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Synthesis and Catalytic Activity of (3,4-Diphenylcyclopentadienone)Iron Tricarbonyl Compounds in Transfer Hydrogenations and Dehydrogenations

Abstract

Four (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds were synthesized, and their activities in transfer hydrogenations of carbonyl compounds and transfer dehydrogenations of alcohols were explored and compared to those of the well-established [2,5-(SiMe3)2-3,4-(CH2)4(η4-C4C═O)]Fe(CO)3 (**3**). A new compound, [2,5-bis(3,5-dimethylphenyl)-3,4-diphenylcyclopentadienone]iron tricarbonyl (**7**), was the most active catalyst in both transfer hydrogenations and dehydrogenations, and compound **3** was the least active catalyst in transfer hydrogenations. Evidence was found for product inhibition of both **3** and **7** in a transfer dehydrogenation reaction, with the activity of **3** being more heavily affected. A monomeric iron hydride derived from **7** was spectroscopically observed during a transfer hydrogenation, and no diiron bridging hydrides were found under reductive or oxidative conditions. Initial results in the transfer hydrogenation of *N*-benzylideneaniline showed that **3** was a significantly less active catalyst in comparison to the (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds.

Keywords

catalysis, iron, bifunctional, transfer hydrogenation, transfer dehydrogenation

Disciplines

Chemistry

Comments

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Synthesis and Catalytic Activity of (3,4-Diphenylcyclopentadienone)Iron Tricarbonyl Compounds in Transfer Hydrogenations and Dehydrogenations

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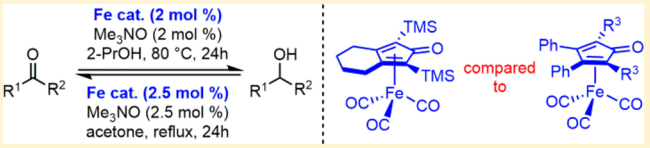
Supporting Information

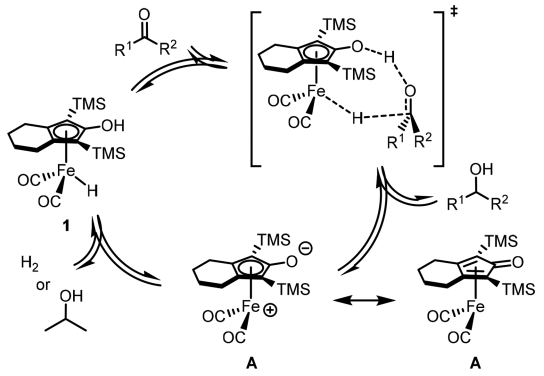
ABSTRACT: Four (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds were synthesized, and their activities in transfer hydrogenations of carbonyl compounds and transfer dehydrogenations of alcohols were explored and compared to those of the well-established [2,5-$(SiMe_3)_2$-3,4-$(CH_2)_4$(η^4-$C_4C{=}O$)]$Fe(CO)_3$ (**3**). A new compound, [2,5-bis(3,5-dimethylphenyl)-3,4-diphenylcyclopentadienone]iron tricarbonyl (**7**), was the most active catalyst in both transfer hydrogenations and dehydrogenations, and compound **3** was the least active catalyst in transfer hydrogenations. Evidence was found for product inhibition of both **3** and **7** in a transfer dehydrogenation reaction, with the activity of **3** being more heavily affected. A monomeric iron hydride derived from **7** was spectroscopically observed during a transfer hydrogenation, and no diiron bridging hydrides were found under reductive or oxidative conditions. Initial results in the transfer hydrogenation of *N*-benzylideneaniline showed that **3** was a significantly less active catalyst in comparison to the (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds.



INTRODUCTION

While (cyclopentadienone)iron tricarbonyl compounds have been known since the 1950s,[1] it was not until 2007 that a report on their catalytic activity in carbonyl reductions was published.[2] Initial experimental[3] and computational[4] mechanistic studies of the iron hydroxycyclopentadienyl hydride **1**[5] supported bifunctional reactivity, where both the iron and the oxygen of the cyclopentadienone carbonyl were involved in a concerted hydrogen transfer (Scheme 1). This reactivity is similar to that observed for Shvo's catalyst (**2**, Figure 1).[6] Compound **1** is sensitive to oxygen, but the catalytic cycle can also be entered by removing a carbonyl ligand from air-stable (cyclopentadienone)iron tricarbonyl **3**[7] using basic water,[8] light,[9] or trimethylamine *N*-oxide,[10] which generates unsaturated species **A** in solution.

Scheme 1. Proposed Mechanism Using 1: Clockwise for Carbonyl Reduction and Counterclockwise for Alcohol Oxidation



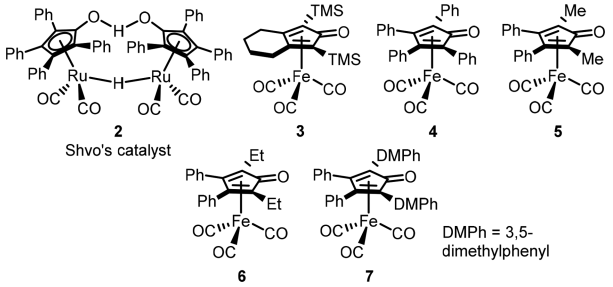


Figure 1. Catalytically important iron and ruthenium carbonyl compounds.

Iron compounds **1** and **3** and derivatives of **3** have been shown to react in a variety of oxidative and reductive transformations,[11] and recent studies have taken advantage of their ability to catalyze both oxidations and reductions using the borrowing hydrogen approach.[12] In general, compounds **1** and **3** have been used the most often, but when other catalysts are used, a majority of them contain a bicyclic cyclopentadienone.[8b,10,12d,i,13] Relatively few catalysts without rings fused to the cyclopentadienone have been explored, and of those that have,

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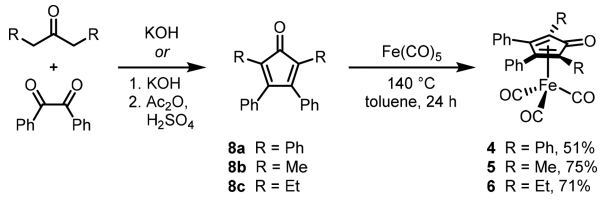
tetraphenylcyclopentadienone compound **4**[1] is the most common.[8a,13b,c,14] A close look at these studies suggests that **4** and its derivatives are less efficient catalysts in comparison to those bearing fused rings in the 3- and 4-positions of the cyclopentadienone in reductions with H_2, but they are competitive with or superior to bicyclic catalysts in transfer oxidations and reductions. To gain more insight into this potential trend, **3**–**7** were synthesized and their activities in the transfer hydrogenation of carbonyl compounds and the transfer dehydrogenation of alcohols were explored. Compounds **4**–**7** were chosen because they offered varying degrees of steric hindrance in the 2- and 5-positions of the cyclopentadienone ring.

RESULTS AND DISCUSSION

Catalyst Synthesis. The general synthetic route for (cyclopentadienone)iron tricarbonyl compounds is shown in Scheme 2. Substituted cyclopentadienones can be purchased or

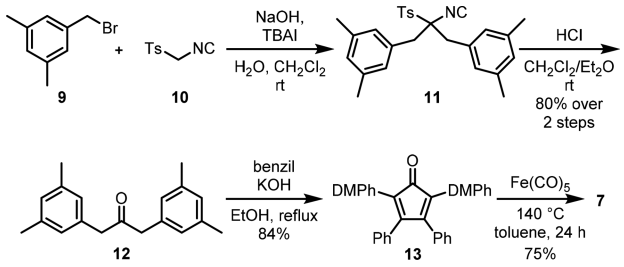
Scheme 2. General Synthesis of Iron Compounds 4–6



synthesized from the corresponding symmetrical ketone and benzil,[15] and they react with iron pentacarbonyl at elevated temperature to afford the desired (cyclopentadienone)iron tricarbonyl compounds as air-stable solids. Compounds **4**[16] and **5**[1c,17] are known, and their corresponding cyclopentadienones are commercially available, with **8b** being a Diels–Alder dimer that undergoes a retro-Diels–Alder process under the reaction conditions.[15b] The diethyl cyclopentadienone **8c** has also been synthesized previously,[15b] but its iron tricarbonyl compound (**6**) has not been reported.

Access to compound **7** required the synthesis of cyclopentadienone **13**,[18] and our approach is shown in Scheme 3.

Scheme 3. Synthesis of Iron Compound 7



There are multiple reports of the synthesis of ketone **12**,[19] and in our hands the two-step TosMIC approach[20] afforded the highest yield and purest product. Ketone **12** reacted with benzil to afford the desired cyclopentadienone **13** in 84% yield, and the procedure outlined in Scheme 2 was used to access **7**.

Iron compounds **4**–**7** were characterized by NMR and IR spectroscopy and mass spectrometry. The atom connectivity of this class of compounds is well established, and X-ray crystal structures of **4**[16a] and other (cyclopentadienone)iron tricarbonyl compounds bearing phenyl groups in the 2- and 5-positions of the cyclopentadienone[13e] have been reported. In these solid-state structures, it varies as to whether or not the phenyl groups in the 2- and 5-positions are coplanar with the cyclopentadienone. Interestingly, the ^{1}H and ^{13}C NMR spectra of **7** at room temperature show that the methyl groups on the DMPh rings are equivalent, indicating that in solution there is free rotation around the C–C bond connecting the cyclopentadienone to these substituents.

Catalyst Activities. The reduction of acetophenone using isopropyl alcohol as the hydrogen source was chosen as a representative transfer hydrogenation, and the reaction progress was monitored over time to gain insight into the catalytic activities of compounds **3**–**7** (Figure 2). Interestingly, the TMS

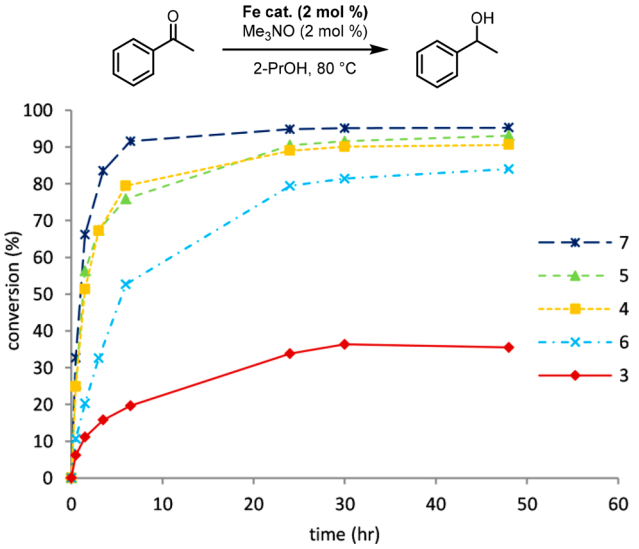


Figure 2. Acetophenone reduction using **3**–**7**. Conversions were determined by GC relative to biphenyl. The consumption of acetophenone (conversion) tracked with the formation of 1-phenylethanol (yield).

catalyst **3** significantly underperformed relative to all four of the (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds under these conditions. Compound **7** was the most active catalyst, resulting in >90% conversion within 6 h, and **4** and **5** had about the same activities and led to 90% conversion over a longer period of time. No clear activity trend based on the size of the substituent in the 2- and 5-positions of the cyclopentadienone ring emerged.

To see if the trend found in acetophenone reduction was general, the activities of catalysts **3** and **7** were explored in the transfer hydrogenation of other carbonyl compounds (Table 1). Overall, ketones were reduced in higher conversions using **7** in comparison to **3** (Table 1, entries 1–7). Substrate electronics affected the reactions, with electron-poor ketones being reduced more readily with both **3** and **7** (Table 1, entries 2 and 3). Aliphatic ketones were also reduced more efficiently by **7** (Table 1, entries 5–7). When an α,β-unsaturated ketone (4-phenyl-3-buten-2-one) and aldehyde (cinnamaldehyde) were used, mixtures of products from carbonyl reduction, alkene reduction, or both were observed with both catalysts (Table 1, entries 8 and 9, respectively), and **3** was more selective at reducing only the carbonyl group relative to **7**. Unhindered aldehydes were reduced in high conversions with both catalysts (Table 1, entries 9, 10, and 13), but **7** outperformed **3** when a hindered aldehyde was used (Table 1, entry 11). Interestingly,

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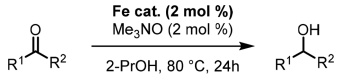
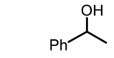
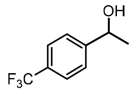
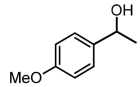
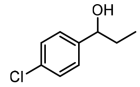
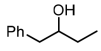
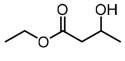
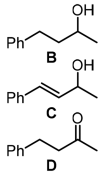
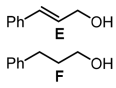
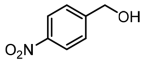
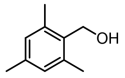
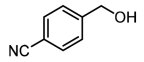
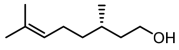
Table 1. Transfer Hydrogenations with 7 and 3[a]



entry	product	conversion (%) with 7[b]	conversion (%) with 3[b]
1		95	34
2		>99	51
3		71	25
4		83	20
5		98 4:1 cis/trans[c]	48 4.7:1 cis/trans[c]
6		77	8
7		97	91
8		50 **B:C:D** 1:5.5:5.9[c]	27 **B:C:D** 1:31:6.6[c]
9		>99 **E:F** 15:1[c]	>99 **E:F** >99:1[c]
10		>99	>99
11		>99	28
12		39	5
13		98	98

[a]Reaction conditions for transfer hydrogenations: ketone or aldehyde (2.5 mmol), iron compound (0.05 mmol), anhydrous trimethylamine *N*-oxide (0.05 mmol), and biphenyl (0.63 mmol) in 5 mL of degassed isopropyl alcohol at 80 °C. [b]Determined by GC relative to biphenyl and matched yield values calculated using ^{1}H NMR spectroscopy. [c]Determined by relative integration values in the ^{1}H NMR spectra.

when the same aldehyde reacted with an acetonitrile derivative of **3** under very similar reaction conditions, a high yield of 2,4,6-trimethylbenzyl alcohol was obtained.[21] Substrates bearing nitriles are known to deactivate this class of catalysts,[2,21] and although **7** was more active than **3**, low conversions were still observed (Table 1, entry 12). While substrates containing a variety of reducible groups were explored, no evidence for reduction of the aryl chloride, ester, nitro, nitrile, or unconjugated alkene was observed (Table 1, entries 4, 7, 10, 12, and 13, respectively).

The same catalysts were used in the oxidation of 4-phenyl-2-butanol (Figure 3). During the first 6 h, catalysts **3**, **5**, and **7** had

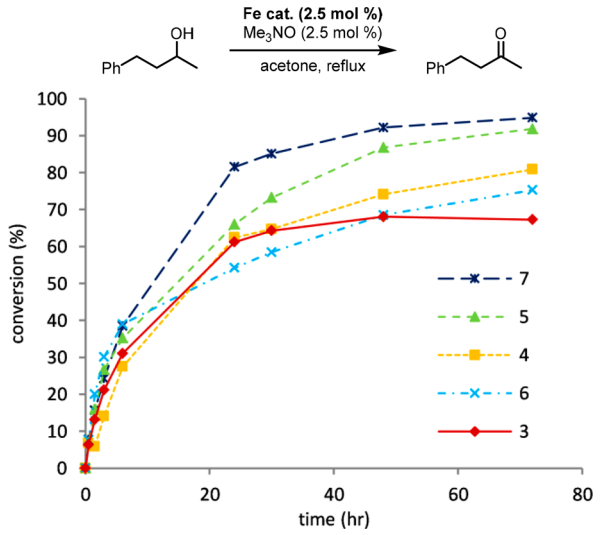


Figure 3. 4-Phenyl-2-butanol oxidation using **3**–**7**. Conversions were determined by GC relative to biphenyl. The consumption of 4-phenyl-2-butanol (conversion) tracked with the formation of 4-phenyl-2-butanone (yield).

similar activities, but ultimately **7** led to higher conversions more quickly than the others. Compound **4** has already been shown to be an active transfer dehydrogenation catalyst, but both **5** and **7** outperformed it under these conditions.[13b] As in the carbonyl reductions, no clear activity trend based on steric hindrance in the 2- and 5-positions of the cyclopentadienone arose. In a recent study of a reaction using **3** as part of a cocatalyst system in a borrowing hydrogen process, an induction period was observed and was proposed to be due to the time needed for catalyst activation by trimethylamine *N*-oxide, but we have found no evidence for an induction period with any of these catalysts, including **3**.[22]

Catalysts **3** and **7** were tested in the transfer dehydrogenation of other alcohols to see if the same activity pattern emerged (Table 2). In alcohol oxidations **7** was as or more active than **3**, although the differences in conversions between the two were not as large as in the carbonyl reductions. Secondary benzylic alcohols were oxidized by both catalysts (Table 2, entries 1–4), but **7** was more active than **3** when an electron-poor aromatic ketone formed (Table 2, entry 2). Catalyst **7** was also more active in the dehydrogenation of acyclic and cyclic secondary aliphatic alcohols (Table 2, entries 5 and 6, respectively). Interestingly, both catalysts reacted preferentially with the cis isomer of 4-*tert*-butylcyclohexanol, but **3** was more selective than **7** (Table 2, entry 6). Due to a disfavored equilibrium, transfer dehydrogenations of primary alcohols to aldehydes are notoriously challenging,[23] and our attempt with 3-phenyl-1-butanol afforded low conversions with both **7** and **3**. In addition to the aldehyde, an ester—from an oxidative coupling—formed with both catalysts;[24] it was the major product with **7** but the minor product using **3**.

Product Inhibition. Figures 2 and 3 show that catalyst **3** does not turn over much beyond 24–30 h, and when some of the reactions with **3** in Tables 1 and 2 were allowed to run for

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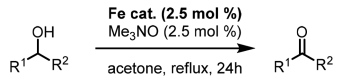
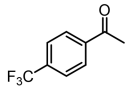
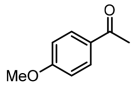
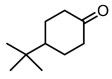
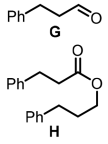
Table 2. Transfer Dehydrogenations with 7 and 3[a]



entry	product	conversion (%) with 7[b]	conversion (%) with 3[b]
1		98	83
2[c]		83	49
3		>99	98
4		>99	>99
5		94	78
6		71 (77% cis and 69% trans)[d]	61 (81% cis and 53% trans)[d]
7		24 **G:H** ~1:2[e]	14 **G:H** ~2:1[e]

[a]Reaction conditions for transfer dehydrogenations: alcohol (2.5 mmol), iron compound (0.063 mmol), anhydrous trimethylamine *N*-oxide (0.063 mmol), and biphenyl (0.63 mmol) in 5 mL of degassed acetone at reflux. [b]Determined by GC relative to biphenyl and matched yield values calculated using ^{1}H NMR spectroscopy. [c]Reaction time was 72 h. [d]Determined by a combination of GC and relative integration values in the ^{1}H NMR spectra; the mixture of 4-*tert*-butylcyclohexanol used had a 2.9/1 trans/cis ratio. [e]Determined by relative integration values in the ^{1}H NMR spectra.

longer times, negligible increases in conversion were observed. Additionally, the rate of acetophenone reduction with **3** was lower than that for all the other catalysts explored. Two possible explanations for this plateauing behavior are catalyst decomposition and product inhibition. To explore if product inhibition was occurring, 1 equiv of 1-phenylethanol was added to acetophenone reduction reactions using **3** or **7**, and conversion over time was monitored (Figure 4). In the case of **7**, the initial rate and final conversion were slightly lower when product was added, but no decrease in rate or final conversion was observed in the reaction using **3**. In fact, the final conversion for the reaction with **3** was about 10% higher when the product was added at the beginning of the reaction. These data suggest that product inhibition is not causing the decreased activity of **3** in the reduction of acetophenone and therefore some other factor—possibly catalyst decomposition—is contributing to its lack of activity after approximately 24 h.[13f]

The same product-inhibition experiments were performed for 4-phenyl-2-butanol oxidations using **3** or **7**: 1 equiv of 4-phenyl-2-butanone product was added at the beginning of the reactions (Figure 5). With **7** the initial rate decreased and the

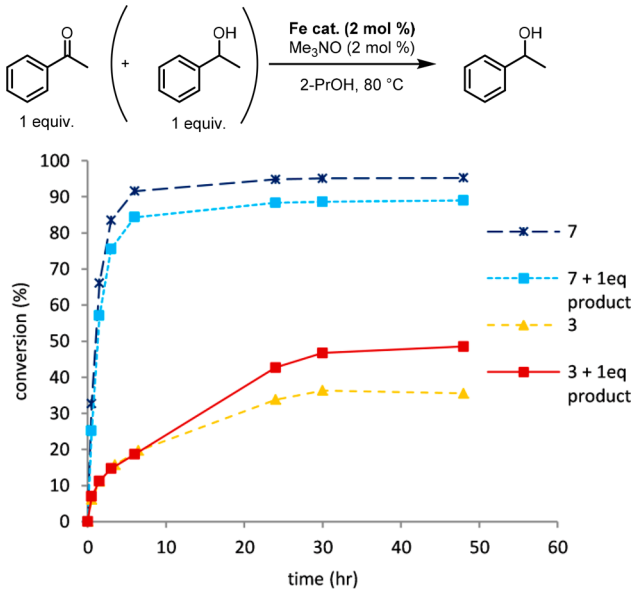


Figure 4. Acetophenone reduction using **3** or **7** with and without 1 equiv of product added at t = 0. Conversions were determined by GC relative to biphenyl. The consumption of acetophenone (conversion) tracked with the formation of 1-phenylethanol (yield).

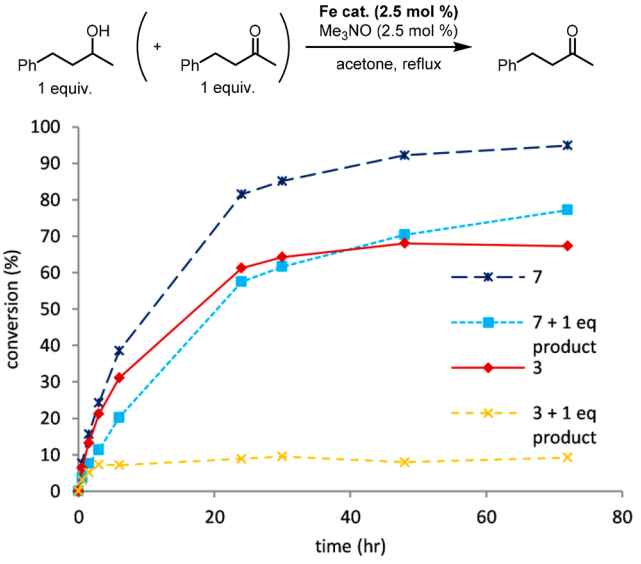


Figure 5. 4-Phenyl-2-butanol oxidation using **3** or **7** with and without 1 equiv of product added at t = 0. Conversions were determined by GC relative to biphenyl. The consumption of 4-phenyl-2-butanol (conversion) tracked with the formation of 4-phenyl-2-butanone (yield).

overall conversion was 15−20% lower when product was added. A much more dramatic decrease was observed in the reaction with **3**, where the product-spiked reaction struggled to reach 10% conversion over 72 h. While some form of product inhibition is occurring in both of these reactions, it is much more dramatic with catalyst **3**. The coordination of alcohols to unsaturated species **A** has been observed in both the solution and solid phases,[3a] but no evidence of an analogous ketone-bound intermediate has been provided. Taken together, these data suggest the observed product inhibition in alcohol oxidations is not due to ketone coordinating to a 16-electron species analogous to **A** but may be due to an increased rate in

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the reverse reaction (reduction of ketone to alcohol) and a shift in the equilibrium of the reaction, both due to increased concentrations of ketone.

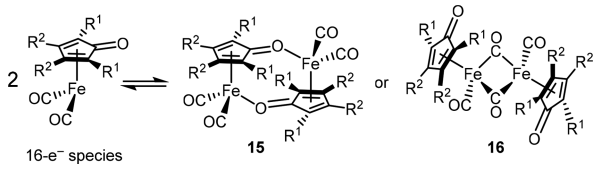
Detection of Iron Hydrides. Next we chose to gain some insight into the active catalyst species present during transfer hydrogenation reactions using **7**. When **7** was treated with 1 equiv of trimethylamine *N*-oxide at 80 °C in 1:1 toluene-d_8/isopropyl alcohol, an iron hydride signal at −10.72 ppm was observed in the ^{1}H NMR spectrum. The chemical shift was similar to that of **1** (−11.62 ppm in C_6D_6)[5] and the analogous ruthenium compound (2,5-diphenyl-3,4-bis(*p*-tolyl)-hydroxylcyclopentadienyl)ruthenium dicarbonyl hydride (−9.76 ppm in THF-d_8),[25] and it suggests that monomeric iron hydride **14** formed in solution (Scheme 4). Diruthenium

Scheme 4. In Situ Formation of Proposed Iron Hydride 14

bridging hydride **2** and its derivatives are formed under similar conditions—by heating (cyclopentadienone)ruthenium tricarbonyl compounds in alcohols—but we found no evidence for a diiron bridging hydride compound similar to **2**, whose hydride is significantly more shielded at −17.75 ppm in C_6D_6.[26] Excess acetophenone was added to our iron hydride solution, and the reaction was monitored at 70 °C by ^{1}H NMR spectroscopy. Catalyst turnover was occurring under these conditions, and the signal at −10.72 ppm remained with no other hydrides appearing. These data are consistent with monomeric iron hydride **14**, not a diiron bridging hydride, being the resting state of the catalyst during the transfer hydrogenation reaction. Increased catalytic activities of (hydroxycyclopentadienyl)iron and ruthenium hydrides bearing sterically bulky TMS groups have been attributed to their inability to form catalytically inactive bridging hydrides, and the sterically bulky 3,5-dimethylphenyl groups may also be inhibiting their formation.[3b,27]

To examine the active catalyst in solution during a transfer dehydrogenation reaction, a solution of **7** in acetone-d_6 was treated with trimethylamine *N*-oxide and excess 4-phenyl-2-butanol at 50−60 °C. Catalyst turnover occurred under these conditions—4-phenyl-2-butanone and isopropyl alcohol-d_6 were observed—and ^{1}H NMR spectroscopy showed very small peaks at −4.87 ppm and −10.82 ppm. No peaks around −20 ppm were present; thus, while the resting state of the catalyst is unclear, no bridging hydrides analogous to **2** were present. If we assume that an unsaturated species analogous to **A** forms in solution, it could dimerize as a way to stabilize itself. Some possible resting state structures based on other dimeric species that have been proposed to form in reactions using structurally similar catalysts are shown in Scheme 5. Compound **15** is analogous to known ruthenium dimers that have a low-energy barrier of dissociation and readily react with a variety of Lewis bases, including alcohols.[28] Alternatively, the formation of iron dimers with bridging carbonyl ligands (**16**) has been proposed as a possible explanation for why certain (cyclopentadienone)iron tricarbonyl compounds bearing phenyl groups in the 2- and 5-positions show poor catalytic activity in reductive aminations.[13c] Catalyst **7** remained active throughout the course of the reaction; therefore, any resting

Scheme 5. Possible Resting State Structures



state structure that forms must not trap it irreversibly. While we did not observe any diiron bridging hydride species using **7**, Guan and co-workers attributed peaks at approximately −22 ppm (in toluene-d_8) to them when they treated crude (2,5-diphenylhydroxycyclopentadienyl)iron dicarbonyl hydrides with acetone.[27]

Preliminary Imine Reduction Study. The difference in activity between **3** and the other catalysts encouraged us to perform an initial experiment comparing their activities in an imine reduction. (Cyclopentadienone)iron tricarbonyl compounds are known to catalyze imine reductions and reductive aminations,[13c−e,h,29] but **4** is the only catalyst bearing a 3,4-diphenylcyclopentadienone that has been used, and it afforded low conversions when it was used in a reductive amination with molecular hydrogen.[13c] In our study the transfer hydrogenation of *N*-benzylideneaniline reached completion within 4 h using catalysts **5** and **6** (Figure 6). The two catalysts with aromatic

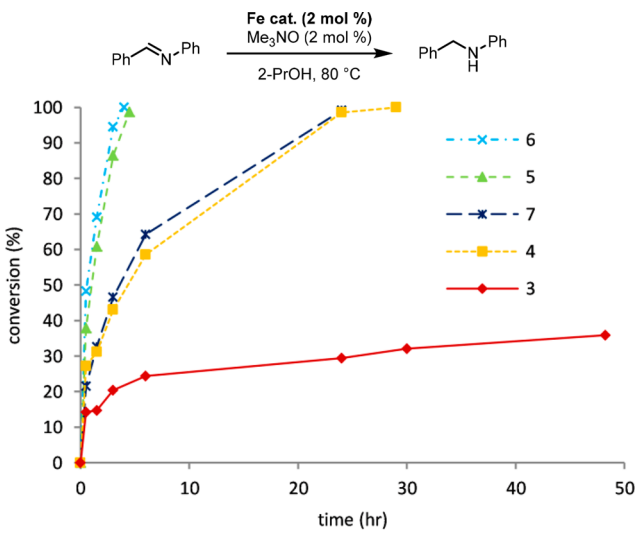


Figure 6. *N*-Benzylideneaniline reduction using **3**−**7**. Conversions were determined by GC relative to biphenyl. The consumption of *N*-benzylideneaniline (conversion) tracked with the formation of *N*-benzylaniline (yield).

substituents in the 2- and 5-positions of the cyclopentadienone (**4** and **7**) afforded complete conversions over a longer period of time, and after 2 days the reaction using **3** had not reached 40% conversion. A recent report by Facchini et al. also showed that **3** was an ineffective catalyst for the transfer hydrogenation of imines with isopropyl alcohol, and their [bis-(hexamethylene)cyclopentadienone]iron tricarbonyl compound was significantly more active.[13h] More thorough, detailed studies are needed, but these initial results suggest that catalysts with sterically small groups in the 2- and 5-positions of the cyclopentadienone are more active than those bearing larger substituents.

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SUMMARY AND CONCLUSIONS

In summary, the activities of four (3,4-diphenylcyclopentadienone)iron tricarbonyl compounds in transfer hydrogenations of carbonyl compounds and transfer dehydrogenations of alcohols were explored and compared to those of commonly used **3**. Compound **3** led to the lowest overall conversions in the reactions that were monitored over time, and compound **7** afforded the highest conversions the most quickly in the same reactions. Catalyst **7** was as active as or more active than **3** in all of the carbonyl reductions and alcohol oxidations tested. Monitoring conversion over time allowed us to see that the activity of **3** decreased dramatically after approximately 24−30 h and that there appeared to be some form of product inhibition in alcohol oxidations. Spectroscopic evidence for the presence of a monomeric iron hydride in transfer hydrogenations using **7** was found, and there was no indication that a diiron bridging hydride analogous to **2** was present in reduction or oxidation reactions with **7**. Finally, initial evidence for dramatic differences in catalyst activity in the transfer reduction of an imine was provided. Overall, these studies illustrate that catalysts with phenyl rings in the 3- and 4-positions of the cyclopentadienone are active in transfer hydrogenations and dehydrogenations and deserve a more comprehensive exploration. Further studies will be focused on understanding why and how cyclopentadienone substitution affects catalytic activity.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.8b00037.

Experimental and synthetic details and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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