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BINAP versus BINAP(O) in Asymmetric Intermolecular Mizoroki–Heck Reactions: Substantial Effects on Selectivities**

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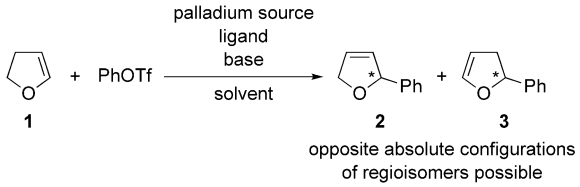
Abstract: 2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) was employed as chiral ligand in the enantioselective intermolecular Mizoroki–Heck reaction, whereas the use of cognate BINAP(O) (monooxidized BINAP) is unprecedented. The regio- and enantioselectivity of the arylation of representative cyclic alkenes changes dramatically in the presence of hemilabile BINAP(O) instead of BINAP. The arylation of 2,3-dihydrofuran is perfectly regiodivergent (98:2 versus 0:100) and the arylation of cyclopentene is only enantioselective with BINAP(O) [60 versus 10% enantiomeric excess (*ee*)]. Use of $[Pd_2(dba)_3]$•dba (dba = dibenzylideneacetone) instead of $Pd(OAc)_2$ produces as high as 86% *ee* in the arylation of cyclopentene.

Keywords: asymmetric catalysis · enantioselectivity · Heck reaction · palladium · regioselectivity

Introduction

Three decades since its discovery,[1] the asymmetric intermolecular Mizoroki–Heck reaction[2] continues to attract attention, largely as a test reaction for new chiral ligands.[3] The mechanism of the original transformation (**1**→**2** and/or **3**, Scheme 1) is also of particular interest because the regiochemical outcome is subtly influenced by several reaction parameters, which include the palladium source and ligand used. Moreover, the enantiomeric excess (*ee*) of the regioisomers formed is profoundly affected by the degree of double-bond migration in a complicated way and opposite absolute configurations for **2** and thermodynamically more stable **3** are possible. A mechanism that involves kinetic resolution of diastereomeric alkene–palladium(II) hydride intermediates has been proposed.[1] Additionally, spectroscopic[4] and quantum-chemical investigations,[5] as well as deuterium-labeling studies,[6] have been devoted to understanding the problem.



Scheme 1. Issues of regio- and enantiocontrol in asymmetric intermolecular Mizoroki–Heck reactions.

The ligand appears to govern the regioselectivity to significant extent.[3] The Hayashi protocol,[1] which uses $Pd(OAc)_2$/2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) and several other bidentate phosphine ligands[7,8] favor double-bond migration (**1**→**3**, Scheme 1). Conversely, predominant formation of **2** (no migration) is observed with bidentate P,N ligands,[9–11] often combined with $[Pd_2(dba)_3]$•dba or $[Pd(dba)_2]$ (dba = dibenzylideneacetone). These well-documented experimental observations[3] are in full accordance with a statement by Hii et al.,[5] who reported that release of the alkene from an intermediate alkene–palladium(II) hydride complex is faster with P,N (no migration) than with P,P (migration) chelating ligands.

In view of the high number of ligands prepared and tested, we found it remarkable that an almost self-evident ligand had been disregarded,[12] BINAP monooxide (BINAP(O)). This omission is particularly intriguing because the reduction of $Pd(OAc)_2$ to palladium(0) in the presence of excess Ph_3P yields Ph_3PO.[13] Likewise, stoichiometric amounts of BINAP(O) [based on $Pd^{II}\rightarrow Pd^0$] are formed from $Pd(OAc)_2$ and BINAP,[14] which is why a twofold excess of BINAP is often used in asymmetric Mizoroki–Heck reactions with $Pd(OAc)_2$.[3,15] The hemilabile mixed phosphine/phosphine oxide ligand[16] BINAP(O) is, therefore, a "common contaminant" in these catalyses but it had never been employed in Mizoroki–Heck reactions as a chiral ligand alone.[12] We now demonstrate that BINAP(O) behaves completely differently to BINAP in representative enantioselective intermolecular Mizoroki–Heck reactions. Both the regio- and enantioselectivity[17] of the transformations are markedly influenced.

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[**] BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl

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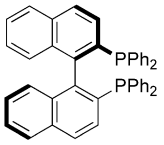
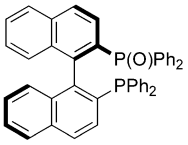


(*R*)-BINAP



(*R*)-BINAP(O)

Results and Discussion

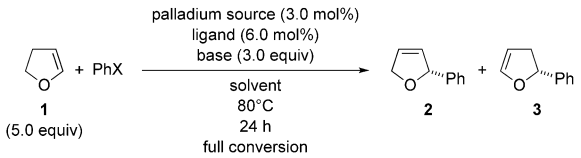
The preparation of BINAP(O),[18,19] as well as its coordination chemistry with palladium(0) and palladium(II),[20] are well established and we successfully followed Gladiali's expedient cross-coupling route.[19] We then decided to reinvestigate the enantioselective arylation of 2,3-dihydrofuran with $Pd(OAc)_2$/BINAP[1] (1:2) and $[Pd_2(dba)_3]$•dba/BINAP (1:2)[21] under various conditions for comparison (Table 1, columns 5–8).

Hayashi et al. had emphasized the crucial role of acetate—introduced with $Pd(OAc)_2$—as a nucleophile in alkene decomplexation by an associative mechanism.[1,8] Its nucleophilicity is dependent on the solvent and base, therefore, we included polar (THF) and nonpolar media (benzene) and organic (iPr$_2$NEt) and inorganic bases (K_2CO_3, KOAc) in our survey. As expected, alkene migration was observed in all cases (**1**→**3**, Table 1, column 6). A single regioisomer was formed in both solvents in the presence of iPr$_2$NEt (Table 1, entries 1 and 4), whereas the slightly diminished regioselectivities when K_2CO_3 or KOAc were used might be interpreted as a hint that a nucleophile is involved in the alkene release step[8] (Table 1, entries 2/5 and 3/6). However, the enantioselectivity was mostly unaffected by both the solvent and base, and the regioisomers (*R*)-**3** (major) and (*R*)-**2** (minor) had the same absolute configuration. Our data do not fully agree with previous findings, from which the formation of (*R*)-**3** (major) and (*S*)-**2** (minor) was reported and rationalized by a kinetic resolution of diastereomeric intermediates (except for Table 1, entry 3, columns 7 and 8).[1] We were, in turn, relieved to see that our results match those of the Keay[21] and Shibasaki[22] groups.

With the reference data in hand (Table 1, columns 5–8), we tested BINAP(O) under otherwise identical reaction conditions (Table 1, columns 9–12). Double the amount of BINAP(O), based on $Pd(OAc)_2$, was used and we assumed that the BINAP dioxide ($BINAP(O)_2$), generated in situ, does not act as a ligand. The outcome was unexpected; alkene migration to give **3** was now the minor pathway (**1**→**2**, Table 1, column 10). With iPr$_2$NEt as the base (Table 1, entries 1 and 4), the arylation was perfectly regiodivergent for BINAP(O) (**1**→**2**) and BINAP (**1**→**3**). The preference for formation of **2** versus **3** resembles that of P,N ligands;[9,11] hemilabile BINAP(O) is also a ligand with a stronger and weaker donor atom (PPh_2 and $P(O)Ph_2$).[16] A similar result had been obtained with 2-diphenylarsino-2′-diphenylphosphino-1,1′-binaphthyl (BINAPAs), a BINAP analogue with a PPh_2 group and a poorly donating $AsPh_2$ group (**2**/**3**= 62:38).[23] There is also a base effect on regioselectivity. Partial alkene migration is seen with inorganic bases K_2CO_3 and KOAc (Table 1, entries 2/5 and 3/6). This finding is inconsistent with the supposed role of a nucleophile in the associative alkene decomplexation in $Pd(OAc)_2$/BINAP-catalyzed reactions.[1]

Dissociation of the alkene–palladium(II) hydride complex is fast in $Pd(OAc)_2$/BINAP(O) catalysis,[5] and we believe that the rate of reductive elimination of the palladium(II) hydride is the branching point.[24] With fully soluble organic bases (homogeneous system) reductive elimination is more facile than with less soluble inorganic bases (heterogeneous system).[25] That longer lifetime in the latter scenario could make the hydride complex available for subsequent alkene insertion. An alternative explanation is provided by Gottumukkala et al. (albeit in a different context).[26] The authors

Table 1. Enantioselective arylation of 2,3-dihydrofuran (**1**) employing either (*R*)-BINAP or (*R*)-BINAP(O).



1 (5.0 equiv) **2** **3**

	Palladium source	X	Base	Solvent	(*R*)-BINAP				(*R*)-BINAP(O)			
					Yield [%][a]	Ratio (**2**/**3**)[b]	*ee* of **2** [%][c]	*ee* of **3** [%][c]	Yield [%][a]	Ratio (**2**/**3**)[b]	*ee* of **2** [%][c]	*ee* of **3** [%][c]
1	$Pd(OAc)_2$	OTf	iPr$_2$NEt	THF	68	0:100	–	66 (*R*)	80	98:2	92 (*R*)	–
2	$Pd(OAc)_2$	OTf	K_2CO_3	THF	78	16:84	80 (*R*)	64 (*R*)	65	85:15	70 (*R*)	48 (*R*)
3	$Pd(OAc)_2$	OTf	KOAc	THF	75	6:94	32 (*S*)	72 (*R*)	56	75:25	24 (*R*)	26 (*R*)
4	$Pd(OAc)_2$	OTf	iPr$_2$NEt	benzene	75	1:99	–	64 (*R*)	70	88:12	88 (*R*)	76 (*R*)
5	$Pd(OAc)_2$	OTf	K_2CO_3	benzene	65	2:98	–	66 (*R*)	58[d]	75:25	68 (*R*)	46 (*R*)
6	$Pd(OAc)_2$	OTf	KOAc	benzene	78	12:88	16 (*R*)	84 (*R*)	79	88:12	20 (*R*)	18 (*R*)
7	$[Pd_2(dba)_3]$•dba	OTf	iPr$_2$NEt	THF	56[d]	5:95	–	60 (*R*)	65	92:8	92 (*R*)	86 (*R*)
8	$[Pd_2(dba)_3]$•dba	OTf	iPr$_2$NEt	benzene	56[d]	1:99	–	66 (*R*)	80	95:5	94 (*R*)	92 (*R*)
9	$Pd(OAc)_2$	I	iPr$_2$NEt	THF	58	0:100	–	0	62	0:100	–	0

[a] Yield refers to analytically pure product isolated after purification by flash chromatography on silica gel. [b] Ratio of regioisomers was determined by achiral GLC analysis. [c] The *ee* values were determined by chiral GLC analysis (baseline-separated peaks). [d] Incomplete conversion.

suggested that the amine base acts as a ligand for palladium(II) after alkene dissociation, which prevents recoordination of the alkene. Less soluble inorganic bases are, in turn, present in lower concentration and coordination of the palladium(II) hydride will be less efficient. As a result, re-establishment of the alkene–palladium(II) hydride complex is more likely.

The enantioselectivity under $Pd(OAc)_2$/BINAP(O) catalysis also deserves attention. The *ee* values are high in the presence of iPr_2NEt (92 and 88% *ee*, Table 1, entries 1 and 4), but poor in the presence of KOAc (24 and 20% *ee*, Table 1, entries 3 and 6). We are aware that the degree of asymmetric induction in the enantioselectivity-determining step might be blurred by a late-stage kinetic resolution,[1,5] but the substantial loss of enantioinduction with excess KOAc indicates that BINAP(O) might act as a monodentate chiral ligand in this case. Acetate is likely to replace the labile $P(O)Ph_2$ group at the palladium(II) center.

A change of the palladium source from $Pd(OAc)_2$ to $[Pd_2(dba)_3]$·dba had little effect on the regio- and enantiocontrol (Table 1, entries 7 and 8).[27] Reaction with phenyl iodide produced the thermodynamically more stable regioisomer in racemic form independent of the chiral ligand (**1**→**3**, Table 1, entry 9).[1]

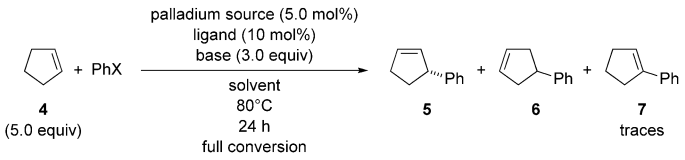
We next turned to the intermolecular arylation of cyclopentene (**4**→**5**/**6**, Table 2). This asymmetric Mizoroki–Heck reaction is more challenging than those of heterocycles such as **1** due to extensive double-bond migration, and only a few effective catalyses with P,N ligands have been reported.[9a,b,11c,e] Screening with BINAP as the ligand confirmed these known problems (Table 2, columns 5–7). Conversely, both the regio- and enantioselectivity were again superior when BINAP(O) was used (Table 2, columns 8–10). An excellent regioisomeric ratio (**5**/**6** = 94:6) and a decent enantiomeric excess (60% *ee*) was obtained in THF with iPr_2NEt as the base (Table 2, entry 1). The effect of inorganic bases on these selectivities followed the same trends as the arylation of **1** (Table 2, entries 2/5 and 3/6). $[Pd_2(dba)_3]$·dba performed even better (**5**/**6** = 94:6, 86% *ee*, Table 2, entry 8).[27]—Phenyl iodide reacted with similar regiocontrol, yet without any asymmetric induction (Table 2, entry 9).

The mutual dependence of regio- and enantiocontrol complicates the interpretation of the literature and our data. The model of an associative mechanism[28] of alkene decomplexation from diastereomeric 16e square-planar alkene–palladium(II) hydride intermediates helps to understand the degree of alkene migration and the proposed kinetic resolution.[1,8] Hemilabile BINAP(O) falls into the category of phosphinooxazoline-type (PHOX) ligands and alkene release is a facile step.[5,28] Prediction of the absolute stereocontrol is difficult with nonsymmetric chelating ligands and mechanistic models are scarce.[8,9k] A recent quantum-chemical study even showed that, in one example, the migratory insertion of **1** occurs from the least-favored intermediate.[29] The consistently high *ee* values obtained with iPr_2NEt as base corroborate, at least, that BINAP(O) acts as a bidentate ligand, and the minor deviations in the *ee* values of **2** and **3** (both *R* configuration) do not support a kinetic-resolution pathway.

Conclusion

The use of BINAP and BINAP(O) as chiral ligands in the asymmetric intermolecular Mizoroki–Heck reaction of representative cyclic alkenes affords quite different (sometimes reverse) selectivities. Arylation of 2,3-dihydrofuran (**1**) is regiodivergent (**1**→**3** versus **1**→**2**) and arylation of cyclopentene (**4**) is only regio- and enantioselective when BINAP(O) is used (**4**→**5**, with a maximum of 86% *ee*). We are currently

Table 2. Enantioselective arylation of cyclopentene (**4**) employing either (*R*)-BINAP or (*R*)-BINAP(O).



	Palladium source	X	Base	Solvent	(*R*)-BINAP			(*R*)-BINAP(O)		
					Yield [%][a]	Ratio (**5**/**6**)[b]	*ee* of **5** [%][c]	Yield [%][a]	Ratio (**5**/**6**)[b]	*ee* of **5** [%][c]
1	$Pd(OAc)_2$	OTf	iPr_2NEt	THF	52	75:25	10 (*R*)	50[d]	94:6	60 (*R*)
2	$Pd(OAc)_2$	OTf	K_2CO_3	THF	65	85:15	50 (*R*)	53[d]	92:8	18 (*R*)
3	$Pd(OAc)_2$	OTf	KOAc	THF	47[d]	83:17	8 (*R*)	31[d]	98:2	26 (*R*)
4	$Pd(OAc)_2$	OTf	iPr_2NEt	benzene	41[d]	74:26	6 (*R*)	75	90:10	80 (*R*)
5	$Pd(OAc)_2$	OTf	K_2CO_3	benzene	69	78:22	38 (*R*)	60	94:6	34 (*R*)
6	$Pd(OAc)_2$	OTf	KOAc	benzene	17[d]	68:32	32 (*R*)	66	85:15	14 (*R*)
7	$[Pd_2(dba)_3]$·dba	OTf	iPr_2NEt	THF	33[d]	74:26	24 (*R*)	69	92:8	84 (*R*)
8	$[Pd_2(dba)_3]$·dba	OTf	iPr_2NEt	benzene	24[d]	62:38	14 (*R*)	75	94:6	86 (*R*)
9	$Pd(OAc)_2$	I	iPr_2NEt	THF	27	78:22	0	70	87:13	0

[a] Yield refers to analytically pure product isolated after purification by flash chromatography on silica gel. [b] Ratio of regioisomers was determined by achiral GLC analysis. [c] The *ee* values were determined by chiral GLC analysis (not fully baseline-separated peaks). [d] Incomplete conversion.

testing BINAP(O) in intramolecular[15a] and desymmetrizing[15b] Mizoroki–Heck reactions.

Experimental Section

All reactions were performed in either flame-dried glassware by using Schlenk techniques under a static pressure of argon or in sealed tubes. Liquids and solutions were transferred by syringe. Solvents were purified and dried prior to use following standard procedures: CH_2Cl_2, MeOH, and DMF were distilled over calcium hydride and benzene and THF were distilled over potassium. Solvents were degassed by freeze–pump–thaw cycles (×3) or by passing through argon for 15 min. Technical-grade solvents for extraction and chromatography (cyclohexane, *n*-pentane, CH_2Cl_2, diethyl ether, and ethyl acetate) were distilled prior to use. Analytical TLC was performed on silica gel SIL G-25 glass plates (Macherey–Nagel). Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM, Merck) with the indicated solvents. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded in $CDCl_3$ on Bruker AV300 and Bruker AV400 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual solvent resonance as the internal standard ($CHCl_3$: $\delta = 7.26$ ppm, $CDCl_3$: $\delta = 77.16$ ppm). Data are reported as follows: chemical shift, multiplicity (d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), integration. IR spectra were recorded on a Varian 3100 FTIR spectrophotometer equipped with an attenuated total reflectance (ATR) unit and are reported (vw = very weak, w = weak, m = medium, s = strong) in wavenumbers ($\tilde{\nu}$, cm^{-1}). Achiral gas–liquid chromatography (GLC) was performed on a Shimadzu GC-17A gas chromatograph equipped with a CS-Chromatographie Service SE-54 capillary column (30 m × 0.32 mm, 0.25 μm film thickness) by using the following program: N_2 carrier gas, injection temperature 250 °C, detector temperature 300 °C; temperature program: start temperature 40 °C, heating rate 10 °C min^{-1}, end temperature 280 °C for 5 min. Chiral GLC was performed on a Shimadzu GC-17A gas chromatograph equipped with a CS-Chromatographie Service FS-Cyclodex β-I/P capillary column (25 m × 0.32 mm) by using the following program: N_2 carrier gas, injection temperature 250 °C, detector temperature 300 °C; temperature program: 115 °C isothermal. Alternatively, chiral GLC was performed on an Agilent Technologies 6890N gas chromatograph equipped with a Supelco Chiraldex G-TA capillary column (30 m × 0.25 mm, 0.12 μm film thickness) by using the following program: N_2 carrier gas, injection temperature 200 °C, detector temperature 220 °C; temperature program: 70 °C isothermal. Optical rotations were measured on a Perkin–Elmer 341 polarimeter. Melting points (m.p.) were determined with a Thompson Scientific apparatus and are uncorrected. HRMS, electron-spray-ionization mass spectrometry (ESI-MS), and electron ionization (EI) mass spectrometry were performed by the Analytical Facility at the Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster.

General procedure for the enantioselective intermolecular Mizoroki–Heck reaction with $Pd(OAc)_2$ (GP1):[1a] Under an argon atmosphere, a flame-dried sealed tube was successively charged with $Pd(OAc)_2$ (6.0–10 μmol, 3.0–5.0 mol %), ligand (12–20 μmol, 6.0–10 mol %), and inorganic base—if used—(0.60 mmol, 3.0 equiv). The tube was then briefly evacuated and backfilled with argon, followed by the addition of a solution of PhOTf (0.20 mmol, 1.0 equiv), alkene **1** or **4** (1.0 mmol, 5.0 equiv), and iPr$_2$NEt (0.60 mmol, 3.0 equiv)—if used—in the degassed solvent (2 mL). The reaction tube was sealed and the reaction mixture was maintained at 80 °C for 24 h. Addition of silica gel to the reaction mixture, followed by solvent evaporation under reduced pressure, and purification by flash column chromatography on silica gel with either cyclohexane/ethyl acetate or *n*-pentane as eluent afforded **2** and/or **3** as well as **5**–**7**.

General procedure for the enantioselective intermolecular Mizoroki–Heck reaction with $[Pd_2(dba)_3]$·dba (GP2):[11e] Under an argon atmosphere, a flame-dried sealed tube was successively charged with $[Pd_2(dba)_3]$·dba (6.0–10 μmol, 3.0–5.0 mol %) and ligand (12–20 μmol, 6.0–10 mol %). The tube was then briefly evacuated and backfilled with argon. Degassed solvent (1 mL) was added and the reaction mixture was maintained at ambient temperature for 5 min. A solution of PhOTf (0.20 mmol, 1.0 equiv), alkene **1** or **4** (1.0 mmol, 5.0 equiv), and iPr$_2$NEt (0.60 mmol, 3.0 equiv) in the degassed solvent (1 mL) was subsequently added. The reaction tube was sealed and the reaction mixture was maintained at 80 °C for 24 h. Addition of silica gel to the reaction mixture, followed by solvent evaporation under reduced pressure, and purification by flash column chromatography on silica gel with either cyclohexane/ethyl acetate or *n*-pentane as eluent afforded **2** and/or **3** as well as **5**–**7**.

(*R*)-2-Phenyl-2,5-dihydrofuran [(*R*)-2]: According to GP1 (twofold scale for full characterization), analytically pure (*R*)-**2** (40 mg, 69 %) was obtained from PhOTf (91 mg, 0.40 mmol, 1.0 equiv) and 2,3-dihydrofuran (**1**, 0.150 mL, 140 mg, 2.00 mmol, 5.00 equiv) by using $Pd(OAc)_2$ (2.7 mg, 0.012 mmol, 3.0 mol %), (*R*)-BINAP(O) (15.3 mg, 0.0240 mmol, 6.00 mol %), and iPr$_2$NEt (0.210 mL, 155 mg, 1.20 mmol, 3.00 equiv) in degassed THF (4 mL). Purification by flash column chromatography on silica gel (cyclohexane/ethyl acetate = 50:1) afforded (*R*)-**2** as a yellow oil. $R_f = 0.06$ (cyclohexane/ethyl acetate 50:1); GLC (achiral): retention time (t_R) = 9.5 min; $[\alpha]_D^{20} = +245.3$ ($c = 0.985$ in $CHCl_3$) for 92 % *ee* ($[\alpha]_D^{20} = +282$ ($c = 0.92$ in $CHCl_3$) for 96 % *ee*[9c]); GLC (FS-Cyclodex β-I/P, column temperature 115 °C isothermal, flow rate 0.5 mL min^{-1}): t_R = 23.1 min [(*S*)-**2**], t_R = 23.6 min [(*R*)-**2**]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.78 (dddd, J = 12.8, 4.2, 2.6, 1.6 Hz, 1H), 4.89 (dddd, J = 12.8, 6.0, 2.4, 1.6 Hz, 1H), 5.80 (m_c, 1H), 5.90 (dddd, J = 6.5, 2.4, 2.4, 1.5 Hz, 1H), 6.04 (dddd, J = 6.2, 2.4, 1.6, 1.6 Hz, 1H), 7.27–7.38 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 76.0, 88.1, 126.5, 126.8, 128.0, 128.7, 130.1, 142.2 ppm; IR (ATR): $\tilde{\nu}$ = 3030 (vw), 2850 (m), 1602 (vw), 1492 (m), 1453 (m), 1080 (w), 1063 (s), 841 (w), 701 cm^{-1} (m); HRMS (ESI): *m*/*z*: calcd for $C_{10}H_{10}ONa$ ($[M+Na]^+$): 169.06239; found: 169.06249.

(*R*)-2-Phenyl-2,3-dihydrofuran [(*R*)-3]: According to GP1 (twofold scale for full characterization), analytically pure (*R*)-**3** (40 mg, 68 %) was obtained from PhOTf (91 mg, 0.40 mmol, 1.0 equiv) and 2,3-dihydrofuran (**1**, 0.150 mL, 140 mg, 2.00 mmol, 5.00 equiv) by using $Pd(OAc)_2$ (2.7 mg, 0.012 mmol, 3.0 mol %), (*R*)-BINAP (14.9 mg, 0.0240 mmol, 6.00 mol %), and iPr$_2$NEt (0.210 mL, 155 mg, 1.20 mmol, 3.00 equiv) in degassed THF (4 mL). Purification by flash column chromatography on silica gel (cyclohexane/ethyl acetate 50:1) afforded (*R*)-**3** as a yellow oil. $R_f = 0.15$ (cyclohexane/ethyl acetate 50:1); GLC (achiral): t_R = 9.0 min; $[\alpha]_D^{20} = -28.7$ (c = 0.955, $CHCl_3$) for 66 % *ee* ($[\alpha]_D^{20} = -64.3$ ($c = 1.2$, $CHCl_3$) for 93 % *ee*[1a]); GLC (FS-Cyclodex β-I/P, column temperature 115 °C isothermal, flow rate 0.5 mL min^{-1}): t_R = 18.3 min [(*S*)-**3**], t_R = 18.7 min [(*R*)-**3**]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.61 (dddd, J = 15.2, 8.4, 2.4, 2.4 Hz, 1H), 3.09 (dddd, J = 15.3, 10.7, 2.4, 2.4 Hz, 1H), 4.96 (ddd, J = 2.5, 2.5, 2.5 Hz, 1H), 5.52 (dd, J = 10.7, 8.4 Hz, 1H), 6.46 (ddd, J = 2.5, 2.5, 2.5 Hz, 1H), 7.27–7.37 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.0, 82.5, 99.2, 125.7, 127.8, 128.7, 143.2, 145.5 ppm; IR (ATR): $\tilde{\nu}$ = 3031 (vw), 2926 (vw), 2858 (vw), 1620 (m), 1494 (m), 1451 (w), 1135 (m), 1050 (s), 698 cm^{-1} (m); HRMS (ESI): *m*/*z*: calcd for $C_{10}H_{10}ONa$ ($[M+Na]^+$): 169.0624; found: 169.0622.

(*R*)-3-Phenylcyclopentene [(*R*)-5]: According to GP1 (twofold scale for full characterization), analytically pure (*R*)-**5** (34 mg, 59 %) was obtained from PhOTf (91 mg, 0.40 mmol, 1.0 equiv) and cyclopentene (**4**, 0.180 mL, 136 mg, 2.00 mmol, 5.00 equiv) by using $Pd(OAc)_2$ (2.7 mg, 0.012 mmol, 3.0 mol %), (*R*)-BINAP(O) (25.5 mg, 0.0400 mmol, 10.0 mol %), and iPr$_2$NEt (0.210 mL, 155 mg, 1.20 mmol, 3.00 equiv) in degassed THF (4 mL). Purification by flash column chromatography on silica gel (*n*-pentane) afforded (*R*)-**5** as a colorless oil. $R_f = 0.56$ (*n*-pentane); GLC (achiral): t_R = 8.9 min; $[\alpha]_D^{20} = +184.7$ ($c = 0.990$, $CHCl_3$) for 84 % *ee* ($[\alpha]_D^{20} = +90$ ($c = 1$, $CHCl_3$) for 42 % *ee*[30]); GLC (G-TA-Chiraldex, column temperature 70 °C isothermal, flow rate 1.1 mL min^{-1}): t_R = 39.6 min [(*R*)-**5**], t_R = 40.6 min [(*S*)-**5**]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68–1.78 (m, 1H), 2.35–2.56 (m, 3H), 3.86–3.94 (m, 1H), 5.76–5.80 (m, 1H), 5.92–5.96 (m, 1H), 7.27–7.38 ppm (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.7, 33.9, 51.5, 126.1, 127.4, 128.5, 132.1, 134.4, 146.7 ppm; IR (ATR): $\tilde{\nu}$ = 3056 (s), 3027 (s), 2940 (s), 2850 (s), 1601 (s), 1490 (s), 1451 (s), 1355 (m) 1259 (w), 1145 (w), 1076 (s), 1029 (w), 1009 (m), 985 (w), 914 (s), 754 (s), 696 (s), 567 cm^{-1} (m); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{12}$ ($[M]^+$): 144.0939; found: 144.0922.

4-Phenylcyclopentene (6): Depending on the reaction conditions for GP1, the minor regioisomer **6** was formed in various amounts from the reaction of PhOTf (45 mg, 0.20 mmol, 1.0 equiv) and cyclopentene (**4**, 0.090 mL, 68 mg, 1.0 mmol, 5.0 equiv). It was not possible to separate **6** from the major isomer (*R*)-**5** by conventional flash chromatography on silica gel. GLC (achiral): $t_R = 9.0$ min; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 2.35–2.56 (m, 2H), 2.83 (m, 2H), 3.47 (tt, $J = 7.1$, 9.0 Hz, 1H), 5.77–5.80 (m, 2H), 7.27–7.38 ppm (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 41.5$, 43.3, 125.9, 127.1, 128.5, 130.0 ppm (the *ipso*-carbon atom of the phenyl group was not detected in the ^{13}C NMR spectrum); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{12}$: 144.0939; found: 144.0910.

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