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Tetrahedron Letters 49 (2008) 110–113

Tetrahedron Letters

Highly efficient catalytic system for hydrosilylation of ketones with iron(II) acetate–thiophenecarboxylate

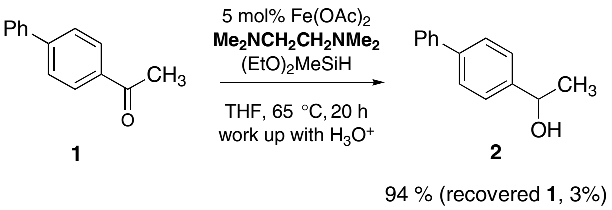
Akihiro Furuta and Hisao Nishiyama*

Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa, Nagoya 464-8603, Japan

Received 13 September 2007; revised 31 October 2007; accepted 1 November 2007
Available online 4 November 2007

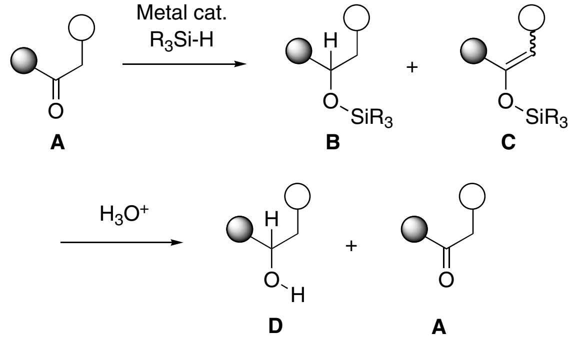
Abstract—A combination of a catalyst derived from ferrous acetate and sodium thiophene-2-carboxylate efficiently promoted hydrosilylation of aromatic and aliphatic ketones to give the corresponding secondary alcohols in high yields with extremely high selectivity.

Efficient reduction of simple ketones to secondary alcohols is an important subject for organic synthesis.[1] Potent methods for the reduction to meet social demands such as environmentally sound and inexpensive ones have been quested continuously. In this context, we have recently reported catalytic hydrosilylation of ketones with iron catalysts, which consist of commercially available $Fe(OAc)_2$ and a nitrogen-based ligand, *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (Scheme 1).[2] However, the selectivity of hydrosilylative reduction giving the desired secondary alcohols largely fluctuated to recover the starting ketones (ca. 2–50%) derived from dehydrogenative silylation depending on substrate ketones. In general, metal-catalyzed hydrosilylation of ketones **A** thus also suffers from dehydrogenative silylation to form silyl enol ether **C**, which regenerates the starting ketone **A** after hydrolytic work up (Scheme 2).



Scheme 1. Iron–TMEDA catalyst for hydrosilylation of ketones.

During our continuous search for efficient ligands for catalytic hydrosilylation, we have been fascinated with the sulfur atom making preferable bonding to iron atom not only as shown in some enzymes but also organometallic iron complexes.[3] We have focused on thiophene derivatives as ligands. First, we confirmed that ferrous acetate itself gave only a trace amount of reduction product (Table 1, entry 1). Next, we examined thiophene **3a** as a ligand to find that hydrosilylation of 4-phenylphenyl methyl ketones **1** with 5 mol % of ferrous acetate and diethoxymethylsilane (2.0 equiv) took place, but it gave the reduction product **2** in only 15% of the yield at 65 °C for 24 h (Scheme 3, entry 2 of Table 1), where 85% of the starting ketone remained unreacted and was recovered. Addition of dithiophene **3b** and thiophenecarboxylic acid **3c** also did not work well (entries 3 and 4). However, when we adopted sodium thiophene-2-carboxylate (**3d**, STC) as an additive, we eventually found almost complete selectivity in high yield (entry 5). Where, the conversion was 100%, and no starting ketone was recovered. In place of $(EtO)_2MeSiH$,



Scheme 2. Metal-catalyzed hydrosilylation of ketones.

Keywords: Iron; Thiophene; Hydrosilyation; Ketone; Reduction.

* Corresponding author. Fax: +81 52 789 3209; e-mail: hnishi@apchem.nagoya-u.ac.jp

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doi:10.1016/j.tetlet.2007.11.002

Table 1. Iron-catalyzed hydrosilylation of ketones[a]

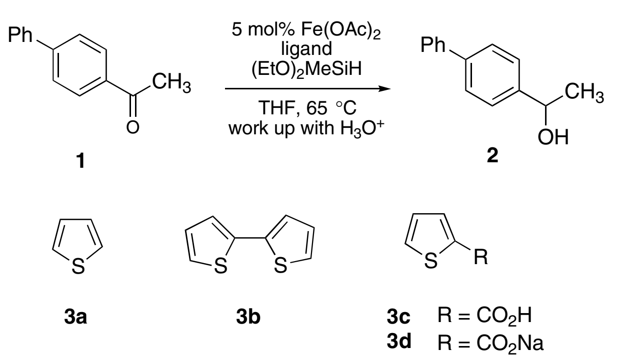
Entry	Metal salt (mol %)	Ligand (mol %)	°C/h	Yield of **2** (%)	Recovered ketone **1** (%)
1	$Fe(OAc)_2$ (5)	—	65/24	4	94[b]
2	$Fe(OAc)_2$ (5)	**3a** (10)	65/24	15	85[b]
3	$Fe(OAc)_2$ (5)	**3b** (10)	65/24	10	89[b]
4	$Fe(OAc)_2$ (5)	**3c** (10)	65/24	20	76[b]
5	$Fe(OAc)_2$ (5)	**3d** (10)	65/24	99	0
6[c]	$Fe(OAc)_2$ (5)	**3d** (10)	65/24	90	7[d]
7	$Fe(OAc)_2$ (2)	**3d** (4)	65/36	98	0
8	—	**3d** (10)	65/24	No react	—
9	$FeCl_3$ (5)	**3d** (10)	65/24	No react	—
10	$Fe(acac)_3$ (5)	**3d** (10)	65/24	No react	—

[a] 4-Phenylphenyl methyl ketone (**1**) (1.0 mmol), THF (3 mL), $(EtO)_2MeSiH$ (2.0 mmol).

[b] Ketone **1** remained unreacted and then recovered.

[c] PMHS (ca 2.0 mmol) in place of $(EtO)_2MeSiH$.

[d] Conversion was ca 100%. The ketone was recovered after hydrolysis.



Scheme 3. Iron–thiophene derivatives catalyzed hydrosilylation of ketones.

polymethylhydrosiloxane (PMHS) worked similarly but formed some amounts of the starting ketone after hydrolysis (entry 6). The reduction with 2 mol % of $Fe(OAc)_2$ sufficiently proceeded for 36 h to give **2** in 98% (entry 7). We also confirmed that in the absence of $Fe(OAc)_2$, only STC did not cause the hydrosilylation (entry 8). The combination of $FeCl_3$ and $Fe(acac)_3$ with STC showed no catalytic activity (entries 9 and 10). Thus, we have found that almost complete selective reduction of ketones with the catalyst derived from ferrous acetate and sodium thiophene-2-carboxylate and diethoxymethylsilane as a hydrogen donor.

Under the standard condition adopted for entry 5 in Table 1, other ketones were subjected to the hydrosilylation to furnish the corresponding secondary alcohols (Table 2). Substituted acetophenones **4a**–**f** were reduced in high yields 95–99% of **5a**–**f** (conversion = 100%) with no formation of starting ketones after acidic work up except *p*-methoxyphenyl ketone and *p*-phenoxyphenyl ketone (Table 2, entries 1–6). Ester and bromo groups survived under the reduction condition. Although β-acetonaphthone (**4h**) was efficiently reduced, α-acetonaphthone (**4g**) resulted in a decrease of the yield to 89% and regeneration of the ketone (5%) (entries 7 and 8). Alkyl phenyl ketones **4i** and **4j** were reduced to 94% and 99%, respectively (entries 9 and 10). α-Tetralone (**4k**) was reduced to 93% giving a small amount of the ketone, respectively (entry 11). Benzyl ketone **4m**, phenethyl ketone **4n** and 2-tridecanone (**4o**) efficiently gave only the secondary alcohols (entries 13–15).

Comparing to our previous results with $Fe(OAc)_2$/TMEDA catalyst,[2] the yields and the selectivity described here in Table 2 were extremely improved; for representative examples with $Fe(OAc)_2$/TMEDA catalyst and $(EtO)_2MeSiH$, the substrate ketones [yield (%) of the corresponding secondary alcohol/yield (%) of recovered ketone]; **4g** [67/31], **4j** [89/10], **4k** [55/42], **4m** [48/51] and **4n** [88/5] (Chart 1).

In turn, α,β-unsaturated ketones **6** were examined under the same condition to give mainly the corresponding 1,2-reduction products in 93% of **7a** with a small amount of 1,4-reduction product (Scheme 4). Chalcone **6b** resulted in lower yield (57%).

Table 2. Iron-catalyzed hydrosilylation of other ketones[a]

Entry	Ketone	Alcohol	Reaction time (h)	Yield (%) (recovered)
1	**4a**	**5a**	24	96 (0)
2[b]	**4b**	**5b**	24	95 (4)[c]
3[b]	**4c**	**5c**	24	97 (<1)[c]
4	**4d**	**5d**	19	99 (0)
5	**4e**	**5e**	24	98 (0)
6[b]	**4f**	**5f**	24	97 (0)
7	**4g**	**5g**	40	89 (5)[d]
8	**4h**	**5h**	24	95 (0)
9	**4i**	**5i**	24	94 (0)
10	**4j**	**5j**	24	99 (0)
11	**4k**	**5k**	40	93 (3)[d]
12	**4l**	**5l**	48	96 (4)[d]
13[b]	**4m**	**5m**	24	94 (0)
14	**4n**	**5n**	20	99 (0)
15	**4o**	**5o**	24	97 (0)

[a] Ketone (1.0 mmol), $Fe(OAc)_2$ (5.0 mol %), STC **3d** (10 mol %), $(EtO)_2MeSiH$ (2.0 mmol), THF (3.0 mL), 65 °C.

[b] Work up was performed with TBAF (1 M, 1 mL) and KF (2 mmol) instead of aq HCl.

[c] Conversion was almost 100%. The ketone was detected after work up.

[d] The ketone remained unreacted.

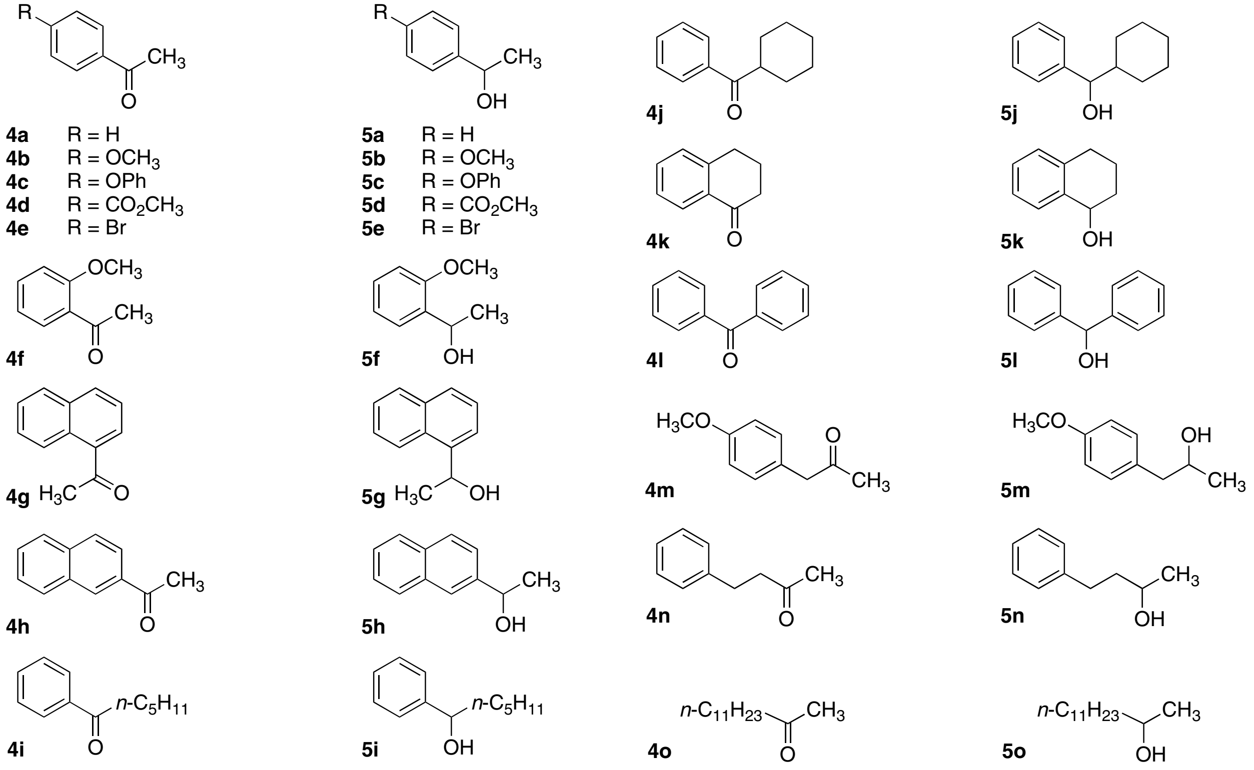
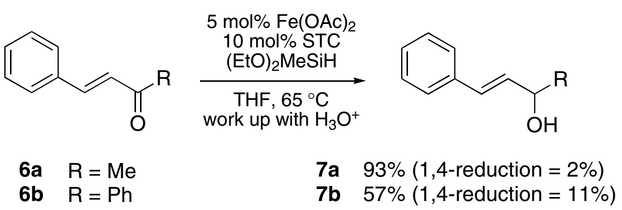
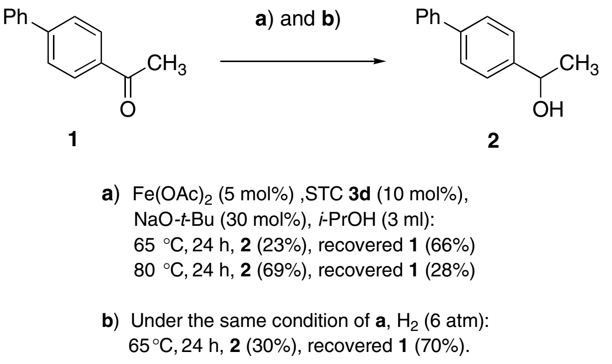


Chart 1.



Scheme 4. Iron-catalyzed hydrosilylation of α,β-unsaturated ketone.

In terms of iron-catalyzed reduction of ketones, transfer hydrogenation with iron–phosphine catalysts has been reported by Beller and co-workers.[4] In addition, Casey and Guan recently reported an iron–hydroxycyclopentadienyl complex for hydrogenation of ketones.[5] These works prompted us to check an ability of iron–thiophenecarboxylate catalyst for the transfer hydrogenation (Scheme 5, a) and hydrogenation of ketone (Scheme 5, b). The transfer hydrogenation with ketone **1** with Fe(OAc)$_2$ (5 mol %), STC (10 mol %) and NaO*t*-Bu (30 mol %) in isopropyl alcohol proceeded to give alcohol **2** in only 23% yield (unreacted ketone, 66% recovered) at 65 °C for 24 h. At 80 °C for 24 h, the yield increased to 69% yield (recovered ketone, 28%). Under molecular hydrogen atmosphere (6 atm), a very weak acceleration was observed to form alcohol **2** in 30% yield (recovered ketone, 70%) at 65 °C for 24 h. Therefore, we conclude that the iron–thiophenecarboxylate system proved to be not so sufficient for transfer hydrogenation and hydrogenation.



Scheme 5. Iron-catalyzed transfer hydrogenation and hydrogenation.

In summary, we have thus found a highly efficient method for catalytic hydrosilylation of ketones with iron–thiophenecarboxylate.[6] At this stage, although we cannot clearly explain the effect of thiophenecarboxylate (STC), we think that one or two STC moieties can strongly bind to iron as a bidentate ligand through S atom and COO$^-$ skeleton to prevent from undesirable dehydrogenative silylation.[7]

Acknowledgements

This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan (460:18065011), the Japan Society for the Promotion of Science (18350049) and Mitsubishi Foundation.

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6. Other metal acetates (5 mol %) in the combination with STC were examined to show lower catalytic activity: [yield (%) of **2**/recovered **1**], $Pd(OAc)_2$ [15/76], $Sn(OAc)_2$ [18/80], $Co(OAc)_2$ [37/58] and $Cu(OAc)_2$ [no react]. On the other hand, the set of $Zn(OAc)_2$ and STC exhibited high activity [98/0]. Under the same standard reaction condition (at 65 °C, 10 h), *p*-methoxybenzaldehyde was also reduced to *p*-methoxybenzyl alcohol in 96% yield.
7. *Typical procedure. Hydrosilylation of methyl 4-phenylphenyl ketone* (**1**): A mixture of ferrous acetate (8.7 mg, 0.05 mmol), ketone **1** (196 mg, 1.0 mmol), sodium thiophene-2-carboxylate (**3d**) (15.0 mg, 0.10 mmol) in absolute THF (3.0 mL) was stirred for ca 10 min at 65 °C to form an orange homogenous solution. Then, $(EtO)_2MeSiH$ (0.32 mL, 2.0 mmol) was added by a syringe. The mixture was stirred at 65 °C for 24 h. After confirming consumption of **1** by TLC examination, aq HCl (2 N, 2 mL) was added at 0 °C. The mixture was extracted with ethyl acetate, and the extract was dried over Na_2SO_4. After concentration, the residue was purified by silica-gel column chromatography to give the desired alcohol **2** (196 mg, 0.99 mmol) in 99% yield. The product was analyzed by ^1H and ^{13}C NMR. 2-Thiophenecarboxylic acid sodium salt was purchased from Aldrich (28897-7) and Wako (325-75571).