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Manganese Catalyzed Selective Hydrogenation of Cyclic Imides to Diols and Amines

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Herein we report the selective hydrogenation of cyclic imides to diols and amines, homogeneously catalyzed for the first time by a complex of an earth-abundant metal, a manganese pincer complex. A plausible catalytic cycle is proposed based on informative mechanistic experiments.

Hydrogenation is a green and sustainable method for organic transformation and therefore hydrogenation of polar bonds, in particular organic carbonyl compounds, is of much interest. In the past, we and others have reported the catalytic hydrogenation of a variety of carbonyl compounds such as ketones, esters, acids, anhydrides, amides, carbonates, carbamates and urea derivatives, as reviewed.[1-9] Although examples of hydrogenation of cyclic imides were reported, selective hydrogenation of cyclic imides to diols and amines have received scant attention. Partial hydrogenation of cyclic imides to hydroxyamides were reported by Ikariya[10-11] and Bergens[12] using ruthenium catalysts. Drago,[13] Bruneau,[14] Beller[15] and Agbossou-Niedercorn[16] have independently reported on the hydrogenative C-O bond cleavage of cyclic imides to form lactams or cyclic amines (Scheme 1). Regarding the hydrogenative cleavage of both imide C-N bonds Lv and Zhang[17] reported hydrogenation of a single substrate, N-benzylphthalimide, to 1,2-benzenedimethanol and benzyl amine. Recently we reported a general hydrogenation of cyclic imides to diols and amines using a ruthenium pincer catalyst (Scheme 1).[18] Additionally, we employed this method for the development of a fundamentally new Liquid Organic Hydrogen Carrier (LOHC), thereby implicating additional importance for this mode of hydrogenation of cyclic imides.[18]

In order to develop cost-effective and sustainable catalytic processes, catalysts based on earth-abundant metals are highly desirable. Indeed, there has been great interest in past few years in the development of earth-abundant-based metal complexes as catalysts of (de)hydrogenation reactions. Base-metal catalysts for the hydrogenation of most of the carbonyl compounds were well reviewed.[19] Manganese catalyzed hydrogenation of aldehydes, ketones, esters, amides,[20] as well as the most challenging substrates, organic carbonates,[21] carbamates and urea derivatives,[22] have been reported. On the other hand, hydrogenation of cyclic imides using base-metal catalysts have not received much attention. The research groups of García[23] and Beller[24] reported partial hydrogenation of cyclic imides with Ni(0) and Co-based complexes, respectively, which involve C=O bond cleavage (Scheme 1). However, a homogeneous catalyst based on earth-abundant metal for the hydrogenation of cyclic imides all the way to diols and amines via both C-N bond cleavage is still unknown. Here we present such a reaction, homogeneously catalyzed by a pincer complex of earth-abundant manganese.
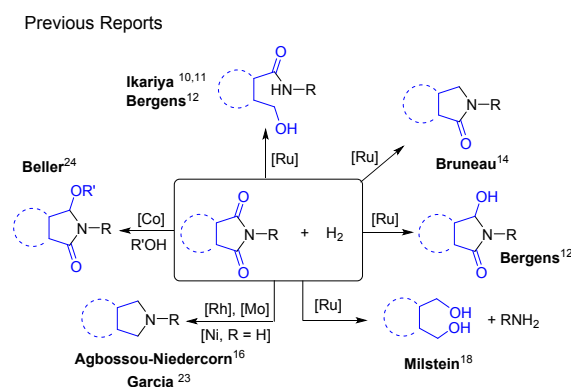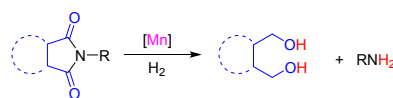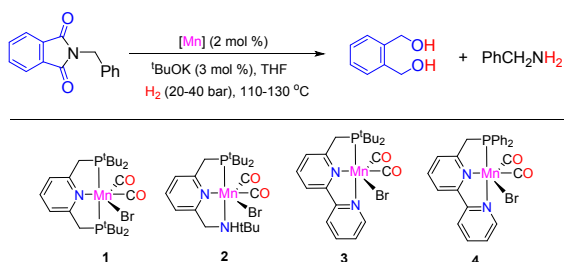

Scheme 1. Hydrogenation of cyclic imides.

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Scheme 2. Manganese catalyzed hydrogenation of cyclic imides and the manganese complexes (**1**-**4**) employed in this study.

Table 1. Optimization of the catalytic conditions for hydrogenation of N-benzylphthalimide.[a]

ent ry	[**Mn**]	H_2 (bar)	temp (°C).	t (h)	Conv. (%)[b]	yield (%) of diol/amine[b]
1	**1**	40	110	24	-	-
2	**2**	40	110	24	-	-
3	**2**	40	130	36	43	35/40
4	**3**	40	110	24	-	-
5	**4**	40	130	24	78	68/73
6	**4**	40	130	36	90	75/87
7	**4**	**30**	**130**	**48**	**>99**	**98(94)[c]/99(92)[c]**
8	**4**	20	130	48	>99	65[d]/99

[a]Reaction conditions: Catalyst [**Mn**] (0.02 mmol), [t]BuOK (0.03 mmol), N-benzylphthalimide (1 mmol), THF (2 mL), H_2 (20-40 bar). [b]Conversion of N-benzylphthalimide and yields of diols and amines were determined by GCMS and/or ^{1}H NMR spectroscopy using mesitylene as an internal standard. [c]Isolated yields. [d]Phthalide is minor product.

We started our investigation by screening manganese pincer catalysts developed in our laboratory that have been previously utilized for (de)hydrogenation reactions (Scheme 2, SI).[25] Under the catalytic conditions of 2 mol% complex **1**, **2** or **3**, [t]BuOK (3 mol%), H_2 (40 bar) at 110 °C in THF, no conversion of N-benzylphthalimide was observed in 24 h (Table 1, entries 1,2, 4).

However, upon raising the temperature to 130 °C, using precatalyst **2** and keeping the remaining conditions the same, 43% of N-benzylphthalimide was hydrogenated to 1,2-benzenedimethanol (35%) and benzyl amine (40%, Table 1, entry 3). Interestingly, using our recently reported[26] complex **4** at 130 °C, keeping the remaining conditions same, 78% of N-benzylphthalimide was hydrogenated to 1,2-benzenedimethanol (68%) and benzyl amine (73%, Table 1, entry 5). The best results were obtained using complex **4** (2 mol %), [t]BuOK (3 mol %), H_2 (30 bar) at 130 °C for 48 h, resulting in 99% conversion of N-benzylphthalimide to form 1,2-benzenedimethanol (98%) and benzyl amine (99%, Table 1, entry 7). A comparison of the catalytic activity of the complexes in different solvents, including toluene, dioxane and p-xylene showed that THF was the best solvent, and complex **4,** bearing a PPh₂ group, was the best catalyst (See SI, Table S1). One reason for that might be that replacing of the P[t]Bu₂ group,

present in the other complexes, by PPh₂ in **4**, results in lower steric hindrance, and in higher Lewis acidity of the Mn centre, thus enhancing the binding of the carbonyl compounds.

Optimizing the reaction conditions, we explored the substrate scope of this catalytic process. As described in Table 2, a variety of N-benzylphthalimides bearing substituted benzyl amines were successfully hydrogenated to afford excellent yields of 1,2-benzenedimethanol and amines (Table 2, entries 1-6). N-phenylphthalimide as well as N-hexylphthalimide were also hydrogenated almost quantitatively to produce 1,2-benzenedimethanol and the corresponding amines in excellent yields (Table 2, entries 7 and 8). Additionally, N-substituted succinimides were also hydrogenated to produce 1,4-butanediol and corresponding amines in excellent yields (Table 2, entries 9-12). Interestingly, N-phenylmaleimide underwent hydrogenation of both the C=O and C=C bonds to yield 1,4-butanediol and aniline (Table 2, entry 13). Finally, N-benzylglutamide was hydrogenated in 83% yield to afford 1,5-pentanediol and benzylamine in 77% and 80% yields, respectively (Table 2, entry 14). However, attempted hydrogenation of phthalimide resulted in recovery of the starting material, indicating that the N-H group is detrimental, perhaps due to its acidity, which may result in catalyst deactivation.

Table 2. Manganese catalyzed hydrogenation of cyclic imides.[a]

entry	cyclic imide	conversion(%)[b]	yield(%)[b] of diol/amine
1	X = H	99	98(94)[c]/99(92)[c]
2	= CH₃	98	89/98
3	= F	90	84/89
4	= Cl	89	83/86
5	= OMe	91	85/90
6	= CF₃	75	70/73
7		99	89/99
8		99	95(90)[c]/99(95)[c]
9		99	93/97
10	Y = H	99	96(85)[c]/98(93)[c]
11	= OMe	96	90/95
12	= F	90	85/90
13		98	87[d]/96
14		83	77/80%

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aReaction conditions: Complex **4** (0.02 mmol), tBuOK (0.03 mmol), cyclic imides (1 mmol), H_2 (30 bar), THF (2 mL), 130 °C (bath temperature), reaction time: 48h. bConversion and yields of amines and diols were determined by GC-MS and/or ^{1}H NMR spectroscopy using mesitylene as an internal standard. cIsolated yields. d1,4-butanediol was the alcohol product.
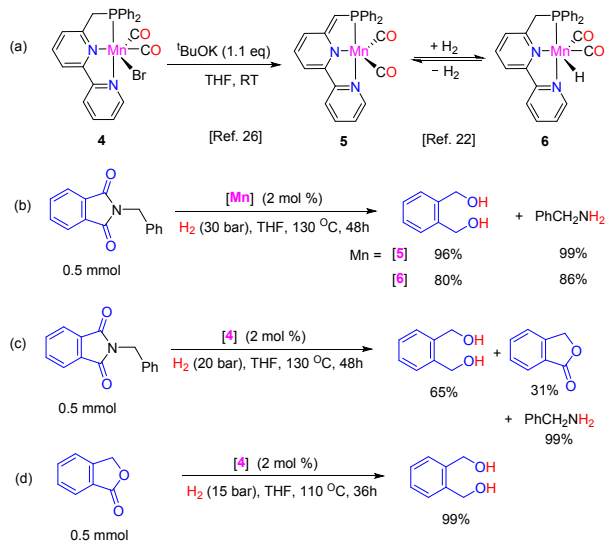

Scheme 3. Mechanistic study.

In order to gain mechanistic insight we carried out preliminary investigations. We have previously demonstrated that complex **4** in the presence of 1.1 equivalent of tBuOK forms the dearomatized manganese complex **5** which readily reacts with hydrogen to form manganese hydride complex **6** (Scheme 3a).[22, 26] Interestingly, when hydrogenation of N-benzylphthalimide was carried using complex **5** (2 mol %), in absence of base (the remaining conditions as in Table 1, entry 7), almost quantitative yields of benzylamine and 1,2-benzenedimethanol were obtained (Scheme 3b). Similarly, performing the same hydrogenation reaction in the presence of complex **6** (2 mol %) resulted in excellent yields of benzylamine and 1,2-benzenedimethanol (Scheme 3b). These experiments indicate that complexes **5** and **6** are catalytically competent and are likely involved in the catalytic cycle for the hydrogenation of cyclic imides. Additionally, when catalytic hydrogenation of N-benzylphthalimide was performed under lower pressure (20 at, Table 1, entry 8), formation of phthalide was observed in 31% yield in addition to the formation of benzylamine (99%) and 1,2-benzenedimethanol (65%)(Scheme 3c). This experiment is suggestive of a lactone being an intermediate during hydrogenation of the cyclic imide. Indeed, catalytic hydrogenation of phthalide occurred with great ease even under milder conditions of H_2 (15 bar), 110 °C, 36 h and produced quantitative yield of 1,2-benzenedimethanol (Scheme 3d).

Based on these observations, we propose a mechanism for the hydrogenation of cyclic imides as outlined in Scheme 4.

Insertion of a carbonyl bond of cyclic imide into the Mn-H bond of complex **6** results in the formation of complex **7**. Deprotonation of the side arm proton by the -NR moiety results in the formation of a dearomatized complex **8**. Addition of hydrogen to complex **8** results in the formation of an aromatized alkoxy amide complex **9**. Assisted by metal-ligand cooperativity, attack of alkoxide group at the C=O group of the amide group results in the elimination of amine and formation of a lactone along with generation of the dearomatized complex **5** that immediately reacts with hydrogen to form complex **6**. In presence of catalyst and H_2 the lactone undergoes hydrogenation to the diol in a similar way of ester hydrogenation.
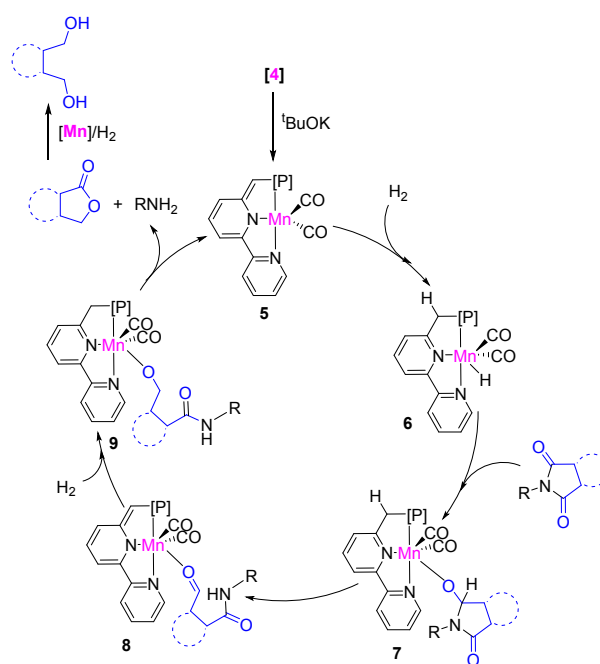
Scheme 4. Proposed mechanism for the hydrogenation of cyclic imides.

In conclusion, hydrogenation of cyclic imides to diols and amines was accomplished, for the first time, using a catalyst based on an earth-abundant-metal. The reaction proceeds under homogeneous conditions, catalyzed by the Mn(I) complex **4** in the presence of catalytic base, as well as by the dearomatized complex **5**, with no added base. Our mechanistic investigations suggest that the hydrogenation reaction proceeds via metal-ligand cooperativity and a proposed mechanism is outlined in Scheme 4.

Conflicts of interest

There are no conflicts to declare.

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