

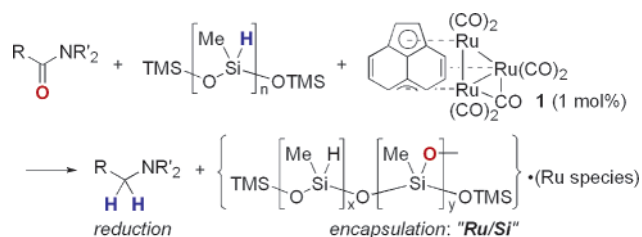
# Self-Encapsulation of Homogeneous Catalyst Species into Polymer Gel Leading to a Facile and Efficient Separation System of Amine Products in the Ru-Catalyzed Reduction of Carboxamides with Polymethylhydrosiloxane (PMHS)

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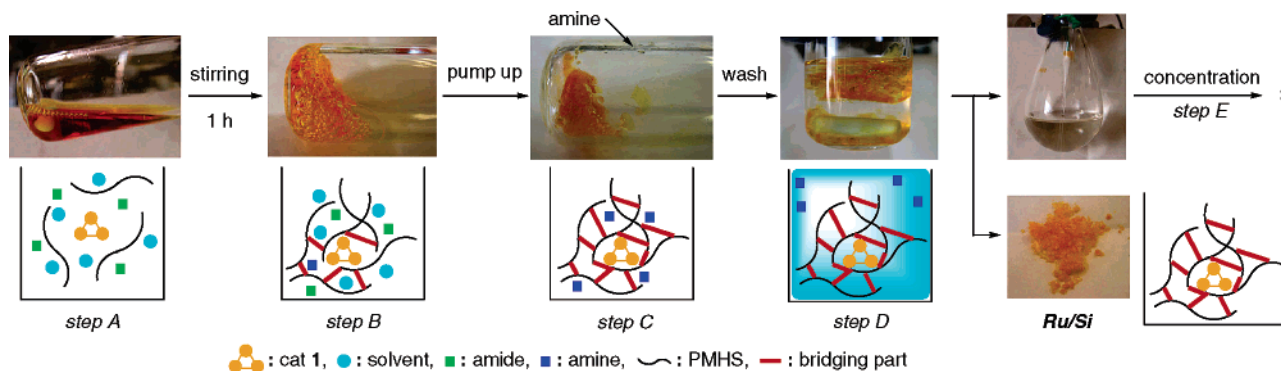
Reduction of carboxamides is a crucially important method in organic synthesis for the production of amines. Alkali metal hydrides have long been the reagents of choice for the reaction, and its utility has been demonstrated innumerable times.<sup>1</sup> However, there still remain drawbacks which should be improved from the viewpoint of safe and environmentally benign chemical processes: a stoichiometric quantity of an air- and moisture-sensitive reagent, which sometimes causes ignition, must be used, and production of metal hydroxide or oxide wastes makes the isolation of the product from the reaction mixture difficult. Reduction with air- and moisture-stable hydrosilanes is one of the solutions;<sup>2,3</sup> in particular, we have recently reported the reduction of amides using trialkylsilanes catalyzed by a ruthenium cluster, ( $\mu_3, \eta^2, \eta^3, \eta^5$ -acenaphthylene)- $\text{Ru}_3(\text{CO})_7$  (**1**).<sup>4</sup> In this catalytic reaction, the reaction is exothermic and efficiently proceeds even at room temperature and can be used for production of a large quantity of amines.<sup>4c</sup> The siloxane waste can be removed from the amines by a workup process using strong acids and bases through the corresponding ammonium salts of the products formed. In contrast, the acid–base treatment only partially contributes to removing the ruthenium species (ca. 90%) from the crude amine product. In other words, removal of metal residues from the product remains a problem needing improvement, and for the solution, it is desirable to avoid harsh conditions, such as strong acids and bases.



As a new concept to resolve these problems, we were interested in encapsulation of metal species by polymers.<sup>5</sup> Elegant work by Kobayashi and co-workers recently established that encapsulation of metal species into an organic polymer by "microcapsulation techniques" led to new types of metal catalysts dispersed on the polymer supports.<sup>6</sup> Our idea is not the usage of polymer-supported heterogeneous catalysts but that of the microcapsulation technique itself for removal of the catalyst species from the product. In the catalytic reduction of amides with polymer-reducing reagents containing Si–H groups, such as polymethylhydrosiloxane (PMHS),<sup>7</sup> the catalytically active ruthenium species generated by the reaction of **1** with PMHS contributes to producing the desired amines. At the same time, the active ruthenium species takes part in cross-linking the PMHS, resulting in formation of polymer gel,

to which the catalyst species is effectively self-encapsulated. After the reaction is complete, the amine product, soluble in appropriate organic solvents, is readily separated from the insoluble polymer gel containing the catalyst species. This idea is actually realized using a commercially available PMHS. The initial solution contains an amide, PMHS, ruthenium complex **1**, and a small amount of a solvent in order to make the solution homogeneous (Figure 1, *step A*). As the hydride reduction of the amide proceeds, the oxygen atom originating from the amide contributes to bridging the polymer chains of the siloxane. This produces a polymer gel with highly cross-linked siloxane networks (*step B*).<sup>8</sup> After the reaction is complete, removal of the solvent affords a silicone resin insoluble in common organic solvents in which the catalyst species is encapsulated, but the amine product is not (*step C*).<sup>9</sup> As a result, the product is obtained by washing the silicone resin (solid) with an appropriate solvent without contamination by the metal residue as well as silicon waste (*step D*). In a typical example, reaction of *N,N*-dimethyl-3-phenylpropionamide **2a** (1 mmol) with PMHS ( $M_w = 1500$ – $1900$ ;  $n = 25.6$  (average); Si–H = 4.4 equiv to **2a**) and **1** (1 mol % based on **2a**) was carried out using tetrahydropyran (THP) as the solvent (0.5 mL) at 30 °C. After 1 h, the homogeneous solution set to gel (*step B*). After 15 h, removal of the solvent from the gel under reduced pressure, a silicone resin, and an amount of liquid product was obtained (*step C*). Washing the mixture with ether gave a clear, colorless solution containing the amine **3a** (88% yield determined by NMR) and a light orange solid (*step D*).<sup>11</sup> It is important that the orange metal species is only in the silicone resin (**Ru/Si**) and not in the amine obtained. In fact, ICP mass analysis of the amine at *step E* contained less than 15 ppm of the ruthenium, which means that >99.95% of the ruthenium species has been encapsulated by the silicone resin, and does not contaminate the amine product! Interestingly, the encapsulated catalyst species is still active in the silicone resin and is reusable; the recovered ruthenium-containing resin (**Ru/Si**: 1 mol % of Ru species) catalyzed the reduction of **2a** (1 mmol) with PMHS (Si–H = 3.3 equiv to **2a**) at 30 °C for 15 h to give the amine **3a** in 75% yield.

The reduction of **2a** efficiently proceeds in  $\text{Et}_2\text{O}$ , THP, dimethoxyethane (DME), cyclopentyl methyl ether (CPME), and toluene. Washing the resinous materials with ether, hexane, or toluene gave **3a** in 82–95% yields with the ruthenium content of 15–43 ppm. In other words, 99.95–99.85% of the ruthenium was encapsulated into the silicon resin. The present process can apply to reduction of various amides **2b–e** (5 mmol) using **1** (1 mol % to **2**) and PMHS (Si–H = 4.4 equiv to **2**) in THP (Table 1). The amides were completely consumed after 15 h, and washing the formed gel with ether afforded the corresponding amine (NMR analysis showed the yield to be 93–98%). Subsequent distillation afforded the



**Figure 1.** Photos and images of the reduction of carboxamides with PMHS catalyzed by  $(\mu_3, \eta^2, \eta^3, \eta^5\text{-acenaphthylene})\text{Ru}_3(\text{CO})_7$  **1**.

**Table 1.** Reduction of Various Carboxamides<sup>a</sup>

entry	amide	product	yield (%) <sup>b</sup>
1			79
2 <sup>c</sup>	<b>2a</b>	<b>3a</b>	70
3			74
4 <sup>d</sup>			80
5 <sup>d</sup>			77
6			81

<sup>a</sup> All reactions were carried out using 5 mmol of **2**, 1.5 mL (Si–H = 22 mmol) of PMHS, 0.05 mmol of **1** in 2.5 mL of THP at 30 °C for 15 h. <sup>b</sup> After distillation. <sup>c</sup> Compound **2a** (56 mmol) was used. <sup>d</sup> At 40 °C for 15 h.

product (>98% purity by GLC analysis) in 74–81% yields. The present procedure was adaptable to a large quantity of reaction: 6.42 g of **3a** was obtained from 10 mL (56 mmol) of **2a** (entry 2).

Thus, the present reduction of amides with PMHS offers a solution as an environmentally benign production of amines, namely, an efficient catalytic process involving facile separation of catalyst species and silicone byproducts from the product. The self-encapsulation of catalyst species into the silicone resin is considered to be one of the methods for microencapsulation of molecular catalysts into polymer supports. However, new and particular features of this process include the following: (1) the immobilization technique itself is the catalytic process; (2) the active catalytic species is self-encapsulated into the insoluble polymer during the reduction; (3) separation of both the catalyst species and silicone byproducts can be achieved; and (4) recovered silicone resin can be used as the catalyst for the reduction. This may be a good entry to a new field of environmentally benign chemical processes, in which catalytic activation of polymer reagents leads to both efficient chemical transformation of organic compounds and removal of catalyst species and polymer byproducts from the desired products. Work on this line as well as detailed mechanistic studies on the encapsulation is actively underway.

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**Supporting Information Available:** Detailed experimental procedures and results, characterization data of amides **2a–e** and amines **3a–d**, photos of Figure 1, IR and <sup>29</sup>Si NMR spectra of siloxane gel. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (8) Evidence for the formation of cross-linked silicone was obtained from the solid-state <sup>29</sup>Si NMR. The <sup>29</sup>Si CP/MAS NMR spectrum showed four signals at  $\delta$  10.4, –35.0, –56.5, and –64.8 ppm assignable to –OSiMe<sub>3</sub>, –OSi(H)Me<sub>2</sub>, Si in the trisiloxane ring, and –OSiMe(O–)<sub>2</sub>, respectively; the latter two of which are due to the cross-linked silicones (see Supporting Information). The integral values of these peaks suggest the proportion of cross-linked silicone to be ca. 45%. See: (a) Engelhardt, G.; Jancke, H.; Lippmaa, E.; Samoson, A. *J. Organomet. Chem.* **1981**, *210*, 295. (b) Satyanarayana, N.; Alper, H. *Macromolecules* **1995**, *28*, 281 and references therein.
- (9) We have reported that the silane reduction of carbonyl compounds catalyzed by **1** and its analogue is investigated by the oxidative addition of the triruthenium species to a Si–H bond. In fact, the oxidative adducts having a Ru–Si bond were isolated, and their role in catalysis is investigated (refs 4a and 10). The ruthenium-containing silicone resin (**Ru/Si**) showed two characteristic  $\nu_{\text{CO}}$  absorptions identical to those seen for the oxidative adducts (see Supporting Information); these suggest that the ruthenium species may be immobilized by the Ru–Si bond. In contrast, there is no chemical interaction between the amine product and the silicone resin. This provides facile extraction of the amine by ether. For a related work in which a palladium nanoparticle is stabilized in the cross-linking PMHS, see: Chauhan, B. P. S.; Rathore, J. S.; Bando, T. *J. Am. Chem. Soc.* **2004**, *126*, 8493.
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- (11) The crude amine contains a small amount of oligomeric hydrosiloxanes and low cross-linking PMHS; the former are generally contained in commercially purchased PMHS. We believe that contamination of the siloxane residue can be minimized by using PMHS without containing hydrosiloxane oligomers and careful control of the charged ratio of PMHS and the amide.

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