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Rh Soaked in Polyionic Gel: An Effective Catalyst for Dehydrogenative Silylation of Ketones

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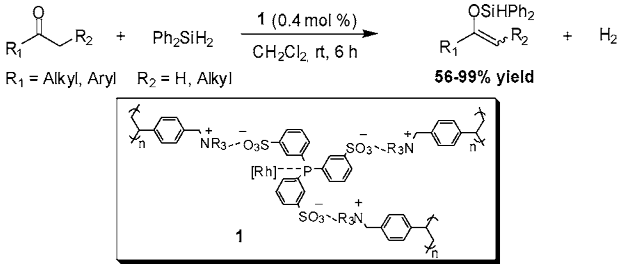
ABSTRACT



A polyionic gel-soaked Rh catalyst allows the formation of synthetically useful diphenylsilyl (DPS) enols under mild conditions. The reaction proceeds through dehydrogenative silylation of ketones, affording the kinetic silyl enol ether in good to excellent yields. The in situ formed DPS enols were directly involved, without purification, in one-pot aldol and Mannich condensations.

Silyl enol ethers are key intermediates in a number of C−C and C−X bond-forming reactions.[1] Since the introduction of these sensitive intermediates to organic synthesis, continuous studies have been devoted to improve their synthesis. The most widely used method for their preparation relies on the *O*-silylation of lithium enolates.[2]

Interest has been recently directed toward the development of milder and more selective metal-based reagents. In particular, magnesium and calcium bisamide bases enable highly regio- and stereoselective silyl enol ether formation.[3] Also, thermally induced silyl migration provides an interesting route to silyl enol ethers under neutral conditions.[4] These approaches require stoichiometric amounts of base and silylating agent.

To the best of our knowledge, only two catalytic processes for the synthesis of silyl enol ethers were reported in the literature, i.e., the transition-metal-catalyzed dehydrogenative silylation of ketones[5] and the catalytic 1,4-hydrosilylation of α,β-unsaturated enones.[6,7]

The transition-metal-catalyzed dehydrogenative silylation of ketones using hydrosilanes is an attractive and convenient method. Indeed, H_2 is the sole byproduct generated in the course of the reaction, and no base is required. The absence

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[1] For silyl enol ether preparation, see: (a) Brownbridge, P. *Synthesis* **1983**, 1. (b) Chan, T.-H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, p 595. For C−C reactions, see: (a) Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafini, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779. (b) Carreira, E. M. In *Comprehensive Asymetric Catalysis*; Springer: Berlin, 1999; Vol. 3, p 997. For reviews, see: (a) Mukaiyama, T. *Angew. Chem., Int. Ed.* **1977**, *16*, 817. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203. For C−X reactions, see: Brook, M. A. In *Silicon in Organic, Organometallic and Polymer Chemistry*; Wiley: Toronto, 2000; pp 215−239.

[2] (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462. (b) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324. For kinetic control, see: Henderson, K. W.; Kerr, W. J.; Moir, J. H. *Tetrahedron* **2002**, *58*, 4573. For thermodynamic control, see: Yamamoto, Y.; Matui, C. *Organometallics* **1997**, *16*, 2204.

[3] (a) Henderson, K. W.; Kerr, W. J. *Chem.−Eur. J.* **2001**, *7*, 3430. (b) He, X.; Allan, J. A.; Noll, B. C.; Kennedy, A. R.; Henderson, K. W. *J. Am. Chem. Soc.* **2005**, *127*, 6920.

[4] (a) Kuo, Y.-N.; Yahner, J. A.; Ainsworth, C. *J. Am. Chem. Soc.* **1971**, *93*, 6321. (b) Choi, J.; Imai, E.; Mihara, M.; Oderaotoshi, Y.; Minakata, S.; Komatsu, M. *J. Org. Chem.* **2003**, *68*, 6164.

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of other side products is a particularly interesting feature as silyl enol ethers are sensitive intermediates which are difficult to isolate. Using catalytic systems such as $Co_2(CO)_8$−pyridine,[5a] a dimeric tungsten complex,[5b] $RhCl_3$(pybox)−AgOTf,[5c] a combination of metal−Et_2NH−EtI,[5d] or a diphosphinidenecyclobutene-coordinated platinum complex,[5e] the reaction afforded silyl enol ether in high yield. In addition, under these reaction conditions, the thermodynamic isomer is formed as the major product.

In addition to these known methods, silyl enol ethers are often obtained as minor side products in the rhodium-catalyzed hydrosilylation of ketones.[8] Here, we report that the polyionic gel-soaked rhodium **1** preferentially catalyzes the dehydrogenative silylation of ketones leading to silyl enol ethers as major products, with high selectivity toward the kinetic isomer. This mild catalytic process enables the preparation of sensitive and synthetically useful intermediates.

Recently, we reported that polyionic gels are suitable heterogeneous media for metal scavenging and catalysis. Indeed, a polyionic gel-soaked Pd proved to be a highly active catalyst for Suzuki couplings.[9] As an extension to this work, we investigated the reactivity of polyionic gel-soaked rhodium complexes in the dehydrogenative silylation of ketones. We prepared two heterogeneous Rh catalysts[10] **1** and **2** from the dimeric $[Rh(cod)Cl]_2$ and the Wilkinson's ($RhCl(PPh_3)_3$) precursors, respectively (Figure 1). Catalytic efficiencies of **1** and **2** were compared to the corresponding homogeneous rhodium precursors, as well as to Sakurai's[5a] and Fuchikami's[5d] catalyst systems (Table 1).

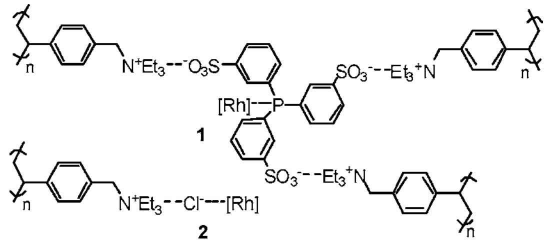
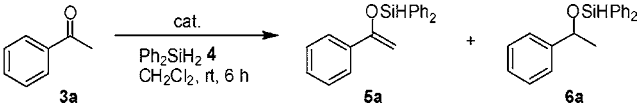


Figure 1. Polyionic gel-soaked Rh catalysts.

Table 1. Dehydrogenative Silylation of Acetophenone **3a** with Various Catalysts[a]



entry	catalyst	**5a/6a**	conv[b]
1	cat. **1**	84:16	95
2	cat. **2**	1:99	70
3	$RhCl(PPh_3)_3$	1:99	>99
4	$[Rh(cod)Cl]_2$	24:76	90
5	$[Rh(cod)Cl]_2/PPh_3$[c]	1:99	96
6	$[Rh(cod)Cl]_2$/TPPTS/NBu_4Cl[d]	22:78	77
7	Co_2CO_8−pyridine[e]	54:46	43
8	Pd/C−Et_2NH−EtI[f]	95:5	6
9	$Ir_4(CO)_{12}$−Et_2NH−EtI[f]	95:5	5

[a] **3a** (0.44 mmol) and **4** (0.88 mmol) were stirred in CH_2Cl_2 (4 mL) in the presence of catalyst (0.4 mol % of metal) at rt for 6 h under argon. [b] Determined by ^1H NMR spectroscopy of the crude reaction mixture. [c] 1.7 mol % of PPh_3 was used. [d] 1.7 and 4.8 mol % of TPPTS and NBu_4Cl, respectively, were used. [e] 0.4 mol % of pyridine was used. [f] 2.0 and 2.0 mol % of Et_2NH and EtI were used.

We performed as a model reaction the hydrosilylation of acetophenone **3a** with diphenylsilane **4** under standard conditions: **4** (2 equiv) in CH_2Cl_2 at rt for 6 h in the presence of 0.4 mol % of catalyst.[11] After completion of the reaction, the catalyst was filtered off, and the filtrate was concentrated under reduced pressure. ^1H NMR spectroscopy of the reaction mixtures showed the presence of diphenylsilyl (DPS) enol **5a**, silylalkyl ether **6a**, unreacted ketone **3a**, and an excess of **4**.

By using the ionic gel-stabilized Rh catalyst **1**, the DPS enol **5a** was predominantly formed (**5a**/**6a** = 84:16 with over 95% conversion, entry 1). In contrast, heterogeneous catalyst **2** prepared from the polyionic gel and the Wilkinson's precursor showed high selectivity in favor of **6a** (entry 2). As expected, homogeneous reactions involving either the Wilkinson's or the dimeric $[Rh(cod)Cl]_2$ precursors gave hydrosilylated derivative **6a** as the major product (entries 3 and 4). No change was observed upon addition of either 1.7 mol % of PPh_3 or the combination of NBu_4Cl (4.8 mol %) and TPPTS (1.7 mol %), which was added to mimic the ionic environment exhibited by the polyionic gel (entries 5 and 6). In comparison, in the presence of Sakurai's or Fuchikami's catalyst, reactions resulted either in a poor selectivity or in low yields under our conditions (Table 1, entries 7−9). However, under the reported original conditions,[12a,b] they respectively afforded a 35:65 mixture of **5a**/**6a** in 88% yield and selectively **5a** in 74% yield.

We then investigated the scope and limitations of **1** toward various substituted acetophenones **3** (Table 2). Strong electron-donating substituents proved to be detrimental to the dehydrogenative silylation and favored the reductive

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(5) (a) Sakurai, H.; Miyoshi, K.; Nakadaira, Y. *Tetrahedron Lett.* **1977**, *18*, 2671. (b) Fuchikami, T.; Ubukata, Y.; Yanaka, Y. *Tetrahedron Lett.* **1991**, *32*, 1199. (c) Nagashima, H.; Ueda, T.; Nishiyama, H.; Itoh, K. *Chem. Lett.* **1993**, 347. (d) Igarashi, M.; Sugihara, Y.; Fuchikami, T. *Tetrahedron Lett.* **1999**, *40*, 711 and references therein. (e) Ozawa, F.; Yamamoto, S.; Kawagishi, S.; Hiraoka, M.; Ikeda, S.; Minami, T.; Ito, S. *Chem. Lett.* **2001**, 972.

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(7) For the Lewis acid-catalyzed version, see: Blackwell, J. M.; Morrison, D. J.; Piers, W. E. *Tetrahedron* **2002**, *58*, 8247.

(8) (a) Benes, J.; Hetflejs, J. *Collect. Czech. Chem. Commun.* **1976**, *41*, 2264. (b) Payne, N. C.; Stephan, D. W. *Inorg. Chem.* **1982**, *21*, 182. (c) Brunner, H.; Becker, R.; Riepl, G. *Organometallics* **1984**, *3*, 1354. (d) Kromm, K.; Osburn, P. L.; Gladysz, J. A. *Organometallics* **2002**, *21*, 4275. (e) Reyes, C.; Prock, A.; Giering, W. P. *J. Organomet. Chem.* **2003**, *671*, 13. (f) Chianese, A. R.; Crabtree, R. H. *Organometallics* **2005**, *24*, 4432.

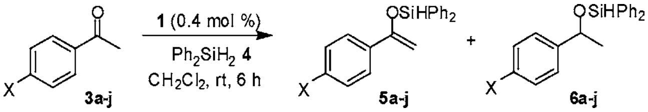
(9) Thiot, C.; Schmutz, M.; Wagner, A.; Mioskowski, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 2868.

(10) See the Supporting Information.

(11) Recycling was also performed. See the Supporting Information.

(12) (a) Sakurai's conditions: CH_2Cl_2, 50 °C, 2 h, $PhMe_2SiH$, $Co_2(CO)_8$−pyridine: 2.0−2.0 mol %. (b) Fuchikami's conditions: toluene, 100 °C, 16 h, Et_3SiH, $Ir_4(CO)_{12}$−Et_2NH−EtI: 1.0−5.0−5.0 mol %.

Table 2. Effect of Substituent on Acetophenones **3**



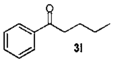
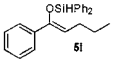
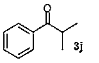
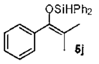
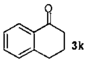
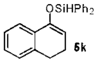
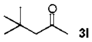
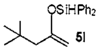
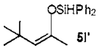
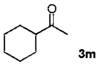
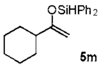
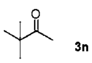
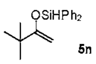
entry	ketone **3**	**5/6**	conv^a
1	**3a** (X = H)	84:16	95
2	**3b** (X = *p*-Me)	48:52	61
3	**3c** (X = *p*-MeO)	0:100	65
4	**3d** (X = *p*-Br)	91:9	96
5	**3e** (X = *p*-CF$_3$)	98:2	99
6	**3f** (X = *p*-CO$_2$Et)	99:1	97
7	**3g** (X = *p*-OTf)	99:1	98
8	**3h** (X = 2-naphthyl)	77:23	96

[a] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture.

elimination (entries 2 and 3). In contrast, reactions performed with acetophenones bearing *p*-electron-withdrawing substituents resulted in highly selective formation of DPS enols **5d**−**g**, with almost complete conversion (entries 4−7). The same holds true for naphthyl methyl ketone **3h** to give **5h** (entry 8). Noteworthy under similar reaction conditions, acetophenones bearing *p*-NO$_2$ and *p*-CN groups as well as *N*-heteroaryl ketones failed to react. This nonreactivity was attributed to the deactivation of the catalyst via heteroatom chelation. Reaction with an aldehyde such as 3-phenylpropionaldehyde afforded only, as expected, the corresponding silylalkyl ether in >95% yield. Heterogeneity tests indicated that the catalysis is carried out by heterogeneous Rh catalyst.[11] The turnover frequency of Rh catalyst **1** was determined to be 124 h^{-1} for **3f**.[11]

We next examined the selectivity of catalyst **1** toward aryl alkyl and dialkyl ketones **3i**−**n** (Table 3). The selectivity of the reaction appeared to be strongly governed by steric factors in two ways. First, for aryl alkyl ketones **3i**−**k**, upon increasing steric hindrance of the alkyl side chain, an increased amount of silylalkyl ether (arising from the reductive elimination pathway) was observed (entries 1−3). In addition, for dialkyl ketones, the less substituted DPS enol was predominantly formed (85−91% yields, entries 4 and 5).

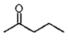
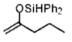
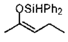
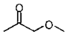
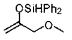
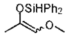
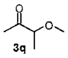
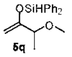
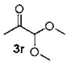
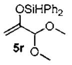
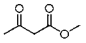
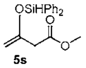
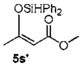
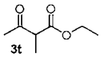
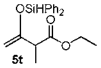
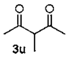
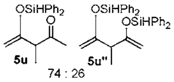
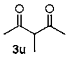
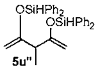
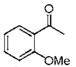
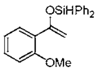
Table 3. **1**-Catalyzed Dehydrogenative Silylation of Ketones **3**

entry	ketone **3**	kinetic : thermodynamic **5**^{a}			yield (%)^b
1	 3i	 5i		-	56
2	 3j	 5j		-	0^c
3	 3k	 5k		-	75
4	 3l	 5l	 5l'	90 : 10	91
5	 3m	 5m		100 : 0	85
6	 3n	 5n		-	98

[a,b] Measured by ^{1}H NMR spectroscopy using benzofuran as an internal standard of the crude reaction mixture. [c] Only silylalkyl ether was formed.

It appeared that the efficiency for the DPS enol formation and the selectivity for the kinetic isomer are further improved for substrates containing both coordinating oxygen atoms and a steric hindrance (Table 4). While reaction with pent-2-one **3o** resulted in a mixture of DPS enols together with a large amount of the corresponding silylalkyl ether, the corresponding ketone **3p** bearing an oxygen atom afforded predominantly enol **5p** in high yield (entries 1 and 2). It was found that strong coordinating groups favor the formation of DPS enols.[11] Oxygen atoms appear to have a beneficial effect on selectivity, presumably due to an intramolecular Si−O interaction that favors transition state leading to *β*-hydride elimination. By adding an alkyl or extra coordinating methoxy group in **3q** or **3r** (α-position of the carbonyl group), the corresponding kinetic enols **5q** and **5r** were exclusively formed in high yield (entries 3−4). Noteworthy by using the Co$_2$(CO)$_8$−pyridine and Ir$_4$(CO)$_{12}$−Et$_2$NH−EtI catalytic systems, no reaction occurred for substrate **3r** under our conditions.[13]

Table 4. Effect of Coordinating Groups

entry	ketone **3**	kinetic : thermodynamic **5**^{a}			yield (%)^b
1	 3o	 5o	 5o'	31 : 69	28^c
2	 3p	 5p	 5p'	63 : 37^d	88
3	 3q	 5q		100 : 0	95
4	 3r	 5r		100 : 0	98
5	 3s	 5s	 5s'	76 : 24	81
6	 3t	 5t		100 : 0	82
7^e	 3u	 5u 5u'' 74 : 26		100 : 0	81
8	 3u	 5u''		100 : 0	98
9	 3v	 5v	-	-	63^f

[a,b] Measured by ^{1}H NMR spectroscopy using benzofuran as an internal standard of the crude reaction mixture. [c] The corresponding silylalkyl ether was formed in 56% yield. [d] *E*/*Z* = 35/65. [e] 4 equiv of **4** was used. [f] The corresponding silylalkyl ether was formed in 19% yield.

Unsymmetrical ketones **3t** and **3u** bearing chelating groups provided regioselectively the expected kinetic enols in good

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[13] As a control, in the reported original conditions (see ref 12), Sakurai's catalyst gave no reaction from **3r**, whereas reaction with Ir$_4$(CO)$_{12}$−Et$_2$NH−EtI afforded a 21:79 mixture of kinetic silyl enol/silyl alkyl with complete conversion.

yields (entries 6 and 7). Substrate **3u** gave a mixture of mono- and bis-silyl enol ethers. It was not possible to form selectively **5u** either at low temperatures or by slow addition of the silane. However, the use of an excess of Ph_2SiH_2 **4** exclusively afforded the bis-silyl enol ether **5u″** without carbonyl hydrosilation (entry 8).

To illustrate the synthetic potential of this catalytic dehydrogenative silylation for silyl enol ether preparation, the crude mixture containing the DPS enol **5** was directly engaged without purification in one-pot Mukaiyama aldol[14] and Mannich-type condensations[15] (Figure 2). The in situ formed kinetic enols **5r** and **5t** react, respectively, with pyridine-2-carboxaldehyde and 3,4,5-trimethoxybenzaldehyde to afford **9** and **10**, two potential precursors for the synthesis of biologically relevant molecules.[16,17]

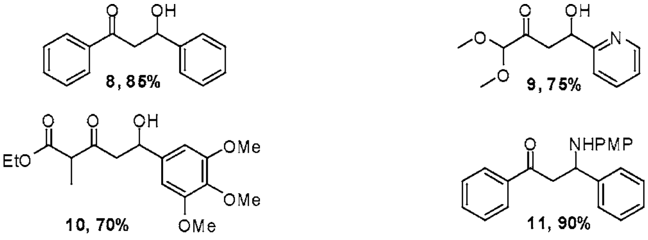
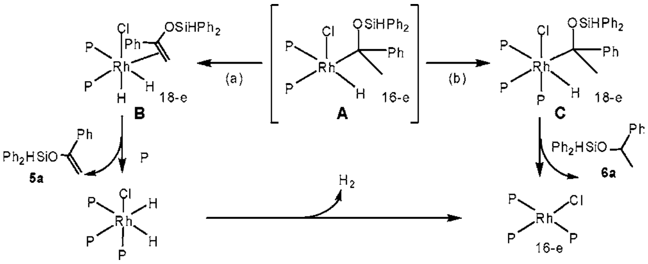


Figure 2. Structures of condensation products.

The generally accepted mechanism is depicted in Scheme 1.[18,19] According to our experimental data, it appears that the ratio **5a**/**6a** is influenced by phosphine steric hindrance (Tolman cone angle) (see the Supporting Information, p S7). To corroborate this postulate, we carried out reactions with soluble phosphines bearing various cone angles (PPh_3 (145°), P(*o*-tol)$_3$ (194°), P(mesityl)$_3$ (212°)). As expected, it has been observed that an increase in the cone angle induces better silyl enol selectivities (the ratios **5a**/**6a** were, respectively, 1:99, 24:76, and 38:62). We assume that as the result of strong steric interactions between the polymeric matrix that ligates the phosphine through ionic ammonium−sulfonate bonds, the cone angle of the supported TPPTS is larger than this of its free counterpart. We suggest that phosphines exhibiting both large cone angle and entropic constrains arising from polymeric rigidity disfavor the formation of intermediate **C** (b), thus allowing the open coordination site at the catalytic Rh center in **B** that is necessary for the β-H elimination (a).

Scheme 1. Competitive Catalytic Pathways



In summary, we report that ionic resin soaked Rh **1** efficiently catalyzes the dehydrogenative silylation of ketones. This process appears to be a valuable route, particularly for electron-deficient acetophenones and sterically hindered and chelating methyl ketones. It allows under mild conditions the formation of kinetic silyl enol ethers, which can be directly involved in one-pot condensation reactions without isolation.

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Supporting Information Available: General procedures and spectra of the obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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