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NOVEL SYNTHESES OF 1-(TRIALKYLSILYL)-1,3-DIYNES AND 1,4-BIS-SILYL-1,3-BUTADIYNES FROM (Z)-1-METHOXY-1-BUTEN-3-YNE

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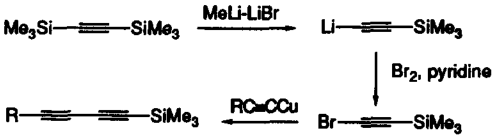
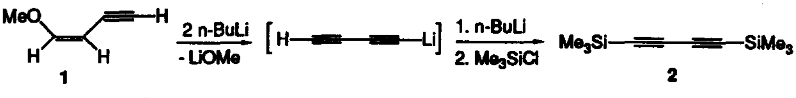
Abstract: Alkylation or silylation of lithiated *(Z)*-1-methoxy-1-buten-3-yne affords the corresponding substituted methoxyenynes which, upon sequential treatment with lithium diisopropylamide followed by chlorotrialkylsilanes, furnish 1-(trialkylsilyl)-1,3-diynes and 1,4-bis-silyl-1,3-butadiynes, respectively.

The 1,3-butadiyne structural feature is frequently embodied in many natural products and fungal metabolites.[1] Furthermore, it is a potential synthetic precursor for stereodefined enynes and dienes. The usefulness of 1,3-diynes in organic synthesis, however, depends on whether the triple bonds may be reacted chemoselectively with electrophilic and nucleophilic reagents. We have recently shown that the presence of a trimethylsilyl moiety imparts appreciably different reactivities to the triple bonds of 1-(trimethylsilyl)-1,3-diynes in reactions with hydrometallating[2,3] and dimetallating agents.[4] The required diynes were synthesized via a modified coupling reaction[5] of copper(I) acetylides with (bromoethynyl)trimethylsilane.[6,7]

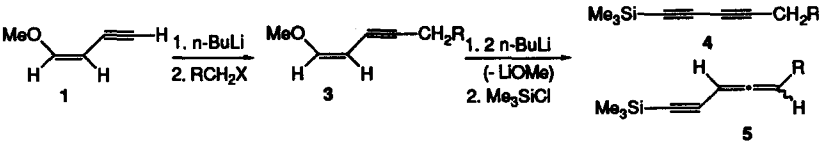


In connection with our ongoing studies of the utility of 1,3-diynes as intermediates in organic synthesis, it was important to have ready access to silyl-diynes having various alkyl groups attached to silicon. We had previously shown that treatment of the methoxyenyne **1** with *n*-butyllithium, followed by quenching the reaction mixture with chlorotrimethylsilane, affords the 1,4-bis(trimethylsilyl)-1,3-butadiyne **2**.[8]



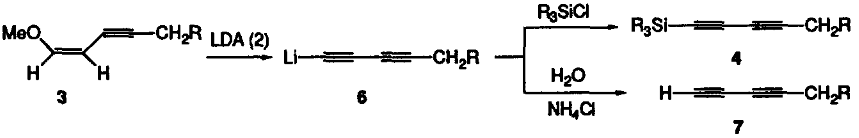
Since *(Z)*-1-methoxy-1-buten-3-yne **1** is commercially available at low cost, we have now also investigated its use as a precursor for the preparation of 1-(trialkylsilyl)-1,3-diynes **4**. Our plan for the conversion of **1** into the diynes **4** was to prepare the alkyl-substituted enynes **3** and then subject them to a sequence of metallation-elimination-metallation-silylation reactions.

Treatment of **1** with one equivalent of *n*-BuLi produced the lithium alkynylide, which could be alkylated with an appropriate primary alkyl halide[9] in the presence of HMPA (hexamethylphosphoramide) to furnish the alkyl-substituted methoxyenyne **3** in good yield. It should be noted here that the alkylation may also be carried out in the presence of DMPU (1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone)[10,11] as activator, thus avoiding use of the carcinogenic HMPA. Attempted conversion of **3** (R=*n*-hexyl) into the diyne **4** by successive treatment with 2 equivalents of *n*-BuLi followed by chlorotrimethylsilane under similar experimental conditions to those used for the preparation of the trimethylsilyl-substituted enyne **2** resulted, however, in a 28:72 mixture of the desired diyne **4** and the allene-yne **5**.



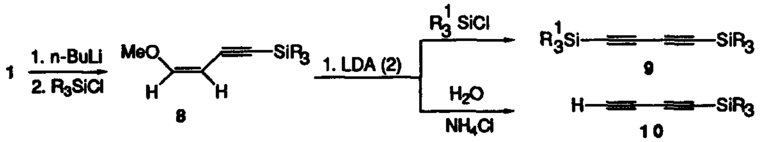
Apparently, deprotonation at the propargylic position by *n*-butyllithium competes favorably with deprotonation at the C-2 vinylic carbon of **3**.

Fortunately, this problem could be obviated by carrying out the deprotonation with lithium diisopropylamide (LDA) instead of *n*-butyllithium. Thus, when **3** was reacted with two equivalents of LDA at -40°C for 2 h and the resultant 1-lithio-1,3-diyne **6** was trapped with either chlorotrimethylsilane, chlorodimethyl-*t*-butylsilane or chlorodimethylthexylsilane, the desired diynes **4** were obtained in good yields and free of the corresponding allene-ynes **5**. The choice of temperature for the deprotonation with LDA is critical. Thus, at low temperature (-78°C) metallation of **3** with LDA was sluggish, whereas at higher temperature (> -40°C) propargylic deprotonation became an increasingly important side reaction.



This novel methodology is also amenable to the preparation of hydrogen-substituted 1,3-diynes **7** by quenching the reaction mixture, after deprotonation with LDA, with aqueous ammonium chloride instead of with chlorotrialkylsilanes.

Returning to the lithiated methoxyenyne **1**, silylation with chlorotrimethylsilane or chlorodimethylthexylsilane does not require the presence of an activator. The resulting trialkylsilyl-substituted enynes **8** may serve as precursors for 1,4-bis-silyl-1,3-butadiynes. Specifically, we were interested in the preparation of diynes in which the two silyl moieties would exhibit different nucleophilicities so they could be elaborated in a sequential manner. This was accomplished by treatment of **8** (R_3=thexylMe$_2$) with 2 equivalents of LDA and then with chlorotrimethylsilane, as exemplified by the preparation of the unsymmetrically-substituted butadiyne **9** (R_3=dimethylthexyl; $R^1{}_3$ =Me$_3$). Moreover, mono-substituted silyl-1,3-butadiynes **10** are available from the silyl-enynes **8** by protonation of the intermediate lithiated diynes with aqueous ammonium chloride.



From the results obtained in this investigation, it is evident that the commercially available methoxyenyne **1** provides a convenient access both to 1-(trialkylsilyl)-1,3-diynes and to the nucleophilic 1,4-bis-silyl-1,3-butadiynes. The latter constitute a stable source of butadiyne, an extremely useful, but unstable synthon. A summary of methoxyenyne starting material and 1,3-diyne yields obtained in this study is shown in the Table.

Table. Yields of (*Z*)-1-Methoxy-1-buten-3-ynes and 1,3-Diynes

R	R^1 [a]	products, % [b,c] (*Z*)-MeOCH=CHC≡CR	$R^1C{\equiv}CC{\equiv}CR$
n-C_6H_{13}	A	89	88
	B		87
	C		83
	H		82
$(CH_2)_3CH{=}CH_2$	B	95	82
Me_3Si	A	89	75
thexylMe_2Si	A		97
	B	87	82
	H		90

[a] A=Me_3Si; B=Me_2thexylSi; C=Me_2-*t*-BuSi. [b] Isolated yields. [c] The IR, ^{1}H NMR, ^{13}C NMR, and mass spectral data of the compounds are consistent with the assigned structures.

The following procedures for the preparation of (*Z*)-methoxyenynes are representative. To freshly distilled (CaH_2) **1**[8] (15 mmol) was added a 1.60 M solution of *n*-BuLi (15 mmol) in hexanes while maintaining the temperature during the addition at -50°C ($CaCl_2$/Dry Ice bath).[12] The mixture was stirred for 30 min, treated at -50°C with a solution of the appropriate alkyl halide (15.8 mmol) in HMPA (6 mL), warmed to 0°C, stirred for 2 h, and then poured into ice water. The alkyl-substituted methoxyenynes **3** formed were extracted with pentane, the combined extracts were washed with 1N HCl (2x10 mL) and brine, dried ($MgSO_4$), filtered, concentrated, and distilled. For the preparation of silyl-substituted methoxyenynes **8**, the chorotrialkylsilane (15.8 mmol) was added to the lithiated enyne at -78°C in the absence of HMPA. The mixture was then warmed to 0°C, stirred for 3.5 h, then poured into saturated aqueous NH_4Cl. The silyl-substituted methoxyenyne obtained was worked up as described above.

The following procedures for the preparation of 1,3-diynes are representative. To a solution of *freshly* distilled (CaH_2) methoxyenyne **3** or **8** (5 mmol) in THF (9 mL) was added dropwise a 0.6 M solution of LDA (10.0 mmol) in THF while maintaining the temperature during the addition between -40° and -50°C. The mixture was stirred at this temperature for 2 h, the bath was removed, and the mixture was stirred for an additional 15 min to insure complete elimination of MeOLi. For the preparation of the hydrogen-substituted 1,3-diynes **7** or **10**, the intermediate lithio-1,3 diynes **6** were cooled to -50°C, then treated with an aqueous solution of NH_4Cl. The aqueous layer was extracted with pentane, the combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, concentrated, and distilled. For the preparation of the silyl-substituted 1,3-diynes **4** and **9**, the lithio-1,3-diynes **6** were cooled between -40°C and -50°C, then treated with chlorotrimethylsilane (20 mmol) or with chlorodimethyl-*t*-butylsilane (10 mmol). The reaction mixture was stirred at this temperature for 15 min, then poured into an aqueous solution of NH_4Cl. Silylation with chlorodimethylthexylsilane (10 mmol) was also carried out between -40°C and -50°C for 15 min, but then the mixture was warmed to room temperature and stirred for 30 min before being poured into an aqueous solution of NH_4Cl. The layers were separated and the aqueous layer was extracted with pentane. The organic extracts were dried ($MgSO_4$), filtered, concentrated, and the liquid rèsidue obtained was purified by flash chromatography[13] on silica gel (60-200 mesh) using *n*-hexane as an eluent and distilled. The solid, symmetrically-substituted bis-silyl diynes were recystallized from ethyl acetate/methanol.

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