α,β-Unsaturated Acyl Silanes

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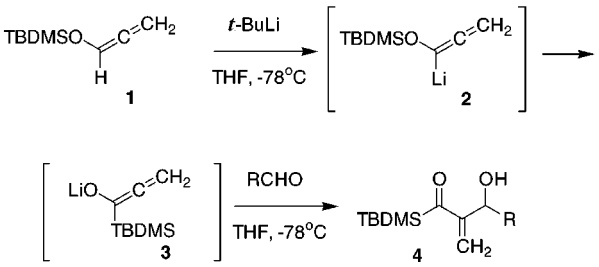
A rapid method for the synthesis of α,β-unsaturated acyl silanes from allenyl trialkylsilyl ethers and aldehydes or ketones has been developed. The method is general and leads to the acyl silane products in good to excellent yields.

α,β-Unsaturated acyl silanes have been widely used in organic synthesis,[1] as Michael acceptors with organocuprates,[2] in $TiCl_4$-promoted allylations,[3] and in conjugate additions of silylated nucleophiles.[4] They are also reactive as Diels−Alder dienophiles[2] and undergo a variety of [1,3]-dipolar cycloadditions.[5] They react in [3 + 2] annulations with allenylsilanes[5] and with ketone enolates[6a,b] and are also reactive in [3 + 4] annulations with α,β-unsaturated methyl ketone enolates.[6c,d] Many transformations are specific to the acyl silane function, including Brook rearrangements,[2,7] oxidation to carboxylic acids,[8] and fluoride-promoted conversions to aldehydes and ketones.[8] Despite their utility in synthesis, there was no convenient method for preparing α-functional α,β-unsaturated acyl silanes. Methods requiring multiple steps have been described. For example, the double bond has been introduced via a Peterson olefination,[8,9] Horner−Wadsworth−Emmons condensation,[10] dehydration,[11] or dehydrohalogenation reactions.[12] Preparation of the acyl silane unit has been accomplished by hydrolysis of an α-silyl enol ether,[2,7a,13] oxidation of an allylic carbinol,[14] silyl cuprate addition to an acyl chloride,[15] enyne hydroboration−oxidation,[16] or use of the benzotriazole acyl anion methodology.[17]

We recently reported the generation of lithium silaacrolein enolate anion **3**, which produced TBDMS acyl silanes **4** upon addition to aldehydes (eq 1).[18] Anion **3**



[1]

results from a reverse Brook rearrangement of allenyllithium **2**, which is presumably formed first from the α-deprotonation of allene **1** with *t*-BuLi.[19] There is precedence for this oxygen-to-carbon anionic silicon migration in the syntheses of allylic α-trialkylsilyl alcohols[14] and propargyl α-silyl alcohols[20] from the corresponding silyl ethers.

The methodology summarized in eq 1 was useful for the synthesis of TBDMS acyl silanes; however, there were shortcomings. Enolizable aldehydes led to low yields (53−64%) of product, and all attempts to add lithium enolate **3** to ketones led to very low yields (<20%) of the corresponding acyl silane accompanied by an acetylenic byproduct. In this work, we report optimal conditions for the addition of silaacrolein enolates to enolizable aldehydes and ketones.

The formation of the silyl allene ethers is summarized in Scheme 1. The reaction sequence involves protection of propargyl alcohol **5** as a silyl propargyl ether **6**,[21] which is subsequently isomerized to the allene with catalytic potassium *tert*-butoxide.[22] We attempted to form silyl allene ethers ranging from the sensitive triethylsilyl (TES) group to the significantly less labile TIPS and *tert*-butyldiphenylsilyl (TBDPS) groups.

(1) (a) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647−660. (b) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 147−195.
(2) Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949−960.
(3) Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2509−2512.
(4) Ricci, A.; Degl'Innocenti, A.; Borselli, G.; Reginato, G. *Tetrahedron Lett.* **1987**, *28*, 4093−4096.
(5) Danheiser, R. L.; Fink, D. M. *Tetrahedron Lett.* **1985**, *26*, 2513−2516.
(6) (a) Takeda, K.; Nakajima, A.; Yoshii, E. *Synlett* **1997**, 255−256. (b) Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc.* **1993**, *115*, 9351−9352. (c) Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc.* **1995**, *117*, 6400−6401. (d) Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *120*, 4947−4959.
(7) (a) Reich, H. J.; Kelly, M. J. *J. Am. Chem. Soc.* **1982**, *104*, 1119−1120. (b) Reich, H. J.; Eisenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791−7800.
(8) Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc.* **1981**, *103*, 6217−6219.
(9) (a) Yanagisawa, A.; Habaue, S.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 5198−5200. (b) This area has been reviewed: Ager, D. J. *Synthesis* **1984**, 384−398.
(10) Nowick, J. S.; Danheiser, R. L. *J. Org. Chem.* **1989**, *54*, 2798−2802.
(11) Plantier-Royon, R.; Portella, C. *Synlett* **1994**, 527−529.
(12) Cunico, R. F.; Kuan, C.-P. *J. Org. Chem.* **1985**, *50*, 5410−5413.
(13) (a) Leroux, Y.; Mantione, R. *Tetrahedron Lett.* **1971**, *12*, 591−592. (b) Clinet, J.-C.; Linstrumelle, G. *Tetrahedron Lett.* **1980**, *21*, 3987−3990.
(14) Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y.-M.; Szczepanski, S. W. *J. Org. Chem.* **1985**, *50*, 5393−5396.
(15) Capperucci, A.; Degl'Innocenti, A.; Faggi, C.; Ricci, A.; Dembech, P.; Seconi, G. *J. Org. Chem.* **1988**, *53*, 3612−3614.
(16) Hassner, A.; Soderquist, J. A. *J. Organomet. Chem.* **1977**, *131*, C1−C4.
(17) Katritzky, A. R.; Wang, Z.; Lang, H. *Organometallics* **1996**, *15*, 486-490.
(18) Tius, M. A.; Hu, H. *Tetrahedron Lett.* **1998**, *39*, 5937−5940.
(19) Zimmer, R. *Synthesis* **1993**, 165−178, and references cited.
(20) Kruithof, K. J. H.; Klumpp, G. W. *Tetrahedron Lett.* **1982**, *23*, 3101−3102.
(21) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190−6191.
(22) Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916−924.

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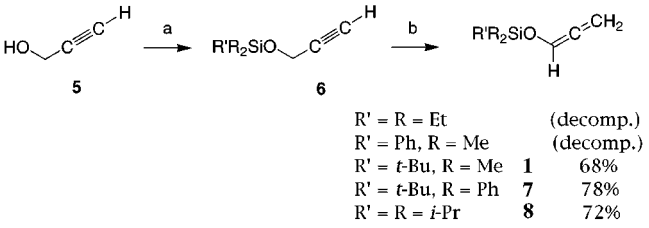
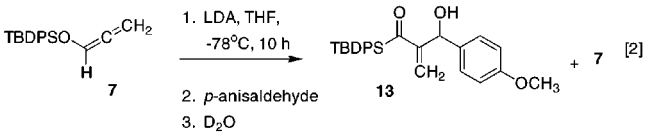
Scheme 1[a]



[a] Key: (a) $R'R_2SiCl$, imidazole, DMAP, THF, 0 °C to room temperature, 1 h; (b) *t*-BuOK, 60 °C.

The results suggest that the isomerization step is successful only for robust silyl groups. Whereas formation of the TES and phenyldimethylsilyl propargyl ethers proceeded in high yield, the attempted isomerization reaction to the corresponding allenes led only to cleavage of the silyl groups. However, the TBDPS and the TIPS propargyl ethers completely isomerized to the corresponding allene ethers (**7** and **8**) after 3 h. Two experimental observations are noteworthy. First, temperature control is critical to the success of the isomerization reaction, which must be carried out in a stirring oil or water bath. Use of a sand bath, which forms hot spots leading to uneven heating, resulted in low yields of allene, presumably due to competing thermal decomposition of the product. Second, when extreme care was taken to ensure anhydrous reaction conditions, the reaction time was significantly longer (80% completion after 35 h for **7**). Less fastidious technique resulted in complete isomerization within 3 h, suggesting that the isomerization requires a proton source.

The first step in conversion of silyl allene ethers **1**, **7**, and **8** to acyl silanes is α-deprotonation. TIPS allene ether **8** was deprotonated with *t*-BuLi and stirred for 1.5 h. Addition to nonenolizable aldehydes led to products **9**−**12** in high yield (Table 1, entries 1−3). Treatment of TBDPS allene ether **7** under the same conditions failed to produce acyl silanes. Furthermore, treatment of **7** with *t*-BuLi followed by D_2O showed no evidence of deuterium incorporation in the recovered allene. The surprising conclusion is that α-deprotonation of **7** with *t*-BuLi did not take place. Similarly, reaction of **7** with *n*-BuLi followed by *p*-anisaldehyde resulted in only trace amounts of acyl silane. It was observed that treatment of **1** with LDA followed by *p*-anisaldehyde led to acyl silane in 84% yield. When **7** was treated with LDA followed by *p*-anisaldehyde, acyl silane **13** was isolated in 23−56% yield, depending on the reaction time (eq 2). Allowing the anion



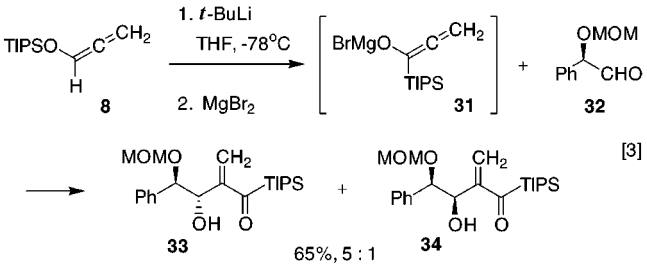
[2]

to age for 10 h prior to addition of the aldehyde gave the best yield of acyl silane. The reaction was quenched with D_2O, but NMR spectra showed no incorporation of deuterium in the recovered allene. This suggests that deprotonation is the slow step, not the rearrangement. This is supported by the observation that no silaacrolein was ever detected in the reaction mixtures.

The addition of the silaacrolein enolate anion **3** to ketones took place in low yield (<20%). We surmised that the basicity of **3** allowed enolization to compete with addition; therefore, our approach was to solve the problem by transmetalation. Transmetalation to the Ce^{III} enolate using $CeCl_3$ led to no improvement in the reaction with aldehydes or ketones, whereas the Zn^{II} enolate reacted with aldehydes, but did not add to ketones. The reduced basicity of the Zn enolate suggested that it would be a good choice for addition to enolizable aldehydes, which proved to be the case. Deprotonation of **1** or **8** with *t*-BuLi in THF at −78 °C followed by addition to $ZnCl_2$−TMEDA (or fused $ZnCl_2$) and addition of an enolizable aldehyde led to acyl silanes in high yield (Table 1, entries 4−7). The lowest yield was 73% (entry 7, **19**), which is from the most readily enolizable aldehyde of the series.

Transmetalation from Li to Mg^{II} by adding lithium enolate **3** to a solution of $MgBr_2$[23] led to the most effective nucleophile for addition to ketones. Yields varied according to the ketone substrate (Table 1, acyl silanes **20**−**30**): more readily enolizable ketones gave lower yields of acyl silane. Entries 11 and 12 were the most challenging cases. Cyclopentanone (entry 11) led to the desired acyl silane in 57% yield, and 4-methoxytetralone (entry 12) gave only 27% yield. No acyl silane was isolated from addition to camphor. These results define the limits of the current method. The magnesium enolate also added to enolizable aldehydes in good yield (70−80%), but the reaction was not as clean as with the zinc enolate. Attempts were made to deprotonate the silyl allene ethers with isopropylmagnesium chloride in THF in order to access the magnesium enolate directly, but the only product isolated from these experiments was derived from addition of the Grignard reagent to the aldehyde.

A single experiment was performed to probe the diastereofacial selectivity of the addition reaction to (*R*)-mandelaldehyde derivative **32** (eq 3). Both the Mg^{II} and



[3]

the Zn^{II} enolates of **8** were used, and both cases exhibited only modest stereoselectivity. The addition of the magnesium enolate gave a 5:1 diastereomeric mixture, presumably favoring the (*R*,*S*) diastereomer **33**, which arises from chelation control. The Zn enolate gave rise to an approximately 1:2 mixture but was selective for syn diastereomer **34**. The potential utility of the method is indicated by the fact that hydroxyl-directed homogeneous hydrogenation[24] of the methylene double bond in **33** is predicted to give the (*R*,*S*,*R*) stereotriad, which is found in synthetic precursors of unit A of the cryptophycins.[25]

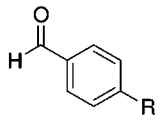
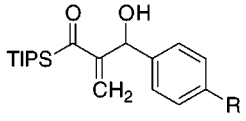
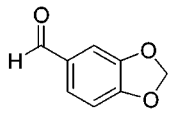
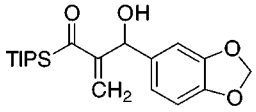
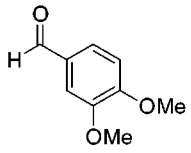
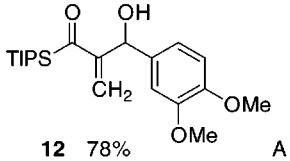
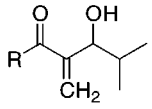
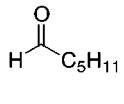
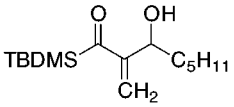
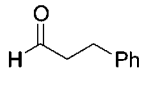
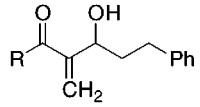
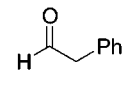
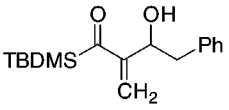
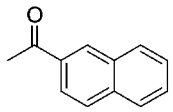
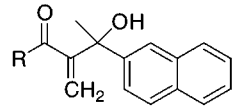
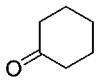
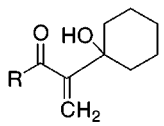
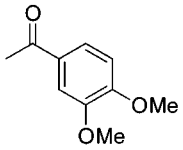
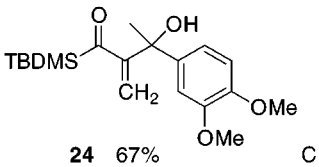
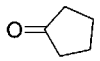
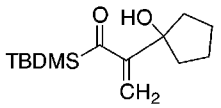
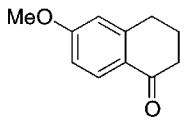
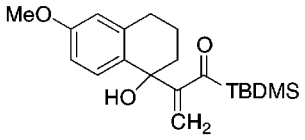
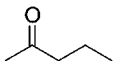
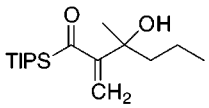
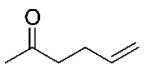
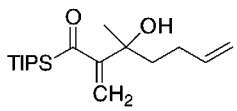
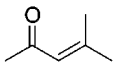
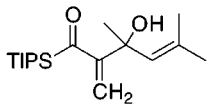
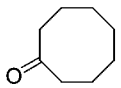
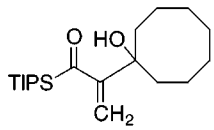
In conclusion, TBS and TIPS α,β-unsaturated acyl silanes can be derived from nonenolizable aldehydes by

(23) Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1256−1268.

(24) (a) Evans, D. A.; Morrissey, M. M. *J. Am. Chem. Soc.* **1984**, *106*, 3866−3868. (b) Farrington, E.; Franchini, M. C.; Brown, J. M. *J. Chem. Soc., Chem. Commun.* **1998**, 277−278. (c) This area has been reviewed: Brown, J. M. *Ang. Chem., Int. Ed. Engl.* **1987**, *26*, 190−203.

(25) Barrow, R. A.; Hemscheidt, T.; Liang, J.; Paik, S.; Moore, R. E.; Tius, M. A. *J. Am. Chem. Soc.* **1995**, *117*, 2479−2490.

Table 1. Acyl Silanes

Entry	Electrophile	Acyl Silane, Yield	Conditions[a]
1		 **9** R = NMe_2 81% **10** R = OMe 74%	A A
2		 **11** 71%	A
3		 **12** 78%	A
4		 **14** R = TBDMS 88% **15** R = TIPS 91%	B B
5		 **16** 89%	B
6		 **17** R = TBDMS 92% **18** R = TIPS 79%	B B
7		 **19** 73%	B
8		 **20** R = TBDMS 77% **21** R = TIPS 84%	C C
9		 **22** R = TBDMS 72% **23** R = TIPS 92%	C C
10		 **24** 67%	C
11		 **25** 57%	C
12		 **26** 27%	C
13		 **27** 77%	C
14		 **28** 66%	C
15		 **29** 87%	C
16		 **30** 77%	C

[a] 0.9 equiv *t*-BuLi, THF, −78 °C, followed by the following: (A) 0.8 equiv of RCHO, THF, −78 °C; (B) (a) 1.0 equiv of $ZnCl_2$−TMEDA, THF, −78 °C; (b) 0.75 equiv of RCHO, THF, −78 °C; (C) (a) 1.2 equiv of $MgBr_2$, Et_2O, THF, −78 °C; (b) 0.33 equiv of ketone, THF, −78 °C.

lithiation of allenyl ethers **1** and **8**, respectively. Transmetalation to zinc provides access to acyl silanes from enolizable aldehydes. For reaction of the anions derived from **1** and **8** with ketones, transmetalation to magnesium is optimal. On the basis of a limited number of experiments, it appears that slow deprotonation of TBDPS allene ether **7** limits its practical utility. The simple and convenient methods that have been described suggest that this chemistry will be useful in synthesis.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded in deuteriochloroform ($CDCl_3$) at 300 MHz ^{1}H and 75 MHz ^{13}C unless otherwise noted. IR spectra were recorded neat. MS data are reported in the form of *m*/*z*. TLC was performed on Sigma−Aldrich precoated silica gel 60 F-254 analytical plates (0.25 mm). ICN silica gel (0.032−0.063 mm) or Florisil (60−100 mesh) was used for normal-phase flash column chromatography. HPLC was performed using a 5 μm Phenomenex silica column (150 × 4.60 mm). Purity and homogeneity of all materials was determined chromatographically and from ^{1}H NMR and ^{13}C NMR, combustion analysis, and HPLC. THF and diethyl ether were distilled from sodium−benzophenone ketyl. Benzene was distilled from CaH_2. Diisopropylamine was distilled from CaH_2 and stored over KOH. Other reagents were obtained commercially and used as received. All reactions were performed under static nitrogen atmosphere in flame-dried glassware. Elemental analyses were performed by Desert Analytics, Inc.

General Procedure for the Synthesis of Allene Ethers 1, 7, and 8. To a solution of 2.4 mL (40 mmol) of propargyl alcohol **5** in 40 mL of THF at 0 °C was added 3.4 g (50 mmol) of imidazole, 0.5 g (4 mmol) of DMAP, and 9.4 mL (44 mmol) of triisopropylchlorosilane. The reaction mixture was stirred at room temperature for 1 h, diluted with pentane, and filtered through a short pad of silica gel. Solvent was evaporated, and 0.5 g (4 mmol) of potassium *tert*-butoxide was added at room temperature. The heterogeneous mixture was stirred at room temperature for 10 min, placed on a 60 °C oil bath, and stirred for 2 h. The reaction was cooled to room temperature, and the residue was distilled under vacuum to give 7.0 g (72% yield) of 1-triisopropylsilyloxy-1,2-propadiene **8**: colorless oil; bp 45−50 °C (5 mmHg); IR 1960 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.65 (t, J = 5.9 Hz, 1H), 5.22 (d, J = 5.9 Hz, 2H), 1.16 (sept, J = 5.9 Hz, 3H), 1.11 (d, J = 5.9 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 115.7, 86.3, 17.8, 12.2.

General Procedure for the Synthesis of TIPS Acyl Silanes 9−12. A solution of 275 mg (1.29 mmol) of allene **8** in 4 mL of THF at −78 °C was treated with a solution of 0.72 mL of *t*-BuLi (1.6 M in pentane, 1.16 mmol) dropwise. After 1.5 h, a solution of *p*-*N*,*N*-dimethylaminobenzaldehyde (153 mg, 1.03 mmol) in 1.5 mL of THF was added dropwise. The reaction was stirred at −78 °C for 45 min and then quenched by addition of saturated aqueous KH_2PO_4 and diluted with ether and pentane (1/1, v/v). Extraction with ether followed by drying ($MgSO_4$) and solvent evaporation provided the crude product, which was purified by flash column chromatography on silica gel to produce 294 mg of 1-triisopropylsilyl-2-[[4-(dimethylamino)phenyl]hydroxymethyl]prop-2-en-1-one **9** (81% yield) as a yellow oil: R_f = 0.29 (15% EtOAc in hexanes); IR 3450, 1620, 1600, 1520 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 8.7 Hz, 2H), 6.13 (s, 1H), 6.03 (s, 1H), 5.49 (br s, 1H), 2.95 (br s, 1H), 2.14 (s, 6H), 1.30 (sept, J = 7.3 Hz, 3H), 1.04 (d, J = 7.3 Hz, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 239.0, 156.9, 150.1, 129.6, 127.6, 127.2, 112.5, 72.4, 40.7, 18.7, 12.3; mass spectrum *m*/*z* 361 (M^+, 27), 318 (30), 150 (74); exact mass calcd for $C_{21}H_{35}NO_2Si$ 361.2437, found 361.2437.

Procedure for the Synthesis of 1-*tert*-Butyldiphenylsilyl-2-[hydroxy(4-methoxyphenyl)methyl]prop-2-en-1-one 13. To a solution of LDA (0.61 mmol) in 5 mL of THF at −78 °C was added a solution of allene **7** (200 mg, 0.68 mmol) in 2 mL of THF. The reaction was stirred at −78 °C for 10 h, and then a solution of *p*-anisaldehyde (69 mg, 0.51 mmol) in THF (1 mL) was added. The reaction was stirred at −78 °C for 1 h, quenched with D_2O, and diluted with ether and pentane (1/1, v/v). Extraction with ether followed by drying with $MgSO_4$ and solvent evaporation provided the crude product, which was purified by flash column chromatography on silica gel to produce 123 mg (56% yield) of **13** as a yellow oil: R_f = 0.10 (10% EtOAc in hexanes); IR 3450, 1600, 1520 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, J = 6.4 Hz, 2H), 7.53 (d, J = 6.4 Hz, 2H), 7.44−7.26 (m, 6H), 7.22 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.88 (s, 1H), 5.72 (s, 1H), 5.57 (br d, J = 4.4 Hz, 1H), 3.80 (s, 3H), 2.93 (d, J = 4.9 Hz, 1H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 236.3, 159.0, 154.4, 136.04, 136.01, 133.7, 132.7, 130.3, 129.7, 129.6, 127.9, 76.8, 55.3, 27.4, 18.9; mass spectrum *m*/*z* 373 ($M^+ - C_4H_9$, 18); exact mass calcd for $C_{27}H_{30}O_3Si$ 430.1964, found 430.1948; HPLC (5% EtOAc in hexanes, 1.0 mL/min) t_R = 6.6 min.

General Procedure for the Addition to Enolizable Aldehydes (Formation of Acyl Silanes 14−19). A 220 mg (1.29 mmol) portion of allene **1** in 4 mL of THF at −78 °C was treated with 0.72 mL of *t*-BuLi (1.6 M in pentane, 1.16 mmol) dropwise. After 0.5 h, the anion solution was added to a stirring heterogeneous mixture of $ZnCl_2$−TMEDA (292 mg, 1.16 mmol) in THF at −78 °C. The reaction mixture was stirred at −78 °C for 15 min until it became homogeneous, and then isobutyraldehyde (63 mg, 0.87 mmol) was added as a solution in 1 mL of THF. The reaction was stirred for 1 h at −78 °C and then quenched by addition of saturated aqueous KH_2PO_4 and diluted with ether and pentane (1/1, v/v). Extraction with ether followed by drying ($MgSO_4$) and solvent evaporation provided the crude product, which was purified by flash column chromatography on silica gel to produce 185 mg (88% yield) of 1-*tert*-butyldimethylsilyl-2-(1-hydroxy-2-methylpropyl)prop-2-en-1-one **14** as a yellow oil: R_f = 0.21 (7.5% EtOAc in hexanes); IR 3480, 1580, 1470 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.14 (s, 1H), 6.07 (s, 1H), 4.05 (t, J = 7.3 Hz, 1H), 2.65 (d, J = 7.6 Hz, 1H), 1.76 (sept, J = 6.6 Hz, 1H), 0.92 (s, 9H), 0.89 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H), 0.254 (s, 3H), 0.251 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 239.4, 154.8, 129.4, 77.3, 32.7, 26.7, 19.7, 17.6, 16.8, −4.4, −4.6; mass spectrum *m*/*z* 185 ($M^+ - C_4H_9$, 2), 73 (64); exact mass calcd for $C_9H_{17}O_2Si$ 185.0997, found 185.1011; HPLC (5% EtOAc in hexanes, 1.0 mL/min) t_R = 13.0 min.

General Procedure for Addition to Ketones (Synthesis of Acyl Silanes 20−30). A 220 mg (1.29 mmol) portion of allene **1** in 4 mL of THF at −78 °C was treated with 0.72 mL of *t*-BuLi (1.6 M in pentane, 1.16 mmol) dropwise. After 0.5 h, the anion solution was added to a stirring heterogeneous mixture of $MgBr_2$ (2.5 mL of 0.56 M solution in 10% benzene in diethyl ether, 1.4 mmol) in 3 mL of THF at −78 °C. The reaction was stirred for 2 h at −78 °C until it became homogeneous, and then acetonaphthone (65 mg, 0.38 mmol) was added as a solution in 1 mL of THF. The reaction was stirred for 1 h at −78 °C and then quenched by addition of saturated aqueous KH_2PO_4 and diluted with ether and pentane (1/1, v/v). Extraction with ether followed by drying ($MgSO_4$) and solvent evaporation provided the crude product, which was purified by flash column chromatography on silica gel to produce 99 mg of 1-*tert*-butyldimethylsilyl-3-(1-hydroxy-1-(2-naphthyl)ethyl)prop-2-en-1-one **20** (77% yield) as a yellow oil: R_f = 0.33 (10% EtOAc in hexanes); IR 3460, 3060, 1580, 1465, 1475 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84−7.75 (m, 4H), 7.47−7.42 (m, 3H), 6.42 (s, 1H), 6.21 (s, 1H), 5.07 (s, 1H), 1.68 (s, 3H), 0.82 (s, 9H), 0.24 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 243.0, 156.8, 144.3, 133.1, 132.3, 128.8, 128.1, 127.8, 127.4, 125.9, 125.6, 123.3, 123.1, 76.7, 29.1, 26.5, 16.8, −4.68, −4.72; mass spectrum *m*/*z* 340 (M^+, 10), 283 ($M^+ - C_4H_9$, 100); exact mass calcd for $C_{21}H_{28}O_2Si$ 340.1858, found 340.1849.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra, IR spectra, mass spectra and product characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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