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

H.-J. Kreuzfeld*, Chr. Döbler

Academy of Sciences of the GDR, Central Institute of Organic Chemistry, Division of Complex Catalysis, Buchbinderstr. 5/6, Rostock 1, DDR 2500 (G.D.R.)

and H.-P. Abicht

Martin-Luther-Universität Halle-Wittenberg, Sektion Chemie, Weinbergweg 16, Halle/Saale, DDR 4050 (G.D.R.)

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Abstract

Trans-2,3-bis-(diphenylphosphinomethyl)-norbornene-(5), *trans*-2,3-bis-(diphenylphosphinomethyl)-7-oxanorbornane, and (−)-/2((*S*)-1-dimethylaminoethyl)-phenyl/-diphenylphosphine have been used as ligands for the nickel and palladium catalyzed asymmetric Grignard cross-coupling reaction giving the coupling product (*E*)-1,3-diphenyl-1-butene.

Chemical yields from 60 to 95% and optical yields up to 40% were obtained, depending on the types of ligand coordinated.

Introduction

The asymmetric Grignard cross-coupling of secondary racemic Grignard reagents with vinyl halides to give optically active olefines has been intensively studied. The use of chiral phosphine and aminophosphine nickel and palladium chloride complexes as catalysts can provide optical yields of up to 83% ee [1–6].

Kellogg and coworkers recently prepared further types of ligands by making use of sulfur-containing amino acids according to a procedure by Kumada [4]. Besides nitrogen- and sulfur-bearing macrocycles they also made compounds containing nitrogen, sulfur, and phosphorus, respectively [7,8].

In continuation of our studies on the structure and efficiency of chiral catalysts we investigated the title reaction in the presence of nickel and palladium chloride complexes of two chiral bicyclic diphosphines [9,10] and the aminophosphine (*S*)-AMPHOS [11].

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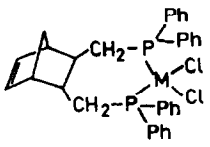
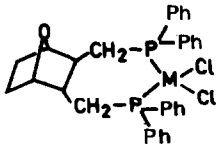


(1)



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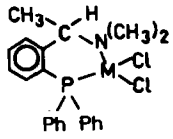


(3)

M = Ni , Pd

It is hoped that the oxygen atom in catalyst **2** has a stabilizing influence during complexation with the Grignard reagent.

As demonstrated by Kumada et al. [5] P/N ligands compared with P/P ligands transfer chirality particularly well. They concluded that a large substituent and a dimethylamino group at the chiral carbon atom would be very efficient. Thus we selected AMPHOS which is similar to the well known PPFA [4], different only in that it has a simple aromatic system as backbone for the donor groups instead of the ferrocene sandwich with its additional chirality.

The formation of the nickel chloride complexes **1** and **2** by mixing the ethanolic solutions of nickel chloride and phosphine under argon, as described by Chatt and Booth [12], leads to well-formed violet crystals. We were, however, unable to isolate nickel complex **3**. The palladium chloride complexes were prepared by a ligand exchange reaction with dichlorobis(benzonitrile)palladium(II) in benzene solution. The compounds isolated pure did not show the nitrile band of the starting complex at 2289 cm^{-1} in its infrared spectrum (Nujol).

It is noteworthy that the formation of the Grignard reagent is always accompanied by a large amount of diphenylbutanes. For this reason the solutions were titrated prior to use and in most cases the real concentration was 60 to 65% of the theoretical.

Results and discussion

With the exception of **3**, where M is Ni, all catalysts were used as isolated complexes. A mixture of catalyst, (*E*)-β-bromostyrene, and the Grignard reagent under argon at −45 °C was stirred for 20 h at 0 °C. The usual molar ratio of catalyst/bromostyrene/Grignard reagent was 1/200/400.

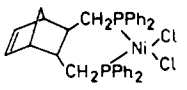
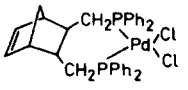
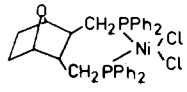
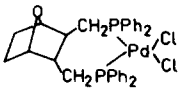
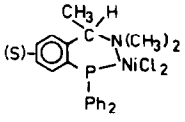
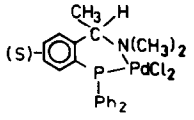
The values given in Table 1 represent the calculated average from six independent runs.

The most surprising result is the very small enantioselectivity of the nickel catalysts, since from the literature the nickel complexes are known to exhibit higher ee's than their palladium counterparts (see for example [5], [13]). The expected stabilizing and selectivity increasing influence of the oxygen atom in catalyst **2** was observed only in the case of the nickel complex. This effect is clear and reproducible, but takes place in a range of insufficient enantiomeric excesses.

From a comparison of the bicyclic palladium complexes with respect to their optical induction, the oxanorbornane derivative turns out to be significantly less effective. So we see that in the nickel catalyzed reaction, ligand **2** is more effective; whereas palladium catalyzed ligand **1** realizes the higher enantioselectivity.

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 (configuration)	Catalyst	Chem. yield (%)	Optical yield % ee (configuration)
	58	2 (S)		62	24 (S)
	60	5 (S)		60	14 (S)
	no reaction	——		95	40 (R)

The best result obtained in this study is an optical yield of about 40% ee under AMPHOS-$PdCl_2$ catalysis. This result is comparable with those found by Kumada et al. [4] for BPPFA-$PdCl_2$, as it induces 46% ee in the same reaction.

As mentioned before all attempts to isolate nickel complex **3** failed. Different nickel(II) salts, such as $NiCl_2 \cdot 4EtOH$, $NiCl_2 \cdot 6H_2O$, and $NiCl_2$ were used, and complex formation using various solvents, such as ethanol, dimethyl ether, dioxane, THF, and benzene, respectively was also attempted. All these experiments were unsuccessful, and the solutions, most of them pale violet in colour, were unreactive to the cross-coupling reaction.

A likely way of circumventing these difficulties seemed to be the ligand exchange reaction, which was used to prepare the palladium complexes. The well formed royal blue crystals of dichlorobis(acetonitrile)nickel(II), described by Kern [14], react with a benzene solution of AMPHOS to give an intense violet solution. But this sample also turned out to be inactive in the cross-coupling reaction.

Experimental

Optical rotations were measured by use of a Zeiss-Polamat A instrument. Gas chromatographic data were obtained using a HP 5880 A chromatograph, equipped with a 12 m quartz capillary, 0.2 mm internal diameter, modified with OV 101, carrier gas argon at 1 ml/min, FID. Toluene was used as an internal standard. The micropreparative isolation of (*E*)-1,3-diphenyl-1-butene was carried out on a Chro-

matron GCHF 18.3-4 chromatograph equipped with a 2 m OV 101 packed column (8% on chromosorb W, AW/DMCS, 80–100 mesh), internal diameter 4 mm, argon 3 ml/min, FID, 160 °C isotherm, 100 injections. The sample thus isolated was found to be 96% pure, based on GLC (HP 5880 A).

The preparation of each ligand has been published previously [9–11]. 1-Phenylethyl alcohol [15], 1-phenylethyl chloride [16], and (*E*)-β-bromostyrene [17] were prepared by published procedures. Solvents were purified and dried over sodium benzophenone-ketyl, and most of the operations were carried out under argon.

Preparation of the catalysts

1-$NiCl_2$. To a solution of 238 mg (1.0 mmol) of $NiCl_2 \cdot 6H_2O$ in 5 ml of ethanol was added a hot solution of 491 mg (1.0 mmol) of *trans*-2,3-bis-(diphenylphosphinomethyl)-norbornene-(5), $[\alpha]_D^{25}$ – 11.9° ($c = 1.0$, benzene), m.p. 78–79 °C, in 100 ml of ethanol.

After 5–6 h at room temperature under argon, the violet crystals that had separated were collected by filtration, washed with ethanol, and dried in vacuo. Yield: 540 mg (87%).

Anal. Found: C, 63.69; H, 5.08; Cl, 12.00; P, 10.1; Ni, 9.15. $C_{33}H_{32}Cl_2NiP_2$ (620.2) calc: C, 63.91; H, 5.20; Cl, 11.43; P, 9.98; Ni, 9.46%.

2-$NiCl_2$. To a solution of 238 mg (1.0 mmol) of $NiCl_2 \cdot 6H_2O$ in 5 ml of ethanol was added a hot solution of 485 mg (1.0 mmol) of *trans*-2,3-bis-(diphenylphosphinomethyl)-7-oxanorbornane, $[\alpha]_D^{25}$ −13.0° ($c = 1.0$, benzene), m.p. 104–108 °C, in 100 ml of ethanol under argon. After isolation, as described above had been carried out, 560 mg (90%) of violet crystals were obtained.

Anal. Found: C, 61.30; H, 5.06; Cl, 11.60; P, 10.5; Ni, 9.10. $C_{32}H_{32}Cl_2NiOP_2$ (624.2) calc: C, 61.58, H, 5.17; Cl, 11.36; P, 9.92; Ni, 9.41%.

1-$PdCl_2$. To a suspension of 236 mg (0.62 mmol) of dichlorobis(benzonitrile)-palladium(II) in 9 ml of dry benzene under argon was added with stirring a solution of 309 mg (0.63 mmol) of *trans*-2,3-bis(diphenylphosphinomethyl)-norbornene-(5) in 8 ml of benzene. After 20 h at room temperature the yellow complex which formed was isolated by filtration under argon, washed with benzene, and dried in vacuo. The complex was used without further purification. Yield: 400 mg (95%).

Anal. Found: C, 59.81; H, 4.93; Cl, 11.10; P, 8.90; Pd, 15.52. $C_{33}H_{32}Cl_2P_2Pd$ (667.9) calc: C, 59.35; H, 4.82; Cl, 10.61; P, 9.28; Pd, 15.93%.

2-$PdCl_2$. To a suspension of 236 mg (0.62 mmol) of dichlorobis(benzonitrile)-palladium(II) in 9 ml of dry benzene under argon was added with stirring a solution of 311 mg of *trans*-2,3-bis-(diphenylphosphinomethyl)-7-oxanorbornane in 8 ml of benzene. After isolation, as described above had been carried out, 350 mg (83%) of a white powder was obtained.

Anal. Found: C, 57.90; H, 4.82; Cl, 10.40; P, 8.78; Pd, 15.30. $C_{32}H_{32}Cl_2OP_2Pd$ (672.3) calc: C, 57.16; H, 4.79; Cl, 10.55; P, 9.21; Pd, 15.89%.

3-$PdCl_2$. To a suspension of 376 mg (0.98 mmol) of dichlorobis(benzonitrile)-palladium(II) in 15 ml of dry benzene under argon was added a solution of 333 mg (1.0 mmol) of (−)-/2((*S*)-1-dimethylaminoethyl)-phenyl/-diphenylphosphine in 20 ml of benzene. The mixture was stirred for two days at room temperature. A yellow powder was isolated by filtration under argon. After the mixture had been stirred with fresh benzene at 50–60 °C for 10 min, and filtered the complex was free from benzonitrile. Yield 420 mg (82%).

Anal. Found: C, 52.31; H, 4.84; Cl, 13.50; N, 2.85; P, 5.80; Pd, 20.31. $C_{22}H_{24}Cl_2NPPd$ (510.7) calc.: C, 51.74; H, 4.74; Cl, 13.88; N, 2.74; P, 6.06; Pd, 20.83%.

Asymmetric Grignard cross-coupling reaction

A 30-ml Schlenk tube containing 8.3 mg (0.0125 mmol) of **1**-$PdCl_2$ was evacuated and filled with argon. After 0.32 ml (2.48 mmol) of (*E*)-β-bromostyrene had been added, and cooled to −70°C, about 10 ml of a filtered and precooled Grignard solution, prepared from 0.5 g of magnesium and 2.68 ml (20 mmol) of 1-phenylethyl chloride in 25 ml of ether, was added. The mixture was then stirred under a slight excess argon pressure for 20 h at 0°C. The reaction was stopped by the addition of 5 ml of 10% hydrochloric acid. The aqueous phase was separated and extracted with 20 ml of ether. After the combined ether solutions had been washed with saturated $NaHCO_3$ solution and water, and dried over Na_2SO_4, the solvent was removed by use of a rotary evaporator. Yield: 1.32 g of an oily product, which contained 23.6% (*E*)-1,3-diphenyl-1-butene (60% chem. yield) based on GLC analysis. The crude product, dissolved in 10 ml of benzene, showed an optical rotation α_D −0.4°. The specific rotation based on this value was $[\alpha]_D^{20}$ −12.8° ($c = 3.12$, benzene). Compared with the highest reported optical rotation [4] the enantiomeric excess is 24.2%. The procedure described was also modified in the following manner. Before removal of the solvent, the ethereal solution was frozen, and at −80°C *meso*-diphenylbutane-(2,3) partly separated out in crystalline state by filtration. After the crystals had been washed with a small amount of precooled ether the filtrate was dried and the solvent removed as described. In a typical run using **3**-$PdCl_2$ the following data were obtained: yield: 0.79 g of an oily product, containing 63.5% of (*E*)-β-1,3-diphenyl-1-butene (96% chem. yield); dissolved in 10 ml of benzene the measured optical rotation was α_D +1.14°, the specific rotation based on this value was $[\alpha]_D^{20}$ +22.4° ($c = 5.0$, benzene), enantiomeric excess: 42%. This result was confirmed after GLC isolation as described before, together with measurement of the optical rotation. The isolated sample (32.2 mg, 96% purity, r.t. 24.6 min) showed an $[\alpha]_D^{20}$ value of +22.0° ($c = 1.24$, benzene) consistent with a 41.6% ee.

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