Tetrahedron Letters 51 (2010) 2044–2047

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

From tropos to atropos: 5,5′-bridged 2,2′-bis(diphenylphosphino)biphenyls as chiral ligands for highly enantioselective palladium-catalyzed hydrogenation of α-phthalimide ketones

Changqing Wang, Guoqiang Yang, Jing Zhuang, Wanbin Zhang *

School of Chemistry and Chemical Technology, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, PR China

ARTICLE INFO

Article history:
Received 5 January 2010
Revised 7 February 2010
Accepted 10 February 2010
Available online 13 February 2010

ABSTRACT

A class of atropisomeric diphosphine ligands with a wide range of dihedral angles has been developed. X-ray study of the Pd(II) complexes of these ligands showed that as the bridge length increased, the dihedral angles and the ligand bite angles increased as well, while an excessive increase in bridge length had a reverse effect. It was found that there was a correlation between the ligand dihedral angles and the enantioselectivity in Pd-catalyzed asymmetric hydrogenation of α-phthalimide ketones, and excellent enantioselectivities of up to 99% ee were afforded.

© 2010 Elsevier Ltd. All rights reserved.

Atropisomeric diphosphines are well-known versatile and indispensable chiral inducers in many enantioselective transformations.[1] Since the development of BINAP,[2] many excellent chelating diphosphines with an atropisomeric biaryl scaffold, such as MeO-BIPHEP,[3] SEGPHOS,[1d,4] TunePhos,[5] and P-Phos,[1e,6] have been reported. The structural variations of the biaryl backbone are responsible for the wide diversity of atropisomeric diphosphines. Despite the extensive design of the biaryl core, the existing atropisomeric biaryl diphosphine ligands possess at least one ortho substituent at the biaryl skeleton,[1f,h] and if the substituent is too small, the ligands become tropos due to the free rotation around the axis. It is considered that such tropos diphosphine ligands as 2,2′-bis(diphenylphosphino) biphenyl (BIPHEP) can provide a wider range of dihedral angles than atropisomeric ligands due to the minimal steric hindrance of the ortho hydrogen atoms. In view of the significant influence of dihedral angles on asymmetric control,[3–7] it is conceptually interesting to design and synthesize a class of atropisomeric diphosphine ligands while maintaining the small size of the ortho substituents, as it may ideally provide a wide range of dihedral angles. To our knowledge, such a class of ligands remains unexplored in the course of development of atropisomeric diphosphines.

As part of our continued efforts to design new axial chiral ligand scaffolds,[8] we herein present a novel class of diphosphine ligands **1** (Fig. 1), in which the tropos BIPHEP is restricted by a bridge with variable length at 5,5′-positions. Ligands **1** are expected to provide a wide range of dihedral angles due to the lack of substituents at 6,6′-positions. It is well known that a subtle variation of the ligand dihedral angle can have a significant effect on the reactivity and selectivity of the reactions. As a result, excellent ligands with high reactivity and enantioselectivity for particular substrates could be developed. Moreover, as each of the ligands **1** is restricted by a bridge with variable length, this new class of ligands should be rigid and have tunable bite angles. These properties provide us a golden opportunity to study systematically the influence of the dihedral angle of atropisomeric diphosphines on the reactivity and selectivity of asymmetric reactions.

Our synthetic approach to enantiopure (*R*)- and (*S*)-5,5′-alkyldioxy-2,2′-bis(diphenylphosphino)biphenyls (**1a–e**) is depicted in Scheme 1. Bromination of the commercially available 4-methoxyphenol with Br_2 furnished **2**. Reaction of **2** with $(CF_3SO_2)_2O$ in the presence of pyridine gave its triflate derivative **3** almost quantitatively. Phosphine oxide **4** was obtained by phosphinylation of triflate **3** with the aid of a Pd catalyst. The bis(diphenylphosphine oxide) **5** was obtained via Ullmann coupling of the phosphine oxide **4**. Reaction of **5** with BBr_3 provided **6** in high yield. Treatment of **6** with alkyl dihalides in the presence of excess anhydrous K_2CO_3 in DMF furnished **7a–e** in good yields. The optical resolution of (*RS*)-**7a–e** was by chiral preparative HPLC using Daicel Chiracel AD-H

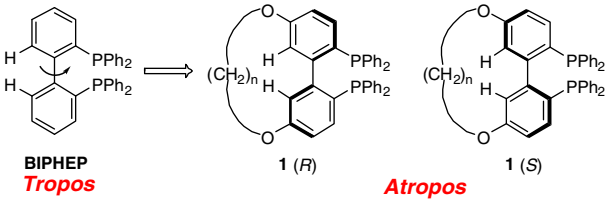
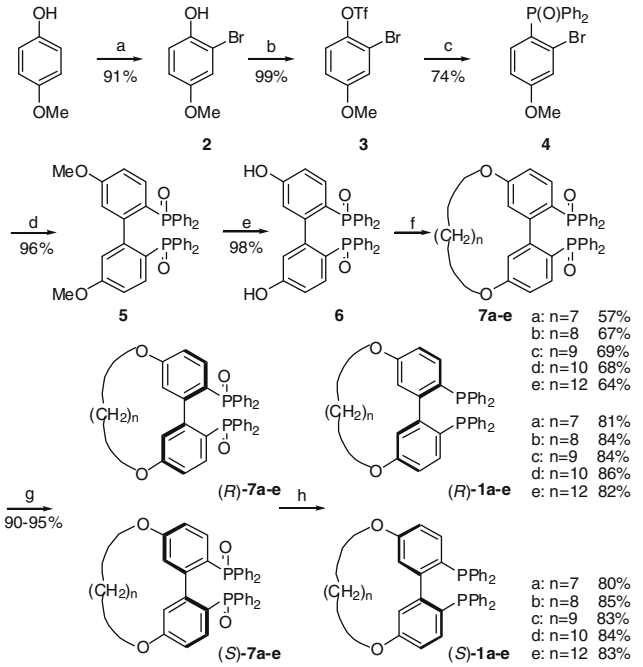


Figure 1. Atropisomeric ligands with a bridge across the 5,5′-positions of the biphenyl.

* Corresponding author. Tel./fax: +86 21 5474 3265.
E-mail address: wanbin@sjtu.edu.cn (W. Zhang).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.02.055



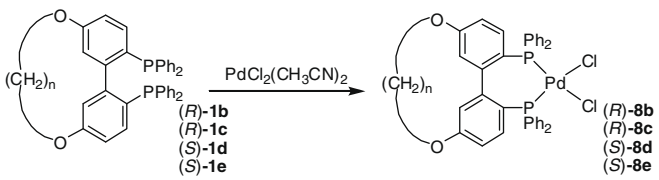
[a] Br_2, CH_2Cl_2. [b] Tf_2O, Py, CH_2Cl_2. [c] $Ph_2P(O)H$, $Pd_2(dba)_3.CHCl_3$, dppp, DIPEA, PhMe. [d] Cu, DMF. [e] BBr_3, CH_2Cl_2. [f] $Br(CH_2)_nBr$, K_2CO_3, DMF. [g] Prep. Chromatogr. [h] $HSiCl_3$, $PhNMe_2$, PhMe.

Scheme 1. Synthesis of ligands.

Column in about 90% yield based on (*RS*)-**7a–e**. The target diphosphine ligands (*R*)**1a–e** and (*S*)**1a–e** were easily obtained by the reduction of their resolved oxides **7a–e** with an excess of $HSiCl_3$ in 80–86% yields.[9] Noteworthy is the fact that no racemization of these diphosphines took place even after refluxing in toluene under N_2 for 12 h.

To understand the effects of the variable bridge length on metal coordination and ligand performance in catalysis, the newly synthesized ligands were reacted with a stoichiometric amount of $PdCl_2(CH_3CN)_2$ to afford the corresponding palladium dichloride adducts (Table 1). X-ray crystal structure analysis of (*R*)-**8b**, (*R*)-**8c**, (*S*)-**8d**, and (*S*)-**8e** allowed for a direct comparison with the known BINAP structure (Fig. 2).[10,11] As expected, (*R*)-**8b** has almost the narrowest dihedral angle (59.7°), followed by (*R*)-**8c** (64.1°) and (*S*)-**8d** (72.4°). These results are in agreement with our hypothesis. Directly related to these are the ligand bite angles (∠P–Pd–P): 91.8° **[**(*R*)-**4b**], 92.8° **[**(*R*)-**4c**], and 95.3° **[**(*S*)-**4d**]. Interestingly, the further increase of the length of the bridges led to the decrease of the dihedral angle (65.0° [(*S*)-**4e**]) and the bite angle (92.2° [(*S*)-**4e**]). This is the first study of a series of diphosphine complexes with tunable dihedral angles by X-ray crystal structure analysis.

Table 1
Structural parameters for $PdCl_2$ complexes



Entry	Phosphine	Dihedral angle (°)	Bite angle (°)
1	BINAP	68.4	92.8
2	(*R*)-**1b** (*n* = 8)	59.7	91.8
3	(*R*)-**1c** (*n* = 9)	64.1	92.8
4	(*S*)-**1d** (*n* = 10)	72.4	95.3
5	(*S*)-**1e** (*n* = 12)	65.0	92.2

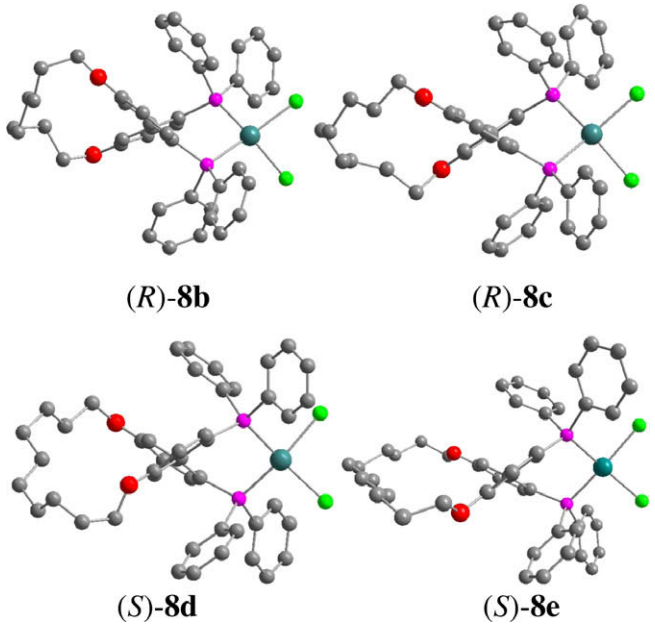


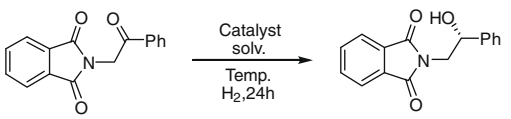
Figure 2. Crystal structures of $PdCl_2$ complexes **8b–e**.

Chiral amino alcohols are important compounds as biologically active molecules and as chiral auxiliaries. Consequently, much effort has been devoted to the development of efficient methods for the asymmetric synthesis of this structural motif.[12] High enantioselectivity has been achieved via the key step of Ru-catalyzed asymmetric hydrogenation of α-phthalimide ketones.[13] Zhou and co-workers have recently reported a method for the synthesis of chiral amino alcohols using homogeneous palladium catalysts, where up to 92.2% ee was achieved.[14] To demonstrate the asymmetric induction efficiency of chiral ligands **1a–e**, the Pd-catalyzed asymmetric hydrogenation of *N*-phenacyl-phthalimide (**9a**) was employed as a model reaction. Initially, we carried out several experiments employing a $Pd(CF_3CO_2)_2$/(*R*)-**1d** system in 2,2,2-trifluoroethanol (TFE) to screen optimal conditions for hydrogenation. A dramatical increase of enantioselectivity upon the hydrogenation of **9a** was observed as increase in H_2 pressure and reaction temperature. For example, 53% ee was obtained under 35 atm of H_2 at room temperature, while up to 98% ee with more than 99% conversion was observed when high hydrogen pressure (100 atm) and high temperature (80 °C) were employed (Table 2, entry 4). However, by further increasing the temperature, the enantioselectivity dropped slightly to 96% ee (entry 5). The effect of solvent was also investigated. As reported by Zhou and co-workers, this reaction was strongly solvent-dependent and only TFE was the most effective in terms of the conversion and enantioselectivity. Dichloromethane and other solvents such as acetone, toluene, methanol, ethanol, 2-propanol, and THF led to low activity.

Under the optimized conditions, ligands (*R*)-**1a–e** were employed to test the effect of the dihedral angle of the chiral biaryl ligands on the enantioselectivity of the reaction. The obtained enantioselectivities were particularly interesting (Table 2, entries 6–9): as the dihedral angles increased, the best result was observed when (*R*)-**1d** was used (98% ee), while the enantioselectivity was the lowest (90% ee) with (*R*)-**1e**.

With the optimized ligand and reaction conditions, other α-phthalimide ketones including an alkyl ketone were examined

Table 2
Optimization of reaction conditions for Pd-catalyzed hydrogenation of *N*-phenacylphthalimide[a]



9a **10a**

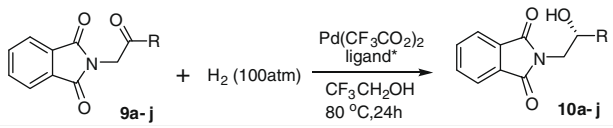
Entry	Ligand	Temp. (°C)	H_2 (atm)	Conv.[b] (%)	ee[c] (%)
1	(*R*)-**1d**	rt	35	34	53
2	(*R*)-**1d**	rt	70	51	67
3	(*R*)-**1d**	50	70	83	81
4	(*R*)-**1d**	80	100	>99	98
5	(*R*)-**1d**	90	100	>99	96
6	(*R*)-**1a**	80	100	>99	93
7	(*R*)-**1b**	80	100	>99	96
8	(*R*)-**1c**	80	100	>99	97
9	(*R*)-**1e**	80	100	>99	90

[a] Reaction conditions: $Pd(CF_3CO_2)_2$ 2.0 mol %, (*R*)-**1** 2.4 mol %.
[b] Determined by ^1H NMR analysis of the crude products.
[c] The enantiomeric excesses were determined by chiral HPLC using a Daicel Chiralcel OJ-H column. The *R* absolute configurations were assigned by comparison of optical rotations with the literature data.[13]

for possible use in the hydrogenation with Pd-(*R*)-**1d** catalyst. Both electron-deficient and electron-rich aryl ketones could be hydrogenated with high conversions and enantioselectivities (Table 3, entries 1–9). For example, hydrogenated products with 98% ee were obtained for *para*-substituted **9b** (entry 2) and **9d** (entry 4). The highest enantioselectivity (99%) was also achieved upon hydrogenation of *m*-methoxy-substituted phenyl ketone **9e** (entry 5), which was comparable to the best result obtained with Ru–phosphine complexes.[13] Alkyl ketone **9j** also worked well, giving high enantioselectivity (entry 10). To our knowledge, these enantioselectivities are the highest achieved so far for the homogeneous Pd-catalyzed asymmetric hydrogenation of α-phthalimide ketones.[14]

In conclusion, we have developed a new class of atropisomeric diphosphine ligands with a wide range of dihedral angles. X-ray study of the Pd(II) complexes of these ligands showed that as the bridge length increased, the dihedral angles and the ligand bite angles increased as well, while an excessive increase in bridge length had a reverse effect. These ligands afforded excellent enantioselectivities when utilized in the Pd-catalyzed asymmetric hydrogenation of α-phthalimide ketones.

Table 3
Asymmetric hydrogenation of α-phthalimide ketones[a]



9a-j **10a-j**

Entry	Substrate	Conv.[b] (%)	ee[c] (%)
1	**9a** (R = Ph)	>99	98
2	**9b** (R = *p*-$CH_3C_6H_4$)	>99	98
3	**9c** (R = *p*-PhC_6H_4)	>99	93
4	**9d** (R = *p*-FC_6H_4)	>99	98
5	**9e** (R = *m*-$CH_3OC_6H_4$)	>99	99
6	**9f** (R = *p*-ClC_6H_4)	87	88
7	**9g** (R = *m*-ClC_6H_4)	>99	92
8	**9h** (R = *o*-ClC_6H_4)	>99	78
9	**9i** (R = 2-naphthyl)	93	94
10	**9j** (R = Me)	>99	91

[a] Reaction conditions: $Pd(CF_3CO_2)_2$ 2.0 mol %, (*R*)-**1d** 2.4 mol %.
[b] Determined by ^1H NMR analysis of the crude products.
[c] The enantiomeric excesses were determined by chiral HPLC using a Daicel Chiralcel OJ-H column. The *R* absolute configurations were assigned by comparison of optical rotations with the literature data.[13,14]

Acknowledgments

This work was supported by the National Natural Science Foundation of China (No. 20772081), Science and Technology Commission of Shanghai Municipality (Nos. 08431901700, 09JC1407800), and Nippon Chemical Industrial Co., Ltd. We thank Prof. Tsuneo Imamoto for helpful discussion.

References and notes

1. (a) For representative reviews, see: *Asymmetric Catalysis in Organic Synthesis*; Noyori, R., Ed.; Wiley: New York, 1994; (b) *Comprehensive Asymmetric Catalysis I–III*; Jacobson, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: New York, 1999; (c) *Principles and Applications of Asymmetric Synthesis*; Lin, G.-Q., Li, Y.-M., Chan, A. S. C., Eds.; Wiley: New York, 2001; (d) Shimizu, H.; Nagasaki, I.; Saito, T.. In *Phosphorus Ligands in Asymmetric Catalysis*; Börner, A., Ed.; Wiley-VCH: Weinhem, 2008; Vol. 1, pp 207–260; (e) Li, Y.-M.; Yu, W.-Y.; Chan, A. S. C.. In *Phosphorus Ligands in Asymmetric Catalysis*; Börner, A., Ed.; Wiley-VCH: Weinhem, 2008; Vol. 1, pp 260–283; (f) Otero, I.; Börner, A.. In *Phosphorus Ligands in Asymmetric Catalysis*; Börner, A., Ed.; Wiley-VCH: Weinhem, 2008; Vol. 1, pp 307–329; (g) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40; (h) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029; (i) Shimizu, H.; Nagasaki, I.; Saito, T. *Tetrahedron* **2005**, *61*, 5405.
2. (a) Miyashita, A.; Yasuda, H.; Takaya, H.; Toriumi, K.; Ito, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932; (b) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.
3. (a) Schmid, R.; Cereghetti, M.; Heiser, B.; Schonholzer, P.; Hansen, H.-J. *Helv. Chim. Acta* **1988**, *71*, 897; (b) Schmid, R.; Broger, E. A.; Cereghetti, M.; Crameri, Y.; Foricehr, J.; Lalonde, M.; Muller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. *Pure Appl. Chem.* **1996**, *68*, 131.
4. Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264.
5. (a) Zhang, Z.; Qian, H.; Longmire, J.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 6223; (b) Wu, S.; Wang, W.; Tang, W.; Lin, M.; Zhang, X. *Org. Lett.* **2002**, *4*, 4495; (c) Lei, A.; Wu, S.; He, M.; Zhang, X. *J. Am. Chem. Soc.* **2004**, *126*, 1626; (d) Wang, C.-J.; Sun, X.; Zhang, X. *Angew. Chem.* **2005**, *117*, 5013. *Angew. Chem., Int. Ed.* **2005**, *44*, 4933; (e) Raghunath, M.; Zhang, X. *Tetrahedron Lett.* **2005**, *46*, 7017; (f) Wang, C.-J.; Sun, X.; Zhang, X. *Synlett* **2006**, 1169.
6. Pai, C.-C.; Lin, C.-W.; Lin, C.-C.; Chen, C.-C.; Chan, A. S. C. *J. Am. Chem. Soc.* **2000**, *122*, 11513.
7. (a) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Tetrahedron Lett.* **2003**, *44*, 823; (b) Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Org. Proc. Res. Dev.* **2003**, *7*, 399; (c) Jeulin, S.; Duprat de Paule, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 320; (d) Wu, J.; Ji, J.-X.; Chan, A. S. C. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 3570; (e) Qiu, L.; Kwong, F. Y.; Wu, J.; Lam, W. H.; Chan, S.; Yu, W.-Y.; Li, Y.-M.; Guo, R.; Zhou, Z.; Chan, A. S. C. *J. Am. Chem. Soc.* **2006**, *128*, 5955; (f) Shintani, R.; Yashio, K.; Nakamura, T.; Okamoto, K.; Shimada, T.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2772.
8. (a) Wang, F.; Zhang, Y. J.; Wei, H.; Zhang, J.; Zhang, W. *Tetrahedron Lett.* **2007**, *48*, 4083; (b) Wei, H.; Zhang, Y. J.; Wang, F.; Zhang, W. *Tetrahedron: Asymmetry* **2008**, *19*, 482; (c) Zhang, Y. J.; Wei, H.; Zhang, J. M.; Zhang, W. *Tetrahedron* **2009**, *65*, 1281.
9. *5,5′-Heptamethylenedioxy-2,2′-bis(diphenylphosphino) biphenyl* (**1a**). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.09 (m, 22H, ArH), 6.82 (dd, *J* = 3.0, 8.2 Hz, 2H, ArH), 6.36 (d, *J* = 8.2 Hz, 2H, ArH), 4.19 (m, 2H, OCH), 3.86 (m, 2H, OCH), 1.93–1.29 (m, 10H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.73, 149.81, 138.99, 138.94, 138.87, 135.92, 134.01, 133.90, 133.79, 133.62, 133.52, 133.42, 128.32, 128.30, 128.27, 128.24, 128.04, 127.03, 117.81, 116.44, 67.45, 26.78, 24.69, 22.13; ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): δ = −15.3; HRMS (ESI): Calcd for $C_{43}H_{40}O_2P_2$ $[M]^+$ 650.2504, found: 650.2506. For (*R*)-**1a**: $[\alpha]_D^{27}$ −131 (*c* 0.50, $CHCl_3$). For (*S*)-**1a**: $[\alpha]_D^{27}$ 130 (*c* 0.50, $CHCl_3$). *5,5′-Octamethylenedioxy-2,2′-bis(diphenylphosphino)biphenyl* (**1b**). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.10 (m, 20H, ArH), 6.96 (dt, *J* = 2.4, 8.8 Hz, 2H, ArH), 6.76 (dd, *J* = 3.8, 5.2 Hz, 2H, ArH), 6.39 (d, *J* = 3.8 Hz, 2H), 3.89 (dd, *J* = 1, 2 Hz, 4H, OCH), 1.86–1.15 (m, 12H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.28, 149.28, 149.08, 148.89, 138.73, 138.66, 138.59, 138.54, 138.48, 135.28, 134.22, 134.12, 134.01, 133.72, 133.62, 133.58, 133.51, 128.42, 128.40, 128.37, 128.31, 128.28, 128.24, 128.21, 128.13, 127.44, 127.41, 117.82, 115.23, 115.19, 115.15, 65.98, 28.99, 28.89, 25.25; ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): δ = −14.4; HRMS (ESI) Calcd for $C_{44}H_{42}O_2P_2$ $[M]^+$ 664.2660, found: 664.2664. For (*R*)-**1b**: $[\alpha]_D^{27}$ −123 (*c* 0.50, $CHCl_3$). For (*S*)-**1b**: $[\alpha]_D^{27}$ +123 (*c* 0.50, $CHCl_3$). *5,5′-Nonamethylenedioxy-2,2′-bis(diphenylphosphino)biphenyl* (**1c**). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.10 (m, 20H, ArH), 6.98 (d, *J* = 8.4 Hz, 2H, ArH), 6.79 (d, *J* = 8.4 Hz, 2H, ArH), 6.33 (s, 2H, ArH), 4.00 (m, 2H, OCH), 3.65 (m, 2H, OCH), 1.78–0.83 (m, 14H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.15, 135.31, 134.19, 134.10, 133.67, 133.58, 133.47, 128.60, 128.56, 128.51, 128.37, 128.31, 128.10, 117.54, 117.42, 68.02, 28.34, 28.22, 27.01, 24.51; ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): δ = −14.8; HRMS (ESI)

Calcd for $C_{45}H_{44}O_2P_2$ $[M-1]^+$ 677.2738, found: 677.2743. For (*R*)-**1c**: $[\alpha]_D^{27}$ −114 (*c* 0.50, $CHCl_3$). For (*S*)-**1c**: $[\alpha]_D^{27}$ +114 (*c* 0.50, $CHCl_3$). *5,5′-Decamethylenedioxy-2,2′-bis(diphenylphosphino)biphenyl* (**1d**). Yield 86%; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 20H, ArH), 6.96 (dd, *J* =1.2, 8.4 Hz, 2H, ArH), 6.78 (dd, *J* = 2.4, 8.4 Hz, 2H, ArH), 6.37 (s, 2H, ArH), 3.89 (m, 2H, OCH), 3.64 (m, 2H, OCH), 1.70–1.12 (m, 16H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.68, 135.41, 134.22, 134.12, 134.01, 133.69, 133.59, 133,49, 128.37, 128.07, 116.96, 116.18, 116.13, 67.50, 28.78, 28.71, 27.85, 24.91; ^{31}P NMR (162 Hz, $CDCl_3$, 85% H_3PO_4): δ = −15.1; HRMS (ESI) Calcd for $C_{46}H_{46}O_2P_2$ $[M]^+$ 692.2973, found: 692.3002. For (*R*)-**1d**: $[\alpha]_D^{27}$ −75.7 (*c* 0.50, $CHCl_3$). For (*S*)-**1d**: $[\alpha]_D^{27}$ 79.7 (*c* 0.50, $CHCl_3$). *5,5′-Dodecamethylenedioxy-2,2′-bis(diphenyl phosphino)biphenyl* (**1e**). Yield 82%; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.21 (m, 20H, ArH), 6.97 (dt, *J* = 1.6, 8.8 Hz, 2H, ArH), 6.77 (dd, *J* = 2.4, 8.4 Hz, 2H, ArH), 6.42 (dd, *J* = 2.4, 4.0 Hz, 2H, ArH), 3.78(m, 2H, OCH), 3.63(m, 2H, OCH), 1.64–1.15 (m, 20H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.69, 135.62, 134.15, 134.06, 133.96, 133.66, 133.56, 133.46, 128.45, 128.42, 128.38, 128.34, 128.03, 116.34, 116.09, 67.50, 29.18, 28.76, 28.47, 27.78, 24.86; ^{31}P NMR (162 MHz, $CDCl_3$, 85% H_3PO_4): δ = −15.3; HRMS (ESI) Calcd for $C_{48}H_{50}O_2P_2$ $[M]^+$ 720.3286, found: 720.3272. For (*R*)-**1e**: $[\alpha]_D^{27}$ −30.3 (*c* 0.50, $CHCl_3$). For (*S*)-**1e**: $[\alpha]_D^{27}$ 30.3 (*c* 0.50, $CHCl_3$).

10. Crystallographic data for (*R*)-**4b**: $C_{47}H_{48}Cl_8O_2P_2Pd$, M_r = 1096.79, *T* = 296(2) K, monoclinic, *P*2(1), *a* = 13.488(2) Å, *b* = 12.6229(19) Å, *c* = 14.890(2) Å, β = 96.663(2)°, *V* = 2518.1(6) Å^3, *Z* = 2, ρ_{calcd} = 1.447 Mg m^{-3}, μ = 0.893 mm^{-1}, 13050 reflections collected, 8669 independent reflections (R_{int} = 0.0242), Final *R* indices [$I > 2\sigma(I)$]: R_1 = = 0.0478, wR_2 = 0.1260. Compound (*R*)-**4c**: $C_{46}H_{46}Cl_4O_2P_2Pd$, M_r = 940.97, *T* = 293(2) K, Orthorhombic, P2(1)2(1)2(1), *a* = 12.146(5) Å, *b* = 16.190(6) Å, *c* = 23.877(10) Å, β = 90°, *V* = 4695(3) Å^3, *Z* = 4, ρ_{calcd} = 1.331 Mg m^{-3}, μ = 0.725 mm^{-1}, 19527 reflections collected, 8191 independent reflections (R_{int} = 0.0507), Final *R* indices [$I > 2\sigma(I)$]: R_1 = 0.0483, wR_2 = 0.1045. Compound (*R*)-**4d**: $C_{46}H_{46}Cl_2O_2P_2Pd$, M_r = 870.07, *T* = 293(2) K, monoclinic, P2(1)/c, *a* = 14.6665(9) Å, *b* = 12.2499(8) Å, *c* = 22.8437(14) Å, β = 97.0920(10)°, *V* = 4072.8(4) Å^3, *Z* = 4, ρ_{calcd} = 1.419 Mg m^{-3}, μ = 0.703 mm^{-1}, 24152 reflections collected, 9205 independent reflections (R_{int} = 0.0398), Final *R* indices [$I > 2\sigma(I)$]: R_1 = 0.0447, wR_2 = 0.1006. Compound (*R*)-**4e**: $C_{49}H_{58}Cl_4O_5P_2Pd$, M_r = 1037.09, *T* = 296(2) K, monoclinic, *P*2(1)/*c*, *a* = 18.252(2) Å, *b* = 12.7537(14) Å, *c* = 28.133(2) Å, β = 128.557(4)°, *V* = 5121.1(9) Å^3, *Z* = 4, ρ_{calcd} = 1.345 Mg m^{-3}, μ = 0.676 mm^{-1}, 26002 reflections collected, 9021 independent reflections (R_{int} = 0.0420), Final *R* indices [$I > 2\sigma(I)$]: R_1 = 0.0561, wR_2 = 0.1560. CCDC 749256 (*R*)-**4b**, 749257 (*R*)-**4c**, 749258 (*R*)-**4d**, and 749259 (*R*)-**4e** contain 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. Ozawa, F.; Kubo, A.; Matsumoto, Y.; Hayashi, T.; Nishioka, E.; Yanagi, K.; Moriguchi, K. *Organometallics* **1993**, *12*, 4188.
12. (a) Bergmeier, S. C. *Tetrahedron* **2000**, *56*, 2561; (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835; (c) Bogevig, A.; Pastor, I. M.; Adolfsson, H. *Chem. Eur. J.* **2004**, *10*, 394; (d) Petra, D. G. I.; Reek, J. N. H.; Handgraaf, J. W.; Meijer, E. J.; Dierkes, P.; Kamer, P. C. J.; Brussee, J.; Schoemaker, H. E.; Van Leeuwen, P. W. N. M. *Chem. Eur. J.* **2000**, *6*, 2818.
13. Hu, A.; Lin, W. *Org. Lett.* **2005**, *7*, 455.
14. Wang, Y.-Q.; Lu, S.-M.; Zhou, Y.-G. *Org. Lett.* **2005**, *7*, 3235.