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Hydrosilylation of Carbonyl-Containing Substrates Catalyzed by an Electrophilic η^1-Silane Iridium(III) Complex

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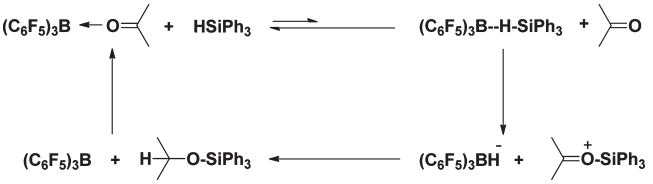
Hydrosilylation of a variety of ketones and aldehydes using the cationic iridium catalyst (POCOP)-Ir(H)(acetone)$^+$, **1** (POCOP = 2,6-bis(di-*tert*-butylphosphinito)phenyl), is reported. With triethyl silane, all but exceptionally bulky ketones undergo quantitative reactions employing 0.5 mol % catalyst in 20−30 min at 25 °C. Hydrosilylation of esters and amides results in over-reduction and cleavage of C−O and C−N bonds, respectively. The diastereoselectivity of hydrosilylation of 4-*tert*-butyl cyclohexanone has been examined using numerous silanes and is highly temperature dependent. Using $EtMe_2SiH$, analysis of the ratio of cis:trans hydrosilylation products as a function of temperature yields values for $\Delta\Delta H^{\ddagger}$ ($\Delta H^{\ddagger}$(trans) − $\Delta H^{\ddagger}$(cis)) and $\Delta\Delta S^{\ddagger}$ ($\Delta S^{\ddagger}$(trans) − $\Delta S^{\ddagger}$(cis)) of −2.5 kcal/mol and −6.9 eu, respectively. Mechanistic studies show that the ketone complex (POCOP)Ir(H)(ketone)$^+$ is the catalyst resting state and is in equilibrium with low concentration of the silane complex (POCOP)Ir(H)($HSiR_3$)$^+$. The silane complex transfers R_3Si^+ to ketone, forming the oxocarbenium ion $R_3SiOCR'_2{}^+$, which is reduced by the resulting neutral dihydride **3**, (POCOP)Ir$(H)_2$, to yield product $R_3SiOCHR'_2$ and (POCOP)IrH^+, which closes the catalytic cycle.

Introduction

Hydrosilylation of carbonyl functionalities is an extensively explored and widely used synthetic methodology.[1] This process provides an alternative to hydride reductions of ketones and aldehydes as well as a convenient one-step process for converting these substrates directly to protected alcohols, which circumvents the normal two-step procedure: reduction to alcohol followed by silyl protection. Several different hydrosilylation mechanisms have been shown to operate, dependent on the nature of the catalyst. Late metal catalysts typically proceed through a "Chalk−Harrod" pathway, in which the key step involves oxidative addition of the silane to a low-valent metal center.[2] Early metal catalysts where oxidative addition is disfavored proceed via σ bond metathesis mechanisms.[3]

Scheme 1



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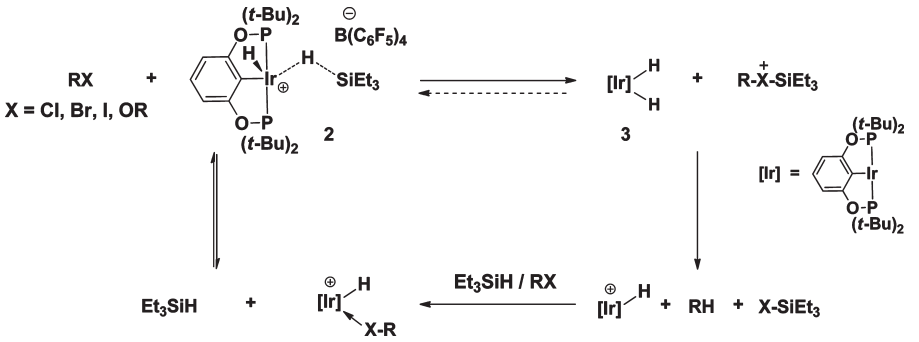
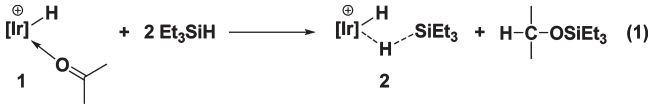
Scheme 2



Recently, high-valent metal oxo complexes have been shown to serve as hydrosilylation catalysts. Abu-Omar reported that the $Re(O)(hoz)_2^+$ (hoz = 2-(2′-hydroxyphenyl)-2-oxazoline) catalyst operates via a σ bond metathesis mechanism.[3m−o] Through extensive mechanistic studies Toste and Bergman established that hydrosilylations catalyzed by $(PPh_3)_2Re(O)_2I$ occur by a unique mechanism that involves addition of the silane across the Re═O bond, insertion of the carbonyl functionality into the resulting Re−H bond, and elimination of the hydrosilylation product, which closes the cycle and regenerates the Re═O bond.[3g−j] Piers has reported that Ph_3SiH in combination with catalytic amounts of $(C_6F_5)_3B$ achieves hydrosilylation of carbonyl compounds.[3b,4a,4b] Surprisingly, although the carbonyl compounds exhibit much higher binding affinities to $(C_6F_5)_3B$ than Ph_3SiH, the mechanism involves activation of the *silane* through coordination to $(C_6F_5)_3B$, transfer of Ph_3Si^+ to the carbonyl functionality, and reduction of the resulting $Ph_3SiOC(R)(R')^+$ by $(C_6F_5)_3BH^-$ (Scheme 1).

We have recently reported reduction of R−X bonds (X = Cl, Br, I, OR) using the silane complex **2**, a potent R_3Si^+ donor.[5] The mechanism was shown to involve transfer of R_3Si^+ to X to generate $R_3Si{-}X{-}R^+$ followed by hydride reduction of this species by the iridium dihydride complex **3**, formed upon silyl transfer (see Scheme 2).

The most convenient precatalyst was found to be the stable, crystalline, easily isolated acetone complex, **1**. Treatment with excess triethylsilane rapidly generates silane complex **2** in situ and one equivalent of $Et_3SiOCH(CH_3)_2$, the acetone hydrosilylation product (eq 1). These observations suggested



(1)

that **2** should function as a hydrosilylation catalyst. We report here synthetic and mechanistic details of the catalytic hydrosilylation of a variety of carbonyl-containing compounds employing this system, which proves to be exceptionally active and highly efficient.

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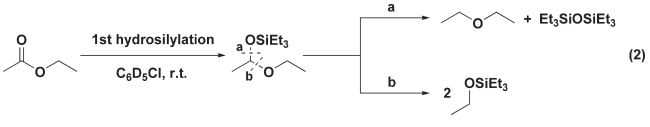
(5) (a) Yang, J.; Brookhart, M. *J. Am. Chem. Soc.* **2007**, *129*, 12656. (b) Yang, J.; White, P. S.; Brookhart, M. *J. Am. Chem. Soc.* **2008**, *130*, 17509. (c) Yang, J.; White, P. S.; Schauer, C; Brookhart, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4141. (d) Yang, J.; Brookhart, M. *Adv. Synth. Catal.* **2009**, *351*, 175.

Results and Discussion

Hydrosilylation of Carbonyl-Containing Substrates Catalyzed by 1. Complex **1**[5a] together with Et_3SiH initiates hydrosilylations of ketones, aldehydes, esters, and amides at room temperature. Results of hydrosilylation of several carbonyl-containing substrates are summarized in Table 1. Ketones undergo hydrosilylation rapidly to attain quantitative conversions in 0.3−0.5 h at room temperature (200 TOs) (Table 1, entries 1−6). Hydrosilylations of ketones bearing exceptionally bulky alkyl substituents, diisopropyl ketone (entry 2) and methyl *tert*-butyl ketone (entry 3), are rapidly and quantitatively achieved. The exceptional efficiency of the hydrosilylation is illustrated by the quantitative hydrosilylation of methyl *tert*-butyl ketone in 30 min using a 0.075 mol % catalyst loading (1330 TOs, entry 4). Hydrosilylation of acetophenone yields 94% of the corresponding silyl alkyl ether and 6% of ethylbenzene, which results from further cleavage of the silyl alkyl ether (entry 5). The competitive hydrosilylation reaction between acetophenone and 4′-(trifluoromethyl)acetophenone (entry 6) shows that the activity of the more basic acetophenone is ca. 4 times greater than that of 4′-(trifluoromethyl)acetophenone. Hydrosilylation of aldehydes with excess silane often results in secondary cleavage of the resultant silyl alkyl ether.[5b] However, using just over 1 equiv of Et_3SiH, benzaldehyde undergoes quantitative hydrosilylation in 0.3 h to yield the silyl benzyl ether (entry 7).

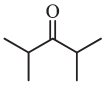
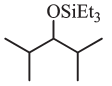
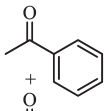
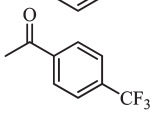
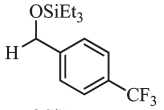
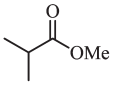
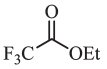
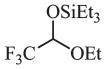
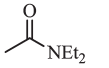
Complex **1** catalyzes the hydrosilylation of ethyl acetate to afford silyl ethyl ether and diethyl ether in 2:1 ratio (entry 8). This results from formation of the acetal and subsequent cleavage of either of the C−O bonds as shown in eq 2.



(2)

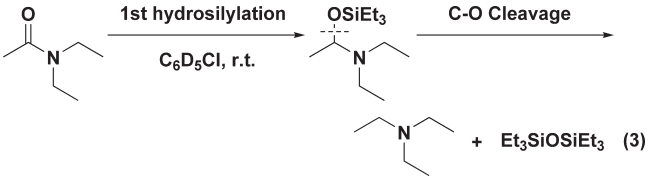
In contrast, the hydrosilylation of methyl isobutyrate exhibits only cleavage of the C−OMe bond of the acetal to give only isobutyl silyl ether and methyl silyl ether (entry 9). This selectivity can be attributed to a sterically demanding environment around oxygen in the C--$OSiEt_3$ bond. Introduction of an electron-withdrawing group into the α-position of the ester enables a single hydrosilylation even with excess Et_3SiH to selectively form the corresponding acetal (entry 10). The preference for single hydrosilylation is likely due to the decreased basicity of the acetal formed via initial hydrosilylation and the decreased tendency for ionization of the silated acetal.

Table 1. Hydrosilylation of Carbonyl Functions by 1[a]

entry	substrate	*t* h	conversion[b] %	product
1		0.3	quant.	
2		0.5	quant.	
3		0.3	quant.	
4[c]		0.5	quant.	
5[d]		0.3	quant.	
6[e,f]	A 	0.5	80	
	B 		20	
7[g]		0.3	quant.	
8		0.3	quant.	$EtOSiEt_3$(70%) + Et_2O(30%)
9		1.5	quant.	*i*-$BuOSiEt_3$(50%) + $MeOSiEt_3$(50%)
10[h]		22	95	
11		16	42	NEt_3 + Et_3Si-O-$SiEt_3$

[a] Reaction conditions: 0.5 mol % **1**, solvent = C_6D_5Cl, 3 equiv of Et_3SiH, and room temperature. [b] Determined by ^1H NMR. [c] 0.075 mol % **1**. [d] 6% of ethylbenzene formed. [e] [A]:[B]:[Et_3SiH]:[**1**] = 100:100:100:1. [f] Minor unidentified signals observed in NMR. [g] 1.2 equiv of Et_3SiH employed. [h] Use of Me_2EtSiH instead of Et_3SiH affords quantitatively the corresponding acetal in only 0.3 h.

N,N-Diethyl acetamide is slowly hydrosilated (42% conversion in 16 h) to give Et_3N together with the disiloxane (entry 11). After 16 h, no further consumption of the amide is observed. The retarded hydrosilylation may result from the deactivation of the electrophilic catalytic Ir species by excess Et_3N formed during reaction. The sequence responsible for product formation is shown in eq 3 and is similar to that proposed for ester reduction.



Stereochemistry of Hydrosilylation of 4-*tert*-Butyl Cyclohexanone. Reductions of 4-*tert*-butyl cyclohexanone by various metal hydrides, especially $LiAlH_4$ and $NaBH_4$, have been extensively studied[6] and found to preferentially give the trans-alcohol via an axial attack of the hydride (eq 4, path a). Several explanations have been advanced for this diastereoselectivity including the straightforward proposition that there are unfavorable eclipsing interactions between the axial C−H bonds at C2 and C6 and the

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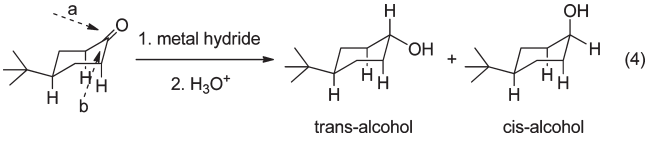
Table 2. Hydrosilylation of 4-*tert*-Butylcyclohexanone with Various Alkylsilanes Catalyzed by 1[a]

entry	catalyst mol %	silane	solvent	*T*, °C	*t*, h	conversion[b] %	*trans*/*cis*[b] %
1	1.0	$EtMe_2SiH$	CD_2Cl_2	22	0.3	quant.	55:45
2	1.0	$EtMe_2SiH$	C_6D_5Cl	22	0.3	quant.	69:31
3	1.0	$EtMe_2SiH$	toluene-d_6	22	0.3	quant.	75:25[c]
4	1.0	Et_2MeSiH	C_6D_5Cl	22	0.3	quant.	74:26
5	1.0	Et_3SiH	C_6D_5Cl	22	0.3	quant.	68:32
6	1.0	*i*-$PrMe_2SiH$	C_6D_5Cl	22	0.3	quant.	76:24
7	1.0	*t*-$BuMe_2SiH$	C_6D_5Cl	80	2	quant.	87:13
8	1.0	$(i\text{-}Pr)_3SiH$	C_6D_5Cl	80	12	quant.	51:49
9	1.0	$(t\text{-}Bu)_2SiH_2$	C_6D_5Cl	22	1.5	quant.	57:43[e]
10	1.39	$EtMe_2SiH$	CD_2Cl_2	−20	0.5	quant.	82:18[f]
11	1.39	Et_3SiH	CD_2Cl_2	−20	0.5	quant.	88:12[f]

[a] Reaction conditions: 3 equiv of silane in C_6D_5Cl (0.3 mL). [b] Determined by NMR spectroscopy. [c] **1** is not completely soluble in toluene-d_8. [e] 39% of di-*tert*-butyl silyl enol ether is observed. [f] 4 equiv of silane used.

incoming hydride reagent during equatorial attack (eq 4, path b).[7]



(4)

The diastereoselectivity of hydrosilylations of cyclohexanones has also received attention. Semmelhack has examined the hydrosilylation of 4-*tert*-butyl cyclohexanone by various di- and trialkylsilanes using classical catalysts $(PPh_3)_3RhCl(I)$ and $(PPh_3)_3RuCl_2(II)$, which operate by the Chalk−Harrod mechanism.[2e] Bulky triethyl- and triphenylsilanes provide predominantly the more stable trans silyl ether with up to 95% diastereoselectivity, whereas the less bulky diethyl- and diphenylsilanes give the corresponding silyl ethers with a trans/cis ratio of ca. 50:50. On the other hand, hydrosilylation by diphenylsilane using $(PPh_3)_4RhH(I)$ has been reported to give a 84:16 (trans/cis) ratio of diasteromers.[2j] A triruthenium carbonyl cluster-catalyzed hydrosilylation of 4-*tert*-butyl cyclohexanone affords predominantly the cis-diastereomer with triethylsilane,[2l] which contrasts with the results of the hydrosilylation by the mononuclear Rh or Ru complexes. Most recently, Toste et al. have obtained silyl ethers with a high trans selectivity (>96%) using the dioxorhenium(V) catalyst $(PPh_3)_2Re(O)_2I$, which operates by the non-Chalk−Harrod mechanism described above.[3j] These studies prompted us to examine the diastereoselectivities of hydrosilylation of 4-*tert*-butyl cyclohexanone using catalyst **1**, where product ratios depend on axial versus equatorial attack of iridium dihydride **3** on the silated ketone (see below).

Results of the hydrosilylation of 4-*tert*-butyl cyclohexanone using various silanes and different solvents are shown in Table 2. In chlorobenzene, there is little difference in diastereoselectivity as the bulk of the silane ranges from dimethylethylsilane (trans/cis = 69:31) to methyldiethylsilane (74:26) to triethylsilane (68:32) to dimethylisopropylsilane (76:24). Dimethyl-*tert*-butylsilane and triisopropylsilane are sufficiently unreactive that the reactions must be carried out at 80 °C; however, quantitative conversions can be obtained and result in 87:13 and 51:49 trans/cis product ratios, respectively. In the case of di-*tert*-butylsilane, selectivity drops to 57:43, but the hydrosilylation products are accompanied by a side reaction to form 39% of the silyl enol ether. (Semmelhack et al. observed the same side product in the hydrosilylation using $(EtO)_3SiH$.[2e])

Solvent effects on diastereoselectivity are also minimal. Hydrosilylation with dimethylethylsilane in methylene chloride, chlorobenzene, and toluene varies from trans/cis = 55:45 to 69:31 to 75:25, respectively. The most dramatic effect on selectivity is seen with variation in reaction temperature. Using dimethylethylsilane in methylene chloride, the selectivity increases from 55:45 at 22 °C to 82:18 at −20 °C, while for triethylsilane the selectivity is 68:22 at 22 °C in chlorobenzene and increases to 88:12 at −20 °C in methylene chloride. Temperature effects are examined in more detail in the next section.

Table 3. Hydrosilylation of 4-*tert*-Butyl Cyclohexanone with $EtMe_2SiH$ at Various Reaction Temperatures[a]

entry	*T*, °C	*t*, h	conversion[b] %	trans/cis ratio[b] %
1	−60	17	quant.	92:8
2	−30	3	quant.	86:14
3	0	1	quant.	77:23
4	17	3	quant.	70:30

[a] Reaction conditions; 4 equiv of $EtMe_2SiH$, 1.39 mol % of **1** in CD_2Cl_2 (1 mL). [b] Determined by ^1H NMR spectroscopy.

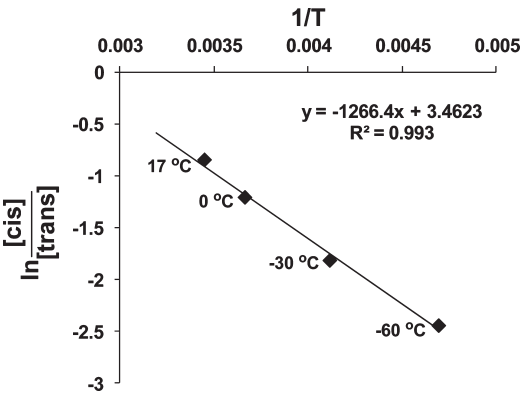


Figure 1. Plot of ln[cis]/[trans] vs $1/T$ using the data from Table 3.

Hydrosilylation of 4-*tert*-Butyl Cyclohexanone: Effect of Reaction Temperature on Diastereoselectivity. Although appreciable efforts have been dedicated to the elucidation of factors affecting the diastereoselectivity of metal hydride reductions of 4-*tert*-butyl cyclohexanone, there have been limited studies of temperature effects on selectivity.[8] Thus, we have examined the diastereoselectivity of hydrosilylation of 4-*tert*-butyl cyclohexanone with dimethylethylsilane over

(7) (a) Coxon, J. M.; Houk, K. N.; Luibrand, R. T. *J. Org. Chem.* **1995**, *60*, 418. (b) Li, H.; le Noble, W. J. *Recl. Trav. Chim. Pays-Bas* **1992**, *111*, 199. (c) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. (d) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. (e) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1973**, 4307.

Table 4. Hydrosilylations of Alkyl-Substituted Cyclohexanone Derivatives Catalyzed by 1[a]

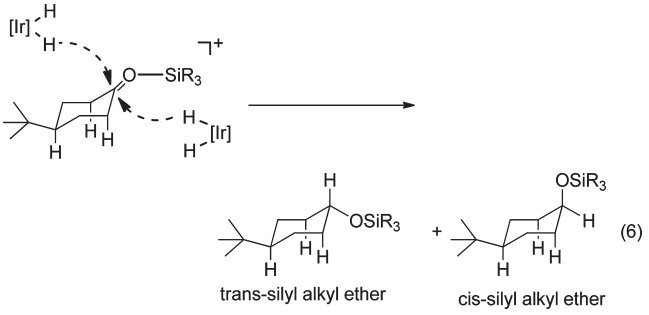
entry	ketone	silane	T, °C	t, h	conversion[b] %	trans/cis ratio[b] %
1	3,3,5-trimethylcyclohexanone	$EtMe_2SiH$	22	0.3	quant.	86:14
2	2-methylcyclohexanone	$EtMe_2SiH$	22	0.5	quant.	29:71
3	2-*tert*-butylcyclohexanone	$EtMe_2SiH$	22	0.5	quant.	24:76
4	camphor	$EtMe_2SiH$	0	2	quant.	21:79[c]

[a] Reaction conditions; 0.5 mol % of **1** and 3 equiv of silane in C_6D_5Cl. [b] Determined by NMR spectroscopy. [c] exo/endo ratio.

a wide range of temperatures. These data provide information concerning differences of enthalpies and entropies of activation for the two pathways. The trans/cis product ratio for the hydrosilylation of 4-*tert*-butyl cyclohexanone in CD_2Cl_2 at various reaction temperatures is shown in Table 3. A plot of ln[cis]/[trans] versus $1/T$ made using the data in Table 3 provides a good linear regression with $R^2 = 0.993$ as shown in Figure 1. By using the relationship shown in eq 5 (derived from the Erying equation), $\Delta\Delta H^{\ddagger}$ ($\Delta H^{\ddagger}$(trans) − $\Delta H^{\ddagger}$(cis)) and $\Delta\Delta S^{\ddagger}$ ($\Delta S^{\ddagger}$(trans) − $\Delta S^{\ddagger}$(cis)) were calculated to be −2.5 kcal/mol and −6.9 eu, respectively.

$$\ln\frac{[\text{cis}]}{[\text{trans}]} = \frac{\Delta H^{\ddagger}(\text{trans}) - \Delta H^{\ddagger}(\text{cis})}{RT} + \frac{\Delta S^{\ddagger}(\text{cis}) - \Delta S^{\ddagger}(\text{trans})}{R} \quad (5)$$

The stereodetermining step is attack of **3** on the silated ketone (eq 6; see below for mechanistic considerations), and thus axial attack is strongly favored enthalpically over equatorial attack but strongly disfavored entropically. Since this is a bimolecular reaction, both activation entropies are no doubt negative, so axial attack must exhibit a more negative entropy of activation relative to equatorial attack. The reasons for these significant differences are not clear.

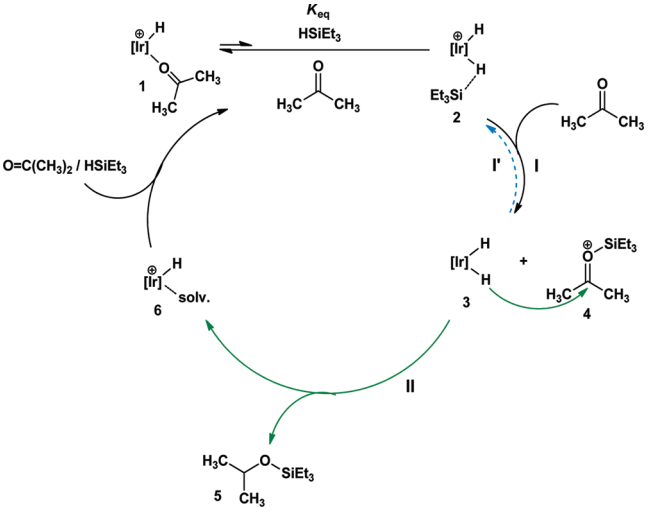


(6)

It is noteworthy that the iridium-catalyzed hydrosilylation of 4-*tert*-butyl cyclohexanone has considerably larger differences in the activation parameters relative to reductions by $LiAlH_4$ and $NaBH_4$ (for $LiAlH_4$, $\Delta\Delta H^{\ddagger} = -0.8$ kcal/mol and $\Delta\Delta S^{\ddagger} = 2.0$ eu).[8d] In these cases the temperature dependence of the product ratio is small and $\Delta\Delta S^{\ddagger}$ is small and positive, in contrast to a large negative value for the hydrosilylation.

Hydrosilylation of Alkyl-Substituted Cyclohexanone Derivatives Catalyzed by 1. We have examined the hydrosilylations of other alkyl-substituted cyclohexanone derivatives to probe the diastereoselectivities in these cases. Results of hydrosilylation of 3,3,5-trimethyl cyclohexanone, 2-methyl cyclohexanone, 2-*tert*-butyl cyclohexanone, and camphor with dimethylethylsilane are summarized in Table 4.

Scheme 3. Proposed Catalytic Cycle for the Iridium-Catalyzed Hydrosilylation of Acetone with Triethylsilane

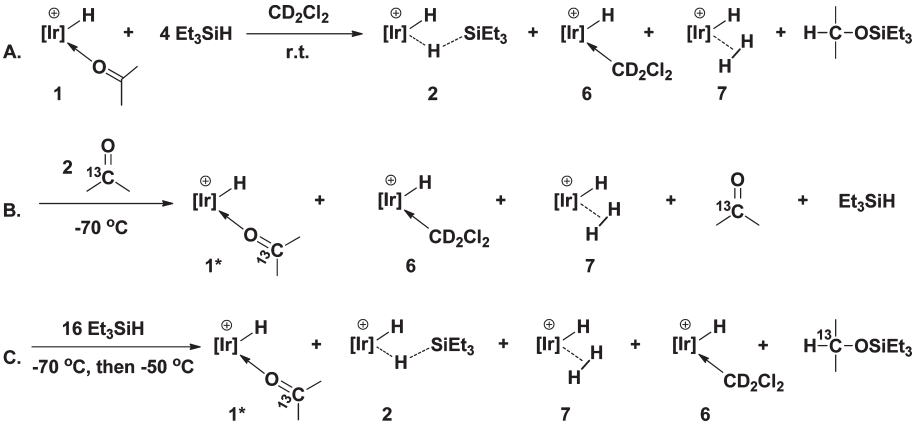


3,3,5-Trimethyl cyclohexanone undergoes quantitative hydrosilylation with dimethylethylsilane in 0.3 h to give the silyl alkyl ether with 86% trans diastereoselectivity (entry 1). The preference for trans stereochemistry can be attributed to blocking of the axial approach of the bulky iridium dihydride by the axial methyl group at C3. (Trans selectivity ranging from 52% to 83% is seen in hydride reductions of 3,3,5-trimethyl cyclohexanone.)[6h,i,n,p] 2-Alkylcyclohexanone derivatives possessing large equatorial alkyl substituents are reported to inhibit axial attack of metal hydrides.[6a,e,l,m] For example, reduction of 2-methyl cyclohexanone by $LiAlH_4$ affords alcohols with a trans/cis selectivity of ca. 73:27. However, when the steric bulk of the C2 substituent is increased to *tert*-butyl, axial approach is somewhat inhibited to yield product alcohols with slight cis selectivity (50−64%). The hydrosilylation of 2-methyl cyclohexanone by **1** at 22 °C proceeds rapidly to give the silyl alkyl ether with 71% cis selectivity (entry 2). The use of 2-*tert*-butyl cyclohexanone in the hydrosilylation leads to a slight increase in the cis selectivity to 76% (entry 3). The steric impact of 2-substituents is significantly greater in these cases compared to the metal reductions. The hydrosilylation of camphor at 0 °C yields the exo and endo isomers in 21:79 ratio, respectively (entry 4). In the $(Ph_3P)_4RhH$-catalyzed hydrosilylation of camphor with diphenylsilane the opposite selectivity is observed, with an exo:endo product ratio of 64:36 reported.[2j]

Mechanistic Investigation of the Hydrosilylation of Ketones. Based on earlier mechanistic investigations of silane reductions of alkyl halides and alkyl ethers using iridium complex **1**, our working hypothesis concerning the catalytic mechanism of hydrosilylation of ketones is shown in Scheme 3 and illustrated with acetone. Binding triethylsilane to the

(8) (a) Lansbury, P. T.; Macleay, R. E. *J. Org. Chem.* **1963**, *28*, 1940. (b) Wigfield, D. C.; Phelps, D. J. *J. Org. Chem.* **1976**, *41*, 2396. (c) Ashby, E. C.; Boone, J. R. *J. Org. Chem.* **1976**, *41*, 2890. (d) Rosenberg, R. E.; Vilardo, J. S. *Tetrahedron Lett.* **1996**, *37*, 2185.

Scheme 4



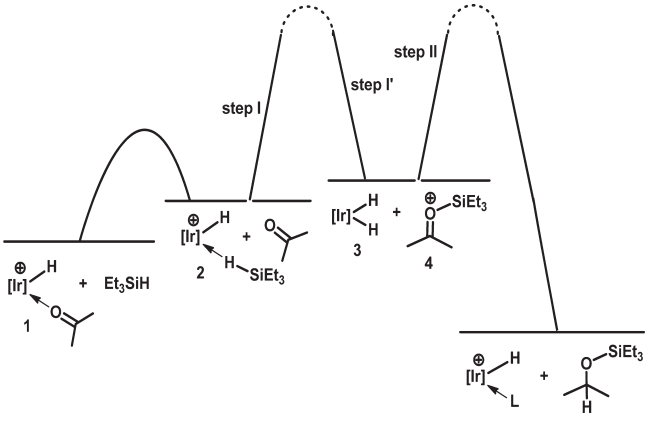
electrophilic iridium center in **2** renders this complex a potent Et_3Si^+ donor, which can transfer Et_3Si^+ to acetone, forming the oxocarbenium ion, **4**, and iridium dihydride, **3**. The dihydride, earlier established as a good hydride donor,[5b] reacts with **4** to produce hydrosilated product, **5**, and the cationic hydride, **6**, which then reenters the catalytic cycle.

Low-temperature reactions were carried out to probe the details of this cycle. ^{13}C-labeled acetone, $(CH_3)_2{}^{13}CO$), was employed to allow monitoring by ^{13}C as well as ^{1}H and ^{31}P NMR spectroscopy. Initially, the equilibrium between **1** and **2** was probed, as shown in Scheme 4. Reaction of **1** (containing unlabeled bound acetone) with triethylsilane (4 equiv) in CD_2Cl_2 at 25 °C rapidly produced 1 equiv of $Et_3SiOCHMe_2$ (^{1}H NMR) and silane complex **2** (21%), CD_2Cl_2 complex **6** (48%), and cationic trihydride **7** (31%) (Scheme 4A). The complexes were identified by ^{31}P NMR shifts. The trihydride results from reaction of **2** with traces of water.[9] This solution was cooled to −70 °C, and $(CH_3)_2$*CO (2 equiv) was added. Acetone immediately displaces silane from **2** and CD_2Cl_2 from **6** to give a solution containing acetone complex **1*** (ca. 64%) and trihydride **7** (ca. 34%) and traces of solvent complex **6** (Scheme 4B). ^{1}H NMR spectroscopy was used to determine the ratio of free acetone (δ 2.13, doublet, J_{13C-H} = 5 Hz) to bound acetone (δ2.57, doublet, J_{13C-H} = 5 Hz) as 64:36. No silane complex can be easily detected (< 0.5%), and no hydrosilylation product is formed. The hydrosilylation product of $(CH_3)_2$*CO, Et_3SiO*$CHMe_2$, can be distinguished from $Et_3SiOCHMe_2$ since the CH resonance at δ3.99 is split into a doublet with J_{13C-H} = 138.5 Hz. These results imply that the equilibrium between **1** and **2**, not surprisingly, lies strongly to the left and that equilibrium is established rapidly relative to product formation.

To quantitatively assess K_{eq}, 16 equiv of Et_3SiH was added to this solution (Scheme 4C). Even under these conditions no silane complex **2** could be detected by ^{31}P NMR spectroscopy. Upon warming this solution in the NMR probe to −50 °C, catalytic hydrosilylation begins as shown by the appearance in the ^{1}H NMR spectrum of Et_3SiO*$CHMe_2$. As acetone is consumed and the ratio of Et_3SiH to free acetone further increases, a point is reached where finally a sufficient quantity of silane complex is formed that the equilibrium constant can be measured. After 10 min at −50 °C, the ratio of free acetone to Et_3SiH is 1:18.9 (^{1}H NMR), and the ratio of acetone complex **1** to silane complex **2** is 37.5:1

(9) The trihydride is inert and is carried through the next sequence of reactions.

Scheme 5. Free Energy Diagram for the Iridium-Catalyzed Hydrosilylation of Acetone with Triethyl Silane



(^{31}P NMR), which yields an equilibrium constant of 1.4×10^{-3} at −50 °C (eq 7):[10]

$$K_{eq} = \frac{[(CH_3)_2C{=}O]}{[Et_3SiH]}\frac{[\mathbf{2}]}{[\mathbf{1}]} = 0.053 \times 0.027$$
$$= 1.4 \times 10^{-3}, -50°C \qquad (7)$$

While these experiments establish a rapid equilibrium between **1** and **2** during catalysis with the ketone complex as the nearly exclusive resting state, they do not provide a decision as to whether step I, silation of acetone, or step II, reduction of **4** by iridium dihydride **3**, is turnover-limiting (Scheme 5). Either scenario predicts that the turnover frequency is zero-order in ketone and first-order in Et_3SiH. Indeed that has been confirmed for reduction of 4-*tert*-butyl cyclohexanone at −60 °C under typical catalytic conditions. Figure 2 (left) shows a typical plot of the initial rate of disappearance of 4-*tert*-butyl cyclohexanone (1.06 M) using Et_3SiH (0.639 M) and complex **1** (6.4 mM) in CD_2Cl_2. Figure 2 (right) shows a

(10) The reaction of acetone-2-^{13}C (3 equiv) with a solution containing **2**, **6**, and **7** in a ratio of 0.68:0.12:0.19 in the presence of excess triethylsilane (90 equiv) at −70 °C leads to hydrosilation (36% conversion) in 5 min to afford Et_3SiO-$^{13}CHMe_2$, **5**. ^{1}H and ^{31}P NMR spectra at −70 °C exhibit the proton resonances for triethylsilane and free acetone-2-^{13}C, and the phosphorus resonances of iridium species **1** (61%) and **2** (9%) as well as **6** (2%) and **7** (28%). On the basis of these NMR data, the equilibrium constant, K (−70 °C), between **1** and **2** can be calculated to be 1.8×10^{-3}, in agreement with the value of 1.4×10^{-3} obtained at −50 °C.

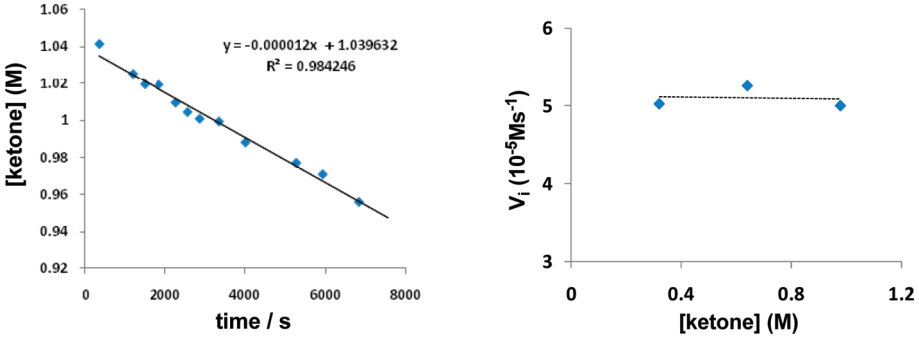


Figure 2. (Left) Plot of concentration of 4-*tert*-butyl cyclohexanones [ketone] vs time for the hydrosilylation of 4-*tert*-butyl cyclohexanone catalyzed by **1** at −60 °C. (Right) Plot of the initial rate, V_i, of 4-*tert*-butyl cyclohexanone vs 4-*tert*-butyl cyclohexanone concentration at −60 °C.

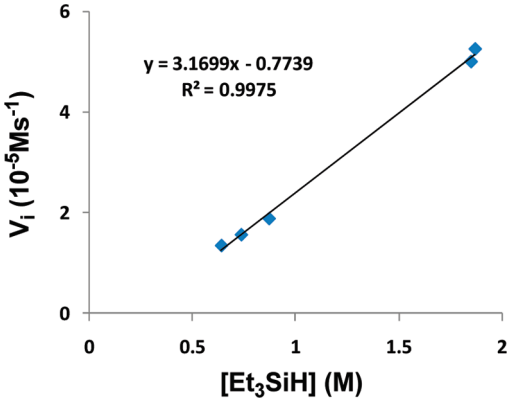


Figure 3. Plot of the initial rate, V_i, of disappearance of 4-*tert*-butyl cyclohexanone vs Et_3SiH concentration at −60 °C.

plot of the initial rates of disappearance of 4-*tert*-butyl cyclohexanone at various concentrations of 4-*tert*-butyl cyclohexanone using 1.87 M Et_3SiH and 6.4 mM **1** in CD_2Cl_2 at −60 °C. This plot establishes that the turnover frequency is zero-order in ketone. Figure 3 shows a plot of the initial rates of disappearance of 4-*tert*-butyl cyclohexanone (0.32−1.06 M) at various concentrations of Et_3SiH using complex **1** (6.4 mM) in CD_2Cl_2 (−60 °C). This plot shows clearly that the turnover frequency is first-order in silane.

Jian et al. has reported the Ir-catalyzed reduction of alkyl halides by Et_3SiH and proposed a quite similar catalytic cycle to Scheme 3 based on the kinetic data, although, as here, they were not able to distinguish whether the silation of alkyl halides, RX, or the transfer of hydride to Et_3SiXR^+ was the turnover-limiting step.[5a]

Conclusions

Iridium complex **1** is a highly active, long-lived catalyst for hydrosilylation of a variety of ketones and aldehydes with trialkylsilanes to afford the corresponding silyl alkyl ethers in excellent yields. Highly hindered ketones such as diisopropyl ketone are effective substrates. The majority of the cases studied here have used Et_3SiH as the silane, but several other silanes including the bulky $(i\text{-}Pr)_3SiH$ have been shown to be effective with cyclohexanone. Hydrosilylation of esters leads to "over-reduction" and cleavage of C−O bonds. Similarly, diethyl acetamide reacts to yield triethylamine. The diastereoselectivity of the hydrosilylation of 4-*tert*-butyl cyclohexanone with **1** and $EtMe_2SiH$ shows unprecedented temperature dependence. Analysis of product ratios as a function of temperature yields values for $\Delta\Delta H^{\ddagger}$ ($\Delta H^{\ddagger}$(trans) − $\Delta H^{\ddagger}$(cis)) and $\Delta\Delta S^{\ddagger}$ ($\Delta S^{\ddagger}$(trans) − $\Delta S^{\ddagger}$(cis)) of −2.5 kcal/mol and −6.9 eu, respectively.

A mechanistic study of the reaction showed that the ketone and silane complexes are in rapid equilibrium relative to the rate of catalytic hydrosilylation and that the ketone complex is strongly favored and can be viewed as the resting state. Catalysis ensues by silation of ketone by the cationic silane complex followed by reduction of this species by the resultant iridium dihydride. Low-temperature mechanistic studies revealed that the ketone complex is the dominant resting state in rapid equilibrium with silane complex **2**. The turnover-limiting step in this catalytic cycle is either silation of ketone by **2** or the reduction of resultant oxocarbenium ion via a hydride transfer from iridium dihydride **3**. The turnover frequency is first-order in silane and zero-order in ketone, in accord with this proposal. This mechanism is similar to that proposed by Piers for hydrosilylation of ketones using $(C_6F_5)_3B/Ph_3SiH$, where the silane is activated by $(C_6F_5)_3B$ and transfers Ph_3Si^+ to ketone.[4a]

Experimental Section

General Procedures. All manipulations were carried out using standard Schlenk, high-vacuum, and glovebox techniques. Argon and nitrogen were purified by passing through columns of BASF R3-11 catalyst (Chemalog) and 4 Å molecular sieves. THF was distilled under a nitrogen atmosphere from sodium benzophenone ketyl prior to use. Pentane, methylene chloride, and toluene were passed through columns of activated alumina[11] and degassed by either freeze−pump−thaw methods or purging with argon. Benzene and acetone were dried with 4 Å molecular sieves and degassed by freeze−pump−thaw methods. Silanes were dried with $LiAlH_4$ or 4 Å molecular sieves and vacuum transferred into a sealed flask. All of the other substrates purchased from Sigma-Aldrich were dried with either K_2CO_3 or 4 Å molecular sieves and vacuum transferred into a sealed flask for the substrate with boiling point less than ca. 110 °C, except that 4-*tert*-butyl cyclohexanone was purified by sublimation at ca. 40 °C. Deuterated solvents (CD_2Cl_2, $C_6D_5CD_3$, C_6D_5Cl) for NMR were dried with CaH_2 or 4 Å molecular sieves and vacuum transferred into a sealed flask. NMR spectra were recorded on Bruker spectrometers (DRX-400, AVANCE-400, AMX-300, and DRX-500). ^1H and ^{13}C NMR spectra were referenced to solvent peaks. $Ph_3C[B(C_6F_5)_4]$,[12]

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(12) Scott, V. J.; Çelenligil-Çetin, R.; Ozerov, O. V. *J. Am. Chem. Soc.* **2005**, *127*, 2852.

(POCOP)Ir(H)$_2$,[13] and [(POCOP)Ir(H)(acetone)]$^+$[B(C$_6$F$_5$)$_4$]$^-$, **1**,[5] were prepared according to published procedures.

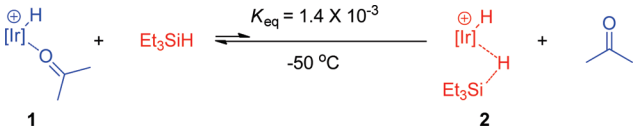
General Procedure for the Hydrosilylation of Substrates with Et$_3$SiH in C$_6$D$_5$Cl. Et$_3$SiH (0.48 mL, 3.00 mmol, 3 equiv) was added to a solution of **1** (6.7 mg, 0.005 mmol, 0.5 mol %) in C$_6$D$_5$Cl (0.3 mL) in a medium-walled J. Young NMR tube, and the contents were well shaken. The substrate (1.00 mmol, 1 equiv) was then added, and the reaction was allowed to stand at room temperature. The progress was followed by NMR spectroscopy. With the exception of diethyl acetamide (entry 11, Table 1) conversions are quantitative and no starting material remains at the end of the reaction. NMR data for the hydrosilated products in Table 1 are available in the Supporting Information.

General Procedure for the Hydrosilylation of 4-*tert*-Butyl Cyclohexanone with Various Silanes in C$_6$D$_5$Cl. Silane (3.00 mmol, 3 equiv) was added to a solution of **1** (6.7 mg, 0.005 mmol, 0.5 mol %) in C$_6$D$_5$Cl (0.3 mL) in a medium-walled J. Young NMR tube, and the contents were well shaken. 4-*tert*-Butyl cyclohexanone (154 mg, 1.00 mmol, 1 equiv) was then added and the reaction was allowed to stand at room temperature for the specified time. The reaction mixture was then analyzed by NMR spectroscopy. NMR data for the hydrosilated products in Table 2 are available in the Supporting Information.

General Procedure for the Hydrosilylation of Alkyl-Substituted Cyclohexanone Derivatives with EtMe$_2$SiH in C$_6$D$_5$Cl. Silane (0.40 mL, 3.00 mmol, 3 equiv) was added to a solution of **1** (6.7 mg, 0.005 mmol, 0.5 mol %) in C$_6$D$_5$Cl (0.3 mL) in a medium-walled J. Young NMR tube, and the contents were well shaken. Alkyl-substituted cyclohexanone derivatives (1.00 mmol, 1 equiv) were then added, and the reaction mixtures were allowed to stand at room temperature or 0 °C for a specific time. The reaction mixtures were then analyzed by NMR spectroscopy. NMR data for the hydrosilated products in Table 4 are available in the Supporting Information.

General Procedure for Kineic Studies (CD$_2$Cl$_2$). Et$_3$SiH was added to a solution of **1** (6.7 mg, 0.005 mmol) in CD$_2$Cl$_2$ in a medium-walled J. Young NMR tube, and the solution was well shaken. The NMR tube was placed in a bath at −100 °C to freeze the solution, and then 4-*tert*-butyl cyclohexanone in CD$_2$Cl$_2$ (0.32−1.06 M) was added on the top of the frozen solution at −100 °C. After briefly shaking, the NMR tube was quickly placed in the NMR probe precooled to −70 °C. The reaction was allowed to warm to −60 °C, and the ratio of 4-*tert*-butyl cyclohexanone to the silyl ether product was monitored with respect to time by ^{1}H NMR. The data were analyzed using the method of initial rates, and the initial reduction rates were obtained from the linear portion of the concentration versus time curve in the early stage of the reaction (Figures 2 and 3).

Scheme 6. Equilibrium between 1 and 2 at −50 °C



Low-Temperature Reaction of 1, Et$_3$SiH, and Acetone-2-^{13}C, −70 to −50 °C. To the solution of **1** (10.05 mg, 0.0075 mmol) in CD$_2$Cl$_2$ in a medium-walled J. Young NMR tube was added 4 equiv of Et$_3$SiH (4.8 μL, 0.03 mmol), and the solution was stirred at 22 °C for 30 min. The solution was cooled to −70 °C, and 1 equiv of acetone-2-^{13}C was added from a stock solution of acetone-2-^{13}C in CD$_2$Cl$_2$. After briefly shaking, the NMR tube was quickly placed in the NMR probe precooled to −80 °C. The reaction was allowed to warm to −70 °C and monitored by NMR spectroscopy. After NMR experiments at −70 °C, 16 equiv of Et$_3$SiH was additionally added to the solution while keeping the temperature at −70 °C, followed by warming the solution to −50 °C. The hydrosilylation of acetone-2-^{13}C with Et$_3$SiH began at −50 °C, and the concentration of all species was monitored by NMR spectroscopy to determine the equilibrium constant between **1** and **2** (Scheme 6).[5a,b]

Acknowledgment. We gratefully acknowledge funding by the National Institutes of Health (Grant No. GM 28939).

Supporting Information Available: Text and figures giving NMR data for hydrosilated products obtained in this work. This material is available free of charge via the Internet at http://pubs.acs.org.

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