Synthesis of Pyrrolidine-Fused 1,3-Dithiolane Oligomers by the Cycloaddition of Polycyclic Dithiolethiones to Maleimides and Evaluation as Mercury(II) Indicators

Pedro Fuertes, María García-Valverde, José V. Cuevas, Borja Díaz de Greñú, Teresa Rodríguez, Josefa Rojo, and Tomás Torroba*

Department of Chemistry, Faculty of Sciences, University of Burgos, 09001 Burgos, Spain

Supporting Information

ABSTRACT: The scandium triflate-catalyzed cycloaddition reaction of polycyclic 1,2-dithiolethiones to maleimides is described. The reaction constitutes an easy approach to linear as well as branched oligomeric cis-fused dihydro[1,3]dithiol[4,5-c]pyrrole-4,6-dione rings interconnected by 3,5-diylidenethiomorpholine-2,6-dithione or ylidene-6-thioxo[1,2]dithiol[3,4-b][1,4]thiazin-3-one groups. The presence of highly colored, highly polarized push–pull αβ unsaturated thione groups in their structures make these compounds sensitive to the presence of mercury(II) cation in organic or mixed organic/aqueous solvents.

INTRODUCTION

Polyheterocyclic compounds bearing 1,3-dithiole1 and 1,3-dithiolane2 moieties are important donor units in new electronic materials and molecular devices such as extended alkenes are known to give unstable adducts that can be trapped by dienophiles such as maleimides. The extensive chemistry developed in the search for these new materials currently used for this chemistry is surprisingly low, being conserved unchanged for a long time. Less common synthetic methods for the preparation of 1,3-dithiole derivatives include 1,3-dipolar cycloadditions of 1,2-dithiole-3-thiones and activated triple bonds, which permit multiple cycloadditions in one pot, thereby giving rise to extended TTF derivatives by very short reaction pathways. Despite the rich chemistry shown by these reactions, related alternatives are scarce. Thus, the photochemical reactions of 1,2-dithiole-3-thiones and nonactivated alkynes are known to give unstable adducts that can be trapped by dienophiles such as N-phenylmaleimide. Notwithstanding the extensive chemistry developed in the field of 1,2-dithiole-3-thiones, their cycloaddition reactions with classical activated double bonds such as maleimides are not known. The only loosely related known reaction is a single example of a thermal cycloaddition of 2,4-diphenylisothiazoline-5-thione and N-phenylmaleimide that was reported long time ago by McKinnon and co-workers. Apparently, the thermal reaction of N-substituted maleimides and 1,2-dithiole-3-thiones does not work under heating in high-boiling-point solvents. Such a reaction, if it should be possible, would constitute a very good approach to dihydro derivatives of the 2-methylene-4H-[1,3]dithiol[4,5-c]pyrrole-4,6(SH)-dione system, an almost unknown system that could be potentially useful in the search for new materials and pharmacological leads. Therefore, in this paper we describe the scandium triflate-catalyzed cycloaddition of polycyclic dithiolethiones to maleimides as an unprecedented approach to branched oligomeric polyheterocyclic 1,3-dithiolanes.

RESULTS AND DISCUSSION

We selected a suitable catalyst, scandium triflate, which was very effective for the 1,3-cycloaddition reactions of polyheterocyclic dithiolethiones and activated alkynes, to study the cycloaddition reaction of the most reactive dithiolethiones we had in hand and commercial or easily synthesized maleimides. Our starting materials, 4-alkylbis[1,2]dithiol[3,4-b:4,3′-c]-[1,4]thiazin-3-oxo-5-thiones and -3,5-dithiones can be prepared in one-pot reactions from Hünig’s base or N,N-(disopropyl)benzylamine in a selective fashion and therefore are fast entries to complex heterocyclic chemistry. We first selected to use 4-ethylbis[1,2]dithiol[3,4-b:4,3′-c][1,4]thiazin-3-oxo-5-thione (1) in catalyzed reactions with commercial maleimides 2a–j. In this way, 1 and 2a–j reacted equimolecularly in refluxing dichloromethane for 1 h in the presence of scandium triflate (25% mol) to give, after workup and column chromatography, the corresponding orange solid adducts, 5-substituted 2-(4-ethyl-3-oxo-6-thioxo[1,2]dithiol[3,4-b][1,4]thiazin-5-yliden)-
dihydro[1,3]dithiolopyrrole-4,6-diones 3a–j, in yields of up to 88% (Scheme 1).

Scheme 1. Reaction of Bisdithioloketothione 1 and Maleimides 2a–j

<table>
<thead>
<tr>
<th>Entry</th>
<th>Maleimide</th>
<th>Cycloadduct</th>
<th>Yield [%]</th>
<th>Conformers ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>2a</td>
<td>3a</td>
<td>68</td>
<td>61/39</td>
</tr>
<tr>
<td>b</td>
<td>2b</td>
<td>3b</td>
<td>77</td>
<td>57/43</td>
</tr>
<tr>
<td>c</td>
<td>2c</td>
<td>3c</td>
<td>81</td>
<td>52/48</td>
</tr>
<tr>
<td>d</td>
<td>2d</td>
<td>3d</td>
<td>88</td>
<td>52/48</td>
</tr>
<tr>
<td>e</td>
<td>2e</td>
<td>3e</td>
<td>52</td>
<td>52/48</td>
</tr>
<tr>
<td>f</td>
<td>2f</td>
<td>3f</td>
<td>64</td>
<td>53/47</td>
</tr>
<tr>
<td>g</td>
<td>2g</td>
<td>3g</td>
<td>72</td>
<td>55/45</td>
</tr>
<tr>
<td>h</td>
<td>2h</td>
<td>3h</td>
<td>59</td>
<td>55/45</td>
</tr>
<tr>
<td>i</td>
<td>2i</td>
<td>3i</td>
<td>38</td>
<td>58/42</td>
</tr>
<tr>
<td>j</td>
<td>2j</td>
<td>3j</td>
<td>51</td>
<td>55/45</td>
</tr>
</tbody>
</table>

Isolated yields.

All of the obtained compounds showed a single spot on the TLC silica plates, but their $^1$H NMR spectra clearly showed two sets of signals, each composed of two doublets at $\delta$ 4.5–6.0, corresponding to the C3a and C6a protons (the pair of cis-bridgehead protons in the dithiopyrrole system) for every compound, in a roughly equimolecular amount, and two complex multiplets for the signals of the methylene protons of the ethyl group. Therefore, the complex $^1$H NMR spectra are due to the slow inversion of the pyramidal nitrogen in the 1,4-thiazine ring and consequently to the presence of nitrogen inversion conformers. Two chiral centers at the C3a and C6a positions are generated by the 1,3-dipolar cycloaddition reaction with the maleimide, causing the $\alpha$-methylene hydrogens atoms of the N-substituent of the starting substrate 1 to become diastereotopic in the cycloadduct and thus to show magnetic nonequivalence in the $^1$H NMR spectra. Therefore, the two protons of the dithiopyrrole system (H3a and H6a) are structurally nonequivalent. Indeed both the endo- and exo-1,3-dipolar cycloaddition reactions lead to enantiomeric dithiopyrrole rings (Scheme 2). In a characteristic example, compound 3f showed a set of two partially superposed sextets centered at $\delta$ 3.24 (ddq, $J = 25.9, 14.2, 6.9$ Hz) for one methylene proton and another set of two partially superposed sextets centered at $\delta$ 3.56 (ddq, $J = 24.7, 14.6, 7.3$ Hz) for the other methylene proton along with four doublets, two at $\delta$ 5.28 and 5.02 ($J = 8.5$ Hz) for the pair of dithiopyrrole protons of one conformer and two at $\delta$ 5.18 and 4.81 ($J = 9.0$ Hz) for the pair of dithiopyrrole protons of the other conformer.

The transformation among the conformational isomers SYN and ANTI was studied by DFT calculations performed on a simplified model of compounds 3a–j. The SYN/ANTI transformation can be explained as an inversion of the configuration of the amine nitrogen atom. In order to avoid complications arising from the simultaneous inversion on the nitrogen atom and the rotation of the C–C bond in the ethyl group, this ethyl group was simplified to a methyl group. In these theoretical calculations, we found that for this simplified model of 3a–j the SYN and ANTI conformers have similar stabilities, with a free energy difference of 0.319 kcal mol$^{-1}$. This small difference is in good agreement with the experimental observation of both conformers in solution, and on the basis of the calculated free energy difference between the conformers, the statistical distribution of the population at 298 K is 63.2% for the ANTI conformer and 36.8% for the SYN conformer (Figure 1). The estimated barrier for the SYN/ANTI transformation in the simplified model is 17.6 kcal mol$^{-1}$, which is high enough to allow the observation of both isomers in the $^1$H NMR experiments at room temperature. Similar calculations performed on a nonsimplified structure of compound 3a afforded populations of 62.7% for ANTI-3a and 37.3% for SYN-3a (61/39 experimental), in good agreement with the experimental results (Figure 2).

All of these compounds decomposed at the melting point in a cycloreversion reaction followed by thermal desulfuration, giving rise to 4-ethylbis[1,2]dithiolopyrrole-3-oxo-5-thione 4, a known product of thermal desulfuration of 1[10b] (Scheme 3). As a characteristic example, upon slow melting of 3c in a heating chamber under a microscope, yellow crystals of 4 were formed by sublimation as 3c melted. Compound 4 was characterized by mass spectrometry and compared to a synthetic sample.

In the same way, 4-benzylbis[1,2]dithiolopyrrole-3,4-bis-4′-[3,4,b'-4,3'-c][1,4]-thiazin-3-oxo-5-thione 5 (S) and commercial maleimides 2a–d reacted equimolecularly in refluxing dichloromethane for 2–4 h in the presence of scandium triflate (25% mol) to give
after workup and column chromatography, the corresponding orange solid adducts, 5-substituted 2-(4-benzyl-3-oxo-6-thioxo-[1,2]dithiolo[3,4-b][1,4]thiazin-5-ylidene)dihydro[1,3]-dithiolo[4,5-c]pyrrole-4,6-diones 6a−c,e−g, in yields of up to 74% (Scheme 4). In this case, the inversion of the pyramidal nitrogen in the 1,4-thiazine ring was evidenced in the \(^1\)H NMR spectra by the presence of two pairs of doublets, one for each of the benzyl methylene protons, and two sets of signals, each composed of two doublets at \(\delta 4.5−6.0\), corresponding to the pair of \(\textit{cis}\)-dithiolopyrrole protons for every compound, in amounts from equimolecular to 2:1. In a characteristic example, the \(^1\)H NMR spectrum of 6f showed two pairs of doublets at \(\delta 4.40/4.12 \,(J = 14.1 \text{ Hz})\) and \(\delta 4.37/4.19 \,(J = 14.1 \text{ Hz})\) in a 2:1 proportion for the two benzyl methylene protons and two pairs of doublets at \(\delta 5.83/5.58 \,(J = 8.9 \text{ Hz})\) and \(\delta 5.66/5.35 \,(J = 9.2 \text{ Hz})\) in a 2:1 proportion for the two pairs of dithiolopyrrole protons.

On the other hand, 4-ethylbis[1,2]dithiolo[3,4-b:4',3'-c]-[1,4]thiazin-3,5-dithione \(^1\) and 2 equiv of commercial maleimides 2b,f,g reacted in refluxing dichloromethane for 1−2 h in the presence of scandium triflate to give, after workup and column chromatography, the corresponding orange solid adducts, \(S,S'\)-disubstituted 2,2'-[(4-ethyl-2,6-dithioxothiomorpholine-3,5-diyldiene)bis(5-methyl{or aryl}dihydro-4\(H\)-[1,3]dithiolo[4,5-c]pyrrole-4,6-dione)s \(^8\) in yields of up to 67% (Scheme 5). In this case, several conformers are expected, therefore complicating the otherwise simple \(^1\)H NMR spectrum of every compound. In this way, the \(^1\)H NMR spectrum of 8b showed four sets of signals (eight doublets) for the dithiopyrrole protons (\(\delta 5.0−6.0\)) in different proportions, whereas 8f showed only two main equimolecular conformers and traces of two others and 8g showed only one main conformer and traces of two others in the same region of the \(^1\)H NMR spectrum, probably for steric reasons.

Moreover, bisdithioloketothione \(^1\) reacted with commercial bismaleimides 9a and 9b and the synthesized bismaleimide \(^9\) in refluxing dichloromethane for 1 h in the presence of scandium triflate to give, after workup and column chromatography, the corresponding adducts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Maleimide</th>
<th>Cycloadduct</th>
<th>Yield[a] [%]</th>
<th>Conformers ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>2a</td>
<td>6a</td>
<td>67</td>
<td>66/34</td>
</tr>
<tr>
<td>b</td>
<td>2b</td>
<td>6b</td>
<td>70</td>
<td>59/41</td>
</tr>
<tr>
<td>c</td>
<td>2c</td>
<td>6c</td>
<td>74</td>
<td>55/45</td>
</tr>
<tr>
<td>e</td>
<td>2e</td>
<td>6e</td>
<td>66</td>
<td>62/38</td>
</tr>
<tr>
<td>f</td>
<td>2f</td>
<td>6f</td>
<td>51</td>
<td>65/35</td>
</tr>
<tr>
<td>g</td>
<td>2g</td>
<td>6g</td>
<td>48</td>
<td>55/45</td>
</tr>
</tbody>
</table>

[a] Isolated yields.
scandium triflate (25% mol) to give, after workup and column chromatography, the corresponding orange solid monoadducts 10a and 10b or the diadducts 11a–c in yields of up to 55% (Scheme 6). The structures of compounds 10a–b and 11a–c are represented in Figure 3. The expected compound 10c was not isolated, probably because of a lack of stability; therefore, in this case only compound 11c was obtained. The presence of two dithiopyrrole heterocycles in 11a–c was evidenced in the $^1$H NMR spectra by again the presence of four sets of signals (eight doublets) for the heterocyclic protons ($\delta 4.5–5.5$). In contrast, the presence of only one dithiopyrrole system in 10a and 10b was evidenced in their $^1$H NMR spectra by the presence of only two sets of signals (four doublets) for the heterocyclic protons ($\delta 4.5–5.5$).

In the case of monoadducts 10, the presence of a maleimide nucleus makes the products suitable for a second cycloaddition reaction. Therefore, bisdithiolodithione$^{16}$ 7 and 2 equiv of maleimide 10a reacted in refluxing dichloromethane for 6 h in the presence of scandium triflate (25% mol) to give, after workup and column chromatography, the corresponding orange solid adduct 12 in 74% yield (Scheme 7). Some traces of the corresponding monoadduct were also recovered from the column, but the compound was not sufficiently stable for a correct characterization. Compound 12 possesses a remarkable stable structure in which all of the spectroscopic characteristics found in the $^1$H NMR spectra of compounds 3f–h and 8f–g are preserved, showing a complex mixture of conformers.

Furthermore, 1, 2, or 3 equiv of bisdithioloketothione$^{16}$ 1 and trismaleimide 13$^{20}$ reacted in refluxing dichloromethane for 4 h in the presence of scandium triflate (25% mol with respect to 1) to give, after workup and column chromatography, the corresponding orange solid monoadduct 14, diadduct 15, or triadduct 16, respectively, in yields of up to 41% (Scheme 8). Variable amounts of the starting materials and adduct were recovered in each case, and the yields given in Scheme 8 are only for the main product obtained in each reaction. In this case, the yields were lower because of the lack of selectivity, but the compounds were reasonably stable and could be characterized by spectroscopy and microanalysis as in the previous cases.

All of these compounds were obtained within a small window between the reactivity of the starting materials and the stability of the products; this series of reactions was possible because of the presence of scandium triflate as the catalyst of the hitherto unknown 1,3-cycloaddition reaction between dithiolethiones and maleimides. The catalysis permitted the reaction to be...
performed at a suitable temperature to allow the formation and recovery of the obtained products in almost all cases. These new compounds are thermally sensitive, undergoing a cycloreversion reaction followed by thermal desulfuration at the melting point. All of these compounds hold in their structure at least one αβ-unsaturated thione group, which is a well-known heterodiene system that is frequently used for hetero-Diels–Alder cycloaddition reactions with activated alkynes. In the present case, all of the attempted reactions under uncatalyzed or catalyzed conditions gave the product of sequential 1,3-dipolar cycloreversion (presumably to give the starting material 1) followed by the 1,3-dipolar cycloaddition of dithiolethione 1 and the new dipolarophile. In a characteristic example, compound 3f was subjected to reaction with dibenzoylecetalene (17) under diverse conditions but only the known compound 18b was obtained with no traces of the expected compound 19 (Scheme 9).

On the other hand, the highly polarized push–pull αβ-unsaturated thione group is responsible for the color exhibited by these compounds. Compounds 3a–j display an orange color in solution that may undergo changes in the presence of the most common cations or anions. All of them behaved similarly when tested with the same cations or anions, independently of the N-alkyl or N-aryl group, and therefore, the behavior of two of the most representative examples, 3f and 8f, is reported. Addition of 1 equiv or more of Hg2+ to 10−4 M solutions of 3f (λmax = 394 nm, ε = 10 946 M−1 cm−1) in MeCN resulted in a dramatic change of color from yellow to maroon. This response was selective for Hg2+, and addition of several equivalents of other cations (Ag+, Ni2+, Sn2+, Cd2+, Zn2+, Pb2+, Cu2+, Fe3+, Sc3+, and Al3+) as their perchlorate or triflate salts resulted in no appreciable changes (Figure 4).

A quantitative UV–vis titration of a 10−4 M solution of 3f in MeCN with Hg2+ (added as the perchlorate salt in MeCN) showed that as Hg2+ was added (up to 2 equiv), the original absorption maximum bands centered at 394 and 345 nm decreased and some new bands appeared at 550, 430, and 310 nm, generating isosbestic points at 290, 333, and 402 nm (Figure 4a). After the addition of more than 2 equiv of Hg2+, the new bands slowly decreased with the disappearance of the isosbestic point at 402 nm. The titration profile fitted nicely to a 1:1 binding model (Figure 5b), and the association constant was calculated as log K = 4.94 ± 0.09. The Job’s plot analysis of the UV–vis titration carried out in MeCN revealed a maximum at a mole fraction of 50% (Figure 5c), in accordance with the proposed 1:1 binding stoichiometry. The Hg2+ detection limit of a 10−4 M solution of 3f in MeCN, calculated in UV–vis (Figure 5d), was 263 ± 5.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Maleimide</th>
<th>No. equiv.</th>
<th>Cycloadduct</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>13</td>
<td>1</td>
<td>14</td>
<td>42</td>
</tr>
<tr>
<td>b</td>
<td>13</td>
<td>2</td>
<td>15</td>
<td>38</td>
</tr>
<tr>
<td>c</td>
<td>13</td>
<td>3</td>
<td>16</td>
<td>43</td>
</tr>
</tbody>
</table>

*Isolated yields.*
The selective sensing action of a 10⁻⁴ M solution of 8f in MeCN and 1 equiv or more of Hg²⁺ in MeCN or water was also very effective, in contrast to the lack of effect of adding 1 equiv or more of other cations (Ag⁺, Ni²⁺, Sn²⁺, Cd²⁺, Zn²⁺, Pb²⁺, Cu²⁺, Fe³⁺, Sc³⁺, and Al³⁺) in MeCN. In this case, a striking color change from yellow to maroon only in the presence of Hg²⁺ was observed (Figure 6).

A quantitative UV–vis titration of a 10⁻⁴ M solution of 8f in MeCN with Hg²⁺ (added as the perchlorate salt in MeCN) showed that addition of Hg²⁺ resulted in the decrease of the original absorption maximum bands centered at 390 and 417 nm and the appearance of a large absorption band from 300 to 600 nm (responsible for the observed color) with no appearance of isosbestic points (Figure 7a). Related titrations performed in acetonitrile/water mixtures showed a similar tendency, but a clear isosbestic point at 365 nm was observed (Figure 7b), thus confirming the appearance of a unique equilibrium complex. The titration profile fitted nicely to a 2:1 binding model (Figure 7c), and the association constants were calculated as log K₁ = 3.42 ± 0.14 and log K₂ = 4.56 ± 0.17. The Job’s plot analysis of the UV–vis titration carried out in MeCN revealed a maximum between mole fractions of 0.60 and 0.70 (Figure 7d), in accordance with the proposed 2:1 binding stoichiometry. The Hg²⁺ detection limit of a 10⁻⁴ M solution of 8f in MeCN, calculated in UV–vis absorption by the blank variability method, was 3.69 × 10⁻⁶ M.

In agreement with previous related chromogenic probes for mercury(II) cation, we assumed that in both cases complexation was probably effected through the thione group, leading to the formation of complexes in which Hg²⁺ extends the conjugation between the 1,3-dithiolane and thione groups, causing in both cases bathochromic shifts of the main UV–vis absorption band in UV–visible. As a representative example, the structure of the complex 3f[Hg²⁺]:MeCN was obtained by DFT calculations (Figure 8). The model found with ligand 3f and a mercury(II) cation showed a preference for coordination of the mercury cation to the thione sulfur and a preferred orientation through the sulfur atom of the thiomorpholine moiety.
Comparison of the HOMOs and LUMOs of 3f and 3f[Ag+·MeCN] showed that the HOMO of 3f is a nonbonding orbital spread through the 5-(1,3-dithiolan-2-ylidene)[1,2]dithiolo[3,4-b][1,4]thiazin-3-oxo-6-thione moiety and the LUMO is an antibonding orbital spread through the 2-(1,3-dithiolan-2-ylidene)dithiocarboxylate moiety. In contrast, the HOMO of 3f[Ag+·MeCN] is a nonbonding orbital on the N-phenylpyrrolidine-2,5-dione moiety and the LUMO of 3f[Ag+·MeCN] is an σ antibonding orbital spread through the 2-(1,3-dithiolan-2-ylidene)dithiocarboxylate–Ag+ moiety (Figure 9), thus proving that the extension of the conjugation between the 1,3-dithiolane group and the complexed thione group is responsible for the bathochromic shift in the UV titration.

CONCLUSION
We have described the scandium triflate-catalyzed cycloaddition of polycyclic dithiolethiones to maleimides. The reaction constitutes an unprecedented approach to linear as well as branched oligomeric cis-fused [1,3]dithiole[4,5-c]pyrrole rings interconnected by 3,5-dihydronitromorpholine-2,6-dithiole-6-thione-1,2-dithiole[3,4-b][1,4]thiazin-3-one groups. Both the 1,4-thiazine core and the cis-fused [1,3]dithiole[4,5-c]pyrrole ring are nonplanar nonaromatic rings that display the presence of inversion conformers of the 1,4-thiazine nitrogen. The presence of highly colored, highly polarized push-pull α,β-unsaturated thione groups in their structures make these compounds sensitive to the presence of mercury(II) cation in organic or mixed organic/aqueous solvents with remarkable selectivity, as shown for two simple derivatives. Therefore, the more structurally complex compounds are good candidates in mercury removal schemes, as absorbants for mercury(II) salts, and as selective indicators. This is due to the enormous number of sulfur heteroatoms (in either acceptor or donor positions) that these new molecular systems display, such as the 1,3-dithioles and the conjugated thione groups.

EXPERIMENTAL SECTION
General. The reactions were conducted under dry nitrogen. The solvents were previously distilled under nitrogen over phosphorus pentoxide, calcium hydride, or sodium filaments. Melting points were not corrected. Infrared spectra were registered in potassium bromide tablets. NMR spectra were recorded in DMSO-d6, CDCl3, CD3CN, or CD3OD. Chemical shifts are reported in parts per million with respect to residual solvent protons, and coupling constants (JX-X') are reported in parts per million. DEPT experiments from selected samples permitted the assignment of 13C NMR chemical shifts. Elemental analyses of C, H, and N were performed for all new products. High-resolution mass spectra were taken in a quadrupole mass spectrometer by electron impact, FAB, or LSIMS. 4-Ethylbis[1,2]dithiole[3,4-b,4'-3'-c'][1,4]-thiazin-3-oxo-5-thione, 4-benzylbis[1,2]dithiole[3,4-b,4'-3'-c'][1,4]-thiazin-3-oxo-5-thione, 4-ethylbis[1,2]dithiole[3,4-b,4'-3'-c'][1,4]-thiazin-3-oxo-5-thione, and bismaleimide 9c were prepared as described in the literature. The Journal of Organic Chemistry dx.doi.org/10.1021/jo500076c | J. Org. Chem. XXX, XXX, XXX−XXX

Figure 7. (a, b) Hg2+ UV−vis titration curves of (a) 10−4 M 8f in MeCN and (b) 5 × 10−4 M 8f in MeCN/water. (c) Titration profile (λmax = 390 nm). (d) Job’s plot (λmax = 295 nm).

Figure 8. DFT-calculated structure of the complex 3f[Hg2+·MeCN].

Figure 9. HOMOs and LUMOs of 3f and the 3f[Hg2+·MeCN] complex.
General Procedure for the Catalytic Cycloaddition of 4-Ethylidene[3,4-b:4,3'-e][1,4]thiazin-3(6H)-yldiene
dihydropyridine-4H-[1,3]-dithiolo[4,5-c]pyrrole-4,6(5H)-dione (3d).

13C NMR (CDCl3, 100 MHz): δ 79.6 (Cq conformer A), 58.6 (CH2 conformer A), 29.7 (3a
H, 201.1, 200.7, 184.8, 184.5, 171.9, 171.7, 171.2, 172.2, 171.1, 162.5, 163.2, 151.1, 150.3, 133.3, 132.5 (CH2 conformer B), 28.1 (3a

Dithiolo[4,5-c]pyrrole-4,6(5H)-dione (3e).

13C NMR and DEPT (CDCl3, 100 MHz): δ 201.1, 200.7, 184.8, 184.5, 171.9, 171.7, 171.2, 172.2, 171.1, 162.5, 163.2, 151.1, 150.3, 133.3, 132.5 (CH2 conformer B), 28.1 (3a

3a,6aS(Z,E)-5-(tert-Butyl)-2-(4-ethyl-3-oxo-6-thioxo-3H,4H-[1,2]
dithiolo[3,4-b:4,3'-e][1,4]thiazin-3(6H)-yldiene)dihydropyridine-4H-[1,3]
dithiolo[4,5-c]pyrrole-4,6(5H)-dione (3f).

20 mg (52%), orange solid, mp 88–89 °C (dec.) (DCM/ EtOAc 98:2). MS (FAB+): m/z (%) 475.9482. Anal. Calcld for C16H16N2O3S6: C 45.36, H 2.76, N 5.49. Found: C 45.38, H 2.76, N 5.48.
(3aR,6aS)(Z/E)-2-(4-Ethyl-3-oxo-6-thioxo-3H,4H-[1,2]-dithiolo[3,4-b][1,4]thiazin-5-(6H)-yldiene)-5-(4-iodophenyl)dihydro-4H-[1,3]dithiolo[4,5-c]pyrrole-4,6(5H)-dione (3g).
9 mg (72%), orange solid, mp 144–145 °C (dec.) (DCM), 55/45 ratio of conformers. IR (KBr): δ = 3289, 2922, 1716, 1644, 1285, 1163 cm⁻¹. H NMR (CDCl₃, 400 MHz): δ 7.85–7.79 (m, 2H, H₂), 7.15–7.09 (m, 2H, H₂), 5.25 (d, δ = 8.4 Hz, 0.55H, CH conformer A), 5.14 (d, δ = 9.0 Hz, 0.45H, CH conformer B), 5.00 (d, δ = 8.4 Hz, 0.55H, CH conformer A), 4.73 (d, δ = 9.0 Hz, 0.45H, CH conformer B), 3.67–3.53 (m, 1H, CH₂ conformer A/B), 3.33–3.18 (m, 1H, CH₂ conformer A/B), 1.16 (t, δ = 7.0 Hz, 3H, CH₃ conformer A/B). ¹³C NMR (CDCl₃, 100 MHz): δ 201.2, 198.8, 184.6, 184.6, 171.7, 171.5, 165.9, 163.8, 152.4, 152.2, 152.1, 151.6, 153.2, 153.1, 136.7, 136.7, 136.5, 130.0, 60.0 (CH₂ conformer A/B), 58.6 (CH₂ conformer A/B). ¹⁹F NMR (CDCl₃, 400 MHz): δ -40.85 (CH₃ conformer A/B), 48.7 (CH₃ conformer A/B), 47.3 (CH₃ conformer A/B), 13.3 (CH₃ conformer A/B). MS (FAB⁺): m/z (%) 601 (M⁺ + 1, 10), 600 (M⁺, 10). HRMS (LSIMS): m/z 600.9616; calcld for [C₃H₇N₅O₆S₂ + H⁺], 600.9625.

Analytical Calcd for C₃H₇N₅O₆S₂: C 47.98, H 2.68, N 9.35. Found: C 48.11, H 2.73, N 9.22.

General Procedure for the Catalytic Cyclodehydration of 4-Benzyl[1,2]dithiolo[3,4-b,4′-3′-e][1]thiazin-3-oxo-5-thione (5) and Maleimides 2a–e–g.

Maleimide 2a–e–g (1 equiv) was prepared using a 5% (600 mg, 0.9 mmol) solution of sodium hydride in dimethylformamide (10 mL), and the mixture was refluxed for 2 h (for 2b, 3b, or 4b for 2g). Then the solution was evaporated under reduced pressure, and the residue was purified by column chromatography (silica 230–400 mesh, eluting with light petroleum to dichloromethane or a 4:24:5 ratio of dichloromethane/ethyl acetate 95:5 mixture for 6a). Analysis was performed by thin-layer chromatography (glass plates, silica 20 cm x 20 cm x 0.1 cm, eluting with dichloromethane/dichloromethane/ethyl acetate mixtures).

General Procedure for the Catalytic Cyclodegradation of 4-Ethylbis[1,2]dithiole-3,4-b[4,3,5]-[1,4]thiazin-3,5-dithione (7) and Maleimides 2b,2f, g

(1H NMR (DMSO-d6, 15N-3O4S7: C 38.49, H 2.69, N 7.48. Found: C 38.36, H 2.77, N 7.40. (Z/E)/2b,2f, 3a,3b, 6a,6a S)-2',2'-4-Ethyl-2,6-dithioxothio-morpholine-3,5-diyldienebis(5-methylidihydro-4H-[1,3]dithiole[4,5-c]-pyrrole-4,6(5H)-dione) (8b). MS (FAB+): m/z 40.35, H 1.91, N 4.09. Found: C 40.44, H 1.83, N 3.98.
(Z)2/E2/E2/E3a,3a”R6a,6a-S”)-2’,2’-(4-Ethyl-2,6-dithioxathiole-3,2’,4(3H)-trione)-2,2-dithioxathiole-3,2’,4(3H),6(a)-dione (8b). 21 mg (15%), light-brown solid, mp 184–185 °C (dec.) (DCM/EtOAc 95:5), 75/70/12/11.2 ratio of conformers. IR (KR): v = 1710, 1640, 1375 cm⁻¹. 1H NMR (DMSO-d₆, 400 MHz): δ (for the main conformer) 7.92–7.88 (m, 2H, HAr), 7.70–7.65 (m, 2H, HAr), 7.21–7.17 (m, 7H, HAr), 7.10–7.07 (m, 2H, HAr), 5.78 (d, J = 8.7 Hz, 2H, CH₂), 5.47 (d, J = 8.7 Hz, 2H, CH₂), 4.75 (q, J = 7.2 Hz, 2H, CH₂). 13C NMR and DEPT (CDCl₃, 100 MHz): δ (for the main conformer) 143.4, 134.4, 141.4, 137.6, 137.5, 134.3, 131.3 (C₂), 129.0 (CH₃), 95.2 (C₂), 60.5 (CH₂), 51.5 (CH), 34.31 (CH₃), 13.0 (CH₃). MS (FAB⁺): m/z (%) 938 (M⁺ + 1, 1). Anal. Calcd for C₃₂H₂₆N₄O₆S₁₂: C 37.72, H 1.98, N 6.12. Found: C 37.69, H 1.89, N 6.07. 1.06H, CH₂ conformer A), 3.63 (m, 1.11H, CH₂ conformer B). 13C NMR and DEPT (CDCl₃, 100 MHz): δ (for the main conformer) 143.4, 134.4, 141.4, 137.6, 137.5, 134.3, 131.3 (C₂), 129.0 (CH₃), 95.2 (C₂), 60.5 (CH₂), 51.5 (CH), 34.31 (CH₃), 13.0 (CH₃). MS (FAB⁺): m/z (%) 938 (M⁺ + 1, 1). Anal. Calcd for C₃₂H₂₆N₄O₆S₁₂: C 37.72, H 1.98, N 6.12. Found: C 37.69, H 1.89, N 6.07.
928 2-(Z/E)(E)-4-ethyl-5-[(3aR,6aS)-5-4-(4-((3aR,6aS)E/Z)-2-(4-
ethyl-3-oxo-6-thioxo-3H-4H-[1,2]dithiole[3,4-b][1,4]thiazin-
5(6H)-ylidene)-4,6-dioxotetrahydro-5H-[1,3]dithiolo[4,5-c]-
pyrrol-5-yl)(benzyl)phenyl]-4,6-dioxotetrahydro-4H-[1,3]-
dithiolo[4,5-c]pyrrolo[4,5-c]pyrrole-4,6(5H)-dione (12). Maleimide 10a (60 mg, 0.088 mmol) and
Sc(OOTf)3 (9 mg, 0.018 mmol) were added under nitrogen to 4-
ethylbis[1,2][dithiole[3,4-b][3,4-c]thiadiene](3.5-5-dihime) (15) (15
mm, 0.044 mmol) dissolved in dry dichloromethane (10 mL), and
the mixture was refluxed for 6 h. Then the solvent was evaporated
under reduced pressure, and the residue was purified by column
chromatography (silica 230–400 mesh, eluting with light petroleum
to dichloromethane/ethyl acetate 50:50) to get 12 (56 mg, 74% yield).

An analytical sample of 12 was obtained by thin-layer chromatography
(glass plates, silica 20 cm × 20 cm × 0.1 cm, eluting with
dichloromethane/ethyl acetate 50:50). Yellow solid, mp 238–239
°C (dec.) (DCM/EtOAc 50:50). IR (KBr): £ = 3429, 2946, 1710,
1532, 1404, 1342 cm

ACKNOWLEDGMENTS

We gratefully acknowledge financial support from the Ministerio
de Economía y Competitividad, Spain (Project CTQ2012-
31611), Junta de Castilla y León, Consejería de Educación y
Cultura y Fondo Social Europeo (Project BU246412-A) and
the European Commission Seventh Framework Programme
(Project SNIFFER FP7-SEC-2012-312411).