A Convenient Synthesis of 1-Trimethylsilyl-1,3-diynes and their Conversion into Terminal 1,3-Diynes

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In connection with ongoing synthetic work, we required ready access to a class of conjugated diynes in which the triple bonds exhibit different reactivities toward electrophilic and nucleophilic reagents. Experiments have revealed that 1-trimethylsilyl-1,3-diynes **5** fulfill this requirement[1]. Unfortunately, published methods for their preparation are either limited in scope or require precursors which are not readily accessible.

Although sequential deprotonation and silylation of terminal 1,3-diynes provides silyldiynes in good yields[2], the method suffers from the lack of convenient procedures for obtaining the diyne precursors[3]. It was reported that oxidative coupling of *trans*-2-ethynylcyclohexanol with trimethylsilylacetylene afforded a fair yield of the corresponding 1-trimethylsilyl-1,3-diynes[4]. However, three equivalents of the silylacetylene had to be employed. The Cadiot-Chodkiewicz coupling of arylacetylenes with (bromoethynyl)-triethylsilane produces the corresponding silyldiynes[5,6] in modest yields only. Also, the reaction is confined to the preparation of 1-triethylsilyl-1,3-diynes. Attempts to synthesize the trimethylsilyl analogs produced the desilylated 1,3-diynes[6]. However, it appeared to us that these shortcomings could be circumvented by using preformed copper(I) acetylenides[7] with (bromoethynyl)-trimethylsilane **(3)**.

Our initial efforts were directed toward developing an efficient synthesis of the (bromoethynyl)-trimethylsilane intermediate **3**[8]. It was known that bis[trimethylsilyl]acetylene **(1)** undergoes monodesilylation when reacted with methyllithium in

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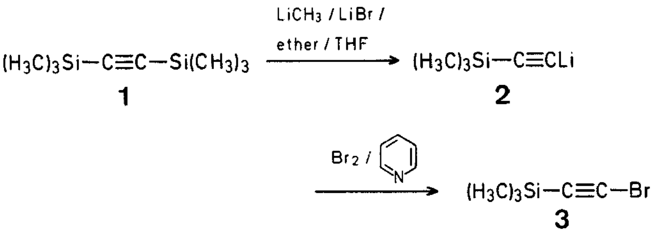
tetrahydrofuran solvent[9]. Thus, it was anticipated that sequential treatment of **1** with methyllithium/lithium bromide in ether followed by bromination of the resultant lithium acetylenide **2** should afford the desired (bromoethynyl)-trimethylsilane **(3)**, and this was borne out by experiment (70% yield of **3**).



1 **2** **3**

Coupling of **3** with dry copper(I) pentynylide[10] in pyridine at 25 °C proceeded exothermally to furnish, after workup, 1-trimethylsilyl-1,3-heptadiyne in nearly quantitative yield (96%) containing only small amounts of the two possible homocoupled by-products, bis[trimethylsilyl]butadiyne (1%) and 4,6-decadiyne (3%). However, since many copper(I) acetylenides are difficult to isolate as solids in high yield, we also investigated the utilization of *in situ* prepared copper(I) acetylenides[11]. These are readily obtained by sequential treatment of 1-alkynes with an alkyllithium followed by the appropriate copper(I) halide[12]. Thus, treatment of 1-octyne dissolved in tetrahydrofuran with *n*-butyllithium in hexane at −78 °C converted it into the lithium acetylenide. To this was added at 0 °C an equimolar amount of copper(I) bromide to produce a slurry of the copper(I) acetylenide **4a**. The solvents were removed under reduced pressure (1 torr) and replaced by dry pyridine[13]. Addition of (bromoethynyl)-trimethylsilane **(3)** at 25 °C afforded, after workup and distillation, the corresponding 1-trimethylsilyl-1,3-diyne **(5a)** in 83% yield containing less than 2% of the corresponding homocoupling products[14].

$$R{-}C{\equiv}CH \xrightarrow{\substack{1.\ n\text{-}C_4H_9Li \\ 2.\ CuBr}} \underset{\textbf{4a-e}}{R{-}C{\equiv}C{-}Cu} \xrightarrow{(H_3C)_3Si{-}C{\equiv}C{-}Br\ (\textbf{3})} \underset{\textbf{5a-e}}{R{-}C{\equiv}C{-}C{\equiv}C{-}Si(CH_3)_3}$$

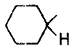
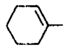
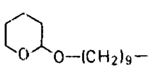
The reaction of *in situ* prepared copper(I) acetylenides **4** with **3** to produce the silyldiynes **5** was found to be of wide utility. Thus, equally high yields of **5** were realized using copper(I) acetylenides derived from primary, secondary, or tertiary alkyl substituted alkynes, as well as from those containing a conjugated double bond (Table).

Finally, desilylation of 1-trimethylsilyl-1,3-diynes **(5)** provides the corresponding terminal 1,3-diynes, which are difficult to obtain by existing methodologies[3]. For example, treatment of crude 1-trimethylsilyl-1,3-decadiyne **(5a)** with an excess of potassium fluoride dihydrate in dimethylformamide[15] afforded 1,3-decadiyne **(6)** in 79% overall yield based on the starting 1-octyne.

$$n\text{-}C_6H_{13}{-}C{\equiv}CH \xrightarrow{\substack{1.\ n\text{-}C_4H_9Li \\ 2.\ CuBr \\ 3.\ (H_3C)_3Si{-}C{\equiv}C{-}Br\ (\textbf{3})}}$$

$$\underset{\textbf{5a}}{n\text{-}C_6H_{13}{-}C{\equiv}C{-}C{\equiv}C{-}Si(CH_3)_3} \xrightarrow{KF\cdot 2\,H_2O/\,DMF} \underset{\textbf{6}}{n\text{-}C_6H_{13}{-}C{\equiv}C{-}C{\equiv}CH}$$

Table. Yields of 1-Trimethylsilyl-1,3-diynes **(5)**

Product 5	R	Yield [%][a,b]	b.p./torr or m.p. [°C]	n_D [°C]	Molecular Formula[c]
a	n-C_6H_{13}	83	65°/0.01	1.4865 (22°)	$C_{13}H_{22}Si$ (206.1)
b		81	71–72°/ 0.02	1.5139 (26°)	$C_{13}H_{20}Si$ (204.1)
c		85	110°/10^{-4} [d]	1.5479 (24°)	$C_{13}H_{18}Si$ (202.1)
d	t-C_4H_9	93	112–113°		$C_{11}H_{18}Si$ (178.1)
e		70[e,f]		1.4895 (24°)	$C_{21}H_{36}O_2Si$ (348.1)

[a] The spectral data of the reported compounds are consistent with the assigned structures.

[b] The isolated trimethylsilyl-1,3-diynes contained less than 2% of the corresponding by-products of homocoupling.

[c] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.25; H, ±0.14.

[d] Kugelrohr distillation.

[e] The reaction mixture was worked up with saturated aqueous sodium chloride instead of 6 molar hydrochloric acid. The pyridine was removed by precipitation with 20% aqueous cadmium chloride.

[f] The compound was purified by column chromatography on Florisil using dichloromethane as the eluent.

(Bromoethynyl)-trimethylsilane (3):
To a well-stirred solution of bis[trimethylsilyl]acetylene (**1**; 13.6 g, 80.0 mmol) in tetrahydrofuran (80 ml) under a nitrogen atmosphere at 0 °C is added dropwise a 1.4 molar solution of methyllithium/lithium bromide (63 ml, 88 mmol) in ether. The mixture is stirred at 0 °C for 30 min, gradually warmed to 25 °C, stirred for 30 min at this temperature, and then cooled to −78 °C and treated sequentially with dry pyridine (12.8 ml, 160 mmol) and a solution of bromine (14 g, 88 mmol) in dichloromethane (20 ml). The resultant mixture is stirred at −78 °C for 15 min, gradually warmed to room temperature, and then poured into 6 molar hydrochloric acid (50 ml). The layers are separated, and the aqueous phase is extracted with pentane (2 x 50 ml). The combined organic extracts are washed with 6 molar hydrochloric acid (3 x 25 ml), 20% aqueous cadmium chloride (20 ml), 10% aqueous sodium sulfite (20 ml), saturated aqueous sodium hydrogen carbonate (20 ml), saturated aqueous sodium chloride (30 ml), and then dried with magnesium sulfate. The solvents are removed by atmospheric pressure distillation through a tantalum spiral column (1 m), and the residue obtained is distilled through a short Vigreux column; yield: 9.93 g (70%); b.p. 74 °C/130 torr; n_D^{25}: 1.4605 (Ref.[8], b.p. 48 °C/50 torr; n_D^{20}: 1.4612).

1-Trimethylsilyl-1,3-decadiyne (5a); Typical Procedure:
A 1.8 molar solution of *n*-butyllithium (28 ml, 50 mmol) in *n*-hexane is added dropwise to a stirred solution of 1-octyne (5.5 g, 50 mmol) in tetrahydrofuran (80 ml) at −78 °C under a nitrogen atmosphere. The mixture is warmed to 0 °C and then treated with dry copper(I) bromide (7.2 g, 50 mmol). The resulting viscous mixture is stirred vigorously at 20–25 °C for 30 min. The volatiles are removed under reduced pressure (1 torr, 30 min), and to the residue obtained is added dry pyridine (100 ml). The vigorously stirred mixture is treated at 25 °C with (bromoethynyl)-trimethylsilane (**3**; 8.85 g, 50.0 mmol), causing the temperature to rise gradually to 50 °C. The resultant brown solution is stirred at ambient temperature for 1 h, then is poured into stirred, ice-cold 6 molar hydrochloric acid (150 ml). The layers are separated, and the aqueous phase is extracted with *n*-hexane (3 x 30 ml). The combined organic extracts are washed successively with 6 molar hydrochloric acid (2 x 25 ml), saturated aqueous sodium hydrogen carbonate (20 ml), saturated aqueous sodium chloride (30 ml), and then dried with magnesium sulfate. The solvent is removed using a rotary vacuum

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evaporator and the residue obtained is distilled through a short Vigreux column; yield 8.6 g (83%); b.p. 65 °C/0.01 torr; n_D^{22}: 1.4865.

$C_{13}H_{22}Si$	calc.	C 75.65	H 10.74
(206.1)	found	75.45	10.67

I.R. (neat): ν=2240, 2120, 1250, 1185, 845, 765 cm^{-1}.

^{1}H-N.M.R. (CCl$_4$): δ=0.10 (s, 9 H); 0.80 (t, 3 H); 1.1–1.5 (m, 8 H); 2.30 ppm (t, 2 H).

1,3-Decadiyne (6):

The organic extract obtained from coupling of 1-octyne (5 mmol) with (bromoethynyl)-trimethylsilane (**3**; 5 mmol) as described in the typical procedure above is concentrated using a rotary vacuum evaporator to remove most of the solvents. The crude 1-trimethylsilyl-1,3-decadiyne (**5a**) obtained is added to a slurry of potassium fluoride dihydrate (0.94 g, 10 mmol) in dimethylformamide (10 ml) at 25 °C. The mixture is stirred for 30 min, then is poured into a separatory funnel containing 3 molar hydrochloric acid (30 ml). The layers are separated, and the aqueous phase is extracted with *n*-hexane (3 × 15 ml). The combined organic extracts are successively washed with 3 molar hydrochloric acid (2 × 15 ml), saturated aqueous sodium hydrogen carbonate (10 ml), saturated aqueous sodium chloride (15 ml), and then dried with magnesium sulfate. The solvents are removed and the residue is distilled (Kugelrohr); yield 0.53 g (79%); b.p. 85 °C/5 torr; n_D^{24}: 1.4727 (Ref.[16], b.p. 57–60 °C/2.7 torr).

$C_{10}H_{14}$ (134.1096).

M.S.: m/e=134.1118.

I.R. (neat): ν=3315, 2945, 2295, 2225 cm^{-1}.

^{1}H-N.M.R. (CCl$_4$): δ=0.8 (t, 3 H); 1.1–1.6 (m, 8 H); 1.80 (t, 1 H); 2.20 ppm (t, 2 H).

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