C. R. Chimie 13 (2010) 353–357

Contents lists available at ScienceDirect

Comptes Rendus Chimie

www.sciencedirect.com

Full paper / Mémoire

Enantioselective hydrosilylation of prochiral ketones catalyzed by chiral BINAP-copper(I) complexes

Jean-Thomas Issenhuth, Samuel Dagorne **, Stéphane Bellemin-Laponnaz *

CNRS, université de Strasbourg, institut de chimie, 1, rue Blaise-Pascal, 67000 Strasbourg, France

ARTICLE INFO

Article history:
Received 8 July 2009
Accepted after revision 4 November 2009
Available online 21 January 2010

Keywords:
Asymmetric catalysis
Hydrosilylation
Copper
Hydride

ABSTRACT

The CuCl/NaO*t*-Bu/BINAP system was found to efficiently catalyze the hydrosilylation of aryl alkyl ketones with excellent enantioselectivities by using phenyl methyl silane as a stoichiometric hydride source. High enantiomeric excesses (up to 97%) and excellent yields (up to 99%) were obtained.

Catalytic asymmetric reduction of prochiral ketones using transition metal complexes is an easy way for the access to chiral non-racemic secondary alcohols, which are very important intermediates in organic synthesis. Although conversion of the ketone in the corresponding alcohol by hydrosilylation requires a two-step reaction (addition of Si-H bond followed by hydrolysis), it is still an attractive method since quantitative yields are usually obtained. It is also a good alternative to hydrogenation, which usually requires H_2 pressure [1].

Investigations on hydrosilylation of ketones with rhodium-phosphine systems [2] have led to the development of efficient catalysts that achieve high levels of enantiomeric excess (above 90%) [3,4]. Ruthenium-based systems may also afford good enantioselectivities [5]. More recently, efficient asymmetric hydrosilylation reactions using cheaper and less toxic metals such as zinc [6], titanium [7], iron [8] and copper [9] have been reported.

The first report on the use of copper hydride along with a chiral phosphine for asymmetric hydrosilylation was published by Brunner and Miehling in 1984 [10]. Almost two decades later, Lipshutz and coworkers accomplished a breakthrough [9,11].[1] Thus, when coordinated by a highly sterically demanding BIPHEP or SEGPHOS-type ligand, CuH appears to be an efficient catalyst for the hydrosilylation of ketones with a high level of enantioselectivity (above 90% ee). Moreover, they showed that inexpensive silanes such as polymethylhydrosiloxane (PMHS) could be used. Among the ligands tested, cheap BINAP was found to lead a somewhat lower level of enantioselectivity (e.g. 75% ee with acetophenone) [12].

We recently reported that the Cu(I)/BINAP catalytic system, when combined with $PhMeSiH_2$ as a reducing agent may allow the reduction of various aryl alkyl ketones with a high-level of enantioselectivity [13]. In this report, we provide a full account of our investigations on the Cu(I)/BINAP-catalyzed hydrosilylation of ketones.

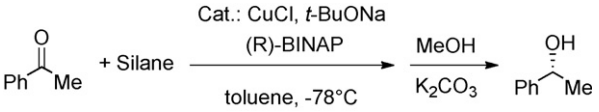
The active species of the system was formed in situ by the now well-established procedure involving CuCl, NaOtBu and diphosphine [4]. Acetophenone was chosen

* Corresponding author.
** Co-corresponding author.
E-mail addresses: dagorne@chimie.u-strasbg.fr (S. Dagorne), bellemin@chimie.u-strasbg.fr (S. Bellemin-Laponnaz).

[1] An efficient asymmetric conjugate reduction of α, β-unsaturated esters or cyclic enones using chiral phosphine/Cu-H systems was also reported.

1631-0748/$ – see front matter
doi:10.1016/j.crci.2009.11.002

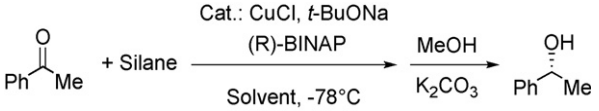
Table 1
Asymmetric hydrosilylation of acetophenone with the (*R*)-BINAP/CuCl/tBuONa system by various silanes.



Entry	Silane	ee (%) at r. t.	ee (%) at −78 °C
1	Ph_2SiH_2	76	80
2	$(Mes)_2SiH_2$	78	79
3	(1-napht)$PhSiH_2$	77	90
4	(o-tol)$PhSiH_2$	79	91
5	$PhMeSiH_2$	81	93
6	Ph*t*BuSiH_2	79	93

Cat.: CuCl, *t*-BuONa, (R)-BINAP (5 mol%); reaction time: 18 hours; ee values were determined by chiral GC analysis.

Table 2
Asymmetric hydrosilylation of acetophenone: solvent effect.



Entry	Silane	Toluene ee (%)	THF ee (%)	Diethyl ether ee (%)
1	(*o*-tol)$PhSiH_2$	91	88	87
2	$PhMeSiH_2$	93	91	88
3	Ph*t*BuSiH_2	93	91	89

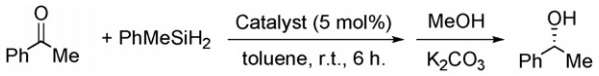
Cat.: CuCl, *t*-BuONa, (R)-BINAP (5 mol%); reaction time: 18 hours; ee values were determined by chiral GC analysis.

as a reference substrate. As an initial study, we screened various silanes as reducing agents and found that the level of enantioselectivity was slightly dependent on the nature of the silane (Table 1). Thus by using various dihydrosilane, the enantiomeric excess of the alcohol product ranged between 76% ee with Ph_2SiH_2 and 81% ee with $PhMeSiH_2$ at room temperature.[2] By lowering the temperature at −78 °C, four dihydrosilanes out of six allowed ee's above 90%. In particular, we found that the hydrosilylation of acetophenone is highly enantioselective in the presence of $PhMeSiH_2$ or Ph(*t*Bu)SiH_2 (93% ee, entries 5–6). The commercial availability of phenylmethylsilane prompted us to use this silane for further studies. A study of solvent effect showed that toluene was the solvent of choice as displayed Table 2. THF and diethyl ether were also found to be good solvents for the reaction albeit with somewhat lower enantioselectivity.

It has been reported that various copper salts (including copper(II)) could be used for hydrosilylation reactions [12]. Thus, we investigated the reaction with different copper sources (Table 3). $(CH_3CN)_4CuBF_4$, $CuCl_2$, $Cu(OAc)_2$ or CuF_2

[2] In our preliminarily communication, we originally got a racemic product when (1-napht)$PhSiH_2$ was used as reducing agent. Reinvestigation of the reaction revealed that our original silane was not pure.

Table 3
Asymmetric hydrosilylation of acetophenone with various copper-based systems.



Entry	Catalyst [a]	ee (%)	Yield (%) [b]
1	CuCl/*t*-BuONa/BINAP	81	99
2	CuCl/BINAP	No reaction	
3	CuCl/*t*-BuONa	No reaction	
4	$(CH_3CN)_4CuBF_4$/*t*-BuONa/BINAP	76	97
5	CuF_2/BINAP	78	98
6	$CuCl_2.2H_2O$/*t*-BuONa/BINAP	78	97
7	$Cu(OAc)_2.H_2O$/BINAP	79	98

[a] (R)-BINAP was used.
[b] Isolated yield.

can be used, however, the level of enantioselectivity was found to be somewhat lower compared to CuCl (entry 1 vs. entries 4–7). Interestingly, no reaction occurred when CuCl/BINAP or CuCl/NaOt-Bu systems were used (entries 2–3). Thus, the system that combines CuCl with NaO*t*-Bu and BINAP appears to be best suited.

We also examined the influence of O_2 onto the catalysis, since Riant et al. showed that the complex fluorotris (triphenylphosphine)copper-bis(methanol) $CuF(PPh_3)_3.2$-MeOH combined with a chiral diphosphine was a good catalyst for the hydrosilylation of ketones especially in the presence of oxygen or air [12b,f]. Fig. 1 displays a parallel experiment under an atmosphere of dioxygen and dinitrogen using CuCl/NaOtBu/BINAP as precatalyst. To some extent, the reaction was found to be slower in the presence of oxygen. However, the enantiomeric excess of the final product remained unchanged (93% in both cases). Thus conducting the reaction under nitrogen seems to be necessary to get the better results.

High enantioselectivities were also obtained in the reduction of a variety of aryl alkyl ketones under the

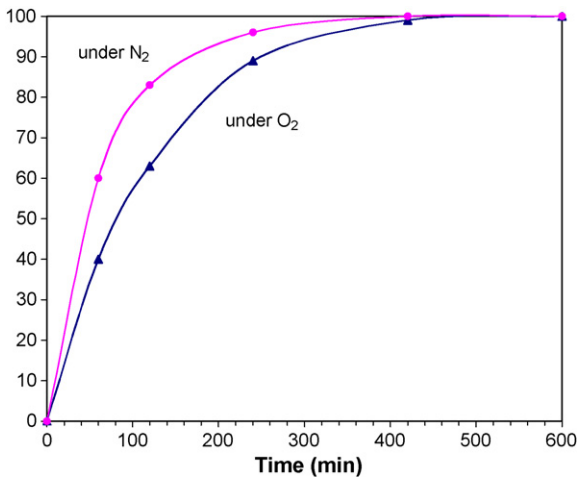
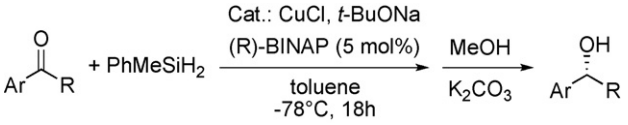
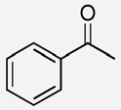
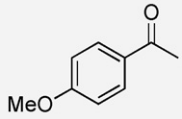
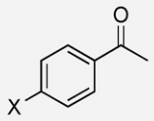
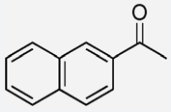
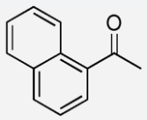
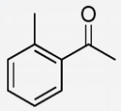
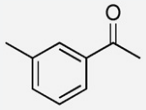
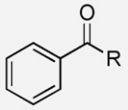
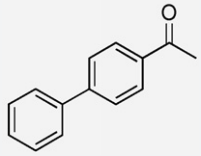
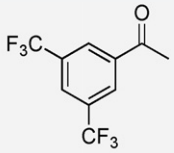
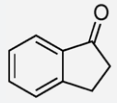
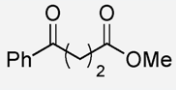
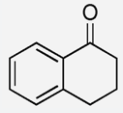


Fig. 1. Asymmetric hydrosilylation of acetophenone catalysed by CuCl/NaOt-Bu/(*R*)-BINAP (5 mol% in toluene). Effect of oxygen.

Table 4
Asymmetric hydrosilylation of aryl alkyl ketones by $PhMeSiH_2$ with the (*R*)-BINAP/CuCl/*t*-BuONa system (5 mol%).



Entry	Substrate	ee [yield] (%)	Entry	Substrate	ee [yield] (%)
1		93 [99]	9	 	92 [75]
2		90 [99]	10	X = F	96 [99]
3		79 [80]	11	X = Cl	97 [99]
4		87 [92]	12	X = Br	97 [90]
5	 	92 [99]	13		94 [99]
6	R = Et	97 [91]	14		92 [99]
7	R = *i*Pr	92 [99]	15		94 [80]
8		85 [80]	16		65 [75]

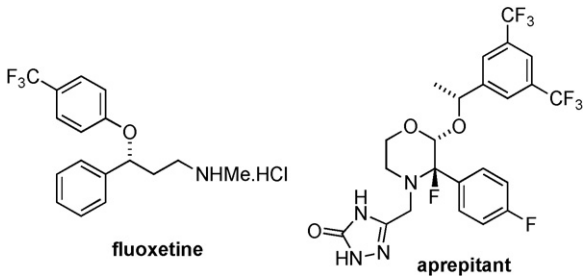


Fig. 2. Structure of fluoxetine (left) and aprepitant (right).

optimized reaction conditions described above.[3] For all substrates listed in Table 4, the reactions were completed within 18 hours using 5 mol% catalyst and two equivalents of phenylmethylsilane. Ketone derivatives exhibiting different steric or/and electronic properties are reduced with exceptional enantioselectivities (up to 97% ee) and yields (up to 99%). Propiophenone and isobutyrophenone are reduced with good enantioselectivities and yields (97 and 92% ee, respectively; entries 6–7). 85% ee and 80% isolated yield were obtained for the keto ester (entry 8), a precursor in the synthesis of the antidepressant fluoxetine (prozac, Fig. 2) [14]. Reaction with 3,5-bis(trifluoromethyl) acetophenone leads the corresponding secondary alcohol in 92% ee and 99% isolated yield (entry 14). This alcohol is also of special interest for the development of some recent NK-1 antagonists including aprepitant (Fig. 2) [15].

As anticipated, the excellent enantioselectivity displayed by CuCl/NaOt-Bu/BINAP system seems to be limited to aryl alkyl ketones. Table 5 displays some examples with dialkyl ketones as substrates. For example, the reduction of phenyl-3-butanone proceeds with a good yield (92%) albeit with low enantioselectivity (5% ee). The use of other silane did not improve the results.

In summary, we have shown that the CuCl/NaO*t*-Bu/BINAP system is an efficient catalytic system for the reduction of prochiral aryl alkyl ketones when phenylmethyl silane was used as reducing agent. High enantiomeric excesses and yields could be achieved with only 5 mol% of the catalytic system generated in situ.

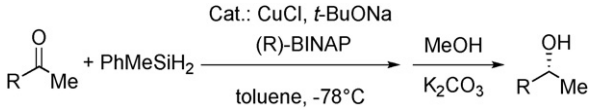
Experimental section

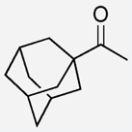
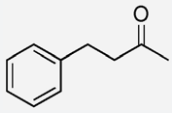
General procedure for the hydrosilylation reaction

A schlenk was charged with CuCl (0.025 mmol), NaO-*t*-Bu (0.025 mmol) and (*R*)-BINAP (0.025 mmol) (Table 1, entry 5). Dry toluene was added under argon (5.0 mL) and the solution was stirred for 20 min at room temperature. After cooling to −78 °C, the silane ($PhMeSiH_2$, 1.0 mmol) was added dropwise followed by the acetophenone (0.5 mmol). The yellow solution was stirred at −78 °C for 16 hours. Upon completion, a solution of K_2CO_3 (or NaOH) in methanol was added and the resulting solution was stirred for 1 h at room temperature. Column chromatography provided the desired alcohol (60.4 mg, 99% yield). GC analysis on a chiral column gave a 93% ee (*R*). Absolute configuration was determined by comparison of optical rotation with literature values.

[3] Two equivalents of silane were used in order to increase the reaction rate. In principle, both hydrides of $PhMeSiH_2$ can be used for the reduction. However, when only 0.5 equivalent of silane was used, 50% of alcohol was isolated indicating that only one H is reactive toward reduction.

Table 5
Asymmetric hydrosilylation of dialkyl ketones by $PhMeSiH_2$ with the (*R*)-BINAP/CuCl/*t*-BuONa system (5 mol%).



Entry	Substrate	ee [yield] (5)
1		25 [80]
2		10 [90]
3		5 [92]

Acknowledgments

We thank the CNRS and the Ministère de l'Education Nationale, de la Recherche et de la Technologie for a Ph.D. grant (J.T.I) and an « ACI Jeunes chercheuses et jeunes chercheurs ».

References

[1] (a) E.N. Jacobsen, A. Pfaltz, H. Yamamoto (Eds.), Comprehensive asymmetric catalysis, Springer, New York, 1999 ;
(b) I. Ojima (Ed.), Catalytic Asymmetric Synthesis, 2nd edition, Wiley-VCH, New York, 2000.
[2] (a) I. Ojima, M. Nihonyanagi, Y. Nagai, J. Chem. Soc., Chem. Commun. (1972) 938 ;
(b) I. Ojima, T. Kogure, M. Nihonyanagi, Y. Nagai, Bull. Chem. Soc. Jpn. 45 (1972) 3506 ;
(c) I. Ojima, T. Kogure, M. Nihonyanagi, Y. Nagai, Bull. Chem. Soc. Jpn. 45 (1972) 3722 ;
(d) R.J.P. Corriu, J.J.E. Moreau, J. Chem. Soc., Chem. Commun. (1973) 38 ;
(e) W. Dumont, J.C. Poulin, T.P. Dang, H.B. Kagan, J. Am. Chem. Soc. 95 (1973) 8295.
[3] (a) H. Nishiyama, H. Sakaguchi, T. Nakamura, M. Horihata, M. Kondo, K. Itoh, Organometallics 8 (1989) 846 ;
(b) M. Sawamura, R. Kuwano, Y. Ito, Y. Angew. Chem., Int. Ed. Engl. 33 (1994) 111 ;
(c) A. Sudo, H. Yoshida, K. Saigo, Tetrahedron: Asymmetry 8 (1997) 3205 ;
(d) B. Tao, G.C. Fu, Angew. Chem., Int. Ed. 41 (2002) 3892 ;
(e) W.L. Duan, M. Shi, G.B. Rong, Chem. Commun. (2003) 2976 ;
(f) D.A. Evans, F.E. Michael, J.S. Tedrow, K.R. Campos, J. Am. Chem. Soc. 125 (2003) 3534 ;
(g) V. César, S. Bellemin-Laponnaz, H. Wadepohl, L.H. Gade, Chem. Eur. J. 11 (2005) 2862.

[4] (a) For reviews on hydrosilylation of ketones, see: J.F. Carpentier, V. Bette, Curr. Org. Chem. 6 (2002) 913 ;
(b) O. Riant, N. Mostefai, Courmacel, J. Synthesis (2004) 2943 ;
(c) C. Deutsch, N. Krause, B.H. Lipshutz, Chem. Rev. 108 (2008) 2916 ;
(d) S. Díez-González, S.P. Nolan, Acc. Chem. Res. 41 (2008) 349.
[5] Y. Nishibayashi, L. Takei, S. Uemura, M. Hidai, Organometallics 17 (1998) 3420.
[6] (a) H. Mimoun, J.Y. de Saint Laumer, L. Giannini, R. Scopelliti, C. Floriani, J. Am. Chem. Soc. 121 (1999) 6158 ;
(b) V. Bette, A. Mortreux, D. Savoia, J.F. Carpentier, Tetrahedron 60 (2004) 2837 ;
(c) V. Bette, A. Mortreux, D. Savoia, J.F. Carpentier, Adv. Synth. Catal. 347 (2005) 289.
[7] J. Yun, S.L. Buchwald, J. Am. Chem. Soc. 121 (1999) 5640.
[8] (a) B.K. Langlotz, H. Wadepohl, L.H. Gade, Angew. Chem. Int. Ed. 47 (2008) 4670 ;
(b) N.S. Shaikh, S. Enthaler, K. Junge, M. Beller, Angew. Chem. Int. Ed. 47 (2008) 2497.
[9] B.H. Lipshutz, K. Noson, W. Chrisman, A. Lower, J. Am. Chem. Soc. 125 (2003) 8779.
[10] H. Brunner, W. Miehling, J. Organomet. Chem. 275 (1984) C17.
[11] (a) D.H. Appella, Y. Moritani, R. Shintani, E.M. Ferreira, S.L. Buchwald, J. Am. Chem. Soc 121 (1999) 9473 ;
(b) Y. Moritani, D.H. Appella, V. Jurkauskas, S.L. Buchwald, J. Am. Chem. Soc. 122 (2000) 6797 ;
(c) J. Yun, S.L. Buchwald, Org; Lett. 3 (2001) 1129.
[12] (a) For other phosphines/copper/silane systems used for the asymmetric hydrosilylation of ketones, see: S. Sirol, J. Courmacel, N. Mostefaï, O. Riant, Org. Lett. 3 (2001) 4111 ;
(b) J. Courmacel, N. Mostefaï, S. Sirol, S. Chopin, O. Riant, Isr. J. Chem. 41 (2002) 231 ;
(c) D.W. Lee, J. Yun, Tetrahedron Lett. 45 (2004) 5415 ;
(d) J. Wu, J.X. Ji, A.S.C. Chan, Proc. Natl. Acad. Sci. 102 (2005) 3570 ;
(e) M.L. Kantam, S. Laha, J. Yadav, P.R. Likhar, B. Sreedhar, B.M. Choudary, Adv. Synth. Catal. 349 (2007) 1797 ;
(f) N. Mostefaï, S. Sirol, J. Courmacel, O. Riant, Synthesis 8 (2007) 1265 ;
(g) M.L. Kantam, S. Laha, J. Yadav, P.R. Likhar, B. Sreedhar, S. Jha, S. Bhargava, M. Udayakiran, B. Jagadeesh, Org. Lett. 10 (2008) 2979 ;
(h) L.M. Kantam, S. Laha, J. Yadav, R.L. Pravin, B. Sreedhar, B.M. Choudary, Adv. Synth. Catal. 349 (2007) 1797 ;
(i) C.T. Lee, B.H. Lipshutz, Org. Lett. 10 (2008) 4187 ;
(j) M.L. Kantam, J. Yadav, S. Laha, P. Srinivas, B. Sreedhar, F. Figueras, J. Org. Chem. 74 (2009) 4608.
[13] J.T. Issenhuth, S. Dagorne, S. Bellemin-Laponnaz, Adv. Synth. Catal. 348 (2006) 1991–1994.
[14] J.W. Hilborn, Z.H. Lu, A.R. Jurgens, Q.K. Fang, P. Byers, S.A. Wald, C.H. Senanayake, Tetrahedron. Lett. 42 (2001) 8919.
[15] K.M.J. Brands, J.F. Payack, J.D. Rosen, T.D. Nelson, A. Candelario, M.A. Huffman, M.M. Zhao, J. Li, B. Craig, Z.J. Song, D.M. Tschaen, K. Hansen, P.N. Devine, P.J. Pye, K. Rossen, P.G. Dormer, R.A. Reamer, C.J. Welch, D.J. Mathre, N.N. Tsou, J.M. McNamara, P.J. Reider, J. Am. Chem. Soc. 125 (2003) 2129.