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Chemoselective hydrosilylation of hydroxyketones

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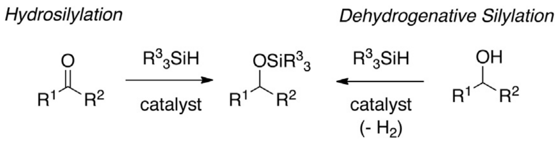
ABSTRACT

A chemoselective method for the hydrosilylation of ketones has been developed, using the combination of triphenylsilane and a catalyst prepared from Ni(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.

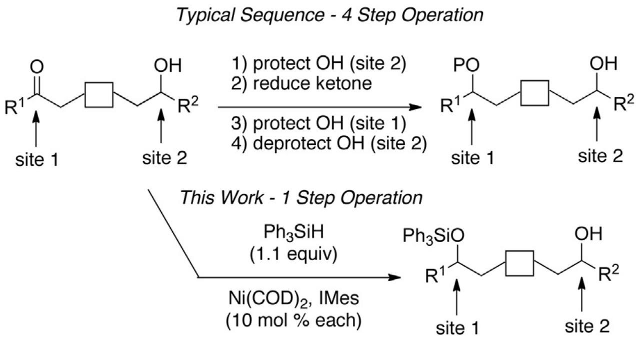
1. Introduction

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).



Scheme 1. Silane additions to ketones or alcohols.

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).



Scheme 2. Selective reduction/protection of hydroxyketones.

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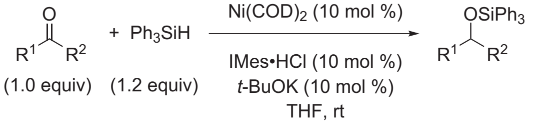
2. Results and discussion

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 catalyst[7] 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 Ph_3SiH 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.

Table 1
Hydrosilylation of simple ketones



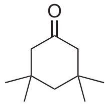
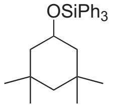
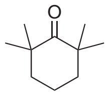
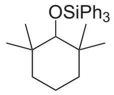
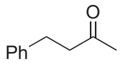
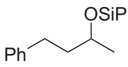
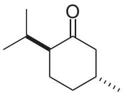
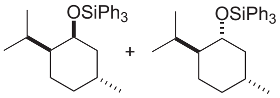
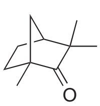
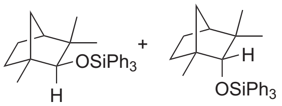
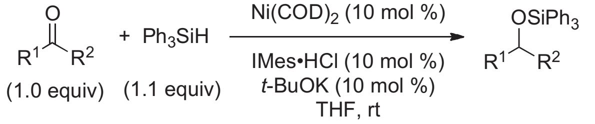
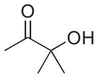
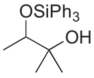
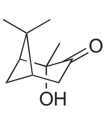
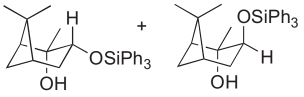
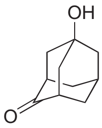
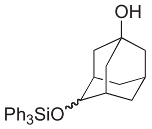
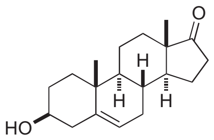
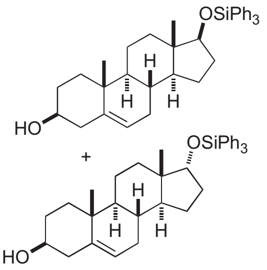
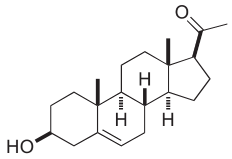
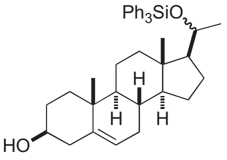
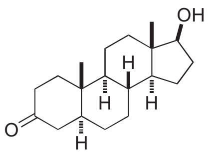
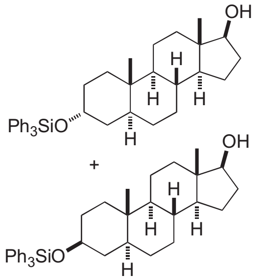
Entry	Substrate	Product (% yield isomer ratio)
1		 (95%)
2		 (98%)
3		 (98%)
4		 (97%, 1.3:1)
5		 (98%, 2.7:1)

Table 2
Hydrosilylation of hydroxyketones



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)