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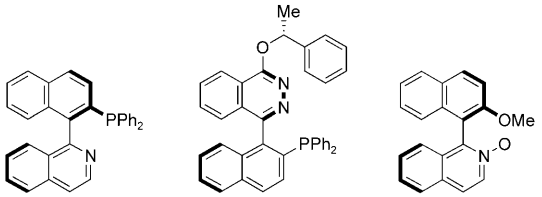
Enantioselective Synthesis of Axially Chiral 1-Arylisoquinolines by Rhodium-Catalyzed [2+2+2] Cycloaddition

Norifumi Sakiyama,[a] Daiki Hojo,[a] Keiichi Noguchi,[b] and Ken Tanaka*[a]

Axially chiral 1-arylisoquinoline and 2-arylpyridine derivatives are valuable compounds as chiral ligands[1] and catalysts[2] for various asymmetric catalytic reactions. However, their conventional syntheses are based on the optical resolution of racemic compounds.[1,2] For example, the axially chiral 1-arylisoquinoline-based P,N ligand quinap was synthesized by optical resolution of its racemate with a stoichiometric amount of a chiral palladium(II) complex.[1d,f,j] The axially chiral 1-aryl-phthalazine-based P,N ligand pinap, was synthesized by separation of two atropisomeric diastereomers derived from a chiral secondary alcohol or amine.[1k] Axially chiral 1-arylisoquinoline-*N*-oxide (quinox) was synthesized by optical resolution of the corresponding 1-arylisoquinoline by using a stoichiometric amount of chiral 1,1′-bi-2-naphthol.[2c,d]



(*R*)-quinap (*R,R*)-O-pinap (*R*)-quinox

In 2004, Gutnov, Heller, and co-workers reported a spectacular approach to axially chiral 2-arylpyridines. They developed the chiral cobalt(I)-complex-catalyzed enantioselective [2+2+2] cycloaddition of aryldiynes with nitriles, to give axially chiral 2-arylpyridines.[3–8] However, this method requires low reaction temperatures to gain high enantioselectivity, and further reaction steps to introduce a phosphorus substituent. Recently, Clayden and co-workers reported the first asymmetric synthesis of a quinap ligand by the dynamic thermodynamic resolution method,[9] whereas catalytic enantioselective synthesis has not been realized to date. Conversely, our research group and others reported the enantioselective synthesis of axially chiral biaryl phosphorus compounds by the cationic rhodium(I)/axially chiral biaryl bisphosphine complex catalyzed atropselective [2+2+2] cycloaddition of diynes with phosphorus-substituted arylalkynes.[10,11] Herein, we report the application of this methodology to the highly enantioselective synthesis of axially chiral 1-arylisoquinolines, which involves the first catalytic enantioselective synthesis of diphenylphosphinoyl-substituted axially chiral 1-arylisoquinolines.

We first investigated the reaction of trimethylsilyl-substituted 1-ethynylisoquinoline **2a** with ether-linked 1,6-diyne **1a** in the presence of the cationic rhodium(I)/(*R*)-binap complex (20 mol%). Excess **1a** (3 equiv) was employed due to its rapid homo-[2+2+2] cycloaddition. Pleasingly, the reaction proceeded at room temperature to give the desired [2+2+2] cycloaddition product **3aa** in good yield with excellent enantioselectivity (Table 1, entry 1). The choice of biaryl bisphosphine ligands appeared to have a modest impact on the product yields, but not on the product enantiomeric excess (*ee*) values (Table 1, entries 1–4). Since the use of H_8-binap and solphos gave **3aa** in high yields, the reaction conditions were further optimized with these ligands (Table 1, entries 5–8). The use of a catalyst loading of 10 mol% and solphos as the ligand, significantly decreased both yield and *ee* value (Table 1, entry 5). An increase of reaction temperature to 80°C also failed to improve the yield of **3aa** (Table 1, entry 6). In contrast, although the use of 5 mol% Rh^I/H_8-binap catalyst at room temperature was

[a] N. Sakiyama, D. Hojo, Prof. Dr. K. Tanaka
Department of Applied Chemistry, Graduate School of Engineering
Tokyo University of Agriculture and Technology
Koganei, Tokyo 184-8588 (Japan)
Fax: (+81) 42-388-7037
E-mail: tanaka-k@cc.tuat.ac.jp

[b] Prof. Dr. K. Noguchi
Instrumentation Analysis Center
Tokyo University of Agriculture and Technology
Koganei, Tokyo 184-8588 (Japan)

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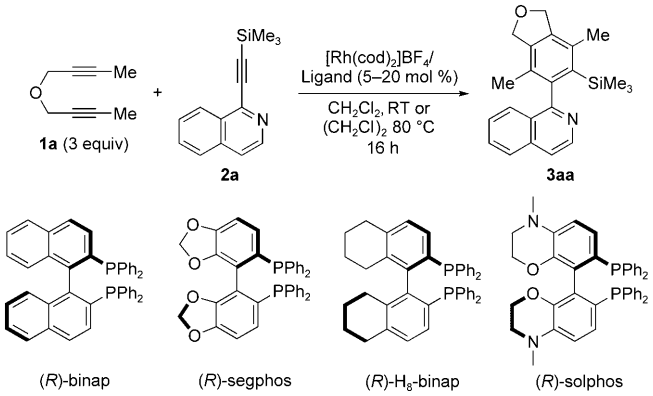
Table 1. Optimization of reaction conditions for rhodium-catalyzed enantioselective [2+2+2] cycloaddition of **1a** with 1-alkynylisoquinoline **2a**.



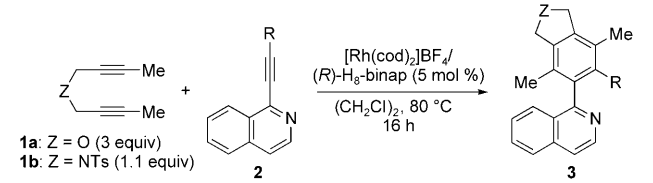
Entry	Ligand	Catalyst [mol %]	*T* [°C]	Yield [%][a]	*ee* [%]
1	(*R*)-binap	20	RT	60	99 (−)
2	(*R*)-segphos	20	RT	64	98 (−)
3	(*R*)-H_8-binap	20	RT	72	99 (−)
4	(*R*)-solphos	20	RT	83	97 (−)
5	(*R*)-solphos	10	RT	26	93 (−)
6	(*R*)-solphos	10	80	17	86 (−)
7	(*R*)-H_8-binap	5	RT	11	99 (−)
8	(*R*)-H_8-binap	5	80	73	93 (−)

[a] Yield of the isolated product.

sluggish (Table 1, entry 7), an increase in the reaction temperature to 80 °C improved the reaction rate to give **3aa** in high yield with a high *ee* value (Table 1, entry 8).

The generality of the reaction was then examined as shown in Table 2. Both ether-linked 1,6-diyne **1a** (Table 2, entry 1) and tosylamide-linked 1,6-diyne **1b** (entry 2) were suitable substrates for this process. In the case of **1b**, 1.1 equivalent was sufficient because of its slow homo-[2+2+2] cycloaddition. With respect to the substituents at the alkyne terminus of 1-ethynylisoquinoline, not only trimethylsilyl-**2a** (Table 2, entries 1 and 2) but also isopropyl- (**2b**, entries 3 and 4), *n*-butyl- (**2c**, entries 5 and 6), and methoxymethyl-substituted 1-ethynylisoquinolines (**2d**, entry 7) could be used.

Table 2. Rhodium-catalyzed enantioselective [2+2+2] cycloaddition of **1a** and **1b** with alkynes **2a**–**2d**.

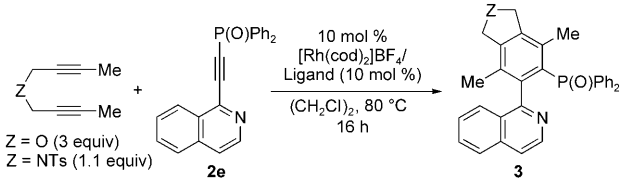


Entry	**1**	**2** (R)	**3**	Yield [%][a]	*ee* [%]
1	**1a**	**2a** ($SiMe_3$)	(−)-**3aa**	73	93
2[b]	**1b**	**2a** ($SiMe_3$)	(−)-**3ba**	78	92
3	**1a**	**2b** (*i*Pr)	(+)-**3ab**	75	94
4	**1b**	**2b** (*i*Pr)	(−)-**3bb**	79	91
5	**1a**	**2c** (*n*Bu)	(+)-**3ac**	84	90
6	**1b**	**2c** (*n*Bu)	(−)-**3bc**	83	89
7	**1a**	**2d** (CH_2OMe)	(+)-**3ad**	71	90

[a] Yield of the isolated product. [b] Catalyst: 10 mol %.

The reactions of diphenylphosphinoyl-substituted 1-ethynylisoquinoline **2e** with tosylamide-linked 1,6-diyne **1b** also proceeded by using a high catalyst loading (10 mol % Rh) and an elevated temperature (80 °C); however, with binap, segphos, and H_8-binap as ligands, the product *ee* values were low (Table 3, entries 1–3). Fortunately, by using solphos as a ligand, the *ee* value was improved with a slight loss of the product yield (Table 3, entry 4). This reaction was also attempted at room temperature with a high catalyst loading (20 mol %) however, the reaction rate was low (Table 3, entry 5). Under the optimum reaction conditions (Table 3, entry 4), the reaction of compound **2e** with ether-linked 1,6-diyne **1a** also proceeded in moderate yield with a good *ee* value (Table 3, entry 6).

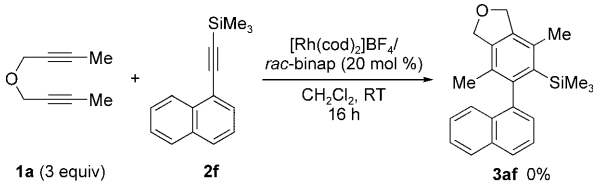
Table 3. Rhodium-catalyzed enantioselective [2+2+2] cycloaddition of 1,6-diynes **1b** and **1a** with diphenylphosphinoyl-substituted 1-ethynylisoquinoline **2e**.



Entry	**1**	Ligand	**3**	Yield [%][a]	*ee* [%]
1	**1b**	(*R*)-binap	(+)-**3be**	86	20
2	**1b**	(*R*)-segphos	(+)-**3be**	36	32
3	**1b**	(*R*)-H_8-binap	(−)-**3be**	77	38
4	**1b**	(*R*)-solphos	(+)-**3be**	65	74
5[b]	**1b**	(*R*)-solphos	(+)-**3be**	22	75
6	**1a**	(*R*)-solphos	(+)-**3ae**	58	77

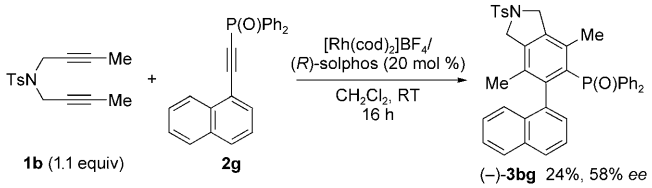
[a] Yield of the isolated product. [b] At RT in CH_2Cl_2, catalyst (20 mol %).

For comparison, the reaction of **1a** with 1-(trimethylsilylethynyl)naphthalene (**2f**) with the Rh^I/*rac*-binap catalyst was examined (Scheme 1). Because of the rapid homo-[2+2+2] cycloaddition reaction of **1a**, the cross-[2+2+2] cycloaddition product **3af** was not obtained. This result clearly indicates that the nitrogen atom of the isoquinoline unit of compound **2a** is essential to promote the desired cross-[2+2+2] cycloaddition with **1a**. On the other hand, the reaction of 1,6-diyne **1b** with 1-(diphenylphosphinoylethynyl)naphthalene (**2g**) using the Rh^I/(*R*)-solphos catalyst gave the



Scheme 1. Rhodium-catalyzed reaction of diyne **1a** with alkyne **2f**.

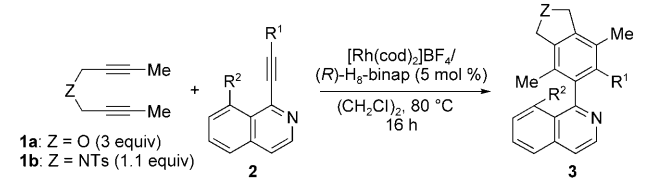
cross-[2+2+2] cycloaddition product **3bg** in almost identical yield, although the *ee* value was lower than that of **3be** (Scheme 2 vs. Table 3, entry 5).



Scheme 2. Rhodium-catalyzed reaction of diyne **1a** with alkyne **2g**.

To obtain 1-arylisoquinolines possessing a configurationally more stable biaryl axis, the reactions of 1-alkynyl-8-methylisoquinolines with 1,6-diynes were examined (Table 4). Interestingly, an 8-methyl substitution is beneficial; 8-methylisoquinolines **3bh** and **3ah** were obtained with higher yields and *ee* values than those of isoquinoline **3aa** (Table 4, entries 1 and 2 vs. entry 3). This positive substituent effect was also found in the reactions of diphenylphosphinoyl-substituted 1-ethynyl-8-methylisoquinoline **2i** with **1b** and **1a**; the desired cycloaddition products **3bi** and **3ai** were obtained with significantly higher yields and *ee* values than those of isoquinoline **3ae**, by using 5 mol% of the rhodium catalysts at 80°C (Table 4, entries 4 and 5 vs. entry 6). Furthermore, biaryl phosphine oxides **3bi** and **3ai** were obtained at room temperature by using 20 mol% of the rhodium catalyst (entries 7 and 8). The absolute configuration of axially chiral biaryl phosphine oxide (+)-**3ai** was unambiguously determined to be *R* by the anomalous dispersion method.[12]

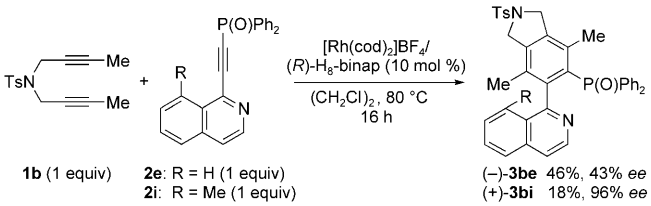
Table 4. Comparison of reactivity and enantioselectivity between 8-methylisoquinolines **2h** and **2i** and isoquinolines **2a** and **2e**.



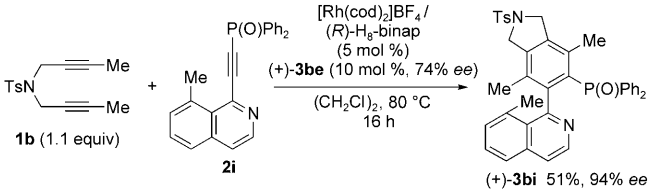
Entry	**1**	**2** (R^1, R^2)	**3**	Yield[%][a]	*ee* [%]
1	**1b**	**2h** ($SiMe_3$, Me)	(−)-**3bh**	87	99
2	**1a**	**2h** ($SiMe_3$, Me)	(−)-**3ah**	80	99
3	**1a**	**2a** ($SiMe_3$, H)	(−)-**3aa**	73	93
4	**1b**	**2i** [$P(O)Ph_2$, Me]	(+)-**3bi**	88	95
5[b]	**1a**	**2i** [$P(O)Ph_2$, Me]	(*R*)-(+)-**3ai**	90	94
6[b]	**1a**	**2e** [$P(O)Ph_2$, H]	(+)-**3ae**	30	33
7[c]	**1b**	**2i** [$P(O)Ph_2$, Me]	(+)-**3bi**	83	95
8[b,c]	**1a**	**2i** [$P(O)Ph_2$, Me]	(*R*)-(+)-**3ai**	87	95

[a] Yield of the isolated product [b] Ligand: (*R*)-binap. [c] At RT in CH_2Cl_2, catalyst (20 mol%).

To clarify the role of the 8-methyl substituent, a competition experiment between **2e** and **2i** was conducted. Although **3bi** was obtained with higher yield than **3be** in separate experiments (Table 4, entry 4 vs. Table 3, entry 3), compound **3be** was obtained with higher yield than **3bi** in the competition experiment (Scheme 3). We anticipated that 1-arylisoquinoline **3be** is more coordinative than 1-aryl-8-methylisoquinoline **3bi**, which might inhibit the reaction. Indeed, the addition of **3be** (10 mol%) to the reaction of 1-alkynyl-8-methylisoquinoline **2i** and **1b** significantly lowered the yield of **3bi** (Scheme 4).

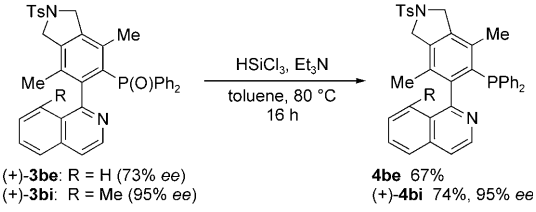


Scheme 3. Competition experiment between **2e** and **2i**.



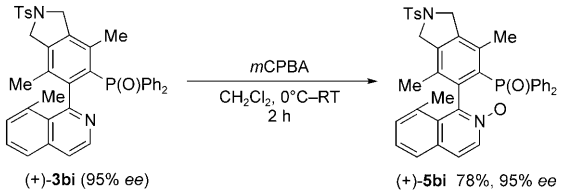
Scheme 4. Rhodium-catalyzed [2+2+2] cycoaddition of **1b** with **2i** in the presence of (+)-**3be**.

Derivatization of axially chiral 1-arylisoquinoline **3** into chiral P,N ligand **4** and chiral isoquinoline-*N*-oxide **5** was readily accomplished. Reduction of phosphine oxide **3be** with $HSiCl_3$ and Et_3N proceeded at 80°C in good yield, whereas the product phosphine **4be** did not possess stable axial chirality at room temperature (Scheme 5).[13] Fortunately, reduction of phosphine oxide **3bi** proceeded under the same reaction conditions to give the corresponding phosphine **4bi**, with stable axial chirality even at 80°C, in good yield and without racemization (Scheme 5). Oxidation of 1-arylisoquinoline **3bi** with *meta*-chloroperbenzoic acid (*m*CPBA) also proceeded to give the corresponding *N*-oxide **5bi** in good yield without racemization (Scheme 6).



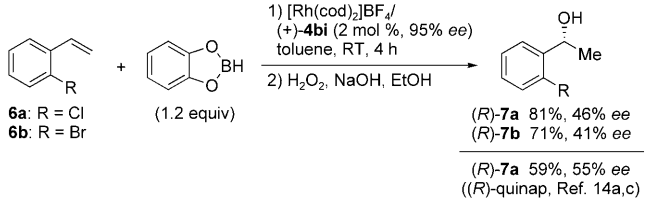
Scheme 5. Synthesis of axially chiral P,N ligands **4be** and (+)-**4bi**.

Finally, preliminary applications of the enantioenriched P,N ligand **4bi** and isoquinoline-*N*-oxide **5bi** in asymmetric catalysis were briefly examined. Since the previously reported rhodium(I)/quinap-catalyzed asymmetric hydroboration

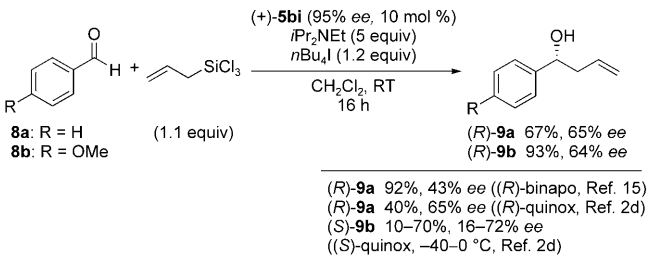


Scheme 6. Synthesis of axially chiral 1-arylisoquinoline-*N*-oxide (+)-**5bi**.

of 2-chlorostyrene proceeds with insufficient yield and enantioselectivity,[14] the rhodium(I)-catalyzed asymmetric hydroboration of 2-chloro- and 2-bromostyrenes **6a** and **6b** was investigated with (+)-**4bi** as a ligand. Although the *ee* values were still moderate, the corresponding chiral secondary alcohols **7a** and **7b** were obtained in high yields (Scheme 7). The asymmetric allylation of benzaldehyde (**8a**) was also examined by using (+)-**5bi** as a catalyst. The corresponding chiral secondary alcohol (*R*)-**9a** was obtained in good yield with a moderate *ee* value (Scheme 8). Comparable results are obtained by using binapo [2-diphenylphosphino-2′-diphenylphosphinyl-1,1′-binaphthalene][15] or quinox[2c,d] as the catalyst.[16] Interestingly, the asymmetric allylation of the less electrophilic 4-methoxybenzaldehyde (**8b**) proceeded in significantly higher yield than that of **8a** (Scheme 8).



Scheme 7. Rhodium-catalyzed asymmetric hydroboration with axially chiral P,N ligand (+)-**4bi**.



Scheme 8. Asymmetric allylation catalyzed by axially chiral 1-arylisoquinoline-*N*-oxide (+)-**5bi**.

In conclusion, we have achieved the enantioselective synthesis of axially chiral 1-arylisoquinolines, which involved the synthesis of diphenylphosphinoyl-substituted arylisoquinolines, by a rhodium-catalyzed [2+2+2] cycloaddition. The new diphenylphosphinoyl-substituted axially chiral 1-arylisoquinolines were successfully derivatized to the corresponding axially chiral P,N ligand and Lewis base catalyst. Future studies will focus on further optimization of chiral ligand/catalyst structures and their applications in various asymmetric catalyses.

Experimental Section

General procedure (Table 4, entry 4): Under an Ar atmosphere, (*R*)-H_8-binap (4.7 mg, 0.0075 mmol) and $[Rh(cod)_2]BF_4$ (3.0 mg, 0.0075 mmol) were dissolved in CH_2Cl_2 (1.0 mL) and the mixture was stirred at room temperature for 30 min. H_2 was added to the resulting solution in a Schlenk tube. After stirring at room temperature for 1 h, the resulting solution was concentrated to dryness. $(CH_2Cl)_2$ (0.5 mL) was then added to the residue at room temperature, followed by a solution of **2i** (55.1 mg, 0.150 mmol) and **1b** (45.4 mg, 0.165 mmol) in $(CH_2Cl)_2$ (1.0 mL). The mixture was stirred at 80 °C for 16 h. The resulting solution was concentrated and purified by preparative TLC (EtOAc) to give (+)-**3bi** (84.6 mg, 0.132 mmol, 88 % yield, 95 % *ee*) as a pale yellow solid.

Acknowledgements

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Keywords: asymmetric catalysis · axial chirality · cycloaddition · isoquinolines · P,N ligand

[1] For reviews, see: a) G. Chelucci, G. Orrù, G. A. Pinna, *Tetrahedron* **2003**, *59*, 9471; b) P. J. Guiry, C. P. Saunders, *Adv. Synth. Catal.* **2004**, *346*, 497; c) Y.-M. Li, F.-Y. Kwong, W.-Y. Yu, A. S. C. Chan, *Coord. Chem. Rev.* **2007**, *251*, 2119. For examples, see: d) N. W. Alcock, J. M. Brown, D. I. Hulmes, *Tetrahedron: Asymmetry* **1993**, *4*, 743; e) J.-M. Valk, T. D. W. Claridge, J. M. Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2597; f) H. Doucet, J. M. Brown, *Tetrahedron: Asymmetry* **1997**, *8*, 3775; g) M. McCarthy, P. J. Guiry, *Tetrahedron* **1999**, *55*, 3061; h) M. McCarthy, R. Goddard, P. J. Guiry, *Tetrahedron: Asymmetry* **1999**, *10*, 2797; i) P. M. Lacey, C. M. McDonnell, P. J. Guiry, *Tetrahedron Lett.* **2000**, *41*, 2475; j) C. W. Lim, O. Tissot, A. Mattison, M. W. Hooper, J. M. Brown, A. R. Cowley, D. I. Hulmes, A. J. Blacker, *Org. Process Res. Dev.* **2003**, *7*, 379; k) T. F. Knöpfel, P. Aschwanden, T. Ichikawa, T. Watanabe, E. M. Carreira, *Angew. Chem.* **2004**, *116*, 6097; *Angew. Chem. Int. Ed.* **2004**, *43*, 5971; l) S. P. Flanagan, R. Goddard, P. J. Guiry, *Tetrahedron* **2005**, *61*, 9808; m) T. Fekner, H. Müller-Bunz, P. J. Guiry, *Org. Lett.* **2006**, *8*, 5109; n) T. Thaler, F. Geittner, P. Knochel, *Synlett* **2007**, 2655; o) T. Fekner, H. Müller-Bunz, P. J. Guiry, *Eur. J. Org. Chem.* **2008**, 5055: p) W. J. Fleming, H. Müller-Bunz, P. J. Guiry, *Eur. J. Org. Chem.* **2010**, 5996.

[2] For reviews, see: a) A. V. Malkov, P. Kočovský, *Eur. J. Org. Chem.* **2007**, 29; b) P. Kočovský, A. V. Malkov, *Pure Appl. Chem.* **2008**, *80*, 953. For examples, see: c) A. V. Malkov, L. Dufková, L. Farrugia, P. Kočovský, *Angew. Chem.* **2003**, *115*, 3802; *Angew. Chem. Int. Ed.* **2003**, *42*, 3674; d) A. V. Malkov, P. Ramírez-López, L. Biedermannová, L. Rulíšek, L. Dufková, M. Kotora, F. Zhu, P. Kočovský, *J. Am. Chem. Soc.* **2008**, *130*, 5341.

[3] a) A. Gutnov, B. Heller, C. Fischer, H.-J. Drexler, A. Spannenberg, B. Sundermann, C. Sundermann, *Angew. Chem.* **2004**, *116*, 3883; *Angew. Chem. Int. Ed.* **2004**, *43*, 3795; b) M. Hapke, K. Kral, C. Fischer, A. Spannenberg, A. Gutnov, D. Redkin, B. Heller, *J. Org. Chem.* **2010**, *75*, 3993.

[4] For a review of atropselective biaryl syntheses by the transition-metal-catalyzed [2+2+2] cycloaddition, see: K. Tanaka, *Chem. Asian J.* **2009**, *4*, 508.

[5] For recent reviews of atropselective biaryl synthesis, see: a) G. Bringmann, A. J. P. Mortimer, P. A. Keller, M. J. Gresser, J. Garner, M. Breuning, *Angew. Chem.* **2005**, *117*, 5518; *Angew. Chem. Int. Ed.* **2005**, *44*, 5384; b) O. Baudoin, *Eur. J. Org. Chem.* **2005**, 4223; c) T. W. Wallace, *Org. Biomol. Chem.* **2006**, *4*, 3197; d) M. Ogasawara, S. Watanabe, *Synthesis* **2009**, 1761; e) M. C. Kozlowski, B. J. Morgan, E. C. Linton, *Chem. Soc. Rev.* **2009**, *38*, 3193.

[6] For recent reviews of the synthesis of nitrogen heterocycles by the transition-metal-catalyzed [2+2+2] cycloaddition, see: a) J. A. Varela, C. Saá, *Synlett* **2008**, 2571; b) B. Heller, M. Hapke, *Chem. Soc. Rev.* **2007**, *36*, 1085; c) Y. Yamamoto, *Chim. Oggi* **2007**, *25*, 108; d) P. R. Chopade, J. Louie, *Adv. Synth. Catal.* **2006**, *348*, 2307; e) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127; f) J. A. Varela, C. Saá, *Chem. Rev.* **2003**, *103*, 3787.

[7] For the enantioselective synthesis of axially chiral 6-aryl-2-pyridones by the rhodium-catalyzed [2+2+2] cycloaddition, see: a) K. Tanaka, A. Wada, K. Noguchi, *Org. Lett.* **2005**, *7*, 4737. For the enantioselective synthesis of axially chiral 4-aryl-2-pyridones by the palladium-catalyzed cycloisomerization, see: b) H. Imase, T. Suda, Y. Shibata, K. Noguchi, M. Hirano, K. Tanaka, *Org. Lett.* **2009**, *11*, 1805.

[8] For the enantioselective synthesis of axially chiral 1-(1-naphthyl)isoquinolines and 1-(1-naphthyl)pyridines through sulfoxide ligand coupling reactions, see: R. W. Baker, S. O. Rea, M. V. Sargent, E. M. C. Schenkelaars, T. S. Tjahjandarie, A. Totaro, *Tetrahedron* **2005**, *61*, 3733.

[9] J. Clayden, S. P. Fletcher, J. J. W. McDouall, S. J. M. Rowbottom, *J. Am. Chem. Soc.* **2009**, *131*, 5331.

[10] a) G. Nishida, K. Noguchi, M. Hirano, K. Tanaka, *Angew. Chem.* **2007**, *119*, 4025; *Angew. Chem. Int. Ed.* **2007**, *46*, 3951. For the enantioselective syntheses of biaryl diphosphonetes and diphosphine oxides by the double [2+2+2] cycloaddition, see: b) G. Nishida, S. Ogaki, Y. Yusa, T. Yokozawa, K. Noguchi, K. Tanaka, *Org. Lett.* **2008**, *10*, 2849; c) S. Doherty, C. H. Smyth, R. W. Harrington, W. Clegg, *Organometallics* **2008**, *27*, 4837. For an example of the enantioselective synthesis of a biaryl monophosphine sulfide, see: d) A. Kondoh, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 6996.

[11] For enantioselective synthesis of axially chiral biaryl phosphorus compounds by the cobalt-catalyzed [2+2+2] cycloaddition, see: B. Heller, A. Gutnov, C. Fischer, H.-J. Drexler, A. Spannenberg, D. Redkin, C. Sundermann, B. Sundermann, *Chem. Eur. J.* **2007**, *13*, 1117.

[12] CCDC-788763 [(*R*)-(+)-**3ai**] contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[13] See the Supporting Information for details.

[14] a) J. M. Brown, D. I. Hulmes, T. P. Layzell, *J. Chem. Soc. Chem. Commun.* **1993**, 1673; b) J. M. Valk, G. A. Whitlock, T. P. Layzell, J. M. Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2593; c) H. Doucet, E. Fernandez, T. P. Layzell, J. M. Brown, *Chem. Eur. J.* **1999**, *5*, 1320; d) E. Fernandez, K. Maeda, M. W. Hooper, J. M. Brown, *Chem. Eur. J.* **2000**, *6*, 1840; e) M. McCarthy, M. W. Hooper, P. J. Guiry, *Chem. Commun.* **2000**, 1333; f) F. Y. Kwong, Q. Yang, T. C. W. Mak, A. S. C. Chan, K. S. Chan, *J. Org. Chem.* **2002**, *67*, 2769; g) D. J. Connolly, P. M. Lacey, M. McCarthy, C. P. Saunders, A.-M. Carroll, R. Goddard, P. J. Guiry, *J. Org. Chem.* **2004**, *69*, 6572; h) A. C. Maxwell, C. Franc, L. Pouchain, H. Müller-Bunz, P. J. Guiry, *Org. Biomol. Chem.* **2008**, *6*, 3848.

[15] a) M. Nakajima, S. Kotani, T. Ishizuka, S. Hashimoto, *Tetrahedron Lett.* **2005**, *46*, 157; b) S. Kotani, S. Hashimoto, M. Nakajima, *Tetrahedron* **2007**, *63*, 3122.

[16] Recently, the synthesis of axially chiral bis(tetrahydroisoquinoline)-*N*,*N*′-dioxides by using a cobalt-catalyzed [2+2+2] cycloaddition was reported and, their application to the enantioselective allylation of aldehydes was explored, see: a) A. Kadlčíková, R. Hrdina, I. Valterová, M. Kotora, *Adv. Synth. Catal.* **2009**, *351*, 1279; b) A. Kadlčíková, I Valterová, L. Ducháčková, J. Roithová, M. Kotora, *Chem. Eur. J.* **2010**, *16*, 9442.

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