Synthesis and novel reactivities of several 1,9-dithiaalkane-bridged thianthrene 10-oxides

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ABSTRACT

The irreversible photolytic axial to equatorial change (**3ax–4ax→3eq–4eq**) and the irreversible thermal equatorial to axial change (**3eq–4eq→3ax–4ax**) of the S–O configuration were first observed. Meanwhile, the shorter 1,9-bridged derivative (**2ax**) exhibited the interesting photolytic degradation, affording 1,9-dithiadibenzothiophene (**5**) by the elimination of SO and ethylene.

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It has been known that thianthrene derivatives are folded along the S–S axis, and exist as 'butterfly structures' in the equilibrium state of two 'flip-flap' conformational isomers.[1] We have been interested in such inherent nature of the thianthrene derivatives so as to apply for potent molecules with regulation of the conformational change. As the basic study, recently, we have reported the stereochemical changes of 10-mono- and 10,10-dioxy-5-sulfilimines,[2] their *N*-bromosulfilimine derivatives,[3] and their fluorothiazyne derivatives[4] under several thermal and nucleophilic conditions on their sulfur atom. These studies indicated the importance of the 'flip-flap' motion of the thianthrene framework and the steric interaction between nucleophiles and the substituent on 5-sulfur atom or peri-hydrogens on thianthrene benzene ring.

In order to study the behavior of thianthrene derivatives with more rigid 'flip-flap' motion, several 1,9-dithiaalkane-bridged thianthrene 10-oxides (**2ax–4ax**) were synthesized. As summarized in Table 1, dilithiation of thianthrene 5-oxide (**1**) with LDA (2.2 equiv), followed by addition of elemental sulfur (1.2 equiv), and subsequently, with the reaction of dibromoalkane (1.2 equiv) was found to afford axial sulfoxides **2ax–4ax** (axial isomer) exclusively, despite the possibility of the formation of **2eq–4eq** (equatorial isomer), besides a small amount of undesired 1,9-di-ω-bromoalkylthia- and 1-mono-ω-bromoalkyl-thianthrene 10-oxide derivatives. It is noteworthy that the yields of **2ax**, **3ax**, and **4ax** were extraordinarily high in 62%, 49%, and 39%, respectively, as ex-

pected in the ordinary intramolecular cyclization reactions. This result probably suggests the importance of the steric hindrance and/or intramolecular Li-coordination with oxygen of S–O group. The compounds were fully characterized by NMR and IR spectroscopies as well as elemental analysis. The determination of the structures of **2ax–4ax** were finally performed by single crystal X-ray crystallographic analyses. The ORTEP drawing for **2ax** is shown in Figure 1.[10]

Concerning the S–O configuration change, Mislow et al. reported the thermal racemization of sulfoxides via the pyramidal inversion at high temperature, generally around 180 °C.[5] They also reported the photolytic pyramidal inversion of sulfoxides.[6] In order to study the photolytic behavior and the effect of 1,9-dithiaalkane linkages of thianthrene 10-oxide, the photolysis of **2ax** was carried out in CH$_2$Cl$_2$ under irradiation of high pressure mercury lamp with

Table 1
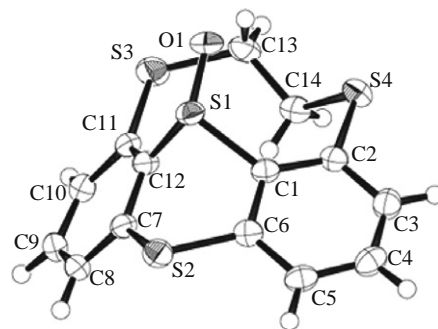Synthesis of 1,9-dithiamethylene-bridged thianthrene derivatives

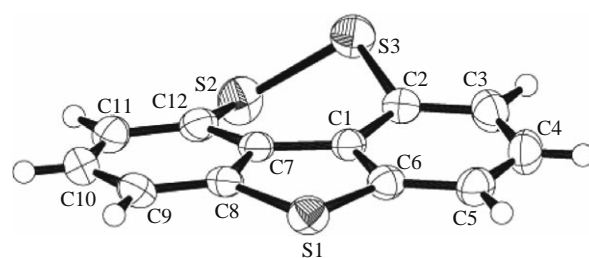| Entry	*n*	Compound	Yield (%)
1	2	**2ax**	62
2	3	**3ax**	49
3	4	**4ax**	39
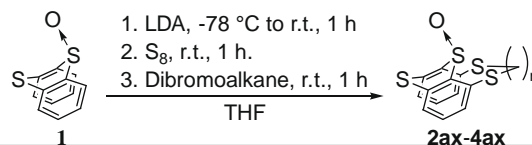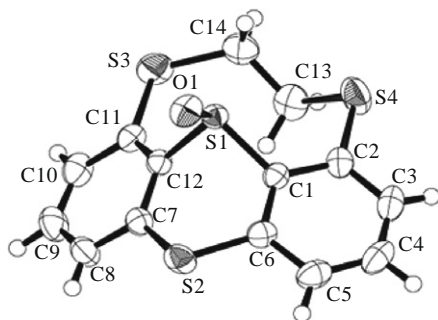
Figure 1. An ORTEP drawing of **2ax** (50% probability ellipsoids). Selected bond lengths (Å) and angles (°). S(1)–O(1), 1.492(1); S(1)–C(1), 1.776(1); S(2)–C(6), 1.760(2); S(3)–C(2), 1.772(2); S(4)–C(13), 1.821(2); O(1)–S(1)–C(1), 107.70(7); O(1)–S(1)–C(12), 107.12(6); C(1)–S(1)–C(12), 93.97(6); C(2)–S(4)–C(13), 101.96(8).
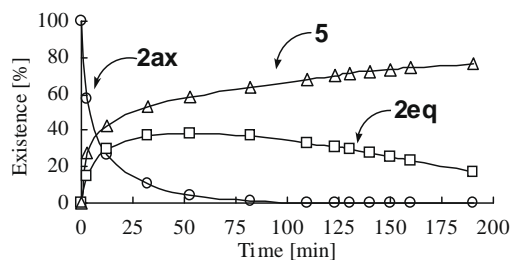

Figure 2. An ORTEP drawing of **2eq** (50% probability ellipsoids). Selected bond lengths (Å) and angles (°). S(1)–O(1), 1.457(2); S(1)–C(1), 1.81(1); S(1)–C(12), 1.781(3); S(2)–C(6), 1.78(1); S(4)–C(14), 1.847(7); O(1)–S(1)–C(1), 113.5(1); C(1)–S(1)–C(12), 94.4(3); C(11)–S(3)–C(13), 110.1(2); S(3)–C(11)–C(12), 129.8(2).

Figure 3. An ORTEP drawing of **5** (50% probability ellipsoids). Selected bond lengths (Å) and angles (°). S(1)–C(6), 1.749(2); S(1)–C(8), 1.751(2); S(2)–S(3), 2.066(1); S(2)–C(12), 1.773(3); S(3)–C(2), 1.775(2); C(1)–C(7), 1.435(3); C(6)–S(1)–C(8), 91.7(1); S(3)–S(2)–C(12), 102.43(8); S(2)–S(3)–C(2), 101.94(8).

Figure 4. Time course of photolysis of **2ax**.

a Pyrex filter. As show in Table 2 (entry 1), S–O inversion product **2eq** was obtained in 27% yield after irradiation for 3 h, and interestingly 1,9-dithiadibenzothiophene (**5**)[7] was formed in 47% yield. The structures of **2eq** and **5** were finally determined by the single crystal X-ray crystallographic analyses as shown in Figures 2[10]3[10], respectively.
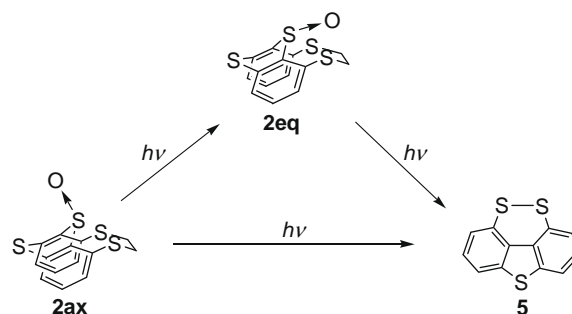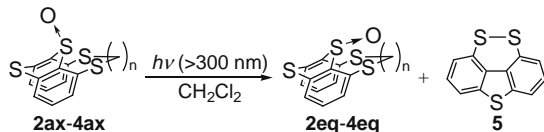
Further, in order to obtain a clue of reaction pathway, the time-course dependence of products was carried out by ^{1}H NMR spectroscopy. The observation of the formation of **5** at very early stage of the photoreaction and the slower reaction rate of **2eq** to **5** compared to the disappearance of **2ax** seems to suggest the existence of the direct path from **2ax** to **5** in Figure 4 and Scheme 1. Additionally, in the measurement of ^{1}H NMR spectra, gradual increase of a singlet peak around 5.40 ppm was observed. This peak was confirmed to be of ethylene when compared with the ^{1}H NMR spectra of the sample prepared authentically. Further, several mechanistic studies for the formation of **5** were carried out as follows: Since SO trapping experiments were reported using diene and acetylene derivatives,[8] the photolysis of **2ax** was carried out in the presence of 2,3-dimethyl-1,3-butadiene, and the formation of the SO-trapped product, that is, 3,4-dimethyl-2,5-dihydrothiophene S-oxide (**6**), was observed in 73% yield (Scheme 2). It is reported that SO exists as the triplet state (biradical state) at ground state and can be excited to the singlet state by UV irradiation.[8a] Therefore, it is interesting to obtain the information about the electronic state of SO formed in the photolysis. Additionally, we carried out the photolysis of **2ax** in the presence of 2,4-hexadiene (contains three isomers). As a result, SO-trapped products, 2,5-dimethyl-3-thiolene S-oxides **7a** (11%), **7b** (22%), and **7c** (13%) were observed (Scheme 3 and Fig. 5). This result may suggest the possibility of generation of the triplet SO by the photolysis of **2ax** forming ethylene and **5**, as similarly reported in the literature.[8a,e,f] Further, in order to make clear the ethylene formation step, we synthesized

Table 2
Photolysis of **2ax–4ax** under irradiation of high pressure mercury lamp with a Pyrex filter

Entry	*n*	Time (min)	Yield (%)	
			Equatorial isomer	**5**
1	2	180	27	47
2	3	20	95	—
3	4	20	98	—

Scheme 1. Photoreaction path-way of **2ax** under irradiation of high pressure mercury lamp with a pyrex filter.

1,9-dithiaethylene-bridged dibenzothiophene **8**, by the reaction of **2ax** with *n*-BuLi (1.5 equiv) following the reported procedure,[9] and carried out the photolysis of **8** under the same conditions as shown in Scheme 3. This result indicated clearly that the photolysis of **2ax** proceeded to form **8** eliminating SO (probably triplet state)
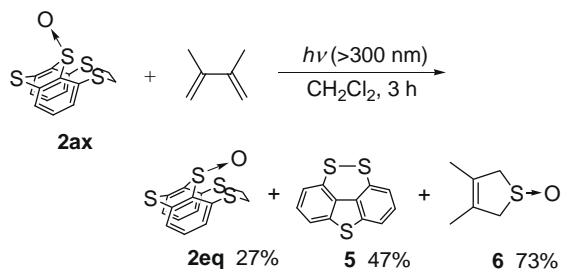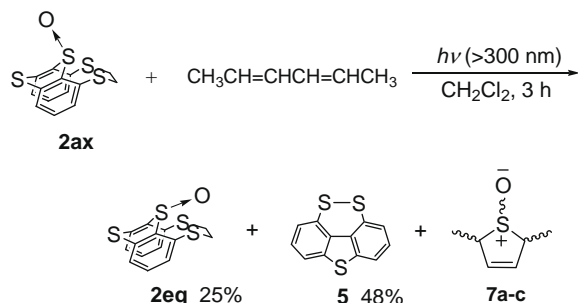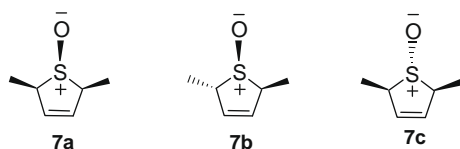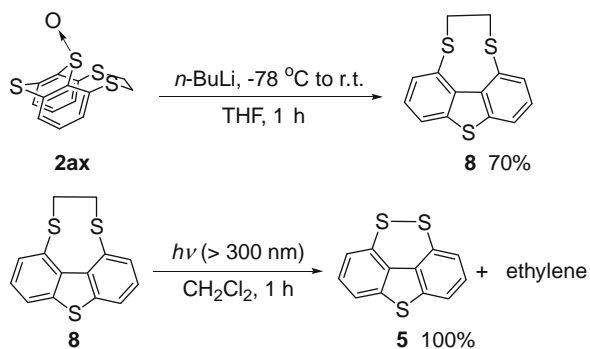
Scheme 2. Photoreaction of **2ax** with 2,3-dimethyl 1,3-butadiene.

Scheme 3. Photoreaction of **2ax** with 2,4-hexadiene.

Figure 5. Isomers of 2,5-dimethyl-3thiolene S-oxide.

Scheme 4. Synthesis of **8** and its photolytic behavior.

and successively, **8** was photolyzed secondarily to form **5** and ethylene exclusively and very rapidly, (Scheme 4) because no initial formation of **8** was observed in the photolysis of **2ax**.

In order to study the photolytic behavior on the S–O bond isomerization depending on the size of 1,9-dithiaalkane-bridged linkages, the photoreactions of **3ax** and **4ax** were carried out under the same conditions. The results are summarized in Table 2 (entries 2 and 3). In the photoreaction of **3ax** and **4ax**, no degraded product **5** was formed, and S-O inversion products **3eq** and **4eq** were formed in 95% and 98% yields, respectively. The photoreactions of the photo-isomerized products **3eq** and **4eq** (equatorial isomers), thus obtained, were carried out. However, the photo S–O inversion to axial isomers in reverse way was not observed,

Table 3
Thermal reaction of **3eq–4eq** in sealed tube

Entry	n	Time (day)	Yield (%)
1	3	5	100
2	4	5	100

resulting in the recovery of **3eq** and **4eq**. Comparing the UV spectral data of the isomers, **3ax** and **4ax,** were found to have a weak UV absorption around 330–350 nm (ε = ca. 0.5), while nothing in the equatorial isomers of **3eq** and **4eq**. This evidence is also one of the reasons for the one-way photo isomerization from **3ax**–**4ax** to **3eq**–**4eq**, together with the steric restriction between S-O bond and the side of chain linkages. The structures of **3eq**–**4eq** were finally determined by a single crystal X-ray crystallographic analysis. As already mentioned earlier, since sulfoxides are known to invert thermally, it is interesting to study the thermal behavior of **3ax** and **4ax,** and **3eq** and **4eq**. In both cases of axial (**3ax** and **4ax)** and equatorial isomers (**3eq** and **4eq**), the decomposition reactions proceeded and resulted in the formation of the complex product mixtures. Under milder conditions in sealed tube at 85 °C for 20 h, the axial isomers **3ax** and **4ax** afforded the complete recovery of the starting material. However, the equatorial isomers **3eq** and **4eq** were revealed to afford the isomerized products **3ax** and **4ax** in high yield at the same temperatures for five days (Table 3). As the results in the 1,9-dithiaalkane-bridged thianthrene 10-oxides **3ax** and **4ax**, we first demonstrated the reversible change of S–O configuration by photolytical axial to equatorial and thermal equatorial to axial ways.

In summary, the irreversible photolytic axial to equatorial change (**3ax**–**4ax**→**3eq**–**4eq**) and the irreversible thermal equatorial to axial change (**3eq**–**4eq**→**3ax**–**4ax**) of the S–O configuration were first observed. Meanwhile, in the photolysis of **2ax**, S–O inversion product **2eq** and 1,9-dithiadibenzothiophene **5** were obtained.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.12.116.

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10. *Crystal data* **2ax**: $C_{14}H_{10}OS_4$, $M = 322.47$, monoclinic, $a = 10.527(4)$, $b = 11.625(3)$, $c = 11.231(1)$ Å, $\beta = 96.46(2)°$, $V = 1365.7(5)$ Å^3, $T = 296.2$ K,

space group $P2_1/n$, $Z = 4$, μ(MoKα) = 6.81 cm^{-1}, 4175 reflection measured, 3345 unique ($R_{int} = 0.015$), $R_I[I > 2s(I)] = 0.031$, R_W(all data) = 0.099; **2eq**: $C_{14}H_{10}OS_4$, $M = 322.47$, monoclinic, $a = 9.38(8)$, $b = 26.15(9)$, $c = 11.14(6)$ Å, $\beta = 107.8(5)°$, $V = 2600(28)$ Å^3, $T = 233.2$ K, space group $P2_1/c$, $Z = 8$, μ(MoKα) = 7.16 cm^{-1}, 8250 reflection measured, 8074 unique ($R_{int} = 0.022$), $R_I[I > 2s(I)] = 0.034$, R_W(all data) = 0.099; **5**: $C_{12}H_6S_3$, $M = 246.36$, monoclinic, $a = 12.003(1)$, $b = 10.990(1)$, $c = 16.392(1)$ Å, $\beta = 109.296(6)°$, $V = 2040.7(3)$ Å^3, $T = 296.2$ K, space group = $P2_1/a$, $Z = 8$, μ(MoKα) = 6.81 cm^{-1}, 6216 reflection measured, 4096 unique ($R_{int} = 0.013$), $R_I[I > 2s(I)] = 0.042$, R_W(all data) = 0.139.