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Hydroformylation of Alkenes Employing Rhodium(I) Complexes and a Phosphine Oxide Ligand

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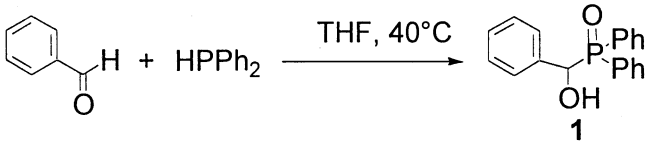
Abstract: Following the facile synthesis of a novel phosphine oxide compound, (diphenylphosphinoyl)phenylmethanol (**1**), this compound was employed as a ligand in the rhodium-catalyzed hydroformylation of alkenes, with good conversions and regioselectivities. This ligand was partially resolved using an enzyme, and enantioselective hydroformylation was carried out with the addition of a rhodium(I) complex. The rhodium(I) complex containing ligand **1** was not isolated, although it was subjected to low-temperature NMR studies.

As hydroformylation is one of the most extensively studied homogeneous catalytic reactions, there has been a large body of research into the ligands used for this transformation. For example, there is increasing interest in the use of mixed bidentate ligands in a variety of metal-catalyzed processes, such as ligands containing P−S, P−N, N−S, N−O, or P−O groups.[1−8] Mixed phosphine−phosphine oxide ligands have been used for the carbonylation of methanol,[9] and mixed amino−phosphine oxide complexes have also out performed their phosphine analogues for the hydroformylation of aryl alkenes.[10,11] However, the use of monodentate phosphine oxides as ligands has received little attention. Indeed, it has been thought that phosphine oxides decrease the rate of hydroformylation and as such have not been further investigated.[12]

We report the successful use of a novel phosphine oxide ligand for olefin hydroformylation. The synthesis of this ligand is extremely facile and the compound is easy to handle due to its lack of sensitivity to air. (Diphenylphosphinoyl)phenylmethanol (**1**) is formed in 67% yield from the reaction of diphenylphosphine and benzaldehyde in tetrahydrofuran (THF) (eq 1).



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This ligand was investigated for the hydroformylation of several substrates catalyzed by chloro(dicarbonyl)-rhodium(I) dimer, and the results are presented in Table 1. The hydroformylation of olefins bearing aryl substituents was performed in chloroform, using a 2:1 ratio of **1**/$[Rh(CO)_2Cl]_2$ and 1:1 CO/H_2 at a total pressure of 600 to 1000 psi and usually at 40 °C. The ratio of substrate to rhodium was 167/1.

The hydroformylation reaction of styrene proceeded well at 40 °C and in good selectivity (96/4 branched/linear aldehydes, Table 1, entry 1). However little conversion occurred at 25 °C (Table 1, entry 2). Note that in the absence of **1**, there is virtually no reaction (Table 1, entry 3). Furthermore, significantly lower conversions, but comparable selectivities (Table 1, entries 4 and 5) were observed if ligand (**1**) was replaced by PPh_3 and $BzP(O)Ph_2$ under the same reaction conditions as entry 1. The hydroformylation reaction, carried out with *p*-methylstyrene and *p*-chlorostyrene as substrates, also proceeded in good conversion and regioselectivity (Table 1, entries 6 and 7). This catalyst system is particularly excellent for phenyl vinyl ether (Table 1, entry 8) and for vinyl benzoate with only the branched aldehyde formed in quantitative yield (Table 1, entry 9). Although the regioselectivity was good for vinyl acetate, the conversion was only 31% (Table 1, entry 10). Nevertheless, the latter result was superior to that obtained using PPh_3 or $BzP(O)Ph_2$ as the ligands (Table 1, entries 11 and 12).

The structure of the active species is not known. The ligand could be coordinated to the rhodium solely through the oxygen of the phosphine oxide or through both the oxygen of the phosphine oxide and the hydroxyl oxygen. It is also conceivable that the ligand may function as a monodenate ligand, with more than one ligand molecule coordinated to the rhodium. Low-temperature ^{31}P NMR suggests that the rhodium is in fact coordinating through the oxygen of the phosphine oxide. All the signals are singlets indicating no coupling to rhodium. A broad singlet at δ 30.9 ppm, recorded at room temperature, splits into two singlets, at δ 32.5 and 48.9, when the spectrum is recorded at −70 °C. The ^{31}P chemical shift of the free ligand (**1**) in DMSO-d_6 occurs at 33.2 ppm, and thus, the chemical shift at 32.5 ppm ($CDCl_3$) was assigned to the phosphorus resonance in the uncoordinated ligand (**1**). These results can be compared to those of Grim and co-workers,[13] who report a complex with phosphine oxide coordination to (1,5−cyclooctadiene)-[bis(diphenylphosphinoyl)(diphenylthiophosphinoyl)-methanido]rhodium(I)-2-propanol. At room temperature, they observe a broad singlet at δ 36.2. However at −50

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TABLE 1. Hydroformylation of Olefins Employing (Diphenylphosphinoyl)phenylmethanol (1)

entry	ligand	substrate[a]	*T* (°C)	pressure[b] (psi)	conversion[c] (%)	(% branched)[d]
1	**1**	styrene	40	600	77	96
2	**1**	styrene	25	600	8	97
3		styrene	40	600	2.5	95
4	PPh_3	sryrene	40	600	15	95
5	$BzP(O)Ph_2$	styrene	40	600	27	96
6	**1**	*p*-chlorostyrene	40	600	93	97
7	**1**	*p*-methoxystyrene	40	600	74	95
8	**1**	phenylvinyl ether	60	600	93	97
9	**1**	vinyl benzoate	50	1000	100	>99
10	**1**	vinyl acetate	40	600	31	97
11	PPh_3	vinyl acetate	40	600	7	90
12	$BzP(O)Ph_2$	vinyl acetate	40	600	26	95

[a] All experiments were run with 2 mmol of substrate, 2 mL of chloroform, 0.012 mmol of $[Rh(CO)_2Cl]_2$, and 0.024 mmol of ligand for 20 h. [b] Total pressure for a 1:1 mixture of CO and H_2. [c] Determined by ^1H NMR/GC. [d] Determined by ^1H NMR/GC, remainder of which is linear aldehyde.

TABLE 2. Enantioselective Hydroformylation

entry	substrate[a]	*T* (°C)	pressure[b] (psi)	time (h)	conversion[c] (%)	(% branched)[d]	% ee of branched aldehyde[e]
1[f]	styrene	40	600	20	15	95	25
2[f]	styrene	60	800	20	22	93	35
3[g]	*p*-chlorostyrene	50	600	20	96	95	23
4[g]	vinyl benzoate	50	1000	20	99	97	52

[a] All experiments were run with 2 mmol of substrate, 2 mL of chloroform, 0.012 mmol of $Rh[(CO)_2Cl]_2$, and 0.024 mmol of ligand. [b] Total pressure always a 1:1 mixture of CO and H_2. [c] Determined by ^1H NMR/GC. [d] Determined by ^1H NMR/GC, remainder of which is linear aldehyde. [e] Determined by the addition of chiral shift reagent into the ^1H NMR sample or chiral GC. [f] Ligand was 18% enantiomerically pure. [g] Ligand was 23% enantiomerically pure.

°C, the singlet splits to give signals at δ 26.5 and 46.3, similar to the data we observed. These results were attributed to the fast exchange between the coordination of the phosphine oxide and then the decomplexation to give the uncoordinated phosphine oxide. Nevertheless, it is conceivable that the labile nature of this ligand explains the excellent regioselectivity seen.

The hydroxyphosphine oxide (**1**) contains a chiral center. The resolution of this alcohol was carried out using porcine pancreatic lipase in a transesterification reaction with methyl propionate. This reaction did not go to completion and therefore the enantiomerically pure alcohol was not obtained, as some racemic alcohol was always present. However, some optically active alcohol with 18−23% ee was extracted from the mixture during two experiments. The optical purity was determined by a combination of chiral HPLC and optical rotation. Several hydroformylation reactions were effected under the same conditions as previously employed using racemic diphenylphosphinoyl)phenylmethanol (Table 2).

With styrene as the substrate, the conversions appear to be lower than with the racemic ligand. However, with both *p*-chlorostyrene and vinyl benzoate (Table 2, entries 3 and 4) the conversions and regioselectivity are comparable to previous hydroformylation reactions. For vinyl benzoate, the enantioselectivity (52%) observed displayed is very encouraging considering the ligand employed is of 23% ee.

In conclusion, (diphenylphosphinoyl)phenylmethanol was prepared and used as a ligand for the rhodium-catalyzed hydroformylation of aryl alkenes. This ligand is not only readily synthesized, but air stable. It enables one to attain aldehydes in high regioselectivity using $[Rh(CO_2)Cl]_2$ as a catalyst.

Experimental Section

(Diphenylphosphinoyl)phenylmethanol. Benzaldehyde (1 mL, 10 mmol) and diphenylphosphine (1.75 mL, 10 mmol) were stirred in a THF (10 mL) solution overnight. The solvent was removed in vacuo, and the resulting off white solid was recrystallized in methanol affording a white crystalline solid (2.069 g, 67%): IR (KBr, cm^{-1}) 3210, 3059, 1435, 1163, 722, 693; ^1H NMR (200 MHz, DMSO-d_6) δ 7.9−7.0 (m, 15H, Ar*H*), δ 5.5 (d, J = 4.6, 1H, C*H*); ^{13}C NMR (75 MHz, DMSO-d_6) 138.1, 131.9 (d, J = 8.5 Hz), 131.6 (m), 131.3 (d, J = 8.8 Hz), 128.3 (d, J = 10.7 Hz), 128.1 (d, J = 10.7 Hz), 127.7 (d, J = 4.4 Hz), 127.5 (d, J = 2.2 Hz), 127.4 (d, J = 2.7 Hz), (Ar*C*), 72.1 (d, J = 86.4 Hz, *C*H); ^{31}P NMR δ 33.2; electrospray MS calc. for $C_{19}H_{17}O_2P$ ($M + H^+$) 309, ($2M + H^+$) 617.

General Hydroformylation. The following is a typical procedure: The catalyst was placed in a stainless steel autoclave with a glass liner equipped with a stirring bar, under a nitrogen atmosphere. The olefin (2 mmol), $[Rh(CO)_2Cl]_2$ (0.012 mmol), and (diphenylphosphinoyl)phenylmethanol (0.024 mmol) were mixed with chloroform (2 mL). The autoclave was purged three times with carbon monoxide, to displace any air, and then charged with a 1:1 ratio of carbon monoxide and hydrogen. The autoclave was placed in an oil bath with sufficient silicone oil to cover the majority of the autoclave and heated to the appropriate temperature. After the reaction was complete, the contents of the autoclave were cooled to room temperature, opened and then passed through a small column of neutral alumina and washed with chloroform. The analysis was carried out without removal of solvent. Identical reaction conditions were employed using 0.024 mmol of benzyldiphenylphosphine oxide or triphenylphosphine as the ligand.

Transesterification of (Diphenylphosphinoyl)phenylmethanol. (Diphenylphosphinoyl)phenylmethanol (0.1 g, 0.325 mmol), methyl propionate (0.035 mL, 0.36 mmol), and porcine pancreatic lipase (0.2 g) were added to diethyl ether (10 mL). This suspension was stirred in a water bath at 30 °C for 3 days. The mixture was then filtered to remove the enzyme and washed with methanol and then ethanol. The washings were concentrated in vacuo to give a white solid.

The experimental data were the same as for the previous compound.

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