

Regioselective synthesis, X-ray structure, and reactivity of a tricyclic tetrasulfone, 1,3,5,7-tetramethyl-2,4,6,8,9,10-hexathiatricyclo[3.3.1.1<sup>3,7</sup>]decane 2,2,4,4,6,6,8,8-octaoxide, derived from tetramethylhexathiaadamantane †

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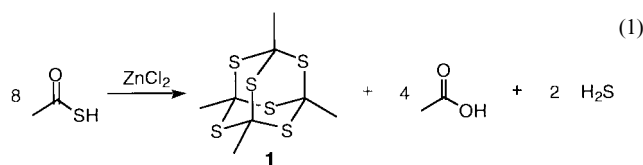
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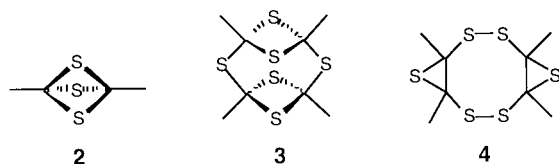
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Enthalpically disfavored tetrasulfone **9** is regioselectively synthesized from hexathiaadamantane **1**; X-ray crystallographic data shows **9** to be compressed relative to **1** along its transannular S9–S10 through space axis containing sulfide functions; **9** exhibits diverse reactivity including thermal extrusion of SO<sub>2</sub>, further oxidation to pentasulfone **10**, and transalkylation to tetradodecyl substituted tetrasulfone **11**.

T<sub>d</sub> symmetric 1,3,5,7-tetramethyl-2,4,6,8,9,10-hexathiatricyclo[3.3.1.1<sup>3,7</sup>]decane (*i.e.*, tetramethylhexathiaadamantane), **1**, was first prepared, albeit without an accurate structural assignment, by Bongartz<sup>1</sup> in 1886 according to eqn. (1).



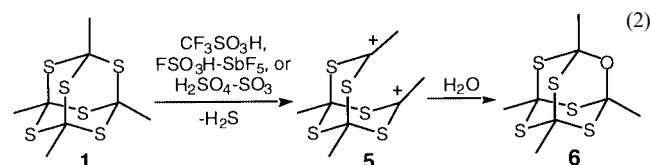
After calculating an empirical formula of C<sub>4</sub>H<sub>6</sub>S<sub>3</sub> for **1**, Bongartz proposed structure **2** for his product. In 1895, Candiana<sup>2</sup> prepared **1** by treating thioacetic acid with HBr. A molecular weight determination suggested that Bongartz' empirical formula should be doubled and Candiana proffered **3** and **4** as prospective C<sub>8</sub>H<sub>12</sub>S<sub>6</sub> structures. In 1901, Fromm and



Mangler<sup>3</sup> independently proposed structure **3** after repeating Bongartz' original synthesis [eqn. (1)]. It was not until 1947 that Fredga<sup>4</sup> correctly identified **1** as a tricyclo[3.3.1.1<sup>3,7</sup>] (adamantane-like) cage structure. Fredga's proposal was not based on new experimental evidence, but rather a re-evaluation of existing evidence. He surmised that **1** was simply too stable a structure to contain either three- or four-membered rings as in **2**, **3**, and **4**. Indeed, **1** and related hexathiaadamantanes (HTAs) are remarkably stable structures resisting both thermal and oxidative degradation. **1** melts without complication at 224 °C and survives prolonged heating in open air at elevated tem-

peratures. In 1986, Pickardt and Rautenberg<sup>5</sup> confirmed Fredga's structure by publishing an X-ray structure analysis for **1** and its PdCl<sub>2</sub> complex. More recently, Hargittai, Miller and co-workers<sup>6</sup> reported a joint computational, gas phase electron diffraction, and spectroscopic investigation of the molecular structure and vibrations of **1**.

Despite its early synthesis and subsequent structural studies, the chemistry of **1** remains largely unexplored. Last year, however, we reported<sup>7</sup> the formation and trapping of long-lived carbocation **5** prepared from **1** in superacid media [eqn. (2)].



Previously unknown oxapentathiaadamantane **6** is generated in modest yield upon quenching dication **5** with ice-water. As part of our ongoing studies of HTA chemistry, we now report our findings concerning the oxidation of **1** to give a variety of oxide adducts including monosulfoxide **7** and various bis- and trisoxides of **1** including monosulfone **8**. Most interesting, however, is the discovery that enthalpically disfavored tetrasulfone **9**, 1,3,5,7-tetramethyl-2,4,6,8,9,10-hexathiatricyclo[3.3.1.1<sup>3,7</sup>]decane 2,2,4,4,6,6,8,8-octaoxide, is regioselectively formed upon reacting **1** with an excess of either *m*-chloroperoxybenzoic acid (*m*CPBA) or KMnO<sub>4</sub>. **9** demonstrates interesting reactivity including thermal extrusion of SO<sub>2</sub>, further oxidation to pentasulfone **10**, and transalkylation to tetradodecyl substituted **11**.

Synthesis and structure of **9**

Oxidation studies on **1** are nearly nonexistent, save an early report by Fromm and Mangler<sup>3</sup> that KMnO<sub>4</sub> oxidation leads to a disulfone, but no higher oxidation products. We find that **1**<sup>8</sup> reacts with 2 equivalents of *m*CPBA to form a complex mixture of oxide adducts including monosulfoxide **7**,<sup>9</sup> traces of monosulfone **8**, and several other as yet incompletely resolved bisoxides and trisoxides. Upon reacting **1** with 25 equivalents of *m*CPBA, regioselective formation of D<sub>2d</sub> symmetric **9**<sup>9</sup> is accomplished in 69% isolated yield. Excepting a small quantity (<1%) of unreacted **1**, this latter reaction yields **9** as the only detectable product after aqueous base work-up. An analogous procedure using 25 equivalents of KMnO<sub>4</sub> yields **9** in 60% isolated yield. **9** is readily recrystallized from hot chloroform allowing an X-ray structure analysis§ to be completed (Fig. 1).

† Analytical data for compounds **1**, **7**, **9–11** are available as supplementary data. For direct electronic access see <http://www.rsc.org/suppdata/p2/b0/b004911p/>

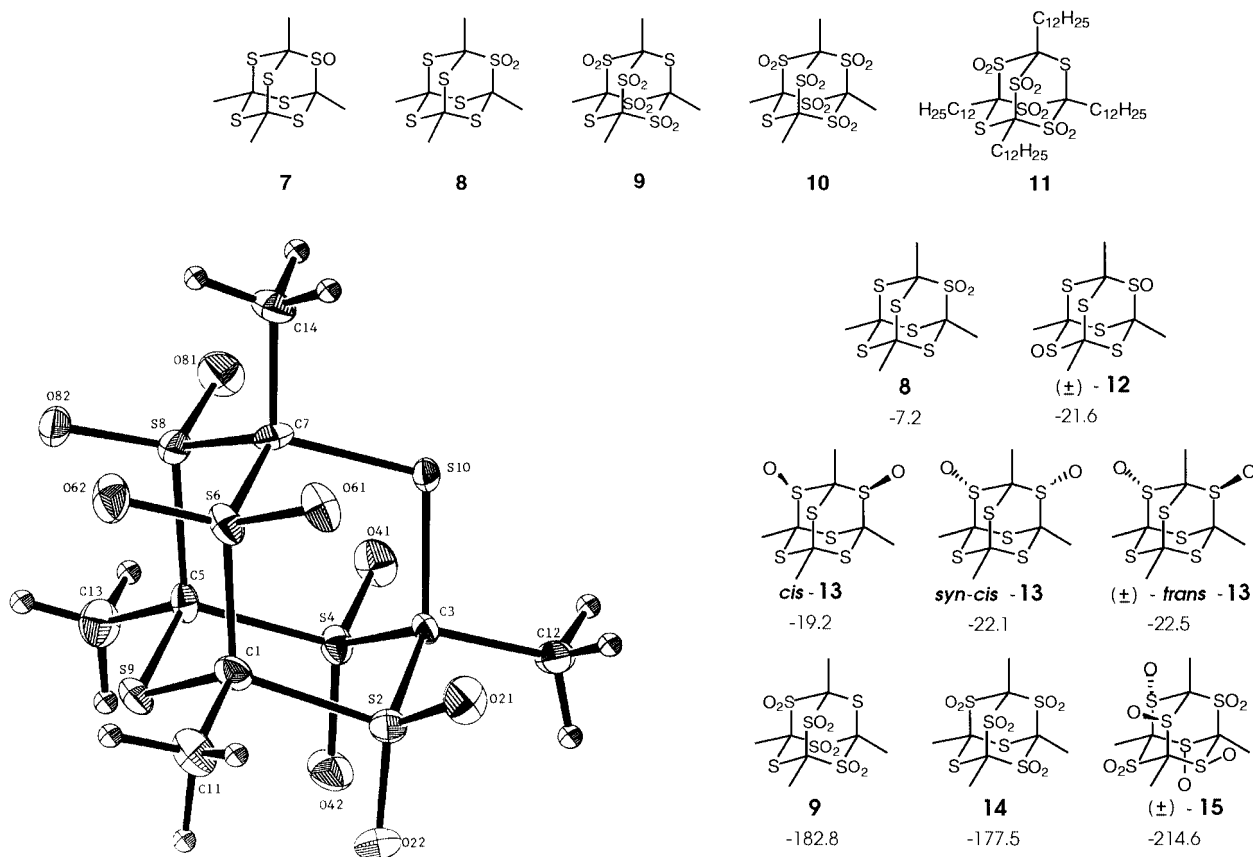
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§ CCDC reference number 188/263.

**Table 1** Geometrical parameters for **1** and **9** from electron diffraction and X-ray crystallography

Parameter	<b>1</b>			<b>9</b>	
	Electron diffraction $^{\circ}/\text{\AA}$ or $^{\circ}$	X-ray $^{\circ}/\text{\AA}$ or $^{\circ}$	3-21G(*) $^{\circ}/\text{\AA}$ or $^{\circ}$	X-ray $^{\circ}/\text{\AA}$ or $^{\circ}$	3-21G(*) $^{\circ}/\text{\AA}$ or $^{\circ}$
C–S	1.820(4)	1.808–1.837(9)	1.82	1.79–1.82(1)	1.82
C–SO <sub>2</sub>				1.80–1.85(1)	1.80
C–CH <sub>3</sub>	1.536(4)	1.50–1.53(1)	1.55	1.52–1.57(2)	1.57
S–O				1.40–1.46(1)	1.43
S9–S10	4.285(5)		4.30	4.15(2)	4.17
C–S–C	102.2(2)	102.7–103.5(4)	102.0	106.6–106.8(5)	103.6
C–SO <sub>2</sub> –C				101.8–103.7(6)	101.8
O–S–O				119.4–120.3(5)	119.8
S–C–S	112.8(2)	111.6–113.5(5)	112.9		
SO <sub>2</sub> –C–SO <sub>2</sub>				112.3–115.4(9)	115.0
SO <sub>2</sub> –C–S				110.3–112.9(7)	111.7

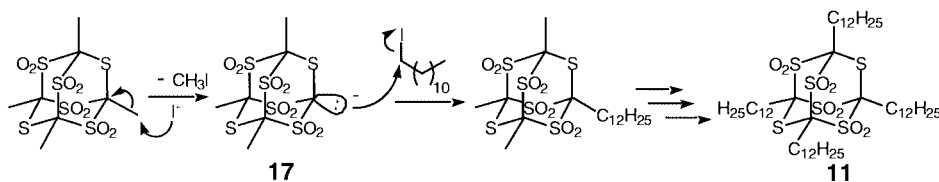
<sup>a</sup> See ref. 6. <sup>b</sup> See ref. 5. <sup>c</sup> MacSpartan's *ab initio* module was utilized for all 3-21G(\*) calculations; ranges are shown as appropriate for X-ray data; estimated standard deviations in the least significant figure are given in parentheses.

**Fig. 1** ORTEP drawing of **9** with 30.0% probability ellipsoids.**Fig. 2** AM1 calculated  $\Delta H_f^\circ$  values ( $\text{kcal mol}^{-1}$ ) for several oxide adducts of **1**.

Select geometrical parameters for both **1** and **9** are listed in Table 1.

Regioselective formation of tetrasulfone **9** from hexasulfide **1** is both striking and unexpected. Since oxidation of **1** using 2 equivalents of *m*CPBA leads to a complex mixture of mono-, bis-, and trisoxides, the initial stages of oxidation leading to **9** are apparently devoid of selectivity. Nonetheless, the first formed oxidation products all manage to converge on **9** in the presence of excess oxidant. AM1 calculations suggest the observed regioselectivity is not driven by thermodynamics. Thus, AM1 calculated  $\Delta H_f^\circ$  values (Fig. 2) show a strong enthalpic bias against sulfone and polysulfone formation on **1**. For example, of five possible bisoxide structures, sulfone **8** is disfavored by at least 12  $\text{kcal mol}^{-1}$ . Multiple octaoxide structures are possible, three of which are depicted in Fig. 2, and all but one is enthalpically preferred to **9** by AM1 calculations. Remarkably, AM1 favored octaoxide **15** is calculated to be nearly 32  $\text{kcal mol}^{-1}$  more stable than **9**. **15** possesses two

transannular sulfone and four sulfoxide functions. The four sulfoxide oxygens in **15** are all *trans* with respect to one another and are positioned over the four unique faces of the tricyclic adamantane cage. The only octaoxide structure enthalpically disfavored to **9** is **14**, the only other tetrasulfone. Both **9** and **14** suffer from van der Waals strain, specifically O–O (due to the proximity of O atoms on neighboring sulfone functions) and O–CH<sub>3</sub> repulsions. AM1 molecular modeling suggests that compression along the S9–S10 transannular axis in *D*<sub>2d</sub> symmetric **9** increases the through space distance between oxygen atoms on neighboring sulfone functions, thus reducing van der Waals strain. Indeed, the X-ray data indicate that tetrasulfone **9** is compressed along its S9–S10 transannular axis relative to **1**. That is, the S9–S10 through space distance is at least 0.11  $\text{\AA}$  shorter in **9** than in **1** resulting in a substantially wider ( $\sim 4^\circ$  wider) C–S9(10)–C bond angle for **9** (Table 1). 3-21G(\*) calculations correctly predict this trend toward S9–S10 transannular compression and provide geometrical



Scheme 1 Formation of **11** via bridgehead carbanion **17**.

parameters which closely match the X-ray data (Table 1), an exception being the C–S–C bond angle in **9**.

Considerable prior work concerning the oxidation of 1,3-dithianes seem to corroborate the AM1 preference for sulfoxide rather than sulfone formation in cyclic aliphatic polysulfides. Several groups<sup>10</sup> have studied the oxidation of 1,3-dithiane using a multitude of traditional oxidants including *m*CPBA, NaIO<sub>4</sub> and O<sub>3</sub>. In those cases where 2 equivalents of oxidant are utilized and/or where reactions are stopped after initial detection of bisoxides,<sup>10c</sup> bissulfoxides are formed to the exclusion of monosulfone. An anomaly is the KMnO<sub>4</sub> oxidation of 1,3-dithiane 1-oxide<sup>10a</sup> which yields monosulfone in excellent yield rather than bissulfoxide product. Enzymatic oxidations of 1,3-dithiane also generally give bissulfoxide<sup>11a,b</sup> in preference to monosulfone, an exception being cyclohexanone monooxygenase<sup>11c</sup> which shows the reverse selectivity.

## Reactivity of **9**

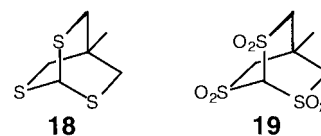
TGA analysis of **9** indicates the onset of thermal decomposition at about 150 °C. Thermal decomposition occurs in three distinct and increasingly significant steps centered at 175 (~12% weight loss), 260 (~20% weight loss) and 305 °C (~58% weight loss). Gas phase FT-IR detection of evolved gases reveals SO<sub>2</sub> liberation during the latter two weight loss steps. Conversely, hexasulfide **1** and monosulfoxide **7** sublime with little or no decomposition under analogous conditions. The van der Waals strain inherent to **9** may account for its reduced thermal stability compared to hexasulfide **1** and monosulfoxide **7**. **1**, **7**, and **9** are impervious to photochemical activation. No changes are detected after separate irradiations with 254 and 185 nm light for 24 h at 25 °C.

Although resistant to further oxidation, **9** is converted to pentasulfone **10**,<sup>9</sup> 1,3,5,7-tetramethyl-2,4,6,8,9,10-hexathiatri-cyclo[3.3.1.1<sup>3,7</sup>]decane 2,2,4,4,6,6,8,8,10,10-decaoxide, in 3–5% yield when treated with an additional 25 equivalents of *m*CPBA added in successive 5 equivalent increments over 25 h of reaction time in refluxing acetic acid. **10** is readily distinguished from **9** on the basis of its <sup>1</sup>H NMR ( $\delta_{\text{H}}$  (CH<sub>3</sub>–C, ppm, CDCl<sub>3</sub>) **9**: 2.23 (12H, s); **10**: 2.29 (6H, s), 2.47 (6H, s)) and CI mass spectrum (*m/z* (M<sup>+</sup> + 1) **9**: 429; **10**: 461). Considering the relative stabilities of **9** and **14** (Fig. 2), it is of little surprise that **9** resists further oxidation to pentasulfone **10**. Like **14**, **10** suffers from serious van der Waals strain that is not abated by simple molecular distortions.

Transalkylation of **9** using 4 equivalents of 1-iodododecane in the presence of 1 equivalent of tetrabutylammonium iodide yields **16**,<sup>9</sup> 1,3,5-tridodecyl-7-methyl-2,4,6,8,9,10-hexathiatri-cyclo[3.3.1.1<sup>3,7</sup>]decane 2,2,4,4,6,6,8,8-octaoxide, in 25% crude yield. **16** is inseparable from lesser substituted (*i.e.*, monododecyl and didodecyl) tetrasulfone product by flash silica chromatography, but can be identified on the basis of its <sup>1</sup>H and <sup>13</sup>C NMR spectra. Upon transalkylating **9** with 10 equivalents of 1-iodododecane and otherwise identical conditions, 1,3,5,7-tetradodecyl-2,4,6,8,9,10-hexathiatri-cyclo[3.3.1.1<sup>3,7</sup>]decane 2,2,4,4,6,6,8,8-octaoxide, **11**,<sup>9</sup> is formed in 65% crude yield with only small quantities of lesser substituted tetrasulfone present. **11** is readily distinguished from **16** and lesser substituted transalkylation products on the basis of its <sup>1</sup>H NMR spectrum, the former lacking a bridgehead methyl singlet at approximately 2.1 ppm.

Bridgehead carbanion **17** is a proposed intermediate in the transalkylation reaction (Scheme 1). Carbanions have long been known to be stabilized by adjacent sulfide or sulfone<sup>12</sup>

functions, and there is general agreement that 3d-orbitals on S play an important role in determining  $\alpha$ -thiocarbanion structure,<sup>13</sup> if not energetics.<sup>14,15</sup> **17** is reminiscent of carbanion intermediates formed via bridgehead deprotonation of bicyclic trithioorthoformate **18**<sup>16</sup> and bicyclic trisulfone **19**.<sup>17</sup> **17** is a



structurally unique carbanion, however, in that its non-bonding electrons are simultaneously adjacent to one sulfide and two electron-withdrawing sulfone functions. Moreover, the formation of carbanion **17** via nucleophilic attack at a bridgehead methyl is, to the best of our knowledge, unprecedented. Relief of O–CH<sub>3</sub> van der Waals strain appears to be an important driving force for the facile demethylation of **9**. Thus, both kinetic and thermodynamic factors favorably influence formation of **17** from **9**.

3-21G(\*) calculations suggest a slightly flattened structure at C1 of **17** (S–C1–SO<sub>2</sub> (°) **9**: 111.7, **17**: 115.5; SO<sub>2</sub>–C1–SO<sub>2</sub> (°) **9**: 115.0, **17**: 120.0) in which the corresponding S–C1 and SO<sub>2</sub>–C1 bond distances are reduced compared to those in **9** (S–C1  $\delta$  (Å) **9**: 1.818, **17**: 1.731; SO<sub>2</sub>–C1  $\delta$  (Å) **9**: 1.799, **17**: 1.686). The large reduction in SO<sub>2</sub>–C1 distances indicates a strong interaction between the non-bonding electrons on C1 and the vacant 3d-orbitals on adjacent sulfone S atoms. Interaction with the adjacent sulfide S appears weaker, but still significant.

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- (CH<sub>2</sub>)<sub>11</sub>-CS(SO<sub>2</sub>)<sub>2</sub>, 1.20–1.45 (72H, br m, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>9</sub>-C<sub>2</sub>H<sub>4</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 1.82 (8H, quintet, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>9</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 3.18 (8H, t, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>10</sub>-CH<sub>2</sub>-CS(SO<sub>2</sub>)<sub>2</sub>); CI-MS (*m/z*) 581, 507, 371, 285, 257, 233, 169, 119, 63, 57; **16**; δ<sub>H</sub>(360 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.89 (9H, t, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>11</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 1.20–1.43 (54H, br m, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>9</sub>-C<sub>2</sub>H<sub>4</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 1.59 (6H, quintet, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>9</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 2.10 (3H, s, CH<sub>3</sub>-CS(SO<sub>2</sub>)<sub>2</sub>), 2.50 (6H, t, CH<sub>3</sub>-(CH<sub>2</sub>)<sub>10</sub>-CH<sub>2</sub>-CS(SO<sub>2</sub>)<sub>2</sub>); CI-MS (*m/z*) 734, 568, 552 (M<sup>+</sup> - 2 C<sub>12</sub>H<sub>25</sub>), 383 (M<sup>+</sup> - 3 C<sub>12</sub>H<sub>25</sub>), 367 (M<sup>+</sup> - 3 C<sub>12</sub>H<sub>25</sub> - O), 233, 217, 169 (C<sub>12</sub>H<sub>25</sub>).
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