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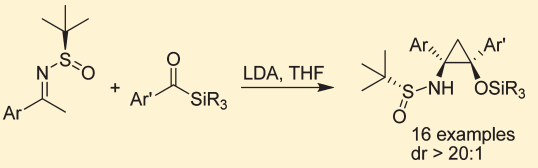
Asymmetric Synthesis of *cis*-2-Aminocyclopropanols by Intramolecular Mannich Addition of Silyloxy Benzyl Carbanions

Bo Liu and Chong-Dao Lu*

Xinjiang Technical Institute of Physics and Chemistry, Chinese Academy of Sciences, Urumqi 830011, China

Supporting Information

ABSTRACT: An efficient, highly diastereoselective method for the preparation of protected *cis*-2-aminocyclopropanols from *N*-*tert*-butanesulfinyl ketimines and various aryl acylsilanes is described. A tandem process for carbon−carbon bond formation via nucleophilic addition to acylsilanes, Brook rearrangement, and intramolecular Mannich reaction has been developed.



Enantiomerically pure 1,2-aminoalcohols are key substructures in a number of bioactive compounds and can serve as useful precursors for several valuable ligands and auxiliaries in asymmetric synthesis.[1−3] Although 2-aminocyclopropanols make up a unique subclass of 1,2-aminoalcohols, they have received little attention, in part because few synthetic methods for their efficient preparation are available. *trans*-2-Aminocyclopropanols have been prepared by irradiation of β-aminoketones,[4] whereas [2+1] cycloaddition reaction of bis(iodozincio)methane with α-ketoimines yields the *cis* isomers.[5] However, such methods give racemic products that are of limited diversity.

Here, we report an efficient method for asymmetric synthesis of *cis*-2-aminocyclopropanols possessing a silyl group on oxygen and an *N*-*tert*-butanesulfinyl group on nitrogen. The synthesis involves the reaction of *N*-*tert*-butanesulfinyl ketimines[6−9] with acylsilanes in the presence of lithium diisopropylamide via nucleophilic addition of lithium enamines to acylsilanes, followed by Brook rearrangement[10] and trapping of the silyloxy benzyl anion by intramolecular Mannich addition (Scheme 1).

A number of synthetically useful methodologies based on Brook rearrangement have been developed by using organometallic reagents as triggers, such as metallocyanide,[11] metallophosphite,[12] vinyl/propargyllic lithium,[13] zinc acetylide,[14] vinyl Grignard reagents,[15] and metalloenolates.[16−18] The related intramolecular transformations initiated by the addition of lithium ketone enolates to acylsilanes and its applications in total synthesis have been disclosed by the Takeda group in recent years.[19−21] However, the reactivity of metalloenamines derived from *N*-*tert*-butanesulfinyl ketimines toward acylsilanes has not been reported. This report serves as the first demonstration of this reactivity.

The results from our preliminary experiments are presented in Table 1. Lithiation of the (R_S)-*N*-*tert*-butanesulfinyl imine of acetophenone **1a** with LHMDS at −78 °C followed by the addition of acylsilane **2a** resulted in *cis*-2-aminocyclopropanol **3a** in 66% isolated yield as a single diastereomer (entry 1). LHMDS as a base is superior to NaHMDS and KHMDS for this reaction (entries 2 and 3, respectively). Further experimentation revealed that LDA (entry 4) gave a better yield than LHMDS (entry 1). Increasing the reaction temperature, which accelerates the 1,2-Brook rearrangement, further improved the yield (entry 5 vs entry 4). The best yield was obtained by using LDA as a base and warming the reaction mixture gradually from −78 to −30 °C over a period of 5 h [84% yield (Table 1, entry 5, and Table 2, entry 1)]. We also observed that the bulkiness of the silyl groups in the acylsilanes significantly influenced the reaction rate. Compared to the example of **1a** and PhCOTBS outlined above, reactions involving acylsilanes with smaller silyl groups proceeded smoothly at lower temperatures with a shorter reaction time. Warming the reaction mixture of **1a** and acylsilane **2b** (PhCOTES) from −78 to −50 °C over a period of 3 h was sufficient to consume **1a** completely (Table 2, entry 2). In addition, acyltrimethylsilane **2c** reacted even faster than its analogue with a slightly bulkier silyl group (**2b**, PhCOTES), reaching completion when the reaction mixture was warmed from −78 to −50 °C over 1.5 h. For further studies of the scope of the reaction, acyltriethylsilanes (**2b**, **2d**, **2e**, and **2f**) were chosen instead of the acyltrimethylsilanes because TES ether products exhibit better tolerance to silica gel chromatography.

We next examined the scope of the addition of *N*-sulfinyl metalloenamines to acylsilanes. As illustrated in Table 2, the reactions generally proceeded in moderate to good yields. *N*-Sulfinyl aryl (or heteroaryl) methyl ketimines **1a**−**1h** served as nucleophiles to attack aryl acylsilanes, and the addition-initiated cascade reactions produced a diverse collection of enantioenriched *cis*-2-aminocyclopropanols with contiguous tertiary carbons bearing identical or different aryl groups. Both electron-rich and electron-deficient aryl-substituted acylsilanes (**2d**−**2f**) proved to be suitable for this reaction.

The absolute configuration of the 2-aminocyclopropan-1-ol **3a** was determined to be (R_S,1*S*,2*R*) by single-crystal X-ray diffraction analysis, with **3b**−**3p** assigned by analogy.[22] The relative configuration between the *t*BS-amine group and the TBS-ether moiety

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Scheme 1. Reactions Involving 1,2-Brook Rearrangement and Intramolecular Mannich Addition

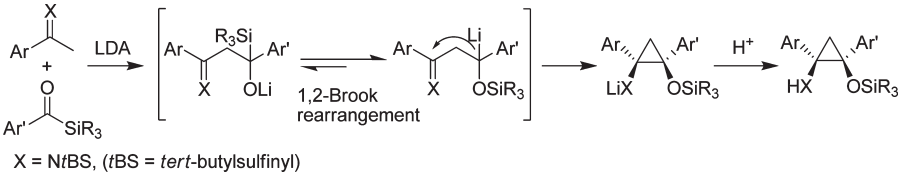
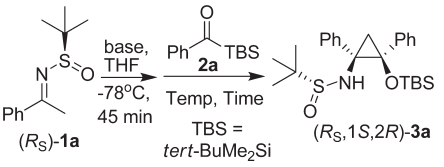


Table 1. Optimization of the Addition of *N*-Sulfinylketimine 1a to Acylsilane 2a[a]



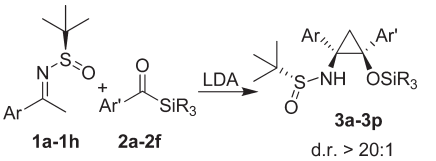
entry	base (equiv)	temp (°C)	time (h)	yield (%)[b]
1	LHMDS (1.05)	−78	8	66
2	NaHMDS (1.05)	−78	8	47
3	KHMDS (1.05)	−78	8	33
4	LDA (1.20)	−78	12	74
5	LDA (1.20)	−78 to −30	5	84

[a] The reaction was performed on a 0.2 mmol scale using 1.5 equiv of **2a**. [b] Isolated yield after column chromatography on silica gel. ^{1}H NMR of the crude reaction mixture detected only one diastereomer.

appeared to be *cis*. The reaction occurred with high diastereoselectivity in all cases (Table 2, dr > 20:1). Although the origin of the high degree of stereocontrol of this reaction is unclear, the observed stereochemistry can be explained in the following way. On the basis of the six- and four-membered bicyclic transition-state model advanced by Ellman in the reaction of metalloenamines and aldehydes (Scheme 2),[8] nucleophilic attack of the lithium enamine on the aryl acylsilane should proceed preferentially from the opposite direction of the *tert*-butyl group. However, according to Ellman and Liu's pioneering studies, this step does not proceed in a highly diastereoselective manner without assistance from additives. In their studies, reactions of lithium enamine derived from *N-tert*-butanesulfinyl imine of acetophenone with phenacyl derivatives (PhCOR′), such as benzaldehyde (R′ = H) and phenyl trifluoromethyl ketone (R′ = CF_3), gave moderate to poor diastereoselectivity without assistance from $ZnBr_2$ (R′ = H, and dr = 73:27; R′ = CF_3, and dr = 59:41).[8,9] The facial selectivity from the aryl acylsilane (R′ = SiR_3; re face or si face) would be low in this case because the competing 1, 3-diaxial interactions in **A** and **A′** are not overwhelmingly different.

It is likely that the silyloxy carbanions **C** (and **C′**), generated from the stereospecific Brook rearrangement via **B** (and **B′**) with retention of configuration, intramolecularly attack azomethine with retention of configuration at the carbanion center for **C** and with inversion for **C′**,[23−26] leading to **3** as the sole product with the requisite stereochemical features. The chair conformation of **C** (and **C′**), together with the significant electron density on both faces of the partially flattened α-oxybenzyl anion,[27] permits the diastereocontrol in the intramolecular Mannich trapping. Prior to formation of the second C−C bond, partial epimerization between carbanions **C** and **C′** could also occur.

Table 2. Addition of *N*-Sulfinyl Metalloenamines to Acylsilanes[a]



1a, Ar = Ph
1b, Ar = *p*-MeOPh
1c, Ar = *o*-MeO-Ph
1d, Ar = *p*-Cl-Ph
1e, Ar = *p*-Br-Ph
1f, Ar = 2-pyridinyl
1g, Ar = 3-pyridinyl
1h, Ar = 2-furanyl

2a, Ar′ = Ph, SiR_3 = TBS
2b, Ar′ = Ph, SiR_3 = TES
2c, Ar′ = Ph, SiR_3 = TMS
2d, Ar′ = *p*-MeOPh, SiR_3 = TES
2e, Ar′ = *p*-MePh, SiR_3 = TES
2f, Ar′ = *p*-ClPh, SiR_3 = TES

entry	sulfinimine **1** (Ar)	acylsilane **2**[b] (Ar′, SiR_3)	product **3**	yield (%)[c]
1	**1a** (Ph)	**2a** (Ph, TBS)	**3a**	84
2	**1a** (Ph)	**2b** (Ph, TES)	**3b**	84
3	**1a** (Ph)	**2c** (Ph, TMS)	**3c**	74
4	**1a** (Ph)	**2d** (*p*-MeOPh, TES)	**3d**	69
5	**1a** (Ph)	**2e** (*p*-MePh, TES)	**3e**	47
6	**1a** (Ph)	**2f** (*p*-ClPh, TES)	**3f**	63
7	**1b** (*p*-MeOPh)	**2a** (Ph, TBS)	**3g**	84
8	**1b** (*p*-MeOPh)	**2b** (Ph, TES)	**3h**	94
9	**1b** (*p*-MeOPh)	**2d** (*p*-MeOPh, TES)	**3i**	77
10	**1b** (*p*-MeOPh)	**2f** (*p*-ClPh, TES)	**3j**	75
11	**1c** (*o*-MeOPh)	**2b** (Ph, TES)	**3k**	74
12	**1d** (*p*-ClPh)	**2b** (Ph, TES)	**3l**	80
13	**1e** (*p*-BrPh)	**2b** (Ph, TES)	**3m**	65
14	**1f** (2-pyridinyl)	**2b** (Ph, TES)	**3n**	62
15	**1g** (3-pyridinyl)	**2b** (Ph, TES)	**3o**	69
16	**1h** (2-furanyl)	**2b** (Ph, TES)	**3p**	67

[a] The reaction was performed on a 0.2 mmol scale using 1.5 equiv of **2**. [b] TBS indicates *tert*-butyldimethylsilyl, TES triethylsilyl, and TMS trimethylsilyl. [c] Isolated yield after column chromatography on silica gel. ^{1}H NMR of the crude reaction mixture indicated that only one diastereomer was observed.

In summary, we have developed a diastereoselective synthesis of protected *cis*-2-aminocyclopropanols by the reaction of *N-tert*-butylsulfinyl ketimines with acylsilanes. A cascade transformation involving the formation of two C−C bonds and an O−Si bond is a key feature of this reaction. A mechanism rationalizing the observed diastereocontrol for the formation of *cis*-2-aminocyclopropanol is proposed.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of *cis*-2-Aminocyclopropanol 3. THF (1.5 mL) and diisopropylamine (33.8 μL, 0.24 mmol)

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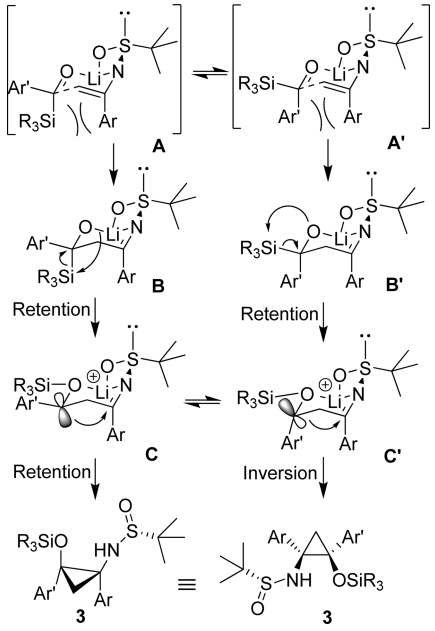
Scheme 2. Rationale for the Observed Stereochemistry



were added to a flame-dried flask equipped with a magnetic stirring bar and purged with nitrogen. The solution was cooled to −10 °C, and *n*-butyllithium (2.5 M in hexane, 96 μL, 0.24 mmol) was added by syringe. The mixture was stirred at this temperature for 45 min and then cooled to −78 °C. *N*-Sulfinyl imine **1**[28,29] (0.2 mmol) in THF (1.5 mL) was added to the reaction mixture at −78 °C, and the mixture was stirred for an additional 45 min. A solution of acylsilane **2**[30,31] (0.3 mmol) in THF (0.5 mL) was added, and the mixture was gradually warmed to the indicated temperature for the indicated time (see the details for each of the examples), at which point the starting material had been completely consumed, based on TLC detection. The reaction was quenched with saturated aqueous ammonium chloride. After being warmed to ambient temperature, the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated by evaporation. The residue was analyzed by ^{1}H NMR (dr > 20:1) and purified by flash column chromatography on silica gel to give the desired product.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1,2-Diphenyl-2-(*tert*-butyldimethylsilyloxy)-cyclopropyl]-2-methylpropane-2-sulfinamide (3a). The reaction mixture was gradually warmed to −30 °C over a 5 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (9:1 to 6:1, v/v) gave 74.1 mg of product **3a** (84% yield) as a white solid: mp 95−97 °C; $[\alpha]^{25}_D$ = −38.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14−6.94 (m, 10H), 4.86 (s, 1H), 2.40 (d, *J* = 7.7 Hz, 1H), 2.02 (d, *J* = 7.7 Hz, 1H), 1.19 (s, 9H), 0.91 (s, 9H), 0.15 (s, 3H), −0.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.5, 129.1, 128.5, 127.7, 127.6, 127.4, 126.6, 64.8, 55.8, 47.6, 26.0, 22.7, 21.5, 18.2, −3.7; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{37}NO_2SSiNa$ $[M + Na]^+$ 466.2212, found 466.2206.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1,2-Diphenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3b). The reaction mixture was gradually warmed to −55 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (9:1 to 6:1, v/v) gave 74.4 mg of product **3b** (84% yield) as a white solid: mp 57−59 °C; $[\alpha]^{25}_D$ = −13.5° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−6.90 (m, 10H), 4.90 (s, 1H), 2.38 (d, *J* = 7.7 Hz, 1H), 2.01 (d, *J* = 7.7 Hz, 1H), 1.20 (s, 9H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.63−0.44 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.7, 129.1, 128.3, 127.7, 127.7, 127.4, 126.6, 64.5, 55.8, 47.6, 22.6, 21.9, 6.9, 5.5; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{37}NO_2SSiNa$ $[M + Na]^+$ 466.2212, found 466.2200.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1,2-Diphenyl-2-(trimethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3c). The reaction mixture was gradually warmed to −55 °C over a 1.5 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (15:1 to 10:1, v/v) gave 59.3 mg of product **3c** (74% yield) as a white solid: mp 88−90 °C; $[\alpha]^{25}_D$ = −24.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−6.91 (m, 10H), 4.89 (s, 1H), 2.36 (d, *J* = 7.7 Hz, 1H), 2.05 (d, *J* = 7.7 Hz, 1H), 1.20 (s, 9H), 0.06 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 138.5, 129.1, 128.1, 127.8, 127.7, 127.3, 126.7, 64.6, 55.8, 47.2, 22.6, 22.1, 1.0; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{31}NO_2SSiNa$ $[M + Na]^+$ 424.1742, found 424.1737.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1-Phenyl-2-(4-methoxyphenyl)-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3d). The reaction mixture was gradually warmed to rt over a 20 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (6:1 to 4:1, v/v) gave 65.3 mg of product **3d** (69% yield) as a slight yellow solid: mp 85−87 °C; $[\alpha]^{25}_D$ = 4.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.8 Hz, 2H), 7.07−7.00 (m, 4H), 6.97 (t, *J* = 7.1 Hz, 1H), 6.58 (d, *J* = 8.8 Hz, 2H), 4.88 (s, 1H), 3.67 (s, 3H), 2.30 (d, *J* = 7.6 Hz, 1H), 1.98 (d, *J* = 7.6 Hz, 1H), 1.20 (s, 9H), 0.87 (t, *J* = 7.6 Hz, 9H), 0.59−0.43 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 139.1, 130.6, 129.5, 128.7, 127.5, 126.3, 112.8, 64.1, 55.6, 55.0, 47.2, 22.4, 21.9, 6.7, 5.2; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{39}NO_3SSiNa$ $[M + Na]^+$ 496.2318, found 496.2312.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1-Phenyl-2-(4-methylphenyl)-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3e). The reaction mixture was gradually warmed to −50 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 43.3 mg of product **3e** (47% yield) as a white solid: mp 86−88 °C; $[\alpha]^{25}_D$ = −25.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.2 Hz, 2H), 7.06−6.94 (m, 5H), 6.84 (d, *J* = 7.9 Hz, 2H), 4.89 (s, 1H), 2.32 (d, *J* = 7.6 Hz, 1H), 2.16 (s, 3H), 1.96 (d, *J* = 7.6 Hz, 1H), 1.18 (s, 9H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.58−0.45 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 136.7, 135.3, 128.9, 128.2, 128.0, 127.4, 126.3, 64.2, 55.6, 47.3, 22.4, 21.8, 21.0, 6.7, 5.2; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{39}NO_2SSiNa$ $[M + Na]^+$ 480.2368, found 480.2363.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1-Phenyl-2-(4-chlorophenyl)-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3f). The reaction mixture was gradually warmed to rt over a 12 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (8:1 to 6:1, v/v) gave 60.4 mg of product **3f** (63% yield) as a slight yellow solid: mp 84−86 °C; $[\alpha]^{25}_D$ = −11.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14−6.94 (m, 9H), 4.83 (s, 1H), 2.33 (d, *J* = 7.8 Hz, 1H), 2.01 (d, *J* = 7.7 Hz, 1H), 1.18 (s, 9H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.62−0.45 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.5, 137.4, 132.9, 129.2, 128.9, 127.7, 127.7, 126.7, 63.7, 55.6, 47.6, 22.4, 21.7, 6.7, 5.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{36}ClNO_2SSiNa$ $[M + Na]^+$ 500.1822, found 500.1817.

(*R*$_S$)-*N*-[(1*R*,2*S*)-1-(4-Methoxyphenyl)-2-phenyl-2-(*tert*-butyldimethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3g). The reaction mixture was gradually warmed to −15 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (8:1 to 6:1, v/v) gave 79.0 mg of product **3g** (84% yield) as a colorless solid: mp 142−144 °C; $[\alpha]^{25}_D$ = −40.0° (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−6.99 (m, 7H), 6.56 (d, *J* = 8.7 Hz, 2H), 4.82 (s, 1H), 3.65 (s, 3H), 2.31 (d, *J* = 7.6 Hz, 1H), 1.96 (d, *J* = 7.6 Hz, 1H), 1.18 (s, 9H), 0.91 (s, 9H), 0.14 (s, 3H), −0.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 138.5, 131.0, 130.1, 128.2, 127.5, 127.1, 112.8, 64.4, 55.5, 54.9, 47.0, 25.8, 22.5, 21.3, 18.0,

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−3.9, −4.0; HRMS (ESI) m/z calcd for $C_{26}H_{39}NO_3SSiNa$ $[M + Na]^+$ 496.2318, found 496.2312.

(R_S)-*N*-[(1*R*,2*S*)-1-(4-Methoxyphenyl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3h). The reaction mixture was gradually warmed to −40 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 89.3 mg of product **3h** (94% yield) as a colorless oil: $[\alpha]^{25}_D = 22.1°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14−7.02 (m, 7H), 6.58 (d, J = 8.7 Hz, 2H), 4.86 (s, 1H), 3.67 (s, 3H), 2.30 (d, J = 7.6 Hz, 1H), 1.96 (d, J = 7.6 Hz, 1H), 1.19 (s, 9H), 0.89−0.81 (m, 9H), 0.63−0.45 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 139.0, 131.2, 130.4, 128.1, 127.7, 127.3, 113.0, 64.3, 55.7, 55.3, 47.4, 22.6, 22.0, 7.0, 5.5; HRMS (ESI) m/z calcd for $C_{26}H_{39}NO_3SSiNa$ $[M + Na]^+$ 496.2318, found 496.2312.

(R_S)-*N*-[(1*R*,2*S*)-1,2-Bis(4-methoxyphenyl)-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3i). The reaction mixture was gradually warmed to −20 °C over a 5 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 77.2 mg of product **3i** (77% yield) as a colorless oil: $[\alpha]^{25}_D = -18.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (dd, J = 8.6, 6.5 Hz, 4H), 6.58 (dd, J = 8.6, 6.9 Hz, 4H), 4.84 (s, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 2.21 (d, J = 7.5 Hz, 1H), 1.90 (d, J = 7.5 Hz, 1H), 1.18 (s, 9H), 0.86 (t, J = 7.9 Hz, 9H), 0.59−0.43 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 157.9, 131.2, 130.9, 130.0, 129.4, 112.9, 112.9, 63.8, 55.5, 55.0, 55.0, 46.9, 22.4, 21.9, 6.7, 5.2; HRMS (ESI) m/z calcd for $C_{27}H_{41}NO_4SSiNa$ $[M + Na]^+$ 526.2423, found 526.2418.

(R_S)-*N*-[(1*R*,2*S*)-1-(4-Methoxyphenyl)-2-(4-chlorophenyl)-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3j). The reaction mixture was gradually warmed to −50 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 75.6 mg of product **3j** (75% yield) as a slight yellow solid: mp 88−89 °C; $[\alpha]^{25}_D = -31.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 4H), 7.01 (d, J = 8.7 Hz, 2H), 6.60 (d, J = 8.7 Hz, 2H), 4.80 (s, 1H), 3.69 (s, 3H), 2.27 (d, J = 7.7 Hz, 1H), 1.96 (d, J = 7.7 Hz, 1H), 1.18 (s, 9H), 0.88 (t, J = 7.9 Hz, 9H), 0.61−0.48 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 137.6, 132.8, 130.5, 130.2, 129.0, 127.8, 113.1, 63.5, 55.5, 55.0, 47.3, 22.5, 21.8, 6.7, 5.3; HRMS (ESI) m/z calcd for $C_{26}H_{38}ClNO_3SSiNa$ $[M + Na]^+$ 530.1928, found 530.1924.

(R_S)-*N*-[(1*R*,2*S*)-1-(2-Methoxyphenyl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3k). The reaction mixture was kept at −78 °C for 4 h, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 70.3 mg of product **3k** (74% yield) as a white solid: mp 62−63 °C; $[\alpha]^{25}_D = -35.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 1H), 7.09 (dd, J = 7.8, 1.7 Hz, 2H), 7.04−6.95 (m, 4H), 6.72 (d, J = 6.9 Hz, 1H), 6.41 (d, J = 6.5 Hz, 1H), 4.72 (s, 1H), 3.50 (s, 3H), 2.23 (s, 1H), 1.91 (d, J = 7.3 Hz, 1H), 1.06 (s, 9H), 0.90 (t, J = 7.9 Hz, 9H), 0.67−0.52 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 139.4, 130.4, 128.7, 127.2, 126.6, 126.5 (overlap), 126.5, 119.3, 109.8, 63.7, 55.3, 54.5, 46.6, 22.2, 6.8, 5.7, 5.4, 5.1; HRMS (ESI) m/z calcd for $C_{26}H_{39}NO_3SSiNa$ $[M + Na]^+$ 496.2318, found 496.2312.

(R_S)-*N*-[(1*R*,2*S*)-1-(4-Chlorophenyl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3l). The reaction mixture was gradually warmed to −25 °C over a 5 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 76.0 mg of product **3l** (80% yield) as a white solid: mp 92−94 °C; $[\alpha]^{25}_D = -25.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−6.91 (m, 9H), 4.87 (s, 1H), 2.32 (d, J = 7.7 Hz, 1H), 2.03 (d, J = 7.8 Hz, 1H), 1.19 (s, 9H), 0.89−0.84 (m, 9H), 0.60−0.43 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.1, 137.7, 132.1, 130.1, 128.0, 127.7 (overlap), 127.4, 64.3, 55.7, 46.9, 22.4, 21.8, 6.7, 5.2; HRMS (ESI) m/z calcd for $C_{25}H_{36}ClNO_2SSiNa$ $[M + Na]^+$ 500.1822, found 500.1817.

(R_S)-*N*-[(1*R*,2*S*)-1-(4-Bromophenyl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3m). The reaction mixture was gradually warmed to −40 °C over a 4 h period, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 68.2 mg of product **3m** (65% yield) as a white solid: mp 102−104 °C; $[\alpha]^{25}_D = -19.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 7.7 Hz, 2H), 7.14−7.02 (m, 5H), 6.98 (d, J = 7.8 Hz, 2H), 4.88 (s, 1H), 2.33 (d, J = 7.7 Hz, 1H), 2.04 (d, J = 9.1 Hz, 1H), 1.20 (s, 9H), 0.90−0.85 (m, 9H), 0.63−0.43 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 138.1, 130.6, 130.5 128.0, 127.7, 127.5, 120.3, 64.3, 55.7, 47.0, 22.4, 21.7, 6.7, 5.2; HRMS (ESI) m/z calcd for $C_{25}H_{36}BrNO_2SSiNa$ $[M + Na]^+$ 544.1317, found 544.1312.

(R_S)-*N*-[(1*R*,2*S*)-1-(Pyridin-2-yl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3n). The reaction mixture was gradually warmed to −35 °C over a 3 h period, giving complete conversion. Elution with a petroleum ether/EtOAc/MeOH mixture (10:1:1, v/v) gave 55.0 mg of product **3n** (62% yield) as a slight yellow oil: $[\alpha]^{25}_D = -24.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 4.8 Hz, 1H), 7.48−7.36 (m, 2H), 7.16 (d, J = 6.6 Hz, 2H), 7.07−6.96 (m, 3H), 6.82−6.76 (m, 1H), 4.93 (s, 1H), 3.01 (d, J = 7.1 Hz, 1H), 2.13 (d, J = 7.1 Hz, 1H), 1.27 (s, 9H), 0.87 (t, J = 7.9 Hz, 9H), 0.53 (q, J = 15.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 148.1, 138.2, 135.5, 128.9, 127.5, 127.3, 123.7, 120.8, 65.8, 56.0, 48.7, 22.7, 22.2, 6.9, 5.4; HRMS (ESI) m/z calcd for $C_{24}H_{36}N_2O_2SSiNa$ $[M + Na]^+$ 467.2164, found 467.2159.

(R_S)-*N*-[(1*R*,2*S*)-1-(Pyridin-3-yl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3o). The reaction mixture was gradually warmed to −25 °C over a 4 h period, giving complete conversion. Elution with a petroleum ether/EtOAc/MeOH mixture (10:1:1, v/v) gave 61.2 mg of product **3o** (69% yield) as a slight yellow oil: $[\alpha]^{25}_D = -37.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 2.0 Hz, 1H), 8.19 (dd, J = 4.8, 1.5 Hz, 1H), 7.33−7.28 (m, 1H), 7.14−7.02 (m, 5H), 6.93 (dd, J = 7.9, 4.8 Hz, 1H), 4.90 (s, 1H), 2.38 (d, J = 7.9 Hz, 1H), 2.09 (d, J = 7.9 Hz, 1H), 1.21 (d, J = 7.2 Hz, 9H), 0.92−0.82 (m, 9H), 0.58−0.45 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.5, 147.4, 137.7, 135.8, 134.9, 128.0, 127.9, 127.6, 122.3, 64.4, 55.8, 45.4, 22.4, 21.3, 6.6, 5.2; HRMS (ESI) m/z calcd for $C_{24}H_{36}N_2O_2SSiNa$ $[M + Na]^+$ 467.2164, found 467.2159.

(R_S)-*N*-[(1*R*,2*S*)-1-(Furan-2-yl)-2-phenyl-2-(triethylsilyloxy)cyclopropyl]-2-methylpropane-2-sulfinamide (3p). The reaction mixture was kept at −78 °C for 2.5 h, giving complete conversion. Elution with a petroleum ether/EtOAc mixture (10:1 to 8:1, v/v) gave 58.3 mg of product **3p** (67% yield) as a white solid: mp 82−84 °C; $[\alpha]^{25}_D = -36.0°$ (c 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, J = 7.3, 2.2 Hz, 3H), 7.20−7.13 (m, 3H), 7.01−6.96 (m, 1H), 6.04 (dd, J = 3.2, 1.8 Hz, 1H), 6.01−5.96 (m, 1H), 4.67 (s, 1H), 2.31 (d, J = 7.3 Hz, 1H), 2.07 (d, J = 7.3 Hz, 1H), 1.25 (s, 9H), 0.94−0.80 (m, 9H), 0.58−0.42 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 141.6, 138.5, 128.6, 127.8, 127.8, 110.3, 108.3, 64.7, 56.0, 42.9, 23.30, 22.6, 6.9, 5.4; HRMS (ESI) m/z calcd for $C_{23}H_{35}NO_3SSiNa$ $[M + Na]^+$ 456.2005, found 456.1999.

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H NMR and ^{13}C NMR spectra for all new compounds synthesized and X-ray structure of compound **1a**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: clu@ms.xjb.ac.cn.

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