DOI: 10.1002/ejoc.200900071

Suzuki Cross-Coupling at the Chiral Groove of 1,1′-Binaphthyl: Stereoconservation versus Deracemization Pathway

Henrich Brath,[a] Michaela Mešková,[a] and Martin Putala*[a]

Keywords: Asymmetric catalysis / Biaryls / C-C coupling / Palladium / P ligands

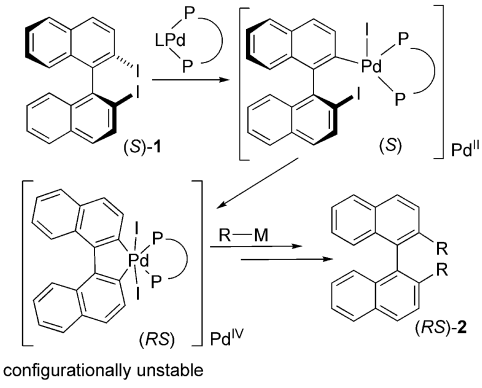
The use of monophos as a ligand in the palladium-catalyzed Suzuki diarylation of 2,2′-diiodo-1,1′-binaphthyl under optimized conditions followed a stereoconservative course. However, some chiral P ligands were found to be capable of inducing stereogenic information during this coupling, regardless of the configuration of the starting diiodide. Among those ligands tested in the deracemization approach, binap exhibited the highest level of asymmetric induction, yielding diarylated product in 83 % *ee* starting from racemic diiodide.

Introduction

Configurationally stable, enantiopure 2,2′-substituted 1,1′-binaphthyl derivatives[1] represent an important group of chiral compounds with applications reported in asymmetric catalysis as ligands,[2] in supramolecular chemistry as building blocks or sensors,[3] and in materials science as compounds with interesting optical and/or electronic properties.[4] The Suzuki reaction has also been applied to prepare binaphthyl derivatives: by diastereoselective[5] or enantioselective[6] coupling of two naphthalene units, or by the attachment of carbon groups to binaphthyl in a stereoconservative manner.[7,8] A deracemization approach has not been reported yet to our best knowledge.

Whereas Suzuki coupling at positions other than the 2- and 2′-positions of 1,1′-binaphthyl derivatives proceeds smoothly without impairment of the enantiomeric purity of the product,[7] at the 2- and 2′-positions, the reaction gives moderate yields of a coupling product that is almost completely racemized under standard conditions.[8] Racemization during Suzuki cross-coupling is most probably caused by the secondary oxidative addition of the common palladium(II) intermediate to the configurationally unstable palladium(IV) intermediate (Scheme 1).[9,10]

Suppressing the expected secondary oxidative addition can be one approach to increase the stereoconservative course of this reaction. Indeed, we have shown that the stereochemical result of Suzuki diarylation at the 2- and 2′-positions of the enantiopure binaphthyl precursor can be significantly affected by the leaving groups at the 2- and 2′-positions; ditolylation by using triphenylphosphane as a ligand and barium hydroxide as a base yielded product **2** with 7 %*ee* from diiodide **1**,[8] 95 %*ee* from dibromide,[10] and >99 %*ee* from diboronic acid.[8] Racemization of the binaphthyl moiety during diarylation of diiodide **1** can be suppressed by the use of less-electron-rich phosphane ligands,[10] which decrease the ability of the palladium(II) intermediate to undergo secondary oxidative addition to the palladium(IV) intermediate. The best results were achieved in the case of trimethyl phosphite and triindol-1-ylphosphane (47 and 65 %*ee* of product **2**, respectively).



Scheme 1. Proposed mechanism of Suzuki coupling of diiodide **1**.

Results and Discussion

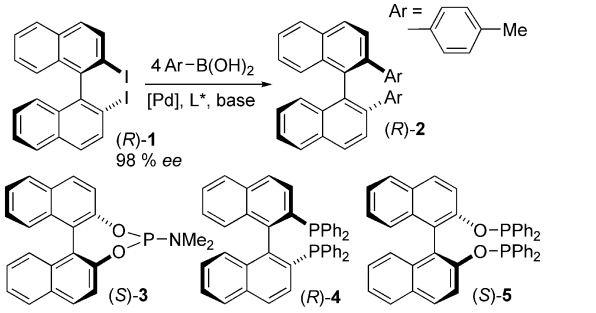
We expected phosphoramidites with similar electronic character as phosphites to give reasonable *ee* values of product **2**. However, starting from diiodide (*R*)-**1** (Table 1), product (*R*)-**2** was obtained with only 3–10 %*ee* when using (*S*)-monophos (**3**) as a ligand. To prevent the possible hydrolysis of the phosphoramidite under the harsh reaction

[a] Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University in Bratislava,
Mlynská dolina CH2, 84215 Bratislava, Slovak Republic
Fax: +421-2-60296337
E-mail: putala@fns.uniba.sk

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200900071.

conditions (heating with barium hydroxide), we switched to using a milder activator of boronic acid/cesium fluoride. No product was formed unless palladium acetate was used as the palladium source in combination with cesium fluoride. Surprisingly, product (*R*)-**2** was then obtained in higher yield and, moreover, in 94%*ee* (Table 1, Entry 4)! The same conditions were required to achieve very high levels of stereoconservation in the case of nonhydrolyzable ligand (*R*)-binap (**4**; Table 1, Entries 6 and 7). The use of phosphinite (*S*)-**5**, which has a donating character between that of **3** and **4**, resulted in product (*R*)-**2** with decreased enantiopurity (35%*ee*). Product **2** was obtained in the highest yield, but in racemic form, when the reaction was performed without a ligand.

Table 1. Effect of reaction conditions and ligand on the stereochemical result of Suzuki tolylation of diiodide (*R*)-**1**.[a]

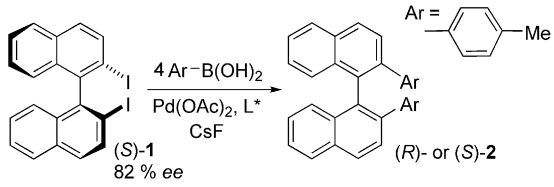


Entry	Ligand	Pd source	Base	Yield [%][b]	*ee* [%][c]
1	(*S*)-**3**	$Pd(dba)_2$	$Ba(OH)_2$	51	3
2	(*S*)-**3**	$Pd(dba)_2$	CsF	0	–
3	(*S*)-**3**	$Pd(OAc)_2$	$Ba(OH)_2$	58	10
4	(*S*)-**3**	$Pd(OAc)_2$	CsF	76	94
5	(*RS*)-**3**	$Pd(OAc)_2$	CsF	80	93
6	(*R*)-**4**	$Pd(dba)_2$	$Ba(OH)_2$	63	10
7	(*R*)-**4**	$Pd(OAc)_2$	CsF	56	94
8	(*S*)-**5**	$Pd(OAc)_2$	CsF	63	35
9	–	$Pd(OAc)_2$	CsF	89	1

[a] Reagents and conditions: (*R*)-**1** (0.1 mmol), *p*-tolylboronic acid (0.4 mmol), $Pd(dba)_2$ or $Pd(OAc)_2$ (0.005 mmol), ligand (0.02 mmol), $Ba(OH)_2 \cdot 8H_2O$ or CsF (0.8 mmol), THF (2 mL), 55 °C, 24 h. [b] Isolated yield. [c] Determined by HPLC with a Chiracel OD column.

The results obtained when using cesium fluoride do not correlate with electronic character of the ligands used. This brought us to investigate whether the chiral ligands tested are really innocent in this reaction. Experiments starting from enriched diiodide (*S*)-**1** (Table 2) revealed that it does depend on the ligand. Application of (*R*)-monophos (**3**) ensures the stereochemical conservation of the reaction − the configuration and the *ee* value of product **2** were the same as those of starting diiodide **1** (within ±7%*ee*), even when (*RS*)-monophos was used (Table 1, Entry 5). However, when (*R*)-binap (**4**) and (*S*)-binop (**5**) were used as ligands, the configuration of product **2** was always (*R*), regardless of the configuration of starting diiodide **1** (Tables 1 and 2). The level of stereoinduction is significantly higher in the case of (*R*)-binap, yielding (*R*)-**2** in 80%*ee* starting from (*S*)-**1** (87%*ee*).

Table 2. Stereochemical result of Suzuki tolylation of enriched diiodide (*S*)-**1** with chiral ligands.[a]

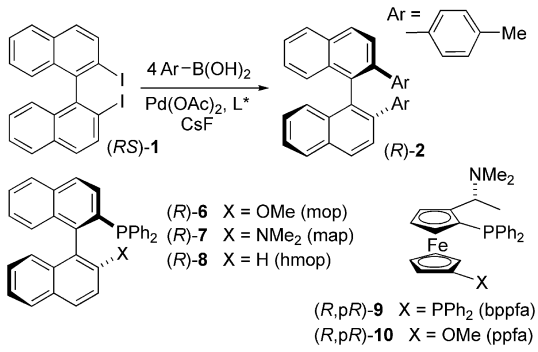


Entry	Ligand	Yield [%][b]	*ee* [%][c]	Configuration
1	(*S*)-**3**	74	89	(*S*)
2	(*R*)-**4**	50	80	(*R*)
3	(*S*)-**5**	64	17	(*R*)

[a] Reagents and conditions: (*S*)-**1** (0.1 mmol), *p*-tolylboronic acid (0.4 mmol), $Pd(OAc)_2$ (0.005 mmol), ligand (0.02 mmol), CsF (0.8 mmol), THF (2 mL), 55 °C, 24 h. [b] Isolated yield. [c] Determined by HPLC with a Chiracel OD column.

On the basis of our observations of the stereoinduction during Suzuki arylation of diiodide **1**, we reasoned that we could obtain enriched product **2** from a racemic substrate. Therefore, we performed a series of Suzuki ditolylations of (*RS*)-**1** under optimized conditions (palladium acetate, chiral ligand, cesium fluoride, THF). Product **2** was indeed obtained in an enantioenriched form. Among the tested ligands, the highest *ee* value (83%) of product **2** was determined with the use of (*R*)-binap (Table 3).

Table 3. Deracemization during Suzuki tolylation of racemic diiodide (*RS*)-**1** with chiral ligands.[a]



Entry	Ligand	Yield [%][b]	*ee* [%][c]	Configuration
1	(*R*)-**3**	78	16	(*R*)
2	(*R*)-**4**	52	83	(*R*)
3	(*S*)-**5**	67	23	(*R*)
4	(*R*)-**6**	40	31	(*R*)
5	(*R*)-**7**	42	16	(*R*)
6	(*R*)-**8**	79	5	(*R*)
7	(*R*,p*R*)-**9**	<3	–	–
8	(*R*,p*R*)-**10**	3	–	–

[a] Reagents and conditions: (*RS*)-**1** (0.1 mmol), *p*-tolylboronic acid (0.4 mmol), $Pd(OAc)_2$ (0.005 mmol), ligand (0.02 mmol), CsF (0.8 mmol), THF (2 mL), 55 °C, 24 h. [b] Isolated yield. [c] Determined by HPLC with a Chiracel OD column.

In order to distinguish between kinetic resolution and deracemization we stopped the Suzuki tolylation of racemic diiodide (*RS*)-**1** with (*R*)-binap at partial conversion and determined the *ee* value of isolated starting diiodide **1** (un-

der those conditions described in Table 3, Entry 2; reaction time 6 h, recovered diiodide **1** 36%). The latter was found to be almost racemic (4%*ee*). This illustrates that stereodiscrimination does not take place during the primary oxidative addition of diiodide **1** to the chiral palladium complex (kinetic resolution) but instead at a later stage of the mechanism, which allows deracemization of the binaphthyl moiety, most probably by the deracemization of the palladium(IV) intermediate.

Conclusions

Experimental studies performed on the Suzuki diarylation of diiodide **1** showed that the use of monophos (**3**) as a ligand suppressed the expected secondary oxidative addition and resulted in a stereoconservative reaction. However, secondary oxidative addition can be advantageous in combination with the use of chiral P ligands capable of stereoinduction, as a deracemization pathway is possible, yielding a significant enantiomeric enrichment (83%*ee*) in the case of binap. We are currently investigating the scope and limitations of the deracemization approach for the preparation of binaphthyl derivatives.

Experimental Section

General Experimental Procedure for Cross-Coupling Reactions: A mixture of 2,2′-diiodo-1,1′-binaphthyl (**1**; 51 mg, 0.1 mmol), *p*-tolylboronic acid (54 mg, 0.4 mmol), cesium fluoride (122 mg, 0.8 mmol) or barium hydroxide (octahydrate, 252 mg, 0.8 mmol), palladium acetate (1.1 mg, 5 mol-%) or bis(dibenzylideneacetone)-palladium (2.9 mg, 5 mol-%), ligand (20 mol-%) in THF (2 mL) was heated to 55 °C for 24 h under an argon atmosphere. The reaction mixture was filtered through a short silica pad (eluted with dichloromethane), and the solvent was evaporated. A sample for HPLC was taken, and the residue was purified by flash chromatography on silica gel (hexanes/ethyl acetate, 10:1). 2,2′-Di-*p*-tolyl-1,1′-binaphthyl (**2**) and 2-*p*-tolyl-1,1′-binaphthyl were obtained as white crystalline solids. The spectroscopic data were in good agreement with reported values.

Supporting Information (see footnote on the first page of this article): General methods, additional information on the experiments, HPLC chromatograms.

Acknowledgments

This work was supported by the Slovak Grant Agency for Science (grant No. 1/3568/06) and Comenius University (grant No. UK/262/2008).

[1] a) M. Putala, *Enantiomer* **1999**, *4*, 243–262; b) C. Rosini, L. Franzini, A. Raffaelli, P. Salvadori, *Synthesis* **1992**, 503–517; c) L. Pu, *Chem. Rev.* **1998**, *98*, 2405–2494.

[2] a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley, New York, **1994**; b) T. Hayashi, *Acc. Chem. Res.* **2000**, *33*, 354–362; c) M. McCarthy, P. J. Guiry, *Tetrahedron* **2001**, *57*, 3809–3844; d) P. Kočovský, Š. Vyskočil, M. Smrčina, *Chem. Rev.* **2003**, *103*, 3213–3245; e) K. Maruoka, T. Ooi, *Chem. Rev.* **2003**, *103*, 3013–3028; f) S. J. Connon, *Angew. Chem. Int. Ed.* **2006**, *45*, 3909–3912.

[3] a) S. G. Telfer, R. Kuroda, *Coord. Chem. Rev.* **2003**, *243*, 33–46. Examples: b) S. J. Lee, W. B. Lin, *Acc. Chem. Res.* **2008**, *41*, 521–537. Recent examples: c) C.-D. Wu, L. Ma, W. Lin, *Inorg. Chem.* **2008**, *47*, 14446–14448; d) T. Ema, D. Tanida, K. Hamada, T. Sakai, *J. Org. Chem.* **2008**, *73*, 9129–9132; e) W. W. Lv, X. M. Zhang, J. T. Lu, X. Y. Zhang, X. Y. Li, J. Z. Jiang, *Eur. J. Inorg. Chem.* **2008**, 4255–4261; f) M. A. Alam, A. Tsuda, Y. Sei, K. Yamaguchi, T. Aida, *Tetrahedron* **2008**, *64*, 8264–8270; g) S. M. Biros, R. M. Yeh, K. N. Raymond, *Angew. Chem. Int. Ed.* **2008**, *47*, 6062–6064; h) R. Nandhakumar, J. Ryu, H. Park, L. Tang, S. Choi, K. M. Kim, *Tetrahedron* **2008**, *64*, 7704–7708; i) Y. Liu, Q. Miao, S. W. Zhang, X. B. Huang, L. F. Zheng, Y. X. Cheng, *Macromol. Chem. Phys.* **2008**, *209*, 685–694; j) Y. Imai, K. Kawaguchi, K. Murata, T. Sato, R. Kuroda, Y. Matsubara, *Org. Lett.* **2008**, *10*, 469–471; k) C. Gautier, R. Taras, S. Gladiali, T. Burgi, *Chirality* **2008**, *20*, 486–493; l) T. Ema, D. Tanida, T. Sakai, *J. Am. Chem. Soc.* **2007**, *129*, 10591–10596; m) Y. Liu, S. W. Zhang, Q. Miao, L. F. Zheng, L. L. Zong, Y. X. Cheng, *Macromolecules* **2007**, *40*, 4839–4847; n) M. Ratajczak-Sitarz, A. Katrusiak, K. Gawronska, J. Gawronski, *Tetrahedron: Asymmetry* **2007**, *18*, 765–773; o) K. S. Kim, E. J. Jun, S. K. Kim, H. J. Choi, J. Yoo, C.-H. Lee, *Tetrahedron Lett.* **2007**, *48*, 2481–2484; p) Q. Wang, X. Chen, L. Tao, L. Wang, D. Xiao, X. Q. Yu, L. Pu, *J. Org. Chem.* **2007**, *72*, 97–101; q) K. Tsubaki, *Org. Biomol. Chem.* **2007**, *5*, 2179–2188.

[4] a) See ref.[3b] Recent examples: b) Y. Zhou, Q. G. He, Y. Yang, H. Z. Zhong, C. He, G. Y. Sang, W. Liu, C. H. Yang, F. L. Bai, Y. F. Li, *Adv. Funct. Mater.* **2008**, *18*, 3299–3306; c) J. Y. Lee, J. Y. Park, S. H. Min, K. W. Lee, Y. G. Baek, *Thin Solid Films* **2007**, *515*, 7726–7731; d) Y. Zhao, W. Chen, J. Zhai, X. L. Sheng, Q. G. He, T. X. Wei, F. L. Bai, L. Jiang, D. B. Zhu, *Chem. Phys. Lett.* **2007**, *445*, 259–264; e) M. Kawamoto, T. Aoki, T. Wada, *Chem. Commun.* **2007**, 930–932; f) Ch. Wang, L. Zhu, Y. Yu, Z. Shuai, D. Zhu, *J. Org. Chem.* **2007**, *72*, 4306–4312; g) M. Juríček, P. Kasák, M. Putala, *Tetrahedron Lett.* **2007**, *48*, 8869–8873.

[5] a) J. M. Burk, J. R. Lee, J. P. Martinez, *J. Am. Chem. Soc.* **1994**, *116*, 10847–10848; b) W. Wang, J. Zhang, Ch. Xiong, V. J. Hruby, *Tetrahedron Lett.* **2002**, *43*, 2137–2140; c) W. Wang, M. Cai, Ch. Xiong, J. Zhang, D. Trivedi, V. J. Hruby, *Tetrahedron* **2002**, *58*, 7365–7374; d) . M. Demchuk, B. Yoruk, T. Blackburn, V. Snieckus, *Synlett* **2006**, *18*, 2908–2913.

[6] a) U. Anton, Ch. Goeltner, K. Muellen, *Chem. Ber.* **1992**, *125*, 2325–2330; b) Ch. D. Braddock, S. C. Tucker, J. M. Brown, *Bull. Soc. Chim. Fr.* **1997**, *134*, 399–410; c) A. N. Cammidge, K. V. L. Crepy, *Chem. Commun.* **2000**, *18*, 1723–1724; d) M. Feuerstein, H. Doucet, M. Santelli, *Tetrahedron Lett.* **2001**, *42*, 6667–6670; e) N. Aoyagi, T. Izumi, *Tetrahedron Lett.* **2002**, *43*, 5529–5532; f) A.-S. Castanet, F. Colobert, P.-E. Broutin, M. Obringer, *Tetrahedron: Asymmetry* **2002**, *13*, 659–666; g) J. Yin, M. P. Rainka, X.-X. Zhang, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 1162–1163; h) N. Kataoka, Q. Shelby, J. P. Stambuli, J. F. Hartwig, *J. Org. Chem.* **2002**, *67*, 5553–5566; i) N. Aoyagi, T. Ohwada, T. Izumi, *Tetrahedron Lett.* **2003**, *44*, 8269–8272; j) K. Mikami, T. Miyamoto, M. Hatano, *Chem. Commun.* **2004**, *18*, 2082–2083; k) A. N. Cammidge, K. V. L. Crepy, *Tetrahedron* **2004**, *60*, 4377–4386; l) D. Drahonovsky, G. Ch. Labat, J. Sevcik, A. von Zelewsky, *Heterocycles* **2005**, *65*, 2169–2179; m) O. Baudoin, *Eur. J. Org. Chem.* **2005**, 4223–4229; n) M. Genov, A. Almorin, P. Espinet, *Chem. Eur. J.* **2006**, *12*, 9346–9352; o) S. S. Moleele, J. P. Michael, Ch. B. de Koning, *Tetrahedron* **2006**, *62*, 2831–2844; p) H. Li, Y. Wu, W. Yan, *J. Organomet. Chem.* **2006**, *691*, 5700–5708; q) N. Marion, O. Navarro, J. Mei, E. D. Stevens, N. M. Scott, S. P. Nolan, *J. Am. Chem. Soc.* **2006**, *128*, 4101–4111; r) P. Wawrzyniak, J. Heinicke, *Tetrahedron Lett.* **2006**, *47*, 8921–8924; s) M. Ciclosi, J. Lloret, F. Estevan, P. Lahuerta, M. Sanau, J. Perez-Prieto, *An-*

gew. Chem. Int. Ed. **2006**, *45*, 6741–6744; t) O. M. Demchuk, B. Yoruk, T. Blackburn, V. Snieckus, *Synlett* **2006**, *18*, 2908–2913; u) M. Genov, A. Almorin, P. Espinet, *Tetrahedron: Asymmetry* **2007**, *18*, 625–627; v) B. Puget, J.-P. Roblin, D. Prim, Y. Troin, *Tetrahedron Lett.* **2008**, *49*, 1706–1709.

[7] Examples: a) At the 3- and 3′-positions: M. Kitamura, Y. Arimura, S. Shirakawa, K. Maruoka, *Tetrahedron Lett.* **2008**, *49*, 2026–2030; b) At the 4- and 4′-positions: A. Hu, H. L. Ngo, W. Lin, *Angew. Chem. Int. Ed.* **2004**, *43*, 2501–2504; c) At the 5- and 5′-positions: L. Wu, L. Zheng, L. Zong, J. Xu, Y. Cheng, *Tetrahedron* **2008**, *64*, 2651–2657; d) At the 6- and 6′-positions: T. Taniguchi, T.-A. Fukuba, S. Nakatsuka, S. Hayase, M. Kawatsura, H. Uno, T. Itoh, *J. Org. Chem.* **2008**, *73*, 3875–3884; e) At the 8- and 8′-positions: D. H. Hua, J. W. McGill, M. Ueda, H. A. Stephany, *J. Organomet. Chem.* **2001**, *637*, 832–836.

[8] a) P. Kasák, H. Brath, M. Dubovská, M. Juríček, M. Putala, *Tetrahedron Lett.* **2004**, *45*, 791–794; b) H. Brath, M. Dubovská, M. Juríček, P. Kasák, M. Putala, *Collect. Czech. Chem. Commun.* **2004**, *69*, 1517–1536.

[9] P. Kasák, R. Mikláš, M. Putala, *J. Organomet. Chem.* **2001**, *637–639*, 318–326.

[10] M. Juríček, H. Brath, P. Kasák, M. Putala, *J. Organomet. Chem.* **2007**, *692*, 5279–5284.

Received: January 22, 2009
Published Online: May 27, 2009

