MHz) δ 2.42–2.61 (m, 3 H), 4.75 (m, 1 H), 5.01–5.20 (m, 2 H), 5.65–5.92 (m, 1 H), 7.00–7.42 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 43.00, 69.72, 118.61, 121.05, 126.00, 126.30, 134.63, 145.78; MS (70 eV, 250 °C) m/z 154 (M^+, 0.88), 137 (M – OH, 11.19), 113 (M – C_3H_5, 83.72), 85 (100), 45 (22.44); IR (neat) 3359 (s), 1635 (m) cm^{-1}.

(*S*)-1-(1-Methyl-2-pyrrolyl)-3-buten-1-ol (16): 78% yield; bp 82–84 °C (0.7 mm); $[\alpha]^{23}D$ = –12.1° (*c* 1.25, EtOH); ≥99% ee by capillary GC analysis; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.30 (m, 1 H), 2.56–2.70 (m, 2 H), 6.56 (m, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.97, 40.67, 65.85, 106.43, 106.77, 118.07, 123.33, 134.44, 135.29; MS (70 eV, 250 °C) m/z 151 (M^+, 4.77), 110 (M – C_3H_5, 100), 82 (M – C_3H_5 – H_2O, 64.28), 67 (22.53); IR (neat) 3386 (s), cm^{-1}. Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.74; H, 8.90; N, 9.19.

(*S*)-1-(2-Pyridyl)-3-buten-1-ol (17): 85% yield; bp 72 °C (0.4 mm) (lit.[14] bp 80 °C (0.1 mm)); $[\alpha]^{23}_D$ = –32.5° (*c* 3.5, EtOH); ≥99% ee by capillary GC analysis; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.35–2.86 (m, 2 H), 4.60–5.46 (m, 4 H), 5.67–6.05 (m, 1 H), 6.48 (m, 1 H), 7.01–7.90 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 42.83, 72.93, 118.04, 120.83, 122.60, 134.71, 137.08, 148.83, 162.86; MS (70 eV, 250 °C) m/z 150 (M + H, 4.62), 130 (M – H – H_2O, 9.84), 108 (M – C_3H_5, 100), 78 (55.43), 53 (16.77); IR (neat) 3306 (s), 1635 (m), 1591 (s), 1568 (m) cm^{-1}.

(*S*)-1-(3-Pyridyl)-3-buten-1-ol (18): 84% yield; bp 110 °C (0.8 mm) (lit.[14] bp 102 °C (0.1 mm)); $[\alpha]^{23}_D$ = –28.0° (*c* 1.03, EtOH); 96% ee by capillary GC analysis; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.42–2.66 (m, 2 H), 4.75 (m, 1 H), 4.95–5.30 (m, 3 H), 5.68–5.94 (m, 1 H), 7.20–7.35 (m, 1 H), 7.75 (m, 1 H), 8.30–8.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 43.79, 71.04, 118.54, 123.82, 134.40, 134.48, 140.72, 147.86, 148.43; MS (70 eV, 250 °C) m/z 150 (M + H, 100), 132 (M + H – OH, 4.51), 108 (M – C_3H_5, 18.80); IR (neat) 3219 (s) 1635 (m), 1588 (m), 1575 (m) cm^{-1}.

(*S*)-1-(4-Pyridyl)-3-buten-1-ol (19): 83% yield; bp 96 °C (0.8 mm) (lit.[14] bp 96 °C (0.1 mm)); $[\alpha]^{23}_D$ = –16.9° (*c* 1.62, EtOH); ≥99% ee by capillary GC analysis; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.50 (t, 2 H, *J* = 7.0 Hz), 4.76 (t, 1 H, *J* = 6.4 Hz), 5.01–5.20 (m, 3 H), 5.68–5.92 (m, 1 H), 7.31 (m, 2 H), 8.42 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 43.54, 71.87, 118.79, 121.53, 134.18, 149.52, 154.65; MS (70 eV, 250 °C) m/z 150 (M + H, 0.76), 122 (M – C_2H_4, 17.34), 108 (M – C_3H_6, 100), 51 (45.49); IR (neat) 3199 (s), 1638 (m), 1598 (s), 1555 (m) cm^{-1}.

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Supplementary Material Available: ^{13}C NMR spectra of 12–19 (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Formylsilanes. Chemoenzymatic and Chemical Syntheses of the 2,4-Dinitrophenylhydrazones of These Apparently Air- and Water-Stable Compounds

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Formylsilanes have long been reported to be notoriously unstable compounds. In fact, no formylsilane has been reported that was stable in air or in water nor are there any known hydrates, imines, or hydrazones of formylsilanes. We have found that monoamine oxidase catalyzes the oxidation of (aminomethyl)-*tert*-butyldimethylsilane in aqueous buffer at pH 9 to give, apparently, either formyl-*tert*-butyldimethylsilane or the corresponding hydrate, which is isolated as the 2,4-dinitrophenylhydrazone. The chemical synthesis of this same compound and the corresponding formyltrimethylsilane was carried out in low yields by a standard route to acylsilanes but in good yields by a new route involving conversion of (1,3-dioxolan-2-yl)tri-*n*-butylstannane to the corresponding silanes followed by acid hydrolysis. Although the formylsilane could not be isolated, it or its hydrate apparently is stable enough in water to survive incubation for several hours prior to the 2,4-dinitrophenylhydrazine trapping reaction.

Introduction

Acylsilanes are well-studied compounds that are useful as intermediates in the preparation of silyl enol ethers,[1] in diastereoselective aldol condensations,[2] in the synthesis of β-hydroxysilanes,[3] and in the stereoselective synthesis of vinylsilanes.[4] The chemistry of formylsilanes, on the other hand, is virtually nonexistent because of the presumed difficulty in their preparation.[5] Until fairly recently the attempted synthesis of formyltrimethylsilane (Me_3SiCHO) had been the subject of decades of unsuccessful research.[5] However, evidence for the existence of Me_3SiCHO at low temperatures was provided more recently by Ireland and Norbeck[6] and by Linderman and Suhr[7] who carried out a Swern oxidation of (trimethylsilyl)methanol at low temperature and isolated the products of nucleophilic attack on the presumed Me_3SiCHO intermediate. Campion et al.[8] identified by NMR spectroscopy Me_3SiCHO as the product of the low-temperature addition of 1 equiv of dry HCl to $Cp_2Zr(\eta^2\text{-}COSiMe_3)Cl$. The only report of a "stable" formylsilane has been for-

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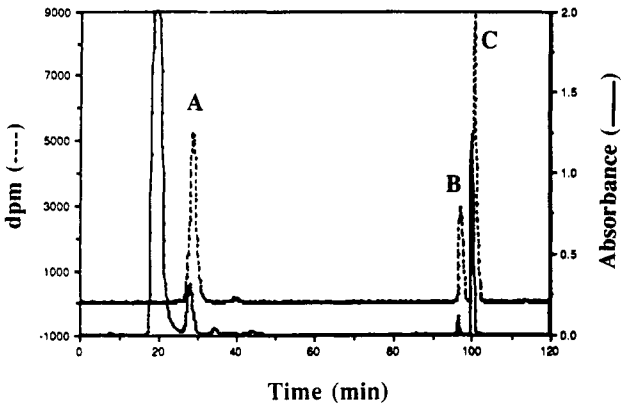

Figure 1. Reversed-phase HPLC chromatogram of the metabolites of monoamine oxidase-catalyzed oxidation of [1-^{3}H](aminomethyl)-*tert*-butyldimethylsilane followed by treatment with 2,4-dinitrophenylhydrazine. See the Experimental Section for details.

myltris(trimethylsilyl)silane [$(Me_3Si)_3SiCHO$], which was synthesized from the corresponding reaction of 1 equiv of dry HCl to the tris(trimethylsilyl)zirconium complex under vacuum in toluene.[9] Pentane extraction in the absence of air gave a product identified as formyltris(trimethylsilyl)silane by a variety of NMR and other spectral techniques and from product analyses after various reactions. However, this compound was reported to decompose instantly and exothermally upon exposure to air.

We have been interested for many years in the reactions and inactivation of mitochondrial monoamine oxidase, an enzyme that catalyzes the oxidation of a variety of amines to the corresponding iminium ions, which are subsequently hydrolyzed to aldehydes. During our studies on the inactivation of monoamine oxidase by (aminomethyl)-*tert*-butyldimethylsilane we noticed an unusual peak in the HPLC of the metabolites of this reaction following a quench with 2,4-dinitrophenylhydrazine. Here we show that this derivatized metabolite is the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane and that it and the corresponding trimethylsilyl analogue can be synthesized by a new synthetic route to formylsilanes as well as by the classical procedure for the synthesis of acylsilanes. No hydrazones, or hydrates of formylsilanes have been reported previously or have any formylsilanes been reported to be stable to air or water. This appears to be the first report of an air- and water-stable formylsilane (or hydrate) and its 2,4-dinitrophenylhydrazone and may be a general route to their synthesis.

Results

Monoamine Oxidase-Catalyzed Synthesis of Formyl-*tert*-butyldimethylsilane. Incubation of mitochondrial monoamine oxidase B with (amino[^{3}H]-methyl)-*tert*-butyldimethylsilane for 4 h followed by quench with acidic 2,4-dinitrophenylhydrazine and HPLC separation of the metabolites (Figure 1) revealed the formation of three radioactive products. Peak A was shown to correspond to the 2,4-dinitrophenylhydrazone of formaldehyde by independent synthesis, peak B corresponded to the 2,4-dinitrophenylhydrazone of 2,2-dimethylpropanal by independent synthesis, and the major peak C was identified as the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (vide infra). The large nonradioactive peak with a t_R at 20 min is excess 2,4-dinitrophenylhydrazine reagent. The NMR and mass spectra

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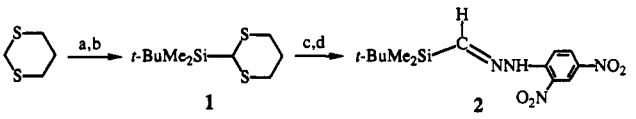
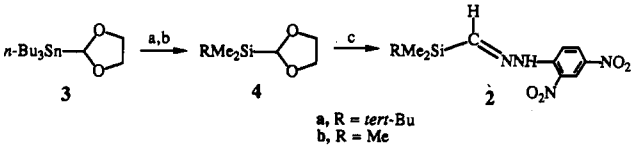
Scheme I. Brook[10]/Corey[11] Synthetic Route to the 2,4-Dinitrophenylhydrazone of Formyl-*tert*-butyldimethylsilane[a]



[a] Key: (a) *n*-BuLi, −25 to 0 °C; (b) *t*-$BuMe_2SiCl$; (c) $HgCl_2$/$CdCO_3$, acetone/H_2O; (d) 2,4-dinitrophenylhydrazine, EtOH/H_3O^+.

Scheme II. New Synthetic Route to Formylsilanes and to the 2,4-Dinitrophenylhydrazone of Formyl-*tert*-butyldimethylsilane[a]



[a] Key: (a) *n*-BuLi, −78 °C; (b) RMe_2SiCl; (c) 2,4-dinitrophenylhydrazine, EtOH/H_3O^+.

corresponded to those of the synthetic compounds (see Figure 2 for a comparison of the ^{1}H NMR spectra of the enzymatic and synthetic products).

Brook/Corey Route to the Synthesis of Formyl-*tert*-butyldimethylsilane. Brook et al.[10] and Corey et al.[11] independently reported the same general method for the synthesis of acylsilanes via the corresponding dithiane. This procedure was utilized for the synthesis of formyl-*tert*-butyldimethylsilane. 2-(*tert*-Butyldimethylsilyl)-1,3-dithiane (**1**) was synthesized by the treatment of 2-lithio-1,3-dithiane with *tert*-butyldimethylchlorosilane[10] (Scheme I). Hydrolysis of the dithiane with cadmium carbonate and mercuric chloride in aqueous acetone[10] for 1 h was followed by evaporation of the solvents, extraction with chloroform, treatment with 2,4-dinitrophenylhydrazine, and HPLC purification as was done with the enzyme reaction. It should be noted that the product was not trapped with 2,4-dinitrophenylhydrazine until after hydrolysis continued for an hour and after extraction into the organic solvent. The same product as was formed by the enzymatic route, namely the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (**2**), was identified in this reaction by HPLC, ^{1}H NMR (Figure 2), ^{13}C NMR, and mass spectrometry. The yield of this reaction, however, was only 2%.

New Synthesis of Formylsilanes. Transmetalation of (1,3-dioxolan-2-yl)-*tert*-butyldimethylstannane[12] (**3**, Scheme II) with *n*-butyllithium followed by reaction with *tert*-butyldimethylchlorosilane gave the corresponding silane **4a**. Hydrolysis in the presence of 2,4-dinitrophenylhydrazine gave the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (**2a**) in a 70% yield. The same reaction with the corresponding trimethylsilyl analogue (**4b**) gave the 2,4-dinitrophenylhydrazone of formyltrimethylsilane (**2b**) in a 46% yield.

Acid Hydrolysis of (1,3-Dioxolan-2-yl)-Substituted Silanes. In order to determine if there is an intrinsic stability difference in the two formylsilanes and to see if the free formylsilanes form upon hydrolysis of the dioxolanes, the acid hydrolyses of (1,3-dioxolan-2-yl)-*tert*-

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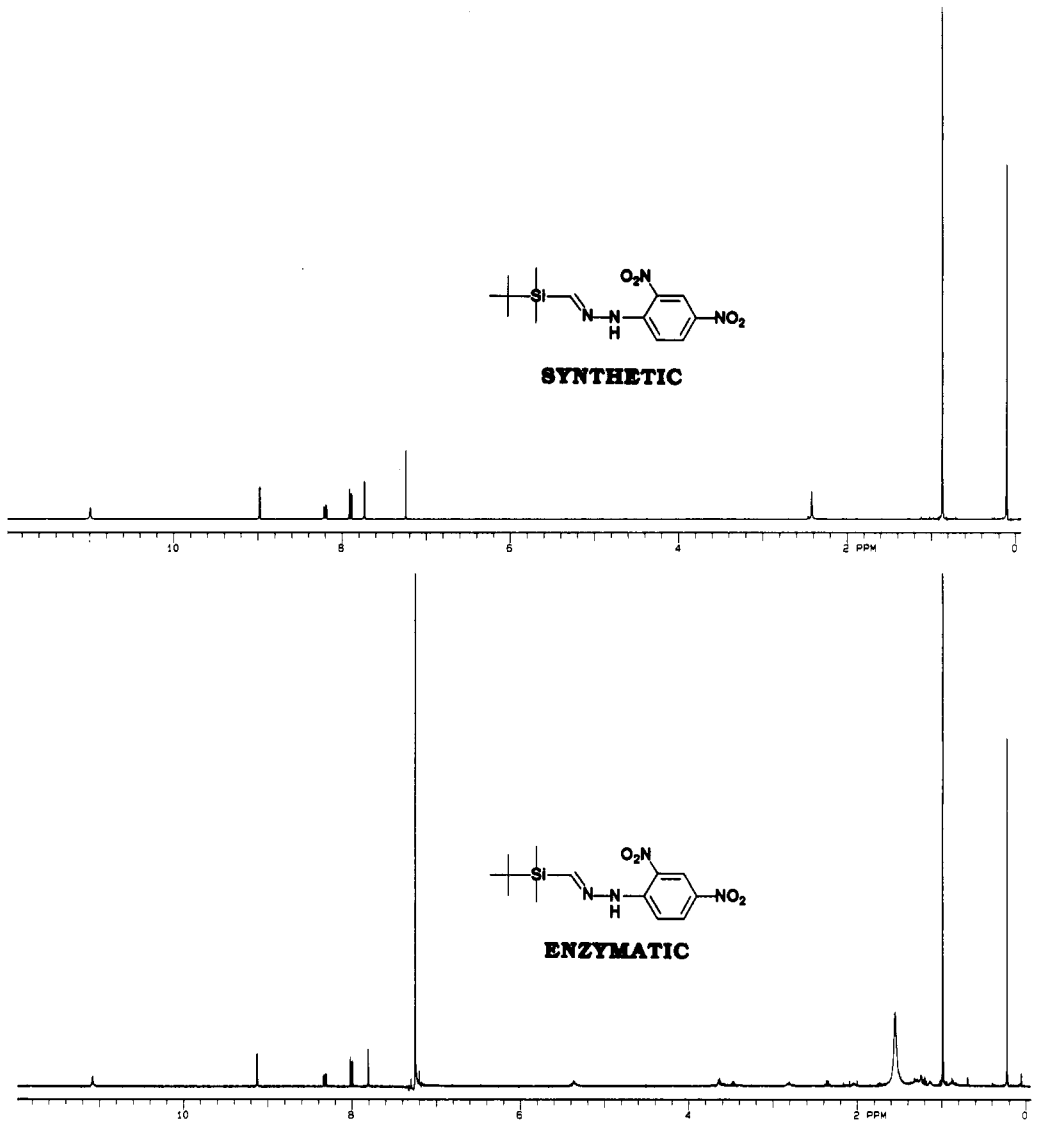

Figure 2. ^1H NMR spectra (400 MHz) of the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane generated synthetically and chemoenzymatically. The peak at 2.4 ppm in the spectrum of the synthetic compound is probably a water peak. The large peak at about 1.6 ppm in the spectrum of the enzymatic compound also may be a water peak. The peak at 7.24 ppm in both spectra is chloroform.

butyldimethylsilane and (1,3-dioxolan-2-yl)trimethylsilane were carried out in one part 0.5% DCl in D_2O and two parts acetone-d_6. The rates of hydrolysis were determined by NMR spectroscopy from the rates of decrease of the C-4 and C-5 protons in the dioxolane ring which correlated with the rates of formation of the ethylene glycol protons. The half-life for the hydrolysis of **4a** was 76 min and for the corresponding trimethylsilane (**4b**) was 34 min. Extraction of the hydrolysis mixtures, however, gave no detectable formylsilane or formylsilane hydrate. Hydrolysis of **4a** in 10% sulfuric acid in 62% aqueous ethanol at 0 °C for 70 min and for 300 min followed by quench with 2,4-dinitrophenylhydrazine produced the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (**2a**) in 75% and 50% yields, respectively. This indicates that the hydrolysis product (either the formylsilane or the corresponding hydrate) is stable to air and water for an extended period of time. Again however, it was not possible to isolate the formylsilane or its hydrate by extraction.

Discussion

Monoamine oxidase is well known to oxidize a variety of amines to the corresponding imines which are then released from the enzyme and hydrolyzed to the corresponding aldehydes. (Aminomethyl)trimethylsilane is a substrate and inactivator of monoamine oxidase.[13] The formylsilane in this case was not trapped by 2,4-dinitrophenylhydrazine, presumably because of the lower stability of this formylsilane relative to that of formyl-*tert*-butyldimethylsilane. The half-life for formyltrimethylsilane in mildly acidic conditions was determined to be about a 0.5 h, and the enzyme incubations are generally run for about 4 h. The greater stability of the *tert*-butyldimethyl analogue, apparently, is sufficient to allow trapping by 2,4-dinitrophenylhydrazine to take place. As is found with (aminomethyl)trimethylsilane, MAO oxidation of (aminomethyl)-*tert*-butyldimethylsilane produces formaldehyde (trapped as the 2,4-dinitrophenylhydrazone; see Figure 1). This metabolite presumably arises from hydrolysis of the formylsilane.[13] The second radioactive peak in the HPLC trace was identified as the 2,4-dinitrophenylhydrazone of 2-methylpropanal by independent synthesis and by comparison of its HPLC retention times and NMR spectrum to those of the standard. It is not

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known how this metabolite arises, but it appears to be the result of a [1,2] migration of the *tert*-butyl group from the silicon to the aminomethyl group.

The metabolite with the longest retention time was identified as the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane by mass spectrometry and by ^1H and ^{13}C NMR spectroscopy. This suggested that it should be possible to chemically synthesize this compound. Although there are no general routes to formylsilanes, the synthesis of acylsilanes is well known.[14] A standard route to acylsilanes is the mercuric ion and cadmium ion hydrolysis of silyl-substituted dithianes.[10,11] This route, followed by a 2,4-dinitrophenylhydrazine quench, yielded none of the 2,4-dinitrophenylhydrazone of formyltrimethylsilane. However, when the corresponding *tert*-butyldimethylsilyl-substituted dithiane was exposed to the mercuric and cadmium hydrolysis method, the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane was obtained in a 2% yield.

A new route to the synthesis of formylsilanes was sought so that sufficient product could be obtained to attempt to isolate it without its trapping as a hydrazone derivative. It was thought that the harshness of the dithiane hydrolysis method may be responsible for the low yields. Consequently, acid hydrolysis of the corresponding acetals was investigated (Scheme II). Transmetalation of (1,3-dioxolanyl)tri-*n*-butylstannane with *n*-butyllithium and then silylation gave the ethylene glycol acetal of the desired formylsilanes (the diethyl acetal derivatives were too unstable to isolate). Mild acid treatment (0.16% HCl in 2:1 acetone–water) resulted in hydrolysis of the acetal; however, the formylsilane could not be isolated. When the ethylene glycol acetal of formyl-*tert*-butyldimethylsilane was treated with acidic 2,4-dinitrophenylhydrazine directly, a 70% yield of the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane was isolated. This product was identical in all respects to the compound isolated from the MAO-catalyzed oxidation of (aminomethyl)*tert*-butyldimethylsilane (by their ^1H NMR (see Figure 2), ^{13}C NMR, mass spectrum, and HPLC). Because these two processes, MAO-catalyzed oxidation of amines and acid hydrolysis of acetals, are well-known to produce aldehydes and the fact that 2,4-dinitrophenylhydrazine is well-known to react with aldehydes to give 2,4-dinitrophenylhydrazones, it must be concluded that the product of both of these reactions is formyl-*tert*-butyldimethylsilane (which may exist in water primarily as the corresponding hydrate). The formylsilanes that are produced enzymatically and chemically are apparently stable to air and water because the 2,4-dinitrophenylhydrazine is not added for several hours after the formylsilanes are produced, but yet the 2,4-dinitrophenylhydrazones still are obtained.

Conclusions

To date formylsilanes have been thought to be highly unstable species in air and water. In fact, there are no known water-stable formylsilanes, nor are there any reported hydrates, imines, or hydrazones of formylsilanes. The results of our studies provide the first evidence to suggest that formation of these compounds under mild conditions (for example, enzymatic or mild acid hydrolysis of acetals) can lead to the isolation and synthetic utilization of these compounds, suggesting that possibly these heretofore presumed highly unstable species may not be so unstable. Although we have been unable to isolate the free formylsilanes, reaction of the products with 2,4-dinitrophenylhydrazine produces the corresponding 2,4-dinitrophenylhydrazones.

Experimental Section

Analytical Methods. Optical spectra and MAO assays were recorded on either a Perkin-Elmer Lambda 1 or Beckman DU-40 UV/vis spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Varian XLA-400 MHz spectrometer. Chemical shifts for ^1H NMR spectra are reported as δ values in parts per million relative to tetramethylsilane which is set to 0. An Orion Research Model 601 pH meter with a general combination electrode was used for pH measurements. Mass spectra were obtained on a VG Instruments VG70-250SE high-resolution mass spectrometer. Elemental analyses were performed either by Galbraith Laboratories, Inc., Knoxville, TN, or by G.D. Searle and Co., Skokie, IL. HPLC was performed using Beckman 110B pumps in series with a Beckman 163 variable-wavelength detector and a Radiomatic Instruments Flo-One/Beta Model CR radioactivity detector utilizing Packard Radiomatic FLO-SCINT II or RPI 3a70B scintillation cocktails for reversed- (C_{18} silica gel) and normal-phase (silica gel) HPLC, respectively. An Alltech Econosil C_{18} 10 μ 10- × 250-mm column was used for semi-preparative HPLC, and either Econosil C_{18} 10 μ 4.6 × 250-mm or Econosil silica 10 μ 4.6 × 250-mm columns were used for analytical HPLC. Liquid scintillation counting was done in a Beckman LS-3133T scintillation counter using 10 mL RPI 3a70B scintillation cocktail. [^3H]Toluene (2.22×10^6 dpm/mL, corrected for first-order decay) from New England Nuclear was used as an internal standard. Amine hydrochlorides were visualized on TLC plates by spraying with a solution of ninhydrin (300 mg) with pyridine (2 mL) in acetone (100 mL) and then heating. Radiopurity of radioactive compounds was assessed by cutting developed TLC plates (Merck Kieselgel 60 plates without fluorescent indicator) into strips and counting each strip with scintillation cocktail in a scintillation counter.

Reagents. 2,4-Dinitrophenylhydrazine reagent was prepared by the standard method.[15] Benzophenone (99+%), *tert*-butyldimethylchlorosilane, *n*-butyllithium (2.0 M in pentane), chloroform-*d*, deuterium chloride (37 wt%, 99 atom % D), deuterium oxide (>99.96 atom % D and 99.8 atom % D), anhydrous diethyl ether, ninhydrin, anhydrous tetrahydrofuran, tetramethylsilane, and triethylaluminum (1.0 M in hexanes) were purchased from Aldrich. [^3H]Water (5.0 C_i/mL) was obtained from Amersham (Arlington Heights, IL). Diethyl ether and tetrahydrofuran for reactions were distilled from sodium with benzophenone ketyl indicator under nitrogen immediately prior to use. HPLC-grade acetonitrile, ethyl acetate, hexane, and water were obtained from Mallinckrodt and were filtered prior to use. Other organic solvents were dried over 3- or 4-Å molecular sieves. All other chemicals were used without further purification. Distilled water was deionized or deionized and redistilled.

(Aminomethyl)-*tert*-butyldimethylsilane·HCl. Benzophenone *N*-methylimine[16] (2.198 g, 88.7 wt %, 10.0 mmol) in tetrahydrofuran (10 mL) was added to a solution of 1.5 M *n*-BuLi (7.0 mL, 10.5 mmol) and tetrahydrofuran (40 mL) at −78 °C while stirring with a magnetic stirrer under a dry nitrogen atmosphere. The blackish-red solution was stirred for 1 h at −60 °C, and then the temperature was lowered again to −78 °C and *tert*-butyldimethylchlorosilane (1.556 g, 10.0 mmol) in tetrahydrofuran (10 mL) was added dropwise over several min. The reaction mixture was stirred under nitrogen and allowed to warm to room temperature overnight. The solution was cooled to 0 °C in an ice/water bath, and ice-cold deionized water (160 mL) was added. The reaction mixture was extracted with diethyl ether (3 × 80 mL), and the combined organic extracts were dried over anhydrous sodium carbonate. The solvent was removed by rotary evaporation in vacuo, yielding a yellowish oil. The oil was dissolved in diethyl ether (75 mL) and 95% ethanol (12.5 mL), and then oxalic acid dihydrate (0.693 g, 5.5 mmol) was added and the mixture was stirred overnight at room temperature. The fluffy white pre-

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cipitate produced was filtered from the greenish supernatant, washed with anhydrous diethyl ether, and allowed to dry. The white solid (1.06 g, 61% yield) was dissolved in a solution of saturated potassium carbonate (10 mL) and deionized water (10 mL) and extracted with diethyl ether (3 × 25 mL). The combined organic extracts were extracted with 1.0 N HCl (3 × 250 mL), and then the combined aqueous layers were rotary evaporated in vacuo to dryness, yielding a white solid, which was recrystallized from absolute ethanol/anhydrous diethyl ether: mp 255–256 °C; ^{1}H NMR (D_2O) δ 0.05 (s, 6 H), 0.81 (s. 9 H), 2.37 (s, 2 H); ^{13}C NMR (^{1}H decoupled, D_2O) 6.39, 16.83, 26.93, 27.07. Anal. Calcd for $C_7H_{20}ClNSi$: C, 46.25; H, 11.09; N, 7.71; Si, 15.45; Found: C, 46.48; H, 11.37; N, 7.74; Si, 15.27.

[1-^{3}H]Benzophenone *N*-((*tert*-Butyldimethylsilyl)-methyl)imine. (Aminomethyl)-*tert*-butyldimethylsilane·HCl was converted to the free amine by basification with aqueous sodium hydroxide followed by extraction with diethyl ether, drying over anhydrous magnesium sulfate, and removal of ether by distillation through a column of glass helices. Triethylaluminum in hexanes (1.0 M, 16 mL, 16 mmol) was dissolved in dry benzene (16 mL) under an argon atmosphere. (Aminomethyl)*tert*-butyldimethylsilane (2.26 g, 15.6 mmol) in dry benzene (5 mL) was added at room temperature while the solution was stirred with a magnetic stirrer. The solution was refluxed for 0.5 h, and then benzophenone (1.95 g, 10.7 mmol) was added. After being allowed to reflux for an additional 1.75 h, the reaction mixture was cooled, and absolute ethanol (2.5 mL) was added. The reaction mixture was poured into an aqueous sodium tartrate solution (50 mL, 10% w/v) and extracted with dichloromethane (50 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed by rotary evaporation in vacuo to yield a clear, slightly yellowish oil (1.95 g, 59% yield). Slight contamination of the benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine by benzophenone was indicated by NMR and TLC: NMR ($CDCl_3$) δ 0.10 (s, 6 H), 1.00 (s, 9 H), 3.45 (s, 2 H), 7.20–8.05 (m, 12 H); TLC gave two spots after visualization by UV and ninhydrin (80:20 hexane/ethyl acetate, R_f = 0.37 and R_f = 0.54; benzophenone standard R_f = 0.37). To anhydrous tetrahydrofuran (25 mL) under argon at −78 °C was added 2.5 M *n*-BuLi in pentane (2.4 mL, 6.0 mmol). Benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine (89.4 wt %, 1.80 g, 5.82 mmol) in tetrahydrofuran (3 mL) was added dropwise while being stirred with a magnetic stirrer. The deep red anion was allowed to stir for 1 h at −78 °C, and then [^{3}H]water (100 μL, 5 Ci/mL, 5.6 mmol) in tetrahydrofuran (2 mL) was added quickly with stirring. The solution was allowed to stir at room temperature for ca. 15 min and then was quenched with cold water (25 mL). The reaction mixture was extracted with diethyl ether (3 × 50 mL), and the combined organic layers were washed with water (2 × 50 mL) and dried ($MgSO_4$). Organic solvents were removed by rotary evaporation in vacuo to yield a clear, yellow oil.

[1-^{3}H](Aminomethyl)-*tert*-butyldimethylsilane·HCl. The oily residue of [1-^{3}H] benzophenone *N*-((*tert*-butyldimethyl)-methyl)imine was dissolved in 95% ethanol (7.3 mL) and anhydrous diethyl ether (43 mL). Oxalic acid dihydrate (0.7572 g, 6.0 mmol) was added, and a flocculent white precipitate was observed after ca. 10 min. The solution was stirred overnight at room temperature. Solvent was removed by rotary evaporation in vacuo to yield a solid which was triturated with anhydrous diethyl ether (20 mL). The solid was neutralized with aqueous sodium hydroxide and extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with water (25 mL) and then extracted with 3 N HCl (3 × 20 mL). The solvent was removed to yield a white solid which was recrystallized from absolute ethanol/anhydrous diethyl ether to a constant specific activity, 2.08 × 10^7 dpm/μmol. TLC showed one spot after visualization (12:5:3 *n*-butanol/water/acetic acid, R_f = 0.65) corresponding to the (aminomethyl)-*tert*-butyldimethylsilane·HCl standard. The radiopurity was determined to be 99.8% by TLC.

2-(*tert*-Butyldimethylsilyl)-1,3-dithiane (1). To 1.14 g (9.5 mmol) of 1,3-dithiane in 24 mL of dry tetrahydrofuran at −25 °C was added dropwise 4 mL (10 mmol) of 2.5 M *n*-butyllithium in hexane. After 1.5 h the suspension was warmed to 0 °C, and 1.51 g (10 mmol) of *tert*-butyldimethylchlorosilane in 15 mL tetrahydrofuran was added over 20 min. The resulting cloudy yellow solution was maintained at 0 °C for 3 h, and then the suspension was worked up with 2% HCl and extracted with diethyl ether. The combined organic layers were dried and distilled to give an oil (1, 1.87 g, 85%): bp 124 °C (5 mmHg); ^{1}H NMR ($CDCl_3$) 0.05 (s, 6 H), 0.92 (s, 9 H), 1.97 (m, 2 H), 2.65 (dd, 2 H), 2.85 (dd, 2 H), 3.75 (s, 1 H); HRMS *m/z* calcd for $C_{10}H_{22}S_2Si$ (M^+) 234.0932, found 234.0933. Anal. Calcd for $C_{10}H_{22}S_2Si$: C, 51.28; H, 9.40. Found: C, 50.94; H, 9.48.

Hydrolysis of 2-(*tert*-Butyldimethylsilyl)-1,3-dithiane (1) and Reaction of the Product with 2,4-Dinitrophenylhydrazine. A solution of 2-(*tert*-butyldimethylsilyl)-1,3-dithiane (1, 0.351 g, 1.5 mmol) in 12.5 mL of acetone and 5 mL of tetrahydrofuran was added to a mixture of cadmium carbonate (2.95 g, 17.5 mmol) suspended in a solution of mercuric chloride (2.03 g, 7.5 mmol) in acetate (7.5 mL) and water (0.62 mL, 34 mmol) under nitrogen at room temperature. After 1 h the solvents were removed from the viscous suspension in vacuo, the resulting white solid was washed thoroughly with chloroform, and then 800 μL of 2,4-dinitrophenylhydrazine reagent was added. The solution was allowed to react overnight, was washed with water, and was evaporated to dryness. After being redissolved in acetonitrile the sample was purified by preparative reversed-phase HPLC (as described below) and preparative normal-phase HPLC (3% ethyl acetate in hexane, 1.4 mL/min, monitoring at 254 nm) which gave 9 mg (2%) of the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (2). See **2,4-Dinitrophenylhydrazone of Formyl-*tert*-butyldimethylsilane** (below) for the characterization of this compound.

(1,3-Dioxolan-2-yl)-*tert*-butyldimethylsilane (4a). A solution of (1,3-dioxolan-2-yl)tri-*n*-butylstannane[12] (3, 363 mg, 1 mmol) in 5 mL of THF was cooled to −78 °C, and *n*-butyllithium (0.63 mL of a 1.6 M hexanes solution, 1.0 mmol) was added dropwise. After being stirred for 20 min at −78 °C HMPA (1.0 mL) and a solution of *tert*-butyldimethylchlorosilane (150.5 mg, 1 mmol) in 0.5 mL of THF was added dropwise. The mixture was stirred at −78 °C for 20 h and at −60 °C for an additional 2 h and then was allowed to warm to ambient temperature overnight. The mixture was poured into 20 mL of 100 mM potassium phosphate buffer, pH 7.0, and extracted with three 20-mL portions of ether. The extracts were combined and dried over sodium sulfate and then filtered and concentrated. The crude product was obtained by Kugelrohr distillation (70 °C (3 mmHg)) and purified further by flash chromatography on silica gel using hexanes and then 10% ethyl acetate in hexanes as eluant (R_f = 0.45 using 10% ethyl acetate in hexanes). The product (4a) was obtained as a colorless oil (150 mg, 80%): ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 6 H), 0.95 (s, 9 H), 3.45 (t, 2 H), 3.78 (t, 2 H), 5.1 (s, 1 H); HRMS (M − 1) calcd for $C_9H_{19}O_2Si$ 187.1154, found 187.1185. Anal. Calcd for $C_9H_{19}O_2Si$: C, 57.45; H, 10.64; Si, 14.89. Found: C, 58.46; H, 10.94; Si, 14.63.

2,4-Dinitrophenylhydrazone of Formyl-*tert*-butyldimethylsilane (2a). To a solution of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane (4a, 19 mg, 0.1 mmol) in ethanol was added 2,4-dinitrophenylhydrazine reagent dropwise, and the stirring was continued at 0 °C overnight. The reaction mixture was extracted with three 20-mL portions of chloroform, and the extracts were combined, dried over magnesium sulfate, filtered, and concentrated. Purification by flash chromatography on silica gel using 10% ethyl acetate in hexanes as eluant gave 22 mg (70% yield) of the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane (2a) as orange-red crystals: mp 139–140 °C; ^{1}H NMR ($CDCl_3$) δ 0.10 (s, 6 H), 0.87 (s, 9 H), 7.73 (s, 1 H), 7.90 (d, 1 H), 8.20 (dd, 1 H), 8.98 (d, 1 H), 10.96 (s, 1 H); ^{13}C NMR (101 MHz decoupled, $CDCl_3$) δ −6.91, 16.54, 26.10, 116.77, 123.05, 128.62, 129.65, 137.87, 144.52, 158.49; MS (EI, 70 eV) *m/z* (relative intensity) 324 (M^+, 33), 240 (66), 194 (15), 183 (15), 167 (6), 142 (15), 115 (44), 75 (63), 73 (100), 59 (18), 57 (7); HRMS calcd for $C_{13}H_{20}N_4O_4Si$ (M^+) 324.1254, found 324.1248. Anal. Calcd for $C_{13}H_{20}N_4O_4Si$: C, 48.15; H, 6.17; N, 17.28. Found: C, 48.06; H, 6.03; N, 17.01.

This product comigrated by reversed-phase HPLC (60% acetonitrile in water, 0.56 mL/min, monitoring at 254 nm) with the 2,4-dinitrophenylhydrazone obtained from the monoamine oxidase B-catalyzed metabolism of (aminomethyl)-*tert*-butyldimethylsilane.

(1,3-Dioxolan-2-yl)trimethylsilane (4b) and Its 2,4-Dinitrophenylhydrazone 2b. (1,3-Dioxolan-2-yl)trimethylsilane

(4b) was prepared by the same procedure described above for the preparation of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane (4a). The crude product, obtained by Kugelrohr distillation (60 °C (5 mmHg)) could not be purified further by flash chromatography on silica gel because of its instability: crude yield 37%; ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 9 H), 3.72 (t, 2 H), 3.88 (t, 2 H), 4.42 (s, 1 H); HRMS (M − 1) calcd for $C_6H_{13}SiO_2$ 145.0694, found 145.0713.

The 2,4-dinitrophenylhydrazone of formyltrimethylsilane (2b) was obtained in a 46% yield as described above for formyl-*tert*-butyldimethylsilane: mp 141–142 °C; ^{1}H NMR ($CDCl_3$) δ 0.23 (s, 9 H), 7.58 (s, 1 H), 7.94 (d, 1 H), 8.31 (dd, 1 H), 9.05 (d, 1 H), 11.03 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ −2.439, 116.87, 123.24, 128.82, 129.78, 138.09, 144.69, 159.91; HRMS calcd for $C_{10}H_{14}N_4O_4Si$ 282.0784, found 282.0785. Anal. Calcd for $C_{10}H_{14}N_4O_4Si$: C, 42.55; H, 4.97; N, 19.86. Found: C, 42.26; H, 4.91; N, 19.73.

Hydrolysis of (1,3-Dioxolan-2-yl)silanes. Hydrolysis of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane (4a) and the corresponding -trimethylsilane (4b) was carried out at 25 °C in one part of 0.5% DCl in D_2O and two parts of acetone-d_6 in an NMR tube. The rates of hydrolysis were determined by following the decrease in the area of the C-4 and C-5 dioxolane protons and the increase in the area of the four ethylene glycol protons with time. The hydrolysis of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane also was examined in one part 30% sulfuric acid in water and two parts ethanol at 0 °C. After 70 and 300 min 2,4-dinitrophenylhydrazine reagent was added, and the solutions were allowed to stand at 0 °C overnight. The 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane was isolated in 75% and 50% yield, respectively.

Enzymes and Assays. Bovine liver MAO B was isolated according to the published method.[17] MAO activity was assayed by the method Tabor et al.[18] The percentage of active enzyme was determined by inactivation with [^{14}C]- or [1-^{3}H]pargyline.[19] Protein assays were done with either Pierce BCA protein assay reagent or Pierce Coomassie protein assay reagent using bovine serum albumin for standard curves. All buffers and enzyme solutions were prepared with doubly distilled deionized water.

Formation of Tritiated Aldehydes During Inactivation of MAO by [1-^{3}H](Aminomethyl)-*tert*-butyldimethylsilane. MAO (100 μM, 25 μL) was incubated with 53 mM [1-^{3}H](aminomethyl)*tert*-butyldimethylsilane·HCl in 200 mM Tris-HCl buffer pH 9.0 (475 μL) at 25 °C. A control without inactivator was run simultaneously at one-fifth the scale. The enzyme was assayed after 4 h and was found to be completely inactive. 2,4-Dinitrophenylhydrazine reagent (200 μL) was added directly to the inactivated enzyme and to a nonenzymatic control, and the solutions were allowed to react overnight at room temperature. Water (3 mL) was added to the solutions which were extracted with chloroform (2 × 5 mL). The combined organic extracts were washed with water (2 × 5 mL) and evaporated. Samples were redissolved in acetonitrile and analyzed using analytical reversed-phase HPLC (60:40 acetonitrile/water 0.25 mL/min; FLO-SCINT II scintillation fluid 0.75 mL/min) monitoring the UV absorbance at 360 nm.

Large-Scale Formation of Aldehydes During Inactivation of MAO by (Aminomethyl)-*tert*-butyldimethylsilane. The procedure for the preparation of tritiated aldehydes during inactivation of MAO by [1-^{3}H](aminomethyl)-*tert*-butyldimethylsilane and the subsequent reaction with 2,4-dinitrophenylhydrazine was followed exactly except that (aminomethyl)-*tert*-butyldimethylsilane was substituted for [1-^{3}H]-(aminomethyl)-*tert*-butyldimethylsilane. Preparative reversed-phase HPLC (60:40 acetonitrile/water for 10 min then 100% acetonitrile with a linear gradient for 2 min at 1.4 mL/min) was used to separate compounds in unknown peaks for mass spectral analysis. The product obtained in the peak corresponding to the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane had a ^{1}H NMR spectrum (Figure 2), a ^{13}C NMR spectrum (data not shown), and mass spectrum (data not shown) the same as those for the synthetic compound. HRMS (EI) calcd for $C_{13}H_{20}N_4O_4Si$ 324.1254, found 324.1269.

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Registry No. 1, 95452-06-5; 2a, 143370-61-0; 2b, 143370-69-8; 3, 118418-21-6; 4a, 143370-62-1; 4b, 143370-68-7; MAO, 9001-66-5; benzophenone *N*-methylimine, 13280-16-5; (*tert*-butyldimethyl)chlorosilane, 18162-48-6; (aminomethyl)-*tert*-butyldimethylsilane·HCl, 143370-63-2; (aminomethyl)-*tert*-butyldimethylsilane, 143370-64-3; benzophenone, 119-61-9; benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine, 143370-65-4; [1-^{3}H]-benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine, 143370-66-5; [1-^{3}H](aminomethyl)-*tert*-butyldimethylsilane·HCl, 143370-67-6; 1,3-dithiane, 505-23-7.

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An Improved Synthesis of Naphthoate Precursors to Olivin

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An improved synthesis of olivin synthetic intermediate **3** is described. The synthesis involves the Horner–Wadsworth–Emmons coupling of **14** and **16**, the diastereoselective vinylcuprate addition to enone **20**, and the condensation of isocoumarin **25** and methyl acetate. A parallel sequence starting from allyl ether **26** has provided naphthoate **35** that is suitably differentiated for glycosylation studies.

Olivomycin A and other clinically active members of the aureolic acid family of anticancer agents are challenging synthetic targets.[1,2] These compounds are inhibitors of DNA-dependent RNA polymerase, and a recent report suggests that they inhibit transcription of the c-myc protooncogene.[3] Available structure–activity data indicate that the two oligosaccharide chains are essential for bio-

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