copherol and linoleoylperoxy radical within the micelle might be unfavorable. However, since there is no significant variation in k_{inh} for the C_1–C_{10} hydrocarbon esters of Trolox, which presumably will have very different solubilization sites if this argument operates, this feature is considered unimportant. The alternative, which we prefer, is that diffusion of the highly lipophilic phenols, e.g., tocopherol, between micelles may be so slow as to limit the scavenging process. The most potent phenols in Table I suppress autoxidation to around 10% of its uninhibited rate at a ratio of phenol molecules to micelles of 1:100. For the phenol to protect ca. 100 micelles so effectively, its intermicellar diffusion (i.e., the frequency with which it "visits" each micelle) must be rapid compared to the lifetime of a linoleoylperoxy radical.[16,17]

In a similar case where the rate of a bimolecular free-radical process was retarded by entrainment within SDS micelles, the rate constant for exit of mesitylthiyl radicals from SDS was estimated at 2×10^3 s^{-1}.[18] The more hydrophobic α-tocopherol should exit more slowly,[19] although the degree of acceleration provided by its amphipathic nature[20] is unclear. We estimate the pseudo-first-order rate constant ($=k_p$[LH]) for the propagation reaction of LOO$^\bullet$ (eq 1) to be 75 s^{-1} in our system, so exit rates of this order, with 100 micelles to be visited, would be rate-limiting. Where exit from the micelle is a rate-controlling step, eq 4 is inapplicable without modification.

Thus, it seems that the hydrophobic phytyl tail of α-tocopherol, apparently chosen by nature to *retain* vitamin E in biomembranes,[21] inhibits intermicellar transfer. In this behavior, micelles can be compared to liposomes where, for example,[22] α-tocopherol has been found to be reluctant to exchange among phosphatidylcholine liposomes—in contrast to analogues that lack the phytyl tail and exchange freely. A requirement for facile diffusion may be one reason why small and relatively polar phenols are often superior to α-tocopherol as food antioxidants.[23,24] We may also be witnessing the onset of such behavior in the series of Trolox esters studied. Values of k_{inh} are fairly constant for the C_1–C_{10} hydrocarbon esters but the highly hydrophobic $C_7F_{15}CH_2$ compound (Table I) is appreciably less effective. We believe that this is due to a hydrophobic effect rather than to steric or electronic effects.

Our uninhibited reactions obey eq 3 in that oxygen uptake is first order in linoleic acid (0.95), half-order in initiator (0.60), and reciprocal three-halves order in micellised SDS (−1.53). Bimolecular termination therefore operates and, since the chance that two autoxidation chains initiate in the same micelle is essentially nil,[25] this is evidence that linoleoylperoxy radicals diffuse freely from one micelle to another.[26] For extremely hydrophobic antioxidants such as α-tocopherol, it is probably the diffusion of the chain-carrying peroxy radical to the phenol rather than the reverse that provides the (rate-limiting) mechanism for encounter and consequent scavenging.[27]

Acknowledgment. We thank the Ministry of Agriculture, Fisheries, and Food for a grant, and the referees for invaluable comments.

Registry No. SDS, 151-21-3; BHT, 128-37-0; BHA, 121-00-6; LOO$^\bullet$, 86683-30-9; linoleic acid, 60-33-3; 2-*tert*-butylphenol, 88-18-6; 2,5-di-*tert*-butyl-4-methoxyphenol, 1991-52-2; α-tocopherol, 59-02-9; trolox, 56305-04-5; phenol, 108-95-2; di-*tert*-butyl hyponitrite, 14976-54-6; trolox methyl ester, 86646-83-5; trolox ethyl ester, 103960-43-6; trolox butyl ester, 103960-44-7; trolox octyl ester, 103960-45-8; trolox (perfluoroheptyl)methyl ester, 103960-46-9; trolox decyl ester, 103960-47-0.

(14) Estimates of k_{inh} for α-tocopherol in homogeneous solution include 3.2×10^6 M^{-1} s^{-1} (polystyrylperoxy in PhCl)[11] and 5.1×10^5 M^{-1} s^{-1} (methyl linoleoylperoxy in *t*-BuOH: Niki, E.; Saito, T.; Kawakami, A.; Kamiya, Y. *J. Biol. Chem.* **1984**, *259*, 4177-4182).

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(24) Poor antioxidant activity of α-tocopherol in aqueous dispersions with a water-soluble initiator has been noted previously.[4]

(25) The initiator[3] partitions almost entirely into the aqueous phase (method of ref 7).

(26) Another indication that each autoxidation chain is not confined within any single micelle is that at low initiation rates, chain lengths in excess of 70 were seen whereas each micelle contains only about 17 linoleic acid molecules.

(27) The exit rate of amphiphilic molecules from their micelles is strongly dependent on their chain length.[20] The value for hexadodecyl sulfate has been estimated at 6×10^4 s^{-1} and the exit rate for linoleate anion from SDS might be expected to be similar.

Carbon Monoxide Cleavage by (silox)$_3$Ta (silox = *t*-Bu$_3$SiO$^-$)

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The initial step in the Fischer–Tropsch (F–T)[1] process is thought to be the dissociative adsorption of CO to provide surface oxide and carbide.[2] The latter surface species are modeled[3] by late metal, carbonyl cluster carbides,[4] whose formation is often accompanied by the release of CO_2 ($2CO \rightarrow$ carbide + CO_2). Although carbonylation of metal alkyls[5] and hydrides[6] has resulted in CO cleavage, existing early metal carbides[7] have not been prepared by direct scission of the carbon–oxygen bond. With CO coupling promoted by low-valent early metal centers providing

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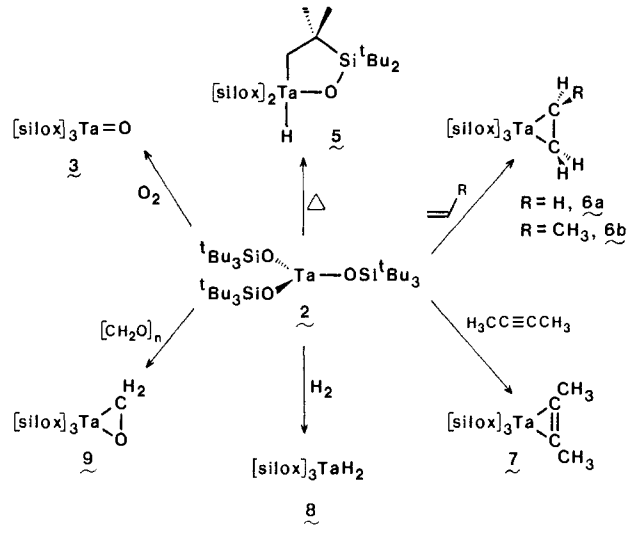
0002-7863/86/1508-6382$01.50/0

Scheme I



precedence,[8] the utilization of a highly reduced, oxophilic metal center proved to be crucial in effecting CO cleavage.

Reduction of (silox)$_3$TaCl$_2$ (**1**,[9,10] silox = *t*-Bu$_3$SiO$^-$)[11] with excess Na/Hg in THF afforded pale blue (silox)$_3$Ta (**2**, 60%)[12] after crystallization from hexane (eq 1). Treatment of **2** in

$$(\text{silox})_3\text{TaCl}_2 \xrightarrow[-2\text{NaCl, THF}]{\text{Na/Hg}} (\text{silox})_3\text{Ta} \qquad (1)$$
1 **2**

benzene solution (25 °C) with 1.00 equiv of carbon monoxide resulted in the uptake of 0.47 CO to provide an approximate 2:1 mixture of (silox)$_3$Ta=O (**3**, 47%)[13] and a sparingly soluble, brick red powder, formulated as [(silox)$_3$Ta]$_2$(μ-C$_2$) (**4**, 46% based on Ta, eq 2). Crystallization from hot THF afforded analytically

$$2(\text{silox})_3\text{Ta} + \text{CO} \rightarrow (\text{silox})_3\text{Ta}{=}\text{O} + {}^1/_2[(\text{silox})_3\text{Ta}]_2(\mu\text{-C}_2) \qquad (2)$$
2 **3** **4**

pure, deep-red **4**.[14] Colorless crystals of the oxo derivative **3** were also obtained upon oxygenation of **2** (43%, Scheme I). ^{1}H NMR spectra of H$_2$O-quenched THF slurries of **4** revealed the presence of ethylene and (silox)H. IR spectra of **4** derived from either CO or C^{18}O exhibited a band at 709 cm^{-1} in addition to absorptions attributable to silox. When ^{13}CO was the substrate, the band shifted to 682 cm^{-1}; from a 1:1 mixture of CO and ^{13}CO, bands at 709, 695 and 682 cm^{-1} were obtained in a ~1:2:1 ratio, consistent with a dicarbide (μ-C$_2$) bridge. The IR band may be assigned as either a Ta=C stretch or TaCCTa rocking vibration.

A single-crystal X-ray investigation of [(silox)$_3$Ta]$_2$(μ-C$_2$) (**4**) confirmed the proposed structure. The molecular core of **4** displayed in Figure 1 is the result of a preliminary refinement ($P\bar{1}$, $Z = 1$, $R = 0.107$).[15] The staggered silox ligands of the pseudo-Td

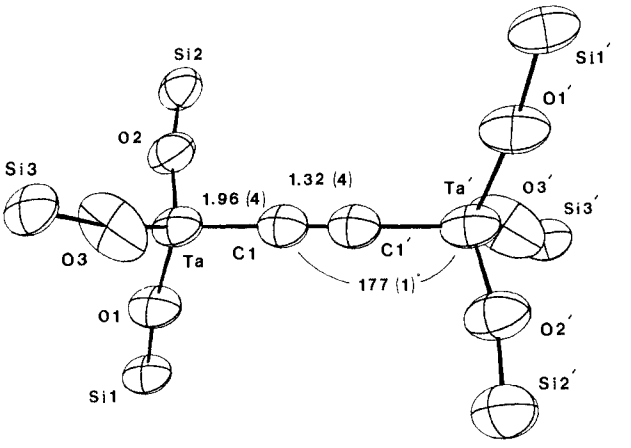


Figure 1. Skeletal view (50% probability ellipsoids) of [(silox)$_3$Ta]$_2$(μ-C$_2$) (**4**). Average bond distances (Å): Ta–O, 1.878 (9); Si–O, 1.68 (3). Average bond angles (deg): O–Ta–O, 111 (5); O–Ta–C, 108 (2); Ta–O–Si, 170 (3).

Ta centers and near-linear Ta–C–C angle (177 (1)°) impart approximate D_{3d} symmetry to the dicarbide (**4**). The 1.32 (4) Å C–C distance is near that of a typical double bond (1.34 Å) and the 1.96 (4) Å Ta–C bond length is similar to known Ta alkylidenes (1.89–2.07 Å).[16] Best described as (silox)$_3$Ta=C=C=Ta(silox)$_3$, **4** possesses π-type molecular orbitals (D_{3d}), consisting of a fully occupied e_u^4 set mostly C–C π^b in character and a half-populated e_g^2 HOMO that is Ta–C localized (π^b), yet partially C–C π^*.[17] The resultant $^3A_{2g}$ ground state of **4** provides a rationale for its unusual chemical shifts,[14] the unobserved (^{13}C NMR) dicarbide signals of [(silox)$_3$Ta]$_2$(μ-^{13}C$_2$) (**4**-^{13}C), and its paramagnetism (μ = 3.0 μ_B, Faraday balance).

Scheme I illustrates various crystalline derivatives of (silox)$_3$Ta (**2**), thus providing a clear indication of its potential reactivity. Cyclometalation[18] to colorless (silox)$_2$(H)TaOSi(*t*-Bu)$_2$CMe$_2$CH$_2$ (**5**) occurs in both solution (benzene, $t_{1/2}$ ~ 90 h, 25 °C) and solid state (84%).[19] Ethylene and propylene react rapidly at 25 °C to form monoolefin species (silox)$_3$Ta(η^2-C$_2$H$_3$R) (**6a**, R = H, yellow-orange, 63%; **6b**, R = Me, orange-red, 56%),[20] while 2-butyne more slowly ($t_{1/2}$ ~ 90 h, 25 °C) generates a colorless alkyne adduct, (silox)$_3$Ta(η^2-C$_2$Me$_2$) (**7**, 38%).[21] Exposure of

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(12) **2**: ^{1}H NMR (C$_6$D$_6$) δ 1.33; ^{13}C{^{1}H} NMR δ 31.75 (CH$_3$), 22.83 (SiC); ^{29}Si{^{1}H} NMR δ 18.63; M_r found 850, calcd 826.

(13) Anal. Calcd for **3**, TaSi$_3$O$_4$C$_{36}$H$_{81}$: C, 51.28; H, 9.68. Found: C, 51.13; H, 9.52. ^{1}H NMR (C$_6$D$_6$) δ 1.28; ^{13}C{^{1}H} NMR δ 30.54 (CH$_3$), 23.71 (SiC); IR (Nujol) ν(Ta=O) = 905 cm^{-1}; M_r found 800, calcd 842.

(14) Anal. Calcd for **4**, TaSi$_3$O$_3$C$_{37}$H$_{81}$: C, 52.95; H, 9.73. Found: C, 52.73; H, 9.58. The following spectral assignments are tentative due to the possibility that trace soluble impurities in highly insoluble **4** may be responsible: ^{1}H NMR (C$_6$D$_6$) δ 2.03; (THF-d_8) 1.88; ^{13}C{^{1}H} NMR (THF-d_8, 40 °C) δ 53.45 (SiC), 44.50 (CH$_3$), μ-^{13}C$_2$ not located; IR (Nujol) (μ-C$_2$) 709 cm^{-1}, (μ-C^{13}C) 695, (μ-^{13}C$_2$) 682.

(15) Dicarbide **4** crystallized in the triclinic system (a = 13.444 (6) Å, b = 13.028 (4) Å, c = 16.149 (6) Å, α = 69.13 (3)°, β = 87.57 (3)°, and γ = 120.03 (3)°). A total of 5981 unique reflections (sin $\theta/\lambda < 0.54$ Å^{-1}, Cu Kα) were measured and 4446 (74%) were judged observed ($|F_o| > 3\sigma(F_o)$). Intensity statistics and successful refinement indicated that the correct space group was $P\bar{1}$ centrosymmetric, $Z = 1$). A residual of 0.094 was obtained but the peripheral Me groups were in unsatisfactory positions. From CRYSTALS, the *t*-Bu groups were constrained and refinement resulted in an R of 0.107; the core of the molecule remained the same. Full details including the latest efforts at modeling this complicated disorder will be reported in the full paper.

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(19) Anal. Calcd for **5**, TaSi$_3$O$_3$C$_{36}$H$_{81}$: C, 52.27; H, 9.87. Found: C, 52.11; H, 9.72. ^{1}H NMR (C$_6$D$_6$) δ 1.27 (s, silox-CH$_3$, 54 H), 1.29 (s, *t*-Bu$_2$, 18 H), 1.37 (s, C(CH$_3$)$_2$, 6 H), 1.89 (s (br), CH$_2$, 2 H), 21.97 (s, TaH, 1 H); ^{13}C{^{1}H} NMR δ 97.04 (CH$_2$), 39.80 (C(*C*H$_3$)$_2$), 33.61 (Si(C(*C*H$_3$)$_3$)$_2$), 30.73 (silox-CH$_3$), 24.93 (*C*(CH$_3$)$_2$), 23.61 (silox-C), 23.52 (Si(*C*(CH$_3$)$_3$)$_2$); ^{29}Si{^{1}H} NMR δ 16.37 (silox), 20.43 (OSi-*t*-Bu$_2$C(CH$_3$)$_2$CH$_2$); IR (Nujol) ν(Ta-H) 1770 cm^{-1}.

(20) Anal. Calcd for **6a**, TaSi$_3$O$_3$C$_{38}$H$_{85}$: C, 53.36; H, 10.02. Found: C, 53.15; H, 9.88. ^{1}H NMR (C$_6$D$_6$) δ 1.23 (s, CH$_3$, 81 H), 2.32 (s, C$_2$H$_4$, 4 H); ^{13}C NMR δ 66.18 (t, C$_2$H$_4$, J_{CH} = 143 Hz), 30.68 (CH$_3$), 23.52 (SiC); M_r found 850, calcd 854. Anal. Calcd for **6b**, TaSi$_3$O$_3$C$_{39}$H$_{87}$: C, 53.88; H, 10.09. Found: C, 53.98; H, 10.02. ^{1}H NMR (C$_6$D$_6$) δ 1.25 (s, CH$_3$, 81H), 1.64 (dd, *t*-*H*HC=, 1 H, ^2J = 10 Hz, ^3J = 12 Hz), 2.30 (ddq, —HC=, 1 H, ^3J = 12, ^3J = 16, ^3J = 7 Hz), 2.73 (d, CH$_3$, 3 H, ^3J = 7 Hz), 2.99 (dd, H*H*$_c$C=, 1 H, ^2J = 10, ^3J = 16 Hz); ^{13}C{^{1}H} NMR δ 77.83, 73.39 (C=C), 30.68 (silox CH$_3$), 26.64 (CH$_3$), 23.47 (SiC). The yields of extremely soluble **6a,b** are >95% by ^{1}H NMR.

2 to dihydrogen and paraformaldehyde provides the previously prepared dihydride $(silox)_3TaH_2$ (**8**, >95%, ^1H NMR) and formaldehyde complex $(silox)_3Ta(\eta^2\text{-}CH_2O)$ (**9**, >95%, ^1H NMR),[10] respectively.

The potent reducing ability of $(silox)_3Ta$ (**2**) in combination with the stability of the $Ta(\mu\text{-}C_2)Ta$ bridge and Ta=O bond appears to mimic the surface properties responsible for the heterogeneous dissociation of CO. Further reactivity studies of **2**, mechanistic investigations pertaining to the formation of the dicarbide **4**, and detailed analyses of the latter will be reported in due course.

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(21) Anal. Calcd for **7**, $TaSi_3O_3C_{40}H_{87}$: C, 54.51; H, 9.95. Found: C, 54.50; H, 9.89. ^1H NMR (C_6D_6) δ 1.27 (s, silox, 81 H), 2.59 (s, $\equiv CCH_3$, 6 H); ^{13}C {^1H} NMR δ 30.68 (silox-CH_3), 23.37 (SiC), 22.05 ($\equiv CCH_3$), $H_3CC\equiv$ not observed.

Radical Cyclization–Trapping in the Synthesis of Natural Products. A Simple, Stereocontrolled Route to Prostaglandin $F_{2\alpha}$

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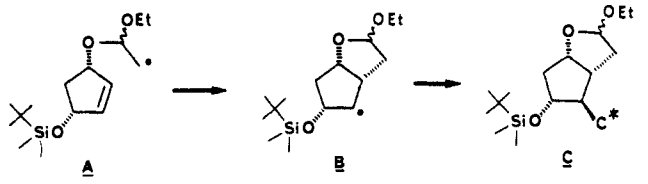
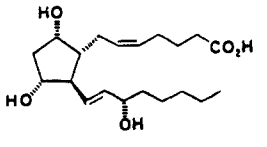
We report here an efficient synthesis of natural (+)-prostaglandin $F_{2\alpha}$ (**1**)[1] in which our recently described radical cyclization–trapping methodology[2] is utilized to add, in a single step, two differentiated carbon-functional appendages (precursors of the two side chains) to a preexisting cyclopentenediol nucleus. The two new carbon–carbon bonds are formed with virtually complete regio- and stereochemical control: The cyclization step (A → B) adds a potential acetaldehyde unit to the proximal end of the double bond and cis to the controlling allylic oxygen. Attachment of C* (B → C), the precursor of the unsaturated alcohol chain,



A B C



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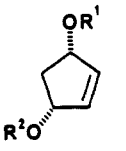
† W.H.O. visiting fellow from the Shanghai Institute of Planned Parenthood Research (1982–1983).

(1) For recent surveys of prostaglandin syntheses, see: Pike, J. E.; Morton, D. R. *Chemistry of Prostaglandins and Leukotrienes*; Raven Press: New York, 1985. Lai, S. M. F.; Manley, P. W. *Nat. Prod. Rep.* **1984**, *1*, 409. Roberts, S. M.; Scheinmann, F. *New Synthetic Routes to Prostaglandins and Thromboxanes*; Academic Press: New York, 1982.

(2) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.

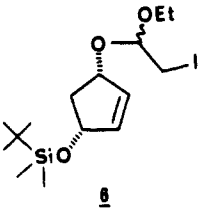
then takes place on the convex face of the bicyclic radical intermediate B. In this particular case, it is likely that the steric bulk of the silyloxy substituent magnifies the normal bias for convex face trapping.

Our synthesis began with cyclopentadiene, which is easily converted to *cis*-2-cyclopentene-1,4-diol (**2**) by photooxygenation–reduction.[3] The corresponding diacetate **3** (acetic anhydride, pyridine, methylene chloride, room temperature; 86%) is a convenient source of the (−)-monoacetate **4**.[4] Protecting group manipulation [(1) *tert*-butyldimethylsilyl chloride, imidazole, methylene chloride, room temperature; (2) potassium cyanide, ethanol, room temperature[5]] gave the monosilyl ether **5** in quantitative yield. The mixed iodoacetal **6**, necessary for radical cyclization–trapping, was obtained in 96% yield from **5** (ethyl vinyl ether, *N*-iodosuccinimide, methylene chloride, −20 °C).[2]

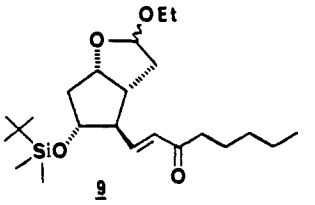


$R^1 = R^2 = H$ **2**
$R^1 = R^2 = Ac$ **3**
$R^1 = Ac, R^2 = H$ **4**
$R^1 = H, R^2 = Si(t\text{-}Bu)Me_2$ **5**

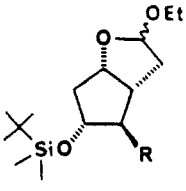
We now describe two sequences from **6** to **9** based on two different catalytic cyclization–trapping reactions. In the first



6



9



R = CN **7**
R = CHO **8**
$R = CH_2CH(TMS)C(=O)C_5H_{11}$ **10**
$R = CH_2CH{=}C(OTMS)C_5H_{11}$ **11**

of these, use of *tert*-butyl isocyanide as the radical trap[2,6] led to **7**, an obvious precursor of enone **9**. In the second sequence, simultaneous transfer of all eight carbons of the enone chain was achieved. We were intrigued by this approach because it required finding a solution to an important problem. Although vinyl ketones are suitable as traps in catalytic cyclization–trapping reactions,[2] use of 1-octen-3-one as the trap would yield a nearly symmetrical saturated ketone. Regiospecific introduction of a conjugated double bond into this ketone would not be simple. We show below that the use of an α-silyl-substituted vinyl ketone, 2-(trimethylsilyl)-1-octen-3-one, provided a solution to the problem.[7]

In the first route, which was carried out on a gram scale, the cyano compound **7** was obtained in 71% yield[8] from **6** (0.1 equiv

(3) Kaneko, C.; Sugimoto, A.; Tanaka, S. *Synthesis* **1974**, 876.

(4) Wang, Y.-F.; Chen, C.-S.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1984**, *106*, 3695. We thank Professor Sih for converting several grams of the diacetate **3** into the monoacetate **4** (97% ee). See also: Laumen, K.; Reimerdes, E. H.; Schneider, M. *Tetrahedron Lett.* **1985**, *26*, 407. Miura, S.; Kurozumi, S.; Toru, T.; Tanaka, T.; Kobayashi, M.; Matsubara, S.; Ichimoto, S. *Tetrahedron* **1976**, *32*, 1893.

(5) Mori, K.; Tominaga, M.; Takigawa, T.; Matsui, M. *Synthesis* **1973**, 790.

(6) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765.

(7) α-Silylated vinyl ketones had previously established their value in solving the problem of regiospecific annulation: Stork, G.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 6152. Boeckman, R. K., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 6179. Stork, G.; Singh, J. *J. Am. Chem. Soc.* **1974**, *96*, 6181. Boeckman, R. K., Jr.; Blum, D. M.; Ganem, B.; Halvey, N. *Org. Synth.* **1978**, *58*, 152. Boeckman, R. K., Jr.; Blum, D. M.; Ganem, B. *Org. Synth.* **1978**, *58*, 158.

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