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BINAPHTHYLCYCLOPENTADIENE: A C_2-SYMMETRIC ANNULATED CYCLOPENTADIENYL LIGAND WITH AXIAL CHIRALITY

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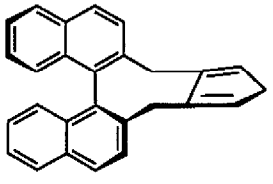
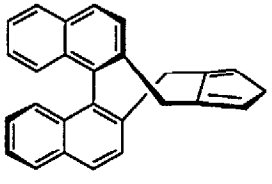
Summary: The asymmetric preparation and metallation of binaphthylcyclopentadiene **1** is described. The key step in this four step synthesis is an asymmetric nickel-catalyzed coupling reaction.

Chiral cyclopentadienyl ligands are becoming recognized as potent chiral auxiliaries for asymmetric organometallic reactions.[1,2] Despite their promise, relatively few chiral cyclopentadienyl ligands have been prepared when compared to the many examples of other chiral ligands such as phosphines, amines and alcohols.[3] Due to the advantages inherent in C_2-symmetric annulated cyclopentadienyl ligands,[4] we are engaged in the design, synthesis and application of such ligands in asymmetric synthesis. In order to provide ligands which are less sterically encumbered than those based on the bicyclo[2.2.2]octane framework,[1a] we undertook the synthesis of a new ligand class based on binaphthyl scaffolding. We report here the facile preparation of either enantiomer of the new C_2-symmetric, axially chiral binaphthylcyclopentadiene ligand **1**.



(S)-(-)-**1**

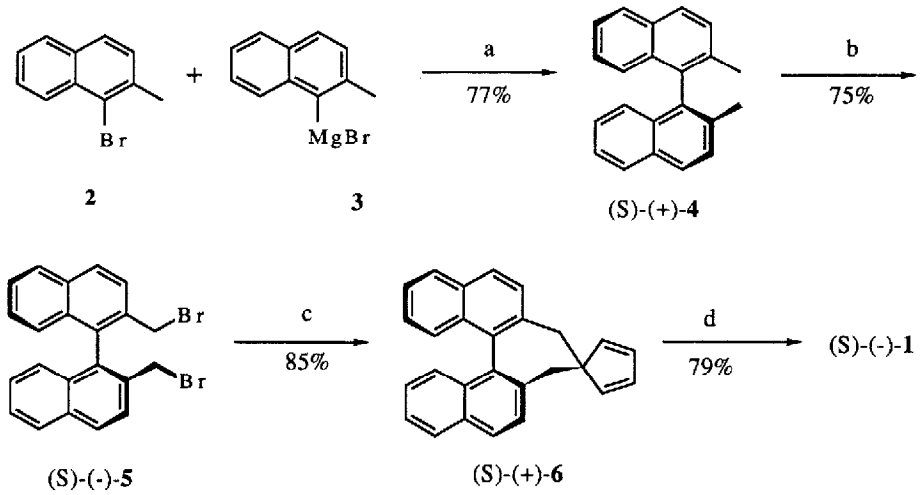


(R)-(+)-**1**

We based our synthetic strategy for the synthesis of **1** on the established bisalkylation of cyclopentadiene[1a,5] by an appropriate binaphthyl moiety. The highly enantioselective coupling of 1-bromo-2-methylnaphthalene (**2**) with its derived Grignard reagent **3** was recently reported to be catalyzed by $NiBr_2$ in the presence of the chiral phosphine PPF-OMe[6] to produce 2,2'-dimethyl-1,1'-binaphthyl (**4**) in 94% enantiomeric excess (Scheme I).[7,8] Taking advantage of this efficient access to the enantiomerically enriched 1,1'-binaphthyl

skeleton, we were able to produce the desired bisalkylating reagent, dibromide **5** via bromination of **4** using N-bromosuccinimide.[7] We have repeated these reactions successfully on 20 g scales. Recrystallization of the dibromide gives enantiomerically pure material (58% yield from **2**). Dibromide (S)-(-)-**5** proved to be a suitable alkylating reagent, forming spirodiene (S)-(+)-**6** in 85% yield upon treatment with cyclopentadiene / sodium hydride. The desired C_2-symmetric, fused, cyclopentadiene (S)-(-)-**1** was produced without racemization[9] by the thermolysis of spirodiene (S)-(+)-**6** in 79% yield.[1a] In addition to the C_2-symmetric diene **1**, a small amount, ca. 3% of a diene isomer was also observed in the ^1H NMR spectrum.[10] The enantiomeric integrity of **1** was established by examining its ^1H NMR spectrum while titrating with a chiral lanthanide-silver shift reagent.[1a,11] This ligand is seen by molecular modeling to be less sterically encumbering than the bicyclo[2.2.2]octane-derived cyclopentadiene ligands.[1a] This four step synthesis produced (S)-(-) -**1** in 40% overall yield from commercially available 1-bromo-2-methylnaphthalene (**2**). The chiral phosphine needed for the asymmetric coupling reaction is available as either enantiomer,[6] enabling a facile, large scale synthesis of both enantiomers of this new chiral cyclopentadiene ligand (S)- or (R)-**1**.

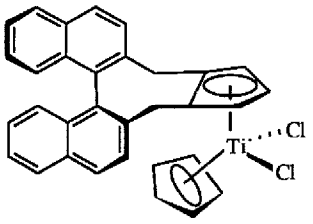
Scheme I[a]



[a]Reagents: (a) $NiBr_2$ (0.03 equiv), (-)-PPF-OMe (0.06 equiv), THF, -5 °C, 5 d; (b) NBS (2.0 equiv), benzoylperoxide (0.02 equiv), CCl_4, hυ, 18 h; (c) cyclopentadiene (1.2 equiv), NaH (2.6 equiv), THF, -30 °C, 2 h; (d) 0.03 M in toluene, 220 °C, 30 h.

In order to demonstrate the suitibility of binaphthylcyclopentadiene **1** as a chiral ligand, we needed to establish that it could be readily metallated. Thus, treatment of the methyllithium-generated anion of cyclopentadiene (S)-(-)-**1** with cyclopentadienyltrichlorotitanium[1a,f] produced the chiral, enantiomerically pure substituted titanocene dichloride (S)-(-)-**7** which was readily characterized spectroscopically.[12] The ^1H NMR

signals due to the four methylene hydrogens are of note in that all are non-equivalent as are those due to the three cyclopentadienyl hydrogens in the substituted ring.



(S)-(-)-**7**

Our facile synthesis of the new axially chiral binaphthylcyclopentadiene ligand (R)- or (S)-**1** by an asymmetric coupling reaction provides the shortest reported access to enantiomerically pure annulated chiral cyclopentadienyl ligands possessing C_2-symmetry. Based on the ease of synthesizing enantiomerically pure **1** and our demonstration of successfully metallating this ligand, we anticipate the widespread use of this chiral cyclopentadiene in new organometallic reagents for asymmetric synthesis. We are pursuing such uses and will report their results in due course.

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References and Notes

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8. Racemic **7** can also be rapidly obtained by a $NiCl_2$ (0.03 equiv) catalyzed coupling of **2** (1 equiv) and **3** (1 equiv) in the presence of PPh_3 (0.06 equiv) (ether, 35 °C, 5 h, 78% yield). Miyano, S.; Okada, S.; Suzuki, T.; Handa, S.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2044.

9. The related 2,2'-dimethyl-1,1'-binaphthyl has a calculated energy barrier to racemization of 35 kcal/mol (Liljefors, T.; Carter, R. E. *Tetrahedron* **1978**, *34*, 1611) and experimentally is configurationally stable at 290 °C (Dixon, W.; Harris, M. M.; Mazengo, R. Z. *J. Chem. Soc. (B)* **1971**, 775).

10. All new compounds were characterized spectroscopically. For example, (S)-(-)-**1**: white crystals (silica gel / petroleum ether), mp 80 °C; IR (thin film) 3060, 2900, 1620, 1600, 1510, 1440, 1370, 1260, 1030, 960, 910, 820, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.5 Hz, 4H), 7.53 (d, J = 8.5 Hz, 2H), 7.43 (ddd, J = 8.0, 6.0, 2.5 Hz, 2H), 7.27 (m, 4H), 6.11 (s, 2H), 3.66 (d, J = 14.0 Hz, 2H), 3.23 (dd, J = 14.0, 1.5 Hz, 2H), 2.83 (d, J = 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.96, 38.79, 125.14, 126.04, 126.80, 127.97, 128.01, 128.20, 128.34, 132.29, 132.42, 135.29, 136.84, 144.69; MS *m/z* (EI, 70 eV, rel intensity) 344 (M^+, 100%), 279 (70), 265 (36); HRMS (EI, 70 eV) calcd for $C_{27}H_{20}$ 344.1565, found 344.1558; $[\alpha]_D^{25}$ -200° (c 0.115, $CHCl_3$).

11. To a solution of **1** (0.04 M in $CDCl_3$) was added portionwise a solution of $Yb(tfc)_3$ (0.10 M) and Ag(FOD) (0.20 M) in $CDCl_3$. The ^1H NMR spectra were recorded. Optimal resolution was achieved at 0.84 equivalents of added shift reagent based on $Yb(tfc)_3$. ^1H NMR (400 MHz, $CDCl_3$) δ 3.37, 3.65 [(S)-(-)-**1**], and 3.45, 3.71 [(R)-(+)-**1**]. Wenzel, T. J.; Sievers, R. E. *J. Am. Chem. Soc.* **1982**, *104*, 382.

12. Red microcrystals ($CHCl_3$/hexane) 24%: mp 312-314 °C; $[\alpha]_D^{25}$ -13.3° (c 0.21, THF); MS, *m/z* (CI, NH_3-CH_4, relative intensity) 543 (M^+ + 15, 51%), 344 (43), 104 (100), 71 (49); ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 4H), 7.63 (d, J = 8.5 Hz, 1H), 7.41 (m, 2H), 7.38 (d, J = 8.5 Hz, 1H), 7.20 (m, 3H), 7.09 (d, J = 8.5 Hz, 1H), 6.67 (t, J = 3.0 Hz, 1H), 6.30 (s, 5H), 6.23 (t, J = 3.0 Hz, 1H), 5.77 (t, J = 3.0 Hz, 1H), 4.16 (d, J = 16.0 Hz, 1H), 3.90 (d, J = 14.0 Hz, 1H), 3.48 (d, J = 14.0 Hz, 1H), 3.45 (d, J = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.52, 35.99, 110.43, 119.81, 120.72, 124.92, 125.47, 125.65, 126.06, 126.49, 126.63, 126.92, 127.10, 128.03, 128.19, 128.36, 128.90, 129.54, 131.94, 132.22, 132.41, 132.61, 133.13, 133.66, 134.95, 135.20, 135.93, 136.95; IR (KBr) 3120, 3060, 2940, 1590, 1510, 1490, 1450, 1370, 1030, 960, 830, 760 cm^{-1}.

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