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Silver-Catalyzed Hydrogenation of Ketones under Mild Conditions

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Abstract. The silver-catalyzed hydrogenation of ketones using H_2 as hydrogen source is reported. Silver nanoparticles are generated from simple silver (I) salts and operate at 25 °C under 20 bar of hydrogen pressure. Various aliphatic and aromatic ketones, including natural products were reduced into the corresponding alcohols in high yields. This silver catalyst allows for the selective hydrogenation of ketones in the presence of other functional groups.

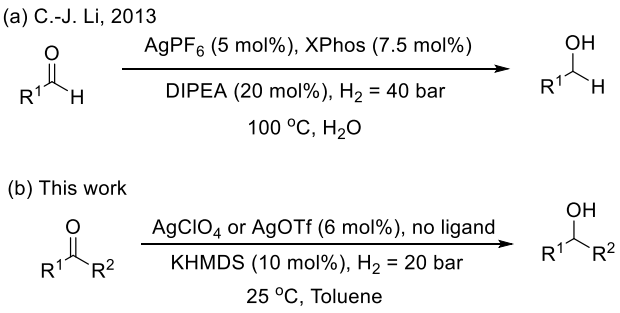
Keywords: Catalysis; Hydrogenation; Ketones; Nanoparticles; Silver

Introduction

Reduction processes play a crucial role in numerous industrial processes and for this reason they have been a topic of continuous intense researches in academia and industry. This situation will very likely persist owing to the growing demand for biosourced compounds yet requiring reduction and hydrogenation protocols.[1] Industrial hydrogenation processes are essentially employing heterogeneous catalysis excepted when highly selective transformations are necessary albeit a number of heterogeneous catalyst display this property. Metal nanoparticles are at the frontier between homogeneous and heterogeneous catalysis as they display in general high activity and selectivity and can be recycled. For these reasons, metal nanoparticles (NPs) have been attracting a strong interest over the past 20 years in catalysis.[2] Among metal-NPs, silver-NPs (Ag-NPs) are receiving attention as an alternative to expensive metal-NPs based on gold, platinum or other noble transition metals.[3] The efficient and selective reduction of aldehydes was extensively studied by Claus since the mid-nineties using Ag-NPs supported on SiO_2 or TiO_2.[4] Ag-NPs have also been reported for the hydrogenation of nitro-aromatics into aniline derivatives[5] and for the selective hydrogenation of amides into alcohols and amines.[6] The hydrogenation of keto-derivatives with Ag-NPs turns to be more difficult and only a few recent results are published. As an illustration, we could mention that during his investigations on the scope of the Ag-NPs hydrogenation of nitroaromatics, Shimizu reported that an acetyl group was not hydrogenated by Ag-NPs supported on alumina when the reaction was conducted at 160 °C under 30 bar of hydrogen pressure.[5a] In another example, Moores and Li reported the hydrogenation of two benzylic ketones using magnetic Ag-F_3O_4 nanoparticles supported on carboxymethyl cellulose. The corresponding alcohols were obtained in moderate to high yield at 100 °C and 40 bar of hydrogen pressure in water.[7] In 2009, De Vos reported polymer stabilized Ag-NPs that reduced a number of unsaturated ketones with moderate to high selectivity at 60 °C and 40 bar of hydrogen pressure.[8] More recently, Moores described the use of plasmonic silver nanocubes for the hydrogenation of ketones and aldehydes. Four ketones were hydrogenated at 80 °C and 1 bar of hydrogen pressure under irradiation at 450 nm.[9]

In our ongoing efforts to produce the biosourced γ–valerolactone by reduction of levulinic acid with iridium complexes,[10] we became interested in using less expensive metals for hydrogenation reactions. Initially inspired by the work of Li[11] on the homogeneous hydrogenation of aldehydes, we focused our attention on the silver-catalyzed hydrogenation of ketones (Scheme 1).

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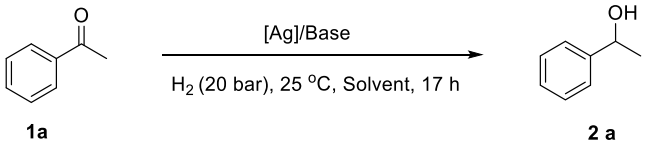
Scheme 1. Silver-catalyzed hydrogenation of carbonyl derivatives

Results and Discussion

Acetophenone was initially selected as a model substrate. Several experimental parameters were screened and optimized. As depicted in Table 1, we first investigated the hydrogenation catalyzed by silver triflate at 25 °C with KHMDS as the base in apolar solvents, in which very good yields were obtained (Table 1, entries1-2). More polar ether solvent resulted in lower yields of 1-phenylethanol (Table 1, entries 3-5). Following this first screening, various silver salts were evaluated emphasizing the superiority of silver perchlorate (Table 1, entries 3-11). Further optimization reactions were then pursued with this catalyst. Interestingly, it was possible to decrease the amount of base to 10 mol% but decreasing the catalyst loading or the hydrogen pressure led to lower yields of alcohol (Table 1, entries 16-17). Various bases were also evaluated (Table 1, entries 18-24) but none of them led to the results obtained with KHMDS. In fact, all those bases led to very poor results indicating a very peculiar role of KHMDS. Finally, experiments conducted in the absence of $AgClO_4$ or KHMDS were found totally ineffective hence demonstrating the necessity of both components (Table 1, entries 25-26).

With these optimized conditions in hand, we performed the hydrogenation of a number of commercially available ketones to highlight the efficacy of the catalytic system. Selected aromatic and aliphatic ketones featuring various steric and electronic demands were thus subjected to the catalytic system at 25 °C. However, in some examples it was necessary to warm the reactions to 60 °C in order to reach good yields. In several cases, full conversions were obtained leading to very clean reaction mixtures. In those cases, the products were isolated by a simple filtration on a short plug of silica. As shown in Table 2, sterically hindered ketones and both electron-withdrawing as well as electron-donating substituted aromatic ketones were hydrogenated in high yields (entries 1-14). Under the standard reaction conditions, *p*-acetyl-acetophenone **1o** was partially hydrogenated furnishing the mono-reduced ketone **2o** in 92% yield (Table 2, entry 15).

Table 1. Ag-catalyzed hydrogenation of acetophenone[a]



1a **2 a**

Entry	Catalyst	Base	Solvent	Yield (%)[b]
1	AgOTf	KHMDS	Pentane	85
2	AgOTf	KHMDS	Toluene	92
3	AgOTf	KHMDS	THF	73
4	AgOTf	KHMDS	CPME	62
5	AgOTf	KHMDS	1,4-Dioxane	82
6	AgCl	KHMDS	Toluene	<5
7	Ag_2O	KHMDS	Toluene	10
8	Ag_2CO_3	KHMDS	Toluene	33
9	$AgPF_6$	KHMDS	Toluene	83
10	$AgSbF_6$	KHMDS	Toluene	89
11	$AgClO_4$	KHMDS	Toluene	99[e]
14	$AgClO_4$	KHMDS (10)	Toluene	99[e](99)[f]
15	$AgClO_4$	KHMDS (5)	Toluene	90
16	$AgClO_4$[c]	KHMDS (10)	Toluene	78
17[d]	$AgClO_4$	KHMDS (10)	Toluene	52
18	$AgClO_4$	LDA(10)	Toluene	<5
19	$AgClO_4$	NaOEt(10)	Toluene	<5
20	$AgClO_4$	Cs_2CO_3(10)	Toluene	<5
21	$AgClO_4$	HCOONa (10)	Toluene	<5
22	$AgClO_4$	*t*BuOK(10)	Toluene	11
23	$AgClO_4$	NaOH(10)	Toluene	<5
24	$AgClO_4$	K_2CO_3(10)	Toluene	<5
25	-	KHMDS(5)	Toluene	0
26	$AgClO_4$	-	Toluene	0

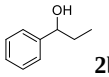
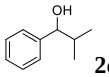
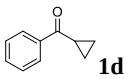
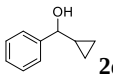
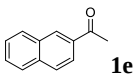
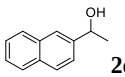
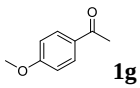
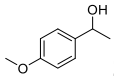
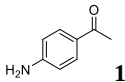
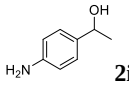
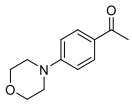
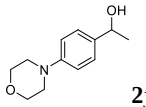
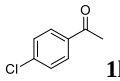
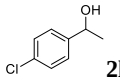
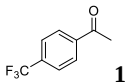
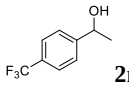
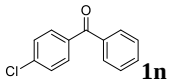
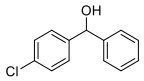
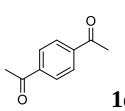
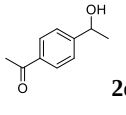
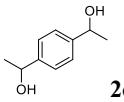
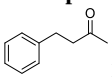
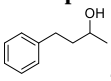
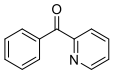
[a] Reaction conditions: acetophenone (0.5 mmol), [Ag] (6 mol%), Base (20 mol% unless other value mentioned), H_2= 20 bar, Solvent (2mL), 25°C (oil bath),17 h. [b] Determined by ^{1}HNMR. [c] 3 mol%. [d] H_2= 10 bar. [e] NMR signals of acetophenone not detected by ^{1}H NMR. [f] isolated yield.

Of note, the fully hydrogenated product **2o'** could be obtained upon heating the reaction at 60 °C. Aliphatic ketones including the naturally occurring and sterically hindered camphor **1r** were also hydrogenated in very good yields (Table 2, entries 16-18). Similarly, heterocyclic keto-compounds were reduced to the corresponding alcohols in high yields. In the case of 3-acetyl-1-methylpyrrole **1u** and 2-benzofuranyl methyl ketone **1v**, a slight heating at 60 °C was necessary to ensure good yields (Table 2, entries 21-22). Finally, the chemoselectivity of the catalytic system was evaluated using a series of bifunctional keto-derivatives. Aldehydes were also introduced in this study in order to demonstrate the applicability of the catalytic system to the hydrogenation of aldehydes. In all cases, the selective reduction of the ketone or aldehyde functional group took place delivering the alcohols in good to high yields (Table 2, entries 23-26). One limitation was

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nevertheless observed with the challenging benzylidene acetone **1aa** which delivered a mixture of alcohol **2aa** and ketone **2aa'**in a 30/70 ratio.[11] Finally, in order to highlight the general applicability of this catalytic system and draw some lines for further developments, we have attempted and succeeded with the selective hydrogenation of benzonitrile**1ab**. If the reaction of nitrile was not observed at room temperature (Table 2, entry 24), raising the temperature to 80 °C and the hydrogen pressure to 40 bar enabled the reduction of benzonitrile **1ab** into benzylamine **2ab** in 83% isolated yield (Table 2, entry 28).

Table 2. Silver-catalyzed hydrogenation of ketones: Substrate scope[a]

Entry	Substrate	Product	Isolated yield (%)[b]
1	 **1a**	 **2a**	>99[c]
2	 **1b**	 **2b**	71
3	 **1c**	 **2c**	87
4	 **1d**	 **2d**	>99[c](73)[d]
5	 **1e**	 **2e**	>99[c] (99)[d]
6	 **1f**	 **2f**	61[e]
7	 **1g**	 **2g**	>99[c] (85)[d]
8	 **1h**	 **2h**	>99 [c]
9	 **1i**	 **2i**	90
10	 **1j**	 **2j**	>99[c]
11	 **1k**	 **2k**	95[e]
12	 **1l**	 **2l**	>99[c,d]
13	 **1m**	 **2m**	99 (99)[d]
14	 **1n**	 **2n**	>99[c,e]
15	 **1o**	 **2o**	92
		 **2o'**	99[e]
16	 **1p**	 **2p**	>99[c]
17	 **1q**	 **2q**	78
18	 **1r**	 **2r**	80
19	 **1s**	 **2s**	79
20	 **1t**	**2t**	>99[c](99)[d]
21	**1u**	**2u**	88[e]
22	**1v**	**2v**	97[e]
23	**1w**		88(99)[d]
24	**1x**	**2x**	93
25	**1y**	**2y**	>99[c](83)[d]
26	**1z**	**2z**	75
		2aa	30[f]
27	**1aa**	**2aa'**	70[f]
28[g]	**1ab**	**2ab**	83

[a] Reaction conditions: substrate (0.5 mmol), $AgClO_4$ (6 mol%), KHMDS (10 mol%), H_2= 20 bar, toluene (2 mL), 25°C (oil bath), 17 h. [b]isolated by coloumn [c]Product isolated by simple filtration on a silica plug. [d]Results in parenthesis obtained with AgOTf as catalyst, 24 h. [e] 60 °C (oil bath). [f]^{1}H NMR ratio. [g]AgOTf (6 mol%), KHMDS (20 mol%), 80 °C, 17 h.

If the use of silver perchlorate in catalytic amounts and small scale syntheses should not present important safety issues, the situation may be different on larger scale syntheses. Considering this potential hazard, we have duplicated some reactions with silver triflate. These reactions performed over an extended reaction time of 24 h led in general to similarly good yields (Table 2, entries 4, 5, 7, 13, 20, 23, 25). It is worth mentioning that the repeatability and reproducibility of the reaction was checked with several substrates.

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Following our investigations on the efficiency and scope of the reaction, we turned our attention to the nature of the catalyst. Although we did not employ any nanoparticle stabilizer or support, the involvement of Ag-NPs was considered seeing the heterogeneous nature of the reaction media at the end of the catalytic transformations. As explained in a review by Finke,[12] there is not a single test leading to unambiguous distinction between homogeneous or metal-NPs catalysis. Hence, we have conducted a series of experiments in order to identify the nature of the catalyst. We have first considered the mercury poisoning test with both silver precursors in the reduction of **1a** (Hg/Ag = 300). However, due to experimental constraint (high pressure reactor), mercury was added at the onset of the reaction. In both cases we observed complete inhibition of the reaction. Next, the reusability of the catalyst was evaluated. Two different procedures were used and in both cases very good yields were obtained in a second run (see SI for details). The kinetic profile of the reaction was also investigated with AgOTf precursor. It was found that the reaction proceeded without induction period hence suggesting a homogeneous catalytic process or fast generation of Ag-NPs (see SI for details).

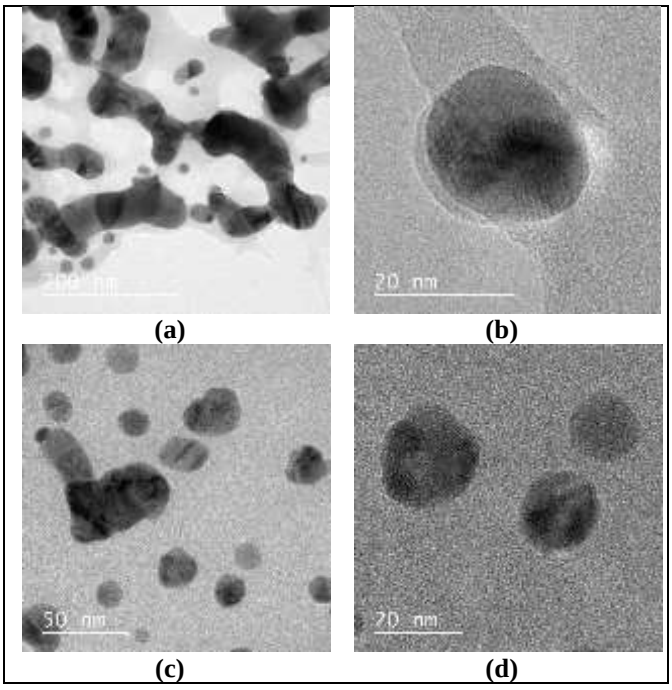


Figure 1: TEM images of reaction mixtures with AgOTf as precursor; (a) and (b) after 15 minutes; (c) and (d) after 17 h.

Finally, the reaction mixture was analyzed by Transmission Electron Microscopy (Figure 1). Two reactions were conducted with AgOTf precursors and stopped after 15 min and 17 h. After decantation, an aliquot of the supernatant liquid of each reaction was taken and deposited onto a TEM copper grid. As depicted in Figure 1, TEM images revealed the formation of nanoparticles with disperse size distribution due to agglomeration. In all cases EDS analyses on several particles for each samples evidenced the formation of silver nanoparticles (see SI for details). The observation of Ag-NPs after only 15 minutes of reaction is in agreement with fast initiation observed in kinetic studies. The unambiguous formation of nanoparticles raises the issue of stabilizers in general necessary to prevent extensive agregation of nanoparticles. Considering that hydrogenation reactions promoted by metal-nanoparticles do not require a base,[5, 7-9, 13] we believe that the bulky potassium hexamethyldisilazide initially introduced as a base necessary for hydrogen activation in an homogeneous catalytic reaction may play the role of stabilizing agent via electrostatic and/or electrosteric effects which are known processes for metal nanoparticle stabilization.[14]

Conclusion

In summary, the unprecedented hydrogenation of ketones with a silver catalyst is reported. These in situ generated silver nanoparticles operate at 25 °C and low hydrogen pressure. High efficacy and selectivity have been achieved in a number of cases involving various ketones. These important characteristics make this process interesting for the synthesis of a broad range of chemicals. Further studies will be carried out to elucidate the non-common formation of nanoparticles and to extend the applicability of these catalysts.

Experimental Section

General procedure for the catalytic hydrogenation of ketones: In an argon-filled glove box, a high pressure reactor was charged sequentially with base (5-20 mol%), silver salt (6 mol%), ketone (0.5 mmol) and 2 mL of dry toluene. The reactor was then charged with H_2 (20 bar) and stirred at the appropriate temperature for 17 h. The reactor was carefully depressurized and the reaction mixture was filtrated through a short plug of silica. The solvent was evaporated and the crude product was analyzed by ^{1}H NMR. This crude product was then purified by flash column chromatography on silica gel using a mixture of heptane and ethyl acetate as the eluent.

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References

[1] (a) P. J. Deuss, K. Barta, J. G. de Vries, *Catal. Sci. Technol*.**2014**, *4*, 1174-1196 ; b) K. Barta, P. C. Ford, *Acc. Chem. Res*. **2014**, *47*, 1503 ; c) M. J. Climent, A. Corma, S. Iborra, *Green Chem*. **2014**, *16*, 516.

Accepted Manuscript

[2] (a) S. Pedro, A. Corma, *ACS Catal*., **2015**, *5*, 7114-7121; (b) C.-J. Jia, F. Schüth, *Phys. Chem. Chem. Phys*. **2011**, *13*, 2457-248; (c) R.Cuenya, *Thin Film Solids*, **2010**, *518*, 3127-3150.

[3] (a) C. Wen, A. Yin, W.-L. Dai, *Appl.Catal.B: Environ.*, **2014**, *160-161*, 730-741; (b) X.-Y. Dong, Z.-W. Gao, K.-F. Yang, W.-Q. Zhang, L.-W. Xu, *Catal. Sci. Technol*., **2015**, *5*, 2554-2574.

[4] (a) P. Claus, H. Hofmeister, *J. Phys. Chem. B*, **1999**, *103*, 2766-2775; (b) W. Grünert, A. Brückner, H. Hofmeister, P. Claus, *J. Phys. Chem. B*, **2004**, *108*, 5709-5717. (c) M. Bron, D. Teschner, A. Knop-Gericke, B. Steinhauer, A. Scheybal, M. Hävecker, D. Wang, R. Födisch, D. Hönicke, A. Wootsch, R. Schlögl, P. Claus, *J. Catal*., **2005**, *234*, 37-47.

[5] (a) K.-i. Shimizu, Y. Miyamoto, A. Satsuma, *J. Catal*., **2010**, *270*, 86-94; (b) Y. Chen, C. Wang, H. Liu, J. Qiu, X. Bao, *Chem. Commun*., **2005**, 5298-5300.

[6] Y. Xie, P. Hu, T. Bendykov, D. Milstein, *Catal. Sci. Technol*. **2018**, *8*, 2784-2788

[7] A. You Li, M. Kaushik, C. J. Li, A. Moores, ACS Sust. Chem. Eng., **2016**, *4*, 965-973.

[8] P. G. N. Mertens, P. Vandezande, X. Ye, H. Poelman, I. F. J. Vankelekom, D. E. De Vos, *Appl. Catal. A: Gen*., **2009**, *355*, 176-183.

[9] M. J. Landry, A. Gellé, B. Y. Meng, C. J. Barret, A. Moores, *ACS Catal.*, **2017**, *7*, 6128-6133.

[10] (a) S. Wang, V. Dorcet, T. Roisnel, C. Bruneau, C. Fischmeister, *Organometallics*, **2017**, *36*, 708-713; b) S. Wang, H. Huang, V. Dorcet, T. Roisnel, C. Bruneau, C. Fischmeister, *Organometallics*, **2017**, *36*, 3152-3162; c) S. Wang, H. Huang, C. Bruneau, C. Fischmeister, *ChemSusChem*, **2017**, *10*, 4150-4154.

[11] Several recent examples highlight the difficulty to perform the selective hydrogenation or transfer hydrogenation of benzylideneacetone : (a) A. Bruneau-Voisine, D. Wang, V. Dorcet, T. Roisnel, C. Darcel, J.-B. Sortais, *Org. Lett*. **2017**, 19, 3656-3659 ; (b) D. Wei, A. Bruneau-Voisine, T. Chauvin, V. Dorcet, T. Roisnel, D. M. Valyaev, N. Lugan, J.-B. Sortais, *Adv. Synth. Catal*. **2018**, *360*, 676-681; (c) D. Wei, T. Roisnel, C. Darcel, E. Clot. J.-B. Sortais, *ChemCatChem*, **2017**, *9*, 80-83; (d) R. Xu, S. Chakraborty, S. M. Bellows, H. Yuan, T. R. Cundari, W. D. Jones, *ACS Catal*. **2016**, *6*, 2127-2135; (e) K. L. Luska, A. Bordet, S. Tricard, I. Sinev, W. Grünert, B. Chaudret, W. Leitner, *ACS Catal*. **2016**, *6*, 3719-3726; (f) K. Farrell, H. Müller-Bunz, M. Albrecht, *Organometallics*, **2015**, *34*, 5723-5733; (g) G. Zhang, S. K. Hanson, *Chem. Commun*., **2013**, *49*, 10151.

[12] J. A. Widegren, R. G. Finke, *J. Mol. Catal. A: Chem*. **2003**, *198*, 317-341.

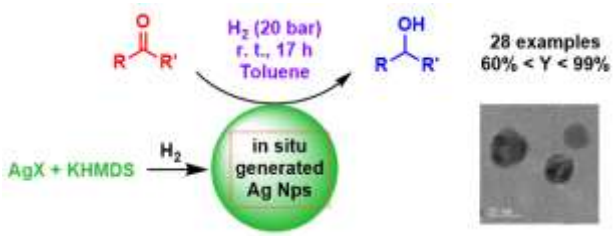
[13] (a) J. Llop Castelbou, E. Bresó-Femenia, P. Blondeau, B. Chaudret, S. Castillón, C. Claver, C. Godard, *ChemCatChem*, **2014**, *6*, 3160-3168; L. Yang, C. Cheng, L. Xia, H. Liu, *RSC Advances*, **2016**, *6*, 31871-31875;

[14] (a) A. Roucoux, *Top. Organomet. Chem*. **2005**, *16*, 261-279; (b) C. Janiak, *Z Naturforschung B*, **2014**, *68*, 1059-1089;

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