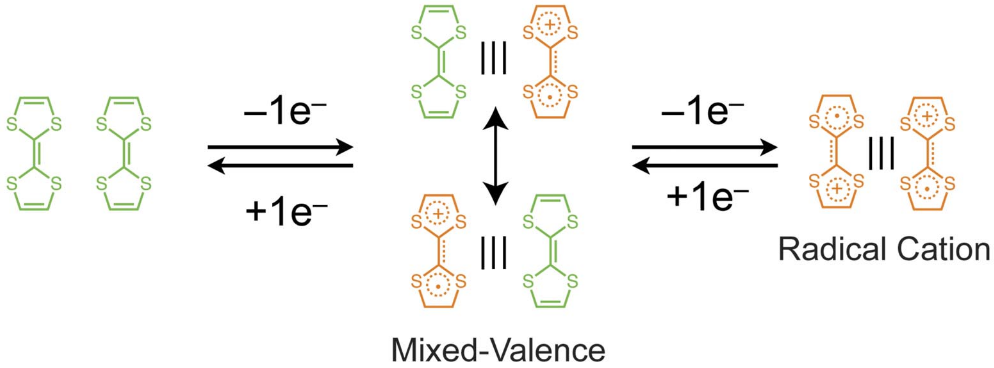

Fig. 3 The stepwise oxidation of adjacent TTF units results in the formation of firstly a mixed-valence dimeric state in which the radical character is shared equally between both units. The second oxidation results in the formation of radical cation π-dimer in which overlapping SOMOs allows radical spin-pairing in this diamagnetic complex.

STABILIZATION THROUGH COVALENT INTERMEDIACY

An alternative approach to inclusion complexation for producing high local concentration of interacting radical species is instead to orient them together covalently in an appropriate cofacial arrangement within the same molecule. When held in such a setting with sufficient flexibility, the electrochemical π-dimerization may even drive conformational switching. For example, when two TTF units are incorporated into flexible crown ethers, the high local concentration of TTF units allows the electrochemical generation of both the mixed-valence and radical cation dimers in reasonable quantities [30]. Sallé and co-workers [31] have utilized a calix[4]arene, doubly functionalized with TTF units on opposite sides of its lower face, to encourage the formation of both mixed-valence and radical cation TTF dimers. The flexibility of the calix[4]arene allows the TTF units to adopt the appropriate relative orientations for association in each state. Interestingly, the calix[4]arene core can be induced to change its conformation when bound to a single sodium cation, an act which operated to dissociate fully the radical π-dimers of $TTF^{•+}$. Swager and co-workers [32] have also taken advantage of the flexibility of a calix[4]arene core to allow sufficient mobility for the formation of radical π-stacks—in this case, using π-dimerization of structurally related oligothiophene units [33]. When elaborated into polymeric materials, the calix[4]arene units act as molecular “hinges”. The oxidatively driven dimerization events of the oligothiophene units within the “hinged” macromolecules enables induced molecular muscle-like contraction/expansion behavior.

The ideal orientation for the noncovalent assembly of discrete TTF π-dimers in solution was also made possible by localizing them as members of glycouril molecular clips. These molecules, designed by Chiu and co-workers [34], lack the flexibility for the TTF members to form intramolecular dimers upon oxidation. The ideal interdigitated planar stacking of four TTF units was attained (Fig. 4), however, during the intermolecular association of two molecular clips. Remarkably, these complexes were formed with very high association constants, following the first oxidation of one of the TTF units, forming a mixed-valence state. The stepwise removal of three more electrons was possible within this intermolecular assembly, with each oxidation state being stabilized by either mixed-valence or radical cation TTF dimeric states. Chemical and electrochemical oxidations were carried out on these molecules in solution; high-level absorption spectroscopy and high-resolution mass spectrometry confirmed the presence of each oxidation state.

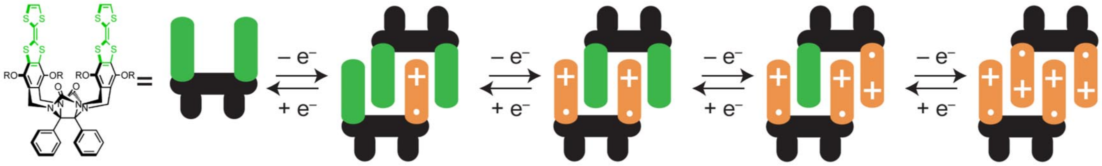

Fig. 4 The TTF molecular clip provides the ideal geometry for clip-dimerization upon oxidation of the TTF units. Amazingly, the complex exists across four distinct oxidation states that were fully addressable and stabilized [34].

SWITCHABLE RADICAL DIMERS IN MECHANICALLY INTERLOCKED MOLECULES

Many of the finest attributes of both covalent systems, as well as complexes, are brought to the fore within mechanically interlocked molecules [35–37]. The simple mechanical interlocking of two distinct macrocycles, forming the prototypical [2]catenane, ensures a lasting connection between both members of the molecule while they each maintain a great deal of conformation freedom [38]. Not only do they possess individual conformational freedom, but the orientation of each member with respect to the other also becomes an important consideration—the term "co-conformation" has been introduced [39] to define this higher-order arrangement between the respective parts of mechanically interlocked molecules. Apart from freely twirling mechanically interlocked rings—in the case of catenanes—specific interactions and affinities may be built into each component to direct the formation of a particular co-conformation. The modulation of these weak interactions permits the controlled co-conformational switching of judiciously designed mechanically interlocked molecules. Moreover, beyond directing the actions of the final mechanically interlocked structures, these same noncovalent binding interactions oftentimes are essential in the template-directed synthesis [40,41] of the elaborate structures in the first place.

An important recognition motif for the production of both functional catenanes and rotaxanes is the stacking of planar aromatic π-donors and π-acceptors. Beyond forming strongly interacting π-stacks, the redox modulation of members of the stack allows the control necessary to achieve switchable systems. The most commonly employed donor–acceptor stacking motif utilized in mechanically interlocked molecules (Fig. 5) involves the inclusion of π-electron-rich guests, such as 1,5-dioxynaphthalene (DNP) and TTF, within the cavity of the π-electron-poor cyclobis(paraquat-*p*-phenylene) (CBPQT^{4+}) [41]. When appropriately elaborated into both switchable catenanes [22] and rotaxanes [37], the higher π-donor capacity of TTF relative to that of DNP is used to establish a co-conformational equilibrium wherein the TTF unit is encircled by the CBPQT^{4+} ring preferentially in the ground state. This arrangement, however, may be completely reversed by the facile oxidation of the TTF unit, either once or twice, such that its recognition by the CBPQT^{4+} ring is turned off completely, and is, in fact, replaced by strong Coloumbic repulsions. Therefore, cycling the oxidation–reduction potential results in reversible switching in which the CBPQT^{4+} ring can be shuttled at will between the TTF and DNP binding stations in a controllable manner. This redox-induced co-conformational switching has

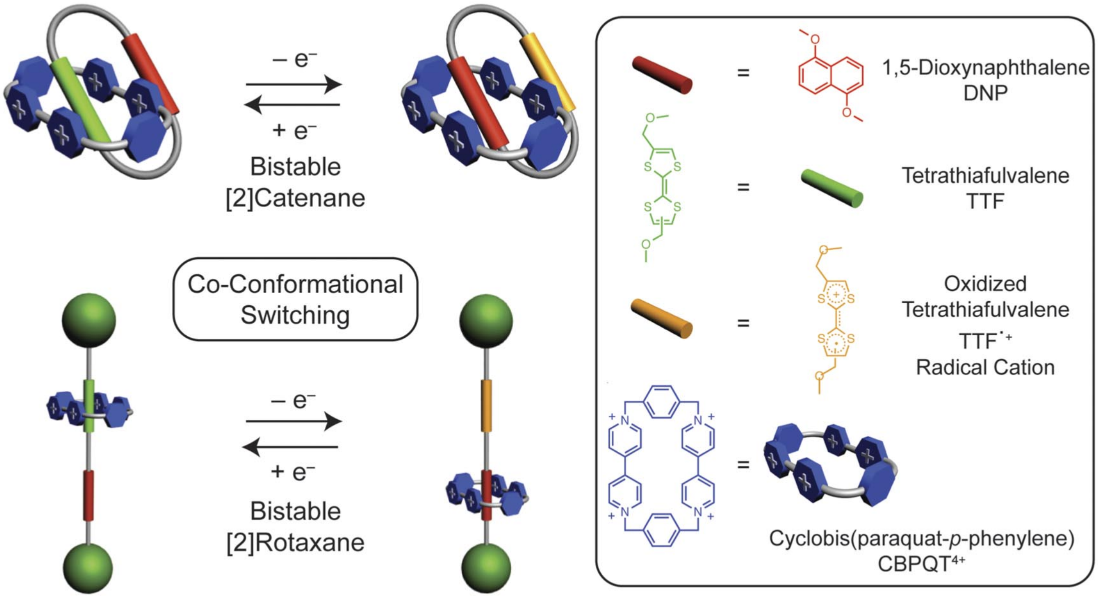

Fig. 5 The prototypical mechanically interlocked molecules bearing only two components—the [2]catenane (top) and [2]rotaxane (bottom). When constructed with specific recognition motifs, triggered co-conformational switching may be achieved. Each structure displayed here contains the donor–acceptor switching motif in which the strongly bound π-electron donor TTF is expelled from within the cavity of the $CBPQT^{4+}$ ring and replaced with the alternative DNP binding station upon oxidation of the TTF unit.

formed the basis of advanced applications such as controlled molecule release [42], electronic information storage [43], and mechanical actuation [44]. While summarized very quickly here, these results represent the culmination of a multitude [43,45–51] of experiments used to develop, not only the basic understanding of mechanically interlocked molecules, but also the detailed fundamentals of donor–acceptor stacking, as well as the fabrication of molecular-based devices.

The efficient synthesis of large quantities of elaborated mechanically interlocked compounds incorporating the $CBPQT^{4+}$ ring is an additional challenge that was met recently [52–55]. Due in part to the high ring strain of this cyclophane and the efficient redox chemistry of its component $BIPY^{2+}$ units, it is very sensitive to common nucleophiles, reducing agents, and bases. This sensitivity had limited the synthesis of mechanically interlocked molecules incorporating this ring system to one, and only one, general technique in which the template-directed double alkylation of the partially formed ring under high pressure (~12 kbar) allows its limited incorporation into fairly simple molecules in reasonable yields. The incorporation of multiple $CBPQT^{4+}$ rings into a single molecule, however, and the production of large quantities of different compounds rapidly had remained a significant challenge. By utilizing very mild and efficient reaction conditions that have recently become ubiquitous to many areas of preparative chemistry—such as the Cu-catalyzed azide-alkyne cycloaddition (CuAAC) click reaction [56]—alternative designs (Fig. 6) have enabled the kinetic trapping of pseudorotaxanes in which the full binding potential of the $CBPQT^{4+}$ ring has been realized prior to and essential for the efficient formation of donor–acceptor catenanes and rotaxanes. These user-friendly protocols have now become standard practice [52,57] for creating large quantities of elaborate mechanically interlocked molecules efficiently. Moreover, they are essential to enabling technologies necessary for the production of compounds that utilize radical π-dimerization as an orthogonal recognition motif for molecular switching.

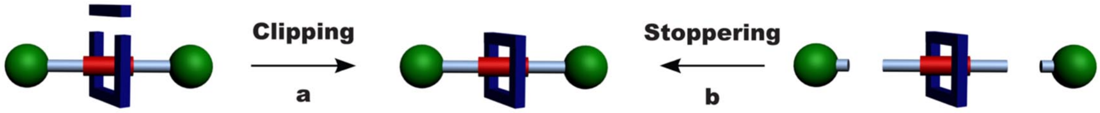

Fig. 6 The two general procedures employed to produce mechanically interlocked molecules incorporating the CBPQT^{4+} ring—illustrated here through the synthesis of a [2]rotaxane. The traditionally "clipping" procedure (a) employs the template-directed double alkylation of a partially formed CBPQT ring to produce the final compound. The more efficient "stoppering" route (b) employs mild and efficient reactions to attach bulky stoppers to a pseudorotaxane where the full binding capacity of the CBPQT^{4+} ring is used.

While the chemistry of CBPQT^{4+} has been explored extensively in the context of donor–acceptor binding, yielding a rich harvest of functional nanosystems, surprises still happen. For example, it was found recently [58] that, when the ring system is doubly reduced to the CBPQT$^{2(\bullet+)}$ diradical dication, it forms (Fig. 7a) a very strong inclusion complex with singly reduced radical cation BIPY$^{\bullet+}$ species. This radical π-dimer—perhaps better described as a trimer—is stabilized strongly with association constants around 10^{12} M^{-1}. The strong association is driven through the same encapsulation effect discussed above in the context of CB8 but also by the perfect alignment of three interacting BIPY$^{\bullet+}$ radical cations in a pseudorotaxane geometry. High-level computational analysis revealed that, while three total radical spins formally comprise the system, two are strongly interacting and paired such that a total $S = 1/2$ (i.e., one free radical) is the lowest-energy electronic arrangement. These data are further supported by the computed geometries of the pseudorotaxane in which the included BIPY$^{\bullet+}$ radical cation is situated off-center within the cavity, interacting more strongly with one face of the CBPQT$^{2(\bullet+)}$ than the other. The complex was characterized experimentally—using cyclic voltammetry under an inert atmosphere—by the fact that changes in the reduction peak potentials indicate the formation of this inclusion complex. By modulating the scanning rate, the formation constant was determined experimentally. Moreover, assembly of the complex is also marked by a very distinctive absorption in the near-IR region.

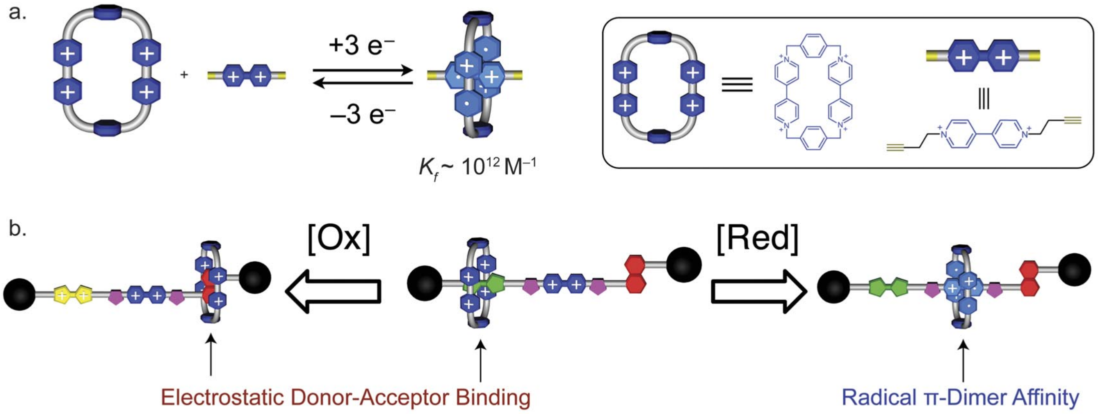

Fig. 7 A "radically" new binding motif (a) was developed in which two normally repulsed components—CBPQT^{4+} and BIPY—are each reduced and self-assemble through radical π-dimerization into a pseudorotaxane complex with exceptionally high affinity [58]. This novel binding motif was used to construct a three-state molecular co-conformational switch in the form of a three-station [2]rotaxane. Two of the states were selected through traditional electrostatic donor–acceptor stacking interactions, while the third was driven by the formation of the stable radical π-dimer.

This interesting redox-driven assembly process has been put to practical use to drive switching within mechanically interlocked molecular rotaxanes [58]. Three different rotaxanes have been prepared using the efficient CuAAC chemistry discussed above in high yields where the templation was driven by traditional donor–acceptor binding of either TTF or DNP with the $CBPQT^{4+}$ cyclophane. Each member of this library of compounds also contains a $BIPY^{2+}$ unit along the thread to be used as a radical binding station, triggered through the electrochemical or chemical reductive formation of $BIPY^{\bullet+}$ radical cation species within both the thread $BIPY^{2+}$ station and the encircling $CBPQT^{4+}$ ring. Interestingly, this alternative radical-based binding motif is completely complementary to the orthogonal donor–acceptor recognition used so commonly within similar systems. Moreover, the use of this radical cation-driven π-dimerization as a recognition motif relies upon the same familiar electroactive components that have already formed the basis for molecular switching, but in a completely different fashion. This reversal in molecular recognition has been described recently [59] as an affinity *umpolung*, wherein an inversion in supramolecular affinity, as opposed to chemical reactivity, is driven by an external stimuli. These concepts are well illustrated by the three-state [2]rotaxane incorporating a TTF, DNP, and $BIPY^{2+}$ binding station along a dumbbell encircled by a $CBPQT^{4+}$ ring (Fig. 7b). Under zero electrochemical bias, the $CBPQT^{4+}$ ring spends the majority of its time localized on the TTF unit, with a small amount located on the DNP unit in the ground state, while the $CBPQT^{4+}$ and $BIPY^{2+}$ units are repelled by Coloumbic interactions. Oxidation of the TTF unit results in the movement of the $CBPQT^{4+}$ ring to the DNP unit as the only other available π-electron donor. This controlled motion is driven by the same donor–acceptor stacking interactions that have prevailed in well-studied systems previously. In this well-designed [2]rotaxane, however, reducing potentials result in the formation of the strong $BIPY^{\bullet+} \subset CBPQT^{2(\bullet+)}$ pair, effectively driving a molecular co-conformational switch by a radical π-dimerization—a completely orthogonal recognition motif. Therefore, a fully reversible, molecular switching assembly was obtained which operates in three different modes based upon three different inputs (neutral, positive, and negative electrochemical bias) utilizing two different and complementary molecular recognition motifs—donor–acceptor stacking and radical π-dimerization.

A similar affinity *umpolung* switch has been devised [59] based upon the oxidative π-dimerization of TTF units encapsulated within a mechanically interlocked [3]catenane. The expanded analogue of $CBPQT^{4+}$ where the phenylene units are replaced with biphenylenes—called cyclobis(paraquat-4,4'-biphenylene)—is known [60,61] to accommodate two π-electron-rich guests within its π-electron-poor expanded cavity. This donor–acceptor binding was used to construct elaborate mechanically interlocked molecules, such as the [5]catenane, dubbed "olympiadane" [62,63]. This compound and even further elaborated heterocatenanes incorporating the cyclobis(paraquat-4,4'-biphenylene) molecular square had been constructed previously using DNP as the primary π-donor component. No studies, however, had been conducted on the double inclusion of π-electron-rich TTF units within its cavity. In fact, the inclusion of two TTF units within the expanded cavity of cyclobis(paraquat-4,4'-biphenylene) is highly favorable and even allows the growth of single crystals of the 2:1 complex. This ternary system forms the supramolecular synthon from which to construct mechanically interlocked molecules bearing the doubly threaded TTF unit (Fig. 8a). Utilizing a Cu^{2+}-catalyzed mild homocoupling of terminal alkynes [64], developed previously to construct donor–acceptor catenanes in high yield [54,65,66], a [3]catenane bearing two independent TTF units was synthesized. This efficient reaction was used to tether the terminal alkyne ends of two bis-alkyne functionalized TTF derivatives around the sides of the templating cyclobis(paraquat-4,4'-biphenylene) molecular square, affording the hetero[3]catenane in good yield. Moreover, because the [3]catenane bears only two types of redox sensitive functions—namely, the TTF units and the $BIPY^{2+}$ components of the cyclophane—it has proved to be the perfect model system to study the interaction of TTF units held in close proximity through a mechanical bond.

Single-crystal X-ray analysis of the ground state of the [3]catenane confirms that the two TTF units are each localized within the π-electron poor cavity of the molecular square. Moreover, the perfect orientation and co-conformational freedom exists within this mechanically interlocked architecture

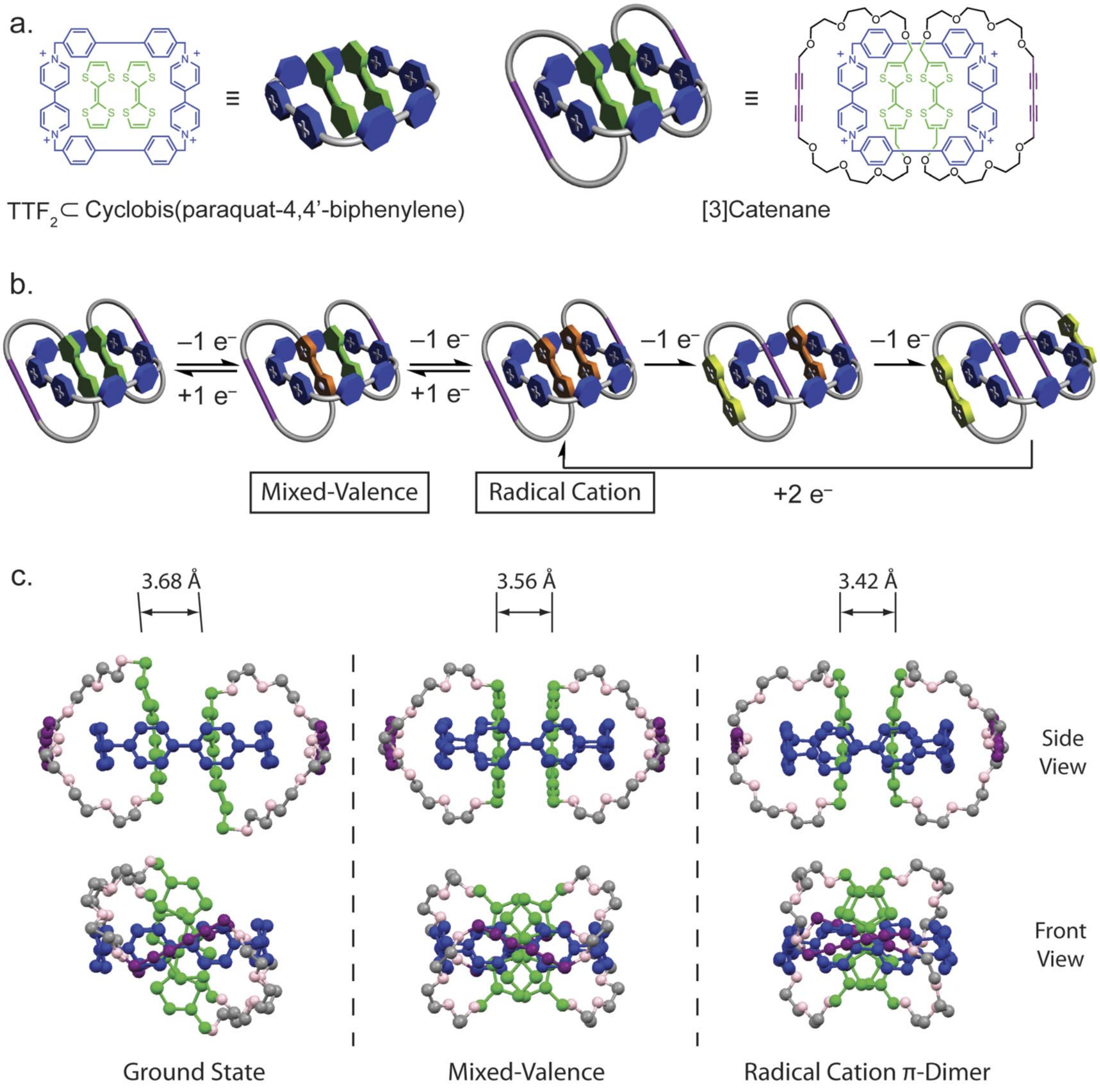

Fig. 8 The large tetracationic cyclophane cyclobis(paraquat-4,4'-biphenylene) forms an effective host for two equivalents of TTF (a). This binding motif has been used to construct a [3]catenane bearing two independent TTF units. A rich redox chemistry and switching mechanism were observed (b) in which five different addressable states were observed, dominated by radical π-dimerization of the two TTF units. The solid-state X-ray crystal structures of the ground state—compared to the first two oxidized states—reveal (c) the strong association of the two encapsulated TTF units, stabilized within the tetracationic cyclophane [59].

for radical π-dimerization to occur between the two encircled TTF units. In fact, a stepwise oxidation mechanism (Fig. 8b) was found to be operative in which the successive removal of electrons from the TTF ring systems results, first of all, in the formation of the mixed-valence $(TTF)^{2\bullet+}$ state and then subsequently of the radical cation π-dimer $(TTF^{\bullet+})_2$. Further oxidation then causes the stepwise ejection of the doubly oxidized TTF^{2+} units one by one. The remarkable stability of both the mixed-valence and the radical cation states of this molecule allowed the successful growth of single crystals suitable for X-ray crystal structural analysis. A comparison of the solid-state structures (Fig. 8c) reveals that the TTF units reorient in perfect registry with one another, as well as draw closer together as the charge is increased in the mixed-valence and radical cation state. Interestingly, each of these charged dimeric states is stabilized within the tetracationic cyclophane, although co-conformational freedom would allow them to circumrotate and escape from the highly charged cavity. Therefore, a real stabilizing effect must be present in each case arising from the mixing of the radical cations between each TTF unit, an effect that outweighs the Coloumbic repulsion arising from their dimerization. Moreover, within the crystals, solvent and/or counterion bridging between the two interacting TTF faces was not observed, indicating that radical interactions alone are sufficient to drive this self-assembly process. Each of these oxidation states can be generated by chemical oxidation in solution under ambient conditions, a feature that facilitates the use of a range of secondary spectroscopies essential for the characterization of this molecular model of discrete TTF radical π-dimerization chemistry.

The nature of each oxidation state of the [3]catenane was probed in detail by employing a variety of spectroscopies. EPR spectroscopy was used to probe the spin properties of each oxidation state. As expected, radical character was observed following the first oxidation to produce the mixed-valence $(TTF)_2^{\bullet+}$ state. The second oxidation results, however, in the disappearance of the radical signal—thus confirming the diamagnetic nature of the SOMO overlapping, spin-paired radical π-dimer $(TTF^{\bullet+})_2$. Furthermore, the ^1H NMR spectrum of the same radical π-dimer $(TTF^{\bullet+})_2$ state containing discrete peaks also confirms that the radicals are spin-paired and localized fully within the TTF dimer system. The characteristic absorbance for each oxidation state was observed within the UV–vis–NIR spectra. Additionally, high-resolution mass spectra also provide additional evidence for the presence and stability of both the mixed-valence $(TTF)_2^{\bullet+}$ and radical cation π-dimer $(TTF^{\bullet+})_2$ states. Each study conducted on this [3]catenane attests to (1) the high stability of radical π-dimers when encapsulated within a large (even charged!) ring system, as well as (2) the ability for this interaction to drive co-conformational switching in a truly practical, unique, and orthogonal manner within appropriately designed mechanically interlocked molecules. One can predict that in the future, functional radical π-dimerization holds promise as an orthogonal and valuable additional recognition motif affording self-assembling molecular machinery.

CONCLUSIONS AND FUTURE PERSPECTIVES

In this article, I have discussed some of the most recent and innovative uses of a novel form of chemical bonding—the radical π-dimerization of planar systems. While these types of interactions have been known and studied for a number of years, the early findings painted them as a chemical curiosity involving a fascinating alternative (yet weak) bonding and not as a robust and active building unit. It is now clear, however, that this mode of chemical bonding, when housed within inclusion complexes, can be used to enable molecular recognition and chemical switching in ways previously unknown, specifically under radical–radical attractive means. The dynamic nature of the bond and the facility of its redox activation—in addition to its strong directing preferences—all position this type of chemical bonding to play an important role in switchable systems for years to come. Perhaps even more powerful is the orthogonality of the radical–radical pair binding mode in relation to existing complementary molecular recognition motifs, such as donor–acceptor binding. Utilization of π-donors and π-acceptors in both electrostatic and radical settings within switchable molecular architectures amounts to an affinity *umpolung*—a concept central to classical covalent chemistry [67], but rather new to the world of noncovalent bonding interactions. The early exploration of this novel concept has already resulted in a number of significant achievements, including the discovery of truly stable encapsulated radical π-dimers and a refined understanding of their attractive interactions as well as the use of radical–radical interactions to direct molecular motion within supramolecular and mechanically interlocked architectures. Research in the future can build upon these achievements and perhaps take advantage of the inherent magnetic properties of the radical pairs to form the basis of spin-operative molecular technologies. An interesting opportunity would be the use of radical-driven heterodimerization—as opposed to the homodimerization discussed throughout this review—in functional nanosystems. While the heterodimerization of different planar radical species would provide many additional tunable parameters for switchable systems, it would also represent the discovery of a unique form of this chemical bond. No matter how this type of novel binding is used in the future, it constitutes a welcome addition to the growing library of robust chemical bonds being employed to direct molecules to perform useful functions as well as to foster new opportunities in fundamental research in chemistry.

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