Asymmetric retro-[1,4]-Brook rearrangement of 3-silyl allyloxysilanes via chirality transfer from silicon to carbon†

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An asymmetric retro-[1,4]-Brook rearrangement of 3-silyl allyloxysilanes has been developed via Si-to-C chirality transfer. Mechanistic studies reveal that the silyl group migrates with retention of configuration. The stereochemical outcome of the newly formed stereogenic carbon center, which has remained a longstanding question, is also clarified, suggesting a diastereoselective Si to C chirality transfer without loss of enantiomeric excess.

Introduction

Intramolecular O-to-C silyl migration, now called retro-Brook (or West) rearrangement, was first reported by Speier and later systematically studied by West.1 The retro-Brook rearrangement occurs only under special circumstances2 and so has been less investigated than Brook rearrangement.3 But, it comprises a powerful synthetic tool because diverse organosilanes could be constructed from more accessible silyl ethers by a rapid and regio- and stereoselective manner. A covalent Si–O bond is cleaved and a Si–C bond is formed via silyl migration. Thus, the stereochemical courses at the migrating silicon center and the stereochemical control at the forming carbon center comprise two important stereochemical issues. Tomooka and co-workers4 reported the first example of practically useful level of retro-[1,4]-Brook rearrangement of allyloxysilane by use of HMPA as a co-solvent. In this work, they also showed, for the first time, that the silyl migration proceeded with retention of configuration at the silicon center (Scheme 1). In contrast, more efforts have been directed toward diastereoselective formation of the Si–C bond to generate synthetically useful chiral organosilanes.

Nearly all previous studies have used stereogenic C1,6−8 C2 (ref. 2h) or C3 (ref. 2a and j) centers in substrate I to control diastereoselective formation of the Si–C bond in III. When the migrating silicon is stereogenic,7 it might be used as a stereochemical controller by Si to C chirality transfer, which was redefined by Oestreich.8 Achieving this in practice is quite challenging. There are only two examples we know come from a preliminary study by Tomooka and co-workers.4 The 3-Me allyloxysilane with SiOMePh−Bu as the migrating silyl group afforded a dr of 83 : 17, while the corresponding 3-SiMe3 allyloxysilane only migrated with a dr of 66 : 34. In both cases, the stereochemistry of the formed stereogenic carbon center were not determined.

Oestreich rationalized the difficulties in achieving high diastereoselectivity during Si-to-C chirality transfer as follows.6 The relatively long Si–C bond favors formation of a compact transition state II, which weakens diastereoselectivity. At the same time, all three substituents on the migrating silyl group can affect the stereochemical course, requiring the careful selection of three substituents that together allow efficient stereochemical control. Despite these difficulties, Oestreich described an intermolecular Pd-catalyzed asymmetric hydroxysilylation using chiral silane (Scheme 2a).7 and Leighton demonstrated an intramolecular Hosomi–Sakurai allylation involving a chiral allylsilane intermediate (Scheme 2b).8 In both

Scheme 1 Diastereoselective retro-Brook rearrangement.
of these cases, either cyclic silanes or acyclic silane with three distinct, sterically demanding substituents were used to achieve the high stereochemical control.

Here we report an asymmetric retro-[1,4]-Brook rearrangement of 3-silyl allyloxysilanes via an efficient Si-to-C chirality transfer (Scheme 2c). The combination of SiMePh-Bu as the migrating silyl group and SiPh3 as the terminal silyl group proved most effective, giving geminal bis(silyl) aldehyde 3 and enol derivatives 4 in good yield with high diastereoselectivity. The overall stereochemical outcome of the migrating silicon center and the newly formed carbon center were clarified by detailed mechanistic studies.

Results and discussion

This project arose from our interest in developing chiral geminal bis(silanes) reagents and synthons. These species contain two different silyl groups, making the carbon to which they are attached a stereogenic center. In previous work, we achieved asymmetric C–C or C–H bonds formation via 3,3-sigma tropic rearrangement of optically pure 3,3-bis(silyl) allylic alcohols, allowing asymmetric synthesis of crotyl geminal bis(silanes). We were curious whether asymmetric C–Si bond formation could be another efficient strategy to construct chiral geminal bis(silanes). Our s-BuLi-promoted retro-[1,4]-Brook rearrangement of 3-silyl allyloxysilanes appeared to be a suitable model to test this possibility. The reaction tolerates a wide range of migrating and non-migrating silyl groups, making it practical for identifying the best pair of silyl groups.

We initially fixed t-BuPhMeSi as the migrating silyl group (Table 1). Entries 1–7 showed an obvious steric bias for the non-migrating silicons (Si1) at the 3-position of 1. When Si1 was an SiMe3 group, geminal bis(silyl) aldehydes 3a were generated as a nearly 1:1 mixture of two diastereomers (entry 1). Even when one methyl was replaced with a phenyl group, dr did not improve for the corresponding products 3b (entry 2). These results imply that the small methyl group does not permit good diastereoechemical control. Diastereoselectivity improved progressively when steric demand at Si2 increased from SiMe3 to SiEt3, Si(n-Pr)3, Si(i-Pr)3, and finally SiPh3 (entries 3–6). The largest SiPh3 group imposed the strongest stereochemical control, providing 3f at the highest dr of 90:10 (entry 6).

Interestingly, an inverse steric bias for Si1 was observed when the migrating silicon was switched from t-BuPhMeSi to t-BuPhMeSi. The largest SiPh3 group afforded a dr of only 65:35, while the smallest SiMe3 provided the best dr of 86:14 (entries 7–9). We also tested the silicon combination in which the t-BuPhMeSi functionalized as a chiral auxiliary, while SiPh3 migrated (entry 10). The reaction gave the aldehyde 3f with a dr of 74:26 lower than that obtained in entry 5.

Next we examined the scope of electrophiles for quenching the lithium enolate intermediate generated from 1f. The reaction tolerated triethylsilyl chloride (entry 1), various acyl chlorides (entries 2–9) and chlorocarbonates (entries 10 and 11) to provide 3,3-bis(silyl) enol derivatives 4 in good yields with high diastereoselectivity (Table 2). The enol double bond formed exclusively with Z-selectivity. The relative stereochemistry of the products was unambiguously established based on X-ray diffraction analysis of 4d crystals. Methyl iodide was also a suitable electrophile, but less reactive than acyl chloride, giving 4l in 40% yield with O-alkylation selectivity (entry 12).

The silicon can migrate with either retention or inversion of configuration. Thus, the relative stereochemistry of 3f may not reflect the stereochemical course of the migrating silicon, or how it controls the stereochemical outcome of the resulting stereochemical center. In particular, if the enanamerically defined silyl group racemizes during migration, the carbon center can be constructed diastereoselectively, but not enantioselectively. The observation by Tomooka and co-workers that silicon migrates with retention of configuration in their simple allyloxy system does not necessarily apply to our case, since the
non-migrating silicon may affect the stereochemical course. To gain a definitive answer to this question, we used enantiomerically defined 10 as a stereochemical probe (Scheme 3). Following the procedure developed by Oestreich, a mixture of 5 was separated by several cycles of silica gel chromatography, affording 6 in diastereomerically pure form. Reduction of 6 with DIBAL-H provided hydrosilane 7 in 77% yield. Subsequent chlorination of 7 with CCl₄ delivered chlorosilane 8, which directly reacted with the potassium salt of 9, giving 10 in 90% yield. The high er of 10 (96 : 4) suggests that transformation from 6 to 10 proceeds in a stereospecific manner at the silicon center, and should follow the known sequence of retention-retention-inversion. Thus, the absolute configuration of the silicon in 10 was assigned as R. Under the optimal retro-[1,4]-Brook rearrangement conditions, 10 was converted into aldehyde 11. The major isomer showed an er of 96 : 4, indicating that the silicon migrated stereospecifically. X-ray diffraction analysis of 11 unambiguously confirmed the R-configuration of the silicon, indicating that migration proceeds with retention of configuration as in Tomooka’s case. The X-ray diffraction analysis of 11 also established the S-configuration of the new stereogenic carbon center. The result revealed that the migration proceeded by a diastereoselective Si to C chirality transfer without loss of enantiomeric excess.

A plausible mechanism to explain our results is proposed in Scheme 4, based on the model we proposed for the racemic version of the reaction. The z-deprotonation of 10 gives the corresponding allylic anion, which adopts the endo-orientation assisted by Li-O coordination. The O-to-C silyl migration takes place irreversibly via two possible pentacoordinated silicate transition states or intermediates, TS-1 and TS-2. In this way, the configuration of the silicon center is retained without

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**Table 2: Scope of Electrophiles**

| Entry | Electrophiles | Product | Yield<sup>b</sup> |
|-------|---------------|---------|------------------|
| 1     | Et₃SiCl       | 4a (60%)|                  |
| 2     | Cl₃C       | 4b (R = H, 65%) |
| 3     | Br₂         | 4c (R = Br, 65%) |
| 4     | NO₂         | 4d (R = NO₂, 60%) |
| 5     | Cl          | 4e (67%) |
| 6     | Me          | 4f (50%) |
| 7     | Me          | 4g (66%) |
| 8     | Me          | 4h (R = Me, 50%) |
| 9     | Ph          | 4i (R = Ph, 55%) |
| 10    | Me          | 4j (R = Me, 70%) |
| 11    | Ph          | 4k (R = Ph, 70%) |
| 12    | Me<sup>d</sup> | 4l (40%) |

<sup>a</sup> Reaction conditions: 1f (0.15 mmol), s-BuLi (0.60 mmol), HMPA (0.6 mmol), 0.5 mL of THF, at −78 °C for 0.5 h, then electrophile at rt for 2 h. <sup>b</sup> Isolated yields. <sup>c</sup> Ratios were determined from crude ¹H NMR analysis of product. <sup>d</sup> 10.0 equiv. of MeI.

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**Scheme 3: Preparation of enantiomerically defined 10 and its retro-[1,4]-Brook rearrangement to form 11.**

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**Scheme 4: Plausible reaction mechanism.**
racermerization. While TS-2 suffers a severely steric repulsion between the Ph group on Si1 and one of the Ph groups on Si2, the interaction between the Me group on Si1 and the Ph group on Si2 appears being tolerable in the case of TS-1. These considerations are supported by the preliminary results from density functional theory calculations, which showed TS-1 to be more stable than TS-2 by 6.2 kJ mol⁻¹. Our model also explains the observed steric bias for substituents on Si2. Substituents smaller than the Ph group might not be large enough to create an appreciable difference between the non-bonded interaction with the Me group in TS-1 and with the Ph group in TS-2. As a result, 3 forms with poor diastereoselectivity (Table 1, entries 1–4).

Conclusions

In summary, Si-to-C chirality transfer has been used as an efficient strategy to achieve asymmetric retro-[1,4]-Brook rearrangement of 3-silyl allyloxysilanes. The SiMePhBu and SiPh3 groups, in which SiMePhBu migrates, function as the best combination to give geminal bis(silyl) aldehyde and enol derivatives with high diastereoselectivity. The silyl group migrates with retention of configuration. Enantioselective generation of the stereogenic carbon center suggests that Si-to-C chirality transfer is a promising method to construct optically pure chiral organosilanes. Further applications of this strategy are being explored in our group.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (a) J. L. Speier, *J. Am. Chem. Soc.*, 1952, 74, 1003; (b) R. West, R. Lowe, H. F. Stewart and A. Wright, *J. Am. Chem. Soc.*, 1971, 93, 282.

2 (a) M. Lautens, P. H. M. Delanghe, J. B. Goh and C. H. Zhang, *J. Org. Chem.*, 1992, 57, 3270; (b) C. Gibson, T. Buck, M. Noltemeyer and R. Brückner, *Tetrahedron Lett.*, 1997, 38, 2933; (c) T. N. Mitchell, M. Schütze and F. Gießelmann, *Synlett*, 1997, 183; (d) J. Bousbaa, F. Ooms and A. Krief, *Tetrahedron Lett.*, 1997, 38, 762; (e) C. Gibson, T. Buck, M. Walker and R. Brückner, *Synlett*, 1998, 201; (f) T. N. Mitchell and M. Schütze, *Tetrahedron*, 1999, 55, 1285; (g) B. M. Comanita, S. Woo and A. G. Fallis, *Tetrahedron Lett.*, 1999, 40, 5283; (h) M. R. Nahm, X. L. Hu, J. R. Potnick, C. M. Yates, P. S. White and J. S. Johnson, *Angew. Chem., Int. Ed.*, 2005, 44, 2377; (i) E. N. Onyeczoli and R. E. Maleczka, *Tetrahedron Lett.*, 2006, 47, 6565; (j) Y. Mori, Y. Futamura and K. Horisaki, *Angew. Chem., Int. Ed.*, 2008, 47, 1091; (k) J. A. Brekan, D. Chernyak, K. L. White and K. A. Scheidt, *Chem. Sci.*, 2012, 3, 1205; (l) Y. P. He, H. T. Hu, X. G. Xie and X. G. She, *Tetrahedron*, 2013, 69, 559; (m) Y. P. He, B. Ma, J. Yang, X. G. Xie and X. G. She, *Tetrahedron*, 2013, 69, 5545; (n) V. Bariak, A. Malastová, A. Almássy and R. Šebesta, *Chem.–Eur. J.*, 2015, 21, 13445; (o) Y. J. Kwon, Y. K. Jeon, H. B. Sim, I. Y. Oh, I. Shin and W. S. Kim, *Org. Lett.*, 2017, 19, 6224; (p) L. Biancalana, S. Zacchini, N. Ferri, M. G. Lupo, G. Pampaloni and F. Marchetti, *Dalton Trans.*, 2017, 46, 16589.

3 For reviews, see: (a) A. G. Brook, *Acc. Chem. Res.*, 1974, 7, 77; (b) P. C. Bulman-Page, S. S. Klair and S. Rosenthal, *Chem. Soc. Rev.*, 1990, 19, 147; (c) P. Jankowski, P. Raubo and J. Wicha, *Synlett*, 1994, 985; (d) M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, John Wiley and Sons, New York, 2000; (e) W. H. Moser, *Tetrahedron*, 2001, 57, 2065; (f) M. Kira and T. Iwamoto, *The Chemistry of Organic Silicon Compounds*, Z. Rappoport and Y. Apeloig, ed. John Wiley and Sons, New York, 2001, pp. 853–948; (g) E. Schaumann and A. Kirschning, *Synlett*, 2007, 177; (h) A. B. Smith and C. M. Adams, *Acc. Chem. Res.*, 2004, 37, 365; (i) H. J. Zhang, D. L. PriebeBenow and C. Bolm, *Chem. Soc. Rev.*, 2013, 42, 8540; (j) M. Sasaki and K. Takeda, *Molecular Rearrangements in Organic Synthesis*, ed. C. M. Rojas, John Wiley and Sons: New York, 2015, pp. 151–183; (k) G. Eppe, D. Didier and I. Marek, *Chem. Rev.*, 2015, 115, 9175.

4 A. Nakazaki, T. Nakai and K. Tomooka, *Angew. Chem., Int. Ed.*, 2006, 45, 2235.

5 For reviews of enantioselective generation of stereogenic silicon center, see: (a) M. Oestreich, *Synlett*, 2007, 1629; (b) L. W. Xu, L. Li, G. Q. Lai and J. X. Jiang, *Chem. Soc. Rev.*, 2011, 40, 1777; (c) L. W. Xu, *Angew. Chem., Int. Ed.*, 2012, 51, 12932; (d) Y. Wu, L. Gao and Z. L. Song, *Chem. Bull.*, 2015, 78, 676; (e) R. Shintani, *Asian J. Org. Chem.*, 2015, 4, 510; (f) J. O. Bauer and C. Strohmann, *Eur. J. Inorg. Chem.*, 2016, 2868; (g) Y. M. Cui, Y. Lin and L. W. Xu, *Coord. Chem. Rev.*, 2017, 330, 37. For selected progresses, see: (h) K. Igawa, J. Takada, T. Shimono and K. Tomooka, *J. Am. Chem. Soc.*, 2008, 130, 16132; (i) Y. Yasutomi, H. Suematsu and T. Katsuki, *J. Am. Chem. Soc.*, 2010, 132, 4510; (j) R. Shintani, H. Otomo, K. Ota and T. Hayashi, *J. Am. Chem. Soc.*, 2012, 134, 7305; (k) J. O. Bauer and C. Strohmann, *Angew. Chem., Int. Ed.*, 2014, 53, 720; (l) R. Shintani, C. Takagi, T. Ito, M. Naito and K. Nozaki, *Angew. Chem., Int. Ed.*, 2015, 54, 1616; (m) R. Shintani, R. Takano and K. Nozaki, *Chem. Sci.*, 2016, 7, 1205; (n) L. Chen, J. B. Huang, Z. Xu, Z. J. Zheng, K. F. Yang, Y. M. Cui, J. Cao and L. W. Xu, *RSC Adv.*, 2016, 6, 67113; (o) K. Igawa, D. Yoshihiro, Y. Abe and K. Tomooka, *Angew. Chem., Int. Ed.*, 2016, 55, 5814; (p) Q. W. Zhang, K. An, L. C. Liu, Q. Zhang, H. F. Guo and W. He, *Angew. Chem., Int. Ed.*, 2017, 56, 1125; (q) X. F. Bai, J. F. Zou, M. Y. Chen, Z. Xu, L. Li, Y. M. Cui, Z. J. Zheng and L. W. Xu, *Chem.–Asian J.*, 2017, 12, 1730; (r) Y. Sato, C. Takagi, R. Shintani and K. Nozaki, *Angew. Chem., Int. Ed.*, 2017, 56, 9211; (s) G. Zhan, H. L. Teng, Y. Luo, S. J. Lou, M. Nishiura and
Z. M. Hou, Angew. Chem., Int. Ed., 2018, 57, 12342; (t) H. Chen, Y. Chen, X. X. Tang, S. F. Liu, R. P. Wang, T. B. Hu, L. Gao and Z. L. Song, Angew. Chem., Int. Ed., 2019, 58, 4695.

6 M. Oestreich, Chem.–Eur. J., 2006, 12, 30.

7 (a) M. Oestreich and S. Rendler, Angew. Chem., Int. Ed., 2005, 44, 1661; (b) S. Rendler and M. Oestreich, Beilstein J. Org. Chem., 2007, 3, 9.

8 D. R. Schmidt, S. J. O’Malley and J. L. Leighton, J. Am. Chem. Soc., 2003, 125, 1190.

9 (a) Q. Luo, C. Wang, Y. X. Li, K. B. Ouyang, L. Gu, M. Uchiyama and Z. F. Xi, Chem. Sci., 2011, 2, 2271; (b) H. Li, L. T. Liu, Z. T. Wang, F. Zhao, S. G. Zhang, W. X. Zhang and Z. F. Xi, Chem.–Eur. J., 2011, 17, 7399; (c) K. Groll, S. M. Manolikakes, X. M. du Jourdin, M. Jaric, A. Bredikhin, K. Karaghiosoff, T. Carell and P. Knochel, Angew. Chem., Int. Ed., 2013, 52, 6776; (d) H. Y. Cui, J. Y. Zhang and C. M. Cui, Organometallics, 2013, 32, 1; (e) S. T. Ding, L. J. Song, L. W. Chung, X. H. Zhang, J. W. Sun and Y. D. Wu, J. Am. Chem. Soc., 2013, 135, 13835; (f) V. Werner, T. Klatt, M. Fujii, J. Markiewicz, Y. Apeloig and P. Knochel, Chem.–Eur. J., 2014, 20, 8338; (g) R. Shintani, H. Kurata and K. Nozaki, Chem. Commun., 2015, 51, 11378; (h) Z. X. Liu, H. C. Tan, T. R. Fu, Y. Xia, D. Qiu, Y. Zhang and J. B. Wang, J. Am. Chem. Soc., 2015, 137, 12800; (i) Z. J. Liu, X. L. Lin, N. Yang, Z. S. Su, C. W. Hu, P. H. Xiao, Y. Y. He and Z. L. Song, J. Am. Chem. Soc., 2016, 138, 1877; (j) T. Kosai, S. Ishida and T. Iwamoto, Angew. Chem., Int. Ed., 2016, 55, 15554; (k) M. Das, A. Manvar, M. Jacolot, M. Blangetti, R. C. Jones and D. F. O’Shea, Chem.–Eur. J., 2015, 21, 8737; (l) M. Das and D. F. O’Shea, Org. Lett., 2016, 18, 336; (m) Y. Mizuhata, S. Fujimori, T. Sasamori and N. Tokitoh, Angew. Chem., Int. Ed., 2017, 56, 4588; (n) H. Kinoshiba, A. Ueda, H. Fukumoto and K. Miura, Org. Lett., 2017, 19, 882; (o) Y. B. Zhang, Q. Y. Guo, X. W. Sun, J. Lu, Y. J. Cao, Q. Pu, Z. W. Chu, L. Gao and Z. L. Song, Angew. Chem., Int. Ed., 2018, 57, 942; (p) H. Hazrati and M. Oestreich, Org. Lett., 2018, 20, 5367; (q) S. Xu, R. Chen, Z. H. Fu, Y. P. Gao and J. B. Wang, J. Org. Chem., 2018, 83, 6186; (r) M. H. Yang, J. Lian, W. Sun, T. Z. Qiao and S. F. Zhu, J. Am. Chem. Soc., 2019, 141, 4579; (s) J. Guo, H. L. Wang, S. P. Xing, X. Hong and Z. Lu, Chem, 2019, 5, 881.

10 (a) Z. W. Chu, K. Wang, L. Gao and Z. L. Song, Chem. Commun., 2017, 53, 3078; (b) Y. Chu, Q. Pu, Z. X. Tang, L. Gao and Z. L. Song, Tetrahedron, 2017, 73, 3707.

11 Z. L. Song, Z. Lei, L. Gao, X. Wu and L. J. Li, Org. Lett., 2010, 12, 5298.

12 CCDC 1901967 [4d] contains the supplementary crystallographic data for this paper.†

13 (a) S. Rendler, M. Oestreich, C. P. Butts and G. C. Lloyd-Jones, J. Am. Chem. Soc., 2007, 129, 502; (b) S. Rendler and M. Oestreich, Angew. Chem., Int. Ed., 2008, 47, 5997; (c) K. Igawa, D. Yoshihiro, N. Ichikawa, N. Kokan and K. Tomooka, Angew. Chem., Int. Ed., 2012, 51, 12745; (d) T. T. Metsänen, P. Hrabaník and M. Oestreich, J. Am. Chem. Soc., 2014, 136, 6912; (e) T. Fallon and M. Oestreich, Angew. Chem., Int. Ed., 2015, 54, 12488.

14 V. T. Trepöhl, R. Fröhlich and M. Oestreich, Tetrahedron, 2009, 65, 6510.

15 Reduction of (R)-10 with DIBAL-H giving (S)-7 in 81% yield. This result supports that the configuration of the silicon center in 10 should be R. See ESI† for details.

16 CCDC 1901968 [11] contains the supplementary crystallographic data for this paper.†

17 (a) W. C. Still and T. L. Macdonald, J. Am. Chem. Soc., 1974, 96, 5561; (b) M. Schlosser and S. Strunk, Tetrahedron, 1989, 45, 2649; (c) A. R. Katritzky, M. Piffel, H. Lang and E. Anders, Chem. Rev., 1999, 99, 665.

18 (a) A. Wright and R. West, J. Am. Chem. Soc., 1974, 96, 3227; (b) T. Kawashima, K. Naganuma and R. Okazaki, Organometallics, 1998, 17, 367; (c) K. Naganuma, T. Kawashima and R. Okazaki, Chem. Lett., 1999, 1139; (d) T. Kawashima, J. Organomet. Chem., 2000, 611, 256; (e) T. Kawashima, Bull. Chem. Soc. Jpn., 2003, 76, 471; (f) E. P. A. Couzijn, M. Schakel, F. J. J. de Kanter, A. W. Ehlers, M. Lutz, A. L. Spek and K. Lammertsma, Angew. Chem., Int. Ed., 2004, 43, 3440; (g) Q. Liu, Y. Chen, X. Zhang, K. N. Houk, Y. Liang and A. B. Smith, J. Am. Chem. Soc., 2017, 139, 8710.