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Asymmetric Homogeneous Hydrogenation of α-Dicarbonyls using New Rhodium Catalyst

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Asymmetric homogeneous hydrogenations of α-keto esters and α-keto amides of the types $PhCOCO_2ME$, $PhCOCO_2Et$, $PhCOCONHCH_2Ph$, $PhCH_2CH_2COCO_2Et$ and $PhCOCONEt_2$ have been carried out under mild conditions using new cationic rhodium catalyst (6) with cyclohexylated diphosphine ligand.

INTRODUCTION

Homogeneous hydrogenation of carbonyl compounds is expected to be a useful method for the preparation of alcohols[1–4], especially optically active alcohols. Wilkinson type catalysts[5, 6], which are quite active for the hydrogenation of olefins and acetylenes, have not been found as effective catalysts for the hydrogenation of carbonyl compounds. Here the hydrogenations of α-keto esters and α-keto amides have been reported which were found to be catalyzed effectively by cationic rhodium complex with more basic cylohexylated diphosphine ligand.

EXPERIMENTAL

Precautions were taken to exclude moisture and air from chemicals and apparatus. Inert atmosphere was maintained during the experiments by nitrogen gas. THF and diethyl ether were distilled from sodium-benzophenone-ketyl radical and benzene was distilled over sodium wire. Methanol was first distilled over sodium methoxide, then over magnesium methoxide. All the reagents used were of analytical grade and purified either by distillation or crystallization before use. $PhCOCONHCH_2Ph$ was prepared by the literature procedure[7]. IR spectra (ν_{Max} in cm^{-1}) were recorded in nujol mull on a Perkin-Elmer 621 spectrometer. NMR spectra were recorded in $CDCl_3$ on a JEOL FX 90 Q spectrometer using TMS as an internal standard. ^{31}P NMR chemical shifts were reported by using 85% H_3PO_4 as an external standard. Optical rotations were recorded on a Yanaco OR-50 polarimeter in 5 mL chloroform using quartz cell (1 = 0.5).

Oxidation of (+)-Norphos

To a stirred solution of (+)-Norphos (1) (0.003 mole) in acetone (20 mL), hydrogen peroxide (1 mL) (35%) was added dropwise at 0°C. The reaction

mixture was stirred at room temperature for 2 h. The completion of the reaction was checked by TLC. Acetone was completely removed. The obtained oxidized product was mixed with cold water and filtered. Precipitate was washed with water (5 × 20 mL) for complete removal of hydrogen peroxide. The product, (+)-Norphos oxide (2) was dried in air, then in *vacuo*. m.p. 200°C, yield 98% (Found: C, 75.31; H, 5.65; P, 12.50%. $C_{31}H_{28}O_2P$ requires C, 75.30; H, 5.66; P, 12.55%); IR (Nujol): 1155 cm^{-1} ν(P=O); $[\alpha]_D^{25}(CHCl_3)$: +58 (c = 1.08); PMR ($CDCl_3$): 5.9–64 (m, 6H ), 7.2–8.0 (m, 20H, Ph) ^{31}P-NMR ($CDCl_3$): –28.56, –31.81.

Preparation of (+)-Cy-norphos oxide (3)

(+)-Norphos oxide (2) (0.005 mole) was dissolved in dry methanol (8 mL) and placed in an autoclave (50 mL capacity). 5% Rh/C (0.12 g) was added to the solution. Autoclave was purged with hydrogen (three times). The hydrogenation was carried out for 80 h at 110°C and 98 kg/cm^2 hydrogen pressure. Catalyst was removed by filtration through celite. Removal of methanol at reduced pressure gave (+)-Cy-Norphos oxide (3). m.p. 105°C, yield 95% (Found: C, 71.51, H, 9.60; P, 11.90%. $C_{31}H_{50}O_2P_2$ requires C, 71.53; H, 9.61; P, 11.92%); IR (Nujol: 1156 cm^{-1} ν(P=O); $[\alpha]_D^{25}(CHCl_3)$: +29.1 (c = 1.24); PMR ($CDCl_3$): 1.39–1.90 (m, 46H, Cy + CHP), 2.7 (m, 8H, ); ^{31}P-NMR ($CDCl_3$): –65.30, –68.92.

Reduction of (+)-Cy-Norphos oxide into (+)-Cy-Norphos (4)

(+)-Cy-Norphos oxide (0.005 mole) was dissolved in benzene (10 mL) and placed in an autoclave (50 mL capacity). Trichlorosilane (0.01 mole) was added into the autoclave under nitrogen atmosphere. The autoclave was closed carefully and the reaction mixture was heated under pressure at 90°C for 20 h. It was cooled down. The reaction mixture was transferred into another flask. It was cooled down to 10°C and treated with 30% deoxygenated caustic soda solution (10 mL). Aqueous layer was washed with benzene (2 × 5 mL). All the benzene extracts were combined and washed with deoxygenated brine solution (6 mL). Organic phase was dried over anhydrous magnesium sulphate and filtered. All the above work up procedures were done under nitrogen atmosphere. Removal of the solvent yielded (+)-Cy-Norphos (4). The reduced product 4 was sensitive to oxygen. It was treated with excess of carbon disulphide and safely stored as CS_2-adduct (5). Free (+)-Cy-Norphos can be easily and quantitatively recovered by refluxing CS_2-aduct in ethanol and used immediately. Yield 90% (Found: C, 76.25; H, 10.21; P, 12.68%. $C_{31}H_{50}P_2$ requires C, 76.22; H, 10.24; P, 12.70%); $[\alpha]_D^{25}$ ($CHCl_3$): +28.0 (c = 1.04); PMR ($CDCl_3$): 1.40–1.90 (m, 46H, Cy + CHP), 2.71 (m, 8H, ); ^{31}P-NMR ($CDCl_3$): –56.33, –59.34.

Synthesis of cationic rhodium precursor (6)

Rh(COD) (acac) (0.005 mole) and perchloric acid (0.005 mole) were treated with 4 (0.005 mole) in THF (20 mL) at room temperature. The reaction mixture was stirred for 0.45 h. The product was precipitated out by adding ether (200

mL). Crystallization of the product from THF and ether (1:8) gave yellow solid which was used immediately for the hydrogenation. The cationic rhodium complex of (+)-Norphos was also prepared by the same above procedure.

General reaction procedure for the hydrogenation of α-dicarbonyl compounds using 6

In a typical experiment, substrate (1.0 mmol) and catalyst 6 (0.02 mmol) were dissolved in methanol (4 mL) in a stainless steel autoclave (50 mL capacity). The solution was purged three times with hydrogen. Finally the hydrogen pressure was maintained at 25 kg/cm^2. The reaction mixture was stirred at room temperature (25°C) for 40 h. The reduced product was purified from the catalyst by chromatography.

SCHEME 1

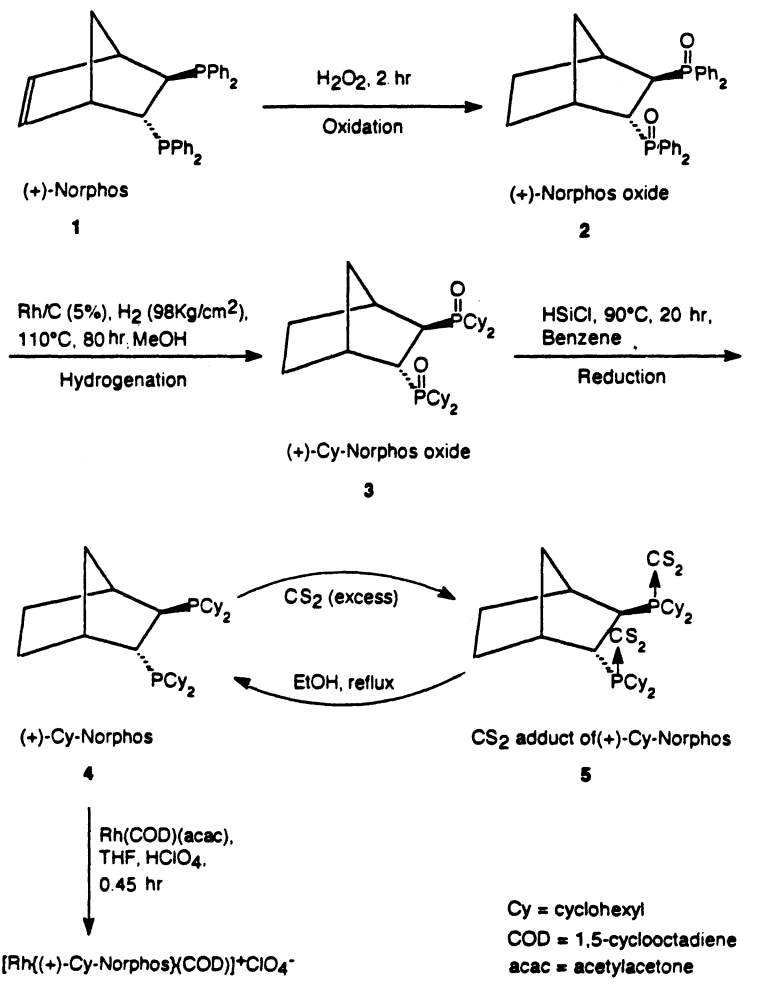

TABLE-1

HYDROGENATION OF α-DICARBONYL COMPOUNDS BY USING RHODIUM(I) COMPLEXES WITH (+)-NORPHOS AND (+)-Cy-NORPHOS[a])

No.	Phosphine ligand	Substrate	Product	Yield (%)	$[\alpha]_D^{25}$	Percentage
1.	(+)-Norphos	$PhCOCO_2Me$	$PhCH(OH)CO_2Me$	89	+6	5.50
2.	(+)-Cy-Norphos	$PhCOCO_2Me$	$PHCH(OH)CO_2Me$	90	+13	11.90
3.	(+)-Cy-Norphos	$PhCOCO_2Et$	$PhCH(OH)CO_2Et$	90	+12	15.00
4.	(+)-Norphos	$PhCOCONHCH_2Ph$	$PhCOCH(OH)NHCH_2Ph$	88	+6	7.50
5.	(+)-Cy-Norphos	$PhCOCONHCH_2Ph$	$PhCOCH(OH)NHCH_2Ph$	87	+34	43.00
6.	(+)-Norphos	$PhCH_2CH_2COCO_2Et$	$PhCH_2CH_2CH(OH)CO_2Et$	90	+2.5	11.98
7.	(+)-Cy-Norphos	$PhCH_2CH_2COCO_2Et$	$PhCH_2CH_2CH(OH)CO_2Et$	89	+3.4	16.29
8.	(+)-Norphos	$PhCOCONEt_2$	PhCH(OH)CONEt	91	+37	30.10
9.	(+)-Cy-Norphos	$PhCOCONEt_2$	PhCH(OH)CONEt	90	+45	36.60
10.	(+)-Norphos	$PhCH_2CH_2COCOO$	—	—	—	—
11.	(+)-Cy-Norphos	—	—	—	—	—

[a]Reaction condition: All the reactions were carried out with 1.0 mmol of substrate and 0.2 mmol of catalyst in 4 mL of methanol. For (+)-Norphos: H_2 pressure = 50 kg/cm^2, Temp. = 60°C, Time = 48 h. For (+)-Cy-Norphos: H_2 pressure = 25 kg/cm^2, Temp. = 25°C (room temperature), Time = 24 h. Concentrations and solvent used for measuring optical rotations of each compound are mentioned under 'Experimental'.

RESULTS AND DISCUSSION

Synthetic route of (+)-cyclohexylated diphosphine [(+)-Cy-Norphos] (4) and its cationic rhodium complex (6) has been shown in Scheme I. Oxidation of (+)-Norphos (1) proceeded smoothly during 2 h. (+)-norphos oxide (2) was hydrogenated in methanol with 98 kg/cm^2 hydrogen pressure at 110°C for 80 h over 5% Rh/C. Reduction of (+)-Cy-Norphos oxide (3) was carried out by trichlorosilane in benzene under nitrogen in an autoclave. The reduced solid product, (+)-Cy-Norphos (4), can be safely stored as a stable carbon disulphide adduct (5). (+)-Cy-Norphos (4) can be easily and quantitatively recovered by refluxing CS_2-adduct in ethanol. The rhodium catalyst precursor (6) was prepared by the reaction of [Rh(COD)(acac) and (+)-Cy-Norphos in the presence of perchloric acid in THF at room temperature and used immediately for hydrogenation.

The results of hydrogenation are summarized in Table-1. As the data in Table-1 show, the reaction condition for the hydrogenation of α-keto esters and α-keto amides are quite milder by cationic rhodium complex with (+)-Cy-Norphos in comparison to rhodium complex with (+)-Norphos. The hydrogenation reaction is markedly dependent on the structure of the substrate used. The stereoselectivity of α-keto amides was found to be better than that of α-keto esters.

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