(Z)-1-Methoxybut-1-en-3-yne. A Versatile Synthon for 1,4-Bis(trimethylsilyl)-1,3-butadiyne as well as for Nucleophilic Aldehyde and Butadiyne Equivalents

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In connection with our ongoing studies on the hydrometalation of functionally substituted alkynes, we examined various synthetic transformations of the commercially available (Z)-1-methoxy-but-1-en-3-yne (1a).[1] We now wish to report our discovery of a simple synthesis of 1,4-bis(trimethylsilyl)-1,3-butadiyne from 1a. Also, convenient routes from the trimethylsilyl derivative 2a to both butadiyne and potential nucleophilic aldehyde equivalents have been uncovered. Clearly such reagents are extremely useful in organic synthesis.

In our initial studies, we examined whether 1a might be converted into the dilithiated methoxy enynes 1b or 1b'[3] by treatment in THF at -72 °C with 2 equiv. of n-butyllithium in n-hexane. However, this resulted solely in deprotonation of the acetylenic hydrogen. Thus, we further investigated the metalation under various conditions. This led to the discovery that sequential treatment of the methoxy enyne 1a in THF at -25 °C with 3 equiv of n-butyllithium followed by Me₃SiCl provides an economical route to 1,4-bis(trimethylsilyl)-1,3-butadiyne (1d), a stable, crystalline source of the synthetically valuable but very unstable butadiyne.[4] The formation of 1d most likely proceeds via a sequence of metalation–elimination–metalation reactions to furnish the dilithio diyne 1c which then reacts with Me₃SiCl to produce 1d (eq 1).
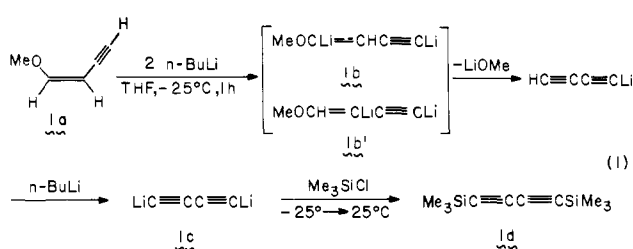
This novel, operationally simple synthesis of 1d involves addition of a solution of n-butyllithium (1.6 M, 75 mmol) in n-hexane to a solution of 1a (25 mmol)[1] in THF (50 mL) cooled to -25 °C (CaCl₂–dry ice bath). The temperature during metalation was maintained between -20 and -25 °C. The mixture was stirred at this temperature for 1 h; then the dilithiated diyne formed was treated with Me₃SiCl (79 mmol)[5] while keeping the temperature during the addition below -20 °C. The mixture was warmed to 25 °C, stirred for 1 h, and then poured into saturated aqueous NH₄Cl. After extraction with n-pentane, the combined organic phases were washed with saturated aqueous NaCl. Drying (MgSO₄) and removal of the solvents yielded 80% of 1d: mp 107 °C after recrystallization from methanol (lit.[4] 107 °C).

Table I. Yields of Products Derived from the Reaction of 2c and 2e with Electrophiles

reagent	electrophile[a] E	reactn time, h[d]	yield of products, %[e]	isomeric purity, %[f]
2c	CH₃OH[b]	0.25	3a, 92	98
	CH₃I	4	3b, 78	99
	n-C₄H₉I	4	3c, 73	93
	(CH₃)₂C=CHCH₂Br	4	3d, 74	97
	C₂H₅CHO	2	3e, 86	99
	(CH₃)₂CO	2	3f, 77	99
2e	H₃O⁺ [c]		4a, 71	
	C₂H₅CHO		4b, 76	
	Me₃SiCl[b]		4c, 80	

[a] 1.1 equiv of the electrophile was used. [b] 2 equiv of the electrophile was used. [c] The reaction mixture was poured into ice-cold 3 N HCl–pentane. [d] The electrophile was added to 2c at -72 °C and the reaction mixture was then maintained at this temperature for the times indicated. For 2e, the electrophile was added at -40 °C and the reaction mixture was then maintained at 25 °C for 1 h prior to workup. [e] Isolated yields. The IR, ¹H NMR, and microanalytical data were consistent with the assigned structures. [f] Determined on either a 30 m SE-54 or on a DB-210 J&W glass capillary column.

In a second area of study, we investigated the lithiation of 2a,[6] the 4-(trimethylsilyl) substituted derivative of the methoxy enyne 1a. Although β-alkyl[3] and -alkenyl[7] substituted enol ethers are metalated α to the alkoxy group, it was anticipated that the strong electron-withdrawing ability of the (trimethylsilyl)ethynyl moiety in 2a would direct lithiation to the β-vinylic carbon to provide the synthetically attractive masked aldehyde enolate 2b. To test this premise, the 4-(trimethylsilyl) substituted (Z)-methoxy enyne 2a (5 mmol) in dimethoxyethane (10 mL) was treated at -72 °C with 1 equiv of n-butyllithium in n-hexane. Quenching the reaction mixture at -72 °C with CH₃OD furnished the deuterated (E)-methoxy enyne 2d with 98% isomeric purity and in 92% yield [¹H
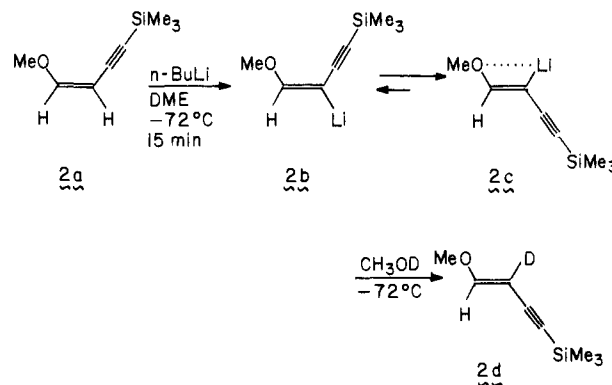
NMR (CCl₄) δ 0.1 (s, 9 H), 3.45 (s, 3 H), 6.75 (t, *J* = 1.8 Hz, 1 H)].[8] The regioselectivity and stereoselectivity observed in formation of 2d imply that the initially formed lithiated methoxy enyne 2b isomerized to the more stable, intramolecularly solvated species 2c,[9,10] which is the actual precursor of 2d.

It is apparent that the organolithium derivative 2c, which represents a novel, functionalized, masked aldehyde enolate, should be amenable to a variety of synthetic transformations. We report

(1) (Z)-1-Methoxybut-1-en-3-yne (97% isomerically pure) is available from Aldrich as a 50% solution in methanol–water. It was purified according to the literature procedure[2] and was distilled from calcium hydride prior to its use. ¹H NMR (CCl₄) δ 2.9 (dd, *J* = 2, 1 Hz, 1 H), 3.8 (s, 3 H), 4.4 (dd, *J* = 7, 2 Hz, 1 H), 6.3 (dd, *J* = 7, 1 Hz, 1 H).

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(5) Since the lithium methoxide formed reacts with Me₃SiCl, an additional equivalent of the silylating agent had to be used.

(6) (Z)-1-Methoxy-4-(trimethylsilyl)but-1-en-3-yne (2a) was prepared by sequential treatment of 1a (30 mmol) in THF (60 mL) at -72 °C with n-butyllithium (30 mmol) followed by Me₃SiCl (32 mmol). The mixture was warmed to 0 °C and stirred for 2 h before being worked up: bp 77–79 °C (12 torr); n_D²¹ 1.4830; ¹H NMR (CCl₄) δ 0.1 (s, 9 H), 3.65 (s, 3 H), 4.30 (d, *J* = 7 Hz, 1 H), 6.0 (d, *J* = 7 Hz, 1 H).

(7) Soderquist, J. A.; Hassner, A. *J. Org. Chem.* **1980**, *45*, 541; *J. Am. Chem. Soc.* **1980**, *102*, 1577.

(8) Lithiation of 2a in THF at -72 °C followed by deuteriolysis produced a 12/88 mixture of the (Z)- and (E)-methoxyenynes.

(9) For an interesting discussion concerning intramolecular solvation of lithium by oxygen in lithiated enol ethers, see: Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, *43*, 1595.

(10) A similar type of isomerization has been observed with lithiated β-(alkylthio) and -(arylthio) substituted vinyl ethers. Vlattas, I.; Vecchia, L. D.; Lee, A. O. *J. Am. Chem. Soc.* **1976**, *98*, 2008.
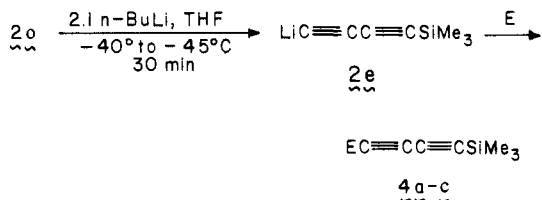
here preliminary studies of its reaction with various electrophiles "E" and its conversion into 4-lithio-1-(trimethylsilyl)butadiyne (**2e**), a nucleophilic butadiyne equivalent.

Treatment of the lithium reagent **2c** in DME at -72 °C with methanol furnished the (E)-methoxy enyne **3a** [E = H; ^{1}H NMR

$$2c \xrightarrow[\text{-72°C, 2-4 h}]{E} \quad \text{3a-f}$$
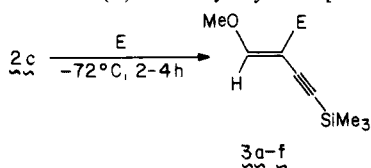
(CCl$_4$) δ 0.1 (s, 9 H), 3.45 (s, 3 H), 4.70 (d, J = 13 Hz, 1 H), 6.75 (d, J = 13 Hz, 1 H)].[11,12] As shown by the results in Table I, **2c** also reacts readily with carbon electrophiles. For example, treatment of **2c** (10 mmol) with a solution of methyl iodide (11 mmol) in DME (1 mL) at -72 °C followed by maintaining the reaction mixture at this temperature for 4 h afforded, after quenching with methanol (1 mL) followed by workup, 78% of **3b**; [E = CH$_3$; ^{1}H NMR (CDCl$_3$) δ 0.17 (s, 9 H), 1.70 (d, J = 1.5 Hz, 3 H), 3.67 (s, 3 H), 6.25 (q, J = 1.5 Hz, 1 H)].[13,14] The synthetic utilities of the 2-substituted methoxy enynes **3** remain to be delineated.

While the lithium reagent **2c** is sufficiently stable at -72 °C to be trapped with electrophiles, at -40 °C it eliminated lithium methoxide to furnish the lithio diyne **2e**[15] together with **2a** as a E/Z mixture. This result suggested that the synthetically important nucleophilic butadiyne equivalent **2e**[16] should be directly accessible from **2a** upon addition of 2 equiv of n-butyllithium. This was borne out by the observation that sequential treatment of **2a** (10 mmol) in THF (10 mL) at -40 to -45 °C with n-butyllithium (21 mmol) in n-hexane followed by Me$_3$SiCl (21 mmol)[5] yielded 80% of the bissilylated butadiyne **4c** (E = SiMe$_3$). Under similar

$$2a \xrightarrow[\substack{-40° \text{ to } -45°C \\ 30 \text{ min}}]{2.1\ n\text{-BuLi, THF}} \quad \text{LiC} \equiv \text{CC} \equiv \text{CSiMe}_3 \xrightarrow{E}$$

$$\text{2e}$$

$$\text{EC} \equiv \text{CC} \equiv \text{CSiMe}_3$$

$$\text{4a-c}$$

conditions, reaction of **2e** with propanal as the electrophile furnished the diynol **4b** (E = C$_2$H$_5$CHOH: ^{1}H NMR (CCl$_4$) δ 0.10 (s, 9 H), 0.8–1.0 (t, J = 7 Hz, 3 H), 1.4–1.8 (m, 2 H), 1.85 (br s, 1 H), 4.20 (t, J = 7 Hz, 1 H)]. Diynols of this type serve as valuable precursors for the preparation of enyne allylic alcohols.[17]

From the preliminary results reported herein it is evident that lithiation of the commercially available methoxy enyne **1a** and its trimethylsilyl derivative **2a** provides a convenient access to the nucleophilic butadiyne synthons 1,4-bis(trimethylsilyl)-1,3-butadiyne (**1d**) and 4-lithio-1-(trimethylsilyl)butadiyne (**2e**) as well as to the potential nucleophilic aldehyde equivalent **2c**. Clearly these intermediates should have considerable value as synthons

for a wide variety of transformations, and many extensions of this work can be envisioned.

Reactivity of Dioxygen with Group 4 Alkoxy Alkyls: Epoxidation via Metal–Alkyl-Mediated Oxygen Atom Transfer

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Controlling and understanding the complex reactivity of dioxygen with homogeneous organotransition-metal species is a demanding task. The activations of O$_2$[1] in homogeneous[2] and heterogeneous[3] oxidation processes, as well as in biological systems,[4] manifest the importance of investigating the reactions of this small molecule. Although considered an anathema in many organometallic transformations, dioxygen has recently been shown to exhibit some striking chemistry. Radical-based oxidative additions of alkyl halides to Pt(II) yield alkylperoxo species when O$_2$ is present[5] and peroxymetallacycles of the type $\overline{\text{MOOCH}(\text{R})\text{CH}(\text{R})}$ have been generated.[6,7] Although the insertion of dioxygen into main-group[8] as well as transition-metal alkyls[9] has been noted, few studies[10] of this fundamental transformation exist. Reported herein are examples of O$_2$ insertions into group 4 metal–alkyl bonds, facile bimolecular methyl for methoxy exchange reactions,[11] and evidence that an M–R bond mediates an oxygen atom transfer from dioxygen.

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(11) It is conceivable that the ethynyl carbon–SiMe$_3$ bond in **3** may be elaborated into a variety of derivatives, thus providing an entry into the hitherto not readily accessible (E)-1-methoxy-1-buten-3-yne systems.[12]

(12) (E)-1-Methoxybutenynes have been isolated from E–Z mixtures by sequential fractional distillation and gas chromatographic purification. Winter, M. *Helv. Chim. Acta* **1963**, *46*, 1754.

(13) The assignment of the E sterochemistry to **3b** was based on the absence of a nuclear Overhauser effect (NOE) between the CH$_3$ and the vinylic hydrogen.

(14) The compound should be stored at low temperature since it slowly decomposes when kept at room temperature.

(15) We have not established whether the organolithium reagent **2b** or **2c** is the actual precursor of **2e**. For pertinent examples of β-eliminations involving simple metalated vinyl ethers, see ref 3 and 9.

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