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Chiral Bicyclo[3.3.0]octa-2,5-dienes as Steering Ligands in Substrate-Dependent Rhodium-Catalyzed 1,4-Addition of Arylboronic Acids to Enones

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Dedicated to Prof. Peter Hofmann on the occasion of his 60th birthday.

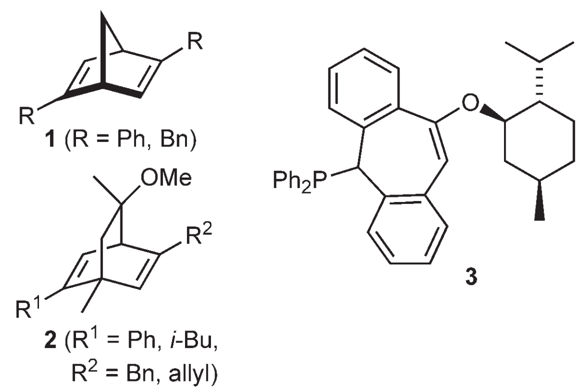
Abstract: The synthesis of disubstituted chiral diene ligands (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10** with a pentalene backbone from the corresponding bicyclo[3.3.0]octa-1,4-diones **7** is described. The latter were accessible by enzymatic resolution of the racemic diol *rac*-**5** and subsequent Swern oxidation. The efficiency of the ligands **10** in the rhodium-catalyzed 1,4-addition of arylboronic acids **12** to cyclic and acyclic enones **11** and **15** could be demonstrated. In the case of cyclic enones **11** the enantiomeric diphenyldienes (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10a** were more selective than the corresponding dibenzyldiene ligands **10b**. When acyclic enones **15** were employed this result, however, reversed. Ligands **10a** were nearly inactive whereas dibenzyldienes **10b** afforded the addition products **16** with enantioselectivities up to 91%.

Keywords: asymmetric catalysis; chirality; diene ligands; enones; rhodium; synthesis

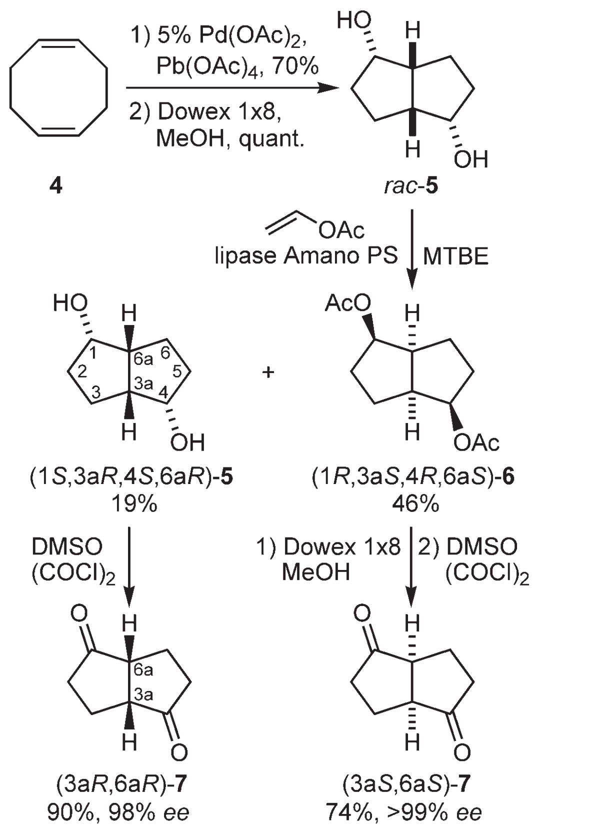
Introduction

In asymmetric catalysis alkenes such as ethylene, propene, 1,4-cyclooctadiene or norbornadiene and derivatives thereof were mainly considered as weak ligands, which do not allow stereochemical control in contrast to P-, N-, O- and S-containing ligands as well as N-heterocyclic carbenes. This situation changed with the recent seminal work of Hayashi,[1] Carreira,[2] and Grützmacher.[3] Their work confirmed the successful application of chiral diene ligands **1**, **2** based on bicycloalkanes, or tropylidenephosphane **3** (Scheme 1), resulting in high selectivities,[4] for example, in the Ir-catalyzed hydrogenation of imines[3d] and allylic substitution,[2c] in the Rh-catalyzed 1,4-addition of phenylboronic acid to enones[1h,l,2d] and fumarates[1k] or in the Rh-catalyzed aryl transfer to sulfonylimines.[1j]

In some cases, however, the synthetic access to the ligands is rather tedious.[1h,k,l] Upon looking for alternative scaffolds which might be easily converted into chiral diene ligands in both enantiomeric forms, we turned our attention to C_2-symmetrical bicyclo[3.3.0]octa-1,4-dione **7** (Scheme 2), whose (3a*R*,6a*R*)-enantiomer has been used as a building block in our total synthesis of the tetramic acid lactam cylindramide.[5] We anticipated that the *convex* roof shape of dione **7**[6] should lead to a diene ligand which bears structural similarities with the known norbornadiene ligands **1**.[1f,5] Further motivation came from a report by Trauner that *convex* phenanthrene ligands resulted in a chiral Pd(0) alkene complex with remarkable sta-



Scheme 1. Some chiral diene **1**,**2** and phosphane olefin ligands **3** reported by Hayashi, Carreira, and Grützmacher.[1–3]



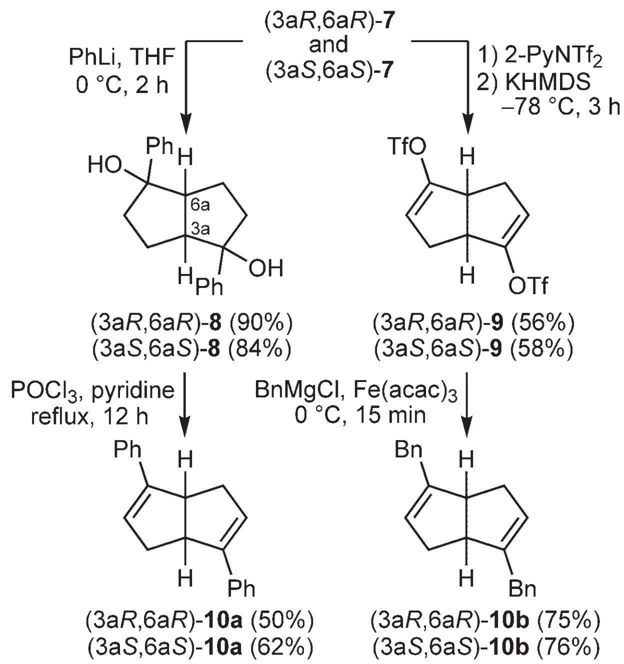
Scheme 2. Preparation of chiral bicyclo[3.3.0]octadiones **7** *via* enzymatic resolution.

bility.[7] Here we report the synthesis of bicyclo-[3.3.0]octadiene ligands and their application in the Rh-catalyzed 1,4-addition of arylboronic acids to enones.[8] Particular emphasis was spent on the influence of the diene substituents on the substrate specificity. The results are described below.

Results and Discussion

Ligand Synthesis

As depicted in Scheme 2, the bicyclo[3.3.0]octa-1,4-diones (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**7** were available starting from cycloocta-1,5-diene **4** by a literature procedure.[5] After transannular Pd-catalyzed ring closure[9] and removal of the acetyl groups,[10] the racemic diol *rac*-**5** was obtained. Diol *rac*-**5** was then submitted to enzymatic resolution with lipase Amano PS and vinyl acetate in methyl *tert*-butyl ether,[5,10,11] as a key step, yielding the diol (1*S*,3a*R*,4*S*,6a*R*)-**5** and the diacetate (1*R*,3a*S*,4*R*,6a*S*)-**6** in 19% and 46%, respectively. The diacetate **6** was separated by chromatography on SiO_2 and deacetylated to the corresponding alcohol (1*R*,3a*S*,4*R*,6a*S*)-**5** by treatment with Dowex 1× 8 in MeOH for 24 h. Swern oxidation[5,12] of both enantiomers **5** with DMSO and $(COCl)_2$ afforded the diones (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**7** with 98% *ee* and >99% *ee*, respectively (Scheme 2).



Scheme 3. Preparation of chiral 3,6-disubstituted bicyclo-[3.3.0]octa-2,5-dienes **10a**,**b**.

As outlined in Scheme 3, the disubstituted bicyclo-[3.3.0]octa-2,5-dienes **10** were prepared analogously to literature procedures. The synthesis of diphenyldiene ligands (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10a** utilized the reaction of both enantiomers **7** with PhLi to give intermediates **8** in 90% and 84% yield, respectively. After dehydration with $POCl_3$ in pyridine at 80°C,[1f] ligands (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10a** were isolated in 50% and 62% yield. Deprotonation of diones (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**7** with KHMDS[13] and subsequent treatment with *N*-(2-*p*yridyl)triflimide[14] (2-$PyNTf_2$) in THF at −78°C gave the bistriflates (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**9** in 56–58% yield. The following Negishi coupling[15] was performed with $Fe(acac)_3$ as the catalyst under the cross-coupling conditions recently described by Hayashi.[13] In this manner, the chiral 3,6-dibenzylated bicyclo-[3.3.0]octadiene ligands (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10b** were accessible in 75% and 76% yield, respectively. This synthesis route allows a variation of the substituent, yielding, for example, also ligand (3a*S*,6a*S*)-**10a** in 62% (see Experimental Section).

Crystallization of (3a*S*,6a*S*)-**10a** from MeOH/CH_2Cl_2 gave single crystals which were suitable for X-ray crystal structure analysis.[16] Figure 1 clearly shows the roof-shape of the bicyclooctadiene with an angle of 115° for the *convex* bicyclic system. The double bonds between C-1/C-2 and C-5/C-6 are not parallel to each other but twisted by 28°, thus being similar to

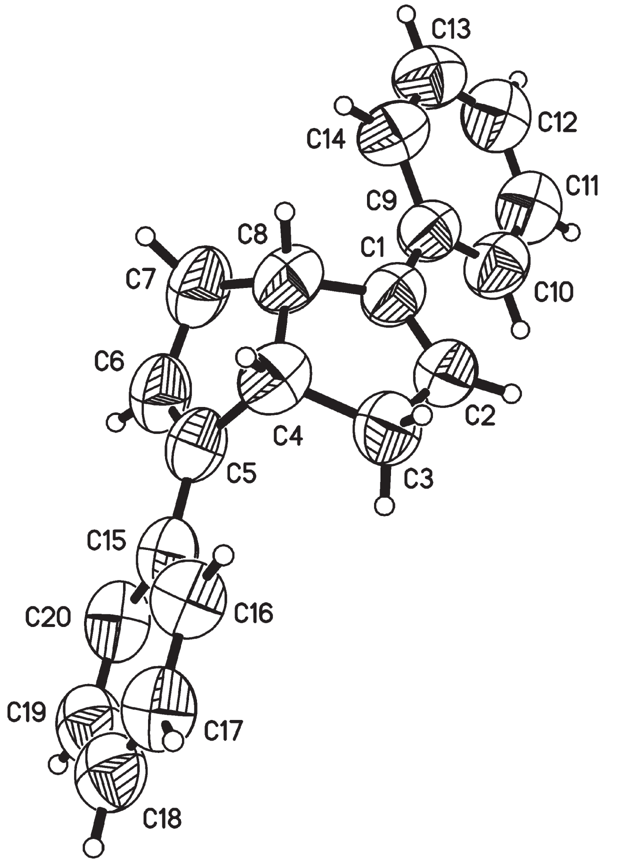


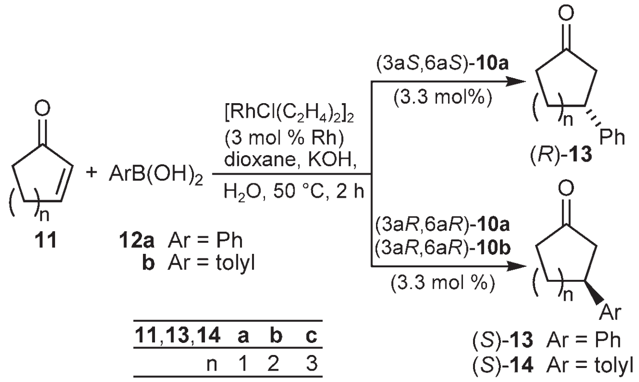
Figure 1. ORTEP plot of ligand 3,6-diphenylbicyclo-[3.3.0]octa-2,5-diene (3a*S*,6a*S*)-**10a**.

Hayashi's 2,6-di(4-methylphenyl)bicyclo[3.3.1]nona-2,6-diene rhodium complex where a twist angle of 23° has been found.[1f]

Asymmetric Rh-Catalyzed 1,4-Addition

First the catalytic properties of the diene ligands **10** were investigated in the Rh-catalyzed 1,4-addition of arylboronic acids **12a**, **b** to the cyclic enones **11a–c** (Table 1). Treatment of cyclopentenone **11a** with phenylboronic acid **12a** in the presence of 3 mol% Rh and 3.3 mol% diphenyldiene ligand (3a*S*,6a*S*)-**10a** and KOH (0.5 equivs.) in aqueous dioxane yielded (*R*)-3-phenylcyclopentanone (*R*)-**13a** in 74% yield and 95% *ee* (entry 1). The enantiomeric ligand (3a*R*,6a*R*)-**10a** gave the corresponding (*S*)-configurated product in 80% yield and 93% *ee* (entry 2). The enantioselectivities decreased with both (3a*S*,6a*S*)- and (3a*R*,6a*R*)-**10a** when cyclohexenone **11b** and cycloheptenone **11c** were employed, while, with exception of product **13c**, good chemical yields were obtained (entries 4, 5, 7, 8). The addition of tolylboronic acid **12b** in the presence of ligand (3a*R*,6a*R*)-**10a** proceeded with similar yields and enantioselectivities

Table 1. Rhodium-catalyzed addition of arylboronic acids **12a**,**b** to cyclic enones **11a–c** using ligands (3a*R*,6a*R*)-**10a**,**b** and (3a*S*,6a*S*)-**10a**.



Entry	Enone	Ligand	Product	Yield [%][a]	% *ee*[b]	Conf.[c]
1	**11a**	(3a*S*,6a*S*)-**10a**	**13a**	74	95	*R*
2	**11a**	(3a*R*,6a*R*)-**10a**	**13a**	80	93	*S*
3	**11a**	(3a*R*,6a*R*)-**10b**	**13a**	73	75	*S*
4	**11b**	(3a*S*,6a*S*)-**10a**	**13b**	95	88	*R*
5	**11b**	(3a*R*,6a*R*)-**10a**	**13b**	93	84	*S*
6	**11b**	(3a*R*,6a*R*)-**10b**	**13b**	78	73	*S*
7	**11c**	(3a*S*,6a*S*)-**10a**	**13c**	47	83	*R*
8	**11c**	(3a*R*,6a*R*)-**10a**	**13c**	51	76	*S*
9	**11a**	(3a*R*,6a*R*)-**10a**	**14a**	85	93	*S*[d]
10	**11b**	(3a*R*,6a*R*)-**10a**	**14b**	81	84	*S*[d]
11	**11c**	(3a*R*,6a*R*)-**10a**	**14c**	71	76	*S*[d]

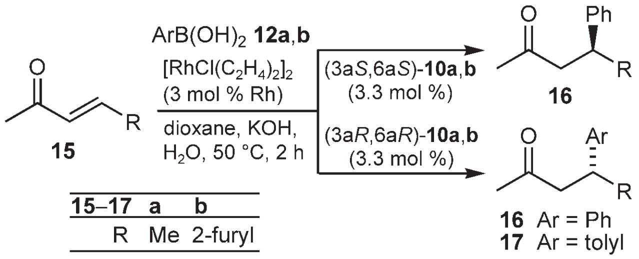
[a] Yields are referred to isolated products.
[b] Enantiomeric excess was determined by GC using chiral stationary phases.
[c] Assignment of the configuration by comparison of optical rotation values with literature data.[17,18]
[d] In analogy to the assignment of products **13**.

(entries 9–11). A considerable drop of the enantioselectivity was observed when dibenzyldiene ligand (3a*R*,6a*R*)-**10b** was used under identical reaction conditions (entries 3, 6).

The most remarkable observation, however, was made during 1,4-addition of boronic acids **12** to acyclic enones **15** (Table 2).

As can be seen in Table 2, diphenyl- and dibenzyl-substituted ligands **10a** and **10b** showed a strikingly different activity. Whereas diphenyldiene ligand (3a*S*,6a*S*)-**10a** and its congener (3a*R*,6a*R*)-**10a** yielded

Table 2. Rhodium-catalyzed addition of arylboronic acids **12a**,**b** to acyclic enones **15a**,**b** using ligands (3a*R*,6a*R*)- and (3a*S*,6a*S*)-**10a**,**b**.



Enone	Ligand	Product	Yield [%][a]	% *ee*[b]	$[\alpha]_D^{20}$ (*c* 1.0, CH_2Cl_2)
15a	(3a*S*,6a*S*)-**10a**	**16a**	< 1[c]	1	-
15a	(3a*R*,6a*R*)-**10a**	**16a**	< 1[c]	0	-
15a	(3a*S*,6a*S*)-**10b**	(*S*)-**16a**[d]	71	91	+29.1
15a	(3a*R*,6a*R*)-**10b**	(*R*)-**16a**[d]	59	89	−31.2
15b	(3a*S*,6a*S*)-**10a**	(+)-**16b**[e]	< 1[c]	16	-
15b	(3a*R*,6a*R*)-**10a**	(−)-**16b**[e]	1[c]	10	-
15b	(3a*S*,6a*S*)-**10b**	(+)-**16b**	73	89	+63.4
15b	(3a*R*,6a*R*)-**10b**	(−)-**16b**	45[f]	88	−49.5
15a	(3a*R*,6a*R*)-**10b**	(*R*)-**17a**[g]	68	89	−30.0
15b	(3a*R*,6a*R*)-**10b**	(−)-**17b**	58	86	−65.2

[a] Yields are referred to isolated products.
[b] Enantiomeric excess was determined by GC using chiral stationary phases.
[c] Starting material **15a** and **15b** was recovered.
[d] Assignment of the configuration by comparison of optical rotation values with literature data.[19]
[e] According to the direction of rotation.
[f] 72% yield with 6 mol% Rh catalyst.
[g] In analogy to the assignment of derivative **16a**.

only trace amounts of the corresponding 1,4-addition products **16a** and **16b** in racemic form, the corresponding dibenzyldienes (3a*S*,6a*S*)- and (3a*R*,6a*R*)-**10b** gave the target products **16a**, **b** in good yields and enantioselectivities of 88–91%. When tolylboronic acid **12b** was employed in the presence of dibenzyldiene ligand (3a*R*,6a*R*)-**10b** comparable results were obtained.[20]

Conclusions

We have demonstrated that chiral bicyclo[3.3.0]octadiene ligands **10a** and **10b** which were easily accessible in optically pure form in a five (or six) step sequence from cycloocta-1,5-diene **4**, could be used in the catalytic asymmetric 1,4-addition of arylboronic acids to enones. More importantly, the substitution pattern of the diene led to complementary activity and substrate specificity of the catalyst. Whereas diphenyldiene ligands **10a** converted cyclic enones **11a–c** with good yields and high enantioselectivities, it turned out to be almost completely inactive towards acyclic enones **15a**, **b**. In contrast, dibenzyldiene ligands **10b** gave decreased selectivities for cyclic enones **11** as compared to the diphenyldiene counterpart **10a**. For acyclic enones **15**, however, ligands **10b** produced good yields and selectivities. Thus, it needs to be explored whether such complementary behaviour of ligands **10a**, **b** is also observed for other catalytic reactions.

Experimental Section

General Remarks

Melting points (uncorrected) were determined on a Büchi SMP 20. Specific rotations were determined on a Perkin–Elmer 241 polarimeter. IR spectra: Bruker Vektor22. Mass spectra: Finnigan MAT 95, Varian MAT 711, and Bruker Daltonics mircOTOFq. NMR spectra: Bruker Avance 300 and Avance 500. The spectra were recorded with TMS as internal standard. TLC: Silica gel 60 F_{254} (Merck). Column chromatography: Fluka Kieselgel 60, grain size 40–63 μm. GC: Fisons HRGC MEGA 8560 and Carlo Erba Strumentazione HRGC 5300. Column and temperature programs are given below.

(3a*R*,6a*R*)- and (3a*S*,6a*S*)-Hexahydropentalene-1,4-diones (7)

Compounds **7** were prepared as described in ref.[5] In order to obtain enantiomerically pure (3a*S*,6a*S*)-**7**, the diacetate (1*R*,3a*S*,4*R*,6a*S*)-**6** obtained from enzymatic resolution with 96% *ee* was submitted to saponification followed by enzymatic acetylation and Swern oxidation.

(3a*R*,6a*R*)-1,4-Diphenyloctahydropentalene-1,4-diol (8)

$CeCl_3{\cdot}7H_2O$ (2.1 g, 5.6 mmol) was heated under vacuum at 140 °C for 2 h and cooled. Then THF (10 mL) was added and the suspension stirred for 1 h at room temperature. The suspension was cooled to −78 °C, PhLi (3.1 mL, 5.6 mmol, 1.8 M in dibutyl ether) was added and the reaction mixture stirred for a further 1 h. After addition of a solution of (3a*R*,6a*R*)-**7** (276 mg, 2 mmol) in THF (2 mL), the reaction mixture was warmed to −40 °C over 6 h. The reaction was quenched with water (20 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3× 50 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was removed under vacuum. Chromatography of the residue on SiO_2 [PE/EtOAc, 4:1→0:1, R_f (PE/EtOAc 5:1)=0.6] afforded **8** as a white solid; yield 531 mg (90%); mp 192 °C; $[\alpha]_D^{20}$: −53.7 (*c* 1.0, CH_2Cl_2). FT-IR (ATR): $\tilde{\nu}$=3326 (s), 2966 (m), 2925 (m), 1734 (m), 1494 (m), 1459 (m), 1444 (m), 1372 (m), 1297 (m), 1249 (m), 1154 (m), 1071 (m), 1037 (m), 927 (m), 756 (s), 697 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.73–1.85 (m, 2H, 3-H_a, 6-H_a), 2.08–2.39 (m, 6H, 2-H, 3-H_b, 5-H, 6-H_b), 2.94–3.07 (m, 2H, 3a-H, 6a-H), 3.64 (s, 2H, O*H*), 7.22–7.39 (m, 2H, *p*-H), 7.31–7.39 (m, 4H, *o*-H), 7.49–7.54 (m, 4H, *m*-H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=20.9 (C-3, C-6), 45.1 (C-2, C-5), 55.4 (C-3a, C-6a), 81.3 (C-1, C-4), 125.3 (*o*-C), 126.9 (*p*-C), 128.3 (*m*-C), 145.0 (*i*-C); GC-MS (EI): *m/z* (%)=295 (1) [M^++H], 276 (15) [M^+−H_2O], 258 (80) [M^+−2H_2O], 230 (20), 156 (40), 143 (50), 129 (45), 115 (43), 105 [M^+−2H_2O−2C_6H_5+H], 90 (50), 77 (25) [C_6H_5]; ESI-MS: *m/z*=317.1517 [M^+], calcd. for $C_{20}H_{22}NaO_2$ 317.1512; anal. calcd. for $C_{20}H_{22}O_2$ (294.38): C 81.60, H 7.53; found: C 81.37, H 7.63.

(3a*S*,6a*S*)-1,4-Diphenyloctahydropentalene-1,4-diol (8): Yield: 84%; $[\alpha]_D^{20}$: +54.1 (*c* 1.0, CH_2Cl_2). The spectroscopic data are in accordance with those of (3a*R*,6a*R*)-**8**.

(3a*R*,6a*R*)-3,6-Diphenyl-1,3a,4,6a-tetrahydropentalene (10a)

To a solution of (3a*R*,6a*R*)-**8** (264 mg, 0.90 mmol) in pyridine (1 mL) at room temperature was added $POCl_3$ (495 μL), and the reaction mixture refluxed for 12 h. After cooling to room temperature, the reaction was quenched with water (10 mL) and extracted with CH_2Cl_2 (3×20 mL). The combined extracts were washed with a 2M solution of NaOH, dried ($MgSO_4$) and concentrated. Chromatography on SiO_2 (PE/Et_2O, 500:1, R_f=0.1) afforded **10a** as a white solid; yield: 132 mg (50%); $[\alpha]_D^{20}$: −406 (*c* 1.0, CH_2Cl_2). FT-IR (ATR): $\tilde{\nu}$=2904 (m), 2837 (m), 1494 (m), 1444 (m), 747 (s), 694 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=2.42 (ddd, *J*=17.8, 5.9, 3.0 Hz, 2H, 3-H_a, 6-H_a), 2.88–2.97 (m, 2H, 3-H_b, 6-H_b), 4.03–4.10 (m, 2H, 3a-H, 6a-H), 6.00–6.04 (m, 2H, 2-H, 5-H), 7.18–7.26 (m, 2H, *p*-H), 7.27–7.37 (m, 4H, *o*-H), 7.41–7.47 (m, 4H, *m*-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 38.6 (C-3, C-6), 48.3 (C-3a, C-6a), 124.4 (C-2, C-5), 126.3 (C-*m*), 126.9 (C-*p*), 128.4 (C-*o*), 135.9 (C-*i*), 145.1 (C-1, C-4); MS (CI, CH_4): *m/z* (%)=258 (100) [M^+], 243 (19), 230 (17), 215 (11), 202 (7), 178 (11), 167 (28), 154 (31), 141 (15), 128 (12), 117 (88), 102 (8), 91 (28), 77 (9) [C_6H_5]; HR-MS (CI, CH_4): *m/z*= 258.1409 [M^+], calcd. for $C_{20}H_{18}$: 258.1409.

(3a*S*,6a*S*)-3,6-Diphenyl-1,3a,4,6a-tetrahydropentalene (10a): Yield: 62%; $[\alpha]_D^{20}$: +396 (*c* 1.0, Et_2O). The spectroscopic data are in accordance with those of (3a*R*,6a*R*)-**10a**.

(3a*R*,6a*R*)-4-{[(Trifluoromethyl)sulfonyl]oxy}-3,3a,6,6a-tetrahydropentalen-1-yl Trifluoromethanesulfonate (9)

A solution of KHMDS (1.32 g, 6.64 mmol) in THF (12 mL) was slowly added to a solution of (3a*R*,6a*R*)-**7** (400 mg, 3.00 mmol) and *N*-(2-*p*yridyl)-bis(trifluoromethanesulfonimide) (2-$PyNTf_2$) (2.49 g, 6.96 mmol) in THF (12 mL) at −78 °C, and the reaction mixture stirred for 3 h. Then a saturated solution of $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with pentane (2×50 mL), the combined organic layers were washed with a solution of 5% NaOH-H_2O, dried ($MgSO_4$) and concentrated. Chromatography on SiO_2 (PE/EtOAc, 25:1, R_f=0.4) afforded triflate **9** as a colorless oil; yield: 675 mg (56%); $[\alpha]_D^{20}$: −45.2 (*c* 1.0, CH_2Cl_2). FT-IR (ATR): $\tilde{\nu}$=2936 (m), 2871 (m), 1964 (m), 1659 (s), 1420 (vs), 1331 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.51 (ddd, *J*=17.4, 5.2, 2.6 Hz, 2H, 3-H_a, 6-H_a), 2.62–2.68 (m, 2H, 3-H_b, 6-H_b), 3.62–3.65 (m, 2H, 3a-H, 6a-H), 5.58–5.66 (m, 2H, 2-H, 5-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ= 30.3 (C-3, C-6), 44.1 (C-3a, C-6a), 115.3 (C-2, C-5), 118.6 (q, *J*=2.6, SO_2CF_3), 149.0 (C-1, C-4) ppm; GC-MS (CI, CH_4): *m/z* (%)=402 (1) [M^+], 269 (9) [M^+−CF_3O_2S], 162 (2), 135 (6), 119 (12), 99 (6), 91 (19), 77 (8), 69 (36) [CF_3], 64 (17) [SO_2], 55 (100); HR-MS (CI, CH_4): *m/z*=401.9647 [M^+], calcd. for $C_{10}H_8F_6O_6S_2$: 401.9666.

(3a*S*,6a*S*)-4-{[(Trifluoromethyl)sulfonyl]oxy}-3,3a,6,6a-tetrahydropentalen-1-yl trifluoromethanesulfonate (9): Yield: 58%; $[\alpha]_D^{20}$: +47.1 (*c* 1.0, CH_2Cl_2). The spectroscopic data are in accordance with those of (3a*R*,6a*R*)-**9**.

(3a*R*,6a*R*)-2,5-Dibenzyl-1,3a,4,6a-tetrahydropentalene (10b)

BnMgCl (0.5 mL, 1 mmol, 2M in THF) was slowly added to a solution of (3a*R*,6a*R*)-**9** (210 mg, 0.52 mmol) and $Fe(acac)_3$ (37 mg, 0.10 mmol, 5 mol%) in THF (5 mL) at 0 °C, and the reaction mixture stirred for 15 min. The reaction was then quenched at 0 °C with a saturated solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL), the combined extracts were dried ($MgSO_4$), and concentrated. Chromatography on SiO_2 (PE/Et_2O, 500:1, R_f=0.2) afforded **10b** as a colorless oil; yield: 111 mg (75%); $[\alpha]_D^{20}$: −49.5 (*c* 1.0, CH_2Cl_2). FT-IR (ATR): $\tilde{\nu}$=3025 (m), 2902 (m), 2844 (m), 1601 (s), 1493 (m), 1452 (m), 1155 (s), 1072 (m), 1029 (m), 819 (m), 752 (m), 696 (s), 614 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ=2.25–2.32 (m, 2H, 3-H_a, 6-H_a), 2.40–2.49 (m, 2H, 3-H_b, 6-H_b), 3.17–3.22 (m, 2H, 3a-H, 6a-H), 3.26 (dd, *J*=15.4, 1.4 Hz, 2H, 7-H_a, 8-H_a), 3.47 (d, *J*= 15.4 Hz, 2H, 7-H_b, 8-H_b), 5.13–5.16 (m, 2H, 2-H, 5-H), 7.08–7.14 (m, 8H, *o*-H, *m*-H) 7.17–7.29 (m, 2H, *p*-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=35.9 (C-3, C-6), 36.0 (C-7, C-8), 49.8 (C-3a, C-6a), 123.3 (C-2, C-5), 125.9 (C-*p*), 128.2 (C-*m*), 129.0 (C-*o*), 140.0 (C-*i*), 145.9 (C-1, C-4); GC-MS (CI, CH_4): *m/z* (%)=286 (40) [M^+], 195 (74) [M^+−C_7H_7], 178 (8), 167 (22), 153 (8), 129 (10), 117 (26), 91 (100) [C_7H_7], 77 (8) [C_6H_5], 65 (14), 51 (6); HR-MS (CI, CH_4): *m/z*=286.1722 [M^+], calcd. for $C_{22}H_{22}$: 286.1721.

(3a*S*,6a*S*)-2,5-Dibenzyl-1,3a,4,6a-tetrahydropentalene (10b): Yield: 76%; $[\alpha]_D^{20}$: +52.8 (*c* 1.0, CH_2Cl_2). The spectroscopic data are in accordance with those of (3a*R*,6a*R*)-**10b**.

(3a*S*,6a*S*)-2,5-Diphenyl-1,3a,4,6a-tetrahydropentalene (10a): According to ref.,[1f,j] from PhMgBr (0.5 mL, 1.49 mmol, 3M in Et_2O), $PdCl_2$(dppf) (1.88 mg, 2.50 μmol), and (3a*S*,6a*S*)-**9** (100 mg, 0.25 mmol) at room temperature, reaction time 16 h; yield: 62%; $[\alpha]_D^{20}$: +379.5 (*c* 1.0, Et_2O).

General Procedure for the Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids 12 to Enones 11 and 15

A solution of $[RhCl(C_2H_4)_2]_2$ (3 mol% Rh) and the respective ligand **10** (3.3 mol%) in degassed dioxane (2 mL) was stirred at room temperature for 15 min. Then a degassed 1 M solution of KOH (0.5 equivs.) was added, and the mixture stirred for a further 10 min. After addition of the respective enones **11** or **15** (1 equiv.) and arylboronic acids **12** (2 equivs.), the reaction mixture was stirred at 50 °C for 2 h. The reaction was then quenched with a saturated solution of NH_4Cl (5 mL), and the aqueous layer was extracted with Et_2O (3×20 mL). The combined organic layers were dried ($MgSO_4$) and the solvent removed under vacuum. The crude products **13**, **14** or **16**, **17** were purified by chromatography on SiO_2 with PE/EtOAc (10:1). GC: cyclic products **13a**,**b**, **14a**,**b**: column Bondex un α (20 m×0.25 mm), 0.4 bar H_2; cyclic products **13c**, **14c**: column Bondex un β (20 m×0.25 mm); acyclic products **16a**,**b**, **17a**,**b**: column Amidex C (0.5% mono-2-undecamethylenepermethyl-β-cyclodextrin, 1.2% *N*-(4-trimethylenoxybenzoyl)-L-valine bornylamide) (20 m×0.25 mm), 0.35 bar H_2.

According to this protocol the following addition products were obtained. The spectroscopic data of **13**, **14** and **16a**, **17a** are in accordance with those in the literature.[17,21]

(*S*)-3-Phenylcyclopentanone (13a): R_f=0.25; $[\alpha]_D^{20}$: −101.7 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**], $[\alpha]_D^{20}$: −73.5 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]; GC: 10 °C min^{-1} gradient from 40 °C to 120 °C, 3 min at 120 °C, then 2 °C min^{-1} gradient to 200 °C, t_{R1}=17.04 min, t_{R2}=17.39 min (major enantiomer).

(*R*)-3-Phenylcyclopentanone (13a): $[\alpha]_D^{20}$: +96.4 (*c* 1.0, CH_2Cl_2) [with (3a*S*,6a*S*)-**10a**]; GC: t_{R1}=17.04 min.

(*S*)-3-Phenylcyclohexanone (13b): R_f=0.3; $[\alpha]_D^{20}$: −15.0 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**]; $[\alpha]_D^{20}$: −14.1 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]; GC: 10 °C min^{-1} gradient from 40 °C to 120 °C, 3 min at 120 °C, then 2 °C min^{-1} gradient to 150 °C, then 10 °C min^{-1} gradient to 200 °C, t_{R1}=19.57 min, t_{R2}=20.02 min (major enantiomer).

(*R*)-3-Phenylcyclohexanone (13b): $[\alpha]_D^{20}$: +8.4 (*c* 1.0, CH_2Cl_2) [with (3a*S*,6a*S*)-**10a**]; GC: t_{R1}=19.57 min.

(*S*)-3-Phenylcycloheptanone (13c): R_f=0.3; $[\alpha]_D^{20}$: −43.0 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**]; GC: 0.5 °C min^{-1} gradient from 80 °C to 130 °C, then 10 °C min^{-1} gradient to 200 °C, t_{R1}=83.88 min (major enantiomer), t_{R2}=84.88 min.

(*R*)-3-Phenylcycloheptanone (13c): $[\alpha]_D^{20}$: +41.4 (*c* 1.0, CH_2Cl_2) [with (3a*S*,6a*S*)-**10a**]; GC: t_{R2}=84.88 min.

(*S*)-3-(4-Methylphenyl)cyclopentanone (14a): R_f=0.2; $[\alpha]_D^{20}$: −89.0 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**]; GC: 10 °C min^{-1} gradient from 40 °C to 120 °C, 3 min at 120 °C, then 2 °C min^{-1} gradient to 200 °C, t_{R1}=22.17 min, t_{R2}=22.45 min (major enantiomer).

(*S*)-3-(4-Methylphenyl)cyclohexanone (14b): R_f=0.23; $[\alpha]_D^{20}$: −19.8 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**]; GC: 10 °C min^{-1} gradient from 40 °C to 120 °C, 3 min at 120 °C, then 2 °C min^{-1} gradient to 200 °C, t_{R1}=24.13 min, t_{R2}=24.62 min (major enantiomer).

(*S*)-3-(4-Methylphenyl)cycloheptanone (14c): R_f=0.28; $[\alpha]_D^{20}$: −29.0 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10a**]; GC: 0.5 °C min^{-1} gradient from 80 °C to 130 °C, then 10 °C min^{-1} to 200 °C, t_{R1}=85.67 min (major enantiomer), t_{R2}=86.54 min.

(*R*)-4-Phenylpentan-2-one (16a): R_f=0.3; $[\alpha]_D^{20}$: −31.2 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]; GC: 1 min at 40 °C, then 2 °C min^{-1} gradient to 200 °C, t_{R1}=27.15 min (major enantiomer), t_{R2}=27.71 min.

(*S*)-4-Phenylpentan-2-one (16a): $[\alpha]_D^{20}$: +29.1 (*c* 1.0, CH_2Cl_2) [with (3a*S*,6a*S*)-**10b**]; GC: t_{R2}=27.71 min.

(−)-4-(2-Furyl)-4-phenylbutan-2-one (16b): R_f=0.28; $[\alpha]_D^{20}$: −49.5 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]. FT-IR (ATR): $\tilde{\nu}$=2361 (m), 2342 (m), 1715 (s), 1586 (m), 1504 (m), 1494 (m), 1453 (m), 1413 (m), 1359 (s), 1158 (s), 1079 (m), 1009 (s), 936 (m), 922 (m), 808 (m), 731 (m), 698 (s), 577 (m), 535 (m), 509 (s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.09 (s, 3H, 1-H), 3.00 (dd, *J*=7.3, 16.7 Hz, 1H, 3-H_a), 3.23 (dd, *J*=7.5, 16.7 Hz, 1H, 3-H_b), 4.59 (dd, *J*=7.5, 7.3 Hz, 1H, 4-H), 5.99 (d, *J*=3.3 Hz, 1H, 3′-H), 6.27 (dd, *J*=1.9, 3.1 Hz, 1H, 4′-H), 7.19–7.32 (m, 6H, aryl-H, 5′-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=30.4 (C-1), 40.2 (C-4), 48.4 (C-3), 105.7 (C-4′), 110.2 (C-3′), 126.9 (C-*p*), 127.7 (C-*m*), 128.6 (C-*o*), 141.6 (C-5′), 141.7 (C-*i*), 156.5 (C-2′), 206.2 (C-2); MS (EI): *m/z* (%)=215 (8) [M$^+$+H], 214 (50) [M$^+$], 171 (12) [$C_{12}H_{11}O$], 157 (100) [$C_{11}H_9O$], 128 (20), 115 (9), 103 (18), 77 (6) [C_6H_6], 43 (17); ESI-MS: *m/z*=237.0886 [M+Na]$^+$, calcd. for $C_{14}H_{14}NaO_2$: 237.0884. GC: 10 min at 100 °C, then 2 °C min^{-1} gradient to 160 °C, 10 min at 160 °C, then 10 °C min^{-1} gradient to 200 °C, t_{R1}=29.91 min, t_{R2}=30.35 min (major enantiomer).

(+)-4-(2-Furyl)-4-phenylbutan-2-one (16b): $[\alpha]_D^{20}$: +63.4 (*c* 1.0, CH_2Cl_2) [with (3a*S*,6a*S*)-**10b**]; GC: t_{R1}=29.91 min.

(*R*)-4-(4-Methylphenyl)pentan-2-one (17a): R_f=0.25; $[\alpha]_D^{20}$: −30.0 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]; GC: 1 min at 40 °C, then 2 °C min^{-1} gradient to 200 °C, t_{R1}=31.85 min (major enantiomer), t_{R2}=32.17 min.

(−)-4-(2-Furyl)-4-(4-methylphenyl)butan-2-one (17b): R_f=0.25; $[\alpha]_D^{20}$: −65.2 (*c* 1.0, CH_2Cl_2) [with (3a*R*,6a*R*)-**10b**]. FT-IR (ATR): $\tilde{\nu}$=2361 (m), 1715 (s), 1588 (m), 1513 (m), 1415 (m), 1358 (m), 1158 (s), 1112 (m), 1009 (m), 966 (s), 884 (m), 802 (s), 732 (s), 547 (m), 518 (m), 505 (m) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.08 (s, 3H, 1-H), 2.29 (s, 3H, CH_3), 2.98 (dd, *J*=7.4, 16.7 Hz, 1H, 3-H_a), 3.21 (dd, *J*=7.4, 16.7 Hz, 1H, 3-H_b), 4.55 (dd, *J*=7.4, 7.4 Hz, 1H, 4-H), 5.96–5.99 (m, 1H, 3′-H), 6.27 (dd, *J*=1.8, 3.1 Hz, 1H, 4′-H), 7.07–7.15 (m, 4H, aryl-H), 7.28 (dd, *J*=0.7, 1.8, 1H, 5′-H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=20.9 (CH_3), 30.3 (C-1), 48.4 (C-3), 49.8 (C-4), 105.5 (C-4′), 110.1 (C-3′), 127.6 (C-*m*), 129.2 (C-*o*), 136.3 (C-*p*), 138.6 (C-5′), 141.7 (C-*i*), 156.5 (C-2′), 206.2 (C-2); MS (EI): *m/z* (%)=229 (8) [M$^+$+H], 228 (40) [M$^+$], 185 (6), 171 (100) [$C_{12}H_{11}O$], 141 (7), 128 (12), 117 (10), 115 (7), 77 (2) [C_6H_6], 43 (5); ESI-MS: *m/z*=251.1043 [M+Na]$^+$, calcd. for $C_{15}H_{16}NaO_2$: 251.1046. GC: 3 min at 100 °C, then 1.5 °C min^{-1} gradient to 160 °C, then 10 °C min^{-1} gradient to 200 °C, t_{R1}=34.99 min, t_{R2}=35.32 min (major enantiomer).

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[16] Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-629398. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax.: (internat.) + 44 1223/336–033; e-mail: deposit@ccdc.cam.ac.uk].

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