Hydrogenation Catalysts

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Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State

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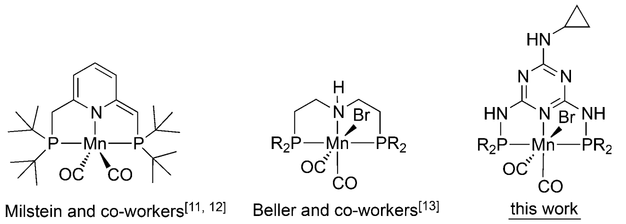
Abstract: *The replacement of expensive noble metals by earth-abundant transition metals is a central topic in catalysis. Herein, we introduce a highly active and selective homogeneous manganese-based C=O bond hydrogenation catalyst. Our catalyst has a broad substrate scope, it is able to hydrogenate aryl–alkyl, diaryl, dialkyl, and cycloalkyl ketones as well as aldehydes. A very good functional group tolerance including the quantitative and selective hydrogenation of a ketone in the presence of a non-shielded olefin is observed. In Mn hydrogenation catalysis, the combination of the multidentate ligand, the oxidation state of the metal, and the choice of the right ancillary ligand is crucial for high activity. This observation emphasizes an advantage and the importance of homogeneous catalysts in 3d-metal catalysis. For coordination compounds, fine-tuning of a complex coordination environment is easily accomplished in comparison to enzyme and/or heterogeneous catalysts.*

The hydrogenation of olefins, imines, and ketones or aldehydes is of high academic and industrial interest. Most of the successfully applied catalysts are based on expensive noble metals, such as Ru, Rh, Ir, Pd, and Pt. The low availability of such metals has stimulated a search for alternative catalysts based on transition metals with significantly higher concentration in the earth crust (base metals).[1] The key motivation for this shift of interest results from the need of the conservation of our elemental resources as a central issue of a more sustainable future. In addition, novel mechanistic pathways permitting new activity/selectivity patterns can be expected based on the different redox and magnetic properties of these metals.[2] The application of homogeneous hydrogenation catalysts is especially promising for the reduction of C=O bonds since a bifunctional mechanism involving the ligand can operate for efficient H_2 activation.[3] Recently, we discovered a highly active cobalt C=O bond hydrogenation catalyst stabilized by PN_5P ligands.[4–6] We have had successfully used such ligands to design iridium catalysts[7] and observed for Co, in contrast to Ir, that only very minor alterations of the catalyst structure strongly influenced the hydrogenation activity. Since PN_5P-ligands and the related PN_3P-ligands,[8] introduced by Haupt and co-workers[9] and intensively used by the Kirchner group in recent years,[10] are simple to vary, ligand or catalyst libraries can be used to identify catalytically active species. A base metal which has been overlooked in recent years with regard to catalytic reactions classically associated with noble metals is the third most abundant transition metal of the earth crust, namely manganese. Very recently, Milstein and co-workers introduced homogeneous Mn catalysts for the imine synthesis from alcohols and amines[11] as well as for alkylation chemistry (Scheme 1, left).[12]



Scheme 1. Recently developed manganese complexes able to catalyze reactions classically mediated by noble metals (left and middle) and the pre-catalyst described herein (right).

Herein, we report on the development of a highly active and selective Mn C=O bond hydrogenation catalyst. The pre-catalyst is easy to synthesize in two steps from commercially available starting materials with almost quantitative yield for both steps. In addition, the pre-catalyst is easy to activate by adding a catalytic amount of a metal base, such as KO^tBu (Bu = butyl). The catalyst is active in the hydrogenation of aldehydes as well as aryl–alkyl, dialkyl, diaryl, and cycloalkyl ketones. In addition, functional groups, such as terminal olefins are tolerated. Most importantly, we show that the right choice of the PN_5P ligand, the right oxidation state of the metal, and the right kind and number of ancillary ligands are requirements for catalytic activity. Parallel to our work, Beller and co-workers introduced a Mn catalyst for C=O bond hydrogenation based on a different multidentate ligand (Scheme 1, middle).[13] To the best of our knowledge, this is the only other example of a Mn catalyst able to hydrogenate C=O bonds efficiently.[14] Our catalyst is 10-times more active than the Beller catalyst, operates under milder conditions, and gives quantitative conversion in significantly shorter reaction times.

We first synthesized a representative number of PN_5P-ligand stabilized manganese(II) dichlorido (**2a**,**b**) and manganese(I) bromido dicarbonyl (**3a**–**d**) complexes (Scheme 2).[15] X-ray crystal structure analysis of **2a** was performed to determine the molecular structure (see Sup-

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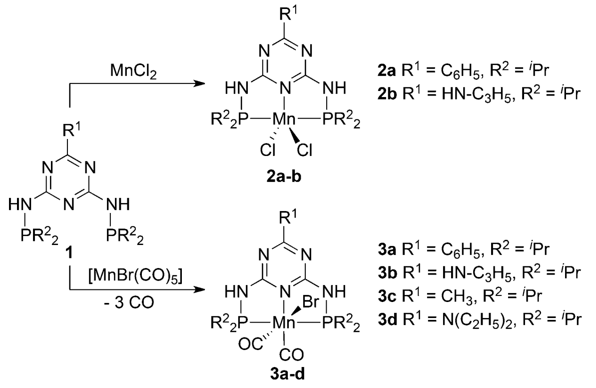
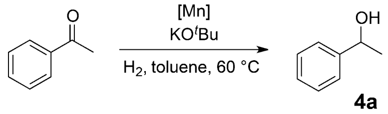


Scheme 2. Synthesis of novel Mn^{II} (**2a**,**b**) and Mn^{I} (**3a**–**d**) complexes.

Table 1: Hydrogenation of acetophenone with several Mn pre-catalysts.



Entry	Pre-catalyst	Yield[c] [%]	Entry	Pre-catalyst	Yield[c] [%]
1	**2a**[a]	0	5	**3c**[b]	31
2	**2b**[a]	0	6	**3d**[b]	55
3	**3a**[b]	38	7	MnCl$_2$	0
4	**3b**[b]	72	8	[MnBr(CO)$_5$]	0

Reaction conditions: [a] 1 mmol acetophenone, 5 mol% pre-catalyst, 100 mol% KO^{t}Bu, 2 mL toluene, 60 bar H$_2$, 60 °C, 16 h. [b] 3 mmol acetophenone, 0.1 mol% pre-catalyst, 1 mol% KO^{t}Bu, 2 mL toluene, 20 bar H$_2$, 60 °C, 4 h. [c] Determined by GC with dodecane as internal standard.

porting Information). Next, we investigated the hydrogenation of acetophenone to 1-phenylethanol **4a** (Table 1) as a suitable test reaction to find an active catalyst and optimal hydrogenation reaction conditions. No activity was observed using 5 mol% of **2a**,**b** in toluene, activated with an excess of KO^{t}Bu, under 60 bar hydrogen pressure and at 60 °C (Table 1, entries 1–2). In contrast, the Mn^{I} bromide complexes **3a**–**d** were able to hydrogenate the model substrate after activation by a base. After finding an initial hydrogenation activity, with the catalyst based on **3b** being the most active one, we optimized the reaction conditions, such as base amount, pressure, temperature, and catalyst loading (see Supporting Information). The molecular structure of **3b** was confirmed by X-ray crystal structure analysis (XRD) because it gave the most active catalyst (Figure 1). XRD revealed a hexacoordinate Mn^{I} complex with a slightly distorted octahedral coordination. The PN$_5$P ligand acts as a neutral ligand, coordinating the Mn in a tridentate manner with a P1-Mn1-P2 angle of 162.17(6)°. The CO ligands are coordinated *cis* to each other with a C1-Mn1-C2 angle of 88.55(3)°. To our delight, 0.1 mol% of complex **3b** afforded 1-phenylethanol (**4a**) in quantitative yield (Table 2, entry 1) under relatively mild reaction conditions (80 °C, 20 bar H$_2$, 4 h). The mildest conditions used by Beller and co-workers to obtain quantitative conversion were 100 °C, 30 bar and 24 h with a catalyst loading of 1 mol%. Our catalyst hydrogenates under milder conditions, in significant shorter time, and with up to 10-times less catalyst loading. The pre-catalyst based on **2b** is completely inactive at these optimized conditions. Since the conditions were optimized for **3b**, we assigned the inactivity of **2b** also to the not optimal reaction conditions. A thorough investigation of the ketone hydrogenation ability of **2b** revealed no activity. Comparing **2b** and **3b**, we see two alterations, the oxidation state [manganese(I) versus (II)] and the presence of the ancillary carbonyl ligands. To see if **2b** becomes active in the +1 oxidation state, reduction of **2b** with one equivalent of potassium graphite was carried out and the corresponding complex was studied in the hydrogenation of the model substrate acetophenone. We could not identify any activity of this carbonyl ligand free “catalyst” and concluded that the combination of the oxidation state and the presence of the ancillary carbonyl ligands is beneficial or even a precondition for ketone hydrogenation activity. The catalytically active species can be formed by the reaction of **3b** with 1 equivalent KO^{t}Bu to form a blue dicarbonyl complex, which reacts with H$_2$ to form a colorless carbonyl hydride complex.[10a]

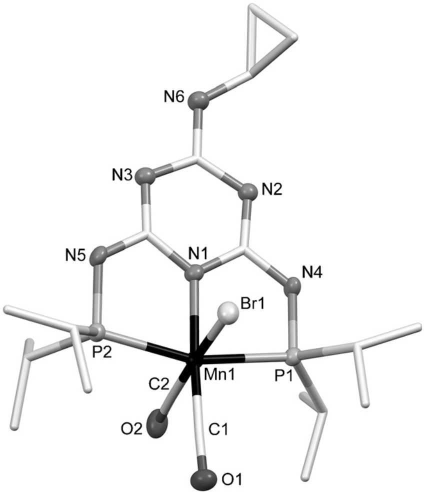
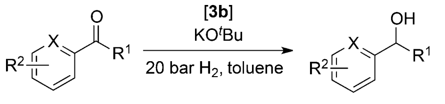


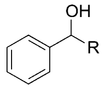
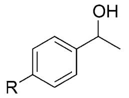
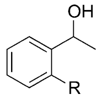
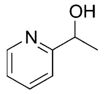
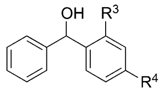
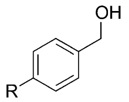
Figure 1. Molecular structure of **3b** is displayed with thermal ellipsoids set at 50% probability.[16] H atoms and one cocrystallized benzene molecule are omitted for clarity. Selected bond lengths [Å] and angles [°]: Mn1–P1 2.265(2), Mn1–P2 2.283(2), Mn1–N1 2.036(4), Mn1–Br1 2.577(1), Mn1–C1 1.800(6), Mn1–C2 1.759(6), P1–N4 1.708(4), P2–N5 1.713(5), C1–O1 1.112(8), C2–O2 1.143(7); P1-Mn1-P2 162.17(6), Mn1-P1-N4 99.67(2), Mn1-P2-N5 100.00(2), P2-Mn1-N1 80.52(1), P1-Mn1-N1 81.78(1), C1-Mn1-Br1 87.35(2), C2-Mn1-Br1 175.89(2), C1-Mn1-N1 174.18(2), C2-Mn1-N1 97.09(2), C1-Mn1-P1 96.75(2), C1-Mn1-P2 100.65(2), C2-Mn1-P1 90.96(2), C2-Mn1-P2 93.31(2), Br1-Mn1-N1 87.01(1).

Next, we explored the substrate scope applicable to this novel manganese-based hydrogenation catalyst. Starting from the acetophenone motif, we first varied the length (**4a**–**d**) and the branching (**4e**,**f**) of the alkyl chain. For increased chain length, the pre-catalyst concentration had to be gradually increased from 0.1 to 1 mol% to reach full conversion. The branched alcohol **4e** could only be obtained quantitatively by increasing the reaction time to 24 h, after which the even bulkier alcohol **4f** could also be obtained in high yields (82%, Table 2, entry 6). A series of 4′-substituted acetophenone derivatives (**4g**–**l**) were then subjected to hydrogenation,

Table 2: Hydrogenation of aryl–alkyl, diaryl carbonyl compounds and aldehydes.[a]

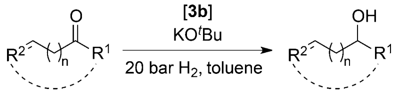


4a-u

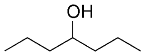
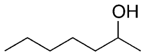
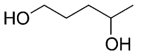
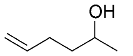
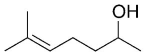
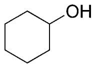
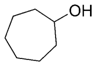
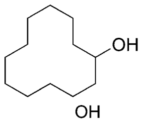
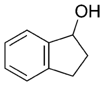
Entry	Product			Cat. loading [%]	Yield[d] [%]
1		R = CH_3	**4a**	0.1	> 99
2		R = CH_2CH_3	**4b**	0.2	97
3		R = $(CH_2)_2CH_3$	**4c**	1	> 99
4		R = $(CH_2)_3CH_3$	**4d**	1	> 99 (98[c])
5		R = $CH(CH_3)_2$	**4e**	1[e]	99
6		R = $C(CH_3)_3$	**4f**	1[e]	82
7		R = Cl	**4g**	0.1	97 (96[c])
8		R = Br	**4h**	0.1	97 (95[c])
9		R = OCH_3	**4i**	0.2	> 99 (91[c])
10		R = CN	**4j**	2	89
11		R = C(O)OMe	**4k**	1	52[c]
12		R = CH_3	**4l**	0.2	> 99
13		R = Cl	**4m**	0.2	98
14		R = F	**4n**	1	> 99 (92[c])
15			**4o**	0.5	> 99 (92[c])
16		R^3 = H, R^4 = H	**4p**	0.5	> 99
17		R^3 = CH_3, R^4 = H	**4q**	0.5	75
18		R^3 = H, R^4 = CH_3	**4r**	0.5	> 99
19		R^3 = H, R^4 = OCH_3	**4s**	0.5	> 99 (93[c])
20		R = H	**4t**	0.1[b]	> 99
21		R = NO_2	**4u**	1	> 99

[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] 40 °C. [c] Yield of isolated product. [d] Determined by GC with dodecane as internal standard. [e] 24 h.

Table 3: Hydrogenation of dialkyl, and cycloalkyl carbonyl compounds.[a]



5a-i

Entry	Product		Cat. loading [%]	Yield[b] [%]
1		**5a**	0.5	> 99
2		**5b**	0.2	95
3		**5c**	1	88
4		**5d**	0.1	> 99 (95[c])
5		**5e**	0.2	98 (86[c])
6		**5f**	0.1	98
7		**5g**	0.2	96
8		**5h**	1	58
9		**5i**	1	97

[a] Reaction conditions: 3 mmol substrate, pre-catalyst **3b**, KO^{t}Bu, 1.5 mL toluene, 20 bar H_2, 80 °C, 4 h. [b] Determined by GC with dodecane as internal standard. [c] Yield of isolated product.

which were quantitatively hydrogenated under very low catalyst loadings. The 2′-substituted acetophenone derivatives (entries 13–14) could also be obtained quantitatively. Compared to acetophenone, the N-heterocyclic relative 2′-acetylpyridine required higher catalyst loadings to reach full conversion into **4o**, which is probably due to the poisoning of the manganese center by the pyridine moiety. The performance of the catalyst was further evaluated using a series of diaryl ketones (**4p–s**). Generally, higher catalyst loadings (0.5 mol %) were required to reach full conversion, but even the bulkier 2-methylbenzhydrol **4q** was obtained in high yields (75 %, Table 2, entry 17). These substrates could be readily reduced to the alcohols under mild conditions, and correspondingly benzaldehyde was hydrogenated to quantitatively yield benzyl alcohol at only 40 °C. To show the full potential of the catalyst system, the synthesis of **4h** (entry 8) was scaled up to a 45 mmol batch using otherwise unchanged parameters (see Supporting Information for details), still yielding 97 % of essentially pure **4h** after filtration over silica. Since the hydrogenation of various demanding ketones went smoothly, the generally more demanding substrate class of dialkyl ketones was investigated (Table 3). The alcohol **5a** was obtained at a rather high pre-catalyst loading of 0.5 mol % most probably because of the position of the C=O bond. Ketones with better accessibility (**5b–e**) of the carbonyl function are reduced very efficiently (**5b**). Ketones bearing a C=C double bond were very selectively converted into the corresponding unsaturated alcohols (**5d**,**e**). Even a rather exposed unsubstituted double bond remained unharmed during the hydrogenation procedure, resulting in nearly quantitative isolation of **5d**. Lastly, cycloalkyl ketones with various ring sizes were subjected to hydrogenation (**5f**–

h). Cycloalkyl ketones with small ring sizes are herein more readily hydrogenated than ketones with larger ring systems, resulting in only 58 % yield of **5h** despite the use of 1 mol % pre-catalyst. The five-membered ring of 1-indanone also required the higher than usual pre-catalyst loading of 1 mol %, but was quantitatively hydrogenated to the corresponding alcohol **5i**.

In summary, we introduced a highly active and easy to synthesize Mn based C=O bond hydrogenation catalyst. The easy modification of the used multidentate ligands makes the catalyst family attractive for fast catalyst identification. Manganese is the third most abundant transition metal in the Earth's crust and we developed a Mn catalyst, which hydrogenates various ketones quantitatively in 4 h with only 0.1 mol % catalyst loading. The substrate scope is broad since aryl–alkyl, diaryl, dialkyl, and cycloalkyl ketones can be hydrogenated smoothly. In addition, we see an impressive functional group tolerance. Hydrogenation of C=O bonds proceeds selectively in the presence of a non-shielded olefin, a nitrile, or a nitro group.

Most importantly, we feel that in Mn hydrogenation catalysis the combination of the multidentate ligand, the oxidation state of the metal, and the choice of the right ancillary ligand is crucial to give high activity. This observation emphasizes an advantage of homogeneous catalysis in the application of base metals as active sites. For coordination compounds, a fine-tuning of a complex coordination environment is easily accomplished in comparison to enzyme catalysis and/or heterogeneous catalysis.

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Keywords: alcohols · base metals · hydrogenation · manganese · PNP ligands

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[16] CCDC 1499551 (**2a**) and 1499552 (**3b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via Cambridge Crystallographic Data Centre.

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