Asymmetric Hydrogenation

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An Additional Coordination Group Leads to Extremely Efficient Chiral Iridium Catalysts for Asymmetric Hydrogenation of Ketones**

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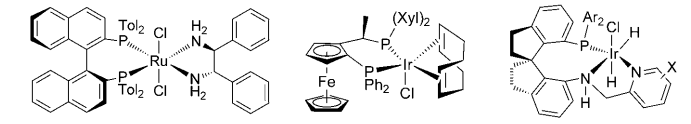
The production of enantiopure chiral compounds is important for pharmaceutical and agrochemical industries because enantiomers can exhibit distinct biological activities. Therefore, processes that directly produce the desired enantiomer are desirable. First reported by Knowles, Horner et al. in 1968,[1] catalytic asymmetric hydrogenation of unsaturated compounds such as olefins, ketones, and imines is one of the most commonly used methods for producing enantiopure chiral compounds.[2] Great progress has been made in this field, and many chiral catalysts are developed for a wide range of unsaturated substrates.

It is noteworthy that some of these synthetic chiral catalysts, which are much smaller and simpler than enzymes, exhibit activities and selectivities comparable to those of enzymes: in some cases, one molecule of catalyst can produce millions of new molecules enantioselectively. For example, the diphosphine/diamine ruthenium catalyst reported by Noyori et al.[3] and the iridium ferrocenyl catalyst Ir-(*R*,*S*)-Xyliphos developed by a team from Novartis[4] (Scheme 1)



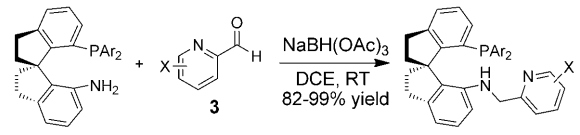
Scheme 1. Examples of exceptionally efficient chiral catalysts.

have turnover numbers (TON, molar ratio of converted substrate to catalyst) as high as 1000000 for the hydrogenation of ketones and imines.[5] However, chiral catalysts with TONs over a million are rare, and most of the reported chiral catalysts have TONs lower than 1000 and are unable to obtain applications in industry.

Chiral iridium complexes with phosphorus–nitrogen ligands are among the most commonly used catalysts in asymmetric hydrogenations.[6] However, these catalysts are easily deactivated by irreversible formation of inactive dimers or trimers under the hydrogenation conditions, and this deactivation prevents the achievement of extremely high TONs.[2b] To overcome this limitation, investigators have employed several strategies, including immobilization, dendrimerization, the use of a bulky counteranion, and the introduction of a bulky or rigid ligand.[7] Although these strategies substantially increased the stability and/or reactivity of chiral Ir/P–N catalysts, the efficiencies were still below the level required for practical use.

We recently developed new chiral iridium catalysts that bear a spiro aminophosphine ligand (SpiroAP; **1**, Scheme 2) and efficiently catalyze the asymmetric hydrogenation of aromatic and α,β-unsaturated ketones under mild conditions.[8] However, these catalysts also tend to lose their activity under hydrogenation conditions.[8b] We attributed the deactivation to the formation of an inactive iridium dihydride complex with two SpiroAP ligands. To inhibit the coordination of a second SpiroAP ligand to the iridium atom of the catalyst, we introduced an additional coordination group to the SpiroAP, making it a tridentate ligand. This modification led to a novel chiral spiro iridium catalyst with exceptionally high stability and activity for ketone hydrogenation. Herein, we report the synthesis, characterization, and application of new iridium catalysts with tridentate spiro ligands, SpiroPAP (**2**), to the hydrogenation of simple ketones. The new catalysts afforded chiral alcohols in up to 99.9% *ee* and with TONs as high as 4550000.

We chose a pyridine moiety as the additional coordination group because the pyridine ring can be easily modified and has suitable coordination ability in many iridium catalysts.[9] Starting from **1**, SpiroPAP ligands **2** were conveniently synthesized in high yields (82–99%) by means of



1 SpiroAP
1a Ar = C_6H_5
1b Ar = 3,5-$(Me)_2C_6H_3$
1c Ar = 3,5-$(tBu)_2C_6H_3$

2 SpiroPAP
2a Ar = C_6H_5, X = H
2b Ar = 3,5-$(Me)_2C_6H_3$, X = H
2c Ar = 3,5-$(tBu)_2C_6H_3$, X = H
2d Ar = 3,5-$(tBu)_2C_6H_3$, X = 6-Me
2e Ar = 3,5-$(tBu)_2C_6H_3$, X = 6-Et
2f Ar = 3,5-$(tBu)_2C_6H_3$, X = 5,6-$(CH)_4$
2g Ar = 3,5-$(tBu)_2C_6H_3$, X = 3-Me
2h Ar = 3,5-$(tBu)_2C_6H_3$, X = 4-*t*Bu

Scheme 2. Synthesis of SpiroPAP ligands.

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a one-step procedure involving reaction with picolinaldehydes (**3**) in dichloroethane (DCE) in the presence of $NaBH(OAc)_3$ as a reducing agent (Scheme 2).

The coordination of ligands **2** to the iridium atom was verified by analysis of the single crystal structure of the complex $[IrH_2((R)\text{-}\mathbf{2c})Cl]$[10] (Figure 1) obtained from the

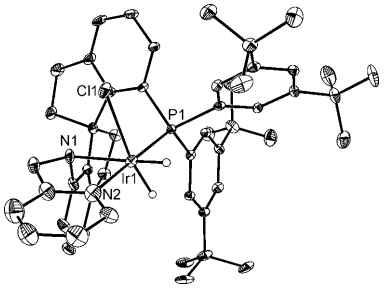
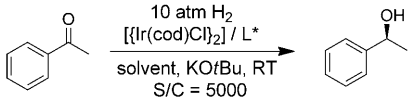


Figure 1. ORTEP diagram of $[IrH_2((R)\text{-}\mathbf{2c})Cl]$. Thermal ellipsoids set at 30% probability. Selected bond lengths [Å] and angles [°]: Ir1-P1 2.224, Ir1-N1 2.228, Ir1-N2 2.033, Ir1-H1 1.403, Ir1-H2 1.405; P1-Ir1-N1 99.98(15), P1-Ir1-N2 178.7(4), N1-Ir1-N2 81.30(4), N1-Ir1-H1 105.00(3), N1-Ir1-H2 166.00(3), H1-Ir1-H2 86.00(4), P1-Ir1-N1-N2 −179.87.

reaction of (*R*)-**2c** with $[\{Ir(cod)Cl\}_2]$ (cod = cyclooctadiene) in MeOH under hydrogen. In the crystal structure of $[IrH_2((R)\text{-}\mathbf{2c})Cl]$, ligand (*R*)-**2c** was coordinated to the iridium atom by means of one phosphorus atom and two nitrogen atoms by a conformationally restricted eight-membered ring and a five-membered heterometal ring. The newly introduced sp^2 nitrogen atom of the pyridine ring was coordinated to the iridium atom in a *trans* orientation relative to the phosphorus atom (P1–Ir1–N2, 178.7°) and was located in the plane defined by the iridium, phosphorus, and sp^3 nitrogen atoms (P1–Ir1–N1–N2 torsion angle, −179.87°). This structural characteristic indicates that $[IrH_2((R)\text{-}\mathbf{2c})Cl]$ for the most part retained the original core structural characteristics of the Ir–SpiroAP catalysts, despite the introduction of the pyridine moiety.[8b] However, the bite angle P–Ir–N(sp^3) (99.98°) in $[IrH_2((R)\text{-}\mathbf{2c})Cl]$ was clearly larger than that in $[Ir((R)\text{-}\mathbf{1c})(cod)]BF_4$ (91.79°). The increased angle brought the Ir atom, the reaction center of the catalyst, closer to the spirobiindane backbone and created a chiral environment around the Ir atom that permitted more efficient catalysis. The fact that no dimer or trimer formation was observed in the preparation of $[IrH_2((R)\text{-}\mathbf{2c})Cl]$ at a hydrogen pressure of 1 atm shows that the iridium catalyst was highly stabilized by the introduction of the pyridine moiety.

The preliminary hydrogenation was carried out under conditions previously optimized for the reaction catalyzed by Ir-(*R*)-**1c** (substrate/catalyst, S/C = 5000, 10 atm H_2, 25–30 °C).[8b] Hydrogenation of the standard substrate, acetophenone (**4a**), over Ir-(*R*)-**2c** generated in situ from 0.01 mol% $[\{Ir(cod)Cl\}_2]$ and 0.022 mol% (*R*)-**2c** afforded (*S*)-**5a** within 1 h with 100% conversion and 96% *ee* (Table 1, entry 2). This enantioselectivity was better than that obtained with Ir-(*R*)-**1c** (92% *ee*, entry 1). Solvent experiments showed that EtOH

Table 1: Optimizing the reaction conditions of the asymmetric hydrogenation of acetophenone.[a]



4a **5a**

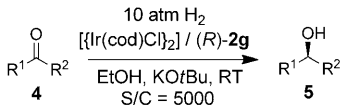
Entry	Ligand	Solvent	*t*	Conv [%][b]	*Ee* [%][c]
1	(*R*)-**1c**	*n*PrOH	10 min	100	92 (*S*)
2	(*R*)-**2c**	*n*PrOH	1 h	100	96 (*S*)
3	(*R*)-**2c**	MeOH	3 min	>99	91 (*S*)
4	(*R*)-**2c**	EtOH	20 min	100	97 (*S*)
5	(*R*)-**2c**	*i*PrOH	4 h	100	86 (*S*)
6	(*R*)-**2c**	Toluene	16 h	100	67 (*S*)
7	(*R*)-**2a**	EtOH	1 h	100	69 (*S*)
8	(*R*)-**2b**	EtOH	1 h	100	76 (*S*)
9	(*R*)-**2d**	EtOH	20 min	100	96 (*S*)
10	(*R*)-**2e**	EtOH	25 min	100	95 (*S*)
11	(*R*)-**2f**	EtOH	18 h	100	85 (*S*)
12	(*R*)-**2g**	EtOH	<20 min	100	98 (*S*)
13	(*R*)-**2h**	EtOH	45 min	100	98 (*S*)
14[d]	(*R*)-**2g**	EtOH	5 h	100	90 (*S*)
15[e]	(*R*)-**2g**	EtOH	6 h	100	92 (*S*)
16[f]	(*R*)-**2g**	EtOH	30 h	100	98 (*S*)
17[g]	(*R*)-**2g**	EtOH	15 days	91	98 (*S*)

[a] Reaction conditions: 7.5 mmol scale, [substrate] = 2.1 M, 0.01 mol% $[\{Ir(cod)Cl\}_2]$, 0.022 mol% ligand, [KO*t*Bu] = 0.02 M , solvent volume = 2.0 mL, room temperature (25–30 °C). [b] Determined by GC. [c] Determined by GC on a Supelco chiral β-dex-225 solid phase. [d] 1 atm H_2. [e] S/C = 100000, 50 atm H_2 (initial). [f] S/C = 1000000, 50 atm H_2 (initial). [g] S/C = 5000000, 100–60 atm H_2.

was the best solvent for Ir-(*R*)-**2c**, and the reaction was completed within 20 min, giving (*S*)-**5a** in 97% *ee* (entry 4). Ligand screening revealed that the substituents on the *P*-phenyl rings and on the pyridine ring of the ligand markedly affected the activity and enantioselectivity of the catalyst (entries 7–13); the ligand (*R*)-**2g**, which has 3,5-*tert*-butyl groups on the *P*-phenyl rings and a 3-methyl group on the pyridine ring, gave the best result (98% *ee*, less than 20 min, entry 12). As we expected, Ir-(*R*)-**2g** was very stable and active. When the catalyst loading was lowered to 0.0001 mol% (S/C = 1000000), the hydrogenation product (*S*)-**5a** was still obtained in 98% *ee* with 100% conversion within 30 h at room temperature under an initial hydrogen pressure of 50 atm (the final hydrogen pressure was about 20 atm). When the catalyst loading was further lowered to 0.00002 mol% (S/C=5000000), the reaction still proceeded well under 100–60 atm of H_2 pressure and provided (*S*)-**5a** in 98% *ee* with 91% conversion within 15 days (TON = 4550000, turnover frequency = 12600 h^{-1}).

A wide range of ketones were hydrogenated over Ir-(*R*)-**2g** under the standard reaction conditions (Table 2). All the tested aromatic ketones (**4a–o**) underwent hydrogenation smoothly to afford the corresponding chiral alcohols (**5a–o**) in high yields (from 96 to >99%) and excellent enantioselectivities (96–99.9% *ee*) (Table 2, entries 1–15). We were pleased to find that 3,5-bis-(trifluoromethyl)acetophenone (**4o**) was hydrogenated to the corresponding alcohol (**5o**) with an *ee* as high as 99.9% (entry 15). When the catalyst

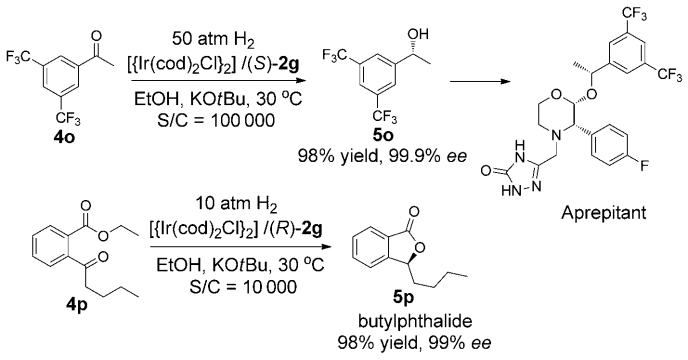
Table 2: Asymmetric hydrogenation of ketones with Ir-(*R*)-**2g**.[a]



Entry	R^1	R^2	Prod	*t*	Yield [%][b]	*Ee* [%][c]
1	C_6H_5	Me	**5a**	20 min	>99	98 (*S*)
2	C_6H_5	Et	**5b**	40 min	>99	96 (*S*)
3	4-MeC_6H_4	Me	**5c**	50 min	>99	98 (*S*)
4	4-$MeOC_6H_4$	Me	**5d**	40 min	98	98 (*S*)
5	4-ClC_6H_4	Me	**5e**	40 min	96	97 (*S*)
6	4-BrC_6H_4	Me	**5f**	40 min	98	96 (*S*)
7	3-MeC_6H_4	Me	**5g**	40 min	96	98 (*S*)
8	3-$MeOC_6H_4$	Me	**5h**	50 min	99	98 (*S*)
9	3-BrC_6H_4	Me	**5i**	50 min	98	98 (*S*)
10	2-MeC_6H_4	Me	**5j**	3 h	99	99.3 (*S*)
11	2-$MeOC_6H_4$	Me	**5k**	40 min	99	99.6 (*S*)
12	2-ClC_6H_4	Me	**5l**	35 min	97	99 (*S*)
13	2-BrC_6H_4	Me	**5m**	4 h	97	98 (*S*)
14	2-naphthyl	Me	**5n**	30 min	97	96 (*S*)
15	3,5-$(CF_3)_2C_6H_3$	Me	**5o**	1.5 h	98	99.9 (*S*)
16[d]	2-$MeOCOC_6H_4$	Bu	**5p**	1 h	99	99 (*S*)
17[e]	cyclohexyl	Me	**5q**	4 h	98	88 (*S*)

[a] Reaction conditions were the same as those listed in Table 1, entry 12. [b] Yield of isolated product. [c] Determined by GC or HPLC on a chiral stationary phase (see the Supporting Information). [d] The product was (*S*)-3-butylisobenzofuran-1(3*H*)-one. [e] S/C = 1000.

loading was reduced to 0.001 mol% (S/C = 100000), hydrogenation of **4o** still proceeded well to give alcohol **5o** in 98% yield and 99% *ee* under 50 atm H_2 (initial). This reaction provided a highly efficient method for the synthesis of (*R*)-**5o**, an important chiral intermediate for a number of pharmaceutically interesting targets such as the NK-1 receptor antagonist aprepitant (Scheme 3).[11] The *ee* for this reaction was better than that obtained by a team from Solvias using a Ru-(phosphinoferrocenyl)oxazoline complex as the catalyst (94.3% *ee* at S/C = 50000).[12] The hydrogenation of ethyl 2-pentanoylbenzoate (**4p**) provided direct access to optically active 3-*n*-butylphthalide (**5p**),[13] which is a medical agent for the treatment of brain-related neurological diseases such as ischemic stroke.[14] When Ir-(*R*)-**2g** was used to catalyze the hydrogenation of **4p**, the corresponding 3-*n*-butylphthalide ((*S*)-**5p**) was obtained in 98% yield and 99% *ee* (entry 16). The catalyst loading could be further lowered to 0.01 mol%



Scheme 3. Asymmetric hydrogenation of **4o** and **4p** with high TONs.

(S/C = 10000) without diminishment of the enantioselectivity of the reaction (Scheme 3). This result provides an efficient approach to the synthesis of optically active 3-*n*-butylphthalide.[15] However, like catalyst Ir-(*R*)-**1c**,[8b] Ir-(*R*)-**2g** was less efficient for the asymmetric hydrogenation of aliphatic ketones such as cyclohexyl methyl ketone (**4q**, entry 17).

In conclusion, we developed a new strategy for inhibiting the deactivation of chiral iridium catalysts by introducing an additional coordination group into the catalysts. This strategy led to the discovery of a highly active and enantioselective chiral iridium catalyst for ketone hydrogenation. With iridium catalyst Ir-(*R*)-**2g**, which has a tridentate spiro P–N–N ligand, the efficiency of the asymmetric hydrogenation has reached a new level.

Experimental Section

General procedure for asymmetric hydrogenation of ketones at S/C = 5000: The catalyst precursor [{Ir(cod)Cl}$_2$] (0.5 mg, 0.75 μmol), ligand (*R*)-**2g** (1.2 mg, 1.6 μmol), and anhydrous EtOH (2 mL) were added under nitrogen to a hydrogenation vessel (20 mL). The mixture was stirred for 1.0 h at 25–30 °C to give a clear yellow solution. The vessel was then placed in an autoclave and purged with hydrogen by pressurizing to 1 atm and releasing the pressure. This procedure was repeated three times and the solution was stirred for 1.0 h under 1 atm of H_2. After releasing the pressure, ketone (7.5 mmol) and a solution of *t*BuOK in EtOH (0.134 mmol mL^{-1}, 0.5 mL, 0.067 mmol) were added through the injection port. The autoclave was then pressurized to 10 atm of H_2 and the reaction mixture was stirred at room temperature (25–30 °C) until no obvious hydrogen pressure drop was observed. After releasing the hydrogen pressure, the reaction mixture was filtered through a short silica gel column, and the filtrate was analyzed by GC to determine the conversion. The solvent in the filtrate was removed to determine the yield. The enantiomeric excess of the product was determined by GC or HPLC on a chiral stationary phase.

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[1] a) W. S. Knowles, M. J. Sabacky, *J. Chem. Soc. Chem. Commun.* **1968**, 1445; b) L. Horner, H. Siegel, H. Büthe, *Angew. Chem.* **1968**, *80*, 1034; *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 942.
[2] a) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029; b) *Handbook of Homogeneous Hydrogenation* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2007**; c) *Catalysis in Asymmetric Synthesis* (Eds.: V. Caprio, J. M. J. Williams), Wiley-VCH, Chichester, **2009**; d) J.-H. Xie, S.-F. Zhu, Q.-L. Zhou, *Chem. Rev.* **2011**, *111*, 1713.
[3] H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya, R. Noyori, *Angew. Chem.* **1998**, *110*, 1792; *Angew. Chem. Int. Ed.* **1998**, *37*, 1703.
[4] a) H.-U. Blaser, H. P. Buser, K. Loers, R. Hanreich, H. P. Jalett, E. Jelsch, B. Pugin, H. D. Schneider, F. Spindler, A. Wagmann, *Chimia* **1999**, *53*, 275; b) H.-U. Blaser, *Adv. Synth. Catal.* **2002**, *344*, 17.
[5] Other examples of asymmetric hydrogenation of acetophenone with TONs as high as 1000000, see: a) A. G. Hu, H. L. Ngo, W. B. Lin, *Org. Lett.* **2004**, *6*, 2937; b) W. Li, X. Sun, L.

Zhou, G. Hou, S. Yu, X. Zhang, *J. Org. Chem.* **2009**, *74*, 1397.
[6] For reviews, see: a) A. Pfaltz, J. Blankenstein, R. Hilgraf, E. Hörmann, S. Mclntyre, F. Menges, M. Schönleber, S. P. Smidt, B. Wüstenberg, N. Zimmermann, *Adv. Synth. Catal.* **2003**, *345*, 33; b) X. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272; c) K. Källström, I. Munslow, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 3194; d) H.-L. Kwong, H.-L. Yeung, C.-T. Yeung, W.-S. Lee, C.-S. Lee, W.-L. Wong, *Coord. Chem. Rev.* **2007**, *251*, 2188.
[7] For selected examples, see: a) D.-S. Wang, J. Zhou, D.-W. Wang, Y.-L. Guo, Y.-G. Zhou, *Tetrahedron Lett.* **2010**, *51*, 525; b) G. H. Liu, M. Yao, J. Y. Wang, X. Q. Lu, M. M. Liu, F. Zhang, H. X. Li, *Adv. Synth. Catal.* **2008**, *350*, 2464; c) Y. Xu, D. M. P. Mingos, J. M. Brown, *Chem. Commun.* **2008**, 199; d) S. Li, S.-F. Zhu, C.-M. Zhang, S. Song, Q.-L. Zhou, *J. Am. Chem. Soc.* **2008**, *130*, 8584; e) Z.-J. Wang, G.-J. Deng, Y. Li, Y.-M. He, W.-J. Tang, Q.-H. Fan, *Org. Lett.* **2007**, *9*, 1243; f) W.-J. Tang, S.-F. Zhu, L.-J. Xu, Q.-L. Zhou, Q.-H. Fan, H.-F. Zhou, K. Lam, A. S. C. Chan, *Chem. Commun.* **2007**, 613; g) S.-F. Zhu, J.-B. Xie, Y.-Z. Zhang, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 12886; h) B. Pugin, H. Landert, F. Spindler, H.-U. Blaser, *Adv. Synth. Catal.* **2002**, *344*, 974; i) H.-U. Blaser, B. Pugin, F. Spindler, A. Togni, *C. R. Chim.* **2002**, *5*, 379.
[8] a) J.-B. Xie, J.-H. Xie, X.-Y. Liu, W.-L. Kong, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2010**, *132*, 4538; b) J.-B. Xie, J.-H. Xie, X.-Y. Liu, Q.-Q. Zhang, Q.-L. Zhou, *Chem. Asian J.* **2011**, *6*, 899.
[9] a) R. H. Crabtree, H. Felkin, G. E. Morris, *J. Organomet. Chem.* **1977**, *141*, 205; b) R. H. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331; For reviews see: c) *Iridium complexes in organic synthesis* (Ed.: C. Claver), Wiley-VCH, Weinheim, **2009**; d) C. G. Arena, G. Arico, *Curr. Org. Chem.* **2010**, *14*, 546; and Ref. [6d].
[10] CCDC 822013 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[11] a) M. M. Zhao, J. M. McNamara, G.-J. Ho, K. M. Emerson, Z. J. Song, D. M. Tschaen, K. M. Brands, U. Dolling, E. J. J. Grabowski, P. J. Reider, *J. Org. Chem.* **2002**, *67*, 6743; b) W. K. Hagmann, *J. Med. Chem.* **2008**, *51*, 4359.
[12] a) F. Naud, F. Spindler, C. J. Rueggeberg, A. T. Schmidt, H. U. Blaser, *Org. Process Res. Dev.* **2007**, *11*, 519; b) F. Naud, C. Malan, F. Spindler, C. Rüggeberg. A. T. Schmidt, H. U. Blaser, *Adv. Synth. Catal.* **2006**, *348*, 47.
[13] a) B. Zhang, M.-H. Xu, G.-Q. Lin, *Org. Lett.* **2009**, *11*, 4712; b) K. Everaere, J.-L. Scheffler, A. Mortreux, J.-F. Carpentier, *Tetrahedron Lett.* **2001**, *42*, 1899.
[14] a) X. X. Huang, D. Hu, Z. W. Qu, J. T. Zhang, Y. P. Feng, *Yaoxue Xuebao* **1996**, *31*, 246; b) X. Z. Zhu, X. Y. Li, J. Liu, *Eur. J. Pharmacol.* **2004**, *500*, 221; c) Q. Chang, X. L. Wang, *Acta Pharmacol. Sin.* **2003**, *24*, 796; d) X. W. Wang, *Drugs Future* **2000**, *25*, 16.
[15] The synthesis of 3-*n*-butylphthalide by asymmetric transfer hydrogenation of ethyl 2-pentanoylbenzoate was reported: using catalyst Ru–TsDBuPEN, 92% yield, 98% *ee* at S/C = 200 (ref. [12a]); using catalyst Ru–TsDPEN, 80% conv., 92% *ee* at S/C = 100 (ref. [12b]).

