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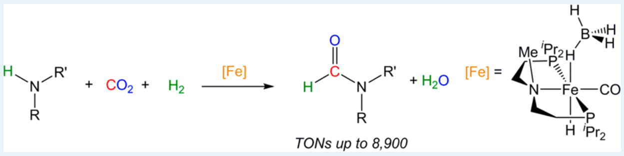
Selective Iron-Catalyzed *N*-Formylation of Amines using Dihydrogen and Carbon Dioxide

Upul Jayarathne,[†] Nilay Hazari,[‡] and Wesley H. Bernskoetter*,[†]

[†]The Department of Chemistry, University of Missouri, Columbia, Missouri 65211, United States
[‡]The Department of Chemistry, Yale University, New Haven, Connecticut 06520, United States

Supporting Information



ABSTRACT: A family of iron(II) carbonyl hydride species supported by PNP pincer ligands was identified as highly productive catalysts for the *N*-formylation of amines via CO_2 hydrogenation. Specifically, iron complexes supported by two different types of PNP ligands were examined for formamide production. Complexes containing a PNP ligand with a tertiary amine afforded superior turnover numbers in comparison to complexes containing a bifunctional PNP ligand with a secondary amine, indicating that bifunctional motifs are not required for catalysis. Systems incorporating a tertiary amine containing a PNP ligand were active for the *N*-formylation of a variety of amine substrates, achieving TONs up to 8900 and conversions as high as 92%. Mechanistic experiments suggest that *N*-formylation occurs via an initial, reversible reduction of CO_2 to ammonium formate followed by dehydration to produce formamide. Several intermediates relevant to this reaction pathway, as well as iron-containing deactivation species, were isolated and characterized.

KEYWORDS: *carbon dioxide, iron, formamide, amine, carbamic acid*

INTRODUCTION

The widespread chemical utilization of carbon dioxide (CO_2) would be a significant step toward realizing the potential of our renewable carbon resources.[1] The conversion of CO_2 into value-added chemicals would also offer an economically beneficial outlet for carbon capture technologies.[2] Unfortunately, despite the low toxicity and widespread availability of CO_2, it is rarely utilized as a C_1 feedstock for synthesizing fine or bulk chemicals.[3] Two prominent exceptions are in the production of salicylic acid and urea.[3e,f] The relative paucity of industrial processes which utilize CO_2 as a renewable synthon is due, in part, to its inherent thermodynamic and kinetic stability. These factors often necessitate harsh reaction conditions and highly reactive catalysts to facilitate chemical transformations with high yields and selectivities, resulting in impractical systems. In recent years, in order to accelerate the discovery of systems for the utilization of CO_2, our laboratories have reported detailed investigations into the hydrogenation of CO_2 to formate by a series of pincer-supported iron catalysts.[4] Herein we describe an extension of these studies and report a system catalyzed by an earth-abundant metal for the production of formamides from CO_2, H_2, and amines, as well as mechanistic experiments which elucidate key features of the reaction pathway.

The *N*-formylation of amines to formamides is performed industrially on a large scale for a number of different applications.[5a] For example, formamides are used as solvents for ionic compounds as well as feedstocks for the synthesis of pharmaceuticals, pesticides, and herbicides.[5] Traditionally, the carbonyl moiety is introduced into a formamide using relatively hazardous reagents such as chlorals, carbon monoxide, acetic formic anhydride, and formic acid.[6] In comparison to these synthetic routes, the reductive functionalization of CO_2 offers a potential environmentally benign alternative for the synthesis of formamides. Likewise, the use of H_2 in lieu of more toxic silane or borane reducing agents is likely to minimize the environmental impact of this approach to *N*-formylation.[7]

Transition-metal-catalyzed *N*-formylation using CO_2 and H_2 was investigated as early as 1970, when Haynes et al. reported that Vaska's complex, $[(Ph_3P)_2Ir(CO)Cl]$, could catalyze the formation of dimethylformamide (DMF) with a maximum turnover number (TON) of 1200.[8] In subsequent years other sporadic syntheses of DMF via CO_2/H_2-derived *N*-formylation appeared in the literature, each using precious metals to facilitate the reaction.[9,10] In 1996, Noyori and co-workers reported a ruthenium catalyst, $[RuCl_2(PMe_3)_4]$, that *N*-formylates dimethylamine into DMF with an impressive TON of 370000. A year later, Baiker and co-workers found that switching the ancillary phosphine ligand from PMe_3 to $Ph_2PCH_2CH_2PPh_2$ (dppe) nearly doubles the production of DMF, and they obtained a TON of 740000 using $[RuCl_2(dppe)_2]$. In 2003, the same laboratory expanded these studies to a wider range of amine substrates, most notably including the formylation of aniline (TON = 930), which has proven to be one of the most challenging substrates. Jessop also reported the synthesis of formanilide from the formylation of aniline using the catalyst $[RuCl_2(PMe_3)_4]$ in the presence of the strong base 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). In

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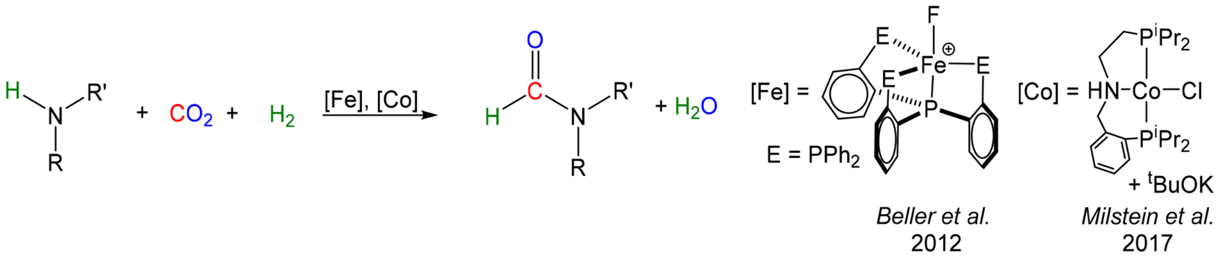
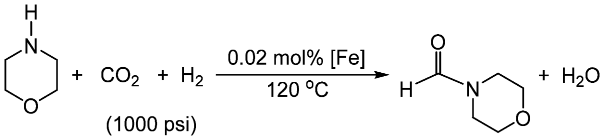


Figure 1. First base metal catalysts for *N*-formylation of amines with CO_2.

Table 1. Solvent Screening for *N*-Formylation of Morpholine Using Precatalysts 1 and 2[a]

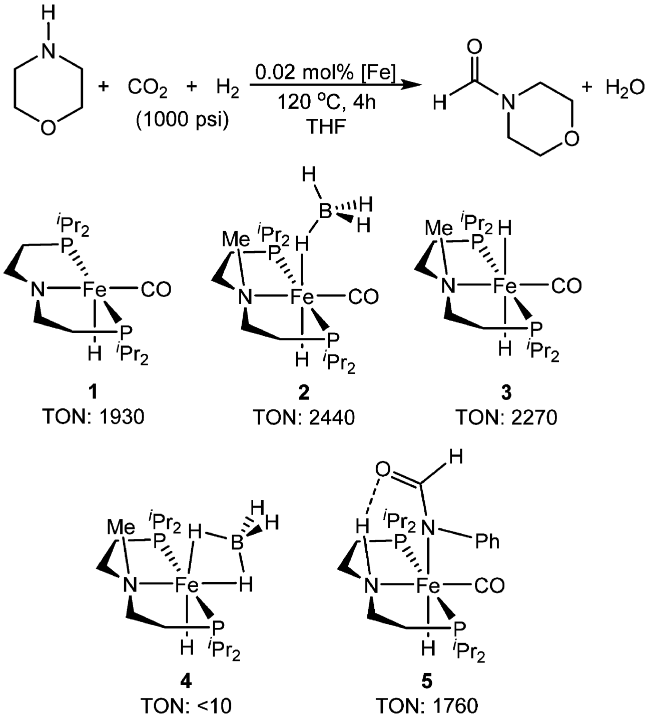


catalyst	THF (TON) 4 h	THF (TON) 16 h	toluene (TON) 4 h	toluene (TON) 16 h	dioxane (TON) 4 h	dioxane (TON) 16 h	ethyl acetate[c] (TON) 4 h	ethyl acetate[c] (TON) 16 h
[(^{iPr}PNP)FeH(CO)] (**1**)	1930[b]	2660	1935	2340	1700		1720	
[(^{iPr}P^{Me}NP)FeH(CO)(BH_4)] (**2**)	2440	3420		3020				

[a] Reaction conditions: P_{H_2} = 500 psi, P_{CO_2} = 500 psi, 5 mL of reaction solution, 2.5 μmol of [Fe], 12.5 mmol of morpholine. [b] TONs based on the amount of 4-formylmorpholine production as determined by GC-FID. Reported values are the average of two or more trials. [c] 1-Morpholinoethanone and ethanol were observed as additional products.

2015, Ding and co-workers reported the most productive *N*-formylation catalyst reported thus far, [(^{Ph}P^{Me}NP)RuClH(CO)], obtaining a TON of 1850000 for the synthesis of 4-formylmorpholine over 3 days under 70 atm of total CO_2/H_2 (1/1) pressure at 120 °C.[10]

There is currently considerable interest in the replacement of toxic precious-metal catalysts with systems containing earth-abundant base metals.[11] In general, the potential for economic and environmental advantages motivates most of these efforts, but the transition to base-metal catalysts also offers the opportunity for new catalytic selectivity, substrate preference, and even improved performance in comparison with precious-metal systems. To date there have been few reports of highly active well-defined base-metal catalysts for the *N*-formylation of amines via reductive CO_2 hydrogenation.[12,13] Two leading examples were independently reported by the laboratories of Beller and Milstein using iron and cobalt catalysts, respectively (Figure 1).[13] Beller and co-workers demonstrated that a tetraphosphine-supported iron(II) complex is an excellent precatalyst for *N*-formylation of dimethyl and diethylamine, achieving TONs up to 5100 over 20 h under 100 bar total pressure of H_2/CO_2 (7/3) at 100 °C. However, the substrate scope was not examined further. Milstein and co-workers reported a more broadly applied cobalt pincer catalyst which transformed a range of primary and secondary amines to the corresponding formamides. Although the cobalt system could produce high conversion for several formamides, the observed productivity was quite modest with a maximum TON of 130 over 36 h under 60 bar total pressure of H_2/CO_2 (1/1) at 150 °C. Our own laboratories have reported similar pincer iron complexes, [(^{iPr}PNP)FeH(CO)] (**1**) and [(^{iPr}PN^{Me}P)FeH(CO)(BH_4)] (**2**) (^{iPr}PNP = N{$CH_2CH_2(P^iPr_2)$}$_2$; ^{iPr}PN^{Me}P = MeN{$CH_2CH_2(P^iPr_2)$}$_2$), which are highly active for the hydrogenation of CO_2 in the presence of Lewis acids and poorly nucleophilic amines, such as DBU.[14b] This activity motivated further examination of these catalysts for *N*-formylation of a diverse group of more nucleophilic amine substrates in search of more productive base-metal catalysts.



1
TON: 1930
2
TON: 2440
3
TON: 2270
4
TON: <10
5
TON: 1760

Figure 2. Pincer iron precatalysts screened for *N*-formylation activity. Reaction conditions are identical with those applied in Table 1.

RESULTS AND DISCUSSION

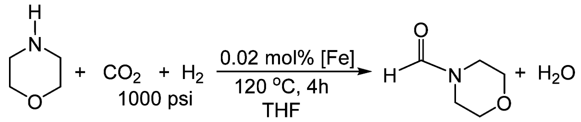
Catalytic *N*-Formylation. Our investigations of *N*-formylation catalysis with CO_2 and H_2 began by screening **1** for activity with three amine substrates, aniline, diphenylamine and morpholine, under conditions similar to those used in catalysis with precious-metal systems.[10] A 0.02 mol % loading of **1** in THF under 1000 psi (~69 bar) total pressure of H_2/CO_2 (4/1) at 120 °C for 16 h only produced formamide in the case of morpholine, although the unoptimized TON of 2700 was quite promising. The absence of conversion using the aromatic amines is perhaps unsurprising, given that these substrates are also problematic for precious-metal catalysts, owing to their relatively weak basicity and nucleophilicity.[9b,c]

The catalytic conversion of morpholine to 4-formylmorpholine was used as a benchmark *N*-formylation reaction to optimize reaction conditions prior to examining substrate scope and exploring mechanistic considerations. Complete details of the reaction optimization are provided in the Supporting Information. A total pressure of 1000 psi (~69 bar) of a 1/1 H_2/CO_2 mixture was the preferred combination of gases, as enriching the mixture in either H_2 or CO_2 decreased conversion. Decreasing the total pressure of the reaction even to 750 psi also produced a substantial drop in TON, suggesting that pressures greater than 1000 psi may enhance the reaction further. However, a limit of 1000 psi was used in this study due to safety considerations. The reaction temperature of 120 °C used in the initial trials was found to be optimal following variation between 100 and 140 °C. Altering the reaction solvent demonstrated that similar catalyst performance is observed in THF and toluene, while TONs diminish slightly in dioxane and ethyl acetate during 4 h reaction trials (Table 1). It is notable that *N*-formylation works well in both ethereal and hydrocarbon solvents.

In recent years, our laboratories and others have developed a number of closely related pincer-supported iron (pre)catalysts for reversible hydrogenation reactions.[14] In many cases, more than one such iron complex proved to be catalytically active, which motivated a comparative catalytic study of a range of well-defined (pre)catalysts (Figure 2). The highest TONs were obtained for the iron complexes bearing an *N*-methyl version of the PNP ligand, $[(^{iPr}PN^{Me}P)FeH(CO)(BH_4)]$ (**2**) and $[(^{iPr}PN^{Me}P)Fe(H)_2(CO)]$ (**3**). These species show very similar activities, which is in agreement with prior experiments demonstrating that **2** rapidly eliminates BH_3 in the presence of excess amine.[14b] The absence of observable catalytic activity using $(^{iPr}PN^{Me}P)Fe(H)(BH_4)$ (**4**) suggests the presence of the ancillary carbonyl ligand is crucial to reductive functionalization of CO_2 in this system. Complex **2** also performed comparably well in toluene (Table 1). These screening results mirror many of those in our prior investigations into the hydrogenation of CO_2 to formate salts using iron catalysts with DBU as an external base.[14b] There too, the best productivity was obtained using **2** and **3**, which contain the tertiary $PN^{Me}P$ ligand.

One notable difference between the two catalytic processes to produce formate salts and formamide is the influence of Lewis acidic lithium salts. In CO_2 hydrogenation to formate, TONs for all catalysts were dramatically enhanced (up to 20-fold) by the addition of lithium triflate (LiOTf); however, the addition of 20 equiv of LiOTf (relative to iron) noticeably reduced formamide production using catalysts **1** and **2** (Table 2; entries 1, 2 and 5, 6). Further consideration of this effect is discussed in the Supporting Information. Hypothesizing that a stronger base may accelerate any potential dihydrogen activation or deprotonation steps in catalysis, we also tested DBU as an additive. Though the presence of this hindered base did marginally improve formamide production, it was deemed not sufficiently effective to warrant its inclusion in the standard reaction conditions.

Table 2. Catalytic Effect of Additives on *N*-Formylation Reaction[a]



entry	catalyst	amt, equiv			TON[b]	yield, %[c]
		LiOTf	DBU	2-fluorophenol		
1	**1**				1930	39
2	**1**	20			1030	21
3	**1**		20		1910	38
4	**1**			20	1680	34
5	**2**				2440	49
6	**2**	20			615	12
7	**2**		20		2530	51
8	**2**			20	1940	39

[a] Reaction conditions: P_{H_2} = 500 psi, P_{CO_2} = 500 psi, 0.14 mmol of [Fe], 7 mmol of morpholine with appropriate additive in 5 mL of THF heated at 120 °C for 4 h. [b] TONs based on the amount of 4-formylmorpholine production as determined by GC-FID. Reported values are the average of two or more trials. [c] Yield reported relative to amine loading.

As a counterpoint to DBU addition, an acidic alcohol, 2-fluorophenol, was tested as an additive. Several other studies of CO_2 hydrogenation have noted an accelerating effect from acidic alcohols,[15] but in this case the phenol had a slight inhibitory influence on TON. The results of the additive experiments indicate that there is no advantage to including these reagents to our standard *N*-formylation; however, the data raise some mechanistic questions which are discussed further in the Supporting Information.

Having empirically devised a set of optimized conditions for *N*-formylation, we examined the amine substrate scope using **2** as the precatalyst (Table 3). For experimental convenience these comparative catalytic trials were conducted over 4 h intervals, though a notable increase in conversion was obtained with several substrates by extending reactions to 16 h (entries 3, 13, 17, and 19). A collection of primary and secondary aliphatic and benzylic amines was successfully converted to formamides, all with essentially complete selectivity (as observed by GC-FID) and with TONs up to ~4600 over 4 h. In one case (entry 15), decreasing the catalyst loading and extending reaction times afforded a remarkable TON of 8900, surpassing the production of formamide from previously reported base-metal catalysts. Several −OR and −OH functionalized amines also exhibited moderate activity (entries 10−12). Overall, the productivity of catalyst **2** for *N*-formylation with CO_2 and H_2 was remarkable in comparison to the handful of other reported first-row-metal catalysts. In many cases, our iron system achieves TONs which are 10−100-fold higher than those reported for well-defined manganese, cobalt, iron, and copper catalysts.[12c,13a,c,12d] It is also notable that, in cases where comparable TONs have been achieved, other existing first-row-metal catalysts require ≥20 h (under similar temperature and pressure) to reach this production, in comparison to only 4 h using catalyst **2**. While the state of the art precious-metal catalysts are still superior to the productivity of **2**, this iron-based system provides a significant advance in the development of base-metal systems.

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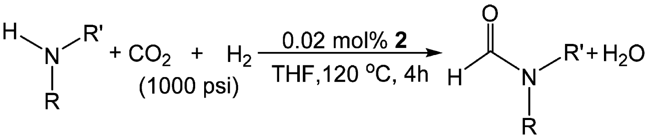
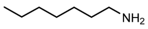
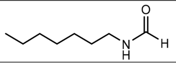
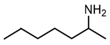
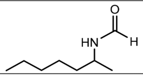
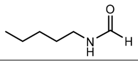
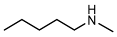
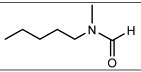
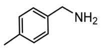
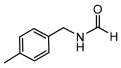
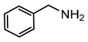
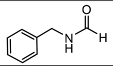
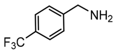
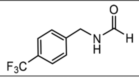
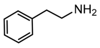
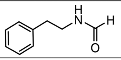
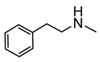
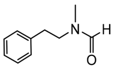
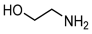
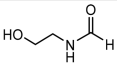
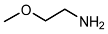
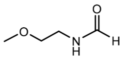
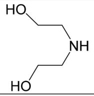
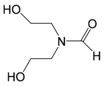
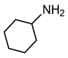
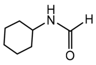
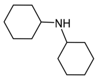
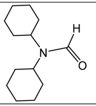
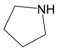
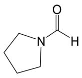
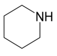
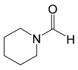
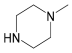
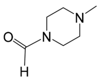
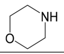
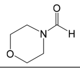
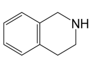
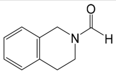
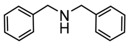
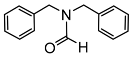
Table 3. Iron-Catalyzed *N*-Formylation via Reductive CO_2 Hydrogenation[a]



Entry	Substrate	Product	TON[b] (Yield)[c]
1			2050 (41%)
2			560 (11%)
3			1930 (38%) 3580 (72%)[d]
4			2630 (53%)
5			1890 (38%)
6			1700 (34%)
7			630 (13%)
8			1750 (35%)
9			2660 (53%)
10			1300 (26%)
11			1000 (20 %)
12			1870 (37 %)
13			900 (18%) 2019 (40%)[d]
14			< 10 (trace)
15			4620 (92%) 8900 (59%)[e]
16			4390 (88%)
17			2830 (57%) 4300 (86%)[d]
18			2440 (49 %)
19			2440 (49%) 2630 (53%)[d]
20			390 (8 %)

[a] Reaction conditions: P_{H_2} = 500 psi, P_{CO_2} = 500 psi, 2.5 μmol of [Fe], 12.5 mmol of amine in 5 mL of THF heated at 120 °C for 4 h. [b] TONs based on the amount of formamide production as determined by GC-FID. Reported values are the average of two or more trials. [c] Yield reported relative to amine loading. [d] TON (yield) after 16 h. [e] TON (yield) after 16 h using 2.5 μmol of [Fe] and 37.5 mmol of amine.

Closer examination of the results in Table 3 indicates several trends in substrate preference. In general, the acyclic secondary amines show higher conversion than the corresponding primary amines as can be observed from comparing entries 3 and 4, 8 and 9, and 10 and 12. However, steric considerations can alter this trend, as seen in entries 6 and 20. The iron-catalyzed *N*-formylation favors amine substrates bearing electron-donating substituents (entries 5–7), which is analogous to the trend observed with more widely studied precious-metal catalysts.[9b,10] This preference for electron-rich amines could arise from either the enhanced basicity of the substrate or improved nucleophilicity. It is often difficult to completely separate these two influences, but certainly enhanced catalytic performance is only loosely correlated with the pK_a of the amine (Table S5). Clearly steric constraints also play a strong role in catalytic efficiency, as cyclohexylamine (entry 13) has a TON of 900 while dicyclohexylamine (entry 14) affords little to no conversion. Similarly, conversion of 1-heptylamine (entry 1) was significantly greater than that of 2-heptylamine (entry 2), where the $-NH_2$ unit is attached to a secondary carbon (entry 2). Steric influences may also contribute to the excellent performance of the cyclic amine substrates (entries 15–19), which exhibit considerable activity over the 4 h reaction period. Notably, when isoquinoline (entry 19) is allowed to react for 16 h, only a modest increase in TON is obtained, suggesting a greater catalyst deactivation with this substrate.

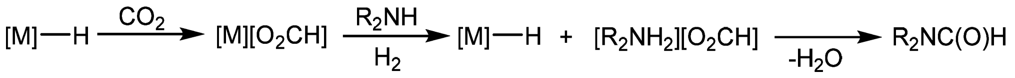
Mechanistic Considerations. Several prior studies of transition-metal-catalyzed *N*-formylation from CO_2 and H_2 have proposed the common mechanistic pathway depicted in Scheme 1.[13a,9g] The pathway begins with a metal hydride promoted reduction of CO_2 to formate. Amine-assisted extrusion of the formate, along with activation of dihydrogen, would then regenerate the metal hydride species and liberate an ammonium formate salt. Finally, dehydration of ammonium formate would yield the observed formamide product followed by extrusion of an ammonium formate salt. Though this oft-proposed route appears quite reasonable, minimal direct evidence in support of the pathway has been gathered to date.[13a,9g]

During the course of catalytic *N*-formylation experiments our laboratories made several observations relevant to elucidating the reaction pathway. Most notably, at the completion of several catalytic trials a colorless precipitate was observed upon cooling, depressurizing, and opening the stainless steel autoclave reactor. This species was initially thought to be the carbamate salt resulting from residual amine substrate reacting with the high pressure of CO_2 (eq 1).

$$\begin{aligned}[R_2NCO_2][R_2NH_2] + H_2 &\rightleftarrows CO_2 + 2R_2NH + H_2 \\ &\rightleftarrows [R_2NH_2][O_2CH] + R_2NH \end{aligned} \qquad (1)$$

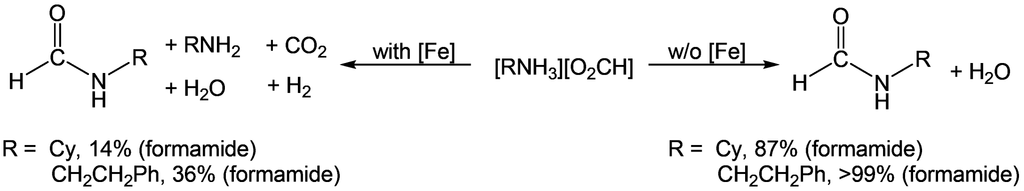
Analysis by NMR spectroscopy confirmed that this was indeed true for most substrates where a precipitate formed. However, in the cases of cyclohexylamine and phenethylamine NMR analysis revealed the solid also contained the

Scheme 1. Generic Pathway for *N*-Formylation of Amines via CO_2 Reduction



$$[M]{-}H \xrightarrow{CO_2} [M][O_2CH] \xrightarrow[H_2]{R_2NH} [M]{-}H + [R_2NH_2][O_2CH] \xrightarrow[-H_2O]{} R_2NC(O)H$$

Scheme 2. Dehydration and Dehydrogenation of Formate Salt in the Presence and Absence of 2[a]



[a] Reaction conditions: P_{H_2} = 500 psi, P_{CO_2} = 500 psi, 2.5 μmol of [Fe], 6.25 mmol of amine in 5 mL of THF heated at 120 °C for 4 h.

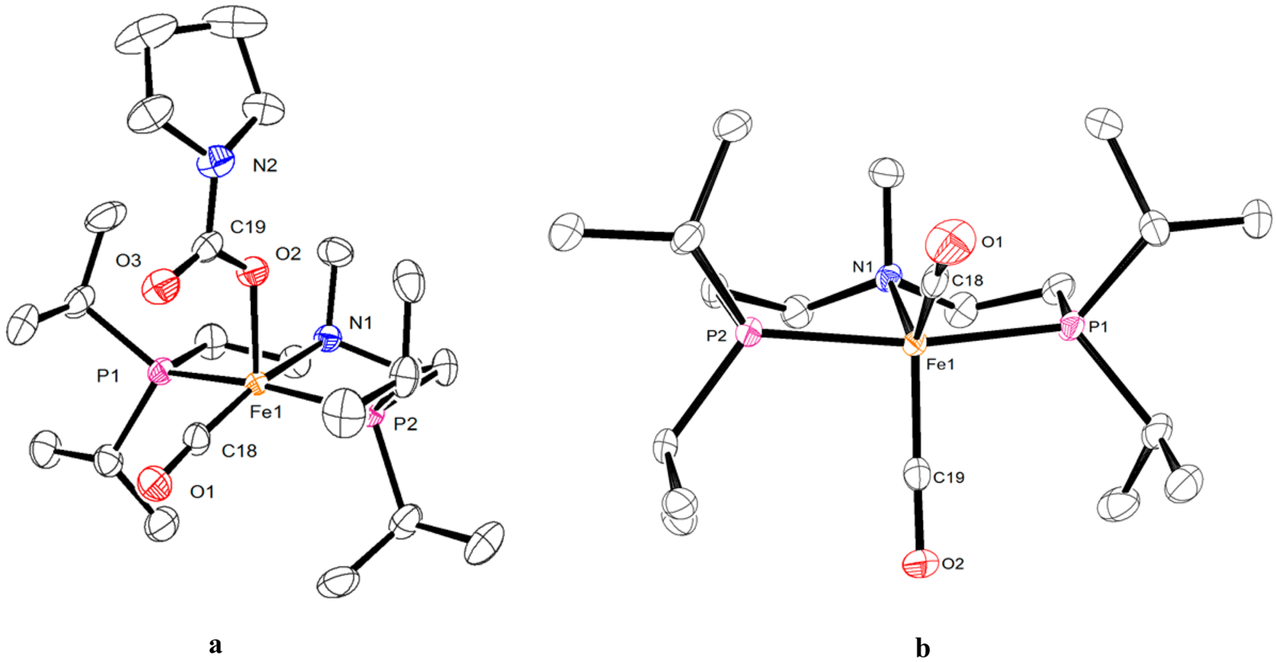
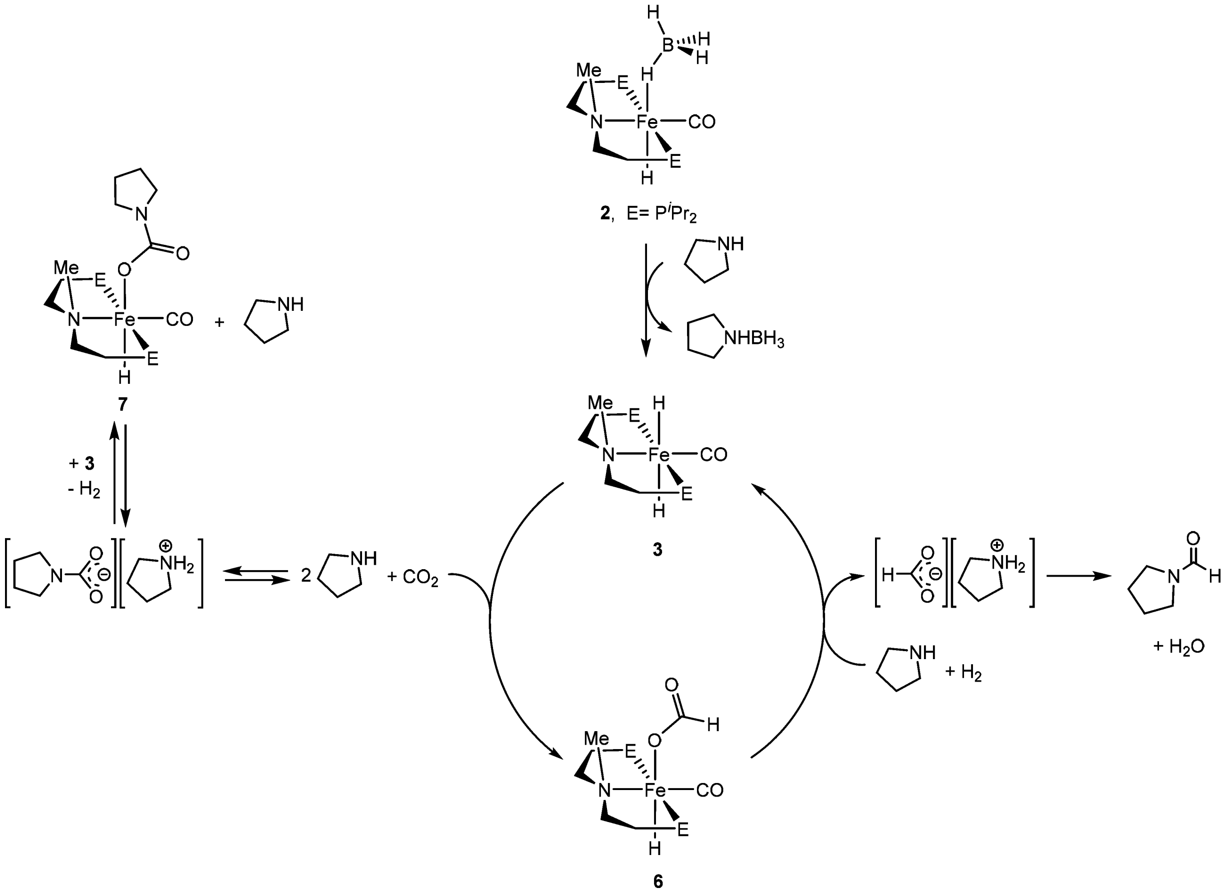


Figure 3. (a) Molecular structure of **7** with ellipsoids at 30% probability. Hydrogen atoms have been removed for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)−P(1) 2.2130(7), Fe(1)−P(2) 2.2081(7), Fe(1)−N(1) 2.1449(2), Fe(1)−C(18) 1.7034(2); P(1)−Fe(1)−P(2) 164.64(3), Fe(1)−O(3)−C(19) 125.9 (2). O(3)−C(19)−O(2) 128.4(2). (b) Molecular structure of **8** with ellipsoids at 30% probability. Most hydrogen atoms have been removed for clarity. Selected bond lengths (Å) and angles (deg): Fe(1)−P(1) 2.205(1), Fe(1)−P(2) 2.209(1), Fe(1)−N(1) 2.18(1), Fe(1)−C(18) 1.726(5), Fe(1)−C(19) 1.736(5); P(1)−Fe(1)−P(2) 166.65(5), C(18)−Fe(1)−C(19) 117.1(2).

corresponding ammonium formate salt, supporting the hypothesis that formate salts are intermediates in the formation of formamides. This possibility was further tested by taking samples of cyclohexylamonium and phenylethylammonium formate[16] and placing them under the catalytic conditions. Surprisingly, the conversion of the formate salt to the corresponding formamide was quite poor in both cases, with the majority of ammonium formate reverting to the amine and CO_2 (Scheme 2). When the same experiments were conducted in the absence of **2**, dehydration to the formamide product was nearly quantitative under the same conditions. This suggests that, while ammonium formate salts are viable and observable intermediates to formamide production, the dehydration step is not metal catalyzed and in fact competes with an iron-mediated dehydrogenation back to the amine and CO_2.

In order to obtain mechanistic details regarding the speciation of the iron complexes, catalytic *N*-formylation experiments were carried out in J. Young NMR tubes under modified reaction conditions. In typical experiments, samples of **2** in benzene-d_6 were treated with ≥6 equiv of pyrrolidine, placed under 2 atm of H_2/CO_2 (1/1), heated at 50 °C, and monitored by ^1H and ^{31}P NMR spectroscopy. Sample spectra from these experiments may be found in the Supporting Information. NMR spectra taken immediately after sample preparation, and prior to gas addition, exhibit resonances identical with those previously reported for the iron(II) dihydride compound **3**.[14b] This confirms that **2** functions as a precatalyst for **3** and is consistent with their near-identical catalytic performances. Pressurizing the sample with H_2 and CO_2 resulted in rapid CO_2 insertion into the Fe−H bond and formation of the previously reported iron(II) formate complex $[(^{iPr}PN^{Me}P)FeH(CO)(HCO_2)]$ (**6**).[14b] In addition to complex **6**, a second iron-containing product was detected with a signature Fe−H resonance at −24.83 ppm in the ^1H NMR spectrum and a peak at 89.7 ppm in the ^{31}P NMR spectrum. This new species was identified as the pyrrolidine carbamate complex $[(^{iPr}PN^{Me}P)FeH(CO)(C_4H_8NCO_2)]$ (**7**). Complex **7** was independently prepared by exposing isolated samples of **6**

Scheme 3. Proposed Reaction Pathway for Catalytic *N*-Formylation



to pyrolidine under an H_2 atmosphere, and its molecular structure is depicted in Figure 3. Similar carbamato structures have been previously reported on biorelevant metals.[17] Continued monitoring of the modified catalytic reaction for 12 h at 50 °C resulted in peaks indicative of 1-formylpyrrolidine formation in the ^1H NMR spectrum along with partial decomposition of the iron species to free ligand and an iron(0) dicarbonyl species, $[(^{iPr}PN^{Me}P)Fe(CO)_2]$ (**8**) (Figure 3).[18] Despite the partial decomposition, complexes **6** and **7** remained the major organometallic species in solution after 12 h.

The dramatic difference between the pressure and temperature conditions of the standard catalytic reaction and the NMR model reaction require some caution in using the NMR data to draw conclusions in regard to the mechanism of catalysis. However, it seems reasonable to use the observations in outlining the general reaction landscape (Scheme 3). The initial activation of **2** to the iron(II) dihydride species **3** by pyrrolidine was self-evident in the NMR spectra and will likely be nearly instantaneous in the catalytic reaction when 5000 equiv of base is present. As has been described in prior studies,[14b] the insertion of CO_2 into **3** to produce the iron(II) formate complex **6** appears to be rapid even at low pressure. The subsequent reaction of **6** with amine to generate an ammonium formate (and later formamide following dehydration) is consistent with isolation of these salts following several catalytic reactions (vide supra). An accompanying activation of H_2 would regenerate **3**. The more surprising observation was the formation of the iron(II) carbamate complex **7**. In the NMR tube and synthetic experiments, **7** was obtained from the reaction of pyrrolidine with **6**. However, under our standard catalytic conditions, we hypothesize that **7** could also originate from the reaction of **3** with the ammonium carbamate salt, which is likely present in significant concentrations and was observed as a precipitate following several catalytic trials. We were initially concerned that formation of complex **7** could be a deactivation pathway, but employing isolated samples of **7** in our standard catalytic reaction afforded a TON of 4200 for pyrrolidine *N*-formylation. This productivity is comparable to that using **2** or **3** as the (pre)catalyst and suggests that **7** is likely a resting state, not a deactivation species. In contrast, formation of the iron(0) dicarbonyl complex **8** does appear to be a deactivating process, as it produced a TON of only 520 under analogous catalytic conditions. The pathway for the formation of **8** is not clear, though the secondary amine ligated congener, $[(^{Cy}PN^{H}P)Fe(CO)_2]$, is proposed to form via H_2 reductive elimination from the corresponding iron(II) dihydride species $[(^{iPr}PN^{H}P)Fe(H)_2(CO)]$.[14f] A similar route for H_2 elimination from **3** (which is present as cis and trans isomers) could account from the formation of **8**.

■ CONCLUDING REMARKS

The catalytic activity of **1** and **2** for the production of formamides from amines, CO_2, and H_2 represents an advance toward the goal of using earth-abundant metals to harness renewable carbon sources. Perhaps more significantly, the superior performance of the tertiary amine ligated **2** over the secondary amine supported **1** demonstrates that metal−ligand bifunctional reactivity is not always required to obtain good activity with these base-metal systems. This is a feature which might be easily overlooked, given the significant recent successes in base-metal−ligand bifunctional catalyst development.[4,13a,14e,19] Precatalyst **2** is remarkably productive for *N*-formylation within the context of base-metal catalysis, achieving TONs in excess of 4500 and high conversions over relatively short reaction times. This level of productivity is essentially state of the art for earth-abundant metals, though further catalyst development will be required to match the performance obtained with precious-metal systems. On the basis of the mechanistic insights outlined here, obviating catalyst deactivation via formation of iron dicarbonyl species is one avenue which may lead to significant TON enhancement. Although the pathway for iron dicarbonyl complex formation has not been fully elucidated, it appears likely to involve a bimolecular event between catalytic species. Approaches such as catalyst site isolation and intermolecular steric repulsion to prevent these events are among the methods currently under consideration in our laboratories. Additionally, the CO_2 reduction technology described here could potentially be coupled with other transformations of formamides to broaden the scope of CO_2 utilization or provide net pathways to CO_2-based chemical hydrogen storage materials.

EXPERIMENTAL SECTION

General Considerations. All manipulations were carried out using standard vacuum, Schlenk, cannula, or glovebox techniques. Hydrogen was purchased from Airgas and used as received. Catalysts **1**−**4** and **6** were prepared as previously described.[14b] All amines were purchased from Aldrich or Fisher Scientific and purified by sublimation or vacuum distillation after drying over CaH_2 or NaH. Inorganic materials were purchased from Strem and isotopically labeled materials from Cambridge Isotope Laboratories. All nonvolatile solids were dried under vacuum at 50 °C overnight. Solvents were dried and deoxygenated using literature procedures.[20] ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker 300 MHz DRX, 500 MHz DRX, or 600 MHz spectrometer at ambient temperature, unless otherwise noted. ^{1}H and ^{13}C chemical shifts are referenced using the solvent resonances; ^{31}P chemical shifts are referenced to an external standard of H_3PO_4. Probe temperatures were calibrated using ethylene glycol and methanol as previously described.[21] High-pressure catalytic hydrogenation reactions were performed using a Parr 5500 series compact reactor with glass insert.

General Method for Catalytic *N*-Formylation of Amines. Inside a glovebox, a glass reactor liner (50 mL) was charged with the amine (12.5 mmol) and THF (5 mL). Then a solution of **1**−**6** (2.5 μmol) in THF was added to this mixture via microsyringe. The Parr reactor was sealed and removed from the glovebox. The reactor was pressurized with commercial-grade CO_2 at ambient temperature (500 psi), followed by commercial-grade H_2 (500 psi). After the allotted time (4−16 h), the reactor was cooled by submersion in an ice bath and the remaining gas was slowly vented. The product solution was then analyzed by ^{1}H NMR spectroscopy and/or GC-FID using mesitylene as a standard. Control experiments using $FeCl_2$ as a catalyst using this procedure gave no detectable conversion.

General Method for the Synthesis of Formate Salts. Inside the glovebox the required amine was measured into a round-bottom flask sealed with a rubber septum. This flask was removed from the glovebox and cooled to 0 °C using an ice bath. Degassed formic acid (1.2 equiv) was transferred to the above flask using a syringe. The mixture was stirred for 1 h and washed with THF (5 mL × 3) and filtered to obtain a white solid. This solid was dried under vacuum overnight.

Synthesis of $[(^{iPr}P^{Me}NP)FeH(CO)(C_4H_8NCO_2)]$ (7). Inside a glovebox the iron formate complex **6** (0.035 g, 0.08 mmol) was measured into a vial and transferred to a 50 mL Schlenk bomb using THF (5 mL). Pyrrolidine (0.127 mL, 1.6 mmol) was added to the bomb, and H_2 (1 atm) was introduced using a high-vacuum line. This mixture was stirred overnight at 50 °C. Upon evaporation of the solvent a yellow solid was obtained. This solid was dissolved in 5 mL of pentane and concentrated to ∼3 mL. After the solution was left overnight at −35 °C, a yellow precipitate formed, which was isolated by filtration. Yield: 0.018 g (44%). This solid contained a small amount of $[(^{iPr}P^{Me}NP)Fe(CO)_2)]$. Crystals of **7** suitable for X-ray diffraction were obtained by leaving a concentrated solution of this solid in pentane at −35 °C overnight. ^{1}H NMR (THF-d_8): δ 3.16 (s, 4H, C*H*$_2$(py)), 2.91−1.91 (br, 11H, ligand C*H*$_2$, overlap with N-*Me*)), 1.64 (br, 4H, C*H*$_2$(py), overlap with *solvent peak*), 1.51−0.74 (br, 28H, ^{i}*Pr*), −24.66 (t, Fe-*H*). ^{31}P{^{1}H} NMR (THF-d_8): δ 89.2 (*major*), 90.2 (*minor*). ^{13}C{^{1}H} NMR (THF-d_8): δ 223.48 ((Fe-CO)), 162.23 (Fe−OCOPy), 65.83 (t, CH_2), 47.23 (s, CH_2), 45.26 (CH_2), 27.06 (t, P^i*Pr*$_2$), 26.58 (t, P^i*Pr*$_2$), 20.38 (s, P^i*Pr*$_2$), 19.74 (s, P^i*Pr*$_2$), 19.18 (s, P^i*Pr*$_2$), 18.08 (s, P^i*Pr*$_2$).

Synthesis of $[(^{iPr}P^{Me}NP)Fe(CO)_2]$. Inside a glovebox a sample of KC_8 (0.039 g, 0.282 mmol, 2.1 equiv) was measured into a vial and transferred to a 100 mL Schlenk bomb using THF (∼5 mL). This mixture was frozen using a cold well, and a crystalline sample of $[(^{iPr}P^{Me}NP)FeCl_2]$, (0.069 g, 0.134 mmol, 1 equiv) was added. The bomb was immediately removed from the box and kept frozen until CO (1 atm) was added. The mixture was then stirred at room temperature for 3 h. The volatiles were removed under reduced pressure, and the residue was extracted with THF (3 mL × 4) and filtered through a bed of Celite. The filtrate was evaporated under reduced pressure, and an orange solid was obtained. This solid was washed with pentane (2 mL × 3) and dried for 4 h to obtain a spectroscopically pure product. Yield: 0.032 g (0.074 mmol, 51%). Crystals suitable for X-ray diffraction were obtained by leaving a concentrated solution of $[(^{iPr}P^{Me}NP)Fe(CO)_2)]$ in THF at −35 °C overnight. ^{1}H NMR (C_6D_6): δ 2.30 (m, 2H, C*H*$_2$), 2.18−2.02 (m, 4H, C*H*$_2$), 2.01−1.89 (m, 2H, C*H*$_2$, overlap with N-*Me*), 1.94 (s, 3H, N-*Me*, overlap with C*H*$_2$), 1.55 (sep, 2H, P^i*Pr*$_2$), 1.06−1.43 (m, 26H, P^i*Pr*$_2$). ^{31}P{^{1}H} NMR (C_6D_6): δ 104.6. ^{13}C{^{1}H} NMR: δ 223.13 (Fe-CO), 220.48 (Fe-CO), 64.64 (t, CH_2), 52.32(s, CH_2), 26.98(t, P^i*Pr*$_2$), 26.24 (t, P^i*Pr*$_2$), 23.42 (t, P^i*Pr*$_2$), 17.96 (s, P^i*Pr*$_2$), 17.67 (s, P^i*Pr*$_2$).

ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.7b03834.

Additional experimental details, discussion, and selected NMR spectra (PDF)

Crystallographic data (CIF)

Crystallographic data (CIF)

Crystallographic data (CIF)

AUTHOR INFORMATION

Corresponding Author

*E-mail for W.H.B.: bernskoetterwh@missouri.edu.

ORCID

Nilay Hazari: 0000-0001-8337-198X

Wesley H. Bernskoetter: 0000-0003-0738-5946

Notes

The authors declare no competing financial interest.

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