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Al Lewis acid-catalyzed regiodivergent 1,2-rearrangement of α-siloxy aldehydes: scope and mechanism

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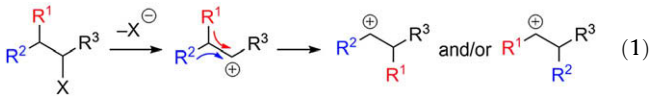
ABSTRACT

Regiodivergent 1,2-rearrangement of α-siloxy aldehydes bearing α-aryl and α-alkyl substituents into α-siloxy ketones has been realized by using different Al Lewis acid catalyst/solvent systems. The scope of this unprecedented protocol has been investigated with various substrates, clearly demonstrating its utility for the selective synthesis of two structural isomers from one substrate. Controlled experiments proved that the regiodivergency resulted from the switch of the migrating group.

1. Introduction

1,2-Rearrangements, represented by pinacol[1] and Wagner–Meerwein[2] rearrangements, are classical yet powerful tools for the structural reorganization of organic molecules through the consecutive or concurrent cleavage and formation of carbon-carbon bonds,[3] often making it feasible to construct otherwise hard-to-access molecular frameworks with simplicity and high level of atom economy.[4] Inducing regiochemistry in such processes, however, leads to a formidable problem in that it requires the control of migrating group (Eq. (1)).



(1)

A common approach to this problem is the design of substrates based on the relative migratory aptitude of substituents,[5] and/or conformational effect,[6] which often establishes selective transformation leading to the most favorable isomers. Nevertheless, this strategy requires the preparatory installation of all the structural features that will drive the rearrangement in the desired direction, and in principle the obtainable product is restricted to only one. In contrast, intentional control of the migratory tendency for the selective synthesis of any isomers from one substrate is attractive yet challenging objective.

In various 1,2-rearrangement, the relative migratory tendency of aryl>alkyl is generally accepted. For instance, phenyl group is well known to have an excellent migrating ability in pinacol and Wagner–Meerwein rearrangement. This large migratory aptitude of aryl group is usually accounted for by participation of π-orbitals delocalizing the developing charge of the carbonium ion into the aromatic ring.[5d,e,7] The stability of the transition states in 1,2-rearrangement, however, depends not only on the activity of the migrating group but also on the steric and/or electronic effects of the non-migrating group.[7] Therefore, the ability of aryl group to conjugatively stabilize a neighboring cation could sometimes cause inverse aptitude to prevail.[8] Indeed, in our previous research on the enantioselective 1,2-rearrangement of differently α,α-disubstituted α-siloxy aldehydes,[9] the reaction of **1a** predominantly afforded siloxy ketone **2a** (Scheme 1), which was interpretable as the result of selective migration of benzyl group over phenyl despite higher migrating ability of phenyl group. In consideration of such a contradiction, we have been interested in the possibility of developing the regiodivergent 1,2-rearrangement via intentional control of migrating group, i.e., switch of migratory tendency.[10,11] Reported herein are the study on the realization of regiodivergency in 1,2-rearrangement of α-siloxy aldehydes and the detailed mechanistic investigations.

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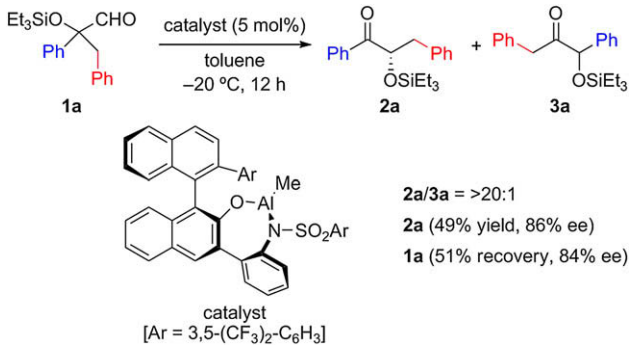


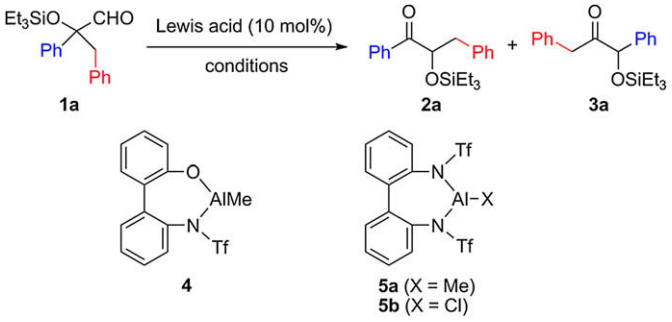
Scheme 1. Kinetic resolution of differently α,α-disubstituted α-siloxy aldehyde.

2. Results and discussion

2.1. Development of regiodivergent 1,2-rearrangement of α-siloxy aldehydes

To examine whether the degree of regioselectivity was dependent only on the structural features of substrate, we initiated our investigation by performing the reaction of α-siloxy aldehydes **1a** with various Al catalysts. Although one of the most conventional Al Lewis acids, Me_2AlCl, promoted the predominant transformation of **1a** to **2a** in toluene at 0 °C, the use of biphenyl-based Al catalyst **4**[12] was found to provide a mixture of two regioisomers, **2a** and **3a**, in a ratio of 5:1 (entries 1 and 2, Table 1). Encouraged by this interesting result, we conducted further examination by using other Al Lewis acids. Switching the catalyst from **4** to comparatively strong Lewis acid **5a**[13] resulted in reducing the proportion of **2a** (entry 3). Moreover, the product distribution was reversed in the reaction under the influence of **5b** with ever higher Lewis acidity (entry 4), which implied that stronger Lewis acid might lead to increase in the ratio of **3a** in the present rearrangement. Although it was assumed that the selectivity was influenced mainly by the steric size of the catalyst rather than its Lewis acidity, this possibility was ruled out by the distinct difference of the regioselectivity between the reactions with methylaluminum bis(2,6-di-*tert*-butyl-4-bromophenoxide) (MABR)[14] and structurally similar, but less Lewis acidic methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)[15,16] (entries 5 and 6). Subsequently, we tuned the reaction parameters for enhancing the preference toward the formation of **3a**. To our delight, use of dichloromethane as a solvent instead of toluene led to improvement of the selectivity (entry 7 vs 4) and **3a** was eventually isolated as a sole product by lowering the reaction temperature to –20 °C (entry 8).

Table 1
1,2-Rearrangement of α-siloxy aldehydes **1a** with several Lewis acids



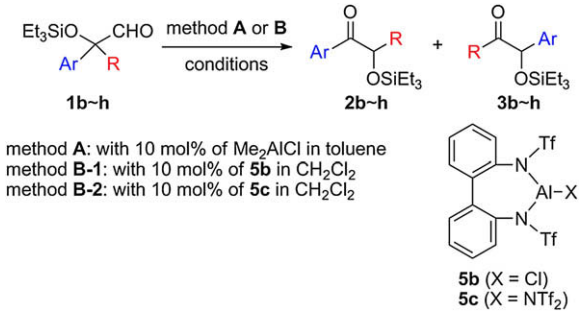
Entry[a]	Lewis acid	Conditions (solvent, °C)	Yield[b] (%)	**2a**/**3a**[c]
1	Me_2AlCl	Toluene, 0	91	>20:1
2	**4**	Toluene, 0	71	5:1
3	**5a**	Toluene, 0	99	3:1
4	**5b**	Toluene, 0	99	1:1.5
5	MABR	Toluene, 0	45	1:1
6	MAD	Toluene, 0	35	5:1
7	**5b**	CH_2Cl_2, 0	99	1:4
8	**5b**	CH_2Cl_2, −20	99	1:>20

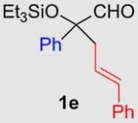
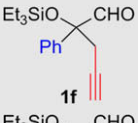
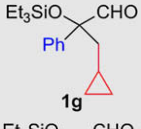
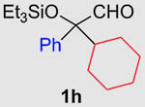
[a] The reaction was carried out with 10 mol% of Lewis acid under the given reaction conditions.
[b] Isolated as a mixture of **2a** and **3a**.
[c] Determined by ^1H NMR analysis.

2.2. Substrate scope

With the protocol for switching the regioselectivity in hand, subsequent experiments were conducted to probe the substrate scope of this unprecedented regiodivergent 1,2-rearrangement (Table 2). In the reactions of α-triethylsiloxy aldehydes bearing

Table 2
Substrate scope



Entry[a]	Substrate	Method	Temp.	Yield[b]	**2**/**3**[c]
1	 **1b**	**A**	0 °C	91	10:1
2		**B-1**	−20 °C	99	1:>20
3	 **1c**	**A**	0 °C	93	>20:1
4		**B-1**	−20 °C	64	1:5
5		**B-2**	−40 °C	98	1:>20
6	 **1d**	**A**	0 °C	61	>20:1
7		**B-1**	−20 °C	71	1:>20
8	 **1e**	**A**	0 °C	99	>20:1
9		**B-1**	−20 °C	99	1:3
10		**B-2**	−50 °C	63	1:>20
11	 **1f**	**A**	rt.	60	>20:1
12[d]		**B-1**	−20 °C	76	1:>20
13	 **1g**	**A**	0 °C	97	11:1
14		**B-1**	−20 °C	99	1:>20
15	 **1h**	**A**	rt.	81	3:1
16		**B-1**	−20 °C	73	1:>20

[a] The reaction was carried out with 10 mol% of Lewis acid under the given reaction conditions.
[b] Isolated as a mixture of **2** and **3**.
[c] Determined by ^1H NMR analysis.
[d] The rearranged product **3f** immediately isomerized to the corresponding allenyl ketone.

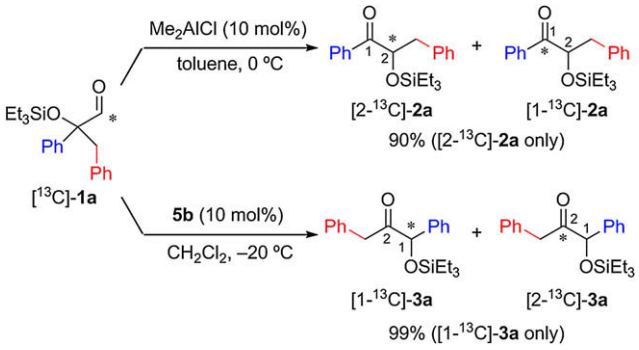
benzyl and various aryl substitutents **1b–d**, the catalytic Me_2AlCl system in toluene (method **A**) was uniformly effective, and α-siloxy ketones **2** were obtained with good to excellent selectivities (entries 1, 3 and 6). In contrast, the reactions with Al catalyst **5b** in CH_2Cl_2 (method **B-1**) proceeded with opposite sense of regioselectivities, leading to the preferential formation of siloxy ketones **3** (entries 2, 4 and 7). Whereas the rearrangement of **1c** with an electron-deficient aryl group exhibited only moderate selectivity under the influence of **5b**, complete selectivity for **3** was achieved with **5c** in CH_2Cl_2 (method **B-2**) at lower temperature (entry 4 vs 5). By the appropriate choice of the method (i.e., method **A**: with Me_2AlCl in toluene, method **B-1**: with **5b** in CH_2Cl_2 and method **B-2**: with **5c** in CH_2Cl_2), the reversals of regioselectivity were also observed in the reactions of phenyl- and various alkyl-substituted α-siloxy aldehydes **1e–h** (entries 8–16). These substrates were also tolerated to afford siloxy ketones **2** with moderate to high selectivities by using method **A** (entries 8, 11, 13 and 15). Although method **B-2** proved to be superior for the selective formation of siloxy ketones **3**, the complicated procedure for the preparation of **5c** led us to employ it only when unsatisfactory results were obtained with **5b**. For instance, the selectivity in the transformation of **1e** having phenyl and allylic substituents to the corresponding siloxy ketone **3** was greatly improved by changing the method from **B-1** to **B-2** (entry 9 vs 10). On the other hand, the use of method **B-1** was sufficient for exclusive production of **3** in the rearrangement of phenyl- and propargyl-, phenyl- and cyclopropylmethyl-, or phenyl- and cyclohexyl-substituted substrates **1f–h** (entries 12, 14 and 16).

2.3. Mechanistic investigation

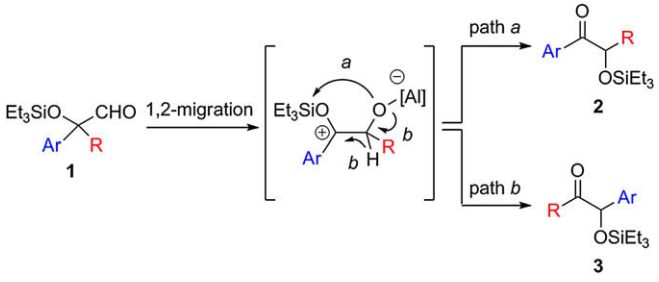
2.3.1. Interrogating the 1,2-hydride shift

The catalytic cycle of 1,2-rearrangement of α-siloxy aldehyde **1** to α-siloxy ketones **2** or **3** would be initiated by the activation of aldehyde via the coordination of Lewis acid, which promotes the nucleophilic migration of α-substituent. Following this initial migration, two mechanistic rationales are conceivable for quenching the remaining cation; one is intra- or intermolecular transfer of the silyl group (path a, Scheme 2) and the other is a 1,2-hydride migration (path b).

In order to clarify whether silyl group transfer or 1,2-hydride migration is involved in quenching the zwitterionic intermediate, the reactions were performed using ^{13}C (C*) labeled substrate [^{13}C]-**1a** (Scheme 3). When aldehyde [^{13}C]-**1a** was treated with 10 mol % of Me_2AlCl in toluene at 0 °C (method **A**), siloxy ketone [2-^{13}C]-**2a** was obtained as a sole product, and the isomer [1-^{13}C]-**2a** was not detected by either ^1H or ^{13}C NMR spectroscopy. Further, upon treatment with **5b** in CH_2Cl_2 at –20 °C (method **B-1**), [^{13}C]-**1a** underwent selective transformation to a product [1-^{13}C]-**3a**, in which ^{13}C was incorporated at the carbon bearing ethereal oxygen. If the 1,2-hydride shift had occurred, the isomers [1-^{13}C]-**2a** and [2-^{13}C]-**3a** incorporating ^{13}C at the carbonyl carbon would have been produced. Thus, these results unequivocally confirmed that the rearrangement exclusively proceeded via silyl transfer process, and the realization of the regiodivergent synthesis of siloxy ketones **2** and **3** essentially stemmed from the switch of the migrating group.



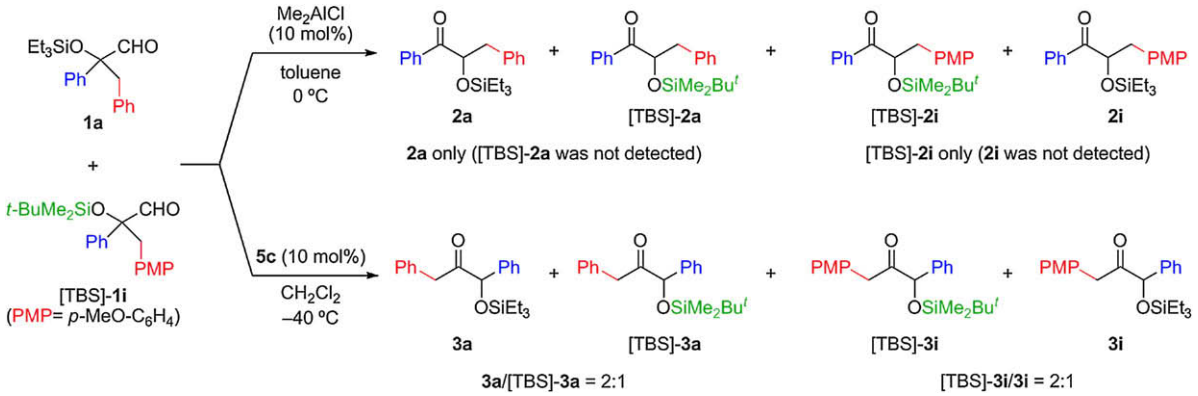
Scheme 3. 1,2-Rearrangement of the ^{13}C-labeled substrate [^{13}C]-**2a**.



Scheme 2. The two possible reaction pathways.

2.3.2. Silyl group transfer pathway

To gain insight into the silyl group transfer, we performed crossover experiments with two siloxy aldehydes, **1a** and [TBS]-**1i**, which were differentiated in the identity of both silyl groups and α-alkyl substituents (Scheme 4). When an equimolar mixture of **1a** and [TBS]-**1i** was treated with 10 mol % of Me_2AlCl in toluene, **2a** and [TBS]-**2i** were obtained in a ratio of 1:1, and neither [TBS]-**2a** nor **2i** was detected by ^1H NMR spectroscopy, revealing that the silyl transfer process takes place intramolecularly. On the other hand, the distribution of silyl groups was observed under the influence of **5c** in dichloromethane,[17] affording a mixture of **3a**, [TBS]-



Scheme 4. Test for the silyl transfer pathway.

3a, [TBS]-**3i** and **3i**. Additional control experiments showed that neither the silyl group of siloxy aldehydes **1a** and [TBS]-**1i** nor that of siloxy ketones **3a** and [TBS]-**3i** was exchanged under similar conditions. These experimental results suggested the involvement of the intermolecular silyl group transfer process. One of the two possible pathways is the intermolecular silyl shift between the zwitterionic intermediates, and the other is the siloxocarbenium ion-promoted 1,2-rearrangement. In the reaction with method **B-2**, the strong coordination of oxygen anion to the highly Lewis acidic Al of **5c** in the intermediate might diminish the nucleophilicity of the alkoxy moiety, and hence both the intra- and intermolecular silyl shift would be suppressed, allowing the generation of highly active siloxocarbenium ion. This cationic silyl species could promote the subsequent rearrangement as a Lewis acid (Fig. 1),[18] from which the distribution of silyl groups might result.

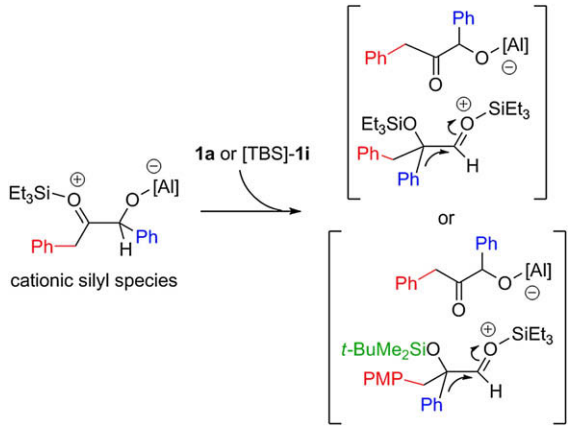
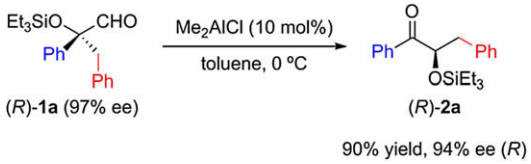


Figure 1. 1,2-Rerarrangement promoted by the siloxocarbenium ion.

2.3.3. *Conformation in transition states*

Finally, to elucidate the preferred conformation of transition states, stereospecific 1,2-rearrangement of optically active α-siloxy aldehyde was tested. Thus, (*R*)-**1a** (97% ee) was treated with 10 mol % of Me_2AlCl in toluene at 0 °C for 24 h, and the rearranged **2a** was isolated in 90% yield with 94% ee (Scheme 5). Its absolute configuration was established as *R* by comparison of the optical rotation with a reported value after desilylation,[9,19] which suggested that the benzyl group migration via '*siloxy*-eclipsed conformation' is operative almost exclusively (Fig. 2). As a result of the selective benzyl shift in such a manner, the zwitterionic intermediate with the alkoxy moiety disposed at *syn* position to the siloxy group would be generated, thereby undergoing the facile intramolecular silyl shift.



Scheme 5. 1,2-Rearrangement of optically active substrate.

Next, we examined the rearrangement of (*R*)-**1a** with method **B-1** and found that the 1,2-migration of phenyl group was concomitant with a significant decrease in ee, resulting in a maximum value of 75% (Scheme 6).

The absolute configuration of the resulting **3a** was determined to be *R* by comparison of the optical rotation with a known literature value[20] after derivatization. This result indicated that, in contrast to the case with method **A**, phenyl migration preferably proceeds via '*benzyl*-eclipsed' conformation. Such 1,2-shift of phenyl

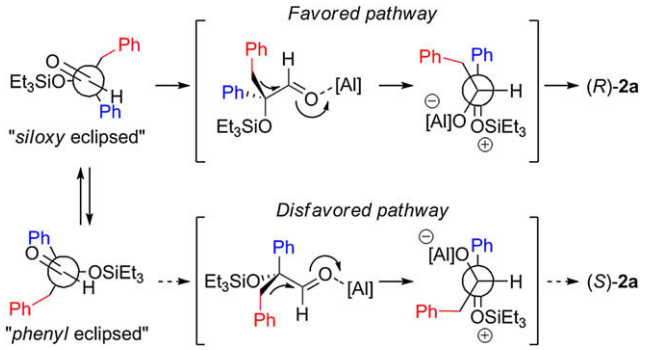
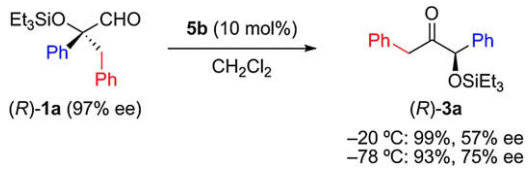


Figure 2. Plausible transition state of 1,2-benzyl migration.



Scheme 6. 1,2-Rearrangement of optically active substrate with **5b**.

group would generate the intermediary zwitterions as shown in Figure 3, in which the alkoxy functionality is aligned at *anti* position to the siloxy group. From this disposition, the intramolecular silyl shift is apparently unfavorable, leading to either the intermolecular silyl shift or the generation of siloxocarbenium ion intermediate.

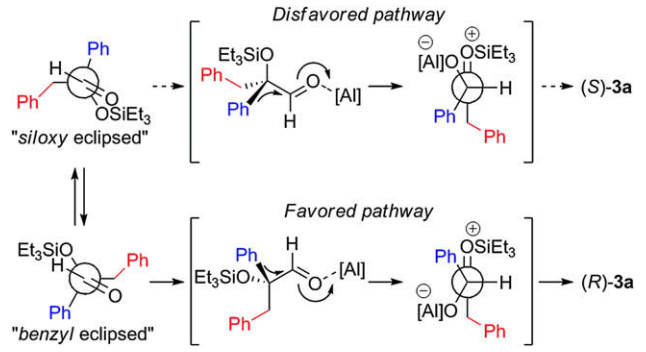


Figure 3. Plausible transition state of 1,2-phenyl migration.

In summary, a complete switch of migratory aptitude in 1,2-rearrangement of differently α,α-disubstituted α-siloxy aldehydes has been realized by using different Al catalysts and conditions, and we have successfully demonstrated that the methods to rigorously control the group migration could be applied to various substrates. The reaction pathways of the 1,2-rearrangements were proposed based on the detailed mechanistic studies. These investigations should pave the way for the development of a new protocol for the selective preparation of any structural isomers from one substrate by switching the migratory tendency in the skeletal rearrangement.

3. Experimental procedures

3.1. General

Infrared (IR) Spectra were recorded on a Shimadzu FT-IR. ^1H and ^{13}C NMR spectra were measured on JEOL JNM-FX400 (400 MHz) and JEOL AL-400 (400 MHz) spectrometers. Chemical shifts of ^1H NMR spectra were reported in ppm relative to tetramethylsilane (δ 0). Chemical shifts of ^{13}C NMR spectra were reported in ppm

relative to the residual solvent (chloroform, δ 77.07). Analytical high performance liquid chromatography (HPLC) was performed on a Shimadzu LC-10AT instrument equipped with a column of Daicel Chiralcel OD-H and OJ-H. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. The high-resolution mass spectra (HRMS) were measured on an BRUKER DALTONICS micro-TOF focus-KR spectrometer. Analytical thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) throughout this work. Flash column chromatography was performed on silica gel 60 (Merck 1.09386.9025, 230–400 mesh). EYELA PSL-1400 and EYELA PSL-1800 constant temperature baths were used for low temperature 1,2-rearrangement reactions.

All air- and moisture-sensitive reactions were performed under an atmosphere of argon in flame-dried, round bottom flasks fitted with rubber septa. The manipulations for Al-catalyzed 1,2-rearrangements were carried out with standard Schlenk techniques under nitrogen. In experiments requiring dry solvent, toluene and CH_2Cl_2 were purified by both A2 alumina and Q5 reactant using a GlassContour solvent dispensing system. Tetrahydrofuran (THF) was purchased from Kanto Chemical Co., Ltd. as 'dehydrated'. Me_3Al and Me_2AlCl were kindly supplied from Tosoh-Finechem Co., Ltd., Japan. Other simple chemicals were purchased and used as such.

3.2. Preparation of α-siloxy aldehyde 1a

3.2.1. 2-Phenyl-2-(triethylsiloxy)acetonitrile

To a solution of benzaldehyde (1.0 mL, 10 mmol) and triethylsilylcyanide (1.4 g, 10 mmol) in CH_2Cl_2 (30 mL) was added iodine (253.8 mg, 1.0 mmol) at 0 °C under argon. After stirring for 1 h, the reaction mixture was quenched with satd Na_2SO_3 and extractive workup was conducted with EtOAc. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration, the resulting liquid was used for next step without any purification. ^{1}NMR of the title compound (400 MHz, $CDCl_3$) δ 7.47–7.49 (2H, m, Ph-H), 7.38–7.44 (3H, m, Ph-H), 5.51 (1H, s, CHCN), 0.98 (9H, t, J=8.0 Hz, CH_3CH_2Si), 0.67–0.74 (6H, m CH_3CH_2Si).

3.2.2. 2,3-Diphenyl-2-(triethylsiloxy)propanenitrile

To a solution of diisopropylamine (1.7 mL, 12 mmol) in THF (10 mL) was added a 1.5 M hexane solution of *n*-BuLi (8.0 mL, 12 mmol) at −78 °C under argon, and the mixture was stirred for 15 min. A solution of crude 2-phenyl-2-(triethylsiloxy)acetonitrile in THF (10 mL) was transferred into this mixture at the same temperature and the resulting mixture was kept for 30 min. After addition of benzyl bromide (1.4 mL, 12 mmol), the whole reaction mixture was stirred for additional 1 h at −78 °C. Then, the solution was poured into water and extracted with EtOAc. The organic extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of solvents and drying under vacuum, the resulting crude oil was used for next step without any purification. ^{1}NMR of the title compound (400 MHz, $CDCl_3$) δ 7.44–7.47 (2H, m, Ph-H), 7.33–7.37 (3H, m, Ph-H), 7.23–7.25 (3H, m, Ph-H), 7.09–7.11 (2H, m, Ph-H), 3.24 (1H, d, J=13.6 Hz, $PhCH_2$), 3.12 (1H, d, J=13.6 Hz, $PhCH_2$), 0.81 (9H, t, J=8.0 Hz, CH_3CH_2Si), 0.45–0.62 (6H, m, CH_3CH_2Si).

3.2.3. 2,3-Diphenyl-2-(triethylsiloxy)propanal ***1a***

To a solution of crude 2,3-diphenyl-2-(triethylsiloxy)propanenitrile in CH_2Cl_2 (20 mL) under argon was introduced a 1 M toluene solution of DIBAH (20 mL, 20 mmol) at −78 °C, and the reaction mixture was stirred for 1 h at the same temperature. Then, the mixture was quenched with 1 N HCl and extracted with ether. The organic extracts were washed with brine and dried over anhydrous Na_2SO_4, and concentrated. The residual oil was purified by column chromatography on silica gel (CH_2Cl_2/hexane=1:4 as eluant) to give the title compound (2.8 g, 8.2 mmol, 82% yield for three steps) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (1H, s, CHO), 7.26–7.33 (5H, m, Ph-H), 7.12–7.14 (3H, m, Ph-H), 6.95–6.98 (2H, m, Ph-H), 3.32 (1H, d, J=14.2 Hz, $PhCH_2$), 3.25 (1H, d, J=14.2 Hz, $PhCH_2$), 0.89 (9H, t, J=8.0 Hz, CH_3CH_2Si), 0.58 (6H, q, J=8.0 Hz, CH_3CH_2Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 139.4, 135.4, 130.7, 128.2, 127.6, 127.5, 126.3, 126.0, 85.1, 44.9, 7.0, 6.8; IR (neat) 2954, 2937, 2910, 2875, 2808, 1734, 1496, 1454, 1242, 1143, 1076, 1008, 956, 761, 729, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{21}H_{28}NaO_2Si$ ($[M+Na]^+$): 363.1751. Found: 363.1762.

α-Siloxy aldehydes **1b**,[11] **1c**,[9] **1d**,[11] **1e**,[9] and **1f**–**h**[11] showed the identical spectra according to the literature.

3.3. General procedure for 1,2-rearrangement of α,α-disubstituted α-siloxy aldehydes

3.3.1. With dimethylaluminum chloride

To a solution of **1a** (170.3 mg, 0.5 mmol) in toluene (5.0 mL) was added a 1 M toluene solution of Me_2AlCl (50 μL, 0.05 mmol) at 0 °C under nitrogen. After stirring for 24 h, sodium fluoride (8.4 mg, 0.2 mmol) and water (2.7 μL, 0.15 mmol) were added and the whole mixture was stirred for 30 min at room temperature. To remove precipitates, filtration through Celite with EtOAc was carried out. Concentration of the filtrate and purification by column chromatography on silica gel (CH_2Cl_2/hexane=1:4 as eluant) afforded a mixture of **2a** and **3a** (154.9 mg, 0.455 mmol, 91% yield, **2**/**3**=>20:1) as colorless oil. **2a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.07 (2H, m, Ph-H), 7.56 (1H, t, J=7.6 Hz, Ph-H), 7.45 (2H, t, J=7.6 Hz, Ph-H), 7.21–7.29 (5H, m, Ph-H), 4.95 (1H, dd, J=9.0, 4.0 Hz, SiOCH), 3.10 (1H, dd, J=13.6, 4.0 Hz, $PhCH_2$), 3.00 (1H, dd, J=13.6, 9.0 Hz, $PhCH_2$), 0.75 (9H, t, J=8.0 Hz, CH_3CH_2Si), 0.39 (6H, q, J=8.0 Hz, CH_3CH_2Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 137.5, 134.9, 133.0, 129.6, 129.1, 128.3, 128.1, 126.5, 78.6, 42.2, 6.4, 4.4; IR (neat) 2954, 2910, 2875, 1697, 1680, 1454, 1278, 1240, 1109, 1004, 771, 744, 731, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{21}H_{28}NaO_2Si$ ($[M+Na]^+$): 363.1751. Found: 363.1749.

3.3.2. With Al catalyst ***5b***

To a solution of 2,2′-bis(trifluoromethanesulfonylamino)-1,1′-biphenyl (24.6 mg, 0.055 mmol) in CH_2Cl_2 (5.0 mL) was added a 1 M toluene solution of Me_2AlCl (50 μL, 0.05 mmol) was added at room temperature under positive nitrogen pressure and the resulting mixture was kept for 30 min with stirring. Then, this solution was cooled to −20 °C, and **1a** (170.3 mg, 0.5 mmol) was introduced into it. After stirring for 12 h at the same temperature, sodium fluoride (8.4 mg, 0.2 mmol) and water (2.7 μL, 0.15 mmol) were added and the whole mixture was stirred for 30 min at room temperature. To remove precipitates, filtration through Celite with EtOAc was carried out. Concentration of the filtrate and purification by column chromatography on silica gel (Et_2O/hexane=1:10 as eluant) afforded a mixture of **2a** and **3a** (169.9 mg, 0.5 mmol, 99% yield, **2**/**3**=1:>20) as colorless oil. **3a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, J=7.0 Hz, Ph-H), 7.18–7.36 (6H, m, Ph-H), 7.01 (2H, d, J=7.0 Hz, Ph-H), 5.18 (1H, s, SiOC*H*), 3.90 (1H, d, J=16.6 Hz, $PhCH_2$), 3.72 (1H, d, J=16.6 Hz, $PhCH_2$), 0.91 (9H, t, J=8.0 Hz, CH_3CH_2Si), 0.59 (6H, q, J=8.0 Hz, CH_3CH_2Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.3, 138.4, 134.1, 129.6, 128.4, 128.2, 128.0, 126.6, 125.9, 80.7, 42.6, 6.6, 4.6; IR (neat) 2954, 2937, 2910, 2875, 1726, 1494, 1452, 1413, 1240, 1188, 1130, 1095, 1068, 1004, 864, 727, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{21}H_{28}NaO_2Si$ ($[M+Na]^+$): 363.1750. Found: 363.1755.

3.3.3. With Al catalyst ***5c***

An oven-dried Schlenk tube equipped with direct light excluded was charged with $AgNTf_2$ (19.4 mg, 0.05 mmol) and CH_2Cl_2

(3.0 mL). A 1 M toluene solution of Me_2AlCl (50 μL, 0.05 mmol) was added under nitrogen and the resulting mixture was stirred at room temperature for 12 h. To this mixture was added a solution of 2,2′-bis(trifluoromethanesulfonylamino)-1,1′-biphenyl (24.6 mg, 0.055 mmol) in CH_2Cl_2 (1.0 mL) and stirred for another 1 h. After being cooled to −40 °C, a solution of **1c** (179.3 mg, 0.5 mmol) in CH_2Cl_2 (1.0 mL) was transferred into this mixture and the stirring was maintained at −40 °C for 24 h. Then, the reaction mixture was quenched with 1 N HCl and extracted with EtOAc. The organic extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation, the residual oil was purified by column chromatography on silica gel (CH_2Cl_2/hexane=1:4 as eluant) to afford a mixture of **2c** and **3c** (175.9 mg, 0.49 mmol, 98% yield, **2**/**3**=1:>20) as colorless oil. **3c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.41 (2H, m, Ar-H), 7.19–7.26 (3H, m, Ar-H), 7.00–7.05 (4H, m, Ar-H), 5.15 (1H, s, SiOC*H*), 3.88 (1H, d, *J*=16.2 Hz, $PhCH_2$), 3.74 (1H, d, *J*=16.2 Hz, $PhCH_2$), 0.91 (9H, t, *J*=8.0 Hz, CH_3CH_2Si), 0.59 (6H, q, *J*=8.0 Hz, CH_3CH_2Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.3, 162.6 (d, J_{C-F}=247 Hz), 134.3 (d, J_{C-F}=2.5 Hz), 133.9, 129.5, 128.3, 127.6 (d, J_{C-F}=8.2 Hz), 126.6, 115.4 (d, J_{C-F}=22.2 Hz), 80.0, 42.7, 6.6, 4.6; IR (neat) 2956, 2877, 1726, 1506, 1222, 1085, 1014, 862, 819, 731, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{21}H_{27}FNaO_2Si$ ([M+Na]$^+$): 381.1656. Found: 381.1653.

Compounds **2b**,[11] **2c**,[9] **2d**,[11] **2e**,[9] **2f**–**2h**,[11] **3b**[11] and **3d**–**3h**[11] showed the identical spectra according to the literature.

3.4. Synthesis of ^{13}C labeled substrate

Benzaldehyde (510 μL, 5.0 mmol) was slowly added to a stirred solution of sodium hydrogensulfite (58% assay, mixture of $NaHSO_3$ and $Na_2S_2O_5$, 1.8 g, 10 mmol) in distilled water (3.0 mL) at room temperature to afford a white precipitate. The mixture was allowed to stir for 2 h once addition was complete, at which point the mixture was cooled to 0 °C and a solution of potassium cyanide-^{13}C (>99.5 atom % ^{13}C, 650 mg, 10 mmol) in water (2.0 mL) was added. After being warmed up to room temperature, this mixture was stirred for additional 2 h, and the precipitate gradually disappeared. The reaction mixture was extracted with ether and the ethereal extracts were washed with brine and then dried over Na_2SO_4. After filtration and evaporation, further drying of residue in vacuo was conducted. To a solution of this crude compound and *N*,*N*-diisopropylethylamine (1.0 mL, 6.0 mmol) in CH_2Cl_2 (15 mL) was added triethylsilyl chloride (1.0 mL, 6.0 mmol) at 0 °C under argon. The reaction mixture was warmed up to room temperature and maintained for 2 h with stirring. Then, this mixture was poured into water and extracted with EtOAc. The combined organics were washed with brine and dried over anhydrous Na_2SO_4. Filtration, removal of solvents and further drying under vacuum afforded almost pure 2-phenyl-2-(triethylsiloxy)acetonitrile in which ^{13}C was incorporated in cyano position. Further, the same manipulations for the preparation of **1a** gave the ^{13}C labeled substrate [^{13}C]-**1a**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (1H, d, J_{C-H}=178.4 Hz, ^{13}CHO), 7.26–7.32 (5H, m, Ph-H), 7.12–7.13 (3H, m, Ph-H), 6.95–6.97 (2H, m, Ph-H), 3.31 (1H, dd, *J*=14.4, J_{C-H}=3.6 Hz, $PhCH_2$), 3.25 (1H, dd, *J*=14.4, J_{C-H}=2.4 Hz, $PhCH_2$), 0.89 (9H, t, *J*=8.0 Hz, CH_3CH_2Si), 0.58 (6H, q, *J*=8.0 Hz, CH_3CH_2Si).

3.5. Test for silyl group transfer pathway

3.5.1. Experimental procedure for the reaction with Me_2AlCl

To a solution of **1a** (85.1 mg, 0.25 mmol) and [TBS]-**1i** (92.6 mg, 0.25 mmol) in toluene (5.0 mL) was added a 1 M toluene solution of Me_2AlCl (50 μL, 0.05 mmol) at 0 °C under nitrogen. After stirring for 24 h, sodium fluoride (8.4 mg, 0.2 mmol) and water (2.7 μL, 0.15 mmol) were added and the whole mixture was stirred for 30 min at room temperature. To remove precipitates, filtration through Celite with EtOAc was carried out. Concentration of the filtrate and purification by column chromatography on silica gel (CH_2Cl_2/hexane=1:4, then Et_2O/hexane=1:10 as eluant) afforded separated products, **2a** (77.4 mg, 0.23 mmol, 91% yield, [TBS]-**2a** was not detected) and [TBS]-**2i** (87.0 mg, 0.24 mmol, 94% yield, **2i** was not detected). **2a** TLC (EtOAc/hexane=1:10): R_f 0.5, [TBS]-**2i**: R_f 0.3.

3.5.2. With catalyst ***5c***

To a mixture of $AgNTf_2$ (19.4 mg, 0.05 mmol) in CH_2Cl_2 (3.0 mL) was added 1 M toluene solution of Me_2AlCl (50 μL, 0.05 mmol) under nitrogen and the resulting mixture was stirred at room temperature for 12 h. To this mixture was added a solution of 2,2′-bis(trifluoromethanesulfonylamino)-1,1′-biphenyl (24.6 mg, 0.055 mmol) in CH_2Cl_2 (1.0 mL) and stirred for another 1 h. After being cooled to −40 °C, a solution of **1a** (85.1 mg, 0.25 mmol) and [TBS]-**1i** (92.6 mg, 0.25 mmol) in CH_2Cl_2 (1.0 mL) was transferred into this mixture and the stirring was maintained at −40 °C for 48 h. Then, the reaction mixture was quenched with 1 N HCl and extracted with EtOAc. The organic extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation, the residual oil was purified by column chromatography on silica gel (CH_2Cl_2/hexane=1:4, then Et_2O/hexane=1:10 as eluant) to give products, a mixture of **3a** and [TBS]-**3i** (84.8 mg, 0.25 mmol, 99% yield, **3a**/[TBS]-**3a**=2:1), and a mixture of [TBS]-**3i** and **3i** (92.0 mg, 0.25 mmol, 99% yield, [TBS]-**3i**/**3i**=2:1). A mixture of **3a** and [TBS]-**3a** TLC (EtOAc/hexane=1:10): R_f 0.5, [TBS]-**3i** and **3i**: R_f 0.3.

3.5.3. 2-(tert-Butyldimethylsiloxy)-3-(4-methoxyphenyl)-2-phenylpropanal [TBS]-***1i***

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (1H, s, CHO), 7.26–7.33 (5H, m, Ph-H), 6.91 (2H, d, *J*=9.2 Hz, Ar-H), 6.68 (2H, d, *J*=9.2 Hz, Ar-H), 3.73 (3H, s, $MeOC_6H_4$), 3.35 (1H, d, *J*=14.6 Hz, $ArCH_2$), 3.22 (1H, d, *J*=14.0 Hz, $ArCH_2$), 0.94 (9H, s, *t*-BuSi), 0.04 (3H, s, MeSi), −0.05 (3H, s, MeSi); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 158.1, 139.3, 131.7, 128.3, 127.7, 127.5, 126.3, 113.1, 85.2, 55.1, 43.5, 26.2, 18.9, −2.2, −2.4; IR (neat) 2954, 2929, 2856, 1734, 1514, 1253, 1141, 1037, 958, 912, 831, 777, 700 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{22}H_{30}NaO_3Si$ ([M+Na]$^+$): 393.1856. Found: 393.1865.

3.5.4. 2-(tert-Butyldimethylsiloxy)-3-(4-methoxyphenyl)-1-phenylpropan-1-one [TBS]-***2i***

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.07 (2H, m, Ph-H), 7.53–7.57 (1H, m, Ph-H), 7.43–7.47 (2H, m, Ph-H), 7.13–7.16 (2H, m, Ar-H), 6.80–6.84 (2H, m, Ar-H), 4.86 (1H, dd, *J*=9.2, 4.0 Hz, SiOCH), 3.78 (3H, s, $MeOC_6H_4$), 3.05 (1H, dd, *J*=14.0, 4.0 Hz, $ArCH_2$), 2.95 (1H, dd, *J*=14.0, 9.2 Hz, $ArCH_2$), 0.76 (9H, s, *t*-BuSi), −0.20 (3H, s, MeSi), −0.22 (3H, s, MeSi); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 158.4, 134.9, 133.0, 130.7, 129.6, 129.2, 128.3, 113.6, 79.5, 55.2, 41.4, 25.6, 18.1, −5.2, −5.5; IR (neat) 2953, 2929, 2856, 1724, 1512, 1300, 1247, 1178, 1132, 1095, 1068, 1037, 877, 837, 779, 746, 700 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{22}H_{30}NaO_3Si$ ([M+Na]$^+$): 393.1856. Found: 393.1857.

3.5.5. 1-(tert-Butyldimethylsiloxy)-3-(4-methoxyphenyl)-1-phenylpropan-2-one [TBS]-***3i***

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.44 (2H, m, Ar-H), 7.29–7.36 (3H, m, Ar-H), 6.90 (2H, d, *J*=8.4 Hz, Ar-H), 6.77 (2H, d, *J*=8.4 Hz, Ar-H), 5.17 (1H, s, SiOCH), 3.81 (1H, d, *J*=17.8 Hz, $ArCH_2$), 3.75 (3H, s, $MeOC_6H_4$), 3.69 (1H, d, *J*=17.8 Hz, $ArCH_2$), 0.95 (9H, s, *t*-BuSi), 0.08 (3H, s, MeSi), 0.01 (3H, s, MeSi); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 158.3, 138.4, 130.5, 128.4, 128.0, 126.0, 125.9, 113.7, 80.9, 55.1, 41.6, 25.7, 18.2, −4.9, −5.0; IR (neat) 2953, 2929, 2856, 1724, 1512, 1300, 1247, 1178, 1132, 1095, 1068, 1037, 877, 837, 779, 746, 700 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{22}H_{30}NaO_3Si$ ([M+Na]$^+$): 393.1856. Found: 393.1859.

3.6. For stereospecific 1,2-rearrangement

3.6.1. Preparation of optically active substrate via kinetic resolution[9]

To a solution of (*S*,*S*)-2-hydroxy-2′-[3,5-bis(trifluoromethyl)] phenyl-3-{2-[3,5-bis(trifluoromethyl)]benzenesulfonylamino}phenyl-1,1′-binaphthyl (233.5 mg, 0.275 mmol) in toluene (25 mL) was added a 1 M toluene solution of Me_3Al (250 μL, 0.25 mmol) at room temperature under nitrogen and stirred for 30 min. After being cooled to −20 °C, **2a** (1.7 g, 5.0 mmol) was added to this solution and the stirring was maintained at −20 °C for 18 h. Then, sodium fluoride (42.0 mg, 1.0 mmol) and water (13.5 μL, 0.75 mmol) were added and the whole mixture was stirred for 30 min at room temperature. To remove precipitates, filtration through Celite with EtOAc was carried out. Concentration of the filtrate and purification by column chromatography on silica gel (CH_2Cl_2/hexane=1:4 as eluant) afforded (*R*)-**2a** (646.3 mg, 1.9 mmol, 38% recover, 97% ee).

3.6.2. Data for chiral siloxy ketones

(*R*)-**2a** $[\alpha]_D^{25}$ +39.1 (*c* 1.47, $CHCl_3$, 94% ee); HPLC condition: DAICEL Chiralcel OD-H, hexane/*i*-PrOH=99:1, flow rate=0.3 mL/min, λ=210 nm, retention time: 15.4 min (*S*), 16.9 min (*R*).

(*R*)-**3a** $[\alpha]_D^{28}$ −40.9 (*c* 1.03, $CHCl_3$, 75% ee); HPLC condition: DAICEL Chiralcel OJ-H, hexane/*i*-PrOH=99:1, flow rate=0.3 mL/min, λ=220 nm, retention time: 18.8 min (*S*), 20.6 min (*R*). Absolute configuration was established by comparison of the optical rotation with a known literature value[20] after derivatization as follow.

A solution of **3a** (68.1 mg, 0.2 mmol, 75% ee) in THF (2.0 mL) was treated with 1 N HCl (1.0 mL) with vigorous stirring. After being kept for 2 h, the reaction mixture was extracted with EtOAc, and the organic extracts were washed with brine and dried (Na_2SO_4). Filtration, evaporation and further drying under vacuum were conducted. Then, to a solution of this crude compound and acetic anhydride (38 μL, 0.4 mmol) in dichloromethane (1.0 mL) was added copper(II) trifluoromethanesulfonate (1.8 mg, 5.0 μmol) at room temperature under argon. After being stirred for 1 h, the mixture was quenched by the addition of satd $NaHCO_3$. Extractive workup was performed with EtOAc and the combined organics were washed with water, brine and dried over anhydrous Na_2SO_4. After concentration, resulting crude product was purified by column chromatography on silica gel (EtOAc/hexane=1:4 as eluant) to afford pure 2-oxo-1,3-diphenylpropyl acetate (48.8 mg, 0.18 mmol, 90% yield for two steps).

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