Chiral Cyclopentadienone Fe-Complexes for the Catalytic Asymmetric Hydrogenation of Ketones

Piotr Gajewski,[a, b] Marc Renom-Carrasco,[a, b] Sofia Vailati Facchini,[c] Luca Pignataro,[a]* Laurent Lefort,[b] Johannes G. de Vries,[e] Raffaella Ferraccioli,[d] Alessandra Forni,[d] Umberto Piarulli[c]* and Cesare Gennari[a]*

Abstract: Three chiral cyclopentadienone Fe-complexes derived from (*R*)-BINOL (**CK1-3**) were synthesized and their structure unambiguously confirmed by X-ray analysis (**CK3**). Under suitable conditions for the in situ conversion into the corresponding Fe-hydroxycyclopentadienyl hydrides (Me_3NO, H_2), the new chiral complexes were tested in the catalytic asymmetric hydrogenation of ketones, showing moderate to good enantioselectivity. In particular, the complex bearing methoxy substituents at the 3,3'-positions of the binaphthyl moiety (**CK2**) proved remarkably more enantioselective than the unsubstituted one (**CK1**) and reached the highest level of enantioselectivity (up to 77% *ee*) ever obtained with chiral cyclopentadienone Fe-complexes.

Asymmetric hydrogenation (AH) is by far the most industrially relevant enantioselective transformation, owing to its operational simplicity and 100% atom economy. During its 40 year-long history, thousands of homogeneous catalysts have been developed, allowing the hydrogenation of many substrates with high enantioselectivity.[1] However, most of the AH catalysts rely on very expensive and toxic precious metals (e.g., Ru, Rh, Ir, Pd), which may prevent in some cases their implementation on large scale.[2] For this reason, developing new catalysts relying on cheap 'base metals' (e.g., Fe, Co, Ni, Cu) constitutes the next frontier to unleash the full potential of AH. In particular, Fe appears to be the most appealing base metal due to its abundance (5% of Earth's crust), low cost and scarce toxicity.[3] In spite of these attractive features, the application of Fe in AH is still very limited:[4] a few chiral catalysts have been developed for the hydrogenation of ketones[5] and ketoimines,[5b,6] while no examples were reported with olefins.[7]

[a] P. Gajewski, M. Renom-Carrasco, Dr. L. Pignataro, Prof. Dr. C. Gennari
Università degli Studi di Milano, Dipartimento di Chimica
Via C. Golgi, 19, I-20133, Milan (Italy)
E-mail: luca.pignataro@unimi.it
cesare.gennari@unimi.it
http://www.chimica.unimi.it/ecm/home
[b] P. Gajewski, M. Renom-Carrasco, Dr. L. Lefort
DSM Innovative Synthesis BV,
P.O. box 18, 6160 MD Geleen (The Netherlands)
[c] S. Vailati Facchini, Prof. Dr. U. Piarulli
Università degli Studi dell'Insubria,
Dipartimento di Scienza e Alta Tecnologia,
Via Valleggio, 11, I-22100, Como (Italy)
E-mail: umberto.piarulli@uninsubria.it
[d] Dr. R. Ferraccioli, Dr. A. Forni
CNR, Istituto di Scienze e Tecnologie Molecolari (ISTM)
Via C. Golgi, 19, I-20133, Milan (Italy)
[e] Prof. Dr. J. G. de Vries
Leibniz-Institut für Katalyse e. V.
Albert-Einstein-Str., 29 a 18059 Rostock (Germany)

In our quest for new chiral Fe-catalysts for the AH of ketones, our attention was captured by cyclopentadienone and hydroxycyclopentadienyl iron complexes, whose catalytic properties are currently the object of a growing interest.[8] Although iron cyclopentadienone complexes are known since the 1950s,[9] it was only in 1999 that Knölker and co-workers were able to isolate and characterize the hydroxycyclopentadienyl activated complex ***act*-K1**, obtained from Fe-cyclopentadienone **K1** by Hieber base reaction (Figure 1 a).[10] The catalytic potential of complex ***act*-K1** was discovered some years later by Casey and co-workers,[11a] who reported its ability to promote the hydrogenation of carbonyl compounds and proposed a concerted outer-sphere mechanism.[11b] One limitation of ***act*-K1**-type complexes is their sensitivity to air and moisture. However, it has been recently shown that this problem can be circumvented by generating complexes ***act*-K** *in situ* from their precursors **K** (stable to air, moisture and chromatography) in the presence of Me_3NO,[12] UV light[5c] or K_2CO_3[13] (Figure 1 b). Therefore, unlike most other Fe-complexes used in homogeneous hydrogenation,[5b,e-f,14] cyclopentadienone complexes **K** are stable pre-catalysts which do not require inert or dry atmosphere (e.g., use of a glovebox) to be handled. This attractive feature makes them suitable candidates for practical industrial use. Chiral Fe-cyclopentadienone complexes have been obtained either by replacing one of the CO ligands of a **K** complex with a chiral phosphoramidite,[5c] or by inserting a stereocenter on the ring fused to the cyclopentadienone.[12d] However, despite their theoretical interest, both these approaches met limited success in terms of enantioselectivity (up to 31% *ee* in ketone AH and up to 25% *ee* in ketone asymmetric transfer hydrogenation, respectively).

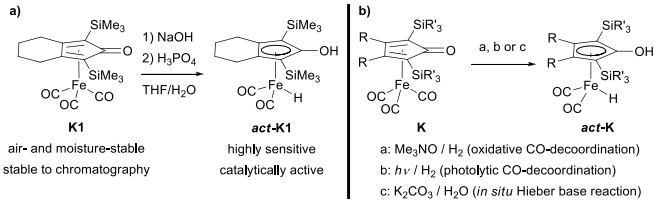


Figure 1. Knölker's synthesis of Cp-Fe activated complex ***act*-K1** (a) and reported methods for in situ formation of Cp-Fe activated complexes ***act*-K** (b).

Our approach to the development of chiral **K**-type complexes (**CK**) envisages the use of BINOL-derived chiral cyclopentadienone ligands (Figure 2), whose design was inspired by the chiral Cp-ligands recently reported by Cramer et al. for Rh(III) catalysis.[15]

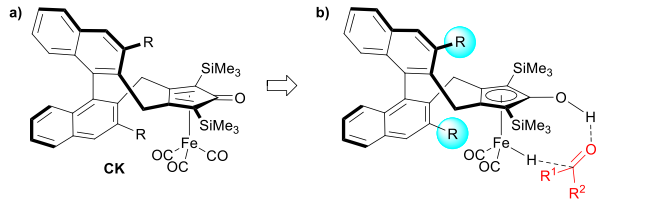
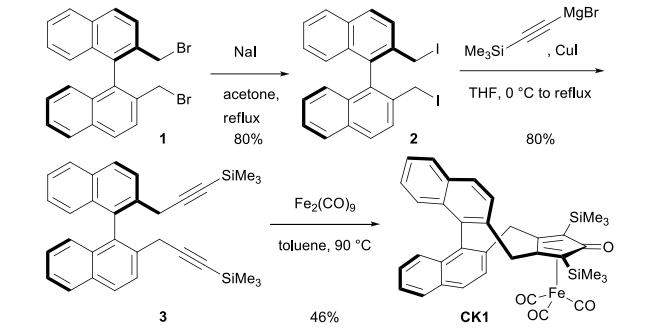


Figure 2. General structure of chiral pre-catalysts **CK** (A) and expected importance of binaphthyl 3,3'-substituents in AH (B).

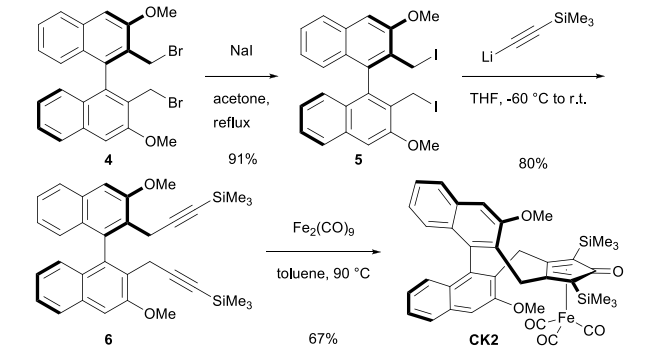
The synthesis of the 3,3'-unsubstituted complex (*R*)-**CK1** (Scheme 1) was carried out in three steps starting from the commercially available compound (*R*)-**1**.[16]



Scheme 1. Synthesis of the pre-catalyst (*R*)-**CK1**.

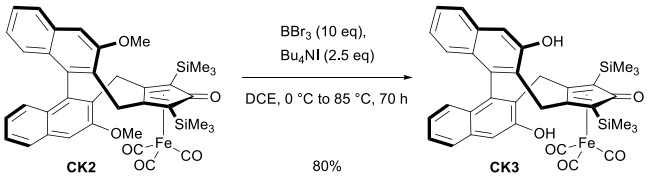
Bis-bromide (*R*)-**1** was converted into the more reactive bis-iodide (*R*)-**2**, which was treated with [(trimethylsilyl)ethynyl]magnesium bromide in the presence of CuI[17] to yield the diyne (*R*)-**3**. The latter compound was then cyclized under the conditions reported by Renaud et al.[12a] [$Fe_2(CO)_9$ at 90 °C in toluene] to yield the complex (*R*)-**CK1**, which proved to be stable in air as expected, and could be purified by chromatography.

Considering the previously reported BINOL-derived catalytic systems[15,18] and the commonly accepted mechanism of the act-**K**-catalyzed reductions,[11b] we envisioned that 3,3'-substituents on the binaphthyl moiety would be needed to ensure an efficient transfer of stereochemical information from the catalyst's stereoaxis to the substrate. Indeed, in the commonly accepted TS[11b] (see Figure 2 b), the substrate is located at a remarkable distance from the cyclopentadienone-fused ring, where the stereogenic unit of **CK** complexes is located. For this reason, we decided to synthesize a 3,3'-substituted complex as shown in Scheme 2.



Scheme 2. Synthesis of the 3,3'-disubstituted pre-catalyst (*R*)-**CK2**.

The bis-bromomethyl derivative (*R*)-**4**, prepared from (*R*)-BINOL as described by Maruoka et al.,[16] was converted into the corresponding bis-iodide (*R*)-**5**, which was then reacted with [(trimethylsilyl)ethynyl]lithium to yield the diyne (*R*)-**6** in 80% yield.[19] Remarkably, this double alkynylation only proceeded in the presence of methoxy groups in the 3,3'-positions, which prevented us from preparing other 3,3'-substituted derivatives. Compound (*R*)-**6** was then cyclized in the presence of $Fe_2(CO)_9$ to yield the 3,3'-dimethoxy substituted pre-catalyst (*R*)-**CK2**. Attempts to grow crystals of complexes **CK1** and **CK2** failed due to their high solubility in the most common organic solvents. We thus decided to convert **CK2** in the corresponding 3,3'-dihydroxy derivative **CK3** (Scheme 3), as we expected the latter to be easier to crystallize in apolar solvents. Quite harsh reaction conditions (BBr_3 at 85 °C with Bu_4NI as activator[20]) were necessary to achieve full deprotection. Nevertheless, compound (*R*)-**CK3** could be obtained in good yield (80%), which confirmed the remarkable stability of the iron cyclopentadienone complex.



Scheme 3. Synthesis of complex (*R*)-**CK3** by demethylation of (*R*)-**CK2**.

To our delight, crystals suitable for X-ray diffraction analysis could be obtained by slow diffusion of hexane into a DCM solution of complex **CK3**.[21]

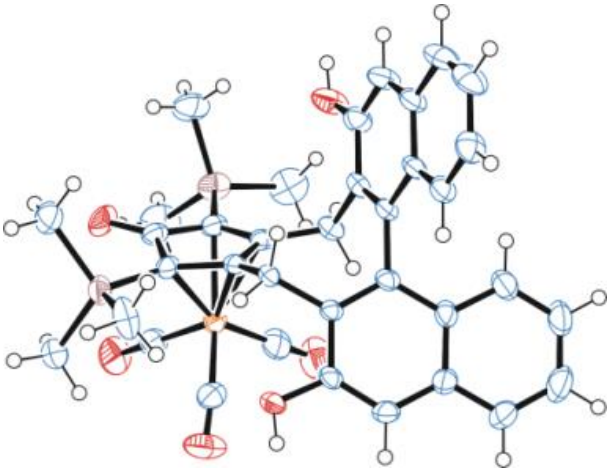


Figure 3. ORTEP diagram of the molecular structure of (*R*)-**CK3** (thermal ellipsoids set at the 50% probability level). Co-crystallized solvent molecules are omitted for clarity.

Pre-catalysts **CK1**, **CK2** and **CK3** were initially tested in the AH of acetophenone **S1** (Table 1, entry 1-3) under the conditions described by Beller and co-workers,[13] i.e. employing K_2CO_3 as activator to form the corresponding complexes ***act*-CK** in situ (see Figure 1 b). In each of the three experiments a moderate conversion (54-68%) was obtained, along with enantioselectivity in favor of (*S*)-**1**-phenylethanol **P1**.[22] Very low conversions (< 5%) were observed in the absence of H_2 suggesting that the hydrogenation pathway is predominant over the transfer hydrogenation from *i*PrOH.[13a,23] In agreement with our expectation, substitution at the 3,3'-positions of the binaphthyl moiety strongly affects the level of enantioselectivity: the observed *ee* follows the same trend of the steric bulk of 3,3'-

substituents: H (**CK1**, entry 1) << OH (**CK3**, entry 3) < OMe (**CK2**, entry 2).

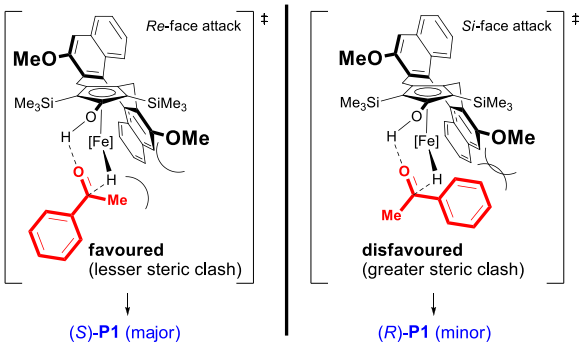
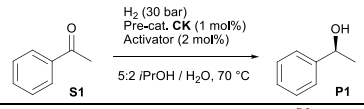


Figure 4. Stereoselection model based on the commonly accepted TS of ***act*-K**-catalyzed AH.[11b]

Remarkably, the observed stereochemical preference for (*S*)-**P1** is consistent with a pericyclic TS[11b] where **S1** orients its larger substituent (Ph) away from the binaphthyl 3-substituent (OMe) to minimize steric clash (Figure 4). The most enantioselective pre-catalyst **CK2** was selected for further optimization of the reaction parameters. First of all, a series of different activators were screened (Table 1, entry 4-11): while K_2CO_3 confirmed to be the most efficient inorganic base in terms of conversion (entry 2 vs. entry 4-10), the oxidative CO decomplexation with Me_3NO[12] turned out to be the most efficient activation methodology, leading to high conversion (entry 11).

Table 1. Test of **CK** pre-catalysts in the AH of acetophenone **S1** and screening of different activators.[a]

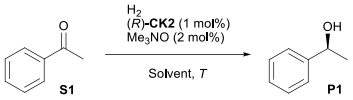


Entry	CK	Activator	Conv. (%)[b]	*ee* (%)[b,c]
1	**CK1**	K_2CO_3	62	8
2	**CK2**	K_2CO_3	54	49
3	**CK3**	K_2CO_3	68	47
4	**CK2**	Li_2CO_3	9	52
5	**CK2**	Na_2CO_3	25	53
6	**CK2**	Cs_2CO_3	29	51
7	**CK2**	LiOH	49	51
8	**CK2**	NaOH	35	50
9	**CK2**	KOH	30	52
10	**CK2**	K_3PO_4	23	53
11	**CK2**	Me_3NO	84	50

[a] Reaction conditions: **S1**/**CK**/activator = 100:1:2, P_{H2} = 30 bar, solvent = 5:2 *i*PrOH/H_2O, c_0 (**S1**) = 1.43 M, *T* = 70 °C, reaction time = 18 h. [b] Determined by GC equipped with a chiral capillary column (MEGADEX DACTBSβ, diacetyl-*t*-butylsilyl-β-cyclodextrin). [c] Absolute configuration: *S* in all cases (assigned by comparison of the optical rotation sign with literature data[22]).

The optimization was continued by assessing the effect of changing H_2 pressure, temperature and solvent (Table 2). We found that neither increasing pressure (entry 2) nor temperature (entry 3) led to full conversion, which instead could be obtained by increasing the catalyst loading to 2 mol% (entry 5; isolated yield = 94%). Lowering the temperature to 50 °C increased the *ee* to 55%, but at the cost of conversion (entry 4). We next screened several different solvents (entry 7-15), but all of them gave lower conversions compared to the 5:2 *i*PrOH/H_2O mixture. In particular, the presence of water turned out to be beneficial for the conversion (*cf.* entry 1 and 7).

Table 2. Optimisation of reaction parameters of the AH of acetophenone **S1** promoted by pre-catalyst **CK2**.[a]



Entry	Solvent	*P* (bar)	*T* (°C)	Conv. (%)[b]	*ee* (%)[b,c]
1	5:2 *i*PrOH/H_2O	30	70	84	50
2	5:2 *i*PrOH/H_2O	50	70	85	51
3	5:2 *i*PrOH/H_2O	30	80	59	50
4	5:2 *i*PrOH/H_2O	30	50	33	55
5[d]	5:2 *i*PrOH/H_2O	30	70	100[e]	50
6[f]	5:2 *i*PrOH/H_2O	30	70	58	51
7	*i*PrOH	30	70	15	54
8	5:2 EtOH/H_2O	30	70	21	49
9	5:2 CF_3CH_2OH/H_2O	30	70	74	42
10	5:2 DME/H_2O	30	70	56	52
11	5:2 dioxane/H_2O	30	70	56	52
12	5:2 CH_3CN/H_2O	30	70	3	53
13	5:2 DMF/H_2O	30	70	26	54
14	5:2 DCE/H_2O	30	70	34	54
15	5:2 toluene/H_2O	30	70	8	53

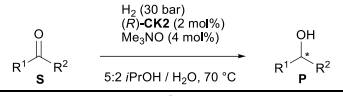
[a] Reaction conditions: **S1**/**CK2**/Me_3NO = 100:1:2, P_{H2} = 30 bar, c_0 (**S1**) = 1.43 M. [b,c] See the footnotes of Table 1. [d] 2 mol% **CK2** (4 mol% Me_3NO) employed. [e] Yield of the isolated product **P1** = 94%. [f] c_0 (**S1**) = 0.72 M.

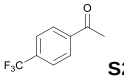
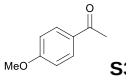
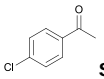
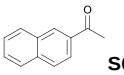
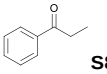
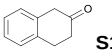
Having established the optimal reaction conditions for the ***act*-CK2**-catalyzed AH, we assessed the scope of the reaction (Table 3).

As expected, electron-poor acetophenone derivatives (**S2** and **S4**) were more reactive than electron-rich 4'-methoxyacetophenone **S3** (Table 3, entry 2 vs entries 1 and 3). As a general trend for the methyl ketones (Table 3, entries 1-6 and 11-13), *S*-selectivity was always observed and the *ee* increased along with the steric bulk of the other C=O substituent (*t*Bu > 1-Np > Cy > 2-Np ≈ Ph ≈ Py ≈ *p*-X-C_6H_4 >> *i*Bu). Unfortunately, the most hindered substrates also gave lower conversions (e.g., Table 3, entry 4 and 13). The hydrogenation of 3-acetylpyridine **S7** also proved to be sluggish (Table 3, entry 6), possibly due to its ability to coordinate iron. A similar trend was observed for cyclic ketones, with 1-tetralone **S9** giving much higher *ee* (77%) and lower conversion than 2-tetralone **S10** (Table 3, entry 8 vs 9). Surprisingly, the reduction of **S10** and **S11** showed opposite stereochemical preference (*R*- instead of *S*-product). Propiophenone **S8** (Table 3, entry 7) gave similar conversion and slightly better *ee* than acetophenone **S1** (Table 2, entry 4).

In summary, we have developed new BINOL-derived chiral cyclopentadienone iron complexes (**CK**), which display high stability to air, moisture and chromatography. The new compounds can be converted in situ into the corresponding hydroxycyclopentadienyl complexes ***act*-CK**, which catalyze the AH of ketones with better enantioselectivities (up to 77% *ee*) than any other reported chiral cyclopentadienone iron complex.[5c,12d] As the obtained enantioselectivity increases with the steric bulk of the binaphthyl 3,3'-substituents of **CK**, future work will focus on the synthesis of new complexes with various 3,3'-substituents starting from the 3,3'-dihydroxysubstituted complex **CK3**.

Table 3. Substrate screening for the ***act*-CK2**-catalyzed AH.[a]



Entry	Subst.	Conv. (%)[b]	*ee* (%),[c] abs. conf.[d]
1	 **S2**	100	46, *S*
2	 **S3**	64	50, *S*
3	 **S4**	100	51, *S*
4	 **S5**	43	68, *S*
5	 **S6**	99	51, *S*
6	 **S7**	35	50, *S*
7	 **S8**	97	57, *S*
8[e]	 **S9**	25	77, *S*
9	 **S10**	100	13, *R*
10	 **S11**	78	59, *R*
11	 **S12**	89	61, *S*
12	 **S13**	76	0
13	 **S14**	22	77, *S*

[a] Reaction conditions: substrate/**CK2**/Me_3NO = 100:2:4, P_{H2} = 30 bar, solvent = 5:2 *i*PrOH/H_2O, c_0 (substrate) = 1.43 M, T = 70 °C, reaction time = 18 h. [b] Determined by GC equipped with a chiral capillary column (see the Supporting Information). [c] Determined by GC or HPLC equipped with a chiral capillary column (see the Supporting Information). [d] Assigned by comparison of the sign of optical rotation with literature data (see the Supporting Information). [e] Substrate/**CK2**/Me_3NO = 100:5:10.

Experimental Section

General procedure for the asymmetric hydrogenation. Hydrogenations were run in a 450 mL Parr autoclave equipped with a removable aluminum block that can accommodate up to fifteen magnetically stirred 7 mL-glass vials. The catalyst (0.005 mmol – 1 mol%, or 0.01 mmol – 2 mol%) was weighed in the glass vials, which were accommodated in the aluminum block after adding magnetic stirring bars in each of them. The block was put in a Schlenk tube, where it was subjected to three vacuum/nitrogen cycles. *i*PrOH (0.25 mL) was added in each vial and stirring was started. Me_3NO (0.01 mmol – 2 mol%, or 0.02 mmol – 4 mol%) was added into each vial as a H_2O solution (0.1 mL). After stirring for 10 min at R.T. under nitrogen, the substrate (0.5 mmol) was added to the mixtures. Each vial was capped with a Teflon septum pierced by a needle, the block was transferred into the autoclave and stirring was started. After purging four times with hydrogen at the selected pressure, heating was started. The reactions were stirred overnight under pressure of hydrogen and then analyzed for conversion and *ee* determination.

Acknowledgements

We thank the European Commission [ITN-EID “REDUCTO” PITN-GA-2012-316371] for financial support and for predoctoral fellowships (to P. Gajewski and M. Renom-Carrasco). L. Pignataro thanks the Dipartimento di Chimica, Università di Milano, for financial support (Piano di sviluppo dell’Ateneo—anno 2014—Linea B.1—grants for young researchers).

Keywords: asymmetric catalysis • asymmetric hydrogenation • chiral Fe-complexes • homogeneous catalysis • ketone reduction

[1] For a comprehensive review of the topic, see: J. G. de Vries, C. J. Elsevier, *Handbook of Homogeneous Hydrogenation*, Wiley-VCH, Weinheim, **2007**.

[2] a) D. J. Ager, A. H. M. de Vries, J. G. de Vries, *Chem. Soc. Rev.* **2012**, *41*, 3340-3380; (b) *Asymmetric Catalysis on Industrial Scale, 2nd ed. Challenges, Approaches, Solutions*, H.-U. Blaser, H.-J. Federsel, Wiley-VCH, Weinheim, **2010**.

[3] For general reviews on iron catalysis, see: a) M. Darwish, M. Wills, *Catal. Sci. Technol.* **2012**, *2*, 243-255; b) S. Enthaler, K. Junge, M. Beller, *Angew. Chem.* **2008**, *120*, 3363-3367; *Angew. Chem. Int. Ed.* **2008**, *47*, 3317-3321.

[4] For selected reviews covering Fe-catalyzed AH, see: (a) K. Gopalaiah, *Chem. Rev.* **2013**, *113*, 3248-3296; (b) K. Junge, K. Schröder, M. Beller, *Chem. Commun.* **2011**, *47*, 4849-4859; (c) R. H. Morris, *Chem. Soc. Rev.* **2009**, *38*, 2282-2291.

[5] a) Y. Li, S. Yu, X. Wu, J. Xiao, W. Shen, Z. Dong, J. Gao, *J. Am. Chem. Soc.* **2014**, *136*, 4031-4039; b) P. O. Lagaditis, P. E. Sues, J. F. Sonnenberg, K. Y. Wan, A. J. Lough, R. H. Morris, *J. Am. Chem. Soc.* **2014**, *136*, 1367-1380; c) A. Berkessel, S. Reichau, A. von der Höh, N. Leconte, J.-M. Neudörfl, *Organometallics* **2011**, *30*, 3880-3887; d) Y. Wang, M. Zheng, X. Li, L. Si, D. He, Y. Zhao, *Int. J. Chem.* **2011**, *3*, 118-122; e) C. Sui-Seng, F. N. Haque, A. Hadzovic, A.-M. Pütz, V. Reuss, N. Meyer, A. J. Lough, M. Zimmer-De Iuliis, R. H. Morris, *Inorg. Chem.* **2009**, *48*, 735-743; f) C. Sui-Seng, F. Freutel, A. J. Lough, R. H. Morris, *Angew. Chem.* **2008**, *120*, 954-957; *Angew. Chem. Int. Ed.* **2008**, *47*, 940-943.

[6] S. Zhou, S. Fleischer, K. Junge, M. Beller, *Angew. Chem.* **2011**, *123*, 5226-5230; *Angew. Chem. Int. Ed.* **2011**, *50*, 5120-5124.

[7] Iron dialkyl complexes with chiral bidentate phosphines were used in the hydrogenation of olefins, but no enantioselectivity was observed with prochiral substrates, see: J. M. Hoyt, M. Shevlin, G. W. Margulieux, S. W. Krska, M. T. Tudge, P. J. Chirik, *Organometallics* **2014**, *33*, 5781-5790.

[8] For a recent review on iron cyclopentadienone complexes, see: A. Quintard, J. Rodriguez, *Angew. Chem.* **2014**, *126*, 4124-4136; *Angew. Chem. Int. Ed.* **2014**, *53*, 4044-4055.

[9] G. N. Schrauzer, *J. Am. Chem. Soc.* **1959**, *81*, 5307-5310.

[10] H.-J. Knölker, E. Baum, H. Goesmann, R. Klauss, *Angew. Chem.* **1999**, *111*, 2196-2199; *Angew. Chem. Int. Ed.* **1999**, *38*, 2064-2066.

[11] a) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2007**, *129*, 5816-5817; b) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2009**, *131*, 2499-2507.

[12] a) S. Moulin, H. Dentel, A. Pagnoux-Ozherelyeva, S. Gaillard, A. Poater, L. Cavallo, J.-F. Lohier, J.-L. Renaud, *Chem. Eur. J.* **2013**, *19*, 17881-17890; b) D. S. Mérel, M. Elie, J.-F. Lohier, S. Gaillard, J.-L. Renaud, *ChemCatChem* **2013**, *5*, 2939-2945; c) A. Pagnoux-Ozherelyeva, N. Pannetier, M. D. Mbaye, S. Gaillard, J.-L. Renaud, *Angew. Chem.* **2012**, *124*, 5060-5064; *Angew. Chem. Int. Ed.* **2012**, *51*, 4976-4980; d) J. P. Hopewell, J. E. D. Martins, T. C. Johnson, J. Godfrey, M. Wills, *Org. Biomol. Chem.* **2012**, *10*, 134-145.

[13] a) S. Fleischer, S. Zhou, K. Junge, M. Beller, *Angew. Chem.* **2013**, *125*, 5224-5228; *Angew. Chem. Int. Ed.* **2013**, *52*, 5120-5124; b) A. Tlili, J. Schranck, H. Neumann, M. Beller, *Chem. Eur. J.* **2012**, *18*, 15935-15939.

[14] a) T. Zell, Y. Ben-David, D. Milstein, *Angew. Chem.* **2014**, *126*, 4773-4777; *Angew. Chem. Int. Ed.* **2014**, *53*, 4685-4689; b) D. Srimani, Y. Diskin-Posner, Y. Ben-David, D. Milstein, *Angew. Chem.* **2013**, *125*, 14381-14384; *Angew. Chem. Int. Ed.* **2013**, *52*, 14131-14134; c) R. Langer, M. A. Iron, L. Konstantinovski, Y. Diskin-Posner, G. Leitus, Y. Ben-David, D. Milstein,

Chem. Eur. J. **2012**, *18*, 7196-7209; d) R. Langer, G. Leitus, Y. Ben-David, D. Milstein, *Angew. Chem.* **2011**, *123*, 2168-2172; *Angew. Chem. Int. Ed.* **2011**, *50*, 2120-2124; e) P. J. Chirik, K. Wieghardt, *Science* **2010**, *327*, 794-795; f) R. J. Trovitch, E. Lobkovsky, E. Bill, P. J. Chirik, *Organometallics* **2008**, *27*, 1470-1478; g) S. C. Bart, E. J. Hawrelak, E. Lobkovsky, P. J. Chirik, *Organometallics* **2005**, *24*, 5518-5527.

[15] a) B. Ye, N. Cramer, *Angew. Chem.* **2014**, *126*, 8030-8033; *Angew. Chem. Int. Ed.* **2014**, *53*, 7896-7899; (*b*) B. Ye, N. Cramer, *J. Am. Chem. Soc.* **2013**, *135*, 636-639.

[16] T. Ooi, M. Kameda, K. Maruoka, *J. Am. Chem. Soc.* **2003**, *125*, 5139-5151.

[17] Conditions previously reported for the synthesis of a related biphenyl compound, see: R. R. Singidi, A. M. Kutney, J. C. Gallucci, T. V. RajanBabu, *J. Am. Chem. Soc.* **2010**, *132*, 13078-13087.

[18] a) D. Kampen, C. Reisinger, B. List, *Top. Curr. Chem.* **2009**, *291*, 1-37; b) M. Terada, *Chem. Commun.* **2008**, 4097-4112.

[19] The reaction run under the conditions (copper catalysis) adopted for preparing the 3,3'-unsubstituted compound (*R*)-**3** did not show any conversion in this case.

[20] P. R. Brooks, M. C. Wirtz, M. G. Vetelino, D. M. Rescek, G. F. Woodworth, B. P. Morgan, J. W. Coe, *J. Org. Chem.* **1999**, *64*, 9719-9721.

[21] For full crystallographic data, selected distances/angles, and a comparison with related complexes, see the Supporting Information.

[22] Absolute configuration assigned by comparison of the sign of optical rotation with literature data, see: R. Patchett, I. Magpantay, L. Saudan, C. Schotes, A. Mezzetti, F. Santoro, *Angew. Chem.* **2013**, *125*, 10542-10545; *Angew. Chem. Int. Ed.* **2013**, *52*, 10352-10355.

[23] It is well-known that Fe-hydroxycyclopentadienyl complexes ***act*-K** (either pre-isolated or generated *in situ*) can also promote ketone transfer-hydrogenation and alcohol dehydrogenation processes, see a) Refs. 8, 11a, 12d; b) S. A. Moyer, T. W. Funk, *Tetrahedron Lett.* **2010**, *51*, 5430-5433.