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Novel chiral xylofuranose-based phosphinooxathiane and phosphinooxazinane ligands for palladium-catalyzed asymmetric allylations

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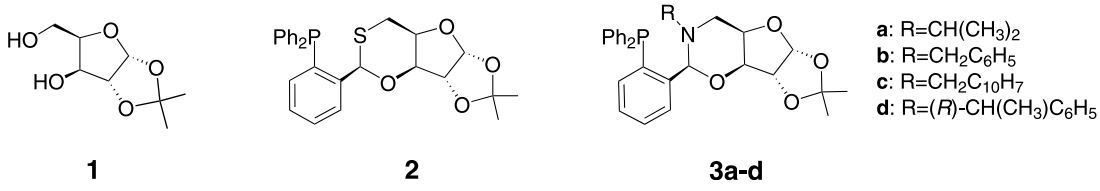
Abstract—Novel chiral xylofuranose-based phosphinooxathiane and phosphinooxazinane ligands were found to provide high levels of enantioselectivity (up to 94% ee) in palladium-catalyzed asymmetric allylic alkylations and aminations.

1. Introduction

Palladium-catalyzed allylation[1] is one of the most important methods for carbon–carbon bond formation in synthetic organic chemistry. As such its asymmetric version using a chiral ligand has also been extensively studied over the last decade.[2,3] Generally, the combination of a donor atom and a rigid backbone in a ligand is very important for realizing high levels of asymmetric induction in the reaction. 1,2-*O*-Isopropylidene-D-xylofuranose **1** is a readily available and highly functionalized compound with several stereogenic centers, allowing for a systematic regio- and stereoselective introduction of different functionalities in the synthesis of a series of chiral ligands. For this reason, several xylofuranose-based chiral ligands have recently been explored and their potential utility in asymmetric reactions such as palladium-catalyzed allylation,[4] hydrogenation,[5] hydroformylation,[6] and copper-catalyzed addition[7] of dialkylzinc to enones has been demonstrated. More recently, we have also explored a new type of chiral phosphinooxathiane[8] **2** and phosphinooxazinane ligands **3a–d** by fusing a xylofuranose ring and have shown their utility in palladium-catalyzed tandem allylations[9] (Scheme 1). Herein, we report the application of these ligands to Pd-catalyzed allylic alkylations and aminations.



1 **2** **3a-d**

Scheme 1.

2. Results and discussion

2.1. Synthesis of phosphinooxathiane and phosphinooxazinane ligands

Phosphinooxathiane **2** and phosphinooxazinane **3a–d** ligands were synthesized easily from commercially available 1,2-*O*-isopropylidene-D-xylofuranose **1** (Scheme 2). Diol **1** was converted to **4** by monotosylation[10] followed by acetylation. The displacement of the tosylate group with potassium thioacetate and the treatment of **6** with potassium carbonate afforded the mercapto-alcohol **7**. The condensation of **7**

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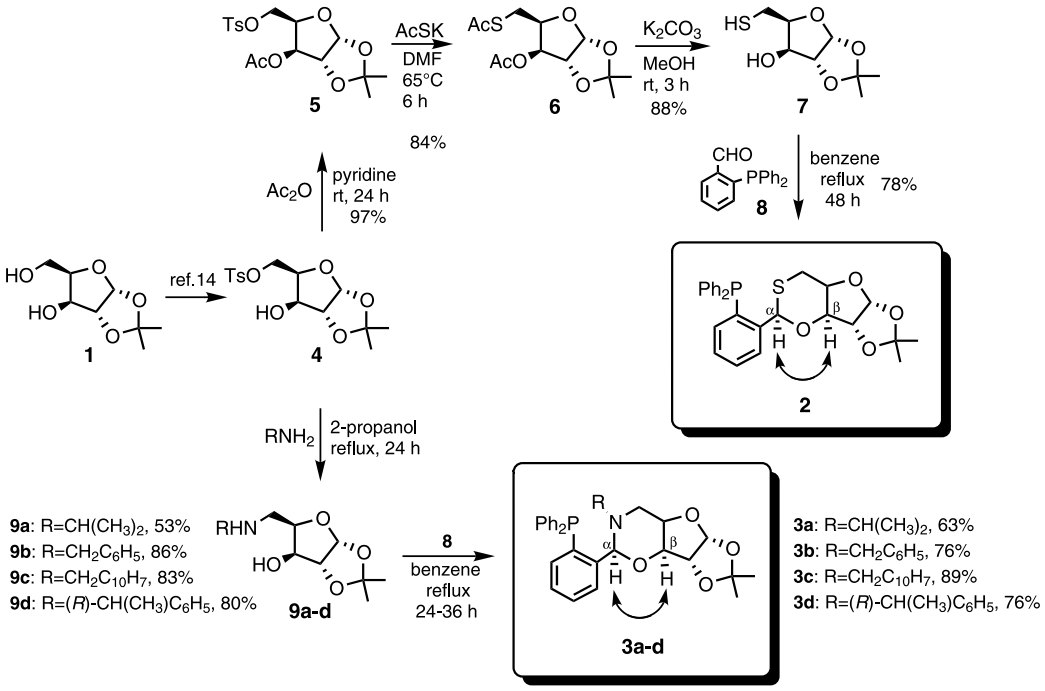


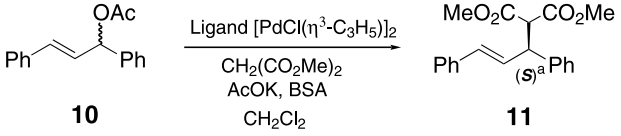
Scheme 2.

with 2-(diphenylphosphino)benzaldehyde **8** gave the desired chiral phosphinooxathiane ligand **2** in 43% yield. Similarly, chiral ligands **3a–d** were also easily prepared by the reaction of tosylate **4** with the corresponding amines followed by the condensations of **9a–d** with **8** in good yields (63–89%). In all five cases **2** and **3a–d**, the assigned stereochemistry at the α-position of the 1,3-oxathiane ring was determined by the NOE difference spectrum (NOEDS). Enhancements were observed between the hydrogen at the α-position and the hydrogen at the β-position when the α- and β-protons were irradiated, respectively (Scheme 2).[8,9]

2.2. Palladium-catalyzed asymmetric allylic alkylations

The palladium-catalyzed allylic alkylation of 1,3-diphenyl-2-propenyl acetate **10** with dimethyl malonate using chiral phosphinooxathiane ligand **2** and phosphinooxazinane ligands **3a–d** were examined in the presence of π-allylpalladium chloride dimmer $[PdCl(\eta^3\text{-}C_3H_5)]_2$, *N*,*O*-bis(trimethylsilyl)acetamide (BSA),[11] and potassium acetate (entries 1–8) in dichloromethane to give the allylation product **11**. The results are summarized in Table 1. The reaction using phosphinooxathiane ligand **2** (5 mol%) gave the

Table 1. Asymmetric Pd-catalyzed allylic alkylation of acetate **10**



Entry	Ligand	Ligand (mol%)	Temp. (°C)	Time (h)	Yield[b] (%)	Ee[c] (%)
1	**2**	5	rt	6	93	90
2	**2**	2	rt	24	91	91
3	**2**	1	rt	24	87	84
4	**2**	2	0	48	90	70
5	**3a**	2	rt	24	67	46
6	**3b**	2	rt	24	64	75
7	**3c**	2	rt	24	75	49
8	**3d**	2	rt	24	17	73

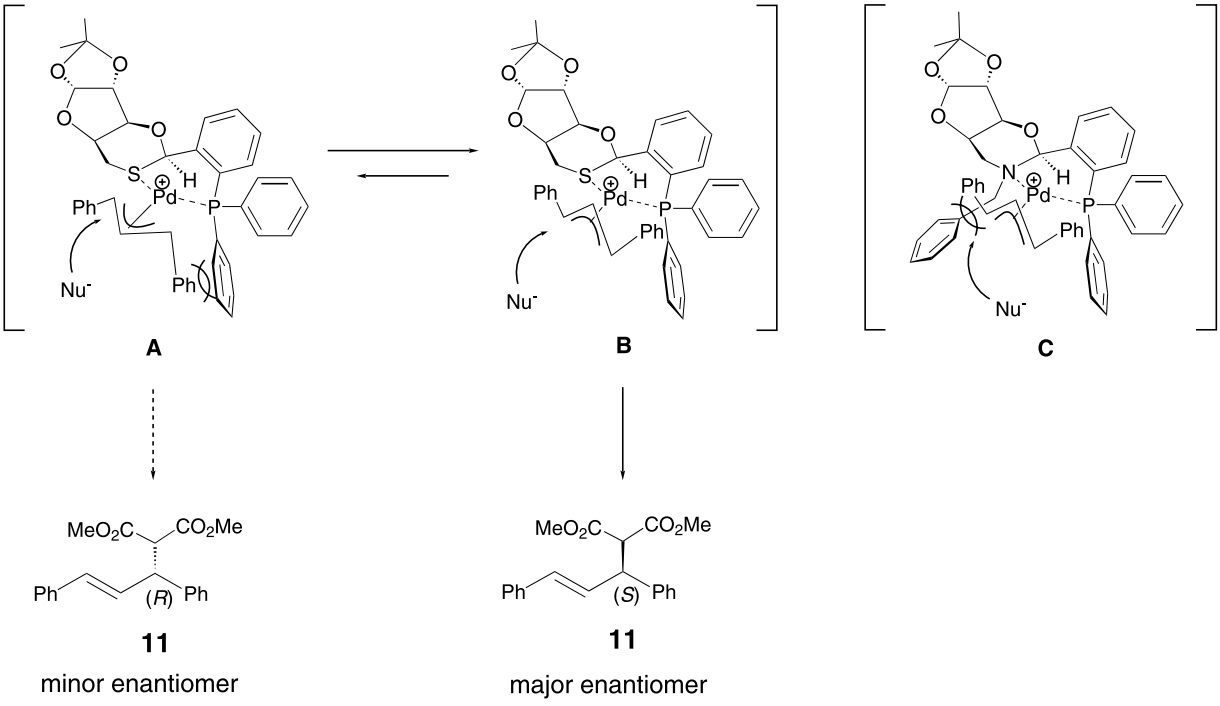
[a](*S*)-Configurations based on the specific rotation with literature data.[3b]
[b]Isolated yields.
[c]Determined by HPLC analysis using a DAICEL Chiralcel OD-H.

product **11** in 93% yield and 90% enantiomeric excess (ee) (entry 1). Decreasing the catalyst loading of **2** from 5 mol% to 2 mol% afforded almost the same results as entry 1 (91%, 91% ee) (entry 2). However, a further decrease in catalyst loading to 1 mol% led to a decrease in ee (entry 3). In addition, decreasing the temperature also brought about a decrease in ee (70% ee) (entry 4). Reactions with chiral phosphinooxazinane ligands **3a**–**d** under the same conditions as entry 2 using ligand **2** gave only low to moderate yields and enantioselectivities (entries 5–8). The best result was obtained when the reaction was carried out with *N*-benzylated ligand **3b** (64%, 75% ee) (entry 5). Based on the above results, chiral phosphinooxathiane ligand **2** was more effective than phosphinooxazinane ligands **3a**–**d** for this allylic alkylation.

It is considered that the enantiodifferentiation step in Pd-catalyzed allylic alkylation and amination involves the substitution of π-allyl complexes with nucleophiles, and nucleophilic attack occurs predominantly at the allyl terminus from *trans* to the better π-acceptor (P> S).[8b,12] Due to the (*S*)-product being obtained as the major enantiomer, the reaction probably proceeded through an M-type **A** rather than a W-type **B** intermediate (Scheme 3). In addition, the differentiation of chemical yields and enantiomeric excesses for the oxathiane ligand **2** and oxazinane ligands **3a**–**d** may be explained by steric differences. Thus, the ligands **3a**–**d** have bulky alkyl- or arylmethyl groups on the nitrogen atom in the oxazinane ring that obstructs construction of the π-allyl palladium complex **C**.

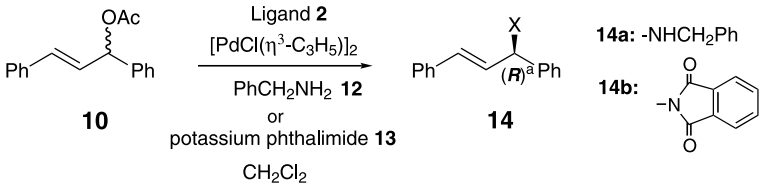
2.3. Palladium-catalyzed asymmetric allylic aminations

We next examined the palladium-catalyzed allylic amination[13] of acetate **10** with benzylamine **12** acting as the nucleophile using the chiral phosphinooxathiane ligand **2**, which showed an efficient ability in allylic alkylation. The reaction was carried out in CH_2Cl_2 using a catalyst generated by mixing 1 or 2.5 mol% of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ with 2 or 5 mol% of chiral ligand **2**, respectively, to give the aminated product **14a**. The results are summarized in Table 2. When the reaction was carried out at room temperature using 2 mol% of ligand **2** and 2.5 equiv. of benzylamine **12** to a substrate **10**, the product **14a** was obtained in low chemical yield (43%), but with good ee (89% ee) (entry 1). Increasing the nucleophile loading of **12** from 2.5 to 25 equiv. at room temperature did not give a significant increase in the chemical yield (53%, entry 2). At 45°C the reaction proceeded almost to completion (98%), but with a low enantioselectivity (52% ee) (entry 3). Decreasing the temperature to 0°C led to a substantial decrease in both chemical yield (13%) and enantioselectivity (79% ee, entry 4). However, varying the catalyst loading to 5 mol% of chiral ligand **2** brought about an increase in chemical yield (60%) without the substantial decrease in the enantioselectivity (85% entry 5). Furthermore, the same reaction was examined using potassium phthalimide **13** as a bulky, reactive nitrogen nucleophile (entries 6–8). The reaction at room temperature gave the product **14b** an excellent chemical yield (98%) and enantioselectivity (94% ee entry 6). Cooling to 0°C led to a decrease in chemical yield (31%) (entry 7). Varying



Scheme 3.

Table 2. Asymmetric Pd-catalyzed allylic amination of acetate **10**



Entry	Nucleophile	Ligand (mol%)	Nucleophile (equiv. to **10**)	Temp. (°C)	Time (h)	Yield[b] (%)	Ee[c] (%)
1	**12**	2	2.5	rt	48	43	89
2	**12**	2	25	rt	48	53	88
3	**12**	2	25	45	6	98	52
4	**12**	2	25	0	96	13	79
5	**12**	5	25	rt	48	60	85
6	**13**	2	3	rt	48	98	94
7	**13**	2	3	0	48	31	92
8	**13**	5	3	0	48	90	90

[a](*R*)-Configurations based on the specific rotation with literature data.[3b]
[b]Isolated yields.
[c]Determined by HPLC analysis using a DAICEL Chiralcel OD-H column.

the catalyst loading to 5 mol% of chiral ligand **2** gave a good chemical yield (90%) and enantioselectivity (90% ee), even at 0°C (entry 8). From these results, it appears that the chemical yield and the enantioselectivity depend on both the amount of catalyst and the reaction temperature in the reactions using nucleophiles **12** and **13**. Increasing the reaction temperature gave an excellent chemical yield, but enantioselectivity was poorer. However, increasing the catalyst loading of **2** accelerated the reaction rate without the substantial decrease in the enantioselectivity. In particular, this was observed in the reaction using imide **13** as the nucleophile. For reasons that are not clear, it might be considered that imide **13** has both weaker basicity and more rigid structure when compared to amine **12**.

3. Conclusions

The chiral xylofuranose-based phosphinooxathiane **2** and phosphinooxazinane **3a–d** ligands have been exploited, and applied to Pd-catalyzed asymmetric alkylations and aminations. From these results it can be seen that the S–P type chiral oxathiane ligand **2** was effective in both reactions. In particular an excellent chemical yield and high enantiomeric excess were obtained when chiral ligand **2** was used in Pd-catalyzed aminations. It is expected that both **2** and **3** could act as good ligands in other catalytic asymmetric reactions. Further applications and modifications of these ligands are in progress.

4. Experimental

4.1. General methods

Melting points are uncorrected. IR spectra were recorded as KBr pellets (solids) or thin films (liquids). The ^{1}H and ^{13}C NMR spectra were recorded at 270 and 67.5 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta=0$) for ^{1}H NMR and relative to the central $CDCl_3$ resonance ($\delta=77.0$) for ^{13}C NMR. Mass spectra were obtained by EI. The enantiomeric excesses (ee) of the products were determined by chiral HPLC. Optical rotations were recorded at the sodium D line with a polarimetar at room temperature. Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Chromatography refers to flash chromatography on silica gel (230–400 mesh), unless otherwise noted.

4.2. 3-*O*-Acetyl-1,2-*O*-isopropylidene-5-*p*-toluenesulfonyl-3,5-dioxy-α-D-xylofuranose 5

To a solution of **4**[14] (1.0 g 2.91 mmol) in anhydrous pyridine (15 mL) was added acetic anhydride (0.33 mL, 3.49 mmol) at 0°C. After being stirred at room temperature for 24 h, the reaction mixture was concentrated under reduced pressure. The residue was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (hexane/EtOAc = 2/1 as eluent) to give the pure product **5** (1.1 g, 97%): $[\alpha]_D^{23}=-16.4$ (*c* 1.9, $CHCl_3$). IR (film) cm^{-1}: 3021, 1749, 1375, 1216, 1178. ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.47 (s, 3H), 2.03 (s, 3H), 2.45 (s, 3H), 4.11–4.26 (m, 2H), 4.40–4.46 (m, 1H), 4.49 (d, $J=3.6$ Hz, 1H), 5.19 (d, $J=3.1$ Hz, 1H), 5.86 (d, $J=3.6$ Hz, 1H), 7.35 (d, $J=8.4$ Hz, 2H), 7.79 (d, $J=8.4$ Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 21.13, 22.18, 26.72, 27.18, 66.31, 76.15, 76.51, 83.63, 105.23, 112.88, 128.37, 130.26, 132.96, 145.42, 169.81. HRMS *m*/*z* calcd for $C_{17}H_{22}O_8S$ (M^+): 386.1035. Found: 386.1037.

4.3. 3-*O*-Acetyl-5-deoxy-1,2-*O*-isopropylidene-5-thioacetyl-α-D-xylofuranose 6

To a solution of **5** (1.0 g, 2.59 mmol) in DMF (5 mL) was added potassium thioacetate (592 mg, 5.18 mmol) under Ar. After being stirred at 65°C for 6 h under Ar, the reaction mixture was quenched with water and extracted with ether. The organic layer was washed with saturated aqueous Na_2CO_3, dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (hexane/EtOAc = 2/1 as eluent) to give the pure product **6** (633 mg, 84%): $[\alpha]_D^{23} = -13.2$ (*c* 1.7, $CHCl_3$). IR (film) cm^{-1}: 1746, 1695, 1224. ^1H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.50 (s, 3H), 2.12 (s, 3H), 2.34 (s, 3H), 3.15 (dd, $J = 7.1$ Hz, 1.6 Hz, 2H), 4.35 (dt, $J = 7.1$ Hz, 2.9 Hz, 1H), 4.50 (d, $J = 3.8$ Hz, 1H), 5.19 (d, $J = 3.0$ Hz, 1H), 5.90 (d, $J = 3.8$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 20.82, 26.24, 26.66, 26.70, 30.51, 76.20, 77.88, 83.43, 104.64, 112.12, 169.52, 194.29. HRMS *m*/*z* calcd for $C_{12}H_{18}O_6S$ (M^+): 290.0824. Found: 290.0847.

4.4. 5-Deoxy-1,2-*O*-isopropylidene-5-mercapto-α-D-xylofuranose 7

A mixture of **6** (500 mg, 1.72 mmol) and K_2CO_3 (1.2 g, 8.62 mmol) in MeOH (9 mL) was stirred at room temperature for 4 h under Ar, and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (hexane/ether = 1/2 as eluent) to give the pure product **7** (313 mg, 88%): mp 66–68°C. $[\alpha]_D^{23} = -50.0$ (*c* 1.2, $CHCl_3$). IR (KBr) cm^{-1}: 3366, 2580. ^1H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.51 (s, 3H), 2.06 (d, $J = 5.7$ Hz, 1H), 2.70–2.93 (m, 2H), 4.21–4.28 (m, 1H), 4.31–4.34 (m, 1H), 4.53 (d, $J = 3.6$ Hz, 1H), 5.93 (d, $J = 3.6$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 21.97, 26.28, 26.81, 74.75, 81.50, 85.12, 104.79, 111.77. HRMS *m*/*z* calcd for $C_8H_{14}O_4S$ (M^+): 206.0613. Found: 206.0585. Anal. calcd for $C_8H_{14}O_4S$: C, 46.58; H, 6.84. Found: C, 46.63; H, 6.67.

4.5. (1*S*,3*R*,6*R*,8*R*,9*R*)-2,7-Dioxa-3-(2-diphenylphosphino)phenyl-8,9-*O*-isopropylidenethiabicyclo[4.3.0]-nonane 2

Compound **7** (100 mg, 0.49 mmol), 2-(diphenylphosphino)benzaldehyde **8** (140 mg 0.49 mmol), camphor-10-sulfonic acid (15 mg) and benzene (10 mL) were placed in a flask equipped with a Dean–Stark trap and the mixture refluxed for 48 h. The solvent was removed under reduced pressure and the residue purified by preparative TLC (hexane/EtOAc = 15/1) to give the product **2** (181 mg, 43%): mp 78–80°C. $[\alpha]_D^{23} = -78.0$ (*c* 1.0, $CHCl_3$). IR (KBr) cm^{-1}: 746, 697. ^1H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.48 (s, 3H), 3.13 (dd, $J = 14.8$ Hz, 3.0 Hz, 1H), 3.45 (dd, $J = 14.8$ Hz, 2.6 Hz, 1H), 4.03 (d, $J = 2.1$ Hz, 1H), 4.10 (d, $J = 3.6$ Hz, 1H), 4.12–4.15 (m, 1H), 5.98 (d, $J = 3.6$ Hz, 1H), 6.35 (d, $J = 7.6$ Hz, 1H), 6.92–6.97 (m, 1H), 7.20–7.41 (m, 12H), 7.67–7.72 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 25.97, 26.58, 29.76, 68.15, 80.93, 81.30, 83.71, 105.18, 111.52, 127.16, 127.23, 128.45, 128.48, 128.55, 128.59, 128.72, 128.82, 129.06, 129.48, 133.56, 133.78, 133.85, 133.98, 134.06, 142.39, 142.73. HRMS *m*/*z* calcd for $C_{27}H_{27}O_4PS$ (M^+): 478.1368. Found: 478.1390.

4.6. General procedure for synthesis of 5-deoxy-1,2-*O*-isopropylidene-5-*N*-monoalkylamino-α-D-xylofuranoses 9a–d

To a solution of **4**[10] (1.0 g, 2.91 mmol) in 2-propanol (6 mL) was added amines (11.62 mmol) and the reaction mixture refluxed for 24 h. The solvent was removed under reduced pressure. The residue was diluted with EtOAc and washed with saturated aqueous Na_2CO_3. The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (hexane/EtOAc = 1/1 as eluent) to give the pure products **9a–d**.

4.6.1. 5-Deoxy-5-isopropylamino-1,2-*O*-isopropylidene-α-D-xylofuranose 9a[14]. Yield 53%.

4.6.2. 5-Benzylamino-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose 9b[14]. Yield 86%.

4.6.3. 5-Deoxy-1,2-*O*-isopropylidene-5-naphthylmethylamino-α-D-xylofuranose 9c. Yield 83%; $[\alpha]_D^{23} = +6.7$ (*c* 1.3, $CHCl_3$). IR (film) cm^{-1}: 770. ^1H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.47 (s, 3H), 3.12 (dd, $J = 12.9$ Hz, 1.2 Hz, 1H), 3.49 (dd, $J = 12.9$ Hz, 3.5 Hz, 1H), 4.22–4.27 (m, 4H), 4.46 (d, $J = 3.6$ Hz, 1H), 5.90 (d, $J = 3.6$ Hz, 1H), 7.40–7.58 (m, 4H), 7.79 (m, 1H), 7.84 (d, $J = 9.1$ Hz, 1H), 8.00 (d, $J = 8.2$ Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 26.11, 26.81, 48.26, 51.44, 78.00, 85.80, 104.84, 111.28, 123.02, 125.05, 125.89, 126.24, 126.42, 128.20, 128.59, 131.38, 133.66, 133.87. HRMS *m*/*z* calcd for $C_{19}H_{21}NO_4$ (M^+): 329.1627. Found: 329.1607.

4.6.4. 5-(*R*)-Phenylmethylamino-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose 9d. Yield 80%; $[\alpha]_D^{23} = +40.8$ (*c* 2.2, $CHCl_3$). IR (film) cm^{-1}: 3320, 770. ^1H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.38 (d, $J = 6.6$ Hz, 3H), 1.45 (s, 3H), 2.79 (dd, $J = 12.9$ Hz, 1.3 Hz, 1H), 3.23 (dd, $J = 12.9$ Hz, 3.5 Hz, 1H), 3.70 (q, $J = 6.6$ Hz, 1H), 4.12–4.17 (m, 2H), 4.49 (d, $J = 3.6$ Hz, 1H), 5.99 (d, $J = 3.6$ Hz, 1H), 7.22–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$) δ 24.33, 26.20, 26.86, 46.44, 58.69, 77.12, 77.99, 85.89, 104.95, 111.33, 126.62, 127.31, 128.58, 143.33. HRMS *m*/*z* calcd for $C_{16}H_{23}NO_4$ (M^+): 293.1627. Found: 293.1603.

4.7. General procedure for synthesis of phosphinooxazinane ligands 3a–d

Amino alcohols (0.5 mmol), 2-(diphenylphosphino)benzaldehyde (130 mg 0.45 mmol), and benzene (10 mL) were placed in a flask equipped with a Dean–Stark trap and the mixture refluxed for 24–36 h. The reaction mixture was passed through on celite 454 and the filtrate concentrated under reduced pressure to give the producs **3a–d**. Compounds **3b** and **3c** were recrystallized from hexane. Compound **3d** was purified by preparative alumina TLC (hexane/EtOAc = 15/1).

4.7.1. (1*S*,3*S*,6*R*,8*R*,9*R*)-4-Aza-2,7-dioxa-3-(2-diphenylphosphino)phenyl-4-isopropyl-8,9-*O*-isopropylidenebicyclo[4.3.0]nonane 3a. Yield 63%; mp 66–69°C. $[\alpha]_D^{23}=+17.9$ (*c* 1.2, $CHCl_3$). IR (KBr) cm^{-1}: 746, 745, 698. ^1H NMR ($CDCl_3$) δ 0.65 (d, $J=6.6$ Hz, 3H), 0.99 (d, $J=6.6$ Hz, 3H), 1.28 (s, 3H), 1.47 (s, 3H), 2.69 (m, 1H), 2.93 (dd, $J=14.0$ Hz, 2.7 Hz, 1H), 3.34 (d, $J=14.0$ Hz, 1H), 3.78 (d, $J=2.0$ Hz, 1H), 4.16 (d, $J=2.0$ Hz, 1H), 4.32 (d, $J=3.6$ Hz, 1H), 5.68 (d, $J=7.7$ Hz, 1H), 5.98 (d, $J=3.6$ Hz, 1H), 6.90–6.94 (m, 1H), 7.12–7.72 (m, 12H), 7.75–7.79 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 16.18, 16.27, 26.27, 26.83, 42.90, 47.44, 73.26, 79.21, 83.80, 89.56 ($J_{pc}=26.8$ Hz), 105.62, 111.31, 127.81, 128.11, 128.13, 128.24, 128.38, 128.42, 128.50, 128.67, 128.92, 129.15, 133.35, 133.64, 133.84, 134.13, 135.56, 136.31, 142.81, 143.13. HRMS *m*/*z* calcd for $C_{30}H_{34}NO_4P$ (M^+): 503.2226. Found: 503.2196. Anal. calcd for $C_{30}H_{34}NO_4P$: C, 71.55; H, 6.81; N, 2.78. Found: C, 71.80; H, 6.91; N, 2.66.

4.7.2. (1*S*,3*S*,6*R*,8*R*,9*R*)-4-Aza-4-benzyl-2,7-dioxa-3-(2-diphenylphosphino)phenyl-8,9-*O*-isopropylidenebicyclo-[4.3.0]nonane 3b. Yield 76%; mp 79–81°C. $[\alpha]_D^{23}=+79.8$ (*c* 1.3, $CHCl_3$). IR (KBr) cm^{-1}: 746, 697. ^1H NMR ($CDCl_3$) δ 1.33 (s, 3H), 1.46 (s, 3H), 2.91 (dd, $J=15.0$ Hz, 2.6 Hz, 1H), 3.06 (d, $J=12.9$ Hz, 1H), 3.17 (d, $J=15.0$ Hz, 1H), 3.78 (d, $J=12.9$ Hz, 1H), 4.03 (d, $J=1.3$ Hz, 1H), 4.20 (d, $J=2.0$ Hz, 1H), 4.59 (d, $J=3.6$ Hz, 1H), 5.99 (d, $J=6.6$ Hz, 1H), 6.08 (d, $J=3.6$ Hz, 1H), 6.70–6.73 (m, 2H), 7.00–7.15 (m, 4H), 7.17–7.42 (m, 12H), 7.80–7.84 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 26.31, 26.81, 47.85, 51.57, 73.34, 80.23, 84.16, 89.71 (d, $J_{pc}=25.2$ Hz), 105.14, 111.42, 126.25, 127.20, 127.28, 127.75, 128.11, 128.19, 128.28, 128.55, 128.66, 128.76, 128.80, 128.88, 128.92, 133.05, 133.33, 134.14, 134.45, 135.36, 136.02, 138.24, 138.26, 142.93, 143.26. HRMS *m*/*z* calcd for $C_{34}H_{34}NO_4P$ (M^+): 551.2225. Found: 551.2241. Anal. calcd for $C_{34}H_{34}NO_4P$: C, 74.03; H, 6.21; N, 2.54. Found: C, 74.31; H, 6.47; N, 2.36.

4.7.3. (1*S*,3*S*,6*R*,8*R*,9*R*)-4-Aza-2,7-dioxa-3-(2-diphenylphosphino)phenyl-8,9-*O*-isopropylidene-4-naphthylmethylbicyclo[4.3.0]nonane 3c. Yield 89%; mp 90–93°C. $[\alpha]_D^{23}=+73.5$ (*c* 1.2, $CHCl_3$). IR (KBr) cm^{-1}: 793, 747, 699. ^1H NMR ($CDCl_3$) δ 1.33 (s, 3H), 1.45 (s, 3H), 2.92 (dd, $J=14.8$ Hz, 2.4 Hz, 1H), 3.37 (d, $J=14.8$ Hz, 1H), 3.68 (d, $J=13.9$ Hz, 1H), 4.06 (s, 1H), 4.12 (d, $J=1.8$ Hz, 1H), 4.27 (d, $J=13.9$ Hz, 1H), 4.57 (d, $J=3.6$ Hz, 1H), 5.93 (d, $J=5.6$ Hz, 1H), 6.13 (d, $J=3.6$ Hz, 1H), 6.97–7.01 (m, 1H), 7.13–7.57 (m, 16H), 7.63 (d, $J=8.1$ Hz 1H), 7.75 (d, $J=8.2$ Hz, 2H), 7.87–7.91 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 26.20, 26.68, 49.13, 49.35, 73.26, 80.02, 83.95, 90.18 (d, $J_{pc}=22.9$ Hz), 105.13, 111.34, 123.75, 124.94, 125.18, 125.24, 126.61, 126.80, 127.49, 127.57, 128.21, 128.31, 128.37, 128.42, 128.52, 128.67, 128.76, 131.82, 133.13, 133.37, 133.42, 133.76, 133.99, 134.28, 135.46, 135.71, 135.99, 137.20, 142.36, 142.68. HRMS *m*/*z* calcd for $C_{38}H_{36}NO_4P$ (M^+): 601.2382. Found: 601.2352. Anal. calcd for $C_{38}H_{36}NO_4P$: C, 75.86; H, 6.03; N, 2.33. Found: C, 75.79; H, 6.15; N, 2.35.

4.7.4. (1*S*,3*S*,6*R*,8*R*,9*R*)-4-Aza-2,7-dioxa-3-(2-diphenylphosphino)phenyl-8,9-*O*-isopropylidene-4-((*R*)-phenylethyl)bicyclo[4.3.0]nonane 3d. Yield 76%; mp 70–73°C. $[\alpha]_D^{23}=+46.9$ (*c* 1.3, $CHCl_3$). IR (KBr) cm^{-1}: 763, 747, 723, 698. ^1H NMR ($CDCl_3$) δ 1.21–1.27 (m, 6H), 1.43 (s, 3H), 2.81 (dd, $J=13.5$ Hz, 2.5 Hz, 1H), 3.04 (dd, $J=13.5$ Hz, 1.9 Hz, 1H), 3.74 (d, $J=1.8$ Hz, 1H), 3.87 (q, $J=6.8$ Hz, 1H), 4.13 (d, $J=2.1$ Hz, 1H), 4.28 (d, $J=3.6$ Hz, 1H), 5.84 (d, $J=7.7$ Hz, 1H), 6.00 (d, $J=3.6$ Hz, 1H), 6.87–6.92 (m, 1H), 7.14–7.41 (m, 15H), 7.46 (d, $J=8.1$ Hz, 2H), 7.88–7.93 (m, 1H). ^{13}C NMR ($CDCl_3$) δ 26.21, 26.75, 43.55, 54.07, 73.67, 78.65, 83.53, 88.96 (d, $J_{pc}=27.9$ Hz), 105.68, 111.27, 126.10, 127.06, 127.61, 127.82, 128.10, 128.15, 128.19, 128.36, 128.46, 128.48, 128.63, 128.74, 129.49, 133.34, 133.63, 133.78, 134.08, 135.55, 136.20, 136.50, 136.64, 142.58, 142.92, 143.23. HRMS *m*/*z* calcd for $C_{35}H_{36}NO_4P$ (M^+): 565.2382. Found: 565.2412. Anal. calcd for $C_{35}H_{36}NO_4P$: C, 74.32; H, 6.42; N, 2.48. Found: C, 74.04; H, 6.47; N, 2.45.

4.8. General procedure for the palladium-catalyzed allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate 10 with dimethyl malonate

A mixture of the ligand (0.008 mmol) and $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.004 mmol) in dry CH_2Cl_2 (1 mL) was stirred at room temperature for 1 h under Ar. The solution was added to a mixture of 1,3-diphenyl-2-propenyl acetate **10** (0.4 mmol) and potassium acetate (0.008 mmol) in dry CH_2Cl_2 (1 mL) followed by the addition of dimethyl malonate (1.2 mmol) and BSA (1.2 mmol). The reaction mixture was stirred at a temperature and reaction time as shown in Table 1. The mixture was diluted with ether and quenched with saturated aqueous NH_4Cl. The organic layer was washed with brine and dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue purified by preparative TLC (hexane/ether = 5/1) to give the product **11**. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, 0.5 mL/min, hexane/2-propanol = 98/2). The absolute configuration was determined by the specific rotation.[8b]

4.9. General procedure for the palladium-catalyzed allylic amination of *rac*-1,3-diphenyl-2-propenyl acetate 10 with benzylamine 12

A mixture of the ligand (0.008 mmol) and $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.004 mmol) in dry CH_2Cl_2 (1 mL) was stirred at room temperature for 1 h under Ar. To this was added a solution of 1,3-diphenyl-2-propenyl acetate **10** (0.4 mmol) in CH_2Cl_2 (1 mL) and benzylamine **12** (10 mmol). The reaction mixture was stirred at a temperature and reaction time as shown in Table 2. The mixture was subjected directly to column chromatography on silica gel (hexane/EtOAc = 5/1 as eluent) to give the product **14a**. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, 0.5 mL/min, hexane/

2-propanol = 199/1). The absolute configuration was determined by the specific rotation.[8b]

4.10. General procedure for the palladium-catalyzed allylic amination of *rac*-1,3-diphenyl-2-propenyl acetate 10 with potassium phthalimide 13

A mixture of the ligand (0.008 mmol) and $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (0.004 mmol) in dry CH_2Cl_2 (1 mL) was stirred at room temperature for 1 h under Ar. The solution and the CH_2Cl_2 solution (1 mL) of 1,3-diphenyl-2-propenyl acetate **10** (0.4 mmol) were added to the suspension of potassium phthalimide **13** (1.2 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred at a temperature and a reaction time as shown in Table 2. The mixture was quenched with water and extracted with ether. The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a residue, which was chromatographed on silica gel (hexane/EtOAc = 5/1 as eluent) to give the pure product **14b**. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, 0.5 mL/min, hexane/2-propanol = 98/2). The absolute configuration was determined by the specific rotation.[8b]

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