Silylacetic Esters: Enolate Reactions and Polyol Preparation

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Introduction

Organosilanes are increasingly employed in organic synthesis, as precursors to alkenes via the Peterson olefination[1] and as precursors to alcohols via the Tamao[2] and Fleming oxidations.[3] Recently, Landais demonstrated that α-silyl ester enolates can be readily alkylated and that 1,2-diols can be obtained following reduction of the ester and oxidation of the alkoxysilyl substituent.[4] α-Silyl ester and α-silyl ketone enolates[5] have been employed more commonly as starting materials in the Peterson olefination, via aldol reactions which eliminate silanol to yield α,*β*-unsaturated esters.[6] Larchevêque, for example, isolated a series of *β*-hydroxy-α-trimethylsilyl esters in the stereoselective syntheses of α,*β*-unsaturated esters, but no characterization data were reported for these potentially sensitive compounds. In general, however, workers have not isolated the *β*-hydroxy-α-silyl compounds but have directly converted the aldol products to α,*β*-unsaturated esters by treatment with base. In these instances, the silyl substituent was trimethylsilyl, which is not easily oxidized. Although Larson reported difficulty in isolating alcohols via an aldol route with a diphenylmethylsilyl substituent,[7] Kita obtained *β*-hydroxy-α-silyl esters by reaction of (*tert*-butyldimethylsilyl)ketene with alkoxystannanes followed by condensation with aldehydes.[8] The Peterson olefination via α-silylcarbanions has been applied to imines as well, but there has been little attempt to isolate the *β*-amino-α-silyl compounds.[9]

The oxidation chemistry of silanes has been exploited more frequently in natural product syntheses, as silicon's ability to act as a "masked" hydroxyl group allows it to be used in situations in which an alcohol is not desired.[10] The Tamao oxidation employs a fluoride source and hydrogen peroxide and requires at least one alkoxy substituent on the silane. Fleming oxidations are conducted under acidic conditions ($AcOH/AcO_2H$ or HBF_4), and the silane must have an aryl substituent at the outset. Basic conditions (KH, *tert*-butylhydroperoxide, and TBAF) have been elucidated recently which are compatible with a wide range of alkyl and aryl substituents on silicon.[11]

By exploiting the versatility of the silyl moiety, we report aldol condensation/silyl oxidation and condensation/protodesilylation sequences which complement existing methods for the preparation of polyhydroxylated natural products. Diols can be prepared in an anti fashion by aldol reactions of α-hydroxycarbonyl compounds[12] and in a syn relationship by dihydroxylation reactions.[13] Secondary alcohols can be prepared by various methods,[14] including aldol reaction/reduction of an α-thioether.[15] However, no single precursor yields both mono- and dihydroxylated materials with ease. We detail reliable conditions for the synthesis of *β*-hydroxy-α-silyl esters and their subsequent conversion to α,*β*-dihydroxy esters, *β*-hydroxy esters, and bis-protected triols. Such a sequence of condensation and, ultimately, oxidation or protodesilylation requires that the silyl moiety be disposed toward oxidation, and thus ethyl (dimethylphenylsilyl)acetate (**1**)[16] was utilized as starting material, with the aim of employing one of Fleming's reported one-pot methods for oxidation of the arylsilane as a key step in the sequence.

A systematic study of reaction conditions reveals that the preparation of *β*-hydroxy-α-silyl esters can be performed cleanly by reaction of **1** with lithium diisopropylamide (LDA) to form the ester enolate at −78 °C, followed by exchange of the counterion with $MgBr_2{\cdot}OEt_2$.[17] After allowing 60 min for the Li−Mg exchange to take place, the aldehyde is added. Under these conditions, the *β*-hydroxy-α-silyl condensation product is isolated with minimal formation of the alkene (Scheme 1). Apparently, the more covalent Mg−O bond suppresses tendency toward elimination.[6] Three sources of magnesium were investigated ($MgBr_2{\cdot}OEt_2$, anhydrous $MgBr_2$ (both obtained from Aldrich), and $MgBr_2$ generated in situ from

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Scheme 1

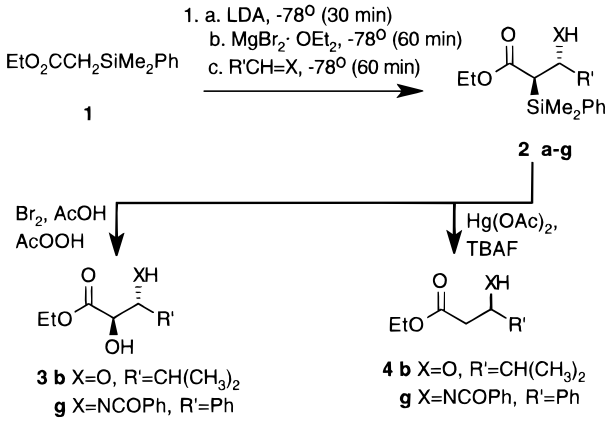

Table 1. Reaction of Ethyl Dimethylphenylsilyl acetate 1 with Aldehydes and Imines

entry	R'	X	product	yield (%)
1	Ph	O	**2a**	76
2	i-Pr	O	**2b**	64
3	Bu	O	**2c**	72
4	PhCH=CH	O	**2d**	70
5	t-Bu	O	**2e**	(alkene)
6	Ph	NBoc	**2f**	43
7	Ph	NCOPh	**2g**	60

Mg and 1,2-dibromoethane[18]), and the stable dietherate gave consistently superior results. Variation of the Mg^{2+} stoichiometry confirmed that it plays a critical role in suppressing the Peterson olefination: use of 0.5 equiv gave predominantly the alkene product, and greater than 1.25 equiv did not improve the yield of alcohol. Other bases (LHMDS, magnesium bromide diisopropylamide) as well as Lewis acids (Bu_2BOTf and $TiCl_4$) were studied, but these reagents yielded crude materials which were contaminated with many other reaction byproducts.

A variety of aldehydes and imines were reacted with the ester enolate in good yield, as shown in Table 1. Peterson olefination byproducts were observed in the crude mixtures, but in very low yield (<10%). In reaction with cinnamaldehyde, the β-hydroxy-α-silyl product is isolated, and none of the diene is observed in the crude product. In only one instance (**2e**) did the alkene predominate, presumably because the steric bulk of the *tert*-butyl and dimethylphenyl substituents causes the elimination pathway to be favored. Although the yields of reaction of the enolate with imines are low, the imines for entries 6 and 7 are hydrolytically unstable and were used in the condensation immediately after preparation without purification. Treatment of the enolate with a less electrophilic imine (*N*-phenylbenzylidene)[19] yielded unreacted starting materials.

The substituents on silicon also influence the aldol reaction toward elimination, and the dimethylphenylsilane was found to have less of this tendency. Bearing in mind that we ultimately wished to oxidize the silicon, it had to bear at least one alkoxy or aryl substituent that would allow oxidation by Tamao's or Fleming's method, respectively. Four α-silylacetates were prepared from ethyl diazoacetate by the methods of Doyle[16] and Landais.[4] The silyl substituents included $-SiMe_2Ph$, $-SiMePh_2$, $-SiMe_2(O-Pr-i)$, and $-SiMe(OEt)_2$. The bulk of two phenyl groups greatly hindered the aldol reaction,[7] and the alkoxy groups enhanced the elimination, despite the presence of magnesium. Commercially available ethyl (trimethylsilyl)acetate also showed a greater propensity toward elimination than the dimethylphenyl analogue.

Table 2. Oxidation and Protodesilylation of Condensation Products

entry	R'	X	product	yield (%)	product	yield (%)
1	$CH(CH_3)_2$	O	**3b**	63	**4b**	48
2	Ph	NCOPh	**3g**	72	**4g**	99

The condensation gives only the anti diastereomer, with the syn diastereomer undetectable by ^1H NMR and GC analysis of the crude materials. The anti assignment can be made on the basis of the α-methine proton coupling to the β-methine proton ($J = \sim 3.5$ Hz), precedent from earlier work that found that use of Mg^{2+} in aldol condensations yields only the anti diastereomer,[17] and comparison of the ^1H NMR spectrum of compound **3g** that has been confirmed to be the anti diastereomer.[20] Molecular modeling[21] of the enolate and Zimmerman-Traxler transition state support the experimental results. Experimentally, the *Z* enolate of ethyl (dimethylphenylsilyl)acetate should be formed under kinetic conditions by treatment with LDA due to the bulk of the $-SiMe_2Ph$ and $-OEt$ groups, and modeling confirms that the *Z* enolate is thermodynamically preferred as well. Comparison of the chair conformations of the aldol transition state involving the *Z* enolate indicates that anti addition is favored.

The utility of these condensations lies in the subsequent chemistry of the silyl moiety to obtain polyfunctionalized compounds by oxidation and reduction (Scheme 1). The results of these studies are found in Table 2. First, we investigated a variety of one-pot oxidation methods[3c,11] on β-hydroxy ester **2b** and β-amino ester **2g**. Treatment of these condensation products with 1.0 M Br_2 in $AcOH/AcO_2H$ at 0 °C as described by Fleming[3c] yielded α,β-dihydroxy ester **3b** and β-amino-α-hydroxy ester **3g**. The anti configuration at the α-center was retained as determined by ^1H NMR coupling constants for the α- and β-protons and is precedented for these arylsilane oxidations. Other one-pot methods ($Hg(OAc)_2/AcO_2H$ and $KBr/AcO_2H/NaOAc/AcOH$) were less successful with these substrates and, in the case of buffered KBr, did not go to completion. The oxidation was potentially problematic, as the retroaldol reaction could become competitive without protection of the extant hydroxyl group, but no evidence of the retroaldol was observed in the ^1H NMR of the crude materials. However, both products decomposed to a minor extent during purification by column chromatography, diminishing the yields somewhat. Nonetheless, this condensation/oxidation sequence provides highly functionalized compounds diastereoselectively and concisely. Note that **3g** is an analogue of the unnatural amino acid phenylisoserine, and the route should be applicable to the synthesis of other natural products. The sequence has advantages over earlier, lengthier synthe-

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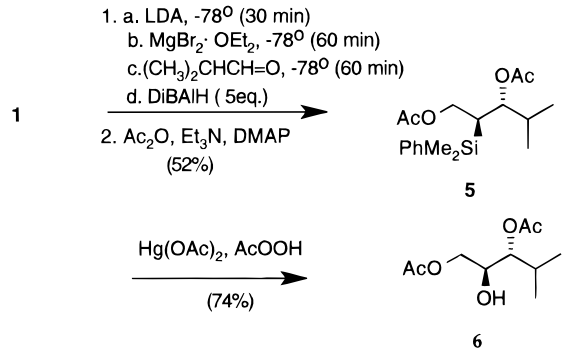
Scheme 2



ses of 1,2-amino alcohols via silyl oxidation which required protection of the amine and employed a two-step silyl oxidation protocol.[8]

Next, we investigated the protodesilylation chemistry of the condensation products. Treatment with 1.2 equiv each of $Hg(OAc)_2$ and 1.0 M TBAF in 1:1 THF−MeOH at 0 °C cleanly and quickly effected the protodesilylation within 15 min. The starting materials did not need to be protected prior to this reaction, and again, no retroaldol was observed. The reaction appears to be facilitated by the presence of the ester, perhaps via an incipient enolate, as attempts to perform protodesilylation on (dimethylphenylsilyl)octane resulted in no reaction. The isolated yield was higher for **4g** which possesses chromophores that facilitated its detection by UV during column chromatography. The use of this combination of reagents to effect protodesilylation has not been reported and is notable in that other one-pot protodesilylation methods require either the presence of an alkoxy group on silicon[22] or strongly basic conditions.[23] Ongoing efforts in our lab are directed at investigating the scope of this reaction.

Last, bis-protected triol **6** can be obtained via the aldol condensation/oxidation sequence if the intermediate aldolate is reduced in situ with diisobutylaluminum hydride (Scheme 2). The reduction takes advantage of the "protection" of the alcohol afforded by the magnesium counterion, and little or no elimination and retroaldol are observed. An alternative route of isolation of the β-hydroxy ester, protection, and reduction was complicated by the tendency of the hydroxy ester to undergo a retroaldol reaction during the protection attempt; thus in situ reduction is more efficient. Oxidation of silane **5** is effected by $Hg(OAc)_2$ in peracetic acid in this case, yielding the bis-protected triol **6**.

In conclusion, enolate reactions of ethyl(dimethylphenylsilyl)acetate with aldehydes and imines provide access to polyfunctionalized alcohols and amines by suppression of the Peterson olefination. The use of $MgBr_2{\cdot}OEt_2$ stabilizes the aldolate intermediate and results in anti diastereoselectivity. One-pot oxidation of the β-hydroxy- and β-aminosilyl esters can be performed without protection of the β-substituent, offering an efficient route to substitution patterns found in many natural products. Last, a bis-protected triol was prepared from the aldol intermediate by ester reduction, diol protection, and, finally, silane oxidation. Thus the condensation product provides direct access to three substitution patterns: α,β-disubstituted and β-monosubstituted esters and α,β,γ-triols.

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Experimental Section

General Experimental Methods. All reactions were conducted in oven-dried glassware, needles, syringes, and stir bars that were cooled in a desiccator over $CaSO_4$. All reactions were conducted under an atmosphere of N_2. THF was dried and distilled from potassium under an atmosphere of N_2. Amines (triethylamine (Et_3N) and diisopropylamine (i-Pr_2NH) were distilled from KOH under N_2 prior to use. All aldehydes were distilled from anhydrous $CaSO_4$ powder under N_2 immediately prior to use. Peracetic acid was obtained from Aldrich as a 32 wt % solution in dilute acetic acid and was used at this concentration. Other chemical reagents were used as received from Aldrich without further purification. "Drying" of extracts refers to drying with $MgSO_4$. NMR was obtained on a Bruker A300 at 300 MHz (^{1}H) and 75 MHz (^{13}C). Shifts are recorded in ppm and were obtained in and referenced to $CDCl_3$ at δ 7.24 for ^{1}H NMR and δ 77.00 for ^{13}C NMR. High-resolution mass spectra (HRMS) were obtained at the University of Iowa. Elemental analyses (C, H) were performed by MHW Laboratories of Phoenix, AZ, and agree within ±0.4% of the calculated values.

Representative Procedure for Aldol Condensation. In a typical procedure, diisopropylamine (1.10 mmol) was added to THF (5 mL) at −78 °C followed by n-BuLi (1.10 mmol, 1.1 M in hexane). After 5 min, the silyl ester **1**[16] (1.00 mmol) was added neat, dropwise by syringe. After 30 min, a suspension of $MgBr_2{\cdot}OEt_2$ (1.25 mmol) in THF (5 mL) was added, and the mixture was stirred for another 60 min. Neat, freshly distilled aldehyde (1.20 mmol) was added, and the reaction mixture was maintained at −78 °C. After the reaction was quenched with 5 mL of satd aq NH_4Cl, the bath was removed and the heterogeneous mixture was stirred at room temperature for at least 15 min, until the phases melted and separated. The organic phase was decanted; the heterogeneous aqueous phase was diluted with 3 mL of water and extracted with Et_2O (3 × 5 mL). The combined organic phases were dried, filtered, and concentrated by rotary evaporation to yield the crude β-hydroxy-α-silyl ester. The crude alcohol was purified by flash column chromatography on silica gel.

2-(Dimethylphenylsilyl)-3-hydroxyphenylpropanoic acid, ethyl ester (2a): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22−7.51 (m, 10 H), 4.90 (d, 1 H, J = 5.5 Hz), 3.95 (q, 2 H, J = 7.3 Hz), 2.83 (d, 1 H, J = 5.5 Hz), 1.04 (t, 3 H, J = 7.3 Hz), 0.46 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 143.8, 134.0, 129.6, 128.2, 127.8, 127.3, 127.1, 125.9, 72.5, 60.2, 46.0, 14.0,−3.30, −3.40; FTIR (neat) cm^{-1} 3451 (br, OH), 1717 (s, C=O). Anal. Calcd for $C_{19}H_{24}O_3Si$: C, 69.47; H, 7.36. Found: C, 69.64; H, 7.09.

2-(Dimethylphenylsilyl)-3-hydroxy-4-methylpentanoic acid, ethyl ester (2b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.56 (m, 5 H), 4.00 (q, 2 H, J = 7.3 Hz), 3.26 (dd, 1 H, J = 3.0, 8.1 Hz), 2.54 (d, 1 H, J = 3.0 Hz), 1.60 (m, 1 H), 1.14 (t, 3 H, J = 7.3 Hz), 0.90 (d, 3 H, J = 6.8 Hz), 0.80 (d, 3 H, J = 6.8 Hz), 0.46 (s, 3 H), 0.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 136.5, 134.1, 129.6, 127.9, 60.1, 41.0, 34.7, 19.7, 18.9, 14.2, −3.00, −3.30; FTIR (neat) cm^{-1} 3501 (br, OH), 1693 (s, C=O). Anal. Calcd for $C_{16}H_{26}O_3Si$: C, 65.26; H, 8.90. Found: C, 65.06; H, 8.61.

2-(Dimethylphenylsilyl)-3-hydroxyheptanoic acid, ethyl ester (2c): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.57 (m, 5 H), 4.03 (q, 3 H, J = 7.0 Hz), 3.67 (m, 1 H), 2.37 (d, 1 H, J = 3.5 Hz), 1.52 (m, 1 H), 1.25 (m, 6 H), 1.13 (t, 3 H, J = 7.0 Hz), 0.82 (t, 3 H), 0.45 (s, 3 H), 0.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 136.2, 134.0, 129.5, 127.8, 70.6, 60.0, 43.6, 37.4, 28.3, 22.4, 14.1, 13.9, −3.10, −3.40; FTIR (neat) cm^{-1} 3487 (br, OH), 1696 (s, C=O). Anal. Calcd for $C_{17}H_{28}O_3Si$: C, 66.19; H, 9.15. Found: C, 66.00; H, 8.82.

(*E*)-2-(Dimethylphenylsilyl)-3-hydroxy-5-phenyl-4-pentenoic acid, ethyl ester (2d): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22−7.56 (m, 10 H), 6.45 (d, 1 H, J = 15.8 Hz), 6.12 (dd, 1 H, J = 6.6, 15.8 Hz), 4.46 (dd, 1 H, J = 5.3, 6.6 Hz), 4.06 (q, 2 H, J = 7.0 Hz), 2.58 (d, 1 H, J = 5.3 Hz), 1.16 (t, 3 H, J = 7.0 Hz), 0.49 (s, 3 H), 0.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6,

136.5, 135.9, 134.1, 131.3, 130.4, 129.6, 128.4, 127.8, 127.6, 126.5, 71.4, 60.3, 44.6, 14.2, −3.1, −3.5; FTIR (neat) cm^{-1} 3460 (br, OH), 1716 (s, C=O), 1631 (s, C=C). Anal. Calcd for $C_{21}H_{26}O_3Si$: C, 71.15; H, 7.39. Found: C, 71.30; H, 7.20.

3-[(*tert*-Butoxycarbonyl)amino]-2-(dimethylphenylsilyl)phenylpropanoic acid, ethyl ester (2f): ^1H NMR (300 MHz, $CDCl_3$) δ 7.20−7.50 (m, 10 H), 6.46 (br d, 1 H), 4.95 (br d, 1 H, J = 3.4 Hz), 3.85 (q, 2 H, J = 6.8 Hz), 2.75 (d, 1 H, J = 3.4 Hz), 1.43 (s, 9 H), 0.97 (t, 3 H, J = 6.8 Hz), 0.46 (s, 3 H), 0.45 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 154.9, 145.5, 135.9, 134.0, 129.6, 128.3, 127.9, 126.8, 125.9, 79.2, 60.1, 44.4, 28.4, 14.0, −3.40, −3.60; FTIR (neat) cm^{-1} 3427 (br, OH), 1706 (s, C=O). Anal. Calcd for $C_{24}H_{33}NO_4Si$: C, 67.41; H, 7.78; N, 3.28. Found: C, 67.47; H, 7.83; N, 3.18.

3-(Benzoylamino)-2-(dimethylphenylsilyl)phenylpropanoic acid, ethyl ester (2g): mp 98−102 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.65 (d, 1 H, J = 8.8 Hz), 7.18−7.78 (m, 15 H), 5.60 (d, 1 H, J = 8.8 Hz), 4.10 (q, 2 H, J = 7.0 Hz), 2.93 (d, 1 H, J = 2.6 Hz), 1.09 (t, 3 H, J = 7.0 Hz), 0.56 (s, 3 H), 0.54 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 165.4, 142.9, 133.7, 131.3, 129.5, 128.6, 128.3, 127.8, 126.9, 125.6, 60.3, 50.8, 43.6, 14.3, −3.40, −3.60; FTIR (KBr) cm^{-1} 3408 (br, −NH), 1703 (s, C=O), 1670 (s, C=O). Anal. Calcd for $C_{26}H_{29}NO_3Si$: C, 72.35; H, 6.77; N, 3.24. Found: C, 72.37; H, 6.83; N, 3.06.

Representative Fleming Oxidation Procedure. A solution of hydroxysilane **2b** (0.0782 g, 0.265 mmol) in peracetic acid (32 wt % solution; 2.6 mL) at 0 °C was treated dropwise with Br_2 (0.50 mL; 1 M in acetic acid). The mixture was warmed to room temperature slowly over 3.5 h as the ice−water bath melted and then stirred for an additional 1.5 h. The reaction mixture was diluted with EtOAc (10 mL), and 2 mL of satd aq $Na_2S_2O_3$ was added slowly, dropwise, until the pale-orange color dispersed. The phases were separated, and the organic phase was carefully washed with H_2O (3 mL) and satd aq $NaHCO_3$ (4 × 3 mL). The combined aqueous phases were back-extracted with EtOAc (10 mL). After drying, the combined organic phases were filtered and concentrated by rotary evaporation. The crude oil was purified by flash column chromatography (Florisil, 10:1 hexanes−ethyl acetate) to yield diol **3b** (0.0295 g, 0.167 mmol, 63%).

2,3-Dihydroxy-4-methylpentanoic acid, ethyl ester (3b): mp 31−33 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.26 (2 H, ABX_3, J = 7.0, 7.5 Hz), 4.24 (1 H, d, J = 3.5 Hz), 3.46 (1 H, dd, J = 3.5, 7.5 Hz), 2.08 (1 H, br s), 1.86 (1 H, m), 1.30 (3 H, ABX_3, J = 7.0, 7.5 Hz), 0.99 (3 H, d, J = 7.0 Hz), 0.96 (3 H, d, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 78.7, 72.3, 62.0, 30.0, 19.2, 18.5, 14.2; FTIR (KBr) cm^{-1} 3440 (br, OH), 1742 (s, C=O); MS (EI) 133 (M − $CH(CH_3)_2$), 104, 76, 72, 43. Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.33; H, 8.94.

***β*-(Benzoylamino)-α-hydroxybenzenepropanoic acid, ethyl ester (3g):** mp 138−140 °C (lit.[20] mp 161−163 °C); ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (1 H, d, J = 8.8 Hz), 7.24−7.49 (10 H, m), 5.60 (1 H, dd, J = 3.5, 8.8 Hz), 4.66 (1 H, d, J = 3.5 Hz), 4.13 (2 H, ABX_3, J = 7.0, 7.5 Hz), 1.23 (3 H, t, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 166.6, 136.4, 134.0, 131.7, 128.5, 128.2, 127.6, 127.0, 72.3, 62.2, 55.4, 14.3; FTIR (KBr) cm^{-1} 3345 (s, −NH, −OH), 1718 (s, C=O), 1645 (s, C=O). Anal. Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.87; H, 6.01; N, 4.19.

General Procedure for the Protodesilylation. A solution of the silyl alcohol **2b** (0.0686 g, 0.209 mmol) in 1:1 THF−MeOH (2.0 mL) at 0 °C was treated with $Hg(OAc)_2$ (0.0795 g, 0.250 mmol) followed by 1.0 M TBAF (250 μL, 0.250 mmol). The yellow homogeneous solution was stirred for 15 min and then diluted with EtOAc (10 mL). The mixture was washed with 3 mL each of satd NH_4Cl, H_2O, and brine. A yellow precipitate which formed upon addition of EtOAc dissolved upon addition of the NH_4Cl solution. The organic phase was dried and concentrated by rotary evaporation to yield an oil which was purified by flash column chromatography (eluted with 5:1 hexanes−EtOAc).

3-Hydroxy-4-methylpentanoic acid, ethyl ester (4 b): ^1H NMR (300 MHz, $CDCl_3$) δ 4.14 (q, 2 H, J = 7.0 Hz), 3.74 (br m, 1 H), 2.90 (br s, 1 H), 2.47 (dd, 1 H, J = 2.6, 16.3 Hz), 2.34 (dd, 1 H, J = 9.7, 16.3 Hz), 1.67 (m, 1 H), 1.25 (t, 3 H, J = 7.0 Hz), 0.92 (d, 3 H, J = 6.6 Hz), 0.90 (d, 3 H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 72.7, 60.7, 38.4, 33.1, 18.3, 17.7, 14.2. Anal. Calcd for $C_8H_{16}O_3$: C, 59.97; H, 10.06. Found: C, 59.95; H, 9.88.

***β*-(Benzoylamino)benzenepropanoic acid, ethyl ester (4g):** white solid, mp 83−86 °C; ^1H NMR (300 MHz, $CDCl_3$) 7.90−7.20 (m, 10 H), 5.62 (dd, 1 H, J = 5.3, 5.7 Hz), 4.06 (q, 2 H, J = 7.0 Hz), 2.96 (dd, 1 H, J = 15.8, 5.3 Hz), 2.89 (dd, 1 H, J = 15.8, 5.7 Hz), 1.15 (t, 3 H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 166.5, 140.5, 134.2, 131.7, 128.6, 127.6, 127.0, 126.2, 60.9, 49.8, 39.9, 14.0; MS (EI) 297, 252, 192, 105, 77.

1,3-Diacetoxy-2-(dimethylphenylsilyl)-4-methylpentane (5). Following addition of the aldehyde and stirring for 60 min at −78 °C, the reaction mixture of the aldol condensation prepared as described above was treated with DIBALH (1.0 M in toluene; 5.0 mL, 5.0 mmol), and immediately warmed to 0 °C, and stirred for another 60 min. The reaction was quenched with saturated aq NH_4Cl (5 mL), and the mixture stirred 30 min and was further treated with saturated aq K·Na tartrate (5 mL). After stirring for 1.5 h, the phases were separated and the milky, heterogeneous aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic phases were dried, filtered, and concentrated by rotary evaporation to yield 300 mg of crude, clear oil. A portion of this crude mixture (0.1943 g, 0.77 mmol; assuming 100% conversion for the previous reaction) was added to a stirred solution of Et_3N (214 μL, 1.54 mmol), DMAP (0.0188 g, 0.154 mmol), and acetic anhydride (145 μL, 1.54 mmol) in CH_2Cl_2 at −10 °C. This reaction mixture was concentrated by rotary evaporation after 60 min without workup and purified by flash column chromatography (10:1 hexanes−EtOAc). The diacetate (0.1351 g, 0.400 mmol, 52%) was isolated as a clear, colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.27−7.51 (5 H, m), 4.97 (1 H, AMX, J = 5.7, 6.1 Hz), 4.28 (1 H, dd, J = 4.0, 11.4 Hz), 4.16 (1 H, dd, J = 6.2, 11.4 Hz), 1.94 (3 H, s), 1.86 (3 H, s), 1.83 (1 H, m), 1.64 (1 H, m), 0.83 (3 H, d, J = 6.6 Hz), 0.70 (3 H, d, J = 6.60 Hz), 0.35 (6 H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.5, 137.2, 133.7, 129.2, 127.8, 76.7, 62.5, 31.8, 29.0, 21.0, 20.89, 19.7, 17.5, −3.0, −3.7. Anal. Calcd for $C_{18}H_{28}O_4Si$: C, 64.25; H, 8.39. Found: C, 64.06; H, 8.54.

1,3-Diacetoxy-4-methyl-2-pentanol (6). Mercuric acetate (0.0350 g, 0.110 mmol) was added to silane **5** (0.0342 g, 0.102 mmol) in peracetic acid (1.0 mL; 32 wt % solution), and the mixture was stirred at 20 °C for 40 min. Ether (15 mL) was added to the solution, and the mixture was treated dropwise with 5 mL of satd aq $Na_2S_2O_3$ (**caution** − vigorous reaction!). The layers were separated, and the organic phase was extracted with 5 mL each of H_2O, satd aq Na_2CO_3, and brine. Following drying, the organic phase was concentrated in vacuo to yield alcohol **6** (0.016 g, 0.074 mmol, 74%) which required no purification: ^1H NMR (300 MHz, $CDCl_3$) δ 4.81 (t, 1 H, J = 6.15 Hz), 4.20 (dd, 1 H, J = 2.2, 11.9 Hz), 4.05 (dd, 1 H, J = 6.6, 11.9 Hz), 3.95 (dt, 1 H, J = 2.2, 6.6 Hz), 2.08 (s, 3 H), 2.07 (s, 3 H), 2.02 (m, 1 H), 0.94 (d, 3 H, J = 7.0 Hz), 0.90 (d, 3 H, J = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 171.1, 77.97, 69.49, 65.6, 28.7, 20.8, 19.3, 17.0; HRMS (EI) m/z calcd for $C_{10}H_{17}O_4$ $(M - OH)^+$ 201.2446, found 201.1133.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for compounds **3g** and **4g** (4 pages). This material is contained in 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.

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