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New catalyst systems for iron-catalyzed hydrosilane reduction of carboxamides[†]

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A heptanuclear iron carbonyl cluster, $[Fe_3(CO)_{11}(\mu-H)]_2$ -Fe(DMF)₄ (4), is found to be a highly efficient catalyst for the reduction of various carboxamides by 1,2-bis(dimethylsilyl)benzene (BDSB), which makes possible reducing the amount of the catalyst, shortening the reaction time, and lowering the reaction temperatures.

In increasing concern to environmentally benign chemical processes for production of organic molecules, homogeneous catalysis by iron compounds has become more important for a solution to the residual metal problems in the product.^{1,2} One of the solutions to this issue is the use of iron catalysts, and we and Beller's group have recently reported $Fe(CO)_5$ or $Fe_3(CO)_{12}$ to be a catalyst for hydrosilane reduction of secondary or tertiary amides.^{3,4} The process has synthetic merits in the successful use of iron catalysts and shows unique chemoselectivity different from the analogous ruthenium or platinum-catalyzed hydrosilane reduction of amides; however, it is desirable to improve because the reaction generally requires long time (24 h) at high temperature (100 °C) even in the presence of relatively large amounts of iron carbonyls (6-30 mol% for Fe).[‡] In this paper, we wish to report a solution to this problem, in which a new iron carbonyl catalyst makes possible the efficient reduction of amides with an appropriate hydrosilane, 1,2-bis(dimethylsilyl)benzene (BDSB). Discovery of the new catalyst actually shortens the reaction time even with lower catalyst concentration at lower temperatures compared with the previous iron-catalyzed hydrosilane reduction of amides.

As described above, a typical thermal reaction process of hydrosilane reduction of amides is treatment of p-MeOC₆H₄-CONMe₂ with TMDS in the presence of Fe(CO)₅ (10 mol% for Fe) at 100 °C for 24 h. The corresponding amine was obtained in 81% yield.⁴ Our first trial to mitigate the reaction conditions is exploration of appropriate hydrosilanes. As shown in Table 1, the reaction with 5 mol% of Fe(CO)₅ at

Table 1 Reduction of N,N-dimethyl-p-methoxybenzamide (1a) with various hydrosilane catalyzed by $Fe(CO)_5$ (5 mol%) in toluene at 80 °C

	0	Fe(Co , (5 mo equiv.) toluene,	D)5 1%) 80°C	H H N 2a			
		Yield of 2	Yield of $2a^a$ (%)				
Entry	"Si–H"	0.5/h	3/h	24/h			
1	Me ₂ PhSiH	<1	<1	<1			
2	(EtO) ₃ SiH	<1	<1	<1			
3	TMDS	6	17	52			
4	BDSB	<1	>99	—			
^{<i>a</i>} Determi standard.	ned by ¹ H NMR a	nalysis with f	errocene as a	n internal			

80 °C showed that PhMe₂SiH and (EtO)₃SiH did not work, whereas TMDS gave the product in 52% yield after 24 h. The best result so far obtained is 1,2-bis(dimethylsilyl)benzene (BDSB); after the induction period (0.5–1 h), the reaction proceeded quickly to give the amine quantitatively after 3 h.

Appropriate catalyst design provided us further improvement of the reaction conditions. As shown in Scheme 1, coordinatively unsaturated Fe(CO)₃ species is considered to be involved in the catalytic cycle, which is generated by thermolysis or photolysis of Fe(CO)₅ or Fe₃(CO)₁₂. There are two possible reaction pathways from $Fe(CO)_3$; one is the double oxidative addition of Si-H groups in BDSB to form the disilaferracyclic intermediate A,⁵ whereas the other is the reaction with amides producing the iron-amide species B. Fink's disilaferracycle $[Me_2SiC_6H_4SiMe_2]Fe(CO)_4$ (3) has an analogous structure to A and can be synthesized as a colorless crystal with ease.⁶ This is one of the candidates for the improved catalyst. A new heptanuclear iron carbonyl cluster 4, which could produce the intermediate \mathbf{B} by thermal disproportionation, was obtained by treatment of Fe(CO)₅ with DMF at 65 °C in 48% yield as a dark purple crystal.

Identification of paramagnetic **4** was carried out by X-ray diffraction analysis. The ORTEP drawing was depicted in Fig. 1, and the selected bond distances and angles are summarized in the ESI.† The molecular structure of **4** is analogous to a heptanuclear iron carbonyl cluster, $Fe(THF)_4[Fe_3(H)(CO)_{11}]_2$, reported by Brook and coworkers.⁷

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University, 6-1 Kasugakoen, Kasuga, Fukuoka, 816-8580, Japan † Electronic supplementary information (ESI) available: Experimental procedure and details of crystallographic data for 4. CCDC 808120. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc10636h



Scheme 1 Proposed reaction mechanism.



Fig. 1 Molecular structure of **4** with 50% probability ellipsoid. Hydrogen atoms except for the bridging hydride atoms were omitted for clarity.

IR spectrum of $\mathbf{4} [\nu_{CO(terminal)} = 1950-2070 \text{ cm}^{-1}, \nu_{CO(bridging)} = 1592 \text{ cm}^{-1}, \nu_{CO} \text{ of DMF} = 1654 \text{ cm}^{-1}]$ and elemental analysis are in accord with the molecular structure of $\mathbf{4}$.

Superior catalytic activity of **3** and **4** to Fe(CO)₅ and Fe₃(CO)₁₂ is clearly demonstrated in the reduction of *p*-MeOC₆H₄CONMe₂ (**1a**) with BDSB at 50–80 °C as shown in Table 2. The reaction in the presence of 5 mol% of the catalyst at 80 °C for 30 min showed that the yield of *p*-MeOC₆H₄CH₂NMe₂ (**2a**) is increased in the order, Fe(CO)₅ < Fe₃(CO)₁₂ < **3** (75%) < **4** (99%). At lower temperatures than 70 °C, conversion of **1a** was lower than 40% in the reaction with Fe(CO)₅ and Fe₃(CO)₁₂ after 19 h. Fink's complex **3** showed good activity at 70 °C; however, the yield of the product did not exceed *ca.* 30% at 60 °C, and deactivation of the catalyst was observed after a few hours. It is noteworthy that the reaction catalyzed by **4** proceeded even at 50 °C. No catalyst deactivation was observed, and the yield of the product reached 99% after 19 h.





			Yield of $2a^a$ (%)							
Entry	Fe cat.	$Temp/^{\circ}C$	0.5/h	1/h	3/h	5/h	12/h	19/h		
1	Fe(CO) ₅	50	<1	<1	<1	<1	<1	<1		
2	Fe(CO) ₅	60	<1	<1	<1	<1	<1	<1		
3	Fe(CO) ₅	70	<1	<1	<1	14	20	24		
4	Fe(CO) ₅	80	<1	31	>99			_		
5	$Fe_3(CO)_{12}$	50	<1	<1	<1	<1	<1	<1		
6	$Fe_3(CO)_{12}$	60	<1	<1	<1	<1	6	6		
7	$Fe_3(CO)_{12}$	70	<1	<1	20	28	32	34		
8	$Fe_3(CO)_{12}$	80	<1	42	>99			_		
9	3	50	<1	<1	<1	<1	8	9		
10	3	60	<1	13	15	29	29	30		
11	3	70	25	58	85	>99				
12	3	80	75	88	>99			_		
13	4	50	<1	<1	<1	4	47	>99		
14	4	60	<1	<1	32	>99				
15	4	70	82	>99				_		
16	4	80	>99	—	—	—		—		
^a Determined by ¹ H NMR analysis with ferrocene as an internal										

"Determined by 'H NMR analysis with ferrocene as an internal standard.

The high catalytic efficiency of 4 is also shown in the reduction of several tertiary and secondary amides in the presence of 0.5 mol% (based on one Fe atom) of 4 as summarized in Table 3. With BDSB (2.2 equivalent to 1) in toluene at 100 °C, the reactions shown in the table proceeded smoothly, and the amide was converted to the corresponding amine in high yields within 30 min. A sterically crowded amide 1g and a secondary amide 1j required prolonged reaction time for completion of the reduction, but the reaction time is no longer than 3 h (Table 3, entry 7, 10). Amides containing a chloride, bromide, or ester as the functional group also underwent the reduction with these reducible functional groups remaining intact, giving the corresponding amines 2c, 2d, and 2e in high yields (entries 3, 4, and 5). Reduction of benzylic chloride was seen as a side reaction for the reduction of 1i; 1i was converted to a mixture of 2i and dehalogenated product (entry 9). Attempted reduction of primary amides was not successful. For instance, treatment of benzamide with BDSB at 100 °C for 3 h resulted in formation of benzonitrile by dehydration in 15% yield with a recovery of benzamide.^{8,9}

Success of the reaction using a small amount of catalyst (0.5 mol%) led to effective removal of the iron species in the product. In a typical example, reduction of **1a** (10 mmol) with **BDSB** in the presence of **4** (0.05 mmol of Fe) is followed by the work up described in the ESI.† The crude product (95% yield) contained no spectroscopically-detectable silicon wastes and 0.7 ppm of Fe residue (ICP-mass); this means almost all of the silicon residue and the Fe species (>99.6%) charged can be removed without purification of the crude product by chromatography or distillation. Efficiency to remove the iron residue is much better than that of the previously reported $Fe(CO)_{5^-}$ catalyzed process with PMHS, in which 95% of iron species was soaked up to a siloxane resin produced by the reaction.^{4,10}

Table 3 Reduction of various carboxamides catalyzed by 4^a



^{*a*} All reactions were carried out with **1** (1 mmol), **4** (0.5 mol% for Fe), and BDSB (2.2 mmol) in toluene (0.5 mL) at 100 °C. ^{*b*} Isolated yield. ^{*c*} ¹H NMR spectrum of the crude product revealed the formation of enamine in *ca.* 3% yield. ^{*d*} Dehalogenated product was isolated in 47% yield.

A question is why the combination of the iron cluster 4 and BDSB reduces the catalyst loading and shortens the reaction time. Several findings provide clues for solving this question, which is related to a strong affinity of CO ligands to the iron center. First, addition of PPh3 to the solution in which the catalytic reaction by 4 (5 mol% for Fe) is smoothly running at 60 °C instantly terminated the reaction, and Fe(CO)₃(PPh₃)₂ was recovered from the reaction mixture. This suggests Fe(CO)₃ is involved in the catalytic cycle. Second, the catalytic reduction of 1a with BDSB in the presence of 5 mol% of Fink's complex 3 afforded a slightly red-violet solution; its NMR spectrum showed that >95% of 3 remained unreacted, whereas UV-vis spectrum of the reaction mixture indicates the existence of a homologue of 4, of which amount is *ca*. 1.8% from the ε of $\lambda_{max} = 499$ nm. This indicates a reaction pathway from 3 to Fe(CO)₃, which is trapped by amides in the catalytic reaction to form 4. The cluster 4 behaves as a dormant species which reversibly generates a catalytically active $Fe(CO)_3(\kappa^1-amide)$ (**B**). Third, the reaction catalyzed by Fink's complex 3 at 60 °C showed catalyst deactivation after a while. The catalyst was able to reactivate by heating the reaction mixture at 100 °C. A reasonable interpretation of this result is that the net catalytic activity of Fe(CO)₃ is facilely killed by coordination of CO.§ In other words, the iron

complex with the number of CO ligands close to 3 is a key to find a good catalyst for this reduction. In this sense, it is noteworthy that the ratio of CO to the Fe is decreased in the order, Fe(CO)₅ (CO/Fe = 5) > Fe₃(CO)₁₂ and Fink's complex (3) (CO/Fe = 4) > 4 (CO/Fe = 3.1). Apparently, 4 efficiently generates catalytically active species Fe(CO)₃ easily reacting with amide and BDSB, but does not produce CO, which deactivates the catalysis by contact with the catalytically active Fe(CO)₃.

In conclusion, we have found a new efficient iron catalyst and a better hydrosilane for reduction of carboxamides. The discovery makes possible to lower the catalyst concentration and reduce the reaction time.¶ The use of iron is a target for development of environmentally benign organic processes. Even if iron is indeed a harmless element, facile removal of the residual iron is desirable. Discovery of **4** provides one clear solution to the residual metal problem for the hydrosilane reduction of amides, and also affords a strategy for the catalyst design, *i.e.* pursuing the lower CO/Fe ratio.

Notes and references

[‡] Improvement in the efficiency of the iron catalyst is a problem recently pursued: for example, Tilley have reported hydrosilylation of ketones occurring at room temperature with a small amount of a catalyst.¹¹ § For the experimental evidence suggesting the importance of a lower CO/Fe ratio in the catalytic species, we examined the reduction of **1a** with BDSB catalyzed by **3** or **4** under a CO atmosphere (1 atm) at 80 °C for 3 h. In both cases, application of CO completely inhibited the reduction. ¶ Although the reaction at lower than 100 °C is also possible, we recommend the application at 100 °C for obtaining reproducible results when less than 1 mol% of **4** is used. When concentration of the catalyst is low, only a small amount of CO existing in the reaction medium easily kills the catalytically active species. Conversion of the starting amide sometimes does not reach >99%. At 100 °C, the deactivated species can be reactivated by dissociation of CO.

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