

# Homolytic 1,5-transfer of chiral organosilicon groups from an enoxy oxygen to an alkoxy oxygen—implications for mechanism

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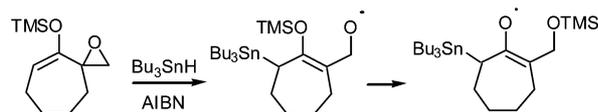
Reaction of the optically active silanes, ((*S*<sub>Si</sub>)-(-)-**6**), formed by treatment of racemic 2-methylenecycloheptanone oxide with LDA followed by (*R*)-(+)-chloromethyl(1-naphthyl)phenylsilane, with tributyltin hydride under standard radical conditions affords (2*R*/2*S*)-[(*S*)-(methyl(1-naphthyl)phenylsilyloxy)methyl]cycloheptanone, (*S*<sub>Si</sub>)-(-)-**7**, providing strong evidence that homolytic 1,5-transfers of organosilicon groups from enoxy oxygen to alkoxy oxygen proceed with retention of configuration, most likely through a *frontside* attack mechanism rather than *via* a hypervalent intermediate.

During the past few decades, many synthetically useful radical rearrangements by atom and group transfer have been reported.<sup>1</sup> It is well established that homolytic 1,5- and 1,6-Bu<sub>3</sub>Sn group transfers from allylic carbon and enoxy oxygen to alkoxy oxygen are greatly favoured over 1,5- and 1,6-hydrogen atom transfer (HAT) reactions,<sup>2,3</sup> while analogous transfers between allylic and alkyl carbon atoms were competitive with HAT.<sup>4</sup> In addition we demonstrated 1,5-Me<sub>3</sub>Si and Ph<sub>3</sub>Ge group transfer from enoxy oxygen to alkoxy oxygen, while very recently we reported the first examples of the 1,5-transfer of the Bu<sub>3</sub>Sn group from enoxy oxygen and allylic carbon to nitrogen.<sup>5</sup> A typical example is depicted in Scheme 1.

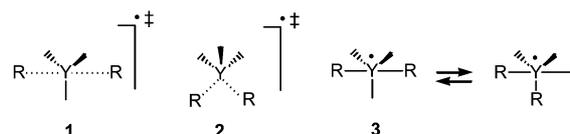
Unlike reactions involving the chalcogens<sup>6</sup> and halogens,<sup>7</sup> recent computational work involving intermolecular homolytic substitution has revealed the existence of both *backside* (**1**) and *frontside* (**2**) transition states and that these are of similar energy for reactions involving silicon, germanium and tin.<sup>8</sup> In addition to pathways involving **1** and **2**, hypervalent structure (**3**) should also be considered as a possible intermediate in these reactions. While recent calculations performed for some 1,5-transfers involving silicon, germanium and tin failed to provide any evidence for the existence of hypervalent intermediates in this translocation chemistry,<sup>9</sup> to the best of our knowledge there are no reports of any experimental evidence for either mechanistic preference.

We now report that 1,5-translocations of chiral organosilicon groups from an enoxy oxygen to alkoxy oxygen proceed with retention of configuration, a result that suggests that the mechanistic pathway for intramolecular homolytic transfer of silyl substituents most likely involves a *frontside* mechanism that does not include a hypervalent intermediate.

We began our quest for mechanistic information by considering a chiral version of the transformation depicted in Scheme 1. We rationalised that if we began with a silane in which the absolute configuration of the silicon atom was known, then the stereochemistry of the translocated product would provide important information regarding the mechanism of the reaction.

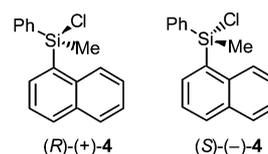


Scheme 1



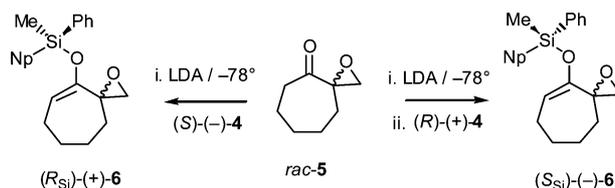
Specifically, *backside attack* would lead to inversion of configuration, *frontside attack* to retention of configuration, while racemization through pseudorotation would be the most likely outcome should an intermediate such as **3** be involved.

Chloromethyl(1-naphthyl)phenylsilane (**4**) was prepared and resolved according to the procedure of Sommer and coworkers.<sup>10</sup> In our hands, (*R*)-(+)-**4** was measured to have an optical rotation, [ $\alpha$ ]<sub>D</sub><sup>20</sup>, of +5.6° (cyclohexane), while its enantiomer, (*S*)-(-)-**4**, had a value of -5.1° (cyclohexane). These values are to be compared with the literature value of -6.3° for (-)-**4** (pentane) and +6.4° for (+)-**4** (pentane).<sup>10</sup>



Following our previously published procedure, racemic 2-methylenecycloheptanone oxide (**5**)<sup>3</sup> was treated with LDA in THF/HMPA (-78 °C) followed by addition of either isomer of **4** to afford the silylated epoxide (**6**) as optically active pairs of diastereoisomers in 54% yield after workup and chromatography (Scheme 2). Compounds (**6**) obtained in this manner from either enantiomer of **4** display separate signals for the alkene proton in each isomer at  $\delta$  5.15 and 5.24 (each signal appeared as a triplet, *J* 6.6 Hz), while the diastereotopic oxirane protons were observed to resonate at  $\delta$  2.44, 2.49, 3.00 and 3.10, each signal appearing as a doublet (*J* 5.9 Hz) of equal intensity. These silanes (**6**) proved to decompose on standing as evidenced by a decline in the quality of their <sup>1</sup>H NMR spectra and were consequently characterised by HRMS.<sup>†</sup>

Importantly, the equi-mixture of silanes (**6**) derived from (*S*)-(-)-**4** was observed to have an optical rotation, [ $\alpha$ ]<sub>D</sub><sup>20</sup>, of +4.6° (cyclohexane), while the optically active mixture derived from (+)-**4** had a value of -4.0°. These diastereoisomeric mixtures will be referred to as (+)-**6** and (-)-**6** respectively throughout and presumably contain (*R*) and (*S*) silicon configurations

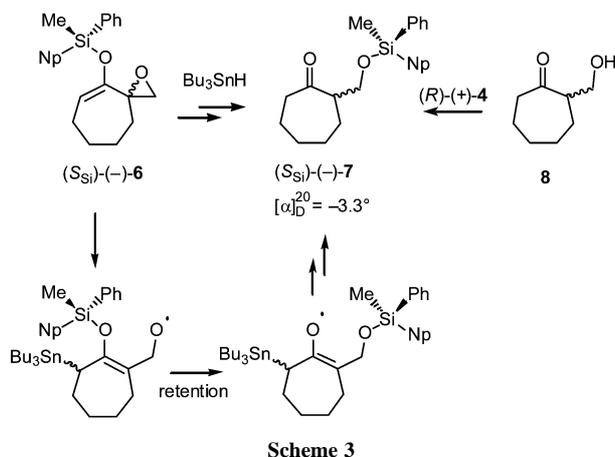


Scheme 2

respectively.<sup>‡</sup> Unfortunately, both sets of chiral silanes (**6**) are viscous oils that failed to provide crystals suitable for X-ray crystallographic analysis.

When (*S*<sub>Si</sub>)-(-)-**6** was reacted with tributyltin hydride as described in our previous publication,<sup>2</sup> the translocated silane, 2-[(methyl(1-naphthyl)phenylsilyloxy)methyl]cycloheptanone (**7**) was isolated as a mixture of diastereoisomers in 78% yield after workup and chromatography (Scheme 3). When prepared in this manner, **7** proved to be a viscous oil with a measured optical rotation, [ $\alpha$ ]<sub>D</sub><sup>20</sup>, of  $-3.3^\circ$  (cyclohexane) that failed to provide crystals for X-ray analysis.<sup>§</sup>

An authentic sample of (*S*<sub>Si</sub>)-**7** was prepared from racemic 2-(hydroxymethyl)cycloheptanone (**8**)<sup>3</sup> by reaction with (*R*)-(+)-chloromethyl(1-naphthyl)phenylsilane, (*R*)-(+)-**4**.<sup>‡</sup> This authentic diastereomeric mixture proved to have identical <sup>1</sup>H and <sup>13</sup>C NMR spectra to those of **7** obtained from the translocation chemistry.<sup>¶</sup> Most importantly, **7** obtained in this manner displayed an optical rotation, [ $\alpha$ ]<sub>D</sub><sup>20</sup>, of  $-3.3^\circ$  (cyclohexane), in excellent agreement with that measured for the compound obtained from the translocation reaction (Scheme 3). In the analogous enantiomeric series of reactions, (*R*<sub>Si</sub>)-(+)-**6** provided a translocated silane (**7**) with an optical rotation of  $+3.3^\circ$  when reacted with tributyltin hydride in the manner described above, strongly suggesting that the translocated product is (*R*<sub>Si</sub>)-(+)-**7**. We conclude from these observations that, in agreement with our computational data,<sup>9</sup> the translocated products (**7**) are in all likelihood formed from **6** in mechanisms involving *frontside* homolytic substitution at the silicon atom (transition state **2**) resulting in retention of configuration rather than through a *backside* mechanism or a pathway involving a hypervalent intermediate such as **3**.



We are currently examining similar chiral translocations involving germanium and tin. We thank the Australian Research Council for support.

## Notes and references

<sup>†</sup> HRMS (ESI: [M + Na]<sup>+</sup>): C<sub>21</sub>H<sub>26</sub>O<sub>2</sub>Si requires 409.1600, found 409.1617.

<sup>‡</sup> While there is evidence to suggest that substitution at silicon by oxygen-centred nucleophiles occurs with inversion of configuration (ref. 10), this assumption is not necessary to the overall stereochemical argument; all that is required is the reasonable assumption that both **5** and **8** react with **4** with the same stereochemical preference.

<sup>§</sup> We were unable to determine whether or not epimerisation at the silicon atom had occurred by chiral-phase HPLC. While we were able to separate the diastereoisomeric pairs of **7** generated during this reaction on several different columns, all attempts to separate the pairs of enantiomers generated by reaction of **8** with racemic **4** failed.

<sup>¶</sup> NMR data (pair of diastereoisomers): <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.71 (3H, s), 1.18–1.48 (4H, m), 1.70–1.87 (4H, m), 2.35–2.39 (2H, m), 2.63–2.68 (1H, m), 3.61–3.71 (1H, m), 3.84–3.93 (1H, m), 7.25–7.43 (6H, m), 7.51 (2H, d, *J* 5.8 Hz), 7.69 (1H, t, *J* 6.1 Hz), 7.78 (1H, d, *J* 7.5 Hz), 7.85 (1H, d, *J* 7.5 Hz), 8.02–8.05 (1H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  -2.25, 24.1, 27.7, 28.65, 28.68, 29.5, 43.8, 54.3, 64.33, 64.35, 125.0, 125.5, 125.9, 127.9, 128.5, 128.7, 129.8, 130.7, 133.2, 133.7, 134.2, 135.1, 136.4, 136.9.

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