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Tuning the Chiral Environment of C_2-Symmetric Diene Ligands: Development of 3,7-Disubstituted Bicyclo[3.3.1]nona-2,6-dienes

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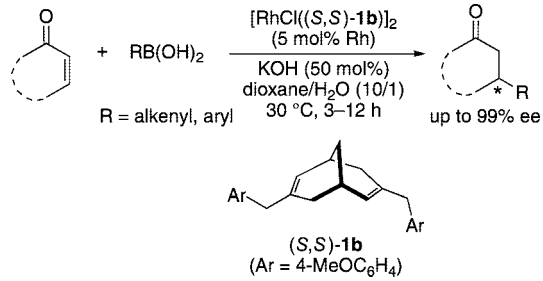

Through the structural analysis of bicyclo[3.3.1]nona-2,6-dienes, new C_2-symmetric chiral diene ligands **1** based on 3,7-disubstituted bicyclo[3.3.1]nona-2,6-diene framework have been designed and synthesized. These chiral ligands readily bind to rhodium(I) and provide a different chiral environment from the existing chiral dienes. The rhodium complexes thus obtained act as effective catalysts for 1,4-addition of alkenyl- and arylboronic acids to various α,β-unsaturated ketones, including several combinations that were previously difficult to provide high enantioselectivity.

Introduction

Chiral dienes have been recently recognized as effective ligands for transition metal-catalyzed asymmetric reactions and several research groups have witnessed the superiority of these ligands to conventional phosphorus- and/or nitrogen-based chiral ligands in some transformations.[1] Among the chiral diene ligands developed to date, the ones with C_2-[2,3a−m,4−6] or pseudo-C_2-symmetry[3n−t] have provided a particularly effective chiral environment for asymmetric carbon−carbon bond-forming reactions such as rhodium-catalyzed asymmetric 1,4-addition reactions. Their effectiveness is considered to be based on the rigid (pseudo-)C_2-symmetry of the ligand framework, but unfortunately, due to the high rigidity, currently available chiral dienes cannot accommodate all the asymmetric catalysis one wishes to accomplish with high stereoselectivity.

For example, we previously reported the use of 2,6-diarylbicyclo[3.3.1]nona-2,6-dienes, such as (*R*,*R*)-Ph-bnd*, as effective ligands for the rhodium-catalyzed asymmetric arylation of imines,[4a] but these ligands provided only moderate enantioselectivity for 1,4-addition to electron-deficient olefins.[4b] By analyzing the three-dimensional structure of 2,3,6,7-tetramethylbicyclo[3.3.1]nona-2,6-diene (**A**) as a model, two alkenes, C2−C3 and C6−C7, are twisted by ca. 27.6° with each other (Figure 1, right), and as a result, methyl groups on C3 and C7 (Cα and Cα′, respectively) are located closer to a metal (M)

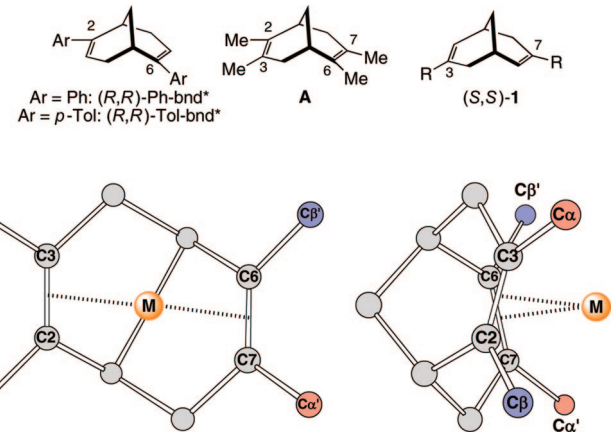

FIGURE 1. Chem3D representation of 2,3,6,7-tetramethylbicyclo-[3.3.1]nona-2,6-diene (**A**) (left: front view; right: side view; M is a transition metal, placed at the same distance from two olefins without optimization).

(1) For reviews, see: (a) Johnson, J. B.; Rovis, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 840. (b) Defieber, C.; Grützmacher, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482.

(2) Bicyclo[2.2.1]hepta-2,5-dienes:(a) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508. (b) Shintani, R.; Ueyama, K.; Yamada, I.; Hayashi, T. *Org. Lett.* **2004**, *6*, 3425. (c) Berthon-Gelloz, G.; Hayashi, T. *J. Org. Chem.* **2006**, *71*, 8957.

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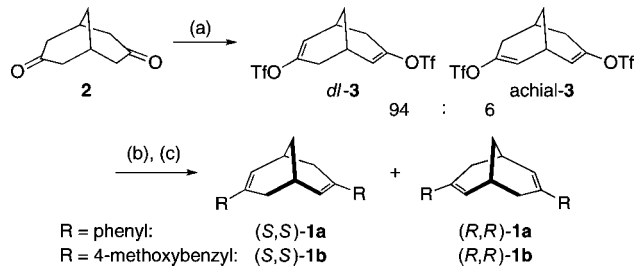
SCHEME 1[a]



[a] Conditions: (a) 2-PyNTf$_2$ (2.4 equiv), KN(SiMe$_3$)$_2$ (2.3 equiv), THF, −78 °C; 82%. (b) NiCl$_2$(dppp) (2 mol %), RMgBr (6.0 equiv), THF, reflux; 70% for **1a**, 85% for **1b**. (c) HPLC resolution (chiralcel OD-H for **1a**, chiralcel OJ for **1b**).

than those on C2 and C6 (Cβ and Cβ', respectively) when this diene forms a chelating metal complex. This simple analysis using model compound **A** led us to design new C_2-symmetric chiral dienes, 3,7-disubstituted bicyclo[3.3.1]nona-2,6-dienes **1**, which are expected to provide a closer and more effective chiral environment in their transition metal complexes.

Results and Discussion

Preparation of 3,7-Disubstituted Bicyclo[3.3.1]nona-2,6-dienes 1. The synthesis of 3,7-disubstituted bicyclo[3.3.1]nona-2,6-dienes **1** begins with readily available bicyclo[3.3.1]nonane-3,7-dione[7] (**2**) in a straightforward manner (Scheme 1). Thus, selective formation of ditriflate *dl*-**3** followed by nickel-catalyzed cross-coupling with an appropriate Grignard reagent gives dienes **1a** (R = phenyl) and **1b** (R = 4-methoxybenzyl) as racemates. The racemic mixtures can be resolved by a preparative chiral HPLC to give each enantiomer of **1a** and **1b**.

Structure of a Rhodium Complex Coordinated with 1. A ligand exchange reaction of [RhCl(C$_2$H$_4$)$_2$]$_2$ with (*S*,*S*)-**1a** in chloroform at 50 °C cleanly produced [RhCl((*S*,*S*)-**1a**)]$_2$ and recrystallization of this complex from THF/hexane afforded single crystals suitable for X-ray analysis.[8] The monomeric

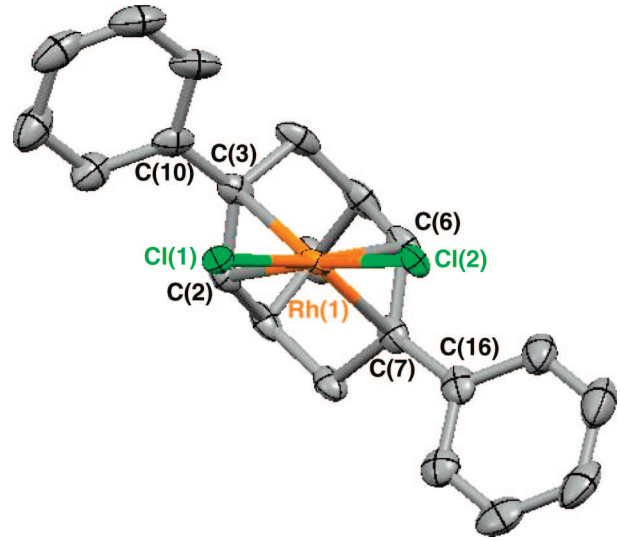
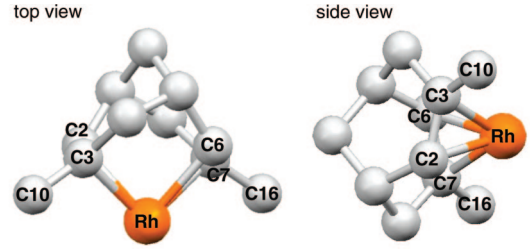
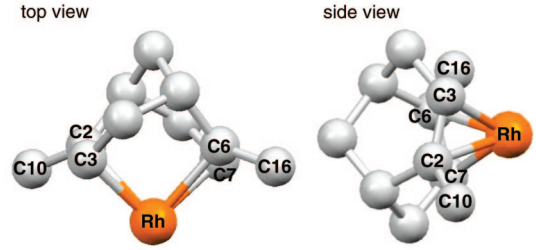


FIGURE 2. X-ray structure of [RhCl((*S*,*S*)-**1a**)]$_2$ with thermal ellipsoids drawn at the 50% probability level (shown as a monomer; hydrogen atoms are omitted for clarity).



Rh–C2 = 2.13 Å, Rh–C3 = 2.14 Å, Rh–C10 = 2.99 Å, C2–C3 = 1.41 Å
∠C2–Rh–C6 = 84°, ∠C3–Rh–C7 = 104°, ∠C10–Rh–C16 = 158°
∠(C2–C3)/(C6–C7) = 21°



Rh–C2 = 2.21 Å, Rh–C3 = 2.09 Å, Rh–C10 = 3.13 Å, C2–C3 = 1.41 Å
∠C2–Rh–C6 = 87°, ∠C3–Rh–C7 = 103°, ∠C10–Rh–C16 = 137°
∠(C2–C3)/(C6–C7) = 23°

FIGURE 3. Selected bond distances and angles for [RhCl((*S*,*S*)-**1a**)]$_2$ (top) and [RhCl((*R*,*R*)-Tol-Bnd*)]$_2$ (bottom).

structure is shown in Figure 2 and its selected bond distances and angles are summarized in Figure 3 along with those of [RhCl((*R*,*R*)-Tol-bnd*)]$_2$ for comparison.[4b] The core bicyclo-[3.3.1]nona-2,6-diene structures are similar between these two complexes: two double bonds C2−C3 and C6−C7 are not parallel but twisted by 21−23°, and as a result, the C3−Rh−C7 angle (103−104°) becomes much larger than that of C2−Rh−C6 (84−87°). Because (*S*,*S*)-**1a** has substituents at C3 and C7, rather than at C2 and C6, the most significant structural difference between [RhCl((*S*,*S*)-**1a**)]$_2$ and [RhCl((*R*,*R*)-Tol-bnd*)]$_2$ is the

(3) Bicyclo[2.2.2]octa-2,5-dienes:(a) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584. (b) Otomaru, Y.; Okamoto, K.; Shintani, R.; Hayashi, T. *J. Org. Chem.* **2005**, *70*, 2503. (c) Shintani, R.; Kimura, T.; Hayashi, T. *Chem. Commun.* **2005**, 3213. (d) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909. (e) Shintani, R.; Okamoto, K.; Hayashi, T. *Org. Lett.* **2005**, *7*, 4757. (f) Hayashi, T.; Tokunaga, N.; Okamoto, K.; Shintani, R. *Chem. Lett.* **2005**, 1480. (g) Chen, F.-X.; Kina, A.; Hayashi, T. *Org. Lett.* **2006**, *8*, 341. (h) Nishimura, T.; Yasuhara, Y.; Hayashi, T. *Org. Lett.* **2006**, *8*, 979. (i) Tokunaga, N.; Hayashi, T. *Adv. Synth. Catal.* **2007**, *349*, 513. (j) Duan, W.-L.; Imazaki, Y.; Shintani, R.; Hayashi, T. *Tetrahedron* **2007**, *63*, 8529. (k) Shintani, R.; Sannohe, Y.; Tsuji, T.; Hayashi, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 7277. (l) Shintani, R.; Ichikawa, Y.; Hayashi, T.; Chen, J.; Nakao, Y.; Hiyama, T. *Org. Lett.* **2007**, *9*, 4643. (m) Sörgel, S.; Tokunaga, N.; Sasaki, K.; Okamoto, K.; Hayashi, T. *Org. Lett.* **2008**, *10*, 589. (n) Defieber, C.; Paquin, J.-F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873. (o) Paquin, J.-F.; Defieber, C.; Stephenson, C. R. J.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 10850. (p) Paquin, J.-F.; Stephenson, C. R. J.; Defieber, C.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 3821. (q) Fessard, T. C.; Andrews, S. P.; Motoyoshi, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 9331. (r) Miura, T.; Murakami, M. *Org. Lett.* **2005**, *7*, 3339. (s) Miura, T.; Murakami, M. *Chem. Commun.* **2005**, 5676. (t) Miura, T.; Takahashi, Y.; Murakami, M. *Chem. Commun.* **2007**, 595.

(4) Bicyclo[3.3.1]nona-2,6-dienes: (a) Otomaru, Y.; Tokunaga, N.; Shintani, R.; Hayashi, T. *Org. Lett.* **2005**, *7*, 307. (b) Otomaru, Y.; Kina, A.; Shintani, R.; Hayashi, T. *Tetrahedron: Asymmetry* **2005**, *16*, 1673.

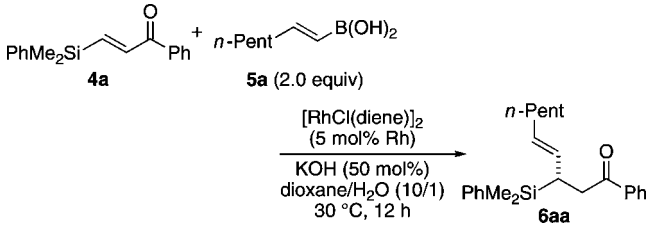
(5) Bicyclo[3.3.0]octa-2,5-dienes: (a) Wang, Z.-Q.; Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336. (b) Helbig, S.; Sauer, S.; Cramer, N.; Laschat, S.; Baro, A.; Frey, W. *Adv. Synth. Catal.* **2007**, *349*, 2331.

(6) Cycloocta-1,5-dienes: (a) Kina, A.; Ueyama, K.; Hayashi, T. *Org. Lett.* **2005**, *7*, 5889 See also. (b) Läng, F.; Breher, F.; Stein, D.; Grützmacher, H. *Organometallics* **2005**, *24*, 2997.

(7) Zalikowski, J. A.; Gilbert, K. E.; Borden, W. T. *J. Org. Chem.* **1980**, *45*, 346. This diketone is also commercially available (e.g, Aldrich).

(8) The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 683881). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

TABLE 1. Rhodium-Catalyzed Asymmetric 1,4-Addition of (*E*)-1-Heptenylboronic Acid (5a) to (*E*)-3-Dimethylphenylsilyl-1-phenyl-2-propen-1-one (4a)



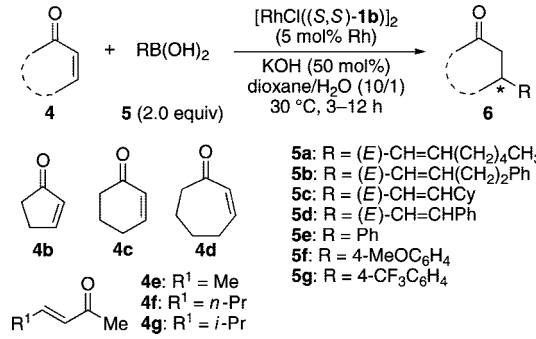
entry	diene	ee (%)[a]
1	(*R*,*R*)-Ph-bod*	52
2	(*R*,*R*)-Bn-bod*	43
3	(*R*,*R*)-Mb-bod*	44
4	(*S*,*S*)-Ph-bnd*	30
5	(*S*,*S*)-Bn-bnd*	6
6	(*S*,*S*)-Mb-bnd*	7
7	(*S*,*S*)-**1a**	75
8	(*S*,*S*)-**1b**	97

[a] Ee was determined by HPLC on a Chiralpak AD-H column with hexane/2-propanol = 100/1.

positions of C10 and C16. Thus, the C10−Rh−C16 angle and the Rh−C10 distance for [RhCl((*S*,*S*)-**1a**)]$_2$ are 158° and 2.99 Å, respectively, whereas the corresponding angle and distance for [RhCl((*R*,*R*)-Tol-bnd*)]$_2$ are 137° and 3.13 Å, respectively. These data clearly show that the substituents on the olefins of (*S*,*S*)-**1a** are indeed located closer to the rhodium metal, thereby creating a more effective C_2-symmetric chiral environment around it compared to previously developed (*R*,*R*)-Tol-bnd*. In addition, the deviation of C10 from the Cl(1)−Rh(1)−Cl(2) plane in [RhCl((*S*,*S*)-**1a**)]$_2$ (1.89 Å) and that in [RhCl((*R*,*R*)-Tol-bnd*)]$_2$ (1.17 Å) are also very different from each other. These structural differences observed here might indicate the possibility of achieving higher stereoselectivity with ligand **1** in the reactions where existing chiral dienes such as bnd* and bod* [3a−m] can induce only moderate enantioselectivity.

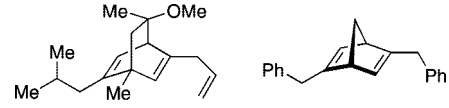
Asymmetric 1,4-Addition Reactions Catalyzed by Rh/(*S*,*S*)-1. To evaluate the potential of newly synthesized ligand **1**, we initially examined a rhodium-catalyzed asymmetric 1,4-addition[9] of linear 1-alkenylboronic acids to β-silyl α,β-unsaturated ketones for the synthesis of chiral allylsilanes,[10] which we previously attempted by using linear 1-alkenylsilicon reagents as the nucleophile, achieving only up to 56% ee with

TABLE 2. Rh/(*S*,*S*)-1b-Catalyzed Asymmetric 1,4-Addition of Organoboronic Acids 5 to α,β-Unsaturated Ketones 4



entry	4	5	product	yield (%)[a]	ee (%)[b]
1	**4a**	**5a**	**6aa**	91	97 (*S*)
2	**4a**	**5b**	**6ab**	72	92 (*S*)
3	**4a**	**5c**	**6ac**	82	87 (*S*)
4	**4a**	**5d**	**6ad**	86	96 (*S*)
5	**4b**	**5d**	**6bd**	94	99 (*R*)
6[c] (ref 3n)	**4b**	**5d**	**6bd**	97	90 (*R*)
7	**4c**	**5a**	**6ca**	91	99 (*R*)
8[d] (ref 2a)	**4c**	**5a**	**6ca**	73	88 (*R*)
9	**4c**	**5d**	**6cd**	95	99 (*R*)
10	**4d**	**5d**	**6dd**	89	99 (*R*)
11[e]	**4e**	**5d**	**6ed**	81	95 (*S*)
12[f] (ref 3n)	**4e**	**5d**	**6ed**	78	89 (*R*)
13[e]	**4f**	**5d**	**6fd**	63	93 (*S*)
14[e,g]	**4g**	**5d**	**6gd**	52	96 (*R*)
15	**4b**	**5e**	**6be**	87	96 (*R*)
16	**4c**	**5e**	**6ce**	91	98 (*R*)
17	**4c**	**5f**	**6cf**	83	98 (*R*)
18	**4c**	**5g**	**6cg**	86	97 (*R*)

[a] Isolated yield. [b] Ee was determined by chiral HPLC with hexane/2-propanol. [c] Data from ref 3n, using (*R*,*R*)-**7** as a ligand at 25 °C. [d] Data from ref 2a, using (*R*,*R*)-Bn-nbd* as a ligand at 50 °C. [e] The reaction was conducted with 3 equiv of **5d** in the presence of 10 mol % catalyst. [f] Data from ref 3n, using (*S*,*S*)-**7** as a ligand at 25 °C. [g] The reaction was conducted at 20 °C.



(*S*,*S*)-Ph-bod* as the ligand.[3l] The reaction of (*E*)-3-dimethylphenylsilyl-1-phenyl-2-propen-1-one (**4a**) with (*E*)-1-heptenylboronic acid (**5a**) was conducted in the presence of a Rh/chiral diene catalyst (5 mol % Rh) at 30 °C and the results are summarized in Table 1. As was the case with linear 1-alkenylsilicon reagents as the nucleophile, the use of (*R*,*R*)-Ph-bod* as the ligand gave 1,4-adduct **6aa** with moderate enantioselectivity (52% ee; entry 1), and somewhat lower ee was observed by using structurally similar (*R*,*R*)-Bn-bod* or (*R*,*R*)-Mb-bod* (43% ee and 44% ee, respectively; entries 2 and 3). The use of (*S*,*S*)-Ph-bnd* resulted in even lower enantioselectivity (30% ee; entry 4), and (*S*,*S*)-Bn-bnd* or (*S*,*S*)-Mb-bnd* also gave **6aa** with low ee (6% ee and 7% ee, respectively; entries 5 and 6). In contrast, significantly higher enantioselectivity was realized by employing (*S*,*S*)-**1a** as the ligand (75% ee; entry 7). The best ee was achieved by changing the substituent of ligand **1** from phenyl to 4-methoxybenzyl ((*S*,*S*)-**1b**) (97% ee; entry 8).[11]

Under the conditions with (*S*,*S*)-**1b** as a ligand, not only 1-heptenyl but some other alkenyl groups can be installed to

(9) For reviews on rhodium-catalyzed asymmetric 1,4-additions, see: (a) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, 1279. (b) Hayashi, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 13. (c) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829. (d) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (e) Bolm, C.; Hildebrand, J. P.; Muñiz, K.; Hermanns, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 3284.

(10) For examples of transition metal-catalyzed asymmetric synthesis of chiral allylsilanes, see: (a) Hayashi, T.; Konishi, M.; Okamoto, Y.; Kabeta, K.; Kumada, M. *J. Org. Chem.* **1986**, *51*, 3772. (b) Hayashi, T.; Han, J. W.; Takeda, A.; Tang, J.; Nohmi, K.; Mukaide, K.; Tsuji, H.; Uozumi, Y. *Adv. Synth. Catal.* **2001**, *343*, 279. (c) Hayashi, T.; Ohno, A.; Lu, S.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 4221. (d) Hayashi, T.; Iwamura, H.; Uozumi, Y. *Tetrahedron Lett.* **1994**, *35*, 4813. (e) Ohmura, T.; Taniguchi, H.; Suginome, M. *J. Am. Chem. Soc.* **2006**, *128*, 13682. (f) Kacprzynski, M. A.; May, T. L.; Kazane, S. A.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 4638. See also: (g) Kacprzynski, M. A.; Kazane, S. A.; May, T. L.; Hoveyda, A. H. *Org. Lett.* **2007**, *9*, 3187.

(11) The methoxy groups were introduced for the purpose of chiral HPLC resolution of **1**.

enone **4a** with high efficiency (72−91% yield, 87−97% ee; Table 2, entries 1−4). Addition of alkenylboronic acids under the present conditions is applicable to various simple α,β-unsaturated ketones as well, and particularly high enantioselectivities are observed for cyclic enones regardless of their ring sizes (99% ee; entries 5, 7, 9, and 10). The use of acyclic enones also gives the 1,4-adducts with high enantioselectivity (93−96% ee; entries 11, 13, and 14), but the chemical yields are somewhat diminished even with a higher catalyst loading. It is worth noting that the enantioselectivities achieved with (*S*,*S*)-**1b** are significantly higher than those reported with ligands (*R*,*R*)- or (*S*,*S*)-**7** (89−90% ee; entries 6 and 12)[3n] and (*R*,*R*)-Bn-nbd* (88% ee; entry 8).[2a] In addition to alkenyl nucleophlies, arylboronic acids can also be employed to give the corresponding β-aryl ketones in high yield and ee (83−91% yield, 96−98% ee; entries 15−18).

Conclusions

We have designed and synthesized 3,7-disubstituted bicyclo[3.3.1]nona-2,6-dienes **1** as new C_2-symmetric chiral diene ligands to provide a different chiral environment from the previously described chiral dienes. These chiral ligands **1** readily bind to rhodium(I) and the rhodium complexes thus obtained act as effective catalysts for 1,4-addition of alkenyl- and arylboronic acids to various α,β-unsaturated ketones, including several combinations that were previously difficult to provide high enantioselectivity.

Experimental Section

Preparation of Chiral Dienes 1. *dl*-3,7-Bis(trifluoromethanesulfonyloxy)bicyclo[3.3.1]nona-2,6-diene (*dl*-3). $KN(SiMe_3)_2$ (46.0 mL, 23.0 mmol; 0.50 M solution in toluene) was slowly added to a solution of bicyclo[3.3.1]nona-3,7-dione (1.52 g, 9.99 mmol) and *N*-(2-pyridyl)triflimide (8.63 g, 24.1 mmol) in THF (30 mL) at −78 °C, and the resulting mixture was stirred for 1 h at −78 °C. The reaction was quenched with saturated aq $NaHCO_3$ and the mixture was warmed to room temperature. After extraction with Et_2O, the organic layer was washed with 10% aq NaOH, dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/20 to afford compound **3** as a white solid (3.39 g, 8.14 mmol; 82% yield (*dl*/achiral = 94/6)).

^{1}H NMR ($CDCl_3$) δ 5.84 (dd, $^3J_{HH}$ = 6.3 Hz and $^4J_{HH}$ = 1.6 Hz, 2H), 2.92−2.86 (m, 2H), 2.68 (dd, $^2J_{HH}$ = 17.2 Hz and $^3J_{HH}$ = 5.5 Hz, 2H), 2.23 (d, $^2J_{HH}$ = 17.4 Hz, 2H), 1.77 (t, $^3J_{HH}$ = 2.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 149.3, 120.9, 118.6 (q, $^1J_{CF}$ = 320 Hz), 32.7, 28.2, 26.7. Anal. Calcd for $C_{11}H_{10}O_2F_6S_2$: C, 31.74; H, 2.42. Found: C, 31.74; H, 2.34.

(1*S*,5*S*)-3,7-Diphenylbicyclo[3.3.1]nona-2,6-diene ((*S*,*S*)-1a). Phenylmagnesium bromide (2.20 mL, 2.18 mmol; 0.99 M solution in THF) was added to a solution of compound **3** (151 mg, 0.363 mmol) and $NiCl_2$(dppp) (3.9 mg, 7.2 μmol) in THF (1.5 mL) at room temperature. The mixture was refluxed for 17 h and the reaction was quenched with saturated aq NH_4Cl at room temperature. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/50 and further purified by GPC with chloroform to afford (±)-**1a** as a white solid (68.8 mg, 0.253 mmol; 70% yield). (±)-**1a** was resolved into each enantiomer by preparative HPLC, using a Daicel Chiralcel OD-H column with hexane/2-propanol = 500/1, flow = 8.0 mL/min. Retention times: 24 min [(1*S*,5*S*)-enantiomer], 30 min [(1*R*,5*R*)-enantiomer]. $[\alpha]^{25}_D$ +27.4 (*c* 0.99, $CHCl_3$). The absolute configuration was determined by X-ray crystallographic analysis of its rhodium complex [RhCl((*S*,*S*)-**1a**)]$_2$ (see Supporting Information for details).

^{1}H NMR ($CDCl_3$) δ 7.38 (d, $^3J_{HH}$ = 7.9 Hz, 4H), 7.29 (t, $^3J_{HH}$ = 7.6 Hz, 4H), 7.21 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.2 Hz, 2H), 6.22 (dd, $^3J_{HH}$ = 6.0 Hz and $^4J_{HH}$ = 1.7 Hz, 2H), 2.90−2.84 (m, 2H), 2.74−2.67 (m, 2H), 2.42 (d, $^2J_{HH}$ = 17.1 Hz, 2H), 1.85 (t, $^3J_{HH}$ = 2.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 142.2, 135.0, 128.7, 128.3, 126.8, 125.3, 33.3, 29.3, 28.4. Anal. Calcd for $C_{21}H_{20}$: C, 92.60; H, 7.40. Found: C, 92.38; H, 7.57.

(1*S*,5*S*)-3,7-Bis(4-methoxylbenzyl)bicyclo[3.3.1]nona-2,6-diene ((*S*,*S*)-1b). 4-Methoxybenzylmagnesium bromide (2.20 mL, 1.45 mmol; 0.66 M solution in THF) was added to a solution of compound **3** (101 mg, 0.243 mmol) and $NiCl_2$(dppp) (2.6 mg, 4.8 μmol) in THF (1.0 mL) at room temperature. The mixture was refluxed for 17 h and the reaction was quenched with saturated aq NH_4Cl at room temperature. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/50 and further purified by GPC with chloroform to afford (±)-**1b** as a white solid (74.7 mg, 0.207 mmol; 85% yield). (±)-**1b** was resolved into each enantiomer by preparative HPLC, using a Daicel Chiralcel OJ column with hexane/2-propanol = 98/2, flow = 15 mL/min. Retention times: 27 min [(1*R*,5*R*)-enantiomer], 43 min [(1*S*,5*S*)-enantiomer]. $[\alpha]^{25}_D$ +158 (*c* 0.99, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ 7.05 (d, $^3J_{HH}$ = 8.7 Hz, 4H), 6.83 (d, $^3J_{HH}$ = 8.7 Hz, 4H), 5.44 (d, $^3J_{HH}$ = 5.2 Hz, 2H), 3.81 (s, 6H), 3.22 (d, $^2J_{HH}$ = 14.8 Hz, 2H), 3.18 (d, $^2J_{HH}$ = 14.8 Hz, 2H), 2.49−2.40 (m, 2H), 2.10 (dd, $^2J_{HH}$ = 16.9 Hz and $^3J_{HH}$ = 5.2 Hz, 2H), 1.72 (d, $^2J_{HH}$ = 17.1 Hz, 2H), 1.62 (t, $^3J_{HH}$ = 2.9 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 157.9, 135.6, 132.6, 129.9, 127.5, 113.7, 55.4, 43.3, 34.1, 29.1, 28.8. Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.29; H, 7.83. Found: C, 83.03; H, 7.96.

Preparation of [RhCl((*S*,*S*)-1)]$_2$. A solution of [RhCl(C_2H_4)$_2$]$_2$ (138 mg, 0.710 mmol Rh) and (*S*,*S*)-**1** (0.620 mmol) in chloroform (30 mL) was stirred for 4 h at 50 °C. The reaction mixture was directly passed through a pad of silica gel with chloroform and the solvent was removed under vacuum to afford crude [RhCl((*S*,*S*)-**1**)]$_2$, which was further purified as described below.

[RhCl((*S*,*S*)-1a)]$_2$. The product was recrystallized from THF/hexane under nitrogen to afford pure [RhCl((*S*,*S*)-**1a**)]$_2$ as red crystals (72% yield). $[\alpha]^{25}_D$ −682 (*c* 0.24, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ 7.70−7.40 (m, 4H), 7.29 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.21 (t, $^3J_{HH}$ = 7.6 Hz, 4H), 4.22 (d, $^3J_{HH}$ = 4.6 Hz, 2H), 3.67 (dd, $^2J_{HH}$ = 15.2 Hz and $^3J_{HH}$ = 3.8 Hz, 2H), 2.26−2.17 (m, 2H), 2.07 (d, $^2J_{HH}$ = 15.3 Hz, 2H), 1.15 (br s, 2H). ^{13}C NMR ($CDCl_3$) δ 144.4, 127.7, 127.6, 127.4, 93.1 (d, $^1J_{CRh}$ = 11.9 Hz), 66.8 (d, $^1J_{CRh}$ = 13.4 Hz), 45.9, 31.6, 27.8. Anal. Calcd for $C_{42}H_{40}Cl_2Rh_2$: C, 61.41; H, 4.91. Found: C, 61.45; H, 4.88.

[RhCl((*S*,*S*)-1b)]$_2$. The product was chromatographed on silica gel with EtOAc/hexane = 1/20 to afford pure [RhCl((*S*,*S*)-**1b**)]$_2$ as an orange solid (81% yield). $[\alpha]^{25}_D$ −182 (*c* 0.20, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ 7.20 (d, $^3J_{HH}$ = 8.5 Hz, 4H), 6.84 (d, $^3J_{HH}$ = 8.6 Hz, 4H), 4.09 (d, $^3J_{HH}$ = 5.7 Hz, 2H), 3.87 (d, $^2J_{HH}$ = 13.9 Hz, 2H), 3.80 (s, 6H), 3.18 (d, $^2J_{HH}$ = 13.8 Hz, 2H), 3.06 (dd, $^2J_{HH}$ = 15.4 Hz and $^3J_{HH}$ = 3.7 Hz, 2H), 2.06−1.97 (m, 2H), 1.89 (d, $^2J_{HH}$ = 15.3 Hz, 2H), 0.81 (br s, 2H). ^{13}C NMR ($CDCl_3$) δ 158.2, 132.9, 129.7, 113.9, 100.4 (d, $^1J_{CRh}$ = 13.4 Hz), 72.1 (d, $^1J_{CRh}$ = 13.4 Hz), 55.4, 47.9, 45.6, 31.3, 27.3. HRMS (ESI-TOF) calcd for $C_{50}H_{56}O_4Cl_3Rh_2$ (M + Cl^-) 1031.1360, found 1031.1382.

Preparation of (1*R*,4*R*)-2,5-Bis(4-methoxybenzyl)bicyclo[2.2.2]-octa-2,5-diene ((*R*,*R*)-Mb-bod*). 4-Methoxybenzylmagnesium chloride (12.0 mL, 3.61 mmol; 0.301 M solution in THF) was added to a solution of *dl*-2,5-bis(trifluoromethanesulfonyloxy)bicyclo[2.2.2]octa-2,5-diene (241 mg, 0.600 mmol) and $PdCl_2$(dppf) (8.8 mg, 12 μmol) in Et_2O (3.0 mL) at room temperature. The mixture was stirred for 9 h at 45 °C and the reaction was quenched with saturated aq NH_4Cl at room temperature. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel preparative TLC with EtOAc/hexane = 1/10 and further purified by GPC with chloroform to afford (±)-Mb-bod* as a white solid (143 mg, 0.412 mmol; 69%

yield). (±)-Mb-bod* was resolved into each enantiomer by a preparative HPLC, using a Daicel Chiralpak AD-H column with hexane/2-propanol = 150/1, flow = 15 mL/min. Retention times: 11 min [(*S*,*S*)-enantiomer], 17 min [(*R*,*R*)-enantiomer]. $[\alpha]^{20}_{D}$ +86.0 (*c* 0.64, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ 7.04 (d, $^3J_{HH}$ = 8.5 Hz, 4H), 6.81 (d, $^3J_{HH}$ = 8.5 Hz, 4H), 5.80 (d, $^3J_{HH}$ = 6.1 Hz, 2H), 3.79 (s, 6H), 3.39 (d, $^2J_{HH}$ = 15.5 Hz, 2H), 3.35 (d, $^2J_{HH}$ = 15.4 Hz, 2H), 3.24−3.22 (m, 2H), 1.26−1.18 (m, 2H), 1.13−1.08 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 158.0, 147.7, 131.9, 130.0, 128.1, 113.7, 55.4, 41.2, 39.4, 26.2. Anal. Calcd for $C_{24}H_{26}O_2$: C, 83.20; H, 7.56. Found: C, 83.22; H, 7.69.

Preparation of (1*S*,5*S*)-2,6-Dibenzylbicyclo[3.3.1]nona-2,6-diene ((*S*,*S*)-Bn-bnd*). Benzylmagnesium bromide (22.0 mL, 24.2 mmol; 1.1 M solution in Et_2O) was added to a solution of *dl*-2,6-bis(trifluoromethanesulfonyloxy)bicyclo[3.3.1]nona-2,6-diene (1.70 g, 4.08 mmol) and $NiCl_2$(dppp) (44 mg, 81 μmol) in THF (15 mL) at room temperature. The mixture was refluxed for 6 h and the reaction was quenched with saturated aq NH_4Cl at room temperature. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/50 and further purified by GPC with chloroform to afford (±)-Bn-bnd* as a white solid (790 mg, 2.63 mmol; 64% yield). (±)-Bn-bnd* was resolved into each enantiomer by a preparative HPLC, using a Daicel Chiralcel OJ column with hexane/2-propanol = 100/1, flow = 14 mL/min. Retention times: 15 min [(*R*,*R*)-enantiomer], 22 min [(*S*,*S*)-enantiomer]. $[\alpha]^{20}_{D}$ −110 (*c* 1.02, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ 7.31−7.27 (m, 4H), 7.22−7.17 (m, 6H), 5.37 (d, $^3J_{HH}$ = 4.9 Hz, 2H), 3.37 (d, $^2J_{HH}$ = 15.0 Hz, 2H), 3.28 (dd, $^2J_{HH}$ = 15.0 Hz and $^4J_{HH}$ = 1.6 Hz, 2H), 2.28−2.21 (m, 4H), 2.02 (dd, $^2J_{HH}$ = 16.2 Hz and $^3J_{HH}$ = 4.0 Hz, 2H), 1.57 (t, $^3J_{HH}$ = 2.4 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 140.7, 140.4, 129.1, 128.3, 126.0, 121.5, 42.6, 30.8, 30.04, 29.96. Anal. Calcd for $C_{23}H_{24}$: C, 91.95; H, 8.05. Found: C, 92.11; H, 8.18.

Preparation of (1*S*,5*S*)-2,6-Bis(4-methoxylbenzyl)bicyclo[3.3.1]nona-2,6-diene ((*S*,*S*)-Mb-bnd*). 4-Methoxybenzylmagnesium chloride (7.31 mL, 6.00 mmol; 0.821 M solution in THF) was added to a solution of *dl*-2,6-bis(trifluoromethanesulfonyloxy)bicyclo-[3.3.1]nona-2,6-diene (415 mg, 0.997 mmol) and $NiCl_2$(dppp) (11 mg, 20 μmol) in THF (2.0 mL) at room temperature. The mixture was refluxed for 20 h and the reaction was quenched with saturated aq NH_4Cl at room temperature. After extraction with Et_2O, the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel preparative TLC with CH_2Cl_2/hexane = 1/1 and further purified by GPC with chloroform to afford (±)-Mb-bnd* as a white solid (252 mg, 0.698 mmol; 70% yield). (±)-Mb-bnd* was resolved into each enantiomer by a preparative HPLC, using a Daicel Chiralcel OD-H column with hexane/2-propanol = 100/1, flow = 12 mL/min. Retention times: 43 min [(*S*,*S*)-enantiomer], 47 min [(*R*,*R*)-enantiomer]. $[\alpha]^{20}_{D}$ −97.3 (*c* 1.05, $CHCl_3$).

^{1}H NMR ($CDCl_3$) δ7.08 (d, $^3J_{HH}$ = 8.5 Hz, 4H), 6.82 (d, $^3J_{HH}$ = 8.7 Hz, 4H), 5.33 (d, $^3J_{HH}$ = 3.8 Hz, 2H), 3.78 (s, 6H), 3.28 (d, $^2J_{HH}$ = 15.0 Hz, 2H), 3.21 (d, $^2J_{HH}$ = 15.0 Hz, 2H), 2.23−2.19 (m, 4H), 2.00 (dd, $^2J_{HH}$ = 16.4 Hz and $^3J_{HH}$ = 4.2 Hz, 2H), 1.54 (t, $^3J_{HH}$ = 2.8 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 158.0, 140.8, 132.8, 130.0, 121.2, 113.8, 55.4, 41.7, 30.8, 30.0. Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.29; H, 7.83. Found: C, 83.26; H, 7.94.

General Procedure for Rh/(*S*,*S*)-1b-Catalyzed Asymmetric 1,4-Addition (Table 2). KOH (0.10 mL, 0.10 mmol; 1.0 M aqueous) was added to a solution of [RhCl((*S*,*S*)-**1b**)]$_2$ (4.7 mg, 10 μmol Rh) in 1,4-dioxane (1.0 mL), and the resulting solution was stirred for 5 min at room temperature. $RB(OH)_2$ **5** (0.40 mmol) and α,β-unsaturated ketone **4** (0.20 mmol) were then added to it, and the resulting mixture was stirred for 3−12 h at 30 °C. After passing through a pad of silica gel with EtOAc, the solvent was removed under vacuum. The residue was purified by silica gel preparative TLC with EtOAc/hexane to afford 1,4-adduct **6**.

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Supporting Information Available: Analytical data for 1,4-adducts **6** and X-ray data for [RhCl((*S*,*S*)-**1a**)]$_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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