ORGANIC LETTERS

2007
Vol. 9, No. 7
1371−1374

Ag^{+}-Assisted Hydrosilylation: Complementary Behavior of Rh and Ir Catalysts (Reversal of Enantioselectivity)

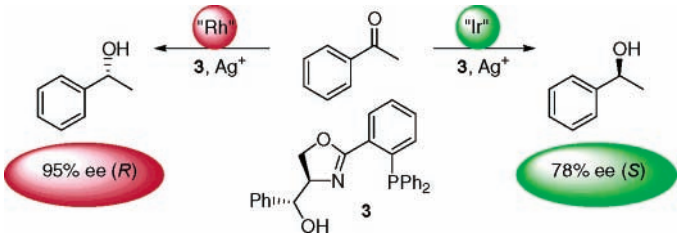
Anders Frölander and Christina Moberg*

KTH School of Chemical Science and Engineering, Organic Chemistry, SE 100 44 Stockholm, Sweden

kimo@kth.se

Received February 2, 2007

ABSTRACT



The presence of a suitably situated hydroxy function in a PHOX ligand leads to an enhancement of the enantioselectivity in Rh-catalyzed hydrosilylations of prochiral ketones in the presence of $AgBF_4$ (95% ee for acetophenone as compared to 75% using *i*-Pr−phosphinooxazoline (PHOX)). Exchanging Rh for Ir affords the product with the opposite absolute configuration (78% ee).

The introduction of functional groups capable of taking part in secondary interactions with the metal ion in transition-metal catalysts may occasionally lead to enhanced selectivity in catalytic reactions.[1] The presence of internal hydroxy groups has, for example, been shown to provide significant effects on the selectivity in catalytic reactions. An early example was provided by Knowles and co-workers, who demonstrated that substitution of methoxy for hydroxy groups in DIPAMP led to increased enantioselectivity in Rh-catalyzed hydrogenations, probably as a result of coordination of oxygen to Rh.[2] Several examples have subsequently been described, whereby the oxygen atom in a hydroxy group takes part in coordination to the metal center in a catalytically active complex. This may result in conformational restrictions and, as a consequence, enhanced enantioselectivity, although occasionally at the expense of the reactivity.[3]

In addition to serving as hemilabile oxygen ligands to metal ions, hydroxy groups can be engaged in hydrogen bonding to electron-rich heteroatoms and, in some cases, to low valent metal ions.[4] We have been able to show that Pd(0) serves as a hydrogen-bond acceptor in π−olefin complexes with ligands containing properly situated hydroxy groups, thereby affecting the conformation and, consequently, the stereochemistry in palladium-catalyzed allylic alkylations.[5] Major differences were also found between hydroxy- and methoxy-containing phosphinooxazoline[6] (PHOX) ligands **1**−**4** (Figure 1) in palladium- and iridium-catalyzed allylations.[7] These differences may also be explained by a hydrogen bond with the metal ion acting as the proton acceptor. PHOX ligands containing properly situated hydroxy

(1) Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 857−871.
(2) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106−112.
(3) Börner, A. *Eur. J. Inorg. Chem.* **2001**, 327−337 and references therein.
(4) (a) Epstein, L. M.; Shubina, E. S. *Coord. Chem. Rev.* **2002**, *231*, 165−181. (b) Brammer, L.; Zhao, D.; Lapido, F. T; Braddock-Wilking, J. *Acta Crystallogr., Sect. B* **1995**, *51*, 632−640. (c) Braga, D.; Grepioni, F.; Tedesco, E.; Biradha, K.; Desiraju, G. R. *Organometallics* **1997**, *16*, 1846−1856.
(5) Hallman, K.; Wondimagegn, T.; Frölander, A.; Svensson, M.; Moberg, C. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5400−5404.
(6) (a) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566−568. (b) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769−1772. (c) Dawson, G. J.; Frost, C. G.; Williams, J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149−3150.
(7) Frölander, A.; Lutsenko, S.; Privalov, P.; Moberg, C. *J. Org. Chem.* **2005**, *70*, 9882−9891.

10.1021/ol0702730 CCC: $37.00
Published on Web 02/27/2007

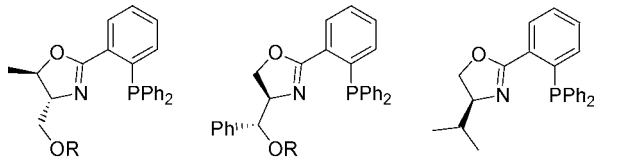


Figure 1. Phosphinooxazoline ligands.

groups can therefore be expected to interact with both low valent metal ions (via hydrogen bonding) and high valent metal ions (via oxygen coordination). Both types of interactions may be expected to have an influence on the stereochemistry of catalytic reactions.

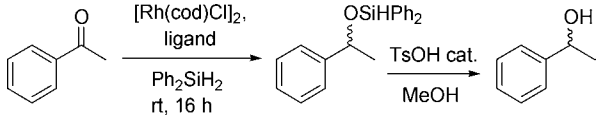
Having access to these functionalized PHOX ligands, we decided to investigate their behavior in Rh- and Ir-catalyzed hydrosilylations of prochiral ketones.[8] Metal-catalyzed hydrosilylations of ketones have emerged as highly versatile reactions, affording enantioenriched products under mild conditions, using complexes based on Rh, Ir, Ti, Zn, and Cu.[9]

PHOX ligands were early employed in hydrosilylations of ketones and resulted in moderate to high enantioselectivities.[10] Reduction of acetophenone with diphenylsilane, often used as a benchmark reaction, resulted in 73−82% ee using a Rh catalyst containing *i*-Pr−PHOX (**5**). Improved selectivity was achieved using an aminoindanol-derived PHOX (94% ee)[11] and an oxazolylferrocene−phosphine ligand (Rh, 91%; Ir, 96% ee).[9b,12] The particular aim of our study was to examine whether an interaction of the hydroxy group in **1** and **3** with the metal ion would influence the stereochemistry of the reaction.

Rh-catalyzed hydrosilylations are known to proceed by oxidative addition of the silane to Rh(I) followed by coordination of the substrate and insertion of the carbonyl bond into the rhodium−silicon bond and subsequent reductive elimination.[13] Because the enantiodetermining step involves Rh(III) complexes only, it is highly unlikely that hydrogen bonding between the hydroxy group and the metal affects the stereochemistry of the product. Coordination of oxygen to the metal is a more likely secondary interaction which might be of importance for the enantioselectivity.

First, Rh-catalyzed hydrosilylation of acetophenone was performed employing diphenylsilane together with $[Rh(cod)Cl]_2$ and ligands **1**−**4**. Moderate enantioselectivities were observed (entries 1, 3, 5, and 8, Table 1), indeed lower than those reported using **5** and other standard PHOX ligands.[10]

Table 1. Hydrosilylations of Acetophenone Using $[Rh(cod)Cl]_2$



entry[a]	ligand	conv (%)[b]	ee (%)[c]	abs conf[d]
1	**1**	100	12	*S*
2	**1**[e]	100	63	*S*
3	**2**	100	70	*S*
4	**2**[e]	100	60	*S*
5	**3**	100	66	*R*
6	**3**[e]	97	91	*R*
7	**3**[e,f]	100	95	*R*
8	**4**	100	56	*R*
9	**4**[e]	100	87	*R*
10	**5**	100	73	*R*
11	**5**[e]	91	69	*R*

[a] Reaction conditions unless otherwise noted: $[Rh(cod)Cl]_2$ (0.5 mol %), ligand (2 mol %), acetophenone (1.0 mmol), diphenylsilane (1.2 mmol), THF (1 mL), 16 h reaction time, rt. [b] Determined by NMR. Yield of silyl enol ether: 2−10%. [c] Determined by chiral GC. [d] Assigned by comparing the sign of optical rotation with the literature data. [e] $AgBF_4$ (2 mol %) added. [f] Reaction performed at 0 °C. Yield of silyl enol ether: <4%.

To favor coordination of oxygen to the metal ion, cationic rhodium complexes, obtained by abstraction of the chloride ion by $AgBF_4$, were then employed for the reaction. We were pleased to find that under these conditions, the product was obtained with considerably higher enantioselectivity, the best result (91% ee, entry 6, Table 1) being obtained with **3**. An even higher ee was obtained at 0 °C under otherwise identical conditions (95% ee, entry 7). The counterion evidently had an effect because addition of other silver salts led to inferior results (AgOTf, 79% ee; $AgPF_6$, 80% ee). Other experimental details were also found to be important: employing only 1 equiv of the ligand gave 83% ee at room temperature, and using the alternative Rh precursor $Rh(cod)_2BF_4$ resulted in only 58% ee.

To determine whether these intriguing effects accompanying the addition of $AgBF_4$ were connected to our PHOX ligands or were the result of some more general phenomenon, we subjected the standard *i*-Pr−PHOX ligand **5** to the hydrosilylation of acetophenone. With the neutral rhodium complex, the result achieved was in agreement with those published[10] (73% ee, entry 10, Table 1; 75% ee at 0 °C). Together with $AgBF_4$, this ligand afforded a slightly *lower* ee (69%, entry 11),[14] indicating that the ee enhancement for ligands **1** and **3** as well as **4** is somehow linked to the oxygen-

(8) (a) Nishiyama, H.; Itoh, K. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley: New York, 2000. (b) Riant, O.; Mostefaï, N.; Courmarcel, J. *Synthesis* **2004**, 2943−2958.

(9) For representative examples, see: (a) Tao, B.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3892−3894. (b) Nishibayashi, Y.; Segawa, K.; Takada, H.; Ohe, K.; Uemura, S. *Chem. Commun.* **1996**, 847−848. (c) Yun, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 5640−5644. (d) Bette, V.; Mortreux, A.; Savoia, D.; Carpentier, J.-F. *Tetrahedron* **2004**, *60*, 2837−2842. (e) Lipshutz, B. H.; Noson, K.; Chrisman, W. *J. Am. Chem. Soc.* **2001**, *123*, 12917−12918.

(10) (a) Newman, L. M.; Williams, J. M. J.; McCague, R.; Potter, G. A. *Tetrahedron: Asymmetry* **1996**, *7*, 1597−1598. (b) Langer, T.; Janssen, J.; Helmchen, G. *Tetrahedron: Asymmetry* **1996**, *7*, 1599−1602.

(11) Sudo, A.; Yoshida, H.; Saigo, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3205−3208.

(12) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486−5487.

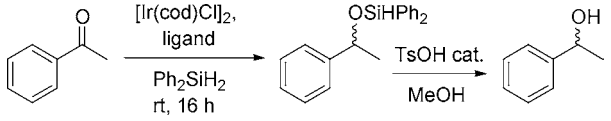
(13) Imamoto, T.; Itoh, T.; Yamanoi, Y.; Narui, R.; Yoshida, K. *Tetrahedron: Asymmetry* **2006**, *17*, 560−565 and references therein.

(14) This is consistent with previous observations; see ref 10a.

containing substituents. A probable explanation for the observed results is that the oxygen atom coordinates to rhodium(III), thereby increasing the rigidity of the catalyst and therefore the enantiodiscriminating power.

Use of our ligands together with $[Ir(cod)Cl]_2$ in the hydrosilylation of acetophenone led to products with moderate ee's (entries 1, 3, 5, and 8, Table 2). Addition of $AgBF_4$ also in this case substantially improved the enantioselectivities. The best result at room temperature was again obtained with ligand **3** (77% ee, entry 6). To our surprise, this product had the opposite absolute configuration to those of the product obtained in the Rh-catalyzed process. The Rh- and Ir-catalyzed processes do thus exhibit complementary behavior. Such behavior has previously been observed for an oxazolylferrocene−phosphine[9b,12] as well as for a few other less selective ligands.[15] In analogy to what was observed in the Rh-catalyzed reactions, a less pronounced selectivity improvement was observed when AgOTf or $AgPF_6$ was added in place of $AgBF_4$. The enantioselectivities in Ir-catalyzed reactions with ligand **5** were low in both the presence and absence of $AgBF_4$ (entries 10 and 11).

Table 2. Hydrosilylations of Acetophenone Using $[Ir(cod)Cl]_2$



entry[a]	ligand	conv (%)[b]	ee (%)[c]	abs conf[d]
1	**1**	99	2	*S*
2	**1**[e]	99	22	*R*
3	**2**	100	8	*S*
4	**2**[e]	98	26	*R*
5	**3**	97	33	*S*
6	**3**[e]	98	77	*S*
7	**3**[e,f]	97	78	*S*
8	**4**	100	16	*R*
9	**4**[e]	98	53	*S*
10	**5**	98	8	*R*
11	**5**[e]	99	32	*S*

[a] Reaction conditions unless otherwise noted: $[Ir(cod)Cl]_2$ (0.5 mol %), ligand (2 mol %), acetophenone (1.0 mmol), diphenylsilane (1.2 mmol), THF (1 mL), 16 h reaction time, rt. [b] Determined by NMR. Yield of silyl enol ether: 2−15%. [c] Determined by chiral GC. [d] Assigned by comparing the sign of optical rotation with the literature data. [e] $AgBF_4$ (2 mol %) added. [f] Reaction performed at 0 °C. Yield of silyl enol ether: <5%.

To find evidence for the assumption that oxygen coordinates to the metal center, the Ir(I) complex **6** (Figure 2) was prepared by stirring **3** with $[Ir(cod)Cl]_2$ followed by anion exchange with $AgBF_4$. Although the complex has not yet been fully characterized, its ^1H and ^{13}C NMR spectra have been assigned. Large downfield shifts were observed for H_a (from 4.11 to 5.91 ppm) and C_a (from 77.4 to 84.0 ppm) in the complex compared to the free ligand, consistent with

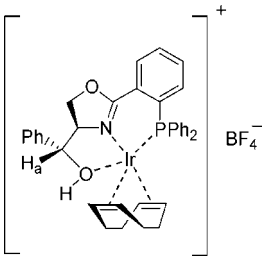
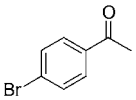
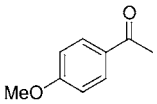
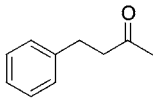
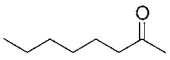


Figure 2. Complex **6**.

the proposed interaction of the hydroxy group with the cationic metal. A signal for the hydroxy proton (at 3.66 ppm at −40 °C) shows that the ligand is not deprotonated.

Encouraged by the results for acetophenone, we decided to subject a number of prochiral ketones to the hydrosilylation using ligand **3** and either $[Rh(cod)Cl]_2$ or $[Ir(cod)Cl]_2$ (Table 3). We found that for all ketones the two catalytic systems gave rise to products with different absolute configurations. For 4-bromoacetophenone and 4-methoxyacetophenone, the ee's were good but somewhat lower than that for acetophenone (entries 1−4, Table 3). For benzylacetone and 2-octanone, good ee's were observed in the rhodium-catalyzed reactions, but low ee's were observed in the iridium system.

Table 3. Hydrosilylations of Various Ketones Using $[Rh(cod)Cl]$ or $[Ir(cod)Cl]_2$ and **3**

entry[a]	ketone	M	conv (%)[b]	ee (%)[c]	abs conf[d]
1		Rh	91	81	*R*
2		Ir	98	69	*S*
3		Rh	100	85	*R*
4		Ir	97	62	*S*
5		Rh	95	67	*R*
6		Ir	98	13	*S*
7		Rh	94	55	*R*
8		Ir	100	9	*S*

[a] Reaction conditions unless otherwise noted: $[M(cod)Cl]_2$ (0.5 mol %), ligand **3** (2 mol %), $AgBF_4$ (2 mol %), ketone (1.0 mmol), diphenylsilane (1.2 mmol), THF (1 mL), 16 h reaction time, rt. [b] Determined by NMR. Yield of silyl enol ether, entries 1−4: <6%, entries 5−8: <3%. [c] Determined by chiral GC or HPLC. [d] Assigned by comparing the sign of optical rotation with the literature data.

In conclusion, we have found that, in the presence of $AgBF_4$, PHOX ligand **3**, easily available in two steps from commercial starting materials, provides an excellent enantioselectivity in the Rh-catalyzed hydrosilylation of acetophenone, due to involvement of the oxygen function. The

(15) (a) Faller, J. W.; Chase, K. J. *Organometallics* **1994**, *13*, 989−992. (b) Kinting, A.; Kreuzfeld, H.-J.; Abicht, H.-P. *J. Organomet. Chem.* **1989**, *370*, 343−349.

analogous catalyst based on Ir was shown to exhibit complementary behavior, giving the opposite enantiomer of the product also with good enantioselectivity.

Acknowledgment. This work was financed by the Swedish Research Council.

Supporting Information Available: Experimental procedures for the catalytic reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0702730