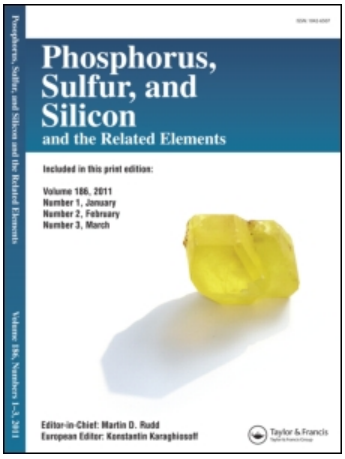

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Atropisomerism of the 1,3-cyclohexadiene Derivatives Induced by Steric Congestion

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ATROPISOMERISM OF THE 1,3-CYCLOHEXADIENE DERIVATIVES INDUCED BY STERIC CONGESTION

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3,4-Di-*tert*-butyl-2,5-dimethylthiophene 1-oxide (2) reacted with maleic anhydride to give the Diels–Alder adduct quantitatively. Oxidation of the sulfinyl group of the adduct and the thermal extrusion of sulfur dioxide from the resulting sulfone furnished 4,5-di-*tert*-butyl-3,6-dimethyl-3,5-cyclohexadiene-1,2-dicarboxylic acid anhydride (8) quantitatively. 8 showed atropisomerism that originates from the inhibited ring inversion of the cyclohexadiene ring by steric congestion. Mixtures of atropisomers were also obtained from the adducts of 2 and 1,4-benzoquinones.

Keywords Atropisomerism; Diels–Alder reaction; 3,4-di-*tert*-butyl-2,5-dimethylthiophene 1-oxide; steric congestion; X-ray diffraction analysis

INTRODUCTION

3,4-Di-*tert*-butylthiophene 1-oxide (**1**) has two π-faces, that is, *syn*- and *anti*-faces with respect to the S=O bond[1] (Figure 1). The 1-oxide **1** is thermally stable but highly reactive, and thus undergoes Diels–Alder reactions with a wide range of dienophiles under mild conditions. These Diels–Alder reactions took place at the *syn*-π-face with respect to the S=O bond without any exceptions.[2–6] The reactions also afforded the *endo*-adducts exclusively or preferentially. By using **1** as the starting material, we have synthesized a variety of sterically congested compounds, in which two *tert*-butyl groups are placed at the vicinal positions of the double bond with *cis*-orientation. We have now synthesized 3,4-di-*tert*-butyl-2,5-dimethylthiophene 1-oxide (**2**) in order to obtain more congested compounds by use of this compound as the starting material. Thus, the synthesis with **2** led to the interesting finding that the ring inversion of 4,5-di-*tert*-butyl-3,6-dimethyl-3,5-cyclohexadiene-1,2-dicarboxylic acid anhydride (**8**), prepared through Diels–Alder reaction of **2** with maleic anhydride, and those of the related compounds are frozen, thereby inducing a new atropisomerism.

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Dedicated to Professor Naomichi Furukawa on the occasion of his 70th birthday.
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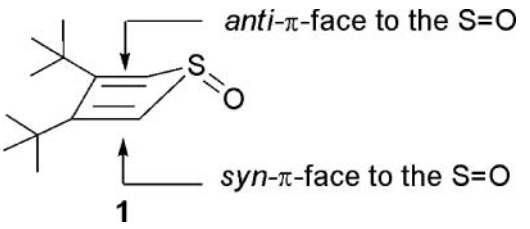
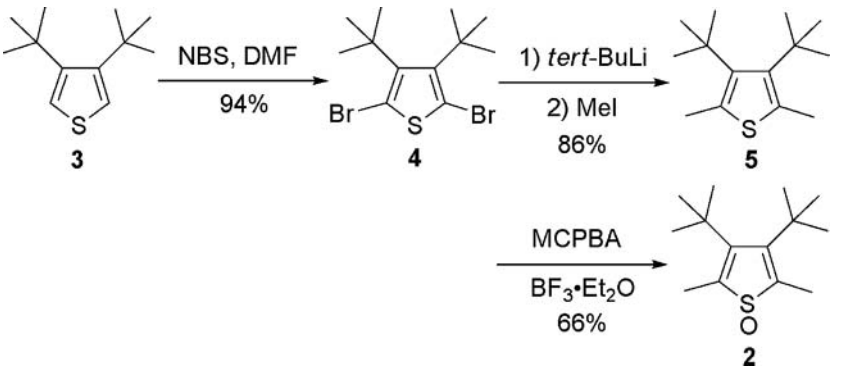


Figure 1 Two π-faces of **1**.

RESULTS AND DISCUSSION

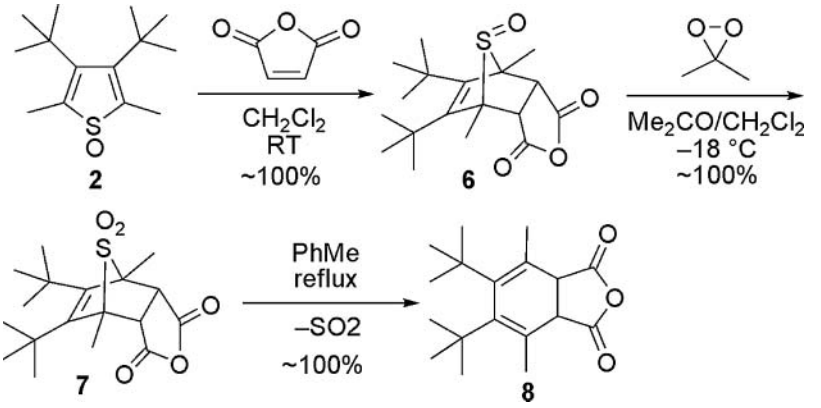
Thiophene 1-oxide **2** was prepared satisfactorily by the method shown in Scheme 1. Bromination of **3**[7] with two molar amounts of *N*-bromosuccinimide in *N,N*-dimethylformamide afforded dibromothiophene **4** in 94% yield. Thiophene **4** was previously obtained as a minor product (8%) of bromination of 3,4-di-*tert*-butylthiophene with an equimolar amount of *N*-bromosuccinimide in acetic acid.[7] Dilithiation of **4** with *tert*-butyllithium followed by treatment with methyl iodide provided dimethyl derivative **5** in 86% yield. Finally oxidation of **5** with *m*-chloroperbenzoic acid in the presence of boron trifluoride etherate, the method developed by the Furukawa group,[8–10] furnished the desired 1-oxide **2** in 66% yield.



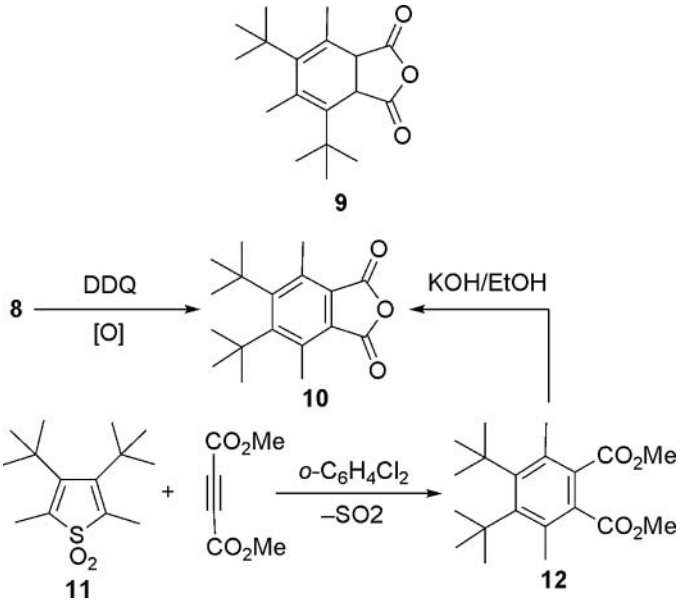
Scheme 1

A titled compound, 4,5-di-*tert*-butyl-3,6-dimethyl-3,5-cyclohexadiene-1,2-dicarboxylic acid anhydride (**8**), was prepared by the method shown in Scheme 2. The *syn*- and *endo*-selective Diels–Alder reaction of **2** with maleic anhydride occurred quickly to give the adduct **6** quantitatively. The reaction was complete within several minutes at room temperature. The conversion of **6** to the sulfone **7** was done quantitatively by using dimethyldioxirane (DMD) as the oxidizing agent. The sulfone **7**, which smells of sulfur dioxide, readily extruded sulfur dioxide to furnish the target compound **8** quantitatively when heated in refluxing toluene for several minutes.

As discussed below, the NMR data of cyclohexadiene **8** indicated that the compound might have the isomeric unsymmetrical structure **9**. Therefore, the following conversion was done to prove that this is not the case (Scheme 3). Thus, **8** was dehydrogenated to furnish phthalic anhydride **10** by heating with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone



Scheme 2



Scheme 3

(DDQ) in refluxing toluene. Previously we synthesized **10** from dimethyl phthalate **12** that was obtained by Diels–Alder reaction of thiophene 1,1-dioxide **11** with dimethyl acetylenedicarboxylate (DMAD) under forcing conditions.[11] The compounds obtained in these two ways were shown to be identical by comparison of the ^{1}H NMR data.

For the ^{1}H NMR spectrum of **8** in $CDCl_3$, the two *tert*-butyl groups, two methyl groups, and two methines all appeared as two nonequivalent signals. Thus, the two *tert*-butyl groups resonated at δ 1.27 (s) and 1.30 (s), two methyl groups at δ 1.99 (d, $J = 1.6$ Hz) and 2.12 (s), and two methines at δ 3.35 (d, $J = 6.6$ Hz) and 3.47 (d/q, $J = 1.6, 6.6$ Hz). The ^{13}C NMR spectrum showed 14 peaks, in accordance with the ^{1}H NMR spectrum, thus indicating that no mirror plane exists any longer in its structure. Incidentally, compounds **6** and **7** showed the NMR spectra that were expected from their symmetrical structures.

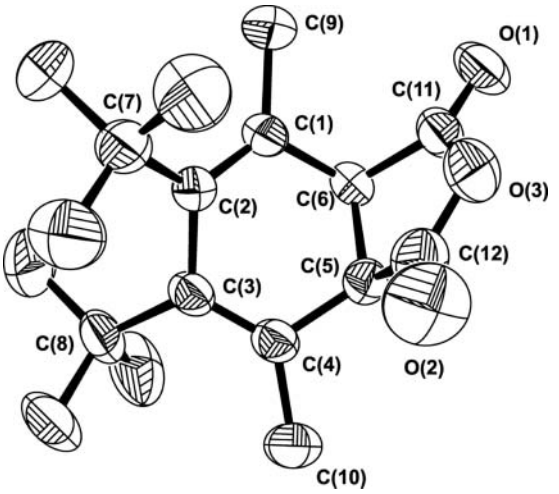


Figure 2A Molecular structure of **8** (top view).

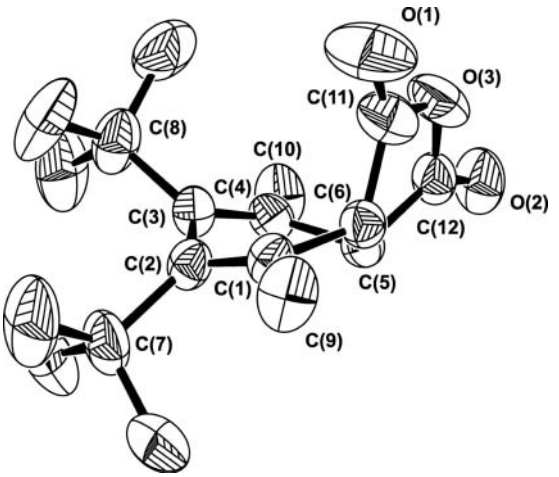


Figure 2B Molecular structure of **8** (side view).

X-ray single crystal structure analysis of **8** was done in order to know more about its structure. The molecular structure of **8**, viewed from two directions, is given as Figures 2A and 2B.

These show that the cyclohexadiene ring adopts a highly twisted chair form. Thus, if the ring is frozen at this conformation, the mirror plane is lost, and hence the molecule comes to show molecular chirality, allowing the existence of a pair of enantiomers. The bond distances, bond angles, and dihedral angles data are given in Table I. The three dihedral angles of the diene part are shown in Figures 3A–3C. The twist angle of the two double bonds is as large as 42.4(3)° (Figure 3A), and the twist angle of the two *tert*-butyl groups is much larger 66.7(3)° (Figure 3B). The *tert*-butyl group at C_2 and the methyl group at C_1 are twisted with a dihedral angle of 28.0(4)° (Figure 3C).

Table I Selected bond lengths, bond angles, and dihedral angles for **8**

Bond lengths [Å]			
C(1)−C(2)	1.343(3)	C(3)−C(8)	1.568(3)
C(1)−C(6)	1.517(3)	C(4)−C(5)	1.504(3)
C(1)−C(9)	1.507(3)	C(4)−C(10)	1.497(3)
C(2)−C(3)	1.508(3)	C(5)−C(6)	1.525(3)
C(2)−C(7)	1.566(3)	C(5)−C(12)	1.487(3)
C(3)−C(4)	1.338(3)	C(6)−C(11)	1.503(3)
Bond angles [°]			
C(2)−C(1)−C(6)	118.98(17)	C(3)−C(4)−C(5)	117.06(17)
C(6)−C(1)−C(9)	113.52(18)	C(5)−C(4)−C(10)	113.78(18)
C(9)−C(1)−C(2)	127.5(2)	C(10)−C(4)−C(3)	129.02(19)
C(1)−C(2)−C(3)	118.25(17)	C(4)−C(5)−C(6)	114.58(16)
C(3)−C(2)−C(7)	120.32(17)	C(6)−C(5)−C(12)	101.99(18)
C(7)−C(2)−C(1)	120.55(19)	C(12)−C(5)−C(4)	119.20(19)
C(2)−C(3)−C(4)	116.95(18)	C(1)−C(6)−C(5)	109.01(16)
C(4)−C(3)−C(8)	120.41(18)	C(5)−C(6)−C(11)	100.76(17)
C(8)−C(3)−C(2)	121.22(18)	C(11)−C(6)−C(1)	107.70(16)
Dihedral angles [°]			
C(6)−C(1)−C(2)−C(3)	−19.2(3)	C(3)−C(4)−C(5)−C(6)	−28.8(3)
C(6)−C(1)−C(2)−C(7)	150.0(2)	C(3)−C(4)−C(5)−C(12)	92.4(2)
C(9)−C(1)−C(2)−C(7)	−28.0(4)	C(10)−C(4)−C(5)−C(6)	147.34(19)
C(9)−C(1)−C(2)−C(3)	162.8(2)	C(10)−C(4)−C(5)−C(12)	−91.5(2)
C(1)−C(2)−C(3)−C(4)	42.4(3)	C(4)−C(5)−C(6)−C(1)	48.2(2)
C(1)−C(2)−C(3)−C(8)	−124.0(2)	C(4)−C(5)−C(6)−C(11)	161.30(17)
C(7)−C(2)−C(3)−C(4)	−126.8(2)	C(12)−C(5)−C(6)−C(1)	−82.04(19)
C(7)−C(2)−C(3)−C(8)	66.7(3)	C(12)−C(5)−C(6)−C(11)	31.1(2)
C(2)−C(3)−C(4)−C(5)	−15.8(3)	C(2)−C(6)−C(1)−C(5)	−23.8(3)
C(2)−C(3)−C(4)−C(10)	168.8(2)	C(2)−C(6)−C(1)−C(11)	−132.3(2)
C(8)−C(3)−C(4)−C(5)	150.8(2)	C(9)−C(6)−C(1)−C(5)	154.43(19)
C(8)−C(3)−C(4)−C(10)	−24.7(4)	C(9)−C(6)−C(1)−C(11)	45.9(3)

Thus, conjugation between the two double bonds C_1-C_2 and C_3-C_4 is practically impossible, thereby causing the elongation of the C_2-C_3 bond to 1.508(3) Å compared to the corresponding bond length (1.468 Å) of the parent 1,3-cyclohexadiene.[12] The C_1-C_2 and C_3-C_4 double bond lengths are 1.343(3) and 1.338(3) Å, respectively, and are close to the double bond length 1.33 Å of the parent ethylene, indicating again that no conjugation exists between the two double bonds. As to the bond angles, large deviation from 120° is not observed around the C_2 and C_3 partly due to the buttressing effect of the methyl groups at C_1 and C_4, but deviation is prominent around the C_1 and C_4. Thus, the bond angle

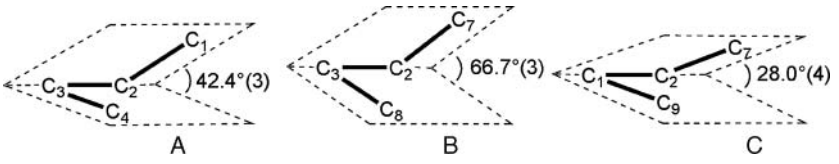


Figure 3 Dihedral angles of the diene part of **8**.

$C_2-C_1-C_9$ is as large as 127.5(2), but the bond angle $C_6-C_1-C_9$ is as small as 113.52 (18) instead.

The UV spectrum of **8** in hexane showed the absorption maximum at 254 nm (ε 4090). This value is close to the absorption maximum (256 nm) of the parent 1,3-cyclohexadiene and is longer than those of tetra-substituted alkenes (for example, 196 nm for 2,3-dimethyl-2-butene in heptane).[13] Since no conjugation exists practically between the double bonds of **8**, the absorption should be ascribed to π–π^* of the isolated double bond. The large bathochromic shift would originate from the destablization of the ground state of the double bonds caused by distortion due to steric congestion.

To sum up the above finding, the two *tert*-butyl groups exist in a largely twisted state caused by the buttressing effect of the methyl groups, in addition to their own bulkiness. As a result, the cyclohexadiene ring is distorted to such a great extent that no ring inversion takes place at least at room temperature, thus inducing the molecular chirality to **8** (Figure 4).

The diene **8** was inert to Diels–Alder reaction because of steric hindrance and non-conjugation between the double bonds. Thus, **8** failed to react with dimethyl acetylenedicarboxylate and maleic anhydride even when heated in *o*-dichlorobenzene at 170°C for 17 h.

The Diels–Alder reaction of **2** with 1,4-benzoquinone also occurred at room temperature to give **13** quantitatively (Scheme 4). The oxidation of **13** with DMD gave the sulfone **14**. When heated briefly in refluxing toluene, **14** extruded sulfur dioxide to furnish dihydronaphthoquinone **15** in 92% yield. The NMR spectra of **15** revealed that no mirror plane exists in the structure, whereas **13** and **14** gave the NNR spectra just expected from their symmetrical structures. Thus, for the ^{1}H NMR spectrum of **15** in $CDCl_3$, the two *tert*-butyl groups, two methyl groups, two methines, and two vinyl protons all showed two nonequivalent signals. Thus, the signals of the *tert*-butyl groups appeared at δ 1.19 (s) and 1.29 (s), methyl groups at δ 1.81 (d, $J = 1.6$ Hz) and 2.07 (s), methines at δ 2.99 (d, $J =$ 4.4 Hz) and 3.34–3.38 (m), and vinyl protons at δ 6.60 (d, $J = 10.3$ Hz) and 6.68 (d/d, $J =$ 1.6, 10.3 Hz). The ^{13}C NMR spectrum showed 16 peaks, in accordance with the ^{1}H NMR spectrum and also with its unsymmetrical twisted structure.

The above facts indicate that the introduction of methyl group into the two-position of **15** would result in the formation of a pair of diastereomers **18a** and **18b** (Scheme 5).

In order to verify this hypothesis, **16** was prepared starting from the Diels–Alder reaction of **2** with 2-methyl-1,4-benzoquinone. Oxidation of the resulting adduct **16** to **17** and the sulfur dioxide extrusion of **17** satisfactorily provided **18** in good overall yield. As

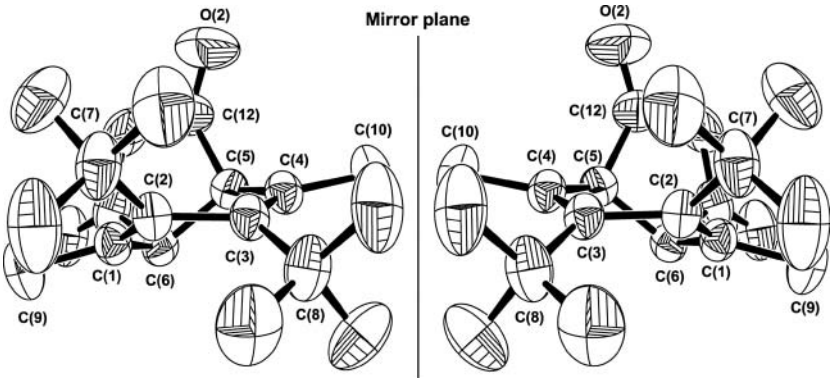
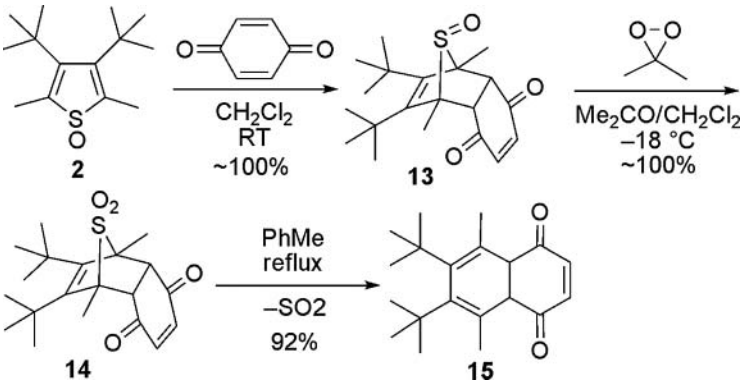
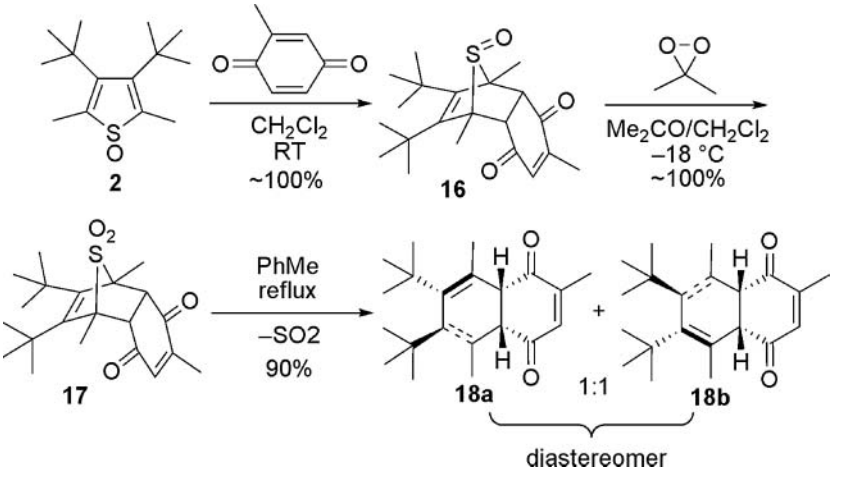


Figure 4 A pair of enantiomers of **8**.



Scheme 4



Scheme 5

expected, **18** was formed as a mixture of **18a** and **18b** in the ratio 1:1. Thus, for the ^{1}H NMR spectrum, *tert*-butyl groups appeared at δ 1.16 (s, 9H), 1.18 (s, 9H), and 1.28 (s, 18 H, accidental coincidence of two peaks); methyl groups at C_6 and C_8 at δ 1.73 (d, 3H, $J =$ 1.8 Hz), 1.79 (d, 3H, $J = 1.8$ Hz), 1.92 (d, 3H, $J = 1.5$ Hz), and 2.00 (d, 3H, $J = 1.8$ Hz); methyl group at C_2 at δ 2.07 (s, 6H, accidental coincidence of two peaks); methines at δ 2.93–2.96 (m, 2H), 3.30–3.34 (m, 1H), and 3.37–3.42 (1H, m); and vinyl protons at δ 6.47–6.50 (m, 1H) and 6.50–6.53 (m, 1H). The ^{13}C NMR spectrum showed 29 peaks in accordance with the observation by ^{1}H NMR, although the 34 expected peaks were not observed because of accidental coincidence of the peaks.

In conclusion, we have found a 1,3-cyclohexadiene system that shows atropisomerism ascribable to the frozen ring-inversion by steric congestion.

EXPERIMENTAL

3,4-Di-*tert*-butyl-2,5-dimethylthiophene (5)

A solution of 2,5-dibromo-3,4-di-*tert*-butylthiophene (**4**) (1.05 g; 30 mmol) in 30 mL of tetrahydrofuran was cooled at −78°C and stirred under argon. To this solution, 8.4 mL (150 mmol) of a 13.2 *M* hexane solution of *tert*-butyllithium was added slowly through a rubber septum. The mixture was stirred for 3 h, during which it was warmed to 0°C. To this mixture 0.90 mL (15 mmol) of methyl iodide was added. After the mixture had been stirred for 0.5 h, ice water was added. The resulting mixture was extracted with ether, and the ether extracts were treated in the usual way to give a crude solid product. It was purified by silica gel column chromatography to give 0.58 g (86%) of **5**: mp 79–80°C (from pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 18H), 2.46 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.8, 34.0, 36.9, 129.0, 146.3. Anal. Calcd for $C_{14}H_{24}S$: C, 74.93; H, 10.78. Found: C, 74.81; H, 10.93.

3,4-Di-*tert*-butyl-2,5-dimethylthiophene 1-oxide (2)

A solution of 2,5-dimethyl-3,4-di-*tert*-thiophene (**5**) (0.58 g; 26 mmol) in 20 mL of dichloromethane was cooled at −18°C and stirred under argon. To this solution, 1.6 mL (130 mmol) of boron trifluoride etherate ($BF_3 \bullet Et_2O$) was added slowly through a rubber septum. The mixture was stirred for 10 min at that temperature, and then a solution of 0.48 g (31 mmol) of *m*-chloroperbenzoic acid in 10 mL of dichloromethane was added slowly to this mixture. After the mixture had been warmed to room temperature and stirred for 3 h, aqueous sodium hydrogen carbonate was added. The resulting mixture was extracted with dichloromethane, and the dichloromethane extracts were treated in the usual way to give a crude product. It was subjected to silica gel column chromatography, and elution of the column with hexane:ethyl acetate (1:1) gave 0.41 g (66%) of **2**: mp 112.5–113.5°C (from pentane/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 18H), 2.26 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.7, 32.1, 36.7, 141.0, 151.5; IR (KBr) 1039 cm^{-1} (S=O). Anal. Calcd for $C_{14}H_{24}OS$: C, 69.94; H, 10.06. Found: C, 69.82; H, 10.82.

Preparation of Sulfoxide 6 by Diels–Alder Reaction of 2 with Maleic Anhydride

A mixture of 50 mg (0.21 mmol) of **2** and 21 mg (0.21 mmol) of maleic anhydride in 2 mL of dichloromethane was stirred for 5 min at room temperature and evaporated to give 71 mg (100%) of practically pure **6**: mp 243–244°C (dec.) (from pentane/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 18H), 1.98 (s, 6H), 3.70 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.6, 34.7, 36.9, 54.5, 75.6, 146.4, 170.7; IR (KBr) 1074 (S=O), 1782, 1859 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{26}O_4S$: C, 63.88; H, 7.74. Found: C, 63.69; H, 7.72.

Preparation of Sulfone 7 by Oxidation of 6

To a stirred solution of 71 mg (0.21 mmol) of **6** in 5 mL of dichloromethane, 6.3 mL of a 0.63 m*M* acetone solution of dimethyldioxirane (0.40 mmol) was added under stirring at −18°C. The mixture was stirred at room temperature for 12 h, and then evaporated under reduced pressure to give 74 mg (100%) of practically pure **7**. Compound **7** has a smell of

sulfur dioxide, indicating that it undergoes extrusion of sulfur dioxide, though slowly, even in the solid state and at room temperature. **7**: mp 91–92°C (dec.) (from pentane/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 18H), 2.09 (s, 6H), 3.47 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.1, 34.1, 37.6, 50.4, 70.6, 147.7, 168.7; IR (KBr) 1163, 1305 (SO_2), 1782, 1861 cm^{-1} (C=O). Elemental analysis of **7** did not give satisfactory results because sulfur dioxide extrusion occurred during storage of the sample. Anal. Calcd for $C_{18}H_{26}O_5S$: C, 60.99; H, 7.39. Found: C, 61.95; H, 7.51.

Preparation of 4,5-Di-*tert*-butyl-3,6-dimethyl-3,5-cyclohexadiene-1,2-dicarboxylic Acid Anhydride (8) by Extrusion of Sulfur Dioxide from 7

A solution of 71 mg (0.21 mmol) of **7** in 5 mL of toluene was heated at reflux for 5 min and evaporated to give 61 mg (100%) of practically pure **8**. When a solution of **7** in $CDCl_3$ was allowed to stand at room temperature, after one week **7** turned into **8** completely by sulfur dioxide extrusion. **8**: mp 107–108°C (from pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (s, 9H), 1.30 (s, 9H), 1.99 (d, 3H, J = 1.6 Hz), 2.12 (s, 3H), 3.35 (d, 1H, J = 6.6 Hz), 3.47 (d/q, 1H, J = 1.6/6.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.2, 23.2, 32.2, 32.3, 37.1, 37.6, 52.4, 52.5, 123.2, 123.4, 150.3, 153.1, 171.0, 172.2; IR (KBr) 1783, 1859 cm^{-1} (C=O); UV (hexane) λ_{max} (ε) 254 (4090). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.36; H, 9.07.

Oxidation of 8 to 4,5-Di-*tert*-butyl-3,6-dimethylphthalic Anhydride 10

The oxidation by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was sluggish probably because the dehydration was hampered by steric hindrance. Thus, a mixture of 7.0 mg (0.024 mmol) of **8** and 21.5 mg (0.094 mmol) of DDQ was heated in refluxing toluene for 8 h. The mixture was evaporated and the residue was analyzed by ^{1}H NMR ($CDCl_3$), which revealed 20% conversion of **8** to **10**; the signals due to **10** appeared at δ 1.50 (s, 18H, *tert*-Bu) and 2.81 (s, 6H, Me). The authentic sample, obtained from **11** via **12**, showed the same ^{1}H NMR spectrum.

Preparation of Sulfoxide 13 by Diels–Alder Reaction of 2 with 1,4-Benzoquinone

The reaction of 51 mg (0.21 mmol) of **2** and 23 mg (0.21 mmol) of 1,4-benzoquinone in 2 mL of dichloromethane for 5 min at room temperature furnished 74 mg (100%) of practically pure **13** after evaporation of the solvent: mp 166–167°C (dec.) (pale yellow crystals from hexane/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 18H), 1.97 (s, 6H), 3.34 (s, 2H), 6.72 (s, 2H); ^{13}C NMR (50 MHz, C_6D_6) δ 19.6, 34.7, 36.5, 54.2, 77.2, 142.6, 145.8, 197.4; IR (KBr) 1059 (S=O), 1669 cm^{-1} (C=O). Anal. Calcd for $C_{20}H_{28}O_3S$: C, 68.93; H, 8.10. Found: C, 68.87; H, 8.34.

Preparation of Sulfone 14 by Oxidation of 13

Sulfoxide **13** (74 mg, 0.21 mmol) was oxidized by DMD in the same way as the oxidation of **6** to **7** to give 77 mg (100%) of practically pure **14**: mp 113–114°C (dec.) (pale yellow crystals from pentane/Et_2O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 18H), 2.05 (s, 6H), 3.32 (s, 2H), 6.72 (s, 2H); ^{13}C NMR (50 MHz, C_6D_6) δ 14.7, 34.2, 37.0, 52.3,

72.2, 142.4, 146.4, 194.4; IR (KBr) 1162, 1306 (SO_2), 1669 m^{-1} (C=O). Anal. Calcd for $C_{20}H_{28}O_4S$: C, 65.90; H, 7.74. Found: C, 65.90; H, 7.78.

Preparation of 9,10-Dihydro-6,7-di-*tert*-butyl-5,8-dimethyl-1,4-naphthoquinone 15 by Extrusion of Sulfur Dioxide from 14

A solution of 77 mg (0.21 mmol) of **14** in 5 mL of toluene was heated at reflux for 20 min and evaporated to give 61 mg (92%) of practically pure **15**: mp 111–112°C (pale yellow crystals from pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.29 (s, 9H), 1.81 (d, 3H, $J = 1.6$ Hz), 2.07 (s, 3H), 2.99 (d, 1H, $J = 4.4$ Hz), 3.34–3.38 (m, 1H), 6.60 (d, 1H, $J = 10.3$ Hz), 6.68 (dd, 1H, $J = 1.6/10.3$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.6, 22.6, 32.1, 32.5, 36.3, 36.5, 58.0, 58.5, 128.0, 129.5, 139.9, 140.0, 147.8, 151.6, 201.7, 20.18; IR (KBr) 1667 cm^{-1} (C=O); UV/Vis (hexane) λ_{max} (ε) 256 (4010), 353 nm (166). Anal. Calcd for $C_{18}H_{26}O_2$: C, 79.96; H, 9.39. Found: C, 79.77; H, 9.59.

Preparation of Sulfoxide 16 by Diels–Alder Reaction of 2 with 2-Methyl-1,4-benzoquinone

The reaction of 49 mg (0.20 mmol) of **2** and 25 mg (0.21 mmol) of 2-methyl-1,4-benzoquinone in 2 mL of dichloromethane for 5 min at room temperature furnished 74 mg (100%) of practically pure **16** after evaporation of the solvent: mp 165–166°C (dec.) (pale yellow crystals from hexane/CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 9H), 1.31 (s, 9H), 1.95 (s, 3H), 1.96 (s, 3H), 2.00 (d, 3H, $J = 1.1$ Hz), 3.32 (d, 1H, $J = 9.2$ Hz), 3.37 (d, 1H, $J = 9.2$ Hz), 6.61 (q, 1H, $J = 1.1$ Hz); ^{13}C NMR (50 MHz, C_6D_6) δ 16.4, 19.7, 19.8, 34.6, 34.7, 36.5, 36.6, 54.2, 54.8, 77.2, 77.3, 140.9, 145.8, 146.1, 151.8, 196.8, 197.8; IR (KBr) 1074 (S=O), 1669 cm^{-1} (C=O). Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.57; H, 8.34. Found: C, 69.57; H, 8.42.

Preparation of Sulfone 17 by Oxidation of 16

Sulfoxide **16** (74 mg, 0.20 mmol) was oxidized by DMD in the same way as the oxidation of **6** to **7** to give 79 mg (100%) of practically pure **17**; mp 123–124°C (dec.) (pale yellow crystals from hexane/MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 1.34 (s, 9H), 1.96 (s, 3H, $J = 1.1$ Hz), 2.04 (s, 3H), 2.05 (s, 3H), 3.30 (d, 1H, $J = 8.8$ Hz), 3.34 (d, 1H, $J = 8.8$ Hz), 6.61 (q, 1H, $J = 1.1$ Hz); ^{13}C NMR (50 MHz, C_6D_6) δ 14.8, 14.9, 16.3, 34.2, 34.3, 37.0, 37.1, 52.3, 53.0, 72.4, 72.5, 140.7, 146.3, 146.7, 151.6, 193.9, 194.9; IR (KBr) 1164, 1301 (SO_2), 1663 m^{-1} (C=O). Anal. Calcd for $C_{21}H_{30}O_4S$: C, 66.63; H, 7.99. Found: C, 65.56; H, 8.04.

Formation of a Diasteromeric Mixture of 9,10-Dihydro-6,7-di-*tert*-butyl-2,5,8-trimethyl-1,4-naphthoquinone 18 by Extrusion of Sulfur Dioxide from 17

A solution of 77 mg (0.21 mmol) of **17** in 5 mL of toluene was heated at reflux for 20 min and evaporated to give 57 mg (90%) of a 1:1 diastereomeric mixture of **18a** and **18b**: mp 113–116°C (pale yellow crystals from pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 9H), 1.18 (s, 9H), 1.28 (s, 18H), 1.73 (d, 3H, $J = 1.8$ Hz), 1.79 (d, 3H, $J = 1.8$ Hz), 1.92

(d, 3H, $J = 1.5$ Hz), 2.00 (d, 3H, $J = 1.5$ Hz), 2.07 (s, 3H), 2.93–2.96 (m, 2H), 3.30–3.34 (m, 1H), 3.37–3.42 (m, 1H), 6.47–6.50 (m, 1H), 6.50–6.53 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.2, 20.3, 20.6, 22.6, 22.7, 32.1, 32.5, 36.2, 36.4, 36.5, 58.0, 58.4, 58.7, 128.4, 128.5, 129.7, 129.8, 136.9, 137.2, 147.4, 149.6, 149.9, 151.0, 201.5, 201.8, 202.4; IR (KBr) 1678 cm^{-1} (C=O). Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.11; H, 9.77.

X-Ray Crystallographic Analysis of 8

Crystal data for **8** were recorded on a Bruker SMART APEX CCD area detector by using 0.30°-wide ω scans and graphite-monochromated Mo-$K\alpha$ radiation ($\lambda = 0.71073$ Å). Frame data (4 sec, 0.30°-wide ω scans) were collected using the Bruker SMART software package. Peak integration was performed by the Bruker SAINT-Plus software package. Absorption correction was made by the software SADABS. Space group determination was done by the software XPREP. All calculations were performed by the Bruker SHELXTL-NT software package. The structure was solved by direct methods and refined with full-matrix least-squares by all independent reflections. The nonhydrogen atoms were refined anisotropically, and hydrogen atoms were placed at calculated positions.

8: $C_{18}H_{26}O_3$, Mw = 290.39, monoclinic, space group *P2/c*; $a = 14.435(6)$, $b = 6.639(3)$, $c = 17.721(8)$ Å, $\beta = 93.275(10)$ deg; $Z = 4$; $V = 1695.5(13)$ Å^3; Dc = 1.138 g/cm^3, $\mu = 0.076$ mm^{-1}; measured reflections 11891, independent reflections 4055 [R(int) = 0.0360], $R1 = 0.0703$, w$R2 = 0.1804$, GOF = 1.019.

Crystallographic data for the structural analysis have been deposited at the Cambridge Crystallographic Data Center, CCDC No. 712258. Copies of this information can be obtained from The Director, DDCD, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.ac.uk or http://www.ccdc.cam.ac.uk).

REFERENCES

1. J. Nakayama, T. Yu, Y. Sugihara, and A. Ishii, *Chem. Lett.*, **26**, 499 (1997).
2. For reviews on the chemistry of thiophene 1-oxides, see (a) J. Nakayama and Y. Sugihara, *Sulfur Reports*, **19**, 349 (1996); (b) J. Nakayama, *Bull. Chem. Soc. Jpn.*, **73**, 1 (2000); (c) J. Nakayama, *Sulfur Reports*, **22**, 123 (2000); (d) J. Nakayama, *J. Synth. Org. Chem., Jpn.*, **61**, 66 (2003).
3. T. Otani, J. Takayama, Y. Sugihara, A. Ishii, and J. Nakayama, *J. Am. Chem. Soc.*, **125**, 8255 (2003).
4. J. Takayama, S. Fukuda, Y. Sugihara, A. Ishii, and J. Nakayama, *Tetrahedron Lett.*, **44**, 5159 (2003).
5. J. Takayama, Y. Sugihara, T. Takayanagi, and J. Nakayama, *Tetrahedron. Lett.*, **46**, 4165 (2005).
6. K. Iguchi, Y. Sugihara, and J. Nakayama, *Bull. Chem. Soc. Jpn.*, **81**, 304 (2008).
7. J. Nakayama, S. Yamaoka, and M. Hoshino, *Tetrahedron Lett.*, **29**, 1161 (1988).
8. N. Furukawa, S.-Z. Zhang, S. Sato, and M. Higaki, *Heterocycles*, **44**, 61 (1996).
9. N. Furukawa, S.-Z. Zhang, E. Horn, O. Takahashi, and S. Sato, *Heterocycles*, **45**, 793 (1997).
10. S.-Z. Zhang, S. Sato, E. Horn, and N. Furukawa, *Heterocycles*, **48**, 227 (1998).
11. J. Nakayama, R. Hasemi, K. Yoshimura, Y. Sugihara, S. Yamaoka, and S. Nakamura, *J. Org. Chem.*, **63**, 4912 (1998).
12. H. Oberhammer and S. H. Bauer, *J. Am. Chem. Soc.*, **91**, 10 (1969).
13. E. Pretsch, P. Bühlmann, and C. Affolter, *Structure Determination of Organic Compounds* (Springer, Berlin, 2000), Chap. 8.