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Gallium Trichloride-Catalyzed Exhaustive α-Ethynylation Reaction of 1-Silylacetylenes

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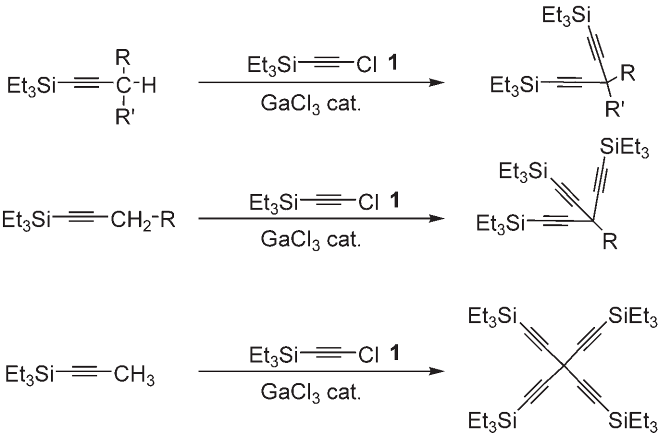
Abstract: Gallium trichloride ($GaCl_3$) catalyzes the ethynylation reaction of a 1,4-enyne with chlorosilylacetylene at the propargyl position giving a triethynylvinylmethane. This catalytic method can be applied to the exhaustive α-ethynylation of 1-silylacetylenes possessing less acidic propargyl protons, and mono-, di-, and triethynylated products are obtained depending on the structure of the starting materials.

Keywords: deprotonation; 1,4-enynes; ethynylation; gallium trichloride; propargylgallium; 1-silylacetylenes

A stoichiometric amount of butyllithium or lithium amide deprotonates the propargyl position of alkynes, and subsequent reactions with electrophiles give functionalized acetylenes.[1] The propargyllithiums in some cases are transmetalated to other metal species to control their reactivity.[2] The direct formation of propargylmetals other than the lithium derivative using a metal base catalyst may be more preferable, since the resultant species can exhibit a novel reactivity depending on the metal. Little, however, is known about such a catalytic method: Yamamoto reported the palladium-catalyzed C–C bond formation of acetylenes *via* allenes giving substituted alkenes.[3] Teuben developed lanthanum- and cerium-catalyzed cyclodimerizations of methylacetylenes *via* propargyl activation.[4]

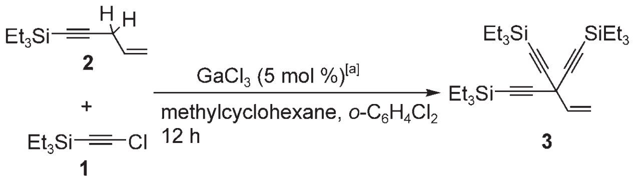
Previously, we reported the $GaCl_3$-promoted ethynylation reaction of 1,4-enynes and 1,4-diynes with chlorotriethylsilylacetylene **1**.[5,6] $GaCl_3$ deprotonated the substrates at the propargyl position activated by two unsaturated groups, and the resultant propargylgallium underwent regioselective ethynylation at the 3-position. The addition of silanol and 2,6-di(*tert*-butyl)-4-methylpyridine retarded the decomposition of the products and substrates. Although the reaction, involving the regeneration of $GaCl_3$, was potentially catalytic, a stoichiometric amount of $GaCl_3$ was required. In this study, diethynylation was found to proceed catalytically, and the catalytic method could be applied to 1-silylacetylenes possessing less acidic propargyl protons. Exhaustive α-ethynylation occurred giving mono-, di-, and triethynylated products depending on the structure of the substrate (Scheme 1).

It was previously observed that $GaCl_3$ itself, in the absence of silanol and 2,6-di(*tert*-butyl)-4-methylpyridine, promoted the diethynylation of the 5-triethylsilyl-1-penten-4-yne **2** with **1** giving 5-triethylsilyl-3,3-bis(triethylsilylethynyl)-1-penten-4-yne **3**,[5] and this reaction was employed to study the catalytic version. The treatment of **2** and **1** (4.0 equivs. against **2**) in a mixture of methylcyclohexane and *o*-dichlorobenzene in the presence of $GaCl_3$ (5 mol% against **1**) at 130 °C for 12 h gave **3** in 3% yield (based on **2**) (Table 1, entry 1). The use of excess **2** (2.0 equivs. against **1**) improved the yield to 21% (based on 1/2 the amount



Scheme 1.

Table 1. Catalytic diethynylation of **2**.



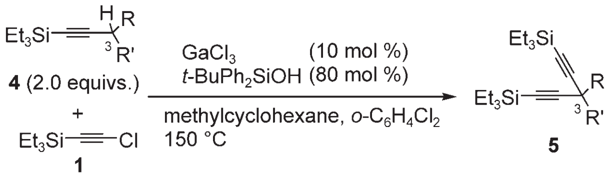
Entry	**2** [equivs.]	Temperature [°C]	Yield [%][b]
1	0.25	130	3[c]
2	1.0	130	9
3	2.0	130	21
4	2.0	150	56

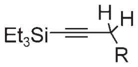
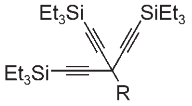
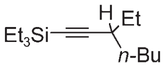
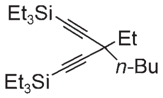
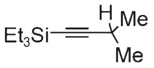
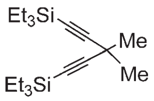
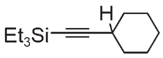
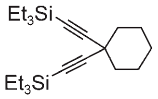
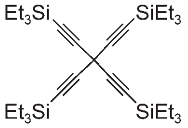
[a] Amount of $GaCl_3$ against **1**.
[b] Yield based on 1/2 the amount of **1**.
[c] Yield based on **2**.

of **1**) (entry 3). This may be due to a decrease in the amount of free $GaCl_3$ caused by complexation with **2**, which retarded the decomposition of **1**, **2**, and **3**. The yield of **3** increased to 56% at 150 °C (entry 4). It was calculated that 1 mole of $GaCl_3$ was used for 11 courses of ethynylation. Although the addition of silanol and pyridine improved the yield of the stoichiometric reaction,[5] the catalytic reaction proceeded in their absence.

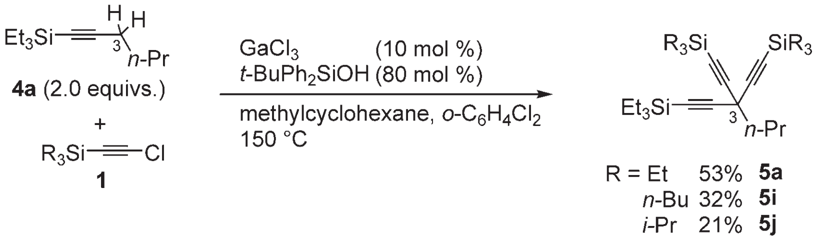
The propargyl ethynylation of 1-silylacetylenes also proceeded with a catalytic amount of $GaCl_3$ (Table 2). The reaction of 1-triethylsilyl-1-hexyne **4a** (2.0 equivs.) and **1** in the presence of $GaCl_3$ (10 mol%) at 150 °C for 12 h gave 1-triethylsilyl-3,3-di(triethylsilylethynyl)-1-hexyne **5a** in 22% yield (Table 2, entry 3). The addition of *tert*-butyldiphenylsilanol (80 mol% and 20 mol%) improved the yield

Table 2. Catalytic α-ethynylation of 1-silylacetylenes.

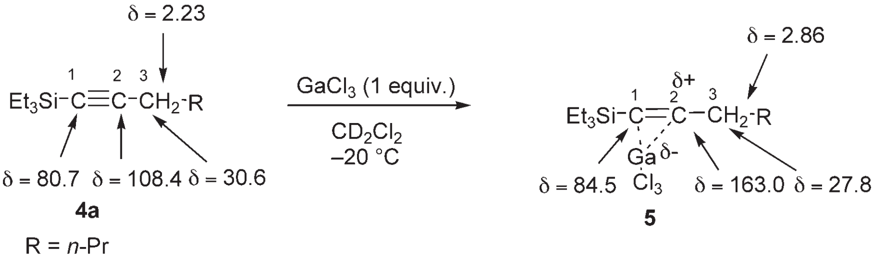


Entry	Substrate			Product	Time [h]	Yield [%]
1	**a**		R = *n*-Pr		12	53[a]
2					12	45[a,b]
3					12	22[a,c]
4	**b**		R = Me		12	52[a]
5	**c**		R = C_7H_{15}		12	53[a]
6	**d**		R = Ph		12	32[a]
7	**e**				24	56[d]
8	**f**				24	52[d]
9	**g**				24	33[d]
10	**h**	$Et_3Si{-}C{\equiv}C{-}CH_3$			24	18[e]

[a] Yield based on 1/2 the amount of **1**.
[b] 20 mol% of t-$BuPh_2SiOH$ against **1** was used.
[c] In the absence of t-$BuPh_2SiOH$.
[d] Yield based on **1**.
[e] Yield based on 1/3 the amount of **1**.



Scheme 2.



Scheme 3.

to 53% and 45% in this case (entries 1 and 2). $GaCl_3$ deprotonated the propargyl position of 1-silylacetylenes, which was activated by only one unsaturated group. Several 1-triethylsilyl-1-alkynes **4b–4d** with different chain lengths were diethynylated at the α-position in the presence of $GaCl_3$ (10 mol%) and *tert*-butyldiphenylsilanol (80 mol%) (entries 4–6). The reaction of the 3,3-dialkylated 1-triethylsilyl-1-propynes **4e–4g** gave the monoethynylated products **5e–5g** (entries 7–9). 1-Triethylsilyl-1-propyne **4h** was triethynylated giving tetraethynylmethane **5h** in 18% yield (based on 1/3 the amount of **1**) (entry 10), in which $GaCl_3$ deprotonated and ethynylated **4h** three times at the propargyl position. Ethynylation, however, did not proceed with 4-octyne indicating an essential role of the silyl group in this reaction. The silicon substituent on the chloroacetylene is also important, and the yield lowered with tributylsilyl (32%) and triisopropylsilyl (21%) derivatives (Scheme 2).

Since the complex formation of **4a** and $GaCl_3$ was considered to play an important role, NMR studies were conducted (Scheme 3).[7] When **4a** and $GaCl_3$ (1 equiv.) were mixed at –20 °C, the propargyl proton 3-H NMR signal shifted from $\delta = 2.23$ to $\delta = 2.86$, and acetylene carbons C-1 and C-2 appeared at 84.5, and 163.0, respectively. It should be noted that C-2 of **4a** shifted 55 ppm to low field by complex formation,[8] which suggested the electron deficient nature of C-2. It might have increased the acidity of the propargyl proton.

To summarize, a 1,4-enyne was catalytically ethynylated at the propargyl position using $GaCl_3$, and this catalytic method could be applied to the exhaustive α-ethynylation of 1-silylacetylenes. $GaCl_3$ was shown to function as a base that catalytically deprotonates and ethynylates propargyl protons.

Experimental Section

Catalytic Diethynylation of 2

Under an argon atmosphere, $GaCl_3$ (0.025 mmol, 5 mol%) in *o*-dichlorobenzene (0.2 mL) and methylcyclohexane (0.25 mL) was added to a mixture of **2** (1 mmol, 180.4 mg) and **1** (0.5 mmol, 87.4 mg) in *o*-dichlorobenzene (0.2 mL) at 0 °C. The mixture was then stirred at 150 °C for 12 h, when water (2 mL) was added. The organic materials were extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane) to give **3**; yield: 63.8 mg (55%).

Typical Procedure for α-Ethynylation of 1-Silylacetylenes

Under an argon atmosphere, to a solution of *tert*-butyldiphenylsilanol (0.4 mmol, 102.4 mg) in *o*-dichlorobenzene (0.2 mL) and methylcyclohexane (0.2 mL) was added a solution of $GaCl_3$ (1.0M, 0.05 mmol, 10 mol%) in methylcyclohexane (0.05 mL) at 0 °C. Then, a solution of **4a** (1.0 mmol, 196.4 mg) and **1** (0.5 mmol, 87.4 mg) in *o*-dichlorobenzene (0.2 mL) was added at the temperature. The mixture was heated at 150 °C for 12 h, when water (2 mL) was added. The organic materials were extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography (petroleum ether) to give **5a**; yield: 64.5 mg (53%).

Acknowledgements

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