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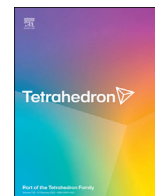
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Incorporating sulfur into redox-active reagents and materials

Sebastian B. Beil^{*1}, Marco B.S. Wonink¹, Ben L. Feringa^{**}

University of Groningen, Stratingh Institute for Chemistry, Nijenborgh 7, 9747 AG, Groningen, the Netherlands



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ABSTRACT

Small sulfur-containing heterocycles, like thianthrenes and tetrathiafulvalenes, together with their larger π -extended counterparts, represent a long-known structural motif and offer reversible redox chemistry at low potentials. Recently these motifs gained an increasing interest in a variety of fields circulating organic chemistry ranging from molecular switches and redox reagents in synthesis to supramolecular aggregates. We anticipate fruitful developments from these versatile building blocks in modern technologies based on their reversible redox properties.

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1. Introduction

Sulfur-containing heterocycles are common structural motifs in organic electronics and materials [1]. Incorporating sulfur heteroatoms into purely carbon-based polycyclic aromatic hydrocarbons offers opportunities by (i) modulating the π -conjugation, (ii) elongating the C–S bond compared to the C–C bond, (iii) distorting the structure and deflating, (iv) lowering of oxidation potentials, and (v) stabilizing (radical) cationic species. Two long-known examples of sulfur-rich heterocycles, we think are currently under-represented with regards to their reversible redox properties, are thianthrene (TT) and tetrathiafulvalene (TTF) as well as their respective π -extended counterparts (e.g., bithioxanthylidene or exTTF). These molecules have been reviewed extensively [2] thus allowing us to highlight their distinct application in selected fields, such as application in organic methodology or molecular switches, and providing inspiration for future applications.

Both thianthrene and tetrathiafulvalene heterocycles undergo an efficient and facile redox-cycling via the radical-cationic intermediate to the stable dicationic state (Fig. 1). Upon single-electron oxidation thianthrene converts into the radical-cation $\text{TT}^{\bullet+}$ at a low potential of +0.80 V vs. the ferrocene redox couple (FcH/FcH⁺) in

acetonitrile (MeCN), whereas tetrathiafulvalene reaches this state already at +0.73 V (TTF^{•+}) [3]. This trend continues towards the dicationic state which is reached at a higher positive potential of +1.40 V (TT²⁺) and +1.10 V (TTF²⁺) vs. FcH/FcH⁺ in MeCN, respectively [4]. Both TT²⁺ and TTF²⁺ are planar aromatic states with achieved aromaticity as thermodynamic driving force [5]. This reversible twofold oxidation at low potentials rationalizes their applications in redox-active or redox-responsive materials as compared to dimethyl viologen (paraquat), which is converted from its dicationic state in two redox steps to the neutral state. The first reduction occurs at –0.43 V and the second at –0.84 V vs. FcH/FcH⁺ in MeCN [6].

Since TT and TTF stand out as thermodynamically stable and fast electrochemically switchable compounds they are well-suited to be incorporated into molecular switches. Molecular switches typically constitute of two stable states, which differ by their electric, magnetic, or optical properties and can be alternated by reversible interconversion induced by external stimuli [7]. An applied voltage produces no waste and can be easily modulated in space, time, and magnitude [8]. These single molecule switches are frequently the basis for more advanced multicomponent switches such as rotaxanes where directed translational motion can be fueled by electricity [9].

Moreover, the reversible low oxidation potential enables the use of TT as redox mediator in organic synthesis, thus giving access to mild and selective oxidation reactions. Preferentially these implementations give access to the conversion of otherwise unreactive or labile functional groups and generate new chemical reactivities.

* Corresponding author.

** Corresponding author.

E-mail addresses: s.b.beil@rug.nl (S.B. Beil), b.l.feringa@rug.nl (B.L. Feringa).

¹ Contributed equally.

Reversible redox properties

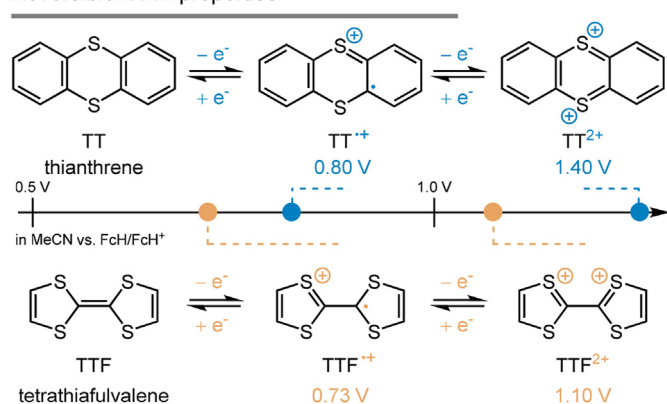


Fig. 1. Thianthrene (TT) and tetrathiafulvalene (TTF) and their respective reversible redox behaviors.

2. Thianthrenes

Thianthrenes offer a broad structural diversity based on simple preparation procedures, such as oxidative dimerization of thiophenols [10]. In the ground state, TT features a distinct structural distortion in which both phenyl rings have a folding angle of 128° facilitating a bent shape available for convex-concave interactions (*vide infra*).

Recently, TT received considerable attention in organic synthesis due to its highly regioselective monocationic thianthrenium adduct formation with aromatic substrates under redox conditions, which could then be used for further functionalization (Fig. 2) [11]. For a fluorinated TT analogue the *para/ortho* (*p/o*) selectivity for the adduct formation by aromatic substitution was as record high as 520:1 [12]. This remarkably selective formation was utilized in subsequent functionalizations, such as fluorination or amination reactions among others (Fig. 2a) [11]. In addition, the Ritter group also found that thianthrenium adducts allow the selective formation of secondary (*E*)-allylic amines, an otherwise challenging and oxidatively labile motif [13]. This photochemical procedure was

amenable to couple primary amines with terminal olefins selectively. Concomitantly, the Wickens group discovered the electrochemical activation of TT and olefins to access aziridines in the presence of primary amines [14] and likewise performing an allylic amination with secondary amines [15]. Upon oxidation of TT, the dicationic adduct (Fig. 1, TT²⁺) with olefins was isolated and proved to be a key intermediate in the reaction. The formation of (*Z*)-allylic amines under the electroorganic conditions is an impressive feature and thus further highlights the high complementarity to the seminal photochemical work by the Ritter group [16].

The extended counterpart of TT is bithioxanthylidene (Fig. 2b), a subclass of overcrowded alkenes. Such motifs can adopt different conformations [17], which originate in the non-planarity of the two tricyclic units on both sides of the olefinic bond [18]. This non-planarity is induced by the steric crowding in the fjord region and can be adapted by twisting around the central double bond or the folding of the tricyclic moieties [19]. Four major geometries are possible: anti-folded, syn-folded, twisted, and orthogonal twisted, allowing for a molecular switch [19]. Different geometries can be individually addressed by external stimuli (e.g. thermal, photo-, and electrochemical stimulants), which may lead to photo, electro-, and mechano-chromic behavior [20]. An example is the reversible switching of bithioxanthylidenes where an anti-folded conformer can be electrochemically oxidized to a dicationic orthogonally twisted conformer showcasing electrochromism (Fig. 2b) [20a]. The change in geometry upon oxidation can be unambiguously confirmed by cyclic voltammetry, which is in line with earlier observations on bisanthrones by Evans et al. [21].

Ultimately, incorporating electroactive thianthrenes into molecular switches may give access to the formation of a molecular electromotor. The unidirectional rotary molecular motor developed in the Feringa group is traditionally based on photochemical *E/Z* isomerizations and thermal helix inversions [22]. Advances have been made to use a second generation molecular motor and drive it with electricity instead of light [23]. The oxidation of the molecular motor results in the formation of the dicationic state which is analogous to the electrochemistry of the aforementioned bithioxanthylidenes. However, this oxidation is immediately followed by a deprotonation and the point chirality of the methyl

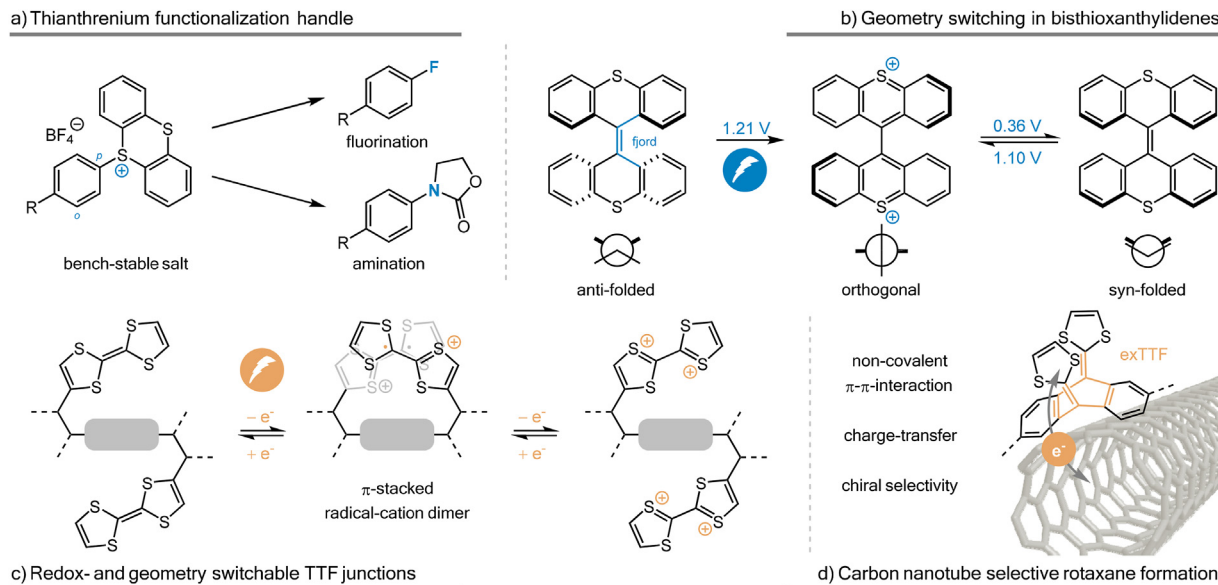


Fig. 2. Possible applications of TT and TTF small molecules in synthesis and materials. Uses range from leaving group properties (a) to intrinsic geometry distortions upon redox modulation (b, c) up to non-covalent functionalization of carbon nanotubes (d).

group is lost. The latter, however, is essential to the unidirectional rotation and further research is therefore required to prevent this deprotonation event.

To incorporate a multi-stimuli responsiveness to the parent bithiathoxanthylidene switch a three-state switching system of an anthracene extended bithiathoxanthylidene was established afterwards, which forms highly stable diradical states [24]. Three individually addressable states can be interconverted by electrochemical, thermal, and photochemical reactions, respectively. Reversible electrochemical switching was found between an orthogonal dicationic and orthogonal, kinetically stabilized, diradical. Furthermore, reversible switching by heating and irradiation between the open- and folded-closed-shell state was demonstrated successfully.

3. Tetrathiafulvalene

TTF is an organic redox switch that showcases exceptional thermodynamically stable oxidation states [2b]. For instance, neutral TTF is a strong π -donor, which decreases with successive oxidation steps, and thus interactions with other parts of a molecule or system can be reversibly tuned by electrochemical means. Reversible dimerization can occur for the neutral TTF and its radical cation (mixed-valence dimer), but also for two radical cations by radical pairing showing profound covalent character (radical-cation dimer, Fig. 2c). Many multicomponent supramolecular systems, such as rotaxane based molecular machines, take advantage of these interactions [25]. The conformation of molecules can be redox switched between an unfolded and folded geometry by the incorporation of two TTF 'arms' [26]. Depending on the solvent/anion combination a two-electron oxidation can lead to the folding of the molecule induced by the dimerization of two radical cation moieties. Upon a second two-electron oxidation step this folding is undone and the initial unfolded conformation is attained to minimize the repulsion between the two doubly charged TTF units.

Another important use of TTF was found to be as semiconductor utilizing its singly oxidized form [2a]. Additionally, metallic-like behavior was discovered when TTF was combined with tetracyanoquinodimethane (TCNQ) moieties creating charge-transfer (CT) complexes that have shown high conductivities [2a,5]. Exploiting the individual addressable redox states of TTF was achieved by its annulation to a porphyrin [27]. In the neutral state the TTF moiety quenches the fluorescence of the porphyrin, but upon oxidation it is transformed into a fluorescent species as electron transfer from the TTF^{•+} unit to the porphyrin is absent. Similarly, TTF was coupled to two anthracene moieties and the fluorescence could be modulated by successive oxidation and reduction steps [28].

Finally, the anthracene-extended counterpart of TTF, called exTTF, features a similar bent shape as discussed for thianthrenes, however, with a larger π -system. Various applications of this exTTF motif have been described such as the non-covalent functionalization of advanced materials like single-walled carbon nanotubes (SWCNT). This strategy was pioneered by the Pérez group who utilized a bis-exTTF macrocycle precursor which undergoes ring-closing metathesis in the presence of the nanotubes [29]. Due to the templated concave-convex π - π -interaction a high loading of macrocycles onto the nanotubes was achieved. Nevertheless, this system lacks error correction and results in oligomerization upon metathesis reaction. To overcome the irreversible formation of the olefin bond, the von Delius group introduced two disulfide units into the bis-exTTF macrocycle (Fig. 2d). This macrocycle was subsequently utilized under dynamic disulfide exchange conditions in the presence of SWCNT [30]. The catalytic nature of the reactions combined with the distinct supramolecular control improved the loading of exTTF rings, allowed for recovery of these rings, and

finally enabled the purification of specific chirality nanotubes from the bulk mixture. The charge-transfer redox interactions between exTTF and SWCNT were unambiguously proven by transient absorption spectroscopy.

4. Conclusion & outlook

The utility as redox mediator in complex organic synthesis makes thianthrene and its extended counterparts remarkable structural units. We anticipate the adaption of these recent synthetic developments towards further protocols accessing sensitive functional groups. Considerations into thianthrene-based molecular electromotors will remain a promising area, since many molecular switches are powered by (photo-)chemical energy while electrical energy driven switching is underexplored. Due to the advantage of selective electrochemical switching over photochemical stimuli, it is a matter of time before these will become more dominant in (commercial) redox addressable smart molecular electronic devices.

For the full utilization of tetrathiafulvalene as organic redox switch in molecular ensemble junctions and organic batteries key challenges remain. With regards to organic batteries the energy density of these molecules needs to be increased while maintaining high stability and reversibility. Future research in the purification of nanoscopic structures like nanotubes or fullerenes with the use of redox-active macromolecules will enable a new era of organic electronics. However, due to the versatility and tunability of the cost-efficient TTF-based organic redox switches it is expected that they will have a bright future in the design of functional devices.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Sebastian B. Beil obtained his M.Sc. in Chemistry from the Christian Albrechts University of Kiel (Germany) in 2015. As a Ph.D. student he worked in the lab of Siegfried Waldvogel in Mainz and Phil Baran at Scripps Research in La Jolla (USA). His research focus were new avenues in organic electro-oxidations and -reductions. After graduation in 2019, he was a postdoctoral fellow with Max von Delius in Ulm and joined the MacMillan lab as a postdoctoral fellow supported by the Leopoldina National Academy of Sciences in 2020, where he explored new avenues in decarboxylative transformations. Recently, his independent career started at the Stratingh Institute for Chemistry at the University of Groningen in 2021 where he develops redox transformations in synthesis and within materials.



Marco B. S. Wonink obtained his M.Sc. in Chemistry and M.Sc. in Chemical Engineering at the University of Groningen in the Netherlands in 2016 having worked in the labs of Prof. Edwin Otten (University of Groningen) and Prof. Yuriy Román-Leshkov (Massachusetts Institute of Technology, USA), respectively. Under the guidance of Prof. Ben Feringa he then continued with his Ph.D. at the University of Groningen where he worked on organic electrochemical conversions and graduated in 2022.



Ben L. Feringa obtained his PhD degree in 1978 at the University of Groningen in the Netherlands under the guidance of Prof. Hans Wynberg. After working as a research scientist at Shell he was appointed full professor at the University of Groningen in 1988 and named the distinguished Jacobus H. van't Hoff Professor of Molecular Sciences in 2004. He was elected foreign honorary member of the American Academy of Arts and Sciences and member of the Royal Netherlands Academy of Sciences. His research interests include stereochemistry, organic synthesis, asymmetric catalysis, molecular switches and motors, photopharmacology, self-assembly and nanosystems.