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SYNTHESIS AND RESOLUTION OF A NEW TYPE OF CHIRAL BISPHOSPHINE LIGAND, trans-BIS-1,2-(DIPHENYLPHOSPHINO)CYCLOBUTANE, AND ASYMMETRIC HYDROGENATION USING ITS RHODIUM COMPLEX

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Oxidative coupling of the 1,4-dicarbanions derived from bis-1,4-(diphenylphosphinyl)butane gave (±)-trans-bis-1,2-(diphenylphosphinyl)cyclobutane. Asymmetric hydrogenation of dehydroamino acids using rhodium complex of the optically active bisphosphine obtained by reduction of the resolved bisphosphine oxide afforded hydrogenated products in high optical yields.

Although a variety of optically active bisphosphines as chelating agents for homogeneous catalysts have been synthesized,¹⁾ most of them have disadvantages such as difficulty and requirement of many steps in the synthesis. On the other hand, we have recently reported a new synthesis of 1,2-bisylidenecyclobutanes using an intermediate 2-(diethoxyphosphinyl)cyclobutylphosphonium ylide.²⁾ In connection with our continuing interest in the synthesis and the utilization of cyclobutanes having phosphorus residues, we developed the simple synthesis of a new type of chiral bisphosphine ligand, trans-bis-1,2-(diphenylphosphino)cyclobutane (abbreviated DPCB) and applied its rhodium complex in asymmetric hydrogenation.

A typical experimental procedure for the synthesis of trans-bis-1,2-(diphenyl-phosphinyl)cyclobutane 2 is as follows.³⁾ To a solution of bis-1,4-(diphenylphosphinyl)butane 1 (11.46 g, 25 mmol) in dry THF was added n-BuLi in hexane (70 mmol) with stirring at 0 °C and the solution was stirred at this temperature for 0.5 h. After dry CuCl (0.50 g, 5 mmol) was added to the solution and the mixture was stirred for 0.5 h, dry CuCl_2 (7.54 g, 55 mmol) was added keeping the temperature at 0 °C. Further, the reaction mixture was stirred at 0 °C for 0.5 h, then the mixture was warmed to room temperature and was continued to stir for 8 h, followed by saturation with O_2 for 0.5 h. After hydrolysis with concd HCl, the reaction mixture was concentrated in vacuo and extracted with CHCl₃, and organic layer was washed with dil. aqueous NH₃ and evaporated. Preparative thin layer chromatography of the residue with ethyl acetate-methanol (19:1) as the eluent gave pure 2^{4} in 4.22 g (37%) yield, mp 214-214.5 °C, together with l-chloro-1,4-di(diphenylphosphinyl)butane 3^{5} (3.45 g, 28%), mp 153-154 °C (Scheme 1).



Similar to the resolution of (±)-Norphos oxide,⁶⁾ treatment of a solution of the racemic mixture of DPCB oxide (3.00 g, 6.6 mmol) in methanol with a stoichiometric quantity of L-(-)-dibenzoyltartaric acid (abbreviated DBT) in methanol resulted in the formation of the precipitate, in which diastereoisomer (-)-DPCB oxide/(-)-DBT is enriched. After separation of (-)-DPCB oxide by KOH-treatment of the precipitate, three times a repetition of the similar resolution procedure for the separated (-)-DPCB oxide gave a 1.40 g (3.1 mmol) yield of pure (-)-DPCB oxide (-)-2, $[\alpha]_D^{22}$ =-7.38° (c 1.25, CH₃OH).⁷⁾ Reduction of the optically pure bisphosphine oxide (-)-2 (2.00 g, 4.4 mmol) in dry benzene (20 ml) with trichlorosilane (1.0 ml, 10 mmol) in a sealed tube (8 h at 110 °C) gave optically active (+)-trans-bis-1,2-(diphenylphosphino)cyclobutane (DPCB) $\underline{4}^{8}$ in quantitative yield, mp 116 °C (from CH₂Cl₂-CH₃OH), $[\alpha]_D^{24}=6.27°$ (c 2.92, CHCl₃).



The absolute configuration of (+)-4 was unambiguously determined by X-ray analysis of its NiCl₂ complex 5. The preparation of the complex 5 was as follows.

Treatment of a solution of (+)-4 (0.50 g, 1.1 mmol) in CH_2Cl_2 with a solution of NiCl_2 (0.14 g, 1.1 mmol) in aqueous ethanol at room temperature, followed by the usual work-up and recrystallization from $CH_2Cl_2-Et_2O$, gave a 0.49 g (80%) yield of pure 5, mp 264.5-266 °C.

Crystal data: $C_{28}H_{26}Cl_2P_2Ni$, M=554.1, triclinic, space group Pl, a=9.635(5), b=9.165(5), c=8.678(4) Å, α =67.12(4), β =95.15(4), γ =109.60(5)°, U=664.4 Å³, Z=1, D_c =1.385 g.cm⁻³. Intensities of 1950 independent reflection were measured ($2\theta_{max}$ =120°) on a Rigaku four-circle diffractmeter using Ni-filtered Cu-K α radiation. The structure was solved by the heavy-atom method and refined by the blockdiagonal least-squares method.⁹⁾ The absolute configuration was confirmed by the Bijvoet method. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms isotropically. Current R-value is 0.075 (R_w =0.090) for 1872 reflections with I>2 σ (I). The atomic scattering factors were taken from Ref. 10. Molecular structure of the complex 5 was illustrated in Fig. 1.



Fig. 1. Molecular structure of the NiCl₂ complex 5. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°) are: Ni-P(1) 2.191(4), Ni-P(2) 2.202(4), Ni-Cl(1) 2.186(4), Ni-Cl(2) 2.192(4); P(1)-Ni-P(2) 90.4(1), P(1)-Ni-Cl(1) 85.8(1), P(2)-Ni-Cl(2) 90.6(2), Cl(1)-Ni-Cl(2) 93.3(2).

With optically pure (+)-DPCB, we have examined the asymmetric hydrogenation of (Z)- α -(benzamido)cinnamic acid and (Z)- α -(benzamido)- β -(4-hydroxy-3-methoxyphenyl)acrylic acid catalyzed by the cationic rhodium (I) complex [Rh·(+)-DPCB· (1,5-COD)]⁺BF⁻₄ (COD: cyclooctadiene). The optical yields of the hydrogenated products, N-benzoyl-(S)-phenylalanine and N-benzoyl-3-(4-hydroxy-3-methoxyphenyl)-(S)-alanine, were found to be 82% ee and 90% ee, respectively, determined by optical rotation¹¹⁾ and by ¹H-NMR (270 MHz) of their methyl esters using a chiral shift reagent.

Thus, trans-bis-1,2-(diphenylphosphinyl)cyclobutane 2 prepared via an intramolecular oxidative cyclization was successfully resolved into an optically pure enantiomer (-)-2. The phosphine oxide (-)-2 can be readily converted into a new type of optically active bisphosphine ligand which is applicable as asymmetric hydrogenation catalyst.

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