Journal of Organometallic Chemistry, 344 (1988) 249–252
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

Asymmetric Grignard cross-coupling reaction between (E)-β-bromostyrene and 1-phenylethylmagnesium chloride. II *

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(Received September 30th, 1987)

Abstract

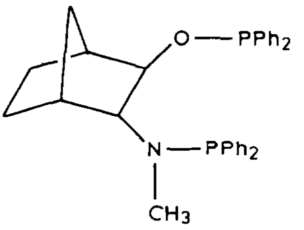
Enantiomers of *cis*- and *trans*-O,N-bis-(diphenylphosphino)-2-hydroxy, 3-methylamino-norbornane have been prepared from the corresponding aminoalcohols and Ph_2PCl. These compounds have been used as ligands for the Pd and Ni complexes and were tested in asymmetric Grignard cross-coupling reaction between (E)-β-bromostyrene and 1-phenylethylmagnesium chloride. Optical yields of up to 13% were obtained.

Introduction

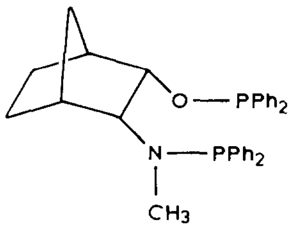
Various types of chiral nickel and palladium complexes, of which the most preferable were those with bidentate P/N and P/P ligands, have been synthesized as catalysts for the asymmetric Grignard cross-coupling of secondary racemic Grignard reagents with vinyl halides to give optically active olefines.

In a previous paper [1] we reported the results of the asymmetric coupling reaction making use of nickel and palladium complexes derived from bicyclic diphosphines.

Here we report the results obtained by two further ligands of the norbornane system containing N–P/O–P donor groups which, to the best of our knowledge, have not been used before in asymmetric cross coupling reactions:



A



B

For part I see ref. 1.

Results and discussion

Preparation

The new ligands *trans*- and *cis*-*O*,*N*-bis(diphenylphosphino)-2-hydroxy, 3-methylamino-norbornane (**A** and **B**) were prepared from the *trans*- and *cis*-2-hydroxy, 3-methylamino-norbornanes, respectively, by reaction with diphenyl chlorophosphine. The preparation of the *trans*-ligand **A**, starting from the 2-*exo*-hydroxy, 3-*endo*-methylamino-norbornane has been described previously [2]. We converted the (+)- and (−)-*trans*-methylamino-norbornanols to their *cis*-isomers, via the *N*-benzoyl derivatives with inverted C2-chirality. This procedure had been applied by Kovar et al. [3] to the racemic aminocyclohexanols and by Pracejus et al. [4] to *trans*-2*R*-methylaminocyclohexan-1*R*-ol and led, in our hands to (+)- and (−)-*cis*-2-*endo*-hydroxy, 3-*endo*-methylamino-norbornanes, respectively.

The existence of only two significant signals in the ^{31}P NMR spectrum of the *cis*-amino-alcohol derivative indicates that there is high stereospecific conversion *.

Palladium and nickel complexes

Well defined solid complexes $PdCl_2$(ligand) were prepared by a ligand exchange reaction of **A** and **B** with dichlorobis(benzonitrile)palladium in benzene solution. In contrast we were unable to isolate an exactly defined complex by the reaction of nickel chloride with either ligand **A** or **B** in dimethyl ether. During complex formation the color changed from green to yellow, then to orange and finally to brick-red. The precipitate was then collected, but in all cases the contents of nickel and chlorine were found to be too high and consequently too low for all other elements. So, the composition of these nickel complexes is uncertain.

Cross-coupling reaction

After the catalyst together with (*E*)-β-bromostyrene and the Grignard reagent had been mixed under argon at −45 ° C, the mixture was stirred at 20 ° C for 20 h. The molar ratio of catalyst/bromostyrene/Grignard reagent was 1/200/400. The values given in Table 1 represent the calculated average of four independent runs.

The isolated palladium complexes $PdCl_2L^\star$ of *trans*-ligand **A** and the *cis*-ligand **B** were examined for their stereoselectivity in the cross-coupling reaction.

The experiments with nickel complexes were difficult. The nickel complexes generated in situ by mixing nickel chloride and ligand in a 1/1 ratio were inactive in this reaction. The isolated but unidentified complexes showed bad reproducibility, though some activity by these ligands in the cross-coupling reaction is evident.

From the comparison of the bicyclic palladium complexes of *trans*- or *cis*-ligand with respect to their optical induction we can state, that the inverted C2-chirality has no significant influence. The chemical yields are unexpectedly different.

The most surprising result, is the reduced enantioselectivity of the nickel catalysts, and especially the very low ee's of the *cis*-ligand **B** complex, with inverted configuration of the reaction product.

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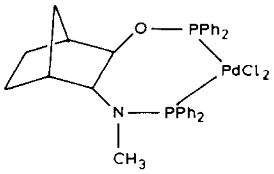
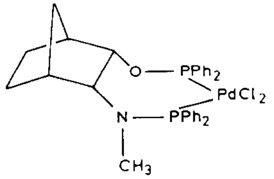
* This *O*,*N*-bis(diphenylphosphino) derivative is an active ligand in the asymmetric hydrogenation of amino acid precursors with nearly 90% ee.

Table 1. Asymmetric cross-coupling of 1-phenylethylmagnesium chloride with (*E*)-*β*-bromostyrene catalyzed by chiral nickel or palladium complexes

Catalyst	Chem. yield (%)	Optical yield (% ee) (config.)	Catalyst	Chem. yield (%)	Optical yield (% ee) (config.)
	90 [a]	13 (*S*)		35	10 (*S*)
Ni/(+)-**A** complex	60–80	4–7 (*S*)	Ni/(+)-**B** complex	50–70	1–2 (*R*)

[a] For a reaction temp. of 0 °C: 85% chem. yield and 14% ee.

Experimental

Optical rotations were measured with a Zeiss-Polamat A. Gas chromatographic data were recorded with a HP 5880 A chromatograph. Toluene was used as an internal standard for the GLC analysis of (*E*)-1,3-diphenyl-1-butene. Details of the reaction analysis have been published previously [1].

(+)- and (−)-cis-2-endo-hydroxy,3-endo-methylaminonorbornane (IIIa and IIIb)

The benzoyl derivatives of (+)- and (−)-*trans*-2-*exo*-hydroxy,3-*endo*-methylaminonorbornane (Ia and Ib) [2] were prepared by use of the general procedure of Leffler and Adams [5], chemical yield 95%, m.p. 150–152 °C.

Ia $[\alpha]_D^{25}$ +57° ($c = 1$, EtOH) Ib $[\alpha]_D^{25}$ −56° ($c = 1$, EtOH). To 10 ml of redistilled thionyl chloride was added in small portions, 5.0 g (0.02 mol) of the *trans*-benzoyl compound Ia or Ib with swirling and cooling during 1 h. The flask was then immersed in a bath at 52–54 °C for 5 h. The reaction mixture was cooled and poured into 200 ml of anhydrous ether, whereupon an oil separated. After standing in the cold for 20 h the ether layer was decanted from the oil. The oil was then dissolved in 50 ml of conc. hydrochloric acid and heated under reflux for 30 h. The solution was chilled, the benzoic acid which crystallized was removed by filtration, and the filtrate evaporated to dryness at 15–20 mmHg. The resulting white residue was crystallized from ethanol/acetone to give 3 g (83% yield) of (+)- or (−)-2-*endo*-hydroxy,3-*endo*-methylamino-norbornane hydrochloride (IIa or IIb), m.p. 270–272 °C.

IIa $[\alpha]_D^{25}$ +5° ($c = 1$, EtOH) IIb $[\alpha]_D^{25}$ −4° ($c = 1$, EtOH).

The hydrochlorides were converted into the free bases (IIIa and IIIb) by treatment with a calculated amount of ethanolic sodium hydroxide at 0 °C. After 2 h at 0 °C, the mixture was filtered to remove sodium chloride, and evaporated to dryness to give 2.2 g (92% yield) white crystals, m.p. 62–64 °C.

IIIa $[\alpha]_D^{25}$ −25° ($c = 1$, EtOH) $[\alpha]_D^{25}$ +15.1° ($c = 1$, benzene)
IIIb $[\alpha]_D^{25}$ +24.8 ($c = 1$, EtOH) $[\alpha]_D^{25}$ −14.5° ($c = 1$, benzene)

*(+)-cis-O,N-bis(diphenylphosphino)-2-endo-hydroxy,3-endo-methylamino-norbornane (ligand **B**)*

To a magnetically stirred solution of 282 mg (2 mmol) of IIIb and 0.79 ml (5.7 mmol) of triethylamine in 8 ml dry benzene was added a solution of 0.71 ml (4 mmol) of Ph_2PCl in 6 ml of benzene at 45–50 °C under argon. The mixture was stirred for 1 h at this temperature and then for 2 h at room temperature. After inert filtration on a small amount of Celite 545 the solvent was removed under reduced pressure to give 850 mg (83%) of an oil, which later crystallized, m.p. 88–100 °C (decomp.). $[\alpha]_D^{25}$ +67.6° ($c = 1.33$, benzene). ^{31}P NMR (vs. H_3PO_4, ppm): $P_{(O)}$ (O-bonded PPh_2) 111.11, $P_{(N)}$ (N-bonded PPh_2) 32.94. Anal. Found: C, 75.75; H, 6.72; N, 2.95; P, 11.68. $C_{32}H_{33}NOP_2$ (509.6) calc: C, 75.36; H, 6.53; N, 2.75; P, 12.15%.

(+)-trans-O,N-bis(diphenylphosphino)-2-exo-hydroxy,3-endo-methylamino-norbornane [2] (ligand A)

$[\alpha]_D^{25}$ +6.7° ($c = 1$, benzene). ^{31}P NMR $P_{(O)}$ 107.34; 107.18. $P_{(N)}$ 52.67; 52.46 (ppm) *.

Preparation of the catalysts

$PdCl_2$[(+)-ligand A]. To a stirred suspension of 322 mg (0.84 mmol) of dichlorobis(benzonitrile)palladium(II) in 10 ml of dry benzene was added a solution of 428 mg (0.84 mmol) of (+)-*O,N*-bis(diphenylphosphino)-2-*exo*-hydroxy,3-*endo*-methylamino-norbornane, $[\alpha]_D^{25}$ +6.7° ($c = 1$, C_6H_6), in 10 ml of benzene under argon. After 6 h at room temperature, the yellow precipitate formed was collected by anaerobic filtration, washed with benzene and dry hexane, and dried in vacuo. The yield of isolated material is about 500 mg (87%) and can be increased by addition of hexane to the filtrate. The complex is analytically pure without further purification and free from traces of starting complex as determined by IR spectroscopy.

Anal. Found: C, 55.40; H, 5.00; Cl, 11.2; N, 2.36; P, 8.6; Pd, 15.89. $C_{32}H_{33}Cl_2NOP_2Pd$ (686.9) calc: C, 55.95; H, 4.84; Cl, 10.32; N, 2.0; P, 9.02; Pd, 15.49%.

$PdCl_2$[(+)-ligand B]. This complex was prepared similarly starting from the isomeric *cis*-ligand (+)-*O,N*-bis(diphenylphosphino)-2-*endo*-hydroxy,3-*endo*-methylamino-norbornane.

Anal. Found: C, 55.75; H, 4.87; Cl, 11.3; N, 2.23; P, 8.5; Pd, 15.54%.

Acknowledgement

The authors thank Mrs. E. Lampe and Mrs. R. Lilienthal for help in the experimental work.

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* The fact that there are two doublets is surprising and has not been observed for the corresponding cyclohexane derivative [4]. To discover the origin of this coupling further investigations are under way.