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Generation and Reactions of Trifluoromethylethenyl Titanium(II) Species

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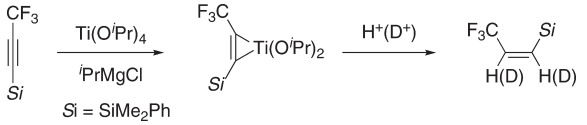
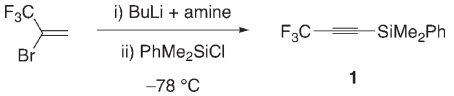


The reaction of (trifluoromethyl)dimethylphenylsilylacetylene and (η^2-propene)Ti(O^iPr)$_2$ generated in situ smoothly proceeded giving the corresponding (η^2-1-dimethylphenylsilyl-2-trifluoromethylalkyne)Ti(O^iPr)$_2$, which reacted with aldehydes and ketones to afford the corresponding addition products in good yields with good to excellent regioselectivity.

Transition metal−alkyne complexes are very useful synthetic intermediates for the preparation of functionalized olefins.[1] They are well-accepted to behave as 1,2-dianionic species. Among them, an alkyne−titanium complex, (η^2-alkyne)Ti(O^iPr)$_2$, developed by Sato and co-workers is a versatile synthetic intermediate and has been employed in a wide variety of reactions.[1a,2] On the other hand, we have been working on the development of versatile fluorine-containing building blocks prepared from easily available fluorinated molecules.[3] Very recently, we reported the synthesis and reactions of β-trifluoromethylvinyl sulfides as a potential synthetic intermediate.[4] Although the smooth generation of β-trifluoromethylvinyl anion species achieved by using sulfanyl group as a scaffold on the olefin, that of α-*trifluoromethylvinyl anion species* remains as an important problem due to easy elimination of fluorine.[5] If we could transform trifluoromethyl-containing alkynes into the corresponding alkyne−titanium complex, we may have a chance to perform the α-trifuoromethylvinylation reaction without loss of fluorine. Here we wish to report the first generation and reaction of (η^2-trifluoromethylated dimethylphenylsilylalkyne)Ti(O^iPr)$_2$ to afford the corresponding functionalized allylic alcohols with high regioselectivity.

TABLE 1. Preparation of 1 under Various Conditions[a]



entry	solvent	amine	additive[b]	yield[c] (%)
1	THF	DIA	none	52
2	Ether	DEA	none	0
3	THF	DEA	none	0
4	THF	DIA	HMPA	69
5	THF	HMDS	HMPA	85

[a]All reactions were conducted using BuLi (2.4 equiv) and amine (2.4 equiv) at −78 °C. [b]HMPA (15 mol %) was used. [c]Isolated yield after distilltion.

We planned our study by investigating the reactivity of (trifluoromethyl)dimethylphenylsilylacetylene **1** toward the alkyne−titanium complex (η^2-alkyne)Ti(O^iPr)$_2$. According to a procedure reported by Yamazaki and co-workers, **1** was prepared by using LDA and 2-bromo-3,3,3-trifluoropropene at −78 °C followed by addition of chloro(dimethylphenyl)silane in 52% isolated yield.[6] However, we soon encountered difficulty in reproducing similar results. Therefore, prior to investigation of our study, a practical procedure for the preparation of **1** was required. After many slightly modified experiments, we noticed the following two problems: (i) The incomplete conversion to **1** was confirmed on the basis of the GC calibration curve method. (ii) The workup procedure often resulted in partial decomposition of **1**, decreasing the yield. The former was settled by the addition of HMPA to the reaction mixture to enhance the reactivity of the corresponding lithium acetylide toward chloro(dimethylphenyl)silane. The latter was solved by the addition of a large amount of hexane to the reaction mixture prior to quench. Thus, we established the synthetic procedure of **1** in 85% isolated yield shown in Table 1.

According to a reported procedure for the preparation of (η^2-alkyne)Ti(O^iPr)$_2$ from [Ti(O^iPr)$_4$/^{i}PrMgCl/acetylene = 1.2:2.4:1], we attempted to generate the corresponding trifluoromethylsilylacetylene complex **1a** (Scheme 1). To our delight, the formation of trifluoromethylsilylacetylene complex **1a** was

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SCHEME 1. Generation and Protonation of the Ti(II) Complex 1a

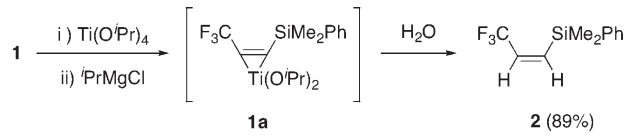
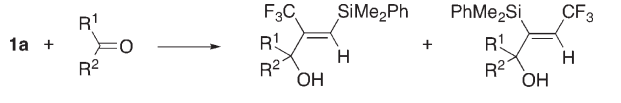


TABLE 2. Reaction of 1a with Various Carbonyl Compounds



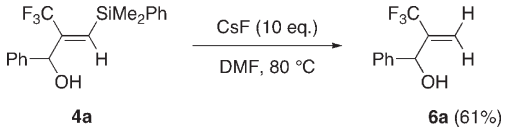
entry	carbonyl compound	yield[a] (%)	ratio (**4**:**5**)[b]
1	benzaldehyde (**3a**)	77	86:14
2	4-methylbenzaldehyde (**3b**)	76	75:25[c]
3	4-chlorobenzaldehyde (**3c**)	73	89:11
4	2-naphthaldehyde (**3d**)	43	93:7
5	decanal (**3e**)	69	73:27
6	2-ethylbutanal (**3f**)	68	88:12
7	acetone (**3g**)	58	100:0
8	cyclohexanone (**3h**)	46	100:0
9	acetophenone (**3i**)	47	100:0

[a]Isolated yield. [b]Determined by GC−MS except for entry 2. [c]Determined by ^{19}F NMR.

indirectly supported by hydrolysis of the reaction mixture exclusively giving the *cis*-vinylsilane **2** along with a small amount of **1**. When we employed double-fold of reagents to **1** [Ti(O^{i}Pr)$_4$/^{i}PrMgCl/acetylene = 2.4:4.8:1], the reaction completely proceeded giving **2** in 89% yield.[7] The stereochemistry of **2** was determined in comparison with the ^{1}H NMR data of the corresponding *trans*-vinylsilane.[8] Under the same reaction conditions, the reaction with deuterium oxide (D_2O) also proceeded giving *cis*-bis-deuterated olefin in 75% yield as well as high D incorporation (96:4).[9] With regard to reducing reagent, the use of BuLi instead of ^{i}PrMgCl was not effective for this reaction, giving almost no desired products.[10]

With the optimized reaction conditions established, the scope and limitation of this reaction were continuously studied. The reaction of **1a** with a variety of carbonyl compounds (**3a**−**i**) proceeded efficiently to afford the corresponding *cis*-allylic alcohols with good regioselectivity. The regioselectivity was determined by GC−MS analysis using a crude reaction mixture prior to chromatographic purification except for entry 2. The IR spectrum of these alcohols showed typical hydroxyl group absorption at around 3400 cm^{-1}. The results are summarized in Table 2. A wide range of aromatic aldehydes were suitable for this transformation in good yields regardless of electronic and steric effects (entries 1−4). In the same manner, linear and branched aliphatic aldehydes successfully underwent addition reaction to give the corresponding *cis*-allylic alcohols in good yields (entries 5 and 6). Interestingly, ketones regardless of whether they were acyclic, cyclic, or aromatic reacted with **1a** to provide a single regioisomer in each case, albeit in moderate yields (entries 7−9). The regiochemistry of the *cis*-allylic alcohols was mainly assigned on the basis of their ^{19}F NMR spectra. As we expected, the major regioisomer **4** showed a single peak, indicating that a trifluoromethyl group is attached to a vinylic carbon having no hydrogen. On the other hand, the minor regioisomer **5** showed a doublet peak. In addition to the carbonyl compounds, other electrophiles such as iodine, iodomethane, chlorotributylstannane, and benzoyl chloride were examined under the same reaction conditions; however, no addition products were obtained, and **2** was mostly obtained after aqueous workup.

SCHEME 2. Transformation of 4a



Finally, the transformation of the silyl group in the final product **4a** was briefly examined. The fluoride ion-assisted desilylation−protonation proceeded giving the corresponding allylic alcohol **6a** in 61% yield,[5f] which means that further functionalization of the final product should be possible (Scheme 2).

In summary, we have developed a new protocol for efficient preparation of trifluomethylated *cis*-allylic alcohols in good yields. The reaction proceeds under mild conditions with a wide range of aldehydes and ketones with high regioselectivity. This methodology should aid in fluoroorganic synthesis.

Experimental Section

3,3,3-Trifluoro-1-(dimethylphenylsilyl)propyne[6] **(1).** A 100 mL two-neck flask equipped with a magnetic stir bar, a stopcock, and a three-way stopcock was charged with 10 mL of THF under argon. To this solution were added HMDS (1.76 mL, 8.43 mmol), HMPA (90 μL, 0.517 mmol), and BuLi (2.64 M in hexane solution, 3.20 mL, 8.45 mmol) dropwise in this order via syringe at 0 °C. Another 25 mL two-neck flask equipped with a magnetic stir bar, a stopcock, and a three-way stopcock was charged with 3 mL of THF under argon. To this solution was added 2-bromo-3,3,3-trifluoropropene (0.40 mL, 3.87 mmol) dropwise via syringe at 0 °C. Both solutions were cooled to −78 °C, and then the second solution was transferred to the first solution via cannula at this temperature. After the solution was stirred for 30 min, chlorodimethylphenylsilane (0.58 mL, 3.51 mmol) was added via syringe. After the mixture was stirred for 30 min, *hexane* (*70 mL*) *was added to the mixture prior to warming to room temperature*. To the resulting solution was carefully added saturated NH_4Cl aqueous solution (15 mL). After the organic layer was separated, additional extraction with hexane was repeated twice. The combined solution was dried over sodium sulfate. The solution was concentrated in vacuo, and the residual oil was *quickly* purified by short-path distillation to give the desired product **1** as colorless oil (679.6 mg, 85%): bp 30 °C/1 mmHg (bath temperature). Anal. Calcd for $C_{11}H_{11}F_3Si$: C, 57.87; H, 4.86. Found: C, 58.16; H, 5.15.

(*Z*)-3,3,3-Trifluoro-1-(dimethylphenylsilyl)propene (2). A 25 mL two-neck flask equipped with a magnetic stir bar, a stopcock, and a three-way stopcock was charged with **1** (90.3 mg,

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0.396 mmol) and [Ti(O^iPr)$_4$] (0.30 mL, 0.963 mmol) in ether (7 mL) under argon. To this solution was added ^{i}PrMgCl (2.0 M in ether, 0.95 mL, 1.90 mmol) at −78 °C, and then the solution was warmed to −50 °C over 30 min, during which time it turned dark red. After the mixture had been stirred at −50 °C for an additional 2 h, water (50 μL, 2.8 mmol) was added. After the mixture was stirred for 1 h, the reaction was quenched with 1 M HCl. After the organic layer was separated, additional extraction with hexane/ether = 3/1 was repeated twice. The combined solution was dried over sodium sulfate. The solution was concentrated in vacuo, and the residual oil was *quickly* purified by silica gel chromatography (hexane/ether = 10/1) to give the desired product **2** as a colorless oil (80.9 mg, 89%): IR (neat) 3073, 2961, 1626, 1376, 1288, 1199, 1120, 849, 817, 786 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.46 (6H, q, J = 0.9 Hz), 6.32 − 6.47 (2H, m), 7.35−7.41 (3H, m), 7.48−7.54 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −2.0 (q, J = 2.5 Hz), 122.9 (d, J = 271.5 Hz), 127.9, 129.3, 133.5, 133.6 (d, J = 34.9 Hz), 137.6, 141.3 (d, J = 5.6 Hz); ^{19}F NMR ($CDCl_3$, 283 MHz) δ −62.7 (d, J = 6.8 Hz); GC−MS m/z 215 [M^+ − 15 (Me), 0.2], 171 (7), 153 (2), 133 (42), 115 (77), 91 (17), 77 (100). Anal. Calcd for $C_{11}H_{13}F_3Si$: C, 57.37; H, 5.69. Found: C, 57.75; H, 5.77.

Acknowledgment. We greatly thank F-Tech Co., Ltd. for a gift of 2-bromo-3,3,3-trifluoropropene.

Supporting Information Available: Characterization of new compounds **4a**−**i**. The material is available free of charge via the Internet at http://pubs.acs.org.