From inconsistent results to high speed hydrosilylation

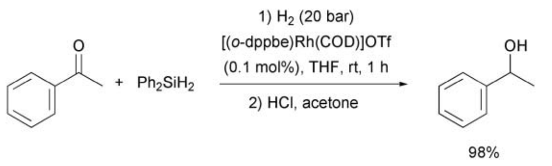
Virginie Comte,* Cédric Balan, Pierre Le Gendre* and Claude Moïse

Received (in Cambridge, UK) 29th November 2006, Accepted 19th December 2006
First published as an Advance Article on the web 10th January 2007
DOI: 10.1039/b617413b

After noting that the presence of dihydrogen, generated *in situ* from the partial hydrolysis of a silane with residual water, significantly enhances the rate of the rhodium-catalysed hydrosilylation of acetophenone, we developed a high speed hydrosilylation reaction under dihydrogen pressure.

Rhodium complexes associated with chiral diphosphine ligands have been widely applied for the asymmetric hydrosilylation of carbonyl compounds.[1] Despite the large number of papers in this area, only a few deal with catalysis in high enantiomeric excess (ee).[2,3] Examination of the literature revealed that high optical yields are generally reached when the reaction is conducted at low temperature. Indeed, efficient precatalysts have been shown to promote the reduction in the temperature range 0 to −60 °C with reasonable loadings and reaction times.[4] This can be detrimental to the development of an efficient asymmetric process, since the latter requires a good catalyst activity. It can thus be assumed that most of the diphosphine ligands tested to date have not yet lived up to their full potential. In line with this conclusion, we decided to focus first on catalytic activity and revisit this reaction using an achiral diphosphine ligand. We first examined the reaction of acetophenone with diphenylsilane in the presence of [(*o*-dppbe)Rh(COD)]OTf.[5] Serendipitously we have found that water markedly enhances the rate of the reaction. The determination of its exact role allowed us to tune the reaction conditions in order to obtain high speed hydrosilylation. The scope of this reaction with several aromatic and aliphatic ketones, along with a preliminary experiment using optimised conditions and a rhodium complex associated with a chiral diphosphine (Deguphos),[6] is discussed in this contribution.

The hydrosilylation of acetophenone with diphenylsilane was achieved in THF at 25 °C using 0.1 mol% [(*o*-dppbe)Rh(COD)]OTf. The reaction was stopped after 5 h and the conversion determined by ^{1}H NMR analysis of the crude product obtained after desilylation. Using such conditions, hydrosilylation readily proceeded, but the yields were found to be low and irreproducible (5–20%). Envisaging that adventitious traces of water could be responsible for the erratic yields, we carried out experiments in which various quantities of water were added. To our surprise, we found that small amounts of water had a favourable effect on the activity of the catalyst. Indeed, while only 5% of phenylethanol was obtained under dry conditions (*i.e.* flame dried vessel, dry THF), an optimum conversion of 56% was achieved in the presence of 10 mol% water. At this point, it is worth mentioning that the addition of diphenylsilane to the "wet" mixture was accompanied by vigorous bubbling. It is reasonable to assume that this gas evolution results from the partial hydrolysis of the silane, leading to the formation of H_2 and siloxane $(Ph_2SiH)_2O$.[7] Therefore the higher conversion might be due to water, siloxane or H_2. The hydrosilylation reactions carried out in the presence of a sub-stoichiometric amount of $(Ph_2SiH)_2O$ showed no improvement in conversion. On the contrary, runs performed under an optimised pressure of 20 bar H_2 led consistently to phenylethanol in 98% yield after only 1 h (Scheme 1).



Scheme 1 Hydrosilylation of acetophenone under dihydrogen pressure.

This rate enhancement in the hydrosilylation of acetophenone was further confirmed by comparing the kinetics of the reaction under normal and optimised conditions (Fig. 1). The initial turnover frequency (TOF) was determined to be 1700 h^{-1} after 30 min at 20 bar H_2, whereas the same catalyst under N_2 gave only a TOF of 40 h^{-1}. This value is comparable to those found for the most active rhodium catalysts described so far in the literature.[2,3,8]

Interestingly, we found that the yield dropped upon using both lower and higher dihydrogen pressures (the hydrosilylation of acetophenone performed at 10 and 25 bar H_2 afforded phenylethanol in 90% and 84% yields after 1 h, respectively).

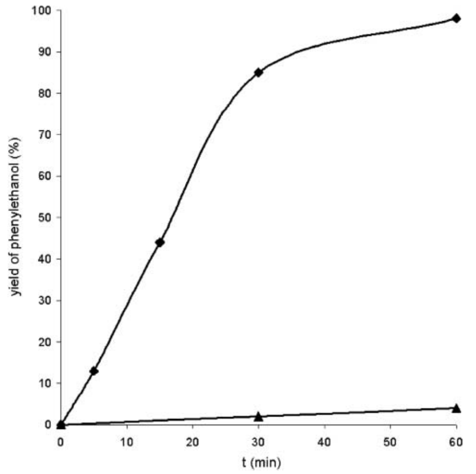


Fig. 1 Conversion into phenylethanol *vs.* time (◆ = reaction under 20 bar H_2, ▲ = reaction under N_2 atmosphere).

Laboratoire de Synthèse et Electrosynthèse Organométalliques LSEO-UMR 5188, Faculté des Sciences Mirande, Dijon, France.
E-mail: virginie.comte@u-bourgogne.fr;
pierre.le-gendre@u-bourgogne.fr; Fax: +33 3 8039 6098;
Tel: +33 3 8039 9048 Tel: +33 3 8039 6082

Moreover, we noticed that the dihydrogen pressure remained constant throughout the reaction, giving evidence that dihydrogen is not consumed. This data is in accordance with the fact that the rhodium complex [(*o*-dppbe)Rh(COD)]OTf does not catalyse the hydrogenation of acetophenone under these conditions. Finally, it is worth mentioning that a constant dihydrogen pressure was required to maintain the high catalytic activity of the rhodium complex. Indeed, a run partially conducted under dihydrogen pressure for 15 min (20 bar H_2), depressurized to 1 bar and finally stopped after 1 h afforded phenylethanol in a moderate yield (50%). Nevertheless, depressurization did not "shut down" definitively the catalytic activity of the rhodium centre. Thus, a run conducted successively at 20 bar (15 min), 1 bar (30 min) and 20 bar (15 min) led to phenylethanol in good yield (90%). One might claim that the rate enhancement was due to the pressure and not to dihydrogen itself. However, this possibility is excluded by the fact that the catalytic hydrosilylation of acetophenone under 20 bar N_2 led to a very poor yield.

According to the literature, hydrosilylation is often accompanied by the undesired dehydrogenative silylation of the enol of acetophenone (silyl enol ether).[1,9] In the subsequent hydrolysis step, the silyl enol ether reverts to the original acetophenone. However, this side reaction, which represents a major drawback, would have no impact on the yield of the reaction if a subsequent catalytic hydrogenation of the silyl enol ether occurred. This would also rationalize why dihydrogen is, overall, not consumed, since silylation of the enol is accompanied by the evolution of molecular hydrogen. To check this hypothesis, we measured the ^{1}H NMR spectrum of the crude product before hydrolytic work-up. The spectrum of the product obtained after a hydrosilylation reaction run under "normal" conditions (*i.e.* under an inert atmosphere) showed signals corresponding to the hydrosilylated product (silyl ether) together with those of residual acetophenone. No trace of silyl enol ether was detected. According to the NMR spectrum, the hydrosilylation of acetophenone under 20 bar H_2 also led exclusively to the hydrosilylated product. Moreover, attempts to hydrogenate the trimethylsilyl enol ether derived from acetophenone in the presence of a catalytic amount of [(*o*-dppbe)Rh(COD)]OTf remained unsuccessful. These results, combined with those discussed above, strongly suggest that dihydrogen is not the stoichiometric reducing agent.

To elucidate the positive role of dihydrogen on the kinetics, we examined the hydrosilylation of acetophenone at 20 bar H_2 with Ph_2SiD_2. Surprisingly, under these conditions, the silyl ether was obtained with only 40% deuterium incorporation. Moreover, the addition of H_2 (20 bar) to a THF solution of Ph_2SiD_2 in the presence of a catalytic amount of the rhodium complex resulted in the partial conversion of Ph_2SiD_2 to $Ph_2SiD_{2-n}H_n$ (n = 1 or 2, product containing only 33% of deuterium after 1 h). These results of H/D exchange strongly suggest that both H_2 and Ph_2SiD_2 undergo an oxidative addition to the same metal centre to give a cationic rhodium(V) adduct.[10–12] Subsequent repeated sequences of reductive elimination–oxidative addition would allow the conversion of Ph_2SiD_2 to Ph_2SiH_2. Since this kind of isotopic exchange occurs in the presence of the ketone, we suspect that Rh(V) species would also be involved in the hydrosilylation process. This hypothesis is supported by previous studies, suggesting that mechanisms of hydrosilylation involving Rh(V) species are reasonable.[13] An important suggestion in these reports is that generally accepted Rh(III) intermediates can undergo a second oxidative addition of another molecule of silane, facilitating the final reductive elimination step of the product. Based on these previously reported mechanistic studies, we propose that dihydrogen replaces here the second molecule of silane in the generation of the oxidative Rh(V) adducts. These complexes would then exist in solution, but only if the local concentration of dihydrogen was sufficient. This hypothesis explains all of the experimental results described above. Further experiments, notably ^{1}H NMR spectroscopy under dihydrogen pressure, are in progress aiming to provide support for this hypothesis.

Using our experimental protocol (*i.e.* under 20 bar H_2), we hydrosilylated a range of aromatic and aliphatic ketones, the results of which are presented in Table 1. For comparative purposes, hydrosilylation reactions under an inert atmosphere were carried out in parallel and quenched after the same reaction time. Yields were determined by ^{1}H NMR spectroscopy of the crude products after desilylation. The hydrosilylation of propiophenone, α-tetralone and pinacolone provided the corresponding alcohols in almost quantitative yields after only 1 h. In contrast, the same catalyst under N_2 gave the products in much lower yields (5, 7 and 4% yields, respectively). Although the hydrosilylation of cyclohexanone and acetone led to moderate yields (46 and 32%, respectively), these reactions were still, respectively, 11 and 16 times faster compared to those performed under an inert atmosphere. When the rhodium complex [(dppe)Rh(COD)]OTf was used as the catalyst precursor, a significant rate enhancement under dihydrogen pressure was also observed (Table 1, results in brackets).[14] It is noteworthy that this structurally comparable complex shows different efficiencies depending on the ketone used. While results were comparable with acetophenone, α-tetralone and pinacolone, a lower yield was obtained with propiophenone as the substrate. On the other hand, the rhodium complex with dppe as the ligand was found to be more efficient for the hydrosilylation of cyclohexanone and acetone.

Since the hydrosilylation of ketones can be highly accelerated by using different ligands, we envisioned taking advantage of this phenomenon for an asymmetric version of this reaction. Preliminary experiments were performed with [((*R*,*R*)-Deguphos)Rh(COD)]OTf as the chiral catalyst and acetophenone as the substrate. A significant rate enhancement associated with dihydrogen pressure was again observed. While only a 27% yield was obtained after 5 h under an inert atmosphere, the reaction went to completion after 1 h if run under 20 bar H_2. Interestingly, the reaction product (phenylethanol) was obtained with a higher ee

Table 1 Catalytic hydrosilylation of various ketones[a]

Entry	Substrate	Yield (%)[b]	
		Under 20 bar H_2	Under N_2
1	Acetophenone	98 (94)	4 (5)
2	Propiophenone	95 (57)	5 (2)
3	α-Tetralone	92 (90)	2 (3)
4	Pinacolone	99 (99)	4 (6)
5	Cyclohexanone	46 (96)	4 (5)
6	Acetone	32 (62)	2 (6)

[a] Conditions: [(*o*-dppbe)Rh(COD)]OTf (0.1 mol%), ketone (2.2 mmol), Ph_2SiH_2 (2.4 mmol), THF (2 mL), rt, 1 h. [b] The yields in brackets correspond to reactions performed with [(dppe)Rh(COD)]OTf as the catalyst.

by carrying out the reaction under dihydrogen pressure (22% ee at 20 bar H_2 *vs.* 11% ee under N_2). Finally, the increased reactivity of the catalyst under dihydrogen pressure allowed the hydrosilylation to be run at a lower temperature, generally resulting in a higher selectivity. Unfortunately, when the temperature was lowered to −40 °C, no influence on the enantioselectivity was seen. Despite the modest level of enantioselectivity, this preliminary result confirms that a sluggish catalyst can be converted into a highly active species simply by conducting the hydrosilylation reaction under a dihydrogen pressure.

In summary, the activity of rhodium complexes associated with common diphosphines such as dppbe or ddpe is several orders of magnitude higher under dihydrogen pressure than under an inert atmosphere. To the best of our knowledge, this phenomenon has never been reported before. Further work aimed at elucidating the mechanism of this acceleration and screening other chiral rhodium catalysts is currently in progress.

Notes and references

1 O. Riant, N. Mostefaï and J. Courmacel, *Synthesis*, 2004, 2943; H. Brunner, in *Transition Metals in Organic Synthesis*, ed. M. Beller and C. Bolm, Wiley-VCH, Weinheim, 1998, pp. 131–140; R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, 1994.

2 For the highly enantioselective rhodium-catalysed hydrosilylation of ketones using diphosphine ligands, see: T. Imamoto, T. Itoh, Y. Yamanoi, R. Narui and K. Yoshida, *Tetrahedron: Asymmetry*, 2006, **17**, 560; T. Imamoto, N. Oohara and H. Takahashi, *Synthesis*, 2004, 1353; R. Kuwano, T. Uemura, M. Saitoh and Y. Ito, *Tetrahedron: Asymmetry*, 2004, **15**, 2263; Y. Yamanoi and T. Imamoto, *J. Org. Chem.*, 1999, **64**, 2988; M. Sawamura, R. Kuwano and Y. Ito, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 111.

3 The most successful results have been obtained using other kinds of chiral ligands. See, for example: V. César, S. Bellemin-Laponnaz, H. Wadepohl and L. H. Gade, *Chem.–Eur. J.*, 2005, **11**, 2862; D. A. Evans, F. E. Michael, J. S. Tedrow and K. R. Campos, *J. Am. Chem. Soc.*, 2003, **125**, 3534; B. Tao and G. C. Fu, *Angew. Chem., Int. Ed.*, 2002, **41**, 3892; D. K. Heldmann and D. Seebach, *Helv. Chim. Acta*, 1999, **82**, 1096; Y. Nishibayashi, K. Segawa, K. Ohe and S. Uemura, *Organometallics*, 1995, **14**, 5486; H. Nishiyama, M. Kondo, T. Nakamura and K. Ito, *Organometallics*, 1991, **10**, 500.

4 Lowering the temperature generally results in higher enantioselectivity (see ref. 2 and ref. 3). Nevertheless, some exceptions have been reported: C. G. Arena and R. Pattacini, *J. Mol. Catal. A: Chem.*, 2004, **222**, 47; K. Kromm, P. L. Osburn and J. A. Gladysz, *Organometallics*, 2002, **21**, 4275; D. Haag, J. Runsink and H. D. Scharf, *Organometallics*, 1998, **17**, 398.

5 *o*-dppbe = *ortho*-Bis(diphenylphosphino)benzene.

6 Deguphos = 3,4-Bis(diphenylphosphino)-1-benzylpyrrolidine.

7 T. C. Bedard and J. Y. Corey, *J. Organomet. Chem.*, 1992, **428**, 315.

8 Highly active mono(phosphine)rhodium catalysts for the hydrosilylation of ketones have been recently described: O. Niyomura, T. Iwasawa, N. Sawada, M. Tokunaga, Y. Obora and Y. Tsuji, *Organometallics*, 2005, **21**, 4275; O. Niyomura, M. Tokunaga, Y. Obora, T. Iwasawa and Y. Tsuji, *Angew. Chem., Int. Ed.*, 2003, **42**, 1287.

9 C. Reyes, A. Prock and W. P. Giering, *J. Organomet. Chem.*, 2003, **671**, 13.

10 M. D. Curtis and P. S. Epstein, *Adv. Organomet. Chem.*, 1981, **19**, 213; R. Goikhman and D. Milstein, *Chem.–Eur. J.*, 2005, **11**, 2983.

11 A H/D exchange from Et_2SiH_2 and D_2 *via* a cationic Ir(V) complex has been recently described: L. Turculet, J. D. Feldman and T. D. Tilley, *Organometallics*, 2004, **23**, 2488.

12 A mechanism analogous to the one described by Fryzuk, involving the formation of dinuclear rhodium complexes, cannot be completely ruled out. However, the low concentration of the rhodium complex in the reaction mixture strongly supports a mechanism occurring at a rhodium centre: M. D. Fryzuk, L. Rosenberg and S. J. Rettig, *Organometallics*, 1996, **15**, 2871.

13 M. J. Fernandez, P. M. Bailev, P. O. Bentz, J. S. Ricci, T. F. Koetzle and P. M. Maitlis, *J. Am. Chem. Soc.*, 1984, **106**, 5458; S. B. Duckett and R. N. Perutz, *Organometallics*, 1992, **11**, 90; H. Nagashima, K. Tatebe, T. Ishibashi, A. Nakaoka, J. Sakakibara and K. Itoh, *Organometallics*, 1995, **14**, 2868.

14 dppe = Bis(diphenylphosphino)ethane.