DOI: 10.1002/adsc.200700582

Biphasic Aqueous Organometallic Catalysis Promoted by Cyclodextrins: How to Design the Water-Soluble Phenylphosphane to Avoid Interaction with Cyclodextrin

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Received: October 12, 2007; Revised: January 10, 2008; Published online: February 25, 2008

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

Abstract: The ability of cyclodextrin to interact with *meta*-trisulfonated triphenylphosphane derivatives bearing one or two methyl (or methoxy) groups on the aromatic ring has been investigated by NMR and UV-vis spectroscopy. In the case of native β-cyclodextrin (β-CD), the presence of one methyl or methoxy group in the *ortho*-position on each aromatic ring is necessary to hamper the formation of an inclusion complex between the β-CD and *meta*-trisulfonated triphenylphosphane derivatives. In the case of methylated β-CD, the formation of an inclusion complex is only observed when the *meta*-trisulfonated triphenylphosphane contains a methyl group in the *para*-position. The poor affinity of methylated β-CD towards modified trisulfonated triphenylphosphanes was attributed to the steric hindrance generated by the methyl groups on the CD secondary face. The absence or presence of an interaction between phosphanes and methylated β-CD was also confirmed by catalytic experiments. Thus, the phosphanes that do not interact with the methylated CD were the most efficient mass-transfer promoters in an aqueous biphasic palladium-catalyzed Tsuji–Trost reaction.

Keywords: aqueous phase catalysis; cyclodextrin; phosphanes; supramolecular chemistry

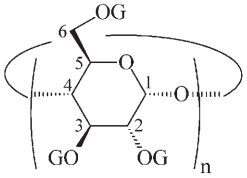
Introduction

Aqueous organometallic catalysis appears to be an environmentally friendly method to produce organic chemicals due to the low cost and toxicity of water. Furthermore, the catalyst that is immobilized into the aqueous phase by water-soluble ligands can be easily recovered by simple separation of the aqueous and organic phases.[1] The most commonly used water-soluble ligand is the sodium salt of *meta*-trisulfonated triphenylphosphane [TPPTS; $P(m\text{-}C_6H_4SO_3Na)_3$] which was originally developed by Rhone-Poulenc for use in the aqueous-phase hydroformylation of propylene.[2] Although appropriate for water-soluble substrates, the aqueous organometallic catalysis suffered from a huge loss of attractiveness when hydrophobic substrates were considered because of mass-transfer limitations.[3]

Cyclodextrins (CDs) have been widely used in aqueous organometallic catalysis to overcome mass-transfer limitations. Indeed, CDs can improve the mass transport across the interface by forming inclusion complexes with highly hydrophobic substrates.[4] Among the different CDs used, the randomly methylated β-CD (Rame-β-CD) appeared to be the most efficient (Table 1).[5]

Indeed, Rame-β-CD notably increased the reaction rates, while avoiding the formation of an emulsion and the partition of the catalyst between the organic and aqueous phases. Nevertheless, this β-CD derivative forms an inclusion complex with the TPPTS ligand.[6] The formation of such inclusion complexes induces a decrease in the linear to branched aldehyde ratio during the rhodium-catalyzed hydroformylation reaction.[7] In fact, the Rame-β-CD is able to dissociate TPPTS from the rhodium species and leads to the formation of low-coordinated phosphane species responsible for this decrease in regioselectivity. In addition, it has been shown that the ability of Rame-β-CD

Table 1. Structure of CD and Rame-β-CD.



G = H or CH_3

Abbreviation	n	Substituent (G)	Carbon bearing the OCH_3 group	Average number of OCH_3 group by CD
β-CD	7	H	(–)	0
Rame-β-CD	7	CH_3	2, 3 and 6	12.6

to bind to the TPPTS ligand can contribute to decrease the reaction rates. Indeed, when the TPPTS/Rame-β-CD ratio is too high, the CD cavity is poisoned by the ligand and the substrate transfer is diminished.[8] As approaches based on the use of α-CD derivatives[9] or chemically modified β-CD[10,11] have not given full satisfaction to solve the above problems, strategies based on phosphane modification are now explored.[12]

In this work, we examined the potential of bulky TPPTS derivatives in aqueous organometallic catalysis promoted by CD. As tri- or tetrasubstituted aromatic rings are largely less associated with CDs than mono- or disubstituted ones, it was expected that attachment of substituents groups on the aromatic ring of the TPPTS would be sufficient to hamper the formation of an inclusion complex between β-CD and the phosphane.[13] So, we have synthesized TPPTS derivatives bearing one or two methyl (or methoxy) groups on each aromatic ring and investigated by NMR and UV-vis spectroscopy the influence of the group position and/or the group number on the inclusion phenomenon. Finally, the behavior of these phosphanes in a model reaction has been examined to confirm the presence or absence of interactions between the phosphanes and cyclodextrins.

The water-soluble phosphanes used in this work are schematically presented in the Table 2.

It should be noticed that tris(*p*-Me)TPPTS, tris(*m*,*p*-diMe)TPPTS, bis(*o*-Me)TPPTS and tris(*o*-Me)TPPDS have never been described in the literature, in contrast to tris(*o*,*p*-diMe)TPPTS[14], tris(*o*-Me)TPPTS[15], tris(*p*-OMe)TPPTS[16] and tris(*o*-OMe)TPPTS.[15] Interestingly, some catalysts based on these ligands have given interesting results in aqueous organometallic catalysis. Hence, tris(*o*,*p*-diMe)TPPTS and tris(*o*-Me)TPPTS provided active catalysts in the hydrogenation of aldehydes,[17] Heck and Suzuki couplings of aryl bromide[18] or Suzuki couplings of unprotected halonucleosides.[19] In addition, tris(*o*-Me)TPPTS has been employed as ligand during the Tsuji–Trost reaction[20] and tris(*p*-OMe)TPPTS or tris(*o*-OMe)TPPTS during the hydroformylation reaction.[21]

Results and Discussion

Synthesis of the Water-Soluble Phosphanes

The various water-soluble phosphanes were synthesized according to procedures described in the literature. Briefly, the methylated or methoxylated derivative of the triphenylphosphane was dissolved in a mixture sulfuric acid/oleum for sulfonation. After hydrolysis of SO_3, trioctylamine was added to extract the reaction product. Finally, the sodium salt was obtained by addition of NaOH (Scheme 1).

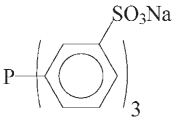
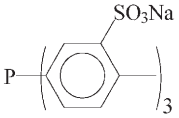
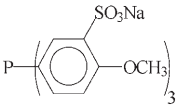
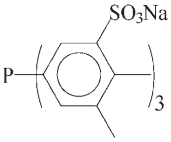
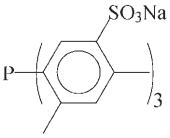
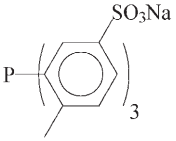
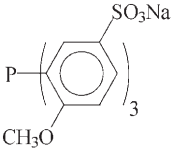
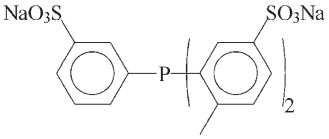
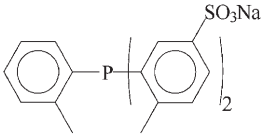
The purity of these water-soluble phosphanes was carefully controlled. In particular, ^1H and $^{31}P\{^1H\}$ NMR analysis indicated that for each phosphane only less than 5% of its oxide was present.

Studies of β-CD/Phosphane Interactions

NMR and UV-vis spectroscopic studies have been performed to provide information concerning the potential interactions between these water-soluble phosphanes and β-CD in aqueous medium. When an interaction was evidenced, the stoichiometry and the association constant were determined. T-ROESY experiments were also performed to determine whether the phosphane is deeply included into the β-CD cavity. The main results are gathered in Table 2. For comparison, the data concerning the inclusion complex between β-CD and TPPTS are also indicated.

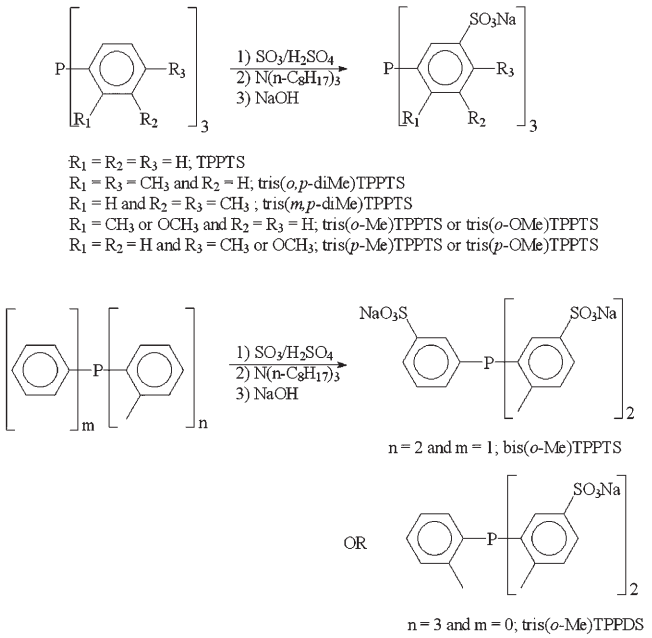
Our first studies were devoted to TPPTS derivatives bearing a methyl or a methoxy group in a *para* position [tris(*p*-Me)TPPTS or tris(*p*-OMe)TPPTS, respectively]. As an illustrative experiment, the case of β-CD and tris(*p*-Me)TPPTS is fully described. For mixtures of tris(*p*-Me)TPPTS and β-CD, the $^{31}P\{^1H\}$ and ^1H NMR spectra exhibited chemical shift variations compared to the spectra of these two compounds alone. These results clearly indicate an interaction between the two compounds. The stoichiometry of the inclusion complex was provided by NMR titrations using the continuous variation technique (Job's method – see Supporting Information).[22] The

Table 2. Structure and abbreviation of the water-soluble phosphanes. Values of association constant[a] (K) and presence of cross peaks in T-ROESY spectra for the β-CD/phosphane couple.

Structure	Name, Abbreviation	K (M^{-1})	T-ROESY cross peaks[c]
	tris(3-sulfonatophenyl)phosphane sodium salt, **TPPTS**	1200	Yes
	tris(4-methyl-3-sulfonatophenyl)phosphane sodium salt, **tris(*p*-Me)TPPTS**	2750	Yes
	tris(4-methoxy-3-sulfonatophenyl)phosphane sodium salt, **tris(*p*-OMe)TPPTS**	400	Yes
	tris(4,5-dimethyl-3-sulfonatophenyl)phosphane sodium salt, **tris(*m*,*p*-diMe)TPPTS**	140	No
	tris(4,6-dimethyl-3-sulfonatophenyl)phosphane sodium salt, **tris(*o*,*p*-diMe)TPPTS**	(–)[b]	No
	tris(6-methyl-3-sulfonatophenyl)phosphane sodium salt, **tris(*o*-Me)TPPTS**	(–)[b]	No
	tris(6-methoxy-3-sulfonatophenyl)phosphane sodium salt, **tris(*o*-OMe)TPPTS**	(–)[b]	No
	bis(6-methyl-3-sulfonatophenyl)(3-sulfonatophenyl)phosphane sodium salt, **bis(*o*-Me)TPPTS**	110	No
	bis(6-methyl-3-sulfonatophenyl)(2-methylphenyl)phosphane sodium salt, **tris(*o*-Me)TPPDS**	50	No

[a] When an interaction between the phosphane and β-CD was observed, the stoichiometry of the adduct or inclusion complex has been determined to be equal to 1:1.
[b] No inclusion complex was evidenced.
[c] The term *Yes* is used when marked cross-peaks between protons of the water-soluble phosphane and β-CD were observed in the T-ROESY spectra at 298 K.

Job's plot shows a maximum at r = 0.5 and a highly symmetrical shape, indicating that the stoichiometry of inclusion complex is 1:1. The association constant was evaluated at 298 K from UV-Vis spectroscopic data (spectral displacement method – see Supporting Information) and was found to be equal to 2750 M^{-1}. It must be pointed out that this value is higher than that found for the β-CD/TPPTS complex (K = 1200 M^{-1}). This result was clearly unexpected as the introduction of a methyl group was initially thought to decrease the affinity of the phosphane for the CD! The structure of the β-CD/tris(*p*-Me)TPPTS inclusion



Scheme 1. General procedure for the synthesis of the water-soluble phosphanes.

complex was elucidated by a two-dimensional T-ROESY NMR experiment (Figure 1).

The strongest interactions are observed between the internal protons of the β-CD (H-3 and H-5) and the three aromatic protons of tris(*p*-Me)TPPTS. In addition, the protons of the methyl groups of tris(*p*-Me)TPPTS are correlated with the H-3, H-5 and H-6 protons. Interestingly, the absence of an interaction between the H-6 protons of β-CD and the aromatic protons of tris(*p*-Me)TPPTS indicates clearly that the inclusion occurs by the secondary face of β-CD.

By using the same methodology, the association constant for the 1:1 inclusion complex between the β-CD/tris(*p*-OMe)TPPTS couple was evaluated at $400\,M^{-1}$. Contrary to tris(*p*-Me)TPPTS, the introduction of a methoxy group clearly decreases the affinity of the phosphane for β-CD. The tris(*p*-OMe)TPPTS is probably more encumbered than tris(*p*-Me)TPPTS, and a deep penetration inside the β-CD cavity is likely more difficult. This assumption was supported by T-ROESY experiments. Indeed, the absence of interaction between the H-5 proton of the β-CD and the protons of the phosphane in the T-ROESY spectra indicate clearly a shallow inclusion (see Supporting Information).

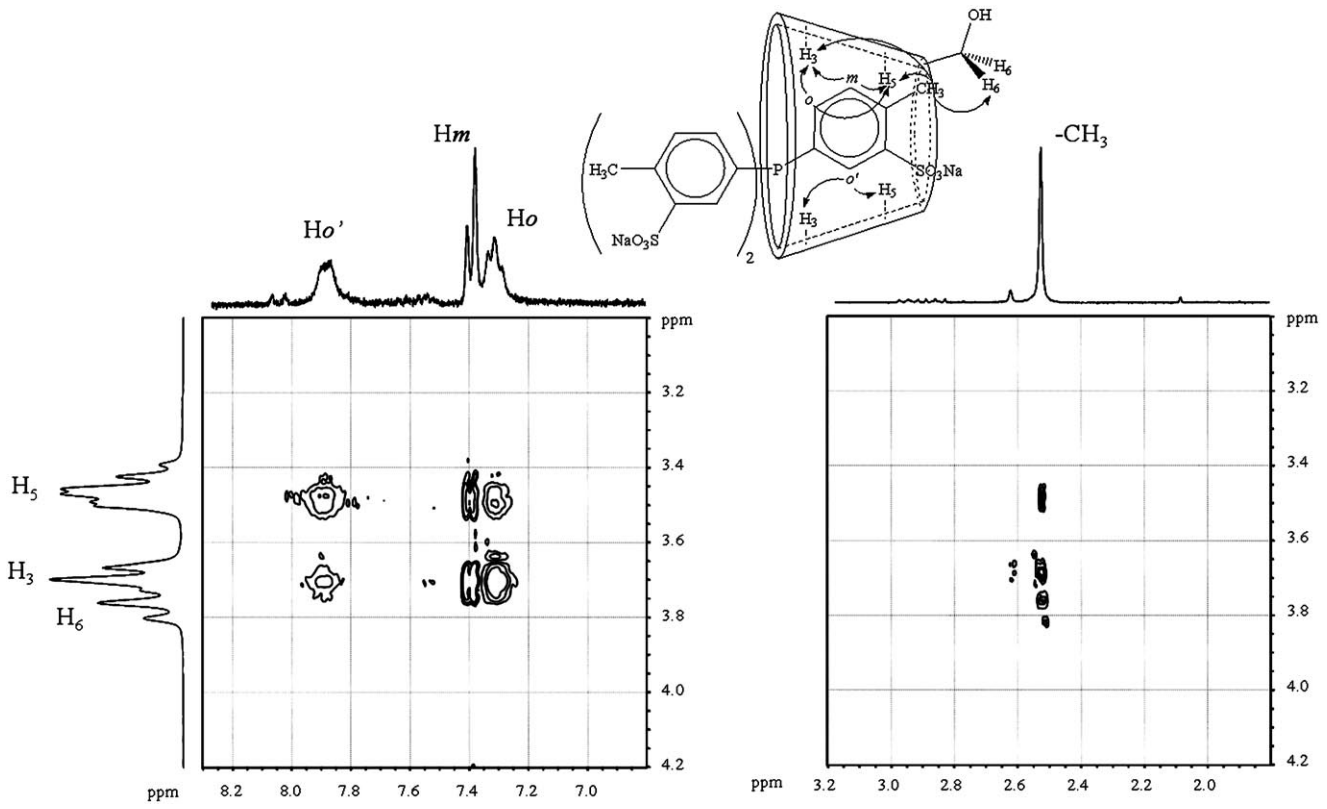


Figure 1. Partial contour plot of the T-ROESY spectrum of a solution containing β-CD (10 mM) and tris(*p*-Me)TPPTS (10 mM) in D_2O at 298 K with a 300 ms mixing time. The interactions observed in the T-ROESY spectrum are indicated by arrows. The deduced orientation of tris(*p*-Me)TPPTS in β-CD cavity is shown.

From the above results, it appears that the presence of one methyl or methoxy group in the *para* position on each aromatic ring of the TPPTS is not sufficient to prevent the formation of an inclusion complex with β-CD. In these conditions, we decided to introduce two methyl groups on each aromatic cycle in the *para/meta* positions [tris(*m*,*p*-diMe)TPPTS] or in the *para/ortho* positions [tris(*o*,*p*-diMe)TPPTS]. The association constant of the 1:1 complex β-CD/tris(*m*,*p*-diMe)TPPTS was evaluated as $140\,M^{-1}$ that is synonymous of a weakly associated inclusion complex. For the β-CD/tris(*o*,*p*-diMe)TPPTS mixture, no spectral modification was observed during NMR or UV-vis experiments, indicating that this phosphane did not interact with β-CD. These results were also confirmed by T-ROESY experiments. In the two cases, no marked cross-peaks between the β-CD and phosphane protons have been observed on the T-ROESY spectrum, proving a not very deep or an absence of an inclusion phenomenon. Consequently, it can be concluded that the presence of two methyl groups in *meta*/*para* or in *ortho*/*para* positions on each aromatic ring blocks the penetration inside the β-CD cavity with a more pronounced effect in the case of tris(*o*,*p*-diMe)TPPTS.

The importance of methyl groups in the *ortho* position was demonstrated by NMR and UV-vis spectroscopy experiments on mixtures of β-CD and tris(*o*-Me)TPPTS. Indeed, no interaction between tris(*o*-Me)TPPTS and β-CD can be evidenced. The same experiments performed with tris(*o*-OMe)TPPTS and β-CD have equally concluded to the absence of interactions. The methylation or methoxylation in the *ortho* position for each aromatic ring is therefore sufficient to generate a constraint preventing the penetration of these water-soluble phosphanes inside the β-CD cavity.

To determine the required number of methyl group in the *ortho* positions to prevent the inclusion process, the behavior of a TPPTS bearing a methyl group in the *ortho* position on only two aromatic rings [bis(*o*-Me)TPPTS] was examined. This phosphane was found to weakly interact with β-CD as the association constant was equal to $110\,M^{-1}$ and no cross-peak correlation was observed on the T-ROESY spectrum. This result undoubtedly demonstrates that the presence of three methyl groups is necessary to obtain a non-interacting phosphane. However, it must be pointed out that the sulfonato group contributes also to impede the formation of inclusion complex. Indeed, we have found that a *meta*-disulfonated triphenylphosphane bearing a methyl group in the *ortho* position on each aromatic ring [tris(*o*-Me)TPPDS interacts with the β-CD ($K = 50\,M^{-1}$)]. However, this interaction does not lead to the formation of a genuine inclusion complex as no cross-peak has been observed on the T-ROESY NMR spectrum.

From these experimental data, it appears that the formation of an inclusion complex between β-CD and a TPPTS derivative can be avoided by introducing a substituent on each ring in the *ortho* position of the phosphane. In the next part, the behavior of the TPPTS derivatives towards Rame-β-CD was investigated to evaluate the effects of the methyl groups of CD on the inclusion processes.

Studies of Rame-β-CD/Phosphane Interactions

In the case of Rame-β-CD, inclusion of the phosphane into the CD cavity is clearly more difficult. Indeed, NMR and UV-vis spectroscopic studies indicate that Rame-β-CD interacts only with TPPTS and tris(*p*-Me)TPPTS phosphanes. The 1:1 association constant values were evaluated as $840\,M^{-1}$ and $960\,M^{-1}$ for Rame-β-CD/TPPTS and Rame-β-CD/tris(*p*-Me)TPPTS inclusion complexes, respectively. It must also be pointed that these values are lower than those observed with native β-CD. This decrease is largely more marked in the case of tris(*p*-Me)TPPTS ($2750\,M^{-1}$ with β-CD *vs.* $960\,M^{-1}$ with Rame-β-CD) than in the case of TPPTS ($1200\,M^{-1}$ with β-CD *vs.* $840\,M^{-1}$ with Rame-β-CD).

These results demonstrate that the inclusion capacity of β-CD is markedly altered by introduction of methyl groups. The steric hindrance generated by the methyl groups on the CD secondary face impedes inclusion of the more encumbered water-soluble phosphanes. These results are in line with those obtained with the native β-CD. Indeed, it has been observed with the native β-CD that most of the phosphanes were not deeply included in the cavity suggesting that a supplementary steric constraint would suppress the inclusion. This result is very promising as the Rame-β-CD is the most efficient mass transfer agent in aqueous organometallic catalysis. So, except for TPPTS and tris(*p*-Me)TPPTS, the other phosphanes should be valuable ligands for aqueous organometallic catalysis promoted by methylated β-CDs. Some experiments in catalysis have been performed to support this assumption.

Catalytic Experiments

The removal of the allyloxycarbonyl group from an allylic carbonate (allyl undecyl carbonate) was chosen as the model reaction to evaluate the behavior of water-soluble phosphanes in the presence of Rame-β-CD (Figure 2). This reaction was catalyzed by a palladium/water-soluble phosphane combination in the presence of diethylamine as allyl scavenger.[23]

The presence or absence of an interaction between the phosphane and Rame-β-CD can be easily detect-

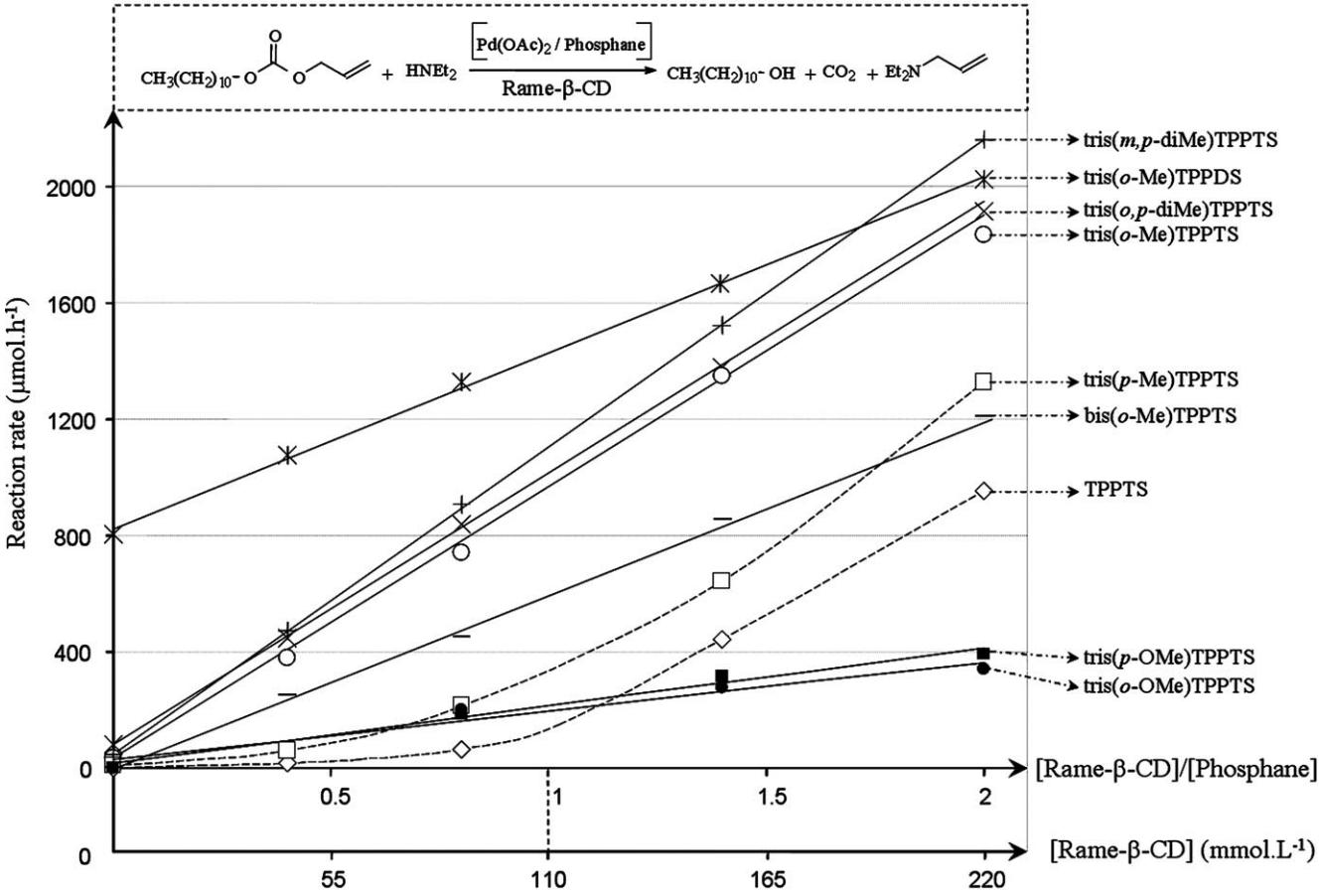


Figure 2. Influence of the Rame-β-CD/phosphane ratio on the reaction rate for different water-soluble phosphanes.

ed by examining the effect of increasing amounts of Rame-β-CD on the reaction rate. In fact, the reaction rate linearly increases with the Rame-β-CD concentration when no interaction occurs between the phosphane and Rame-β-CD.[8] In contrast, when the phosphane interacts with the Rame-β-CD, Rame-β-CD is trapped by the phosphane ligand and is unable to participate in the mass-transfer process at low CD/phosphane ratios (excess of ligand relative to CD). In these conditions, a significant rate increase can only be observed at high CD/phosphane ratios when the amounts of CD are higher than those of ligand (i.e., for a CD/ligand ratio > 1). The results obtained in the presence of various amounts of Rame-β-CD are shown in Figure 2.

Before examining the effect of Rame-β-CD on the reaction rate, it should be pointed out that the activity of the catalytic system in the absence of Rame-β-CD strongly depends on the phosphane (Figure 2 – [Rame-β-CD]/[Phosphane] $= 0$). Concerning the different TPPTS derivatives, the activities are low as the reaction rates were equal to 2, 2, 7, 11, 35, 46 and 81 μmol/h for tris(*o*-OMe)TPPTS, tris(*p*-OMe)TPPTS, bis(*o*-Me)TPPTS, tris(*p*-Me)TPPTS, tris(*o*-Me)TPPTS, tris(*m,p*-diMe)TPPTS and tris(*o,p*-diMe)TPPTS, respectively. In the case of tris(*o*-Me)TPPDS, the reaction rate was higher than those observed with the other phosphanes and was equal to 803 μmol/h. This higher activity is likely connected with the more pronounced hydrophobic character of this phosphane. Indeed, compared to the other TPPTS derivatives, the tris(*o*-Me)TPPDS phosphane contains only two sulfonate groups. Consequently, this phosphane is preferentially situated at the interface facilitating the contact between the catalyst and the substrate.[24]

As expected for a mass-transfer limited reaction, the addition of Rame-β-CD increases the reaction rates (Figure 2). However, effect of the Rame-β-CD on the reaction rate depends on the phosphane. In fact, the plot of reaction rate *vs.* Rame-β-CD/phosphane ratio is linear for tris(*p*-OMe)TPPTS, tris(*m,p*-diMe)TPPTS, tris(*o,p*-diMe)TPPTS, tris(*o*-Me)TPPDS, tris(*o*-OMe)TPPTS), bis(*o*-Me)TPPTS and tris(*o*-Me)TPPTS) and appears exponential for TPPTS and tris(*p*-Me)TPPTS. These results are totally in agreement with our spectroscopic studies. Indeed, the shape of the curves appears directly relat-

ed to the nature of interaction between Rame-β-CD and the phosphane. The reaction rate linearly increases when the water-soluble phosphanes do not interact with Rame-β-CD as expected for a non-interacting system. In contrast, the reaction rate significantly increases when the CD/phosphane ratio is higher than 1 in the case of the TPPTS and tris(*p*-Me)TPPTS, confirming the interaction of these two phosphanes with the Rame-β-CD.

Conclusions

We have demonstrated by spectroscopic studies and catalysis experiments that bulky TPPTS derivatives can be valuable water-soluble phosphanes for aqueous organometallic catalysis promoted by modified cyclodextrins. Indeed, each compound can fully play its own role without mutual interaction: the water-soluble bulky phosphane as a ligand for the metal and the CD as an efficient mass transfer promoter.

Experimental Section

General Remarks

The ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded at 300.13, 75.47 and 121.49 MHz on a Bruker Avance DRX spectrometer, respectively. Mass spectra were recorded on a MALDI TOF TOF Bruker Daltonics Ultraflex II. The 2D T-ROESY experiments were run using the software supplied by Bruker. T-ROESY experiments were preferred to classical ROESY experiments as this sequence provides reliable dipolar cross-peaks with a minimal contribution of scalar transfer. Mixing times for T-ROESY experiments were set at 300 ms. The data matrix for the T-ROESY was made of 512 free induction decays, 1 K points each, resulting from the co-addition of 32 scans. The real resolution was 1.5–6.0 Hz/point in F2 and F1 dimensions, respectively. They were transformed in the non-phase-sensitive mode after QSINE window processing. UV-vis spectroscopy was performed on a Perkin–Elmer Lamba 2S spectrometer. The cell used was placed in a cuvette holder and the temperature was kept constant at 298 ± 0.1 K by means of a thermostated bath. Gas chromatographic analyses were carried out on a Shimadzu GC-17A gas chromatograph equipped with a methyl silicone capillary column (30 m × 0.32 mm) and a flame ionization detector (GC:FID).

D_2O (99.95% isotopic purity) was obtained from Merck. All reactants were purchased from Aldrich Chemicals or Acros in their highest purity and used without further purification. Rame-β-CD was purchased from Aldrich Chemicals. This CD was partially methylated. Methylation occurred at positions 2, 3, or 6 and 1.8 OH groups per glucopyranose unit were statistically modified. Distilled deionized water was used in all experiments. All solvents and liquid reagents were degassed by bubbling N_2 for 15 min before each use or by two freeze-pump-thaw cycles before use.

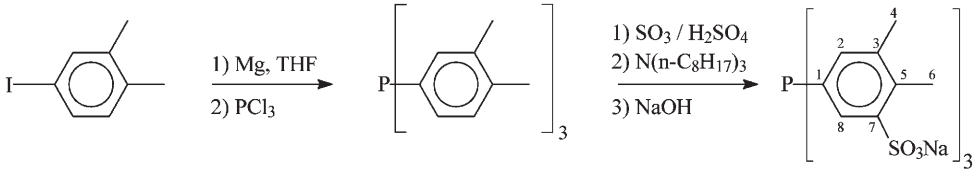
Preparation of Water-Soluble Phosphanes

TPPTS,[25] tris(*o*-Me)TPPTS,[15] tris(*p*-OMe)TPPTS[16] and tris(*o*-OMe)TPPTS[15] were prepared as reported in the literature. Tris(*o,p*-diMe)TPPTS was obtained from Strem. The purity of these water-soluble phosphanes was controlled by ^{1}H, ^{13}C and $^{31}P\{^{1}H\}$ NMR analysis and MALDI-TOF. For the other water-soluble phosphanes, the procedures are described in the following. The full ^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ spectra of tris(*p*-Me)TPPTS, tris(*m,p*-diMe)TPPTS, bis(*o*-Me)TPPTS and tris(*o*-Me)TPPDS are given in the Supporting Information.

Trisodium Salt of Tris(4,5-dimethyl-3-sulfonatophenyl)phosphane [tris(*m,p*-diMe)TPPTS] (Scheme 2)

To a suspension of magnesium (10 g, 0.41 mol, 1.2 equiv.) in 60 mL of anhydrous THF was introduced under nitrogen the iodide derivative (27 g, 0.116 mol, 0.33 equiv.). After a few minutes, the reaction began and 55 g (0.235 mol, 0.66 equiv.) of the iodide derivative in THF (240 mL) were added dropwise. The reaction mixture was then heated under reflux for 1 hour. After cooling, phosphorus trichloride (16 g, 0.117 mol, 0.33 equiv.) in THF (50 mL) was added dropwise and then heated under reflux for 1 hour. Once the reaction was complete, the mixture was poured into a mixture of ice (100 g) and water (100 mL). The organic phase was washed with water (3×50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. Yield: 21%.

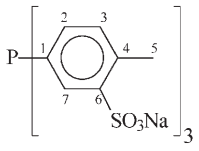
The resulting oil (8.51 g) was then dissolved in 45 mL of 100% concentrated sulfuric acid obtained by mixture of 36 mL of concentrated sulfuric acid (96%) and 9 mL of oleum (65%). After cooling to 5 °C, the oleum (65%, 10.5 mL) was added slowly under vigorous stirring and keeping the temperature below 10 °C. The reaction mixture was then kept at room temperature for 10 h under a nitrogen atmosphere. Excess of SO_3 was transformed to H_2SO_4 by addition of 10 mL of degassed water (***Caution!***). The mixture was poured into a mixture of water and ice (250 mL/250 g), and trioctylamine (27 g, 75.6 mmol) was then added. The ammonium salt of the sulfonated phosphane was recovered from the acidic aqueous layer by addi-



Scheme 2. Synthesis of [tris(*m,p*-diMe)TPPTS].

tion of chloroform (3×30 mL) and the organic layer was washed with water up to neutral pH. The sulfonated salt was recovered by a succession of extractions with NaOH solution (2N). Each fraction was analyzed by $^{31}P\{^1H\}$ NMR spectroscopy and the fractions where a unique signal was observed were concentrated under vacuum and a white solid was obtained. Yield: 7%. ^1H NMR (300 MHz, D_2O, 25°C): $\delta=2.23$ (s, 9H, H-4), 2.49 (s, 9H, H-6), 7.20 (d, $^3J_{P,H}=7.8$ Hz, 3H, H-2), 7.66 (d, $^3J_{P,H}=8.10$ Hz, 3H, H-8); $^{13}C\text{-}\{^1H\}$ NMR (75.5 MHz, D_2O, 25°C): $\delta=16.24$ (s, C-6), 19.86 (s, C-4), 129.88 (d, $^2J_{P,C}=23.4$ Hz, C-8), 132.93 (d, $^3J_{P,C}=7.5$ Hz, C-3), 136.81 (s, C-5), 137.62 (d, $^2J_{P,C}=16.6$ Hz, C-2), 140.75 (d, $^1J_{P,C}=6.0$ Hz, C-1), 141.83 (d, $^3J_{P,C}=7.5$ Hz, C-7); $^{31}P\text{-}\{^1H\}$ NMR (121.5 MHz, D_2O, 25°C): $\delta=-7.38$ (s); MS (MALDI-TOF): $m/z=1327.21$ $[2P+Na]^+$, 1305.22 $[2P+H]^+$, 675.10 $[P+Na]^+$, 653.12 $[P+H]^+$; elemental analysis calcd. (%) for $C_{24}H_{24}Na_3O_9PS_3\cdot3H_2O$ (706.6): C 40.79, H 4.28; found: C 40.65, H 4.20.

Trisodium Salt of Tris(4-methyl-3-sulfonatophenyl)phosphane [tris(*p*-Me)TPPTS]



The procedure described above was used for the sulfonation of tris(*p*-Me)TPP. Yield: 45%. ^1H NMR (300 MHz, D_2O, 25°C): $\delta=2.52$ (s, 9H, H-5), 7.13 (t, $^3J_{P,H}=^3J_{H\text{-}2,H\text{-}3}=7.2$ Hz, 3H, H-2), 7.21 (d, $^3J_{H,H}=7.2$ Hz, 3H, H-3), 7.73 (d, $^3J_{P,H}=8.4$ Hz, 3H, H-7); $^{13}C\text{-}\{^1H\}$ NMR (75.5 MHz, D_2O, 25°C): $\delta=19.82$ (s, C-5), 131.99 (d, $^2J_{P,C}=24.1$ Hz, C-7), 133.12 (d, $^3J_{P,C}=6$ Hz, C-3), 133.58 (d, $^1J_{P,C}=8.3$ Hz, C-1), 136.48 (d, $^2J_{P,C}=16.6$ Hz, C-2), 138.26 (s, C-4), 141.63 (d, $^3J_{P,C}=7.5$ Hz, C-6); $^{31}P\text{-}\{^1H\}$ NMR (121.5 MHz, D_2O, 25°C): $\delta=-7.60$ (s); MS (MALDI-TOF): $m/z=1243.11$ $[2P+Na]^+$, 1221.12 $[2P+H]^+$, 633.07 $[P+Na]^+$, 610.95 $[P+H]^+$; elemental analysis calcd (%) for $C_{21}H_{18}Na_3O_9PS_3\cdot3H_2O$ (664.5): C 37.96, H 3.64; found: C 37.90, H 3.55.

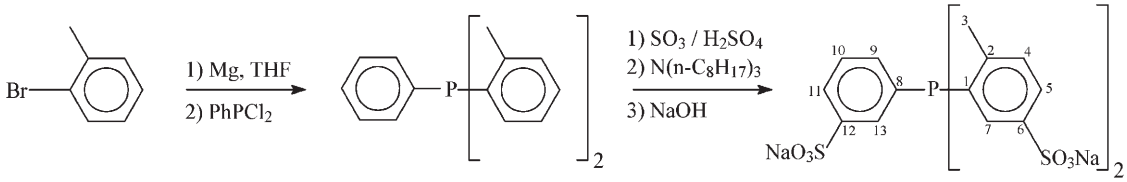
Trisodium Salt of Bis(6-methyl-3-sulfonatophenyl)(3-sulfonatophenyl)phosphane [bis(*o*-Me)TPPTS] (Scheme 3)

To a suspension of magnesium (8.38 g, 0.34 mol, 1.2 equiv.) in 60 mL of anhydrous THF was introduced under nitrogen 1-bromo-2-methylbenzene (16.5 g, 0.0964 mol, 0.33 equiv.). After a few minutes, the reaction began and 33.5 g (0.196 mol, 0.66 equiv.) of the 1-bromo-2-methylbenzene in THF (300 mL) were added dropwise. The reaction mixture was then heated under reflux for 1 hour. After cooling, phenylphosphorus dichloride (26 g, 0.146 mol, 0.5 equiv.) in THF (38 mL) was added dropwise and then heated under reflux for 1 hour. Once the reaction was complete, the mixture was poured into a mixture of ice (100 g) and water (100 mL). The organic phase was washed with water (3×50 mL), dried over anhydrous $MgSO_4$, filtered and concentrated by rotary evaporation. The resulting oil was recrystallized from methanol to give white crystals. Yield: 25%.

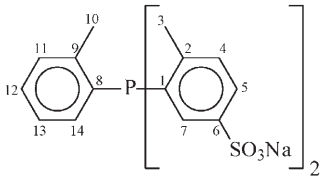
The resulting product (7.08 g) was then dissolved in 17.9 mL of 100% concentrated sulfuric acid obtained by mixture of 14.3 mL of concentrated sulfuric acid (96%) and 3.6 mL of oleum (65%). After cooling to 5°C, the oleum (65%, 19.8 mL) was added slowly under vigorous stirring and keeping the temperature below 10°C. The reaction mixture was then kept at room temperature for 72 h under a nitrogen atmosphere. Excess of SO_3 was transformed to H_2SO_4 by addition of 10 mL of degassed water (***Caution!***). The mixture was poured into a mixture of water and ice (250 mL/250 g), and trioctylamine (26.4 g, 74.6 mmol) was then added. The ammonium salt of the sulfonated phosphane was recovered from the acidic aqueous layer by addition of chloroform (3×30 mL) and the organic layer was washed with water up to neutral pH. The sulfonated salt was recovered by a succession of extractions with a NaOH solution (2N). Each fraction was analyzed by $^{31}P\{^1H\}$ NMR spectroscopy and the fractions where a unique signal was observed were concentrated under vacuum and a white solid was obtained. Yield: 21%. ^1H NMR (300 MHz, D_2O, 25°C): $\delta=2.27$ (s, 6H, H-3), 7.01 (dd, $^3J_{P,H}=4.2$ Hz, $^4J_{H\text{-}5,H\text{-}7}=1.7$ Hz, 2H, H-7), 7.27 (t, $^3J_{P,H}=^3J_{H\text{-}9,H\text{-}10}=7.0$ Hz, 1H, H-9), 7.36 (dd, $^4J_{P,H}=4.6$ Hz, $^3J_{H\text{-}4,H\text{-}5}=8.1$ Hz, 2H, H-4), 7.47 (t, $^3J_{H\text{-}10,H\text{-}11}=^3J_{H\text{-}9,H\text{-}10}=7.7$ Hz, 1H, H-10), 7.62 (dd, $^3J_{H\text{-}4,H\text{-}5}=8.1$ Hz, $^4J_{H\text{-}5,H\text{-}7}=1.7$ Hz, 2H, H-5), 7.76 (d, $^3J_{P,H}=9.1$ Hz, 1H, H-13), 7.77 (d, $^3J_{H\text{-}11,H\text{-}10}=7.7$ Hz, 1H, H-11); $^{13}C\text{-}\{^1H\}$ NMR (75.5 MHz, D_2O, 25°C): $\delta=20.6$ (d, $^3J_{P,C}=19.8$ Hz, C-3), 126.79 (s, C-5), 127.32 (s, C-11), 129.66 (s, C-7), 130.32 (d, $^3J_{P,C}=5.3$ Hz, C-10), 131.37 (s, C-4), 131.5 (d, $^2J_{P,C}=28$ Hz, C-13), 134.41 (d, $^1J_{P,C}=9$ Hz, C-1), 134.56 (d, $^1J_{P,C}=11.3$ Hz, C-8), 137.37 (d, $^2J_{P,C}=12.8$ Hz, C-9), 140.93 (s, C-2), 143.58 (d, $^3J_{P,C}=9.8$ Hz, C-12), 146.63 (d, $^3J_{P,C}=24.1$ Hz, C-6); ^{31}P $\{^1H\}$ NMR (121.5 MHz, D_2O, 25°C): $\delta=-18.67$ (s); MS (MALDI-TOF): $m/z=1215.07$ $[2P+Na]^+$, 1193.09 $[2P+H]^+$, 618.93 $[P+Na]^+$, 596.91 $[P+H]^+$; elemental analysis calcd (%) for $C_{20}H_{16}Na_3O_9PS_3\cdot3H_2O$ (650.5): C 36.93, H 3.41; found: C 36.85, H 3.33.

Disodium Salt of Bis(6-methyl-3-sulfonatophenyl)(2-methylphenyl)phosphane [tris(*o*-Me)TPPDS]

The procedure used to synthesize this product is similar to that described previously. The reaction mixture was kept at room temperature only for 3 h under a nitrogen atmosphere. ^1H NMR (300 MHz, D_2O, 25°C): $\delta=2.30$ (s, 9H H-10, H-3), 6.71 (dd, $^3J_{P,H}=5.4$ Hz, $^3J_{H\text{-}13,H\text{-}14}=7.5$ Hz 1H, H-14), 7.02 (dd, $^3J_{P,H}=4.5$ Hz, $^4J_{H\text{-}5,H\text{-}7}=1.8$ Hz, 2H, H-7), 7.11 (t, $^3J_{H\text{-}13,H\text{-}14}=^3J_{H\text{-}12,H\text{-}13}=7.5$ Hz, 1H, H-13), 7.33 (m, 2H, H-11,



Scheme 3. Synthesis of [bis(*o*-Me)TPPTS].



H-12), 7.39 (dd, $^{4}J_{P,H}=4.5$ Hz, $^{3}J_{H\text{-}4,H\text{-}5}=7.8$ Hz, 2H, H-4), 7.65 (dd, $^{3}J_{H\text{-}4,H\text{-}5}=7.8$ Hz, $^{3}J_{H\text{-}5,H\text{-}7}=1.8$ Hz, 2H, H-5); ^{13}C-{^{1}H} NMR (75.5 MHz, D_2O, 25 °C): $\delta=20.5$ (d, $^{3}J_{P,C}=3$ Hz, C-3), 20.76 (d, $^{3}J_{P,C}=2.3$ Hz, C-10), 126.65 (s, C-5), 127.23 (s, C-13), 129.93 (s, C-7), 130.47 (s, C-12), 130.91 (d, $^{3}J_{P,C}=5.2$ Hz, C-11), 131.27 (d, $^{3}J_{P,C}=4.5$ Hz, C-4), 131.80 (d, $^{2}J_{P,C}=4.5$ Hz, C-9), 133.76 (s, C-14), 134.15 (d, $^{2}J_{P,C}=8.3$ Hz, C-2), 141.02 (s, C-1), 143.47 (d, $^{1}J_{P,C}=26.4$ Hz, C-8), 146.82 (d, $^{3}J_{P,C}=24.9$ Hz, C-6); ^{31}P {^{1}H} NMR (121.5 MHz, D_2O, 25 °C): $\delta=-27.38$ (s); MS (MALDI-TOF): $m/z=1038.74$ $[2P+Na]^+$, 1016.76 $[2P+H]^+$, 530.70 $[P+Na]^+$, 508.72 $[P+H]^+$; elemental analysis calcd (%) for $C_{21}H_{19}Na_2O_6PS_2\cdot 2H_2O$ (544.5): C 46.32, H 4.26; found: C 46.23, H 4.21.

Catalytic Experiments

The water-soluble phosphane (400 μmol, 9 equiv. *vs.* Pd) was dissolved in water (2 g) in a Schlenk tube under a nitrogen atmosphere. This solution was then transferred into another Schlenk tube containing $Pd(OAc)_2$ (44 μmol, 10 mg). After stirring with a magnetic bar for 15 h, the obtained yellow solution was transferred into a mixture of allyl undecyl carbonate (1.12 mmol, 287 mg), diethylamine (2,24 mmol, 165 mg), dodecane (95 mg – GC internal standard), heptane (2 g – solvent) and the required amount of Rame-β-CD. The medium was stirred at 1000 rpm at room temperature and the reaction was monitored by quantitative gas chromatographic analysis of the organic layer. The initial reaction rate ($\mu mol\cdot h^{-1}$) was defined as the amount of allyl undecyl carbonate converted per hour at 20–30% conversion. The Rame-β-CD/phosphane ratio has been calculated by considering the amount of phosphane available in the reaction medium to interact with the cyclodextrin. Indeed, it was considered that only 5 equivalents of the phosphane can interact with the cyclodextrin. In fact, three equivalents were used to stabilize the palladium(0) species $[Pd(TPPTS)_3]$ and one equivalent of the phosphane was oxidized during reduction of the $Pd(OAc)_2$, according to Eq. (1).

$$Pd(OAc)_2 + 9\ TPPTS + H_2O \longrightarrow TPPTS{=}O + Pd(TPPTS)_3 + 5\ TPPTS + 2\ AcOH \quad (1)$$

Acknowledgements

M. Ferreira is grateful to the Ministère de l'Education et de la Recherche for financial support (2005–2008). The authors are grateful to G. Crowyn for NMR analysis and to CAPA (Centre d'Analyse Protéomique de l'Artois) for mass spectrometry analysis. The mass spectrometry facilities used for this study are funded by the European community (FEDER), the Fonds d'Industrialisation du Bassin Minier (FIBM), the ministère de l'éducation nationale, de l'enseignement supérieur et de la recherche and the Université d'Artois.

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