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SYNTHESIS OF PHELLANPHOS, AN EFFICIENT CHIRAL 1,2-DIPHOSPHINE FOR ASYMMETRIC CATALYSIS *

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Summary

A chiral 1,2-diphosphine was prepared in two steps from (-)-a-phellandrene This phosphine phellanphos gives a cationic rhodium complex (phellanphos-cyclooctadienerhodmm hexafluorophosphate) which catalyzes asymmetric reductions. N-Acetylphenylalanme and N-acetylalanme have been prepared in 94—95% enantiomeric excess

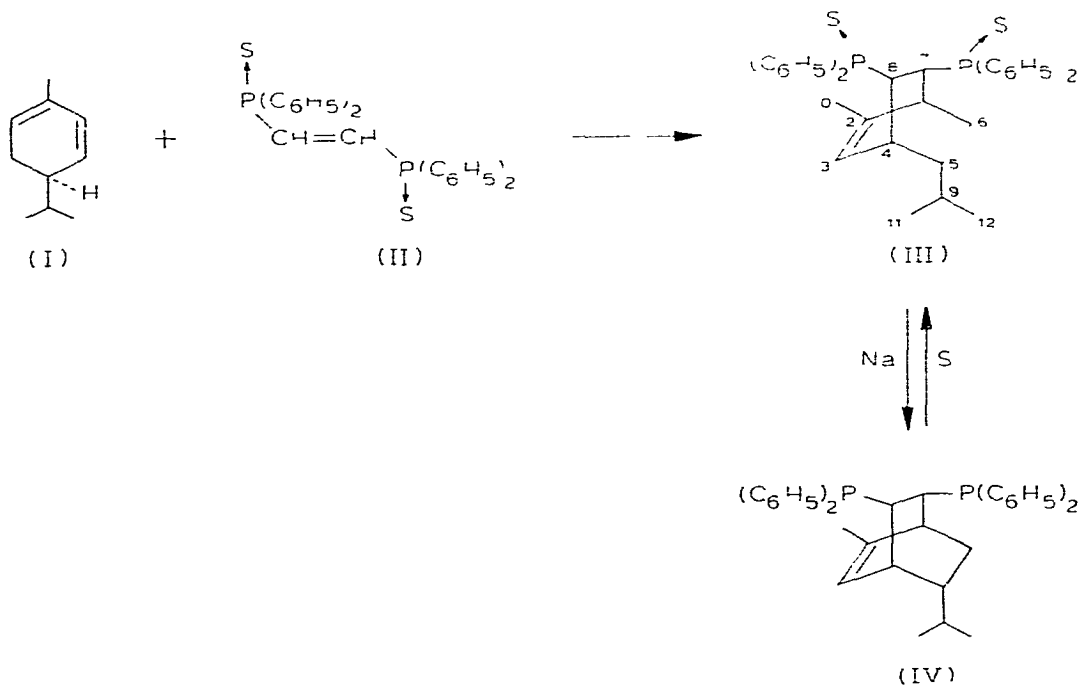
Introduction

Many chiral catalytic systems were obtamed with DIOP, a chiral 1,4-diphosphme [1,2]. The best enantiomeric excess (e e) was in the range 90—92% [3] for some asymmetric hydrogenations Since then many types of chiral 1,4-diphosphines have been prepared, and they are often very useful m asymmetric catalysis ** [2a,2c] More recently 1,2-diphosphines have been synthesized [4,5], and of special interest because of its simplicity is 2,3-bis(diphenylphosphino)butane (chiraphos) studied by Fryzuk and Bosnich [53, unfortunately these types of compound are obtamed in only poor yield because they involve replacement of a vicinal ditosylate or dihalide by a phosphide, and it is difficult to avoid competitive elimination In order to prepare more complicated 1,2-diphosphines than chiraphos it is important to have alternative methods for the introduction of phosphorus atoms m an organic molecule Moreover it is convenient to avoid any resolution step by using a natural product as starting material A good way for creating sunultaneously two asymmetric centers connected to two phosphorus atoms is to start with the P-C=C-P moiety as a Diels-Alder component_ It is known [6] that *trans*-$Ph_2P(O)C{=}CP(O)Ph_2$ under-

* Dedicated to Professor H Normant on the occasion of his 72nd birthday

** For reviews on asymmetric catalysis with various DIOP-complexes see refs 2a—2c

goes a Diels—Alder reaction with cyclopentadiene. We decided to try out such a route to 1,2-diphosphines using a chiral diene. Since phosphine sulfides are known to be much easier to reduce than phosphines oxides [7], we selected *trans*-$Ph_2P(S)C{=}CP(S)Ph_2$ as the dienophile. (—)-α-Phellandrene(I), an easily available monoterpene, was chosen as the chiral diene.



(I) (II) (III) (IV)

Experimental

Chemicals and apparatus

(*E*)-$Ph_2P(S)CH{=}CHP(S)Ph_2$ was prepared according to ref. 8. The (—)-α-phellandrene used originated from a fraction of *Eucalyptus dives* and was kindly given to us by Mane Co., it contained 67% of (—)-α-phellandrene, the other components being α-pinene (2%), *p*-cymene (10%), β-phellandrene (3%). Solvents used in hydrogenation were purified as described in ref. 1. ^1H NMR spectra were recorded in $CDCl_3$ with TMS as internal standard on a R32 Perkin—Elmer spectrometer, and ^{13}C NMR spectra in $CDCl_3$ at 15.08 MHz on a WP-60 Bruker spectrometer using the off-resonance technique.

Polarimetric measurements were performed with a Perkin—Elmer polarimeter model 240. Microanalyses were obtained from CNRS, Centre de Microanalyse at Lyon.

Preparation of Diels—Alder adduct III

A mixture of 7 g of (—)-α-phellandrene and 2.0 g (*E*)-$Ph_2P(S)CH{=}CHP(S)Ph_2$

* Professor H. Brunner (personal communication) informed us that he achieved resolution of the Diels—Alder adduct and was able to prepare the corresponding diphosphine which gives very stereoselective catalysts.

is heated at 160" C for 16 h The resulting brown solution is treated with hexane and the crystals formed are purified by column chromatography on silica (elution by CH_2Cl_2/hexane 1/1) Some $Ph_2P(S)CH{=}CHP(S)Ph_2$ and $Ph_2P(S)$-$CH_2CH_2P(S)Ph_2$ are recovered from the column, being eluted after III The yield is about 700 mg (25%) of pure III. m p >300°C $[\alpha]_D^{20}$ +138° ± 2 (c 1. $CHCl_3$) Analysis Found C, 72 19, H, 6 50, P, 10 51, S, 10 67 $C_{36}H_{28}P_1S_2$ (MW 596 7) calcd. C 72 46, H, 6 42, P, 10 38, S. 10 74%

^{1}H NMR isopropyl group (two doublets at 0 45 and 0 65 ppm), CH_3(C=C) at 1 65 ppm (d, *J* 2 Hz), H(C=C) at 5 35 ppm (d, *J* 7 Hz)

^{13}C NMR Non aromatic carbon atoms of III are numbered from 1 to 10 Then ^{13}C NMR data are described as follows (6 (ppm), d, doublet, q, quartet, *J*(^{13}C^{31}P) coupling constant in Herz) C(10, 11 12) (6 19 S, 20 2, 20 S) C(6) (28 1) triplet in off resonance C(9) (32 5, d, *J* 3), C(S) (36 2, d, *J* 48), C(1) (36 5 d. *J* 3 5), C(4) (39 2, d, *J* 4) C(7) (40 0, q, ^{1}*J* 50, ^{2}*J* 5) *C(5)* (46, d, *J* 14), C(3) (123 4 s), aromatic carbons (6 127—143, multiplet), C(2) (143, d, *J* 14)

Phellanphos (IV)

A mixture of 0 5 g Na and 20 ml toluene is refluxed with vigorous stirring and to the sodium dispersion obtained is added 0 40 g of III in 40 ml hot toluene After 15 h at 110°C the solution is filtered under nitrogen and the solvent evaporated Yield 300 mg (SO%) of a colourless oil which is easily oxidizable

^{1}H NMR Two doublets at 0 75 ppm (isopropyl), doublet (J 3 Hz) at 1 5 ppm (CH_3C=C), doublet at 4 65 ppm (*J* 7 Hz, vinylic proton)

Complex [RhCOD-phellanphos]$^+$[PF_6]$^-$

200 mg of IV in 5 ml CH_2Cl_2 are slowly added to 100 mg $[RhCl(COD)]_2$ in 5 ml CH_2Cl_2 and 150 mg NH_4PF_6 in 3 ml water After stirring under nitrogen 20 mm the organic phase is washed several times with water and evaporated The resulting red solid is treated with 10 ml methanol in which $[RhCl(COD)]_2$ is insoluble $[\alpha]_D^{20}$ +116 4" (c 0 05, $CHCl_3$) Analysis Found C, 58 96, H, 5 71, P, 10 5 $C_{44}H_{50}P_3F_6Rh$ (MW SSS 7) calcd C, 59 47, H, 5.67, P, 10 45%

The complex was obtained as a red material when prepared in complete absence of oxygen Material so prepared was used in the studies described below If oxygen is not carefully excluded, a brown complex is obtained which is less active and less stereospecific

Hydrogenatrom

These were performed at 25°C under one atmosphere of hydrogen in ethanol, according to the general procedure used with the Rhodium-DIOP catalyst [1] The red complex (26 mg, 30 μmol) and the α-aminoacid precursor (3 mmol) were dissolved in ethanol After hydrogen uptake ceased workup gave the crude *N*-acetyl-α-aminoacid in quantitative yield (the NMR showed that all the starting material was consumed) As in ref. 1, optical yields were determined by the values of specific rotation, prior to any crystallisation (*S*)-*N*-Acetylphenylalanine was obtained in *94 5 ± 0.5%* e.e. and (*S*)-*N*-acetylalanine was recovered in 95 ± 1% e.e

Results and discussion

The Diels—Alder reaction between I and II was performed at 160°C and gave III in 25% yield The disulfide III is an easily isolated solid material The yield of the reaction was not optimized The 1,2-bis(diphenylphosphino)ethane disulfide obtained as a by-product (30%) is presumably formed by hydrogen transfer from α-phellandrene to II_ Only one stereoisomer was present in the Drels-Alder adduct. We assigned structure III to this adduct on the basis of its NMR spectrum. The $^3J(^{13}C—^{31}P)$ coupling constants involving C(2) and C(5) are 14 Hz, within the range observed in rigid structures for approximately anticoplanar arrangements [9]. In contrast $^3J(^{13}C—^{31}P)$ for C(3) and C(6) are small. as observed for cisoid conformations [9] These characteristic coupling constants strongly support structure III, which is also favored by comparison of the four competitive transition states of the Diels—Alder reaction Treatment of III with sodium in refluxing benzene gives diphosphine IV in good yield Diphosphine IV can be converted back to III by heating with elemental sulfur Phellanphos IV is readily oxidized, and was stored as the cationic rhodium complex [Rh-COD-phellanphos]$^+$[PF$_6$]$^-$. This orange red complex was prepared by mixing IV in CH_2Cl_2 with $[RhCl(COD)]_2$ and NH_4PF_6 It was used in ethanol as catalyst in homogeneous reduction of (*Z*)-PhCH=C(NHAc)CO_2H and CH_2=C(NHAc)CO_2H at room temperature, under 1 atmosphere of hydrogen (*R*)-*N*-Acetylphenylalanine and (*R*)-*N*-acetylalanine were obtained in quantitative yields in 95% e.e. The turnover numbers (mm^{-1}) are 0 18 and 0 36, respectively_ Phellanphos appears to be amongst the best chiral ligands as far as α-amino synthesis is concerned We are currently investigating its behaviour in other types of reactions as well as using Diels—Alder reactions on chiral dienes for synthesizing new families of chiral phosphines

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