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Fast synthesis and redox switching of di- and tetra-substituted bisthioxanthylidene overcrowded alkenes†

Brian P. Corbet, [iD] Marco B. S. Wonink and Ben L. Feringa [iD] *

A rapid and efficient method for the synthesis of overcrowded alkenes using (trimethylsilyl)diazomethane provides a range of substituted bisthioxanthylidenes. We show large conformational redox switching from folded to orthogonal states, which tolerates many substitution patterns. The facile access to bisthioxanthylidene switches with the potential for further functionalization, in combination with the reliable redox chemistry, provides major opportunities for the design of electrochemically responsive systems.

Overcrowded alkenes[1,2] are an intriguing class of molecules that receive major attention and are particularly attractive in the design of soft actuators[3] and responsive materials.[4] Our group has a long-vested interest in overcrowded alkenes, for example, towards molecular motors[5] and switches, such as bistricyclic aromatic enes (BAEs).[6–8] These BAEs are a subset of overcrowded alkenes and include widely studied motifs, such as bifluorenylidenes,[9] bis(thio-)xanthylidenes,[10] bianthrones[11] and their derivatives (Fig. 1a). For various structures in this class of molecules, fascinating photo-, thermo-, mechano-, and electrochromic behavior as well as dynamic stereochemistry has been demonstrated.[2,12] Previously, our group has demonstrated that bisthioxanthylidenes can be used as electrochromic conformational and luminescence switches, both in solution[7] and on surfaces.[8] Using electrochemical, thermal and photochemical stimuli, multiple states are individually addressable.[7] These properties provide attractive possibilities to design functional dynamic systems and responsive materials.

The characteristic conformational properties found in BAEs, mainly originate from the high steric hindrance around the overcrowded alkene unit.[2,12a,b] There are two ways these molecules accommodate the overcrowding, which are: twisting around the central 9,9′-axis or folding of the tricyclic units. The twisting and folding can introduce helical chirality to these

molecules and is the basis for the four main conformers observed in BAEs (Fig. 1b). The *anti*- and *syn*-folded conformers alleviate strain by folding of the tricyclic units, which can lead to pyramidalization of the central olefin carbon atoms. The twisted and orthogonal conformers have two planar tricyclic units and accommodate the overcrowding by rotation around the central double bond axis.

The *anti*-folded state is the most stable state for neutral bisthioxanthylidenes (Fig. 1, X═Y═S). The strain caused by the overcrowding around the central double bond is relieved by a significant folding of the thiopyran motif.[2] The *syn*-folded and the twisted state experience more strain because of a higher overlap between the two halves. Neutral twisted or orthogonal states, with planar halves are possible, however, with significantly higher energies.[2] Our group previously demonstrated that, by photo-, electrochemical or thermal switching, higher energy conformers are accessible,[4,7] of which the neutral states will rapidly undergo thermal isomerization to the favored *anti*-folded state. We further showed that a stable, orthogonal state is accessible by oxidation towards a dicationic state with increased single bond character for the central C–C bond and two planar halves.[7]

In the synthesis of overcrowded alkenes (Scheme 1), the most challenging reaction is generally the formation of the overcrowded C═C double bond and only a relatively small number of transformations are suitable. Bisthioxanthylidenes
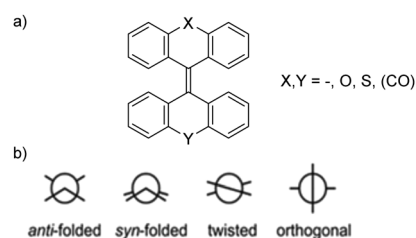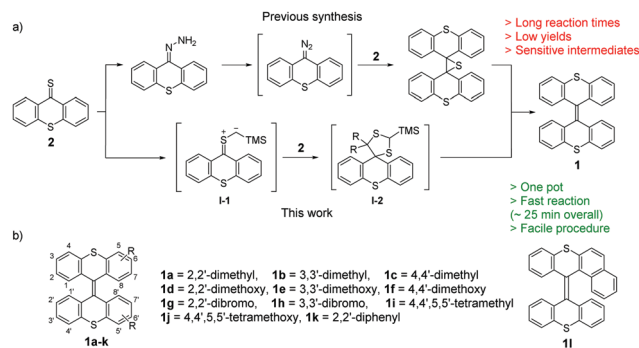
Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, Groningen, 9747 AG, The Netherlands. E-mail: b.l.feringa@rug.nl

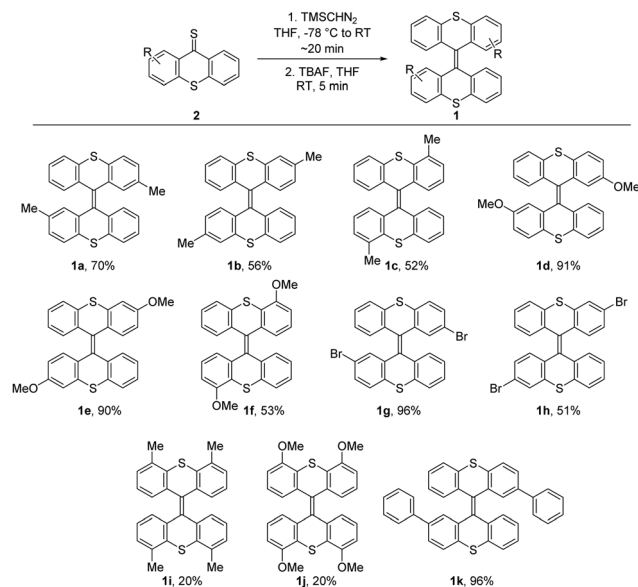† Electronic supplementary information (ESI) available. See DOI: 10.1039/d1cc03098a

Fig. 1 (a) General structure of bistricyclic aromatic enes (BAEs). (b) Schematic representation of the most common conformers of BAEs.

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Scheme 1 (a) Commonly used previous synthesis route (upper) and novel synthesis route (lower) introduced here, to access bisthioxanthylidenes. (b) Schematic overview of bisthioxanthylidenes (**1a–1l**) studied.

are commonly obtained *via* a Barton–Kellogg synthesis,[6a,13] where a diazo compound and a thioketone are used to form olefins *via* an episulfide intermediate (Scheme 1a). The aforementioned diazo compound is obtained from oxidation of a hydrazone, which in turn is frequently obtained, starting from the corresponding thioketone. Long reaction times of typically 12–16 h are required for each step: the hydrazone formation, coupling and desulfurization. Furthermore, the handling of the often very delicate diazo compound is necessary. Faster and easier synthesis routes, such as the one discussed in this work, can contribute to the study of libraries of compounds and serve as an important addition to the toolbox for incorporation of bisthioxanthylidenes as switches in responsive materials.

Here we present an alternative, very facile, synthesis (Scheme 1a) of a variety of substituted bisthioxanthylidenes and their electrochemistry and redox switching (Scheme 1b). By demonstrating a simple, fast synthesis route of substrates with functional handles, in combination with the robust electrochemistry and the intriguing switching modes of bisthioxanthylidenes we expect that these switches will facilitate the development of multi-responsive materials and complex dynamic molecular systems.

Taken inspiration from the recent work of Mlostoń and co-workers,[14] we investigated the use of (trimethylsilyl)-diazomethane (TMSCHN$_2$) for the synthesis of bisthioxanthylidenes *via* dimerization of thioketones. The dimerization reaction cascade likely proceeds *via* a 1,3-dipolar cycloaddition of TMSCHN$_2$ with thioketone **2**, whereupon nitrogen exclusion provides a sulfur ylide (Scheme 1a, **I-1**). This ylide reacts in another 1,3-dipolar cycloaddition with another equivalent of thioketone **2** leading to a 5-membered dithiane (**I-2**). The addition of tetrabutyl ammonium fluoride (TBAF) leads to the deprotection of the silyl group, the elimination of methanedithiolate and the formation of the overcrowded alkene **1**. By optimization of the reaction conditions for dimerization we developed a fast (~25 min) and highly efficient method for sterically demanding bisthioxanthylidene formation. One equivalent of the thioketone is treated with TMSCHN$_2$ at −78 °C. No conversion to the sulfonium ylide is observed at this temperature and the reaction mixture is immediately allowed to warm up to room temperature. The conversion of the strongly colored thioketone **2a–k** can be easily monitored by

Scheme 2 Scope of the dimerization reaction. Compounds **1a** and **1d** are known in literature,[7] compounds **1b**, **1c**, **1e–1k** are novel compounds. For unsymmetrically substituted products only the *E*-isomer is shown for clarity.

TLC analysis or simple observation of the color change. A second equivalent of thioketone was converted within a few minutes after addition. TBAF addition leads to full conversion towards the overcrowded alkene within 5 min. The synthesis of bisthioxanthylidenes from two distinct thioketones is possible. However, this results in a mixture with the homocoupled products (see ESI,† for detailed procedures). The overall time for the complete, one-pot sequence from thioketone to overcrowded olefin is approximately 25 min.

Thioketones **2a–k** could be obtained by thionation of corresponding thioxanthones and were submitted to the dimerization conditions immediately after purification. The dimerization reactions show moderate to excellent isolated yields (Scheme 2), while all conversions proceed rapidly and efficiently. It should be noted that the purification of poorly soluble compounds by chromatographic methods is likely the reason for the most significant loss for some compounds showing lower isolated yields. The dimerization reactions were mostly performed on a 0.18–1.26 mmol scale (see ESI†).

In order to investigate the influence of substitution patterns for bisthioxanthylidenes on electrochemical switching, we synthesized the methyl and methoxy substituted analogues **1a–1f**, substituted at the 2,2′-, 3,3′- and 4,4′-positions. The new method was again highly efficient for the synthesis of these compounds and especially methoxy substituted **1d** and **1e** were obtained in excellent yields. Two bromo substituted bisthioxanthylidenes **1g** and **1h** were prepared, not only to investigate the substituent effect on switching behavior, but in particular to introduce synthetic handles for the further functionalization of these switches or the incorporation in more complex systems. Starting from unsymmetrically substituted thioketones, the obtained bisthioxanthylidenes products were obtained as *E*/*Z*-mixtures with 50 : 50 up to 72 : 28 ratios

(see ESI†). The applicability of this method is underlined by the tolerance for various substitution patterns. Further, the methoxy groups also provide a convenient functional handle for further derivatization. The method is also applicable for tetrasubstituted bisthioxanthylidenes, as observed for **1i** and **1j**, although, for these bisthioxanthylidenes, impurities, which could not be removed by flash column chromatography, were present. In these cases, simple washing steps using Et_2O provided the corresponding products with excellent purity.

The coupling protocol to access sterically demanding bisthioxanthylidenes presented here is a remarkably facile and fast method compared to the previously used Barton-Kellogg reactions. With an efficient method for rapid access to these materials established and a library of compounds (Scheme 1b and Scheme 2, **1a–1l**) in hand, we proceeded to investigate their electrochemical properties.

From cyclic voltammetry (Fig. 2b, see ESI,† for cyclic voltammograms of **1a–1l**) we observe, in the forward, oxidative direction, a current at $E_{p,a}$ = 1.15 V *vs.* saturated calomel electrode (SCE). Initially, **1e** is in its *anti*-folded state and upon oxidation, of overall two electrons, as demonstrated in our previous work,[7] a conformational isomerization to the orthogonal dication **1e^{2+}** occurs. The conformational change within the molecule from the *anti*-folded state with a central double bond proceeds towards an orthogonal state with a central single bond. On the reverse direction, the reduction of **1e^{2+}** is observed at $E_{p,c}$ = 0.25 V *vs.* SCE, where the orthogonal **1e^{2+}** accepts two electrons. This initially leads to a twisted state,[8] which converts relatively quickly, on the timescale of the electrochemical experiment, towards the thermodynamically favorable *anti*-folded state. A small oxidation signal, belonging to the twisted state can be observed at 0.34 V *vs.* SCE. The significant hysteresis between the main oxidation and reduction is caused by the considerable geometrical differences of the *anti*-folded and orthogonal states. Additional to the

different redox response, this geometrical difference aids to explain the differences for the thermal and optical properties.[7]

From the observed redox potentials for the synthesized library of compounds (Table 1, see also ESI†), we can see that the electrochemistry of bisthioxanthylidenes is robust and tolerates several substituents and substitution patterns. The presence of electron donating substituents, either in linear or cross conjugated arrangement, with respect to the central olefin, does not lead to a significant difference in redox potentials. The higher electron density of the methoxy substituted bisthioxanthylidenes (**1d–1f**) has a small effect resulting in a more facile oxidation by stabilization of the dicationic state.

As expected, the bromo-substituted bisthioxanthylidenes (**1g**, **1h**) show a significantly higher oxidation potential of 1.40 and 1.39 V *vs.* SCE, respectively, while still observing the expected geometrical switching. Compound **1g** shows the expected redox behavior, only shifted towards more positive potentials, with a hysteresis comparable to the rest of the compounds in the library. However, 3,3′-dibromo-bisthioxanthylidene (**1h**) shows two closely spaced, significantly smaller reduction signals. This is indicative of a chemical reaction occurring at the dicationic state. We hypothesize that this could be either an oligomerization reaction or nucleophilic attack by water. In **1h**, the bromine substituents are conjugated in a *para* position to the central olefinic bond, which is a plausible explanation for the increased reactivity compared to its regioisomer **1g**.

The tetrasubstituted substrates (**1i, 1j**) show a slight shift towards less positive potentials compared to the disubstituted substrates with a comparable substitution pattern (**1c, 1f**). Both tetrasubstituted bisthioxanthylidenes show a significantly lower solubility. The number of substituents does not show a significant effect on the electrochemical switching. The presence of aromatic substituents, *i.e.* diphenyl bisthioxanthylidene (**1k**), does not interfere with the desired electrochemical
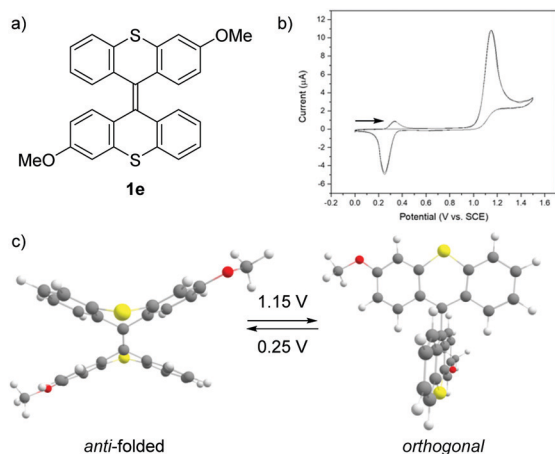

Fig. 2 (a) Structure of **1e**. (b) Cyclic voltammogram of **1e** (1.0 mM), GC, Pt wire, SCE, CH_2Cl_2, scan speed 10 mV s^{-1}, TBAPF$_6$ (0.1 M). (c) Illustration of the conformational switching, optimized geometry structures obtained from DFT calculations at B3LYP/6-31G** level of theory.

Table 1 Peak potentials from cyclic voltammetry[a] for oxidation and reduction

	$E_{p,a}$[b] (V *vs.* SCE)	$E_{p,c}$[b] (V *vs.* SCE)	Hysteresis (V)
1a	1.22	0.34	0.88
1b	1.28	0.38	0.90
1c	1.28	0.38	0.90
1d	1.17	0.33	0.84
1e	1.15	0.25	0.90
1f	1.24	0.40	0.84
1g	1.40	0.56	0.84
1h[c]	1.39	0.47[d]	0.92[d]
1i[e]	1.25	0.34	0.89
1j[e]	1.16	0.31	0.85
1k	1.26	0.45	0.81
1l	1.29	0.46	0.83

[a] **1a–l** (1.0 mM), CH_2Cl_2, TBAPF$_6$ (0.1 M), GC, Pt wire, SCE, 10 mV s^{-1}, room temperature, diffusion limited conditions. [b] $E_{p,a}$ = anodic peak potential; $E_{p,c}$ = cathodic peak potential. [c] For **1h** a different electrochemical response is observed (see text). [d] The first observed wave was selected (see ESI). [e] Measured as saturated solution because of limited solubility.
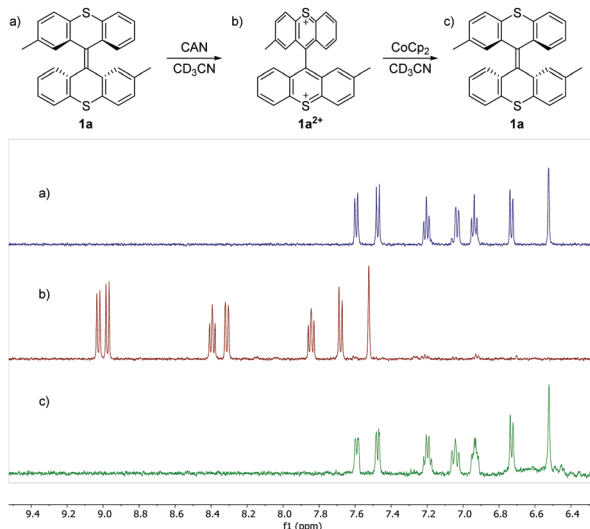
Fig. 3 Chemical redox switching. ^{1}H-NMR spectroscopy (500 MHz, CD$_3$CN) of (a) isomerically enriched **1a**. (b) **1a^{2+}** obtained by oxidation with ceric ammonium nitrate. (c) **1a**, in an equal isomeric ratio, recovered by reduction with cobaltocene. For clarity only the *E*-isomer of **1a** is shown. For further details see ESI.†

switching, with peak potentials at 1.26 and 0.45 V *vs.* SCE. The hysteresis for **1k** (0.81V) is again similar to the hysteresis observed for other substituted bisthioxanthylidenes (Table 1). Finally, the extension of the aromatic core in the non-symmetric 1,2-benzo-compound **1l** (Scheme 1b), results in the expected electrochemical switching.

The dicationic and neutral states of bisthioxanthylidenes can be addressed by electrochemical as well as chemical means. Under ambient conditions in the presence of non-dry solvents, compound **1a** dissolved in CD$_3$CN (Fig. 3a) was readily oxidized by addition of solid ceric ammonium nitrate (Fig. 3b), leading to a highly selective conversion towards the dicationic **1a^{2+}** with a considerable downfield shift for all signals. Subsequent reduction by addition of solid cobaltocene restores the initial spectrum corresponding to the neutral, folded structure of **1a** (Fig. 3c).

We have presented here, a novel, efficient and rapid synthesis method for bisthioxanthylidenes, allowing for various substituent patterns and different regioisomers of these highly overcrowded alkenes. The scope of bisthioxanthylidenes investigated in this study shows that the electrochemical switching is robust and tolerates various substituents. The major geometrically different neutral, *anti*-folded states and dicationic, orthogonal states are readily addressable both by electrochemical and chemical means. As now easily accessible, reliable and functionalizable switches that can be addressed by multiple stimuli, bisthioxanthylidenes have great potential for their use in molecular switching, for example in electrochromic responsive materials.

Conflicts of interest

The authors declare no conflict of interest.

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