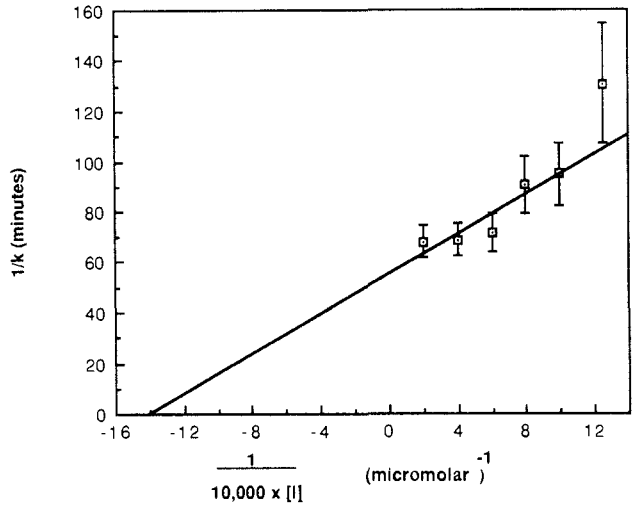

Figure 1. Lineweaver–Burk analysis of time-dependent kinetics with **4**.

Deprotection (K_2CO_3–CH_3OH room temperature) afforded **4**.[14]

At 1 mM concentration, aziridinyltriol **4** showed potent inhibition of green coffee bean α-galactosidase (Sigma; either pH 5 or pH 6.6), but had little or no effect on yeast α-glucosidase (pH 6.6), jackbean α-mannosidase (pH 5), or bovine β-galactosidase (pH 7). Detailed kinetic studies of *p*-nitrophenyl α-D-galactopyranoside hydrolysis at different inhibitor concentrations (pH 6.6) revealed time-dependent first-order inactivation of α-galactosidase.[15] A Lineweaver–Burk plot of $1/k$ vs $1/I$ (Figure 1) gave the dissociation constant of the noncovalent enz-**4** complex [$K_M = 7.1 \pm 2$ μM] as well as the first-order rate constant with which the complex was converted into inactivated enzyme [$k_{inact} = 1.8 \pm 0.51 \times 10^{-2}$ min^{-1}]. In the presence of competitive inhibitor **3**, the enzyme was protected against irreversible inactivation by **4**. Moreover, inactivated enzyme, when treated with 1 M NH_2OH[17] and then $FeCl_3$, gave rise to a strong absorbance at 510 nm characteristic of an enzyme–hydroxamic acid–iron(III) chelate. Controls using fresh enzyme with and without **3** showed no such absorbance, strongly suggesting that inactivation by **4** led to a new ester linkage. Judging from the apparent second-order rate constant for the association of free enzyme and inhibitor [$k_{inact}/K_M = 2540$ min^{-1} M^{-1}], aziridine **4** is, to our knowledge, the most potent and specific α-galactosidase inactivator yet reported.[18] These findings support the proposed orientation of proton-donating and nucleophilic groups at the α-galactosidase active site and may find application in the study of other carbohydrate-processing enzymes.

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(14) For **4**: ^{1}H NMR (300 MHz, D_2O) δ 4.53 (br t, H-5, $J = 5.2, 6.6$ Hz), 3.88 (dd, H-4, $J = 5.6, 6.6$ Hz), 3.77 (m, H-3), 3.09 (m, H-2α, 2β), 2.37 (q, H-6, $J = 5.7, 10.9$ Hz), 1.96 (d, H-7β, $J = 4.1$ Hz), 1.91 (d, H-7α, $J = 6.1$ Hz).

(15) All enzyme assays were conducted in triplicate at 37 °C in citrate–phosphate buffer with added KCl to a constant ionic strength of 0.5 M (ref 16). After interim exposure of enzyme to inhibitor at various concentrations, residual activity was measured by incubating the enzyme with substrate (5 mM) for 15 min in a final volume of 200 μL, the basifying to pH 10.4 and monitoring absorbance at 400 nm.

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(18) For conduritol C epoxide (ref 4a) $k_{inact}/K_M = 6.6$ min^{-1} M^{-1}; for α-D-galactopyranosylmethyl(*p*-nitrophenyl)triazine (ref 4b) $k_{inact}/K_M = 0.96$ min^{-1} M^{-1}.

Preparation of the First Stable Formylsilane, $(Me_3Si)_3SiCHO$, from a Zirconium η^2-Silaacyl Complex

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Despite intent interest in the chemistry and properties of acylsilane derivatives ($RCOSiR'_3$),[1] little has been reported regarding formylsilanes (R_3SiCHO). Early attempts to prepare formylsilanes led to the conclusion that they were unstable under a variety of reaction conditions.[1a,2] Hydrolysis of the ozonide adduct of vinyltrimethylsilane with zinc dust gave trimethylsilanol and formaldehyde, possibly via Me_3SiCHO.[2a] Speier attempted unsuccessfully to prepare Me_3SiCHO by treatment of $Me_3SiCHCl_2$ with potassium acetate and sodium ethoxide and by catalytic dehydrogenation of Me_3SiCH_2OH over copper metal at 260 °C. The latter reaction produced trimethylsilane and carbon monoxide, possible decomposition products of Me_3SiCHO.[2b] Reaction of triphenylsilyllithium with ethyl formate also failed to produce an isolable formylsilane, but Ph_3SiCHO was postulated as an intermediate.[1a] More recently, Ireland and Norbeck have obtained evidence for Me_3SiCHO, generated at low temperature by Swern oxidation of Me_3SiCH_2OH and trapped by reaction with a Wittig reagent.[1h]

A possible route to formylsilanes is suggested by the reported acidification of zirconium acyl derivatives $Cp_2Zr(\eta^2\text{-COR})Cl$ (Cp = η^5-C_5H_5) to produce aldehydes.[3] We have prepared a number of early transition-metal η^2-silaacyl complexes that are potential starting materials for such a synthesis.[4] Indeed, reaction of $Cp_2Zr(\eta^2\text{-COSiMe}_3)Cl$ with 1 equiv of HCl at low temperature generated a product that was identified by NMR spectroscopy as Me_3SiCHO. This species was not thermally stable, however, and decomposed to a number of products above −25 °C.[4d] To obtain a more stable formylsilane derivative, we sought a route to the more sterically hindered $(Me_3Si)_3SiCHO$. Unfortunately, the obvious precursor to this compound, $Cp_2Zr[\eta^2\text{-COSi}(SiMe_3)_3]Cl$, is not available via carbonylation of $Cp_2Zr[Si(SiMe_3)_3]Cl$.[4d] Here we report a successful preparation of an η^2-$COSi(SiMe_3)_3$ derivative of zirconium and its conversion to the first stable, isolable formylsilane $(Me_3Si)_3SiCHO$ (**3**).

The zirconium silyl $CpCp^*Zr[Si(SiMe_3)_3]Cl$ (**1**, $Cp^* = \eta^5$-C_5Me_5) is prepared from $CpCp^*ZrCl_2$[5] and $(THF)_3LiSi(SiMe_3)_3$[6] in benzene.[7] The silaacyl $CpCp^*Zr[\eta^2\text{-COSi}(SiMe_3)_3]Cl$ (**2**)[8] is obtained as pink crystals in 71% yield by reaction of **1** with

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(4) (a) Tilley, T. D. *J. Am. Chem. Soc.* **1985**, *107*, 4084. (b) Arnold, J.; Tilley, T. D. *J. Am. Chem. Soc.* **1985**, *107*, 6409. (c) Arnold, J.; Tilley, T. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1986**, *108*, 5355. (d) Campion, B. K.; Falk, J.; Tilley, T. D. *J. Am. Chem. Soc.* **1987**, *109*, 2049. (e) Arnold, J.; Tilley, T. D.; Rheingold, A. L.; Geib, S. J.; Arif, A. M., manuscript in preparation.

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(7) Elsner, F. H.; Tilley, T. D.; Rheingold, A. L.; Geib, S. J., manuscript in preparation.

(8) For **2**: IR (Nujol) ν(CO) = 1440 cm^{-1}; ^{1}H NMR (benzene-d_6, 22 °C, 300 MHz) δ 0.29 (s, 27 H, $SiMe_3$), 1.73 (s, 15 H, C_5Me_5), 5.70 (s, 5 H, C_5H_5); $^{13}C\{^1H\}$ NMR (benzene-d_6, 22 °C, 75.5 MHz) δ 1.98 ($SiMe_3$), 12.19 (C_5Me_5), 110.58 (C_5H_5), 117.26 (C_5Me_5), 382.79 (ZrCOSi). Anal. ($C_{25}H_{47}ClOSi_4Zr$) C, H.

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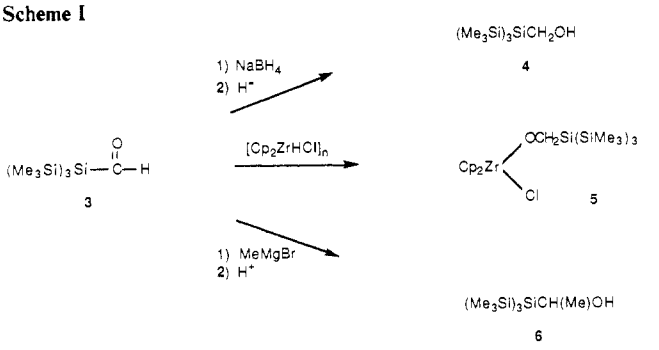
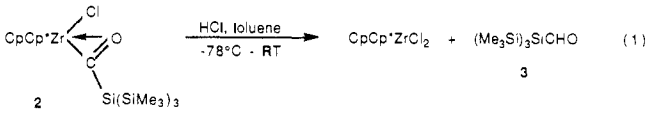
Scheme I



carbon monoxide (100 psi) in pentane. The carbonyl stretching frequency (1440 cm^{-1}) and the ^{13}C NMR shift of the carbonyl carbon for **2** are similar to corresponding values for $Cp_2Zr(\eta^2$-$COSiMe_3)Cl$.[4d] A possible explanation for the greater reactivity of **1** over $Cp_2Zr[Si(SiMe_3)_3]Cl$ toward carbon monoxide is that increased steric interactions about the metal center promote CO insertion in **1**. A similar effect has been observed for Cp_2Zr-$[CH(SiMe_3)_2]Me$, insertion of CO occurring exclusively into the more sterically hindered Zr–C bond.[9]

The formylsilane **3** was prepared by addition of anhydrous HCl gas (1 equiv) to a cold (−78 °C) toluene solution of **2** (0.60 g, 1 mmol), followed by warming to room temperature (eq 1).



(1)

Removal of volatiles under vacuum and extraction of the residue with pentane allowed separation of **3** from $CpCp^*ZrCl_2$, which was isolated in 90% yield. Pentane was removed from the resulting filtrate to afford reasonably pure **3** (≥95% by ^1H NMR) as a colorless oil in 55% yield. Compound **3** may be further purified by distillation under vacuum (70 °C, 10^{-2} mmHg, ca. 80% yield), but this is not necessary for most purposes. Low yields (20–30%) of **3** are also obtained, among other uncharacterized products, by reaction of ethyl formate and $(THF)_3LiSi(SiMe_3)_3$ in pentane at −78 °C (by ^1H NMR).

The ^1H NMR spectrum of **3** consists of singlets at δ 0.20 and 12.36 (benzene-d_6). Labeled [^{13}C]-**3**, prepared from $CpCp^*Zr$-$[\eta^2$-$^{13}COSi(SiMe_3)_3]Cl$ ([^{13}C]-**2**), gave a doublet at δ 12.36. The $^1J_{CH}$ coupling constant of 147 Hz for **3** is rather low for an aldehyde but is consistent with the expected substituent effect of the electropositive silyl group.[10] The carbonyl carbon of [^{13}C]-**3** was observed at δ 243.01 in the ^{13}C NMR spectrum, in the region expected for a $-COSi(SiMe_3)_3$ group.[1g] For comparison, $Me_3Si^{13}CHO$ exhibited a peak at δ 11.77 ($^1J_{CH}$ = 141 Hz) in its ^1H NMR spectrum and a ^{13}C NMR chemical shift at 248.9 ppm.[4d] In addition, ^{29}Si NMR resonances for **3** were observed at −74.68 ($(Me_3Si)_3SiCHO$) and −11.41 ($(Me_3Si)_3SiCHO$) ppm (benzene-d_6). The ν(CO) infrared stretching frequency for compound **3** (1633 cm^{-1}) is slightly higher than values found for acylsilanes $(Me_3Si)_3SiCOR$ (1613–1620 cm^{-1}),[1g] and the ν(CH) stretching frequency (2585 cm^{-1}) is unusually low for an aldehyde. The corresponding infrared stretches for $(Me_3Si)_3SiCDO$, prepared from **2** and DCl, were observed at 1625 and 1950 cm^{-1}, respectively. Mass spectral analysis of **3** using electron ionization techniques gave *m/z* fragments corresponding to M − Me^+ (261 *m/z*) and M − $SiMe_3^+$ (203 *m/z*) but no parent ion as was observed for some analogous acylsilanes.[1g]

Compound **3** decomposes instantly and exothermically upon exposure to air. This may account for the lack of success of some other, more standard attempts to prepare formylsilanes. Formylsilane **3** is thermally stable for weeks under nitrogen. At 100 °C in benzene-d_6, decomposition of **3** is first-order with a half-life of 53.3 h ($k = 3.61 \pm 0.06 \times 10^{-6}$ s^{-1}). A number of uncharacterized decomposition products were observed, including small amounts of $(Me_3Si)_3SiH$ (ca. 10–15%).

Some preliminary reactivity studies of **3** are shown in Scheme I. **3** is readily reduced by $NaBH_4$ to give the alcohol **4**[11] in 90% isolated yield. Reaction with $[Cp_2ZrHCl]_n$ forms zirconium alkoxide **5**[12] quantitatively (by ^1H NMR in benzene-d_6). Compound **5** was independently prepared in 92% isolated yield from $Cp_2ZrMeCl$[13] and **4**. Finally, alkylation of **3** with MeMgBr affords the alcohol **6**,[14] isolated in 89% yield by vacuum sublimation (100 °C, 10^{-2} mmHg).

Acknowledgement is made to the Air Force Office of Scientific Research, Air Force Systems Command, USAF, for support of this work under Grant no. AFOSR-85-0228.

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(12) For **5**: mp 145–147 °C; ^1H NMR (benzene-d_6, 22 °C, 300 MHz) δ 0.32 (s, 27 H, $SiMe_3$), 4.49 (s, 2 H, OCH_2Si), 6.00 (s, 10 H, C_5H_5); $^{13}C\{^1H\}$ NMR (benzene-d_6, 22 °C, 75.5 MHz) δ 1.39 ($SiMe_3$), 67.59 ($ZrOCH_2Si$), 113.38 (Cp); $^{29}Si\{^1H\}$ NMR (benzene-d_6, 22 °C, 59.6 MHz) δ −80.42 ($Si(SiMe_3)_3$), −12.97 ($Si(SiMe_3)_3$). Anal. ($C_{20}H_{39}ClOSi_4Zr$) C, H.

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(14) For **6**: IR (Nujol) ν(OH) = 3460 br; ^1H NMR (benzene-d_6, 22 °C, 300 MHz) δ 0.27 (s, 27 H, $SiMe_3$), 0.60 (br s, 1 H, OH), 1.31 (d, *J* = 7.2 Hz, 3 H, CH_3), 3.82 (q, *J* = 7.2 Hz, 1 H, SiCHO). Anal. ($C_{11}H_{32}OSi_4$) C, H.

Palladium-Mediated Biomimetic Synthesis of Narwedine

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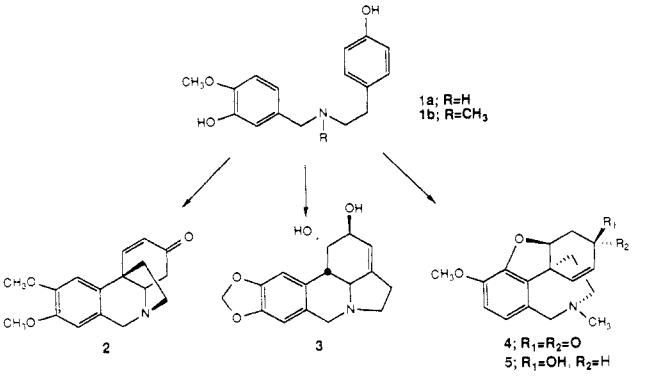
Oxidative phenolic coupling comprises the key step in the biosynthesis of a wide variety of natural products.[2] The three main structural types of the Amaryllidaceae alkaloids, represented by oxomaritidine (**2**), lycorine (**3**), and narwedine (**4**), are all formed in vivo by intramolecular phenolic coupling of norbelladine derivatives **1a** and **1b**.[3]



The first successful laboratory emulation of these processes was reported in 1962 by Barton and Kirby, who obtained narwedine

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