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# Chiral rhodium(I)–(polyether-phosphite) complexes for the enantioselective hydroformylation of styrene: homogeneous and thermoregulated phase-transfer catalysis

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## Abstract

Chiral polyether-phosphite ligands derived from (*S*)-binaphtol were prepared and combined with $[Rh(cod)_2]BF_4$ complex. These systems showed high activity, chemo- and regioselectivity, for the catalytic enantioselective hydroformylation of styrene in thermoregulated phase-transfer conditions. ee Values of up to 25% were obtained and recycling was possible, without loss of enantioselectivity. Catalytic activity of the organic and aqueous phases was studied. © 2000 Elsevier Science B.V. All rights reserved.

*Keywords:* Water-soluble phosphite; Two-phase hydroformylation; Asymmetric catalysis; Rhodium(I) complexes; Styrene; Thermoregulated phase-transfer catalysis

## 1. Introduction

Hydroformylation of propylene in biphasic conditions (Ruhrchemie/Rhône-Poulenc's process) has produced approximately 3 million tons of *n*-butanal in 10 years, which proves the importance of the aqueous phase catalysis [1]. In this process, the Wilkinson catalyst $HRh(CO)(PPh_3)_3$ is modified with the water-soluble ligand TPPTS [tris(3-sulfonatophenyl)-phosphine] as sodium salt. However, the use of water as the second phase suffers from drawbacks: severe mass-transfer limitations appear for substrates with low water-solubility, and a large excess of ligand are sometimes necessary to maintain high activity and selectivity [1].

Bergbreiter et al. previously reported a catalytic system based on nonionic water-soluble phosphine–rhodium complexes [2]. With polyoxoethylene-chains as the hydrophilic group, the complex exhibits a special property of inverse temperature-dependent water-solubility [2]. These 'smart ligands' should control the catalytic activity as a function of temperature: the catalyst is soluble in the aqueous phase at temperatures lower than a critical solution temperature called 'cloud point (Tp)' [2,3] and can transfer into the organic phase at higher temperatures. Such a 'thermoregulated phase-transfer catalyst' should be a convenient system for performing the reaction either in aqueous or organic phase, as well as for the recovery of the catalyst. Thermoregulated phase-transfer catalysis has already been successfully applied to the aqueous/organic two-phase hydroformylation of olefins [3]. Jin et al. described a polyether-phosphite molecule derived from catechol as a 'thermoregulated phase-transfer' ligand. Its rhodium complex showed high catalytic activity, chemo- and regioselectivity in the hydroformylation of styrene [4].

Hydroformylation of functionalized vinylarenes followed by oxidation of the resulting aldehydes can give 2-arylpropionic acids, which represent an important class of analgesics [5,6]. Since only one enantiomer is responsible for the biological activity, the preparation of optically pure product is desired [7–10]. Takaya and co-workers published the results of a highly enantioselective hydroformylation of functionalized alkenes with

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a rhodium–(phosphine–phosphite) catalyst (94% ee) [11–13]. At the same time, Babin et al. reported asymmetric hydroformylation of various alkenes with ee values of up to 90% using a rhodium-diphosphite catalyst based on (2*R*,4*R*)-pentane-diol [14,15].

That prompted us to extend the 'thermoregulated phase-transfer' concept to the enantioselective hydroformylation of styrene. The catalytic activity and the enantioselectivity of rhodium complexes of chiral polyether-phosphite ligands derived from (*S*)-binaphtol have been examined. This paper describes the synthesis of new chiral water-soluble phosphite ligands and their properties for the catalytic aqueous/organic two-phase hydroformylation of styrene using Rh(I) complexes.

## 2. Experimental

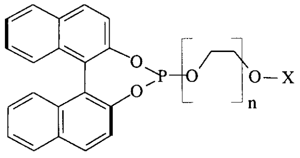
### 2.1. General

All operations were performed under argon atmosphere, using standard Schlenk flask techniques. Solvents were dried and distilled before use.

Melting points (m.p.), noncorrected, were determined with a Kofler apparatus. Elemental analysis (C, H, P) were obtained from the Service Central d'Analyse of the CNRS (Solaize). IR spectra were recorded on a FT Bruker Vektor 22 spectrometer. $^{31}$P-, $^{1}$H- and $^{13}$C-NMR spectra were obtained with a Bruker AC-200 instrument ($^{31}$P 81.015 MHz; $^{1}$H 200.132 MHz; $^{13}$C 50.323 MHz; $\delta$ (ppm); $J$ (Hz); s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; br, broad). Analytical GLC was carried out with a Shimadzu chromatograph fitted with a 15 m EC-5 (SE-54) capillary column or a 30 m β-Dex-225 chiral column (Aldrich, i.d. 0.25 mm). Absolute configuration was determined after reduction with $LiAlH_4$ [15] and comparison with an authentic sample (ACROS). Rotatory power were determined with a Perkin–Elmer 241 polarimeter ($l = 1$ dm; 25°C; concentration in g dm$^{-3}$).

### 2.2. Ligand synthesis

Poly(ethylene glycol)-methyl ether (M*n ca.* 750) or poly(ethylene glycol) (M*n ca.* 200) (Aldrich) were chosen to obtain characterizable molecules, although the polyether chain of average mass 200 is hardly long enough to give a water-soluble molecule. The phosphite ligands, illustrated in Scheme 1, were prepared through conversion of (*S*)-binaphtol to the corresponding phosphochloridite [16]. Slow addition of polyether and triethylamine (THF solution) followed. Filtration of the ammonium chloride and evaporation of the solvent give a foam, which is stripped with dry ether. Separation of the ether phase gives **1** or **2**, as raw products, still containing polyether molecules.



**1** X = Me, n = 16-17

**2** X = $PO_2R$, n = 4-5
[$RO_2H_2$ = (S)-Binol]

Scheme 1.

Complex **1** was obtained as an orange viscous liquid. The estimated cloud point (Tp [2–4]) of the ligand is 100°C [2% (w/w) in water solution]. The yield was corrected to 70% according to the elemental analysis (Calc. for 70% $C_{53.6}H_{80.3}O_{19.3}P$ and 30% $C_{33.6}H_{69.3}O_{17.3}$): C, 58.05 (58.93); H, 7.80 (8.00); P, 2.27% (2.23%). Characteristics of chiral monophosphite ($[\alpha]_D = +67$ ($c = 1.05$; THF)), with different chain-lengths was assessed by NMR and FAB-MS analysis: $^{31}P\{^1H\}$: 143.2–143.1. $^{13}C\{^1H\}$: 152.5–133.5–130.0–129.7–128.6–127.9–127.8–127.6–126.4–126.2–125.8–124.6–124.4–124.2–122.8–121.3–118.1 (arom.); 72.3–71.4–70.0–67.8–65.3 ($CH_2O$); 58.5 ($CH_3$). $^{1}$H: 8.0–7.0 (m, 12H, arom.); 4.1–3.4 (m, 65H); 3.35 (s, 3H, OMe). FAB (NBA) $(M+Na)^+$: 853.1–895.0–939.2–983.2–1027.6–1073.6–1116.0–1159.9–1204.1. IR: $\nu$ (cm$^{-1}$) = 3449 (OH-PEG); 3050 (arom.); 2958; 2870; 1619; 1589; 1507; 1464; 1433; 1384; 1354; 1324; 1213; 1083; 818; 774; 749; 695.

Complex **2** was obtained as an orange viscous liquid. Yield was corrected to 53% according to the elemental analysis (Calc. for 62% $C_{48.3}H_{40.6}O_{9.1}P_2$ and 38% $C_{8.3}H_{18.6}O_{5.1}$): C, 68.08 (67.41); H, 5.50 (5.51); P, 6.47% (6.51%). Characteristics of chiral diphosphite ($[\alpha]_D = +57$ ($c = 1.02$; $CDCl_3$)), with different chain-lengths was assessed by NMR analysis: $^{31}P\{^1H\}$: 140.2–140.1. $^{13}C\{^1H\}$: 152.5–133.5–130.0–129.7–128.6–127.9–127.8–127.6–126.4–126.2–125.8–124.6–124.4–124.2–122.8–121.3–118.1 (arom.); 72.3–71.4–70.0–67.8–65.3 ($CH_2O$). $^{1}$H: 8.0–7.0 (m, 24H, arom.); 3.8–3.4 (m, 16.5H). IR: $\nu$ (cm$^{-1}$) = 3436 (OH-PEG); 3055 (arom.); 2953; 2870; 1620; 1589; 1505; 1462; 1432; 1398; 1328; 1273; 1212; 1069; 1043; 947; 820; 769; 748; 695.

### 2.3. Hydrogenation of itaconic acid

According to the principle of cloud point of the nonionic surfactants, thermoregulated phase separation or precipitation occurs in aqueous system [3]. Increasing molecular weight of a polyethylene glycol induces an increase of the temperature of precipitation from water. Jin et al. reported the cloud points of various polyether-based ligands and of some of their rhodium complexes [3,4]. The activity of the catalyst was measured at various temperatures until the precipitation occurs and the reaction stops. This represents a convenient method to determine the cloud point of a complex [2–4].

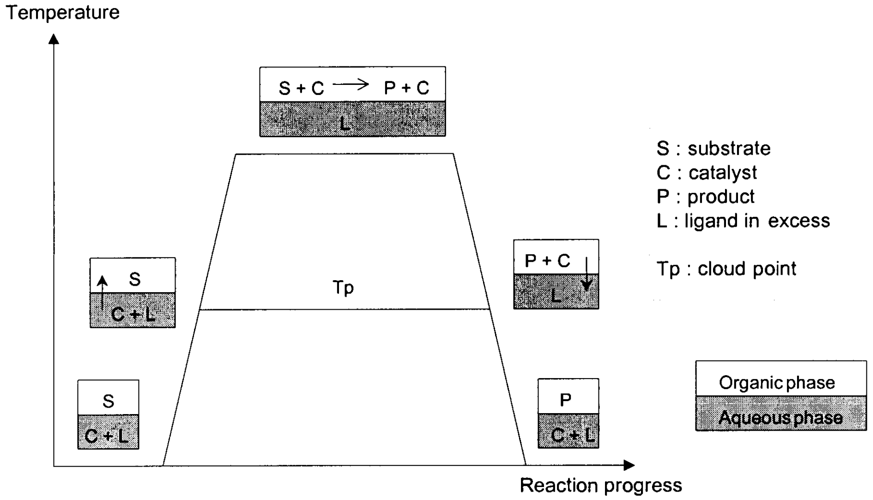


Fig. 1. General principle of thermoregulated phase-transfer catalysis with organometallic species.

The hydrogenation was carried out in a 250 ml double-walled glass flask (Büchi) connected to a Büchi pressflow gas controller. Itaconic acid (5.2 g, 40 mmol), $RhCl_3 \cdot 3H_2O$ (5 mg, 0.02 mmol, acid/Rh = 2000), ligand and water (150 ml, [Rh] = $1.5 \times 10^{-4}$ M) were added to the reactor under argon atmosphere. The system was purged three times with $H_2$, pressurized at 4 bar $H_2$ and checked for leaks. The reactor was then heated or cooled at a precise reaction temperature and the $H_2$ uptake was monitored. The total pressure was maintained at 4 bar during the reaction. After collecting the experimental data, the aqueous solution was acidified to pH 1 and extracted with ether. The organic layer was washed with brine and dried over magnesium sulfate. $SOCl_2$–MeOH was added to the resulting organic layer and the mixture was stirred for 3 h, washed with brine and dried over magnesium sulfate. The resulting ester is used to determine the enantiomeric excess.

### 2.4. Hydroformylation

As the reaction proceeds both in aqueous and organic systems, the experiments were performed in homogeneous as well as in biphasic conditions.

#### 2.4.1. Homogeneous phase experiments

In a typical experiment, a 25 ml stainless-steel autoclave was purged with argon, filled with the catalytic system (4 to $30 \times 10^{-6}$ mol Rh), dry dichloromethane (4 ml) and styrene (2 ml), pressurized with CO–$H_2$ (1:1) and heated. After a selected reaction time (6–96 h), the autoclave was cooled and depressurized. The reaction mixture was analyzed by GC.

#### 2.4.2. Biphasic experiments and recycling

In a typical experiment a 25 ml stainless-steel autoclave was purged with argon, filled with the catalytic system ($18 \times 10^{-6}$ mol Rh), water (4 ml) and styrene (2 ml), pressurised with CO–$H_2$ (1:1) and heated. After a selected reaction time (6–24 h), the autoclave was cooled and depressurized. The reaction mixture looks like a white emulsion. Pentane (ca. 8 ml) was used to transfer the whole emulsion from the autoclave in a Schlenk flask. The organic layer was then separated and the aqueous phase was extracted with pentane (ca. 5 ml). The white aqueous phase was reintroduced into the same autoclave filled with styrene (2 ml) for a further run. The organic layer (ca. 15 ml) was analyzed as for homogeneous experiments and a 2 ml sample was introduced into another autoclave already filled with water (4 ml) and styrene (2 ml) for a new run in biphasic conditions.

## 3. Results and discussion

### 3.1. Cloud point of the catalysts

According to Bergbreiter [2], ‘smart materials’ undergo physical property changes in response to a stimulus, for instance a phase change. Polyether containing molecules are known to have inverse temperature-dependent solubilities in water. Thermoregulated phase separation or precipitation occurs in aqueous systems on heating above the cloud point. Thus the cloud point could be easily estimated [2–4] (Fig. 1).

Lengthening the polyether chains in a molecule is known to increase its water solubility. The cloud point is also dependent on the molecule concentration in the water solution [2]. The exact cloud point of the rhodium catalyst formed using **1** as the ligand is determined by itaconic acid hydrogenation experiments (Fig. 2).

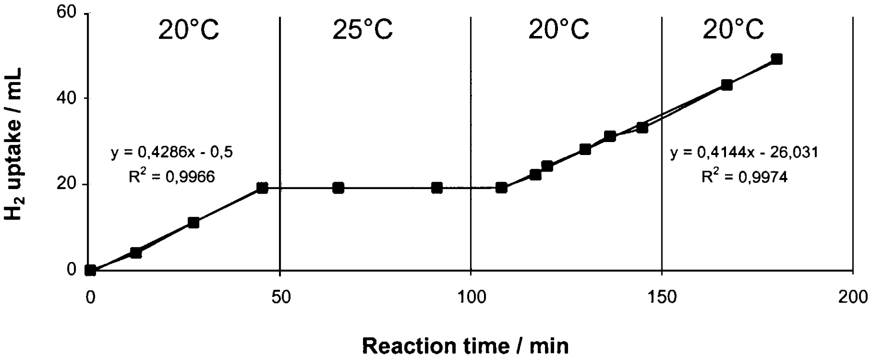


Fig. 2. Hydrogenation of itaconic acid in aqueous system under 4 bar $H_2$ using $RhCl_3{\cdot}3H_2O$/**1** as catalyst. Cloud point of the reactive solution is 22°C; [Rh]: $1.5\times10^{-4}$ M, P/Rh = 10.

Catalytic hydrogenation of itaconic acid was performed under a constant pressure of hydrogen (4 bar), using a complex prepared in situ from $RhCl_3{\cdot}3H_2O$ and ligand **1**. The catalytic activities were observed at various temperatures, according to the amount of $H_2$ consumed.

Fig. 2 shows that when the reaction temperature is below the cloud point of the catalyst, namely 22°C, hydrogenation occurs (ee < 5%). The solution is then clear, while when the temperature is kept above the cloud point (25–50°C), the reaction stops and the reaction medium is cloudy. If the temperature is lowered under the cloud point, the reaction resumes and the solution is clear again. The reaction rate indicates that degradation does not occur. Similar phenomena have already been reported [2–4]. If an extra organic phase containing a water-immiscible substrate is added to the reaction system, the catalyst is extracted from the aqueous phase on heating above its Tp and is transfered into the organic phase. The reaction would then take place into the organic phase.

### *3.2. Thermoregulated phase-transfer enantioselective hydroformylation of styrene*

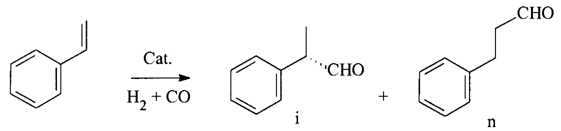
Catalytic reactions were carried out both in homogeneous and biphasic conditions to give a mixture of the branched (*i*, 2-phenylpropanal) and normal (*n*, 3-phenylpropanal) regioisomers (Scheme 2). Only traces of the hydrogenated product were observed (ethylbenzene < 1%) [7–10]. Babin et al. have already reported that the monophosphite derived from (*S*)-binaphtol and (2-*tert*-butyl-4-methoxy)phenol, when combined with $[Rh(acac)(CO)_2]$, was able to induce 10% ee, with high regioselectivity (*i*/*n* = 86/14) in the enantioselective hydroformylation of styrene (9 bar, 45°C) [14]. We have carried out this reaction using $[Rh(cod)_2]BF_4$ as the catalyst precursor and polyether-phosphite **1** (Table 1) or **2** (Table 2) as the ligand.

Under homogeneous conditions ($CH_2Cl_2$ as solvent, Table 1, entries 1–3) the asymmetric induction of the rhodium–ligand **1** (Rh-**1**) catalytic system increases with the molar ligand to metal ratio (from 1 to 10). A total pressure of 20 bar seems to be better for the enantioselectivity despite a decrease of the activity. Increasing further the **1**/Rh ratio (i.e. > 10) should decrease both the activity and the regioselectivity of this system and hitherto its application as catalyst for the hydroformylation of olefins.

Chen et al. have already observed that, under biphasic conditions, the conversion and the yield of aldehyde increase when the polyether-monophosphite to rhodium (P/Rh) ratio goes from 1 to 20 [4]. In addition, the *i*/*n* ratio of aldehyde slightly decreases with an increase of the P/Rh ratio. At P/Rh = 13, the maximum conversion of styrene is reached. Under these conditions, the conversion of styrene and the yield of aldehyde both increase with temperature and total pressure. The *i*/*n* ratio decreases sharply as temperature increases although it remains constant when the total pressure changes. Little effect on the catalytic results is observed with different non-polar solvents (from toluene to *n*-heptane), but rhodium leaching is reduced when *n*-heptane is used [4].

In biphasic conditions (Table 1, entries 5–6), the asymmetric induction of the Rh-**1** catalytic system appears when the ratio equals 9, and reaches 17% ee for 13. Moreover, increasing the molar **1**/Rh ratio makes the system more active. However, this decreases the regioselectivity.

Contrary to the rhodium–ligand **1** (Rh-**1**) catalytic system, in homogeneous conditions, Rh-**2** is more active and enantioselective when the total pressure decreases (Table 2, entries 7–11). Moreover, the regioselectivity is less sensitive to pressure effects with this



Scheme 2.

Table 1
Rhodium catalyzed enantioselective hydroformylation of styrene with ligand **1** [a]

| Entry | Solvent | **1**/Rh | S/Rh | *P* (bar) | *t* (h) | %Conversion [b] | *i*/*n* [b] | %ee [b] |
|---|---|---|---|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | 1.5 | 600 | 40 | 6 | 43 | 93/7 | 1 |
| 2 | $CH_2Cl_2$ | 1.5 | 600 | 20 | 6 | 17 | 91/9 | 3 |
| 3 | $CH_2Cl_2$ | 10 | 600 | 20 | 48 | 43 | 83/17 | 8 |
| 4 | $H_2O$ | 1.5 | 1000 | 40 | 6 | 5 | 92/8 | 0 |
| 5 | $H_2O$ | 9 | 1000 | 40 | 24 | 65 | 92/8 | 3 |
| 6 | $H_2O$ | 13 | 1000 | 40 | 18 | 71 | 76/24 | 17 |

[a] S, styrene = 2 ml; solvent or water: 4 ml; $H_2$: CO (1:1); Rh = $[Rh(cod)_2BF_4]$; $T = 40°C$.
[b] See Section 2; the configuration of the aldehyde is (*S*).

Table 2
Rhodium catalyzed enantioselective hydroformylation of styrene with ligand **2** [a]

| Entry | Solvent | **2**/Rh | S/Rh | P (bar) | *t* (h) | %Conversion [b] | *i*/*n* [b] | %ee [b] |
|---|---|---|---|---|---|---|---|---|
| 7 | $CH_2Cl_2$ | 1.0 | 4000 | 10 | 24 | 26 | 74/26 | 17 |
| 8 | $CH_2Cl_2$ | 1.0 | 4000 | 20 | 48 | 70 | 80/20 | 14 |
| 9 | $CH_2Cl_2$ | 1.5 | 4000 | 20 | 96 | 51 | 80/20 | 27 |
| 10 | $CH_2Cl_2$ | 1.5 | 4000 | 40 | 96 | 25 | 80/20 | 25 |
| 11 | $CH_2Cl_2$ | 3.5 | 4000 | 40 | 96 | 18 | 80/20 | 25 |
| 12 | $H_2O$ | 0.75 | 1000 | 40 | 24 | 98 | 85/15 | 4 |
| 13 | $H_2O$ | 1.5 | 1000 | 40 | 24 | >99 | 84/16 | 16 |
| 14 | $H_2O$ | 3.8 | 1000 | 40 | 24 | >99 | 83/17 | 19 |
| 15 | $H_2O$ | 8.5 | 1000 | 40 | 24 | >99 | 83/17 | 25 |

[a] S, styrene = 2 ml; solvent or water 4 ml; $H_2$: CO (1:1); Rh = $[Rh(cod)_2BF_4]$; $T = 40°C$.
[b] See Table 1.

system, and an *i*/*n* ratio of 80/20 is obtained when L/Rh = 1.5. However, an optimum is reached for 20 bar and a molar **2**/Rh ratio of 1.5 (Table 2, entry 9).

With Rh-**2**, the activity is very high in biphasic conditions. It is now well established that $HRh(CO)_4$ is a very efficient catalyst for the hydroformylation of styrene [17]. Part of the activity should be assigned to unmodified species, as observed for **2**/Rh = 0.75 (Table 2, entry 12). However, when **2**/Rh = 8.5, enantioselectivity reaches up to 25%, which is nearly the value obtained in homogeneous conditions.

In conclusion, the diphosphite **2** is a better ligand for the cationic rhodium catalyst than the monophosphite **1**. Moderate enantioselectivity (17–25% ee) has been obtained in both cases. These molecules are actually acting as ligands. Pressure and ligand to rhodium ratio have to be chosen in order to optimize activity, regio- and enantio-selectivity. Our results compare well with those of Herrmann et al. The authors have obtained 18% ee with a sulfonated-Naphos derivative as ligand in biphasic conditions, instead of 32% for the Naphos in homogenous conditions [18].

### 3.3. Recycling experiments

Recycling experiments were carried out in order to appreciate both the stability of the phosphite–rhodium complexes in water and the rhodium leaching. This allowed us to collect information on the structure of the catalyst: nature of the complex, ligand to rhodium ratio, cloud point of the cationic complex. Thus, the catalytic activity of the organic (biphasic conditions) and aqueous phase were studied (Table 3).

The cloud point of the catalyst obtained with $RhCl_3$ and ligand **1** is 22°C. The cloud point of the cationic complex should be very near from this value since the organic layer is slightly yellow after the first run. However, such a cationic species should be more soluble in water. Lower enantioselectivity and activity are obtained for the recycled aqueous phase with ligand **1**, but the organic phase is even less active and enantioselective. The catalyst is retained into the aqueous phase, with only a small amount extracted. However, this system does not recycle with the same enantioselectivity. The hydrogenation experiment (Fig. 2) has shown that degradation is not observed during the phase transfer. Decomposition of the complex may occur during the transfer from the autoclave into the Schlenk flask, but the L/Rh ratio is also modified. Since the asymmetric induction requires at least a L*/Rh = 9 (Table 1), it is not surprising to obtain a lower enantioselectivity when recycling this system.

Table 3
Enantioselective hydroformylation of styrene: recycling experiments

| Entry | Cycle | Ligand | L/Rh | *t* (h) | %Conversion [b] | *i*/*n* [b] | %ee [b] |
|---|---|---|---|---|---|---|---|
| 16 | 1 [a] | **1** | 13 | 18 | 71 | 76/24 | 17 |
| 17 | 2 d | Aqueous phase | – | 24 | 58 | 82/18 | 8 |
| 18 | 2 [c] | Organic phase | – | 24 | 7 | 90/10 | 3 |
| 19 | 1 [a] | **2** | 8.5 | 24 | >99 | 83/17 | 25 |
| 20 | 2 [c] | Aqueous phase | – | 24 | 35 | 83/17 | 25 |
| 21 | 2 [c] | Organic phase | – | 24 | 65 | 86/14 | 12 |

[a] Reactions were carried out in degazed and deionized water (4 ml); [Rh = [Rh(cod)$_2$BF$_4$]: $18\times10^{-6}$ mol; S, styrene (2 ml); S/Rh: 1000, p($H_2$ + CO) = 40 bar; $T$ = 40°C].

[b] See Table 1.

[c] Recycling of the aqueous phase or the organic phase in biphasic conditions (extraction temperature: 25°C).

With ligand **2**, recycling of the aqueous phase is possible with the same regio- and enantio-selectivity, but with a lower activity. The yellow organic phase also contains catalyst because the polyether chains are too short for a satisfactory water-solubility. The species in the organic phase gives a higher activity but a lower enantioselectivy. Actually, the ee value is close to the one obtained with a **2**/Rh ratio of 1. These results suggest that the catalyst is partially extracted as species containing mainly one diphosphite ligand per rhodium atom. However, the complex retained into the aqueous phase leads to the same enantioselectivity since it does not require a large excess of ligand **2** (Table 2), unlike **1**.

In conclusion, the rhodium–ligand **1** system is kept into the aqueous phase, but it does not recycle with the same enantioselectivity. Contrary to the rhodium–ligand **1** system, the catalyst–ligand **2** is extracted at room temperature from the aqueous phase containing the excess of ligand. When separated from this aqueous phase, the species dissolved into the organic phase affords lower asymmetric induction since it depends on the ligand to rhodium ratio. Nevertheless, recycling of the aqueous phase is possible with ligand **2**, with the same regio- and enantio-selectivity, but with a lower activity. However, it is unlikely that the Rh-**2** catalytic system will give higher ee and a satisfactory re-usable system for the hydroformylation of styrene. The choice of the chain-lengths of the polyether moiety to obtain rhodium complexes with controlled cloud points is currently being examined. The enantioselectivity should also be optimized by using one of the various chiral moiety described for the homogeneous hydroformylation.

## 4. Conclusion

Two chiral polyether-phosphite compounds were synthesized from readily available starting materials. These ligands, combined with [Rh(cod)$_2$]BF$_4$, exhibit high catalytic activity in the enantioselective hydroformylation of styrene. Thermoregulated phase-transfer catalysis gives branched aldehydes with high regioselectivity and enantioselectivity of up to 25%, which is exactly the same value that has been obtained in the homogeneous way. Although this asymmetric induction is modest, it is the highest ever obtained for the hydroformylation of styrene in biphasic conditions. Recycling was possible, but with a lower activity since rhodium leaching can not be avoided. Extraction of the rhodium complexes does not occur at temperatures below the cloud point of the catalyst. Thus, the recyclability should be improved by increasing the chain-length of the polyether moiety. The properties of the organic phase suggest extraction of diphosphite rhodium species for temperatures above the cloud point of the catalyst rather than degradation of the catalyst. This paper demonstrates for the first time the feasibility of enantioselective thermoregulated phase-transfer hydroformylation. It also proves that the catalytic system should be easily improved: firstly, by modifications of the polyether part of the ligand to induce higher cloud points, and secondly, by a proper design of the chiral part of the ligand, which controls the asymmetric induction.

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