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Base-Free Dehydrogenative Coupling of Enolizable Carbonyl Compounds with Silanes

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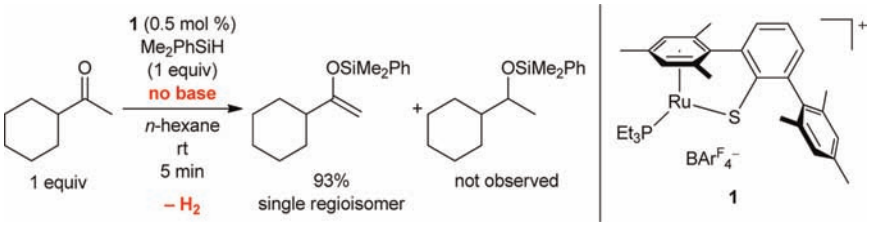
ABSTRACT



A dehydrogenative coupling between enolizable carbonyl compounds and equimolar amounts of triorganosilanes catalyzed by a tethered ruthenium complex with a Ru−S bond is reported. The complex is assumed to fulfill a dual role by activating the Si−H bond to release a silicon electrophile and by abstracting an α-proton from the intermediate silylcarboxonium ion, only liberating dihydrogen as the sole byproduct. Reaction rates are exceedingly high at room temperature with very low loadings of the ruthenium catalyst.

Coordinatively unsaturated late transition metal complexes with a bulky thiolate ligand are particularly active in the reversible splitting of dihydrogen.[1,2] Quantum-chemical calculations indicate that, depending on the transition metal, the activation mechanism is either homolytic (Ir−S bond) or heterolytic (Rh−S bond).[3] For the tethered ruthenium complex **1**[2] (Scheme 1, upper), we believe that the H−H bond is cooperatively activated by the Ru−S bond (Scheme 1, lower).[2,4] By this, dihydrogen is split into a hydride and a proton. The same strategy applied to the chemoselective activation of a Si−H bond produces a metal hydride and a silicon electrophile, likely a sulfur-stabilized silylium ion or silicon-substituted sulfonium ion (Scheme 1, lower);[4] the tether in **1** is absolutely crucial to prevent dissociation of the silylated bulky thiol.

The cooperative activation of Si−H bonds by **1** at ambient temperature is a mild method to generate silicon electrophiles, and our laboratories recently realized its use in C-3-selective indole C−H functionalization.[4] Exclusive bond formation in the C-3 position corroborates an electrophilic aromatic substitution mechanism where the Wheland intermediate is deprotonated to yield an indole along with dihydrogen rather than being reduced to yield an indoline. With no external added base, the neutral ruthenium hydride complex acts as an internal base and not as a reducing agent.

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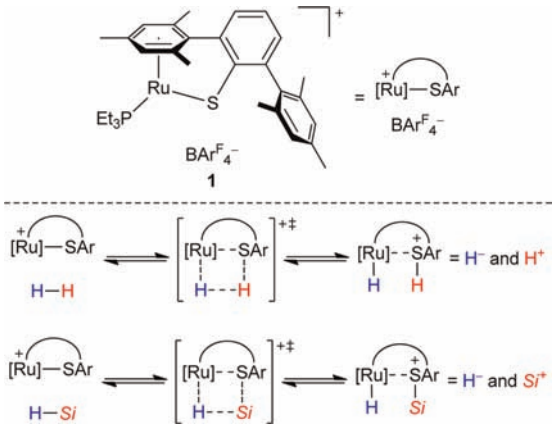
Scheme 1. Tethered Ruthenium Complex **1** with a Polar Ru–S Bond in H–H and Si–H Bond Activation [Ar^F = 3,5-Bis-(trifluoromethyl)phenyl and *Si* = Triorganosilyl]



We, therefore, asked ourselves whether **1** would catalyze, as with dihydrogen,[2,5] the reduction of enolizable carbonyl compounds[6,7] (**I**→**II**→**III**, Scheme 2, left) or would result in the dehydrogenative formation of silyl enol ethers (**I**→**II**→**IV**, Scheme 2, right). The latter, catalyzed by various transition metal complexes, is not unprecedented,[8−17] but there are only a few general protocols.[11,14−17] Moreover, these known systems usually require an external base or thiol whereas our protocol would be base-free with the release of dihydrogen. We report here the dehydrogenative silylation of enolizable carbonyl compounds catalyzed by **1** under neutral conditions to access the synthetically useful class of silyl enol ethers.[18]

Our investigation commenced with a screening of different triorganosilanes **3a**–**3f** in the dehydrogenative coupling of acetophenone (**2a**) catalyzed by **1** (Table 1). The nonhindered silanes **3a** and **3b** showed full conversion at ambient temperature and yielded the desired silyl enol ethers **4a** and **5a** (dehydrogenation path) along with the undesired silyl ether **10a** and **11a** (reduction path) in promising ratios of 85:15 and 83:17, respectively (Table 1, entries 1 and 4). Good chemical yields were obtained in both cases. Those ratios were substantially deteriorated at lower temperatures and remained the same

Scheme 2. Reduction (left) or Dehydrogenation (right) in the Reaction of Enolizable Carbonyl Compounds and Silanes Catalyzed by **1**

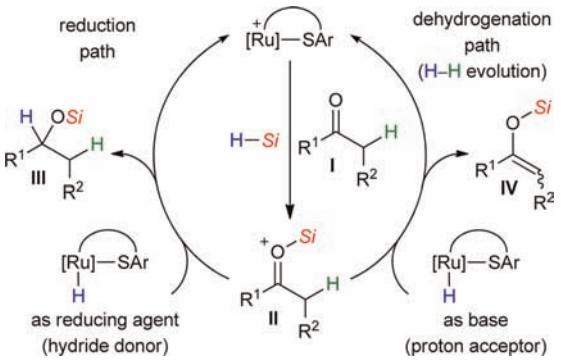
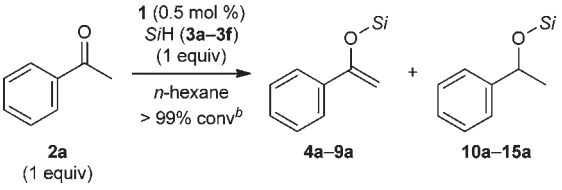


Table 1. Survey of Silanes and Reaction Temperatures in the Dehydrogenative Coupling[a]



entry	*Si*H	temp [°C]	time [min]	compd	chemo-selectivity ratio[c]	yield [%][d]
1	Me_2PhSiH (**3a**)	rt	5	**4a**, **10a**	85:15	93
2		−20	60		53:47	85
3		65	30		84:16	70
4	$MePh_2SiH$ (**3b**)	rt	5	**5a**, **11a**	83:17	89
5	$EtMe_2SiH$ (**3c**)	rt	5	**6a**, **12a**	97:3	91
6	Et_3SiH (**3d**)	65	30	**7a**, **13a**	70:30	87
7	Ph_3SiH (**3e**)	65	30	**8a**, **14a**	80:20	–[e]
8	*t*-$BuMe_2SiH$ (**3f**)	65	30	**9a**, **15a**	–	–[f]

[a] All reactions were conducted according to the general procedure at a concentration of 0.5 M of **3** (cf. the Supporting Information). [b] Conversion was monitored by GLC analysis. [c] Ratio of silyl enol ether (**4a**–**9a**) and silyl ether (**10a**–**15a**) was determined by GLC-MS analysis. [d] Combined yield after catalyst removal. [e] Incomplete conversion. [f] No reaction.

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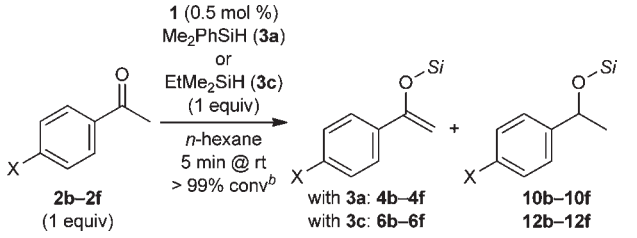
Table 2. Dehydrogantive Coupling of *Para*-Substituted Acetophenones Using Silanes **3a** and **3c**[a]



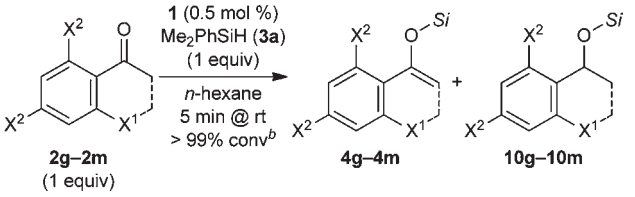
		Me_2PhSiH (**3a**)			$EtMe_2SiH$ (**3c**)		
entry	X compd	compd	ratio of **4**/**10**[c]	yield [%][d]	compd	ratio of **6**/**12**[c]	yield [%][d]
1	OCH_3 **2b**	**4b**, **10b**	10:90	97	**6b**, **12b**	41:59	98
2	CH_3 **2c**	**4c**, **10c**	43:57	96	**6c**, **12c**	91:9	90
3	Cl **2d**	**4d**, **10d**	65:35	93	**6d**, **12d**	98:2	97
4	OTf **2e**	**4e**, **10e**	88:12	91	**6e**, **12e**	90:10	92
5	CF_3 **2f**	**4f**, **10f**	95:5	88	**6f**, **12f**	97:3	82

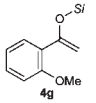
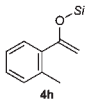
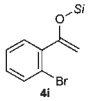
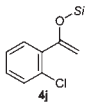
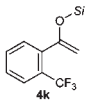
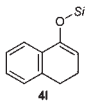
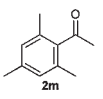
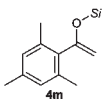
[a] All reactions were conducted according to the general procedure at a concentration of 0.5 M of **3** (cf. the Supporting Information). [b] Conversion was monitored by GLC analysis. [c] Ratio of silyl enol ether (**4b**–**4f** or **6b**–**6f**) and silyl ether (**10b**–**10f** or **12b**–**12f**) was determined by GLC-MS analysis. [d] Combined yield after catalyst removal.

at elevated reaction temperatures (e.g., with **3a**, Table 1, entries 2 and 3); no conversion was seen at −78 °C. We were then delighted to find that, with rarely used silane **3c**, an excellent selectivity of 97:3 in favor of dehydrogenation was obtained (Table 1, entry 5). With a catalyst loading as low as 0.5 mol %, complete conversion and 91% isolated yield were reached within 5 min, requiring neither a base nor a hydrogen acceptor. More bulky silanes **3d**–**3f** either afforded more of the reduced carbonyl compound at slower reaction rate (Table 1, entries 6 and 7) or did not react at all (Table 1, entry 8).

Having established the new catalytic system, we next focused on the substrate scope by using different *para*-substituted acetophenones (**2b**–**2f**, Table 2). We observed a clear trend in the electronic effect of the X group; electron-donating groups steer the catalysis toward reduction while electron-withdrawing X groups favor the dehydrogenation path. The effect is strong with Me_2PhSiH (**3a**, Table 2, columns 3–5) and weaker with $EtMe_2SiH$ (**3c**, Table 2, columns 6–8). A far less pronounced electronic effect is exerted by an X group in the *ortho*-position of the corresponding acetophenones **2g**–**2k** using Me_2PhSiH (**3a**, Table 3, entries 1–5). Only the strongly electron-donating methoxy group is detrimental while the other X groups are tolerated. It is important to note though that the poor 35:65 ratio (**2g**→**4g**/**10g**) with **3a** is dramatically improved to 83:17 (**2g**→**6g**/**12g**) with less hindered silane

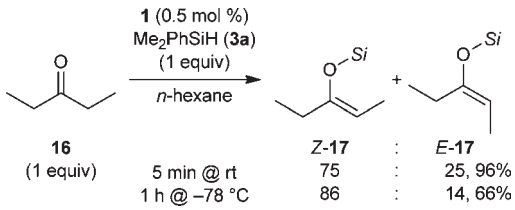
Table 3. Dehydrogenative Coupling of *Ortho*-Substituted Acetophenones and Related Compounds Using Silane **3a**[a]



entry	compd	silyl enol ether	ratio **4**:**10**[c]	yield [%][d]
1	 **2g**	 **4g**	35:65[e]	97
2	 **2h**	 **4h**	>99:1	95
3	 **2i**	 **4i**	>99:1	96
4	 **2j**	 **4j**	98:2	96
5	 **2k**	 **4k**	>99:1	95
6	 **2l**	 **4l**	>99:1	98
7	 **2m**	 **4m**	>99:1	98

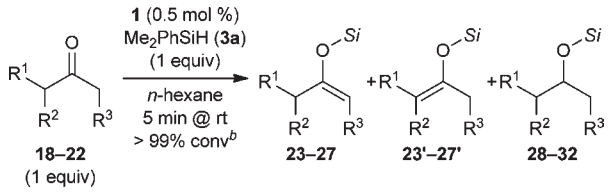
[a] All reactions were conducted according to the general procedure at a concentration of 0.5 M of **3** (cf. the Supporting Information). [b] Conversion was monitored by GLC analysis. [c] Ratio of silyl enol ether (**4g**–**4m**) and silyl ether (**10g**–**10m**) was determined by GLC-MS analysis. [d] Analytically pure product after catalyst removal. [e] The reaction of **2g** with **3c** afforded **6g** and **12g** in a ratio of 83:17 in 96% yield.

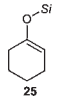
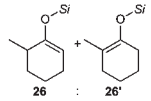
Scheme 3. Probing Diastereoselective Silyl Enol Ether Formation



3c (cf. footnote *e* in Table 3). That example nicely demonstrates that, for critical carbonyl compounds, $EtMe_2SiH$ (**3c**) might even reverse the selectivity found with Me_2PhSiH (**3a**). Our survey also included cyclic substrate **2l**

Table 4. Dehydrogenative Coupling of Dialkyl Ketones: Control of the Regioselectivity[a]



entry	compd	silyl enol ethers	chemoselectivity ratio[c]	yield [%][d]
1	 18	 23	>99:1	90
2	 19	 24	>99:1	94
3	 20	 25	94:6	96
4	 21	 26 : 26' 78 : 22	98:2	86
5	 22	 27	>99:1	93

[a] All reactions were conducted according to the general procedure at a concentration of 0.5 M of **3** (cf. the Supporting Information). [b] Conversion was monitored by GLC analysis. [c] Ratio of silyl enol ethers (**23**–**27**/**23′**–**27′**) and silyl ether (**28**–**32**) was determined by GLC-MS analysis. [d] Analytically pure product after catalyst removal.

(Table 3, entry 6) and hindered acetophenone **2m** (Table 3, entry 7). Comparison of the ratios in Tables 2 and 3 suggests that steric factors might override electronic effects. Moreover, the size of the silicon group is a decisive parameter, and if small enough, it appears to bring forward proton abstraction (**II**→**IV**) rather than hydride transfer (**II**→**III**) by the ruthenium hydride complex (cf. Scheme 2).

The possibility of double bond isomer formation was probed in the dehydrogenative coupling of symmetric ketone **16** (Scheme 3). Diastereocontrol was only moderate at room temperature but could be improved to a reasonable level at −78 °C. Using $MePh_2SiH$ (**3b**) or $EtMe_2SiH$ (**3c**) instead of Me_2PhSiH (**3a**) showed no enhancement of the *Z*/*E* ratio. Other dialkyl ketones **18**–**22** also reacted cleanly according to the dehydrogenation path (Table 4), and those catalyses where regioisomers could form afforded the less substituted double bond isomer with high preference (abstraction of methyl ≫ methylene > methine protons). While cyclohexanone derivative **21** yielded a decent regioisomeric mixture (Table 4, entry 4), methyl-substituted **19** and **22** were converted into single isomers (Table 4, entries 2 and 5).

To summarize, we disclose here a particularly mild method for the dehydrogenative transformation of ketones into silyl enol ethers. The catalysis proceeds within minutes at room temperature with 0.5 mol % of the cationic ruthenium complex **1**, affording high isolated yields. We emphasize that no base must be added and dihydrogen is the sole byproduct. The chemoselectivity, which is either proton abstraction from (dehydrogenation path) or hydride addition to (reduction path) the intermediate silylcarboxonium ion, is dependent on the size of the triorganosilane employed. $EtMe_2SiH$ (**3c**) was found to be superior to routinely used Me_2PhSiH (**3a**) in several cases. By using either of these triorganosilanes, excellent chemoselectivity ratios in favor of dehydrogenation are obtained.

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Supporting Information Available. Experimental details, characterization data, and ^{1}H, ^{13}C, and ^{29}Si NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.