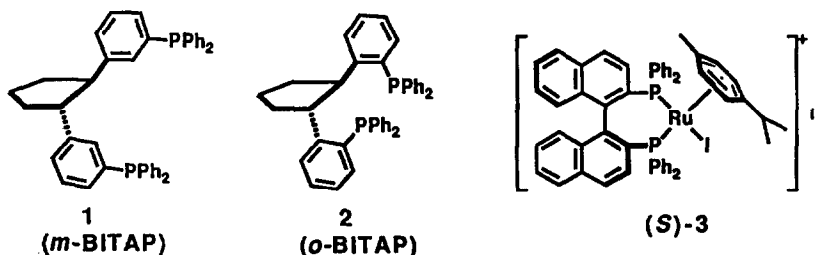


SYNTHESIS OF NEW CHIRAL BIS(TRIARYLPHOSPHINE) LIGANDS BASED ON ASYMMETRIC HYDROGENATION OF 4,5-DIARYL-2-OXOCYCLOPENTANECARBOXYLATES

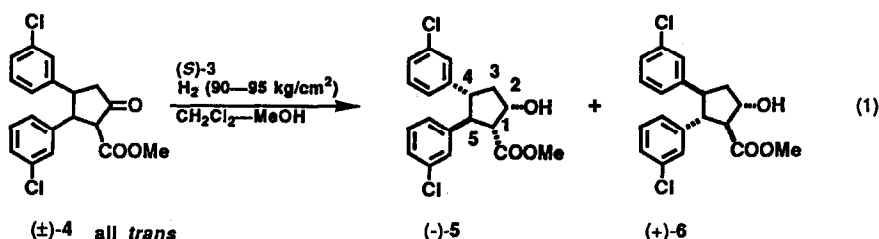
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Summary: New chiral bis(triarylphosphine) ligands, *trans*-bis(3-diphenylphosphino-phenyl)cyclopentane and *trans*-bis(2-diphenylphosphinophenyl)cyclopentane, have been prepared in optically pure forms based on asymmetric hydrogenation of 4,5-diaryl-2-oxocyclopentanecarboxylates catalyzed by the BINAP—Ru(II) complex.

Various kinds of chiral diphosphine ligands have been prepared and their transition metal complexes have been used as catalysts for asymmetric reactions.¹ We reported synthesis of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), an atropisomeric diphosphine, which has been successfully used as chiral ligand for various transition-metal catalyzed asymmetric transformations such as Ru(II)- and Rh(I)-catalyzed asymmetric hydrogenation and 1,3-hydrogen migration.² BINAP is a bis(triarylphosphine), which is one of the characteristics responsible for its high efficiency. The number of chiral, fully arylated diphosphines, however, has been limited. This time, we have prepared two new bis(triarylphosphine) ligands 1 and 2 based on asymmetric hydrogenation of cyclic β -keto esters by use of cationic BINAP—Ru(II) complex 3 as catalyst.^{3,4} The meta-substituted phosphine 1 (abbreviated to *m*-BITAP) will coordinate to metals in a *trans* manner, while formation of *cis*-chelation complex having a large bite angle P—Metal—P is expected for 2 (abbreviated to *o*-BITAP).



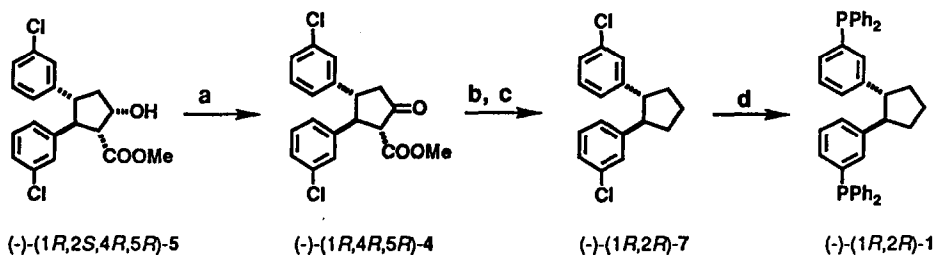
Racemic methyl 4,5-bis(3-chlorophenyl)-2-oxocyclopentanecarboxylate [(\pm)-4] was prepared in one step by the electrochemical cyclodimerization of methyl *m*-chlorocinnamate in 34% isolation yield.⁵ When (\pm)-4 was hydrogenated by use of (*S*)-3 (60 °C, 120 h, H₂ 90—95 kg/cm²), a diastereomeric mixture of (-)-5 and (+)-6 in 1.00:1.16 ratio was obtained quantitatively, which can be easily separated on silica gel column chromatography.^{6,7} The all *trans* structure of (+)-6 has been established by the aid of X-ray crystallography of its *p*-bromobenzoyl derivative.⁸ Oxidation of (-)-5 with CrO₃ followed by recrystallization from methanol gave (-)-4, mp 150—152 °C, [[α]_D³⁰ -155.2° (c



1.12, CHCl_3), 98% *ee*] in 44 % yield. Similar oxidation of (+)-6 gave (+)-4. No racemization has been observed for (+)- and (-)-4 under the catalytic conditions, which shows that the hydrogenation does not belong to dynamic kinetic resolution.⁴

Conversion of the keto ester (-)-4 to the diphosphine (-)-1 $[[\alpha]_D^{30} -139.8^\circ$ (c 0.99, CHCl_3)] was carried out by the procedures shown in Scheme 1. Hydrolysis of (-)-4 followed by decarbonylation and Clemmensen reduction afforded (-)-7 in 55% yield.^{9,10} The optical purity (98%) of (-)-7 was confirmed by HPLC analysis with a chiral column, CHIRALCEL OD (hexane : isopropyl alcohol = 60 : 1). The absolute configuration was determined by conversion of (-)-4 to (+)-(3*R*,4*R*)-3,4-diphenyladipic acid.^{11,12} Treatment of (-)-7 with 1% sodium—lithium alloy in THF at -78 — -60 °C followed by addition of Ph_2PCl afforded (-)-(1*R*,2*R*)-1 in 42% yield.¹³

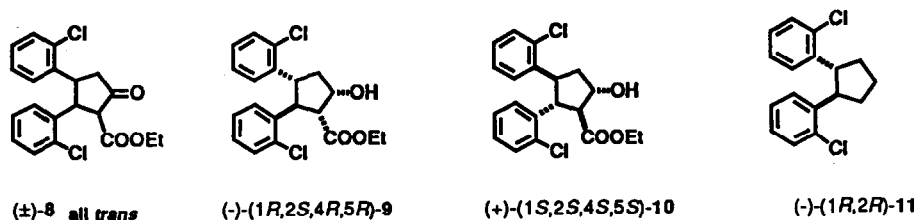
Scheme 1



Reagents and yields: a: CrO_3 , 64% yield. b: HBr , 78% yield. c: HCl — Zn /ether, 71% yield. d: Li (1% Na) dispersion/THF/ -78 °C, then Ph_2PCl , 42% yield.

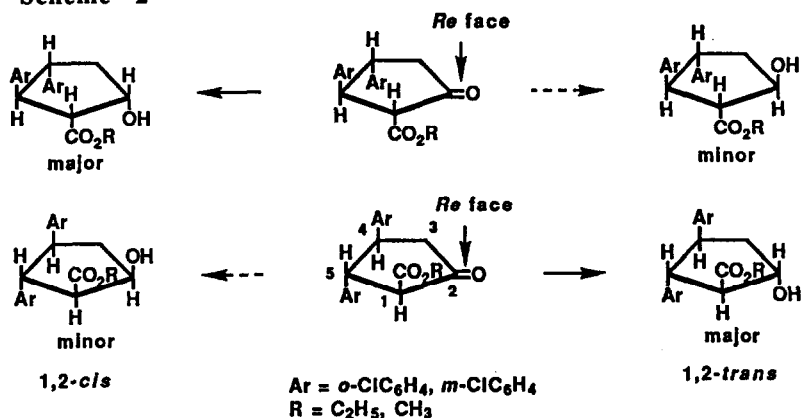
A similar procedure with the *o*-chloro derivative of 4 afforded 2. When the racemic ethyl 4,5-bis(*o*-chlorophenyl)-2-oxocyclopentanecarboxylate (8)¹⁴ was hydrogenated by use of (*S*)-3 (60 °C, 74 h, H_2 90—95 kg/cm^2), a diastereomeric mixture of (-)-9 and (+)-10 was obtained in 1.0:1.6 ratio.^{15,16} The compounds (-)-9 and (+)-10 separated by column chromatography on silica gel have been converted to (-)-8 (97% *ee*) and (+)-8 (61% *ee*), respectively, by CrO_3 oxidation. Simple recrystallization from methanol gave optically pure (+)-8 $[[\alpha]_D^{26} +68.0^\circ$ (c 0.50, CHCl_3)] and (-)-8 $[[\alpha]_D^{24} -66.3^\circ$ (c 1.49, CHCl_3)]¹⁷ in 8% and 13% yield based on (±)-8, respectively.¹⁸

Conversion of (-)-8 to (+)-2 $[[\alpha]_D^{20} +29.6^\circ$ (c 1.02, CHCl_3)] was carried out by the same procedures as shown in Scheme 1. Decarbonylation and Clemmensen reduction of (-)-9 gave (-)-11 in 29% yield,¹⁹ which was lithiated with lithium dispersion in THF at -78 — -60 °C and then treated with Ph_2PCl to afford (+)-2 in 33% yield.²⁰



The stereochemistry of the hydrogenation is shown in Scheme 2, which shows that for both enantiomers the single-handed catalyst bearing (*S*)-BINAP ligand approaches from the *rectus* faces.

Scheme 2



Thus, the present method provides us a convenient route to a new class of chiral bis(triarylphosphine) with *C*₂ chirality. Use of metal complexes of ligands **1** and **2** as catalysts for asymmetric reactions are our further interest.

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- The compound **4** has been prepared by the application of the reported procedure: I. Nishiguchi and T. Hirashima, *Angew. Chem., Int. Ed. Engl.*, **1983**, *22*, 52.
- (-)-**5**: *R*_f = 0.34 (silica gel, CH₂Cl₂). [α]_D³¹ -81.7° (*c* 0.50, CHCl₃) (estimated to be 90% *ee*). ¹H NMR (90 MHz, CDCl₃) δ 2.02 (ddd, *J*_{3a,3b} = 13.9 Hz, *J*_{2,3a} and *J*_{3a,4} = 7.7 Hz and 2.9 Hz, H_{3a}), 2.64 (dt, *J*_{2,3b} = *J*_{3b,4} = 5.3 Hz, H_{3b}), 2.98–3.28 (m, H₁, H₄, and H₅), 3.62 (s, Me), 4.58–4.81 (m, H₂), 6.86–7.26 (m, aromatic protons). Anal. Calcd for C₁₉H₁₈O₃Cl₂: C, 62.48; H, 4.97. Found: C, 62.46; H, 5.01.

7. (+)-6: $R_f = 0.27$ (silica gel, CH_2Cl_2). $[\alpha]_{\text{D}}^{31} +79.0^\circ$ (c 0.65, CHCl_3) (estimated to be 84% *ee*). $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 2.25 (dd, $J_{2,3} = 4.7$ Hz, $J_{3,4} = 8.5$ Hz, H_{3a} and H_{3b}), 3.04 (dd, $J_{1,2} = 9.5$ Hz, $J_{1,5} = 4.2$ Hz, H_1), 3.26—3.57 (m, H_4 and H_5), 3.67 (s, Me), 4.68 (dd, H_2), 7.00—7.19 (m, aromatic protons). Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_3\text{Cl}_2$: C, 62.48; H, 4.97. Found: C, 62.39; H, 4.96.
8. Crystal data for *p*-bromobenzoyl derivative of (+)-6: monoclinic space group A_2 with cell parameters; $a = 20.888(3)$ Å, $b = 7.022(1)$ Å, $c = 18.119(3)$ Å, $\beta = 114.67(1)^\circ$, $U = 2418.5(6)$ Å³; $Z = 4$; $D_{\text{calcd}} = 1.506$; $F.W. = 548.26$. Current R_w value is 5.9%. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, England.
9. (-)-3,4-Bis(3-chlorophenyl)-1-cyclopentanone: $R_f = 0.43$ (silica gel, benzene). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 2.50—2.57 (m, H_{2a} and H_{5a}), 2.83—2.90 (m, H_{2b} and H_{5b}), 3.40—3.51 (m, H_3 and H_4), 6.97—7.26 (m, aromatic protons). Anal. Calcd for $\text{C}_{17}\text{H}_{14}\text{OCl}_2$: C, 63.34; H, 5.31. Found: C, 63.04; H, 5.30.
10. (-)-7: $[\alpha]_{\text{D}}^{27} -201.1^\circ$ (c 1.26, CHCl_3). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.78—1.99 (m, H_3 and H_5), 2.25—2.30 (m, H_4), 2.99—3.07 (m, H_1 and H_2), 7.10—7.26 (m, aromatic protons). Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{Cl}_2$: C, 70.11; H, 5.54. Found: C, 69.94; H, 5.46.
11. The compound (-)-4 ($[\alpha]_{\text{D}}^{28} -131.1^\circ$ (c 1.47, CHCl_3) (84% *ee*) was hydrolyzed with NaOH and then dechlorinated by H_2 —Pd/C to afford (+)-(3*R*,4*R*)-3,4-diphenyladipic acid ($[\alpha]_{\text{D}}^{31} +11.2^\circ$ (c 0.44, EtOH), 78% *ee*).¹²
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13. (-)-1: $[\alpha]_{\text{D}}^{30} -139.82^\circ$ (c 0.99, CHCl_3). $^{31}\text{P NMR}$ (CDCl_3) δ -5.1 ppm. $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 1.61—2.32 (m, H_3 , H_4 , and H_5), 2.80—3.06 (m, H_1 and H_2), 6.92—7.50 (m, aromatic protons). High resolution mass spectrum (FAB) m/z , calcd for $\text{C}_{41}\text{H}_{37}\text{P}_2$ ($\text{M}^+ + \text{H}$); 591.2370, found 591.2306.
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15. (-)-9: $R_f = 0.28$ (silica gel, CH_2Cl_2). $[\alpha]_{\text{D}}^{22} -39.1^\circ$ (c 1.34, CHCl_3). $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 1.03 (t, $J = 7.1$ Hz, Me), 1.91 (ddd, $J_{3a,3b} = 14.3$ Hz, $J_{3a,4} = 7.7$ Hz, $J_{2,3a} = 3.4$ Hz, H_{3a}), 2.79 (ddd, $J_{2,3b} = 6.2$ Hz, $J_{3b,4} = 9.6$ Hz, H_{3b}), 3.19 (dd, $J_{1,5} = 11.2$ Hz, $J_{1,2} = 5.3$ Hz, H_1), 3.48 (d, $J = 2.8$ Hz, OH), 3.89—4.21 (m, CH_2 and H_4), 4.39 (dd, $J_{4,5} = 11.1$ Hz, H_5), 4.74 (ddt, H_2), 6.96—7.80 (m, aromatic protons). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}_3\text{Cl}_2$: C, 63.34; H, 5.31. Found: C, 63.07; H, 5.31.
16. (+)-10: $R_f = 0.18$ (silica gel, CH_2Cl_2). $[\alpha]_{\text{D}}^{31} +18.9^\circ$ (c 1.17, CHCl_3). $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 1.14 (t, $J = 7.1$ Hz, Me), 1.99—2.40 (m, OH and H_3), 2.95—3.13 (m, H_1), 4.01—4.36 (m, CH_2 , H_4 , and H_5), 4.68—4.87 (m, H_2), 6.96—7.60 (m, aromatic protons). Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{O}_3\text{Cl}_2$: C, 63.34; H, 5.31. Found: C, 63.04; H, 5.30.
17. The 100% optical purity of (-)-8 was confirmed by HPLC analysis using a chiral column, CHIRALCEL OD (hexane : isopropyl alcohol = 60 : 1).
18. The absolute configuration of (+)-8 was determined by reduction (treatment with Li dispersion in THF, and then quench with methanol) of (+)-11 to (+)-(1*S*,2*S*)-1,2-diphenylcyclopentane, which was prepared by similar reduction of (+)-(1*S*,2*S*)-7.
19. (-)-11: mp. 126—128 °C. $[\alpha]_{\text{D}}^{22} -4.7^\circ$ (c 0.53, CHCl_3). $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 1.42—2.16 (m, H_3 and H_5), 2.34—2.67 (m, H_4), 3.86—4.11 (m, H_1 and H_2), 7.13—7.59 (m, aromatic protons). Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{Cl}_2$: C, 70.11; H, 5.54. Found: C, 69.90; H, 5.56.
20. (+)-2: mp. 179—181 °C. $[\alpha]_{\text{D}}^{23} +29.6^\circ$ (c 1.02, CHCl_3). $^{31}\text{P NMR}$ (CDCl_3) δ -16.9 ppm. $^1\text{H NMR}$ (90 MHz, CDCl_3) δ 1.12—2.42 (m, H_3 , H_4 , and H_5), 4.14—4.56 (m, H_1 and H_2), 6.47—7.42 (m, aromatic protons). High resolution mass spectrum (FAB) m/z , calcd for $\text{C}_{41}\text{H}_{37}\text{P}_2$ ($\text{M}^+ + \text{H}$); 591.2370, found 591.2367.

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