Arndt, V. V. Burkalov, U. Rosenthal, *Synlett* **1996**, 111 – 118; E. Negishi, T. Takahashi, *Bull. Chem. Soc. Jpn*. **1998**, *71*, 755 – 769.
[2] O. Geis, H.-G. Schmalz, *Angew. Chem*. **1998**, *110*, 955 – 958; *Angew. Chem. Int. Ed.* **1998**, *37*, 911 – 914; S. C. Berk, R. B. Grossman, S. L. Buchwald, *J. Am. Chem. Soc*. **1994**, *116*, 8593 – 8601; F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc*. **1996**, *118*, 11 688 – 11 689; J. Barluenga, R. Sanz, F. J. Fañanás, *Chem. Eur. J*. **1997**, 1324 – 1336; T. Takahashi, S. Huo, R. Hara, Y. Noguchi, K. Nakajima, W.-H. Sun, *J. Am. Chem. Soc*. **1999**, *121*, 1094 – 1095.
[3] H. Urabe, T. Hata, F. Sato, *Tetrahedron Lett*. **1995**, *36*, 4261 – 4264; H. Urabe, T. Takeda, D. Hideura, F. Sato, *J. Am. Chem. Soc*. **1997**, *119*, 11 295 – 11 305.
[4] Z. Zhao, Y. Ding, G. Zhao, *J. Org. Chem*. **1998**, *63*, 9285 – 9291.
[5] To execute this process, transmetalation of the aforementioned Group 4 metallacycles to other appropriate organometallic intermediates (typically a copper reagent) has sometimes been undertaken: Y. Liu, B. Shen, M. Kotora, T. Takahashi, *Angew. Chem*. **1999**, *111*, 966 – 968; *Angew. Chem. Int. Ed.* **1999**, *38*, 949 – 951; M. Kotora, C. Xi, T. Takahashi, *Tetrahedron Lett*. **1998**, *39*, 4321 – 4324. Alternatively, a stepwise sequence by the use of bis-halogenated intermediates that are readily available by the halogenolysis of the metallacycles has also been devised: E. Negishi, S. Ma, T. Sugihara, Y. Noda, *J. Org. Chem*. **1997**, *62*, 1922 – 1923.
[6] H. Urabe, F. Sato, *J. Org. Chem*. **1996**, *61*, 6756 – 6757; S. Yamaguchi, R.-Z. Jin, K. Tamao, F. Sato, *J. Org. Chem*. **1998**, *63*, 10 060 – 10 062; H. Urabe, F. Sato, *J. Am. Chem. Soc*. **1999**, *121*, 1245 – 1255; H. Urabe, *J. Synth. Org. Chem. Jpn*. **1999**, *57*, 492 – 502.
[7] T. Hamada, D. Suzuki, H. Urabe, F. Sato, *J. Am. Chem. Soc*. **1999**, *121*, 7342 – 7344.
[8] F. Sato, H. Urabe, S. Okamoto, *J. Synth. Org. Chem. Jpn*. **1998**, *56*, 424 – 432.
[9] Review on tandem reactions: R. A. Bunce, *Tetrahedron* **1995**, *48*, 13 103 – 13 159; P. J. Parsons, C. S. Penkett, A. J. Shell, *Chem. Rev*. **1996**, *96*, 195 – 206.
[10] Intramolecular addition of alkenyltitanium species to esters to yield ketones has been reported: S. Okamoto, A. Kasatkin, P. K. Zubaidha, F. Sato, *J. Am. Chem. Soc*. **1996**, *118*, 2208 – 2216; H. Urabe, K. Suzuki, F. Sato, *J. Am. Chem. Soc*. **1997**, *119*, 10 014 – 10 027.
[11] Recent reports on the synthesis of cyclopentadienols and related cyclopentadienylamines: S. H. Hong, Y. K. Chung, *Tetrahedron Lett*. **1998**, *39*, 4843 – 4846; L. G. Quan, V. Gevorgyan, Y. Yamamoto, *J. Am. Chem. Soc*. **1999**, *121*, 3545 – 3546; R. Aumann, A. G. Meyer, R. Fröhlich, *Organometallics* **1996**, *15*, 5018 – 5027.
[12] B. J. Wakefield, *Organolithium Methods*, Academic Press, London, **1988**, p. 53; B. H. Lipshutz, S. Sengupta, in *Organic Reactions*, *Vol. 41* (Ed.: L. A. Paquette), Wiley, New York, **1992**, pp. 135 – 631.
[13] Condensed five- and six-membered rings are frequently found in naturally occurring products. Review on the synthesis of polyquinanes: G. Mehta, A. Srikrishna, *Chem. Rev*. **1997**, *97*, 671 – 719; V. Singh, B. Thomas, *Tetrahedron* **1998**, *54*, 3647 – 3692; review on the synthesis of hydrindane rings: P. Jankowski, S. Marczak, J. Wicha, *Tetrahedron* **1998**, *54*, 12 071 – 12 150.

Development of New Chiral P,N Ligands and Their Application in the Cu-Catalyzed Enantioselective Conjugate Addition of Diethylzinc to Enones**

Xinquan Hu, Huilin Chen, and Xumu Zhang*

The conjugate addition of various organometallic reagents to enones is one of the most widely used synthetic methods for carbon – carbon bond formation.[1] Many chiral auxiliaries or stoichiometric reagents have been reported for highly stereoselective 1,4-additions. Great attention has been devoted recently to developing enantioselective catalytic 1,4-addition reactions.[2] Chiral copper, nickel, and other metal complexes have been investigated as catalysts for enantioselective additions of organolithium, Grignard, and diorganozinc reagents to enones.[3] Most notable among these reagents are the chiral phosphorus – Cu^{I} complexes, for example, Feringa's chiral phosphoramidite,[4] which have proven effective for enantioselective conjugate additions to cyclic enones. In addition, several other efficient enantioselective Michael addition reactions with cyclic enones have been described.[5] In contrast to the cyclic enones, highly enantioselective Cu-catalyzed conjugate addition (> 95 % *ee*) to acyclic enones has not been realized (*ee* values around 90 % have been reported in several promising systems[3d, 4a]). Because strong substrate dependence is quite common for asymmetric carbon – carbon bond forming reactions catalyzed by transition metals, the development of new chiral ligands plays a pivotal role for overcoming this substrate limitation. Herein we report the synthesis of novel chiral P,N ligands for highly enantioselective Cu-catalyzed conjugate addition of diethylzinc to acyclic enones. In addition, these P,N ligands are also very efficient for the Cu-catalyzed conjugate addition of diethylzinc to 2-cyclohexen-1-one.

A number of chiral P,N ligands have been developed for transition metal-catalyzed asymmetric reactions.[6] Pfaltz et al.[4c] and Stangeland and Sammakia[7] have applied chiral oxazoline – phosphite and oxazoline – phosphane ligands to Cu-catalyzed conjugate addition of organometallics to enones. We are particularly interested in exploring new chiral motifs to build effective P,N ligands for broad applications in asymmetric catalysis. Chiral 2-amino-2′-hydroxy-1,1′-binaphthyl (NOBIN, **1**; see scheme 1) developed by Kocovsky et al. has proven to be an excellent framework for construct-

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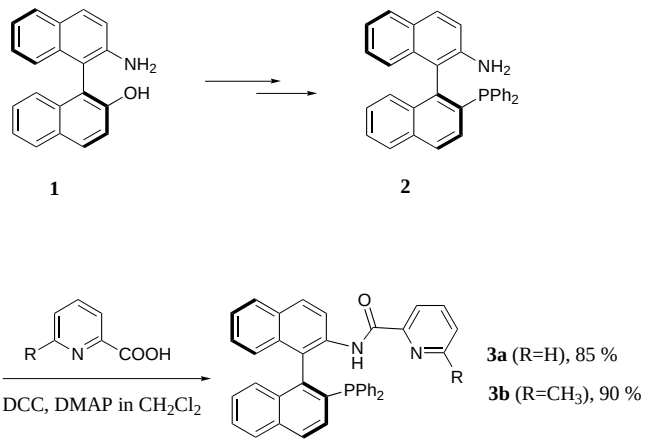
ing chiral ligands.[8] Several synthetic routes and resolution methods have been developed for synthesizing NOBIN in large quantity.[8c, 9] One of the most notable applications is its use as the chiral backbone in the chiral aldol catalyst of Carreira et al.[10] The combination of a diarylphosphane group with a substituted pyridine in a chiral binaphthyl system may lead to useful ligands, and we have derived a new family of chiral P,N ligands from **2** as shown in Scheme 1. The two chiral

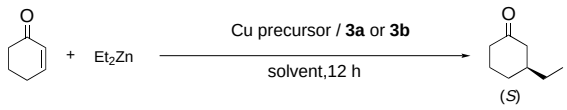


Scheme 1. Synthesis of novel chiral P,N ligands.

P,N ligands (*S*)-(+)-2-(2-pyridinylcarboxamido)-2′-(diphenylphosphanyl)-1,1′-binaphthyl (**3a**) and (*S*)-(+)-2-(6-methyl-2-pyridinylcarboxamido)-2′-(diphenylphosphanyl)-1,1′-binaphthyl (**3b**) are prepared in high yields from the previously reported compound **2**.[8e] A major difference of these chiral P,N ligands (**3**) over other chiral P,N ligands[6] is their relatively large bite angle when binding to transition metals. The rigid amide linker in **3** provides conformational rigidity of the biaryl ligand, which may be important for effective chiral induction.

We selected 2-cyclohexen-1-one as a typical substrate to develop optimal reaction conditions (Table 1). The enantioselective 1,4-addition of diethylzinc to 2-cyclohexen-1-one gives better conversion and enantioselectivity in nonpolar solvents than in coordinating solvents such as THF (entries 1–3 versus entry 4). Mixed solvent systems can also be used to achieve good conversion and enantioselectivity (entries 5–7). Interestingly, removal of the dissociated CH_3CN during catalyst preparation also helps to increase the conversion and enantioselectivity when $[Cu(CH_3CN)_4]BF_4$ is used as the catalyst precursor (entry 6 versus entry 5). By lowering the reaction temperature from 0 to $-20\,^{\circ}C$ (entry 7) an 85 % *ee* could be obtained when **3a** was used as the chiral P,N ligand. Since removing CH_3CN is needed with the $[Cu(CH_3CN)_4]BF_4$ catalyst precursor, we chose to use Cu complexes with noncoordinating ligands such as $Cu(OTf)_2$ and $[Cu(OTf)]_2 \cdot C_6H_6$ (entries 9 and 10). Our results show that $[Cu(OTf)]_2 \cdot C_6H_6$ is an excellent precursor, which gives a quantitative yield of the 1,4-conjugate addition product with high enantioselectivity (entry 10). The conjugate addition can also be carried out at room temperature, albeit with a lower enantioselectivity (entry 11). The optimal reaction temperature for obtaining high enantioselectivity is $-20\,^{\circ}C$ (entries 12 and 13). This enantioselective conjugate addition is apparently a ligand-accelerated process.[11] The enantioselectivity when the ratio of **3a**:Cu = 2.5:1 is significantly higher than the result obtained with the ratio of **3a**:Cu = 1.25:1 (entry 12 versus 14). The addition of more than two equiv-

Table 1. Cu-catalyzed enantioselective 1,4-conjugate addition of Et_2Zn to 2-cyclohexen-1-one.[a]



Entry	Cu precursor	Solvent	T[°C]	**3a**:Cu	Conv.[%][b]	*ee*[%][b]
1	$[Cu(CH_3CN)_4]BF_4$	toluene	0	2.5:1	82	82
2	$[Cu(CH_3CN)_4]BF_4$	$Cl(CH_2)_2Cl$	0	2.5:1	58	78
3	$[Cu(CH_3CN)_4]BF_4$	CH_2Cl_2	0	2.5:1	40	62
4	$[Cu(CH_3CN)_4]BF_4$	THF	0	2.5:1	11	56
5	$[Cu(CH_3CN)_4]BF_4$	toluene/$Cl(CH_2)_2Cl$ (2/1)	0	2.5:1	76	70
6[c]	$[Cu(CH_3CN)_4]BF_4$	toluene/$Cl(CH_2)_2Cl$ (2/1)	0	2.5:1	91	76
7[c]	$[Cu(CH_3CN)_4]BF_4$	toluene/$Cl(CH_2)_2Cl$ (2/1)	−20	2.5:1	95	85
8[c]	$[Cu(CH_3CN)_4]BF_4$	toluene/$Cl(CH_2)_2Cl$ (2/1)	−20	**3b**:Cu = 2.5:1	98	92
9	$Cu(OTf)_2$	toluene	0	2.5:1	100	72
10	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	0	2.5:1	100	82
11	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	25	2.5	100	65
12	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−20	2.5:1	55	87
13	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−40	2.5:1	41	77
14	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−20	1.25:1	72	72
15	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−20	5.0:1	76	91
16[d]	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−20	2.5:1	100	89
17[d]	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene	−20	**3b**: Cu = 2.5:1	100	89
18	$[Cu(OTf)]_2 \cdot C_6H_6$	toluene/$Cl(CH_2)_2Cl$ (2/1)	−20	**3b**:Cu = 2.5:1	100	87

[a] The reaction was carried out at 0 °C for 12 h with 1.0 mmol of the substrate and 1 mol % of Cu precursor in 3 mL of solvent. [b] The conversions were measured by GC analysis and *ee* values were determined by GC on a Cyclodextrin column with a chiral phase; the absolute configuration was determined by comparison with literature values.[12] [c] With removal of CH_3CN under vacuum after preparation of the [Cu(**3a**)] complex. [d] The reaction was run for 48 h. – Tf = trifluoromethanesulfonyl.

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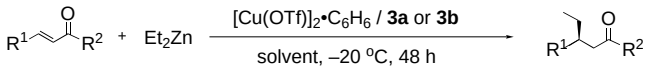
Table 2. Cu-catalyzed enantioselective 1,4-conjugate addition.[a]



Entry	R^1	R^2	Ligand	Solvent	Yield [%]	*ee* [%][b]	Config.[c]
1	Ph	Ph	**3a**	toluene/$Cl(CH_2)_2Cl$ (2/1)	92	83	*S*
2	Ph	Ph	**3b**	toluene/$Cl(CH_2)_2Cl$ (2/1)	85	96	*S*
3	Ph	Ph	**3b**	toluene	72	94	*S*
4	Ph	4-Ch_3O-C_6H_4	**3b**	toluene/$Cl(CH_2)_2Cl$ (2/1)	69	97	– [d]
5	Ph	4-Ch_3O-C_6H_4	**3b**	toluene	10	90	– [d]
6	4-Ch_3O-C_6H_4	Ph	**3b**	toluene/$Cl(CH_2)_2Cl$ (2/1)	97	98	*S*
7	4-Cl-C_6H_4	Ph	**3b**	toluene/$Cl(CH_2)_2Cl$ (2/1)	72	95	+ [d]
8	Ph	4-Cl-C_6H_4	**3b**	toluene/$Cl(CH_2)_2Cl$ (2/1)	70	95	– [d]
9	Ph	CH_3	**3b**	toluene/$Cl(CH_2)_2Cl$(2/1)	70	90	*S*
10	*i*Pr	CH_3	**3b**	toluene	53	86	+ [d]

[a] The reaction was carried out at $-20\,^\circ C$ for 48 h in 1 mL of toluene and 0.5 mL of $ClCH_2CH_2Cl$ (substrate (0.5 mmol):$[Cu(OTf)]_2 \cdot C_6H_6$:ligand = 1:0.01:0.05), or in 1.5 mL of toluene. [b] The *ee* values were determined by chiral-phase HPLC. [c] The absolute configuration was assigned by comparison of the optical rotation with reported data.[3, 4] [d] Sign of the optical rotation.

alents of ligand has only a marginal effect on the enantioselectivity (entry 12 versus entry 15). Finally, replacing **3a** with the sterically more hindered chiral P,N ligand **3b** gives comparable or better results for enantioselective 1,4-conjugate addition to 2-cyclohexen-1-one (entries 7 and 16, entries 8 and 17, respectively). Our experiments indicate that $[Cu(OTf)]_2 \cdot C_6H_6$ is the best copper catalyst precursor and nonpolar solvents such as toluene or $Cl(CH_2)_2Cl$ are desirable. This result is consistent with earlier studies conducted by several research groups.[3, 4]

We have tried to develop effective catalytic systems for a variety of acyclic enones (Table 2). Chalcone was selected as the substrate for testing the reaction conditions. Our experimental results show that enantioselective conjugate addition of diethylzinc to chalcone (entry 2) gives better *ee* values when catalyzed by a [Cu^I(**3b**)] species than those obtained with a [Cu^I(**3a**)] complex (entries 1 and 2). The reaction in the mixed solvent system (toluene/$Cl(CH_2)_2Cl$) works better than that carried out in toluene both in terms of conversion and enantioselectivity (entry 2 versus entry 3), possibly because the substrates are more soluble in the mixed solvent system. This is especially true for a methoxy-substituted chalcone (entry 4 versus entry 5). Under the optimal conditions for enantioselective 1,4-addition of diethylzinc to chalcone (entry 2) several acyclic enones with aryl substituent groups have been successfully converted into the corresponding chiral ketones (entries 4–9, up to 98 % *ee*). To our knowledge, the enantioselectivies achieved in this study are the best yet reported for the Cu-catalyzed enantioselective conjugate addition to acyclic enones. Furthermore, a very promising result has been obtained for an acyclic enone with only aliphatic substituents (entry 10, 86 % *ee*).

Experimental Section

3a: 2-Pyridinecarboxylic acid (0.940 g, 7.64 mmol), 4-(dimethylamino)pyridine (DMAP, 20 mg, 0.164 mmol) and 1,3-dicyclohexylcarbodiimide (DCC, 2.06 g, 10 mmol) were added to a solution of amine **2** (0.863 g, 1.91 mmol) in CH_2Cl_2 (50 mL). The mixture was stirred overnight at RT. Water (20 mL) and AcOH (0.2 mL) were added to this mixture and stirred at RT for 2 h. The solid residue was then filtered and washed with CH_2Cl_2 (10 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on silica gel (80 g) eluting with hexanes/CH_2Cl_2 (1/2) to afford 906 mg (85 %) of **3a** as a white solid, m.p. 185–187 °C. $[\alpha]_D^{25}$ +45.6 (c = 1.0, $CHCl_3$); ^{1}H NMR (CD_2Cl_2): δ = 6.87 (d, J = 8.4 Hz, 1H), 6.93–6.98 (m, 2H), 7.03–7.35 (m, 13H), 7.49–7.53 (m, 2H), 7.76–7.81 (m, 1H), 7.91–8.09 (m, 6H), 8.87 (d, J = 9.0 Hz, 1H), 9.75 (s, 1H); ^{13}C NMR (CD_2Cl_2): δ = 120.15, 122.70, 125.11, 125.26, 125.40, 126.54, 126.73, 126.76, 126.88, 127.05, 127.78, 127.96, 128.67, 128.76, 128.85, 128.96, 128.98, 129.04, 129.18, 129.75, 129.89, 131.13, 131.15, 131.27, 133.55, 133.65, 134.02, 134.05, 134.11, 134.16, 134.38, 134.43, 134.89, 135.50, 135.53, 137.45, 137.61, 137.65, 137.82, 138.17, 138.20, 138.37, 140.62, 141.08, 148.29, 150.49, 162.12; ^{31}P NMR (CD_2Cl_2): δ = –13.71 (s); HR-MS calcd for $C_{38}H_{27}N_2OP$: 559.1939; found: 559.1904.

3b: P,N ligand **3b** (747 mg, 90 %) was prepared from **2** (660 mg, 1.46 mmol) according to the same procedure as used for **3a** and isolated as a white solid, m.p. 208–209 °C. $[\alpha]_D^{25}$ +42.0 (c = 1.0, $CHCl_3$); ^{1}H NMR (CD_2Cl_2): δ = 1.98 (s, 3H), 6.82–6.87 (m, 2H), 6.99–7.30 (m, 13H), 7.30–7.40 (m, 1H), 7.48–7.57 (m, 2H), 7.64 (t, J = 7.7 Hz, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.90–7.98 (m, 2H), 8.06 (t, J = 8.2 Hz, 2H), 8.95 (d, J = 9.0 Hz, 1H), 9.93 (s, 1H); ^{13}C NMR (CD_2Cl_2): δ = 24.06, 119.40, 119.43, 124.36, 124.47, 125.21, 126.42, 126.72, 126.75, 127.10, 127.83, 128.01, 128.60, 128.70, 128.92, 128.95, 129.02, 129.03, 129.06, 129.74, 129.98, 131.08, 131.27, 131.29, 133.58, 133.67, 133.96, 134.00, 134.20, 134.26, 134.47, 135.00, 135.85, 135.88, 137.29, 137.46, 137.90, 138.07, 138.28, 138.52, 138.69, 140.65, 141.10, 149.58, 157.35, 161.95; ^{31}P NMR (CD_2Cl_2): δ = –13.77 (s); HR-MS calcd for $C_{39}H_{29}N_2OP$: 573.2096; found: 573.2051.

General Procedure for asymmetric 1,4-conjugate addition: A solution of $[Cu(OTf)]_2 \cdot C_6H_6$ (10.0 mg, 2 mmol) and **3b** (57.2 mg, 10 mmol) in a mixture of 1,2-dichloroethane (4 mL) and toluene (8 mL) was stirred at RT for 0.5 h in a Schlenk tube in a N_2-filled glovebox. This catalyst solution was used for four separate experiments. Enone (0.5 mmol) and then the catalyst solution (3 mL) were added to a dried Schlenk tube. The solution was stirred at RT for 10 min and then cooled to $-20\,^\circ C$. After the solution was stirred at $-20\,^\circ C$ for 15 min, Et_2Zn (1.0 M solution in hexanes, 0.75 mL, 0.75 mmol) was added slowly. The resulting mixture was stirred at $-20\,^\circ C$ for 48 h and 5 % dilute hydrochloric acid (2 mL) was added. After warming the reaction mixture to RT, Et_2O (10 mL) was added. The organic phase was washed with saturated $NaHCO_3$ (5 mL), dried over anhydrous Na_2SO_4, and concentrated under vacuum. The residue was purified by column chromatography on silica gel and eluted with EtOAc/hexanes (1/40–1/20) to afford the addition product. All chiral 1,4-addition products are known compounds.[3, 4]

Determination of enantiomeric excesses: racemic products were obtained by 1,4-addition of substrates with ethylmagnesium bromide (1.0 M in THF) in THF at RT. The retention times (in minutes) for the racemic products are given in minutes a) chiral capillary GC column: Supelco γ-DEX-225 (30m × 0.25 mm (i.d.)): 3-ethylcyclohexanone: T = 80 °C for 40 min then 120 °C, t_S = 42.93, t_R = 43.27; 4-ethyl-5-methyl-hexan-2-one: T = 80 °C,

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$t_1 = 23.25$, $t_2 = 23.92$, and 4-phenyl-hexan-2-one: $T = 120\,^{\circ}C$, $t_S = 32.25$, $t_R = 33.32$; b) chiral HPLC Columns: Daicel Chiralcel OD and Chiralpak AD, particle size: 5.0 μm, column dimensions: 25 cm (length) × 0.46 cm (i.d.), flow = 1.0 mL min^{-1}. 1,3-diphenyl-pentan-1-one (Chiralpak AD, 2-PrOH/hexanes = 1/99), $t_S = 20.43$, $t_R = 29.55$; 3-(4-methoxyphenyl)-1-phenyl-pentan-1-one (Chiralpak AD, 2-PrOH/hexanes = 10/90), $t_S = 12.65$, $t_R = 16.83$; 1-(4-methoxyphenyl)-3-phenyl-pentan-1-one (Chiralcel OD, 2-PrOH/hexanes = 10/90), $t_S = 19.80$, $t_R = 22.37$; 3-(4-chlorophenyl)-1-phenyl-pentan-1-one (Chiralpak AD, 2-PrOH/hexanes = 5/95), $t_S = 10.73$, $t_R = 13.87$; and 1-(3-chlorophenyl)-4-phenyl-pentan-1-one. (Chiralpak AD, 2-PrOH/hexanes = 1/99), $t_S = 25.73$, $t_R = 34.97$.

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[1] P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon, Oxford, **1992**.
[2] For reviews see a) B. E. Rossiter, N. M. Swingle, *Chem. Rev.* **1992**, *92*, 771; b) N. Krause, A. Gerold, *Angew. Chem.* **1997**, *109*, 194; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186; c) N. Krause, *Angew. Chem.* **1998**, *110*, 295; *Angew. Chem. Int. Ed.* **1998**, *37*, 283.
[3] For selected examples on asymmetric conjugate addition reactions, see a) K. H. Ahn, R. B. Klassen, S. J. Lippard, *Organometallics* **1990**, *9*, 3178; b) D. M. Knotter, D. M. Grove, W. J. J. Smeets, A. J. Spek, G. van Koten, *J. Am. Chem. Soc.* **1992**, *114*, 3400; c) K. Soai, M. Okudo, M. Okamoto, *Tetrahedron Lett.* **1991**, *32*, 95; d) C. Bolm, M. Ewald, M. Felder, *Chem. Ber.* **1992**, *125*, 1205; e) M. Spescha, G. Rihs, *Helv. Chim. Acta* **1993**, *76*, 1219; f) M. Kanai, K. Tomioka, *Tetrahedron Lett.* **1995**, *36*, 4275; g) Q. L. Zhou, A. Pfaltz, *Tetrahedron* **1994**, *50*, 4467; h) S. M. W. Bennett, S. M. Brown, J. P. Muxworthy, S. Woodward, *Tetrahedron Lett.* **1999**, *40*, 1767; i) A. Alexakis, J. Frutos, P. Mangeney, *Tetrahedron: Asymmetry* **1993**, *4*, 2427; j) A. Alexakis, J. Vastra, J. Burton, P. Mangeney, *Tetrahedron: Asymmetry* **1997**, *8*, 3193; k) A. Alexakis, J. Burton, J. Vastra, P. Mangeney, *Tetrahedron: Asymmetry* **1997**, *8*, 3987; l) A. Alexakis, J. Vastra, J. Burton, C. Benhaim, P. Mangeney, *Tetrahedron Lett.* **1998**, *39*, 7869.
[4] a) A. H. M. de Vries, A. Meetsma, B. L. Feringa, *Angew. Chem.* **1996**, *108*, 2526; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2374; b) B. L. Feringa, M. Pineschi, L. A. Arnold, R. Imbos, A. H. M. de Vries, *Angew. Chem.* **1997**, *109*, 2733; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2620; c) A. K. H. Knobel, I. H. Escher, A. Pfaltz, *Synlett.* **1997**, 1429; d) M. Yan, L. W. Yang, K. Y. Wong, A. S. C. Chan, *Chem. Commun.* **1999**, 11; e) R. Naasz, L. A. Arnold, M. Pineschi, E. Keller, B. L. Feringa, *J. Am. Chem. Soc.* **1999**, *121*, 1104.
[5] a) T. Arai, H. Sasai, K. Aoe, K. Okamura, T. Date, M. Shibasaki, *Angew. Chem.* **1996**, *108*, 103; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 104; b) E. Gomez-Bengoa, N. M. Heron, M. T. Didiuk, C. A. Luchaco, A. H. Hoveyda, *J. Am. Chem. Soc.* **1998**, *120*, 7649; c) Y. Takaya, M. Ogasawara, T. Hayashi, M. Sakai, N. Miyaura, *J. Am. Chem. Soc.* **1998**, *120*, 5579.
[6] a) A. Schnyder, L. Hintermann, A. Togni, *Angew. Chem.* **1995**, *107*, 996; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 931; b) A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 3047; *Angew. Chem. Int. Ed.* **1998**, *37*, 2897; c) H. Doucet, E. Fernandez, T. P. Layzell, J. M. Brown, *Chem. Eur. J.* **1999**, *5*, 1320.
[7] E. L. Stangeland, T. Sammakia, *Tetrahedron* **1997**, *53*, 16503.
[8] a) M. Smrcina, M. Lorenc, V. Hanus, P. Kocovsky, *Synlett.* **1991**, 231; b) M. Smrcina, M. Lorenc, V. Hanus, P. Sedmera, P. Kocovsky, *J. Org. Chem.* **1992**, *57*, 1917; c) M. Smrcina, S. Vyskocil, J. Polivkova, J. Polakova, P. Kocovsky, *Collect. Czech. Chem. Commun.* **1996**, *61*, 1520; d) S. Vyskocil, S. Jaracz, M. Smrcina, M. Sticha, V. Hanus, M. Polasek, P. Kocovsky, *J. Org. Chem.* **1998**, *63*, 7727; e) S. Vyskocil, M. Smrcina, V. Hanus, M. Polasek, P. Kocovsky, *J. Org. Chem.* **1998**, *63*, 7738.
[9] a) K. Ding, Q. Xu, Y. Wang, J. Liu, Z. Yu, B. Du, Y. Wu, H. Koshima, T. Matsuura, *Chem. Commun.* **1997**, 693; b) R. A. Singer, S. L. Buchwald, *Tetrahedron Lett.* **1999**, *40*, 1095; c) K. Ding, Y. Wang, H. Yun, J. Lu, Y. Wu, M. Terada, Y. Okubo, K. Mikami, *Chem. Eur. J.* **1999**, *5*, 1734.
[10] a) E. M. Carreira, R. A. Singer, W. Lee, *J. Am. Chem. Soc.* **1994**, *116*, 8837; b) E. M. Carreira, W. Lee, R. A. Singer, *J. Am. Chem. Soc.* **1995**, *117*, 3649; c) R. A. Singer, E. M. Carreira, *J. Am. Chem. Soc.* **1995**, *117*, 12360.
[11] D. J. Berrisford, C. Bolm, K. B. Sharpless, *Angew. Chem.* **1995**, *107*, 1159; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1059.
[12] G. H. Posner, L. L. Frye, *Isr. J. Chem.* **1984**, *24*, 88.

Catalytic Aerobic Oxidation of Cycloalkanes with Nanostructured Amorphous Metals and Alloys**

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The functionalization of unactivated carbon – hydrogen bonds in saturated hydrocarbons has been investigated for both its synthetic and biological interest.[1] Catalytic oxidation of alkanes has been explored using several oxidants,[2] and those reactions with molecular oxygen under mild conditions[3] are especially rewarding goals. The oxidation of cyclohexane turns out to be the least efficient of all major industrial processes.[4]

Typically, cyclohexane is oxidized by air (15 atm) at 160 °C in the presence of cobalt naphthenate as oxidation initiator, giving only 4% conversion with 80% selectivity for cyclohexanone and cyclohexanol.[5] The addition of boric acid to the oxidation mixture allows approximately 10% conversion of cyclohexane with 90% selectivity for cyclohexanone and cyclohexanol.[5] Murahashi et al. have reported the oxidation of cyclohexane with iron powder and observed 11% conversion with 95% selectivity for cyclohexanone and cyclohexanol.[6]

Suslick and co-workers demonstrated the first sonochemical synthesis of amorphous iron particles (10 – 20 nm) by ultrasonic irradiation of $[Fe(CO)_5]$, and the utility of these particles as an efficient catalyst in the Fischer – Tropsch process.[7] They have extended this sonication synthesis to nanophase amorphous cobalt (20 nm) and an amorphous Co/

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