Asymmetric Catalysis

DOI: 10.1002/ange.201106972

Rhodium-Catalyzed, Highly Enantioselective 1,2-Addition of Aryl Boronic Acids to α-Ketoesters and α-Diketones Using Simple, Chiral Sulfur–Olefin Ligands**

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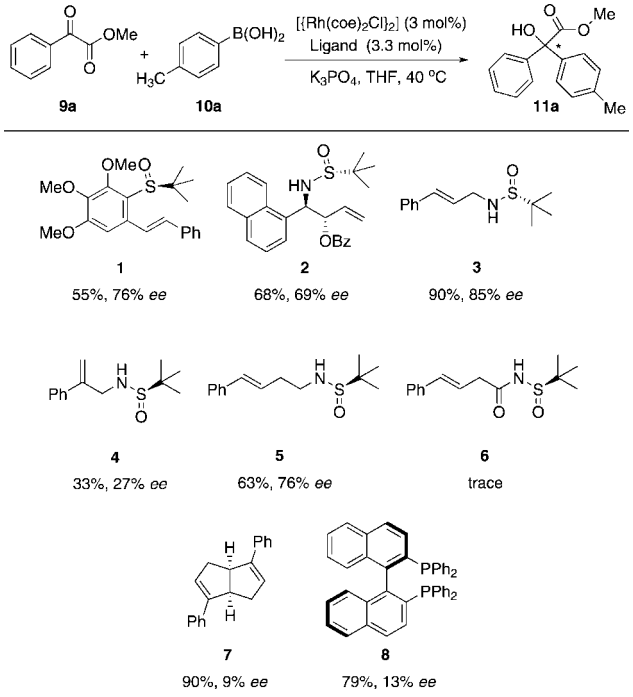
Optically active α-hydroxy carbonyl compounds are not only very important structural motifs in numerous biologically interesting compounds, but also serve as fundamental building blocks for numerous applications in organic synthesis.[1] Over the past decades, various methods have been developed for the synthesis of these valuable chiral compounds.[2–5] Among these, the transition-metal-catalyzed asymmetric nucleophilic addition of organometallic reagents to α-keto carbonyl compounds is a particularly powerful and straightforward approach.[4] In recent years, the use of stable, commercially available aryl boronic acids in place of common organometallic reagents in transition-metal-catalyzed carbon–carbon bond-forming reactions has attracted considerable attention.[5,6] However, despite these successes with asymmetric reactions involving α,β-unsaturated carbonyl compounds[7] and aldimines,[8] the transition-metal-catalyzed asymmetric addition of aryl boronic acids to carbon-oxygen double bonds in ketones (producing enantioenriched tertiary alcohols) remains under-studied and elusive. To date, only very limited progress has been achieved in the rhodium-catalyzed asymmetric addition of these species to isatins (up to 91% *ee*),[5a,b] α-ketoesters (up to 95% *ee*),[5c,d,9] and α-trifluoromethyl ketones (up to 83% *ee*);[10] all methods that employ chiral phosphine, phosphite, or phosphoramidite ligands.[11] With respect to α-diketones, to the best of our knowledge, there are no examples of their catalytic, enantioselective coupling with aryl boronic acids to provide optically active, tertiary α-hydroxyketones.[12] Thus, the development of new catalytic systems that are capable of the efficient synthesis of enantiomerically pure α-hydroxy carbonyl compounds with a quaternary stereogenic center is highly desirable.

We have recently designed a series of chiral sulfinamide/sulfoxide-based olefin ligands and successfully employed them in the rhodium-catalyzed asymmetric 1,4-addition of aryl boronic acids to α,β-unsaturated carbonyl compounds.[13,14] These studies demonstrated that simple and readily available chiral sulfur–olefin hybrid ligands can also display great catalytic activities and enantioselectivities in asymmetric catalysis. We have recently become intrigued by the possibility of their application in the more challenging enantioselective 1,2-addition of aryl boronic acids to more activated ketones, such as α-ketoesters and α-diketones, to provide optically active, functionalized tertiary alcohols. Herein we describe our efforts to address this issue. By employing an extremely simple, chiral *N*-(sulfinyl)cinnamylamine as a ligand, aryl boronic acids were effectively activated under rhodium catalysis to react stereoselectively with both α-ketoesters and α-diketones, giving products with excellent enantioselectivities under exceptionally mild conditions.

In our initial studies, we attempted to test whether our recently designed chiral sulfinamide/sulfoxide–olefins **1–3** can act as chiral ligands in the rhodium-catalyzed 1,2-addition of aryl boronic acids to α-ketoesters (Scheme 1). The addition of methyl phenylglyoxylate (**9a**) with *p*-tolylboronic acid was chosen as a model reaction. To our delight, the reactions all proceeded well in the presence of $[\{Rh(coe)_2Cl\}_2]$ (3 mol%) in aqueous K_3PO_4 (1.5 M)/THF at 40 °C, giving the expected



Scheme 1. Ligand screening. coe = cyclooctene, Bz = benzyl.

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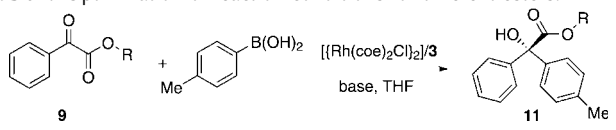
[**] Financial support from the National Natural Science Foundation of China (20972172, 21021063), the Chinese Academy of Sciences, SIMM, and the National Science & Technology Major Project is greatfully acknowledged.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201106972.

tertiary α-hydroxyester **11a** in moderate to good yields with very promising enantioselectivities (69–85% *ee*). Interestingly, the structurally extremely simple chiral *N*-(sulfinyl)cinnamylamine **3**[15] showed the greatest potential, both in terms of catalytic activity and enantiocontrol (90% yield and 85% *ee*).[16] With this result in mind, we further elaborated the ligand structure and designed several new sulfonamide–olefins **4**–**6** for screening. However, these efforts were unsuccessful. In all cases, the new ligands were either less effective or altogether inactive. It should be noted that, although this 1,2-addition reaction could be catalyzed by chiral diene ligand **7** and diphosphine ligand **8** (BINAP), only very low enantioselectivities (9% and 13% *ee*, respectively) were attained. These results highlight the unique catalytic performance of chiral, sulfur-based, olefin-class ligands.

Following up on the encouraging results obtained with chiral *N*-(sulfinyl)cinnamylamine **3**, the reaction conditions, particularly the effect of the ester group in phenylglyoxylate, were thoroughly explored (Table 1). Under conditions similar to those noted above, a survey of solvents indicated that the

Table 1: Optimization of reaction conditions for different esters.[a]



9 **11**

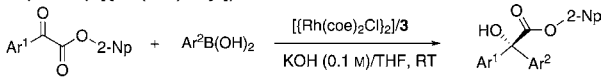
Entry	R	Base[b]	*T* [°C]	**11**	Yield[c] [%]	*ee*[d] [%]
1	Me	K_3PO_4	40	**11a**	90	85
2	Et	K_3PO_4	40	**11b**	96	87
3	*i*Pr	K_3PO_4	40	**11c**	92	85
4	*t*Bu	K_3PO_4	40	**11d**	68	86
5	Bn	K_3PO_4	40	**11e**	81	85
6	Ph	K_3PO_4	40	**11f**	65	92
7	4-ClC_6H_4	K_3PO_4	40	**11g**	33	94
8	1-Np	K_3PO_4	40	**11h**	41	95
9	2-Np	K_3PO_4	40	**11i**	42	94
10	Me	K_3PO_4	RT	**11a**	82	87
11	Me	LiF[e]	RT	**11a**	95	87
12	Et	KOH[f]	RT	**11b**	95	88
13	1-Np	KOH[f]	RT	**11h**	67	93
14	2-Np	KOH[f]	RT	**11i**	86	94

[a] Reactions were carried out with α-ketoester (0.25 mmol) and 1.5 equiv of *p*-tolylboronic acid, in the presence of 3 mol% of [{Rh(coe)$_2$Cl}$_2$], 3.3 mol% of ligand **3**, and base in 1.0 mL of THF. [b] Unless noted, base (1.5 M, 0.5 equiv) was used. [c] Yield of isolated product. [d] Determined by chiral HPLC analysis. [e] 1.2 equiv of LiF (1.5 M) was used. [f] 0.08 equiv of KOH (0.1 M) was used.

use of toluene, CH_2Cl_2, MeOH, or 1,2-dimethoxyethane leads to a decrease in enantioselectivity (60% *ee*, 39% *ee*, 70% *ee*, and 81% *ee*, respectively; not shown in Table 1). Varying the ester substituent from methyl to ethyl, isopropyl, *tert*-butyl, or benzyl did not improve the enantioselectivity of the reaction (Table 1, entries 2–5). Gratifyingly, when phenyl phenylglyoxylate was employed, product **11f** was obtained with improved enantioselectivity (92% *ee*, entry 6), as expected. Further, varying the R group to *p*-chlorophenyl, 1-naphthyl, or 2-naphthyl gave slightly better enantioselectivities (94–95%), but led to a large decrease in yields owing to significant hydrolysis of the aromatic ester substrates (entries 7–9). After extensive studies, we found that the use of even milder conditions employing less base could solve the problem. Finally, 2-naphthyl phenylglyoxylate underwent reaction smoothly, producing tertiary α-hydroxyester **11i** in good yield (86%), with the highest *ee* (94%) obtained in aqueous KOH (0.1M)/THF at room temperature (entry 14).

Having observed that the rhodium/sulfur–olefin-catalyzed addition to 2-naphthyl ester under the above optimized conditions can be highly selective, we then decided to investigate the scope of this process. As summarized in Table 2, a variety of aryl boronic acids with diverse steric and electronic properties were tested with 2-naphthyl α-ketoesters **9i**–**k**. We were pleased to find that the addition reactions consistently gave the expected products in moderate to good yields and excellent *ee* values (90–95%). Unlike the previously reported catalytic system,[5c,d] the addition reaction seems insensitive to the steric effects of the substrates and reagents, as both sterically encumbered 2-naphthyl 2-naphthylglyoxylate and *ortho*-substituted aryl boronic acids could be successfully employed (Table 2, entries 5,6 and 19–21). Notably, the system also allows for the efficient synthesis of products where both Ar^1 and Ar^2 are substituted phenyl or

Table 2: Asymmetric 1,2-addition of arylboric acids to α-ketoesters catalyzed by [{Rh(coe)$_2$Cl}$_2$]/**3**.[a]



9 **10** **11**

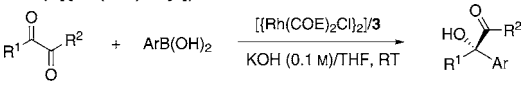
Entry	Ar^1	Ar^2	**11**	Yield[b] [%]	*ee*[c,d] [%]
1	Ph (**9i**)	4-MeC_6H_4	**11i**	86	94 (*S*)
2	Ph (**9i**)	4-ClC_6H_4	**11j**	84	94 (*S*)
3	Ph (**9i**)	4-FC_6H_4	**11k**	86	94 (*S*)
4	Ph (**9i**)	4-$MeOC_6H_4$	**11l**	94	92 (*S*)
5	Ph (**9i**)	2-MeC_6H_4	**11m**	72	92 (*S*)
6	Ph (**9i**)	2-$MeOC_6H_4$	**11n**	73	90 (*S*)
7	Ph (**9i**)	3-MeC_6H_4	**11o**	82	93 (*S*)
8	Ph (**9i**)	3-ClC_6H_4	**11p**	67	95 (*S*)
9	Ph (**9i**)	3-FC_6H_4	**11q**	72	95 (*S*)
10	Ph (**9i**)	3-$MeOC_6H_4$	**11r**	72	93 (*S*)
11	Ph (**9i**)	3,5-$Me_2C_6H_3$	**11s**	74	92 (*S*)
12	Ph (**9i**)	1-naphthyl	**11t**	87	91 (*S*)
13	Ph (**9i**)	2-naphthyl	**11u**	76	92 (*S*)
14	Ph (**9i**)	*n*-PhC_6H_4	**11v**	82	93 (*S*)
15	4-ClC_6H_4 (**9j**)	Ph	**11j′**	66	95 (*R*)
16	4-ClC_6H_4 (**9j**)	4-MeC_6H_4	**11w**	66	92 (*R*)
17	4-ClC_6H_4 (**9j**)	4-FC_6H_4	**11x**	70	95 (*R*)
18	4-ClC_6H_4 (**9j**)	2-naphthyl	**11y**	75	93 (*S*)
19	2-naphthyl (**9k**)	Ph	**11u′**	89	91 (*R*)
20	2-naphthyl (**9k**)	4-ClC_6H_4	**11y′**	87	94 (*R*)
21	2-naphthyl (**9k**)	2-MeC_6H_4	**11z**	54	93 (*S*)

[a] Reactions were carried out with α-ketoester (0.25 mmol) and 1.5 equiv of aryl boronic acid, in the presence of 3 mol% of [Rh], 3.3 mol% of ligand **3**, and KOH (0.1 M, 0.08 equiv) in THF(1.0 mL) for 3 h. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] The absolute configurations of **11i** and **11t** were determined by comparing their optical rotation values with known data[18] after removal of the 2-naphthyl group by ester hydrolysis under basic conditions (2.5 M KOH, see Supporting Information for details); the other configurations were assigned by analogy.

naphthyls groups (entries 16–18 and 20,21). The preparation of such tertiary α-hydroxycarboxylate derivatives by the direct addition of aryl boronic acids to aryl glyoxylates has not been extensively explored before.[17] It is particularly remarkable that a great level of enantiofacial discrimination can be achieved despite only small differences between the aryl groups (entries 16,17). Moreover, by simply switching the corresponding Ar^1 and Ar^2 groups of the α-ketoesters and boronic acids, both enantiomers of the product were obtained with the same high level of enantioselectivity (entries 2 and 15, entries 13 and 19, and entries 18 and 20).

After our success with the 1,2-addition to α-ketoesters, we turned our attention to the more challenging α-diketone substrates in an attempt to generate optically active tertiary α-hydroxyketone derivatives (Table 3).The catalytic enantioselective addition of aryl boronic acids to α-diketones to provide tertiary α-hydroxyketones has not yet been reported. Initially, benzil (**12a**) was examined under the optimized conditions. The reaction led to a 97% yield of the desired product **13a** with an excellent *ee* value of 97% (Table 3, entry 1). Reactions involving other aryl boronic acids with different electronic and steric demands were all found to be successful, giving addition products with similarly high levels of enantioselectivity (up to 99% *ee*; entries 2–7). Furthermore, the substituted benzyl species (such as **12b**, **12c**, and **12d**) also underwent 1,2-addition to afford the corresponding products in very high yields and enantioselectivities (entries 8–10). To further evaluate the substrate scope, the reaction of other commonly used α-diketones with *p*-tolylboronic acid was investigated. In the case of the less sterically hindered aliphatic biacetyl **12e**, a decreased yield and moderate enantioselectivity was obtained (entry 11). Interestingly, when unsymmetrical α-diketone **12f** was employed, our system exhibited both regio- and enantio-selectivity. Products **13l** and **13m** were both observed, with addition to the less hindered and less electron deficient carbonyl group predominating (entry 12). In all of the reaction examples, it is worth noting that no diarylation occurs.

Table 3: Asymmetric 1,2-addition of arylboric acids to α-diketones catalyzed by $[\{Rh(coe)_2Cl\}_2]$/**3**.[a]

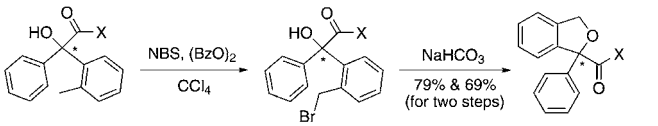


12 **10** **13**

Entry	Substrate	Ar	13	Yield[b] [%]	*ee*[c,d] [%]
1	$R^1=R^2=$Ph (**12a**)	4-MeC_6H_4	**13a**	97	97 (*S*)
2	$R^1=R^2=$Ph (**12a**)	4-$MeOC_6H_4$	**13b**	99	97 (*S*)
3	$R^1=R^2=$Ph (**12a**)	4-ClC_6H_4	**13c**	97	99 (*S*)
4	$R^1=R^2=$Ph (**12a**)	4-FC_6H_4	**13d**	98	98 (*S*)
5	$R^1=R^2=$Ph (**12a**)	4-PhC_6H_4	**13e**	98	97 (*S*)
6	$R^1=R^2=$Ph (**12a**)	3-$MeOC_6H_4$	**13f**	95	97 (*S*)
7	$R^1=R^2=$Ph (**12a**)	2-MeC_6H_4	**13g**	54	95 (*S*)
8	$R^1=R^2=$4-BrC_6H_4 (**12b**)	4-MeC_6H_4	**13h**	93	98 (*R*)
9	$R^1=R^2=$4-FC_6H_4 (**12c**)	4-MeC_6H_4	**13i**	99	96 (*R*)
10	$R^1=R^2=$4-$MeOC_6H_4$ (**12d**)	4-MeC_6H_4	**13j**	98	97 (*R*)
11	$R^1=R^2=$Me (**12e**)	4-MeC_6H_4	**13k**	45	63 (*S*)
12[e]	$R^1=$Me, $R^2=$Ph (**12f**)	4-MeC_6H_4	**13l**	85	80 (*S*)

[a] The reaction was carried out with α-diketone (0.25 mmol) and 1.5 equiv of aryl boronic acid, in the presence of 3 mol% of [Rh], 3.3 mol% of ligand, and 0.1 M aq KOH (0.2 mL, 8% equiv) in 1.0 mL THF. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] The absolute configuration of **13a** was determined by comparing the optical rotation value and HPLC chromatogram with those obtained by Grignard addition of phenylmagnesium chloride to the above-defined tertiary α-hydroxyester (*S*)-**11i**. See Supporting Information for details; the other configurations were assigned by analogy. [e] A regioisomer (**13m**, $R^1=$Ph, $R^2=$Me) was obtained in 10% yield with 76% *ee*.

To demonstrate the synthetic utility of the current method, the addition products **11m** and **13g** were subjected to bromination by NBS/CCl_4 to give the corresponding bromides (**14a** and **14b**). Upon treatment with $NaHCO_3$, the quaternary-carbon-containing, chiral 1,3-dihydroisobenzofuran (phthalan) products **15a** and **15b** were generated in 79% and 69% yield, respectively, without loss of optical purity (Scheme 2). This result is notable because chiral 1,3-dihydroisobenzofuran compounds are valuable pharmacological compounds, as exemplified by the antidepressant drug citalopram.[19] However, they are usually difficult to access through asymmetric catalysis.[20]



11m (X = O-2-Np), 92% *ee* **14a** (X = O-2-Np) **15a** (X = O-2-Np), 91% *ee*
13g (X = Ph), 95% *ee* **14b** (X = Ph) **15b** (X = Ph), 94% *ee*

Scheme 2. Synthesis of chiral 1,3-dihydroisobenzofurans. NBS = *N*-bromosuccinimide, Np = naphthyl.

In summary, we have developed a highly efficient rhodium-catalyzed, asymmetric 1,2-addition of aryl boronic acids to α-ketoesters and α-diketones through the use of extremely simple, chiral *N*-(sulfinyl)cinnamylamine ligand. The method offers easy, general, and practical access to a variety of highly enantioenriched tertiary α-hydroxy carbonyl compounds under exceptionally mild conditions. The catalytic asymmetric addition to α-diketones represents an unprecedented synthesis of optically active, tertiary α-hydroxyketone derivatives. Moreover, aside from their use in 1,4-addition to α,β-unsaturated carbonyl compounds,[13,14] this is the first example of the successful application of the recently developed, chiral sulfur–olefin ligands in asymmetric catalysis, wherein the unique sulfonamide–olefin **3** has been shown to be highly effective. It opens new opportunities for the use of this novel class of readily available ligands in related asymmetric processes. Efforts to realize such a goal are currently underway in our laboratory.

Experimental Section

General procedure for the rhodium-catalyzed asymmetric 1,2-addition: Under an argon atmosphere, a solution of α-dicarbonyl compounds (0.25 mmol), $[\{Rh(coe)_2Cl\}_2]$ (3 mol%, 2.7 mg, 0.0075 mmol of Rh), ligand **3** (2.0 mg, 0.00825 mmol), and aryl

boronic acid (0.375 mmol) in 1.0 mL of THF was stirred at room temperature for 30 minutes. Aqueous KOH (0.2 mL, 0.1M, 0.02 mmol) was then added to this mixture. After being stirred at room temperature for 3 hours, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford the corresponding addition product (**11** or **13**).

Received: October 2, 2011
Published online: December 1, 2011

Keywords: 1,2-addition · α-hydroxy carbonyl compounds · asymmetric catalysis · rhodium · sulfur–olefin ligands

[1] a) G. M. Coppola, H. F. Schuster, *Chiral α-Hydroxy Acids in Enantioselective Synthesis*, Wiley-VCH, Weinheim, **1997**; b) S. Hanessian, *Total Synthesis of Natural Products: The Chiron Approach*, Pergamon, New York, **1983**, Chapter 2.

[2] For reviews, see: a) F. A. Davis, B.-C. Chen, *Chem. Rev.* **1992**, *92*, 919; b) B. Plietker, *Tetrahedron: Asymmetry* **2005**, *16*, 3453; c) J. Christoffers, A. Baro, T. Werner, *Adv. Synth. Catal.* **2004**, *346*, 143.

[3] For representative examples, see: a) F. A. Davis, M. C. Weismiller, *J. Org. Chem.* **1990**, *55*, 3715; b) W. Adam, R. T. Fell, V. R. Stegmann, C. R. Saha-Möller, *J. Am. Chem. Soc.* **1998**, *120*, 708; c) J. L. Wood, G. A. Moniz, D. A. Pflum, B. M. Stoltz, A. A. Holubec, H.-J. Dietrich, *J. Am. Chem. Soc.* **1999**, *121*, 1748; d) N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 6038; e) H. Li, B. Wang, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 732; f) L. C. Akullian, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2006**, *128*, 6532; g) S. Samanta, C.-G. Zhao, *Tetrahedron Lett.* **2006**, *47*, 3383; h) B. E. Howard, K. A. Woerpel, *Org. Lett.* **2007**, *9*, 4651; i) B. M. Trost, J. Xu, T. Schmidt, *J. Am. Chem. Soc.* **2008**, *130*, 11852; j) K. Zheng, J. Shi, X. Liu, X. Feng, *J. Am. Chem. Soc.* **2008**, *130*, 15770; k) J. Luo, H. Wang, X. Han, L.-W. Xu, J. Kwiatkowski, K.-W. Huang, Y. Lu, *Angew. Chem.* **2011**, *123*, 1901; *Angew. Chem. Int. Ed.* **2011**, *50*, 1861; l) T. Ohshima, T. Kawabata, Y. Takeuchi, T. Kakinuma, T. Iwasaki, T. Yonezawa, H. Murakami, H. Nishiyama, K. Mashima, *Angew. Chem.* **2011**, *123*, 6420; *Angew. Chem. Int. Ed.* **2011**, *50*, 6296.

[4] a) E. F. DiMauro, M. C. Kozlowski, *J. Am. Chem. Soc.* **2002**, *124*, 12668; b) B. Jiang, Z. Chen, X. Tang, *Org. Lett.* **2002**, *4*, 3451; c) E. F. DiMauro, M. C. Kozlowski, *Org. Lett.* **2002**, *4*, 3781; d) K. Funabashi, M. Jachmann, M. Kanai, M. Shibasaki, *Angew. Chem.* **2003**, *115*, 5647; *Angew. Chem. Int. Ed.* **2003**, *42*, 5489; e) L. C. Wieland, H. Deng, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2005**, *127*, 15453; f) G. Blay, I. Fernández, A. Marco-Aleixandre, J. R. Pedro, *Org. Lett.* **2006**, *8*, 1287; g) K. Zheng, B. Qin, X. Liu, X. Feng, *J. Org. Chem.* **2007**, *72*, 8478; h) C. Schuster, M. Knollmueller, P. Gaertner, *Tetrahedron: Asymmetry* **2006**, *17*, 2430; i) B. Zheng, S. Hou, Z. Li, H. Guo, J. Zhong, M. Wang, *Tetrahedron: Asymmetry* **2009**, *20*, 2125.

[5] a) R. Shintani, M. Inoue, T. Hayashi, *Angew. Chem.* **2006**, *118*, 3431; *Angew. Chem. Int. Ed.* **2006**, *45*, 3353; b) P. Y. Toullec, R. B. C. Jagt, J. G. de Vries, B. L. Feringa, A. J. Minnaard, *Org. Lett.* **2006**, *8*, 2715; c) H.-F. Duan, J.-H. Xie, X.-C. Qiao, L.-X. Wang, Q.-L. Zhou, *Angew. Chem.* **2008**, *120*, 4423; *Angew. Chem. Int. Ed.* **2008**, *47*, 4351; d) Y. Yamamoto, T. Shirai, M. Watanabe, K. Kurihara, N. Miyaura, *Molecules* **2011**, *16*, 5020.

[6] D. G. Hall, *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*, Wiley-VCH, Weinheim, **2005**.

[7] For reviews, see: a) K. Fagnou, M. Lautens, *Chem. Rev.* **2003**, *103*, 169; b) T. Hayashi, K. Yamasaki, *Chem. Rev.* **2003**, *103*, 2829; c) J. Christoffers, G. Koripelly, A. Rosiak, M. Rossle, *Synthesis* **2007**, 1279.

[8] a) Z.-Q. Wang, C.-G. Feng, M.-H. Xu, G.-Q. Lin, *J. Am. Chem. Soc.* **2007**, *129*, 5336, and references therein; b) Z. Cui, H.-J. Yu, R.-F. Yang, W.-Y. Gao, C.-G. Feng, G.-Q. Lin, *J. Am. Chem. Soc.* **2011**, *133*, 12394.

[9] For non-asymmetric addition of aryl boronic acids to α-ketoesters, see: a) P. He, Y. Lu, C.-G. Dong, Q.-S. Hu, *Org. Lett.* **2007**, *9*, 343; b) P. He, Y. Lu, Q.-S. Hu, *Tetrahedron Lett.* **2007**, *48*, 5283; c) G. R. Ganci, J. D. Chisholm, *Tetrahedron Lett.* **2007**, *48*, 8266; d) S. Miyamura, T. Satoh, M. Miura, *J. Org. Chem.* **2007**, *72*, 2255; For non-asymmetric addition of arylstannanes to α-ketoesters, see: e) S. Oi, M. Moro, H. Fukuhara, T. Kawanishi, Y. Inoue, *Tetrahedron* **2003**, *59*, 4351.

[10] a) S. L. X. Martina, R. B. C. Jagt, J. G. de Vries, B. L. Feringa, A. J. Minnaard, *Chem. Commun.* **2006**, 4093; b) V. R. Jumde, S. Facchetti, A. Iuliano, *Tetrahedron: Asymmetry* **2010**, *21*, 2775.

[11] For an example of palladium-catalyzed, asymmetric intramolecular addition of aryl boronic acids to ketones, see: G. Liu, X. Lu, *J. Am. Chem. Soc.* **2006**, *128*, 16504.

[12] For related non-asymmetric addition examples, see Refs [9c–e].

[13] a) S.-S. Jin, H. Wang, M.-H. Xu, *Chem. Commun.* **2011**, *47*, 7230; b) W.-Y. Qi, T.-S. Zhu, M.-H. Xu, *Org. Lett.* **2011**, *13*, 3410; c) S.-S. Jin, Ph.D. Thesis, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, **2011**.

[14] For other recent reports on using chiral sulfur–olefin ligands for asymmetric 1,4-additions, see: a) T. Thaler, L.-N. Guo, A. K. Steib, M. Raducan, K. Karaghiosoff, P. Mayer, P. Knochel, *Org. Lett.* **2011**, *13*, 3182; b) X. Feng, Y. Wang, B. Wei, J. Yang, H. Du, *Org. Lett.* **2011**, *13*, 3300; c) G. Chen, J. Gui, L. Li, J. Liao, *Angew. Chem.* **2011**, *123*, 7823; *Angew. Chem. Int. Ed.* **2011**, *50*, 7681; d) X. Feng, B. Wei, J. Yang, H. Du, *Org. Biomol. Chem.* **2011**, *9*, 5927; e) F. Xue, X. Li, B. Wan, *J. Org. Chem.* **2011**, *76*, 7256; f) Y. Wang, X. Feng, H. Du, *Org. Lett.* **2011**, *13*, 4954.

[15] Ligand **3** can be prepared on a multi-gram scale in one pot, see the Supporting Information for details.

[16] The use of $[\{Rh(C_2H_4)_2Cl\}_2]$ in place of $[\{Rh(coe)_2Cl\}_2]$ afforded the product in 74% yield and 83% *ee*.

[17] Only one example of Ru/Me-BIPAM-catalyzed asymmetric addition ($Ar^1 = 4\text{-}FC_6H_4$, $Ar^2 = 3\text{-}ClC_6H_4$) is known. See Ref. [5d].

[18] A. I. Meyers, J. Slade, *J. Org. Chem.* **1980**, *45*, 2912.

[19] a) P. Zhang, G. Cyriac, T. Kopajtic, Y. Zhao, J. A. Javitch, J. L. Katz, A. H. Newman, *J. Med. Chem.* **2010**, *53*, 6112; b) J. N. N. Eildal, J. Andersen, A. S. Kristensen, A. M. Jørgensen, B. Bang-Andersen, M. Jørgensen, K. Strømgaard, *J. Med. Chem.* **2008**, *51*, 3045; c) R. G. Lovey, A. J. Elliott, J. J. Kaminski, D. Loebenberg, R. M. Parmegiani, D. F. Rane, V. M. Girijavallabhan, R. E. Pike, H. Guzik, B. Antonacci, T. Y. Tomaine, *J. Med. Chem.* **1992**, *35*, 4221; d) J. F. DeBernardis, D. L. Arendsen, J. J. Kyncl, D. J. Kerkman, *J. Med. Chem.* **1987**, *30*, 178.

[20] For an example of the stereoselective synthesis of 1,3-disubstituted phthalan-$\{Cr(CO)_3\}$ complexes, see: a) S. Zemolka, J. Lex, H.-G. Schmalz, *Angew. Chem.* **2002**, *114*, 2635; *Angew. Chem. Int. Ed.* **2002**, *41*, 2525; For non-asymmetric synthesis examples, see: b) K. Kobayashi, K. Shikata, Y. Fujii, S. Fukamachi, M. Tanmatsu, H. Konishi, *Heterocycles* **2010**, *81*, 1459; c) R. Karmakar, P. Pahari, D. Mal, *Tetrahedron Lett.* **2009**, *50*, 4042; d) B. Chao, D. C. Dittmer, *Tetrahedron Lett.* **2000**, *41*, 6001 and Refs [19].

