

Synthesis of Formylsilanes through Oxidative Cleavage of α -Silyl Glycols

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S Supporting Information

ABSTRACT: A convenient method for the synthesis and isolation of highly reactive formylsilanes by oxidative cleavage of α -silyl glycols is presented. The mild conditions provide an entry to acid- and heat-sensitive members of this theoretically intriguing class of compounds. The utility of the method is demonstrated through the isolation and subsequent diastereoselective derivatization of *t*-BuMe₂- and *t*-BuPh₂-formylsilanes, previously not reported in isolated form.



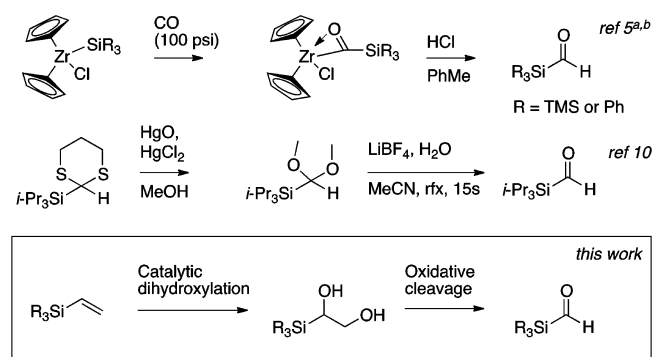
The simplest acylsilanes,¹ formylsilanes, are a class of highly reactive species that are in principle synthetically equivalent to prostereogenic formaldehyde.² While higher acylsilanes are frequently employed in synthesis,³ applications of formylsilanes are surprisingly rare. This paucity is likely a reflection of their challenging synthesis and very high inherent reactivity. When exposed to limited amounts of oxygen, formylsilanes rapidly rearrange to the corresponding silanols with loss of carbon dioxide,⁴ and exposure to the atmosphere has been reported to cause spontaneous ignition.⁵ To advance the chemistry of these potentially useful compounds, general, mild, and operationally convenient procedures that enable isolation of the products are of particular interest.

In a pioneering study, Swern oxidation of trimethylsilylmethanol was used to generate Me₃-formylsilane, which was trapped in situ by reactions with Wittig ylides to produce vinylsilanes.^{6a,7} This procedure was later extended also to reactions with hydrazines and organometallics.^{6b} More recently, (1,3-dioxolan-2-yl)silanes⁸ and benzotriazol(1-yl)carbazol(9-yl)-silylmethane derivatives⁹ have been used in transacetalization reactions with hydrazines and the latter also to generate the electrophile in an aldol condensation.

For more elaborate applications of formylsilanes in synthesis, preparative scale access to such compounds in isolated form is likely a prerequisite. To this end, only two procedures are currently available (Scheme 1): (i) insertion of carbon monoxide into the Zr–Si bond of TMS₃Si– and Ph₃Si–Zr complexes to generate the corresponding η^2 -complexes, which upon exposure to HCl produces the thermally stable Ph₃- and (Me₃Si)₃-formylsilanes,^{5a,b} and (ii) hydrolysis of (dimethoxymethyl)-triisopropylsilane under carefully controlled conditions to form *i*-Pr₃-formylsilane.¹⁰ Importantly, the *i*-Pr₃-formylsilane was in the latter work shown to participate in highly diastereoselective Wittig and aldol reactions.

The potential of using formylsilanes, and by extension their imine derivatives, as homologues to their nonenolizable aliphatic counterparts in multicomponent reactions,¹¹ together with the operational drawbacks of current procedures (high-pressure carbon monoxide and strong acid or elevated temperature and stoichiometric use of mercury) prompted us to investigate alternative methods for their preparation. Herein

Scheme 1. Preparative Synthesis of Formylsilanes



we present an operationally simple procedure for the syntheses of formylsilanes by oxidative cleavage of readily available α -silyl glycols.¹² On a 3 mmol scale, the formylsilane products were obtained in good isolated yields with homogeneities adequate for synthetic applications as demonstrated by diastereoselective aldol and HWE reactions.

The principal byproducts of the reaction, formaldehyde and sodium iodate, are water soluble and can thus be conveniently removed by partitioning the reaction mixture against pentane under an inert atmosphere. The mild conditions (i.e., neutral pH and ambient temperature) enabled the synthesis of *t*-BuMe₂-formylsilane and *t*-BuPh₂-formylsilane, previously not reported in isolated form.

The possibility of using oxidative diol cleavage for formylsilane synthesis was first evaluated by a screening of standard conditions and reagents using α -silyl glycol **1a**¹³ as the substrate (Table 1). NaIO₄ in a mixture of acetonitrile and water (2:1) gave complete consumption of the starting materials within one hour, and the desired formylsilane **2a** was formed in 61% yield along with minor amounts of the corresponding silanol **3a**.¹⁴ Longer reaction times, use of excess NaIO₄, or a more concentrated reaction mixture under

Received: September 25, 2013

Table 1. Reagents and Conditions for Oxidative Cleavage of α -Silyl Glycol **1a**^a

entry	oxidant (equiv)	solvent	time	yield (%) ^b 2a; 3a; 4a
1 ^b	NaIO ₄ (1.0)	MeCN/H ₂ O (2:1)	30 min	49; 5; 0
2 ^b	NaIO ₄ (1.0)	MeCN/H ₂ O (2:1)	1 h	61; 8; 0
3 ^b	NaIO ₄ (1.0)	MeCN/H ₂ O (2:1)	2 h	60; 13; 0
4 ^b	NaIO ₄ /silica (1.0)	DCM	22 h	1; 10; 0
5 ^b	NaIO ₄ (1.0)	EtOAc/H ₂ O (2:1)	22 h	3; 33; 0
6 ^b	H ₃ IO ₆ (1.2)	THF	10 min	0; 67; 0
7 ^c	PIDA (1.2)	DCM	10 min	0; 0; 38
8 ^c	Pb(OAc) ₄ (1.2)	MeCN	10 min	0; 0; 69
9 ^c	Mn(OAc) ₃ (4.0)	MeCN	5 h	0; 0; 37

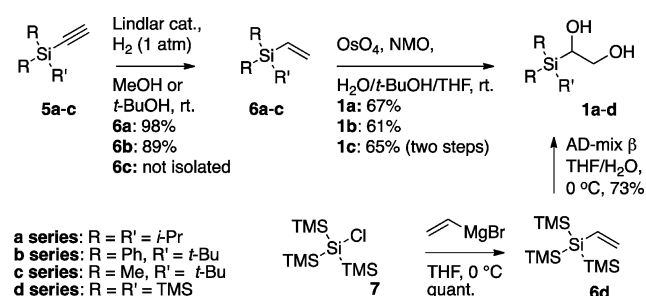
^aGeneral conditions: Diol **2a** (0.1 mmol), organic solvent (1 mL), water (0.5 mL), rt. ^bYield determined by ¹³C NMR using triisopropylsilane as internal standard. ^cYield determined by ¹H NMR using mesitylene as internal standard.

otherwise identical conditions gave lower yields due to increased overoxidation.

Silica-supported NaIO₄¹⁵ or a two-phase solvent system (EtOAc/water), gave very slow conversion and only trace amounts of product. Periodic acid gave a fast consumption of the starting material, even at 0 °C, but no formylsilane formation was detected. Oxidants like PIDA,¹⁶ Pb(OAc)₄¹⁷ and Mn(OAc)₃¹⁸ did not give detectable amounts of product **2a**; instead acyl-silyl acetal **4a**, formed via a radical Brook rearrangement,¹⁹ was obtained (yields are unoptimized).²⁰ The formation of **4a** with hypervalent iodine and Mn(OAc)₃ is noteworthy as these reagents have potential as less toxic alternatives to Pb(OAc)₄ for the generation of α -silyloxy carbon radicals in this context.

The successful cleavage of diol **1a** with NaIO₄ prompted an investigation of the scalability and substrate scope of these conditions. Multigram preparation of α -silyl glycols **1a–c** for this study was performed via a two-step procedure starting with a partial hydrogenation of alkynylsilanes **5a–c** with Lindlar catalyst.²¹ Upjohn-dihydroxylation of the resulting vinylsilanes **6a–c**²² then gave the corresponding α -silyl glycols **1a–c** in good yields over two steps. In contrast, the attempted dihydroxylation of (TMS₃Si)-vinylsilane **6d** gave only a complex mixture with OsO₄/NMO. The desired α -(TMS₃Si)-glycol **1d** could, however, be efficiently formed by dihydroxylation with AD-mix β (Scheme 2).^{23,24}

When conducting the cleavage of α -silyl glycol **1a** on a preparative scale (3 mmol), the reaction was complete in just 20 min, enabling the isolation of formylsilane **2a** in good yield together with only trace amounts of silanol (5%) (Table 2). The same conditions translated well also to the synthesis and isolation of the new *t*-BuPh₂- and *t*-BuMe₂-formylsilanes **2b** and **2c**. Access to these compounds is particularly attractive, as nucleophilic addition to *t*-BuMe₂-formylsilane (**2b**) constitutes an entry to α -(*t*-BuMe₂Si)-alcohols, a motif previously exploited as a chiral primary alcohol equivalent,²⁵ and derivatives carrying a *t*-BuPh₂-group have added value as a masked hydroxyl group.²⁶ Partial evaporation of the semi-

Scheme 2. Synthesis of α -Silyl Glycols **1a–d**Table 2. Preparative Synthesis of Formylsilanes **2a–c**^a

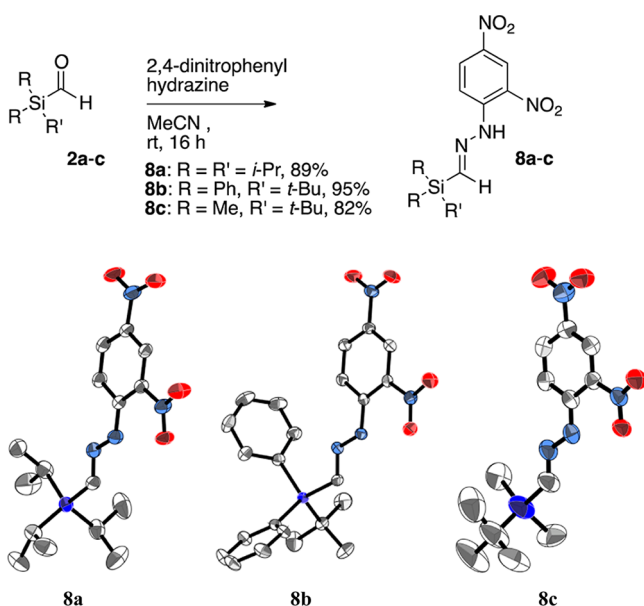
1.	2a, 88% (5%) ^b
2.	2b, 88% (5%) ^b
3.	2c, 61% (4%) ^b
4.	2d, 0%

^aIsolated yields are corrected for silanol content. ^bMol % of silanol in isolated product (¹H NMR).

volatile product and silanol during solvent removal accounts for the somewhat reduced isolated yield in Table 2, entry 3. In contrast to diols **1a–c**, cleavage of α -(TMS₃Si)-glycol (**1d**) gave only unspecific decomposition. This result is attributed, at least in part, to the propensity of TMS₃-silanes to be oxidized at the Si–Si bond.²⁷

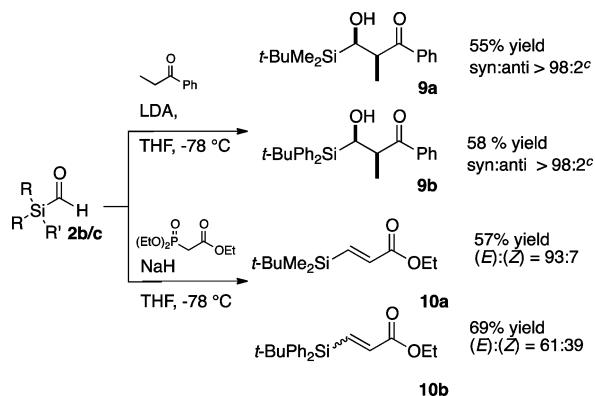
In agreement with the literature data for known formylsilanes, *t*-BuPh₂-formylsilane (**2b**) and *t*-BuMe₂-formylsilane (**2c**) display properties characteristic of a highly polarized C=O bond (**2b**: ¹³C NMR δ = 243 (CO) ppm, IR ν_{CO} = 1650 cm^{−1}; **2c**: ¹³C NMR δ = 246 (CO) ppm, IR ν_{CO} = 1648 cm^{−1}). Molecular ions of the fragile structures were not detected by MS-ESI. For analytical purposes, the isolated formylsilanes were instead converted into their corresponding known 2,4-dinitrophenylhydrazones **8a–c** (Scheme 3).^{8,9} Noteworthy in this context is the essentially quantitative formation of *t*-BuPh₂-derivative **8b** from **2b**. Recrystallization of the hydrazones from MeOH gave single crystals from which the solid-state structures were solved by X-ray crystallography.²⁸ In agreement with the apparent stability of these compounds, virtually no elongation of the C=N bonds (1.27–1.28 Å) were found compared to that of related hydrazone derivatives of aliphatic aldehydes (typically ranging from 1.25 to 1.26 Å).²⁹

The usefulness of the title conditions to provide formylsilanes for applications in synthesis was investigated by subjecting *i*-Pr-formylsilane (**2a**) to the known *syn*-selective aldol reaction with a *Z*-enolate of propiophenone.³⁰ The yield and selectivity of this reaction (64%; *syn:anti* > 98:2) followed that previously reported for this substrate (65%, *syn:anti* > 97:3).^{10a} Formylsilanes **2b** and **2c** were also investigated as substrates in this reaction and were both found to give the

Scheme 3. Synthesis and Crystal Structures of Hydrazones 8a–c^a

^aThermal ellipsoid plots at 30% probability; hydrogen atoms were omitted for clarity.

corresponding aldols with complete diastereoselectivities and moderate isolated yields (Scheme 4). The propensity of the *t*-

Scheme 4. Diastereoselective Derivatization of Formylsilanes 2b and 2c^{a,b}

^aIsolated yields. ^bThe selectivities were quantified by ¹H NMR spectroscopy of the crude reaction mixtures. ^cNo minor diastereomer detected. The relative configuration was assigned by analogy: see ref 10a and references therein.

BuPh₂ group to migrate after addition of the enolate leading to a reduced yield could be suppressed by quenching the reaction immediately after addition of the enolate. The library of available transformations for formylsilanes was also expanded to include *E*-selective olefinations by reacting silanes 2b and 2c under Horner–Wadsworth–Emmons (HWE) conditions.³¹ In this reaction *t*-BuMe₂ formylsilane (2c) gave a good geometric selectivity (*E*:*Z* = 93:7), whereas *t*-BuPh₂ formylsilane (2b) gave only a fair selectivity (*E*:*Z* = 61:39) but a higher isolated yield.

In conclusion, an operationally convenient procedure for the synthesis of formylsilanes by oxidative cleavage of readily available α-silyl glycols with NaIO₄ is described. The conditions

enable access to formylsilanes in isolated form with good to moderate isolated yields. The mildness of the protocol is highlighted by synthesis, isolation, and characterization of the sensitive *t*-BuMe₂- and *t*-BuPh₂-formylsilanes 2b and 2c. The formylsilane products derived from this procedure were shown to efficiently participate in diastereoselective aldol and HWE reactions with up to excellent levels of diastereoselectivity. Studies on expanding this methodology as well as investigations of the properties and applications of these potentially very useful compounds in synthesis are currently under way.

EXPERIMENTAL SECTION

Optimization Study for Oxidative Cleavage of α-Silyl Glycol 1a. For details, see Table 1. To a vial charged with oxidant and a magnetic stir-bar (for entries 1–3 and 5, dissolved in degassed water, 0.5 mL) was added a solution of α-silyl glycol 1a (21.8 mg, 0.1 mmol) in the solvent indicated (1 mL, degassed). The resulting mixture was stirred for the time and temperature indicated, after which pentane (3 mL, degassed) and water (3 mL, degassed) were added sequentially. The aqueous layer was removed by syringe, and the organic layer was concentrated under reduced pressure and then backfilled with nitrogen. The yields were determined by quantitative ¹³C NMR³² for entries 1–6 and ¹H NMR for entries 7–9 using triisopropylsilane and mesitylene, respectively, as internal standard.

2-Hydroxy-1-((triisopropylsilyloxy)ethyl) acetate (4a). The NMR sample used in Table 1 entry 7 was concentrated and purified by silica-gel chromatography eluting with EtOAc/petroleum ether (0–20% EtOAc) to yield acyl-silyl acetal 4a (8.3 mg, 30%) as a clear oil, >95% pure by NMR spectroscopy and a single spot by TLC: *R*_f = 0.53 in 1:3 EtOAc:petroleum ether; ¹H NMR (400 MHz, C₆D₆) δ 6.31 (t, *J* = 4.7 Hz, 1H), 3.57 (t, *J* = 5.3 Hz, 2H), 1.68 (s, 3H), 1.52 (t, *J* = 6.3 Hz, 1H), 1.12–1.04 (m, 21H) ppm; ¹³C NMR (101 MHz, C₆D₆) δ 169.8, 92.4, 65.7, 20.9, 18.1, 18.0, 12.5 ppm; IR (CHCl₃ film) 3020 (m), 2948 (w), 2869 (m), 1734 (s), 1464 (m), 1375 (m) cm⁻¹; HRMS-ESI (*m/z*) [*M* + *K*]⁺ calcd for C₁₃H₂₈KO₄Si, 315.1400, found 315.1394.

General Procedure for the Oxidative Cleavage of α-Silyl Glycols 1a–c. To a gently stirred solution of diol (1 equiv) in MeCN (10 mL/mmol diol, degassed) was added NaIO₄ (1 equiv) dissolved in water (5 mL/mmol diol, degassed) under a nitrogen atmosphere. Within a few minutes the mixture turned yellow, and a white precipitate started to form. After stirring for a total of 20 min (1a) or 30 min (1b and 1c), pentane (20 mL/mmol diol, degassed) and water (10 mL/mmol diol, degassed) were added sequentially. The aqueous layer was removed by syringe, and the remaining organic layer was concentrated in the reaction vessel under reduced pressure (house vacuum 20 mbar), after which it was backfilled with nitrogen to leave the corresponding formylsilanes as yellow oils (2a,b) or a yellow amorphous solid (2c).

Formyltriisopropylsilane (2a).^{10a} Scale: 3.0 mmol of diol 1a. Yield: 556 mg, 88% (5% silanol), isolated as a yellow oil; ¹H NMR (400 MHz, C₆D₆) δ 12.07 (s, 1H), 1.09–1.05 (m, 3H), 0.99 (d, *J* = 6.5 Hz, 18H) ppm; ¹³C NMR (101 MHz, C₆D₆) δ 246.7, 18.5, 10.4 ppm; IR (CHCl₃ film) 1647 (ν_{CO}) cm⁻¹.

Formyl-*tert*-butyldiphenylsilane (2b). Scale: 3.0 mmol of diol 1b. Yield: 743 mg, 88% (5% silanol), isolated as a yellow oil; ¹H NMR (400 MHz, C₆D₆) δ 12.14 (s, 1H), 7.62–7.53 (m, 4H), 7.16–7.09 (m, 6H), 1.09 (s, 9H) ppm; ¹³C NMR (101 MHz, C₆D₆) δ 242.5, 136.5, 131.1, 130.4, 128.5, 27.4, 18.9 ppm; IR (CHCl₃ film) 1650 (ν_{CO}) cm⁻¹.

Formyl-*tert*-butyldimethylsilane (2c). Scale: 5.0 mmol of diol 1c. Yield: 459 mg, 61% (4% silanol), isolated as a yellow amorphous solid; ¹H NMR (400 MHz, C₆D₆) δ 11.89 (s, 1H), 0.81 (s, 9H), –0.08 (s, 6H) ppm; ¹³C NMR (101 MHz, C₆D₆) δ 245.7, 26.4, 16.9, –8.8 ppm; IR (CHCl₃ film) 1648 (ν_{CO}) cm⁻¹.

General Procedure for the Hydrazone Formation. To 2,4-dinitrophenylhydrazine (1.48 g, 5.0 mmol, 33% in H₂O) was added formylsilane (3.05–4.10 mmol) in MeCN (50 mL, degassed) under a

nitrogen atmosphere. The resulting mixture was stirred at ambient temperature for 20 h, and then concentrated, suspended in CHCl_3 (50 mL), and filtered. The filtrate was concentrated and purified by silica-gel chromatography eluting with EtOAc/petroleum ether (0–10% EtOAc) to yield the corresponding hydrazones **8a–c**.

(E)-1-(2,4-Dinitrophenyl)-2-((triisopropylsilyl)methylene)hydrazine (8a).^{9,10a} Scale: 3.34 mmol of formylsilane **2a**. Yield: 1.19 g, 89%, isolated as a yellow solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.74 in 1:10 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 11.10 (s, 1H), 9.14 (d, J = 2.6 Hz, 1H), 8.34 (ddd, J = 9.6, 2.6, 0.6 Hz, 1H), 7.99 (d, J = 9.6 Hz, 1H), 7.82 (d, J = 1.1 Hz, 1H), 1.35–1.25 (m, 3H), 1.15 (d, J = 7.2 Hz, 18H) ppm; IR (CHCl_3 film) 3301 (m), 3021 (m), 2867 (m), 1618 (s), 1595 (m), 1517 (m), 1338 (s), 1317 (s) cm^{-1} ; mp 112.1–112.5 °C (recrystallized from warm MeOH by slow cooling).

(E)-1-((tert-Butyldiphenylsilyl)methylene)-2-(2,4-dinitrophenyl)hydrazine (8b).⁹ Scale: 4.10 mmol of formylsilane **2b**. Yield: 1.75 g, 95%, isolated as a yellow solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.34 in 1:10 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 11.27 (s, 1H), 9.14 (d, J = 2.5 Hz, 1H), 8.33 (dd, J = 9.5, 2.0 Hz, 1H), 8.10 (d, J = 1.1 Hz, 1H), 7.95 (d, J = 9.5 Hz, 1H), 7.74–7.64 (m, 4H), 7.51–7.36 (m, 6H), 1.22 (s, 9H) ppm; IR (CHCl_3 film) 3300 (m), 3019 (m), 2861 (w), 1618 (s), 1596 (m), 1515 (m), 1339 (s), 1317 (s) cm^{-1} ; mp 128.2–128.5 °C (recrystallized from warm MeOH by slow cooling).

(E)-1-((tert-Butyldimethylsilyl)methylene)-2-(2,4-dinitrophenyl)hydrazine (8c).⁹ Scale: 3.05 mmol of formylsilane **2c**. Yield: 809 mg, 82%, isolated as a yellow solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.50 in 1:10 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 11.09 (s, 1H), 9.13 (d, J = 2.6 Hz, 1H), 8.33 (ddd, J = 9.6, 2.6, 0.7 Hz, 1H), 8.01 (d, J = 9.6 Hz, 1H), 7.82 (d, J = 1.1 Hz, 1H), 1.00 (s, 9H), 0.23 (s, 6H) ppm; IR (CHCl_3 film) 3302 (m), 3020 (m), 2862 (w), 1618 (s), 1595 (m), 1517 (m), 1338 (s), 1317 (s) cm^{-1} ; mp 135.1–136.9 °C (recrystallized from warm MeOH by slow cooling).

General Procedure for the Partial Hydrogenation to Alkenes 6a,b. To a stirred solution of silylacetylene (1.0 equiv) and quinoline (0.05 equiv) in methanol (0.8 M) was added Lindlar catalyst (5% Pd on CaCO_3 poisoned with lead, 0.3%), under a nitrogen atmosphere. The atmosphere was changed to H_2 (H_2 from a balloon) and purged three times. Upon complete consumption of the alkyne (TLC control), the mixture was filtered through a plug of Celite and concentrated. The crude mixture was redissolved in petroleum ether, filtered through a plug of silica, and concentrated to yield the corresponding vinyl silanes **6a,b**.

Triisopropyl(vinyl)silane (6a).³³ Yield: 98%, isolated as a clear oil, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.96 in petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 6.10–5.98 (m, 2H), 5.71 (dd, J = 17.5, 7.1 Hz, 1H), 1.07–1.02 (m, 21H) ppm.

tert-Butyldiphenyl(vinyl)silane (6b).³⁴ Yield: 89%, isolated as a clear oil, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.48 in petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 7.67–7.62 (m, 4H), 7.45–7.36 (m, 6H), 6.60 (dd, J = 20.3, 14.8 Hz, 1H), 6.30 (dd, J = 14.8, 3.8 Hz, 1H), 5.74 (dd, J = 20.3, 3.8 Hz, 1H), 1.12 (s, 9H) ppm.

General Procedure for Dihydroxylation of Vinyl Silanes 6a,b. To a stirred solution of alkene (1.0 equiv) and NMO (2.0 equiv) in *t*-BuOH, THF, and water (ratio 1.0:1.4:1.0, 0.6 M) was added OsO_4 (0.005 equiv, 2.5% in *t*-BuOH) under a nitrogen atmosphere. After stirring at ambient temperature for 26 h, the reaction was quenched by addition of Na_2SO_3 (0.3 g/mmol alkene), and the resulting mixture was stirred for an additional 30 min. The reaction was then extracted with petroleum ether (4 mL/mmol alkene), washed with water (2 \times 4 mL/mmol alkene), and concentrated under reduced pressure. The resulting crude product was dissolved in Et_2O (2 mL/mmol alkene), filtered through a plug of silica, and concentrated. Crystallization from pentane (0.5 M) at –78 °C gave the corresponding diols **1a,b**. The mother liquor was concentrated and purified by silica-gel chromatography, eluting with EtOAc/petroleum ether (0–25% EtOAc), to increase the yield.

1-(Triisopropylsilyl)ethane-1,2-diol (1a).¹³ Yield: 67% (60% from crystallization and 7% from chromatography), isolated as a white solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.36 in 1:3 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 3.96–3.74 (m, 3H), 2.01 (bs, 2H), 1.19–1.06 (m, 21H) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 66.6, 66.0, 19.1, 19.0, 10.7 ppm; IR (CHCl_3 film) 3364 (s, br), 2943 (s), 2866 (s), 1434 (m), 1050 (m), 882 (m) cm^{-1} ; HRMS-ESI (m/z) [$M + \text{Na}$]⁺ calcd for $\text{C}_{11}\text{H}_{26}\text{NaO}_2\text{Si}$, 241.1600, found 241.1599; mp 52.5–52.8 °C (recrystallized from pentane at –78 °C).

1-(tert-Butyldiphenylsilyl)ethane-1,2-diol (1b). Yield: 61% (20% from crystallization and 41% from chromatography), isolated as a white solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.32 in 1:3 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 7.75–7.69 (m, 2H), 7.69–7.62 (m, 2H), 7.47–7.30 (m, 6H), 4.23 (dd, J = 10.5, 3.1 Hz, 1H), 3.83–3.63 (m, 2H), 2.09 (bs, 2H), 1.16 (s, 9H) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 136.6, 136.3, 133.2, 132.8, 129.71, 129.69, 128.0, 66.4, 65.7, 28.4, 18.5 ppm. The spectra contain a signal overlap in the aromatic region; IR (CHCl_3 film) 3376 (s, br), 3072 (w), 3013 (w), 2859 (m), 1427 (m), 1105 (m), 1053 (m), 882 (m) cm^{-1} ; HRMS-ESI (m/z) [$M + \text{Na}$]⁺ calcd for $\text{C}_{18}\text{H}_{24}\text{NaO}_2\text{Si}$, 323.1443, found 323.1444; mp 86.6–87.1 °C (recrystallized from pentane at –78 °C).

1-(tert-Butyldimethylsilyl)ethane-1,2-diol (1c). To a stirred solution of *tert*-butyldimethylsilylacetylene (4.94 g, 35.2 mmol, 1 equiv) and quinoline (207 μL , 1.76 mmol, 5%) in *t*-BuOH (35.2 mL) was added Lindlar catalyst (5% Pd on CaCO_3 poisoned with lead, 225 mg, 0.105 mmol, 3%), under a nitrogen atmosphere. The atmosphere was changed to H_2 (purged three times using H_2 from a balloon). After 3 h the mixture was filtered through a plug of Celite. *t*-BuOH (17.6 mL), water (17.6 mL), NMO (50% in water, 14.6 mL, 70.4 mmol, 2 equiv), and OsO_4 (2.5% in *t*-BuOH, 1.78 mL, 0.176 mmol, 0.5%) were added. After stirring at ambient temperature for 1 h the reaction was quenched by addition of Na_2SO_3 (10 g) and stirred for additionally 30 min. The mixture was diluted with water (200 mL), extracted with *tert*-butyl methylether (2 \times 200 mL), and concentrated. Purification by silica-gel chromatography eluting with EtOAc/petroleum ether (0–25% EtOAc) yielded diol **1c** (4.02 g, 65%) as a white solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.18 in 1:3 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 3.83–3.68 (m, 2H), 3.63 (dd, J = 9.4, 3.2 Hz, 1H), 2.05 (s, 2H), 0.94 (s, 9H), 0.05 (s, 3H), –0.03 (s, 3H) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 66.1, 66.0, 27.0, 16.8, –7.4, –8.0 ppm; IR (CHCl_3 film) 3377 (s, br), 2954 (m), 2858 (m), 1464 (m), 1057 (m) cm^{-1} ; HRMS-ESI (m/z) [$M + \text{Na}$]⁺ calcd for $\text{C}_8\text{H}_{20}\text{NaO}_2\text{Si}$, 199.1130, found 199.1136; mp 65.8–66.3 °C (from EtOAc:petroleum ether).

Tri(trimethylsilyl)(vinyl)silane (6d).³⁵ To chlorotris(trimethylsilyl)silane (8.39 g, 30 mmol) was added vinyl magnesium bromide (0.7 M in THF, 64.3 mL, 45 mmol) at 0 °C under a nitrogen atmosphere. The resulting mixture was stirred for 20 min and then quenched by addition of NH_4Cl (aq., sat.). The resulting mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 ($\times 2$). The organic layer was dried using a phaseseparator and concentrated to yield alkene **6d** (8.27 g, 100%) as a white waxy solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.91 in 1:10 EtOAc:petroleum ether; ^1H NMR (400 MHz, CDCl_3) δ 6.08 (dd, J = 19.8, 14.0 Hz, 1H), 5.93 (dd, J = 14.0, 3.8 Hz, 1H), 5.66 (dd, J = 19.8, 3.8 Hz, 1H), 0.17 (s, 27H) ppm.

Tri(trimethylsilyl)silyl)ethane-1,2-diol (1d). To a solution of $\text{K}_3\text{Fe}(\text{CN})_6$ (0.98 g, 3.0 mmol), K_2CO_3 (0.41 g, 3.0 mmol), and (DHQD)₂-PHAL (78 mg, 0.1 mmol) in *t*-BuOH:water 1:1 (14 mL) was added $\text{K}_2\text{OsO}_2(\text{OH})_2$ (7.4 mg, 0.02 mmol). The resulting yellow mixture was cooled to 0 °C (some precipitation was observed). Vinyl silane **6d** (250 mg, 0.91 mmol) was added in one portion dissolved in *t*-BuOH (1.5 mL) followed by addition of water (1.5 mL). The resulting mixture was stirred at 0 °C for 20 h and then quenched by addition of Na_2SO_3 (0.5 g) followed by stirring for an additional 30 min. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 . The combined organic layers were dried with Na_2SO_4 , filtered, and concentrated under reduced pressure.

Purification by silica-gel chromatography, eluting with EtOAc/petroleum ether (3.13–12.5% EtOAc), yielded diol **1d** (204 mg, 73%) as a white solid, >95% pure by NMR spectroscopy and a single spot by TLC; [α]_D²⁵ +7.9 (c = 0.7, CH₂Cl₂); R_f = 0.59 in 1:3 EtOAc:petroleum ether; ¹H NMR (400 MHz, CDCl₃) δ 4.06–3.95 (m, 1H), 3.81–3.68 (m, 2H), 2.01 (bs, 1H), 1.76 (bs, 1H), 0.21 (app. d, J = 2.6 Hz, 27H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 68.5, 67.1, 1.7 ppm; IR (CHCl₃ film) 3401 (s, br), 2949 (m), 2893 (m), 1397 (m), 1059 (m) cm⁻¹; HRMS-ESI (m/z) [M + Na]⁺ calcd for C₁₁H₃₂NaO₂Si₄, 331.1377, found 331.1376; mp 102.0–103.5 °C (from EtOAc:petroleum ether).

General Procedure for Aldol Reaction with Formylsilanes.

To a stirred solution of diisopropylamine (2 equiv) in THF (0.2 M) was added *n*-BuLi (1.6 M in hexanes, 1.5 equiv) at –78 °C under a nitrogen atmosphere. The temperature was raised to 0 °C over 20 min and then reduced back to –78 °C. Propiophenone (1.5 equiv) was added dropwise over 1 min, and the resulting mixture was stirred for 20 min. The resulting enolate solution was then transferred by cannula to a solution of freshly prepared formylsilane (1 equiv, corrected for silanol) in THF (0.2 M) at –78 °C. After complete consumption of the formylsilane (5 s for **2a,b** and 2 h for **2c**) the reaction was quenched by addition of AcOH (10% v/v, in MeOH) or NH₄Cl (aq. sat.), diluted with water (50 mL/mmol formylsilane), extracted with Et₂O (2 \times 50 mL/mmol formylsilane), dried with Na₂SO₄, filtered, and concentrated. Purification of the crude product by silica-gel chromatography, eluting with EtOAc/petroleum ether (0–10% EtOAc), yielded the aldol adduct.

(2*R**,3*R**)-3-(*tert*-Butyldimethylsilyl)-3-hydroxy-2-methyl-1-phenylpropan-1-one (**9a**). Yield: 55%, isolated as a clear oil, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.24 in 1:20 EtOAc:petroleum ether; ¹H NMR (400 MHz, CDCl₃) δ 7.95–7.90 (m, 2H), 7.62–7.56 (m, 1H), 7.52–7.46 (m, 2H), 4.01 (dd, J = 3.3, 1.9 Hz, 1H), 3.57 (qd, J = 7.2, 1.9 Hz, 1H), 2.84 (d, J = 3.4 Hz, 1H), 1.32 (d, J = 7.2 Hz, 3H), 0.96 (s, 9H), 0.15 (s, 3H), 0.05 (s, 3H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 206.4, 135.8, 133.5, 129.0, 128.6, 63.3, 42.6, 26.9, 16.9, 12.9, –6.5, –7.2 ppm; IR (CHCl₃ film) 3516 (m, br), 2952 (m), 2928 (m), 1666 (s), 1449 (m), 972 (m) cm⁻¹; HRMS-ESI (m/z) [M + Na]⁺ calcd for C₁₆H₂₆NaO₂Si, 301.1600, found 301.1598.

(2*R**,3*R**)-3-(*tert*-Butyldiphenylsilyl)-3-hydroxy-2-methyl-1-phenylpropan-1-one (**9b**). Yield: 58%, isolated as a white solid, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.59 in 1:10 EtOAc:petroleum ether; ¹H NMR (400 MHz, C₆D₆) δ 8.13–8.07 (m, 2H), 7.75–7.69 (m, 2H), 7.59–7.55 (m, 2H), 7.24–7.13 (m, 6H), 7.03–6.98 (m, 1H), 6.93–6.87 (m, 2H), 4.70 (dd, J = 2.8, 1.5 Hz, 1H), 3.60 (d, J = 2.8 Hz, 1H), 3.39 (qd, J = 7.2, 1.3 Hz, 1H), 1.22 (s, 9H), 1.19 (d, J = 7.2 Hz, 3H) ppm; ¹³C NMR (101 MHz, C₆D₆) δ 206.4, 137.7, 136.6, 135.9, 134.7, 134.2, 133.2, 129.74, 129.72, 128.8, 128.7, 128.3, 127.8, 65.8, 41.7, 28.6, 18.8, 13.5 ppm; IR (CHCl₃ film) 3510 (w, br), 3017 (m), 2951 (m), 2862 (m), 1665 (s), 1428 (m), 1106 (m) cm⁻¹; HRMS-ESI (m/z) [M + Na]⁺ calcd for C₂₆H₃₀NaO₂Si, 425.1913, found 425.1913; mp 105.8–107.7 °C (from EtOAc:petroleum ether).

(2*R**,3*R**)-3-(*triisopropylsilyl*)-3-hydroxy-2-methyl-1-phenylpropan-1-one (**11**).^{10a} Yield: 64%, isolated as a clear oil, >95% pure by NMR spectroscopy and a single spot by TLC; R_f = 0.60 in 1:10 EtOAc:petroleum ether; ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.91 (m, 2H), 7.62–7.56 (m, 1H), 7.53–7.46 (m, 2H), 4.18 (dd, J = 3.1, 1.5 Hz, 1H), 3.65 (qd, J = 7.2, 1.4 Hz, 1H), 2.93 (d, J = 3.3 Hz, 1H), 1.40 (d, J = 7.2 Hz, 3H), 1.27–1.19 (m, 3H), 1.18–1.11 (m, 18H) ppm.

General Procedure for HWE Olefination of Formylsilanes. To a stirred solution of triethyl phosphonoacetate (2.0 equiv) in THF (0.3 M) was added NaH (60% in mineral oil, 1.5 equiv), under a nitrogen atmosphere, at 0 °C. After stirring for 30 min, the mixture was cooled to –78 °C and transferred by cannula to a solution of formylsilane (1.0 equiv) in THF (0.3 M). After stirring at –78 °C for 2 h, the reaction was quenched by addition of NH₄Cl (aq. sat.). The resulting mixture was poured onto water, extracted with *tert*-butyl methylether (2 \times 60 mL/mmol), dried (MgSO₄), filtered, and concentrated. Purification by

silica-gel chromatography, eluting with EtOAc/petroleum ether (5% EtOAc), yielded the vinyl silane.

(*E*)- and (*Z*)-Ethyl 3-(*tert*-butyldimethylsilyl)acrylate (**10a**). Yield: 57%, (*E*):(*Z*) = 93:7, isolated as a clear oil, >95% pure by NMR spectroscopy and two spots by TLC; R_f major = 0.54; minor = 0.51 in 1:20 EtOAc:petroleum ether; ¹H NMR (400 MHz, CDCl₃) δ (*E*-isomer) 7.27 (d, J = 18.9 Hz, 1H), 6.26 (d, J = 18.9 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 6H) ppm. (*Z*-isomer) 6.59 (d, J = 14.9 Hz, 1H), 6.54 (d, J = 14.9 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H), 0.92 (s, 9H), 0.17 (s, 6H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ (*E*-isomer) 165.8, 147.4, 135.2, 60.5, 26.4, 16.5, 14.3, –6.5 ppm; IR (CHCl₃ film) 2954 (m), 2924 (s), 2855 (m), 1721 (m), 1463 (m), 997 (m) cm⁻¹; HRMS-ESI (m/z) [M + H]⁺ calcd for C₁₁H₂₃O₂Si, 215.1467, found 215.1472.

(*E*)- and (*Z*)-Ethyl 3-(*tert*-butyldiphenylsilyl)acrylate (**10b**). Yield: 69%, (*E*):(*Z*) = 61:39, isolated as a clear oil, >95% pure by NMR spectroscopy and two spots by TLC; R_f major = 0.43; minor = 0.41 in 1:20 EtOAc:petroleum ether; ¹H NMR (400 MHz, CDCl₃) δ (*E*-isomer) 7.68 (d, J = 18.8 Hz, 1H), 7.60–7.54 (m, 4H), 7.45–7.30 (m, 6H), 6.23 (d, J = 18.8 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.1 Hz, 3H), 1.11 (s, 9H) ppm; (*Z*-isomer) 7.70–7.66 (m, 4H), 7.45–7.30 (m, 6H), 6.94 (d, J = 14.9 Hz, 1H), 6.89 (d, J = 14.9 Hz, 1H), 3.40 (q, J = 7.1 Hz, 2H), 0.99 (s, 9H), 0.58 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (101 MHz, CDCl₃) δ (*E*-isomer) 165.8, 143.8, 138.8, 136.4, 133.1, 129.8, 128.0, 60.9, 27.8, 18.5, 14.4 ppm; (*Z*-isomer) 166.1, 142.1, 140.7, 135.5, 133.9, 129.1, 127.6, 60.1, 27.3, 18.5, 13.5 ppm; IR (CHCl₃ film) 2959 (m), 2929 (m), 2858 (m), 1720 (s), 1427 (m), 999 (m) cm⁻¹; HRMS-ESI (m/z) [M + Na]⁺ calcd for C₂₁H₂₆NaO₂Si, 361.1600, found 361.1599.

■ ASSOCIATED CONTENT

Supporting Information

¹H and ¹³C NMR spectra, X-ray diffraction structures, and crystallographic data for compounds **8a–c** in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Swedish Research Council and the Royal Physiographical Society for financial support.

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