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Preparation of 1,4,5,8-tetra-*tert*-butyl-1,3,5,7-cyclooctatetraene by twofold SO_2 extrusion

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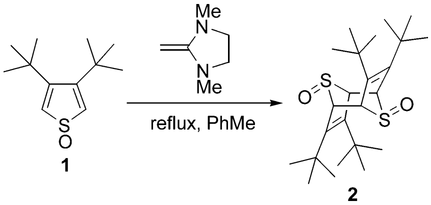
Abstract—Oxidation of *cis*-1-*transoid*-1,2-*cis*-2-3,4,7,8-tetra-*tert*-butyl-9,10-dithiatricyclo[4.2.1.1^{2,5}]deca-3,7-diene 9,10-dioxide (**2**) by dimethyldioxirane gave the corresponding tetraoxide **4** quantitatively, which in turn provided 1,4,5,8-tetra-*tert*-butyl-1,3,5,7-cyclooctatetraene (**6a**) quantitatively by twofold thermal SO_2 extrusion. The molecular structure of **6a** is described on the basis of DFT calculations (B3LYP/6-31G(d) level) and X-ray crystallographic analysis.

Sterically congested compounds have attracted much synthetic and structural interest in their own light. We have been investigating the synthesis of highly congested compounds in which two *tert*-butyl groups occupy vicinal positions of double bond in *cis*-orientation.[1] 3,4-Di-*tert*-butylthiophene, which itself is a congested compound that became readily obtainable,[2] has been used as the starting material of these synthetic studies. Recently we have reported that 3,4-di-*tert*-butylthiophene 1-oxide (**1**), which is obtained by oxidation of 3,4-di-*tert*-butylthiophene in good yield,[3] results in the formation of the [4+4] head-to-head dimer, *cis*-1-*transoid*-1,2-*cis*-2-3,4,7,8-tetra-*tert*-butyl-9,10-dithiatricyclo[4.2.1.1^{2,5}]deca-3,7-diene 9,10-dioxide (**2**),[4] when heated with 2-methylene-1,3-dimethylimidazolidine.[5] Although a number of papers have appeared on the chemistry of multi-*tert*-butyl substituted cyclooctatetraenes, successful synthesis of cyclooctatetraenes in which two *tert*-butyl groups occupy vicinal positions still remains to be developed.[6,7] In addition, preparation of 1,4,5,8-tetra-substituted 1,3,5,7-cyclooctatetraenes, including a tetramethyl derivative,[6e] is laborious. We now report the quantitative conversion of **2** to 1,4,5,8-tetra-*tert*-butyl-1,3,5,7-cyclooctatetraene (**6a**)[7,8] through oxidation followed by twofold SO_2 extrusion. The molecular structure of **6a** is also described on the basis of DFT calculations (B3LYP/6-31G(d) level) and X-ray crystallographic analysis.



A molecular structure of the dimer **2** is shown in Figure 1.[9] ^{1}H NMR analysis of the oxidation products of **2** with an equimolar amount of dimethyldioxirane (DMD)[10] at 0°C revealed that the reaction furnished a mixture of 9,9,10-trioxide **3**,[11] 9,9,10,10-tetraoxide **4**,[11] and the starting material **2**. It is well documented that 2,5-dihydrothiophene 1,1-dioxides undergo thermal extrusion of SO_2 in a concerted disrotatory manner to form 1,3-dienes.[12] Thus, **4** that is composed of two

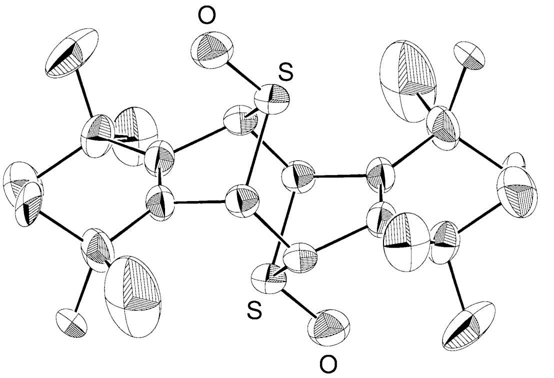


Figure 1. Molecular structure of **2**.

Keywords: cyclooctatetraene; steric congestion; extrusion of SO_2; X-ray crystallographic analysis; DFT calculations.

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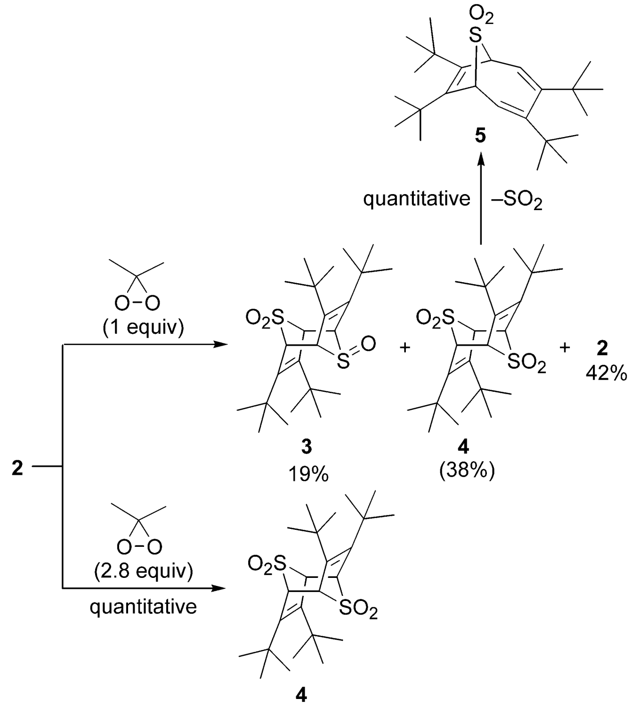
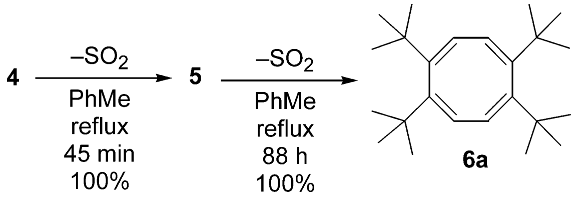
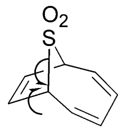
2,5-dihydrothiophene 1,1-dioxide skeletons extruded SO_2, during isolation processes including HPLC, to form **5**[11,13] quantitatively. This led to the isolation of **3**, **5**, and **2** in 19, 38, and 42% yields, respectively.



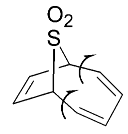
On the other hand, the oxidation of **2** with 2.8 molar amounts of DMD provided the tetraoxide **4** quantitatively, thus allowing easy isolation of pure **4** by mere evaporation of the solvent. Differential scanning calorimetry (DSC) analysis revealed that the crystalline tetraoxide **4** begins to extrude one molecule of SO_2 at about 77°C and another molecule of SO_2 at about 180°C. The first SO_2 extrusion would correspond to the conversion of **4** to **5** and the second one to the conversion of **5** to cylclooctatetraene **6**.



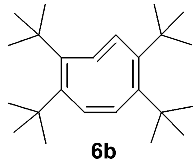
Indeed, heating **4** in refluxing toluene for 45 min produced **5** quantitatively and heating the solution for additional 88 h produced **6**[11] quantitatively. Extrusion of SO_2 of **5** in a thermally allowed [4π+2π] disrotatory mode **A**[12] results in the formation of 1,4,5,8-tetracyclooctatetraene (**6a**). Another thermally allowed process in a [6π+2π] conrotatory mode **B**, which leads to a highly strained isomer (**6b**),[14] would be highly disfavorable. Incidentally, ketone **7** is thermally stable and does not furnish the corresponding cyclooctatetraene even on photolysis,[6c] indicating that SO_2 is a better functional group than CO for extrusion reactions. However, NMR analysis[11] cannot rule out the possibility that, even if **6a** initially formed, it might have isomerized to 1,2,5,6-tetra-*tert*-butylcyclooctatetraene (**6c**) by bond shifting under the thermolytic conditions. We therefore carried out DFT calculations and X-ray crystallographic analysis on **6**.



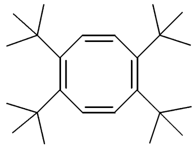
A



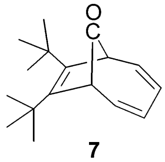
B



6b



6c



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DFT calculations (B3LYP/6-31G(d) level)[15] predicted that, for both **6a** and **6c**, the optimized (energy-minimized) conformation is of a typical tub and the optimized conformation of **6a** (Fig. 2) is more stable than that of **6c** by 24.8 kcal/mol (Fig. 3). As shown in Figure 3, **6c** contains two units of *cis*-1,2-di-*tert*-butylethylene,

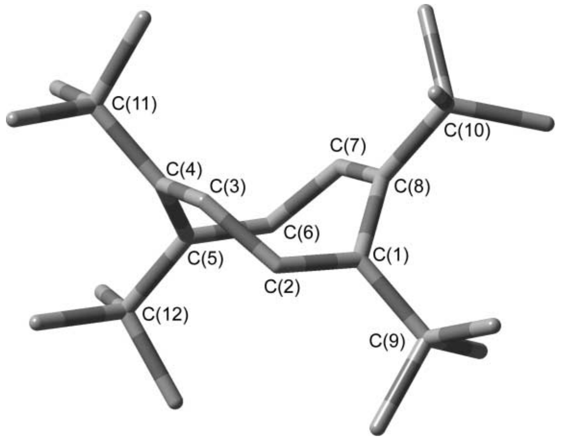

Figure 2. Predicted molecular structure of **6a**. Relevant bond angles (°): C8–C1–C2, 118.8; C1–C2–C3, 125.7; C2–C3–C4, 125.4; C3–C4–C5, 119.3; C4–C5–C6, 119.3; C5–C6–C7, 125.4; C6–C7–C8, 125.7; C7–C8–C1, 118.8; C8–C1–C9, 125.4; C2–C1–C9, 129.9; C7–C8–C10, 120.3(3); C1–C8–C10, 119.8. Dihedral angles (°): C9–C1–C8–C10, 76.8; C11–C4–C5–C12, 78.4. Bond lengths (Å): C1–C2, 1.340; C3–C4, 1.340; C5–C6, 1.340; C7–C8, 1.340; C2–C3, 1.470; C4–C5, 1.500; C6–C7, 1.470; C8–C1, 1.520; C1–C9, 1.550; C8–C10, 1.550.

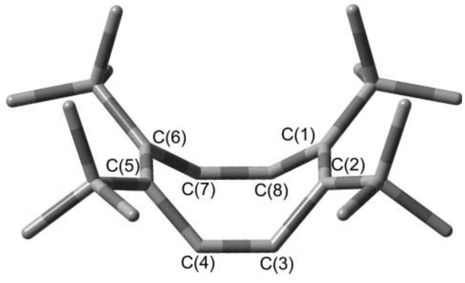

Figure 3. Predicted structure of **6c**.

a typical alkene of established high strain energy, thus high strain energy being imposed on this molecule. In addition, **6c** experiences steric repulsion between *tert*-butyl groups at C1 and C6 (C2 and C5), though this would be much smaller than the former repulsion. Meanwhile, **6a** is nearly free of such repulsion; vicinal *tert*-butyl groups are twisted with dihedral angles of 76.8° and 78.4° (Fig. 2). These would explain the large difference in the heat of formation between **6a** and **6c**. In addition, isomerization of **6a** to **6c** by bond shifting requires a delocalized [8]annulenic *anti*-aromatic planar transition state[16] to take place, where there occurs large expansion of its internal bond angles[17] with a large enhancement of steric repulsion between vicinal *tert*-butyl groups. Thus **6** would exist as **6a** as it formed initially.

Finally, X-ray crystallographic analysis[18,19] revealed unambiguously that **6** exists in the isomeric form of **6a**.[19] Figure 4 shows a molecular structure of **6a** together with the relevant bond angles, dihedral angles, and bond lengths. Although the crystal data of the analysis are not good enough for detailed discussion, it would be safe to conclude the following. (1) Bond alternation exists with double bond lengths in the range 1.336–1.351 Å and single bond lengths in the range 1.470–1.514 Å.[16] (2) Internal bond angles are in the range 117.7–124.8°, characteristic internal bond angle of usual cyclooctatetraenes.[16] (3) Vicinal *tert*-butyl groups are twisted with dihedral angles of 79.7° and 82.3°. (4) DFT calculations well reproduce the experimental strucuture of **6a**.

In conclusion, the new twofold extrusion strategy led to the successful synthesis of **6a** whose structure was established by X-ray crystallographic analysis. In addition, DFT calculations revealed that **6a** is far more stable than **6c**.

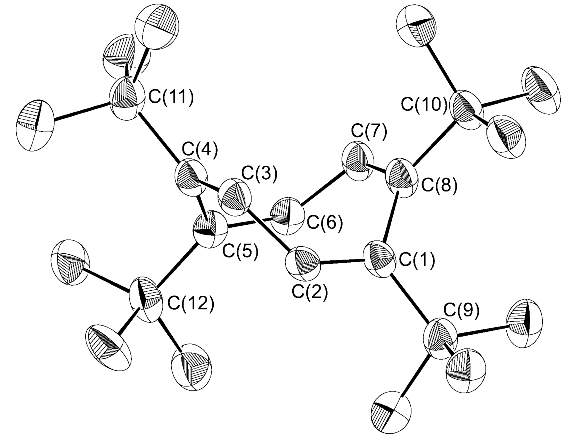

Figure 4. Molecular structure of **6a**. Relevant bond angles (°): C8–C1–C2, 119.2(3); C1–C2–C3, 124.1(3); C2–C3–C4, 124.3(3); C3–C4–C5, 118.6(3); C4–C5–C6, 117.7(3); C5–C6–C7, 124.8(3); C6–C7–C8, 124.1(3); C7–C8–C1, 119.0(3); C8–C1–C9, 120.2(3); C2–C1–C9, 120.3(3); C7–C8–C10, 120.3(3); C1–C8–C10, 120.3(3). Dihedral angles (°): C9–C1–C8–C10, 82.3(4); C11–C4–C5–C12, 79.7(4). Bond lengths (Å): C1–C2, 1.336(5); C3–C4, 1.351(4); C5–C6, 1.344(5); C7–C8, 1.344(4); C2–C3, 1.470(5); C4–C5, 1.507(5); C6–C7, 1.474(5); C8–C1, 1.514(5); C1–C9, 1.540(5); C8–C10, 1.555(5).

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7. Tetra-*tert*-butylcyclooctatetraene **6** was obtained in the laboratory of Professor G. Maier by photolysis of 3,4-di-*tert*-butylcyclobutene-1,2-dicarboxylic acid anhydride; Fritschi, G., Ph.D. Thesis, 1971, Karlsruhe, Germany. Photolysis of the above anhydride produced five hydrocarbons of similar polarity containing **6** (in about 2% yield), in addition to two ketones. It was suggested that 1,4,5,8-tetra-*tert*-butylcyclooctatetraene (**6a**) is sterically a more stable isomer than 1,2,5,6-*tert*-butylcyclooctatetraene (**6c**).
8. Cyclooctatetraene **6** is not registered in Chemical Abstracts. We thank Professor A. Krebs of Hamburg University for providing us the information given in Ref. 7.
9. X-Ray crystallographic data of **2**; $C_{24}H_{40}O_2S_2$, 424.71 g mol^{-1}, triclinic, $P\bar{1}$, $a=6.756(3)$ Å, $b=8.31801(10)$ Å, $c=11.846(2)$ Å, $\alpha=71.920(10)°$, $\beta=73.69(3)°$, $\gamma=77.55(3)°$, $V=601.4(3)$ Å^3, $D_{\text{calcd}}=1.145$ g cm^{-3}, $Z=1$, μ (Mo Kα) = 0.24 mm^{-1}, no. of measured reflections 3003, no. of independent reflections 2767, no. of reflections with $I>2\sigma(I)$ 2213, Parameters = 191, $R_1=0.066$, $wR_2=0.103$ (all), $S=0.709$.

10. Oxidation of **2** with *m*-chloroperbenzoic acid is sluggish and gave a complex mixture.
11. **3**: mp 177.0–177.5°C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 18H), 1.38 (s, 18H), 3.78 (d, $J=8.8$ Hz, 2H), 3.99 (d, $J=8.8$ Hz, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 31.6, 31.7, 34.7, 35.6, 65.1, 68.2, 139.4, 144.7; IR (KBr) 1301, 1124 (SO_2), 1063 (SO) cm^{-1}. **4**: mp 187–196°C (dec.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.37 (s, 36H), 4.00 (s, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.5, 36.0, 69.5, 147.6; IR (KBr) 1289, 1126 cm^{-1} (SO_2). **5**: mp 195.5–196.5°C (dec.); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.26 (s, 18H), 1.33 (s, 18H), 4.16 (d, $J=7.3$ Hz, 2H), 5.82 (d, $J=7.3$ Hz, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 32.6, 32.7, 35.7, 38.4, 69.8, 117.5, 119.4, 126.7; IR (KBr) 1291, 1124 cm^{-1} (SO_2). **6a**: mp 91–92°C (lit.[7] mp 85°C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.10 (s, 36H), 5.89 (s, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) $\delta=32.3$, 35.4, 126.3, 151.4.
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14. Several compounds with this ring system were converted to the corresponding cyclooctatetraenes photochemically or thermally.[13b] See also: Rigby, J. H.; Warshakoon, N. C. *Tetrahedron Lett.* **1997**, *38*, 2049.
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17. Angle modification of 126° to approximately 136° is required: Allinger, N. L.; Sprague, J. T.; Finder, C. J. *Tetrahedron* **1973**, *29*, 2519. The calculated internal bonds angles for **6a** are in the range 118.8–125.7° and for the experimental values, see Figure 4.
18. X-Ray crystallographic data of **6**; $C_{24}H_{40}$, 328.58 g mol^{-1}, triclinic, $P\bar{1}$, $a=9.366$ (2) Å, $b=10.982(2)$ Å, $c=11.624(4)$ Å, $\alpha=92.82(1)°$, $\beta=102.03$ (1)°, $\gamma=111.47(2)°$, $V=1077.8(5)$ Å^3, $D_{\mathrm{calcd}}=1.013$, $Z=2$, μ (Mo Kα) $=0.056$ mm^{-1}, no. of measured reflections 5024, no. of independent reflections 3414, no. of reflections with $I>2\sigma(I)$ 1958, parameters $=218$, $R_1=0.0823$, $wR_2=0.1595$ (all), $S=1.174$, $T=153$ K.
19. X-Ray crystallographic analysis of 1,4,5,8-tetrakis[(*p*-tolyloxy)methyl]-1,3,5,7-cyclooctatetranene was reported. See: Diercks, R.; Stamp, L.; tom Dieck, H. *Chem. Ber.* **1984**, *117*, 1913.