



S0957-4166(96)00016-X

Synthesis, Determination of Enantiomeric Purity and Structural Characterisation of Enantiopure (2R,5R)-(+)-2,5-bis-(diphenylphosphino)-hexane, a Chiral DPPB Analogue

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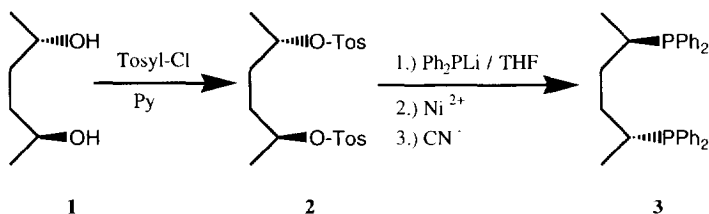
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Abstract: Enantiopure (2R,5R)-(+)-2,5-bis-(diphenylphosphino)hexane, **3**, a chiral analogue of 1,4-bis-(diphenylphosphino)butane was synthesized in two steps from enantiomerically pure (2S,5S)-(+)-hexanediol. The molecular structure of (2R,5R)-**3** was determined by X-ray structure analysis of its nickel-(II)-complex showing a rare dimeric species; NMR analysis of the reaction product of **3** with (+)-di- μ -chloro-bis-{2-[1-(dimethylamino)ethyl]phenyl-*C,N*}-dipalladium allowed to deduce the enantiomeric purity.

Introduction: Diphosphines such as 1,4-bis-(diphenylphosphino)-butane, DPPB, are well established and widely used ligands of various homogeneous transition metal catalysts.¹ Hence, a lot of effort has been put into design and optimisation of their structural, electronic and chemical features. Especially with respect to enantioselective reactions, development of new enantiopure ligands is still of high interest. Our investigations on rhodium catalysed hydroboration have shown that diphosphines like DPPB with a four carbon backbone gave best chemical yields as compared to smaller ligands.² Although the chiral analogues of common 1,2-bis-(diphenylphosphino)-ethane and 1,3-bis-(diphenylphosphino)-propane, Chiraphos and Skewphos, are commercially available, only very recently the preparation of a similar optically active DPPB derivative has been published.³ Here we report an alternative synthesis of enantiopure (2R,5R)-(+)-2,5-bis-(diphenylphosphino)-hexane, the determination of the enantiomeric purity via diastereomeric palladium complexes as well as the molecular structure of its dimeric Ni²⁺ complex.

Results and discussion: The synthesis of diphosphine ligand **3** was achieved by established methods converting enantiomerically pure (2S,5S)-(+)-hexanediol **1** into the corresponding ditosylate **2** which subsequently was reacted with lithium diphenylphosphide to give crude diphosphine **3** (Scheme 1).⁴ Ligand **3** was purified via its Ni²⁺ complex and liberated by addition of sodium cyanide. Final recrystallisation from ethanol gave **3** as a microcrystalline white powder in an overall yield of 53%.⁵

Scheme 1: Synthesis of (2R,5R)-(+)-2,5-bis-(diphenylphosphino)-hexane



To determine the enantiomeric purity, diphosphine ligand **3** was reacted with (+)-di- μ -chloro-bis-{2-[1-(dimethylamino)-ethyl]-phenyl-*C,N*}-dipalladium⁶ and the resulting complex was analysed by NMR-spectroscopy. Both, the ¹H and ³¹P spectra showed that only one of two possible diastereomers was formed, confirming the enantiomeric purity of **3**.⁷ In addition, repeated recrystallisation from ethanol did not change the specific rotation. The absolute configuration of (2*R*,5*R*)-**3** was corroborated by comparison of the CD spectra⁵ of **3** and that of the closely related Skewphos. Surprisingly, the nickel-complex formed^{5,9} was not a monomeric species, like found for most other diphosphine ligands, but dimeric with the two nickel atoms chelated to two molecules of **3** forming a macrocyclic structure⁸ (Figure 1).

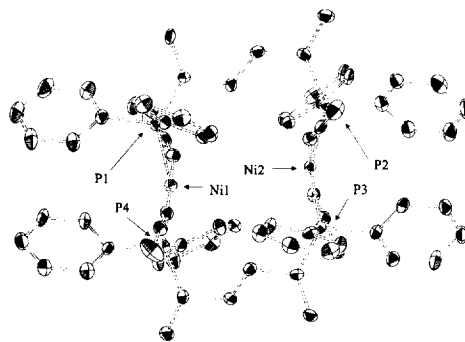


Figure 1: Molecular structure of $[3\text{-Ni}(\text{SCN})_2]_2$

Acknowledgement

Financial support by *Fonds zur Förderung der wissenschaftlichen Forschung* (project : 10474-CHE) is gratefully acknowledged.

References and Notes

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- Synthetic procedure : A solution of 8 mmol of **2**, obtained from **1** and tosylchloride in pyridine (84 % yield, recryst.), in 10 ml THF is added dropwise to a cooled solution of 20 mmol LiPPh₂ in THF and stirred for 16h; water is added and after removal of THF the residue is extracted with ether which subsequently is added to a solution of 2.2g of Ni(ClO₄)₂·6H₂O and 2g NaSCN in 30 ml EtOH and stirred for additional 15 hours. The precipitate is collected, washed, dried (3.4g; 90%) and dissolved in 30 ml THF/EtOH. Aqueous NaCN (1.1g) is added and refluxed until the solution becomes yellow. After workup, the white powder is recrystallised from EtOH to give 1.6g of **3** (70 %).
Selected data for **3** : ¹H-NMR (CDCl₃): δ : 0.92 (6H, dd, 15 Hz, 7 Hz); 1.4 - 1.6 (4H, m); 2.19 - 2.26 (2H, m); 7.29 - 7.36 (8H, m); 7.42 - 7.49 (12H, m); ¹³C-NMR (CDCl₃): δ 15.9 (d, 16 Hz, CH₃); 29.9 (d, 9 Hz, CH); 31.2 (m, CH₂); 128.3 (m, CH); 128.7 (d, 5 Hz, CH); 133.5 (dd, 25 Hz, 19 Hz, CH); 137.2 (t, 13 Hz, C); ³¹P-NMR (CDCl₃): δ -0.7 (s); Anal. Calcd. for C₃₀H₃₂P₂ : C, 79.27; H, 7.10; P, 14.07; Found: C, 79.13; H, 7.28; P, 13.80. [α]_D²¹ : +13.3 ° (c=3.05 in CHCl₃). CD (CH₂Cl₂): [M(Δε)]_D²¹: **3**, [230 (-5.5)]; (2*S*,4*S*)-Skewphos, [230 (+2.9)].
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- ³¹P-NMR (CDCl₃): δ= 46.6 ppm; in case of racemic **3** both diastereomers are formed and observed as well resolved singlets (δ=46.6 and 47.1ppm).
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- Computer programs used: (a) SHELXTL PC: Version 4.1, Siemens Analytical Instruments, Inc., 1990; (b) SHELXL-93: Sheldrick, G. M.; University of Göttingen, 1993; (c) DIFABS: Walker, N.; Stuart, D.; *Acta Crystallogr.*, 1983, A39, 158.