

Hydrogenation

Highly Active Phosphine-Free Bifunctional Iron Complex for Hydrogenation of Bicarbonate and Reductive Amination

Trieu-Tien Thai,^[a] Delphine S. Mérel,^[a] Albert Poater,^{*[b]} Sylvain Gaillard,^[a] and Jean-Luc Renaud^{*[a]}

Abstract: Based on a "transition metal frustrated Lewis pair" approach, a cyclopentadienone iron tricarbonyl complex has been designed and applied in the reductive amination and hydrogenation of bicarbonate. This well-defined phosphine-free complex displays the best activities reported to date for an iron complex in the reduction of bicarbonate into formate and in reductive amination.

Economic constraints and environmental concerns in chemistry have led to increased demand for the replacement of noble metals used in chemical processes by Earth-abundant ones. Iron-catalyzed reduction of polarized C=X bonds and carbonic derivatives has received intensive attention and some iron complexes have shown activities and selectivities that are competitive with those of noble metals.^[1,2] However, exchanging noble metals for cheap, abundant, and biocompatible iron complexes to perform reduction is not the sole criterion to render such complexes attractive for industrial applications;^[3] the catalytic activities and the price of the ligand must also be taken into account. In the context of developing more active and selective iron complexes, the group of $\mathsf{Beller}^{\scriptscriptstyle[4]}$ and our group^[5,6] recently demonstrated that variation of the nature of the substituent on cyclopentadienone iron tricarbonyl complex (Knölker's type complex)^[7,8] improved not only the reactivity but also the chemoselectivity and permitted reduction of unsaturated aldehydes, as well as reductive amination. Thus, we showed that not only does the steric hindrance of the silyl group prevent the dimerization of the iron complex and improve its catalytic activity, but the presence of heteroatom on the backbone of the cyclopentadienone also participates in stabilizing the 16-electron iron species.^[5b] However, despite these promising results, further improvements are required to make such bifunctional iron complexes more competitive. By

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tuning the steric and electronic properties of the iron tricarbonyl complex, we endeavor to improve the catalytic activity. Indeed, considering the 16-electron intermediate with its cyclopentadienone ligand, the vacant site of the iron metal center and one lone pair of the carbonyl moiety of the ligand can be assimilated to a frustrated Lewis pair.^[9] Ligand modifications may thus improve the catalytic activity of such cyclopentadienone iron tricarbonyl complexes. Toward this goal, two series of iron complexes have been envisaged; one based on the modification of the acidic character of the metal center (via the introduction of more π -acidic ligands L) and one based on the variation of the Lewis-basic character of the carbonyl framework located on the cyclopentadienone (Figure 1). As carbonyl ligands are the most π -acidic ligands, we focused our



Figure 1. Cyclopentadienone iron tricarbonyl complexes: a) Transition metal frustrated Lewis pairs; b) the cyclopentadienone tricarbonyl iron(0) complexes used in this study.

attention on the second hypothesis. Herein we report the synthesis of 3,4-ethylenediamino-substituted cyclopentadienone iron tricarbonyl complexes and their application in reductive amination and in hydrogenation of bicarbonate.

To enhance the Lewis base character of the cyclopentadienone iron tricarbonyl complex, we synthesized *N*,*N'*-dimethyl 3,4-ethylenediamino-substituted cyclopentadienone to act as a ligand.^[10] Following the reported procedure,^[10a] the ligand **4** was prepared in two steps, from diethyl oxalate and 1,3-diphenylpropan-2-one, in 65% overall yield (Scheme 1). The complex **5** was then obtained in 69% yield by simple heating of the dienone **4** with [Fe₂(CO)₉] in toluene (Scheme 1).

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Gratifyingly, 5

and **7** in a model reaction between citronellal and *N*-methyl-

benzylamine under 5 bar of

hydrogen in ethanol at 85°C

gave the best yield (23, 67, and

83% for complexes 6, 7 and 5,

respectively; Scheme 2).

(Scheme 2).^[5b]



Scheme 1. Synthesis of 3,4-ethylenediamino-substituted cyclopentadienone tricarbonyl iron(0) complex **5**. Reaction conditions: i) Na, EtOH, ethyl glyoxalate (**2**), 0 °C then RT, 48h; ii) *N*,*N*'-dimethylethylenediamine, MeOH, Δ , 2 h; iii) [Fe₂(CO)₉] (2 equiv.), toluene, Δ , overnight.

To unambiguously establish the atom connectivity in complex **5**, single crystals were grown by slow diffusion of pentane in dichloromethane. Suitable single crystals were obtained and subjected to X-ray diffraction (XRD; Figure 2). This structure presented a C_2 symmetry with a slight distortion of the pipera-



Figure 2. Crystal structures of of complex **5** (left) and **6** (right). Thermal ellipsoids are depicted at 50% probability level. Hydrogen atoms are omitted for clarity.

zine-type ring. However, the most remarkable feature of this complex is that the phenyl rings and the cyclopentadienone ancillary ligand are not coplanar, unlike in the complex **6** (Figures 1 and 2).^[5b] Both phenyl rings in complex **5** are almost perpendicular to the cyclopentadienone (see Table 2 and Table S1 in the Supporting Information). The rotation of the phenyl rings seems to be due to the *N*-methyl substituents. As we have reported previously that steric hindrance around the metal center prevented the formation of a stable and inactive dimer and ensured higher catalytic activities,^[5b] we hypothesized that such rotation might change the catalytic properties of the iron species.

To investigate the electron density on the cyclopentadienone moiety in **5** compared to Knölker's complex **7** (Figure 1), the CO-bond IR stretching frequencies and the bond lengths of the carbonyl ligands were investigated for both complexes. The experimentally measured values validated the initial hypothesis that the electron density was higher on the cyclopentadienone moiety in **5**. The CO stretching frequencies were at 2061, 2053 and 1987 cm⁻¹ in complex **7** (see the Supporting Information of ref. [5b]), whereas they were 2027, 1962 and 1947 cm⁻¹ in **5**, indicating a more significant back donation and thus a more significant electron density on the Fe center (see the Supporting Information). Based on the analysis of the CIF files of **5** and **7**,^[8] the same trends can be drawn. All of the CO ligand bond lengths are longer in complex **5**, indicating again a more significant electron density on the Fe center.

The catalytic activities of complex **5** were first evaluated in reductive amination and compared with those of complexes **6**



Scheme 2. Reductive amination catalyzed by complexes 5, 6, and 7.

Whereas a threshold temperature of 85 °C and catalyst loading of 5 mol% appeared necessary with complex **6** or **7** to ensure efficient reductive amination and to avoid side-product formation, we delineated the optimized reaction conditions (catalyst loading and temperature) with **5**. Whereas no conversion was reached at room temperature, reductive amination proceeded to completion at 44 °C in the presence of only 2.5 mol% of complex **5**. A decreased catalyst loading of 1 mol% provided 50% conversion at 44 °C. All of these results demonstrated that not only the prevention of dimerization of unsaturated iron intermediates by the twisted phenyl rings (highlighting further that steric hindrance around the metal center is a crucial requirement), but also the higher electron density on the cyclopentadienone moiety improves the efficiency of this transition metal frustrated Lewis pair.

The scope of the reductive amination catalyzed by 5 and comparison with that catalyzed by 7 are summarized in Table 1 (5 mol% of catalyst was used to ensure good conversions with all substrates). With the exception of the reaction between citronellal and tetrahydroisoquinoline (Table 1, entry 1), yields were higher with 5 than with 7, regardless of the identity of the carbonyl compounds and the primary or secondary aliphatic amines. More importantly, although aromatic amines did not furnish any alkylated product with 7, we were pleased to isolate in 51% yield the amine from the reductive amination between citronellal and *p*-anisidine in the presence of 5 (Table 1, entry 3). Improved yields were also obtained from less reactive aromatic aldehydes, such as 4-nitro-, 4-fluoro-, or 2methoxybenzaldehyde (Table 1, entries 4-7), although some competitive direct reduction of the carbonyl derivatives was observed (e.g., Table 1, entry 5; the amine/alcohol ratio was 70:30 with 5, whereas with 7 it was 35:65). The hindered ketone norcamphor also reacted smoothly with tetrahydroisoquinoline and the corresponding amine was isolated in 70% yield. The corresponding yield was much lower with 7 (23%;Table 1, entry 9).

DFT calculations for the reductive amination with complex **5** were undertaken and compared to those with complex **7** to

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[a] Conditions: Carbonyl derivative (1 mmol), amine (1.2 mmol), complex **5** (5 mol%), Me₃NO (5 mol%), and H₂ (5 bar) in alcohol at 44 °C; [b] conditions: Carbonyl derivative (1 mmol), amine (1.2 mmol), complex **7** (5 mol%), Me₃NO (5 mol%), and H₂ (5 bar) in alcohol at 85 °C; [c] yield of isolated product; [d] in ethanol; [e] in methanol with NH₄PF₆ (10 mol%).

gain additional information on the catalytic cycle and to elucidate its improved performances.^[17] The energy profile of the reductive amination was obtained according to the previously reported mechanism (Figure 3; for the energy diagram for the reaction with complex 7, see the Supporting Information).^[5b] The energy profiles for oxidative removal of one CO followed by hydrogen coordination (intermediate I to III) and for coordination and hydrogenation of the imine (intermediate IV to VI) are quite similar for complexes 5 and 7. The low energy barrier for H_2 coordination (5.8 kcalmol⁻¹) impedes the potential dimerization of intermediate II (the dimer is $12.5 \text{ kcal mol}^{-1}$ higher in energy than II). Overall, the third step (III to IV, corresponding to hydrogen activation and hydrogen cleavage) seems to be the rate-determining step, with an energy barrier of 25.4 kcal mol⁻¹ (Figure 4). This barrier is 3.4 kcal mol⁻¹ higher in energy with catalyst 7 (see the Supporting Information) than with complex 5. From a structural point of view, this lower energy barrier with **5** appears to be due to a more facile H transfer to the C=O group of the cyclopentadienone ligand, thanks to a shorter H…O distance. Indeed, by comparison of the intermediates III for the two complexes, the calculated H…O(=C) distances is 0.105 Å shorter with **5** than with **7**. The reduction pathway (IV to VI) is another key feature of this energetic diagram as the thermodynamic stability of species IV and VI led to an exothermicity of 3.5 kcalmol⁻¹ for **5** whereas an endothermicity of 2.8 kcalmol⁻¹ was calculated for **7**. Overall, the DFT calculations provide clues to explain both the milder reaction conditions and the higher catalytic performance of catalyst **5** with respect to **7**.

Based on these results and thanks to the enhanced efficiency, we thought that 5 might also be able to reduce less polarized double bonds, such as carbon dioxide or carbonates. Reduction of carbon dioxide offers new opportunities for the synthesis of methanol or formic acid, two important C₁ building blocks in synthesis.^[11] Although the cleavage of H–H bonds requires more energy than that of Si-H or B-H bonds, from an industrial point of view and in term of atom economy, the most appealing reducing agent is molecular hydrogen. However, due to the lower electrophilic character of the carbonyl function, research into carbon dioxide hydrogenation has to date made little progress,^[2] despite great industrial interest in this exciting challenge. The groups of Laurenczy and Beller,^[12,13] Milstein,^[14] and Gonsalvi^[15] have all recently disclosed well-defined iron hydride complexes for the reduction of carbon dioxide into formate or formamides, which hydrogenated bicarbonate was to give formate with turnover numbers (TONs) of up to 727,^[12] 7546,^[13] 320,^[14] and 1229,^[15] respectively. Although these complexes have paved the way to new reactivities in iron chemistry, they contain electron-rich, airand moisture sensitive, and expensive phosphorus ligands. Therefore, we envisaged that our cyclopentadienone iron tricarbonyl complex could provide an alternative iron catalyst for the hydrogenation of bicarbonate (Table 2).

We initially chose water as the solvent because bicarbonate is water-soluble and reduction with cyclopentadienyl iron complexes can operate in this solvent.^[6] Sodium formate was obtained with a TON of 8.5 at 100°C under 10 bar of hydrogen ((Table 2, entry 1). An increase in the pressure to 50 bar enhanced the reactivity (Table 2, entry 2). To further improve the reactivity, several parameters were evaluated, including the solvent and the temperature (Table 2, entries 3, 5, and 6). Again, compared to complex 5, Knölker's complex 7 showed lower activities (Table 2, entries 3 vs. 4). High TONs were attained in alcoholic solvent (Table 2, entries 3-7; see also the Supporting Information). However, the highest activity was obtained in a 1:1 solvent mixture of DMSO and water; a TON of 1246 was attained at 100 °C under 50 bar of hydrogen (Table 2, entry 13). Notably, the reduction could be carried out without Me₃NO as activator and furnished better results (Table 2, entries 8–12).^[16] This result represented the best activity reported to date with a phosphine free iron complex and is competitive with some of the previously reported cases.^[12–15]

In summary, we have synthesized and fully characterized a well-defined phosphine-free iron complex bearing a more

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Figure 3. Energy profile for 5-catalyzed reduction of imine (energies in kcalmol⁻¹). For a 3D representation of the structures with relevant distances, see the Supporting Information.

Table 2. Iron-catalyzed hydrogenation of bicarbonate. ^[a]										
		NaHCO ₃ + H ₂	$\frac{5, \text{ Me}_3\text{NO, solv.}}{\text{H}_2, 7, 20 \text{ h}} HCO_2\text{Na} + \text{H}_2\text{O}$							
Entry	S/C ^[a]	Solvent	P _{H2} [bar]	<i>T</i> [°C]	Me ₃ NO	Conv. [%] ^[b]	TON ^[c]			
1	500	H ₂ O	10	100	yes	1.7	8.5			
2	500	H ₂ O	50	100	yes	6.7	33			
3	500	MeOH	50	100	yes	61.5	307			
4 ^[d]	500	MeOH	50	100	yes	6.1	30			
5	500	MeOH	50	80	yes	5.2	26			
6	500	MeOH	50	120	yes	54	270			
7	500	MeOH/H ₂ O (1:1)	50	100	yes	50.7	253			
8	500	DMSO/H ₂ O (1:1)	50	100	no	100	500			
9	1000	DMSO/H ₂ O (1:1)	50	100	yes	73	730			
10	1000	DMSO/H ₂ O (1:1)	50	100	no	99.6	996			
11	2000	DMSO/H ₂ O (1:1)	50	100	yes	31	620			
12	2000	DMSO/H ₂ O (1:1)	50	100	no	51.6	1032			
13 ^[e]	10000	DMSO/H ₂ O (1:1)	50	100	no	12.5	1246			

[a] S/C = substrate (bicarbonate)/catalyst ratio; [b] bicarbonate (5 mmol), complex 5, Me₃NO (0 or 1 equiv/[Fe]), 5 mL of solvent, 20 h; [c] Determined by ¹H NMR analysis using DMF as an internal standard; [d] complex 7 was used; [e] Bicarbonate (25 mmol).

electron-rich cyclopentadienone framework. Its efficiency was demonstrated in reductive amination of a broad range of carbonyl derivatives and amines and in hydrogenation of bicarbonate. Amines were obtained in moderate to high yields under very mild reaction conditions. Formate was also obtained from bicarbonate with TONs up to 1246 under mild reaction conditions. Further work will be dedicated to extending the application of such transition metal frustrated Lewis pair to the activation of hydrogen and other small molecules in the presence of various unsaturated compounds.

Experimental Section

General conditions for the hydrogenation of bicarbonate: In an autoclave, to a mixture of iron complex (5 or 7; 0.01 mmol), Me₃NO (0.01 mmol), and NaHCO₃ (5 mmol), the degassed solvent (5 mL) was added under argon atmosphere. The autoclave was pressurized with molecular hydrogen to the desired pressure and heated at the desired temperature under stirring for 20 h. After 20 h, the autoclave was cooled down to room temperature, the reactor was vented, and ¹H NMR spectroscopy (in D₂O with DMF as internal standard) of the crude reaction mixture was used to measure the yield of reaction.

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Figure 4. Transition state III–IV for 5 (a) and 7 (b). Selected distances are given in Å.

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