CONFORMATIONAL PREFERENCE IN BENZYLOXY- AND SILOXY-SUBSTITUTED THIANES, THIANE 1-OXIDES, AND THIANE 1,1-DIOXIDES

Yoshimitsu Nagao[a]*, Michimasa Goto[b], Kiyoshi Kida[a], and Motoo Shiro[c]

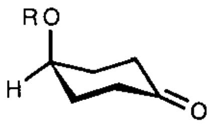
[a]Faculty of Pharmaceutical Sciences, The University of Tokushima, Sho-machi, Tokushima 770, Japan

[b]Chemical Instrument Center, Nagoya University, Chikusa, Nagoya 464-01, Japan

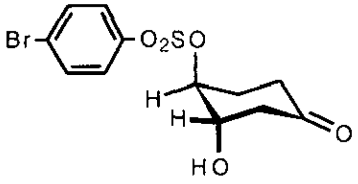
[c]Rigaku Corporation, 3-9-12, Matsubara-cho, Akishima, Tokyo 196, Japan

Abstract- Conformer ratios in 4-benzyloxy- and 4-siloxy-substituted thianes, *cis*- and *trans*-thiane 1-oxides, thiane 1,1-dioxides, and dihydrothiines were revealed on the basis of their low temperature ^1H nmr analyses. Extreme benzyloxy- and siloxy-axial (or -pseudoaxial) conformer preferences in *trans*-thiane 1-oxides, thiane 1,1-dioxides, and dihydrothiines were clearly demonstrated.

Previously, we reported axial (*ax*) conformer preferences (>70% at 25 °C) of alkoxy and siloxy groups in the chair-type cyclohexanones (**1**) and (**2**), glutaric anhydride (**3**: X = O), and glutarimide (**3**: X = NCH_2Ph) not



1 R = CH_2Ph, $Si(Me)_2$*t*-Bu, $Si(Ph)_2$*t*-Bu, $C(Ph)_3$, $SO_2C_6H_4$*p*-Br, COC_6H_4*p*-Br



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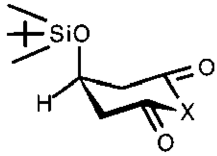
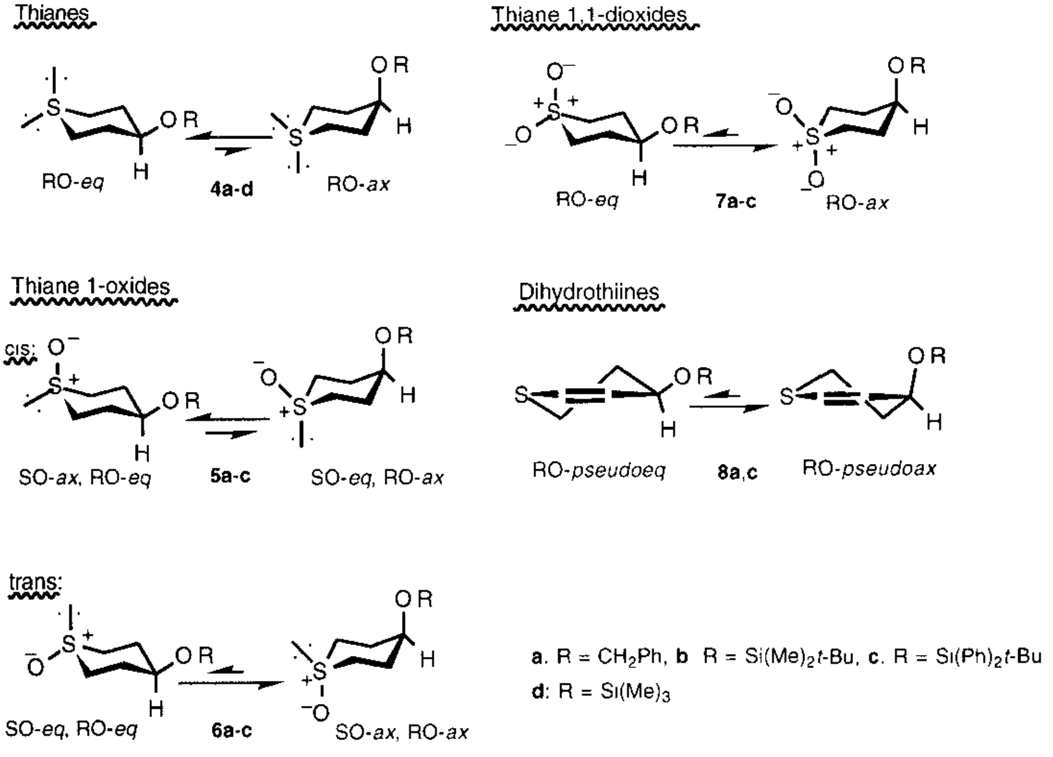


3 X = O, NCH_2Ph

only in their $CDCl_3$ solution but also in the crystalline state.[1] These prochiral compounds (**1**) and (**3**) should be attractive to us from the viewpoint of a new design for the asymmetric induction.[2]

*Significant attention was earlier directed toward the conformational analyses of substituted thianes and their 1-*oxides and 1,1-dioxides. Martin and Ubel reported a conformational preference for the forms having sulfoxide oxygen-*ax* over those with sulfoxide oxygen-equatorial (*eq*) in the *cis*- and *trans*-4-chloro-, 4-hydroxy-, or 4-*p*-toluenesulfonyloxythiane 1-oxides.[3] Ōki and Nogami disclosed interesting evidence of a conformational preference for the forms having Br-*eq* in the 4-bromothiane and its *cis*-1-oxide and for the forms having Br-*ax* in the *trans*-4-bromothiane 1-oxide and its 1,1-dioxide.[4] These results mentioned above prompted us to investigate the systematic conformational analyses of the titled compounds (**4-7**) and dihydrothiines (**8**).



a, R = CH_2Ph, **b** R = $Si(Me)_2t$-Bu, **c**, R = $Si(Ph)_2t$-Bu
d: R = $Si(Me)_3$

Figure 1. Conformational equilibrium modes in 4-RO-substituted thianes, thiane 1-oxides, thiane 1,1-dioxides, and dihydrothiines

The low-temperature ^1H nmr spectra of 4-RO-substituted thianes (**4a-d**),[5] *cis*-thiane 1-oxides (**5a-c**),[5] *trans*-thiane 1-oxides (**6a-c**),[5] thiane 1,1-dioxides (**7a-c**),[5] and 4-RO-dihydrothiine (**8c**)[6] gave rise to two sets of 4-H or 2-H peaks which correspond to the RO-*eq* and RO-*ax* conformers based on the result from their ring interconversion as shown in Figure 1 and Table 1.

Table 1. Conformer ratios in RO-substituted thianes (**4a-d**), *cis*-thiane 1-oxides (**5a-c**), *trans*-thiane 1-oxides (**6a-c**), thiane 1,1-dioxides (**7a-c**), and dihydrothiine (**8c**) based on ^{1}H nmr analysis (400 MHz, CD$_2$Cl$_2$).

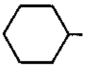
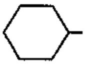
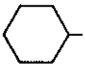
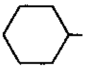
Compound	Conformer Ratio[a)]	δ(ppm) of 4-H		Tc[b)]/°C
	RO-*eq* : RO-*ax*	RO-*eq*	RO-*ax*	
4a	76 : 24	3.23	3.77	-60
4b	69 : 31[c)]	3.46	4.09	-55
4c	47 : 53	3.42	4.03	-50
4d	89 : 11	3.37	4.02	-60
5a	55 : 45	3.45	3.71	-40
5b	34 : 66	3.65	3.97	-40
5c	33 : 67	3.60	3.89	-40
6a	11 : 89	3.40	3.81	-50
6b	4 : 96	3.76	4.10	-50
6c	2 : 98	3.70	4.07	-50
7a	5 : 95	3.59	3.84	-60
7b	2 : 98	3.82	4.10	-70
7c	3 : 97	3.74	4.05	-60
8c	2 : 98[d)]	3.16[e)]	3.57[e)]	-75

a) Unless otherwise, determined at -80 °C. b) Coalescence temp. of 4-H peaks. c) Determined at -90 °C d) Determined at -95 °C. e) δ(ppm) Value of 2-H*ax*.

^{1}H nmr (200 MHz, CDCl$_3$, room temperature) bandwidths (W) of 4-H peaks of **4a-d** exhibited fairly large values (**4a**: 27.6 Hz, **4b**: 25.1 Hz, **4c**: 24.0 Hz, and **4d**: 29.0 Hz), which suggested their RO-*eq* conformer preferences.[1] Then, we examined their 400 MHz ^{1}H nmr analyses at -80 °C and could reveal the details of their conformational ratios (*eq* vs *ax*) in CD$_2$Cl$_2$ solution as shown in Table 1 Interestingly, the order of RO-*eq* conformer preferences among siloxy derivatives (**4b-d**) is shown to be **4d**>**4b**>**4c**. This order must be contrary to that of the bulky size of siloxy groups. Eventually, the order (**4d**>**4a**>**4b**>**4c** and **5a**>**5b**>**5c**) seemed to be in proportion to the basicity (electron density) of the oxygen atom of 4-RO groups. Hence, basicity order of the oxygen atom of the related benzyloxy and siloxy derivatives[7] was tentatively determined on the basis of up-field shift (Δδ ppm) of ^{119}Sn-peak of Me$_2$SnCl$_2$ in the presence of the corresponding cyclohexanol ether as shown in

Table 2. Interestingly, the basicity order (Me_3Si-O>$PhCH_2$-O>*t*-Bu(Me)$_2$Si-O>*t*-Bu(Ph)$_2$Si-O) obtained by our method is perfectly consistent with the order of the RO-*eq* comformer preferences in the compounds (**4**) and (**5**).

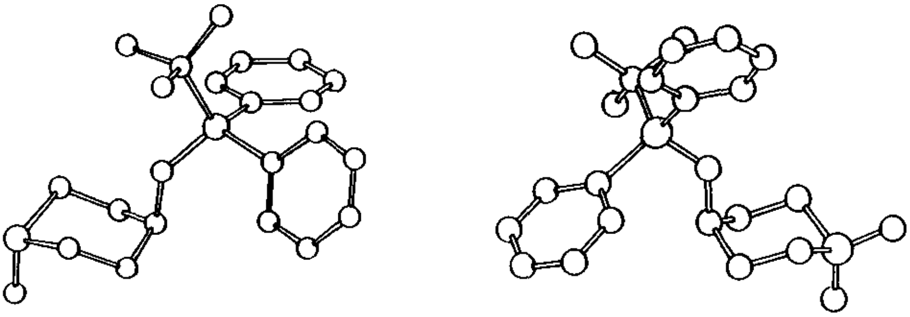
Table 2. Up-field shift (Δδ ppm) of ^{119}Sn-peak (149 MHz, ^{119}Sn nmr) of Me_2SnCl_2 in the presence of ethers in $CDCl_3$ at -50 °C.

Run[a)]	Conditions[a)]	Chemical Shift of ^{119}Sn (δ ppm)[b)]	Δδ ppm[c)]
1)	Me_2SnCl_2 (0.3 mmol)/$CDCl_3$ (2.5 ml)	143.42	—
2)	Me_2SnCl_2 +  -OSi(Me)$_3$	120.09	-23.33
3)	Me_2SnCl_2 +  -OCH_2Ph	131.51	-11.91
4)	Me_2SnCl_2 +  -OSi(Me)$_2$*t*-Bu	138.45	-4.97
5)	Me_2SnCl_2 +  -OSi(Ph)$_2$*t*-Bu	142.92	-0.50

a) In Runs 2-5, a mixture of Me_2SnCl_2 (0.3 mmol) and each ether (0.3 mmol) was determined in $CDCl_3$ (2.5 ml). b) Each chemical shift is indicated in the ppm value relative to the $Me_4{}^{119}Sn$ signal.
c) Δδ ppm = δ ppm ($Me_2{}^{119}SnCl_2$ + ether) - δ ppm ($Me_2{}^{119}SnCl_2$)

In the cases of *cis*-4-RO-thiane 1-oxides (**5a-c**), their RO-*ax* conformer preferences proved to be 45% (**5a**), 66% (**5b**), and 67% (**5c**), respectively, on the basis of their 400 MHz ^{1}H nmr analyses at -80 °C. Each RO-*ax* conformer preference extent of the thiane 1-oxides **5a-c** should be evidently larger than that of the corresponding thianes (**4a-c**) exhibitting the same order aspect **5c>5b>5a** as **4c>4b>4a**. In the cases of *trans*-4-RO-thiane 1-oxides (**6a-c**) and 1,1-dioxides (**7a-c**), the extreme 4-RO-*ax* conformer preference extent of 4-benzyloxy derivatives (**6a** and **7a**) seemes to be little lower than that of the corresponding 4-siloxy ones (**6b**,**c** and **7b**,**c**). Tentative ^{1}H nmr (200 MHz, $CDCl_3$, room temperature) analyses of 4-RO-dihydrothiines (**8a**,**c**) and 1,1-dioxide of **8c** provided the fairly small W values [18.3 Hz (**8a**), 19.7 Hz (**8c**), and 18.6 Hz (1,1-dioxide of **8c**)] due to their 4-H peaks, which should mean their 4-RO-*pseudoax* conformer preferences as we anticipated.[8] The dynamic ^{1}H nmr analysis of **8c** at -95 °C definitly clarified its conformatonal ratio.

Finally, crystalline compounds (**6c** and **7c**) were submitted to the X-ray analysis[9] Perspective views of their crystallographic structures are depicted in Figure 2[9] The thiane 1-oxide and 1,1-dioxide rings adopt a chair form and the siloxy group, in fact, occupies the *ax* site in their molecules.



6c **7c**

Figure 2. Perspectives view of the crystallographic structures of compounds **6c** and **7c**.

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5. Reduction of commercially available 4-ketothiane with $LiAlH_4$ in Et_2O followed by conventional benzylation or silylation employing each corresponding halide gave 4-benzyloxy- or 4-siloxythianes (**4a**-**d**) in a good yield, respectively. Their *cis*- and *trans*-thiane 1-oxides (**5a**-**c** and **6a**-**c**) and thiane 1,1-dioxides (**7a**-**c**) were prepared by oxidation with 1 or 2 mol equiv of *m*-chloroperoxybenzoic acid in CH_2Cl_2. Chromatographic separation of the resultant mixture of *cis*- and *trans*-thiane 1-oxides on a silica gel plate

gave each pure isomer. Assignment of the cis or trans structure should be done by their ^{1}H nmr (200 MHz, $CDCl_3$, room temperature) analyses [W(4-H) = 24.3-25.6 Hz for the *cis*-isomers or W(4-H) = 18.5 - 21.0 Hz for the *trans*-ones; The 3-H peaks of the *cis*-isomers are recognized in the higher magnetic field than those of the corresponding *trans*-ones.] in comparison with the same analyses of the authentic *trans*-(**6c**) and *cis*-(**5c**).

6. 4-Benzyloxy- and 4-siloxydihydrothiines (**8a,c**) were readily prepared by refluxing a mixture of the corresponding *cis*- and *trans*-thiane 1-oxides with Ac_2O in benzene.
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9. The crystallographic data of compounds **6c** and **7c** are as follows **6c**; $C_{21}H_{28}O_2SSi$, M = 372.60, triclinic, P1(#2), a = 10.240(1)Å, b = 12.003(3)Å, c = 9.991(2)Å, α = 111.44(2)°, β = 107.04(1)°, γ = 101.32(1)°, V = 1027.2(4)Å^3, z = 2, Dcalc = 1.205 g/cm^3, R = 0.066, **7c**; $C_{21}H_{28}O_3SSi$, M = 388.597, tetragonal, P4 2/n, a = 20.316 (3)Å, c = 10.302(2)Å, V = 4252(1)Å^3, z = 8, Dcalc = 1.214 g/cm^3, R = 0.066.

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