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An efficient synthesis of 5-silyl-2,3-dihydrofurans via acid-catalyzed ring-enlargement of cyclopropyl silyl ketones and their functionalization

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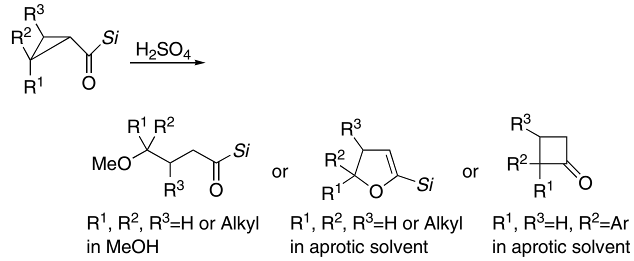
Abstract—Treatment of cyclopropyl silyl ketones with trimethylsilyl trifluoromethanesulfonate as a strong acid having low nucleophilic counter anion gives the corresponding 5-silyl-2,3-dihydrofuran derivatives, exclusively, regardless of substituents on the cyclopropane ring or silicon atom. The resulting 5-silyl-2,3-dihydrofuran derivatives exhibit both reactivities of the vinylsilane and the cyclic enol ether in the subsequent reaction with electrophilic reagents or Heck type reaction.

Acylsilanes are an useful class of compounds in organic synthesis and a number of methods for the preparation of acylsilanes have been developed.[1] Especially, cyclopropyl silyl ketones[2,3] are expected to exhibit the specific reactivities of the silylcarbonyl group and the three-membered ring.[4] Nevertheless, the chemical behavior of cyclopropyl silyl ketones has not yet been fully clarified because of their synthetic difficulty.[1,2] Several years ago, we have already reported facile synthetic method of cyclopropyl silyl ketones[2c] and presented that a series of cyclopropyl silyl ketones reacted with sulfuric acid as a strong acid having low nucleophilic counter anion in methanol to give the corresponding ring opening products, γ-methoxyacylsilanes in high yields, regardless of substituents on the cyclopropyl ring. In contrast, a similar reaction of cyclopropyl silyl ketones with sulfuric acid in aprotic solvents such as dimethoxyethane was found to give two different types of ring-enlargement products, 5-silyl-2,3-dihydrofuran derivatives or cyclobutanones, depending upon the substituents on the three-membered ring (Scheme 1).[3b] Incidentally, the reaction with triflic acid gave 2,3-dihydrofuran derivatives exclusively. However, the above reaction proceeded to give the 5-silyl-2,3-dihydrofuran derivatives in low yield. Furthermore, there have been few reports on the ring-enlargement to dihydrofurans from cyclopropyl ketones under acidic conditions.[5]



Scheme 1. Reaction of cyclopropyl silyl ketones with sulfuric acid.

The above observations led us to attempt the reaction of cyclopropyl silyl ketones with other strong acids having low nucleophilic counter anion in nonpolar solvents, which would afford 5-silyl-2,3-dihydrofuran derivatives effectively.[6] Additionally, the resulting silyl-substituted dihydrofurans are expected to exhibit both reactivities of the vinylsilane[7–10] and the cyclic enol ether[11,12] moieties, thus these would be useful synthetic intermediates as valuable building blocks. Here, we wish to report our findings on the acid-catalyzed ring-enlargement of cyclopropyl silyl ketones as a novel, efficient and facile

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Keywords: Cyclopropyl silyl ketone; Dihydrofurane; Ring enlargement; Heck reaction.

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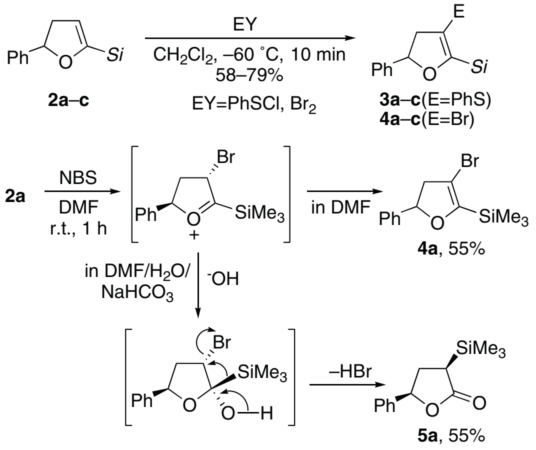
synthetic method for 5-silyl-2,3-dihydrofuran derivatives. Furthermore, in order to indicate the potential of 5-silyl-2,3-dihydrofuran as a synthetic intermediate, the reaction of them with electrophilic reagent and Heck reaction with iodobenzene were carried out.

The treatment of cyclopropyl silyl ketones **1a**–**h** with trimethylsilyl trifluoromethanesulfonate (TMSOTf)[13] as a strong acid having low nucleophilic counter anion in dichloromethane was carried out. The reaction proceeded to give the corresponding 5-silyl-2,3-dihydrofuran derivatives **2a**–**h**, exclusively. The results are summarized in Table 1. The observed yield of this reaction was strongly influenced by the amount of TMSOTf, the reaction temperature and the reaction time. The conditions of the ring enlargement of cyclopropyl trimethylsilyl ketone having a phenyl group on the three-membered ring **1a** were optimized (entries 1–3). It was found that the optimum ratio of TMSOTf to cyclopropyl silyl ketone was 5 equiv and the reaction was complete for 5 min at −78 °C. Under such reaction conditions, the excellent yield for desired product **2a** was observed (entry 1). The reaction of other cyclopropyl silyl ketones proceeded similarly to afford the corresponding five-membered ring products in the excellent yields, regardless of substituents on the cyclopropyl ring or silicon atom (entries 4–9). However, the reaction for **1h** resulted in lower yield because of polymerization (entry 10).

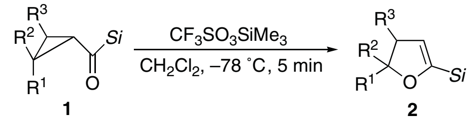


Scheme 2. Reaction of 5-silyl-2,3-dihydrofurans with electrophilic reagents.

The resulting silyl-substituted dihydrofuran derivatives **2a**–**c** were treated with various electrophilic reagents (Scheme 2). In the reaction with PhSCl or Br_2,[7] silyl-substituted dihydrofuran **2** acts as a enol ether, not a vinylsilane. Therefore, the electrophilic substitution proceeded to afford the corresponding 4-substituted 5-silyldihydrofuran derivatives **3** and **4** in good yields. On the other hand, the treatment of **2a** with *N*-bromosuccinimide[8] in DMF gave bromo-substituted **4a** in moderate yield. Noteworthy, in the presence of 1.5 equiv of $NaHCO_3$ and water, the exclusive formation of *cis*-isomer of α-silylated γ-lactone derivative **5a** was observed.[14] This reaction would proceed via attack of hydroxide ion to the resulting oxonium cation intermediate, followed by anionotropic migration of the silyl group in an S_N2' manner.

Next, Heck reaction of silyl-substituted dihydrofuran derivatives **2a**–**f** with iodobenzene was investigated.[9,11] The results are summarized in Table 2. In all cases, a mixture of two regioisomers, 2-phenyl-2,5-dihydrofuran derivatives **6** and 4-phenyl-2,3-dihydrofuran derivatives **7** was obtained as products. The reaction of dihydrofuran derivatives having a trimethylsilyl group gave the corresponding products with preference of 2-phenyldihydrofuran derivatives in good yields (entries 1 and 4). On the other hand, 4-phenyldihydrofuran derivatives was preferentially formed by the reaction of dihydrofuran derivatives having a dimethylphenylsilyl group in moderate yields (entries 2 and 5). Whereas the high regioselectivity was observed, the reaction of

Table 1. Reaction of cyclopropyl silyl ketones with TMSOTf



Entry	Substrate	R^1	R^2	R^3	*Si*	Product	Yield[a] (%)
1	**1a**	H	Ph	H	$SiMe_3$	**2a**	>99
2[b]	**1a**	H	Ph	H	$SiMe_3$	**2a**	47
3[c]	**1a**	H	Ph	H	$SiMe_3$	**2a**	88
4	**1b**	H	Ph	H	$SiMe_2{}^tBu$	**2b**	>99
5	**1c**	H	Ph	H	$SiMe_2Ph$	**2c**	>99
6	**1d**	Me	Me	H	$SiMe_3$	**2d**	>99
7	**1e**	Me	Me	H	$SiMe_2{}^tBu$	**2e**	>99
8	**1f**	Me	Me	H	$SiMe_2Ph$	**2f**	>99
9	**1g**	H	$-(CH_2)_4-$		$SiMe_3$	**2g**	>99
10	**1h**	Me	H	Me	$SiMe_3$	**2h**	24

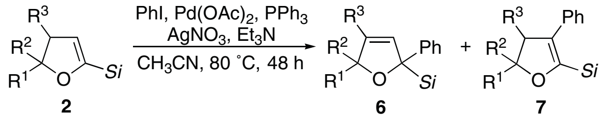
Molar ratio: acylsilanes/$CF_3SO_3SiMe_3$/CH_2Cl_2 = 1:5:400.

[a] Isolated yield.

[b] Reaction was carried out for 0.5 h at −40 °C with an equimolar amount of $CF_3SO_3SiMe_3$.

[c] 3 equiv of $CF_3SO_3SiMe_3$ was used at −40 °C.

Table 2. Heck reaction of 5-silyl-2,3-dihydrofurans



Entry	Substrate	R^1	R^2	R^3	*Si*	Product	Yield[a] (%)	Ratio[b]
1	**2a**	H	Ph	H	$SiMe_3$	**6a**, **7a**	64	70:30
2	**2b**	H	Ph	H	$SiMe_2Ph$	**6b**, **7b**	30	38:62
3	**2c**	H	Ph	H	$SiMe_2{}^tBu$	**6c**, **7c**	22	94:6
4	**2d**	Me	Me	H	$SiMe_3$	**6d**, **7d**	58	73:27
5	**2e**	Me	Me	H	$SiMe_2Ph$	**6e**, **7e**	44	38:62
6	**2f**	Me	Me	H	$SiMe_2{}^tBu$	**6f**, **7f**	13	74:26

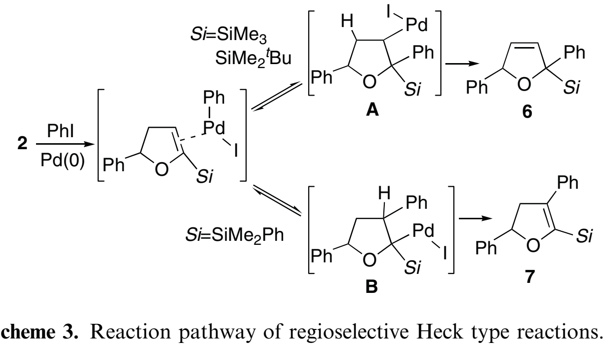
[a] Isolated yield.

[b] Determined by ^1H NMR analysis (270 MHz).

2c or **2f** resulted in the lower yields (entries 3 and 6). In these reactions, when the steric bulkiness of the silyl group was increased, the reactivity was decreased.

A reasonable reaction pathway is shown in Scheme 3. In the palladation of Heck reaction, when silyl-substituted dihydrofuran **2** acts as a cyclic enol ether,[11] palladium atom adds C-3 position to give the intermediate **A**. The following β-elimination of palladium with hydrogen atom gives 2-phenyl-2,5-dihydrofuran **6**. On the other hand, when **2** acts as a vinylsilane,[9] palladium atom adds C-2 position to give the intermediate **B** leading to 4-phenyl-2,3-dihydrofuran **7**. In the reaction of **2b** or **2e** bearing a phenyl group on silicon atom, addition of palladium at C-2 position may be assisted by the coordination of π-electron of the phenyl group to palladium atom.

In conclusion, the development of a novel, efficient and facile synthetic method for 5-silyl-2,3-dihydrofuran derivatives has been described. The reaction of cyclopropyl silyl ketones with trimethylsilyl trifluoromethanesulfonate in dichloromethane proceeded to afford the corresponding 5-silyl-2,3-dihydrofuran derivatives, exclusively. In the subsequent reaction with electrophilic reagents or Heck type reaction, the resulting 5-silyl-2,3-dihydrofuran derivatives exhibited both reactivities as a vinylsilane and a cyclic enol ether, depending upon the substituents on silicon atom. Further studies are aimed at expanding the scope of these reactions in our laboratory. The results will be reported in due course.



Scheme 3. Reaction pathway of regioselective Heck type reactions.

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