

# Twist Boat Conformation of Thiane S-Oxide Both in Solid State and in Solution

Dong Ju Jeon\* and Ikyon Kim

Center for Medicinal Chemistry, Korea Research Institute of Chemical Technology, Yuseong, Daejeon 305-600, Korea

\*E-mail: djjeon@kRICT.re.kr

Received April 4, 2008

A stable twist boat conformation of thiane S-oxide **1a** in solid state and in solution was unambiguously determined by single crystal X-ray crystallography and solution NMR analyses. On the contrary, the thiane S-dioxide **2** which was obtained from the oxidation of corresponding thiane S-oxide **1a** was confirmed to adopt a regular chair conformation.

**Key Words** : Twist boat, Conformational analysis, X-ray crystallography, Thiane S-oxide

## Introduction

It is well-established from calculation studies<sup>1</sup> and some experimental work<sup>2</sup> that the twist boat conformer is ~5 kcal/mol higher energy state than that of the chair form in cyclohexane ring system. This energy difference, not surprisingly, reflects the preference for the chair conformation over twist boat form. Although some factors are known to be involved in changing this pattern, the literature discloses only a few cases in which a nonchair conformation is observed as a stable form in solution or solid state. In particular, twist-boat conformers in a solid state are rarely known in certain cyclohexanes or saturated 6-membered heterocycles.<sup>3</sup>

In the course of our study on the reaction of thiane S-oxide with various electrophiles, we found that 4-*tert*-butyl-2-diphenylcarbinol thiane S-oxide (**1a**) exists in a twist boat conformation both in a solid state and in solution, while *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane S-dioxide (**2**), bearing a sulfone group in place of the sulfoxide of **1**, exists in a chair form. Herein we wish to report our analysis on the twist boat structure of thiane S-oxide determined by both X-ray crystallography and solution NMR spectroscopy.

## Experimental Section

**Chemistry.** <sup>1</sup>H NMR and <sup>13</sup>C NMR were recorded on JEOL GSX-400 (400 MHz <sup>1</sup>H, 100 MHz <sup>13</sup>C), JEOL EX-270 (270 MHz <sup>1</sup>H, 67.8 MHz <sup>13</sup>C) spectrometers. Tetramethylsilane was used as an internal standard. IR spectra were recorded on Jasco IRA-1 or Jasco IR Report-100 spectrometers. Peaks are reported in units of cm<sup>-1</sup>. Mass spectra (LMS) were recorded on a JEOL JMS-01 mass spectrometer, and HRMS were recorded on a DX-300 mass spectrometer under electron impact (EI) conditions. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm Merck silicagel plates (60F-254) with UV light. Melting points were determined on a Buchi 510 melting point apparatus and are uncorrected. For anhydrous reactions, THF, ether, DME, and toluene were distilled from sodium metal benzophenone ketyl.

## Synthesis of *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane-S-oxide (**1a**) and *cis*-4-*tert*-butyl-2-diphenylcarbinol thiane-S-oxide (**1b**):

To a stirred solution of diisopropyl amine (0.46 mL, 3.3 mmol) in THF (30 mL), precooled at -78 °C under nitrogen atmosphere, was added a 1.62 *N* solution of *n*-BuLi in hexane (2.0 mL, 3.3 mmol). After the resulting solution was stirred at -78 °C for 30 min, a solution of *trans*-4-*tert*-butylthiane S-oxide (0.47 g, 2.8 mmol) in THF (3 mL) was added dropwise during a period of about 3 min. After stirring for 30 min at -78 °C, benzophenone (1.3 g, 7.3 mmol) was added, and the whole was stirred for 1 h at -78 °C. The reaction mixture was quenched with satd. aq. NH<sub>4</sub>Cl and allowed to warm to room temperature. After addition of 5% hydrochloric acid and followed by extraction with ethyl acetate three times, the combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and evaporated. The crude products were purified by silica gel column chromatography (ethyl acetate/MeOH = 20/1) to give **1a** (0.31 g, 33%) and **1b** (0.37 g, 39%) as a colorless solid.

Spectra of *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane-S-oxide (**1a**): <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.70-7.76 (10H, m, Ar), 5.55 (1H, s, OH), 3.48 (1H, dd, *J* = 10, 4 Hz, C<sub>2</sub>-H), 3.17 (1H, ddd, *J* = 14, 7, 4 Hz, C<sub>6</sub>-H<sub>eq</sub>), 2.69 (1H, ddd, *J* = 14, 10, 4 Hz, C<sub>6</sub>-H<sub>ax</sub>), 2.46 (1H, ddd, *J* = 15, 10, 7 Hz, C<sub>3</sub>-H<sub>eq</sub>), 2.05-1.92 (2H, m, C<sub>4</sub>-H, C<sub>5</sub>-H<sub>eq</sub>), 1.61 (1H, dt, *J* = 15, 5 Hz, C<sub>3</sub>-H<sub>ax</sub>), 1.40 (1H, m, C<sub>5</sub>-H<sub>ax</sub>), 0.74 (9H, s, *t*-Bu); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>): δ 145.86 (s), 144.55 (s), 128.41 (d), 128.18 (d), 127.24 (d), 126.83 (d), 125.80 (d), 125.18 (d), 80.70 (s), 56.14 (d), 46.45 (t), 40.33 (d), 33.59 (s), 27.32 (q), 18.69 (t), 17.20 (t); MS: *m/z* 356 (M<sup>+</sup>); IR (KBr) (ν<sub>max</sub>): 3400, 1598, 1050, 985, 978, 945 cm<sup>-1</sup>; mp: 171-171.5 °C. Spectra of *cis*-4-*tert*-butyl-2-diphenylcarbinol thiane-S-oxide (**1b**): <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.56-7.26 (10H, m, Ar), 6.06 (1H, s, OH), 3.65 (1H, d, *J* = 12 Hz, C<sub>2</sub>-H<sub>ax</sub>), 3.39 (1H, ddd, *J* = 12, 4, 3 Hz, C<sub>6</sub>-H<sub>eq</sub>), 2.91 (1H, ddd, *J* = 12, 12, 3 Hz, C<sub>6</sub>-H<sub>ax</sub>), 2.10 (2H, m, C<sub>3</sub>-H<sub>eq</sub>, C<sub>5</sub>-H<sub>eq</sub>), 1.46-1.33 (2H, m, C<sub>4</sub>-H<sub>ax</sub>, C<sub>5</sub>-H<sub>ax</sub>), 1.07 (1H, ddd, *J* = 15, 12.2, 12 Hz, C<sub>3</sub>-H<sub>ax</sub>), 0.78 (9H, s, *t*-Bu); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>): δ 143.58 (s), 141.96 (s), 128.25 (d), 127.85 (d), 127.82 (d), 126.76 (d), 127.73 (d), 127.55 (d), 82.21 (s),

71.56 (d), 52.31 (t), 48.23 (d), 32.40 (s), 28.21 (t), 27.23 (q), 24.87 (t); MS:  $m/z$  356 ( $M^+$ ); IR (KBr) ( $\text{cm}^{-1}$ ): 3300, 1598, 1030, 1018, 1000; mp: 168–169 °C.

**Synthesis of *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane-*S*-dioxide (2):** To a stirred solution of *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane-*S*-oxide (1a) (0.19 g, 0.53 mmol) in methylene chloride (5 mL) added slowly 70% MCPBA (2.00 g, 0.79 mmol) at cooling with an ice bath. After stirring for 3 h at room temperature, aqueous 15% NaOH solution (3 mL) was slowly added and the mixture was extracted with ethyl acetate (10 mL) twice. The combined organic layer was washed with aqueous 15% NaOH solution and brine twice respectively, and dried over anhydrous sodium sulfate, evaporated to obtain 2 as a colorless solid (0.25 g, 67%).

Spectra of *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane *S*-dioxide (2):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.58–7.17 (10H, m, Ar), 4.37 (1H, m,  $\text{C}_2\text{-H}$ ), 3.81 (1H, s, OH), 3.37 (1H, td,  $J = 13, 4$  Hz,  $\text{C}_6\text{-H}_{\text{eq}}$ ), 2.69 (1H, m,  $\text{C}_6\text{-H}_{\text{ax}}$ ), 2.11–1.71 (5H, m,  $\text{C}_{3,4,5}\text{-H}$ ), 0.59 (9H, s, *t*-Bu);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  146.36 (s), 144.02 (s), 128.39 (d), 128.29 (d), 127.40 (d), 126.93 (d), 125.80 (d), 125.42 (d), 79.00 (s), 64.64 (d), 53.14 (t), 39.31 (d), 32.58 (s), 27.37 (q), 26.84 (t), 24.30 (t); MS:  $m/z$  372 ( $M^+$ ); IR (KBr) ( $\text{cm}^{-1}$ ): 3458, 1597, 1338, 1292, 1285, 1161, 1142, 1111  $\text{cm}^{-1}$ ; mp: > 230 °C.

## Results and Discussion

As shown in Scheme 1, treatment of *trans*-4-*tert*-butylthiane *S*-oxide<sup>4</sup> with LDA at  $-78$  °C followed by benzophenone in THF produced a mixture of diastereomers, *trans*-4-*tert*-butyl-2-diphenylcarbinol thiane *S*-oxide (1a) and *cis*-4-*tert*-butyl-2-diphenylcarbinol thiane *S*-oxide (1b), which were separated by silica gel column chromatography in 33% and 39% yields, respectively.<sup>5</sup>

Compound 1a was recrystallized from methanol to obtain the colorless crystals, mp 171–171.5 °C. Elemental analysis was obtained within + 0.3 of calculated value. *Trans*-4-*tert*-butyl-2-diphenylcarbinol thiane *S*-dioxide (2) was synthe-

sized by the oxidation of 1a using mCPBA in dichloromethane at room temperature and recrystallized from a mixture of isopropyl alcohol and chloroform (2:1) as a solvent to give the colorless crystals in 83 % yield, mp > 230 °C. C and H analyses within + 0.3 of calculated value were obtained.

Single-crystal X-ray diffraction analyses for 1a and 2 were performed by a P4 X-ray diffractometer (Siemens Co.) and the crystal data and structure refinement are listed in Table 1.<sup>6</sup>

The thiane ring of 1a is highly distorted, as shown in Figure 1, and the examination of the torsional angles in Table 2 reveals that the *tert*-butyl and diphenylcarbinol group of 1a occupy the pseudoequatorial positions, while a sulfoxide group the pseudoaxial position. To the best of our knowledge, twist boat form as a preferred structure in the thiane *S*-oxide system is unprecedented. The twisted conformation of the thiane ring of 1a is further reflected in the long bond for S(1)–C(1) (1.812 Å), S(1)–C(5) (1.812 Å), C(3)–C(4) (1.531

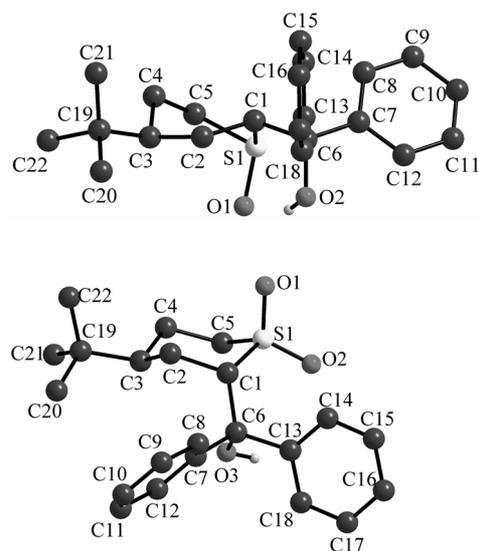
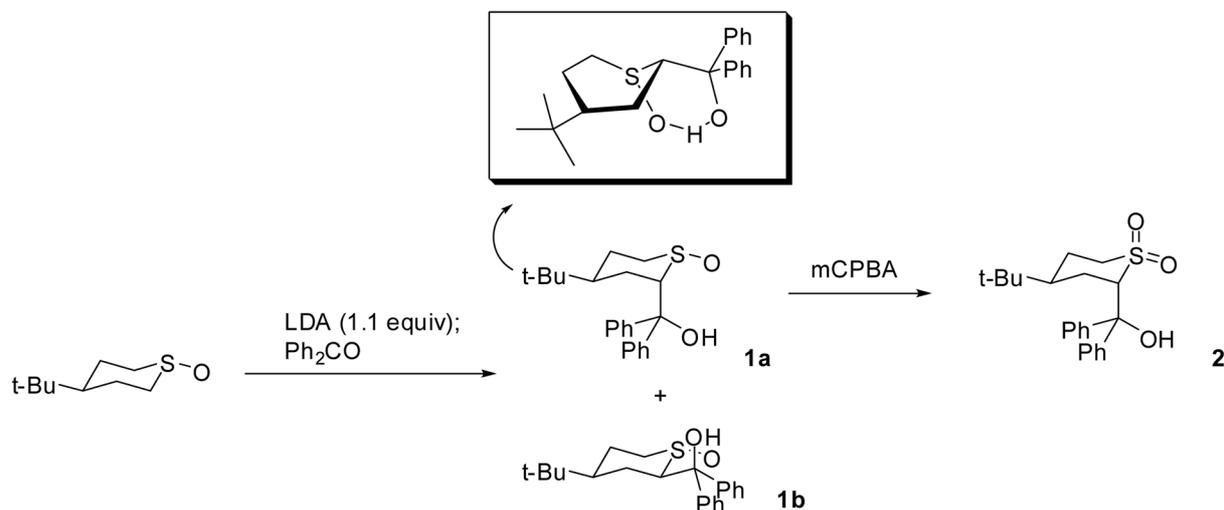


Figure 1. ORTEP drawings of 1a and 2.



Scheme 1. Synthesis of 1 and 2.

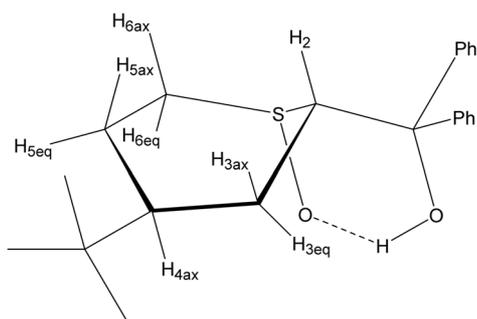
**Table 1.** Crystal Data for **1a** and **2**

	<b>1a</b>	<b>2</b>
formula	C <sub>22</sub> H <sub>28</sub> O <sub>2</sub> S	C <sub>22</sub> H <sub>28</sub> O <sub>3</sub> S
formula weight	356.50	372.50
crystal size (mm)	0.3 × 0.3 × 0.3	0.4 × 0.3 × 0.2
space group	p2 <sub>1</sub> /c	p2 <sub>1</sub> /c
unit cell dimensions	a = 10.4870 (14) Å b = 10.6344 (12) Å c = 18.273 (2) Å α = 90° β = 103.20 (2)° γ = 90°	a = 10.929 (2) Å b = 11.064 (2) Å c = 16.204 (3) Å α = 90° β = 91.388 (12)° γ = 90°
density (calculated)	1.193 Mg/m <sup>3</sup>	1.263 Mg/m <sup>3</sup>
wavelength	0.71073 Å	0.71073 Å
data/restraints/parameters	3498/0/226	3443/0/236
final R indices [I > 2(I)]	R1 = 0.0505 wR2 = 0.1095	R1 = 0.0618 wR2 = 0.1364
R indices (all data)	R1 = 0.0909 wR2 = 0.1274	R1 = 0.1115 wR2 = 0.1588
goodness-of-fit on F <sup>2</sup>	1.016	1.024
max./min. transmission	0.3106 / 0.2925	0.2653 / 0.2426

A), and C(4)-C(5) (1.535 Å). The unusually large bond angles for C(2)-C(1)-S(1) (116.8°) and C(3)-C(4)-C(5) (116.8°) in the ring also clarifies the twisted conformation.

On the other hand, the thiane ring of **2** exists in a chair conformation, where the *tert*-butyl group occupies the equatorial position and diphenylcarbinol group exists in the axial position.

Although structural differences between **1a** and **2** only stem from the difference in oxidation state (sulfoxide vs. sulfonyl group), the conformations are twist boat and chair forms in **1a** and **2**, respectively. Since sulfoxide prefers to occupy the axial position,<sup>7</sup> it seemed to play some role in taking twisted conformation in **1a**, but the preference energy of the axial type of sulfoxide to an equatorial type in the thiane S-oxide is generally known to be ~0.2 kcal/mol,<sup>8</sup> which is too small when compared with the preference energy of chair form over twist boat form (~5 kcal/mol) in the cyclohexane ring system. Another factor for taking the twist form in **1a** is seen in the intramolecular hydrogen bonding between the sulfoxide oxygen and the hydroxyl groups, which is observed in the crystal structure of Figure 1

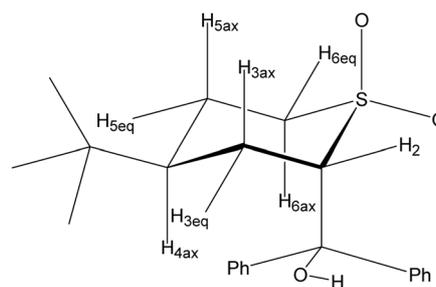
**Figure 2.** Structures of **1a** and **2**.**Table 2.** Torsional Angles for Thiane Ring of **1a** and **2**

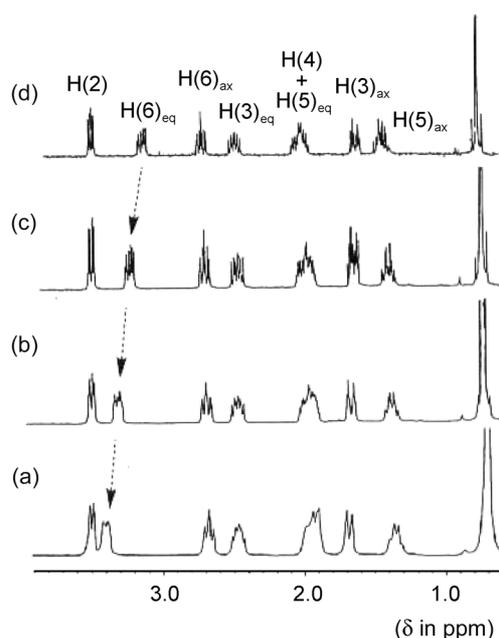
	<b>1a</b>	<b>2</b>
C(5) - S(1) - C(1) - C(2)	21.35(0.24)	-49.56(0.33)
S(1) - C(2) - C(3) - C(4)	38.54(0.30)	59.06(0.41)
C(1) - C(2) - C(3) - C(4)	-69.55(0.28)	-62.04(0.41)
C(2) - C(3) - C(4) - C(5)	28.12(0.31)	65.86(0.40)
C(3) - C(4) - C(5) - S(1)	37.80(0.28)	-59.16(0.34)
C(4) - C(5) - S(1) - C(1)	-58.99(0.20)	46.67(0.27)

for O(1)-H-O(2) (O(1)-H distance: 2.280 Å; O(1)-H-O(2) angle: 129.37°), whereas hydroxyl of **2** does not engage in the intramolecular hydrogen bonding with the sulfoxide functionality.

Internal hydrogen bonding of the hydroxy proton of **1a** was also detected in solution (CDCl<sub>3</sub>) as follows: the hydroxy proton chemical shift (5.6 ppm) of **1a** appeared down field compared with the hydroxy proton of **2** (3.8 ppm); moreover, the hydroxy proton of **1a** was unchanged in various concentrations (0.1 M-0.01 M). Conclusively, we suggest that three factors such as (1) axial preference of sulfoxide, (2) equatorial preference of diphenylcarbinol, and (3) hydrogen bonding between sulfoxide oxygen and hydroxyl, which forms like a [6,6] bicyclic structure (S(1)-C(1)-C(2)-C(3)-C(4)-C(5)-C(10)-O(2)-H-O(1)) work cooperatively for twist boat conformation of **1a**.<sup>9</sup>

The conformation of **1a** in solution (CDCl<sub>3</sub>) was examined as well. Indeed, solution NMR study indicated that the preferred conformation of **1a** in CDCl<sub>3</sub> is a twist boat form like the one observed in the crystal for the following reasons: (1) The sulfoxide of **1a** (Figure 2) is confirmed to be oriented axially<sup>10</sup> since large upfield shifts of C<sub>2</sub>-H (3.48 ppm) and C<sub>6e,6a</sub>-H (3.17, 2.69 ppm) of **1a** were observed, which is comparable to those of the C<sub>2</sub>-H (3.65 ppm) and C<sub>6e,6a</sub>-H (3.39, 2.91 ppm) of **1b** in <sup>1</sup>H NMR. In addition, large upfield shifts of C<sub>2</sub> (56.07 ppm) and C<sub>6</sub> (46.42 ppm) of **1a** were observed in <sup>13</sup>C NMR as were C<sub>2</sub> (71.50 ppm) and C<sub>6</sub> (52.33 ppm) of **1b**.<sup>11</sup> (2) Downfield shifts of C<sub>4</sub>-H (1.96 ppm) and C<sub>3a,3e</sub>-H (2.46, 1.62 ppm) in **1a** in <sup>1</sup>H NMR [C<sub>4</sub>-H (1.37 ppm), C<sub>3a,3e</sub>-H (1.07, 2.10 ppm) in **1b**] are in harmony with the X-ray crystal structure, where C<sub>4</sub>-H and C<sub>3</sub>-H are in the position affecting anisotropy of sulfoxide.<sup>12</sup> (3) Some coupling constants of the thiane ring in **1a** represent the





**Figure 3.**  $^1\text{H}$  NMR of **1a** at various temperatures (a)  $-70\text{ }^\circ\text{C}$  (b)  $-40\text{ }^\circ\text{C}$  (c)  $0\text{ }^\circ\text{C}$  (d)  $60\text{ }^\circ\text{C}$ .

twisted conformation in  $^1\text{H}$  NMR where internal dihedral angles are inclined to be small as seen in the crystal structure, and by the Karplus equation, the vicinal proton coupling constants of axial-axial relationship of **1a** are to be smaller than those of **1b** ( $J_{2a3a} = 10\text{ Hz}$  and  $12\text{ Hz}$  in **1a** and **1b**,  $J_{5a6a} = 10\text{ Hz}$  and  $12\text{ Hz}$  in **1a** and **1b**, respectively) while the vicinal proton coupling constants of axial-equatorial protons of **1a** are to be larger than those of **1b** ( $J_{5a6e} = 7\text{ Hz}$  and  $3\text{ Hz}$  in **1a** and **1b**,  $J_{5e6a} = 4\text{ Hz}$  and  $3\text{ Hz}$  in **1a** and **1b**, respectively).<sup>13</sup>

We also monitored NMR spectra in various temperatures from  $+60\text{ }^\circ\text{C}$  to  $-70\text{ }^\circ\text{C}$  in  $\text{CDCl}_3$  in  $^1\text{H}$  NMR and from  $+20\text{ }^\circ\text{C}$  to  $-80\text{ }^\circ\text{C}$  in  $\text{CD}_2\text{Cl}_2$  in  $^{13}\text{C}$  NMR to exclude the possibility that equilibrium state of different conformations in solution could give one conformation in NMR.

As shown in Figure 3, no noticeable change was observed

**Table 3.** Bond lengths [Å] and angles [deg] for **1a** and **2**

	<b>1a</b>	<b>2</b>
S(1)-O(1)	1.513(2)	1.432(3)
S(1)-C(1)	1.812(3)	1.756(4)
S(1)-C(5)	1.812(2)	1.793(3)
O(2)-C(10)	1.432(3)	
C(1)-C(2)	1.519(4)	1.520(5)
C(2)-C(3)	1.528(3)	1.517(5)
C(3)-C(4)	1.531(3)	1.539(4)
C(3)-C(6)	1.548(4)	1.562(5)
C(4)-C(5)	1.535(3)	1.547(4)
C(5)-C(10)	1.551(3)	1.553(5)
C(6)-C(8)	1.527(4)	1.537(5)
C(6)-C(7)	1.530(4)	1.506(5)
C(6)-C(9)	1.534(4)	1.503(6)
C(10)-C(11)	1.533(3)	1.533(5)
C(10)-C(17)	1.534(3)	1.540(4)

**Table 3.** Continued

	<b>1a</b>	<b>2</b>
C(11)-C(16)	1.377(3)	1.385(5)
C(11)-C(12)	1.382(4)	1.371(5)
C(12)-C(13)	1.375(4)	1.400(6)
C(13)-C(14)	1.377(4)	1.361(7)
C(14)-C(15)	1.361(4)	1.356(7)
C(15)-C(16)	1.381(4)	1.375(5)
C(17)-C(18)	1.383(4)	1.379(5)
C(17)-C(22)	1.386(4)	1.387(4)
C(18)-C(19)	1.379(4)	1.375(5)
C(19)-C(20)	1.369(5)	1.370(5)
C(20)-C(21)	1.359(5)	1.368(6)
C(21)-C(22)	1.391(4)	1.386(5)
S(1)-O(2)		1.438(3)
O(3)-C(10)		1.431(4)
O(1)-S(1)-C(1)	107.70(13)	108.4(2)
O(1)-S(1)-O(2)		117.5(2)
O(1)-S(1)-C(5)	105.20(11)	111.3(2)
C(1)-S(1)-C(5)	97.26(12)	104.3(2)
O(2)-S(1)-C(5)		106.1(2)
C(2)-C(1)-S(1)	116.8(2)	113.9(3)
C(1)-C(2)-C(3)	112.0(2)	112.3(3)
C(2)-C(3)-C(4)	109.6(2)	108.8(3)
C(2)-C(3)-C(6)	114.3(2)	113.1(3)
C(4)-C(3)-C(6)	111.7(2)	112.4(3)
C(3)-C(4)-C(5)	116.8(2)	116.8(3)
C(4)-C(5)-C(10)	112.1(2)	117.0(3)
C(4)-C(5)-S(1)	112.0(2)	107.3(2)
C(10)-C(5)-S(1)	109.4(2)	114.7(2)
C(8)-C(6)-C(7)	108.7(3)	106.6(4)
C(8)-C(6)-C(9)	109.5(3)	108.4(4)
C(7)-C(6)-C(9)	108.0(3)	109.9(4)
C(8)-C(6)-C(3)	111.9(3)	109.6(3)
C(7)-C(6)-C(3)	109.5(2)	112.1(3)
C(9)-C(6)-C(3)	109.1(2)	110.1(3)
O(2)-C(10)-C(11)	107.0(2)	
O(2)-C(10)-C(17)	109.3(2)	
C(11)-C(10)-C(17)	109.7(2)	106.9(2)
O(2)-C(10)-C(5)	109.1(2)	
C(11)-C(10)-C(5)	108.5(2)	107.7(3)
C(17)-C(10)-C(5)	113.1(2)	115.2(3)
C(16)-C(11)-C(12)	118.0(2)	118.4(4)
C(16)-C(11)-C(10)	121.4(2)	119.2(3)
C(12)-C(11)-C(10)	120.6(2)	122.4(3)
C(13)-C(12)-C(11)	121.0(3)	119.7(5)
C(12)-C(13)-C(14)	120.3(3)	120.5(5)
C(15)-C(14)-C(13)	119.2(3)	120.4(5)
C(14)-C(15)-C(16)	120.6(3)	119.5(5)
C(11)-C(16)-C(15)	120.9(3)	121.5(4)
C(18)-C(17)-C(22)	117.6(2)	117.8(3)
C(18)-C(17)-C(10)	122.7(2)	117.2(3)
C(22)-C(17)-C(10)	119.7(2)	124.8(3)
C(19)-C(18)-C(17)	121.2(3)	121.3(3)
C(20)-C(19)-C(18)	120.6(3)	120.6(4)
C(21)-C(20)-C(19)	119.2(3)	119.1(4)
C(20)-C(21)-C(22)	120.8(3)	120.7(4)
C(17)-C(22)-C(21)	120.5(3)	120.5(4)
O(3)-C(10)-C(5)		109.4(2)
O(3)-C(10)-C(11)		108.1(3)
O(3)-C(10)-C(17)		109.2(3)

in spectral patterns except for line broadening at low temperature in  $^1\text{H}$  NMR, confirming that **1a** adopts a twist boat form in solution as one conformer.

In summary, a stable twist boat conformation of thiane S-oxide **1a** in solid state and solution was unambiguously determined by X-ray crystal and solution NMR analyses, respectively. This is the first example where a twist boat form is experimentally observed as a preferred structure in the thiane S-oxide system. In contrast, the corresponding thiane S-dioxide **2** produced by the oxidation of thiane S-oxide **1a** was confirmed to adopt a chair form. Further studies to prepare other stable nonchair conformers are underway in our laboratory.

**Acknowledgments.** We thank Korea Research Institute of Chemical Technology for generous financial support.

### References

- (a) Hendrickson, J. B. *J. Am. Chem. Soc.* **1961**, *83*, 4537. (b) Beckett, C. W.; Pitzer, K. S.; Spitzer, R. *J. Am. Chem. Soc.* **1947**, *69*, 2488. (c) Beckett, C. W.; Freeman, N. K.; Pitzer, K. S. *J. Am. Chem. Soc.* **1948**, *70*, 4227. (d) Turner, R. B. *J. Am. Chem. Soc.* **1952**, *74*, 211. (e) Howlett, K. E. *J. Chem. Soc.* **1957**, 4353.
- (a) Johnson, W. S.; Margrave, J. L.; Baucer, V. J.; Frish, M. A.; Dreger, L. H.; Hubbard, W. N. *J. Am. Chem. Soc.* **1960**, *82*, 1255. (b) Allinger, N. L.; Freiberg, L. A. *J. Am. Chem. Soc.* **1960**, *82*, 2393.
- (a) Hutchins, R. O.; Maryanoff, B. E.; Castillo, M. J.; Hargrave, K. D.; McPhail, A. T. *J. Am. Chem. Soc.* **1979**, *101*, 1600. (b) Bajwa, G. S.; Bentrude, W. G.; Pantaleo, N. S.; Newton, M. G.; Hargis, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 1602. (c) Ramalingam, K.; Berlin, K. D.; Powell, D. R.; Helm, D. *J. Org. Chem.* **1987**, *52*, 2108.
- For the synthesis of *trans*-4-*tert*-butylthiane S-oxide, see: Johnson, C. R.; McCants, D. Jr. *J. Am. Chem. Soc.* **1965**, *87*, 1109.
- For the stereochemistry to the electrophilic reaction of cyclic  $\alpha$ -lithio sulfoxides, see: Chassaing, G.; Lett, R.; Marquet, A. *Tetrahedron Lett.* **1978**, 471, and references therein.
- CCDC 651189 and CCDC 651188 contain the supplementary crystallographic data for compounds **1a** and **2**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
- Freeman, F.; Asgari, N.; Entezam, B.; Gomarooni, F.; Mac, J.; Nguyen, M. H.; Nguyen, N. N. T.; Nguyen, T. P.; Pham, N. B.; Sultana, P.; Welch, T. S.; Shainyan, B. A. *Int. J. Quantum Chem.* **2005**, *101*, 40.
- (a) Lambert, J. B.; Keske, R. G. *J. Org. Chem.* **1966**, *31*, 3429. (b) Allinger, N. L.; Kao, J. *Tetrahedron* **1976**, *32*, 529. (c) Allinger, N. A.; Hirsh, J. A.; Miller, M. A.; Tyminski, L. J. *J. Am. Chem. Soc.* **1969**, *91*, 337.
- For the twist boat conformations by hydrogen bonding, see: (a) Stolow, R. D. *J. Am. Chem. Soc.* **1961**, *83*, 2592. (b) Wolfe, J. J.; Nelson, S. F.; Powell, D. R. *J. Org. Chem.* **1991**, *56*, 5908.
- If the thiane S-oxide ring of **1a** would adopt a chair form, the sulfoxide should be oriented equatorially.
- Chemical shifts of adjacent  $\alpha$ -carbons and protons of axial type sulfoxide in the thiane S-oxide ring appear at upfield in comparison with those of equatorial type sulfoxide; see: (a) Buchanan, G. W.; Durst, T. *Tetrahedron Lett.* **1975**, 1683. (b) Lett, R.; Marquet, A. *Tetrahedron* **1974**, *30*, 3379. (c) Lett, R.; Marquet, A. *Tetrahedron Lett.* **1975**, 1579.
- For the anisotropy of sulfoxide, see: (a) Poster, A. B.; Duxbury, J. M.; Inch, T. D.; Webber, J. M. *Chem. Comm.* **1967**, 881. (b) Edmundson, R. S. *Tetrahedron Lett.* **1965**, 1649.
- From vicinal proton coupling constants by the Karplus method, R value could be calculated and the structural conformation prospected in solution ( $R = J_{\text{trans}}/J_{\text{cis}} = J_{\text{aa}} + J_{\text{ee}}/J_{\text{ae}} + J_{\text{ea}}$ ,  $R = 1.9\text{--}2.2$ : usual chair form,  $<1.9$ : twist boat,  $>2.2$ : puckered chair). In **1a** and **1b**,  $R_{1a} = J_{5a6a} + J_{5e6e}/J_{5a6e} + J_{5e6a} = 10 + 4/7 + 4 = 1.27$  (twist boat),  $R_{1b} = J_{5a6a} + J_{5e6e}/J_{5a6e} + J_{5e6a} = 12 + 4/3 + 3 = 2.67$  (puckered chair). see, (a) Lambert, J. B. *Acc. Chem. Res.* **1971**, *4*, 87. (b) Lambert, J. B. *J. Am. Chem. Soc.* **1967**, *89*, 1836.