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A Molecularly-defined Manganese Catalyst for Low Temperature Hydrogenation of Carbon Monoxide to Methanol.

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ABSTRACT: Methanol synthesis from syngas (CO/H₂ mixtures) is one of the largest manmade chemical processes with annual production reaching 100 million tons. The current industrial method proceeds at high temperatures (200–300°C) and pressures (50–100 atm) using a copper-zinc-based heterogeneous catalyst. In contrast, here we report a molecularly-defined manganese catalyst that allows for low temperature/low pressure (120-150 °C, 50 bar) carbon monoxide hydrogenation to methanol. This new approach was evaluated and optimized by quantum mechanical simulations virtual high throughput screenings. Crucial for this achievement is the use of amine-based promoters, which capture carbon monoxide to give formamide intermediates, which then undergo manganese-catalyzed hydrogenolysis, regenerating the promoter. Following this conceptually new approach, high selectivity towards methanol and catalyst turnover numbers (up to 3170) were achieved. The proposed general catalytic cycle for methanol synthesis is supported by model studies and detailed spectroscopic investigations.

INTRODUCTION

Methanol is one the most important basic chemicals and a central C1 building block, which is used as fuel additive and raw material for the production of formaldehyde, formic and acetic acids, dimethylether (DME) and others.¹ Additionally, methanol-to-olefin (MTO) and methanol-to-gasoline (MTG) processes are used for the preparation of aliphatic and aromatic hydrocarbons on million-ton scale. Due to its properties (liquid at rt, 12.6% hydrogen content), methanol is also considered a promising hydrogen carrier in the context of the hydrogen economy and alternative energy technologies.² Due to its high energy density, it is also considered as a synthetic combustion fuel for applications where battery technology cannot compete. The first industrial syngas to methanol process was developed in the 1920s and operated at 300-400°C and pressures above 300 atm using a zinc chromite (Cr₂O₃-ZnO) catalyst. The current industrial method makes use of a state-of-the-art Cu/ZnO/Al₂O₃ catalyst, which still operates at elevated pressures (50–100 atm) and temperatures (200–300°C). Despite a century of gradual catalyst improvements, there is a strong interest in next generation methanol processes. In fact, today methanol production is among the top 3 chemicals responsible for greenhouse gas emissions and energy consumption.³ Thus, key challenges for future technologies are "low temperature/low pressure processes" and improved catalyst activity/stability. To achieve such goals, the development of milder reaction conditions for syngas conversion is highly desired.



A. Direct and indirect CO hydrogenation to methanol

$$CO + 2 H_2 \xrightarrow{Ru-MACHO-BH} CH_3OH$$

Conditions: 145°C, 80 bar (CO/H₂)

TON - up to 539 (after 168 h), TOF - 2.7 h⁻¹



D. This work: CO hydrogenation via N-formylazoles



Figure 1. Development of indirect CO hydrogenation to methanol.

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In general, homogeneous catalysts are recognized over their heterogeneous counterparts for higher selectivity and efficiency, and they can potentially be used for low temperature carbon monoxide hydrogenation. However, until very recently no defined transition metal complex for homogeneous syngas to methanol conversion was known.⁴ The first attempts to develop such a system trace back to 1950, when DuPont described a cobalt carbonyl species for carbon monoxide hydrogenation at extremely high pressures (1500-5000 atm).^{5,6} Later in the 1970s and 1980s, mainly more expensive noble metal based systems were investigated; nevertheless, high pressures (>1000 atm) were required (Scheme 1A, eq. 2).^{7, 8, 9, 10} These extreme reaction conditions are a result of high bond strength (BDE_{CO} = 1076 kJ mol⁻¹), which is the strongest bond found in a neutral molecule. ¹¹ Furthermore, a key elementary step in the (direct) carbon monoxide reduction – a migratory insertion of CO into an M–H bond is a highly endothermic process.¹² Not surprisingly, under current industrial conditions with Cu/ZnO/Al₂O₃ catalyst, syngas conversion to methanol via direct CO hydrogenation occurs only to a minor extent. Isotope labeling experiments and DFT calculations show that hydrogenation of in situ generated CO₂ (via WGSR) attributes for $\sim 2/3$ of the methanol produced (Figure 1A).^{13,14}

In principle, a similar strategy for the development of a homogeneous methanol process via indirect CO hydrogenation for syngas conversion can be envisioned. Already in 1919, the Danish chemist Jens A. Christiansen proposed the idea converting CO to methyl formate (MF),^{15,16} which might be hydrogenated to methanol under milder reaction conditions.¹⁷ Nevertheless, the first catalytic examples following this concept appeared only in the 1980s. In particular, two systems based on nickel^{18,19} and copper²⁰ catalysts have been designed. However, the volatility and high toxicity of the Ni(CO)₄ formed during the reaction makes its use in industrial settings unlikely. On the other hand, the less toxic copper-based systems suffer from low activity (TONs <10).^{21,22}

Here, we present a molecularly-defined manganese complex for carbon monoxide hydrogenation in the presence of amine promotors (Figure 1D). In this process, basecatalyzed carbonylation affords formamides as key intermediates, which are subsequently hydrogenated to give methanol under comparably mild conditions. Formamides are attractive due to their convenient handling and fast formation from CO.²³ However, hydrogenolysis of (form)amides remained an unsolved goal for many decades. A breakthrough in this field occurred in 2010 when Milstein and co-workers presented a highly selective catalytic hydrogenolysis to corresponding amines and alcohols, promoted by ruthenium complexes.²⁴ Since then, a number of other systems based on Ru ^{25,26,27,28,29,30,31,32,33} Fe^{34,35,36,37} Ag³⁸, Mo³⁹ and Mn⁴⁰ for amide C-N hydrogenation have been suggested.⁴¹ In addition, hydrogenation of formamides has created significant attention in the context of carbon dioxide reduction.^{42,43,44,45} Notably, Prakash and co-workers reported a dramatic drop in activity for formamide hydrogenation in the presence of even trace amounts of CO,⁴⁶ indicating the serious challenge of CO to methanol hydrogenation (Figure 1B). During the preparation of this manuscript, the Prakash group reported the homogeneous hydrogenation of CO to methanol via formamide hydrogenolyisis using a Ru-Macho-BH as a catalyst (Figure 1C).⁴ The highest TON of 539 (TOF = 2.7h⁻¹) was achieved after 7 days at 145°C, 80 bar CO/H₂ pressure, indicating that this class of catalysts is much less suited for CO hydrogenation, compared to CO₂ (TON = 9900 at 145°C, 75 bar CO₂/H₂).⁴⁶

RESULTS AND DISCUSSION

Reaction and Catalyst Design

For identifying a more suitable catalyst with improved tolerance for carbon monoxide and a suitable promoter, initially quantum mechanical simulations⁴⁷ were performed. To get an insight at the molecular scale, 10 different approaches for alternative methanol routes were investigated by evaluating the thermodynamics and the potential rate limiting steps. The most feasible approach, the amine carbonylation and amide hydrogenation, was selected and investigated by a virtual high throughput screening. Here, the goal was to find a promotor, where the Gibbs energy is close to zero along the transformation of the amine to formamide (eq. I) and the subsequent hydrogenation (eq. II) and the release of formaldehyde (eq. III). The latter is known to be easily hydrogenated to methanol. An overview of the Gibbs energy is shown in Table 1.

Table 1. Gibbs energy [kJ/mol] for three reaction steps of the amine carbonylation (I), hydrogenation (II), and formalde-hyde elimination (III).^a

| | R₂NH + CO | \rightarrow R ₂ N(| CO)H (I) | |
|-------|--|---------------------------------|-------------------------|-------|
| | R ₂ N(CO)H + H ₂ | → R ₂ N | ICH(OH)H (II) | |
| | R ₂ NCH(OH)H | R ₂ NH + | CH ₂ O (III) | |
| entry | Promoter | (I) | (II) | (III) |
| 1 | MeNH ₂ | -21.1 | 29.8 | 12.9 |
| 2 | $EtNH_2$ | -21.4 | 30.8 | 12.1 |
| 3 | Me ₂ NH | -37.6 | 36.7 | 22.4 |
| 4 | Piperidine | -34.8 | 42.5 | 13.8 |
| 5 | $PhNH_2$ | -6.5 | 16.3 | 11.6 |
| 6 | $(Ph)_2NH$ | -0.9 | 27.6 | -5.2 |
| 7 | Pyrrole | 8.8 | -5.0 | 17.7 |
| 8 | Indole | 9.2 | -3.0 | 15.3 |
| 9 | Scatole | 1.3 | 0.2 | 19.9 |
| 10 | Carbazole | 0.4 | 1.4 | 19.7 |

^aMethod: DSD-PBE-NL/def2-QZVP//PBE0-D3(BJ)/def2-TZVP. Accuracy: CO + $H_2 \rightarrow$ CH₂O. ΔH_{R^c} = -9.4 kJ/mol (simu1

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lation) $\Delta H_{R^{\circ}} = -12.1 \text{ kJ/mol}$ (experiment, 1933), $\Delta H_{R^{\circ}} = -5.37 \text{ kJ/mol}$ (experiment, 1984+1998).

Table 2. Gibbs energy [kJ/mol] for four reaction steps. ^a

| | | | | - |
|-----------------|--------------------|-----------|---|----------|
| | M-imi2: N | | ר א | |
| (L)M — N | + H ₂ — | | H N (| 1) |
| (L)M — N | + co — | -► (L)M=N | u (| 2) |
| (L)M—N | + RH — | → (L)M→N | R= C ₄ H ₄ N(R= OMe (| 3) 4) |
| Catalyst | (1) | (2) | (3) | (4) |
| Mn-imi2 | 92.6 | 20.1 | -8.5 | 9.8 |
| Fe-imi2 | 10.8 | -15.8 | -43.0 | -9.6 |
| Ru-imi2 | -28.5 | -124.0 | -63.7 | -18.7 |
| Mn-1 | 14.8 | -35.7 | -46.7 | -9.8 |
| Fe-1 | -42.7 | -47.3 | -49.0 | -13.0 |
| Ru-1 | -116.0 | -146.0 | -89.4 | -67.6 |

^aMethod: DSD-PBE-NL/def2-QZVP//PBE0-D3(BJ)/def2-TZVP.

Compared to alkylamines or anilines, the evaluated pyrrole derivatives were thermodynamically more suitable. For example, 3-methylindole and carbazole have Gibbs energies for the first 2 steps close to 0 kJ/mol, which would lead to an equilibrium with a substrate distribution of approximately 1:1. Here, the release of formaldehyde is less favored in contrast to anilines or alkylamines. On the other hand, having a hydrogenation catalyst in the solution would continuously push the equilibrium to the formaldehyde side, via the formation of methanol as the final product.

After identification of pyrrole derivatives as promising promotors a suitable catalyst had to be found. To quantify the impact of the metal on potential key reaction steps, at first a comparison of Fe, Ru and Mn carbonyl complexes with a di-imidazole-pincer ligand was performed (M-imi2) (Table 2). This model ligand, without a significant steric effect, was chosen to determine the impact of the metal on the reaction steps (1)-(4). Obviously, the catalyst should have the ability to activate H₂ by addition to the metal amido bond (Table 2, eq. 1), moreover it should have low COadsorption energy (Table 2, eq. 2) and not be inhibited by the promotor and product (Table 2, eq. 3 and 4). Interestingly, the virtual screening showed that the model Fe- and Ru-complexes bind H₂ and CO much stronger than the corresponding Mn-complex. Thus, from a thermodynamic point of view the Ru-complex is the least suited complex for the hydrogenation step. For hydrogenation of the Nformylazole intermediates a catalyst with a weaker hydrogen and CO affinity would be more suitable.

The energy differences for CO adsorption (2) and pyrrole addition (3) to the different metal-amido complexes are much higher for the Ru-complex than for the Fe- and Mncomplexes. Finally, product inhibition of the three potential catalysts was investigated as well (4). Also for this step the **Mn-imi2** has superior properties. For comparison, thermodynamic data for **Mn-1**, **Fe-1** and **Ru-1** was calculated (Table 2). For these catalysts, a trend similar to a model system with imidazole-based ligand has been observed for every evaluated elementary step. In general, Mn complexes offer the most promising thermodynamic properties for the hydrogenation of CO to methanol.

Reaction development

To verify the hypothesis vide supra, we experimentally investigated the hydrogenolysis of model substrate 1 with H_2/CO (45:5 bar) mixture in the presence of different PNP metal complexes known to promote hydrogenolysis in the absence of CO (Table 3, entries 1-3). In agreement with our calculations, Ru-1 was inactive in the presence of CO. Catalysts Fe-1, Mo-1 gave very poor conversions and proved to be unstable under the reaction conditions. However, to our delight catalyst Mn-1,48 gave promising conversion of 44%, resulting in formation of the amine and methanol as the only products (entry 4). In the absence of carbon monoxide, cleavage of the formamide 1 with Mn-1 is quantitative (Table S1). ⁴⁹ Other PNP (and PNN) Mn-based catalysts Mn-2⁴⁰, Mn-3,⁵⁰ Mn-4⁵¹, Mn-5⁵² proved to be inefficient for amide hydrogenolysis under the studied reaction conditions (entries 5-8).

Having identified catalyst Mn-1 as being tolerant to CO, we attempted the implementation of the amine carbonylation in the catalytic cycle. Systematic studies of reaction parameters, such as pressure, H₂/CO ratio, temperature, solvent, base, amount and nature of N-based promoter, revealed that the effect of the latter is the most significant in the hydrogenation of carbon monoxide (Table 4). In the absence of an amine promoter under the working conditions $(150^{\circ}C, 50 \text{ bar CO/H}_2 (1:4))$ with potassium phosphate as base and Mn-1 as a catalyst no methanol was formed (Table 4, entry 1). On the other hand, in the presence of morpholine partial carbonylation (<5%) occurred, giving small amounts of methanol (entry 2). Aromatic amines were also inefficient promoters for syngas conversion (entries 3 and 4). To our delight, indole showed good activity and significant amounts of methanol ($TON_{MeOH} > 500$), along with methyl formate (TON_{MF} of 22) were formed (entry 5). At this point, it should be mentioned that methyl formate can be consecutively converted to two molecules of methanol under the standard conditions. Scatole and pyrrole proved to be the best of the tested promoters giving TON_{MeOH} of >3000 and 2500 (entries 6 and 7). Due to practicability and price, pyrrole was selected as the main promoter for further studies. It is important to note that under optimized reaction conditions, CO hydrogenation to methanol is catalytic both in metal complex and *N*-promoter.

Table 3. Hydrogenation of formamides with CO/H_2^a



^aReaction conditions: **1** (0.25 mmol), H_2 (45 bar at rt), CO (5 bar at rt), **Cat**. (5 µmol), *t*-BuOK (0.025 mmol), C_6H_{12} (2 mL), 120 °C, 18 h. ^bYields and conversions calculated from GC analysis using *n*-hexadecane as internal standard.

Table 4. Hydrogenation of CO to methanol in the presence of N-Promoter^a

| CO + 0 bar 4(| H ₂ H ₂ H ₂ H ₂ H ₂ H ₂ H ₁ H ₁ H ₂ H ₁ | 25 mmol μmol 32 mmol 7 mL | ^H + H _H O- |
|-------------------------|--|------------------------------------|---|
| entry | Promoter | $\mathrm{TON}_{\mathrm{MeOH}}^{b}$ | $\mathrm{TON}_{\mathrm{MF}}{}^{\mathrm{b}}$ |
| 1 | - | 0 | 0 |
| 2 | | 2 | 0 |
| 3 | | 2 | 0 |
| 4 | | 1 | 0 |
| 5 | | 546 | 22 |
| 6 | | 3170 | 0 |
| 7 | ⟨Ŋ | 2550 | 112 |

^aReaction conditions: CO (10 bar at rt), H₂ (40 bar at rt), , **Mn-1** (5 µmol), *N*-promoter (4.32 mmol), K₃PO₄ (0.75 mmol), C₆H₁₂ (1.7 mL), 150 °C, 18 h. ^bQuantities of MeOH and MF were calculated from GC analysis using *n*-hexadecane as internal standard.

From the experimental results we conclude that the amine promoter has an effect on both steps of methanol synthesis: a) carbonylation of the amine and b) subsequent hydrogenation of the respective formamide. Increasing nucleophilicity of the amine leads to faster carbonylation rate; however, this results in the formation of a stronger amide bond, which impedes hydrogenolysis. Thus, the success of the overall hydrogenation process depends on a fine balance between C-N bond formation (carbonylation) and C-N bond breaking (hydrogenolysis), with the amine promoter playing a critical role (Scheme 1). In this respect, intrinsic properties of azole derivatives (Table 1, eq. 1-2) makes them suitable for the hydrogenation of CO.

Scheme 1. Effect of the promoter on carbonylation and hydrogenolysis rate



In order to better understand the role of the pyrrole promoter, related compounds were tested under optimized reaction conditions (Table 5). As expected, N-methylpyrrole which is incapable of forming an amide- gave only trace amounts of methanol (entry 1). Interestingly, potassium pyrrole resulted in a highly active system, further supporting the hypothesis of nucleophilic attack of a nitrogen atom to carbon monoxide (entry 2). Apparently, N-formylpyrrole is an intermediate in the hydrogenation process, however it was never detected by GC and NMR in our experiments due to high rate of hydrogenolysis.53 To our delight, independently prepared N-formylazoles, subjected to the standard reaction conditions resulted in a catalytic process, supporting the hypothesis of formamide intermediacy (entries 3-5). Generation of N-formylpyrrole in situ is further supported by detection of trace amounts (<0.1%) of N-methyl pyrrole and 1,1-di(Npyrrolyl)methane in the reaction mixture. Both compounds originate from undesired C-O bond cleavage of Nformylpyrrole, rather than C-N hydrogenolysis.

As demonstrated above, the choice of metal and ligand played a critical role in achieving high catalytic activity, thus the ligand effect was investigated in greater detail (Table 6). **Mn-6**⁵⁴ with diphenylphosphine units proved to be inefficient, while dialkylphosphine-based catalysts **Mn-7** and **Mn-9** resulted in a high catalytic activity, giving TONs of 1560 and 1868, respectively. On the other hand, cationic complex **Mn-8** with bulky *tert*-butyl substituents gave only trace 1

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amounts of methanol. Two related complexes neutral - **Mn-9** and a tricarbonyl cationic complex **Mn-10**, showed similar activity (TONs of 1869 and 1807, respectively), while an *N*methylated **Mn-11** gave only TON of 3.⁵⁵

 Table 5. Control experiments: Probing of potential intermediates in CO hydrogenation^a

| <u> </u> | + | Ha | 150 K ₃ PO ₄ - | 0°C 0.75 mmol | 0 | • |
|----------|---|--------|--|------------------------------------|---------------------|-----|
| 10 bar | т | 40 bar | Mn-1 promote C ₆ H ₁₂ | - 5 μmol r 1.0 mmol ₂ 1.7 mL | меон + н | `0´ |
| entr | у | Pr | omoter | TON _{MeOH} | b TON _{MF} | Ь |
| 1 | | | N Me | 25 | 2 | |
| 2 | | | | 425 | 36 | |
| 3 | | | N I <p< td=""><td>1700</td><td>34</td><td></td></p<> | 1700 | 34 | |
| 4 | | Ç | | 1103 | 48 | |
| 5 | | | | 1094 | 43 | |

^aReaction conditions: CO (10 bar at rt), H₂ (40 bar at rt), , **Mn-1** (5 µmol), *N*-promoter (1.0 mmol), K₃PO₄ (0.75 mmol), C₆H₁₂ (1.7 mL), 150 °C, 18 h. ^bQuantities of MeOH and MF were calculated from GC analysis using *n*-hexadecane as internal standard.

Table 6. Ligand effect in Mn-catalyzed CO hydrogenation

| CO 10 ba | + H ₂ r 40 bar | 150°C K ₃ PO ₄ - 0.75 mmol Mn-cat - 5 μmol Pyrrole 0.3 mL C ₆ H ₁₂ 1.7 mL | меон + <mark>н</mark> Чо́́ |
|-------------------------------------|--|---|---|
| | $ \frac{H}{CO} = \frac{H}{Ph_2} = \frac{H}$ | $ \frac{Br}{CO} = \frac{H}{CO} = \frac{H}{CO} = \frac{H}{CO} = \frac{Br}{CO} = \frac{Br}{$ | $ \begin{array}{c} H \\ \Psi_{2} \\ H \\ \Psi_{2} \\ H \\ $ |
| MD | | $\begin{array}{c} H_{\text{L}} & \text{Mn-} \\ H_{\text{L}} & \text{PEt}_{2} \\ & \text{PEt}_{2} \\ & \text{Co} \\ \\ & \text{Co} \\ \end{array} \begin{array}{c} \text{Mn-} \\ & \text{Mn-} \\ & \text{Mn-} \\ & \text{Co} \\ & \text{Co} \\ \end{array} \begin{array}{c} \text{Mn-} \\ & \text$ | |
| | Mn-9 | Mn-10 | Mn-11 |
| entry | Mn-9 Mn-cat | Mn-10 ${ m TON}_{ m MeOH}^{ m b}$ | Mn-11 TON _{MF} ^b |
| entry 1 | Mn-9 Mn-cat Mn-1 | Mn-10 TON _{MeOH} ^b 2550 | Mn-11 TON _{MF} ^b 112 |
| entry 1 2 | Mn-9 Mn-cat Mn-1 Mn-6 | Mn-10 TON _{MeOH} ^b 2550 19 | Mn-11 TON _{MF} ^b 112 1 |
| entry 1 2 3 | Mn-9 Mn-cat Mn-1 Mn-6 Mn-7 | мп-10 ТОЛ _{МеОН} ^b 2550 19 1560 | Mn-11 TON _{MF} ^b 112 1 77 |
| entry 1 2 3 4 | Mn-9 Mn-cat Mn-1 Mn-6 Mn-7 Mn-8 | Mn-10 TON _{MeOH} ^b 2550 19 1560 7 | Mn-11 TON _{MF} ^b 112 1 77 0 |
| entry 1 2 3 4 5 | Mn-9 Mn-cat Mn-1 Mn-6 Mn-7 Mn-8 Mn-9 | мп-10 ТОN _{MeOH} ^b 2550 19 1560 7 1869 | Mn-11 TON _{MF} ^b 112 1 77 0 0 0 |
| entry 1 2 3 4 5 6 | Mn-9 Mn-cat Mn-6 Mn-7 Mn-8 Mn-9 Mn-10 | Mn-10 TON _{MeOH} ^b 2550 19 1560 7 1869 1807 | Mn-11 TON _{MF} ^b 112 1 77 0 0 0 40 |

^aReaction conditions: CO (10 bar at rt), H₂ (40 bar at rt), , **Mn-cat** (5 µmol), pyrrole (4.32 mmol/0.3 mL), K₃PO₄ (0.75 mmol), C₆H₁₂ (1.7 mL), 150 °C, 18 h. ^bQuantities of MeOH and MF were calculated from GC analysis using *n*-hexadecane as internal standard.

On the basis of the above results, and our previous reports on the chemistry of Mn-based pincer complexes,⁵⁶ we propose the following possible mechanism for the hydrogenation of carbon monoxide to methanol (Scheme 2). In the presence of a base, Mn-1 undergoes hydrodebromination giving an amido intermediate Mn-AM, which upon treatment with hydrogen gas gives a key dihydride Mn-DH complex.⁴⁸ Indeed, generation of dihydride Mn-DH occurs even in the presence of CO: upon treatment of Mn-AM with CO/H_2 mixture two new signals at +109.6 ppm and +107.5 ppm were observed by ³¹P NMR, which were assigned as *cis*and trans-isomers of Mn-DH, respectively. In addition to dihydride signals, a new peak at +94.9 ppm was observed, which arose from coordination of carbon monoxide to an amido intermediate Mn-CO. The same species were detected when Mn-AM was treated with pure CO in the absence of H_2 (Table S8, Figure S4).

Carbon monoxide hydrogenation is assisted by the pyrrole promoter, which forms the crucial N-formylpyrrole intermediate in the presence of the base. Subsequent addition of H₂ equivalent across C=O bond, provides 1-pyrrolylmethanol, which in the presence of base gives back the promoter as well as one molecule of formaldehyde.⁵⁷ Formaldehyde or its equivalents in solution (1-pyrrolylmethanol, 1methoxymethanol) will undergo a second hydrogenation in the presence of the dihydride Mn-DH to form methanol. In fact, the reaction of N-formylcarbazole with 2.5 equiv. of Mn-DH in THF-d8 at room temperature resulted in the formation of free carbazole and methanol, regenerating the amido complex Mn-AM. Interestingly, upon completion of the reaction, cis-Mn-DH was fully consumed, while trace amounts of the trans- isomer were still observed by NMR. Such reactivities of the dihydride complexes Mn-DH suggest its intermediacy in the catalytic hydrogenation mechanism.

N-formylpyrrole is involved in several other side-reactions, namely C-O bond cleavage, which forms small amounts of catalytically inactive *N*-methylpyrrole and 1,1-di(*N*pyrrolyl)methane. Moreover, nucleophilic displacement of *N*-formylpyrrole with methoxide gives methyl formate. Alternatively, it can be formed via direct base-catalyzed carbonylation of methanol. Notably, all these intermediates (methyl formate, *N*-formylpyrrole, and formaldehyde) produce methanol under these reaction conditions.⁴⁸ Scheme 2 Proposed general mechanism for the catalytic hydrogenation of CO with Mn-1 and N-promoter



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CONCLUSIONS

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In conclusion, we have demonstrated the first hydrogenation of carbon monoxide to methanol in the presence of a molecularly-defined manganese complex tolerant to CO. Within 3 months, the specific reaction system was designed based on quantum mechanical simulations and experimentally verified.^{58,59} Optimal results for this transformation were realized using catalytic amounts of specific azole promoters, which allow for fast formation of the corresponding formamide and its selective hydrogenolysis to methanol.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website. General information and experimental details (PDF)

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