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Chemoselective hydrosilylation of hydroxyketones

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Abstract

A chemoselective method for the hydrosilylation of ketones has been developed, using the combination of triphenylsilane and a catalyst prepared from $\text{Ni}(\text{COD})_2$ and the simple *N*-heterocyclic carbene IMes. The most notable feature of this method is that free hydroxyls are largely unaffected, thus providing a simple one-step procedure for the conversion of hydroxyketones to mono-protected diols, wherein the protecting group is exclusively installed on the ketone-derived hydroxyl. The process is typically high yielding with both simple ketones and more complex hydroxyketone substrates.

Keywords

Hydrosilylation; Site-selective; Chemoselective; Nickel; Dehydrogenative silylation

1. Introduction

The addition or condensation of trialkylsilanes to either ketone or alcohol functional groups has been widely developed using the catalytic properties of a range of transition metal and Lewis acid catalysts.¹ The hydrosilylation of ketones proceeds by direct addition of the silicon–hydrogen bond across the carbonyl functionality,² whereas the catalyzed addition of trialkylsilanes to alcohols proceeds with the extrusion of hydrogen gas by a dehydrogenative silylation.³ Therefore, irrespective of the oxidation state of the starting material employed (ketone or alcohol), a simple silyl ether results (Scheme 1).

Despite the large number of reports describing either the hydrosilylation of ketones or the dehydrogenative silylation of alcohols, little attention has been placed on the development of the chemoselective addition of silanes to hydroxyketones. Of the few reports that address this issue, the dehydrogenative silylation of alcohols typically proceeds faster than the competing hydrosilylation of carbonyls.⁴ The direct silylation of alcohols in the presence of carbonyl functionality is straightforward using electrophilic silylation reagents, such as chlorides or triflates. However, general protocols for the hydrosilylation of ketones in the presence of unprotected alcohols have not been developed. In many cases, such a transformation requires four distinct operations: alcohol protection, ketone reduction, orthogonal protection of the newly formed hydroxyl, then removal of the initially installed protecting group (Scheme 2). Devising a one-step process that accomplishes this conversion would streamline synthetic routes that require this conversion. Herein, we describe that ketone hydrosilylations readily proceed in the presence of free hydroxyls with the specific combination of a nickel–*N*-heterocyclic carbene catalyst with triphenylsilane, thus providing an efficient one-step process for this commonly-used chemical conversion (Scheme 2).

2. Results and discussion

In the course of screening conditions for the hydrosilylation of ketones in connection with a program devoted to the reductive glycosylation of ketones,⁵ we observed that carbohydrate-derived silanes were effective in both the hydrosilylation of ketones and the dehydrogenative silylation of alcohols when nickel(0) complexes of *N*-heterocyclic carbenes were employed as the catalyst. In contrast, triphenylsilane was especially effective in the nickel-catalyzed hydrosilylation of ketones, but was relatively ineffective for the dehydrogenative silylation of alcohols. We therefore anticipated that the combination of triphenylsilane with Ni(0)–NHC catalysts might be effective for chemoselective ketone hydrosilylations of hydroxyketone substrates.

When examining the potential for chemoselective ketone hydrosilylations using hydroxyketone substrates, common hydrosilylation catalysts, such as Cu–IMes complexes,² Wilkinson's catalyst,⁶ and Karstedt's catalyst⁷ typically produced complex reaction mixtures. In these cases, the alcohol dehydrogenative silylation pathway was typically preferred, and substantial bis-silylation of both the alcohol and ketone functionality was observed in reactions carried out with complete consumption of the hydroxyketone substrate. In contrast, the use of Ph₃SiH with a catalyst derived from a mixture of Ni(COD)₂, 1,3-bis-(2,4,6-trimethylphenyl)imidazolium hydrochloride (IMes·HCl), and *t*-BuOK (0.1 equiv of each) provided a highly active combination for ketone hydrosilylations at rt, with minimal competing reactivity of the hydroxyl functionality when hydroxyketones substrates were employed.^{8,9}

Several examples of simple hydrosilylations of cyclic and acyclic ketones were conducted to illustrate that a range of substitution patterns are tolerated in the process. For example, an unhindered enolizable cyclohexanone derivative underwent facile hydrosilylation in near quantitative yield (Table 1, entry 1), as did a much more hindered derivative that possessed quaternary substitution at both α-positions (Table 1, entry 2). A simple acyclic methyl ketone also underwent high-yielding hydrosilylation to afford the corresponding triphenylsilyl ether (Table 1, entry 3). Both menthone and fenchone underwent high-yielding hydrosilylation as well, although diastereoselectivities were modest to poor in these cases (Table 1, entries 4 and 5). A limitation of this process is that strong back-bonding ligands inhibit the catalyst reactivity. For this reason, conjugated enones were generally unreactive, and their presence in polyfunctional molecules prevented efficient reduction of isolated ketones that would otherwise be reactive.

Following these studies with simple ketones, a range of hydroxyketones were examined (Table 2). By employing only 1.1 equiv of Ph₃SiH, complete conversion was noted in most cases, with very high selectivity for ketone hydrosilylation. Under these conditions, very little dehydrogenative silylation of the alcohol functionality was observed.

With a simple hydroxyketone substrate, hydrosilylation of the methyl ketone was observed in good yield (Table 2, entry 1), and only 4% of the bis-silylated derivative was observed. With 2-hydroxy-3-pinanone, highly diastereoselective ketone hydrosilylation was observed to afford the mono-protected *syn*-diol derivative in a 13:1 ratio with the *anti* diastereomer as a minor component of the reaction mixture (Table 2, entry 2). With a hydroxyadamantanone derivative, highly chemoselective ketone hydrosilylation was observed to provide monosilylated product in 84% as a 1.2:1 ratio of diastereomers, with only 2% of the bis-silylated derivative observed (Table 2, entry 3).

A set of steroid derivatives were also examined and uniformly provided chemoselective ketone hydrosilylation. Hydrosilylation of a D-ring ketone proceeded to provide a 2:1 ratio of diastereomers without affecting the A-ring hydroxyl (Table 2, entry 4). Similarly, a

simple methyl ketone was hydrosilylated with 2.8:1 diastereoselectivity also without affecting the A-ring hydroxyl (Table 2, entry 5). Finally, chemoselective hydrosilylation of the A-ring ketone in a saturated derivative proceeded in 2.4:1 diastereoselectivity to provide the anticipated monosilylated product (Table 2, entry 6).

Given the air-sensitive nature of $\text{Ni}(\text{COD})_2$, the corresponding procedure employing stable and inexpensive $\text{Ni}(\text{acac})_2$ as pre-catalyst was also developed. Reduction of $\text{Ni}(\text{acac})_2$ with DIBAL-H in the presence of cyclooctadiene afforded $\text{Ni}(\text{COD})_2$ in situ,¹⁰ which was washed with ether and then used in the procedure as described above in the hydrosilylation of 5-hydroxy-2-adamantanone (500 mg) with triphenylsilane. By this protocol, an 82% yield (1.3:1 dr) of the expected mono-protected diol was obtained along with 14% of the corresponding bis-protected diol.

3. Summary and conclusions

In summary, a highly chemoselective ketone hydrosilylation reaction has been developed employing triphenylsilane and a nickel NHC catalyst. In contrast to most catalytic ketone hydrosilylation methods, this procedure occurs chemoselectively in the presence of free hydroxyls. Therefore the procedure provides a convenient one-step procedure for the conversion of hydroxyketones to mono-protected diols, with selective installation of the protecting group onto the ketone-derived hydroxyl. We anticipate that this feature will be beneficial in streamlining synthetic sequences that require this common operation.

4. Experimental

4.1. General

All reagents were used as received unless otherwise noted. Tetrahydrofuran (THF), dichloromethane (DCM), diethyl ether (Et_2O), and *N,N*-dimethylformamide (DMF) were treated under nitrogen using a solvent purification system (Innovative Technology, Inc., Model # SPS-400-3 and PS-400-3). $\text{Ni}(\text{COD})_2$ (Strem Chemicals Inc., used as received), potassium *tert*-butoxide (*t*-BuOK), and 1,3-bis-(2,4,6-trimethyl-phenyl)imidazolium chloride (IMes·HCl) were stored and weighed in an inert atmosphere glovebox. All reactions were conducted in flame-dried glassware under an oxygen-free atmosphere of nitrogen. ^1H and ^{13}C spectra were recorded in CDCl_3 at rt (25 °C), on a Varian Inova 400 or Varian MR400. Chemical ^1H NMR shifts were recorded in parts per million (ppm) on the δ scale and referenced to residual chloroform peak (7.27 ppm). Chemical ^{13}C NMR shifts are reported in CDCl_3 solution and referenced to the central signal of CDCl_3 (77.00 ppm). IR spectra were conducted on a Perkin–Elmer FT-IR BX Spectrometer. High resolution mass spectra were obtained on a VG-70-250-s mass spectrometer manufactured by Micromass Corp. (Manchester, UK) at the University of Michigan Mass Spectrometry Laboratory.

4.2. General procedure for nickel-catalyzed hydrosilylation of carbonyl compounds

To a round-bottom flask placed inside a glovebox were added $\text{Ni}(\text{COD})_2$ (0.10 equiv), 1,3-bis-(2,4,6-trimethylphenyl)imidazolium hydrochloride (IMes·HCl) (0.10 equiv), and potassium *tert*-butoxide (0.10 equiv). The flask was then sealed with a rubber septum, removed from the glovebox, and placed under a positive nitrogen atmosphere. THF (1.5 mL) was added and the resulting dark green/blue mixture was stirred for 15 min at rt. This solution was then added via gas-tight syringe to a stirring solution of triphenylsilane (1.2 equiv for hydrosilylation of simple ketones and 1.1 equiv for hydroxy-ketones) and the corresponding carbonyl compound (1 equiv) under nitrogen. The reaction mixture was stirred at rt and was monitored by TLC until total consumption of the corresponding carbonyl compound was noted. Upon completion, the reaction was exposed to air, silica gel

was added, solvent was evaporated in vacuo, and the resulting residue was directly loaded on a silica column and purified.

4.2.1. Triphenyl(3,3,5,5-tetramethylcyclohexyloxy)silane (Table 1, entry 1)—

According to general procedure described above, 3,3,5,5-tetramethylcyclohexanone (77 mg, 0.5 mmol), Ph_3SiH (156 mg, 0.6 mmol), $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), $\text{IMes}\cdot\text{HCl}$ (17 mg, 0.05 mmol), and $t\text{-BuOK}$ (6 mg, 0.05 mmol) were reacted to yield, after purification of the crude product (SiO_2 , hexanes), 197 mg (95%) of triphenyl(3,3,5,5-tetramethylcyclohexyloxy)silane as a white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 7.72 (m, 6H), 7.56–7.31 (m, 9H), 4.10 (tt, $J=3.9$, 11.2 Hz, 1H), 1.70–1.65 (m, 2H), 1.28 (t, $J=11.9$ Hz, 2H), 1.16 (dt, $J=13.6$, 1.9, 1.6 Hz, 1H), 1.07 (d, $J=13.6$ Hz, 1H), 0.92 (s, 6H), 0.81 (s, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.4, 135.0, 129.9, 127.8, 68.1, 51.4, 48.6, 35.1, 32.5, 27.6; IR (film, cm^{-1}) 3067, 2950, 1589, 1428, 1115, 1069; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{34}\text{OSi}$ $[\text{M}]^+=414.2379$, found 414.2373.

4.2.2. Triphenyl(2,2,6,6-tetramethylcyclohexyloxy)silane (Table 1, entry 2)—

2,2,6,6-Tetramethylcyclohexanone (77 mg, 0.5 mmol), Ph_3SiH (156 mg, 0.6 mmol), $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), $\text{IMes}\cdot\text{HCl}$ (17 mg, 0.05 mmol), and $t\text{-BuOK}$ (6 mg, 0.05 mmol) were reacted following the general procedure. After purification of the crude product thus obtained (SiO_2 , hexanes), triphenyl(2,2,6,6-tetramethylcyclohexyloxy)silane was afforded as a white solid (207 mg, 98%). ^1H NMR (CDCl_3 , 400 MHz) δ 7.64 (m, 6H), 7.48–7.39 (m, 9H), 3.11 (s, 1H), 1.58 (qt, $J=13.6$, 3.2 Hz, 1H), 1.44–1.39 (m, 2H), 1.28 (dq, $J=13.6$, 3.6 Hz, 1H), 1.20 (s, 6H), 1.02 (td, $J=13.6$, 3.6 Hz, 2H), 0.78 (s, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.8, 135.4, 129.5, 127.6, 87.0, 40.4, 36.8, 32.9, 20.5, 18.3; IR (film, cm^{-1}) 3067, 2925, 1589, 1428, 1113, 1072; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{34}\text{OSi}$ $[\text{M}]^+=414.2379$, found 414.2392.

4.2.3. Triphenyl(4-phenylbutan-2-yloxy)silane (Table 1, entry 3)—

Benzylacetone (45 mL, 0.3 mmol), Ph_3SiH (94 mg, 0.36 mmol), $\text{Ni}(\text{COD})_2$ (8 mg, 0.03 mmol), $\text{IMes}\cdot\text{HCl}$ (10 mg, 0.03 mmol), and $t\text{-BuOK}$ (3 mg, 0.03 mmol) were reacted under nitrogen following general procedure. After purification of the crude product (SiO_2 , hexanes/ethyl acetate: 10:1), the desired product was achieved as a colorless oil (122 mg, 98%). ^1H NMR (CDCl_3 , 400 MHz) δ 7.55 (m, 6H), 7.34–7.24 (m, 9H), 7.12–7.03 (m, 3H), 6.94 (m, 2H), 3.96 (sex, $J=6.4$ Hz, 1H), 2.62–2.45 (m, 2H), 1.84–1.75 (m, 1H), 1.71–1.62 (m, 1H), 1.12 (d, $J=5.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 142.3, 135.5, 135.0, 129.8, 128.3, 128.2, 127.8, 125.6, 69.5, 41.1, 31.8, 23.5; IR (film, cm^{-1}) 3067, 2025, 2968, 2927, 1589, 1428, 1115, 1060, 1025; HRMS (ESI, Na^+ added) m/z calculated for $\text{C}_{28}\text{H}_{28}\text{OSi}$ $[\text{M}+\text{Na}]^+=431.1807$, found 431.1815.

4.2.4. ((2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyloxy)triphenylsilane (Table 1, entry 4)—

(–)-Menthone (77 mg, 0.5 mmol) was reacted with Ph_3SiH (156 mg, 0.6 mmol) in the presence of $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), $\text{IMes}\cdot\text{HCl}$ (17 mg, 0.05 mmol), and $t\text{-BuOK}$ (6 mg, 0.05 mmol) following general procedure (12 h). The crude product thus obtained was purified (SiO_2 , 3% ethyl acetate in hexanes) to give ((2*S*,5*R*)-2-isopropyl-5-methylcyclohexyloxy)triphenylsilane as a mixture of isomers (201 mg, 97%, dr 1.3:1). The establishment of the relative stereochemistry of both isomers was made by reacting the crude with $n\text{-Bu}_4\text{NF}$ (3 equiv of a 0.2 M solution in THF, rt, overnight) and comparing the crude thus obtained with the known corresponding alcohols (menthol vs neomenthol).¹¹ ^1H NMR (CDCl_3 , 400 MHz) δ 7.68–7.65 (m, 12H), 7.47–7.37 (m, 18H), 4.28 (m, 1H) major isomer, 3.56 (m, 1H) minor isomer, 2.41 (qd, $J=7.2$, 2.7 Hz, 1H), 1.99–1.90 (m, 1H), 1.79–1.54 (m, 7H), 1.37 (m, 2H), 1.20 (m, 2H), 0.92–0.74 (m, 17H), 0.55 (d, $J=6.8$ Hz, 3H), 0.42 (d, $J=6.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 400 MHz) δ 135.6, 135.3, 135.2, 129.8, 127.8, 127.7,

73.9, 70.0, 50.3, 49.6, 45.4, 42.5, 35.3, 34.5, 31.6, 28.6, 26.0, 25.3, 24.5, 22.6, 22.3, 22.1, 21.4, 21.2, 20.9, 15.4, IR (film, cm^{-1}) 3068, 3049, 2952, 2919, 1589, 1428, 1115, 1082, 1064, 1050; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{34}\text{OSi}$ [M^+]=414.2379, found 414.2380.

4.2.5. Triphenyl(1,3,3-trimethylbicyclo[2.2.1]heptan-2-yloxy)silane (Table 1, entry 5)—Following the general procedure, (*R*)-(-)-fenchone (76 mg, 0.5 mmol), Ph_3SiH (156 mg, 0.6 mmol), $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), IMes-HCl (17 mg, 0.05 mmol), and *t*-BuOK (6 mg, 0.05 mmol) were reacted under nitrogen (5 h) to afford, after purification of the crude product (SiO_2 , 2% ethyl acetate in hexanes), triphenyl(1,3,3-trimethylbicyclo[2.2.1]heptan-2-yloxy)silane as an inseparable mixture of diastereomers (206 mg, 98%, dr 2.7:1) Assignment of stereochemistry was made by reacting the crude mixture with *n*- Bu_4NF (3 equiv of a 0.2 M solution in THF, rt, 2 h) and comparing the crude with the known corresponding alcohols.¹² ^1H NMR (CDCl_3 , 400 MHz) δ 7.72 (m, 6H), 7.48–7.39 (m, 9H), 3.56 (d, $J=1.6$ Hz, 1H) major isomer, 3.44 (d, $J=1.6$ Hz, 1H) minor isomer, 2.13 (m, 1H), 2.03 (dq, $J=9.6$, 1.9 Hz, 1H), 1.80 (m, 1H), 1.62 (m, 1H), 1.53–1.30 (m, 4H), 1.09–1.00 (m, 3H), 0.98 (s, 3H) minor isomer, 0.91 (s, 3H) minor isomer, 0.88 (d, $J=1.9$ Hz, 3H) major isomer, 0.63 (s, 3H) minor isomer; 0.62 (s, 3H) major isomer; ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.9, 135.8, 135.1, 135.1, 129.7, 129.7, 127.6, 87.4, 86.5, 49.9, 49.9, 48.6, 48.3, 44.5, 41.5, 41.1, 39.9, 33.5, 29.8, 26.3, 25.7, 25.5, 24.9, 21.9, 20.2, 18.8; IR (film, cm^{-1}) 3067, 2952, 1588, 1427, 1114, 1089; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{32}\text{OSi}$ [M^+]=412.2222, found 412.2219.

4.2.6. 2-Methyl-3-(triphenylsilyloxy)butan-2-ol (Table 2, entry 1)—3-Hydroxy-3-methylbutan-2-one (31 mg, 0.3 mmol), Ph_3SiH (86 mg, 0.33 mmol), $\text{Ni}(\text{COD})_2$ (8 mg, 0.03 mmol), IMes-HCl (10 mg, 0.03 mmol), and *t*-BuOK (3 mg, 0.03 mmol) were reacted following the general procedure. After purification of the crude (SiO_2 , hexanes/ethyl acetate: 10:1), 2-methyl-3-(triphenylsilyloxy)butan-2-ol was achieved as a colorless oil (79 mg, 75%). ^1H NMR (CDCl_3 , 400 MHz) δ 7.69–7.66 (m, 6H), 7.50–7.40 (m, 9H), 3.85 (q, $J=6.4$ Hz, 1H), 2.35 (s, 1H), 1.22 (s, 3H), 1.18 (s, 3H), 1.15 (d, $J=6.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.5, 134.4, 130.0, 127.9, 76.9, 73.1, 26.0, 23.8, 18.5; IR (film, cm^{-1}) 3446, 3068, 2978, 1589, 1428, 1115; HRMS (ESI, Na^+ added) m/z calculated for $\text{C}_{23}\text{H}_{26}\text{O}_2\text{Si}$ [$\text{M} + \text{Na}$] $^+$ =385.1600, found 385.1586. Note: in this reaction a 4% yield of the bis-silylated compound was also observed.

4.2.7. 2,6,6-Trimethyl-3-(triphenylsilyloxy)bicyclo[3.1.1]heptan-2-ol (Table 2, entry 2)—Following general procedure (1*S*,2*S*,5*S*)-(-)-2-hydroxy-3-pinanone (84 mg, 0.5 mmol), Ph_3SiH (143 mg, 0.55 mmol), $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), IMes-HCl (17 mg, 0.05 mmol), and *t*-BuOK (6 mg, 0.05 mmol) were reacted under nitrogen to give, after purification of the crude product (SiO_2 , hexanes/ethyl acetate 10:1), 2,6,6-trimethyl-3-(triphenylsilyloxy)bicyclo[3.1.1]heptan-2-ol (186 mg, 87%) as a 13:1 mixture of two diastereomers. Both isomers were isolated and fully characterized (Assignment of stereochemistry was made on the basis of NOE experiments for both isomers).

Major diastereomer. ^1H NMR (CDCl_3 , 400 MHz) δ 7.70 (m, 6H), 7.50–7.40 (m, 9H), 4.23 (dd, $J=9.2$, 5.2 Hz, 1H), 4.13 (s, 1H, OH), 2.21–2.16 (m, 1H), 2.07–2.03 (m, 1H), 2.00 (t, $J=5.6$ Hz, 1H), 1.83–1.74 (m, 2H), 1.59 (d, $J=10.4$ Hz, 1H), 1.33 (s, 3H), 1.22 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.5, 133.7, 130.3, 128.0, 73.1, 71.8, 53.8, 40.5, 38.4, 38.2, 29.8, 28.5, 28.0, 24.2; IR (film, cm^{-1}) 3498, 3068, 2906, 1587, 1426, 1117, 1058; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{32}\text{O}_2\text{Si}$ [M^+]=428.2172, found 428.2175.

Minor diastereomer. ^1H NMR (CDCl_3 , 400 MHz) δ 7.71 (m, 6H), 7.48–7.40 (m, 9H), 4.41 (dd, $J=9.9$, 5.9 Hz, 1H), 2.27 (ddd, $J=13.9$, 10.4, 4.4 Hz, 1H), 2.06 (dddd, $J=16.4$, 10.4, 5.9, 1.6 Hz, 1H), 1.85–1.82 (m, 3H), 1.37 (s, 3H), 1.32 (d, $J=10.4$ Hz, 1H), 1.23 (s, 3H), 1.06 (s,

3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.6, 134.6, 130.1, 127.9, 78.5, 76.0, 54.1, 40.1, 39.0, 36.6, 27.3, 26.1, 25.3, 23.0; IR (film, cm^{-1}) 3569, 3068, 2905, 1588, 1427, 1116, 1106, 1082; HRMS (EI) m/z calculated for $\text{C}_{28}\text{H}_{32}\text{O}_2\text{Si}$ $[\text{M}]^+ = 428.2172$, found 428.2176.

4.2.8. 4-(Triphenylsilyloxy)adamantan-1-ol (Table 2, entry 3)—According to the general procedure, 5-hydroxy-2-adamantanone (100 mg, 0.6 mmol), Ph_3SiH (172 mg, 0.66 mmol), $\text{Ni}(\text{COD})_2$ (16 mg, 0.06 mmol), $\text{IMes}\cdot\text{HCl}$ (20 mg, 0.06 mmol), and $t\text{-BuOK}$ (7 mg, 0.06 mmol) were reacted under nitrogen. After purification of the crude product thus obtained (SiO_2 , hexanes/ethyl acetate 2:1), 4-(triphenylsilyloxy)adamantan-1-ol was obtained as white solid (213.9 mg, 84%, 1.2:1 dr). Both diastereomers were isolated and fully characterized. (2% of the bissilylated product was also observed.)

Major diastereomer: ^1H NMR (CDCl_3 , 500 MHz) δ 7.64–7.62 (m, 6H), 7.46–7.37 (m, 9H), 3.91 (t, $J=2.9$ Hz, 1H), 2.33 (d, $J=11.5$ Hz, 2H), 2.04 (m, 2H), 1.99 (m, 1H), 1.67 (m, 2H), 1.58 (m, 2H), 1.47 (d, $J=11.5$ Hz, 2H), 1.42–1.37 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.3, 134.8, 129.9, 127.8, 74.0, 67.8, 45.05, 39.3, 37.6, 34.8, 29.4; IR (film, cm^{-1}) 3325, 3066, 2909, 1588, 1427, 1115, 1096, 1067; HRMS (ESI, formic acid added) m/z calculated for $\text{C}_{28}\text{H}_{31}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+ = 427.2093$, found 427.2083.

Minor diastereomer: ^1H NMR (CDCl_3 , 400 MHz) δ 7.66–7.64 (m, 6H), 7.48–7.38 (m, 9H), 4.08 (t, $J=2.8$ Hz, 1H), 2.31 (d, $J=12.4$ Hz, 2H), 2.16 (m, 1H), 1.95 (m, 2H), 1.73 (m, 2H), 1.61 (m, 4H), 1.37 (d, $J=12.0$ Hz, 2H), 1.28 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.3, 134.9, 129.9, 127.8, 74.8, 67.6, 45.4, 43.5, 36.5, 30.0, 29.9; IR (film, cm^{-1}) 3355, 3066, 2916, 1589, 1427, 1115, 1102, 1073; HRMS (ESI, formic acid added) m/z calculated for $\text{C}_{28}\text{H}_{31}\text{O}_2\text{Si}$ $[\text{M}+\text{H}]^+ = 427.2093$, found 427.2080.

4.2.9. 5-Ene-17-(triphenylsilyloxy)-3b-andostranol (Table 2, entry 4)—Following the general procedure, 5-andostren-3b-hydroxy-17-one (100 mg, 0.35 mmol), Ph_3SiH (108 mg, 0.42 mmol), $\text{Ni}(\text{COD})_2$ (10 mg, 0.03 mmol), $\text{IMes}\cdot\text{HCl}$ (12 mg, 0.03 mmol), $t\text{-BuOK}$ (4 mg, 0.03 mmol) were reacted under nitrogen for 3 h. The reaction crude was purified (SiO_2 , 1:3 ethyl acetate/hexanes) to afford the desired compound as a 2:1 mixture of diastereomers (175 mg, 91%). The stereochemistry of both isomers was established by reacting the mixture with $n\text{-Bu}^4\text{NF}$ (3 equiv of a 0.2 M solution in THF, rt, overnight) and comparing the resulting crude to known compounds. 13 ^1H NMR (CDCl_3 , 400 MHz) δ 7.64–7.60 (m, 6H), 7.45–7.36 (m, 9H), 5.38 (m, 1H) minor isomer, 5.32 (m, 1H) major isomer, 4.01 (d, $J=5$ Hz, 1H) minor isomer, 3.79 (t, $J=8$ Hz, 1H) major isomer, 3.69 (m, 1H), 2.31–2.21 (m, 2H), 1.85–1.42 (m, 14H), 1.28–1.03 (m, 3H), 1.01 (s, 3H), 0.92 (s, 3H), 0.78 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 140.8, 140.7, 135.6, 135.5, 135.0, 129.8 ($\times 2$), 127.7, 121.7, 121.4, 82.6, 81.3, 77.2, 71.8, 71.7, 50.6, 50.2, 49.9, 49.6, 45.7, 43.4, 42.3, 42.2, 37.3, 37.2, 36.6, 36.5, 33.1, 32.2 ($\times 2$), 32.1, 31.9, 31.6, 31.5, 31.4, 30.8, 24.9, 23.6, 20.7, 19.4 ($\times 2$), 16.8, 11.7; IR (film, cm^{-1}) 3338, 3066, 2933, 188, 1428, 1115, 1083, 1060; HRMS (EI) m/z calculated for $\text{C}_{37}\text{H}_{44}\text{O}_2\text{Si}$ $[\text{M}]^+ = 548.3111$, found 548.3121.

4.2.10. 5-Ene-20-(triphenylsilyloxy)-3b-pregmol (Table 2, entry 5)—Pregn-5-ene-3b-ol, 20-one (100 mg, 0.32 mmol) was reacted with Ph_3SiH (92 mg, 0.35 mmol) in the presence of $\text{Ni}(\text{COD})_2$ (9 mg, 0.03 mmol), $\text{IMes}\cdot\text{HCl}$ (11 mg, 0.032 mmol), and $t\text{-BuOK}$ (4mg, 0.032 mol) following general procedure. After total consumption of the starting material (16 h), the crude mixture was purified to yield the desired compound as a white solid (172 mg, 94%, 2.8:1 mixture of two diastereomers). ^1H NMR (CDCl_3 , 400 MHz) δ 7.66 (m, 6H), 7.46–7.37 (m, 9H), 5.33 (m, 1H), 3.93 (m, 1H), minor isomer, 3.91 (m, 1H) major isomer, 3.53 (m, 1H), 2.33–2.24 (m, 3H), 2.16–1.96 (m, 2H), 1.85 (m, 3H), 1.63–1.40 (m, 10H), 1.23 (d, $J=6$ Hz, 2H), 1.16–1.00 (m, 6H), 0.99 (m, 3H), 0.51 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 140.8, 140.7, 135.6, 135.5, 135.3, 135.2, 129.7, 129.6, 127.6, 127.6,

121.6, 121.5, 72.9, 72.4, 71.1, 71.6, 58.7, 58.3, 56.6, 56.3, 50.1, 50.0, 42.2, 42.2, 42.0, 41.3, 39.4, 38.8, 37.2, 31.2, 36.5, 31.9, 31.8, 31.7, 31.6, 31.5, 31.4, 27.2, 25.5, 24.3, 24.2, 24.1, 23.7, 20.8, 20.7, 19.4, 19.3, 12.3, 12.0; IR (film, cm^{-1}) 3354, 3066, 2931, 1588, 1427, 1114, 1078, 1040; HRMS (EI) m/z calculated for $\text{C}_{39}\text{H}_{48}\text{O}_2\text{Si}$ $[M]^+ = 576.3424$, found 576.3437.

4.2.11. 17-Hydroxy-3-(triphenylsilyloxy)-androstane (Table 2, entry 6)—

Following general procedure, 17-hydroxy-3-androstanone (145 mg, 0.5 mmol), Ph_3SiH (143 mg, 0.55 mmol), $\text{Ni}(\text{COD})_2$ (14 mg, 0.05 mmol), $\text{IMes}\cdot\text{HCl}$ (17 mg, 0.05 mmol), and $t\text{-BuOK}$ (6 mg, 0.05 mol) were reacted under nitrogen for 1 h, yielding the corresponding carbonyl-hydrosilylated product (purification achieved using 1:5 ethyl acetate/hexanes as eluent) as a mixture of two diastereomers in a 2.4:1 ratio (258 mg, 94%). The stereochemistry of both isomers was determined by $n\text{-Bu}_4\text{NF}$ deprotection of the crude and comparison of the product thus obtained with known diols.¹⁴ ^1H NMR (CDCl_3 , 400 MHz) δ 7.61–7.58 (m, 12H), 7.42–7.32 (m, 18H), 4.18 (m, 1H), 3.73 (m, 2H), 3.62 (t, $J=8$ Hz, 1H) minor isomer, 3.56 (t, $J=8$ Hz, 1H) major isomer, 2.08–1.95 (m, 1H), 1.79–1.71 (m, 2H), 1.70–1.43 (m, 15H), 1.41–1.27 (m, 8H), 1.26–1.10 (m, 8H), 1.01–0.81 (m, 5H), 0.79 (s, 3H) major isomer, 0.76 (m, 2H), 0.72 (s, 3H) minor isomer, 0.71 (s, 3H) minor isomer, 0.68 (m, 3H) major isomer, 0.50 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 135.4, 135.3, 135.1, 135.0, 129.8, 129.7, 127.7, 82.0, 81.9, 77.2, 73.0, 68.4, 54.4, 51.0, 50.9, 44.8, 43.0, 42.9, 39.3, 38.3, 37.0, 36.7, 36.2, 36.1, 35.6, 35.4, 35.4, 32.6, 31.7, 31.6, 30.5, 29.3, 28.5, 28.4, 23.3, 20.7, 20.4, 12.3, 11.4, 11.1, 11.0; IR (film, cm^{-1}) 3373, 3066, 2928, 1428, 1374, 1115, 1073, 1026; HRMS (EI) m/z calculated for $\text{C}_{37}\text{H}_{46}\text{O}_2\text{Si}$ $[M]^+ = 550.3267$, found 550.3254.

4.3. Catalytic hydrosilylation of carbonyl compounds using $\text{Ni}(\text{acac})_2$

In a round-bottom flask, $\text{Ni}(\text{acac})_2$ (77 mg, 0.3 mmol) was heated briefly under vacuum with a heating gun. After cooling and establishing a positive nitrogen atmosphere, 1 mL THF and 1,5-cyclooctadiene (146 mL, 1.2 mmol) were added, and the resulting green slurry was cooled to -78°C in a dry ice/acetone bath. At this temperature DIBAL-H (0.75 mL of a 1.0 M solution in toluene) was added dropwise to give a brown solution, which was stirred at -78°C for another 30 min, and then at 0°C for another 30 min. THF was then removed under vacuum and the resulting brownish oil was washed with ether (1 mL portions) until all brown residues were removed to give a bright yellow solid remaining ($\text{Ni}(\text{COD})_2$).

The 'in situ' generated $\text{Ni}(\text{COD})_2$ was dissolved in THF (5 mL) and was transferred by cannula under nitrogen to a stirring solution of $\text{IMes}\cdot\text{HCl}$ (102 mg, 0.3 mmol) and $t\text{-BuOK}$ (34 mg, 0.3 mmol) in THF (5 mL). The resulting dark green/blue solution was stirred under nitrogen for 15 min and was then added by gas-tight syringe to a stirring solution of 5-hydroxy-2-adamantanone (500 mg, 3 mmol) and Ph_3SiH (859 mg, 3.3 mmol) in THF (20 mL). After total consumption of the starting ketone (30 min), the reaction mixture was opened to air, silica gel was added, the solvent was evaporated in vacuo, and the crude mixture was directly loaded onto a silica column and purified (ethyl acetate/hexanes: 2:1). This afforded the desired product as a mixture of two isomers (dr: 1.3:1) (1.04 g, 82%), as well as the bis-silylated product (319 mg, 14%). (See Section 4.2.8 for characterization).

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Hydrosilylation *Dehydrogenative Silylation*

Scheme 1.
Silane additions to ketones or alcohols.

Typical Sequence - 4 Step Operation *This Work - 1 Step Operation*

Scheme 2.
Selective reduction/protection of hydroxyketones.

Table 1

Hydrosilylation of simple ketones

$ \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{R}^2 \\ (1.0 \text{ equiv}) \end{array} + \text{Ph}_3\text{SiH} \begin{array}{c} \xrightarrow[\text{THF, rt}]{\text{Ni(COD)}_2 (10 \text{ mol } \%), \\ \text{IMes}\cdot\text{HCl} (10 \text{ mol } \%), \\ t\text{-BuOK} (10 \text{ mol } \%) } \end{array} \begin{array}{c} \text{OSiPh}_3 \\ \text{R}^1-\text{CH}-\text{R}^2 \end{array} $ (1.2 equiv)		
Entry	Substrate	Product (% yield isomer ratio)
1		(95%)
2		(98%)
3		(98%)
4		+ (97%, 1.3:1)
5		+ (98%, 2.7:1)

Table 2

Hydrosilylation of hydroxyketones

$ \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{R}^2 \\ (1.0 \text{ equiv}) \end{array} + \text{Ph}_3\text{SiH} \begin{array}{c} (1.1 \text{ equiv}) \end{array} \xrightarrow[\text{THF, rt}]{\begin{array}{c} \text{Ni(COD)}_2 (10 \text{ mol } \%) \\ \text{IMes}\cdot\text{HCl} (10 \text{ mol } \%) \\ t\text{-BuOK} (10 \text{ mol } \%) \end{array}} \begin{array}{c} \text{OSiPh}_3 \\ \text{R}^1-\text{C}-\text{R}^2 \end{array} $		
Entry	Substrate	Product (% yield isomer ratio)
1		(75 %)
2		(87%, 13:1)
3		84%, (1.2:1)
4		91% (2:1)
5		94% (2.8:1)
6		94% (2.4:1)