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Oxidation of 2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane and Its Oxidation Products: An Important Role of 1,3-Transannular Interaction in the 1,3-Dithietane Part

Akihiko Ishii, Meng-Xin Ding, Kiyoto Maeda,
Juzo Nakayama,* and Masamatsu Hoshino
Department of Chemistry, Faculty of Science, Saitama University, Urawa, Saitama 338
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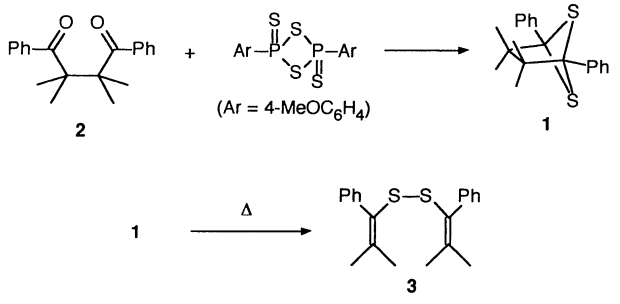
Oxidation of 2,2,3,3-tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]hexane with *m*-chloroperbenzoic acid gives two isomeric *endo*- (**4a**) and *exo*-sulfoxides (**4b**), three *S,S'*-dioxides (*endo, exo*-**5a**, *exo, exo*-**5b**, and *endo, endo*-**5c**), and an *S,S,S'-trioxide* (**6**). The relative reactivity to further oxidation is **4b**≫**4a** and **5b**>**5a**, which suggests that the attractive 1,3-transannular interaction operative in 1,3-dithietane part of **4a** and **5a** decreases the reactivity of **4a** and **5a**. **4b** isomerizes to **4a** on standing over silica gel at room temperature and also **5b** is converted to **5a** on heating. Heating **6** in refluxing toluene yields 3,3,4,4-tetramethyl-1,2-diphenylcyclobutene, 2,5-dimethyl-3,4-diphenyl-2,4-hexadiene, and the isomeric trioxide.

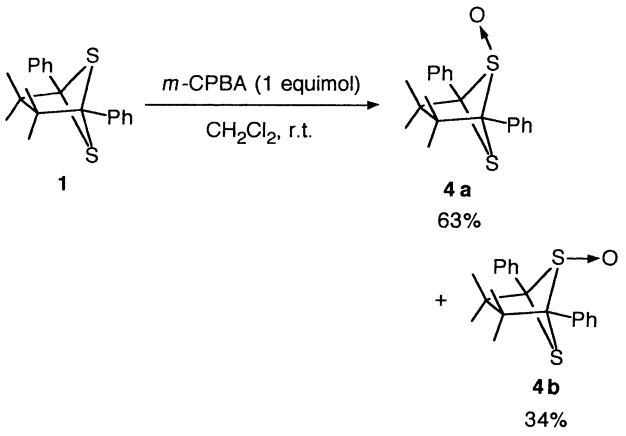
We recently reported that the title compound **1** was obtained by the reaction of 2,2,3,3-tetramethyl-1,4-diphenylbutane-1,4-dione (**2**) with the Lawesson's reagent and was thermally labile to isomerize to disulfide **3**.[1] A 5,6-dithiabicyclo[2.1.1]hexane, the basic skeleton of **1**, is unique in structure because 1,3-dithietane and thiolane ring systems reside together in it. It was reported that the parent 1,3-dithietane is slightly puckered in the solid state and nearly planar in the gas phase[2,3] and the parent thiolane adopts twist conformations.[4] However, the bicyclic framework of the 5,6-dithiabicyclo[2.1.1]hexane forces the 1,3-dithietane and the thiolane to take puckered and envelope conformations, respectively,[5] which interests us in its chemical and physical behavior.



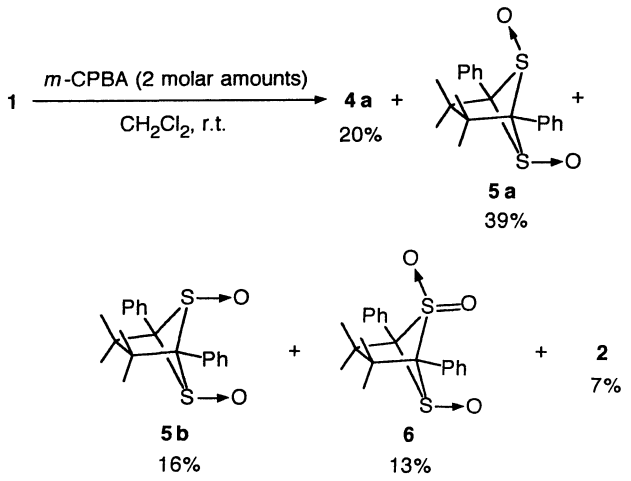
In spite of such interesting features, the chemistry of 5,6-dithiabicyclo[2.1.1]hexanes has not been developed until Bayer and Block reported the isolation of 2,3-dimethyl-5,6-dithiabicyclo[2.2.1]hexane *S*-oxides (zwiebelanes) from onion extract in 1989.[6] The zwiebelanes were reported to show an inhibition of thrombin-induced TXB_2 biosynthesis in human platelet rich plasma. We report here the oxidation of **1** and also discuss the orientation and the relative reactivity of the oxidation products to further oxidation and their relative stability.

Results and Discussion

Oxidation of **1** with an equimolar amount of *m*-chloroperbenzoic acid (*m*-CPBA)[7] in dichloromethane at room temperature gave two isomeric sulfoxides. The structures of the sulfoxides were assigned to *endo*-sulfoxide **4a** (63%) and *exo*-sulfoxide **4b** (34%), respectively. When the oxidation was carried out using 2 molar amounts of *m*-CPBA, two *S,S'*-dioxides (39 and 16%, respectively) and a *S,S,S'*-trioxide (11%) were obtained along with **4a** (20%) and diketone **2** (7%). The major *S,S'*-dioxide was assigned to *S-endo,S'-exo-S,S'*-dioxide **5a** and the minor one to symmetric, *S-exo,S'-exo-S,S'*-dioxide **5b**. The structure of the *S,S,S'*-trioxide was assigned to **6**.



The structure elucidation of **4a**, **4b**, **5a**, **5b**, and **6** was enabled by their ^1H and ^{13}C NMR spectra, infrared spectra, and elemental analyses. The configuration of each of the sulfoxide groups was determined by $Eu(fod)_3$ shift reagent and aromatic solvent induced shift studies in the ^1H NMR (Table 1). The first criterion is that the methyl groups cis to the *endo*-sulfoxide bridge are



deshielded in greater magnitude than those cis to the *exo*-sulfoxide bridge by coordination of the Eu atom on the sulfoxide oxygen.[6,8] For example, a singlet at δ=1.47 of **4a**, which is already deshielded by anisotropic effect of the *endo* sulfoxide group, shows larger downfield shift than the other one (δ=1.12) of **4a** and a singlet peak (δ=1.33) of **4b**. Thus, the configurations on the sulfoxide groups of **4a** and **4b** were assigned to *endo* and *exo*, respectively.[9] The second one is that the aromatic molecule (C_6D_6) coordinates to the positive end (sulfur atom) of a sulfoxide group to provide shielding effect.[6,8b,10] The assignment arrived at by the former criterion is consistent with the consideration by the latter in all compounds. Meanwhile, the assignment of symmetric *S,S'*-dioxide **5b** and *S,S,S'*-trioxide **6** could be also accomplished by the consideration of their derivation; **5b** from **4b** and **6** from **5b** (see below).

As mentioned above, in the case of the oxidation using 2 molar amounts of *m*-CPBA, only **4b** was completely subject to second oxidation and a part of **4a** remained unchanged, while a part of *S,S'*-dioxide was further oxidized to **6**. This result suggests that there is fair difference in reactivity among **4a**, **4b**, **5a**, and **5b** to further oxidation.

Therefore, oxidation of each of these compounds with *m*-CPBA was next examined. Oxidation of *exo*-sulfoxide **4b** with an equimolar amount of *m*-CPBA in dichloromethane at room temperature was complete in 20 min to yield two *S,S'*-dioxides, **5a** (22%) and **5b** (38%), and *S,S,S'*-trioxide **6** (9%) accompanying with isomerization of **4b** to *endo*-sulfoxide **4a** (13%). In contrast to the high reactivity of **4b**, oxidation of **4a** was considerably sluggish. Thus, the reaction of **4a** with an equimolar amount of *m*-CPBA at room temperature for 1.5 h yielded 23% of *S-endo,S'-exo-S,S'*-dioxide **5a**, 1.4% of *S,S,S'*-trioxide **6**, and 4% of diketone **2** with recovery of 40% of **4a**. Regarding this reaction, it is also remarkable that **5a** was the sole *S,S'*-dioxide obtained. On the other hand, oxidation of **5b** with an equimolar amount of *m*-CPBA at room temperature for 1.5 h gave 72% of **6** along with 20% of recovery of **5b**. Oxidation of **5a** under similar conditions provided a mixture of *S,S,S'*-trioxide **6** (39%) and the starting *S,S'*-dioxide (61%). Thus, the relative rate of the oxidation could be estimated to be **4b**$\gg$**4a** and **5b**>**5a**.

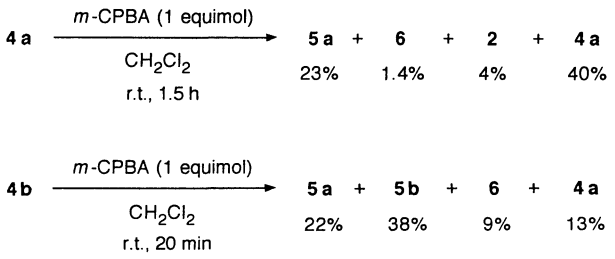
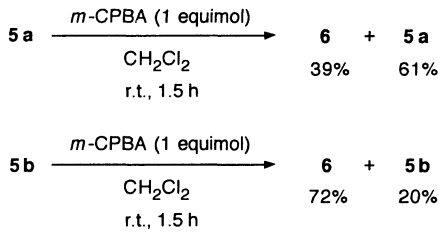


Table 1. The Chemical Shifts of the Methyl Groups of **1**, **4a**, **4b**, **5a**, **5b**, and **6** in the ^{1}H NMR

Compounds	δ_{Me}	$\delta_{Me}(\Delta\delta)$	$\delta_{Me}(\Delta\delta)$, Molar ratio of Eu(fod)$_3$			
	$CDCl_3$	C_6D_6–$CDCl_3$ (1 : 1)	0.1	0.2	0.3	0.4
1	1.24					
4a	1.12	1.02	1.39	1.66	1.96	2.19
		(−0.10)	(+0.27)	(+0.54)	(+0.84)	(+1.07)
	1.47	1.45	2.13	2.80	3.55	4.12
		(−0.02)	(+0.66)	(+1.33)	(+2.09)	(+2.66)
4b	1.33	1.10	1.41	1.51	1.64	1.73
		(−0.23)	(+0.08)	(+0.18)	(+0.31)	(+0.40)
		1.15	1.42	1.55	1.70	1.81
		(−0.18)	(+0.09)	(+0.22)	(+0.37)	(+0.48)
5a	1.14	0.86	1.42	1.68	1.90	2.09
		(−0.28)	(+0.28)	(+0.54)	(+0.76)	(+0.95)
	1.49	1.37	2.01	2.53	2.97	3.34
		(−0.12)	(+0.52)	(+1.04)	(+1.48)	(+1.85)
5b	1.32	0.99	1.51	1.66	1.84	2.01
		(−0.33)	(+0.19)	(+0.34)	(+0.52)	(+0.69)
6	1.28	0.92	1.39	1.54	1.65	1.72
		(−0.36)	(+0.11)	(+0.26)	(+0.37)	(+0.45)
	1.40	1.19	1.56	1.76	1.91	2.01
		(−0.21)	(+0.16)	(+0.36)	(+0.51)	(+0.61)



Johnson reported that the oxidations of 4-substituted thianes and 3-substituted thietanes with peroxy reagents involve steric approach control.[11,12] In this case, however, there seems only a small energy difference between endo and exo approaches because the formation ratio of **4a** and **4b** on oxidation of **1** and that of **5a** and **5b** on oxidation of **4b** are ca. 1.9:1 and 0.6:1, respectively. *m*-CPBA is an electrophilic oxidation agent under the reaction conditions employed so that the reaction rates would depend mainly on the electron density on the sulfur atom to be oxidized. In the infrared spectra the absorptions due to the S=O group occur at 1083 and 1077 cm^{-1} for **4a** and at 1096 cm^{-1} for **4b**. The decrease of the absorption frequency in **4a** is suggestive of an attractive interaction between the positively polarized sulfinyl sulfur(5) and the transannular sulfur(6),[13] which results in decrease of electron density on the sulfur to be oxidized (Fig. 1). Incidentally the X-ray analysis discloses that the nonbonded S···S distance of **4a** is 2.497 Å,[9] which is not only shorter than twice the van der Waals radius of sulfur (1.85 Å) but also ca. 0.1 Å shorter than the reported value of 1,3-dithietane 1-oxide (2.600 Å).[2] It has been reported that 1,3-transannular interaction exists in 2-substituted 1,3-dithiane 1-oxides. In these cases, the interaction appears as decrease of the S(O)CS angle and the nonbonded S···S distance of the trans isomer (Fig. 2).[14] On the other hand, there would exist repulsive interaction between the negatively polarized sulfinyl oxygen and the sulfenyl sulfur.[14b]

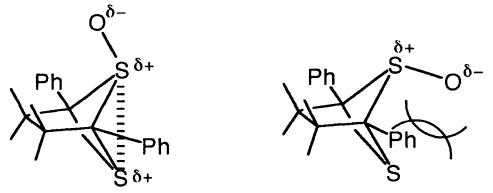


Fig. 1. Transannular interaction in **4a** and **4b**.

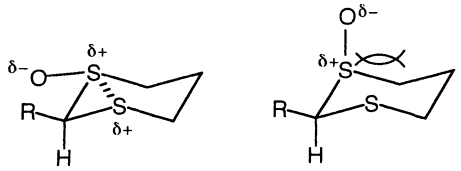
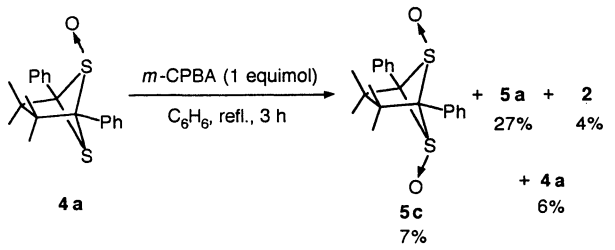


Fig. 2. Transannular interaction in 2-substituted 1,3-dithiane 1-oxide.

Such transannular interactions on **4a** and **4b** is considered to affect not only the reaction rates but also the orientation of oxidation. While two possible *S,S'*-dioxides (**5a** and **5b**) were formed by the oxidation of **4b**, only one isomer (**5a**) was obtained in the case of **4a**. This selectivity would be ascribed to the fact that lone pair electrons on the sulfenyl sulfur in **4a** spread to the *exo* side in greater extent than the *endo* side due to the attractive transannular interaction. By the way, another symmetric *S,S'*-dioxide, *S-endo,S'-endo-S,S'*-dioxide **5c**, was obtained, though in a low yield (7%), by the oxidation of **4a** with an equimolar amount of *m*-CPBA in refluxing benzene along with **5a** (27%), **2** (4%), and **4a** (6%).



There could exist in **5a** the attractive interaction between the *exo*-sulfinyl oxygen and the *endo*-sulfinyl sulfur. In contrast to this, the large dipole-dipole repulsive interaction must be operative between the *exo*-sulfinyl groups of **5b** (Fig. 3).[15] This consideration also explains well the lower reactivity of **5a** than **5b** and the absorptions due to the S=O groups in the infrared spectra (**5a**: 1080 cm^{-1}; **5b**: 1100 cm^{-1}).

The attractive and repulsive transannular interaction illustrated above would be attributable to thermodynamic stability. The isomerizations of **4b** and **5b** are described in the next section.

Oxidation of **1** with 4 molar amounts of *m*-CPBA in dichloromethane at room temperature gave **5a** (16%), **5b** (3%), and **6** (30%). The formation of *S,S,S',S'*-tetraoxide was not observed. An attempt to oxidize *S,S,S'*-trioxide **6** to the *S,S,S',S'*-tetraoxide by the reaction with *m*-CPBA in refluxing benzene failed to result in recovery of the starting material. Block obtained 1,3-dithietane 1,1,3,3-tetraoxide by oxidation of the corresponding *S,S,S'*-trioxide with peracetic acid at 100 °C.[2] However, when *S,S,S'*-trioxide **6** was ex-

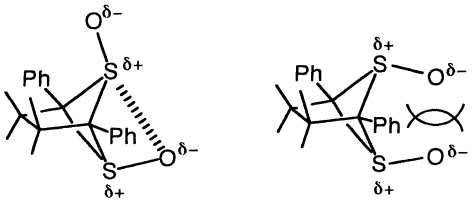
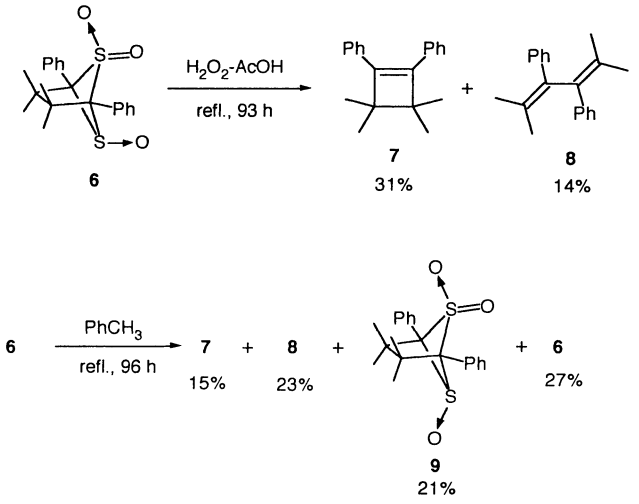


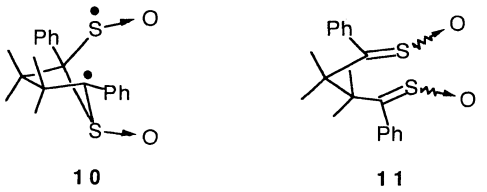
Fig. 3. Transannular interaction in **5a** and **5b**.

posed to H_2O_2 in refluxing acetic acid for 93 h, cyclobutene **7**[16] and hexadiene **8** were obtained in 31 and 14% yields, respectively. The controlled experiment in which **6** was heated in refluxing acetic acid–water for 119 h gave again **7** (29%) and **8** (28%). It was also confirmed that **7** isomerized to **8** in refluxing acetic acid in an appropriate rate. Therefore, it seems reasonable to consider that cyclobutene **7** is derived from **6** by a two-fold extrusion process.[17] It was reported that 1,3-dithietane 1,1,3,3-tetraoxide is planar and almost square.[2] The large dipole–dipole repulsion expected in the puckered 1,3-dithietane part would hinder the formation of the tetraoxide of **1**. Interestingly heating of **6** in refluxing toluene gave **7** (15%), **8** (23%), and another *S,S,S',S'*-tetraoxide **9** (21%) with recovery of **6** (27%).



Isomerizations of 4b to 4a and 5b to 5a. When the separation of *endo*-sulfoxide **4a** and *exo*-sulfoxide **4b** was performed by silica-gel chromatography, the fraction of **4b** always contains ca. 10% of **4a**. This observation indicates that **4b** gradually isomerizes to **4a** on silica gel. Actually, **4b** completely isomerized to **4a** when a solution of a mixture of **4b** and **4a** (91 : 9) in dichloromethane was allowded to stand over silica gel at room temperature for 14 h. By the way, *m*-chlorobenzoic acid is a by-product of oxidation reactions using *m*-CPBA under neutral conditions. The presence of *m*-chlorobenzoic acid, however, was not responsible for the isomerization, while addition of a small amount of concd sulfuric acid induced the rapid isomerization. On the other hand, stirring **4b** in hydrochloric acid–dioxane at room temperature for 30 min brought about a complex reaction to provide only 10% of **4a**, 56% of diketone **2**, and a reduction product **1** (11%). The stereomutation of sulfoxides by various acids was widely studied and in some cases reduction takes place as a side reaction.[18] The ready isomerization of **4b** to **4a** is ascribed to the thermodynamic stability of **4a** due to the effective 1,3-transannular interaction mentioned above.

The isomerization of *S-exo,S'-exo-S,S'*-dioxide **5b** to *S-endo,S'-exo-S,S'*-dioxide **5a** also takes place, though thermally. The isomerization of **5b** to **5a** occurred quantitatively (96%) in refluxing benzene under nitrogen. The yield, however, decreased to 79% when heated in benzene under air, which suggests that the reaction involves a biradical intermediate like **10**.[18] The isomerization obeyed first-order kinetics and the rate was $1.01\times10^{-5}\,s^{-1}$ at 70 °C in C_6D_6–$CDCl_3$. Mislow proposed three distinct mechanisms for the thermal stereomutation of sulfoxides; pyramidal inversion, homolytic scission, and cyclic rearrangement mechanisms and the reaction rate increases in this order.[18] The present rate of isomerization lies between those of the homolytic scission and the cyclic rearrangement mechanisms.[19] By the way, 1,3-dithietane 1,3-dioxide was reported to decompose to two molecules of sulfine ($H_2C{=}S{=}O$) at 750 K in the gas phase.[2] Thus, it is another possible mechanism that the isomerization proceeds via disulfine intermediate **11** and the process of the ring opening of **5b** and/or ring closure to **5a** involves a biradical intermediate.[2] In any event, release from the large dipole–dipole repulsion should be the driving force for the isomerization and lower the isomerization temperature. On the other hand, the isomerization of **5b** did not occur by treatment with concd HCl in dioxane at room temperature probably because the formation of a tetrahedral intermediate[18] is unfavorable due to steric hindrance of another *exo*-sulfoxide group.



In summary, we obtained two *S*-oxides, three *S,S'*-dioxides, and two *S,S,S'*-trioxides by the oxidation of **1** and its oxidation products and identified their structures unequivocally. The relative reactivity and the relative thermodynamic stability among them suggests that the 1,3-transannular interaction in the 1,3-dithietane part, fixed puckered, plays an important role.

Experimental

General. Melting points were determined on a MEL-TEMP capillary tube apparatus and are uncorrected. ^1H (400 MHz) and ^{13}C (100.6 MHz) NMR spectra were obtained on a Bruker AM400 spectrometer using $CDCl_3$ as the solvent. IR spectra were taken on a Hitachi 270-50 spectrometer. Low- and high-resolution mass spectra were measured with a JEOL JMS-DX303 spectrometer operating at 70 eV in the EI mode. Dry column chromatography was performed with

using a 1 : 5 mixture of Merck Kieselgel 60 F_{254} (70—230 mesh) and Merck Kieselgel 60 (70—230 mesh) packed in a seamless cellulose tubing and visualized with a 254-nm UV lamp. Solutions were dried with anhydrous $MgSO_4$. Elemental analyses were performed by Chemical Analysis Center of Saitama University, for which we thank Professor M. Sato, Mr. M. Kubo, and Mrs. E. Morikubo.

Commercially purchased *m*-chloroperbenzoic acid (*m*-CPBA) was purified before use by washing with a phosphate buffer at pH 7.4 several times and drying.[20]

Oxidation of 2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]hexane (1) with Equimol of *m*-CPBA. To a solution of **1** (225 mg, 0.689 mmol) in dichloromethane (10 mL) was added *m*-CPBA (85%, 139.8 mg, 0.689 mmol as *m*-CPBA) by portions at room temperature. The mixture was stirred for 10 min. Aqueous $NaHCO_3$ was added and the organic layer was separated. The aqueous layer was extracted with dichloromethane and the combined organic layer was washed with water and dried. *S-exo,S'-exo-S,S'*-dioxide **5b** was detected by TLC. The solvent was evaporated and the residue was subjected to column chromatography (basic aluminum oxide, activity V, CH_2Cl_2). The first fraction was 145 mg (62%) of *endo*-sulfoxide **4a**. The second fraction was 11.5 mg of a mixture of *endo*-**4a** and *exo*-sulfoxides **4b** and *S'-exo-S,S,S'*-trioxide **6**. The ratio **4a** : **4b** : **6** was determined by the ^1H NMR to be 2.6 (1.4%) : 5.1 (2.9%) : 1(0.6%). The third fraction was 73 mg (31%) of *exo*-sulfoxide **4b**.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane 5-*endo*-oxide (**4a**): Colorless crystals, mp 199—200 °C decomp (hexane); ^1H NMR δ=1.12 (s, 6H), 1.47 (s, 6H), and 7.35 (s, 10H); ^{13}C NMR δ=20.7 (q), 26.7 (q), 53.0 (s), 95.6 (s), 127.9 (d), 128.0 (d), 128.6 (d), and 134.5 (s); IR (KBr) 2964, 2932, 1494, 1454, 1395, 1371, 1143, 1122, 1083 (s), 1077 (s), 759, 715, 696, 514 cm^{-1}; MS *m/z* (rel intensity) 342 (M^+, 1), 294 (100), 279 (76), 264 (19), 251 (13), and 131 (38). Found: C, 70.05; H, 6.65%. Calcd for $C_{20}H_{22}OS_2$: C, 70.13; H, 6.47%.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane 5-*exo*-oxide (**4b**): Colorless crystals, mp 196—197 °C decomp (hexane); ^1H NMR δ=1.33 (s, 12H), 7.04—7.07 (m, 4H), and 7.30—7.39 (m, 6H); ^{13}C NMR δ=23.6 (q), 24.1 (q), 49.4 (s), 89.6 (s), 127.2 (d), 128.1 (d), 128.3 (d), and 131.6 (s); IR (KBr) 2972, 1494, 1446, 1398, 1370, 1120, 1096 (s), 762, 708, 694, and 514; MS *m/z* (rel intensity) 342 (M^+, 1.5), 326 (1.5), 294 (100), 279 (67), 264 (15), 251 (10), and 131 (33). Found: C, 69.60; H, 6.45%. Calcd for $C_{20}H_{22}OS_2$: C, 70.13; H, 6.47%.

Oxidation of 1 wish 2 Molar Amounts of *m*-CPBA. To a solution of **1** (163 mg, 0.5 mmol) in dichloromethane (15 mL) was added *m*-CPBA (70%, 246 mg) by portions. The mixture was stirred for 3 h and aqueous Na_2CO_3 was added. The organic layer was separated, dried, and concentrated. The residue was purified by column chromatography (silica gel, CH_2Cl_2 and then Et_2O). The first fraction was 10 mg (7%) of 2,2,3,3-tetramethyl-1,4-diphenylbutane-1,4-dione (**2**) and the second one was 34 mg (20%) of *endo*-sulfoxide **4a**. A mixture of *S-endo, S'-exo-S,S'*-dioxide **5a** and *S'-exo-S,S,S'*-trioxide **6** was the third fraction, which was separable by column chromatography (silica gel) using Et_2O–hexane (1 : 2) as eluent to give 70 mg (39%) of *S-endo,S'-exo-S,S'*-dioxide **5a** and 24 mg (13%) of *S'-exo-S,S,S'*-trioxide **6**. The last fraction, eluted with Et_2O, was 28 mg (16%) of *S-exo,S'-exo-S,S'*-dioxide **5b**.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane 5-*endo*,6-*exo*-dioxide (**5a**): Colorless crystals, mp 224—225 °C decomp (hexane–CH_2Cl_2); ^1H NMR δ=1.14 (s, 6H), 1.49 (s, 6H), 7.44—7.52 (m, 6H), and 7.66 (d, *J*=7.6 Hz, 4H); ^{13}C NMR δ=22.3 (q), 25.6 (q), 49.0 (s), 104.0 (s), 129.0 (d), 129.1 (d), 129.3 (d), and 130.9 (s); IR (KBr) 2976, 1496, 1448, 1402, 1372, 1120, 1080 (s), 764, 720, 698, and 508 cm^{-1}; MS *m/z* (rel intensity) 294 (M^+–64, 8), 278 (88), 263 (68), and 131 (100). Found: C, 66.84; H, 6.16%. Calcd for $C_{20}H_{22}O_2S_2$: C, 67.00; H, 6.19%.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane 5-*exo*,6-*exo*-dioxide (**5b**): Colorless crystals, mp 200—201 °C decomp (EtOH); ^1H NMR δ=1.32 (s, 12H), and 7.44—7.57 (m, 10H); ^{13}C NMR δ=23.7 (q), 42.6 (s), 87.8 (s), 127.4 (s), 128.7 (d), 129.1 (d), and 129.2 (d); IR (KBr) 2980, 1496, 1450, 1404, 1378, 1110 (s), 1084, 1074, 758, 706, and 694 cm^{-1}; MS *m/z* (rel intensity) 294 (M^+–64, 19), 278 (48), 263 (48), and 131 (100); Found: C, 66.72; H, 6.13%. Calcd for $C_{20}H_{22}O_2S_2$: C, 67.00; H, 6.18%.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane *S'-exo-S,S,S'*-trioxide (**6**): Colorless crystals, mp 224—225 °C decomp (EtOH); ^1H NMR δ=1.28 (s, 6H), 1.40 (s, 6H), and 7.45—7.52 (m, 10H); ^{13}C NMR δ=22.4 (q), 25.5 (q), 42.7 (s), 112.8 (s), 125.4 (s), 129.3 (two peaks overlapped, both d), and 129.8 (d); IR (KBr) 2984, 1496, 1452, 1406, 1380, 1312 (s), 1170 (s), 1138 (s), 1118 (s), 756, 710, 694, and 550 cm^{-1}; MS *m/z* (rel intensity) 310 (M^+–64, 3), 294 (48), 279 (56), 262 (59), 247 (61), 232 (33), 219 (75), and 131 (100); Found: C, 63.76; H, 5.86%. Calcd for $C_{20}H_{22}O_3S_2$: C, 64.14; H, 5.92%.

Oxidation of *endo*-Sulfoxide 4a with Equimol of *m*-CPBA. (a) At Room Temperature in Dichloromethane. To a solution of *endo*-sulfoxide **4a** (157 mg, 0.458 mmol) in CH_2Cl_2 (7 mL) was added *m*-CPBA (92.8 mg, 0.457 mmol) by portions at room temperature. The mixture was stirred for 1.5 h at ambient temperature and aqueous $NaHCO_3$ was added. The mixture was extracted with CH_2Cl_2 and the organic layer was separated and dried. After removal of the solvent, the residue was subjected to dry column chromatography (silica gel, CH_2Cl_2). The first fraction was 62.4 mg (40%) of recovery of **4a**. The second fraction was diketone **2** (5.1 mg, 4%) and the third fraction was a 16 : 1 mixture (39.4 mg) of *S-endo,S'-exo-S,S'*-dioxide **5a** (23%) and *S'-exo-S,S,S'*-trioxide **6** (1.4%).

(b) In Refluxing Benzene. A solution of *m*-CPBA (0.72 g, 2.92 mmol) in benzene (20 mL) was added to a solution of **4a** (1.00 g, 2.92 mmol) in refluxing benzene in a period of 25 min. The mixture was cooled to room temperature and additional *m*-CPBA (720 mg, 2.92 mmol) and benzene (10 mL) were added. The mixture was refluxed for additional 3 h and the solvent was removed under reduced pressure. To the residue were added dichloromethane, aqueous $NaHSO_3$, and aqueous $NaHCO_3$. The organic layer was separated, washed with water, dried, and evaporated to remove a pale yallow solid. The solid was subjected to dry column chromatography (silica gel, dichloromethane–hexane 2 : 1) to provide 76.9 mg (7%) of *S-endo,S'-endo-S,S'*-dioxide **5c**, 57 mg (6%) of **4a**, 30 mg (4%) of diketone **2**, and 288 mg (27%) of *S-endo,S'-exo-S,S'*-dioxide **5a**.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane 5-*endo*,6-*endo*-dioxide (**5c**): Colorless crystals, mp 198—199 °C decomp (hexane); ^1H NMR δ=1.52 (s, 12H),

7.47—7.49 (m, 6H), and 7.72—7.75 (m, 4H); ^{13}C NMR δ=23.1 (q), 55.7 (s), 101.3 (s), 127.4 (d), 128.5 (d), 129.1 (d), and 134.3 (s); IR (KBr) 2972, 1496, 1448, 1398, 1372, 1149, 1140, 1118, 1061 (s), 760, 718, 697, and 504 cm^{-1}; MS *m/z* (rel intensity) 294 (M^+−64, 16), 278 (93), 263 (68), and 131 (100). Found: C, 66.58; H, 6.35%. Calcd for $C_{20}H_{22}O_2S_2$: C, 67.00; H, 6.18%.

Oxidation of *exo*-Sulfoxide 4b with Equimol of *m*-CPBA. To a solution of *exo*-sulfoxide **4b** (31.0 mg, 0.091 mmol) in dichloromethane (5 mL) was added *m*-CPBA (18.5 mg, 0.091 mmol) by portions at room temperature. The mixture was stirred at ambient temperature for 20 min. Aqueous $NaHCO_3$ and CH_2Cl_2 were added and the organic layer was separated, dried, and evaporated. The colorless residue was subjected to dry column chromatography (silica gel, CH_2Cl_2 and then CH_2Cl_2–Et_2O 50 : 1). The first fraction was 4 mg (13%) of *endo*-sulfoxide **4a**. The second fraction was 10 mg of a mixture of *S-endo,S'-exo-S,S'*-dioxide **5a** and *S'-exo-S,S,S'*-trioxide **6** and the ratio was 2.5 : 1 from the ^{1}H NMR (22% and 9%, respectively). The third fraction was 12 mg (38%) of *S-exo,S'-exo-S,S'*-dioxide **5b**.

Oxidation of *S-endo,S'-exo-S,S'*-Dioxide 5a wish Equimol of *m*-CPBA. To a solution of *S-endo,S'-exo-S,S'*-dioxide **5a** (30 mg, 0.085 mmol) in dichloromethane (4.5 mL) was added *m*-CPBA (17 mg, 0.084 mmol) by portions at room temperature. The solution was stirred at ambient temperature for 1.5 h and aqueous $NaHCO_3$ and dichloromethane were added. The organic layer was separated, dried, and evaporated. The residue was a 1 : 1.57 mixture of *S'-exo-S,S,S'*-trioxide **6** (39%) and **5a** (61%) (determined by ^{1}H NMR).

Oxidation of *S-exo,S'-exo-S,S'*-Dioxide 5b with Equimol of *m*-CPBA. To a solution of **5b** (54 mg, 0.15 mmol) in dichloromethane (8 mL) was added *m*-CPBA (30.5 mg, 0.15 mmol) by portions at room temperature. The solution was stirred at ambient temperature for 1.5 h and aqueous $NaHCO_3$ and dichloromethane were added. The organic layer was separated and dried. After removal of the solvent a colorless residue was subjected to column chromatography (silica gel, CH_2Cl_2–Et_2O 20 : 1) to give *S'-exo-S,S,S'*-trioxide **6** (40 mg, 72%) and **5b** (11 mg, 20%).

Attempts to Oxidize *S'-exo-S,S,S'*-Trioxide 6 to *S,S,S',S'*-Tetraoxide. (a) *m*-CPBA in Refluxing Benzene. A solution of *S'-exo-S,S,S'*-trioxide **6** (83.9 mg, 0.224 mmol) and *m*-CPBA (55.2 mg, 0.224 mmol) in benzene (20 mL) was heated under reflux for 18 h. The mixture was taken up with ether after addition of aqueous $NaHCO_3$ and aqueous $NaHSO_3$. The organic layer was washed with water, dried, and evaporated to give 45.5 mg of the starting material.

(b) H_2O_2 in Refluxing Acetic Acid. To a solution of **6** (151.8 mg, 0.405 mmol) in acetic acid (25 mL) was added 4.5 mL of 30% H_2O_2. The solution was refluxed for 93 h and poured into water. The mixture was extracted with ether and the organic layer was washed with aqueous $NaHCO_3$ and then water, dried, and evaporated. The residue was subjected to preparative TLC. (silica gel, hexane) to give 33.2 mg (31%) of cyclobutene **7** and 10.3 mg (14%) of hexadiene **8**.

3,3,4,4-Tetramethyl-1,2-diphenylcyclobutene (**7**):[16] Colorless crystals, mp 93.5—95.5 °C; ^{1}H NMR δ=1.31 (s, 12H), 7.21 (t, *J*=7.2 Hz, 2H), 7.27 (t, *J*=7.4 Hz, 4H), and 7.37 (d, *J*=7.2 Hz, 4H); ^{13}C NMR δ=22.9 (q), 47.4 (s), 127.0 (d), 127.1 (d), 128.3 (d), 135.2 (s), and 145.5 (s); MS *m/z* (rel intensity) 262 (M^+, 100), 247 (49), 232 (28), 219 (99), and 204 (23). Found: *m/z* 262.1695. Calcd for $C_{20}H_{22}$: M, 262.1721.

2,5-Dimethyl-3,4-diphenyl-2,4-hexadiene (**8**): Colorless oil; ^{1}H NMR δ=1.72 (s, 6H), 1.91 (s, 6H), 6.96 (d, *J*=6.8 Hz, 4H), 7.09 (t, *J*=6.7 Hz, 2H), and 7.17 (t, *J*=6.7 Hz, 4H); ^{13}C NMR δ=21.3 (q), 22.1 (q), 125.8 (d), 127.5 (d), 129.3 (d), 129.9 (s), 137.0 (s), and 141.8 (s); MS *m/z* (rel intensity) 262 (M^+, 100), 247 (38), 232 (24), and 219 (89); Found: *m/z* 262.1703. Calcd for $C_{20}H_{22}$: M, 262.1721.

Thermal Decomposition of *S'-exo-S,S,S'*-Trioxide 6. (a) In Refluxing Acetic Acid–Water. A solution of **6** (50 mg, 0.13 mmol) in acetic acid (8 mL) and water (1.5 mL) was refluxed for 119 h. The mixture was poured into water and taken up with ether. The organic layer was washed with aqueous $NaHCO_3$ and then water, dried, and evaporated. The residue was subjected to dry column chromatography (silica gel, hexane) to provide 10.2 mg (29%) of cyclobutene **7** and 9.8 mg (28%) of hexadiene **8**.

(b) In Refluxing Toluene. A solution of **6** (50 mg, 0.13 mmol) in toluene (10 mL) was refluxed for 96 h. The solvent was removed under reduced pressure. The residue was purified by dry column chromatography (silica gel, hexane and then CH_2Cl_2) to provide 5.3 mg (15%) of cyclobutene **7**, 8.1 mg (23%) of hexadiene **8**, 10.4 mg (21%) of *S-endo,S,S,S'*-trioxide **9**, and 13.7 mg (27%) of **6**.

2,2,3,3-Tetramethyl-1,4-diphenyl-5,6-dithiabicyclo[2.1.1]-hexane *S'-endo-S,S,S'*-trioxide (**9**): Colorless needles, mp 207—210 °C decomp (EtOH); ^{1}H NMR δ=1.45 (s, 6H), 1.55 (s, 6H), 7.49 (br s, 6H), and 7.56 (br s, 4H); ^{13}C NMR δ=20.0, 25.2, 49.9, 110.1, 127.5, 128.8, 128.9, and 129.7; IR (KBr) 3060, 2928, 1498, 1472, 1448, 1402, 1376, 1314(s), 1162(s), 1136(s), 1122(s), 1092(s), 1078(s), 758, 712, 694(s), 570, 548, 532, and 496 cm^{-1}; MS *m/z* (rel intensity) 326 (M^+−48, trace), 310 (8), 293 (10), 277 (13), 253 (27), 247 (52), 232 (21), 219 (15), 205 (46), 190 (38), 173 (23), 163 (45), 157 (48), 131 (76), 121 (71), 115 (42), 105 (100), and 91 (60). Found: C, 63.60; H, 5.91%. Calcd for $C_{20}H_{22}O_3S_2$: C, 64.14; H, 5.92%.

Thermal Isomerization of Cyclobutene 7. A solution of **7** (11.5 mg, 0.044 mmol) in acetic acid (5 mL) was heated under reflux for 70 h and then poured into water. The mixture was extracted with dichloromethane and the organic layer was washed with aqueous $NaHCO_3$ and then water, dried, and evaporated. The ^{1}H NMR showed the residue (13.5 mg) was a 6.25 : 1 mixture of hexadiene **8** (86%) and cyclobutene **7** (14%).

Isomerization of *exo*-Sulfoxide 4b to *endo*-Sulfoxide 4a. (a) Over Silica Gel. A solution of a 91 : 9 mixture (18.5 mg, 0.054 mmol) of **4b** and **4a** in dichloromethane (4 mL) was allowed to stand over 1 g of silica gel (Merck Kieselgel 60 (70—230 mesh)) for 14 h. The silica gel was removed by filtration and the filtrate was evaporated to give 17.4 mg of a solid. The ^{1}H NMR of the solid showed that the residue was exclusively *endo*-sulfoxide **4a**.

(b) In HCl–Dioxane. To a solution of **4b** (22.9 mg, 0.067 mmol) in dioxane (5 mL) was added 2.5 mL of 36% HCl. Then the solution turned yellow. The mixture was stirred at room temperature for 30 min, poured into water, and extracted with dichloromethane twice. The combined organic layer was washed with aqueous $NaHCO_3$ and then water, dried, and evaporated. The residue was subjected to dry column chromatography (silica gel, CH_2Cl_2–CCl_4 1 : 1) to give 2.5 mg (11%) of **1** and 13.4 mg of a mixture of diketone **2** and *endo*-sulfoxide **4a**. The ratio **2** : **4a** was determined by the ^{1}H NMR to be 5.4 (56%) : 1 (10%).

Isomerization of *S-exo,S'-exo-S,S'*-Dioxide 5b to 5a. (a)

In Refuxing Benzene under N_2. A solution of **5b** (50 mg, 0.14 mmol) in benzene (60 mL) was degassed under reduced pressure with vigorous stirring and then N_2 was introduced. The solution was refluxed under N_2 for 45 h and the solvent was removed under reduced pressure. The residue was purified by dry column chromatography (silica gel, CH_2Cl_2) to give 47.8 mg (96%) of *S-endo,S'-exo-S,S'*-dioxide **5a**.

(b) In Refluxing Benzene under Air. A solution of **5b** (50 mg, 0.14 mmol) in benzene (10 mL) was refluxed under air for 40 h. The solvent was removed under reduced pressure and the residue was purified by dry column chromatography (silica gel, CH_2Cl_2) to give 39.2 mg (79%) of **5a**.

(c) Kinetics. A part of a solution (1.4 mL) of *S-exo,S'-exo-S,S'*-dioxide **5b** (18.9 mg, 0.0528 mmol) in 1:1 v/v C_6D_6–$CDCl_3$ (0.377 M, 1 M=1 mol dm^{-3}) was transferred to an NMR tube ($CDCl_3$ was passed through silica gel and alumina to remove acidic impurities before use). The solution was degassed by freeze-thaw cycle several times and N_2 was introduced at last. The solution was heated in an air bath (70 °C) and the ratio **5b**:**5a** was determined by the ^{1}H NMR every an hour. The reaction preceded cleanly and 74% of **5b** isomerized to **5a** after 39 h. A least-squares regression analysis of $\ln\{([\mathbf{5b}]+[\mathbf{5a}])/[\mathbf{5b}]\}$ vs. reaction time (h) gave a straight line with a slope (k) of 0.034 h^{-1} ($=1.01\times10^{-5}$ s^{-1}), an intercept of −0.0274, and a correlation coefficient of 0.994.

(d) In HCl-Dioxane. To a solution of **5b** (26.2 mg, 0.073 mmol) in dioxane (5 mL) was added 2.5 mL of 36% HCl. The solution was stirred at room temperature for 6 h and poured into water. The mixture was extracted with dichloromethane twice. The combined organic layer was washed with aqueous $NaHCO_3$ and then water, dried, and evaporated. The ^{1}H NMR and the TLC analyses showed that the residue was exclusively **5b**.

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