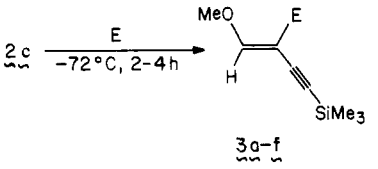
here preliminary studies of its reaction with various electrophiles "E" and its conversion into 4-lithio-1-(trimethylsilyl)butadiyne (**2e**), a nucleophilic butadiyne equivalent.

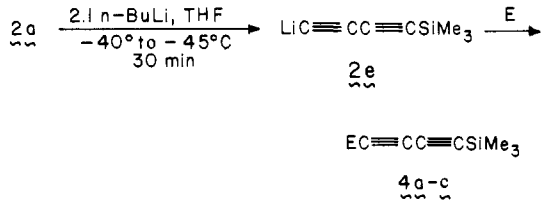
Treatment of the lithium reagent **2c** in DME at -72 °C with methanol furnished the (**E**)-methoxy enyne **3a** [E = H; ^{1}H NMR



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-butyllitium (21 mmol) in n-hexane followed by Me_3SiCl (21 mmol)[5] yielded 80% of the bissilylated butadiyne **4c** (E = $SiMe_3$). Under similar



conditions, reaction of **2e** with propanal as the electrophile furnished the diynol **4b** (E = C_2H_5CHOH: ^{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.

Acknowledgment. We are grateful to the National Science Foundation for supporting this research and to Frank Bobe for carrying out the NOE experiments.

Registry No. 1a, 3685-19-6; **1d**, 4526-07-2; **2a**, 93782-17-3; **2b**, 94203-37-9; **2c**, 94203-38-0; **2d**, 94203-39-1; **2e**, 73084-25-0; **3a**, 94203-40-4; **3b**, 94203-41-5; **3c**, 94203-42-6; **3d**, 94203-43-7; **3e**, 94203-44-8; **3f**, 94203-45-9; **4a**, 4526-06-1; **4b**, 94203-46-0; CH_3OH, 67-56-1; CH_3I, 74-88-4; n-C_4H_9I, 542-69-8; $(CH_3)_2C{=}CHCH_2Br$, 870-63-3; C_2H_5CHO, 123-38-6; $(CH_3)_2CO$, 67-64-1; HCl, 7647-01-0; Me_3SiCl, 75-77-4.

Supplementary Material Available: IR, ^{1}H NMR, and boiling or melting points of **1a**, **2a**, **3a-g**, and **4a-c** (2 pages). Ordering information is given on any current masthead page.

(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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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 $\overline{O_2}$ is present[5] and peroxymetallacycles of the type $\overline{MOOCH(R)CH(R)}$ 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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Table I. Comparative ^1H and $^{13}C\{^1H\}$ NMR Data (C_6D_6) for $HOCMe_2\overline{CHCH_2O}$ and $(tritox)_2Zr(OMe)(OCMe_2\overline{CHCH_2O})$ (**12**)[a]

	OC	Me_2	CH	CH_2	other
			$^{13}C\{^1H\}$, δ[b]		
$HOCMe_2\overline{CHCH_2O}$	67.7	25.1, 27.2	58.7	43.8	
12	77.3	27.8, 28.2	58.8	44.8	33.5, 46.0, 96.0 (tritox), 60.1 (OMe)
			^1H, δ, J(Hz)[c]		
$HOCMe_2\overline{CHCH_2O}$		0.96, 1.06	2.49 (dd, ^3J_t = 2.7, ^3J_c = 3.9)	2.45 (dd, ^3J_t = 2.7, ^2J = 5.3); 2.21 (dd, ^3J_c = 3.9, ^2J = 5.3)	1.39 (OH)
12		1.24, 1.38	2.90 (dd, ^3J_t = 2.9, ^3J_c = 4.2)	2.52 (dd, ^3J_t = 2.9, ^2J = 4.8); 2.87 (dd, ^3J_c = 4.2, ^2J = 4.8)	1.42 (tritox), 3.90 (OMe)

[a] All resonances considered singlets unless otherwise noted (300 MHz). [b] Referenced to C_6D_6 at δ 128.0. [c] Referenced to Me_4Si.

Treatment of $(tritox)_2MMe_2$ (M = Ti, **1**; Zr, **2**;[12] tritox = $((CH_3)_3C)_3CO$)[13] with dry dioxygen afforded (>87%) the corresponding white, crystalline, methoxy complexes $(tritox)_2M(OMe)_2$ (M = Ti, **3**; Zr, **4**),[14] according to eq 1. In a similar

$$(tritox)_2MMe_2 + O_2 \rightarrow (tritox)_2M(OMe)_2 \quad (1)$$
1, M = Ti — **3**, M = Ti
2, M = Zr — **4**, M = Zr

fashion, stoichiometric additions of O_2 to $(tritox)TiMe_3$ (**5**)[12] resulted in the formation of three different crystalline methoxides in 70–95% isolated yields (eq 2): orange $(tritox)TiMe_2(OMe)$

$$(tritox)TiMe_3 + (n/2)O_2 \rightarrow (tritox)Ti(CH_3)_{3-n}(OCH_3)_n \quad (2)$$
5 — **6**, n = 1; **7**, n = 2; **8**, n = 3

(**6**), yellow $(tritox)TiMe(OMe)_2$ (**7**) and white $(tritox)Ti(OMe)_3$ (**8**).[15]

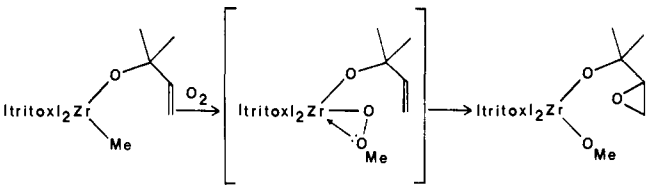
The observation that **5** incorporates only one oxygen atom of O_2 in the formation of $(tritox)TiMe_2(OMe)$ (**6**) implicated the existence of bimolecular methyl for methoxy exchange processes.[11] In accord with this proposal, **6** was formed quantitatively when equimolar amounts of **5** and **7** were mixed. Likewise, **6** and **8** conproportionate to form **7**, and **5** and **8** proceed to generate an approximate 1:1 mixture of **6** and **7**. Upon monitoring the reaction of $(tritox)TiMe_3$ (**5**) with $^1/_2O_2$ at −78 °C (via ^1H NMR and color changes), **7** was observed to form initially; a subsequent conproportionation with unreacted **5** resulted in the conversion to $(tritox)TiMe_2(OMe)$ (**6**).

The O–O bond is severed in each of the insertion processes above. Although the nature of the initial insertion step has not been established, a plausible intermediate common to all of the transformations is a methylperoxy methyl ($M(\eta^2$-OOMe)Me) species.[10,16] Subsequent transfer of an oxygen atom[17,18] from the incipient methylperoxy linkage to a neighboring methyl provides the means by which the methoxy ligands are formed. Analogous bimolecular processes, such as those observed by Schwartz[10] ($Cp_2ZrCl(R) + {}^1/_2O_2 \rightarrow Cp_2ZrCl(OR)$), cannot be ruled out. In order to demonstrate the feasibility of this purported η^2-methylperoxy intermediate, a substrate capable of accepting an oxygen atom other than a nearby M–R was sought. Since the coordination sphere of these species is similar to intermediates in Sharpless' Ti-catalyzed epoxidation,[19,20] $(tritox)_2ZrMe(OCMe_2CH{=}CH_2)$ (**10**) was prepared from the O_2-stable chloride, **9** (eq 3).[21] When **10** was exposed to excess dioxygen, the

$$(tritox)_2ZrCl(OCMe_2CH{=}CH_2) \xrightarrow[-LiCl]{MeLi} (tritox)_2ZrMe(OCMe_2CH{=}CH_2) \quad (3)$$
9 — **10**

epoxy alkoxide complex $(tritox)_2Zr(OMe)(OCMe_2\overline{CHCH_2O})$ (**12**) was obtained (16 h, 25 °C) as a colorless oil in >90% yield (Scheme I). Although **12** decomposes over a period of days,[22] the spectral data obtained show characteristic epoxide resonances (^{13}C and ^1H NMR compared to $HOCMe_2\overline{CHCH_2O}$,[23] Table I) that clearly corroborate its formulation. From the ^{13}C NMR data, it appears that the epoxide oxygen of **12** is not directly bound to the zirconium, yet substantial chemical shift differences (with respect to parent epoxy alcohol) are observed in the ^1H NMR.

Scheme I



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(14) Anal. Calcd for **3**, $TiO_4C_{28}H_{60}$: C, 66.11; H, 11.89. Found: C, 66.25; H, 11.87. ^1H NMR (C_6D_6) δ 1.46 (s, tritox, 54 H), 4.02 (s, $(OCH_3)_2$, 6 H). Anal. Calcd for **4**, $ZrO_4C_{28}H_{60}$: C, 60.92; H, 10.96. Found: C, 60.84; H, 10.83. ^1H NMR (C_6D_6) δ 1.41 (s, tritox, 54 H), 3.84 (s, $(OCH_3)_2$, 6 H).

(15) Anal. Calcd for **6**, $TiO_2C_{16}H_{36}$: C, 62.32; H, 11.77. Found: C, 62.20; H, *Found*: C, 62.20; H, 11.63. M_r found: 316 (calcd 308). ^1H NMR (C_6D_6) δ 1.35 (s, tritox, 27 H), 1.08 (s, $(CH_3)_2$, 6 H), 4.06 (s, OCH_3, 3 H). Anal. Calcd for **7**, $TiO_3C_{16}H_{36}$: C, 59.25; H, 11.19. Found: C, 59.39; H, 11.05. ^1H NMR (C_6D_6) δ 1.44 (s, tritox, 27 H), 1.08 (s, CH_3, 3H), 4.12 (s, $(OCH_3)_2$, 6 H). Anal. Calcd for **8**, $TiO_4C_{16}H_{36}$: C, 56.46; H, 10.66. Found: C, 56.64; H, 10.78. ^1H NMR (C_6D_6) δ 1.46 (s, tritox, 27 H), 4.13 (s, $(OCH_3)_3$, 9 H).

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(21) Addition of $LiOCMe_2CH{=}CH_2$ to $(tritox)_2ZrCl_2$[12] produced **9** (88%). Anal. Calcd for **9**, $ZrClO_3C_{31}H_{63}$: C, 60.99; H, 10.40; Cl, 5.81. Found: C, 60.76; H, 10.28; Cl, 5.65. ^1H NMR (C_6D_6) δ 1.39 (s, tritox, $(CH_3)_2$, 60 H), 5.97 (dd, —CH=, 1 H, ^3J = 17, 11 Hz), 5.06 (dd, =C*H*H, 1 H, ^3J = 17 Hz, ^2J < 1.5 Hz), 4.83 (dd, =CH*H*, 1 H, ^3J = 11 Hz, ^2J < 1.5 Hz). Anal. Calcd for **10** (77% yield), $ZrO_3C_{32}H_{66}$: C, 65.13; H, 11.27. Found: C, 63.47; H, 10.57. ^1H NMR (C_6D_6) δ 1.38 (s, tritox, 54 H), 0.71 (s, $ZrCH_3$, 3 H), 1.40 (s, $(CH_3)_2$, 6 H), 6.02 (dd, —CH=, 1 H, ^3J = 17.5, 10.5 Hz), 5.07 (dd, =C*H*H, 1 H, ^3J = 17.5 Hz, ^2J = 1.2 Hz), 4.84 (dd, =CH*H*, 1 H, ^3J = 10.5 Hz, ^2J = 1.2 Hz); $^{13}C\{^1H\}$ NMR (C_6D_6) δ 33.5, 45.8, 97.2(tritox), 27.3 ($ZrCH_3$), 80.5 ($OC(CH_3)_2$), 31.2 (CH_3)$_2$, 147.1 (—CH=), 110.3 (=CH_2). The ^{13}C NMR indicated that less than 1.5% tritox containing impurities were present.

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When subjected to H_2O, the epoxy alcohol and (tritox)H are cleaved from the zirconium; the cleaved material was correlated with authentic $HOCMe_2\overline{CHCH_2O}$[23]via ^1H NMR (300 MHz) and capillary GC.

The observations above complement the proposed mechanism[20] for Sharpless' epoxidation procedure.[19] The presumed transient methylperoxy species $(tritox)_2Zr(\eta^2\text{-}OOMe)(OCMe_2CH{=}CH_2)$ (**11**) as well as the zirconium alkoxy epoxide complex **12** models intermediates in the Ti-catalyzed process. Since the epoxidation above was carried out under rigorously anhydrous conditions, the premise that a $Ti(\eta^2\text{-}OO\text{-}t\text{-}Bu)$ and *not* a bound *t*-BuOOH species is responsible for the O-atom transfer step in the Sharpless system is further substantiated. The facile dioxygen insertion reactions are of potential relevance to heterogeneous oxidation processes; the results suggest that surface alkyls may react directly with O_2, thus obviating the need for dissociative absorption of dioxygen.[24] Attempts to observe M-OOR complexes from the treatment of other $(tritox)_2(R'O)MR$[25] species with O_2, further exploitation of the oxygen transfer mediation by early metal-alkyls, and mechanistic studies of the insertion and exchange processes are currently under way.

Acknowledgment. Support from the Research Corporation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, the National Science Foundation (CHE-8308272), and Cornell University is gratefully acknowledged. We thank the National Science Foundation Instrumentation Program (CHE-7904825, PCM-8018643) for support of the Cornell Nuclear Magnetic Resonance Facility.

Registry No. 1, 89958-92-9; **2**, 89958-91-8; **3**, 94136-93-3; **4**, 94136-94-4; **5**, 89958-93-0; **6**, 94136-95-5; **7**, 94136-96-6; **8**, 94136-97-7; **9**, 94136-98-8; **10**, 94136-99-9; **12**, 94137-00-5; $HOCMe_2\overline{CHCH_2O}$, 19482-44-1; $LiOCMe_2CH{=}CH_2$, 94137-01-6; $(tritox)ZrCl_2$, 94137-02-7; O_2, 7782-44-7.

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Cytidine-5′-triphosphate Synthetase Catalyzes the Phosphorylation of Uridine 5′-Triphosphate by Adenosine 5′-Triphosphate

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Cytidine-5′-triphosphate (CTP) synthetase from *Escherichia coli* catalyzes the following irreversible reaction:[1,2]

$$UTP + ATP + NH_3 \xrightarrow{Mg^{2+}} ADP + P_i + CTP$$

(1) Abbreviations: ADP, adenosine 5′-diphosphate; ATP, adenosine 5′-triphosphate; UTP, uridine 5′-triphosphate; CTP, cytidine 5′-triphosphate; EDTA, ethylenediaminetetraacetic acid; Tris, tris(hydroxymethyl)aminomethane; Hepes, *N*-(2-hydroxyethyl)piperazine-*N*′-2-ethanesulfonic acid; PIX, positional isotope exchange; ●, ^{18}O.
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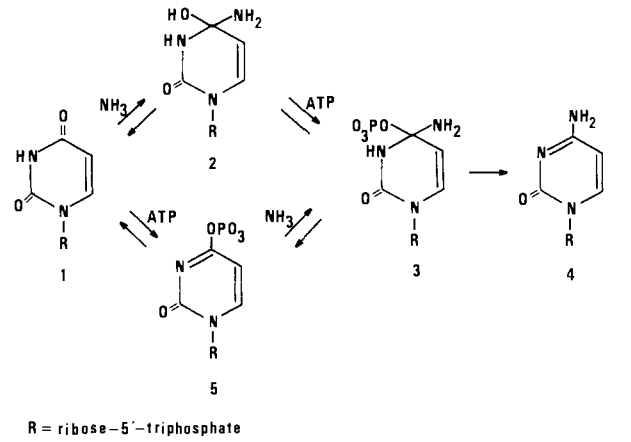
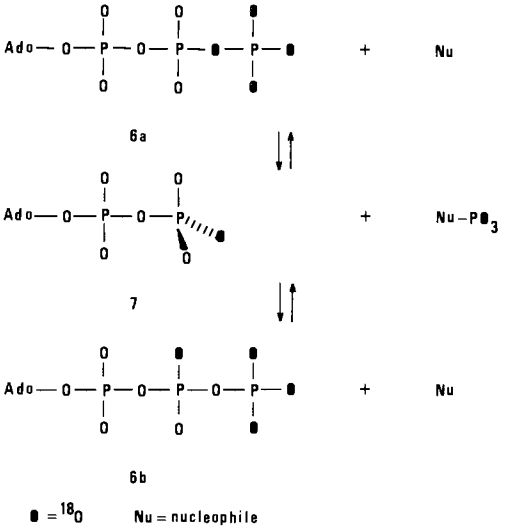
Scheme I



Scheme II



The lack of ATP/ADP exchange leads to the conclusion that ammonia attacks UTP (**1**) to form the carbinol amine **2**, which is then phosphorylated by ATP. Subsequent release of phosphate from **3** yields CTP (**4**) (Scheme I, upper pathway).[2b] We present evidence that CTP synthetase catalyzes the direct phosphorylation of UTP by ATP in the absence of ammonia (Scheme I, lower pathway).

One reason for the failure to observe ATP/ADP exchange could be that the catalytic reaction follows an ordered mechanism, in which the products (including ADP) are released only after the addition of all substrates (including ammonia). Therefore, we designed a positional isotope exchange (PIX) experiment to answer the question of whether ATP phosphorylates UTP (**1**). This experiment has an advantage over ATP/ADP-exchange experiments in that exchange of ADP between enzyme and solution is not necessary. The strategy for the PIX experiment is as follows.

During the catalytic reaction of CTP synthetase, ATP is cleaved between the β-γ-bridge oxygen atom and the γ-phosphorus atom. The nucleophile accepting the phosphate group might either be the enzyme, UTP (**1**), or the carbinol amine **2**. Cleavage in the absence of UTP and ammonia would provide evidence that a group on the enzyme becomes phosphorylated, whereas cleavage in the presence of UTP and absence of ammonia would likely result from the phosphorylation of UTP (Scheme I, lower pathway). For these experiments $[\gamma\text{-}^{18}O_4]ATP$ (**6a**) is used and in each case leads to $[\beta\text{-}^{18}O]ADP$ (**7**). If the terminal phosphate group of **7** rotates fast, the ^{16}O and ^{18}O atoms have equal probability to attack the phosphorylated intermediate in the back reaction to reform ATP and UTP. The result is that $[\beta\text{-}^{18}O,\gamma\text{-}^{18}O_3]ATP$ (**6b**) is produced (Scheme II). The relative amounts of the labeled ATP molecules **6** are conveniently determined by NMR spectroscopy owing to the influence of ^{18}O on the chemical shifts of the ^{31}P nucleus.[3]

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