C_1-Symmetric Bicyclo[2.2.2]octa-2,5-diene (bod*) Ligands in Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to Enones and 1,2-Addition to *N*-[(4-Nitrophenyl)sulfonyl]imines

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Dedicated to Prof. *Dieter Seebach* on the occasion of his 75th birthday

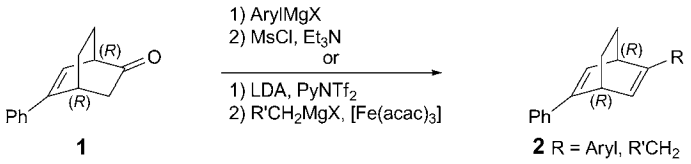
A set of ten C_1-symmetric chiral bicyclo[2.2.2]octa-2,5-dienes (bod*) **2** (*Fig. 1*) were tested as ligands in Rh-catalyzed arylation reactions. The 1,4-addition of arylboronic acids to cyclohex-2-en-1-one, cyclopent-2-en-1-one, and *tert*-butyl cinnamate proceeded smoothly with excellent enantioselectivities (up to 99% ee; *Tables 1–3*). The challenging 1,2-addition of triphenylboroxine to *N*-[(4-nitrophenyl)-sulfonyl]imines yielded the product in high yield and in good enantioselectivity (up to 92% ee; *Table 4*). Generally, the use of C_1-symmetric chiral bod* ligands bearing bulky substituents resulted in lower enantioselectivities, whereas several electron-poor and electron-rich bod* ligands gave higher enantioselectivities than the benchmark ligands reported in literature.

Introduction. – Chiral dienes have been established as an own class of chiral ligands for asymmetric synthesis (for reviews on chiral diene ligands, see [1]). Based on the pioneering work by *Hayashi* and co-workers [2a] and *Carreira* and co-workers [2b], a multitude of different ligands are known today. However, the synthesis of enantiomerically pure chiral dienes remains a challenge – simple and inexpensive syntheses to access the different types of ligands are still not available today[1]). Process research chemists at *Actelion Pharmaceuticals Ltd.* have developed simple and scalable syntheses of (1*R*,4*R*)-5-phenylbicyclo[2.2.2]oct-5-en-2-one (**1**) [3a][3b] (for a synthesis of *rac*-5-phenylbicyclo[2.2.2]oct-5-en-2-one (*rac*-**1**) on a 180 kg scale, see [3c]). The (1*R*,4*R*)-phenylbicyclo[2.2.2]oct-5-en-2-one (**1**) is a crystalline key intermediate, also

[1]) Costs according to the *Sigma–Aldrich* catalogue: *Hayashi*'s (*R*,*R*)-Ph-bod* (**2c**): 743 CHF/500 mg; *Carreira*'s ligand (1*R*,4*R*,8*R*)-5-benzyl-2-isobutyl-8-methoxy-1,8-dimethylbicyclo[2.2.2]octa-2,5-diene (=(+)-dolefin; **III**): 272.50 CHF/100 mg.

available in its enantiomeric forms, for the preparation of chiral C_1-symmetric bicyclo[2.2.2]octa-2,5-diene (bod*) ligands **2** (*Scheme*)[2]).

Scheme



We now report the first application of these new bod* ligands **2** (*Fig. 1*) in four Rh-catalyzed arylation reactions, comprising the 1,4-addition to enones and the 1,2-addition to a *N*-[(4-nitrophenyl)sulfonyl]imine. *Fig. 2* depicts the different types of known chiral dienes that are mentioned in the text for comparison. At the outset, we were interested to check the influence of the residue at the 2-position of the bicyclo[2.2.2]octa-2,5-diene scaffold in these C_1-symmetric dienes **2** on the enantioselectivity. In all four test reactions, the commercially available C_2-symmetric (*R*,*R*)-Ph-bod* (**2c**) was used for comparison with our C_1-symmetric dienes. Mono-substituted chiral dienes of the type **IV** have shown similar enantioselectivities in Rh-catalyzed 1,4-

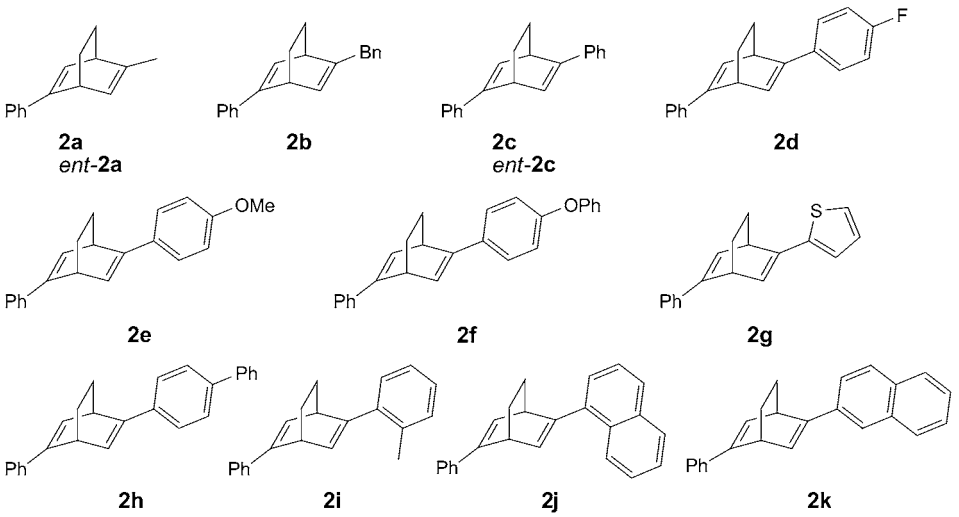


Fig. 1. *Chiral dienes* **2a**–**2k**, *used as chiral ligands in the asymmetric addition reactions* (*Tables 1–4*). All dienes are solids, except for **2a** and **2j** [3a].

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[2]) The 2-aryl-5-phenyl-substituted dienes are accessible from **1** by *Grignard* addition to the ketone, followed by *in situ* elimination of the mesylate of the ensuing alcohol, whereas the 2-alkyl-5-phenyl substituted dienes are synthesized by cross-coupling of the enol triflate derived from **1** (treatment with lithium diisopropylamide (LDA)/(pyridin-2-yl)N(SO_2CF_3)$_2$) with alkylmagnesium bromides, see [3a].

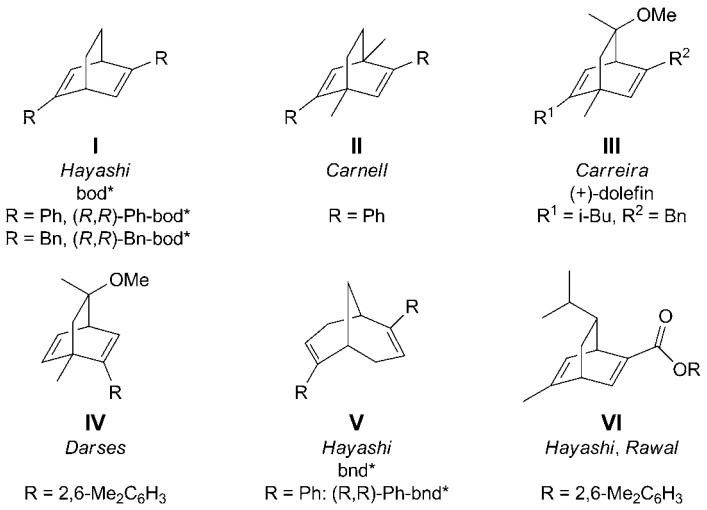


Fig. 2. *Types of chiral dienes that have been reported to give highest ee in the test reactions* (*Tables 1–4*). The C_2-symmetric type-**I** dienes are obtained either by fractional crystallization of diastereoisomeric dihydrazones of (*R*)-5-(1-phenylethyl)semioxamazides or by racemate resolution with chiral HPLC of the C_2-symmetric bicyclo[2.2.2]octane-2,5-dione [4]. The C_2-symmetric type-**II** dienes are accessible by a chemoenzymatic approach [5]. The C_1-symmetric type-**III** and -**IV** dienes are derived from carvone [6][7]. The C_2-symmetric bicyclo[2.2.1]nona-2,6-diene ligands of type **V** are obtained *via* a separation by chiral HPLC [8]. The C_1-symmetric ligands of type **VI** are obtained from (*R*)-α-phellandrene and propiolic acid (= prop-2-ynoic acid) esters by a [4 + 2] cycloaddition [9].

addition reactions as compared to disubstituted dienes. Hence, it was reckoned that C_2-symmetry was not mandatory for high enantioselectivities in these reactions [7][3]).

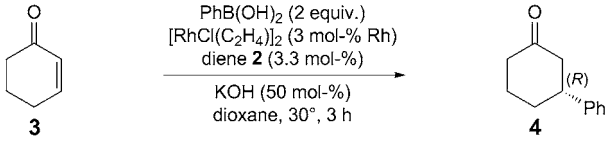
Results and Discussion. – There is ample precedence for the asymmetric addition of phenylboronic acid to cyclohex-2-en-1-one (**3**) and cyclopent-2-en-1-one (**5**) [4][6]. These two substrates were chosen for testing the chiral-diene ligands **2** in asymmetric catalysis. Enantioselectivities of > 95% ee are reported for these substrates both with C_2-symmetric *Hayashi* bod* dienes **I** [4] and with one of *Carreira*'s chiral dienes, *i.e.*, (+)-dolefin (**III**) [6]. *Carnell*'s type **II** ligand gave 99% ee [5]. Similarly, under slightly different conditions, *Darses* reported an ee of 96 and 98% for cyclopentenone and cyclohexenone with ligands of type **IV** [7].

Our results of the addition of phenylboronic acid to cyclohex-2-en-1-one (**3**) to give ketone **4** by means of the new chiral dienes **2** are summarized in *Table 1*. The active catalyst (3 mol-%) was prepared *in situ* by mixing the chiral ligand **2** with $[RhCl(C_2H_4)]_2$. A twofold excess of phenylboronic acid with respect to **3** was used in dioxane and 50% aqueous KOH solution at 30° for 3 h [4]. In general, very good enantioselectivities were achieved with all C_1-symmetric chiral bod* dienes **2**. The highest ee (97%) was obtained with the mother bod* **2c** and with 4-MeO-substituted diaryldiene **2e**. The result with **2c** corresponds well with the result published by *Hayashi*

[3]) This is further corroborated by *Carreira*'s seminal paper [2b].

and co-workers [4]. Surprisingly, variation of the substituent at the *para*-position of the diaryl-substituted dienes had no influence on the enantioselectivity: H- (**2c**), F- (**2d**), MeO- (**2e**), PhO- (**2f**), or Ph-substituted (**2h**) diaryldienes gave similar results independent of their electronic effect! The use of triphenylboroxine ($(PhBO)_3$) as aryl source gave an identical result (*Entry 5*). The two dienes with alkyl residues, **2a** and **2b**, led to lower enantioselectivity – the same was observed for sterically demanding ligands, like the 2-methylphenyl-substituted ligand **2i** (*Entry 12*) or the naphthalen-1-yl ligand **2j** (*Entry 13*). This effect was also described in [4] with the C_2-symmetric 2-methylphenyl-bod* diene. Interestingly, the naphthalen-2-yl-substituted ligand **2k** performed much better than the naphthalen-1-yl-substituted ligand **2j**, probably due to less steric hindrance in the transition state [4][10]. The yields of adduct **4** isolated after chromatography were in the range of 58 to 97% – *Hayashi* and co-workers reported 95% [4]. The yields were not further optimized.

Table 1. *Enantioselective Addition of Phenylboronic Acid to Cyclohex-2-en-1-one* (**3**)*, Catalyzed by Chiral Rh/Diene* **2** *Complexes*



3 **4**

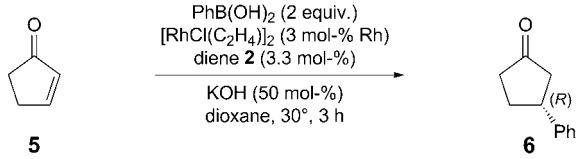
Entry	Diene	Yield [%][a])	ee [%][b])	*Entry*	Diene	Yield [%][a])	ee [%][b])
1	**2a**	75	92	*8*	**2e**	58	97
2	*ent*-**2a**	72	−92	*9*	**2f**	70	96
3	**2b**	65	92	*10*	**2g**	79	96
4	**2c**	90	97 (96[c]))	*11*	**2h**	76	96
5[d])	**2c**	94	97	*12*	**2i**	93	91
6	*ent*-**2c**	70	−97	*13*	**2j**	97	86
7	**2d**	86	96	*14*	**2k**	86	96

[a]) Yield of isolated **4** after chromatography. [b]) Determined by chiral HPLC (210 nm) of isolated **4**. [c]) Value reported by *Hayashi* and co-workers [4]. [d]) With $(PhBO)_3$ instead of $PhB(OH)_2$.

The same protocol was used for the addition of phenylboronic acid to cyclopent-2-en-1-one (**5**) to give ketone **6** (*Table 2*). In general, very good enantioselectivities were achieved with all C_1-symmetric chiral dienes **2**. Again, the best result (99% ee) was achieved with the 4-MeO substituted diaryldiene **2e**. With this *Michael* acceptor, the bulky ligands **2i** and **2j** (*Entries 11* and *12*) showed very good enantioselectivities as well, whereas the two alkyl-substituted bod* dienes **2a** and **2b**, and the [biphenyl]-4-yl-substituted diene **2h** gave slightly lower enantioselectivities. The yields of 1,4-adduct **6** were in the range of 53 to 95% after chromatography – slightly lower than for adduct **4**.

Next, we studied the 1,4-addition of (4-methoxyphenyl)boronic acid to the acyclic enone *tert*-butyl cinnamate (=*tert*-butyl (2*E*)-3-phenylprop-2-enoate; **7**) to give propanoate **8** (*Table 3*). Some important drug substances are derived from chiral

Table 2. *Enantioselective Addition of Phenylboronic Acid to Cyclopent-2-en-1-one* (**5**)*, Catalyzed by Rh/Diene* **2** *Complexes*



5 **6**

Entry	Diene	Yield [%][a])	ee [%][b])	*Entry*	Diene	Yield [%][a])	ee [%][b])
1	**2a**	95	94	*8*	**2f**	80	98
2	*ent*-**2a**	87	−93	*9*	**2g**	55	97
3	**2b**	73	95	*10*	**2h**	65	94
4	**2c**	63	98 (99[c]))	*11*	**2i**	53	97
5	*ent*-**2c**	71	−98	*12*	**2j**	60	97
6	**2d**	75	98	*13*	**2k**	77	98
7	**2e**	73	99				

[a]) Yield of isolated **6** after chromatography. [b]) Determined by chiral HPLC (210 nm) of isolated **6**. [c]) Value reported by *Hayashi* and co-workers [4].

diarylmethines of the type of **8**[4]). *Carreira* and co-workers reported enantioselectivites of 93% ee with the carvon derived dienes of type **III**. To date, ligands of type **I** (bod*) have not been tested with cinnamate **7** [11][12][5]). Thus, the active catalyst (3 mol-%) was prepared *in situ* by mixing chiral ligand **2** with $[RhCl(C_2H_4)]_2$, and a twofold excess of 4-methoxyphenylboronic acid with respect to **7** was used in the presence of 1.5M aqueous KOH at 50° for 16 h. For this reaction, MeOH/H_2O 10:1 was found to be superior to dioxane/H_2O [11]. Gratifyingly, excellent enantioselectivities (98–99% ee) were achieved with several bod* ligands **2**, except for the ligands **2i** and **2j** carrying bulky substituents (*Entries 11* and *12*) and the two aryl-alkyl-substituted dienes **2a** and **2b** (*Entries 1* and *2*). The use of less equiv. of (4-methoxyphenyl)boronic acid (*Entry 4:* 1.2 equiv. of boronic acid as compared to 2 equiv.) resulted in a slightly lower yield but a similar enantioselectivity. The conversion **7** → **8** could be easily determined by ^{1}H-NMR spectroscopy by comparison the signals of the *tert*-butyl esters – in general complete conversion was observed within 16 h. The yields after isolation by chromatography were in the range of 56 to 97%[6]) – *Carreira* an co-workers reported yields of 80–95% for the carvone derived ligands **III** [11]. In some cases, the homocoupling product of (4-methoxyphenyl)boronic acid, the 4,4′-dimethoxy-1,1′-biphenyl could be identified as a minor by-product.

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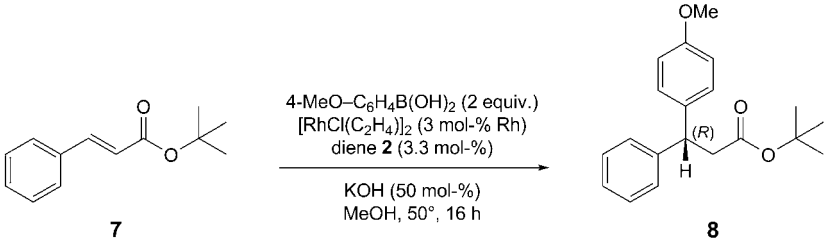
4) For example, the antidepressant sertraline or the antimuscarinic drug tolterodine.

5) A recent paper by *Hayashi* and co-workers [12] describes the Rh-catalyzed 1,4-addition of sodium tetraarylborates to β,β-disubstituted α,β-unsaturated esters with high ee. Even though bod* ligands showed the highest ee's, they have not further been employed in that work, probably due to availability issues. Moreover, this reaction required 45 h at 60° for completion which makes screening more cumbersome.

6) The explicit low yields in *Entries 2* and *10* can be explained by un-optimized seperation during column chromatography.

Table 3. *Enantioselective Addition of* (*4-Methoxyphenyl)boronic Acid to* tert-*Butyl Cinnamate* (**7**), *Catalyzed by Rh/Diene* **2** *Complexes*



7 **8**

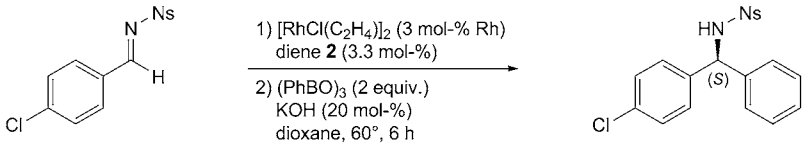
Entry	Diene	Conversion [%][a])	Yield [%][b])	ee [%][c])
1	**2a**	> 95	95	92
2	**2b**	60	20[b])	91
3	**2c**	> 95	78	99
4[d])	**2c**	90	56	98
5	*ent*-**2c**	> 95	78	– 97
6	**2d**	70	56	99
7	**2e**	> 95	97	99
8	**2f**	75	79	98
9	**2g**	> 95	94	98
10	**2h**	> 95	30[b])	98
11	**2i**	> 95	69	93
12	**2j**	> 95	89	89
13	**2k**	> 95	63	98

[a]) Determined by ^{1}H-NMR of the crude product. [b]) Yield of isolated **8** after chromatography. [c]) Determined by HPLC (230 nm) of isolated **8**. [d]) With 1.2 instead of 2 equiv. of 4-MeO–$C_6H_4B(OH)_2$.

Finally, *N*-[(4-nitrophenyl)sulfonyl]aldimine **9** was chosen as test substrate for the 1,2-addition of triphenylboroxine to afford chiral (diarylmethyl)amine derivative **10** (*Table 4*). This product is a precursor for the synthesis of notable pharmacologically active substances[7]). *N*-[(4-Nitrophenyl)sulfonyl]imines are very challenging substrates: *Hayashi*'s bod* ligands **I** gave a maximum ee of 90%. Highest enantioselectivities (98% ee) were reported with bnd* ligands of type **V** [8] or with the phellandrene derived ligands of type **VI** [9]. For this reaction, we prepared the active catalyst separately prior to use in the various reactions. The enantioselectivities were generally lower than those obtained with the preceding substrates: 88–92% ee were obtained with five of the C_1-symmetric dienes **2** (*Entries 3*, *5*, and *7–9*). This is in good agreement with the result disclosed by *Hayashi* and co-workers for **2c** (*Entry 3*). Likewise, the bulky 2-methylphenyl- and naphthalen-1-yl-substituted ligands **2i** and **2j** (*Entries 10* and *11*), respectively, gave the lowest enantioselectitivities (*ca.* 70% ee), and the aryl-alkyl substituted dienes **2a** and **2b** showed significantly lower selectivities than the aryl-aryl substituted dienes. Interestingly, a heteroaryl substituted C_1-symmetric diene ligand, the thienyl-substituted diene **2g**, gave the best result (92%

7) For example, the antihistamine cetirizine or the anti-emetic meclozine.

Table 4. *Enantioselective Addition of Triphenylboroxine to* N-*[(4-Nitrophenyl)sulfonyl]aldimine* **9**, *Catalyzed by Rh/Diene* **2** *Complexes* (Ns = nosyl = (4-nitrophenyl)sulfonyl)



9 **10**

Entry	Diene	Yield [%][a])	ee [%][b])	*Entry*	Diene	Yield [%][a])	ee [%][b])
1	**2a**	87	81	*7*	**2f**	82	88
2	**2b**	88	78	*8*	**2g**	93	92
3	**2c**	69	88 (89[c]))	*9*	**2h**	92	89
4	*ent*-**2c**	85	−88	*10*	**2i**	93	69
5	**2d**	90	89	*11*	**2j**	98	68
6	**2e**	94	84	*12*	**2k**	95	87

[a]) Yield of isolated **10** after chromatography. [b]) Determined by HPLC (210 nm) of isolated **10**. [c]) Value reported by *Hayashi* and co-workers [8].

ee). The yields of isolated amine **10** were in the region of 69–98%, which correspond quite well with the yields of 88–99% reported in [8].

Conclusions. – In summary, C_1-symmetric bicyclo[2.2.2]octa-2,5-diene ligands **2** were successfully tested in Rh-catalyzed arylation reactions of different substrates with phenylboronic acids. The highest enantioselectivities reported so far with benchmark diene ligands were achieved or exceeded with several dienes **2** when applied to the addition to cyclohex-2-en-1-one, cyclopent-2-en-1-one, and *tert*-butyl cinnamate (*Tables 1–3*). The C_1-symmetric 4-fluorophenyl-, 4-methoxyphenyl-, 4-phenoxyphenyl-, and 2-thienyl-substituted dienes **2d**, **2e**, **2f**, and **2g**, respectively, gave similar enantioselectivities as *Hayashi*'s 'mother diene ligand' Ph-bod* **2c**. The aryl-alkyl-substituted C_1-symmetric dienes **2a** and **2b** showed generally slightly lower selectivities than the aryl-aryl-substituted dienes. The 2-methylphenyl- and naphthalen-1-yl-substituted dienes **2i** and **2j**, respectively, with sterically demanding residues gave consistently lower selectivities – except for the 1,4-addition to cyclopent-2-en-1-one (**5**) where all C_1-symmetric aryl-aryl-substituted ligands gave high ee (>97%). The thienyl-substituted diene **2g** was the best chiral diene for the arylation of *N*-[(4-nitrophenyl)sulfonyl]aldimine **9**, albeit with lower enantioselectivity (92% ee) than the best ligand reported by *Hayashi* and co-workers [8][9] for this reaction (98% ee with bnd*-diene ligands).

The isolated yields of pure products of the 1,4-additions to enones were typically in the range of 53–97% (*Tables 1–3*), *i.e.*, slightly lower than for the 1,2-addition to imine **9** (69–98%, *Table 4*). It must be mentioned that these are un-optimized yields, and in this work, all reactions were performed by a scale-up of 10 compared to the experimental procedures reported in [4][6][8].

Although one aryl residue of **2** is fixed (Ph), this array of stable C_1-symmetric diene ligands **2** displays differences in reactivity and selectivity and allows for a systematic

screening of reaction conditions [13] with more complex substrates. The availability of the common precursor (1*R*,4*R*)-5-phenylbicyclo[2.2.2]oct-5-en-2-one (**1**) on a multi-kg scale is an important asset for the simple and expeditious synthesis of a large variety of novel ligands.

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Experimental Part

General. All reactions were performed under Ar in dried glassware and anh. solvents, except for reactions with aq. reagents. All chemicals and solvents were reagent-grade and used as supplied, unless stated otherwise. Anal. TLC: pre-coated *Merck* silica gel *60 F_{254}* plates (SiO_2; 0.25 mm). Column chromatography (FC): *Fluka* SiO_2 *60* (230–400 mesh). HPLC: normal-phase *Daicel-Chiralpak* anal. columns (4.6 × 250 mm; 5 μm) of the *AS-H* or *AD-H* type, *Chiralpak-AY-3* anal. column (4.6 × 100 mm; 3 μm), or *Chiralcel-OD-H* anal. column (4.6–250 mm; 5 μm). M.p.: *Büchi-510* melting-point apparatus; uncorrected. Optical rotations ($[\alpha]_D^{20}$): *Perkin-Elmer 241* polarimeter; enantiomer excesses (ee) by HPLC analyses; t_R in min. ^{1}H- and ^{13}C-NMR Spectra: *Bruker-Avance* instrument; at 300 (^{1}H) and 75 MHz (^{13}C).

*(3*R*)-3-Phenylcyclohexanone* (**4**). A soln. of $[RhCl(C_2H_4)_2]_2$ (14 mg, 0.072 mmol Rh, 0.03 equiv. of Rh), chiral ligand **2** (0.08 mmol, 0.033 equiv.), and phenylboronic acid (600 mg, 4.92 mmol, 2 equiv.) in 1,4-dioxane (10 ml) was stirred at r.t. for 5 min. To this mixture was added cyclohex-2-en-1-one (**3**; 2.46 mmol, 1 equiv.) and aq. 1.5M KOH (1.25 mmol, 0.85 ml, 0.50 equiv.). The mixture was stirred at 30° for 3 h. Then the mixture was filtered over a pad of SiO_2, the pad washed with Et_2O, and the solvent was evaporated. Purification by FC (SiO_2, hexane/AcOEt 3:1 (R_f 0.56)) yielded **4** as a liquid. Anal. data: corresponding to literature data [13]. HPLC (*Chiral-Pak AS-H*, heptane/i-PrOH 90:10, 0.8 ml min^{-1}, 210 nm): t_R(minor) 13.4, t_R(major) 14.4, 97% ee, *Entry 8*, *Table 1*. $[\alpha]_D^{20} = +23.1$ ($c = 1.1$ $CHCl_3$), ((*R*)-enantiomer [14]: $[\alpha]_D^{20} = +20.9$ ($c = 1.0$, $CHCl_3$), 99% ee).

*(3*R*)-3-Phenylcyclopentanone* (**6**). As described for **4**, with cyclopent-2-en-1-one (**5**; 2.46 mmol, 1 equiv.). Purification by FC (SiO_2, hexane/AcOEt 4:1 (R_f 0.7)) yielded **6** as liquid. Anal. data: corresponding to literature data [13]. HPLC (*Chiralpak AY-3*, heptane/i-PrOH (0.05% Et_2NH) 90:10, 0.8 ml min^{-1}, 220 nm): t_R(major) 4.3, t_R(minor) 5.4; 97% ee, *Entry 12*, *Table 2*. $[\alpha]_D^{20} = +86.6$ ($c = 2.5$, $CHCl_3$) ((*R*)-enantiomer [14]: $[\alpha]_D^{20} = +87.3$ ($c = 1.0$, $CHCl_3$), 99% ee).

tert-*Butyl (3*R*)-3-(4-Methoxyphenyl)-3-phenylpropanoate* (=*1,1-Dimethylethyl (β*R*)-4-Methoxy-β-phenylbenzenepropanoate*; **8**). $[RhCl(C_2H_4)]_2$ (2.8 mg, 0.014 mmol Rh, 0.3 equiv. Rh) and diene **2** (0.016 mmol, 0.3 equiv.) were dissolved in MeOH (1.6 ml). The soln. was stirred for 15 min, followed by the addition of aq. 1.5M KOH (0.245 mmol, 165 μl, 0.5 equiv.). After stirring for 15 min, 4-$MeOC_6H_4B(OH)_2$ (149 mg, 0.98 mmol, 2 equiv.) was added, followed by *tert*-butyl cinnamate (**7**; 100 mg, 116 μl, 0.49 mmol, 1 equiv.), and the mixture was stirred at 50° for 16 h (reaction monitoring by ^{1}H-NMR by comparing the *tert*-butyl signal of **7** (δ(H) 1.55) with that of **8** (δ(H)1.27). Then, sat. NH_4Cl soln. was added, the aq. layer extracted with Et_2O (3×), and the combined org. layer washed with brine, dried ($MgSO_4$), and concentrated to give the crude product. Purification by FC (SiO_2, Et_2O/cyclohexane 1:20 (R_f 0.20)) yielded **8** as an off-white solid. M.p. 70–71.5° ([11]: 70–71°). Anal. data: corresponding to literature data [11]. HPLC (*Chiralpak AD-H*, heptane/i-PrOH (0.05% Et_2NH) 90:10, 0.8 ml min^{-1}, 230 nm): t_R(minor) 6.1, t_R(major) 7.1; 99% ee, *Entry 7*, *Table 3*. $[\alpha]_D^{20} = -1.06$ ($c = 0.94$, MeOH) ((*S*)-enantiomer [11]): $[\alpha]_D^{26} = +1.6$ ($c = 0.96$, MeOH), 93% ee).

N-*[(*S*)-(4-Chlorophenyl)phenylmethyl]-4-nitrobenzenesulfonamide* (**10**). A soln. of $[RhCl(C_2H_4)_2]_2$ (13.5 mg, 0.07 mmol Rh, 0.09 equiv.) and chiral diene **2** (0.03 mmol, 0.037 equiv.) in CH_2Cl_2 (1 ml) was stirred at r.t. for 1 h. The mixture was first filtered on a pad of *Celite*, then through a pad of SiO_2 (eluent CH_2Cl_2, then THF). The solvents were evaporated to afford the [Rh(diene)] complex as an orange solid that was directly used as catalyst for the arylation reaction. The [Rh(diene)] complex (*ca.* 0.03 equiv.) was dissolved in 1,4-dioxane (2.3 ml) and aq. 3.1M KOH (0.155 mmol, 50 μl, 0.2 equiv.) was added. After

5 min, this soln. was added to a suspension of *N*-[(4-nitrophenyl)sulfonyl]imine **9** (prepared according to [15]; 250 mg, 0.77 mmol, 1 equiv.) and triphenylboroxine (290 mg, 0.92 mmol, 1.2 equiv.) in 1,4-dioxane (3.9 ml). The mixture was stirred at 60° for 6 h. Then, it was passed through a pad of SiO_2 (pre-treated with MeOH, eluent: AcOEt). The filtrate was evaporated, and the residue was subjected to FC (SiO_2, cyclohexane/AcOEt 2:1 (R_f 0.48)): **10** as an off-white solid. M.p. 180–183° ([16]: 180.7–181.5°). Anal. data: corresponding to literature data [17]. HPLC (*Chiralcel OD-H*, heptane/EtOH 1:1, 0.8 ml min^{-1}, 210 nm): t_R(major) 5.7, t_R(minor) 7.9; 92% ee, *Entry 8*, *Table 4*. $[\alpha]_D^{20} = +2.1$ ($c = 1.16$, $CHCl_3$) ((*S*)-enantiomer [17]: $[\alpha]_D^{20} = +3.3$ ($c = 0.94$, $CHCl_3$), 98.5% ee).

REFERENCES

[1] a) F. Glorius, *Angew. Chem., Int. Ed.* **2004**, *43*, 3364; b) C. Defieber, H. Grützmacher, E. M. Carreira, *Angew. Chem., Int. Ed*. **2008**, *47*, 4482; c) J. B. Johnson, T. Rovis, *Angew. Chem., Int. Ed*. **2008**, *47*, 840; d) R. Shintani, T. Hayashi, *Aldrichim. Acta* **2009**, *42*, 31.

[2] a) T. Hayashi, K. Ueyama, N. Tokunaga, K. Yoshida, *J. Am. Chem. Soc*. **2003**, *125*, 11508; b) C. Fisher, C. Defieber, T. Suzuki, E. M. Carreira, *J. Am. Chem. Soc*. **2004**, *126*, 1628.

[3] a) S. Abele, R. Inauen, D. Spielvogel, C. Moessner, *J. Org. Chem.* **2012**, *77*, 4765; b) S. Abele, R. Inauen, J.-A. Funel, T. Weller, *Org. Process Res. Dev.* **2012**, *16*, 129; c) J.-A. Funel, G. Schmidt, S. Abele, *Org. Process Res. Dev.* **2011**, *15*, 1420.

[4] Y. Otomaru, K. Okamoto, R. Shintani, T. Hayashi, *J. Org. Chem.* **2005**, *70*, 2503.

[5] Y. Luo, A. J. Carnell, *Angew. Chem., Int. Ed.* **2010**, *49*, 2750.

[6] C. Defieber, J.-F. Paquin, S. Serna, E. M. Carreira, *Org. Lett.* **2004**, *6*, 3873.

[7] T. Gendrineau, O. Chuzel, H. Eijsberg, J.-P. Genet, S. Darses, *Angew. Chem., Int. Ed.* **2008**, *47*, 7669.

[8] Y. Otomaru, N. Tokunaga, R. Shintani, T. Hayashi, *Org. Lett*. **2005**, *7*, 307.

[9] K. Okamoto, T. Hayashi, V. H. Rawal, *Chem. Commun*. **2009**, 4815.

[10] N. Takunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584.

[11] J.-F. Paquin, C. R. J. Stephenson, C. Defieber, E. M. Carreira, *Org. Lett.* **2005**, 7, 3821.

[12] R. Shintani, T. Hayashi, *Org. Lett.* **2010**, *13*, 350.

[13] Y. Luo, N. G. Berry, A. J. Carnell, *Chem. Commun.* **2012**, *48*, 3279.

[14] T. Minuth, M. M. K. Boysen, *Org. Lett*. **2009**, *11*, 4212.

[15] B. E. Love, P. S. Raje, T. C. Williams II, *Synlett* **1994**, 493.

[16] Y. Nakao, M. Takeda, J. Chen, T. Hiyama, Y. Ichikawa, R. Shintani, T. Hayashi, *Chem. Lett*. **2008**, *37*, 290.

[17] Z.-Q. Wang, C.-G. Feng, M.-H. Xu, G.-Q. Lin, *J. Am. Chem. Soc*. **2007**, *129*, 5336.

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