New Ring-opening Reactions of Four-membered Carbo- and Sila-cyclic Compounds and Synthesis of 2-Alkoxy-1,3-dienes from Propargylic Alcohol Derivatives

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Preface

The studies in this thesis have been carried out under the direction of Professor Masahiro Murakami at Kyoto University from April 2012 to March 2013 and from April 2015 to March 2018. The studies are concerned with new ring-opening reactions of four-membered carbo- and sila-cyclic compounds and synthesis of 2-alkoxy-1,3-dienes from propargylic alcohol derivatives.

The author would like to express his sincerest gratitude to Supervisor, Professor Masahiro Murakami for his continuous guidance, encouragement, and stimulating discussions throughout this study. All the works in this thesis could be achieved with his constant supervisions.

The author deeply indebted to his advisor, Assistant Professor Naoki Ishida for his constant support, invaluable suggestion, and enthusiasm. The author would also like to thank Associate Professor Tomoya Miura, Dr. Akira Yada, and Assistant Professor Yusuke Masuda for their helpful suggestions, directions, and encouragement.

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Contents

Overview of Present Thesis

This thesis summarizes new five reactions the author developed. The author describes new ring-opening reactions of four-membered ring in chapter 1-4, and a new shynthestic method of 2-alkoxy-1,3-dienes from propargylic alcohol derivatives in chapter 5. Shown below is overview of the present thesis.

Chapter 1.
## Palladium-catalyzed Intermolecular Exchange between C–C and C–Si σ-Bonds
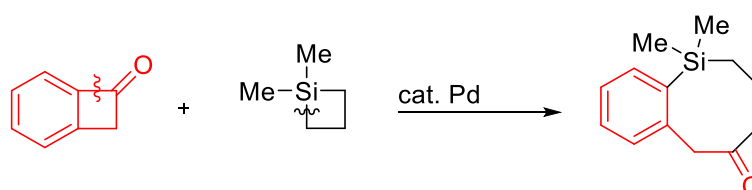
In chapter 1, the author describes palladium catalyzed intermolecular σ-bond exchange between a C–C bond of benzocyclobutenone and a C–Si bond of silacyclobutane.

σ bonds of low polarity such as C–C and C–Si bonds are difficult to cleavage. There are few examples of a reaction to cleave such stable two σ-bonds and to exchange them intermolecularly (σ-bond metathesis type reaction)[1-3]

A C–C bond of benzocyclobutenone[4] and a C–Si bond of silacyclobutane[5] oxidatively add onto transition metals. When a mixture of benzocyclobutenone and silacyclobutane was treated with a palladium isocyanide complex, intermolecular σ-bond exchange between a C–C bond of benzocyclobutenone and a C–Si bond of silacyclobutene occurred. It is assumed that the reaction proceeds through sequential oxidative addition of the C–C and the C–Si bond onto a palladium followed by sequential reductive elimination forming a $C(sp^2)$–Si bond and a C(carbonyl)–$C(sp^3)$ bond. As a result, two four-membered rings merge into an eight-membered ketone that is difficult to synthesize in conventional method.

Chapter 2.

Site- and Regio-selective Incorporation of Carbon Dioxide into the C(sp²)–Si Bond of Benzosilacyclobutenes
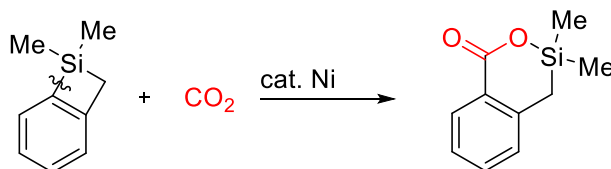

In chapter 2, the author describes site- and regio-selecive incorporation of carbon dioxide into the $C(sp^2)$–Si bond of benzosilacyclobutenes

C–Si bonds of organosilicon compounds are not so nuclephilic, and thus, normally do not react with carbon dioxide directly. Direct reactions of a C–Si bond with carbon dioxide are limited to significantly nucleophilic derivatives such as a lithiated (phosphacyclopentadienyl)silane,[6a] a zincated pyridylsilane,[6b] and a trimethylsilyl cation–*N*-heterocyclic carbene adduct.[6c] The addition of neutral organosilicon compounds onto carbon dioxide requires assistance of an excess amount of an aluminum Lewis acid[7] or cesium fluoride.[8]

When a benzosilacyclobutene was treated with a nickel catalyst under an atmospheric pressure of CO₂, the $C(sp^2)$–Si bond of benzosilacyclobutene reacted with carbon dioxide in a site- and regio-selective manner to afford a benzoic acid derivative. Stoichiometric additives such as a fluoride anion are not required.

Chapter 3.

2-Arylsilacyclobutane as Latent Nucleophile Attacking CO₂
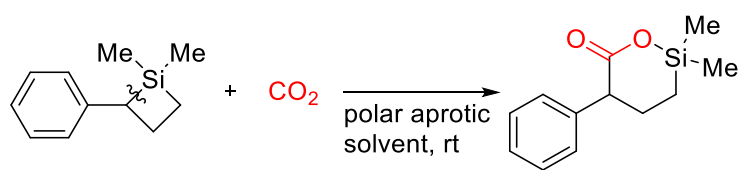
In chapter 3, the author describes direct nucleophilic addition[6] of benzylic C–Si bond of 2-arylsilacyclobutane to carbon dioxide in polar aprotic solvent.

When *cis*-2-phenyl-3-methylsilacyclobutane was dissolved in DMF-*d₇*, epimerization proceeded to afford *trans*-2-phenyl-3-methylsilacyclobutane via ring opening. Building on the discovery, the author found the benzylic C–Si bond of a 2-phenylsilacyclobutane reacted with carbon dioxide directly in a polar aprotic solvent to furnish a silalactone. Transition metal catalysis, Lewis acids, and bases are not required.

Chapter 4
Ring-opening Fluorination of Cyclobutanols and Cyclopropanols Catalyzed by Silver
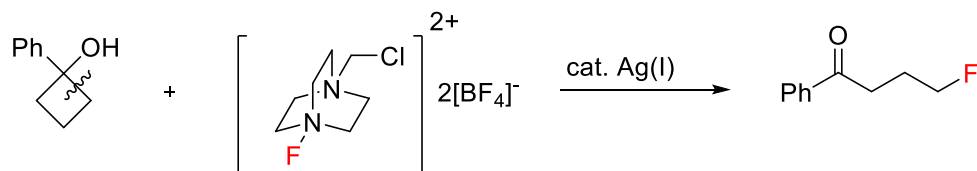
In chapter 4, the author describes ring-opening fluorination of cyclobutanols and cyclopropanols catalyzed by silver.

Organofluorine compounds have attracted significant attention in pharmaceuticals, agrochemicals, and materials science.[9] It is demanded to develop a method to site-selectively introduce a fluorine atom into organic compounds.[10]

Cyclobutanols undergo ring-opening reactions by assistance of transition metal catalysis[11] or oxidants[12]. Ring-opening reactions of cyclobutanols enable to functionalize a position of γ to the keto group. The author found that ring-opening fluorination of a cyclobutanol occurred to furnish a γ-fluoro ketone when treated with Selectfluor® in the presence of a silver salt. Cyclopropanols also undergo the analogous ring-opening fluorination to afford β-fluoroketones

Chapter 5
Synthesis of 2-Alkoxy-1,3-dienes from Propargylic Alcohol Derivatives
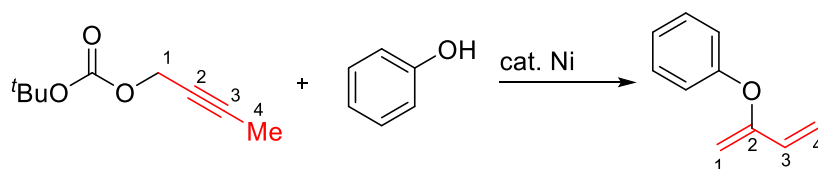
In chapter 5, the author describes a new synthetic method of 2-alkoxy-1,3-dienes from propargylic alcohol derivatives and alcohols catalyzed by nickel.

1,3-Dienes are versatile intermediates which undergo various transformations such as the Diels-Alder reaction.[13] Although a number of synthetic methods of 1,3-dienes have been reported, new synthetic methods from more readily available substances are still in demand.[14]

Propargylic carbonates are readily synthesized from terminal alkynes, aldehydes, and decarbonates,[15, 16] and thus are attractive as starting substances. The author discovered that a propargylic carbonate reacted with an alcohol in the presence of a nickel catalyst to afford a 2-alkoxy-1,3-diene efficiently. A wide variety of functional groups were tolerated.

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Chapter 1

Palladium-catalyzed Intermolecular Exchange between C–C and C–Si σ-Bonds

Abstract

A palladium−isocyanide complex opens the two four-membered rings of benzocyclobutenone and silacyclobutane to merge them into an eight-membered ring skeleton. The present reaction provides a unique example of an intermolecular cross metathesis-type reaction between covalent σ-bonds of low polarity.

Introduction

π-Symmetric orbitals of alkenes and alkynes facilely interact with frontier orbitals of metals. This interaction prompts a variety of metal-catalyzed organic transformations. For example, the C−C double bonds of two alkene molecules are exchanged by the action of a metal carbene complex to furnish differently combined alkenes.[1] It is significantly more difficult that σ-symmetric orbitals of covalent bonds of low polarity like C−C and C−Si interact with metal orbitals. Notwithstanding the difficulty, the last two decades have witnessed the emergence of metal-catalyzed reactions cleaving such a σ-bond.[2−5] Yet, it remains a formidable challenge of considerable novelty to cleave two σ-bonds and to exchange them, with a limited number of successful examples having appeared.[6,7] Murakami group has recently reported that intramolecular exchange of C−C and C−Si σ-bonds occurs when a benzene substrate ortho-disubstituted by cyclobutanone and silacyclobutane is treated with a palladium−trialkylphosphine complex.[8] In this example, the two σ-bonds to be cleaved are confined in close proximity by an ortho-phenylene linker to facilitate exchange between them. Herein, the author reports an intermolecular exchange reaction between C−C and C−Si σ-bonds. A C(aryl)−C(carbonyl) bond of benzocyclobutenones and a C(sp^3)−Si bond of silacyclobutanes are cleaved by action of a palladium−isocyanide complex, and then exchanged to form C(aryl)−Si and C(carbonyl)− C(sp^3) bonds, furnishing an eight-membered skeleton. The present study provides a unique example of a cross metathesis type reaction between two covalent σ-bonds of low polarity. Of note is that the intermolecular reaction dispenses with the need of any linker or directing group which brings about a proximity effect between the two exchanging σ-bonds.

Results and Discussion

Benzocyclobutenone oxidatively adds onto metals like cobalt(I), rhodium(I) and gold(I) either at the C(sp^3)−C(carbonyl) or at the C(aryl)−C(carbonyl) bond.[9] Catalytic reactions through the C−C bond cleavage have also been reported.[10] The C−Si bond of silacyclobutane adds oxidatively onto metals.[11] Metal-catalyzed reactions cleaving the C−Si bond have been developed.[12] These precedents on cleavage of C−C and C−Si bonds led the author to take on a challenge to achieve the intermolecular metathesis-type reaction between these σ-bonds of low polarity. Gratifyingly, an extensive screening identified the palladium-isocyanide complex as the suitable catalyst system. When benzocyclobutenone **1a** and silacyclobutane **2a** were treated with CpPd(π-allyl) (2 mol %) and ^{t}octyl isocyanide (8 mol %) in toluene at 100 °C for 24 h, the two four-membered rings were opened to merge into eight-membered silacycle **3a** in 85% yield

(eq 1). In addition, aldehydes **4** and **5** (each less than 1%) were identified as the minor products.

3a 85%   **4** <1%   **5** <1%
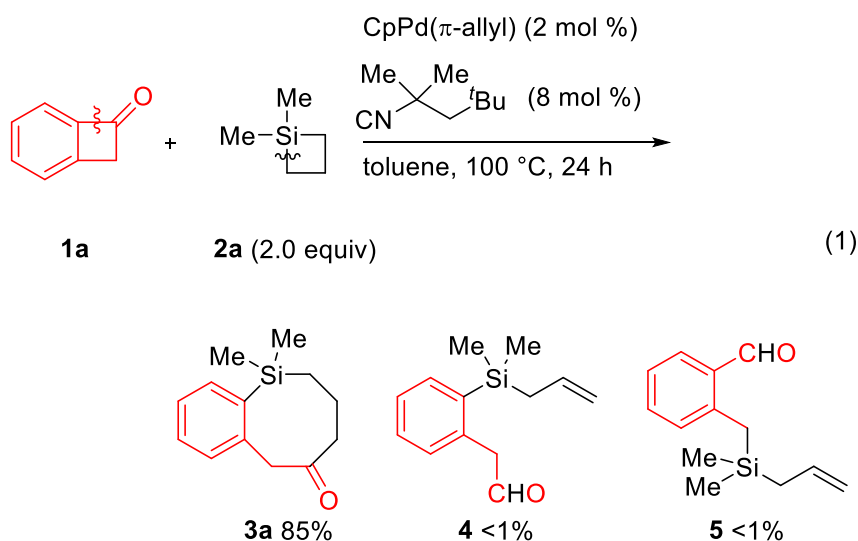
Analogous result was obtained when the isolated palladium-isocyanide complex **6** (eq 2) was used as the catalyst.[13] The bulky trialkylphosphine $P(1\text{-}Ad)_2{}^nBu$, which was the catalyst of choice for the intramolecular reaction previously reported,[8] was ineffective. Sterically less-demanding trialkylphosphines like PMe_3 and P^nBu_3 produced the aldehyde **4** as the major product.
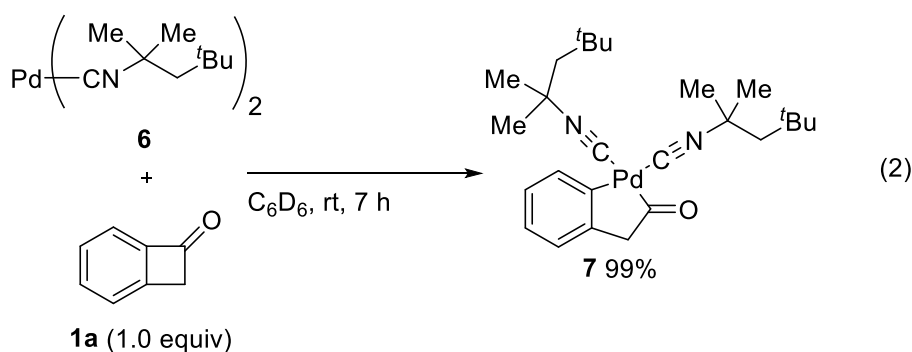
Next, benzocyclobutenone **1a** and silacyclobutane **2a** were separately subjected to a stoichiometric reaction with the isolated palladium-isocyanide complex **6**. No reaction took place when **2a** was treated with an equimolar amount of **6** in C_6D_6 at room temperature. On the other hand, **1a** did undergo oxidative addition under analogous conditions, and after 7 h, the five-membered palladacycle **7** was produced in quantitative yield (eq 2). Recrystallization from a toluene/hexane solution generated a single crystal, which was analyzed by an X-ray structural study. The crystal structure confirms site-selective insertion of palladium into the C(aryl)−C(carbonyl) linkage (Figure 1). Two isocyanide ligands take *cis* positions of the square-planar geometry. The distances to

palladium are slightly different among the two isocyanide ligands. The one *trans* to the acyl carbon is located more distant from palladium (2.071 Å) than the one *trans* to the aromatic carbon (2.050 Å). A similar deviation has been reported with the analogous squareplanar gold(III) complex.[9d] The author assumes the longer distance is suggestive of the stronger trans influence of the acyl carbon than the aryl carbon.
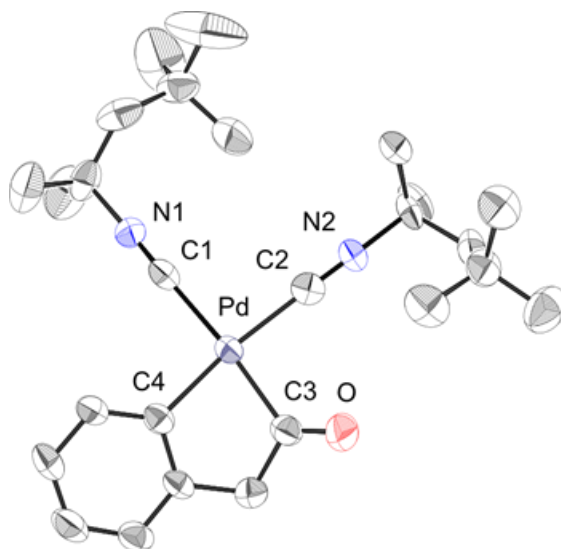

Figure 1. ORTEP Drawing of Palladacycle **7** (50% thermal ellipsoid, hydrogen atoms omitted for clarity) Selected bond lengths (Å) and angles (deg): Pd−C1 2.071(8), Pd−C2 2.050(9), Pd−C3 2.034(8), Pd−C4 2.028(8), C1−N1 1.148(9), C2−N2 1.153(9), C1−Pd−C2 92.6(3), C2−Pd−C3 92.3(3), C3−Pd−C4 80.7(3), C1−Pd−C4 94.4(3).

The palladium−isocyanide complex **6** is unique in that it inserts into the C(aryl)−C(carbonyl) linkage almost exclusively. With the Wilkinson's complex and its cobalt analog, oxidative addition occurs both at the C(sp^3)−C(carbonyl) and at the C(aryl)−C(carbonyl) bond and a mixture of two oxidative adducts results.[9a,b] In the case of a rhodium(I)-PBP pincer complex, it occurs exclusively at the C(sp^3)−C(carbonyl) bond.[9c] With a gold(I)-diphosphine complex, oxidative addition at the C(aryl)−C(carbonyl) bond is kinetically favored, and the oxidative adduct at the C(sp^3)−C(carbonyl) bond is thermodynamically more stable. The oxidative adduct at the C(aryl)−C(carbonyl) bond is initially formed and then gradually isomerizes to the latter.[9d]

The silacyclic product **3a** was obtained in 67% yield when the palladacycle **7** was heated with silacyclobutane **2a** (2.0 equiv) at 100 °C in C$_6$D$_6$ for 48 h (eq 3). Palladium black precipitated during the course of the reaction.
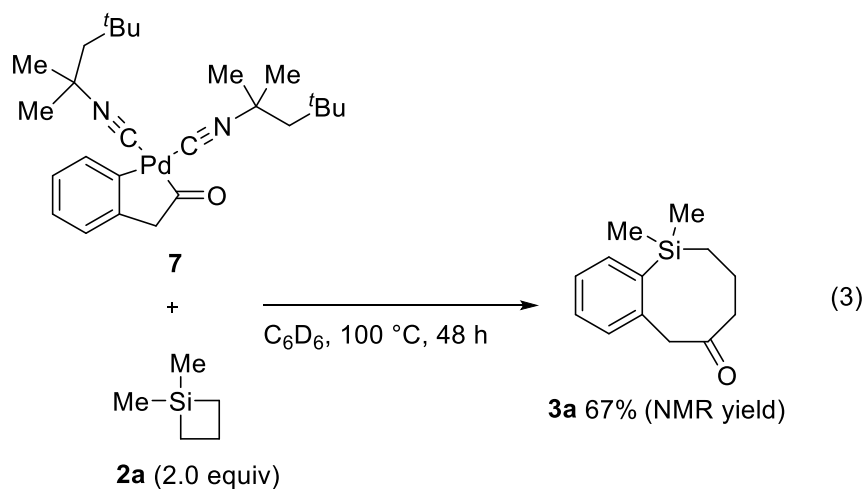
Several mechanistic scenarios are conceivable for the formation of **3a** from **1a** and **2a**.[14, 15] Shown in Scheme 1 is one of the mechanisms that are consistent with the results of the stoichiometric reactions described above. Benzocyclobutenone **1a** undergoes oxidative addition onto palladium(0) site-selectively at its C(aryl)−C(carbonyl) bond to furnish palladacycle(II) intermediate **A**. Next, the C−Si bond of silacyclobutane **2a** undergoes transmetalation with the C−Pd bond of **A**, possibly through a sequence of oxidative addition and reductive elimination to give the nine-membered palladacycle **C**. Reductive elimination then follows to form the eight-membered silacycle **3a**. Simultaneously, the palladium(0) species is regenerated and the next catalytic cycle ensues. The author assumes that the step from **A** to **B** is the rate-determining step because no intermediary palladium species was observed in the reaction mixture when the palladacycle **A** was reacted with silacyclobutane **2a** even at lower temperatures.
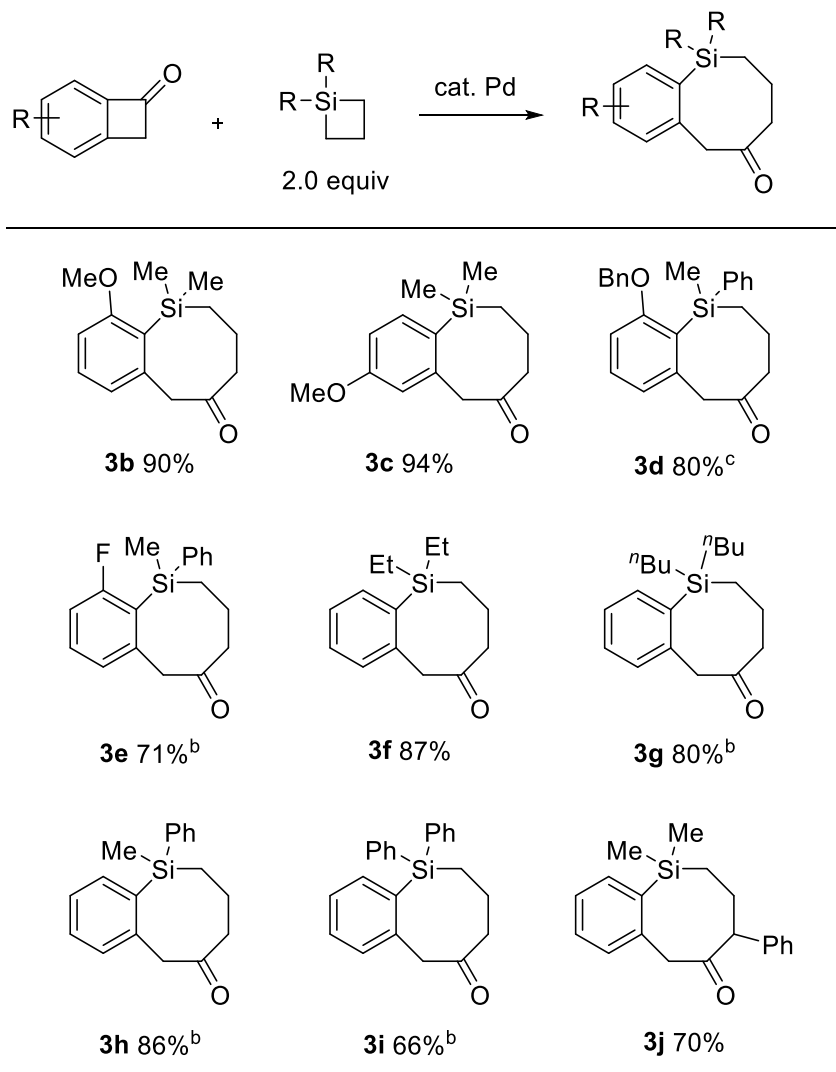
Scheme 1. Possible Mechanistic Pathways
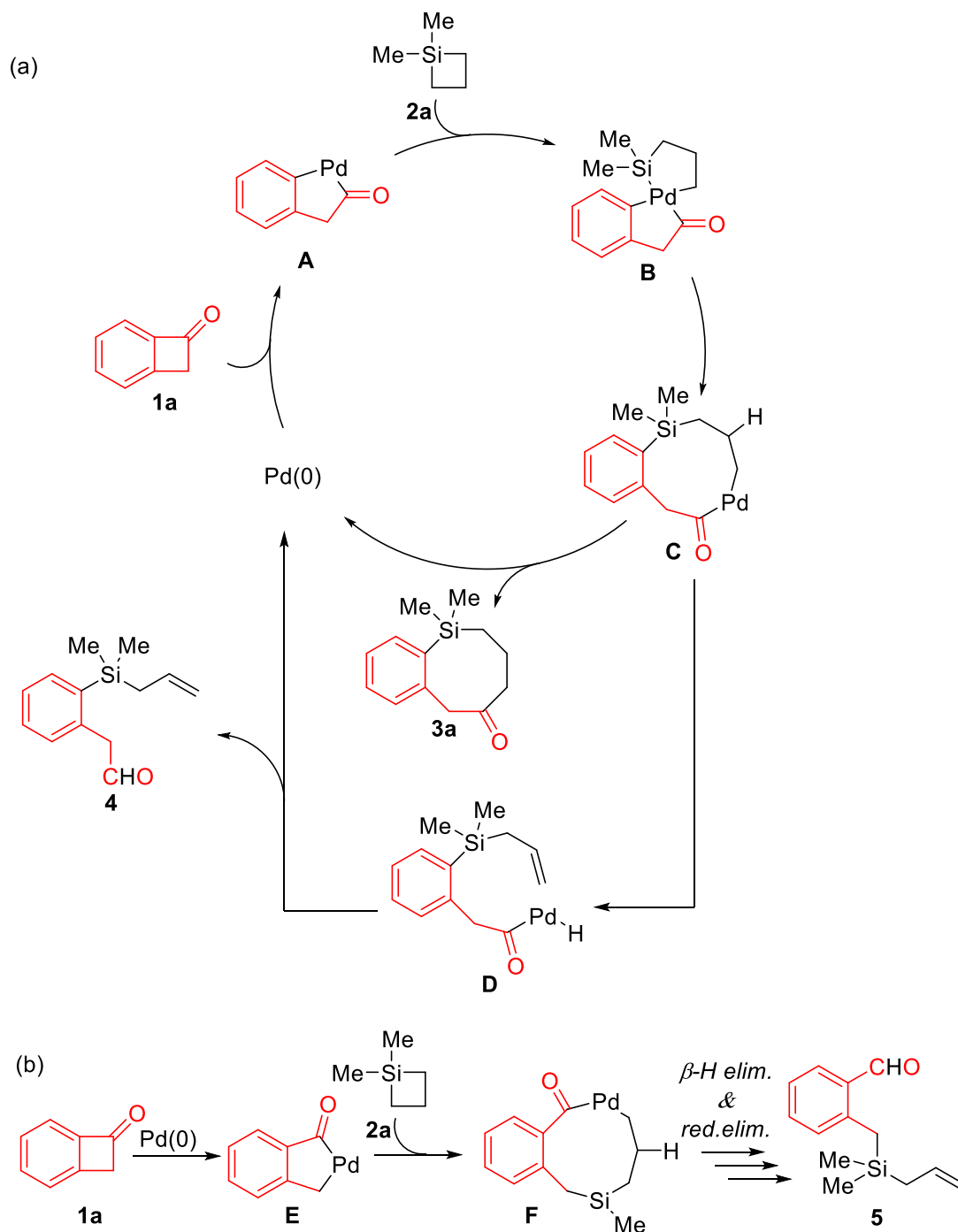
The formation of the aldehyde **4** as the byproduct may support the intermediacy of the palladacycle **C**. [16] Its formation can be justified by assuming that *β*-hydride elimination occurs with **C** and that reductive elimination follows. In case of the isocyanide ligand, the

intermediate **C** favors reductive elimination over *β*-hydride elimination, possibly because of the electron-accepting character of the isocyanide ligand if compared with trialkylphosphine ligands. The electron accepting isocyanides would facilitate the palladium center to be reduced. On the other hand, electron-donating trialkylphosphines would retard reductive elimination, allowing the Pd−C−C−H linkage with a greater chance to take a *syn*-periplanar conformation, which leads to the formation of **4** through *β*-hydride elimination. The formation of **5** can be accounted for by assuming that the palladacycle **E** is formed as the minor oxidative adduct at the elevated temperature and that a transmetallation/*β*-hydride elimination/reductive elimination pathway follows (Scheme 1b).

Listed in Table 1 were the results of the reaction using various benzocyclobutenones and silacyclobutanes. Benzocyclobutenones having an alkoxy or a fluoro substituent on the aromatic ring successfully gave the corresponding eight-membered silacycle **3b**−**3e**. α-Methylbenzocyclobutenone failed to participate the reaction. Silacyclobutanes with phenyl substituents on silicon were also eligible substrates. In the case of nonsymmetrical 2-phenylsilacyclobutane **2j**, the C(benzylic)−Si bond was site-selectively cleaved in preference to the sterically less-hindered C(methylene)−Si bond, furnishing the product **3j** in 70% yield.

To conclude, the author has developed the intermolecular σ-bond exchange reaction between C−C and C−Si σ-bonds. The σ-bonds between the group 14 elements contained in the four-membered ring substrates are site-selectively cleaved and exchanged by action of a palladium−isocyanide complex. The two four-membered rings are merged into an eight-membered skeleton in an atom-economical manner. The intermediate mechanistically assumed was isolated by a stoichiometric reaction of benzocyclobutenone with palladium(0). The present reaction provides a unique example of intermolecular cross metathesis-type reaction between covalent σ-bonds of low polarity.

Table 1. Scope of the σ-Bond Exchange Reaction[a]

3b 90%   **3c** 94%   **3d** 80%[c]

3e 71%[b]   **3f** 87%   **3g** 80%[b]

3h 86%[b]   **3i** 66%[b]   **3j** 70%

[a] Reaction conditions: CpPd(π-allyl) (2 mol %), *t*octyl isocyanide (8 mol %), toluene (1.6 M), 100 °C, 24 h. [b]Mesitylene instead of toluene, 160 °C. [c]0.67 M.

Experimental Section

General Methods

All reactions were carried out under nitrogen atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECZ400S/L1 (^{1}H at 400.44 MHz and ^{13}C at 100.69 MHz) and JNM-ECZ500R (^{1}H at 500.16 MHz and ^{13}C at 125.77 MHz). NMR data were obtained in CDCl$_3$ or C$_6$D$_6$. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm (CHCl$_3$), and 7.16 ppm (C$_6$D$_6$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.16 ppm (CDCl$_3$), and 128.06 ppm (C$_6$D$_6$). IR measurements were performed on FTIR SHIMADZU Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter. High-resolution mass spectra were recorded on a Thermo Scientific Exactive (APCI, EI) spectrometer. Preparative thin-layer chromatography was performed on silica gel plates with PF254 indicator (Merck). Flash column chromatography was performed with diol-silica gel DIOL MB 100–40/75 (Fuji Silysia Chemical Ltd.) or silica gel 60N (Kanto).

Materials

Toluene and Mesitylene were distilled from sodium/benzophenone ketyl. CpPd(π-allyl)[17], and Pd(^{t}octyl isocyanide)$_2$[13b] were prepared according to the literature procedures. ^{t}Octyl isocyanide, and dimethylsilacyclobutane **2a** was obtained from the commercial sources. Other silacyclobutanes[18,19] and all benzocyclobutenones[3o, 20, 21] were prepared according to the literature procedures. Other chemicals were obtained from commercial suppliers.

A Typical Procedure for σ-Bond Exchange between a C–C Bond of Benzocyclobutenone and a C–Si Bond of Silacyclobutane

| **1a** | **2a** | **3a** | **4** | **5** |
| 1.6 M | (2.0 equiv) | 85% | < 1% | < 1% |
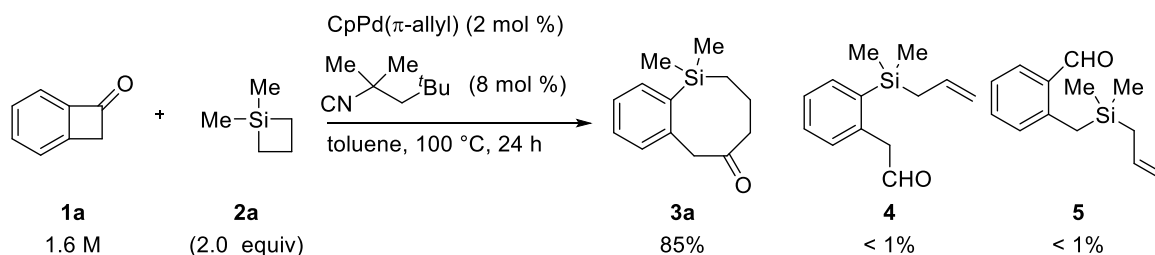
To a solution of CpPd(π-allyl) (0.86 mg, 0.0040 mmol, 2 mol %) and ^{t}octyl isocyanide (2.3 mg, 0.016 mmol, 8 mol %) in toluene (1 mL) was added benzocyclobutenone **1a** (23.3 mg, 0.20 mmol) and silacyclobutane **2a** (40.4 mg, 0.40 mmol, 2.0 equiv). The reaction mixture was stirred at 100 °C for 24 h. After being cooled to room temperature,

the reaction mixture was passed through a pad of Florisil® with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to produce **3a** and a trace amount of **4** and **5** (< 1%). The residue was purified by flash column chromatography with diol-silica gel (hexane/ethyl acetate = 20/1) to give benzosilaoctenone **3a** (36.4 mg, 0.17 mmol, 85%).
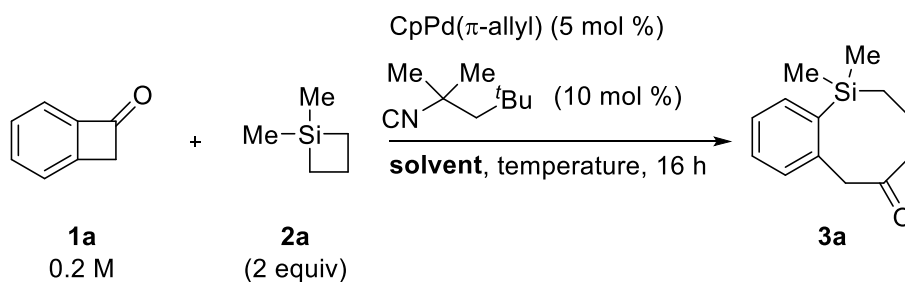
Screening of Solvents

Table 2. Screening of Solvents

Entry	Solvent	Temperature / °C	NMR yield 3a /%
1	toluene	100	90[a]
2	CHCl$_3$	60	0
3	THF	60	5
4	CH$_3$CN	80	35
5	MeOH	100	0
6	DMSO	100	27
7	DMF	100	22

[a]isolated yield

Screening of Ligands
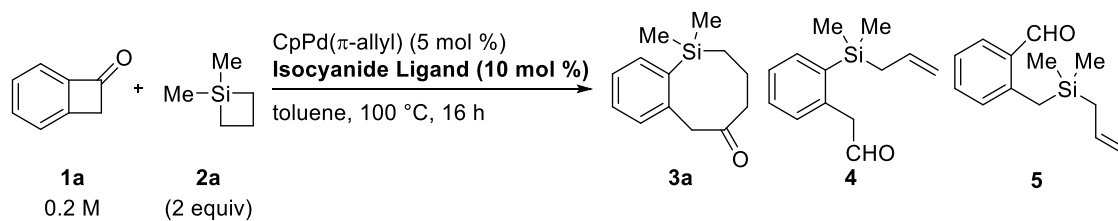
Table 3. Screening of Isocyanide Ligands

Entry	Ligand	NMR yield		
		3a /%	**4** /%	**5** /%
1	1-Adamantyl isocyanide	55	< 1	< 1
2	Cyclohexyl isocyanide	45	< 1	< 1
3	^{n}Butyl isocyanide	19	0	< 1
4	^{t}Butyl isocyanide	45	< 1	< 1
5	2,6-Xylyl isocyanide	45	<1	< 1
6	Benzyl isocyanide	2	0	0
7	^{t}Octyl isocyanide	90[a]	< 1	< 1

[a]isolated yield

Adamantyl isocyanide   Cyclohexyl isocyanide ^{n}Butyl isocyanide

^{t}Butyl isocyanide   2,6-Xylyl isocyanide   Benzyl isocyanide

17
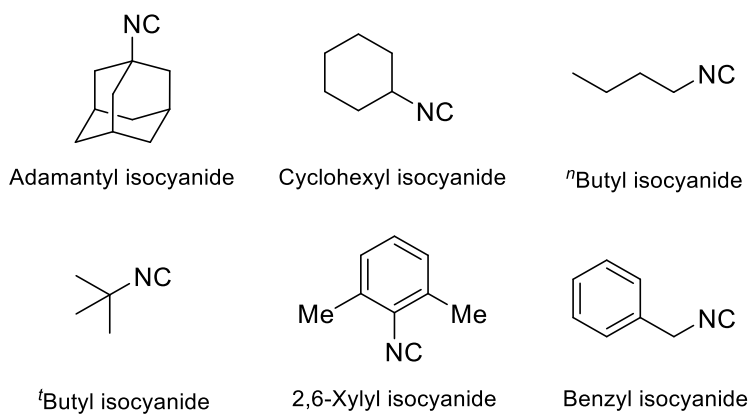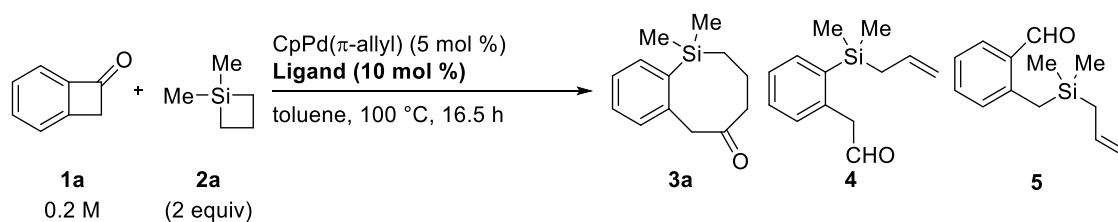
Table 4. Screening of Other Ligands

Entry	Ligand	NMR yield		
		3a /%	**4** /%	**5** /%
1	PPh$_3$	32	33	8
2	P^{t}Bu$_3$	6	38	2
3	PMe$_3$ (20 mol %)	6	56	< 1
4	P(1-Ad)$_2$(^{n}Bu)^a	< 1	< 1	< 1
5	dppf (5 mol %)	11	2	36
6	dppe (5 mol %)	1	0	< 1
7	IPr	1	< 1	< 1

^{a}16 h

Mechanistic Studies

Pd isocyanide complex **6** was synthesized from CpPd(π-allyl) and ^{t}octyl isocyanide[13b]
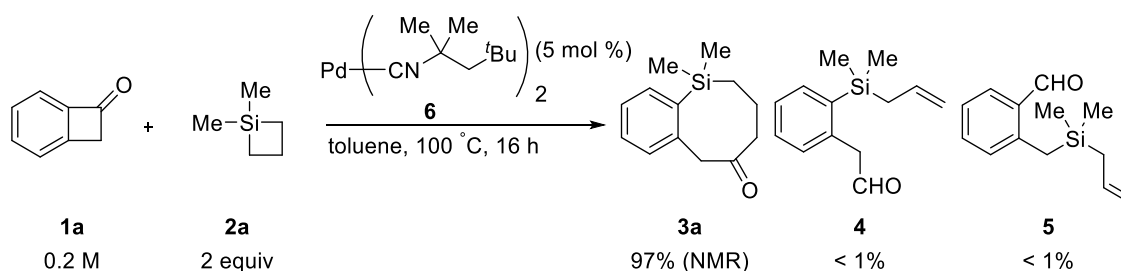
To a solution of CpPd(^{t}octyl isocyanide)$_2$ **6** (3.8 mg, 0.0099 mmol, 5 mol %) in toluene (1 mL) was added benzocyclobutenone **1a** (23.6 mg, 0.20 mmol) and silacyclobutane **2a** (40.7 mg, 0.41 mmol, 2 equiv). The reaction mixture was stirred at 100 °C for 16 h. After cooled to room temperature, the reaction mixture was passed through a pad of Florisil® with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford **3a** in 97 % NMR yield. The trace amount of **4** and **5** (< 1%) were also produced.
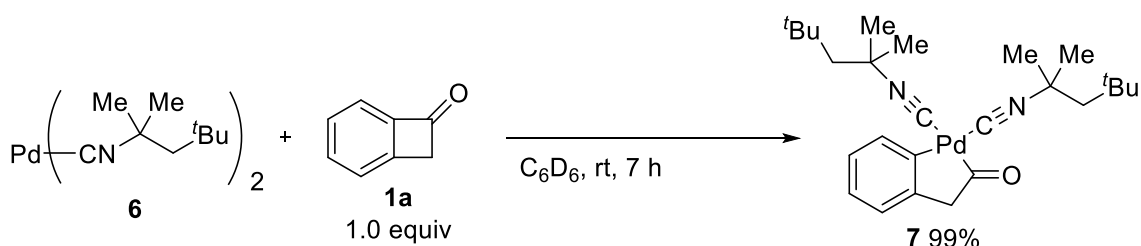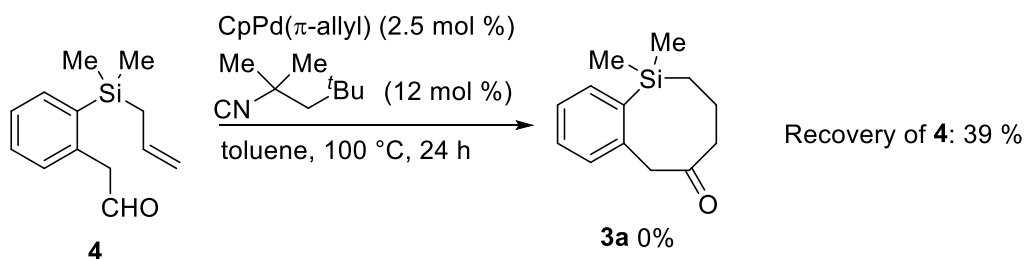
To a solution of CpPd(^{t}octyl isocyanide)$_2$ **6** (75.5 mg, 0.20 mmol,) in C$_6$D$_6$ (0.8 mL) was added benzocyclobutenone **1a** (24.1 mg, 0.20 mmol, 1.0 equiv). After 7 h, evaporation of the resulting solution gave **7** (101.4 mg, 0.20 mmol, 99%)
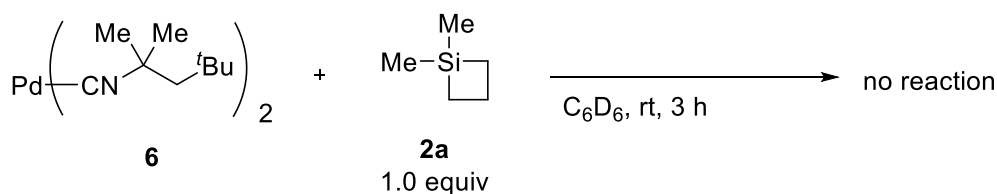
To a solution of Pd(^{t}octyl isocyanide)$_2$ **6** (39.0 mg, 0.10 mmol) in C$_6$D$_6$ (0.8 mL) was added dimethylsilacyclobutane **2a** (10.0 mg, 0.10 mmol, 1.0 equiv). The reaction mixture was stirred at room temperature. After 3 h, no reaction occurred.
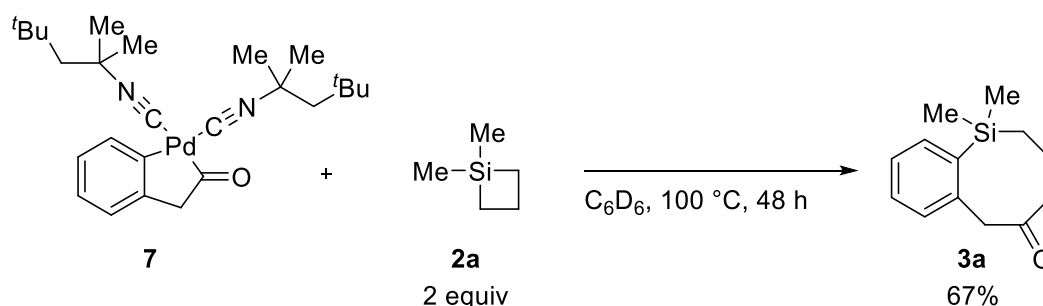
To a solution of Pd complex **7** (101.4 mg, 0.20 mmol) in C$_6$D$_6$ (0.8 mL) was added dimethylsilacyclobutane **2a** (40.1 g, 0.40 mmol, 2.0 equiv). The reaction mixture was stirred at room temperature. After 7.5 h, only trace amount of **3a** was produced (< 1%) and most starting materials remained. Then, the reaction mixture was heated at 100 °C. After 48 h, the reaction mixture was passed through a pad of Florisil® with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure. The residue was analyzed by ^{1}H NMR using 1,1,2,2-tetrachloroethane as an internal standard. The silacycle **3a** was produced in 67 % NMR yield. Other products were **4** (< 1%), **5** (< 1%), and a dimer of silacyclobutane[22] (26% NMR yield).

Recovery of **4**: 39 %

3a 0%

4

To a solution of CpPd(π-allyl) (0.41 mg, 0.0019 mmol, 2.5 mol %) and ᵗoctyl isocyanide (1.3 mg, 0.0095 mmol, 12 mol %) in toluene (0.062 mL) was added 2-(2-allyldimetylsilyl)phenyl)acetaldehyde **4** (16.6 mg, 0.076 mmol). The reaction mixture was stirred at 100 °C for 24 h. After being cooled to room temperature, the reaction mixture was passed through a pad of Florisil® with ethyl acetate as the eluent. The residue was analyzed by ¹H NMR. **3a** was not detected, and 39 % of **4** remained.

Possible Mechanisms[15]

Several mechanistic scenarios are conceivable for the formation of **3a**. Listed below are possible pathways that are consistent with the outcomes of stoichiometric reactions.

Scheme 2. A Reaction Mechanism via Four-membered Cyclic Interaction between Ar–Pd and Si–C(sp³)

Four-membered cyclic interaction
between Ar–Pd and Si–C(sp³)
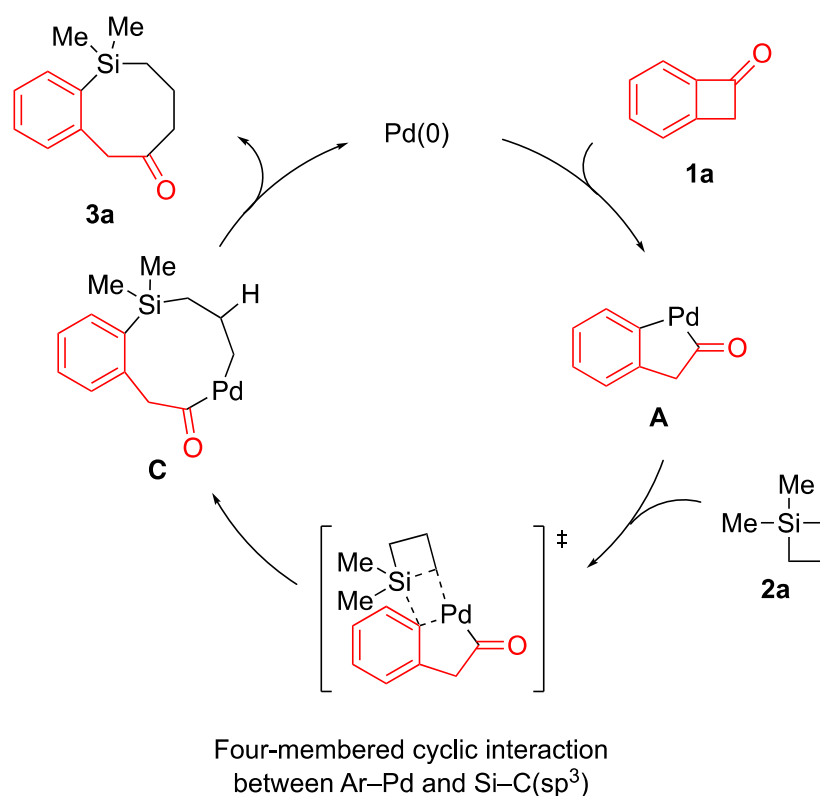
**Scheme 3.** A Reaction Mechanism via Intermediate G
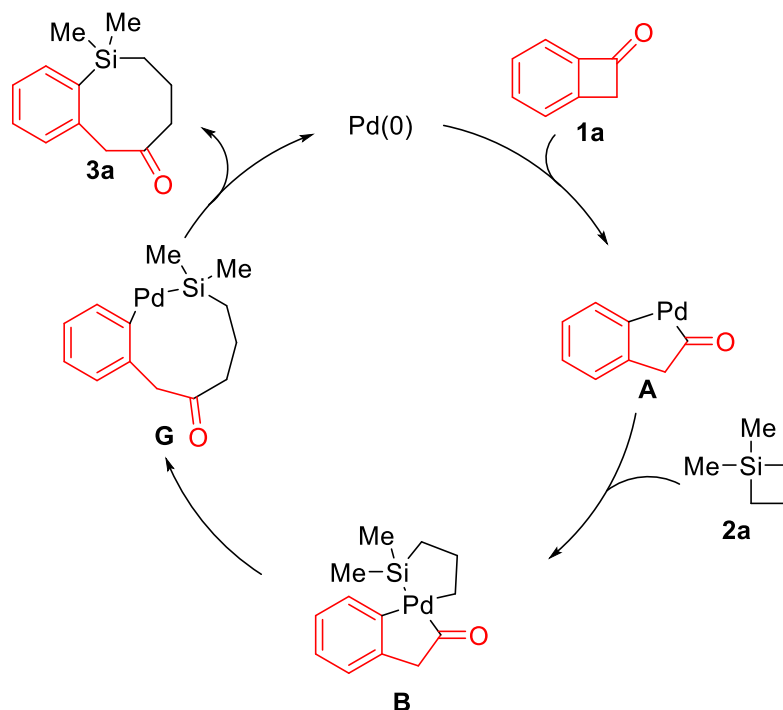
    Although the intermediate **B** possibly undergoes reductive elimination forming a Si–C(carbonyl) bond, such a byproduct was not observed. This is presumably due to the electronic reasons; electronically positive Si would prefer electronically negative Ar carbon over electronically positive carbonyl carbon.

Spectroscopic Data of 3a-3j and 4-7

3a
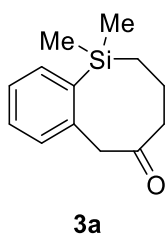
    ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.33 (s, 6H), 1.00-1.03 (m, 2H), 1.99-2.05 (m, 2H), 2.43 (t, J = 6.4 Hz, 2H), 3.81 (s, 2H), 7.19 (dd, J = 7.6, 0.8 Hz, 1H), 7.26 (td, J = 7.2, 1.2 Hz, 1H), 7.32 (td, J = 7.2, 1.6 Hz, 1H), 7.54 (dd, J = 7.2, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = - 1.4, 17.0, 20.0, 42.1, 50.6, 126.5, 129.7, 130.5, 135.1, 139.2, 141.0, 212.0; HRMS(APCI$^+$): Calcd for C$_{13}$H$_{19}$OSi, [M+H]$^+$ 219.1200, Found m/z 219.1191; IR (ATR): 1699, 1248, 824, 737 cm^{-1}.
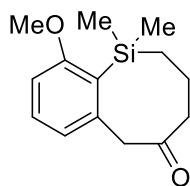
3b

^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.31 (s, 6H), 1.17 (t, *J* = 7.2 Hz, 2H), 1.96 (quint., *J* = 7.2 Hz, 2H), 2.51 (t, *J* = 6.8 Hz, 2H), 3.81 (s, 3H), 3.83 (s, 2H), 6.74 (d, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.2, 17.9, 20.6, 40.8, 54.2, 55.3, 108.8, 124.1, 127.1, 130.8, 142.6, 165.2, 212.0; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{21}$O$_2$Si, [M+H]$^+$ 249.1305, Found m/z 249.1294; IR (ATR): 1697, 1456, 1242, 795 cm^{-1}.


3c
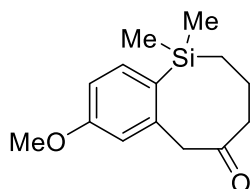
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.30 (s, 6H), 0.96-1.00 (m, 2H), 1.96-2.02 (m, 2H), 2.42 (t. *J* = 6.4 Hz, 2H), 3.78 (s, 2H), 3.80 (s, 3H), 6.75 (d, *J* = 2.8 Hz, 1H), 6.81 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.3, 17.1, 20.0, 42.0, 50.7, 55.2, 112.1, 116.3, 129.9, 136.6, 142.7, 160.8, 211.8; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{21}$O$_2$Si, [M+H]$^+$ 249.1305, Found m/z 249.1294; IR (ATR): 1699, 1593, 1240, 1078, 822 cm^{-1}.


3d
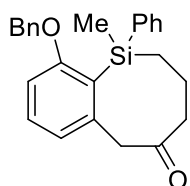
^{1}H NMR (400 MHz, CDCl$_3$): δ =0.53 (s, 3H), 1.25-1.43 (m, 2H), 1.80-2.01 (m, 2H), 2.48-2.54 (m, 1H), 2.62-2.69 (m, 1H), 3.89 (d, *J* = 15.6 Hz, 1H), 4.03 (d, *J* =16.0 Hz, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.90 (d, *J* = 11.6 Hz, 1H), 6.81-6.91 (m, 4H), 7.18-7.40 (m, 9H); ^{13}C NMR (125 MHz, CDCl$_3$): δ = -2.7, 17.9, 20.4, 40.9, 54.0, 70.1, 109.7, 124.3, 124.6, 127.4, 127.57, 127.59, 128.2, 128.6, 131.3, 133.5, 136.3, 138.5, 143.6, 164.3, 211.8; HRMS(APCI$^+$): Calcd for C$_{25}$H$_{27}$O$_2$Si, [M+H]$^+$ 387.1775, Found m/z 387.1765;

IR (ATR): 1697, 1244, 696 cm^{-1}.

3e
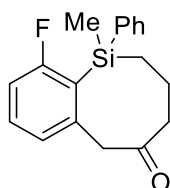
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.67 (d, J = 3.6 Hz, 3H), 1.27-1.34 (m, 1H), 1.43-1.51 (m, 1H), 1.89-2.06 (m, 2H), 2.41-2.47 (m, 1H), 2.59-2.66 (m, 1H), 3.77 (d, J = 16.0 Hz, 1H), 3.99 (d, J = 15.6 Hz, 1H), 6.94 (t, J = 9.2 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 7.32-7.48 (m, 6H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.9 (d, J = 7.7 Hz), 16.9, 20.3, 41.2, 52.9, 114.1 (d, J = 26.8 Hz), 123.1 (d, J = 26.9 Hz), 127.2 (d, J = 1.9 Hz), 128.1, 129.5, 132.1 (d, J = 9.5 Hz), 133.7, 136.8, 143.7 (d, J = 9.6 Hz), 168.2 (d, J = 240.5 Hz), 211.1; HRMS(APCI$^+$): Calcd for C$_{18}$H$_{20}$FOSi, [M+H]$^+$ 299.1262, Found m/z 299.1258; IR (ATR): 1699, 1227, 799, 698 cm^{-1}.


3f
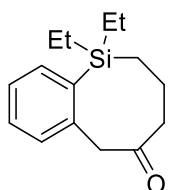
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.81-0.89 (m, 4H), 0.95-1.00 (m, 6H), 1.06-1.10 (m, 2H), 1.97-2.04 (m, 2H), 2.44 (t, J = 6.4 Hz, 2H), 3.80 (s, 2H), 7.18 (dd, J = 7.2, 0.8 Hz, 1H), 7.25 (td, J = 7.2, 1.2 Hz, 1H), 7.31 (td, J = 7.2, 1.6 Hz, 1H), 7.52 (dd, J = 7.2, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 5.1, 7.6, 12.6, 20.2, 41.8, 51.7, 126.3, 129.6, 130.7, 135.6, 137.5, 141.7, 212.1; HRMS(APCI$^+$): Calcd for C$_{15}$H$_{23}$OSi, [M+H]$^+$ 247.1513, Found m/z 247.1502; IR (ATR): 1699, 710 cm^{-1}.
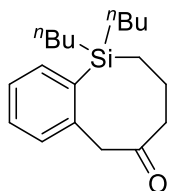

3g

^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.80-0.90 (m, 10H), 1.08 (t, J = 6.8 Hz, 2H), 1.24-1.39 (m, 8H), 1.96-2.03 (m, 2H), 2.44 (t, J = 6.4 Hz, 2H), 3.80 (s, 2H), 7.17 (d, J = 7.2

Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.2 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 13.4, 13.6, 13.8, 20.3, 26.1, 26.8, 41.7, 51.8, 126.3, 129.5, 130.7, 135.5, 138.0, 141.6, 212.0; HRMS(APCI$^+$): Calcd for C$_{19}$H$_{31}$OSi, [M+H]$^+$ 303.2139, Found m/z 303.2132; IR (ATR): 1701, 1196, 737 cm^{-1}.
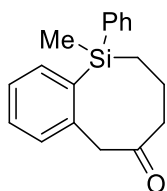

3h

^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.58 (s, 3H), 1.11-1.19 (m, 1H), 1.46-1.53 (m, 1H), 1.97-2.15 (m, 2H), 2.47 (t, J = 6.8 Hz, 2H), 3.61 (d, J = 14.8 Hz, 1H), 3.94 (d, J = 14.8 Hz, 1H), 7.27-7.46 (m, 8H), 7.55 (d, J = 7.6 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$): δ = -2.0, 15.7, 19.6, 42.1, 50.1, 126.4, 128.0, 129.3, 130.1, 130.5, 134.1, 136.2, 136.3, 136.9, 141.5, 211.4; HRMS(APCI$^+$): Calcd for C$_{18}$H$_{21}$OSi, [M+H]$^+$ 281.1356, Found m/z 281.1346; IR (ATR): 1697, 1427, 1109, 795, 698 cm^{-1}.
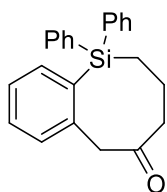
3i

^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.61-1.65 (m, 2H), 2.13-2.18 (m, 2H), 2.54 (t, J = 5.2 Hz, 2H), 3.76 (s, 2H), 7.17-7.27 (m, 2H), 7.32-7.49 (m, 12H); ^{13}C NMR (100 MHz, CDCl$_3$): δ =14.6, 19.5, 43.0, 49.4, 126.4, 128.3, 129.8, 130.5, 130.8, 134.9, 135.1, 135.4, 138.2, 141.9, 211.3; HRMS(APCI$^+$): Calcd for C$_{23}$H$_{23}$OSi, [M+H]$^+$ 343.1513, Found m/z 343.1500; IR (ATR): 1713, 1427, 1111, 700 cm^{-1}.

3j
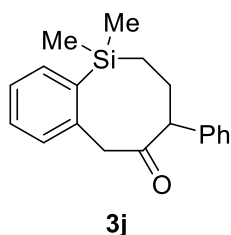
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.32 (s, 3H), 0.40 (s, 3H), 0.91-1.00 (m, 1H), 1.16-1.24 (m, 1H), 2.22-2.30 (m, 1H), 2.41-2.50 (m, 1H), 3.53 (d, *J* = 16.4 Hz, 1H), 3.96 (dd, *J* = 11.6, 5.2 Hz, 1H), 4.09 (d, *J* = 16.4 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.23-7.38 (m, 7H), 7.56 (dd, *J* = 7.2, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.6, -1.3, 15.0, 27.3, 48.6, 58.1, 126.5, 127.3, 128.1, 128.7, 129.8, 131.0, 135.1, 138.9, 139.3, 141.3, 211.1; HRMS(APCI$^+$): Calcd for C$_{19}$H$_{23}$OSi, [M+H]$^+$ 295.1513, Found m/z 295.1502; IR (ATR): 1703, 1125, 741, 704 cm^{-1}.


4
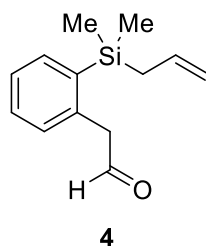
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.34 (s, 6H), 1.81 (d, *J* = 8.0 Hz, 2H), 3.82 (d, *J* = 2.0 Hz, 2H), 4.84-4.90 (m, 2H), 5.68-5.79 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.30 (td, *J* = 7.2, 0.8 Hz, 1H), 7.39 (td, *J* = 7.6, 1.6 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 1H), 9.74 (t, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.5, 24.3, 51.1, 114.2, 126.9, 130.0, 130.5, 134.3, 135.8, 137.7, 138.4, 200.1; HRMS(APCI$^+$): Calcd for C$_{13}$H$_{19}$OSi, [M+H]$^+$ 219.1208, Found m/z 219.1197; IR (ATR): 1724, 1630, 1258, 835 cm^{-1}.


5
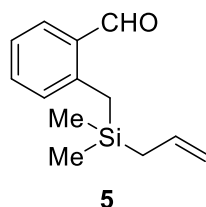
^{1}H NMR (400 MHz, CDCl$_3$): δ = -0.05 (s, 6H), 1.55 (dt, *J* = 8.0, 1.2 Hz, 2H), 2.73 (s, 2H), 4.83-4.85 (m, 1H), 4.87-4.89 (m, 1H), 5.69-5.78 (m, 1H), 7.09 (dt, *J* = 7.6, 0.4 Hz, 1H), 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 7.43 (td, *J* = 7.6, 1.6 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.2 Hz, 1H), 10.16 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -3.7, 22.4, 23.1, 113.7, 124.8,

131.0, 132.9, 133.4, 133.5, 134.5, 144.1, 193.2; HRMS(APCI[+]): Calcd for $C_{13}H_{19}OSi$, [M+H][+] 219.1208, Found m/z 219.1194; IR (ATR): 1695, 1601, 833 cm^{-1}.


6
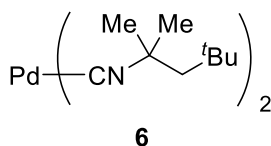
^{1}H NMR (400 MHz, C_6D_6): δ = 1.15 (br, 18H), 1.48 (br, 12H), 1.62 (br, 4H); ^{13}C NMR (125 MHz, C_6D_6): δ = 31.7, 31.8, 32.0, 54.7, 58.7, 156.4; IR (ATR): 2106, 1778, 1211 cm^{-1}; Anal calcd for $C_{18}H_{34}N_2Pd$: C, 56.17; H, 8.90; N, 7.28; Found; C, 56.01; H, 9.11; N, 7.24.

7
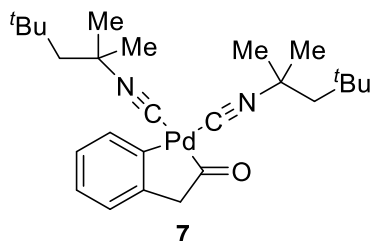
^{1}H NMR (400 MHz, C_6D_6): δ = 0.93 (br, 18H), 1.12 (br, 12H), 1.23 (br, 4H), 4.21 (s, 2H), 7.28 (td, *J* = 7.2, 1.6 Hz, 1H), 7.34 (tdt, *J* = 7.2, 1.6, 0.8 Hz, 1H), 7.40 (dtd, *J* = 7.2, 1.6, 0.8 Hz, 1H), 8.02 (dd, *J* = 7.2, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6): δ = 30.7, 31.0, 31.7, 53.2, 59.2, 72.9, 121.9, 124.5, 126.0, 140.1, 148.0, 163.1, 239.1, two carbons of isocyanides are missing due to the quadrupolar relaxation; Anal calcd for $C_{26}H_{40}N_2OPd$: C, 62.08; H, 8.02; N, 5.57; Found; C, 62.32; H, 8.31; N, 5.95.

Synthesis of Benzocyclobutenones 1a-1e

Benzocyclobutenone **1a-1e** were synthesized according to the literature[3o, 20, 21]
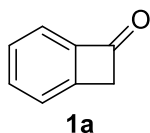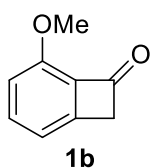
1a

Spectral data were in agreement with literature values.[23]

1b

Spectral data were in agreement with literature values.[20]

1c

Spectral data were in agreement with literature values. [24]

1d

Spectral data were in agreement with literature values. [21]

1e
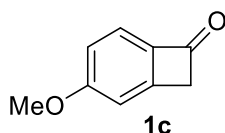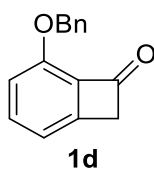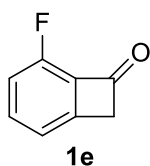
Spectral data were in agreement with literature values.[20]

Synthesis of Silacyclobutane 2b-2e

Silacyclobutane **2b-2e** were synthesized according to the literature.[18,19]

2b
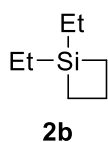
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.70 (q, *J* = 8.0 Hz, 4H), 0.97 (t, *J* = 8.0 Hz, 4H), 1.03 (t, *J* = 8.0 Hz, 6H), 2.05 (sept, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 6.7, 7.3, 11.3, 18.5; HRMS(EI$^+$): Calcd for C$_7$H$_{16}$Si, [M]$^+$ 128.1021, Found m/z 128.1017; IR (ATR): 1458, 1118, 725 cm^{-1}.
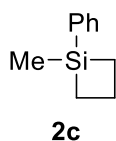
Ph
|
Me—Si—⌐
       └⌐

2c

Spectral data were in agreement with literature values.[25]

Ph
|
Ph—Si—⌐
       └⌐

2d

Spectral data were in agreement with literature values.[25]

Me
|
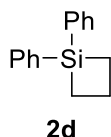Me—Si—⌐
       └⌐
Ph

2e
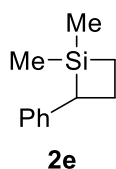
Spectral data were in agreement with literature values.[19]

Details for X-ray Crystallography of 3i and 7

Single crystal of **3i** was obtained from a hexane/dichloromethane solution. The data was collected on a Rigaku R-AXIS with graphite-monochromated Mo Kα radiation. All the following procedure for analysis, Yadokari-XG[26] was used as a graphical interface. The structure was solved by direct methods with SHELXL-2013[27] and refined by full-matrix least-squares techniques against F2 (SHELXL-2013).[27] All non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms were calculated, and their contributions in structural factor calculations were included.

Single crystal of **7** was obtained from a hexane/toluene solution. The data was collected on a Rigaku Saturn 724+ with graphite-monochromated Mo Kα radiation. All the following procedure for analysis, CrystalClear was used as a graphical interface. The structure was solved by direct methods with SHELXL-97[27] and refined by full-matrix least-squares techniques against F2 (SHELXL-97).[27] All non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms were calculated, and their contributions in structural factor calculations were included.
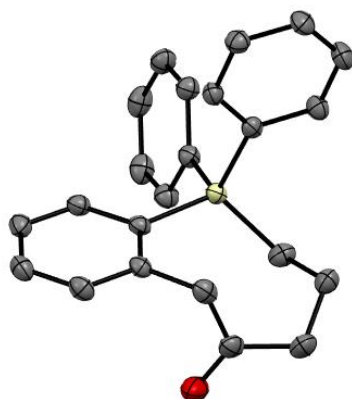
Figure 2. ORTEP Diagram of **3i**

Table 5. Crystallographic Data and Structure Refinement Details for **3i**

3i	
formula	$C_{23}H_{22}OSi$
fw	342.49
T (K)	100(2)
cryst syst	triclinic
space group	*P*-1
a, (Å)	9.8592(5)
b, (Å)	10.2085(6)
c, (Å)	10.9817(7)
α, (Å)	64.914(2)
β, (Å)	78.901(2)
γ, (Å)	65.9140(14)
V, (Å^3)	913.62(9)
Z	2
Dcalc, (g/cm^3)	1.245
μ (mm^{-1})	0.136
F (000)	364
cryst size	0.40×0.20×0.20
radiation λ (Å)	0.71075
reflns collected	8954
indep reflns / Rint	4159/0.0184
params	226
GOF on F^2	1.102
R1, wR2 [I>2σ(I)]	0.0426, 0.1264
R1, wR2 (all data)	0.0564, 0.1687
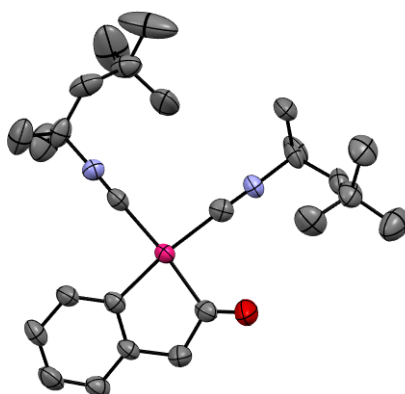
Figure 3. ORTEP Diagram of **7**

Table 6. Crystallographic Data and Structure Refinement Details for **7**

	7
formula	$C_{26}H_{40}N_2OPd$
fw	503.00
T (K)	193(2)
cryst syst	monoclinic
space group	$P2_1/c$
a, (Å)	6.411(3)
b, (Å)	15.344(7)
c, (Å)	27.897(13)
α, (Å)	90.00
β, (Å)	96.217(7)
γ, (Å)	90.00
V, (Å^3)	2728(2)
Z	4
Dcalc, (g/cm^3)	1.225
μ (mm^{-1})	0.697
F (000)	1056
cryst size	0.20×0.20×0.20
radiation λ (Å)	0.71075
reflns collected	21634
indep reflns / Rint	6244/0.1480
params	281
GOF on F^2	1.014
R1, wR2 [I>2σ(I)]	0.0843, 0.1729
R1, wR2 (all data)	0.1546, 0.2104

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Chapter 2

Site- and Regio-selective Incorporation of Carbon Dioxide into the C(sp^2)–Si Bond of Benzosilacyclobutenes

Abstract

A reaction of benzosilacyclobutenes with carbon dioxide is catalyzed by a nickel complex having an *N*-heterocyclic carbene ligand. Carbon dioxide inserts into the C(sp^2)–Si bond in a site- and regio-selective manner to form a carbon–carbon bond, furnishing benzoic acid derivatives.

Introduction

Carbon dioxide is an inert molecule, but its carbon is electrophilic enough to be able to accommodate organometallic reagents of considerable polarity like organomagnesiums. The C–Si bond of organosilicon compounds is not so much polarized in electronics, and thus, is far less reactive towards carbon dioxide than other polar organometallic compounds. Organosilicon compounds which directly fix carbon dioxide at the C–Si bonds are limited to a (phosphacyclopentadienyl)silane,[1] a zincated pyridylsilane,[2] a silene,[3] and a trimethylsilyl cation–*N*-heterocyclic carbene adduct.[4] There are organosilicon compounds which can add to carbon dioxide when assisted by a stoichiometric amount of aluminum Lewis acids[5] or cesium fluoride.[6-8] Some of the fluoride-assisted reactions necessitate a further assistance of a silver-[7] and a copper catalyst.[8] Herein reported is a unique example of a reaction incorporating carbon dioxide into organosilicon compounds through a nickel catalysis,[9] which dispenses with the use of a stoichiometric amount of additives. Carbon dioxide directly inserts into the $C(sp^2)$–Si bond of benzosilacyclobutenes in a site- and regio-selective manner to furnish benzoic acid derivatives.

Results and Discussion

Benzosilacyclobutene exhibits unique reactivities which ordinary organosilicon compounds don't show, being driven by the relief of the ring strain of the four-membered ring.[10,11] For example, the $C(sp^2)$–Si bond undergoes oxidative addition onto a cobalt(I) complex.[11h] 1,2-Addition of the $C(sp^2)$–Si bond across the carbonyl double bond of an aldehyde is promoted by a nickel–phosphine complex.[10e] This study commenced with screening ligands for a nickel(0) complex in a reaction of naphthosilacyclobutene **1a** with an atmospheric pressure of carbon dioxide in toluene at 90 °C for 3.5 h (Table 1). Naphthosilacyclobutene **1a** was used instead of simple benzosilacyclobutene to avoid the potential production of phenylacetic acid, which is illegal. The reaction was quenched by adding 2 N HCl, and the reaction mixture was purified by acid-base extraction. Almost no carboxylated product was formed when phosphine ligands such as PPh₃, PCy₃, and DPPE were employed (entries 1-5). Nitrogen ligands such as 2,2'-bipyridines were also totally ineffective (entries 6-8). On the other hand, the use of IMes successfully gave benzoic acid **2a** in 32% yield (entry 9). The yield was improved to 34% when IPr was used in place of IMes (entry 10). SIPr (entry 11) and IʳBu (entry 12) gave inferior results. Finally, **2a** was obtained in 70% yield when the reaction was carried out at 160 °C using mesitylene as the solvent and the reaction time was elongated to 5.5 h (entry 13).

Table 1. Incorporation of Carbon Dioxide into **1a**[a]
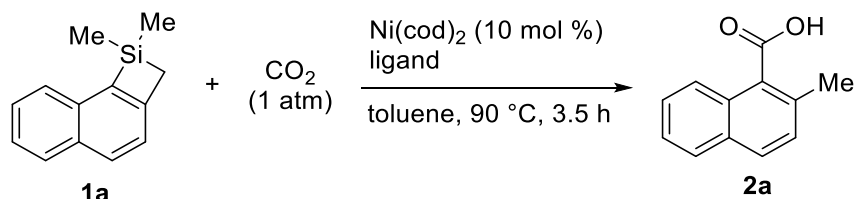
Entry	Ligand (mol %)	Yield of **2a** / %
1	PPh₃ (20)	0
2	PCy₃ (20)	trace
3	DPPE (10)	0
4	DPPF (10)	0
5	*rac*-BINAP (20)	0
6	2,2'-bipyridine (10)	0
7	2-phenylpyridine (10)	0
8	dtbpy (10)	0
9	IMes (20)	32
10	IPr (20)	34
11	SIPr (20)	18
12	I^{t}Bu (20)	2
13[b]	IPr (10)	70[c]

[a] Reaction conditions: **1a** (0.10 mmol), $Ni(cod)_2$ (0.01 mmol, 10 mol %), ligand (the amount is shown in table), toluene (2.0 mL), carbon dioxide (1 atm, balloon), 90 °C, 3.5 h. [b] Mesitylene instead of toluene, 160 °C, 5.5 h. [c] Isolated yields. DPPE = 1,2-bis(diphenylphosphino)ethane, DPPF = 1,1'-bis(diphenylphosphino)ferrocene, BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, dtbpy = 4,4'-di(*tert*-butyl)-2,2'-bipyridine, IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene, IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene, I^{t}Bu = 1,3-di(*tert*-butyl)imidazol-2-ylidene.

Several control experiments were conducted to gain mechanistic insights. No carboxylated product was formed when **1a** was heated at 160 °C in the presence of only IPr without $Ni(cod)_2$. This result indicates that the incorporation reaction of carbon dioxide is promoted by a nickel complex rather than the nucleophilic catalysis of IPr.[12] When the reaction was quenched after 1 h and the mixture was analyzed by ^{1}H NMR using CDCl₃ as the solvent, silalactone **3a** (52%) was produced in addition to the

carboxylic acid **2a** (23%) (Eq 1). Subsequent purification of the mixture by GPC followed by removal of the solvent under vacuum gave white solids. IR and elemental analysis revealed the solid was dicarboxylic acid **3a'**, which was a siloxane dimer of the silalactone **3a**. When the dicarboxylic acid **3a'** was dissolved in CDCl$_3$, the silalactone **3a** was re-generated through hydrolysis induced by a water impurity. The carboxylic acid **2a** was not formed upon simple heating of the isolated **3a'** at 160 °C and the treatment with 2 N HCl under the quenching conditions. On the other hand, heating **3a'** in the presence of a catalytic amount of IPr (10 mol %) at 160 °C for 5.5 h induced its desilylation to afford **2a** in 85% yield (Eq 2). These results indicate desilylation occurred with the assistance of IPr.
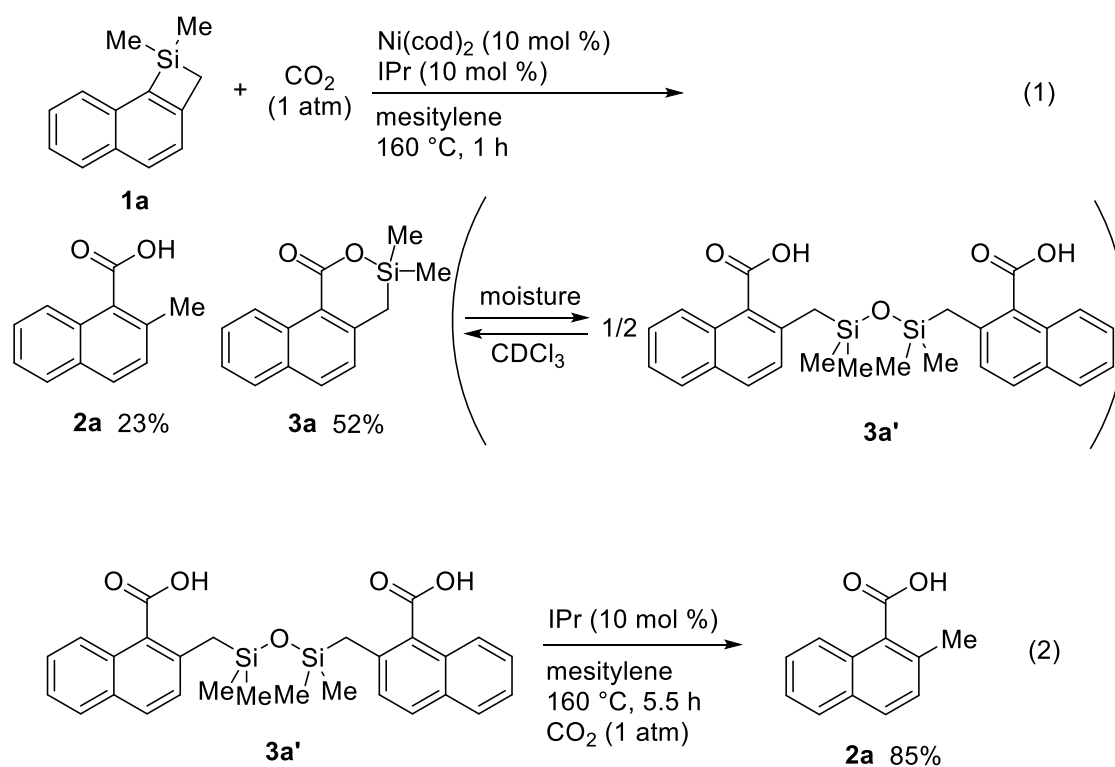
The five-membered derivative 1-silaindane **4** (Figure 1) and the silacyclobutane **5** lacking the fused benzene ring were subjected to the identical reaction conditions. However, no carboxylation reaction occurred. These results suggest that release of the ring strain of the four-membered ring and π-coordination at the ipso carbon of the benzene ring (vide infra) are key requisites for the carboxylation reaction.
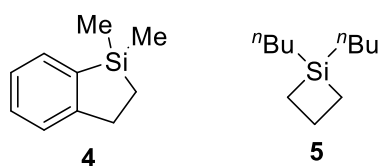
Figure 1. Other Silacyclic Compounds Examined

Shown in Scheme 1 is one of the possible mechanistic scenario for the incorporation of carbon dioxide into the $C(sp^2)$–Si bond of **1a**. Initially, carbon dioxide coordinates to the nickel(0) center with its π-bond to produce the π-complex **A**, which is analogous to the Aresta's complex.[14,15] The π-complex **A** can be regarded as the oxanickellacyclopropane species **A'** consisting of the nickel–carbon and nickel–oxygen σ-bonds. Transmetalation occurs at the nickel–oxygen bond of **A'** and the aromatic carbon–silicon bond of **1a** in a site- and regio-selective manner to generate the seven-membered nickellacycle **C**. The site-selectivity can be ascribed to the interaction of the nickel center with the π-orbital on the ipso carbon of **1a**. Reductive elimination follows to give the silalactone **3a**.[16]

Scheme 1. Possible Reaction Mechanism
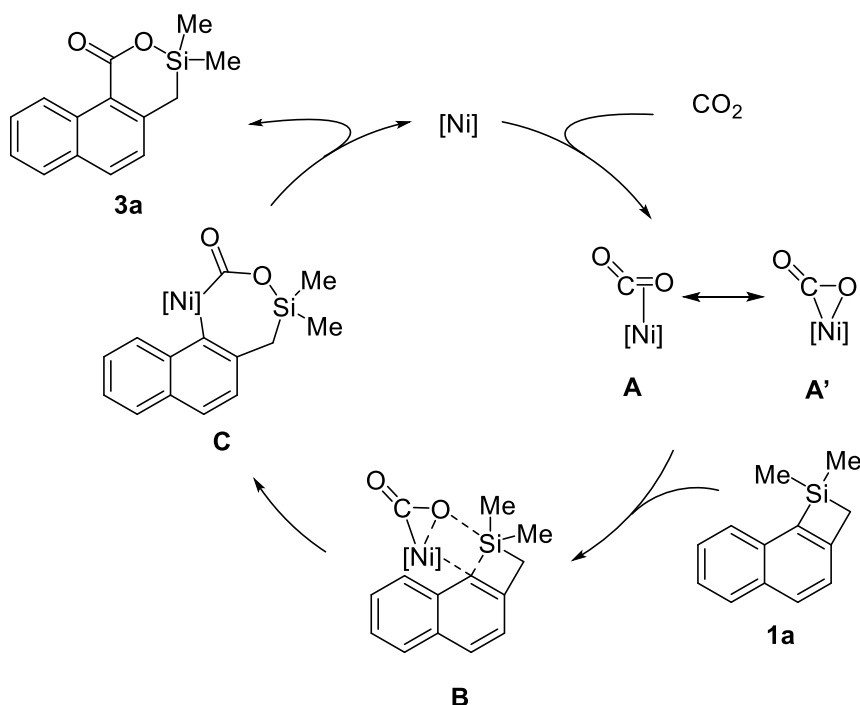
Several benzosilacyclobutenes were subjected to the carboxylation reaction (Eqs 3-6). Ethyl and phenyl groups were tolerated on silicon (Eqs 3 and 5). In addition to naphthosilacyclobutenes **1a** and **1b**, benzo-derivatives **1c-e** successfully participated in

the carboxylation reaction (Eqs 4-6). A fluorine (Eq 4) and a methoxy group (Eq 5) were allowed on the aromatic ring. Carboxylation occurred selectively at the $C(sp^2)$–Si linkage even in the case it was sterically hampered by an ortho methyl group (Eq 6).
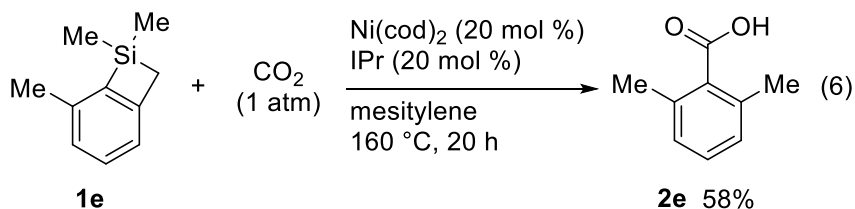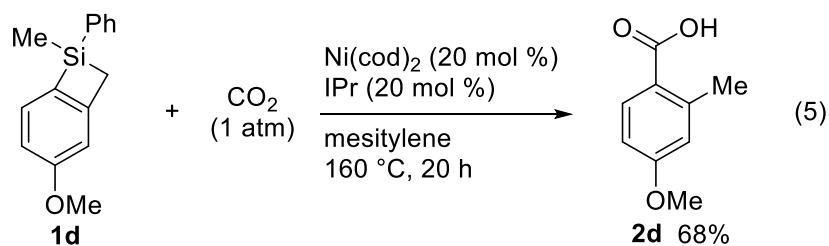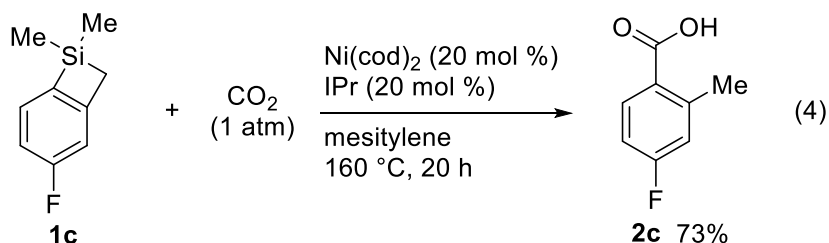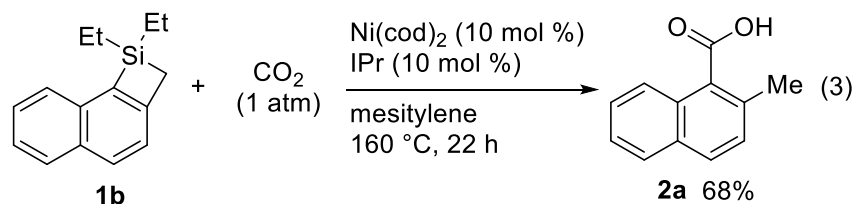
Conclusion

In conclusion, the author found that CO_2 is site-selectively incorporated into the $C(sp^2)$–Si bond of benzosilacyclobutenes with the aid of a nickel complex having an *N*-heterocyclic carbene ligand. The present result demonstrates a unique example of a reaction incorporating CO_2 into a C–Si bond.

Experimental Section

General Methods

All reactions were carried out with standard Schlenk techniques. IR measurements were performed on a FTIR SHIMADZU DR-8000 and FTIR SHIMADZU Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter. IR spectra of a $CDCl_3$ solution of silalactones were measured using the same spectrometer with a fixed cell. ^1H and ^{13}C NMR spectra were recorded on JEOL JNM-ECZ400S/L1 (^1H at 400.44 MHz and ^{13}C at 100.69 MHz). NMR data were obtained in $CDCl_3$. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm ($CHCl_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm ($CDCl_3$). High-resolution mass spectra were recorded on a Thermo Scientific Exactive (APCI, EI) spectrometer. Flash column chromatography was performed with silica gel 60N (Kanto). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9204. Recycling preparative high-performance liquid chromatography (HPLC) was carried out with a Japan Analytical Industry LC-9110 NEXT [SunFire™ Prep Silica OBD™ 5μm (19 x 250 mm)].

Materials

Mesitylene was distilled from sodium/benzophenone ketyl. $Ni(cod)_2$ was recrystallized from a mixture of toluene and 1,5-cyclooctadiene (cod) (toluene/cod = 10:1). IPr was recrystallized from toluene. All benzosilacyclobutenes and benzosilacyclopentene **4**[17], and silacyclobutane **5**[18] were prepared according to the literature procedures. Other chemicals were obtained from commercial suppliers.

A Typical Procedure for Incorporation of CO_2 into $C(sp^2)$–Si Bonds of Benzosilacyclobutenes
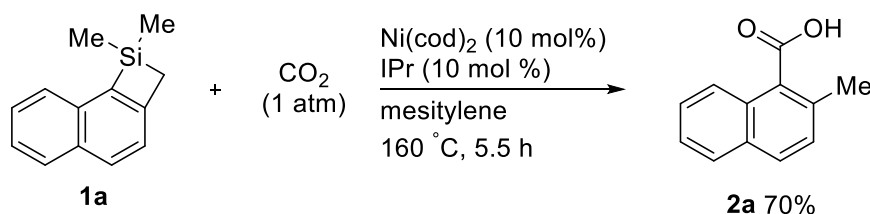

$Ni(cod)_2$ (2.7 mg, 0.01 mmol) and IPr (3.8 mg, 0.01 mmol) were placed in a Schlenk tube and the tube was filled with CO_2 using a balloon. Mesitylene (3 mL) was then added and the reaction mixture was stirred at room temperature for 10 minutes. Then, a liquid of naphthosilacyclobutene **1a** (20.5 mg, 0.10 mmol) was added using a syringe through a

rubber septum. A small amount of **1a** remaining on the inner wall of the vessel was rinsed with additional mesitylene (1 mL). The mixture was then heated at 160 ℃ for 5.5 h. Upon completion of the reaction, the resulting mixture was cooled to room temperature. Saturated $NaHCO_3$ aq was added to quench the reaction, and the resulting mixture was extracted with saturated $NaHCO_3$ aq (3 times). The combined aqueous layer was next acidified with 2 N HCl aq. The organic components were extracted with Et_2O (3 times), washed with water and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford the carboxylic acid **2a** (13.0 mg, 0.07 mmol, 70% yield).

Reaction for 1 h (Eq 1)
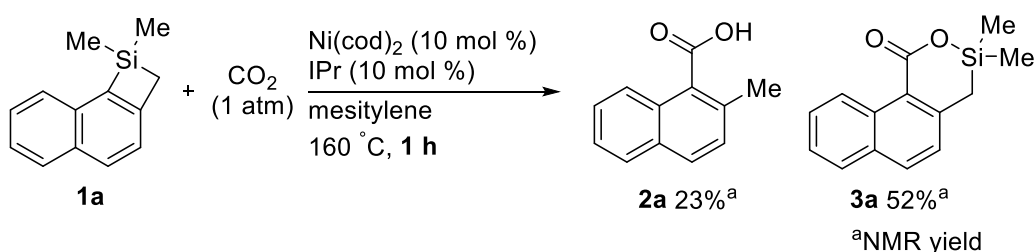
Ni(cod)$_2$ (2.7 mg, 0.01 mmol) and IPr (4.0 mg, 0.01 mmol, 10 mol %) were placed in a Schlenk tube and the tube was filled with CO_2 using a balloon. Mesitylene (3 mL) was then added and the mixture was stirred at room temperature for 10 minutes. Then, a liquid of naphthosilacyclobutene **1a** (20.7 mg, 0.10 mmol) was added using a syringe through a rubber septum. A small amount of **1a** remaining on the inner wall of the vessel was rinsed with additional mesitylene (1 mL). The reaction mixture was then heated at 160 ℃ for 1 h. After being cooled to room temperature, saturated $NaHCO_3$ aq was added. The resulting mixture was extracted with saturated $NaHCO_3$ aq (3 times). The combined aqueous layer was next acidified with 2 N HCl aq. The organic components were extracted with Et_2O (3 times), washed with water and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure. When the residue was dissolved in $CDCl_3$ and analyzed by ^1H NMR, a mixture of the carboxylic acid **2a** and the silalactone **3a** was observed. Subsequent purification of the mixture by GPC (eluent: $CHCl_3$) followed by removal of the solvent under vacuum gave white solids of the dicarboxylic acid **3a'**.

Compound Data of 3a and 3a'


3a   3a'
white solid
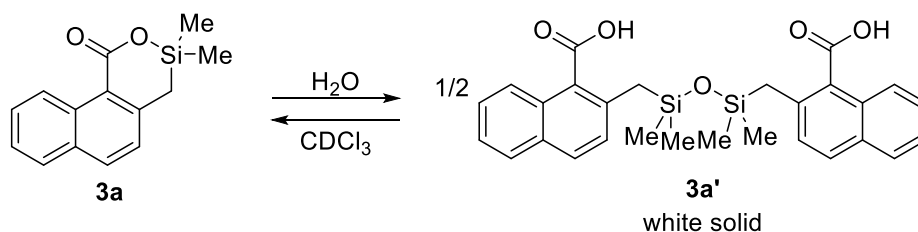
The white solid obtained after GPC was the dicarboxylic acid **3a'**, which was identified by IR and elemental analyses (vide infra). It was difficult to obtain the ^{1}H and ^{13}C NMR spectrum because the dicarboxylic acid **3a'** was rapidly converted into **3a** (less than 5 min.) when dissolved in CDCl$_3$

3a': ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.35 (s, 6H), 2.41 (s, 2H), 7.30 (d, J = 8.4 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.61 (t, J = 8.4 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 8.86 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.7, 21.0, 125.5, 125.7, 126.0, 128.1, 128.2, 128.9, 131.7, 132.6, 133.1, 137.6, 163.5; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{15}$O$_2$Si, [M+H]$^+$ 243.0836, Found m/z 243.0829; IR (Fixed Cell, CDCl$_3$ solution): 1703, 1221 cm^{-1}. (No OH stretching vibrations was detected.)

3a: IR (ATR) 3800-2100, 1686, 1252, 1047, 827 746 cm^{-1}, Anal calcd for C$_{18}$H$_{30}$O$_5$Si$_2$: C, 66.90; H, 6.02; Found; C, 66.24; H, 6.11.

Desilylation of 3a'

3a'   mesitylene, 160 °C, 5.5 h, CO$_2$ (1 atm)   **2a**: 0%   94% recovery of **3a'**
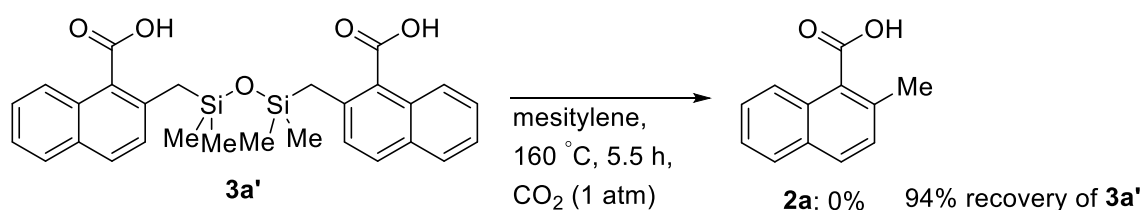
3a' (23.9 mg, 0.048 mmol) was placed in a Schlenk tube, and the tube was filled with CO$_2$ using a balloon. To the tube was added mesitylene (3 mL) and the mixture was stirred at 160 °C for 5.5 h. After being cooled to room temperature, saturated NaHCO$_3$ aq was added. The resulting mixture was extracted with saturated NaHCO$_3$ aq (3 times). The combined aqueous layer was next acidified with 2 N HCl aq. The organic components were extracted with Et$_2$O (3 times), washed with water and brine, and dried over MgSO$_4$. The solvent was removed under reduced pressure to afford dicarboxylic acid **3a'** (22.4 mg, 0.045 mmol, 94%). No **2a** was detected.
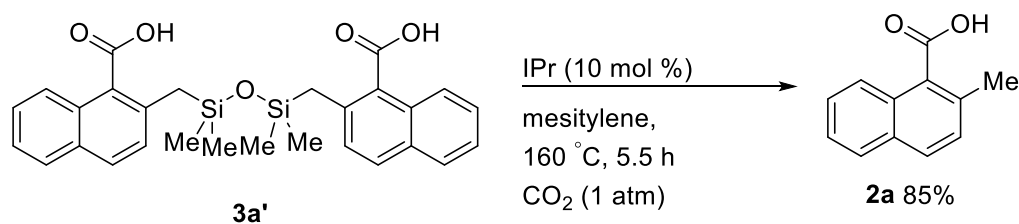
3a' (24.5 mg, 0.049 mmol) and IPr (4.0 mg, 0.010 mmol, 10 mol %) were placed in a Schlenk tube and the tube was filled with CO_2 using a balloon. To the tube was added mesitylene (3 mL) and the mixture was heated at 160 ℃ for 5.5 h. After being cooled to room temperature, saturated $NaHCO_3$ aq was added. The resulting mixture was then extracted with saturated $NaHCO_3$ aq (3 times). The combined aqueous layer was acidified with 2 N HCl aq. The organic components were extracted with Et_2O (3 times), washed with water and brine, and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford only the carboxylic acid **2a** (15.81 mg, 0.085 mmol, 85%).
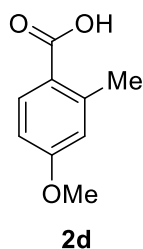
Spectroscopic Data of 2a, 2c, 2d, 2e
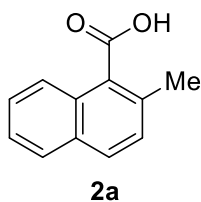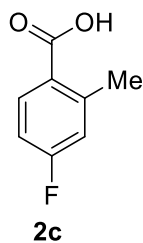
2a

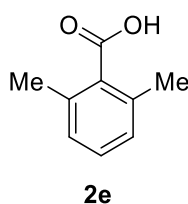Spectral data were in agreement with literature values.[19]

2c

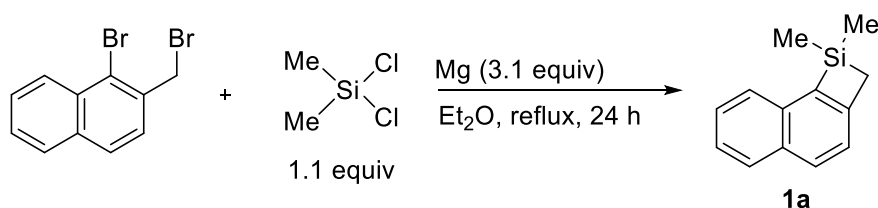Spectral data were in agreement with literature values.[20]

2d

Spectral data were in agreement with literature values.[21]

2e

Spectral data were in agreement with literature values.[22]

## Synthesis of Benzosilacyclobutenes 1a-1e and Benzosilacyclopentene 4

Naphthosilacyclobutene **1a**: A Typical Procedure[17]

An ether (200 mL) solution containing 1-bromo-2-(bromomethyl)naphthalene (12.0 g, 40 mmol) and dichlorodimethylsilane (5.8 g, 46 mmol, 1.1 equiv) was added dropwise to a suspension of magnesium (2.9 g, 122 mmol, 3.1 equiv) in ether (20 mL). The reaction mixture was refluxed for 24 h. The reaction mixture was cooled to room temperature and treated with saturated ammonium chloride aq. The mixture was extracted with Et_2O three times. The combined organic phase was washed with water and brine, and dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the residue was purified by flash column chromatography on silica gel (eluent: hexane) followed by GPC (eluent: $CHCl_3$) to afford naphthosilacyclobutene **1a** (1.4 g, 7.1 mmol, 18%) as colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.57 (s, 6H), 2.24 (s, 2H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 6.8 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = -0.3, 19.8, 125.1, 125.7, 126.3, 127.4, 128.9, 131.2, 132.1, 134.5, 143.9, 149.4; HRMS (EI$^+$): Calcd for $C_{13}H_{14}Si$, [M]$^+$ 198.0859,

Found m/z 198.0863; IR (ATR): 1504, 1246, 825, 745, 700 cm^{-1}.
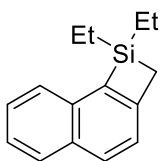
1b

According to the procedure analogous to that described for **1a**, naphthosilacyclobutene **1b** (447.5 mg, 2.0 mmol, 10 %) was prepared from 1-bromo-2-(bromomethyl)naphthalene (6.0 g, 20 mmol) and dichlorodiethylsilane (6.8 g, 44 mmol, 2.2 equiv). Reaction time was 12.5 h. Purified by flash column chromatography on silica gel (eluent: hexane) to give **1b** as colorless oil. Before using in the reaction with CO_2, this compound was further purified by HPLC (eluent: hexane).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.02-1.09 (m, 10H), 2.20 (s, 2H), 7.27 (d, J = 8.0 Hz, 1H), 7.40-7.49 (m, 2H), 7.67 (d, J = 7.6 Hz, 1H), 7.80-7.82 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 6.3, 7.6, 16.5, 125.0, 125.5, 126.3, 127.8, 128.9, 131.0, 132.1, 135.0, 142.6, 150.2; HRMS(EI$^+$): Calcd for C$_{15}$H$_{18}$Si, [M]$^+$ 226.1178, Found m/z 226.1175; IR (ATR): 812, 737, 714 cm^{-1}.
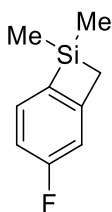
1c

According to the procedure analogous to that described for **1a**, benzosilacyclobutene **1c** was prepared from 2-bromo-5-fluorobenzyl bromide (5.2 g, 20 mmol) and dichlorodimethylsilane (4.4 g, 21 mmol, 1.1 equiv). Reaction time was 14.5 h. Purified by flash column chromatography on silica gel (eluent: hexane) to afford **1c** (1.1 g, 6.7 mmol, 34 %) as colorless oil. Before using in the reaction with CO_2, this compound was further purified by HPLC (eluent: hexane).

^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.47 (s, 6H), 2.13 (s, 2H), 6.86 (d, J = 9.6 Hz, 1H), 6.91 (dd, J = 8.4, 10 Hz, 1H), 7.28 (dd, J = 6.0, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -0.5, 19.9, 113.7 (d, J = 19.2 Hz), 114.3 (d, J = 21 Hz), 132.2 (d, J = 6.3 Hz), 141.0 (d, J = 2.9 Hz), 152.6 (d, J = 5.8 Hz), 165.2 (d, J = 246.3 Hz), HRMS(EI$^+$): Calcd for C$_9$H$_{11}$FSi, [M]$^+$ 166.0614, Found m/z 166.0610; IR (ATR): 1566, 1253, 918, 845, 814,

799, 696 cm^{-1}.
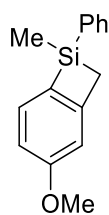
1d

According to the procedure analogous to that described for **1a**, benzosilacyclobutene **1d** (86.2 mg, 0.30 mmol, 3.0%) was prepared from 2-bromo-5-methoxybenzyl bromide (2.8 g, 10 mmol) and dichloro(methyl)phenylsilane (2.4 g, 12 mmol, 1.2 equiv). Reaction time was 13 h. Purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate = 10/1) to give **1d** as colorless oil. Before using in the reaction with CO_2, this compound was further purified by HPLC (eluent: hexane).

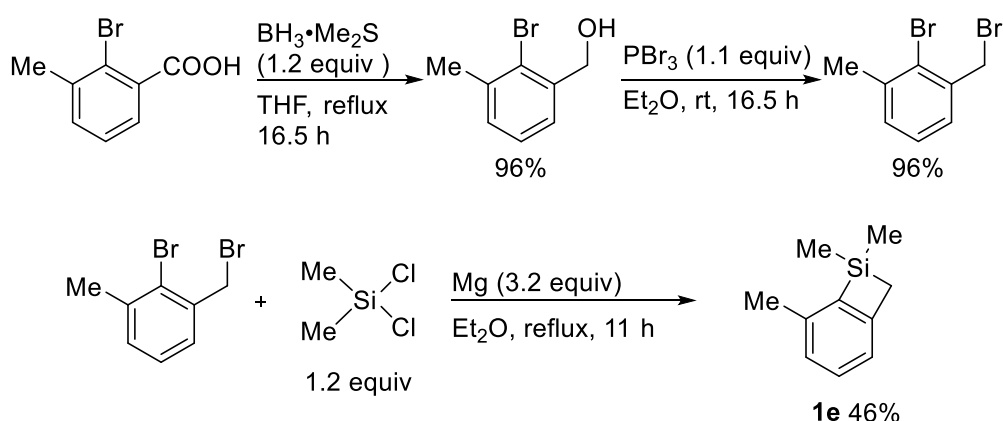^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.75 (s, 3H), 2.31 (s, 2H), 3.82 (s, 3H), 6.78 (s, 1H), 6.84 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.35-7.40 (m, 3H), 7.57-7.60 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -2.6, 20.4, 55.0, 111.23, 114.7, 127.9, 129.8, 132.1, 134.0, 134.9, 136.7, 153.0, 162.4; HRMS(EI$^+$): Calcd for C$_{15}$H$_{16}$OSi, [M+H]$^+$ 239.0898, Found m/z 239.0886; IR (ATR): 1584, 1234, 1045, 812, 698 cm^{-1}.

Synthesis of Benzosilacyclobutene **1e**

BH$_3$· Me$_2$S (11 mL, 116 mmol, 1.2 equiv) was slowly added to a solution of 2-bromo-3-methylbenzoic acid (21.0 g, 98 mmol) in THF (150 mL). The reaction mixture was heated at reflux for 16.5 h. Then, a 2 N solution of NaOH was added and the resulting mixture was stirred for 30 min. The aqueous layer was extracted three times with Et$_2$O. The combined organic layers were washed with water and brine, and dried over MgSO$_4$. Evaporation of the solvent afforded (2-bromo-3-methylphenyl)methanol (18.9 g, 94

mmol, 96% yield).

A solution of (2-bromo-3-methylphenyl)methanol (19 g, 94 mmol) in Et_2O (200 mL) was cooled to 0 °C. To the solution was added phosphorus tribromide (9.4 mL, 103 mmol, 1.1 equiv) dropwise and the mixture was stirred at room temperature for 16.5 h. Methanol (35 mL) and water (100 mL) were added to quench the reaction. The organic phase was washed with water and brine. The organic phase was dried over Na_2SO_4, filtered, and evaporated under reduced pressure to give 2-bromo-1-(bromomethyl)-3-methylbenzene (23.5 g, 90 mmol, 96% yield). Spectral data were in agreement with literature values.[23]

According to the procedure analogous to that described for **1a**, benzosilacyclobutene **1e** (1.5 g, 9.3 mmol, 46%) was prepared from 2-bromo-3-methylbenzyl bromide (5.3 g, 20 mmol) and dichlorodimethylsilane (3.0 g, 23 mmol, 1.2 equiv). Reaction time was 11 h. Purified by flash column chromatography on silica gel (eluent: hexane) to give **1e** as colorless oil. Before using the reactions with CO_2, this compound was further purified by HPLC (hexane).

^1H NMR (400 MHz, $CDCl_3$): δ = 0.47 (s, 6H), 2.10 (s, 2H), 2.27 (s, 3H), 6.95 (d, J = 7.6 Hz, 1H), 6.99 (d, J = 7.6 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = -0.7, 19.6, 21.4, 123.9, 126.3, 130.9, 140.6, 145.9, 150.5; HRMS(EI^+): Calcd for $C_{10}H_{14}Si$, $[M]^+$ 162.0865, Found m/z 162.0863; IR (ATR): 1576, 1460, 1246, 822, 714 cm^{-1}.

Synthesis of Benzosilacyclopentene **4**

36%   **4** 24%
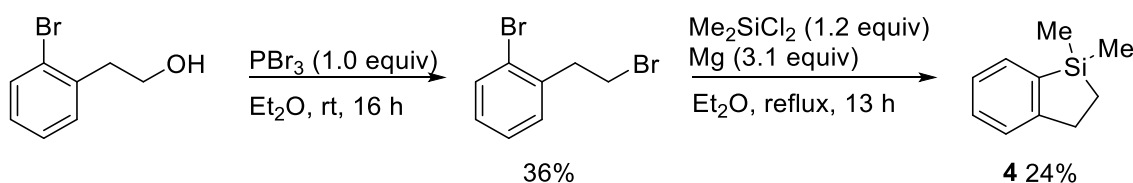
According to the procedure analogous to that described for 2-bromo-1-(bromomethyl)-3-methylbenzene, 1-bromo-2-(2-bromoethyl)benzene (9.7 g, 37 mmol, 36%) was prepared from 2-(2-bromophenyl)ethyl alcohol (20.4 g, 102 mmol) and phosphorus tribromide (9.4 mL, 103 mmol, 1.0 equiv). Reaction time was 16 h. Purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate = 10/1) to give 1-bromo-2-(2-bromoethyl)benzene as colorless oil. Spectral data were in agreement with literature values.[24]

According to the procedure analogous to that described for **1a**, benzosilacyclopentene **4** (396.2 mg, 2.4 mmol, 24%) was prepared from 1-bromo-2-(2-bromoethyl)benzene (2.6 g, 10 mmol) and dichlorodimethylsilane (1.5 g, 12 mmol, 1.2 equiv). Reaction time was 13 h. Purified by flash column chromatography on silica gel (eluent: hexane) to give **4** as

colorless oil.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.30 (s, 6H), 1.01 (t, *J* = 7.2 Hz, 2H), 3.09 (t, *J* = 7.2 Hz, 2H), 7.17-7.31 (m, 3H), 7.53 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -1.7, 11.4, 31.8, 125.5, 125.6, 129.2, 131.9, 139.9, 153.2; HRMS(EI$^+$): Calcd for C$_{10}$H$_{14}$Si, [M]$^+$ 162.0865, Found m/z 162.0865; IR (ATR): 1589, 1441, 1246, 1119, 831, 785, 716 cm^{-1}.

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16. Alternative reaction pathways are also conceivable. For example, a pathway through 1) oxidative addition of the $C(sp^2)$–Si linkage of **1a** onto nickel(0) to form a five-membered nickelacycle intermediate, 2) insertion of carbon dioxide into the resulting $C(sp^2)$–Ni bond to furnish a seven-membered nickelalactone, and 3) O–Si bond forming reductive elimination leads to the formation of **3a**.

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Chapter 3

2-Arylsilacyclobutane as Latent Nucleophile Attacking CO$_2$

Abstract

Four-membered 2-arylsilacyclobutanes generate nucleophilic species at room temperature through cleavage of the benzylic C–Si bond simply when dissolved in polar aprotic solvents such as DMF. The nucleophilic species is capable to attack carbon dioxide to furnish silalactones. The carboxylation reaction is unique in that neither transition metal catalysts, Lewis acids, nor bases are required.

Introduction

Silacyclopropanes and silacyclobutanes exhibit unique ring-opening reactivities that are not available with simple organosilicon compounds, because of the significant strain imposed by the three- and four-membered ring.[1,2] For example, silacyclopropanes adds onto aldehydes through their ring opening when either simply heated,[1b] photolyzed,[1a] treated with a *t*BuOK/18-crown-6,[1b] or treated with a copper salt.[1d] An addition reaction takes place also with formamides upon simple heating.[1c] Silacyclobutanes react with aldehydes in an analogous manner with the assistance of *t*BuOK.[2d] Transition metal catalysts induce cleavage of the C–Si bond of the silacyclopropane and silacyclobutane rings,[3] which have been extended to various ring-opening/-expansion reactions.[4] The author reports that a nucleophilic species is generated from 2-arylsilacycobutanes by a remarkably simple way. When a 2-arylsilacyclobutane is dissolved in an aprotic polar solvent such as *N*,*N*-dimethylformamide (DMF) at room temperature, the four-membered ring is opened at the benzylic C–Si bond to transiently generate a benzylic anion by equilibrium. The anion is capable to undergo nucleophilic attack onto carbon dioxide to furnish a silalactone. Neither catalysts nor bases are required for the carboxylation reaction.

Results and Discussion

This study began with the observation of the surprising behavior of 2-phenylsilacyclobutane *cis*-**1a** in DMF-*d₇* (Scheme 1). *cis*-Enriched **1a** (*cis*:*trans* = 98:2) was dissolved in DMF-*d₇*, and *cis*-to-*trans* epimerization took place albeit slowly (*cis*:*trans* = 48:52 at 805 h). It proceeded faster in the presence of MS4A. The silacyclobutane *cis*-**1a** (only *cis*-isomer) was completely converted into *trans*-**1a** after 92 h in the presence of MS4A. In contrast, no change occurred at all in CDCl$_3$ and C$_6$D$_6$ after 24 h, even in the presence of MS4A.

Scheme 1. Epimerization of *cis*-**1a** to *trans*-**1a**

,

The epimerization is explained by assuming the ring opening/closing process taking place upon the action of the polar DMF molecule (Scheme 2). The Lewis-acidity of the silicon atom of **1a** is enhanced by the four-membered ring structure.[5] Although no

appreciable amount of the corresponding silicate is generated according to the ^{29}Si NMR chemical shift of **1a** in DMF-d_7, the polar solvent DMF would act as the Lewis base to transiently coordinate to the silicon atom of **1a**. The coordination induces ring-opening to generate benzylic anion **A** which is configurationally labile. Recyclization by displacing the DMF molecule on silicon leads to the formation of *trans*-**1a**, which would be thermodynamically far more stable than *cis*-**1a** because of the sterics.

Scheme 2. Possible Mechanism
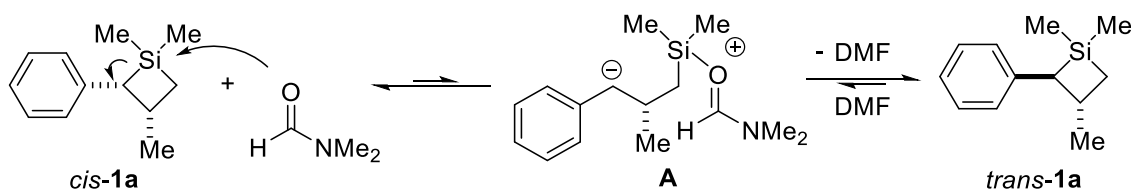
Carbon dioxide is a far less reactive electrophile than aldehydes. Tetraorganosilicon compounds generally fail to add onto carbon dioxide. Addition of organosilicon compounds onto carbon dioxide at the C–Si bond is limited to significantly nucleophilic derivatives such as a lithiated (phosphacyclopentadienyl)silane,[6] a zincated pyridylsilane,[7] and a trimethylsilyl cation–*N*-heterocyclic carbene adduct.[8] Or the addition of neutral organosilicon compounds onto carbon dioxide requires assistance of an excess amount of an aluminum Lewis acid[9] and fluoride[10,11]. Direct incorporation of carbon dioxide into small ring silacycles with carbon dioxide has never been reported until the author's report on a nickel-catalyzed reaction of benzosilacyclobutenes.[12] The ring opening behavior of silacyclobutane **1a** led the author to simply treat 2-phenylsilacyclobutane with carbon dioxide. When a DMF-d_7 solution of **1b** was left under an atmospheric pressure of carbon dioxide at room temperature for 3 h, the signals ascribed to **1b** disappeared and the quantitative formation of silalactone **2b** was observed. The formation of **2b** is explained by assuming that the nucleophilic species generated by the ring opening of **1b** undergoes addition onto carbon dioxide and that the resulting carboxylate displaces the DMF molecule on silicon. The subsequent treatment of the reaction mixture with water afforded the siloxane dimer of the carboxylic acid **3b** in 97% yield. A ^{1}H decoupled quantitative ^{13}C NMR analysis proved the diastereomeric ratio to be 1:1. The choice of the solvent was crucial, as was the case with an epimerization reaction of **1a**. Whereas aprotic polar solvents like DMA and dimethyl sulfoxide (DMSO) effectively promoted the carboxylation reaction (entries 2 and 3)[13], less polar aprotic solvents like toluene, chloroform, acetonitrile and acetone failed to give **3b** even upon heating (entries 4-7). When the reaction was performed in DMA in the presence of MS4A,

the carboxylation reaction completed within 10 min (entry 8). After purification by flash column chromatography on silica gel, **3b** was isolated in 68% yield. Neither silacyclobutane lacking a phenyl group at the 2-position **4** (Figure 1) nor acyclic benzylsilane **5** took in carbon dioxide, indicating that the benzylic C–Si bond contained in the strained four-membered cyclic skeleton was a structural requisite for addition to carbon dioxide.

Table 1. Addition 2-Phenylsilacyclobutane **1a** to CO_2[a]
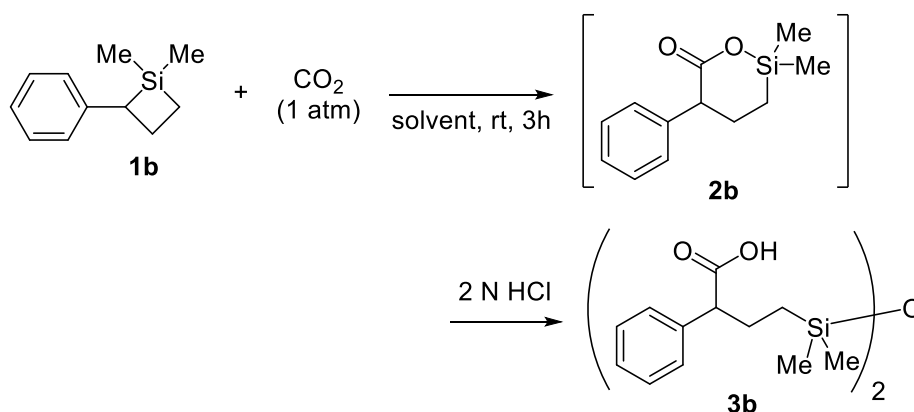
Entry	Solvent	Yield of **3a** / %[b]
1	DMF-d_7	97
2[c]	DMA	86
3	DMSO	86
4[d]	toluene	0
5[d]	chloroform	0
6[d]	MeCN	0
7[d]	acetone	0
8[e]	DMA	90 (68)

[a] Reaction conditions: **1b** (0.10 mmol), solvent (0.5 mL), CO_2 (1 atm, balloon), rt, 3 h; then 2 N HCl. [b] NMR yield. Isolated yield in parenthesis. [c] 0.20 mmol scale. [d] 60 °C, 12 h. [e] 0.20 mmol scale. With MS4A (25 mg), 10 min.
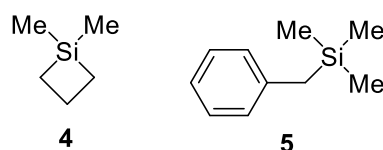
Figure 1. Other Silacyclic Compounds Examined

2-Arylsilacyclobutanes generally added onto carbon dioxide when their DMA solution was simply stirred at room temperature under an atmospheric pressure of carbon dioxide (Table 2). Silacyclobutanes *trans*-**1a** and *cis*-**1a** gave a diastereomeric mixture of dicarboxylic acid **3a** in 63% and 65% yields, respectively (entries 1 and 2). Although it was difficult to determine the ratio of the diastereomers, **3a** was cleanly converted into the silalactone form **2a** when heated at 100 °C in CDCl$_3$ in an NMR tube equipped with a screw cap. The *cis*:*trans* ratio of the carboxylated products was determined by ^{1}H NMR analysis of the silalactone **2a**. In addition to methyl group, ethyl group was tolerated on silicon (entry 3). Methoxy (entry 5) and dioxolane (entry 6) groups were allowed on the aromatic ring.

Table 2. Incorporation Reactions of Carbon Dioxide into 2-Arylsilacyclobutanes[a]

Entry	Substrate	Product[b]
1	*trans*-**1a**	**3a** 63% *cis*:*trans* = 4.5:1.0
2	*cis*-**1a**	**3a** 65% *cis*:*trans* = 2.7:1.0
3	**1c**	**3c** 80%

4	1d	3d 69%
5	1e	3e 67%
6	1f	3f 75%
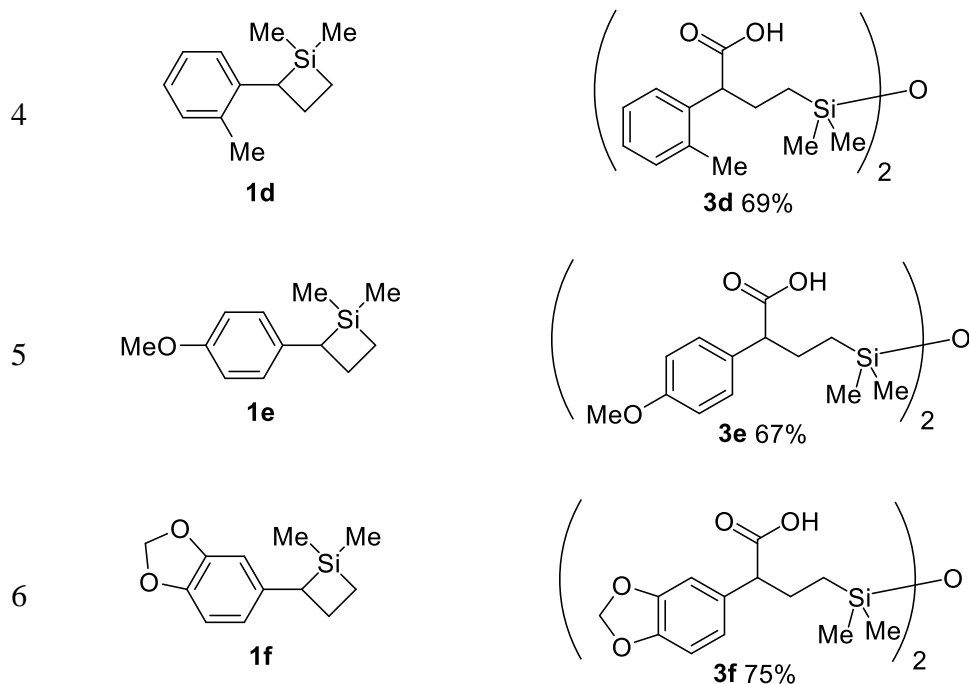
[a] Reaction conditions: 2-arylsilacyclobutane **1** (0.20 mmol), DMA (1 mL), MS4A (50 mg), rt, 3 h; then 2 N HCl. [b] Isolated yield.

Next examined was the reaction of naphthosilacyclobutene **6a**. When a mesitylene solution containing **6a** and a catalytic amount of a nickel–*N*-heterocyclic carbene complex was heated at 160 °C under an atmospheric pressure of carbon dioxide, carbon dioxide is inserted into the C(arene)–Si bond of the **6a** to furnish the silalactone **7a**.[12] By sharp contrast, when a DMA solution of naphthosilacyclobutene **6a** is stirred at room temperature under an atmospheric pressure of carbon dioxide, carbon dioxide was inserted into the benzylic C–Si bond in a site- and regio-selective fashion to furnish six-membered silalactone **8a**. The silalactone **7a** was not observed at all under the present reaction conditions. Silalactone **8a** remained even after the treatment with 2 N HCl unlike the case of **2b**, and purification by base-acid extraction gave **8a** in 68% yield.

Scheme 3. Site-selective Incorporation Reactions of CO_2 into Naphthosilacyclobutene **6a**
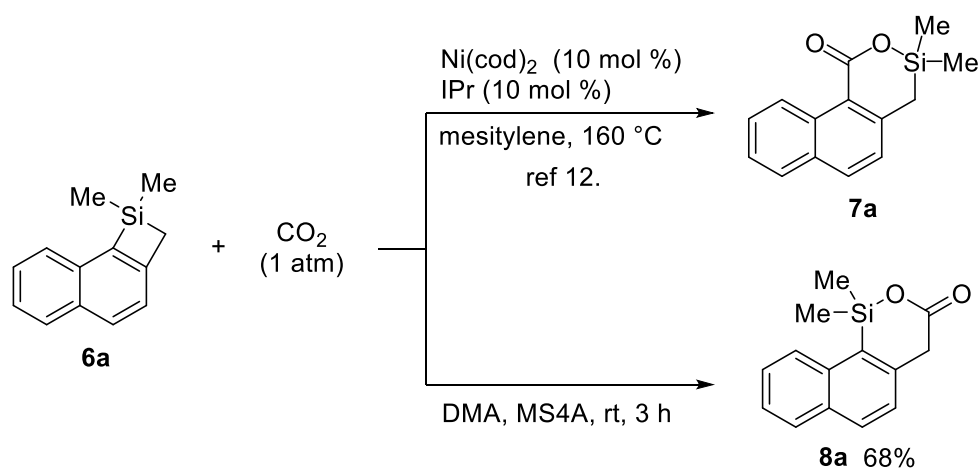
The site-selectivity is general for arene-fused silacyclobutenes examined (Table 3). Not only naphthosilacyclobutenes **6a** and **6b**, but also benzo-derivatives **6c-e** incorporated carbon dioxide site-selectively at their benzylic C–Si bond to furnish **8**. No silalactones **7** and its hydrolyzed products were detected in the reaction mixture.

Table 3. Incorporation Reactions of CO_2 into Arene-fused Silacyclobutanes[a]

Entry	Substrate	Product[b]
1[c]	**6b**	**8b** 92%
2	**6c**	**8c** 79%

3	**6d**	**8d** 80%
4[d]	**6e**	**8e** 55%
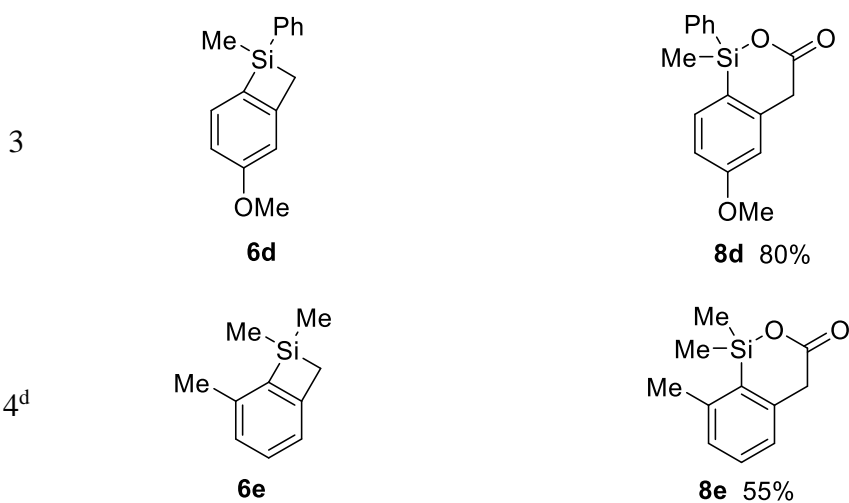
[a] Reaction conditions: benzosilacyclobutene **6** (0.20 mmol), DMA (1 mL), MS4A (50 mg), rt, 3 h; then 2 N HCl. [b] Isolated yield. [c] DMF instead of DMA, 100 °C. [d] DMF instead of DMA, 100 °C, 16 h.

Conclusion

In conclusion, the author has found 2-arylsilacyclobutanes generate nucleophilic species by ring opening simply when dissolved in polar aprotic solvent like DMF. The nucleophilic species attack carbon dioxide to furnish carboxylic acid derivatives. The present reaction is unique in that neither transition metal catalysts, Lewis acids, nor bases are required.

Experimental Section

General Methods

^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECZ400S/L1 (^{1}H at 400.44 MHz and ^{13}C at 100.69 MHz) and JNM-ECA600P (^{29}Si at 119.24 MHz). NMR data were obtained in CDCl$_3$ or DMF-d_7. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm (CHCl$_3$) and 8.03 ppm (DMF). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.16 ppm (CDCl$_3$) and 163.15 ppm (DMF-d_7). Silicon chemical shifts were referenced to the silicon signal of TMS at 0.00 ppm. IR spectra of neat samples were measured on FTIR SHIMADZU Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter. IR spectra of a CDCl$_3$ solution of silalactones were measured using the same spectrometer with a fixed cell. High-resolution mass spectra were recorded on a Thermo Scientific Exactive (APCI, EI) spectrometer. Preparative thin-layer chromatography was performed on silica gel plates with PF254 indicator (Merck). Flash column chromatography was performed with diol-silica gel DIOL MB 100–40/75 (Fuji Silysia Chemical Ltd.) or silica gel 60N (Kanto). Gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC-9204 and LC-5060.

Materials

All 2-phenylsilacyclobutanes[14] and benzosilacyclobutenes[12,15] were prepared according to the literature procedures. Anhydrous *N,N*-dimethylacetamide (Wako Pure Chemical Industries, Ltd) was degassed. Anhydrous *N,N*-dimethylformamide-d_7 (Aldrich) was stored with MS4A under nitrogen atmosphere. MS4A was heated by microwave oven and dried under vacuum (three times) prior to use. Other chemicals were obtained from commercial suppliers and used without further purification.

Epimerization of *cis*-1a to *trans*-1a

  Without MS4A
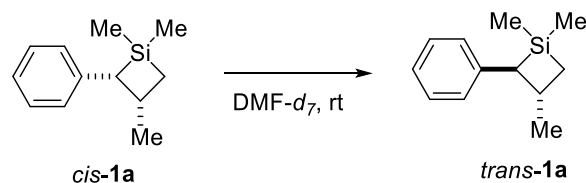
cis-Enriched silacyclobutane **1a** (7.54 mg, 0.04 mmol, (*cis*-**1a**:*trans*-**1a** = 98:2)) and anisole (internal standard, 7.2 mg) were placed in an NMR tube under nitrogen atmosphere, then DMF-d_7 (0.5 mL) was added. Epimerization took place very slowly (*cis*-**1a**:*trans*-**1b** = 48:52 at 805 h).
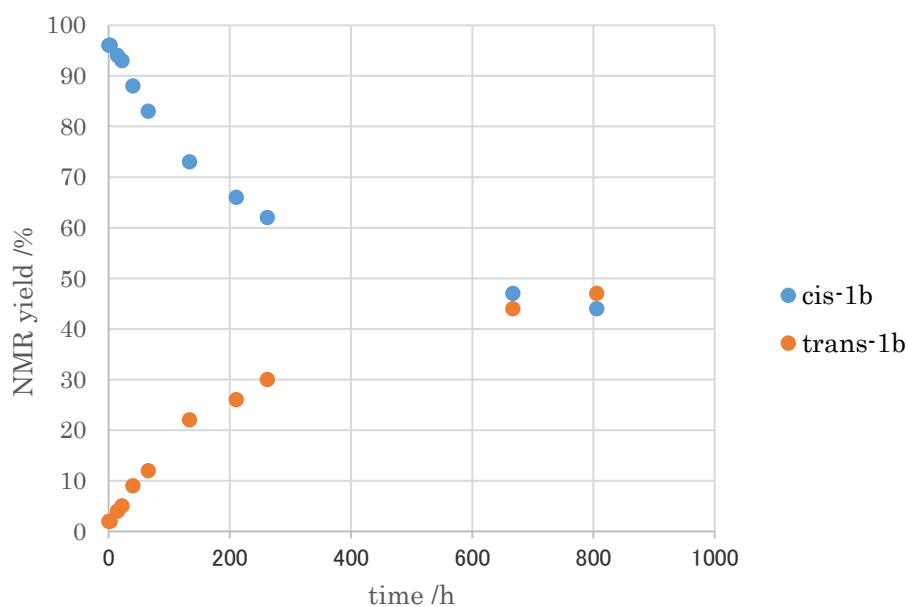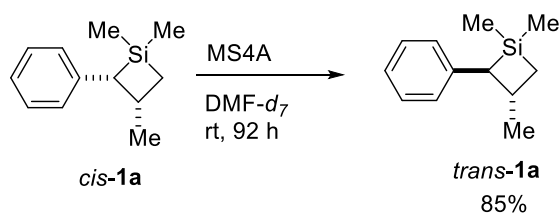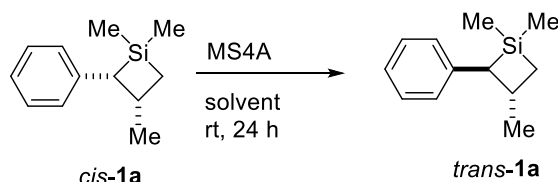

**Figure 2.** Epimerization of *cis*-**1a** to *trans*-**1a**

  With MS4A

cis-Silacyclobutane **1a** (17.5 mg, 0.09 mmol, only *cis*-isomer) and MS4A (25 mg) were placed in a Schlenk tube equipped with a J-Young type screw cap under nitrogen atmosphere. DMF-d_7 (0.5 mL) was added and the reaction mixture was stirred. After 92 h, *cis*-**1a** was completely consumed and *trans*-**1a** was obtained in 85% NMR yield.

Epimerization in CDCl$_3$ and C$_6$D$_6$

Table 4. Epimerization in CDCl$_3$ and C$_6$D$_6$

Entry	Solvent	NMR yield of *trans*-**1a** / %
1	DMF-d_7	36
2[a]	CDCl$_3$	0
3	CDCl$_3$	0
4	C$_6$D$_6$	0

[a]without MS4A,

Epimerization of *trans*-1a to *cis*-1a
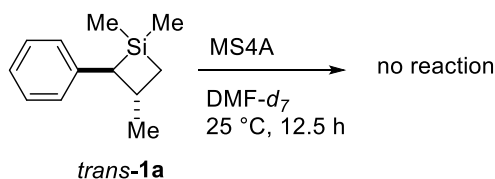
trans-Silacyclobutane **1a** (19.2 mg, 0.10 mmol), MS4A (25 mg) and anisole (internal standard, 10.2 mg) were placed in an NMR tube equipped with a J-Young type screw cap under nitrogen atmosphere. To the mixture was added DMF-d_7 (0.5 mL), and the mixture had been left at 25 °C. No reaction was observed after 12.5 h.

NMR Experiment for Incorporation of CO₂ into 2-Phenylsilacyclobutane 1b
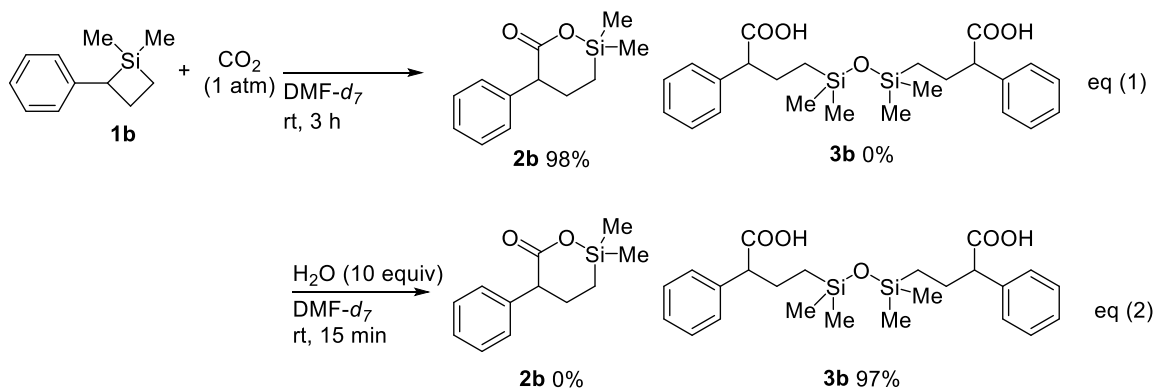
2-Phenyldimethylsilacyclobutane **1b** (17.6 mg, 0.10 mmol) and anhydrous DMF-d_7

(0.5 mL) were placed in an NMR tube equipped with a J-Young type screw cap under nitrogen atmosphere. Then, the reaction vessel was filled with CO_2. After 3 h, cyclohexene was added as an internal standard to the reaction mixture under nitrogen atmosphere. Silalactone **2b** was produced in 98% NMR yield and no dicarboxylic acid **3b** was detected (eq 1).

Then, H_2O (18.49 mg, 1.03 mmol, 10 equiv) was added to the reaction mixture. Hydrolysis of the silalactone **2b** occurred to generate **3b** within 15 min (eq 2).
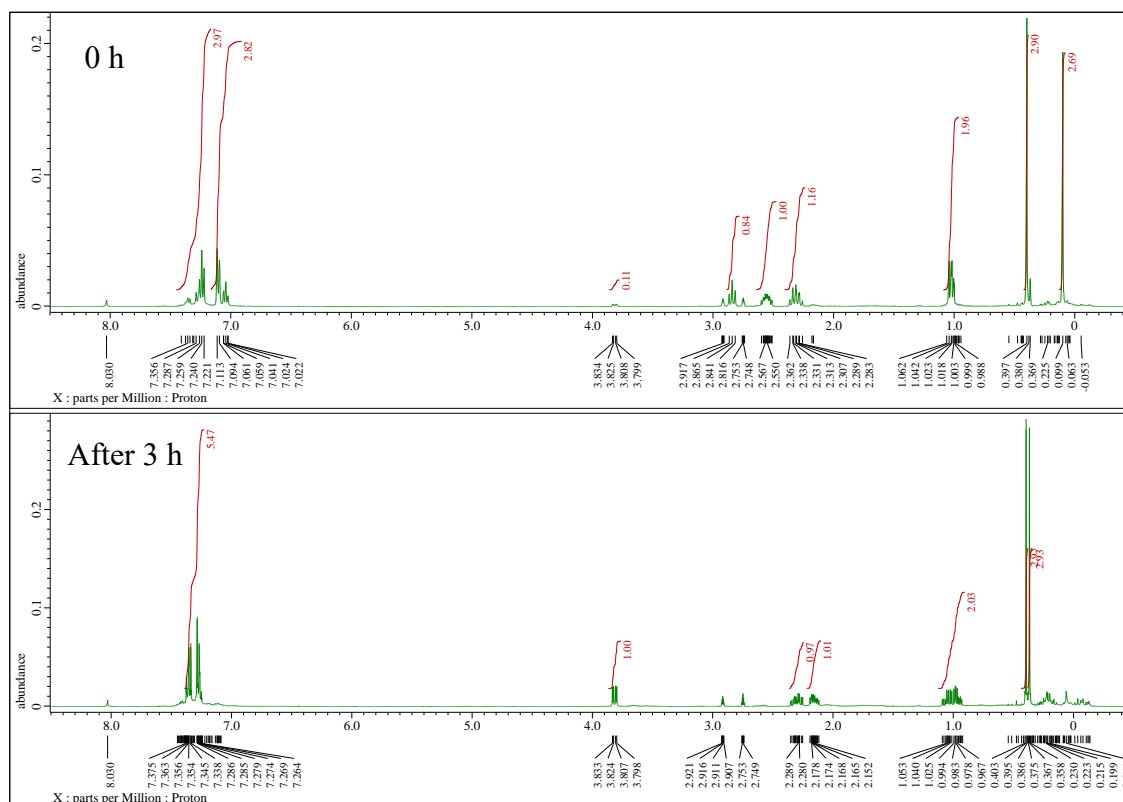
Figure 3. ^1H NMR Spectra of CO_2 Incorporation into **1b** in DMF-d_7
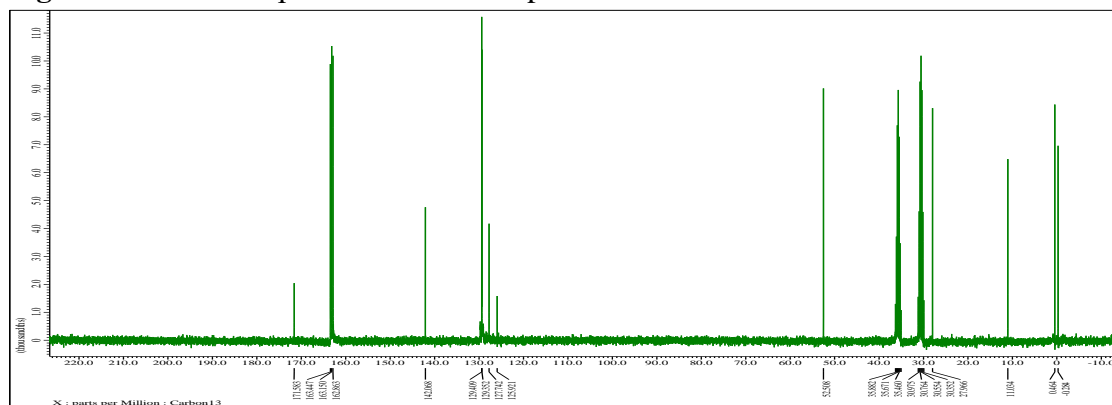

Figure 4. ^{13}C NMR Spectra of **2b** in DMF-d_7

A Typical Procedure for Direct Incorporation of CO₂ into Four-membered Silacycles
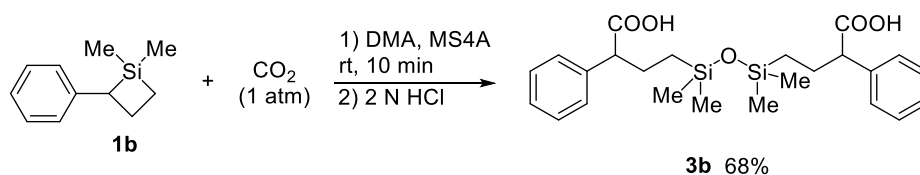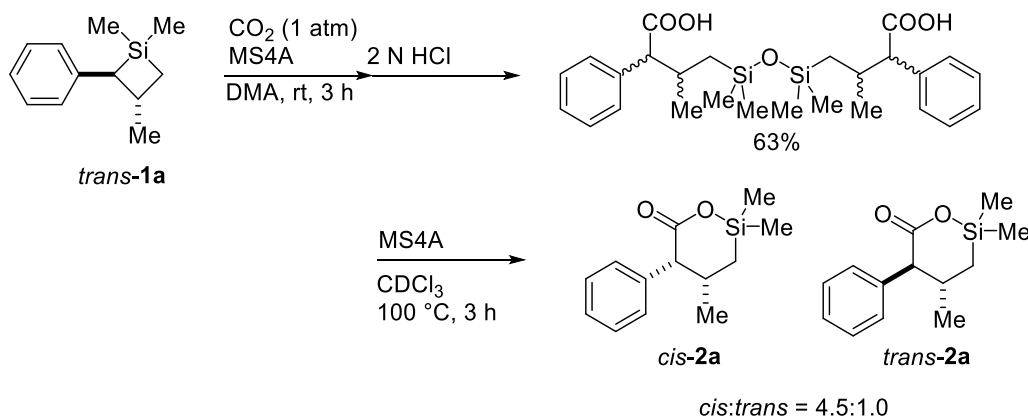

3b 68%

Molecular sieves 4A (50 mg) was placed in a Schlenk tube. The reaction vessel was filled with CO_2 using a balloon, and 2-phenyldimethylsilacyclobutane **1b** (34.2 mg, 0.19 mmol) and DMA (1.0 mL) were then added. The reaction mixture was stirred at room temperature for 10 minutes. Then, 2 N HCl was added to quench the reaction and the resulting mixture was extracted with Et_2O (three times). The combined organic phase was washed with H_2O (twice) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on diol silica gel (hexane/ethyl acetate = 2/1) to give dicarboxylic acid **3b** (30.2 mg, 0.066 mmol, 68%).

Effect of Water

9: 72%   **3b** 7% (NMR)
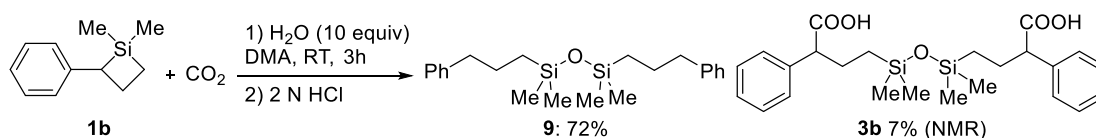
A Schlenk tube was filled with CO_2. To the vessel were added H_2O (36 μL, 2.0 mmol), 2-phenyldimethylsilacyclobutane **1b** (35.87 mg, 0.20 mmol), and DMA (1 mL), and the reaction mixture was stirred at room temperature. After 3 h, 2 N HCl was added to quench the reaction, and the resulting mixture was extracted with Et_2O (three times). The combined organic phase was washed with H_2O (twice) and brine, and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to afford dicarboxylic acid **3b** in 7% NMR yield and disiloxane **9** in 72% NMR yield.

Incorporation of CO₂ into *trans*-1a

Molecular sieves 4A (50 mg) was placed in a Schlenk tube. The reaction vessel was filled with CO_2. Silacyclobutane *trans*-**1a** (38.1 mg, 0.20 mmol) and DMA (1.0 mL) were then added and the reaction mixture was stirred at room temperature. After 3 h, 2 N HCl was added to quench the reaction, and the resulting mixture was extracted with Et_2O (three times). The combined organic phase was washed with H_2O (twice) and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on diol silica gel (hexane/ethyl acetate = 3/1) to give a mixture of dicarboxylic acid (30.7 mg, 0.063 mmol, 63%). This mixture and MS4A (50 mg) were placed in a Schlenk tube equipped with J-Young type screw cap under nitrogen atmosphere, and $CDCl_3$ (1 mL) was added. The reaction mixture was stirred at 100 °C. After 3 h, all carboxylic acid converted to silalactone **2a** (*cis*-**2a**:*trans*-**2a** = 4.5:1.0).
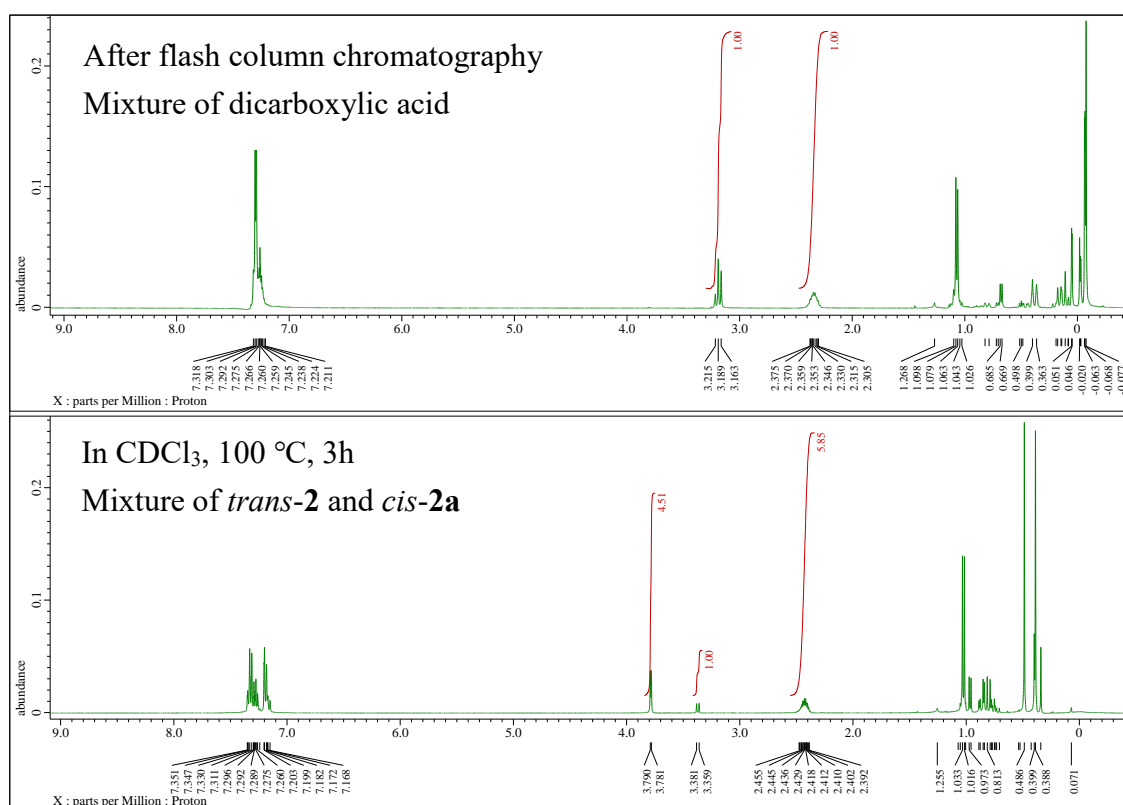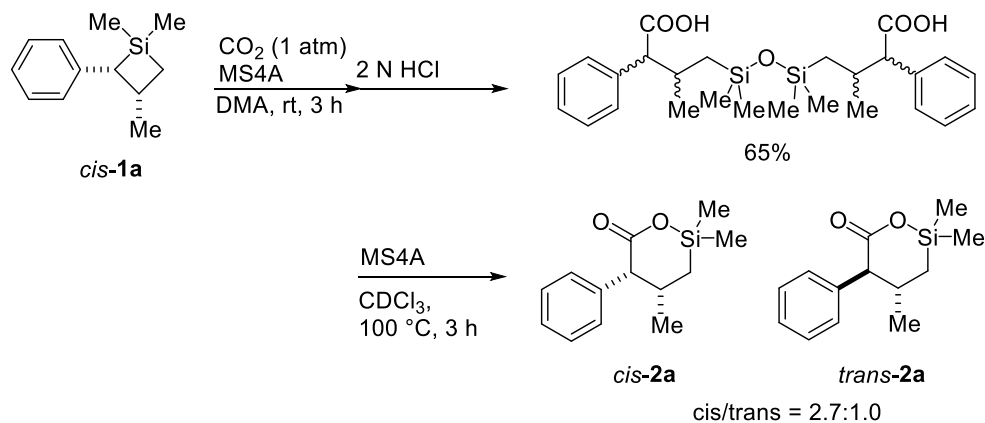
Figure 5. Transformation of Dicarboxylic Acid to Silalactone *trans*-**2a** and *cis*-**2a**

Incorporation of CO₂ into *cis*-1a

Molecular sieves 4A (25 mg) was placed in a Schlenk tube. The reaction vessel was filled with CO$_2$. Silacyclobutane *cis*-**1a** (19.9 mg, 0.10 mmol) and DMA (0.5 mL) were then added and the reaction mixture was stirred at room temperature. After 3 h, 2 N HCl was added to quench the reaction and the resulting mixture was extracted with Et$_2$O (three times). The combined organic phase was washed with H$_2$O (twice) and brine, and then dried over anhydrous MgSO$_4$. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on diol silica gel

67

(hexane/ethyl acetate = 3/1) to give a mixture of dicarboxylic acid (16.2 mg, 0.033 mmol, 65%). This mixture and MS4A (25 mg) were placed in a Schlenk tube equipped with J-Young type screw cap under nitrogen atmosphere and $CDCl_3$ (1 mL) was then added. The reaction mixture was stirred at 100 °C. After 3 h, all carboxylic acid converted to silalactone **2a** (*cis*-**2a**:*trans*-**2a** = 2.7:1.0).
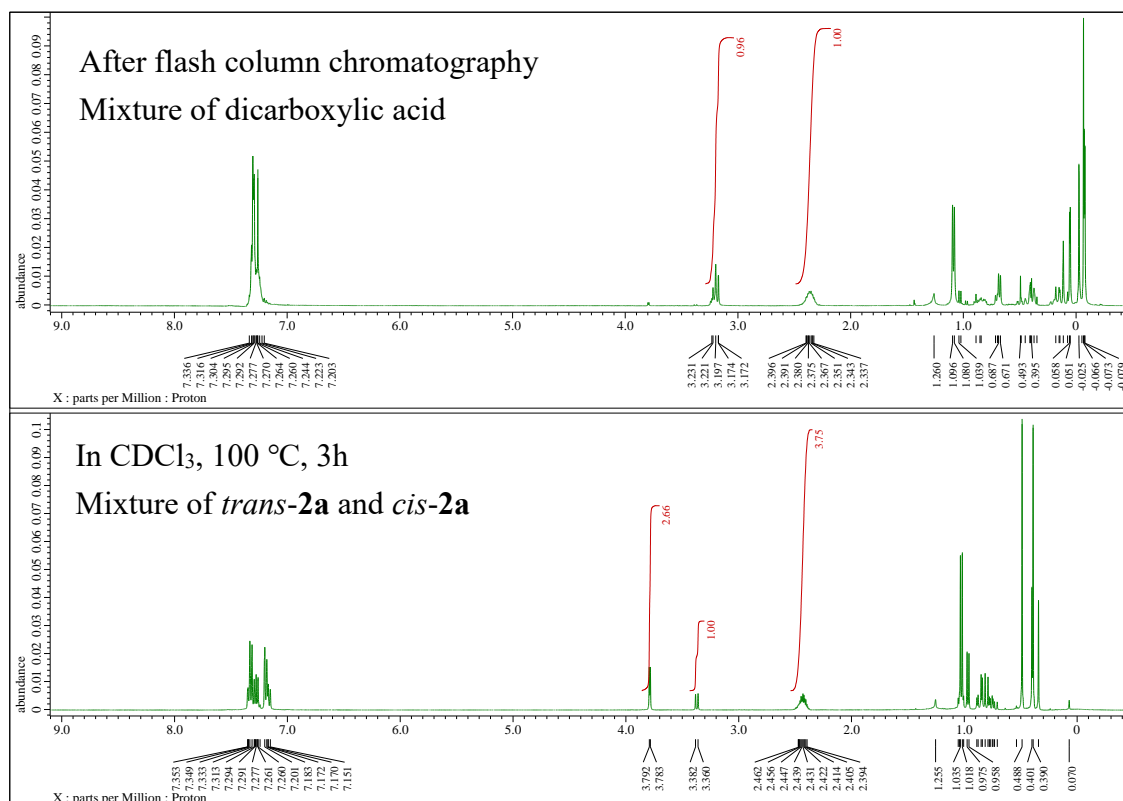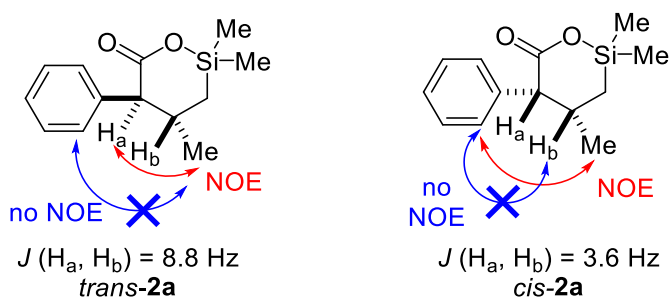

Figure 6. Transformation of Dicarboxylic Acid to Silalactone *trans*-**2a** and *cis*-**2a**

Spectroscopic Data of 2a, 2b, 3b-3f, 8a-8f and 9

^{1}H NMR (400 MHz, $CDCl_3$): *trans*-**2a**: δ = 0.34 (s, 3H), 0.40 (s, 3H), 0.71-0.89 (m, 2H), 0.97 (d, *J* = 6.4 Hz, 3H), 2.40-2.44 (m, 1H), 3.37 (d, *J* = 8.8 Hz, 1H), 7.15-7.35 (m, 5H); *cis*-**2a**: δ = 0.39 (s, 3H), 0.49 (s, 3H), 0.71-0.89 (m, 2H), 1.02 (d, *J* = 6.8 Hz, 3H),

2.40-2.44 (m, 1H), 3.79 (d, J = 3.6 Hz, 1H), 7.15-7.35 (m, 5H); ^{13}C NMR (100 MHz, CDCl$_3$): *trans*-**2a**: δ = -0.1, 1.3, 19.1, 24.2, 32.8, 59.0, 127.2, 128.4, 128.7, 139.0, 171.3; *cis*-**2a**: δ = 0.2, 1.0, 17.2, 21.1, 31.9, 56.7, 127.4, 128.4, 129.6, 136.1, 170.8; HRMS (APCI$^+$) : Calcd for C$_{13}$H$_{19}$O$_2$Si, [M+H]$^+$ 235.1149, Found m/z 235.1141. IR (Fixed Cell, CDCl$_3$ solution): 1721, 1260 cm^{-1}. Although the sample was pure before IR measurement, the sample after IR measurement contained <10% of dicarboxylic acid **3a** by hydrolysis of **2a** with moisture in the air.


2b
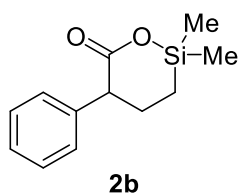
Silalactone **2b**: ^{1}H NMR (400 MHz, DMF-d_7): δ = 0.37 (s, 3H), 0.40 (s, 3H), 0.92-1.09 (m, 2H), 2.12-2.19 (m, 1H), 2.25-2.35 (m, 1H), 3.82 (dd, J = 10.4, 3.6 Hz, 1H), 7.25-7.38 (m, 5H); ^{13}C NMR (100 MHz, DMF-d_7): δ = -0.3, 0.5, 11.0, 28.0, 52.5, 127.7, 129.35, 129.41, 142.1, 171.6; HRMS (APCI$^+$): Calcd for C$_{12}$H$_{17}$O$_2$Si, [M+H]$^+$ 221.0992, Found m/z 221.0987. IR (Fixed Cell, CDCl$_3$ solution): 1721, 1260 cm^{-1}. Although the sample was pure before IR measurement, the sample after IR measurement contained <14% of **3b** by hydrolysis of **2b** with moisture in the air.


3b

cis-**3b** (meso)
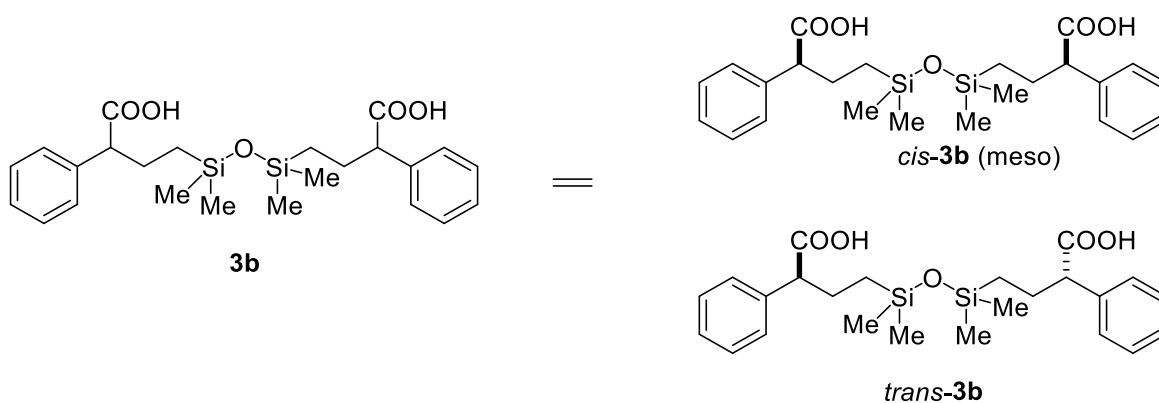
trans-**3b**

Dicarboxylic acid **3b** is a diastereomeric mixture of *cis*-**3b** and *trans*-**3b** (*cis*-**3b**:*trans*-**3b** = 1:1. The ratio was determined by ^{1}H decoupled quantitative ^{13}C NMR). ^{1}H NMR (400 MHz, CDCl$_3$): δ = -0.002-0.013 (m, 12H), 0.37-0.59 (m, 4H), 1.75-1.83 (m, 2H), 2.08-2.15 (m, 2H), 3.48-3.52 (m, 2H), 7.24-7.33 (m, 10H), 11.33 (br, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.2, 0.5, 16.4, 27.4, 54.80, 54.82, 127.5, 128.3, 128.8, 138.6, 180.17, 180.21. Whereas two kinds of methyl carbons on silicon (0.2 and 0.5 ppm), benzyl

carbons (54.80 and 54.82 ppm), and carbonyl carbons (180.17 and 180.21 ppm) were detected, any other peaks overlapped.; HRMS (APCI$^-$): Calcd for $C_{24}H_{33}O_5Si_2$, [M-H]$^-$ 457.1872, Found m/z 457.1873; IR (ATR): 3400-2200, 1697, 1252, 1069, 787 cm^{-1}, Anal calcd for $C_{24}H_{34}O_5Si_2$: C, 62.84; H, 7.47; Found; C, 62.96; H, 7.59.

3c
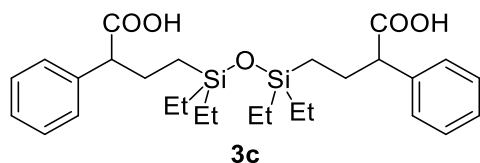
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.39-0.58 (m, 12H), 0.83-0.89 (m, 12H), 1.72-1.82 (m, 2H), 2.04-2.14 (m, 2H), 3.46 (t, J = 6.8 Hz, 2H), 7.23-7.32 (m, 10H), 9.23 (br, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 6.7, 6.8, 12.8, 27.4, 55.1, 127.5, 128.3, 128.7, 138.6, 138.7, 180.4, Whereas two kinds of ipso carbons on silicon (138.6 and 138.7 ppm) were detected, any other peaks overlapped.; HRMS(APCI$^-$): Calcd for $C_{28}H_{41}O_5Si_2$, [M-H]$^-$ 513.2498, Found m/z 513.2493; IR (ATR): 3500-2100, 1701, 1070, 725, 696 cm^{-1}.


3d
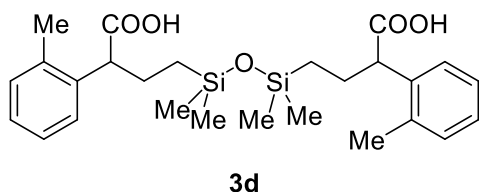
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.03 (s, 12H), 0.43 (td, J = 14.0, 4.4 Hz, 2H), 0.56 (td, J = 13.6, 4.4 Hz, 2H), 1.72-1.79 (m, 2H), 2.07-2.12 (m, 2H), 2.38 (s, 6H), 3.79 (t, J = 7.6 Hz, 2H), 7.13-7.20 (m, 6H), 7.30-7.32 (m, 2H), 9.34 (br, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.3, 0.4, 16.5, 20.1, 26.7, 49.9, 126.56, 126.58, 126.91, 126.93, 127.2, 130.6, 136.6, 136.7, 137.1, 180.51, 180.54. Whereas two kinds of methyl carbons on silicon (0.3 and 0.4 ppm), three aromatic carbons (126.56 and 126.58, 126.91 and 126.93, 136.6 and 136.7 ppm), and carbonyl carbons (180.81 and 180.54 ppm) were detected, any other peaks overlapped.; HRMS (APCI$^-$): Calcd for $C_{26}H_{37}O_5Si_2$, [M-H]$^-$ 485.2185, Found m/z 485.2182; IR (ATR): 3400-2200, 1697, 1070, 785 cm^{-1}.


3e
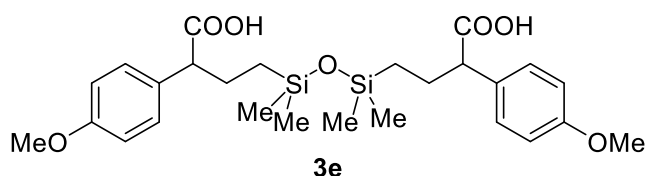
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.01 (s, 12H), 0.40 (td, J = 12.8, 4.8 Hz, 2H), 0.50

(td, J = 12.8, 4.4 Hz, 2H), 1.69-1.79 (m, 2H), 2.02-2.10 (m, 2H), 3.42 (t, J = 7.2 Hz, 2H), 3.78 (s, 6H), 6.84 (d, J = 8.0 Hz, 4H), 7.21 (d, J = 8.8 Hz, 4H), 9.34 (br, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.3, 0.4, 16.3, 27.4, 54.0, 55.4, 114.1, 129.3, 130.7, 159.0, 180.7. Whereas two kinds of methyl carbons on silicon (0.3 and 0.4 ppm) were detected, any other peaks overlapped.; HRMS (APCI[-]): Calcd for C$_{26}$H$_{37}$O$_7$Si$_2$, [M-H][-] 517.2083, Found m/z 517.2080; IR (ATR): 3400-2100, 1701, 1246, 783 cm^{-1}.


3f
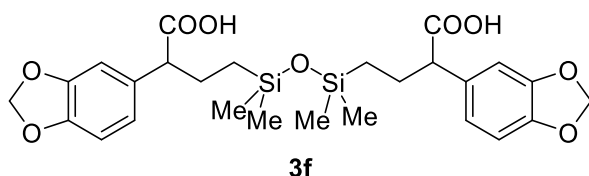
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.02 (s, 12H), 0.37-0.53 (m, 2H), 1.67-1.77 (m, 2H), 1.99-2.08 (m, 2H), 3.39 (t, J = 7.6 Hz, 2H), 5.92 (s, 2H), 5.93 (s, 2H), 6.73 (br, 4H), 6.82 (s, 2H), 10.11 (br, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.3, 0.4, 16.3, 27.4, 54.4, 101.2, 108.39, 108.42, 121.8, 132.3, 147.0, 147.9, 180.47. 180.50. Whereas two kinds of methyl carbons on silicon (0.3 and 0.4 ppm), aromatic carbons (108.39 and 108.42), and carbonyl carbons (180.47 and 180.50) were detected, any other peaks overlapped.; HRMS(APCI[-]): Calcd for C$_{26}$H$_{33}$O$_9$Si$_2$, [M-H][-] 545.1669, Found m/z 545.1669; IR (ATR): 3700-2100, 1703, 1248, 1038, 795 cm^{-1}.

8a
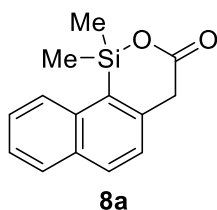
The crude mixture was purified by base-acid extraction. 2 N NaOH and Et$_2$O was added to the crude mixture and the mixture was extracted with 2 N NaOH (three times). The combined aqueous phase was acidified with 2 N HCl and the mixture was extracted with Et$_2$O (three times). The combined organic phase was washed with H$_2$O (twice) and brine, and then dried over anhydrous MgSO$_4$. After removal of the solvent under reduced pressure, **8a** was obtained in pure form. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.74 (s, 6H), 4.07 (s, 2H), 7.23 (d, J = 8.8 Hz, 1H), 7.50-7.60 (m, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.87-7.91 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 1.4. 40.2. 126.1, 126.8, 127.0, 127.1, 127.5, 129.3, 131.6, 132.3, 135.7, 139.2, 168.0; HRMS (APCI[+]): Calcd for C$_{14}$H$_{14}$O$_2$Si, [M][+] 243.0836, Found m/z 243.0829; IR (ATR): 1720, 1254, 980, 791 cm^{-1}.
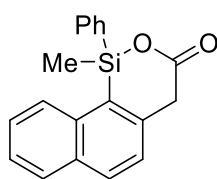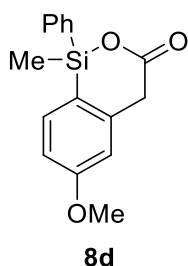
8b

Purified by base-acid extraction according to the procedure analogous to that described for **8a**.^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.03 (s, 3 H), 4.11 (s, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.36-7.51 (m, 5H), 7.58-7.60 (m, 2H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -0.6, 40.6, 125.6, 126.1, 126.9, 127.2, 127.7, 128.6, 129.2, 131.4, 132.1, 132.3, 133.6, 134.3, 136.1, 140.5, 167.8; HRMS (APCI$^+$): Calcd for C$_{19}$H$_{16}$O$_2$Si, [M+H]$^+$ 305.0992, Found m/z 305.0991; IR (ATR): 1732, 1255, 1114, 974, 791, 729, 696 cm^{-1}.
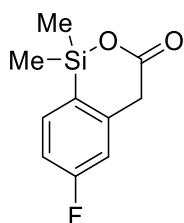

8c

The crude mixture was purified by base-acid extraction according to the procedure analogous to that described for **8a**. The residue was a mixture of **8c** and unknown product (the author assumes this product is a carboxylic acid that is produced by hydrolysis of **8c**). This unknown product was converted to **8c** when the residue was left in CDCl$_3$ (anhydrous) for 4 h. The solvent was then removed by evaporation, where the mixture was kept away from air to avoid hydrolysis by moisture. Silalactone **8c** was thus obtained in pure form.

8c: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.54 (s, 6H), 3.85 (s, 2H), 6.90 (d, *J* = 9.6 Hz, 1H), 7.04 (ddd, *J* = 8.4, 8.4, 2.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -0.4, 40.7, 114.6 (d, *J* = 20.1 Hz), 115.5 (d, *J* = 21.1 Hz), 126.4 (d, *J* = 3.8 Hz), 134.3 (d, *J* = 8.6 Hz), 142.2 (d, *J* = 7.7 Hz), 164.6 (d, *J* = 249.2 Hz), 167.6; HRMS (APCI$^+$): Calcd for C$_{10}$H$_{11}$FO$_2$Si, [M+H]$^+$ 211.0585, Found m/z 211.0585; IR (Fixed Cell, CDCl$_3$ Solution): 1740, 1267 cm^{-1}

8d

The crude mixture was purified by base-acid extraction according to the procedure analogous to that described for **8a**. The residue was a mixture of **8d** and unknown product (the author assumes this product is a carboxylic acid that is produced by hydrolysis of **8d**). This unknown product was converted to **8d** when heated at 100 °C in CDCl$_3$ for 4 h. The solvent was then removed by evaporation, where the mixture was kept away from air to avoid hydrolysis by moisture. Silalactone **8d** was thus obtained in pure form.

8d: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.80 (s, 3H), 3.84 (s, 3H), 3.85 (s, 2H), 6.75 (s, 1H), 6.90 (d, J = 8.0 Hz, 1H), 7.37-7.41 (m, 2H), 7.44-7.46 (m, 2H), 7.54-7.57 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 2.0, 41.4, 55.4, 113.3, 114.0, 119.7, 128.4, 131.2, 133.4, 134.0, 134.7, 142.1, 162.2, 168.3; HRMS (APCI$^+$): Calcd for C$_{16}$H$_{16}$O$_3$Si, [M+H]$^+$ 285.0941, Found m/z 285.0936; IR (Fixed Cell, CDCl$_3$ Solution): 1732, 1260 cm^{-1}
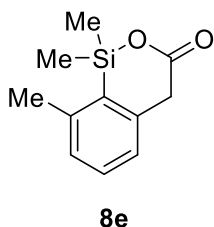

8e

Purified by base-acid extraction according to the procedure analogous to that described for **8a**. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.59 (s, 6H), 2.43 (s, 3H), 3.85 (s, 2H), 6.98 (d, J = 7.6 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.6, 23.2, 40.6, 126.0, 128.6, 129.6, 131.0, 139.9, 142.5, 168.3; HRMS (APCI$^+$): Calcd for C$_{11}$H$_{14}$O$_2$Si, [M+H]$^+$ 207.0836, Found m/z 207.0835; IR (ATR): 1722, 1260, 968, 824, 804, 789, 691 cm^{-1}.

9
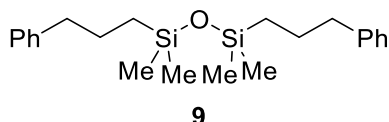
Purified by preparative thin-layer chromatography (hexane/ethyl acetate = 4/1). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.13 (s, 12H), 0.63-0.67 (m, 4H), 1.65-1.73 (m, 4H), 2.65 (t, J = 7.6 Hz, 4H), 7.17-7.20 (m, 6H), 7.27-7.31 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$):

δ = -0.1, 17.7, 25.4, 39.7, 125.8, 128.4, 128.6, 142.6; HRMS (APCI$^+$): Calcd for C$_{22}$H$_{35}$OSi$_2$, [M+H]$^+$ 371.2221, Found m/z 371.2212; IR (ATR): 1252, 1055, 791, 696 cm^{-1}.

**A Typical Procedure for Synthesis of 2-Phenylsilacyclobutane[14]**
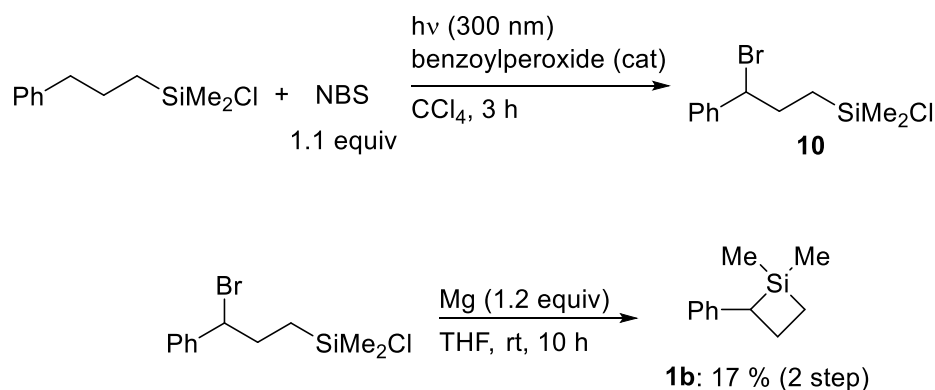
Into an oven-dried flask equipped with a stirrer bar, *N*-bromosuccinimide (5.8 g, 33 mmol, 1.1 equiv) and benzoyl peroxide (a catalytic amount) were placed. The flask was capped with a rubber septum, evacuated and refilled with argon three times. Chlorodimethyl(3-phenylpropyl)silane[16] (6.4 g, 30 mmol) and CCl$_4$ (50 ml) were added by syringe. The reaction mixture was irradiated with an UV lamp (300 nm) for 3 h. The reaction mixture was filtered, and the solvent was removed under reduced pressure to afford 3-bromo-3-phenylpropyldimethylchlorosilane **10**. This product was used for the subsequent Grignard reaction without further purifcation. Spectral data were in agreement with literature values.[14]

In a three-necked flask equipped with a pressure equalizing addition funnel, magnesium (506 mg, 21 mmol, 1.4 equiv) was placed. The flask was capped with a rubber septum, evacuated, and refilled with argon three times. Dry THF (160 mL) was added by syringe. To the mixture, a THF (80 mL) solution of 3-bromo-3-phenyldimethylchlorosilane **10** (4.1g, ca 15 mmol) was added dropwise over 3 h. The mixture was stirred at room temperature. After 10 h, this reaction mixture was cooled at 0 °C, and then was acidified with dilute phosphoric acid. The mixture was extracted with Et$_2$O (three times), washed by water and brine, dried over anhydrous MgSO$_4$, and filtered. After removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on silica gel (eluent: hexane) to afford 2-phenylsilacyclobutane **1b** (910 mg, 5.2 mmol, 17%). Before using in the reaction with CO$_2$, **1b** was further purified by GPC. Spectral data were in agreement with literature

values.[14]

**Spectroscopic Data of 1a and 1c-1f**
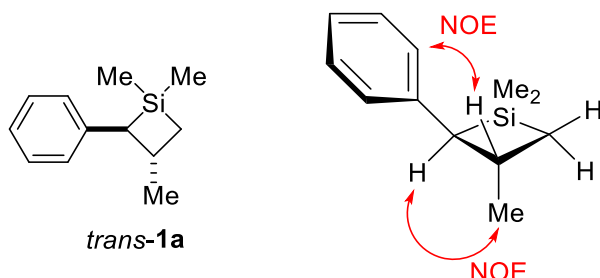
Silacyclobutane **1a** was synthesized as a diastereomeric mixture (*trans*-**1a**:*cis*-**1a** = 12:1) from (3-bromo-2-methyl-3-phenylpropyl)dimethylchlorosilane. The isomers were separated by flash column chromatography (hexane) and GPC. *trans*-**1a**: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.17 (s, 3H), 0.33 (s, 3H), 0.62 (dd, *J* = 14.0, 10.8 Hz, 1H), 1.18 (d, *J* = 6.4 Hz, 3H), 1.25 (ddd, *J* = 14.0, 8.4, 0.8 Hz, 1H), 2.24 (d, *J* = 10.8 Hz, 1H), 2.53-2.65 (m, 1H), 7.04-7.07 (m, 3H), 7.21-7.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -4.4, 1.2, 20.6, 25.3, 34.0, 46.2, 123.9, 126.6, 128.3, 143.9; ^{29}Si NMR (119 MHz, DMF-*d$_7$*) δ = 8.9; HRMS (APCI$^+$): Calcd for C$_{12}$H$_{19}$Si, [M+H]$^+$ 191.1251, Found m/z 191.1247; IR (ATR): 833, 810, 696 cm^{-1}.
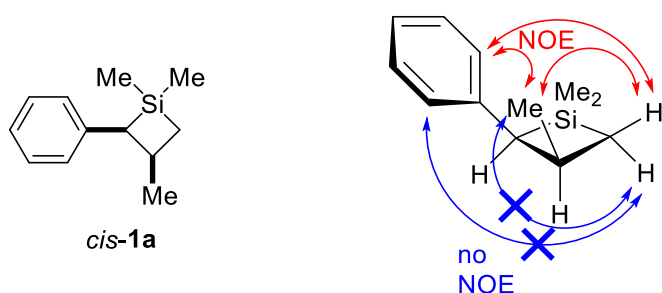

cis-**1a**: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.36 (s, 3H), 0.38 (s, 3H), 0.86 (dd, *J* = 14.4, 6.0 Hz, 1H), 0.95 (d, *J* = 6.8 Hz, 3H), 1.34 (ddd, *J* = 14.0, 8.4, 1.6 Hz, 1H), 2.86-2.98 (m, 2H), 7.08-7.12 (m, 3H), 7.21-7.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.1, 0.9, 20.8, 21.8, 32.8, 41.6, 124.5, 128.0, 129.7, 142.7; ^{29}Si NMR (119 MHz, DMF-*d$_7$*) δ = 14.0; HRMS (EI$^+$): Calcd for C$_{12}$H$_{18}$Si, [M]$^+$ 190.1177, Found m/z 190.1176; IR (ATR): 835, 795, 698 cm^{-1}.

1c
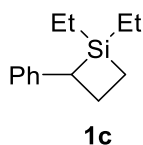
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.55-0.72 (m, 2H), 0.79-0.85 (m, 5H), 1.00-1.04 (m, 2H), 1.09-1.13 (m, 3H), 2.27-2.38 (m, 1H), 2.53-2.62 (m, 1H), 2.92 (t, *J* = 10.0 Hz, 1H), 7.02-7.09 (m, 3H), 7.21-7.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 3.3, 6.9, 7.0, 7.4, 8.0, 24.3, 35.3, 123.7, 126.3, 128.3, 144.8; HRMS (APCI$^+$): Calcd for C$_{13}$H$_{21}$Si, [M+H]$^+$ 205.1407, Found m/z 205.1403; IR (ATR): 1005, 752, 694 cm^{-1}.

1d
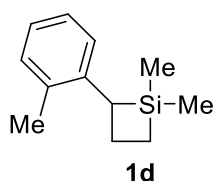
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.02 (s, 3H), 0.45 (s, 3H), 1.00-1.08 (m, 2H), 2.16 (s, 3H), 2.37-2.57 (m, 2H), 2.81 (t, *J* = 9.2 Hz, 1H), 6.96-7.01 (m, 1H), 7.09 (dd, *J* = 7.2, 0.4 Hz, 1H), 7.14-7.16 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -4.4, 1.7, 11.0, 20.5, 22.8, 34.9, 123.6, 124.4, 126.0, 129.6, 134.4, 142.5; HRMS (APCI$^+$): Calcd for C$_{12}$H$_{19}$Si, [M+H]$^+$ 191.1251, Found m/z 191.1246; IR (ATR): 1485, 837, 806, 752 cm^{-1}.

1e
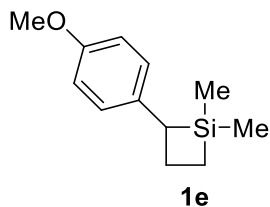
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.15 (s, 3H), 0.36 (s, 3H), 0.97-1.02 (m, 2H), 2.15-2.26 (m, 1H), 2.55-2.64 (m, 1H), 2.73 (t, *J* = 10.0 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.99 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -4.0, 1.2, 11.3, 25.1, 36.3, 55.4, 113.8, 127.2, 136.9, 156.5; HRMS (APCI$^+$): Calcd for C$_{12}$H$_{19}$OSi, [M+H]$^+$ 207.1200, Found m/z 207.1195; IR (ATR): 1508, 1242, 804 cm^{-1}.

1f
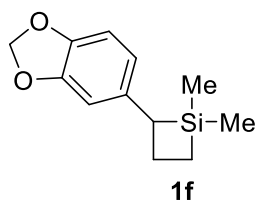
^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.14 (s, 3H), 0.36 (s, 3H), 0.96-1.00 (m, 2H), 2.12-2.22 (m, 1H), 2.53-2.61 (m, 1H), 2.72 (t, J = 10.0 Hz, 1H), 5.89 (s, 2H), 6.50 (dd, J = 8.0, 1.6 Hz, 1H), 6.58 (d, J = 1.6 Hz, 1H), 6.70 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = -4.1, 1.1, 11.2, 25.0, 37.1, 100.7, 107.1, 108.2, 118.6, 138.9, 144.2, 147.6; HRMS (APCI$^+$): Calcd for C$_{12}$H$_{17}$O$_2$Si, [M+H]$^+$ 221.0992, Found m/z 221.0988; IR (ATR): 1503, 1487, 1040, 802 cm^{-1}.

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Chapter 4

Ring-opening Fluorination of Cyclobutanols and Cyclopropanols
Catalyzed by Silver

Abstract

Cyclobutanols and cyclopropanols underwent ring-opening fluorination upon treatment with Selectfluor in the presence of a substoichiometric amount of a silver salt. The reaction provides an efficient method to synthesize γ- and β-fluoroalkyl ketones

Introduction

Organofluorine compounds have attracted significant attention in pharmaceuticals, agrochemicals, and materials science.[1] The strong demand for organofluorine compounds has spurred the development of new synthetic means for organofluorine compounds.[2,3] Herein the author reports a ring-opening fluorination reaction of cyclobutanols and cyclopropanols catalyzed by silver. A fluorine atom is introduced in a site-selective manner to afford the γ- and β-fluoroalkyl ketones.

Results and Discussion

Cyclobutanols are facilely prepared by well-established methods such as [2+2] cycloaddition of alkenes with ketenes followed by an addition reaction of Grignard reagents.[4] They undergo ring-opening reactions upon treatment with transition metal catalysts.[5] Oxidation of cyclobutanols also induces ring opening.[6] As a continuation of Murakami group's previous studies on the ring-opening reactions of cyclobutanol derivatives,[7] the author examined a reaction with fluorinating agents to find that cyclobutanol **1a** underwent a ring-opening fluorination reaction when treated with Selectfluor (4 equiv)[8] in the presence of Ag^{I}F (20 mol %) in a benzene/water biphasic solvent at 60 °C for 5 h (Scheme 1).[3c, 9] γ-Fluoroalkyl ketone **2a** was obtained in 60% isolated yield. Other Ag(I) salts like AgBF$_4$ and AgNO$_3$ exhibited comparable reactivities, and no reaction took place in the absence of Ag(I) salts. Fluorinating agents such as *N*-fluorobenzenesulfonimide and *N*-fluoropyridinium salts were totally ineffective. Treatment of **1a** with a stoichiometric amount of either Ag^{I}F or Ag^{II}F$_2$ in the absence of Selectfluor failed to induce any reactions, suggesting that a reactive species is generated in situ from Ag^{I}F and Selectfluor to initiate the ring-opening fluorination reaction.

Scheme 1. Ring-opening Fluorination of **1a**
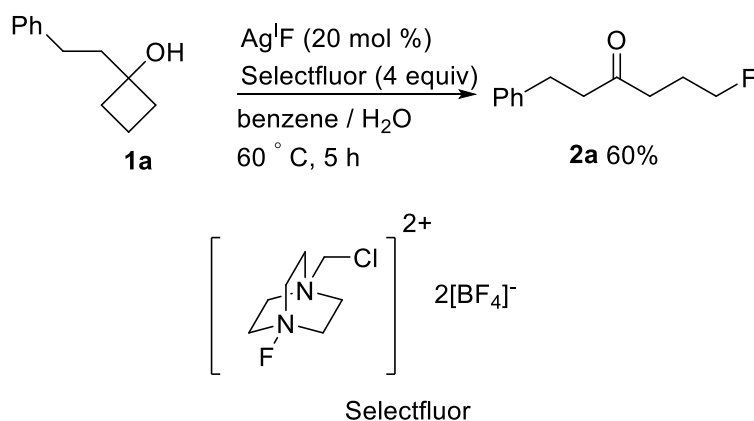
The formation of **2a** from **1a** can be explained by assuming a radical-type reaction mechanism depicted in Scheme 2, although the author has no experimental evidence for it.[10] Initially, Ag(I) is oxidized to Ag(III) by Selectfluor. The resulting Ag(III) reacts with cyclobutanol **1a** to furnish silver cyclobutanolate **A**. One-electron transfer from the cyclobutanolate moiety to Ag(III), i.e., homolytic cleavage of the Ag-O bond induces ring opening to give the alkyl radical intermediate **B** together with Ag^{II}F species. Finally, the carbon-centered radical **B** is fluorinated with the Ag^{II}F, resulting in the formation of **2a** and Ag(I) species, the latter of which re-enters the next cycle.

Scheme 2. Proposed Mechanism
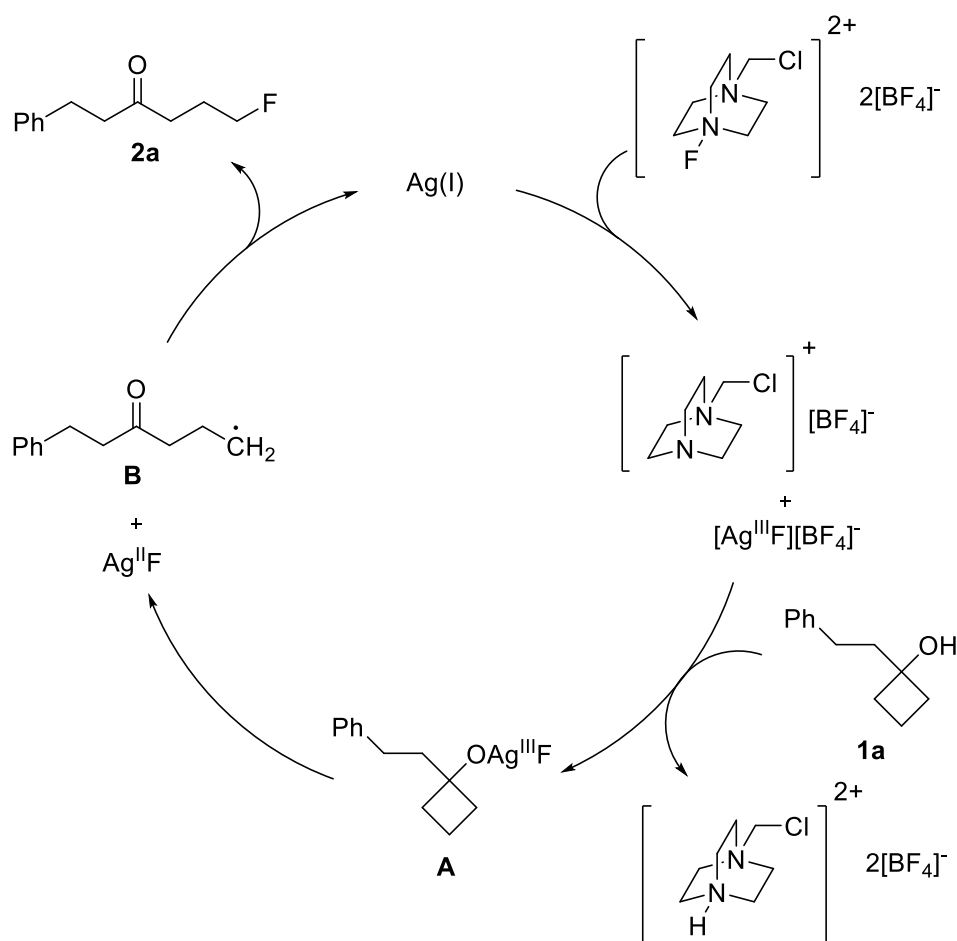
The ring-opening fluorination reaction was significantly dependent on the substituent at the 1-position of cyclobutanols. No reaction was observed with the 1-octadecylcyclobutanol. When a phenyl group is present in the 1-substituent, however, the

fluorination reaction took place. 1-Phenylcyclobutanol (**1b**) underwent the ring-opening fluorination to produce the corresponding γ-fluoroalkyl ketone **2b** in 77% yield (Table 1). 1-Benzylcyclobutanol (**1c**) was also reactive (83% conversion) and **2c** was obtained in 30% yield along with various unidentified by-products. The reaction of 1-(3-phenylpropyl)cyclobutanol (**1d**) was sluggish and transformed only partially under the same reaction conditions. 1-[2-(4-Methoxyphenyl)ethyl]cyclobutanol (**1e**) was so reactive that 1.2 equiv of Selectfluor was enough for full conversion. On the other hand, 1-[2-(4-chlorophenyl)ethyl]-cyclobutanol (**1f**) was unreactive under the same reaction conditions. These results may indicate that the electron-donating phenyl group located in proximity to the hydroxy group facilitates the approach of the catalytically active silver species to the hydroxy group.[11]
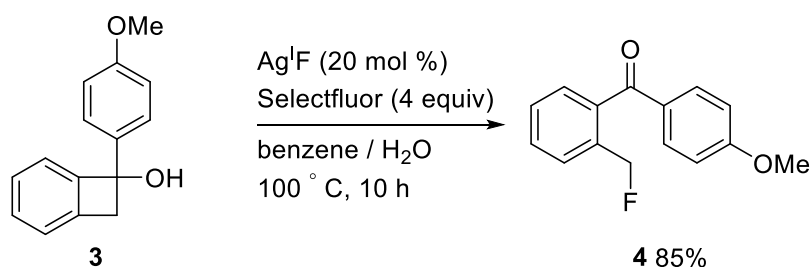
**Table1.** Ring-opening Fluorination of 1-Substituted Cyclobutanols[a]
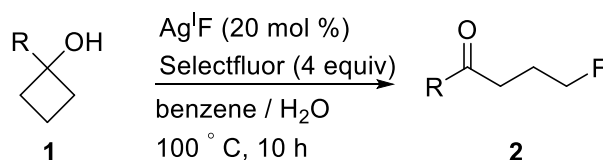
Entry	R	Conversion of **1** /%[b]	Yield of **2** / %[c]
1	Ph- (**1b**)	100	77
2	PhCH$_2$- (**1c**)	83	30
3	Ph(CH$_2$)$_3$- (**1d**)	23	<10
4[d]	4-MeOC$_6$H$_4$(CH$_2$)$_2$- (**1e**)	100	40
5	4-ClC$_6$H$_4$(CH$_2$)$_2$- (**1f**)	<5	<5

[a]Reaction conditions: cyclobutanol **1** (0.20 mmol), AgF (0.04 mmol, 20 mol %), Selectfluor (0.8 mmol, 4 equiv), benzene (1 mL), H$_2$O (1 mL), 100 °C, 10 h. [b] Determined by NMR analysis of the crude reaction mixture. [c] Isolated yield. [d] 1.2 equiv of Selectfluor was used.

When benzocyclobutenol **3** was subjected to the standard reaction conditions in place of cyclobutanol **1**, benzyl fluoride **4** was selectively obtained in 85% isolated yield (Scheme 3). A product derived from cleavage of the C(sp^2)–C(sp^3) bond[12] was not detected in the reaction mixture. This site-selectivity accords with the reported result of the oxidative ring-opening reaction of benzocyclobutenols; a benzocyclobutenoxyl radical undergoes ring opening with site-selective cleavage of the C(sp^3)–C(sp^3) bond to give a benzylic radical intermediate.[13]

Scheme 3. Ring-opening Fluorination of **3**.

Phenyl-substituted cyclopropanols [5a, 5c] also underwent the ring-opening fluorination reaction under the same reaction conditions to afford β-fluoroalkyl ketones (Table 2).[14] In the case of unsymmetrical cyclopropanol **5c**, the ring opening took place site-selectively at the more substituted position to afford sec-alkyl fluoride **6c**. This result is consistent with the proposed radical mechanism, since generation of a more substituted carbon radical would be favored.

Table 2. Ring-opening Fluorination of Cyclopropanols[a]
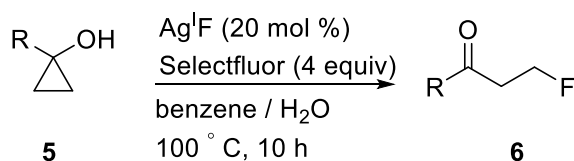
Entry	Cyclopropanol **5**	β-Fluorinated Ketone[b]
1	**5a**	**6a** 78%
2	**5b**	**6b** 55%
3	**5c** dr = 3:1	**6c** 50%

[a]Reaction conditions: cyclopropanol **5** (0.20 mmol), AgF (0.04 mmol, 20 mol %), Selectfluor (0.8 mmol, 4 equiv), benzene (1 mL), H$_2$O (1 mL), 100 °C, 10 h. [b]Isolated yields are shown.

Conclusion

In conclusion, the author has described the silver-catalyzed ring-opening fluorination reaction of cyclobutanols and cyclopropanols. The site-selectivity of the ring-opening process can be rationalized by assuming a radical-type mechanism; the C–C bond is cleaved to generate a more stabilized carbon radical. The present reaction offers a convenient way to synthesize γ- and β-fluorinated ketones.

Experimental Section

General Methods

All reactions were carried out under an argon atmosphere in oven-dried glassware with standard Schlenk techniques. IR measurements were performed on a FTIR SHIMADZU DR-8000. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury-vx400 (^{1}H at 400.44 MHz, ^{13}C at 100.69 MHz, ^{19}F at 376.79 MHz) spectrometer. NMR data were obtained in CDCl$_3$. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm (CHCl$_3$). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.0 ppm(CDCl$_3$). Fluorine chemical shifts were referenced to the signal of the trifluoroacetic acid at -79.0 ppm. High-resolution mass spectra were recorded on a Thermo Scientific Exactive (ESI) spectrometer. Flash column chromatography was performed with silica gel 60N (Kanto). Preparative thin-layer chromatography (PTLC) was performed on silica gel plates with PF254 indicator (Merck).

Materials

Benzene was purchased from Kanto Chemical Co. Distilled water was purchased from Nacalai Tesque. These solvents were degassed by sonication prior to use. Ag(I)F and Selectfluor were purchased from Aldrich. All cyclobutanols[6c] and cyclopropanols[14c] were prepared according to the literature procedures.

## Ring-opening Fluorination of Cyclobutanol 1a: A Typical Procedure
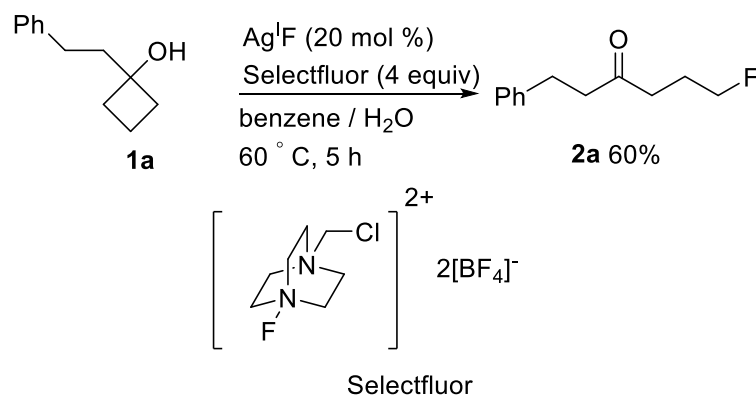
1-(2-Phenylethyl)cyclobutanol **1a** (35.2 mg, 0.20 mmol), AgF (5.0 mg, 0.04 mmol) and Selectfluor (283.4 mg, 0.80 mmol) were placed in a Schlenk tube. The reaction vessel was filled with argon. Benzene (2 mL) and water (2 mL) were then added and the reaction mixture was stirred at 60 °C for 5 h. Upon completion of the reaction, the resulting mixture was cooled to room temperature and extracted with dichloromethane (15 mL × 3). The

combined organic phase was dried over anhydrous MgSO₄. After removal of the solvent under reduced pressure, the crude product was purified by PTLC with ethyl acetate/hexane (1:7) as the eluent to give 6-fluoro-1-phenylhexan-3-one (**2a**) as a yellow oil (23.3 mg, 60% yield).

Characterization Data for New Compounds

2a
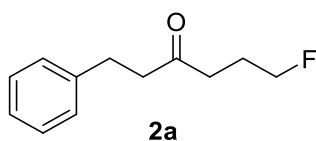
IR (ATR): 1713, 1497, 1373, 1030, 750, 698 cm^{-1}; ^{1}H NMR δ = 1.96 (dtt, J = 26.4, 7.2, 5.6 Hz, 2H), 2.55 (t, J = 7.2 Hz, 2H), 2.76 (t, J = 7.6 Hz, 2H), 2.91 (t, J = 7.6 Hz, 2H), 4.43 (dt, J = 47.2, 6.0 Hz, 2H), 7.17-7.30 (m, 5H); ^{13}C NMR δ = 24.4 (d, J = 19.8 Hz), 29.8, 38.2 (d, J = 4.4 Hz), 44.4, 83.2 (d, J = 163.2 Hz), 126.1, 128.3, 128.5, 140.9, 208.9; ^{19}F NMR δ = -223.2 (tt, J = 47.0, 27.4 Hz); HRMS (ESI): Calcd for C$_{12}$H$_{16}$FO$^+$, [M+H]$^+$ 195.1180. Found m/z 195.1177.


2c
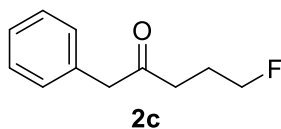
IR (ATR): 1713, 1497, 1454, 1028, 731, 698 cm^{-1}; ^{1}H NMR δ = 1.94 (dtt, J = 26.8, 7.2, 6.0 Hz, 2H), 2.61 (t, J = 7.2 Hz, 2H), 3.71 (s, 2H), 4.41 (dt, J = 47.2, 6.0 Hz, 2H), 7.17-7.30 (m, 5H); ^{13}C NMR δ = 24.4 (d, J = 19.8 Hz), 37.3 (d, J = 4.4 Hz), 50.2, 83.1 (d, J = 163.3 Hz), 127.1, 128.8, 129.4, 134.0, 207.3; ^{19}F NMR δ = -220.2 (tt, J = 53.8, 26.3 Hz); HRMS (ESI): Calcd for C$_{11}$H$_{14}$FO$^+$, [M+H]$^+$ 181.1023. Found m/z 181.1020.


2e
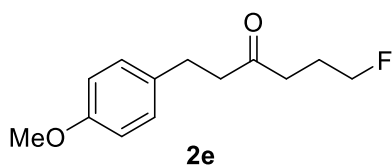
IR (ATR): 2905, 1713, 1512, 1244, 1032, 827 cm^{-1}; ^{1}H NMR δ = 1.95 (dtt, J = 26.8, 7.2, 5.6 Hz, 2H), 2.54 (t, J = 7.2 Hz, 2H), 2.72 (t, J = 7.6 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 3.78 (s, 3H), 4.43 (dt, J = 47.2, 6.0 Hz, 2H), 6.80-6.84 (m, 2H), 7.08-7.11 (m, 2H); ^{13}C NMR δ 24.3 (d, J = 19.8 Hz), 28.9, 38.2 (d, J = 3.7 Hz), 44.6, 55.2, 83.2 (d, J = 163.2

Hz), 113.9, 129.2, 132.9, 157.9, 209.1; ^{19}F NMR δ = -223.1 (tt, J = 49.6, 28.0 Hz); HRMS (ESI): Calcd for $C_{13}H_{18}FO_2^+$, $[M+H]^+$ 225.1285. Found m/z 225.1280.

4
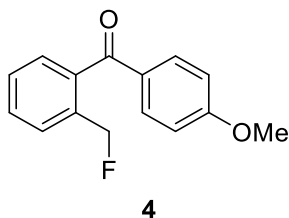
IR (ATR): 2916, 1634, 1597, 1572, 1256, 1151, 993, 741, 611 cm^{-1}; ^{1}H NMR δ = 3.88 (s, 3H), 5.57 (d, J = 47.6 Hz, 2H), 6.94-6.96 (m, 2H), 7.40-7.45 (m, 2H), 7.56 (ddd, J = 7.2, 7.2, 1.2 Hz, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.78-7.81 (m, 2H); ^{13}C NMR δ = 55.5, 82.2 (d, J = 164.7 Hz), 113.7, 127.4 (d, J = 2.2 Hz), 127.7 (d, J = 10.3 Hz), 129.2, 130.2, 130.7, 132.7, 136.6 (d, J = 16.9 Hz), 136.8 (d, J = 3.7 Hz), 163.7, 195.9; ^{19}F NMR δ = -214.9 (t, J = 47.0 Hz); HRMS (ESI): Calcd for $C_{15}H_{14}FO_2^+$, $[M+H]^+$ 245.0972. Found m/z 245.0967.

6b
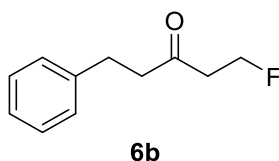
IR (ATR): 1715, 1495, 1389, 1101, 1024, 748, 698 cm^{-1}; ^{1}H NMR δ = 2.78-2.87 (m, 4H), 2.97 (t, J = 7.6 Hz, 2H), 4.75 (dt, J = 43.6, 8.0 Hz, 2H), 7.22-7.35 (m, 5H); ^{13}C NMR δ = 29.4, 43.1 (d, J = 21.2 Hz), 45.0, 78.9 (d, J = 164.0 Hz), 126.2, 128.3, 128.5, 140.7, 206.5 (d, J = 3.6 Hz); ^{19}F NMR δ = -223.3 (tt, J = 45.9, 24.0 Hz); HRMS (ESI): Calcd for $C_{11}H_{14}FO^+$, $[M+H]^+$ 181.1023. Found m/z 181.1019.

6c
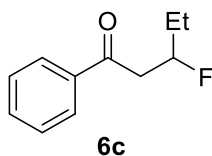
IR (ATR): 2970, 1684, 1448, 1207, 752, 689 cm^{-1}; ^{1}H NMR δ = 1.05 (t, J = 7.2 Hz, 3H), 1.70-1.83 (m, 2H), 3.08 (ddd, J = 26.8, 16.8, 4.8 Hz, 1H), 3.47 (ddd, J = 16.4, 15.6, 7.2 Hz, 1H), 5.11 (dtt, J = 48.0, 6.8, 5.2 Hz, 1H), 7.46-7.50 (m, 2H), 7.58 (tt, J = 6.8, 0.8 Hz, 1H), 7.96 (dd, J = 8.0, 0.8 Hz, 2H); ^{13}C NMR δ = 9.25 (d, J = 5.1 Hz), 28.2 (d, J = 21.2 Hz), 43.4 (d, J = 23.4 Hz), 91.5 (d, J = 167.6 Hz), 128.2, 128.6, 133.4, 136.8, 197.0;

^{19}F NMR δ = -184.4--184.0 (m); HRMS (ESI): Calcd for $C_{11}H_{14}FO^+$, $[M+H]^+$ 181.1023. Found m/z 181.1019.

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8. When 2 equiv of Selectfluor was used, **2a** was obtained in 55% yield and 21% of **1** was recovered.

9. C. Zhu group reported same ring-opening fluorination of cyclobutanols around the same time. Zhao, H.; Fan, X.; Yu, J.; Zhu, C. *J. Am. Chem. Soc.* **2015**, *137*, 3490.

10. TEMPO suppressed the ring-opening fluorination reaction of **2a** significantly, suggesting that a radical intermediate may be involved in the reaction pathway.

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Chapter 5

Synthesis of 2-Alkoxy-1,3-dienes from Propargylic Alcohol Derivatives

Abstract

1-Aryloxybut-2-yne isomerizes to 2-aryloxybuta-1,3-diene through formal 1,2-migration of the aryloxy group when treated with a catalytic amount of a nickel complex. The identical product is obtained from a propargylic carbonate and a phenol under analogous reaction conditions.

Introduction

1,3-Dienes undergo a wide variety of transformations that rapidly increase molecular complexity (e.g. Diels-Alder reaction), and thus, serve as versatile intermediates for the synthesis of complex molecules.[1] Although a number of synthetic methods of 1,3-dienes have been reported, it is still desired to develop a new pathway, particularly those starting from readily available substances.[2] Propargylic alcohols are readily prepared from terminal alkynes and aldehydes,[3] and thus, are attractive as the starting substances. Several 1,3-dienes were synthesized from propargylic alcohol derivatives. 2-Acyloxy-1,3-dienes were synthesized from propargylic acetates via a gold-catalyzed 1,2-acyloxy migration reaction.[4] 1,3-Dienes with a diaryl(cyano)methyl substituent at the 2-position were produced by a palladium-catalyzed addition reaction of diarylacetonitriles to propargyl carbonates.[5] A 2-aryloxy-1,3-diene was formed when a C–O bond forming cross-coupling reaction between but-2-yn-1-ol and 5-bromoisoquinoline was conducted in the presence of a palladium complex and a Josiphos-type bisphosphine ligand.[6] The author reports synthesis of 2-alkoxy-1,3-dienes from propargylic alcohol derivatives through a nickel catalysis.[7] 1-Aryloxybut-2-yne is isomerized into 2-aryloxybuta-1,3-diene. Alcohols are intermolecularly added to propargylic carbonates to produce 2-alkoxy-1,3-dienes in a stereoselective fashion.

Results and Disucussion

This study began with discovery of a nickel-catalyzed isomerization reaction of aryl propargylic ether **1a** to dienyl ether **2a**. When **1a** was treated with Ni(cod)$_2$ (5 mol %), DPPF (8 mol %) in ^{t}BuOH at 80 °C for 24 h, **2a** was produced in almost quantitative yield (Scheme 1).[8] The 1,3-diene **2a** formed also when other bisphosphine was used.[9] DPPB was equally effective. DPPE and DPPPent were less efficient. Monodentate triarylphosphines like PPh$_3$ and bipyridines failed to give **2a**. PCy$_3$ and *N*-heterocyclic carbene ligands like IPr and I^{t}Bu favored cyclotrimerization of the alkyne moiety.

**Scheme 1.** Isomerization of Propargylic Ester **1a** to 2-Aryloxy-1,3-diene **2a**
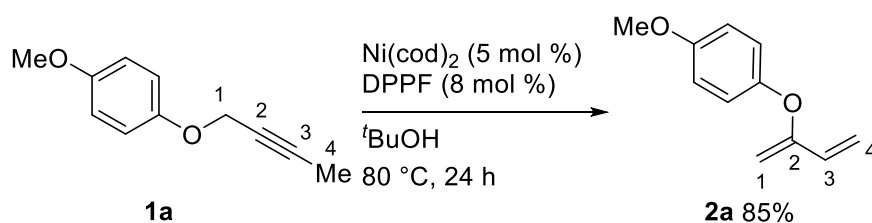
The formation of **2a** from **1a** involves the cleavage of the propargylic carbon–oxygen bond and the formation of a new carbon–oxygen bond at the internal carbon. Formal transfer of a hydrogen on the terminal methyl group to the internal carbon also accompanies. The author next carried out deuterium experiments in order to gain the mechanistic insight (Scheme 2). When the propargylic ether having a CD_3-group **1b-d_3** was subjected to the identical reaction conditions, **2b-d_2** was obtained in 58% isolated yield. This result indicates that the aryloxy group undergoes 1,2-migration onto the next carbon rather than 1,3-migration.[10] Although one deuterium at the methyl terminus of **1b-d_3** shifted away, it was not found on the next internal carbons. This suggests that the hydrogen incorporated into the product comes from ^{t}BuOH solvent rather than the terminal methyl C–H bonds. In fact, when a reaction of non-deuterated substrate **1b** was carried out in ^{t}BuOD, a deuterium was incorporated on the internal carbon (92%D). The terminal enol carbon was also deuterated in part (35%D). A control experiment revealed that the deuterium was incorporated by proton-deuterium exchange between the dienyl ether product and ^{t}BuOD solvent.[11]

Scheme 2. Deuterium Experiments
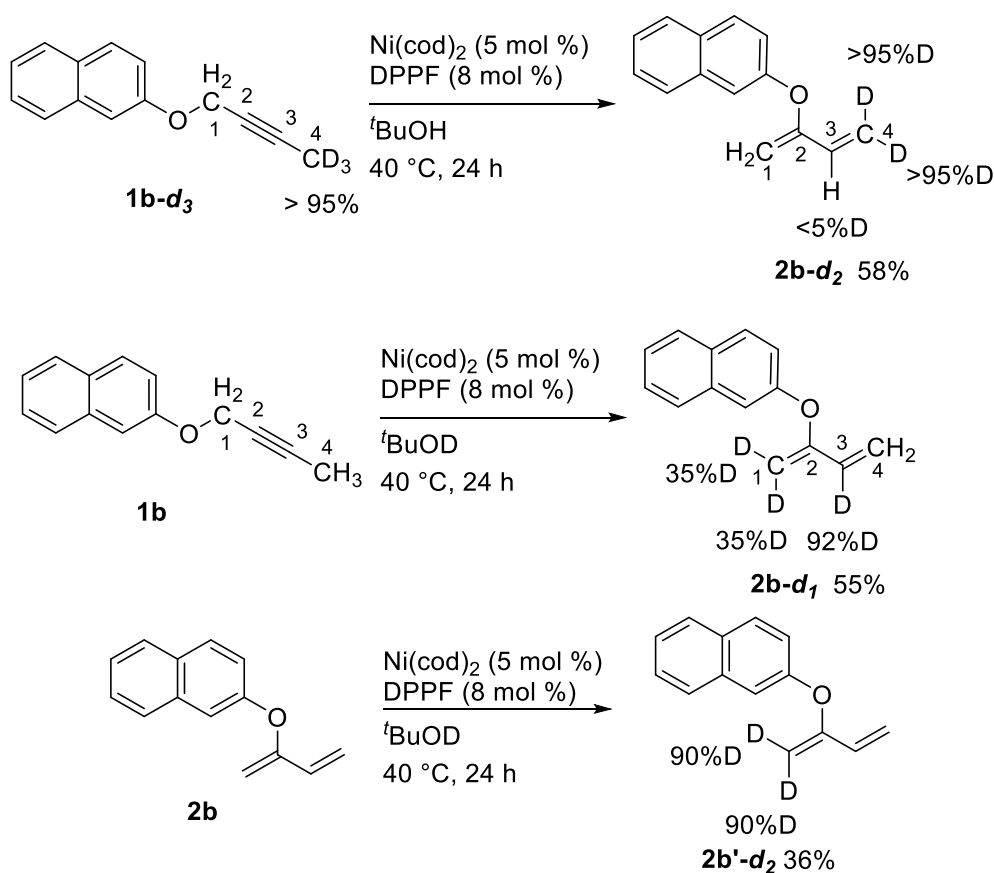
Shown in Scheme 3 is a proposed mechanism for the formation of **2** from **1**. Initially, the propargylic carbon–oxygen bond of **1** undergoes oxidative addition into Ni(0)[12] to afford a propargylic nickel(II) complex. The propargylic ligand possibly takes σ- (**A**) and π-form (**B**).[13] The aryloxide anion then adds onto the central carbon of the propargylic ligand to produce nickellacyclobutene **C**. An analogous nucleophilic addition reaction onto the central carbon of a π-propargylic ligand on rhenium to form rhenacyclobutene was reported.[14] Then, the C(sp²)–Ni linkage undergoes protonolysis to give the σ-allylic nickel intermediate **D**,[15] which is in equilibrium with another σ-allylic nickel intermediate **E**. β-Hydrogen is eliminated from the methyl group to furnish the diene product **2** and *t*BuOH. The Ni(0) species is thus regenerated and enters into the next catalytic cycle.

Scheme 3. Proposed Mechanism
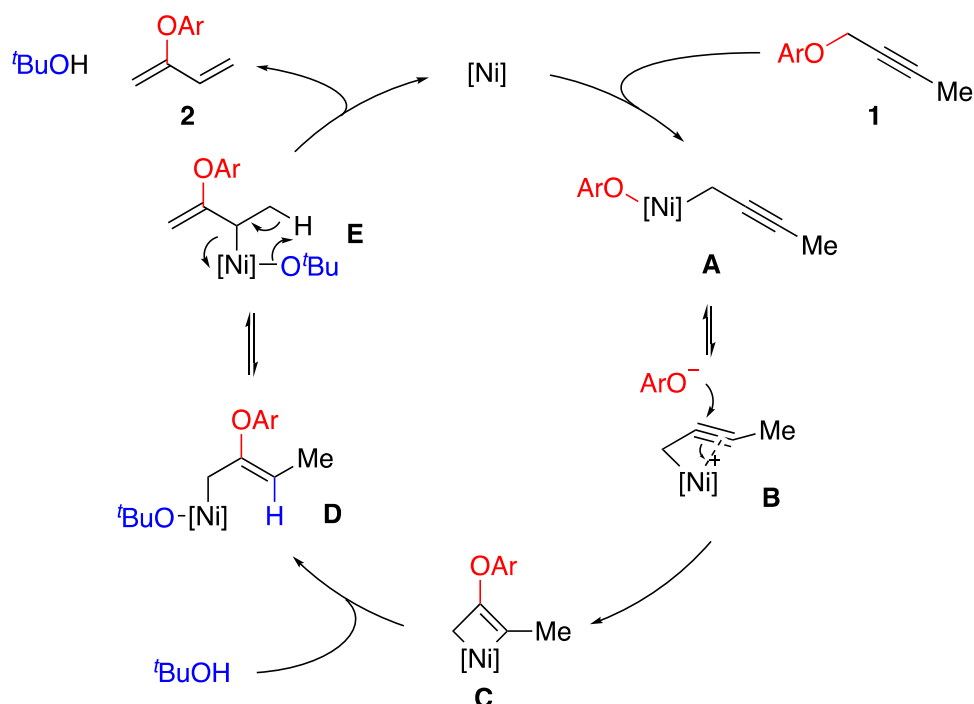
Next examined was intermolecular addition of *p*-methoxyphenol to various propargylic alcohol derivatives in order to enhance the synthetic usefulness (Table 1). Alcohol itself failed to give the adduct **2a** presumably due to the poor leaving ability of the hydroxy group (entry 1). Acetate successfully gave **2a** albeit in 27% yield (entry 2). The yield increased to 72% when methyl carbonate was used as the leaving group (entry 3). The *t*butyl carbonate (**3a**) gave the best result (entry 4). The 1,3-diene **2a** was produced in 91% yield. It was possible to isolate the diene **2a** by passing the reaction mixture through a

short pad of diol-modified silica gel using hexane as the eluent followed by bulb-to-bulb distilation. Analytically pure **2a** was obtained in 82% yield.

**Table 1.** Addition of *p*-Methoxyphenols to Propargylic Electrophiles[a]
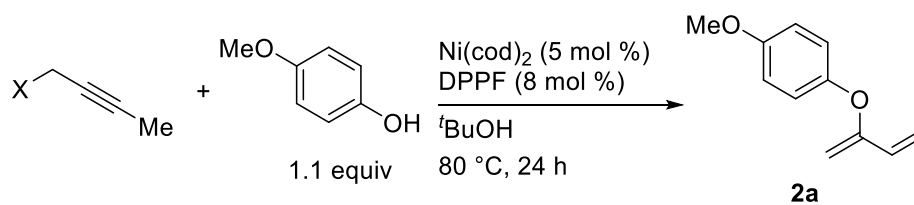
Entry	X	Yield / %[b]
1	HO-	2
2	AcO-	27
3	$MeOCO_2$-	72
4	$^tBuOCO_2$- (**3a**)	91(82)[c]

[a] Reaction conditions: propargylic electrophiles (0.20 mmol), *p*-methoxyphenol (0.22 mmol), Ni(cod)$_2$ (0.01 mmol, 5 mol %), DPPF (0.02 mmol, 8 mol %), ^tBuOH (1.0 mL), 80 °C, 24 h. [b] Determined by NMR analysis of the crude reaction mixture. [c] Isolated yield. The reaction was separately conducted in a 1.0 mmol scale.

    Mechanistically, oxidative addition of **3a** onto nickel (0) is followed by decarboxylation, producing propargylic nickel species. The ^{t}butoxide anion serves as a base to deprotonate *p*-methoxyphenol to generate phenoxides **A** and/or **B**.

    The reaction was examined using other substituted propargylic carbonates. The carbonate **3b**, which is a constitutional isomer of **3a**, afforded **2a** in 53% isolated yield (Scheme 4). Thus, both **3a** and **3b** gave the identical product. This outcome can be explained by a pathway shown in Scheme 4. Oxidative addition of **3b** onto Ni(0) produce the propargyllic nickel **F**. Aryloxide adds onto the central carbon of the π-propargylic ligand to give nickelacyclobutene **G**, which is protonated followed by protonation of the C(sp^2)–Ni bond furnishes the σ-allylnickel intermediate **E**. Intermediate **E** is common with the reaction of **3a**

Scheme 4. Addition of *p*-Methoxyphenol to **3b**
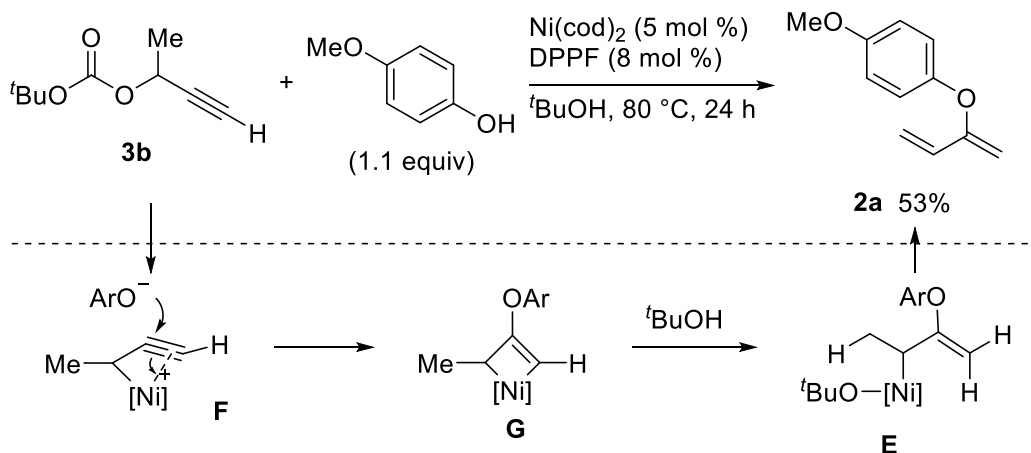
The present result is complimentary to the palladium-catalyzed reaction previously reported.[7] When but-3-yn-2-yl methyl carbonate is reacted with *p*-methoxyphenol in the presence of a palladium catalyst, 2,3-di(*p*-methoxyphenyloxy)but-1-ene is produced as the major product. On the other hand, even when an excess amount of phenol was used for the present nickel-catalyzed reaction, **2a** was obtained as the major product and no 2,3-di(*p*-methoxyphenyloxy)but-1-ene was formed. This dichotomy indicates the greater propensity for *β*-hydride elimination of the π-allylnickel intermediate. Whereas the π-allylpalladium intermediate in the previous case favors addition of *p*-methoxyphenol, the nickel intermediate in the present reaction favors *β*-hydride elimination even in the presence of a phenol nucleophile.

The carbonate **3c** having two methyl groups at the both ends of the propargyl moiety stereoselectively gave the product (*Z*)-**2c** in 88% yield (Scheme 5). The stereochemical outcome can be explained by assuming the *β*-hydride elimination from the *E*-isomer of the σ-allylnickel intermediate **H**. It is generally more favorable than the corresponding *Z*-isomer **J** due to the steric reasons.

Scheme 5. Addition of *p*-Methoxyphenol to **3c**


2c
88% (*Z/E* = 7/1)
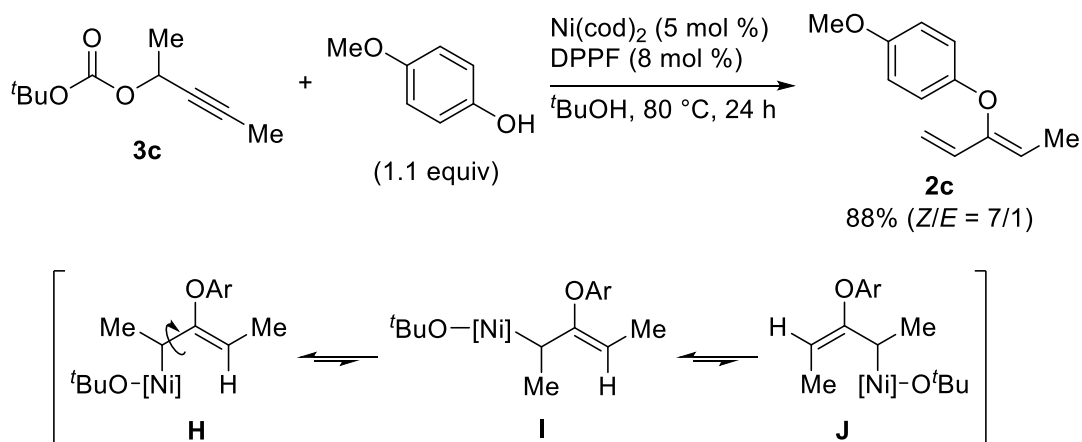
The ethyl-substituted carbonate **3d** gave rise to (*E*)-**2d** stereoselectively (Scheme 6). The selective formation of the *E* isomer can be explained by assuming that *syn-β*-hydrogen elimination takes place with the stereically less congested conformer of the σ-allylnickel intermediate. For *β*-hydrogen elimination, there are two conformers **K** and **L** presumed with which the nickel center and the *β*-hydrogen are located *syn*-periplaner. Among the two conformers having *syn*-periplanar orientation, the two bulkier substituent in juxtaposition overlaps in **K**. Thus, *β*-hydride elimination occurs selectively from **L** to furnish the *E* isomer of **2d**.

Scheme 6. Addition of *p*-Methoxyphenol to **3d**

2d
89% (*E/Z* >20/1)
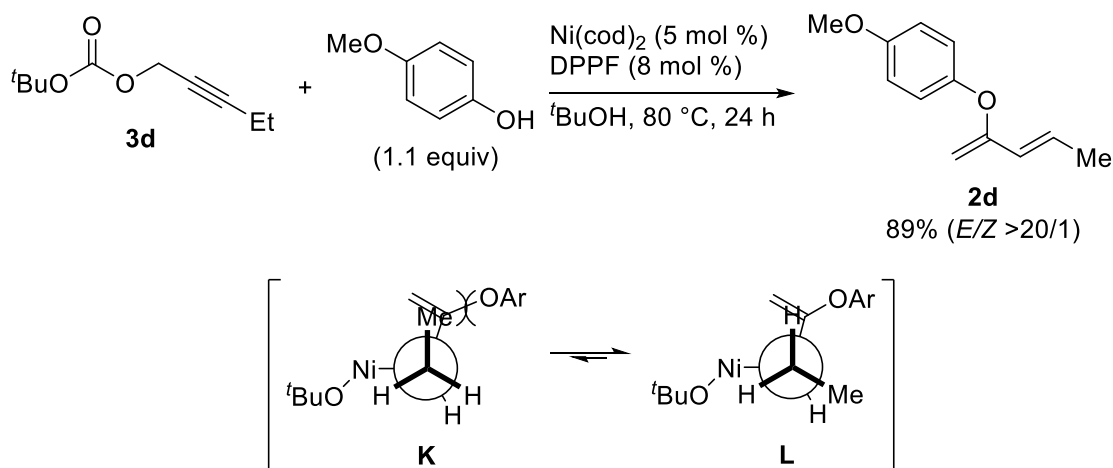
The scope of alcohols was also examined (Table 2). Phenol and trifluoromethyl phenol could be utilized, demonstrating little influence of the electronic perturbation of the aromatic ring (**2e**, **2f**). Bromo, aldehyde, ketone, and amine substituted phenol also gave

the corresponding 1,3-diene **2g-2j**. Sterically hindered ortho-substitued phenol was also eligible (**2k**). On the other hand, *t*BuOH failed to be incorporated, probably due to steric reasons.

Table 2. Addition of Various Alcohols to **3a**[a]

2b	**2e**	**2f**	**2g**
78%	55%	65%	62%

2h	**2i**	**2j**	**2k**
67%	80%	74%[b]	78%
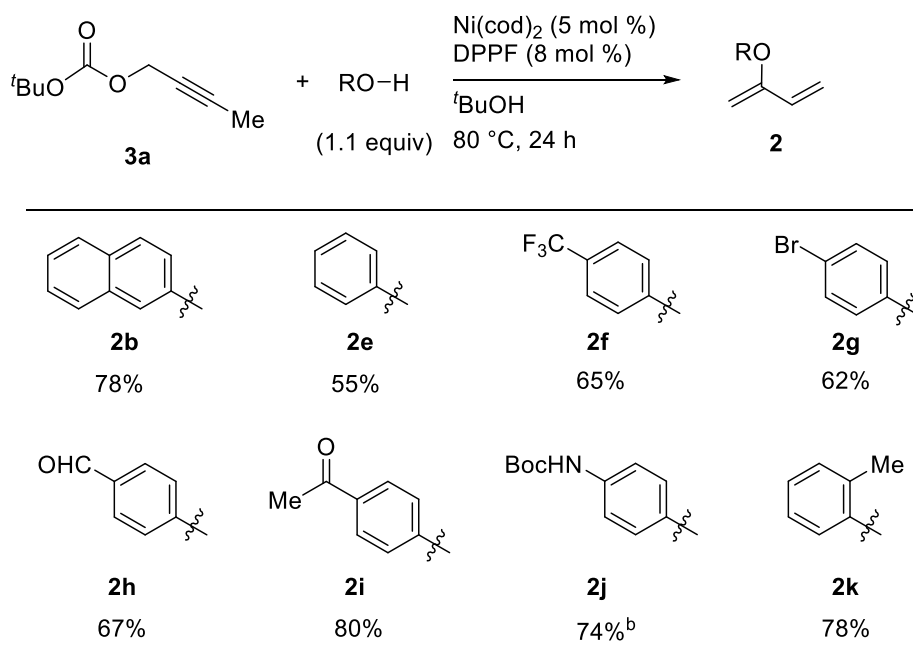
[a] Reaction conditions: Ni(cod)₂ (5 mol %), DPPF (8 mol %), **3a** (1.5 mmol), ROH (1.1 equiv), *t*BuOH (7.5 mL), 80 °C, 24 h. [b] 0.2 mmol scale

Conclusion

In conclusion, the author has developed a nickel-catalyzed reaction that 2-alkoxy-1,3-dienes were produced stereo- and regio-selectively from propargylic alcohol derivatives. Since propargylic alcohols are readily prepared from terminal alkynes and aldehydes, the present method provides an efficient strategy to synthesize 1,3-dienes.

Experimental Section

General Methods

All reactions were carried out under nitrogen atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECZ400S/L1 (^{1}H at 400.44 MHz and ^{13}C at 100.69 MHz) and JNM-ECZ500R (^{1}H at 500.16 MHz and ^{13}C at 125.77 MHz). NMR data were obtained in CDCl$_3$, C$_6$D$_6$ and DMSO-d_6. Proton chemical shifts were referenced to the residual proton signal of the solvent at 7.26 ppm (CHCl$_3$), 7.16 ppm (C$_6$H$_6$), and 2.5 ppm (DMSO). Carbon chemical shifts were referenced to the carbon signal of the solvent at 77.16 ppm (CDCl$_3$), 128.06 ppm (C$_6$D$_6$), and 39.52 ppm (DMSO-d_6). IR measurements were performed on FTIR SHIMADZU Affinity-1S spectrometer fitted with a Pike Technologies MIRacle Single Reflection ATR adapter. High-resolution mass spectra were recorded on a Thermo Scientific Exactive (APCI, ESI) spectrometer. Preparative thin-layer chromatography was performed on silica gel plates with PF254 indicator (Merck). Flash column chromatography was performed with diol-silica gel DIOL MB 100–40/75 (Fuji Silysia Chemical Ltd.) or silica gel 60N (Kanto).

Materials

Toluene and ^{t}BuOH were distilled from sodium/benzophenone ketyl and CaH$_2$ respectively. Anhydrous ^{t}BuOD was purchased from CIL. Ni(cod)$_2$ was recrystallized from a mixture of toluene and 1,5-cyclooctadiene (cod) (toluene/cod = 10:1). DPPF was recrystallized from a mixture of toluene and hexane (toluene/hexane = 2:1). All propargylic ether[16] and all propargylic carbonates[5, 17, 18] were prepared according to the literature procedures. All phenols and other chemicals were obtained from commercial suppliers.

A Typical Procedure for Isomerization of Propargylic Ether to 2-Aryloxy-1,3-Diene
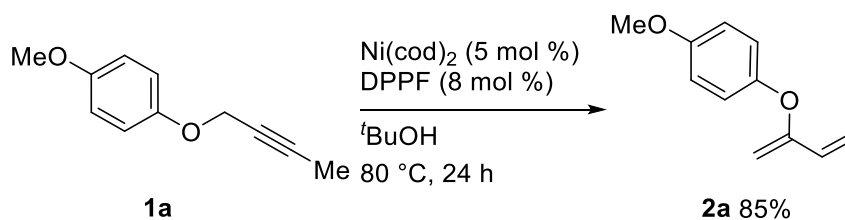
Ni(cod)$_2$ (20.7 mg, 0.075 mmol, 5 mol %) and DPPF (63.5 mg, 0.12 mmol, 8 mol %) were placed in a Schlenk tube equipped with a J-Young type screw cap. ^{t}BuOH (7.5 mL) was then added and the reaction mixture was stirred. After 1 hour, propargylic ether **1a** (258.9 mg, 1.5 mmol) was added. The reaction mixture was stirred at 80 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of diol silica gel with hexane as the eluent (twice). The filtrate was concentrated under reduced pressure to afford 1,3-diene **2a**. The residue was purified by bulb-to-bulb distillation (1.7 torr, 150 °C) to give 1,3-diene **2a** (221.0 mg, 1.26 mmol, 85 %).

Screening of Ligands
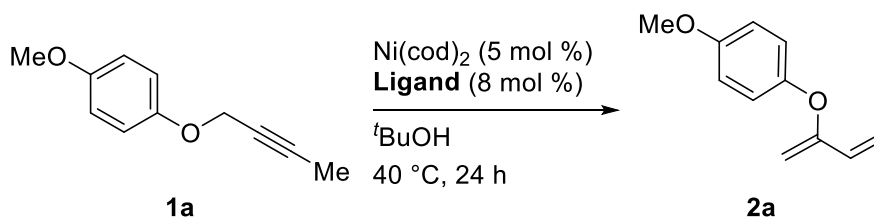
Ni(cod)$_2$ (5 mol %) and Ligand (8 mol %) were placed in a vial. ^{t}BuOH (1.0 mL) was then added and the reaction mixture was stirred. After 10 min, propargylic ether **1a** (0.2 mmol) was added. The reaction mixture was stirred at 40 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of silica gel with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford 1,3-diene **2a**. The NMR yield of **2a** was calculated using 1,1,2,2-tetrachloroethane as an internal standard.

Table 3. Screening of Ligands

Entry	Ligand	NMR yield **2** /%
1	acetylacetonate	0
2	Xantphos	0
3	BINAP	30
4	1,2-Bis(dimethylphosphino)ethane	7

5	1,2-Bis(dichlorophosphino)ethane	0
6	1,2-Bis(diphenylphosphino)ethane	15
7	1,3-Bis(diphenylphosphino)propane	0
8	1,4-Bis(diphenylphosphino)butane	99
9	1,4-Bis(dicyclohexylphosphino)butane	94
10	1,5-Bis(diphenylphosphino)pentane	64
11	1,6-Bis(diphenylphosphino)hexane	0
12	PMe$_3$[a]	79
13	PCy$_3$[a]	0
14	P(^{t}Bu)$_3$[a]	0
15	PPh$_3$[a]	2
16	2-phenylpyridine [a]	0
17	dtbpy	0
18	IPr	0
19	I^{t}Bu	0

(a) 10 mol %
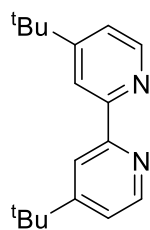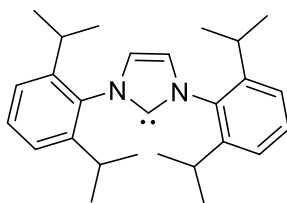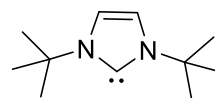
dtbpy   IPr   I^{t}Bu

Deuterium Experiments
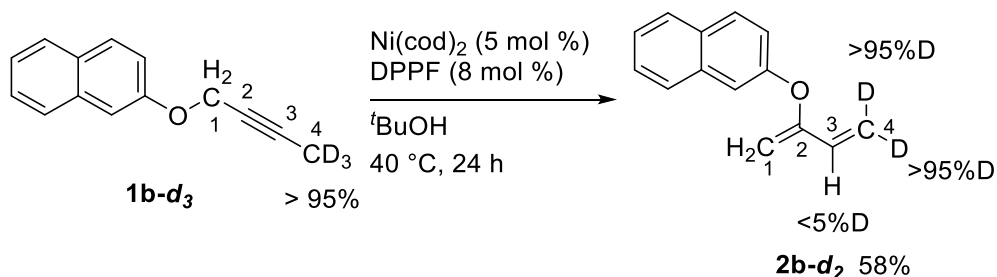
Ni(cod)₂ (2.8 mg, 0.010 mmol, 5 mol %) and DPPF (8.8 mg, 0.016 mmol, 8 mol %) were placed in a vial. ^{t}BuOH (1.0 mL) was then added and the reaction mixture was stirred. After 10 minutes, propargylic ether **1b-*d₃*** (40.9 mg, 0.21 mmol) was added. The reaction mixture was stirred at 40 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of silica gel with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford 1,3-diene **2b-*d₂***. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 50/1) to give **2b-*d₂*** (23.8 mg, 0.12 mmol, 58%).
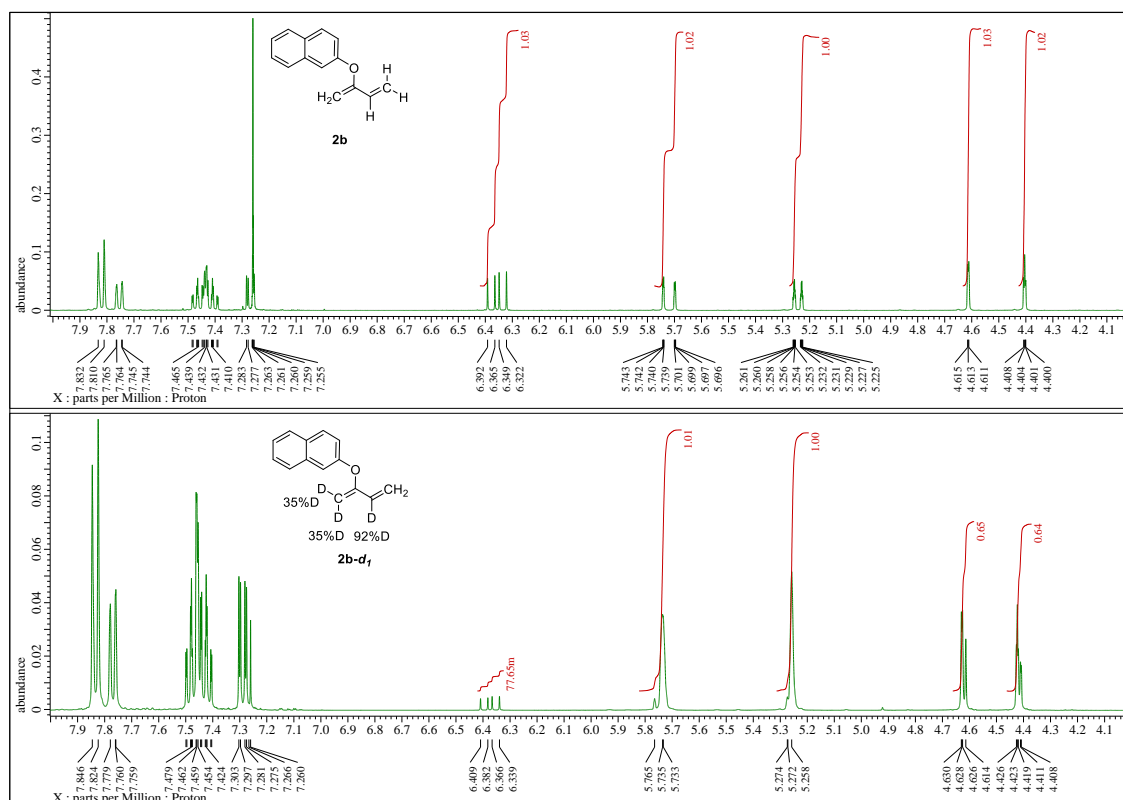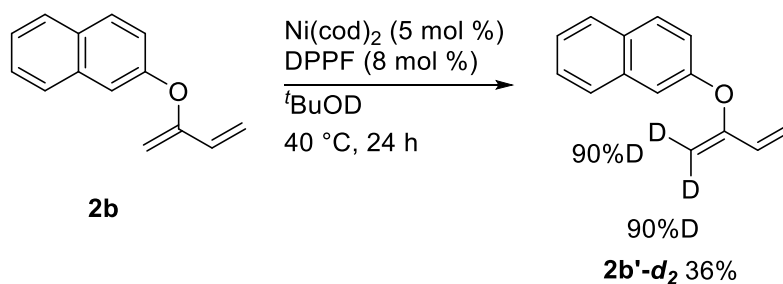

Figure 1. ^{1}H NMR Spectra of **2b** and **2b-*d₂***
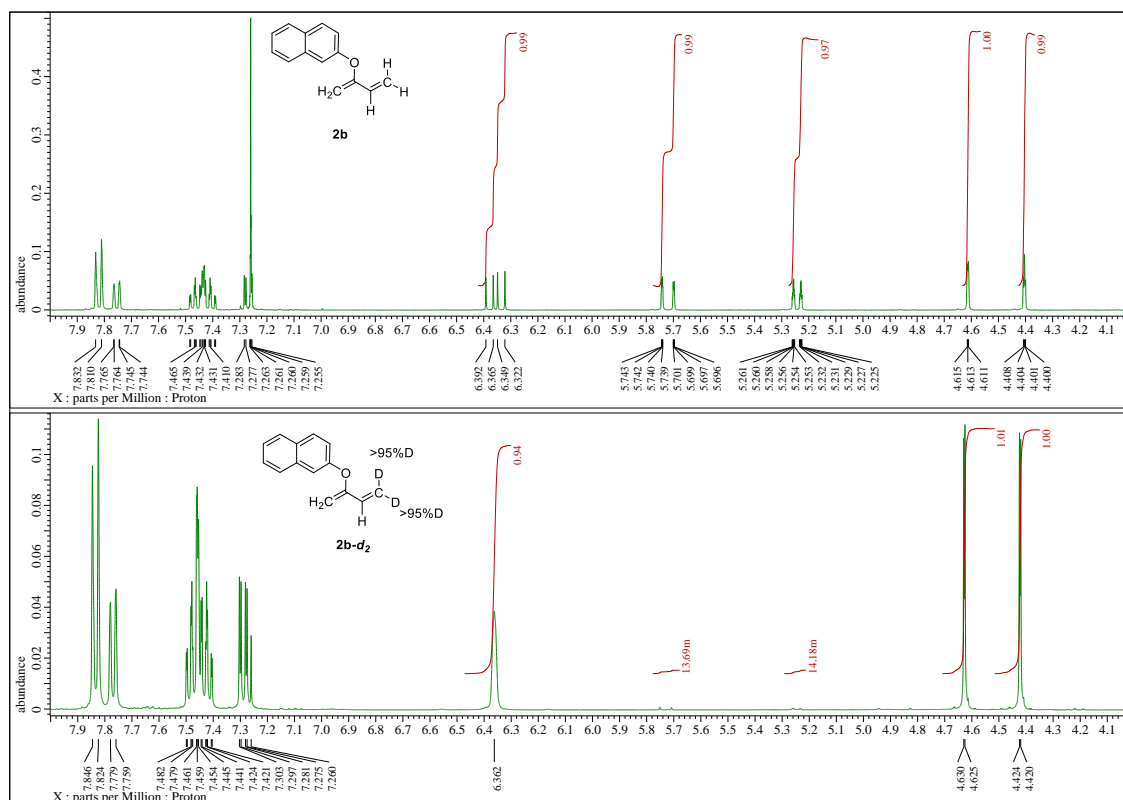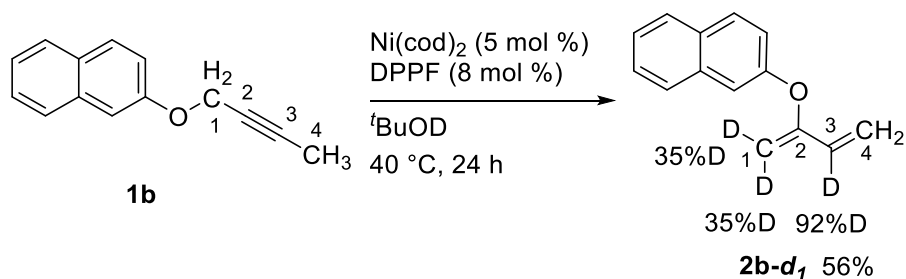
Ni(cod)$_2$ (2.8 mg, 0.010 mmol, 5 mol %) and DPPF (9.0 mg, 0.016 mmol, 8 mol %) were placed in a vial. ^{t}BuOD (1.0 mL) was then added and the reaction mixture was stirred. After 10 minutes, propargylic ether **1b** (39.7 mg, 0.20 mmol) was added. The reaction mixture was stirred at 40 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of silica gel with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford 1,3-diene **2b-*d$_1$***. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 50/1) to give **2b-*d$_1$*** (22.4 mg, 0.12 mmol, 56%).
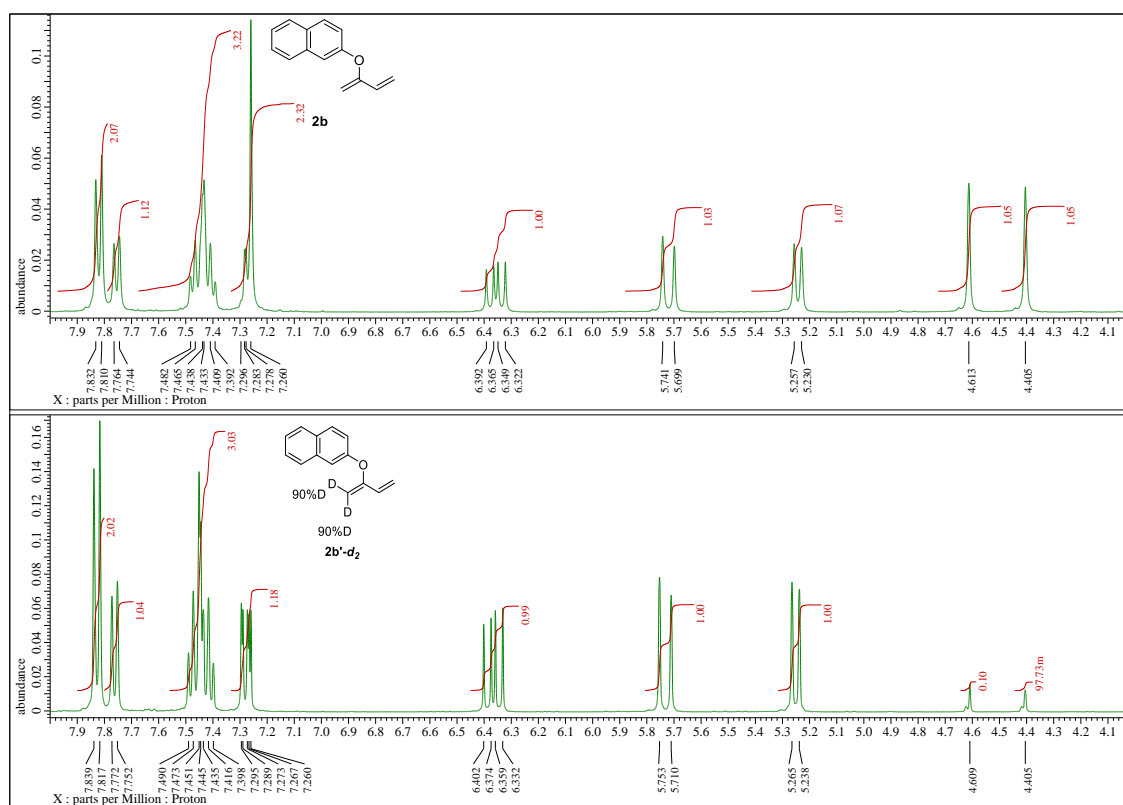

Figure 2. ^{1}H NMR Spectra of **2b** and **2b-*d$_1$***

Ni(cod)$_2$ (3.0 mg, 0.011 mmol, 5 mol %) and DPPF (8.7 mg, 0.016 mmol, 8 mol %) were placed in a vial. ^{t}BuOD (1.0 mL) was then added and the reaction mixture was stirred. After 10 minutes, 1,3-diene **2b** (41.6 mg, 0.21 mmol) was added. The reaction mixture was stirred at 40 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of diol silica gel with ethyl acetate as the eluent (twice). The filtrate was concentrated under reduced pressure to afford 1,3-diene **2b'-d_2**. The residue was purified by preparative thin-layer chromatography (hexane/ethyl acetate = 50/1) to give **2b'-d_2** (15.3 mg, 0.077 mmol, 36%).


Figure 3. ^{1}H NMR Spectra of **2b** and **2b'-d_2**
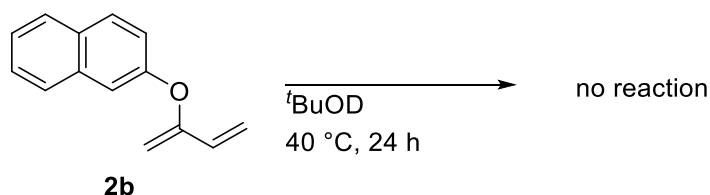
1,3-diene **2b** (36.4 mg, 0.19 mmol) was placed in a vial. ^{t}BuOD (1.0 mL) was then added and the reaction mixture was stirred at 40 °C. After 24 h, the reaction mixture was passed through a pad of diol silica gel with hexane as the eluent (twice). The filtrate was concentrated under reduced pressure. No reaction occurred.

**A Typical Procedure for Intermolecular Reaction of Propargylic Carbonates with Phenols**
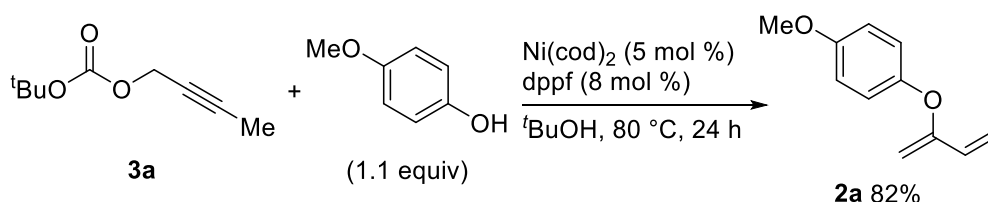
Ni(cod)$_2$ (21.3 mg, 0.077 mmol, 5 mol %), DPPF (64.2 mg, 0.12 mmol, 8 mol %), and *p*-methoxy phenol (205.6 mg, 1.66 mmol, 1.1 equiv) were placed in a Schlenk tube equipped with a J-Young type screw cap. ^{t}BuOH (7.5 mL) was then added and the reaction mixture was stirred. After 1 hour, propargylic carbonate **3a** (256.9 mg, 1.51 mmol) was added. The reaction mixture was stirred at 80 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of diol silica gel with hexane as the eluent (twice). The filtrate was concentrated under reduced pressure to afford 1,3-diene **2a**. The residue was purified by bulb-to-bulb distillation (0.7 torr, 160 °C) to give 1,3-diene **2a** (218.2 mg, 1.24 mmol, 82 %).

Reaction Procedure for Screening of Leaving Group (Table 1)

Ni(cod)$_2$ (5 mol %), DPPF (8 mol %), and *p*-methoxy phenol (1.1 equiv) were placed in a vial. ^{t}BuOH (1.0 mL) was then added and the reaction mixture was stirred. After 10 min, propargylic electrophile (0.2 mmol) was added. The reaction mixture was stirred at 80 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of silica gel with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford 1,3-diene **2a**. The NMR yield of **2a** was calculated using 1,1,2,2-tetrachloroethane as an internal standard.

Spectroscopic Data of 2a-2k
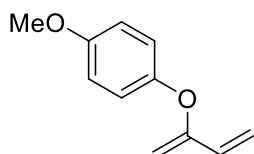
2a

^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.80 (s, 3H), 4.14 (s, 1H), 4.38 (s, 1H), 5.22 (d, J = 10.8 Hz, 1H), 5.74 (d, J = 17.2 Hz, 1H), 6.29 (dd, J = 17.2, 10.8 Hz, 1H), 6.87 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 55.7, 93.8, 114.7, 115.3, 121.7, 132.4, 149.2, 156.2, 159.4; HRMS(APCI$^+$): Calcd for C$_{11}$H$_{13}$O$_2$, [M+H]$^+$ 177.0910, Found m/z 177.0909; IR (ATR): 2835, 1585, 1503, 1209 cm^{-1}.


2b
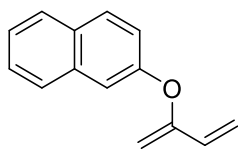
^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.4 (s, 1H), 4.61 (s, 1H), 5.24 (d, J = 10.8 Hz, 1H), 5.72 (d, J = 16.8 Hz, 1H), 6.36 (dd, J = 17.2, 10.8 Hz, 1H), 7.26-7.30 (m, 1H), 7.39-7.48 (m, 3H), 7.75 (d, J = 8.0 Hz, 1H), 7.81-7.83 (m, 2H) ; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 97.2, 115.4, 115.9, 120.6, 124.9, 126.5, 127.3, 127.9, 130.0, 130.5, 132.1, 134.4, 154.0, 158.3; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{13}$O, [M+H]$^+$ 197.0961, Found m/z 197.0956; IR (ATR): 1585, 1246, 976, 808 cm^{-1} .
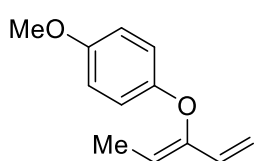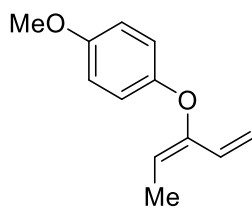

(*Z*)-**2c**　　　　　　(*E*)-**2c**

^{1}H NMR (400 MHz, CDCl$_3$) (*E*/*Z* mixture) (*Z*)-**2c**: δ = 1.63 (d, J = 7.2 Hz, 3H), 3.77 (s, 3H), 4.98 (d, J = 11.2 Hz, 1H), 5.20 (d, J = 17.2 Hz, 1H), 5.41 (q, J = 7.2 Hz, 1H), 6.23 (dd, J = 17.2, 10.8 Hz, 1H), 6.78-6.92 (m, 4H), (*E*)-**2c**: δ = 1.75 (d, J = 7.6, 3H), 3.77 (s, 3H), 5.07 (q, J = 6.0 Hz, 1H), 5.18 (d, J = 10.4 Hz, 1H), 5.53 (d, J = 17.2 Hz, 1H), 6.60 (dd, J = 17.2, 10.8 Hz, 1H), 6.78-6.92 (m, 4H); ^{13}C NMR (100 MHz, CDCl$_3$) (*E*/*Z*

mixture) (*Z*)-**2c**: δ = 11.3, 55.8, 113.8, 114.7, 115.6, 117.2, 132.0, 150.2, 151.6, 154.2, (*E*)-**2c**: δ = 11.6, 55.7, 110.8, 114.6, 115.3, 118.8, 127.1, 151.3, 151.5, 154.9; HRMS(APCI$^+$): Calcd for $C_{12}H_{15}O_2$, [M+H]$^+$ 191.1067, Found m/z 191.1061; IR (ATR) (*E/Z* mixture): 1501, 1206, 826 cm^{-1} .
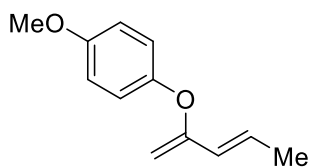

(*E*)-**2d**

^{1}H NMR (400 MHz, C_6D_6): δ = 1.59 (dd, *J* = 6.8, 1.6 Hz, 3H), 3.25 (s, 3H), 4.22 (d, *J* = 26.8 Hz, 2H), 5.95 (dq, *J* = 15.2, 1.6 Hz, 1H), 6.43 (dq, *J* = 15.2, 6.8 Hz, 1H), 6.66 (d, *J* = 9.2 Hz, 2H), 6.99 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, C_6D_6): δ = 17.8, 55.1, 91.3, 115.0, 122.1, 127.2, 127.3, 149.8, 156.6, 160.1; HRMS(APCI$^+$): Calcd for $C_{12}H_{15}O_2$, [M+H]$^+$ 191.1067, Found m/z 191.1062; IR (ATR): 1503, 1209, 955 cm^{-1}.


2e
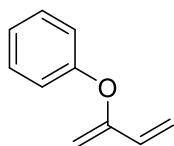
Spectral data were in agreement with literature values.[19]
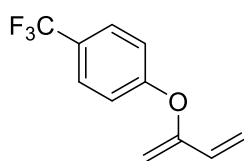
2f

^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.58 (s, 1H), 4.77 (s, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 5.57 (d, *J* = 17.2 Hz, 1H), 6.33 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 101.9, 116.4, 118.1, 123.4 (q, *J* = 31.6 Hz). 124.3 (q, *J* = 270.2 Hz), 127.3 (q, *J* = 3.8 Hz), 131.4, 155.9, 159.4; HRMS(APCI$^+$): Calcd for $C_{11}H_{10}F_3O$, [M+H]$^+$ 215.0678, Found m/z 215.0673; IR (ATR): 1612, 1514, 1323, 1265 cm^{-1} .
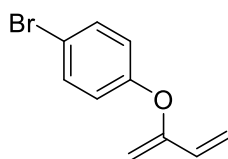
2g

^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.37 (s, 1H), 4.58 (d, *J* = 1.6 Hz, 1H), 5.22 (d, *J* = 10.8 Hz, 1H), 5.63 (d, *J* = 17.2 Hz, 1H), 6.29 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.95 (d, *J* = 10.0 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 97.3, 116.07, 116.12, 121.4, 131.7, 132.7, 155.4, 157.9; HRMS(APCI$^+$): Calcd for C$_{10}$H$_{10}$BrO, [M+H]$^+$ 22.9910, Found m/z 224.9905; IR (ATR): 1584, 1481, 1223 cm^{-1} .
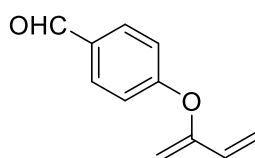
2h

^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.71 (s, 1H), 4.87 (s, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 5.50 (d, *J* = 17.2 Hz, 1H), 6.33 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.16 (d. *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 2H), 9.93 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 101.9, 116.9, 118.0, 131.0, 131.5, 131.9, 156.4, 162.3, 190.9; HRMS(APCI$^+$): Calcd for C$_{12}$H$_{13}$O$_3$, [M+H]$^+$ 205.0859, Found m/z 205.0856; IR (ATR): 1695, 1591, 1229, 1153 cm^{-1}.
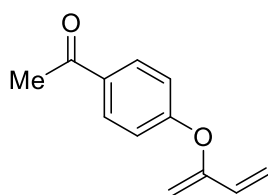

2i

^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.55 (s, 3H), 4.61 (s, 1H), 4.78 (s, 1H), 5.19 (d, *J* = 10.8 Hz, 1H), 5.50 (d, *J* = 17.2 Hz, 1H), 6.28 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 26.6, 100.9, 116.7, 117.8, 130.6, 131.3, 132.2, 156.7, 161.1, 196.9; HRMS(APCI$^+$): Calcd for C$_{12}$H$_{13}$O$_2$, [M+H]$^+$ 189.0910 Found m/z 189.0904; IR (ATR): 1678, 1597, 12233, 1163 cm^{-1}.
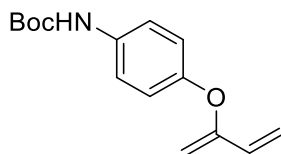
2j

Ni(cod)$_2$ (2.9 mg, 0.011 mmol, 5 mol %), DPPF (8.6 mg, 0.016 mmol, 8 mol %), and 4-*N*-Boc-aminophenol (47.0 mg, 0.23 mmol, 1.1 equiv) were placed in a vial. ^{t}BuOH (1.0 mL) was then added and the reaction mixture was stirred. After 10 min, propargylic carbonate **3a** (35.4 mg, 0.21 mmol) was added. The reaction mixture was stirred at 80 °C for 24 h. After cooled to room temperature, the reaction mixture was passed through a pad of diol silica gel with ethyl acetate as the eluent. The filtrate was concentrated under reduced pressure to afford 1,3-diene **2j**. The residue was purified by flash column chromatography with diol silica gel (hexane/ethyl acetate = 10/1) to give **2j** (40.4 mg, 0.16 mmol. 74%)

^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.52 (s, 9H), 4.22 (s, 1H), 4.43 (s, 1H), 5.20 (d, *J* = 10.8 Hz, 1H), 5.70 (d, *J* = 17.2 Hz, 1H), 6.28 (dd, *J* = 17.2, 10.8 Hz, 1H), 6.49 (br, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 28.5, 80.6, 95.0, 115.5, 120.1, 120.9, 132.2, 134.4, 151.4, 153.1, 158.8; HRMS(ESI$^+$): Calcd for C$_{15}$H$_{19}$NO$_3$Na, [M+Na]$^+$ 284.1257, Found m/z 284.1252; IR (ATR): 1695, 1531, 1155 cm^{-1}.
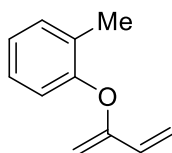

2k

^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.22 (s, 3H), 4.01 (s, 1H), 4.35 (s, 1H), 5.24 (d, *J* = 10.8 Hz, 1H), 5.78 (d, *J* = 17.2 Hz, 1H), 6.31 (dd, *J* = 17.2, 10.8 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.16-7.23 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 15.9, 93.0, 115.3, 121.1, 124.5, 127.1, 130.5, 131.4, 132.2, 153.6, 158.0; HRMS(APCI$^+$): Calcd for C$_{11}$H$_{13}$O, [M+H]$^+$ 161.0961, Found m/z 161.0961; IR (ATR): 1584, 1489, 1231, 745 cm^{-1}.

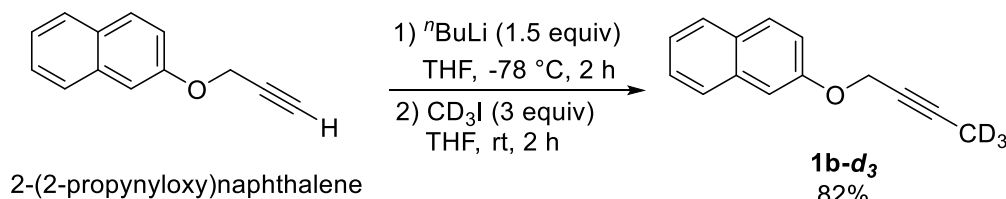**Synthesis of Propargylic Ester 1a, 1b, and 1b-*d₃***

Propargylic ether **1a** and **1b** were synthesized according to the literature procedure.[16]

1a

Spectral data were in agreement with literature values.[20]

1b
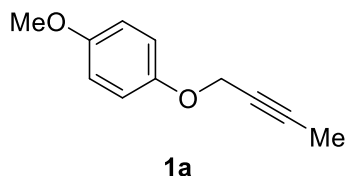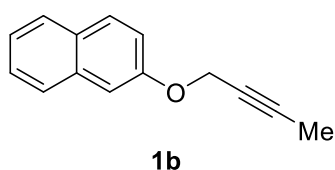
^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.88 (t, J = 2.4 Hz, 3H), 4.77 (q, J = 2.4 Hz, 2H), 7.17-7.22 (m, 2H), 7.33-7.37 (m, 1H), 7.42-7.46 (m, 1H), 7.74-7.78 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 3.7, 56.4, 74.0, 83.9, 107.3, 118.9, 123.9, 126.4, 126.9, 127.7, 129.2, 129.5, 134.4, 155.8; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{13}$O, [M+H]$^+$ 197.0961, Found m/z 197.0962; IR (ATR): 1628, 1597, 1213, 999 cm^{-1}.

2-(2-propynyloxy)naphthalene

1) ^{n}BuLi (1.5 equiv)
 THF, -78 °C, 2 h
2) CD$_3$I (3 equiv)
 THF, rt, 2 h

1b-*d₃*
82%

2-(2-Propynyloxy)naphthalene was synthesized according to the literature procedure.[16] The crude mixture was purified by flash column chromatography (hexane/ethyl acetate = 5:1) to give 2-(2-propynyloxy)naphthalene.

Propargylic ester **1b-*d₃*** was synthesized from 2-(2-propynyloxy)naphthalene according to the literature procedure.[21] The crude mixture was purified by flash column chromatography (hexane/ethyl acetate = 20:1) to afford **1b-*d₃*** in 82% yield. ^{1}H NMR (400 MHz, CDCl$_3$): δ =4.77 (s, 2H), 7.17-7.22 (m, 2H), 7.35 (ddd, J = 8.0, 6.4, 0.8 Hz, 1H), 7.45 (ddd, J = 8.4, 7.2, 1.6 Hz, 1H), 7.74-7.78 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 3.1 (sep, J =20.1 Hz), 56.4, 74.1, 83.8, 107.2, 118.8, 123.8, 126.4, 126.9, 127.7, 129.2, 129.5, 134.4, 155.8; HRMS(APCI$^+$): Calcd for C$_{14}$H$_{10}$D$_3$O, [M+H]$^+$ 200.1149, Found m/z 200.1143; IR (ATR): 3055, 2262, 1213, 995, 741 cm^{-1} .

**Synthesis of Propargylic Carbonates and Propargylic Acetate 3e**

Propargylic carbonates **3a-3d**[17], **3f** [5] and propargylic acetate **3e**[18] were synthesized according to the literature procedure.
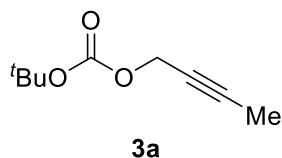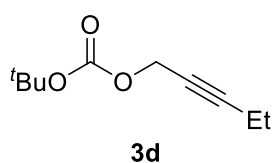

3a

Spectral data were in agreement with literature values.[22]

3b

Spectral data were in agreement with literature values.[23]

3c

Spectral data were in agreement with literature values.[24]

3d
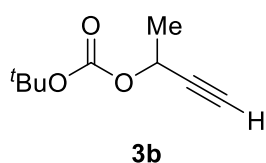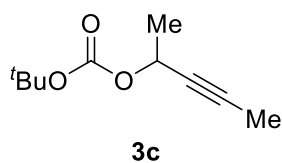
^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.13 (t, J = 7.6 Hz, 3H), 1.49 (s, 9H), 2.22 (qt, J = 7.6, 2.4 Hz, 2H), 4.65 (t, J = 2.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ =12.6, 13.6, 27.8, 55.4, 73.1, 82.7, 89.5, 153.1; HRMS(ESI$^+$): Calcd for C$_{10}$H$_{16}$O$_3$Na, [M+Na]$^+$ 207.0992, Found m/z 207.0992; IR (ATR): 2980, 1744, 1252, 1150 cm^{-1}.

3e
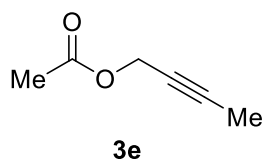
Spectral data were in agreement with literature values.[18]

MeO-C(=O)-O-CH₂-C≡C-Me

3f
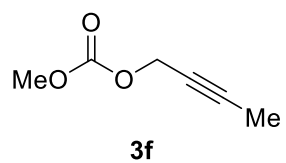
Spectral data were in agreement with literature values.[5]

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8. The diene **2a** was not stable enough to be isolated by flash column chromatography on ordinary silica gel (neutral). It was isolated in 69% yield when diol-modified silica gel was used.

9. See exprimental section for detail.

10. In gold-catalyzed isomerization of propargylic esters, both 1,2- and 1,3-acyloxy migration were observed. See ref. 4

11. See experimental section for detail.

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List of Publications

Chapter 1

Palladium-Catalyzed Intermolecular Exchange between C–C and C–Si σ-Bonds
Shintaro Okumura, Fangzhu Sun, Naoki Ishida, and Masahiro Murakami
J. Am. Chem. Soc. **2017**, *139*, 12414-12417.

Chapter 2

Site- and Regio-Selective Incorporation of Carbon Dioxide into the $C(sp^2)$–Si Bond of Benzosilacyclobutenes
Naoki Ishida, Shintaro Okumura, and Masahiro Murakami
Chem. Lett. **2018**, *47*, 570-572.

Chapter 3

2-Arylsilacyclobutane as Latent Nucleophile Attacking CO_2
Naoki Ishida, Shintaro Okumura, and Masahiro Murakami
To be submitted

Chapter 4

Ring-opening Fluorination of Cyclobutanols and Cyclopropanols Catalyzed by Silver
Naoki Ishida, Shintaro Okumura, Yuuta Nakanishi, and Masahiro Murakami
Chem. Lett. **2015**, *44*, 821-823.

Chapter 5

Synthesis of 2-Alkoxy-1,3-dienes from Propargylic Alcohol Derivatives
Naoki Ishida, Yusaku Hori, Shintaro Okumura, and Masahiro Murakami
To be submitted

Other Publications

C-H/C-F Functionalization by E-Selective Ruthenium(II)-Catalysis
Dhawa, U.; Zell, D.; Yin, R.; Okumura, S.; Murakami, M.; Ackermann, L.
J. Catal. **2018,** in press.

Measurements of production cross sections of ^{10}Be and ^{26}Al by 120 GeV and 392 MeV proton bombardment of ^{89}Y, ^{159}Tb, and ^{nat}Cu targets
Sekimoto, S.; Okumura, S.; Yashima, H.; Matsushi, Y.; Matsuzaki, H.; Matsumura, H.; Toyoda, A.; Oishi, K.; Matsuda, N.; Kasugai, Y.; Sakamoto, Y.; Nakashima, H.; Boehnlein, D.; Coleman, R.; Lauten, G.; Leveling, A.; Mokhov, N.; Ramberg, E.; Soha, A.; Vaziri, K.; Ninomiya K.; Omoto, T.; Shima, T.; Takahashi, N.; Shinohara, A.; Caffee, M.W.; Weltenm, K. C.; Nishiizumi, K.; Shibata, S.; Ohtsuki T.
Nucl. Instr. Meth. B, **2015**, *361*, 685-688.

Measurements of Cross Sections for Production of Light Nuclides by 120 GeV Proton Bombardment of Au
Okumura, S.; Sekimoto, S.; Yashima, H.; Matsushi, Y.; Matsuzaki, H.; Matsumura, H.; Toyoda, A.; Oishi, K.; Matsuda, N.; Kasugai, Y.; Sakamoto, Y.; Nakashima, H.; Boehnlein, D.; Coleman, R.; Lauten, G.; Leveling, A.; Mokhov, N.; Ramberg, E.; Soha, A.; Vaziri, K.; Ninomiya, K.; Shima, T.; Takahashi, N.; Shinohara, A.; Caffee, M. W.; Nishiizumi, K.; Shibata, S.; Ohtsuki T.
JAEA-Conf 2015-003, **2016** 165-171. (doi:10.11484/jaea-conf-2015-003)