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Bisphenylene homologues of BINOL-based phosphoramidites: synthesis, stereostructure, and application in catalysis

Natalia Miklášová [a,†], Ondřej Julínek [b], Michaela Mešková [a], Vladimír Setnička [b], Marie Urbanová [c], Martin Putala [a,*]

[a] Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University in Bratislava, Mlynská dolina, 842 15 Bratislava, Slovak Republic
[b] Department of Analytical Chemistry, Institute of Chemical Technology, Technická 5, 166 28 Prague 6, Czech Republic
[c] Department of Physics and Measurements, Institute of Chemical Technology, Technická 5, 166 28 Prague 6, Czech Republic

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ABSTRACT

Bis-*ortho*- and bis-*meta*-phenylene homologues of BINOL-based *N,N*-dimethylphosphoramidites were prepared from the corresponding diols by treatment with hexamethyltriaminophosphane. Phosphoramidites derived from bulkier secondary amines were synthesized by 5-phenyl-1*H*-tetrazole-promoted amine exchange. All the phosphoramidites were obtained as single diastereomers. Their configurations at the C(naphthyl)–C(phenyl) axes were determined by vibrational circular dichroism (VCD) spectroscopy. Preliminary testing of the ligands in copper-catalyzed conjugate addition of diethylzinc to acyclic enones and nitrostyrene gave the corresponding products in up to 74% ee.

BINOL-based phosphoramidites are privileged ligands in enantioselective organic reactions such as asymmetric rhodium-catalyzed hydrogenations of alkenes,[1] palladium- and nickel-catalyzed hydrovinylations of alkenes,[2] and copper-catalyzed alkylations of imines[3] and activated alkenes (conjugate addition).[4]

Two types of structural modifications of the basic MonoPhos (**1**) structural motif have been reported which affect positively the enantioselectivity of catalyzed reactions (Fig. 1): (a) replacement of the phosphoramidite dimethylamino group with a bulkier secondary amine, including examples containing additional stereogenic center(s) (e.g., **2**);[5,6] (b) introduction of sterically demanding groups to positions 3 and 3′ of the binaphthyl skeleton, for example, **3**.[6,7]

Having developed an effective procedure for the introduction of aryl groups at positions 2 and 2′ of 1,1′-binaphthyl,[8] we aimed to prepare and characterize bisphenylene homologues of BINOL-based phosphoramidites **4** and **5** and explore their potential as ligands in asymmetric catalysis.

For the preparation of BINOL bis-*ortho*-phenylene homologue (*R*)-**6** and bis-*meta*-phenylene homologue (*S*)-**7** (Scheme 1), we exploited the previously described efficient diarylation of diiodide (*R*)- or (*S*)-**8** via Negishi cross-coupling,[8] followed by demethylation of (*R*)-**9** and (*S*)-**10** with excess boron tribromide in dilute dichloromethane solution.[9]

We examined several methods for the preparation of phosphoramidites from diols **6** and **7**: (i) preparation of the corresponding chlorophosphite and in situ reaction with a secondary amine or (ii) direct reaction with aminophosphanyl dichloride (both under various conditions),[10] and (iii) reaction with triaminophosphane.[11]

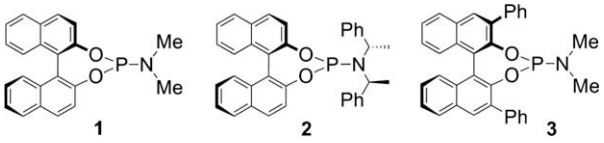
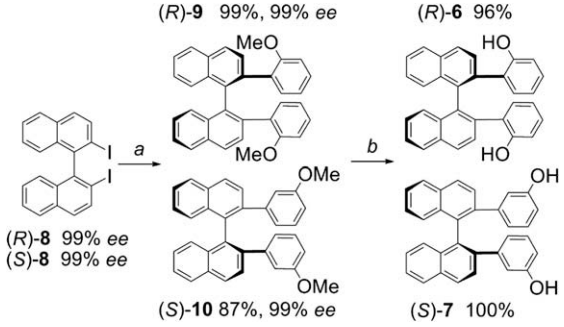


Figure 1. Structural modifications of BINOL-based phosphoramidites.



Scheme 1. Preparation of BINOL bisphenylene homologues (*R*)-6 and (*S*)-7. Reagents and conditions: (a) *o*- or *m*-$MeOC_6H_4ZnCl$ (6 equiv), 5% $Pd(PPh_3)_4$, THF, MW, 120 °C, 40–60 min; (b) BBr_3 (10 equiv), CH_2Cl_2,0 °C, 4 h.

* Corresponding author. Tel.: +421 2 60296323; fax: +421 2 60296337.
E-mail address: putala@fns.uniba.sk (M. Putala).
† Present address: Department of Chemical Theory of Drugs, Faculty of Pharmacy, Comenius University in Bratislava, Kalinčiakova 8, 832 32 Bratislava, Slovak Republic.

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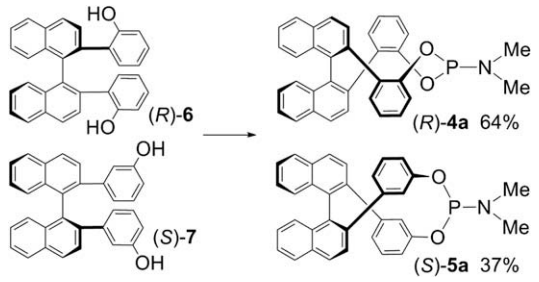
While the first two methods gave complex mixtures of products including oligomers, the latter allowed the preparation of the desired phosphoramidites **4a** and **5a** in reasonable yields (Scheme 2), when hexamethyltriaminophosphane (HMPT)[12] was used. However, reactions with triaminophosphanes derived from bulkier secondary amines did not proceed.

In order to prepare other dialkylphosphoramidites, we treated dimethylphosphoramidites (*R*)-**4a** and (*S*)-**5a** with secondary amines (piperidine and morpholine) in the presence of 5-phenyl-1*H*-tetrazole.[13] The target phosphoramidites (*R*)-**4** and (*S*)-**5** were obtained in low to moderate yields depending on the number of chromatographic steps (Table 1).[14]

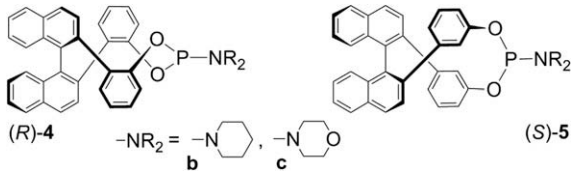
Intermediate methoxy derivatives **9** and **10** exhibit atropisomerization by rotation around the naphthyl–phenyl axes which can be observed in the ^{1}H NMR spectra at decreased temperature. For instance, bis(*ortho*-methoxyphenyl) derivative (*R*)-**9** exists at −50 °C in $CDCl_3$ as a mixture of three interconvertible diastereomers (*R,R,R*), (*R,S,R*), and (*R,S,S*) in the ratio 16:60:24. However, all phosphoramidites **4** and **5** were obtained as single diastereomers, exhibiting sharp signals in ^{1}H NMR spectra within wide temperature ranges. We failed to obtain crystals suitable for X-ray structure analysis. Therefore, the configuration around the naphthyl–phenyl axes was determined using vibrational circular dichroism (VCD) by making a comparison of the experimental with the calculated spectra obtained by density functional theory.[15] We calculated and measured the VCD spectra of the phosphoramidites (*R*)-**4a** and (*S*)-**5a** with the aim of determining the configuration at the naphthyl–phenyl stereogenic axes.

Conformational analysis of the (*S,R,R*), (*S,R,S*), and (*S,S,S*) configurations of **5a** revealed only one abundant conformer with (*R,R*) configuration at the naphthyl–phenyl stereogenic axes, the structure of which is shown in Figure 2a. Conformers with (*R,S*) configuration were energetically unfavorable and their populations were <1%. No conformer with (*S,S*) configuration was found, the connection between the phenyl groups limits the conformational flexibil-



Scheme 2. Preparation of *N,N*-dimethylphosphoramidites (*R*)-4a and (*S*)-5a by reaction with HMPT. Reagents and conditions: $P(NMe_2)_3$ (1.25 equiv), NH_4Cl (2.5 mol %), C_6H_6, rt, 7 h.

Table 1
Preparation of phosphoramidites (*R*)-**4** and (*S*)-**5** by amine exchange[a]



Entry	Amine	Product	Yield (%)
1	Piperidine	(*R*)-**4b**	29
2	Morpholine	(*R*)-**4c**	50
3	Piperidine	(*S*)-**5b**	51
4	Morpholine	(*S*)-**5c**	25

[a] Reagents and conditions: HNR_2 (2 equiv), 5-phenyl-1*H*-tetrazole (1.5 equiv), toluene, reflux, 6–9 h.

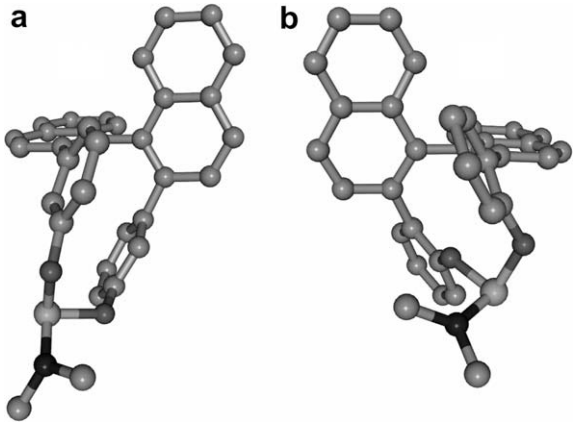


Figure 2. B3LYP/6-31G** structures of the (*S,R,R*)-**5a** (a) and the major conformer, (*R,S,S*)-**4a** (b).

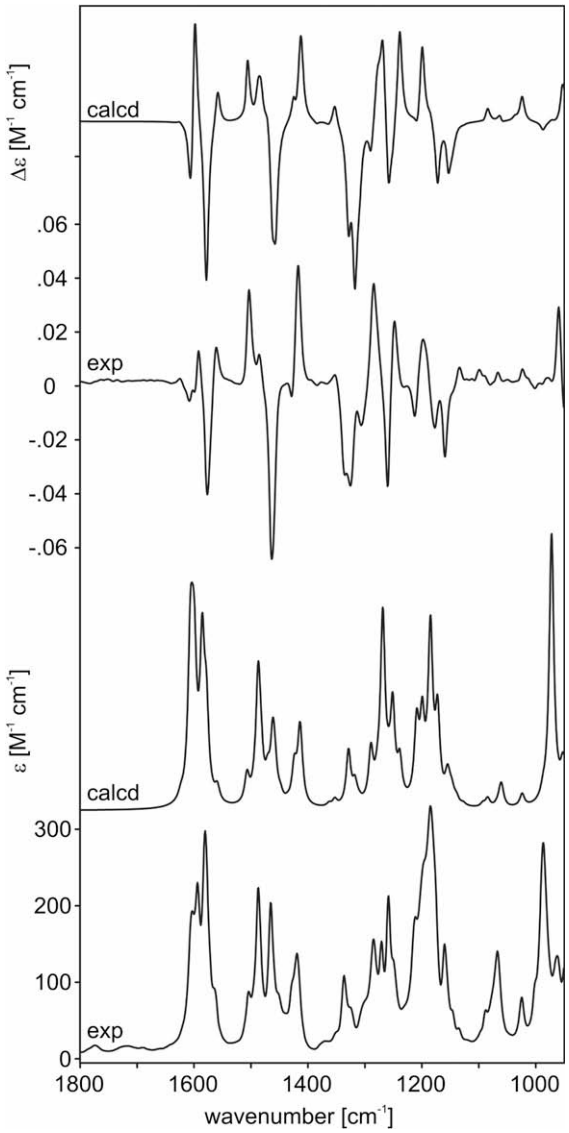


Figure 3. B3LYP/6-31G** IR and VCD spectra of (*S,R,R*)-**5a** and the experimental IR and VCD spectra measured in $CDCl_3$ (0.13 mol L^{-1}).

ity of the molecule and precludes this configuration. The VCD and IR absorption spectra of a single abundant conformer of **5a** with (*S,R,R*) configuration were calculated at the B3LYP/6-31G** level and compared with experimental spectra (Fig. 3). A similar conformational analysis was carried out for (*R,S,S*), (*R,S,R*), and (*R,R,R*)-**4a**. This revealed two conformers, both with (*S,S*) configuration at the naphthyl–phenyl stereogenic axes, differing in the orientation of the lone electron pair at the nitrogen atom, with relative populations of 85% (Fig. 2b) and 15%. Again, the other configurations were either energetically unfavorable or sterically impossible. The IR absorption and VCD spectra of two abundant conformers of **4a** with (*R,S,S*) configuration were calculated at the B3LYP/6-31G** level, weight-averaged and compared with experimental spectra (Fig. 4). An excellent agreement between the calculated and experimental spectra for both the phosphoramidites **4a** and **5a** confirms the exclusive (*R,S,S*) and (*S,R,R*) configurations of **4a** and **5a**, respectively.[16]

Since phosphoramidites have been successfully used as ligands in the stereoselective catalysis of copper-mediated conjugate addition,[4] we tested phosphoramidites **4** and **5** as ligands in conjugate additions of diethylzinc to enones and a nitroalkene. Optimization of the reaction conditions was performed on diethylzinc addition to chalcone with ligand (*S*)-**5a** in toluene as the solvent (Table 2). The results showed that copper(II) triflate was the best copper source (in terms of both the yield and the enantioselectivity, entries 2 and 3). Increasing the catalyst loading improved both the yield and ee of the product (entries 1–3). Decreasing the temperature from −10 °C to −30 °C decreased remarkably the catalyst activity and stereoselectivity (entry 5).

Both copper salts were further examined in experiments with other ligands and on other substrates under optimized conditions (Table 3). In agreement with our previous observations, the reactions with copper(II) triflate gave the best results in general. Results with copper(II) acetate are given when its use resulted in higher yields and/or ee of the corresponding product. The use of copper(II) acetate was found to be beneficial only in combination with the dimethylamino ligand (*R*)-**4a**.

Reasonable levels of enantioselectivity in the copper-catalyzed diethylzinc addition to chalcone and benzalacetone were observed when the dimethylamino ligand (*S*)-**5a** was used (70% and 74% ee).

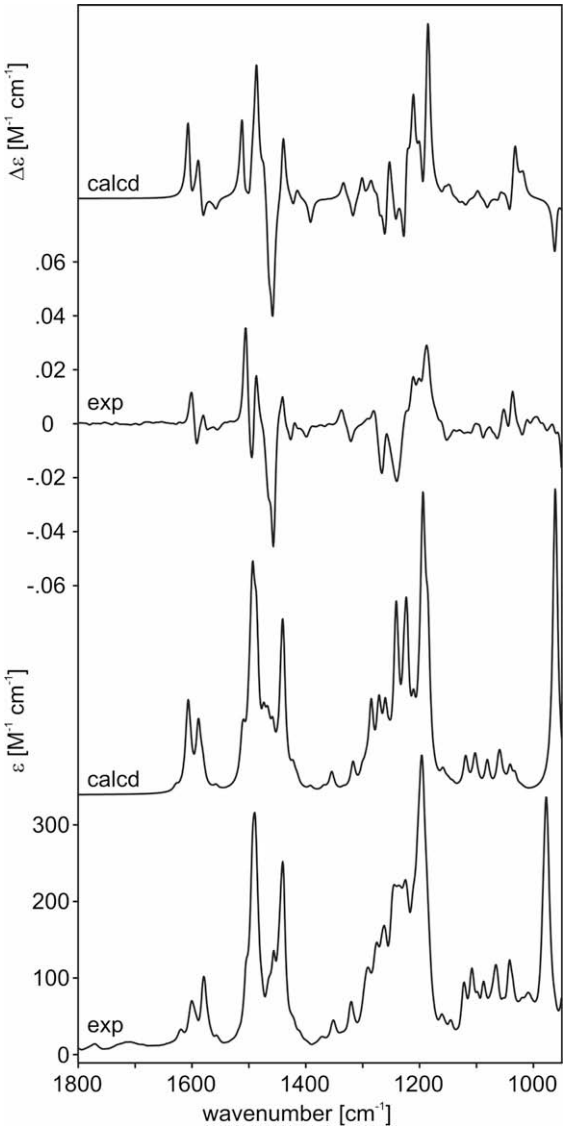
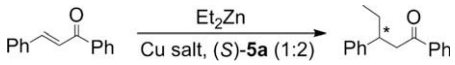


Figure 4. B3LYP/6-31G** IR and VCD spectra of (*R,S,S*)-**4a** and the experimental IR and VCD spectra measured in $CDCl_3$ (0.13 mol L^{-1}).

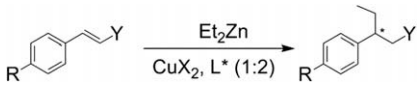
Table 2
Optimization of the reaction conditions in the conjugate addition catalyzed by the copper complex of phosphoramidite (*S*)-**5a**[a]



Entry	Copper source (mol %)	*T* (°C)	Yield[b] (%)	ee % [c]
1	$Cu(OTf)_2$ (0.5)	−10	27	52 (−)
2	$Cu(OTf)_2$ (1)	−10	69	65 (−)
3	$Cu(OTf)_2$ (2)	−10	77	70 (−)
4	$Cu(OAc)_2{\cdot}H_2O$ (2)	−10	27	10 (−)
5	$Cu(OTf)_2$ (2)	−30	10	49 (−)

[a] Reagents and conditions: Et_2Zn (1.7 equiv), CuX_2, (*S*)-**5a**, toluene, 16 h.
[b] ^1H NMR yield with ferrocene as the internal standard.
[c] Determined by HPLC on Chiralcel Daicel OD-H.

Table 3
Conjugate additions catalyzed by the copper complexes of phosphoramidites (*R*)-**4** and (*S*)-**5**[a]



Entry	R	Y	X	L*	Yield[b] (%)	ee % [c]
1	H	COPh	OAc	**4a**	62	39 (+)
2	H	COPh	OTf	**4a**	15	18 (+)
3	H	COPh	OTf	**4b**	99	69 (+)
4	H	COPh	OTf	**4c**	92	57 (+)
5	H	COPh	OTf	**5a**	77	70 (−)
6	H	COPh	OTf	**5b**	66	74 (−)
7	Cl	COMe	OTf	**4a**	55	18[d] (+)
8	Cl	COMe	OTf	**4b**	62	14[d] (+)
9	Cl	COMe	OTf	**5a**	63	15[d] (−)
10	MeO	COMe	OTf	**4a**	47	33[d] (+)
11	MeO	COMe	OTf	**4b**	58	17[d] (+)
12	MeO	COMe	OTf	**5a**	77	21[d] (−)
13	H	COMe	OAc	**4a**	60	28 (+)
14	H	COMe	OTf	**4a**	89	19 (+)
15	H	COMe	OTf	**4b**	55	39 (+)
16	H	COMe	OTf	**5a**	66	74 (−)
17	H	NO_2	OAc	**4a**	65	30[e] (+)
18	H	NO_2	OAc	**5a**	34	24[e] (−)

[a] Reagents and conditions: Et_2Zn (1.7 equiv), CuX_2 (2 mol %), L* (4 mol %), toluene, −10 °C, 16 h.
[b] ^1H NMR yield with ferrocene as the internal standard.
[c] Determined by HPLC on Chiralcel Daicel OD-H.
[d] Determined by HPLC on Chiralcel Daicel AD-H.
[e] Determined by GC on Chiralsil β-Dex.

The latter value is higher than those previously reported with other simple binaphthyl-based phosphoramidites (such as **1**, up to 60% ee),[6,17] although application of chiral amine-based phosphoramidites leads to higher levels of stereoselectivity (e.g., 93% ee in the case of **2**).[5a] Diethylzinc additions to substituted benzalacetones and nitrostyrene occurred with low enantioselectivity, but slightly higher with the dimethylamino ligand (*R*)-**4a** (18–33% ee).

In conclusion, bis-*ortho*- and bis-*meta*-phenylene homologues of BINOL-based phosphoramidites were prepared and their stereochemistry was determined by VCD spectroscopy. Preliminary testing of the prepared ligands in copper-catalyzed conjugate addition of diethylzinc to acyclic enones and nitrostyrene gave the corresponding products in low to moderate ee (up to 74% ee). The design of this group of ligands and their application in enantioselective catalytic transformations are under further investigation.

Acknowledgments

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Supplementary data

General procedures, methods for molecular modelling and characterization data for the products of diethylzinc addition, and NMR spectra of compounds (*R*)-**4**, (*S*)-**5**, (*R*)-**6**, and (*S*)-**7** are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.02.041.

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9. To a stirred solution of (*R*)-**9** or (*S*)-**10** (2.28 mmol, 1 g) in CH_2Cl_2 (30 ml) was added dropwise BBr_3 (22.8 mmol, 22.8 ml, 1 M solution in CH_2Cl_2) at 0 °C. After being stirred at r.t. for 4 h, the reaction mixture was poured into ice-water. The product was extracted with CH_2Cl_2 (3 × 50 ml), washed with brine, and dried over Na_2SO_4. Evaporation of the solvent afforded pure (*R*)-**6** or (*S*)-**7**.
(*R*)-**6**: Yield 96% (0.90 g), off white solid, mp 96–100 °C with decomp., $[\alpha]_D^{20}$ +1.44 (*c* 1; $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 7.5, 8.4 Hz, 4H), 7.54 (ddd, *J* = 7.8, 5.7, 2.1 Hz, 2H), 7.46–7.34 (m, 6H), 7.03 (dd, *J* = 8.4, 8.4 Hz, 2H), 6.90–6.72 (m, 2H), 6.43–6.28 (m, 4H), 3.57 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9 (2C), 132.6 (2C), 129.7 (2C), 129.6 (2C), 129.5 (2C), 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.8 (2C), 127.2 (2C), 127.0 (2C), 126.2 (2C), 119.7 (2C), 116.9 (2C) ppm. IR (KBr): ν = 3446, 2922, 1684, 1653, 1558, 1464, 1395, 1067, 875, 763, 668 cm^{-1}. Anal. Calcd for $C_{32}H_{22}O_2$ (438.52): C, 87.65; H, 5.06. Found: C, 87.24; H, 5.27.
(*S*)-**7**: Yield 100% (0.94 g), off white solid, mp 120–128 °C with decomp., $[\alpha]_D^{20}$ −2.70 (*c* 1; $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.1 Hz, 2H), δ = 7.89 (d, *J* = 8.4 Hz, 2H), 7.49 (ddd, *J* = 7.8, 6.3, 1.5 Hz, 2H), 7.41–7.29 (m, 6H), 6.74 (dd, *J* = 8.1, 7.8 Hz, 2H), 6.54 (dd, *J* = 7.2, 1.8 Hz, 2H), 6.07 (d, *J* = 7.8 Hz, 2H), 5.90 (dd, *J* = 2.1, 1.8 Hz, 2H), 4.63 (br s, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3 (2C), 142.9 (2C), 139.1 (2C), 134.4 (2C), 134.1 (2C), 132.3 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 128.0 (2C), 127.4 (2C), 126.6 (2C), 125.6 (2C), 121.7 (2C), 116.4 (2C), 113.2 (2C) ppm. IR (KBr): ν = 3305, 2923, 1684, 1653, 1559, 1465, 1338, 1191, 810, 782, 677 cm^{-1}. Anal. Calcd for $C_{32}H_{22}O_2$ (438.52): C, 87.65; H, 5.06. Found: C, 87.15; H, 5.32.
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12. To a solution of (*R*)-**6** or (*S*)-**7** (1.14 mmol, 0.50 g) in benzene (10 mL) were added NH_4Cl (0.028 mmol, 1.5 mg) and HMPT (1.42 mmol, 0.23 g). The reaction mixture was heated to reflux for 4 h, then the solvent was removed and the pure phosphoramidites (*R*)-**4a** and (*S*)-**5a** were isolated as white powders by chromatography, using short silica gel columns, neutralized with Et_3N (eluent CH_2Cl_2/hexanes, 5:1).
(*R*)-**4a**: Yield 64% (0.37 g), white solid, mp 97–107 °C with decomp., $[\alpha]_D^{20}$ +1.99 (*c* 1.00; $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.88 (m, 4H), 7.41–7.48 (m, 3H), 7.29–7.36 (m, 5H), 6.87–6.99 (m, 2H), 7.10–7.20 (m, 2H), 6.74–6.80 (m, 2H), 6.67 (ddd, *J* = 7.5, 7.5, 0.8 Hz, 1H), 6.50 (ddd, *J* = 7.5, 7.5, 0.8 Hz, 1H), 2.52 (s, 3H), 2.49 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.37, 149.7, 137.2, 135.7, 135.3, 134.4, 134.1, 133.0 (2C), 132.8, 132.2, 131.2 (2C), 130.1, 129.3 (2C), 128.3 (2C), 127.9 (2C), 127.5 (2C), 127.1 (2C), 125.8 (2C), 125.4 (2C), 121.8, 121.4, 117.4, 117.2, 35.2, 34.9 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 126.0 ppm. IR ($CDCl_3$): ν = 3055, 2840, 2803, 1578, 1488, 1233, 1195, 1079, 820, 752, 710 cm^{-1}. HRMS: no molecular peak observable; calcd for $C_{32}H_{21}O_2P$ $[M-N(CH_3)CH_2]^+$ 468.1279, found 468.2003.
(*S*)-**5a**: Yield 37% (0.22 g), white solid, mp 95–105 °C with decomp., $[\alpha]_D^{20}$ −6.23 (*c* 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.84–7.96 (m, 4 H), 7.40–7.51 (m, 3H), 7.28–7.32 (m, 5H), 6.79 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.73 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.62 (q, *J* = 7.3 Hz, 2H), 6.20 (s, 1H), 6.13 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.00 (d, *J* = 7.3 Hz, 1H), 5.61 (br s, 1H), 2.90 (s, 3H), 2.86 (s, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3, 142.8, 142.5, 139.7, 138.9, 134.5, 134.4, 134.2, 132.3, 132.2, 128.2 (2C), 128.0 (2C), 127.4 (2C), 127.3, 127.2, 127.1, 126.7, 126.6 (2C), 126.5 (2C), 125.5 (2C), 123.1, 122.7, 119.4, 119.2, 118.1 (2C), 35.2, 34.9 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 146.2 ppm. IR ($CDCl_3$): ν = 3050, 2929, 2843, 1578, 1487, 1258, 1182, 1065, 819, 788, 714 cm^{-1}. HRMS: calcd for $C_{34}H_{26}NO_2PH$ $[M+H]^+$ 512.1780, found 512.2352; calcd for $C_{32}H_{21}O_2P$ $[M-N(CH_3)CH_2]^+$ 468.1279, found 468.2641.
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14. General procedure: (*R*)-**4a** or (*S*)-**5a** (0.49 mmol, 0.25 g) dissolved in toluene (12.5 mL) was treated with 2 equiv of the corresponding amine (0.98 mmol), in the presence of 1.5 equiv of 5-phenyl-1*H*-tetrazole (0.71 mmol, 0.10 g). The reaction was carried out under reflux for 6–9 h. Then the solvent was removed and the products were isolated by chromatography on short silica gel columns, neutralized with Et_3N (eluent CH_2Cl_2/hexanes, 5:1).
(*R*)-**4b**: Yield 29% (0.07 g), white solid, mp 97–99 °C, $[\alpha]_D^{20}$ +2.44 (*c* 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.88 (m, 4H), 7.40–7.49 (m, 4H), 7.28–7.34 (m, 2H), 7.09–7.19 (m, 2H), 6.88–6.98 (m, 4H), 6.84 (d, *J* = 7.1 Hz, 2H), 6.70 (dd, *J* = 7.4, 1.2 Hz, 1H), 6.48 (dd, *J* = 7.1, 1.2 Hz, 1H), 2.88 (m, 2H), 1.54 (m, 6H), 1.25 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2, 150.1, 137.4, 135.5, 132.4, 134.8, 133.3 (2C), 132.3, 130.2, 129.6 (2C), 128.1 (2C), 128.0 (2C), 127.9 (2C), 127.8 (2C), 127.6 (2C), 127.3 (2C), 126.0 (2C), 125.6 (2C), 122.0, 121.8, 121.6, 117.6, 44.9, 44.6, 27.0, 26.9, 25.2 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 122.2 ppm. IR ($CDCl_3$): ν = 3058, 2933, 2844, 1577, 1488, 1439, 1275, 1194, 1056, 819, 751, 710 cm^{-1}. HRMS: calcd for $C_{37}H_{30}NO_2PH$ $[M+H]^+$ 552.2092, found 552.2599.
(*R*)-**4c**: Yield 50% (0.13 g), white solid, mp 97–100 °C, $[\alpha]_D^{20}$ +2.0 (*c* 0.010, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.89 (m, 4H), 7.42–7.49 (m, 3H), 7.28–7.36 (m, 3H), 7.10–7.20 (m, 2H), 6.90–7.00 (m, 4H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.71 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.51 (dd, *J* = 7.4, 1.3 Hz, 1H), 3.46 (t, *J* = 4.6 Hz, 4H), 2.95 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.1, 149.5, 136.9, 135.8, 135.2, 134.5, 133.2 (2C), 132.1, 131.2, 129.9, 129.1 (2C), 128.0, 127.8 (2C), 127.6 (2C), 127.1 (2C), 127.0 (2C), 125.9 (2C), 125.6 (2C), 125.5 (2C), 122.2, 121.6, 117.1, 116.8, 67.7 (2C), 44.0, 43.8 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 120.7 ppm. IR ($CDCl_3$): ν = 3062, 2945, 2892, 1579, 1488, 1439, 1245, 1204, 1190, 1112, 1078, 958, 818, 751 cm^{-1}. HRMS: calcd for $C_{36}H_{28}NO_3PH$ $[M+H]^+$ 554.1885, found 554.2612.
(*S*)-**5b**: Yield 51% (0.13 g), white solid, mp 99–101 °C, $[\alpha]_D^{20}$ −8.0 (*c* 0.010, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83–8.08 (m, 4H), 7.28–7.53 (m, 9H), 7.17 (d, *J* = 7.4 Hz, 2H), 6.63–6.90 (m, 2H), 6.53 (m, 1H), 6.28 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.06 (d, *J* = 7.4 Hz, 1H), 2.35 (m, 2H), 1.66 (m, 4H), 1.25 (m, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.7, 154.4, 142.8, 142.5, 139.7, 138.9, 134.5, 134.4, 134.2, 132.2 (2C), 128.2 (2C), 128.0 (2C), 127.4 (2C), 127.2 (2C), 127.1 (2C), 126.5 (2C), 125.5 (2C), 123.1, 122.9, 122.7, 119.4, 119.3, 118.2 (2C), 45.0, 44.7, 27.0, 26.9, 24.9 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 143.1 ppm. IR ($CDCl_3$): ν = 3050, 2924, 2851, 1579, 1487, 1464, 1258, 1192, 1065, 937, 819, 780,

703 cm^{-1}. HRMS: calcd for $C_{37}H_{30}NO_2PH$ $[M+H]^+$ 552.2092, found 552.2426. (*S*)-**5c**: Yield 25% (0.06 g), white solid, mp 96–100 °C, $[\alpha]_D^{20}$ −14.0 (*c* 0.010; $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 8.05–8.08 (m, 2H), 7.80–7.97 (m, 2H), 7.40–7.52 (m, 5H), 7.27–7.36 (m, 7H), 6.53–6.82 (m, 1H), 5.99 (m, 3H), 3.93 (t, *J* = 4.9 Hz, 4H), 3.18 (t, *J* = 4.9 Hz, 4H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.2, 149.2, 137.9, 137.5, 137.4, 137.0, 136.8 (2C), 134.3, 133.6, 133.2, 133.1, 131.1, 130.6, 129.6 (2C), 129.2 (2C), 128.3 (2C), 127.9 (2C), 127.5 (2C), 126.3 (2C), 125.7 (2C), 120.5, 120.4, 118.2, 117.1, 67.8 (2C), 44.5, 43.9 ppm. ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 142.8 ppm. IR ($CDCl_3$): ν = 3051, 2924, 2852, 1580, 1487, 1464, 1259, 1194, 1069, 962, 822, 788, 703 cm^{-1}. HRMS: calcd for $C_{36}H_{28}NO_3PH$ $[M+H]^+$ 554.1885, found 554.2698.

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