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An Environmentally Benign Process for the Hydrogenation of Ketones with Homogeneous Iron Catalysts

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Abstract: Iron complexes generated in situ catalyze homogeneously the transfer hydrogenation of aliphatic and aromatic ketones by utilizing 2-propanol as a hydrogen donor in the presence of base. The influence of different reaction parameters on the catalytic activity is investigated in detail by applying a three-component catalyst system composed of an iron salt, 2,2′:6′,2″-terpyridine, and PPh_3. The scope and limitations of the described catalyst is shown in the reduction of 11 different ketones. In most cases, high conversion and excellent chemoselectivity are obtained. Mechanistic studies indicate a monohydride reaction pathway for the homogeneous iron catalyst.

Keywords: homogeneous catalysis · iron · ketones · ligand effects · transfer hydrogenation

Introduction

Catalysis is a key technology for the advancement of green chemistry, specifically for waste prevention, decreasing energy consumption, achieving high atom efficiency and generating advantageous economics.[1] There is an increasing interest in substituting toxic and expensive late transition metals by readily available and less-toxic metals. In this regard, the use of iron catalysts is especially desirable.[2] So far, homogeneous iron catalysts have been successfully applied for various C–C coupling reactions such as Friedel–Crafts-type reactions, olefin polymerizations, cross-couplings, cycloadditions, and substitution reactions.[3] However, much less is known in the area of industrially important catalytic reductions. Here, comparatively few Fe-catalyzed hydrogenations have been established, mainly for the reduction of olefins[4] and nitro compounds.[5] Clearly, the quest for practical hydrogenation catalysts based on Fe complexes constitutes a major challenge for the development of more sustainable reductions.

Recently, we became interested in applying homogeneous Fe catalysts with respect to C–H functionalization reactions of arenes.[6] Based on that work and our ongoing research in hydrogenation chemistry,[7] we started to explore Fe catalysts for transfer hydrogenations[8] of carbonyl compounds. To the best of our knowledge, only iron carbonyls[9,10] or complexes that contain tetradentate aminophosphines[11] or phosphines[12] have been described for the transfer hydrogenations of ketones and α,β-unsaturated carbonyl compounds. In the latter case, mainly hydrogenation of the olefin occurred.[9,12]

Our goal is to develop a practical Fe hydrogenation catalyst system, which should be easy to prepare and tunable. Thus, the use of commercially available Fe complexes in combination with two different ligands (phosphines and amines) instead of tetradentate ligands seems to be a useful approach. Based on this idea, we report herein the application of new three-component iron catalysts prepared in situ based on iron salts, 2,2′:6′,2″-terpyridine (terpy), and PPh_3. These catalysts give excellent yield and selectivity in the reduction of aromatic and aliphatic ketones to alcohols.

Results and Discussion

As a starting point, 2-propanol-based transfer hydrogenation of acetophenone (**1**) was examined with Fe catalysts in the presence of combinations of nitrogen and phosphorus ligands. In exploratory experiments, terpy and PPh_3 were used as ligands. Typically, the precatalyst was prepared in situ by stirring a solution of $[Fe_3(CO)_{12}]$ (0.3 mol%), terpy (1 mol%), and PPh_3 (1 mol%) in 2-propanol (1.0 mL)

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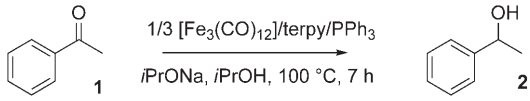
for 16 h at 65 °C. Initially, we investigated the influence of terpy and PPh_3 in the presence of $[Fe_3(CO)_{12}]$, which can be easily handled without special precautions (Table 1). To our

Table 1. Transfer hydrogenation of acetophenone (**1**) with $[Fe_3(CO)_{12}]$/terpy/PPh_3 catalyst.[a]



Entry	Terpy[b]	PPh_3[b]	Yield [%][c]	Selectivity [%][d]
1	–	–	23	>99
2	1	1	78	>99
3	1	–	18	>99
4	–	1	6	>99
5	–	2	21	>99
6	–	10	29	>99
7	5	1	27	>99
8	1	5	24	>99

[a] Reaction conditions: in situ catalyst (0.0038 mmol) ($[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), PPh_3 (0.0038 mmol), 2-propanol (2.0 mL) for 16 h at 65 °C), *i*PrONa (0.019 mmol), 5 min at 100 °C, then addition of **1** (0.38 mmol), 7 h at 100 °C. [b] Ligand to Fe ratio. [c] Yield was determined by GC (50 m Lipodex E, 95–200 °C) with diglyme as internal standard (yield is equivalent to conversion). [d] Selectivity refers to chemoselectivity.

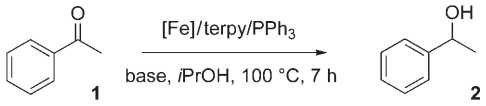
delight, a 1:1 mixture of terpy and PPh_3 gave an active catalyst for the test reaction that was superior to all other combinations (Table 1, entry 2). Notably, low catalytic activity was observed without the use of any ligands (Table 1, entry 1). Increasing the ligand concentration resulted in a significant decrease in activity (Table 1, entries 7 and 8). Importantly, the catalyst systems differ mainly with respect to reactivity, as the chemoselectivity was excellent in all cases.

Next, the influence of base and the iron precatalyst was investigated in more detail (Table 2). The best results were obtained with $[Fe_2(CO)_9]$ and $[Fe_3(CO)_{12}]$ in the presence of catalytic amounts of sodium 2-propylate or sodium *tert*-butylate (Table 2, entries 1, 6, 16). Surprisingly, the most commonly used bases for transfer hydrogenation, such as NaOH, KOH, and *t*BuOK, showed only low activity in this model reaction (Table 2, entries 3–5). Furthermore, different inorganic bases such as K_2CO_3, Cs_2CO_3, and K_3PO_4 (Table 2, entries 7–9) as well as nitrogen-containing organic bases, for instance, pyridine, NEt_3, $N(iPr)_2Et$, DBU, and DABCO (Table 2, entries 10–14), did not prove to be effective. As expected, no transfer of hydrogen was observed in the absence of base (Table 2, entry 15).

To improve the catalytic system, various iron sources with different oxidation states (0, +2, and +3) were tested. Besides $[Fe_2(CO)_9]$ and $[Fe_3(CO)_{12}]$, $FeCl_2$ (Table 2, entry 20) also produced reasonable conversion. To facilitate the formation of active iron hydride complexes, we tested $[Et_3NH][HFe(CO)_4]$[13] as precatalyst, but only limited conversion was detected (Table 2, entry 19).

Following these results, we focused on the nature of the ligands. The results in Table 3 indicate no improvement of

Table 2. Influence of different bases and iron sources in the Fe-catalyzed transfer hydrogenation of **1**.[a]

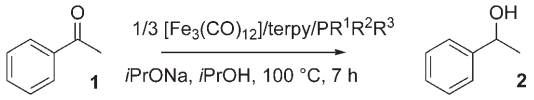


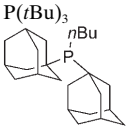
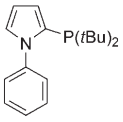
Entry	Iron source	Base	Yield [%][b]
1	$[Fe_3(CO)_{12}]$	*i*PrONa	78
2	$[Fe_3(CO)_{12}]$	LiOH	2
3	$[Fe_3(CO)_{12}]$	NaOH	<1
4	$[Fe_3(CO)_{12}]$	KOH	<1
5	$[Fe_3(CO)_{12}]$	*t*BuOK	12
6	$[Fe_3(CO)_{12}]$	*t*BuONa	76
7	$[Fe_3(CO)_{12}]$	K_2CO_3	3
8	$[Fe_3(CO)_{12}]$	Cs_2CO_3	3
9	$[Fe_3(CO)_{12}]$	K_3PO_4	<1
10	$[Fe_3(CO)_{12}]$	pyridine	1
11	$[Fe_3(CO)_{12}]$	NEt_3	2
12	$[Fe_3(CO)_{12}]$	$N(iPr)_2Et$	<1
13	$[Fe_3(CO)_{12}]$	DBU	<1
14	$[Fe_3(CO)_{12}]$	DABCO	<1
15	$[Fe_3(CO)_{12}]$	–	0
16	$[Fe_2(CO)_9]$	*i*PrONa	84
17	$[Fe(CO)_5]$	*i*PrONa	2
18	$[CpFe(CO)_2I]$	*i*PrONa	3
19	$[Et_3NH][HFe(CO)_4]$	*i*PrONa	11
20	$FeCl_2$	*i*PrONa	45
21	$FeCl_3 \cdot xH_2O$	*i*PrONa	<1
22	$FeBr_2$	*i*PrONa	9
23	$FeSO_4 \cdot 7H_2O$	*i*PrONa	9
24	$Fe(acac)_2$	*i*PrONa	17
25	$Fe(acac)_3$	*i*PrONa	3

[a] Reaction conditions: in situ catalyst (0.0038 mmol) ($[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), PPh_3 (0.0038 mmol), 2-propanol (2.0 mL) for 16 h at 65 °C), base (0.019 mmol), 5 min at 100 °C, then addition of **1** (0.38 mmol), 7 h at 100 °C. [b] Yield was determined by GC (50 m Lipodex E, 95–200 °C) with diglyme as internal standard (yield is equivalent to conversion). acac = Acetylacetonate, Cp = cyclopentadienyl, DABCO = 1,4-diazabicyclo[2.2.2]octane, DBU = 1,8-diazabicyclo[5.4.0]-undec-7-ene.

conversion when PPh_3 was substituted by other phosphorus ligands. Variation in the substitution pattern of PPh_3 with electron-donating (Table 3, entry 2) or electron-withdrawing groups (Table 3, entries 3–5) as well as more-basic and sterically hindered phosphines (Table 3, entries 6–9) decreased the yield of 1-phenylethanol (**2**). We also applied diphosphine ligands in the model reaction. Good activity was obtained with 1,1-bis-(diphenylphosphanyl)methane (dppm) and 1,2-bis(diphenylphosphanyl)ethane (dppe) (Table 3, entries 12–13). Next, we explored the nature of the nitrogen-containing ligand. To our surprise, substituted terpyridines such as 4′-chloro-2,2′:6′,2″-terpyridine (**3**), 6,6′-dibromo-2,2′:6,6′-terpyridine (**4**), and 4,4′,4″-tri-*tert*-butyl-2,2′:6,2″-terpyridine (**5**) led to a significant decrease in alcohol formation (Table 4, entries 1–4). Similarly, the application of structurally related *N*,*N*′,*N*″-ligands **6** and **7** showed no pronounced activity (Table 4, entries 5 and 6). However, in the presence of pyridine (3 mol %) and triphenylphosphine, a reasonable yield of **2** (54 %) was obtained. Clearly, Fe/pyridine/PPh_3 represents one of the least demanding homogenous transfer-hydrogenation catalysts around. Furthermore,

Table 3. Influence of phosphorus ligands in the Fe-catalyzed transfer hydrogenation of **1**.[a]



Entry	Phosphine	Conversion [%][b]
1	PPh_3	78
2	$P(p\text{-MeO-}C_6H_4)_3$	13
3	$P(p\text{-Me-}C_6H_4)_3$	22
4	$P(p\text{-F-}C_6H_4)_3$	23
5	$P(3,4\text{-}CF_3\text{-}C_6H_3)_3$	5
6	PCy_3	11
7	$P(t\text{Bu})_3$	32
8		34
9		31
10	$P(OPh)_3$	8
11	$P(O\text{i}Pr)_3$	7
12	$Ph_2PCH_2PPh_2$	64
13	$Ph_2P(CH_2)_2PPh_2$	50
14	$Ph_2P(CH_2)_4PPh_2$	3
15	$Ph_2P(CH_2)_6PPh_2$	3

[a] Reaction conditions: in situ catalyst (0.0038 mmol) ($[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), phosphorus ligand (0.0038 mmol), 2-propanol (2.0 mL) for 16 h at 65 °C), *i*PrONa (0.019 mmol), 5 min at 100 °C, then addition of **1** (0.38 mmol), 7 h at 100 °C. [b] Yield was determined by GC (50 m Lipodex E, 95–200 °C) with diglyme as internal standard (yield is equivalent to conversion). Cy = cyclohexyl.

the combination of (−)-sparteine and triphenylphosphine provided an active catalyst system (Table 4, entries 11–12).

Next, the optimized general protocol for transfer hydrogenations was applied to aromatic and aliphatic ketones. Here, both $[Fe_3(CO)_{12}]$/terpy/PPh_3 and $FeCl_2$/terpy/PPh_3 were tested for the reduction of 10 different ketones (Table 5). Acetophenone, 4-chloroacetophenone, 2-methoxyacetophenone, and propiophenone were hydrogenated in excellent yield and selectivity (92–99%) (Table 5, entries 1, 2, 5, 6). Acetophenones with electron-donating substituents in the *para* position gave good but somewhat lower yields (75–83%). A chloro substituent in the α position to the carbonyl group proved to be problematic and deactivated both catalysts (Table 5, entry 7). Aliphatic ketones are more challenging substrates than aromatic ketones, but they also react in excellent yield (95–99%).

Notably, similar activities for the reduction of ketones with regard to our $[Fe_3(CO)_{12}]$-based system were reported when other transition-metal carbonyl complexes, for instance, $[Ru_3(CO)_{12}]$-based catalysts, were applied.[14] The $[Fe_3(CO)_{12}]$- and $FeCl_2$-based catalysts showed no significant difference in productivity. Hence, we assume the formation of a similar active species. Indeed, the two catalyst systems produced similar conversion curves (Figure 1). At the start of the reaction, we observe in both cases an induction

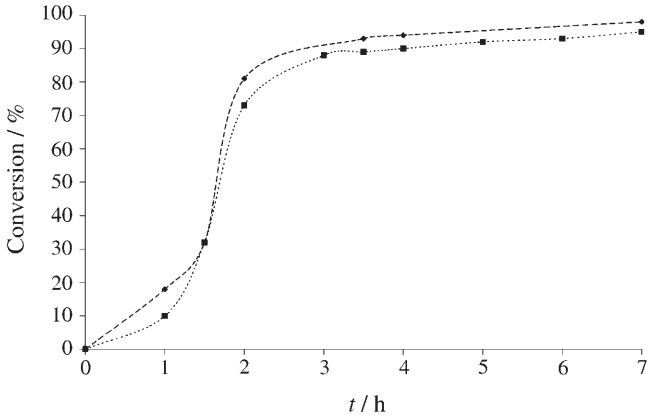


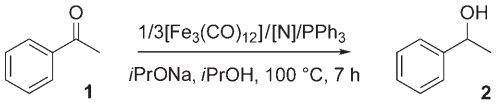
Figure 1. Conversion–time behavior of the different precatalysts containing $[Fe_3(CO)_{12}]$ and $FeCl_2$. Reaction conditions: in situ catalyst (0.0038 mmol) ($[Fe_3(CO)_{12}]$ (0.0013 mmol) or $FeCl_2$ (0.0038 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in 2-propanol (2.0 mL), 16 h at 65 °C), *i*PrONa (0.38 mmol), 5 min at 100 °C, then addition of **1** (0.76 mmol), reaction at 100 °C. Conversion was determined by GC (50 m Lipodex E, 95-200 °C) with diglyme as internal standard (conversion is equivalent to yield). ◆ = $[Fe_3(CO)_{12}]$/terpy/PPh_3, ■ = $FeCl_2$/terpy/PPh_3.

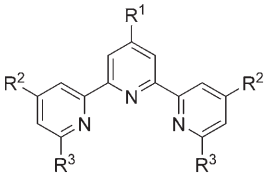
period of nearly one hour, whereby the $FeCl_2$ system showed a slightly lower reaction rate, probably due to the slower elimination of chlorides and the change of oxidation state. The induction period can be shortened by increasing the catalyst preformation time. Thus, when the precatalyst ($[Fe_3(CO)_{12}]$/terpy/PPh_3) was treated with a base for one hour instead of 5 min at the reaction temperature, an increase in conversion into 1-phenylethanol from 18% to 32% in the first hour was recorded.

Next, we focused our attention on the reaction mechanism. To exclude the formation of heterogeneous Fe catalysts,[15] a large excess of Hg(0) was added to the well-stirred reaction mixture after the reaction had proceeded for one hour, so that the "real" catalyst should be formed.[16,17] No significant suppression of the reaction rate in the reduction of **1** was observed (73% yield after 7 h), whereas a positive poisoning of the catalyst should have led to approximately 18% of **2** (see also Figure 1). In another experiment, the reaction was carried out under standard conditions and filtered through celite after one hour.[18] The filtrate was allowed to react for a further six hours. Thereafter, the applied celite was stirred with fresh 2-propanol, sodium 2-propylate, and **1** under reaction conditions for another six hours. The results obtained showed no suppression of reaction rate for the filtrate (92%), whereas no conversion was detected (< 1%) with the celite system. Consequently, both experiments indicate a definite homogeneous catalyst.

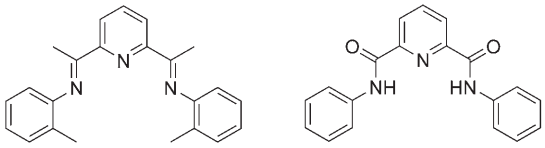
Various methods (^1H, ^{31}P, and ^{13}C NMR and IR spectroscopy and MS) were used for the characterization of the active catalyst species. Unfortunately, the structural composition of the catalyst is still unclear. No evidence for an Fe–H species was detected by ^1H NMR spectroscopy after reaction of the precatalyst with base (5 equiv).[19] The ^{31}P NMR spectrum of the precatalyst in $[D_4]$MeOH or $[D_8]$*i*PrOH showed three singlets with a ratio of 20:1:10 at −5.3 ppm

Table 4. Variation of nitrogen ligands in the Fe-catalyzed transfer hydrogenation of **1**.[a]





3 R^1 = Cl; R^2 = H; R^3 = H
4 R^1 = H; R^2 =Br; R^3 = Br
5 R^1 = *t*Bu; R^2 = *t*Bu; R^3 = *t*Bu



6 **7**

Entry	Ligand	Ligand/metal	Conversion [%][b]
1	terpy	1	78
2	**3**	1	23
3	**4**	1	28
4	**5**	1	14
5	**6**	1	13
6	**7**	1	7
7	2,2′-bipyridine	1	8
8	2,2′-bipyridine	2	6
9	tmeda[c]	1	18
10	tmeda[c]	2	13
11	(−)-sparteine	1	43[d]
12	(−)-sparteine	2	38[d]
13	pyridine	3	54
14	pyridine	6	5

[a] Reaction conditions: in situ catalyst (0.0038 mmol) ([$Fe_3(CO)_{12}$] (0.0013 mmol), nitrogen ligand (0.0038 mmol), PPh_3 (0.0038 mmol), 2-propanol (2.0 mL) for 16 h at 65 °C), *i*PrONa (0.019 mmol), 5 min at 100 °C, then addition of **1** (0.38 mmol), 7 h at 100 °C. [b] Yield was determined by GC (50 m Lipodex E, 95–200 °C) with diglyme as internal standard (yield is equivalent to conversion). [c] tmeda = *N*,*N*,*N*′,*N*′-tetramethylethylendiamine. [d] A racemic mixture of **2** was detected.

(free PPh_3) and two unknown signals at 32.9 and 71.3 ppm.[20] The addition of 5 equivalents of base (sodium 2-propylate) with respect to iron and stirring of the mixture for 5 min at 100 °C did not affect the chemical shift and ratio of the observed ^{31}P NMR signals.[19] Mass spectrometric investigations also gave no clear information about the composition of the precatalyst, because indications for a number of possible candidates or fragments of labile complexes were detected, such as compounds containing terpy, PPh_3, CO, and Fe in a ratio of 1:1:1(2):1 or terpy, CO, and Fe in a ratio of 1:3:1. The utilization of [$Fe_3(CO)_{12}$] represents a potential option for IR spectroscopy. Hence, we recorded the IR spectra of our precatalyst in a solution of 2-propanol. The activation of the precatalyst by sodium 2-propylate (10 equiv) for 5 min at 100 °C resulted in the http://www.dict.cc/?s = disappearance of absorption signals at 1889 and 1718 cm^{-1}. Addition of **1** to the activated precatalyst led to the http://www.dict.cc/?s = disappearance of the signal at 1654 cm^{-1} and emergence of a signal at 1679 cm^{-1}. Interestingly, a similar behavior was described by Gao and co-workers when they followed the formation of the transfer-hydrogenation catalyst composed of [$Fe_3(CO)_{12}$] and tetradentate aminophosphines in 2-propanol in the presence of base.[11]

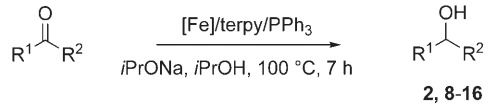
Although the nature of the active Fe–H species remains unclear, we turned our attention to the mechanism of the hydride transfer. To exclude a radical-type reduction, the reaction of cyclopropyl phenyl ketone was examined in more detail ("radical clock" substrate) (Table 5, entry 8). In the presence of [$Fe_3(CO)_{12}$]/terpy/PPh_3 catalyst, the corresponding cyclopropyl phenyl alcohol **14** was detected by ^1H NMR spectroscopy in > 99 % purity. There was apparently no radical-induced reduction, because no opening of the cyclopropyl ring occurred.[21] Consequently, a radical-reduction mechanism promoted by sodium alkoxides, whereby the transition metal plays a marginal role, can also be excluded.[22]

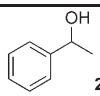
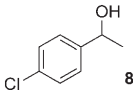
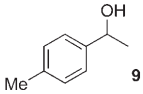
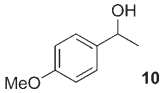
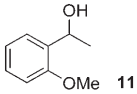
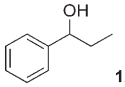
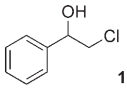
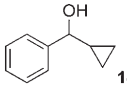
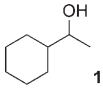
In general, for transition-metal-catalyzed transfer hydrogenation, two mechanisms are accepted: direct hydrogen transfer via formation of a six-membered cyclic transition state composed of metal and hydrogen donor and acceptor, and the hydridic route, which is subdivided into two pathways, the monohydride and the dihydride mechanism (Scheme 1). More specifically, the formation of monohydride metal complexes promote an exclusive hydride transfer from carbon (donor) to carbonyl carbon (acceptor) (Scheme 1, pathway A), whereas a hydride transfer from carbon (donor) to carbonyl carbon (acceptor) as well as carbonyl oxygen (acceptor) was proposed for the formation of dihydride metal complexes (Scheme 1, pathway B).[8a,c,e] Evidence for both pathways (hydridic route) were determined by various researchers when investigating the hydride transfer catalyzed by metal complexes of, for example, Ru, Rh, or Ir.[23] So far nothing is known with respect to iron catalysts in transfer hydrogenations.

To rule out an exchange of hydrogen atoms, for example, by C–H activation, we investigated the transfer hydrogenation with a completely deuterated donor molecule.[24] The [$Fe_3(CO)_{12}$]/terpy/PPh_3 precatalytic system was dissolved in [D_8]*i*PrOH and treated with [D_7]*i*PrONa for 5 min at 100 °C. After addition of **1**, the solution was stirred for 5 h at 100 °C. Only alcohol **17** was detected as product by ^1H NMR spectroscopy (Scheme 2; > 99 %).[25] This result indicates an exclusive transfer of the deuterium into the carbonyl group. Apparently no C–H activation processes and enol formation occurred under the described conditions.[26]

To clarify the pathway of hydrogen transfer from the hydrogen donor to the substrate molecule, we used [D]*i*PrOH (the hydroxy group was deuterated) as solvent/donor and sodium 2-propylate as base in the transfer hydrogenation of **1** (Scheme 2). We obtained a mixture of two different deuterated 1-phenylethanols **18** and **19** in the ratio 85:15.[27]

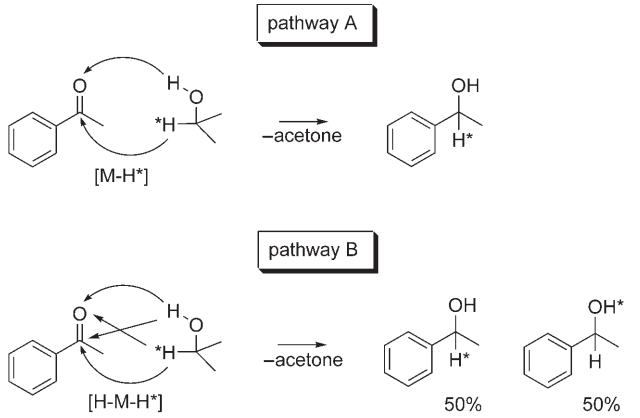
Table 5. $[Fe_3(CO)_{12}]$/terpy/PPh_3- and $FeCl_2$/terpy/PPh_3-catalyzed hydrogenation of ketones.[a]



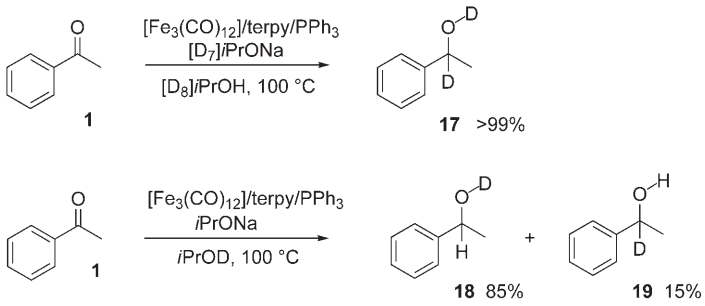
Entry	Alcohol	Yield [%][b] $[Fe_3(CO)_{12}]$	Yield [%][b] $FeCl_2$
1	 **2**	95	91
2	 **8**	>99	97
3	 **9**	84	83
4	 **10**	63	75
5	 **11**	>99	>99
6	 **12**	81	92
7	 **13**	5	8
8	 **14**	48	57
9	 **15**	95	93
10	 **16**	>99	>99

[a] Reaction conditions: in situ catalyst (0.0038 mmol) ($[Fe_3(CO)_{12}]$ (0.0013 mmol) or $FeCl_2$ (0.0038 mmol), terpy (0.0038 mmol), PPh_3 (0.0038 mmol) in 2-propanol (2.0 mL), 16 h at 65 °C), *i*PrONa (0.38 mmol), 5 min at 100 °C, then addition of ketone (0.76 mmol), reaction for 7 h at 100 °C. [b] Yield was determined by GC (**2**: 50 m Lipodex E, 95–200 °C, **8**: 25 m Lipodex E, 100 °C, **9**: 50 m Lipodex E, 90–105 °C, **10**: 25 m Lipodex E, 80–180 °C, **11**, **14**, **15**, and **16**: 30 m, HP Agilent Technologies, 50–300 °C, **12**: 25 m Lipodex E, 90–180 °C, **13**: 50 m Lipodex E, 90–180 °C) with diglyme as internal standard (yield is equivalent to conversion).

This specific migration is in agreement with the described monohydride mechanism, which implies that a major formation of the metal monohydride in the catalytic cycle occurred, albeit with a small amount of **19**.[8c] This H/D scrambling is explained by the reversibility of the hydrogen-transfer process due to the hydrogen-donating ability of 1-phenylethanol (low oxidation potential).[8c]



Scheme 1. Monohydride (pathway A) and dihydride (pathway B) mechanisms of transition-metal-catalyzed transfer hydrogenation of acetophenone.



Scheme 2. Deuterium incorporation into acetophenone (**1**) catalyzed by $[Fe_3(CO)_{12}]$/terpy/PPh_3 in the presence of base.

Conclusions

We have developed the first general homogeneous Fe catalyst system for the transfer hydrogenation of aliphatic and aromatic ketones. In the presence of 1 mol% of $[Fe_3(CO)_{12}]$/terpy/PPh_3 or $FeCl_2$/terpy/PPh_3, the corresponding alcohols are obtained in good to excellent yield and chemoselectivity. The active catalyst systems are easily generated in the presence of cheap available nitrogen and phosphorus ligands. Mechanistic experiments indicate a transfer of hydrogen from the donor molecule to the substrate by a monohydride mechanism. Further work in the direction of stereoselective Fe-based hydrogenation catalysts is under way in our laboratories.

Experimental Section

General

All manipulations were performed under argon atmosphere with standard Schlenk techniques. Unless otherwise specified, all chemicals are commercially available and used as received. 2-Propanol, pyridine, and triethylamine were used without further purification (purchased from Fluka, dried over molecular sieves). Sodium 2-propylate and sodium *tert*-butylate were prepared by treating sodium with 2-propanol or *tert*-butanol under argon atmosphere (stock solution). Ketones **1**, **8**, **9**, **11**, **12**, **14**,

15, and **16** were dried over CaH_2, distilled under vacuum, and stored under argon. Ketones **10** and **13** were treated with vacuum/argon cycles and stored under argon. Tmeda was distilled under Argon. $[Et_3NH][HFeCO_4]$,[13] BuP(adamantyl)$_2$,[28] and *N*-phenyl-2-(di-*tert*-butylphosphanyl)pyrrole[29] were synthesized according to literature protocols. $[D_8]$- and [D]*i*PrOH were dried over CaH_2 and distilled under argon atmosphere.

General Procedure for Transfer Hydrogenation of Ketones

In a Schlenk tube (10 mL), the catalyst (0.0038 mmol) was generated in situ by stirring a solution of $[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in 2-propanol (1.0 mL) for 16 h at 65 °C. The precatalytic system was treated with sodium 2-propylate (0.38 mmol) at 100 °C for 5 min. After addition of the corresponding ketone (0.38 or 0.76 mmol), the reaction mixture was stirred for 7 h at 100 °C. The solution was cooled to room temperature and filtered over a plug of silica. The conversion was measured by GC without further purification.

Procedures for Distinguishing Homogeneous and Heterogeneous Catalysts

Mercury poisoning: In a Schlenk tube (10 mL), a solution of $[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in 2-propanol (1.0 mL) was stirred for 16 h at 65 °C. The precatalyst was treated at 100 °C with sodium 2-propylate (0.38 mmol) in 2-propanol (0.5 mL) for 5 min, followed by **1** (0.76 mmol) in 2-propanol (0.5 mL). The reaction mixture was kept for 1 h at 100 °C. After that, a drop of mercury, which was degassed and stored under argon, was added, and the reaction was continued for 7 h. The reaction mixture was cooled to room temperature and filtered over a plug of silica gel. The conversion was determined by GC without further purification.

Maitlis test: In a Schlenk tube (10 mL), a solution of $[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in 2-propanol (1.0 mL) was stirred for 16 h at 65 °C. The precatalyst was treated at 100 °C with sodium 2-propylate (0.38 mmol) in 2-propanol (0.5 mL) for 5 min, followed by **1** (0.76 mmol) in 2-propanol (0.5 mL). The reaction mixture was kept for 1 h at 100 °C. After that, the solution was filtered under an atmosphere of argon through a filter supported by a plug of celite (heated in vacuum and stored under argon). The filtrate was heated again to 100 °C and the reaction allowed to proceed for another 6 h. The celite phase was transferred into a Schlenk tube (10 mL) and mixed with 2-propanol (1.0 mL), sodium 2-propylate (0.38 mmol) in 2-propanol (0.5 mL), and **1** (0.76 mmol) in 2-propanol (0.5 mL). After the reaction was complete, both mixtures were cooled to room temperature and filtered over a plug of silica gel. The conversion was determined by GC without further purification.

*Transfer Hydrogenation with $[D_8]$i*PrOH as Hydride Source

In a Schlenk tube (10 mL), $[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in $[D_8]$*i*PrOH (1.0 mL) were stirred for 16 h at 65 °C. After mixing the precatalytic solution with $[D_7]$*i*PrONa (0.38 mmol, prepared by reacting sodium (0.38 mmol) with $[D_8]$*i*PrOH (0.5 mL)) at 100 °C for 5 min, a solution of **1** (0.76 mmol) in $[D_8]$*i*PrOH (0.5 mL) was added. The reaction mixture was kept for 5 h at 100 °C, then cooled to room temperature and filtered over a plug of silica. The conversion was determined by ^{1}H NMR spectroscopy.

*Transfer Hydrogenation with [D]i*PrOH as Hydride Source

In a Schlenk tube (10 mL), $[Fe_3(CO)_{12}]$ (0.0013 mmol), terpy (0.0038 mmol), and PPh_3 (0.0038 mmol) in [D]*i*PrOH (1.0 mL) were stirred for 16 h at 65 °C. After mixing the precatalytic solution with sodium 2-propylate (0.38 mmol, prepared by treating sodium (0.38 mmol) with [D]*i*PrOH (0.5 mL)) at 100 °C for 5 min, a solution of **1** (0.76 mmol) in [D]*i*PrOH (0.5 mL) was added. The reaction mixture was kept for 5 h at 100 °C. (To avoid side effects, for instance, scrambling, the reaction was stopped before full conversion.) The solution was cooled to room temperature and filtered over a plug of silica. The solvent was removed under vacuum, and the residue was dissolved in $CDCl_3$. The conversion was determined by ^{1}H NMR spectroscopy. The ratio of **18** to **19** was based on the integrals of the ^{1}H NMR signals of the CH_3 groups.

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[20] The preparation of the precatalyst was carried out in a manner similar to the described procedure, with $[Fe_3(CO)_{12}]$, terpy, and PPh_3, stirring for 16 h at 65 °C in $[D_8]$*i*PrOH or 2-propanol, followed by transfer of the suspension into an NMR tube or removal of 2-propanol and dissolution of the residue in $[D_4]$MeOH, $CDCl_3$, $[D_6]$acetone, or $[D_6]$benzene.
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