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Communication

Simple manganese carbonyl catalyzed hydrogenation of quinolines and imines

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ABSTRACT

Manganese-catalyzed hydrogenation of unsaturated molecules has made tremendous progresses recently benefiting from non-innocent pincer or bidentate ligands for manganese. Herein, we describe the hydrogenation of quinolines and imines catalyzed by simple manganese carbonyls, $Mn_2(CO)_{10}$ or $MnBr(CO)_5$, thus eliminating the prerequisite pincer-type or bidentate ligands.

Sustainable chemistry requires precise and efficient synthesis of various functional molecules and materials in an atom- and step-economical manner. Aiming at this goal, transition metal catalysis has evolved into a powerful tool to discover new reactivity and tune chemo-, regio- and stereoselectivity for synthetic transformations. An illustrative example is transition-metal-catalyzed hydrogenation of unsaturated molecules, which mostly has 100% atom-economy and is potentially a waste-free process [1]. Noble transition metal catalysis has played a predominant role in this field, and very high catalytic turnovers and excellent stereoselectivity have been achieved with structure-defined catalysts [2]. However, the rarity in the earth's crust and intrinsic toxicity limit future wider applications of these metals in hydrogenation reactions. As such, developments of earth abundant and less toxic 3d transition metal catalysts for hydrogenation have gained immense attention recently and are still highly desirable [3].

Manganese, as the third richest transition metal in the earth's crust, is cheap, less toxic and diverse in oxidation states (from -3 to +7) thus being a potential candidate for catalyst development [4,5]. In this context, Beller, Kempe, Sortais, Kirchner *et al*. have elegantly reported hydrogenation of aldehydes/ketones by using manganese-pincer or -bidentate ligand complexes since 2016 (Scheme 1) [6]. Later on, Clarke, Beller, Ding and Zhong further developed asymmetric hydrogenation of ketones with chiral pincer-manganese catalysts [7]. Other carbonyl derivatives such as nitriles [6a,6e,8], carbon dioxide [9], carbonates [10], amides [11] and esters [12] could also be hydrogenated by adopting the related manganese-pincer or -bidentate ligand complexes. Very recently, Milstein and coworkers have nicely demonstrated the hydrogenation of challenging carbamates and ureas with their PNN-pincer manganese catalyst [13]. Meanwhile, Sortais, Kempe and Liu showed the hydrogenation of imines and fused *N*-heterocycles containing C=N bonds respectively, again with bidentate or pincer-type ligand-manganese catalysts [14]. It is generally accepted that these non-innocent pincer ligands cooperate with the manganese centre to enable the hydrogenation processes through an outer-sphere mechanism [5]. In our continuous interest in MnH catalysis [15], we herein describe the hydrogenation of quinolines and imines by using simple manganese carbonyls, $Mn_2(CO)_{10}$ or $MnBr(CO)_5$, which eliminates the previous requirement of pincer-type or bidentate ligands as well as bases (Scheme 2).

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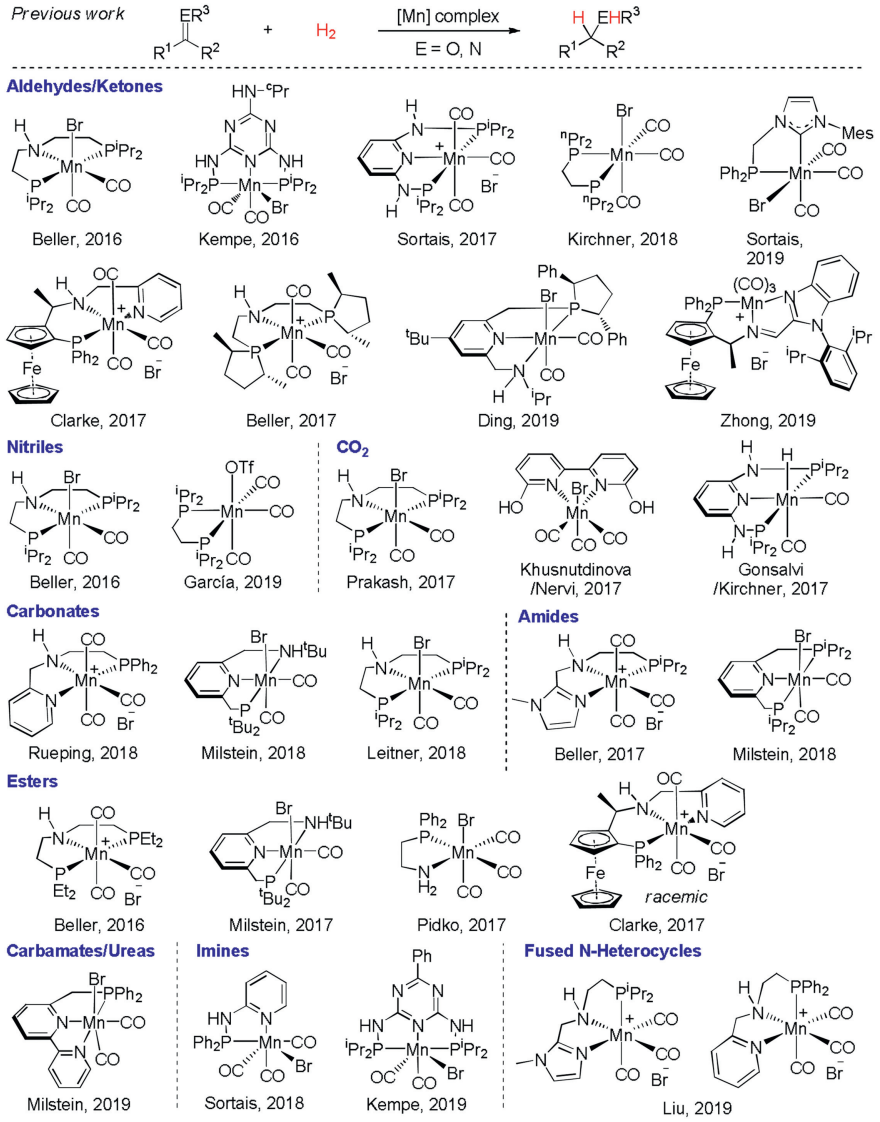
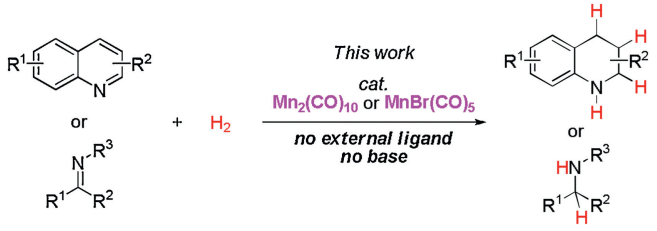


Scheme 1. Pincer or bidentate ligand-manganese complex catalyzed hydrogenation of C = E (E = O, N) containing substrates.



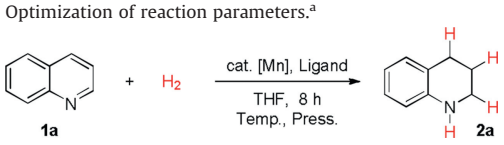
Scheme 2. Simple manganese carbonyl catalyzed hydrogenation of quinolines and imines.

During the preparation of this manuscript, Beller *et al.* elegantly reported a very related work using $MnBr(CO)_5$ as a catalyst for hydrogenation of *N*-heterocycles at a lower temperature [16]. Of note, our results show that $Mn_2(CO)_{10}$ can also act as an efficient catalyst for hydrogenation of quinolines at a higher temperature. Moreover, we demonstrate that imines could be successfully hydrogenated by using simple manganese carbonyl catalysts.

In 2014, we reported a manganese-catalyzed [4 + 2] annulation reaction of *N*-H imines and alkynes with the evolution of H_2 gas [15]. Mechanistic studies indicated the involvement of $MnH(CO)_5$ as a true catalytic species in the reaction. Curious whether the simple $MnH(CO)_5$ species could enable the hydrogenation reactions without using previous external pincer or bidentate ligands, we commenced our study with the hydrogenation of quinoline **1a** by using simple $Mn_2(CO)_{10}$ as a catalyst (Table 1). The expected 1,2,3,4-tetrahydroquinoline **2a** was formed quantitatively when the hydrogenation was carried out with 5 MPa of H_2 and 10 mol% of $Mn_2(CO)_{10}$ in THF at 150 °C (entry 1). While phosphine ligands were detrimental to the reaction, NPh_3 and $AsPh_3$ showed no influence on the reaction outcome (entries 2–6). Changing the reaction temperature suggested that 130 °C was the optimal (entries 7 and 8). Variations on the pressure of H_2 showed that the reaction could proceed at lower pressure even at 1 atm, yet in decreased yields (entries 9–12). The amount of $Mn_2(CO)_{10}$ could be reduced to 5 mol%, however, 1 mol% of the catalyst failed in the reaction (entries 13–14). The use of MnBr bold $(CO)_5$ instead of $Mn_2(CO)_{10}$ gave also a quantitative yield of **2a** (entry 15).

Next, the scope of quinolines was tested with the above-obtained reaction conditions (Scheme 3). It was shown that substitutions on various positions of quinolines **1** had no

Table 1
Optimization of reaction parameters.[a]



Entry	Cat. [Mn] (mol%)	Ligand	T (°C)	P (MPa)	Yield (%)[b]
1	$Mn_2(CO)_{10}$ (10)	–	150	5	100
2	$Mn_2(CO)_{10}$ (10)	PPh_3	150	5	5
3	$Mn_2(CO)_{10}$ (10)	DPPM	150	5	0
4	$Mn_2(CO)_{10}$ (10)	DPPE	150	5	0
5	$Mn_2(CO)_{10}$ (10)	NPh_3	150	5	100
6	$Mn_2(CO)_{10}$ (10)	$AsPh_3$	150	5	100
7	$Mn_2(CO)_{10}$ (10)	–	130	5	100
8	$Mn_2(CO)_{10}$ (10)	–	120	5	0
9	$Mn_2(CO)_{10}$ (10)	–	130	0.1	38
10	$Mn_2(CO)_{10}$ (10)	–	130	1	34
11	$Mn_2(CO)_{10}$ (10)	–	130	2	80
12	$Mn_2(CO)_{10}$ (10)	–	130	3	100
13	$Mn_2(CO)_{10}$ (5)	–	130	3	99
14	$Mn_2(CO)_{10}$ (1)	–	130	3	1
15	$MnBr(CO)_5$ (5)	–	130	3	100

DPPM = Bis(diphenylphosphino)methane, DPPE = 1,2-Bis(diphenylphosphino)ethane.

[a] Unless otherwise noted, all the reactions were carried out with **1a** (0.2 mmol), [Mn] catalyst (10 mol%), Ligand (20 mol%), H_2 (5 MPa) in THF (1.0 mL) for 8 h.

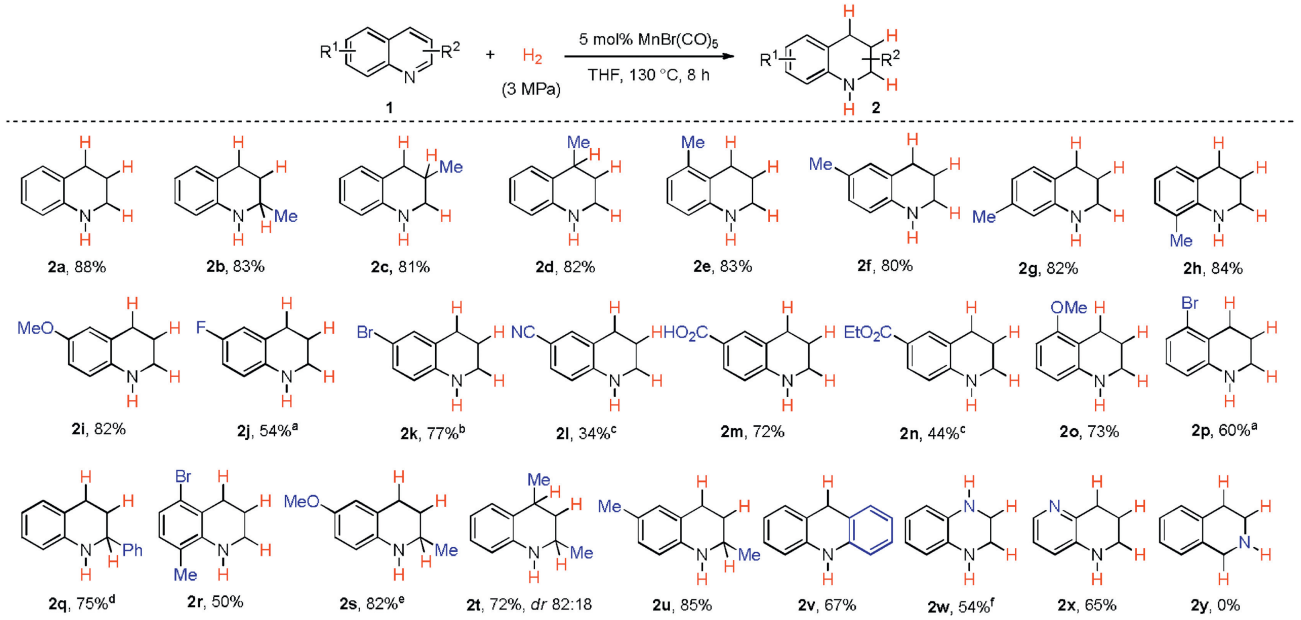
[b] Determined by ^1H NMR analysis with an internal standard.

obvious effect on the reaction outcome giving the corresponding 1,2,3,4-tetrahydroquinolines in high yields (**2a-h**). Both electron-donating and -withdrawing groups were well tolerated in the reactions (**2i-n**). Quinolines bearing other substitution patterns were also applicable to this protocol (**2o-u**). The use of acridine gave 9,10-dihydroacridine (**2v**) smoothly in moderate yield. Quinoxaline and 1,5-naphthyridine led to the expected products successfully (**2w**, **2x**) with the latter only one ring reduced (**2x**). Surprisingly, isoquinoline failed to afford the corresponding product (**2y**) under the current reaction conditions [16].

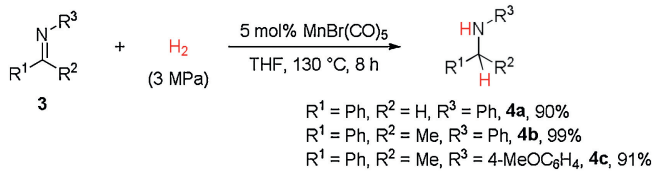
Encouraged by the above success on hydrogenation of quinoline derivatives, we further examined our catalytic system with hydrogenation of imines. As shown in Scheme 4, the hydrogenation of both aldimine and ketimines **3** could give the expected amine products **4** in excellent yields under the same reaction conditions as those of quinolines.

To explore the possible reaction mechanism, a set of experiments was conducted (Scheme 5). First, some additives were added to the reaction in order to probe the possible radical nature of this process. It turned out that TEMPO inhibited the reaction completely and TEMPO-H was detected by GC–MS analysis (Scheme 5a), which may result from the reaction of TEMPO with $MnH(CO)_5$. Other radical scavengers such as butylated hydroxytoluene (BHT) and 1,1-diphenylethylene (1,1-DPE) affected the reaction outcome, however, the expected product **2a** could still be obtained in decreased yields. To further test whether transient radical intermediates were generated in the reduction, cyclopropanyl substituted quinolines at 2-, 3- or 4-positions were subjected to the reactions and no ring-opened products were detected in all cases (Scheme 5b), which suggested the formation of a carbon radical adjacent to the cyclopropanyl group might not occur in the reaction. Remarkably, obvious deuterium-incorporation was found at 2-, 3- and 4-positions of the product with the 3-position being the most when the reaction was carried out in the presence of D_2O (Scheme 5c). It indicated that $MnH(CO)_5$ may undergo H/D exchange with D_2O in the reaction. Interestingly, no D-incorporation was observed in the product when the reaction was conducted in THF-d_8. To probe whether 1,2-reduction species **5a** was the possible reaction intermediate, **5a** was synthesized and subjected to a series of different reaction conditions (Scheme 5d). It was shown that **5a** completely transformed to product **2a** under the standard reaction conditions. Interestingly, disproportionation of **5a** into quinoline **1a** and tetrahydroquinoline **2a** took place even without $MnBr(CO)_5$ or any external base [14c]. Such phenomenon was also found when the reactions were carried out in the absence of H_2. Of note, the yields of **1a** and **2a** were not equal in these reactions, indicating a possible evolution of H_2 during the disproportionation process.

Based on the above results, we prefer an ionic MnH-promoted hydrogenation to a radical mechanism for these reactions and the tentative reaction pathways were depicted in Scheme 6. In the case of $Mn_2(CO)_{10}$ with H_2, $MnH(CO)_5$ was generated first and reacted with quinoline **1** through an either 1,4-addition or 1,2-addition



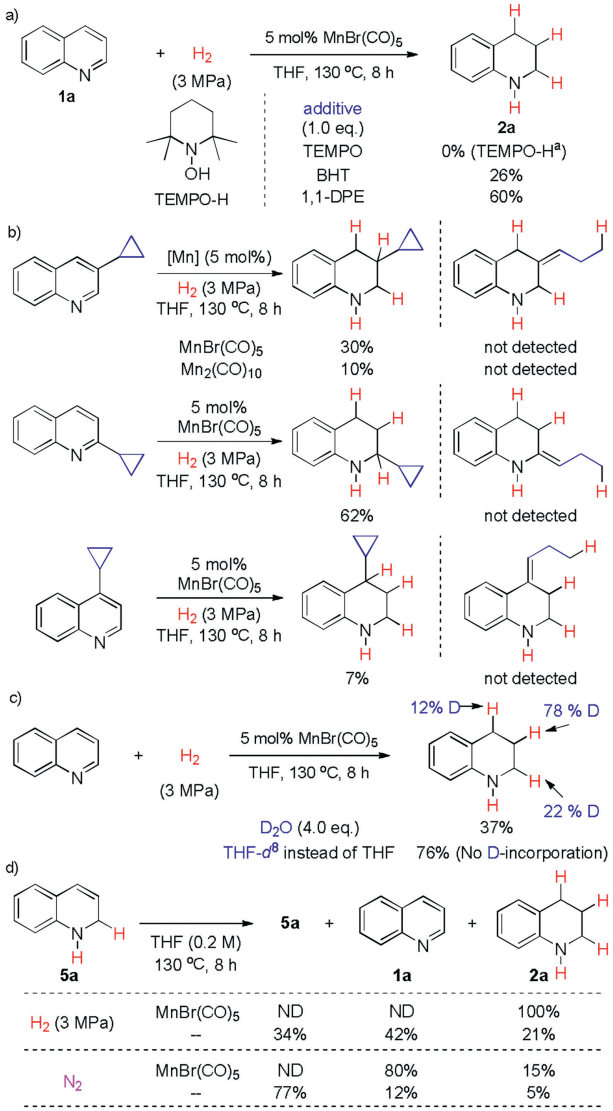
Scheme 3. Simple manganese carbonyl catalyzed hydrogenation of quinolines. Reaction conditions: **1** (0.5 mmol), $MnBr(CO)_5$ (5 mol%), H_2 (3 MPa), 130 °C, THF (2.5 mL), 8 h. [a] 24 h. [b] 150 °C. [c] 1.0 equiv. of CH_3CO_2H was added. [d] H_2 (5 MPa), 24 h. [e] $MnBr(CO)_5$ (10 mol%), H_2 (5 MPa), 24 h. [f] 12 h.



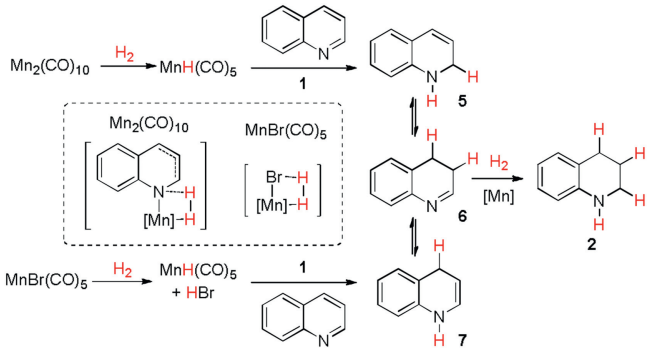
Scheme 4. Simple manganese carbonyl catalyzed hydrogenation of imines. Isolated yields were shown.

way. The resulting [Mn-N] species may cleave H_2 to regenerate $MnH(CO)_5$, which could further reduce the heterocyclic intermediates **5**–**7** to the final tetrahydroquinoline product **2**. In the case of $MnBr(CO)_5$ with H_2, $MnH(CO)_5$ was formed together with HBr, which could activate quinoline **1** by forming a salt [16]. Two sequential steps of reduction would eventually give the tetrahydroquinoline product **2**.

In conclusion, we have developed a simple protocol to achieve the hydrogenation of quinoline derivatives and imines by using commercially available manganese carbonyls, $Mn_2(CO)_{10}$ and



Scheme 5. Mechanistic studies for manganese carbonyl catalyzed hydrogenation of quinolines. Yields were determined by ^1H NMR analysis. [a] Detected by GC–MS analysis. ND = not detected.



Scheme 6. A proposed mechanism.

$MnBr(CO)_5$, which eliminates the need of pincer-type or bidentate ligands previously commonly used. Mechanistic studies suggested the involvement of $MnH(CO)_5$-promoted non-radical reduction process with H_2. Further investigations on $MnH(CO)_5$-enabled catalytic reduction of other substrates and detailed mechanistic studies are underway in our laboratory.

Declaration of competing interest

We herein declare that all the authors have no conflict of interest.

Acknowledgments

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.cclet.2020.02.025.

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