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Stable Diaxial Chair Cyclohexanes due to the Adjacent and Bulky *trans*-Siloxy Groups

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The rings of the (±)-*trans*-1,2-bis(*tert*-butyldiphenylsiloxy)-, (triisopropylsiloxy)-, and (*tert*-butyldimethylsiloxy)cyclohexanes prefer a diaxial chair conformation in the crystal state. The ring of the *tert*-butyldimethylsiloxy derivative switched its chair conformation between the diaxial and a diequatorial conformations in the crystal and in solution, respectively.

Protection of an adjacent diol with bulky trialkyl or alkyldiarylsilyl groups sometimes induces a drastic conformational change. Saito and co-workers have reported the first example of such a conformational control by the introduction of *tert*-butyldimethylsilyl (TBS) groups on acyclic adjacent diols (Fig. 1).[1] The conformational control of rings has also been observed in the tetrahydropyranes of sugars by introducing bulky silyl protecting groups, and the resulting ring-conformations take a chair form with the substituents in axial positions.[2,3] The generated 1,2-disiloxy groups are arranged *anti* to each other and contribute to the induction of a specific stereoselectivity during several reactions.[1,3,4]

The two consecutive bulky siloxy groups on a cyclohexane ring orient axially and restrict even the cyclohexane ring, although A-values of siloxy groups indicate these substituents prefer equatorial orientation.[5] Three kinds of silyl-protected *myo*-inositols stably occur in the axial-rich chair form,[6] and more basically, the preferred 1,2-diaxial chair conformation of the *trans*-1,2-bis(trialkylsiloxy)cyclohexanes (Fig. 2) has been reported by Marzabadi and co-workers based on NMR experiments and MM3 calculations.[7] They have shown that *tert*-butyldiphenylsilyl (TBDPS)- and triisopropylsilyl (TIPS)-protected *trans*-1,2-cyclohexanediol, **1** and **2**, respectively, prefer the diaxial chair form in CD_2Cl_2 and in toluene-d_8. In contrast, the diequatorial chair conformation was the major form when TBS (**3**), triphenylsilyl, and other smaller silyl protecting groups were introduced.

Although the NMR experiments can indicate the existence of conformational isomers, it is generally difficult to obtain proof that the simple cyclohexane rings of the observed con-

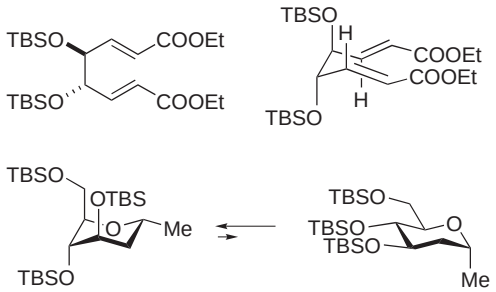

Fig. 1. Example of conformational distribution control due to introduction of bulky silyl protecting groups.[1,2a]

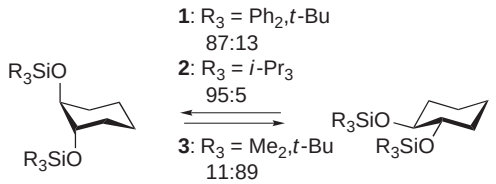

Fig. 2. Ring-conformation of *trans*-1,2-bis(trialkylsiloxy)-cyclohexanes in CD_2Cl_2 at 200 K.[7]

formers are in a chair form. Examples of a stable twist conformer have also been found among compounds that have a six-membered ring with bulky siloxy groups.[8] Furthermore, for a deeper appreciation of such conformational changes, the positional information of the alkyl (or aryl) groups on the silicon atoms are also important, because such conformations vary with the type of the alkyl substituents. Thus, we determined single-crystal X-ray structure of racemic **1**–**3** to obtain detailed information about not only the conformation of the ring, but also the positions of the alkyl groups on the silicon atoms.

The respective cyclohexane rings of **1**–**3** were all in the chair conformation possessing axially oriented C–O bonds (Fig. 3). The dihedral angles of the O–C–C–O in **1**–**3** are 175.0, 173.9, and 173.6° and the H–C–O–Si torsion angles are 13.6 and 15.0°, 9.7 and 15.3° (displayed in Fig. 4), and 4.6 and 8.8°, respectively. Thus, the H–C bond tends to eclipse the O–Si bond, and the view of each model from the direction of the C–O bonds shows that the two O–Si bonds turn slightly out of the two H–C bonds. Generally, the more stable conformer of a 1,2-*trans*-disubstituted cyclohexane derivative is the diequatorial chair form. These obtained results are exceptions to what is normally observed. Marzabadi and co-workers reported a crystal structure of (±)-*trans*-1,2-bis(triphenylsiloxy)-cyclohexane, of which the unit cell contains twelve molecules: four of the twelve molecules took the 1,2-diaxial chair form, and eight molecules took the 1,2-diequatorial chair form.[7] In contrast, each unit cell of TBS-, TIPS-, and TBDPS-protected racemic **1**–**3** contained four molecules, which are all in the axial-rich chair form. These compounds, therefore, entirely take axial-rich chair form.

The substituents on the silicon atoms in each compound located in different directions. In **1**, one *tert*-butyl group faced the cyclohexane ring, and another *tert*-butyl group faced away from the ring (see Fig. 3). It should be noted that the substituents on the silicon atoms in these diaxial chair compounds are not always symmetrical in the solid state. In **2**, a part of the isopropyl groups protruded over both faces of the cyclohexane

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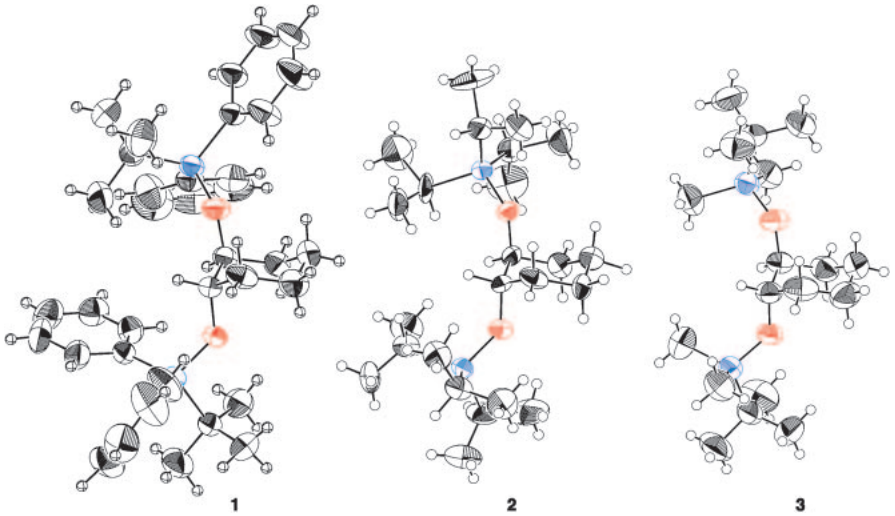

Fig. 3. ORTEP drawings of the crystal structure of (±)-**1**, -**2**, and -**3**. Blue = silicon, red = oxygen.

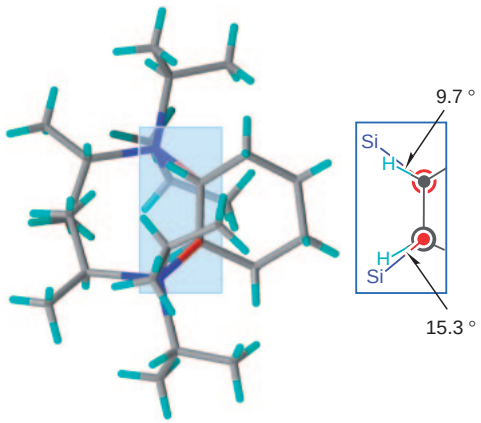

Fig. 4. Top view of **2** with the H–C–O–Si dihedral angles. Blue = silicon, red = oxygen, gray = carbon, cyan = hydrogen.

ring as shown in Fig. 4. In **3**, both of the *tert*-butyl groups were oriented to the cyclohexane ring with an almost C_2 symmetry, and this compound showed an interesting conformational switch.

The ring conformations of **1** and **2** in the crystals were similar to those in solution, but **3** was not. Compound **3** prefers the diequatorial chair conformation in solution (Fig. 2).[7] The conformation is hence controllable by choosing its state; i.e, in solution or in a crystal. Additionally, it was surprising that even two OTBS groups could restrict a cyclohexane ring in the 1,2-diaxial chair form.

In conclusion, we experimentally confirmed that the ring conformations of (±)-**1**–**3** were all in the diaxial chair conformation and the positions of the alkyl groups on the silicon atoms were not always symmetrical in the solid state. Using NMR, it would be difficult to determine that the ring conformations of the observed two conformers are chair, because of the disappearance of the vicinal coupling between the protons on the oxygen-linked carbons due to their C_2 symmetry. The present observations here are the structures in crystals, but they would support the stability of the chair conformations in solution.

Experimental

Crystallizations. Compounds (±)-**1**–**3** were prepared according to Marzabadi's report.[7] The crystallizations of (±)-**1**–**3** were performed in a vial (inside dimensions: 14 mm-diameter × 35 mm-height) covered by aluminum foil with a hole (ca. 0.0075 mm^2). Compound (±)-**1** (200 mg) was dissolved in a mixture of MeOH (0.8 mL) and diethyl ether (2.4 mL), and the mixture was then stored for 28 days at room temperature. Most of the ether evaporated, and in the remaining solution (ca. 0.75 mL), several plate-like single-crystals (mp 58.5–60.5 °C) and a block of an amorphous solid formed. Compound (±)-**2** (100 mg) was dissolved in a mixture of MeOH (0.8 mL) and diethyl ether (2.4 mL), and the mixture was allowed to stand for 14 days at −15 °C. Most of the ether had evaporated, and in the remaining solution (ca. 0.75 mL), several block-like single-crystals (mp 13.8–14.8 °C) were found. Compound (±)-**3** (15 mg) was dissolved in a mixture of hexane (0.5 mL) and diethyl ether (2.0 mL), and the mixture was allowed to stand for 8 days at room temperature. Most of the solvent had evaporated, and several stick-like single-crystals appeared (mp 30.0–31.0 °C).

X-ray Crystallography. Data collections for (±)-**1** and (±)-**3** were carried out at room temperature, and the data of (±)-**2** were collected at 0 °C because of its low melting point. X-ray data were measured on a MacScience dip image plate diffractometer using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). All diagrams and calculations were performed using maXus (Bruker Nonius, Delft & MacScience, Japan). The structure was solved by direct method with SIR-97[9] and refined by a full-matrix least-squares method on F^2 with SHELXS-97.[10]

The crystallographic parameters of (±)-**1**–**3** are as follows. (±)-**1**: $C_{38}H_{48}O_2Si_2$, $M_r = 592.972$, crystal size $0.35 \times 0.25 \times 0.20\,mm^3$, monoclinic, space group $P2_1/a$, $a = 16.4850(5)$, $b = 11.7250(4)$, $c = 18.4930(7)$ Å, $\beta = 95.7050(10)°$, $V = 3556.7(2)$ $Å^3$, $Z = 4$, $D_{calcd} = 1.107\,Mg\,m^{-3}$, $\mu(Mo\,K\alpha) = 0.13\,mm^{-1}$, measured temp. 298 K, $R = 0.062$ ($wR = 0.113$) for 5300 ($I > 3.0\sigma(I)$) reflections. (±)-**2**: $C_{24}H_{52}O_2Si_2$, $M_r = 428.850$, crystal size $0.35 \times 0.30 \times 0.30\,mm^3$, monoclinic, space group Cc, $a = 7.8400(5)$, $b = 15.7120(13)$, $c = 23.329(2)$ Å, $\alpha = 90.00$, $\beta = 97.966(3)$, $\gamma = 90.00°$, $V = 2846.0(4)$ $Å^3$, $Z = 4$, $D_{calcd} = 1.001$ $Mg\,m^{-3}$, $\mu(Mo\,K\alpha) = 0.140\,mm^{-1}$, measured temp. 273 K, $R = 0.0479$ ($wR = 0.1223$) for 1723 ($I > 2.0\sigma(I)$) reflections. (±)-**3**:

$C_{18}H_{40}O_6Si_2$, $M_r = 344.688$, crystal size $0.50 \times 0.30 \times 0.25$ mm^3, triclinic, space group $P2_1/n$, $a = 6.7870(2)$, $b = 13.0310(6)$, $c = 26.2050(12)$ Å, $\alpha = 90.00$, $\beta = 91.198(2)$, $\gamma = 90.00°$, $V = 2317.1(2)$ Å^3, $Z = 4$, $D_{calcd} = 0.988$ Mg m^{-3}, μ(Mo Kα) $= 0.158$ mm^{-1}, measured temp. 298 K, $R = 0.0537$ ($wR = 0.1491$) for 3517 ($I > 2.0\sigma(I)$) reflections.

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition numbers CCDC-227487, -227486, and -227485 for (±)-**1**, (±)-**2**, and (±)-**3**, respectively. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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