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# New Phosphane Based on a β-Cyclodextrin, Exhibiting a Solvent-Tunable Conformation, and its Catalytic Properties

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**Abstract:** A new diphenylphosphane based on a β-cyclodextrin skeleton that exhibits a dual solubility in water and in organic solvent was synthesised. Interestingly, a solvent-dependent conformation change was evidenced by NMR spectroscopy studies; the self-inclusion of a phenyl group of the phosphane moiety into cyclodextrin cavity observed in water disappeared in organic solvents due to a change in conformation. Hydrogenation or hydroformylation reactions performed in water and in organic solvents showed that this ligand was able to stabilise catalytically active rhodium species in solution. In the case of the hydroformylation reaction, it was demonstrated that regioselectivity was influenced by the solvent-dependent conformation of the ligand.

**Keywords:** cyclodextrins · hydroformylation · hydrogenation · self-inclusion · water chemistry

## Introduction

Cyclodextrins (CDs) are cyclic glucose oligomers that can form inclusion complexes with numerous organic compounds and so have found numerous applications in various fields, such as analytical chemistry, agrochemistry, pharmaceuticals, foods, cosmetics and catalysis.[1] In this last field, CDs can be used as a macrocyclic platform to build ligands for organometallic catalytic processes.[2] Several CD-functionalised phosphorous ligands and their organometallic complexes have been described in the literature.[3–24] Nevertheless, only some of these ligands have been used during organometallic catalytic processes either in organic media or in aqueous media. In organic media, asymmetric hydrogenation of various prochiral substrates was performed by using a diphosphite-α-CD (dimethyl itaconate; *ee* 84%),[4] a diphosphane-β-CD (derivatives of cinnamic acid or ester, acrylic acid or ester and itaconic acid or ester; *ee* 49–92%),[24] and a tetraphoshane-α-CD (amino acid precursor, *ee* 25%) as ligands.[21] A diphosphite-α-CD[4] and a monophosphinite-β-CD[3] were exploited in hydroformylation reactions of aryl and alkyl olefins. A diphosphane-α-CD was also used in an ethene and propene dimerisation reaction.[16] In aqueous media, rhodium species based on diphosphane-β-CD were active in the hydrogenation of nitroaromatics[12] and in hydrogenation and hydroformylation of aryl and alkyl olefins.[7,10,11] Alkyl olefins were also hydroformylated by using diphosphane-α-CD as a ligand.[13] To the best of our knowledge, only one diphenyl monophosphane β-CD has been evaluated as a water-soluble ligand in the hydrogenation of olefins.[7] Nevertheless, hydrogenation occurred only under forcing conditions and led to the formation of colloidal rhodium, which then acted as a poor catalyst.

As an original extension of these works, we report the synthesis of a new diphenyl monophosphane β-CD that exhibits a dual solubility in both organic solvents and water. An interesting property of solvent-dependent conformation change was evidenced by NMR spectroscopic studies. Hydrogenation or hydroformylation reactions performed in water or in organic solvents showed that this ligand was able

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to stabilise catalytically active rhodium species in solution. In the case of the hydroformylation reaction, it was demonstrated that regioselectivity was influenced by the solvent-dependent conformation of the ligand.

## Results and Discussion

The monophosphane 6$^{A}$-deoxy-6$^{A}$-diphenylphosphinyl-2$^{A}$,2$^{B}$,2$^{C}$,2$^{D}$,2$^{E}$,2$^{F}$,2$^{G}$,3$^{A}$,3$^{B}$,3$^{C}$,3$^{D}$,3$^{E}$,3$^{F}$,3$^{G}$,6$^{B}$,6$^{C}$,6$^{D}$,6$^{E}$,6$^{F}$,6$^{G}$-eicosa-*O*-methyl-β-cyclodextrin (permethylated β-cyclodextrin monodiphenyl phosphane: PM-β-CD-PPh$_2$) was prepared in three steps from β-CD (Scheme 1). β-CD was treated with tosyl chloride in basic medium to give β-CD-OTs (yield 19%),[25] which was permethylated in the presence of methyl iodide and NaH to give PM-β-CD-OTs (yield 50%).[26] PM-β-CD-OTs was then treated with KPPh$_2$ (2 equiv) in a DMF/THF mixture. After purification by column chromatography under N$_2$, PM-β-CD-PPh$_2$ was obtained as a white amorphous solid (yield 85%).

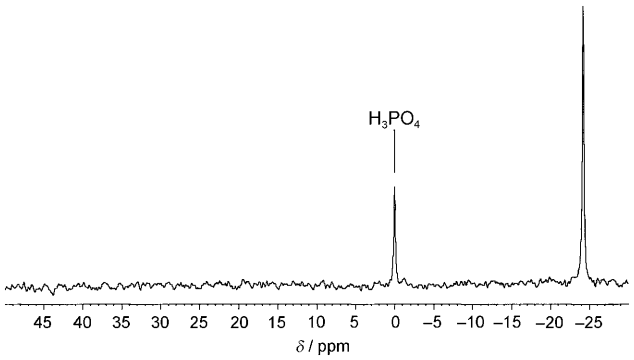
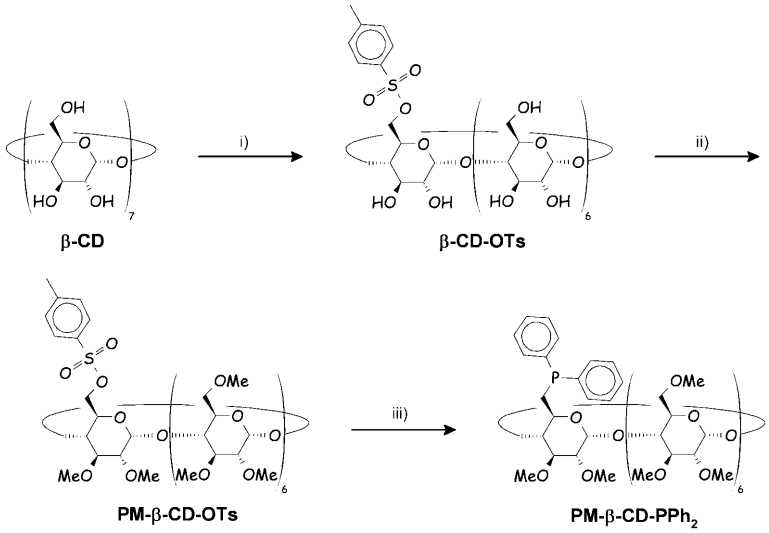



Figure 1. $^{31}P\{^{1}H\}$ NMR spectrum (293.15 K; 121.49 MHz; 1 mM in $D_2O$) of PM-β-CD-PPh$_2$. $H_3PO_4$ was used as external phosphorous reference.




Scheme 1. Synthetic pathway of the cyclodextrin-based phosphane: PM-β-CD-PPh$_2$. Reagents and conditions: i) TsCl, NaOH, $H_2O$, 2 h at RT then HCl (6 N), 24 h at 4 °C, 19%; ii) $CH_3I$, NaH, anhyd DMF, 6 h at 0 °C then 12 h at RT, 50%; iii) KPPh$_2$, anhyd DMF/THF, 18 h at 65 °C, 85%.

PM-β-CD-PPh$_2$ was first characterised by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS). The MS spectrum showed the expected molecular peaks (see the Supporting Information). The first NMR spectroscopic characterisations were performed in pure $D_2O$. The $^{31}P$ NMR spectrum of PM-β-CD-PPh$_2$ showed only one peak at $\delta = -24.3$ ppm, which indicated that no phosphane oxide was present (Figure 1).

The $^{1}H$ and $^{13}C$ NMR spectroscopic assignments were performed by using one and two-dimensional high-resolution experiments (see Figure 2 and the Supporting Information). Surprisingly, the $^{1}H$ and $^{13}C$ NMR spectra showed that the two phenyl groups are non-equivalent (protons $H_b$, $H_c$, $H_d$, $H_{b'}$, $H_{c'}$ and $H_{d'}$ can be distinguished). This phenomenon was explained by T-ROESY experiments. Indeed, the T-ROESY NMR spectra clearly revealed dipolar contacts between the CD and phosphane moieties (Figure 3). More precisely, the strongest contacts were observed between the protons of one aromatic ring ($H_b$ and $H_c$) and the inner CD protons ($H_3$ and $H_5$). This experiment showed that a phenyl group of the phosphane moiety is included into the CD cavity. Additional evidence was found by a $^{1}H$ NMR spectroscopic analysis performed in [D$_6$]DMSO The spectral dispersion of aromatic protons observed in water collapses and only one large peak is observed in DMSO (Figure 4). The strongly solvating power of DMSO for the CD cavity is known to preclude the formation of inclusion complexes.[27,28] These two last experiments undoubtedly show that an inter- or intramolecular complexation phenomenon occurs leading to a distinction between the two phenyl groups.

To provide a distinction between inter- or intramolecular complexes, NMR spectroscopic analyses were performed in aqueous medium at various concentrations (in the range of 0.5 to 3 mM). No displacement of $^{1}H$ or $^{31}P$ NMR signals was observed during these dilution experiments (see the Supporting Information). In addition, temperature increase (up to 50 °C) did not substantially change the spectral characteristics of $^{1}H$ or $^{31}P$ NMR signals (see the Supporting Information). All these observations are in line with the formation of a self-inclusion phenomenon. It is important to underline that a such phenomenon has already been observed for CD possessing a pendant substituent.[8,27–29]

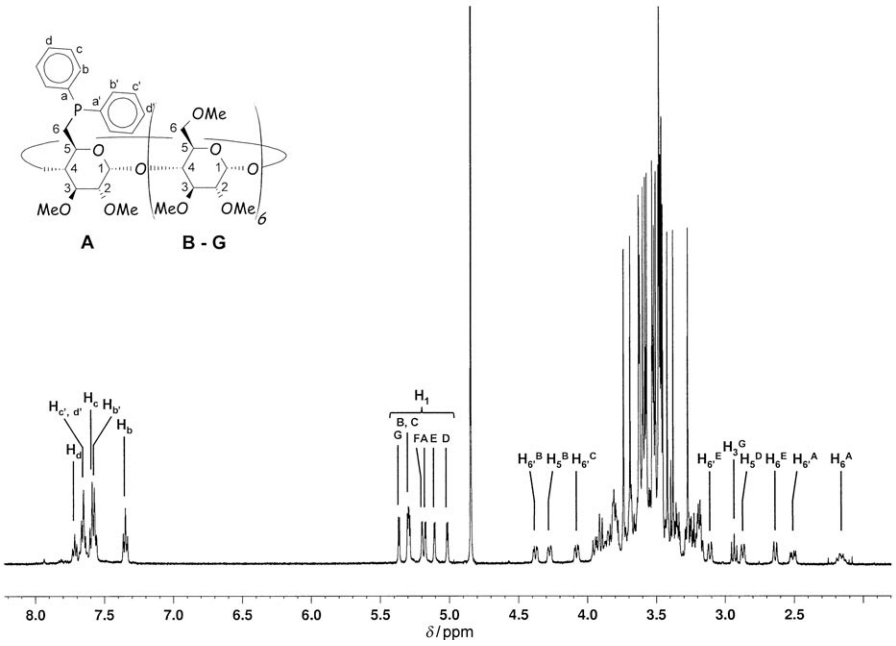



Figure 2. $^1$H NMR spectrum (295.15 K; 500.13 MHz; 1 mM in $D_2O$) of PM-β-CD-$PPh_2$ showing the dispersion of the aromatic and anomeric protons.

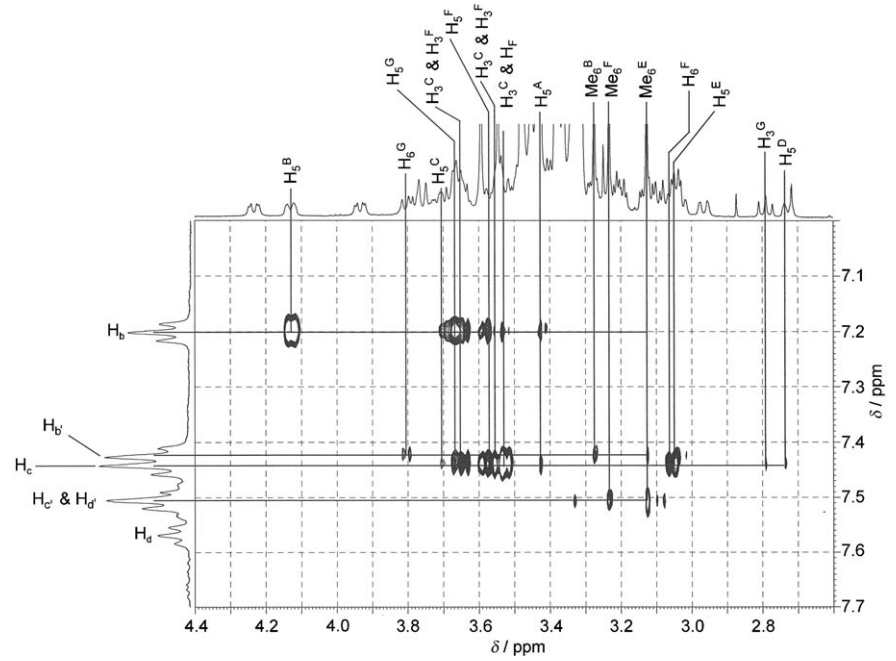



Figure 3. Partial contour plot of a T-ROESY experiment (295.15 K; 500.13 MHz; 1 mM in $D_2O$; spin lock time 500 ms) performed on PM-β-CD-$PPh_2$. Vertical scale: aromatic area, horizontal scale: CD area. See Figure 2 for the atom labelling system.

To estimate the strength of the self-inclusion complex, attempts were made to include an external host in the PM-β-CD-$PPh_2$ cavity. 1-Adamantanecarboxylate sodium salt (ACNa) was selected because of its high affinity for the β-CD cavity. Indeed, the value of association constant for the β-CD/ACNa complex was equal to 30000 M$^{-1}$.[30] The association constant between ACNa and PM-β-CD-$PPh_2$ was determined by NMR spectroscopic studies in aqueous medium and for comparison it was also determined with Trime-β-CD (a permethylated β-CD). Indeed, ACNa is included in the Trime-β-CD cavity by the secondary face (wide side). Because the secondary face of PM-β-CD-$PPh_2$ is similar to that of Trime-β-CD, this latter is a good control. The values of association constants with ACNa are equal to 10700 M$^{-1}$ in the case of Trime-β-CD and 265 M$^{-1}$ in the case of PM-β-CD-$PPh_2$. This lower value signifies that the self-inclusion complex is very strongly stabilised. So, the occupation of the cavity by this aromatic moiety will prevent the formation of stable inclusion complexes with numerous guests.

PM-β-CD-$PPh_2$ is also soluble in various solvents (MeOH, EtOH, $CHCl_3$, $CH_2Cl_2$, THF, DMF, cyclohexane and heptane). Because the main driving forces of self-inclusion phenomena are due to hydrophobic effects, it seemed interesting to study this potential self-inclusion in organic medium. A T-ROESY experiment was performed on PM-β-CD-$PPh_2$ in $C_6D_{12}$ and no dipolar contact was observed (see the Supporting Information). This result suggests that the two phenyl groups are outside the CD cavity. The self-inclusion phenomenon observed in water disappears in organic solvents, and so the conformation of PM-β-CD-$PPh_2$ depends on the solvent. To illustrate the PM-β-CD-$PPh_2$ arrangement in each solvent, a schematic representation is depicted in Figure 5.

This interesting property of dual solubility could allow organometallic catalytic reactions to be performed in aqueous, organic, or aqueous/organic biphasic media. Because PM-β-CD-$PPh_2$ is soluble in water as much as in heptane (3 mM) and because heptane is often used as the organic phase during aqueous biphasic organometallic catalytic processes, the distribution of PM-β-CD-$PPh_2$ in a mixture of heptane/

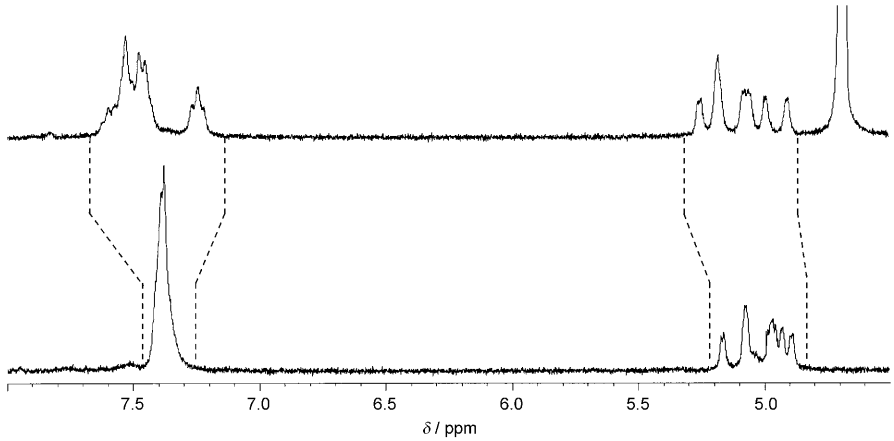



Figure 4. $^1$H NMR spectra (293.15 K; 300.13 MHz; 1 mM) showing the aromatic and anomeric regions of PM-β-CD-$PPh_2$ in water (top) and DMSO (bottom).

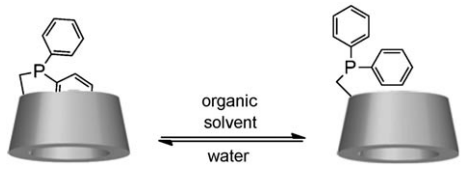



Figure 5. Schematic representation of the PM-β-CD-$PPh_2$ conformation as a function of solvent.

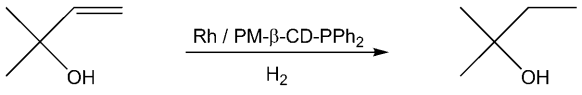
water was determined. The partition coefficient ($P_{ow}$) is equal to 0.48, that is, 68% of PM-β-CD-$PPh_2$ stays in water and 32% moves to the organic layer. These values are not in accordance with the specifications required for an application in biphasic aqueous organometallic catalytic processes because the water-soluble catalyst does not remain in the aqueous layer, which prevents recycling. So, PM-β-CD-$PPh_2$ can be used as a ligand in pure water or in pure organic solvent, but not in a mixture of the two.

We first studied the behaviour of PM-β-CD-$PPh_2$ during the hydrogenation reaction of 2-methyl-3-buten-2-ol in pure water (Table 1). The potential interactions between 2-methyl-3-buten-2-ol and PM-β-CD-$PPh_2$ were studied by using NMR spectroscopy in water (see the Supporting Information). It is important to underline that this substrate does not form an inclusion complex with PM-β-CD-$PPh_2$, which indicates that this latter behaves only as a ligand for the transition metal.

For the catalytic system [Rh(cod)$_2$]$BF_4$/PM-β-CD-$PPh_2$, the conversion was low at 20°C and it was necessary to increase the temperature up to 60°C to reach high conversion after 4 h (Table 1, entries 1 and 2). When [Rh(acac)(CO)$_2$] was used as a catalytic precursor, the conversion was four times lower (Table 1, entry 3). The increase in PM-β-CD-$PPh_2$/Rh ratio decreased the conversion; indeed the catalytic species are the most stable and, therefore, the least active (Table 1, entry 4). In each case, it is important to underline that the aqueous catalytic phase stayed yellow and that no colloidal rhodium particles were observed during or at the end of the reaction. These observations indirectly prove that PM-β-CD-$PPh_2$ is able to stabilise rhodium species in aqueous solution.

We were then interested in the performance of PM-β-CD-$PPh_2$ in the hydroformylation of methyl 4-pentenoate in pure water (Table 2). The hydroformylation reaction was chosen as a model reaction because it is able to provide interesting information concerning activity, chemoselectivity and regioselectivity. By using NMR spectroscopy studies, it was demonstrated that methyl 4-pentenoate is not able to form an inclusion complex with PM-β-CD-$PPh_2$ (see the

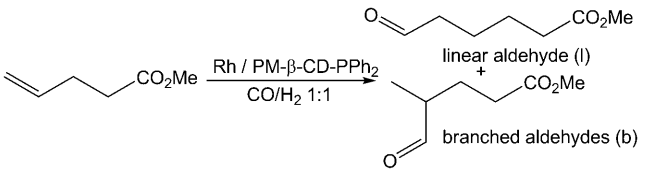
Table 1. Rhodium-catalysed hydrogenation of 2-methyl-3-buten-2-ol in the presence of PM-β-CD-$PPh_2$ as ligand.[a]




| | Catalytic precursor | L/Rh | $T$ [°C] | Conversion[b] [%] |
|---|---|---|---|---|
| 1 | [Rh(cod)$_2$]$BF_4$ | 2 | 20 | 6 |
| 2 | [Rh(cod)$_2$]$BF_4$ | 2 | 60 | 97 |
| 3 | [Rh(acac)(CO)$_2$] | 2 | 60 | 18 |
| 4 | [Rh(cod)$_2$]$BF_4$ | 4 | 60 | 63 |

[a] Experimental conditions: [Rh(cod)$_2$]$BF_4$ or [Rh(acac)(CO)$_2$] ($7.55\times10^{-3}$ mmol), L: PM-β-CD-$PPh_2$; water (12 mL), 2-methyl-3-buten-2-ol (1.89 mmol), 1250 rpm, $P(H_2)=1$ atm; $t=4$ h. [b] Olefin conversion (calculated with respect to the starting olefin).

Table 2. Rhodium-catalysed hydroformylation of methyl 4-pentenoate in the presence of PM-β-CD-$PPh_2$ as the ligand.[a]




| | Solvent | L/Rh | $P$(CO/$H_2$) [bar] | Conversion[b] [%] | Selectivity[c] [%] | l/b ratio[d] |
|---|---|---|---|---|---|---|
| 1 | water | 4 | 50 | 96 | 99 | 1.8 |
| 2 | water | 8 | 50 | 97 | 99 | 1.8 |
| 3 | water | 4 | 25 | 89 | 99 | 1.9 |
| 4 | heptane | 4 | 50 | 83 | 99 | 1.2 |
| 5 | heptane | 8 | 50 | 82 | 98 | 1.2 |
| 6 | heptane | 4 | 25 | 88 | 98 | 1.2 |

[a] Experimental conditions: [Rh(acac)(CO)$_2$] ($1.94\times10^{-3}$ mmol); L: PM-β-CD-$PPh_2$; solvent (6 mL); methyl 4-pentenoate (0.97 mmol); 1500 rpm; $T=80$°C; time: 2 h. [b] Olefin conversion (calculated with respect to the starting olefin). [c] Aldehyde selectivity, i.e., (mol of aldehydes)/(mol of converted olefins)×100. The side products were mainly isomeric olefins. [d] Ratio of linear to branched aldehyde product.

Supporting Information). When PM-β-CD-$PPh_2$ was used as a ligand (Table 2, entry 1), high conversion was reached after 2 h. The aldehyde selectivity was 99%, which shows that no isomerisation or hydrogenation of the double bound occurred. The ratio of linear to branched aldehydes (l/b) was 1.8. When the PM-β-CD-$PPh_2$/Rh ratio was increased from 4 to 8 (Table 2, entries 1 and 2) or the $CO/H_2$ pressure was decreased from 50 to 25 bar (Table 2, entries 1 and 3), no remarkable change was observed. It was interesting to evaluate the catalytic properties of Rh/PM-β-CD-$PPh_2$ in organic medium because PM-β-CD-$PPh_2$ possesses a dual solubility. Heptane was chosen as the reaction solvent and methyl 4-pentenoate as the substrate because it is miscible with heptane, and experiments similar to those described above were performed in heptane (compare Table 2, entries 1–3 and 4–6). The conversions were slightly lower in heptane, but the chemoselectivities were almost unchanged. However, the l/b ratio decreased from 1.8 in water to 1.2 in heptane. To understand this phenomenon, experiments were performed in heptane with triphenylphosphane (TPP) as the ligand, and in water with trisulfonated triphenylphosphane (TPPTS) as the ligand. After a reaction time of 2 h, high conversions (>98%) and selectivities (>99%) were reached with a l/b ratio of 1.8 in the presence of each phosphane. These results suggest that the l/b ratio decrease was not due to a solvent effect. One hypothesis could be a modification of the conformation of PM-β-CD-$PPh_2$. Indeed, the self-inclusion phenomenon observed in water disappears in organic solvents and, therefore, the conformation of PM-β-CD-$PPh_2$ is different in each solvent. PM-β-CD-$PPh_2$ is rigid in water, whereas it is more flexible in heptane because the two phenyl groups are outside the CD cavity.

## Conclusion

PM-β-CD-$PPh_2$ is a valuable ligand for organometallic catalytic processes performed in water or organic solvents. In addition, the conformation of this ligand is solvent-tunable, and this interesting property opens the way to specific selectivity during organometallic processes.

## Experimental Section

**General**: The starting β-cyclodextrin was a generous gift from Roquette Frères (Lestrem, France). Most of the chemical products, reagents and solvents used in this study were purchased from Acros Organics and Sigma–Aldrich in their highest purity and used without further purification. Catalytic precursors, heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin and deuterated solvents were purchased respectively from Strem Chemicals (Bischheim, France), Cyclolab (Budapest, Hungary) and Euriso-Top (Gif sur Yvette, France) in their highest purity and used without further purification. Distilled water was used in all experiments. The sodium salt of TPPTS was synthesised as previously reported.[31] $CO/H_2$ mixture (1:1) and $H_2$ were used directly from cylinders (>99.9% pure; Air Liquide). Analytical thin-layer chromatography plates (TLC silica gel 60 $F_{254}$ aluminium) and silica (Geduran® Si 60 (0.063–0.200 mm)) for preparative column chromatography were purchased from Merck. Compounds were identified by using UV fluorescence and/or staining with a solution of phosphomolybdic acid in aqueous sulfuric acid and EtOH. Characterisation and structure determinations were achieved by NMR spectroscopy experiments by using a Bruker Avance DRX300 spectrometer operating at 300.13 MHz for $^1$H nuclei, 75.47 MHz for $^{13}$C nuclei and 121.49 MHz for $^{31}$P nuclei, or by using a Bruker Avance 500 spectrometer operating at 500.13 MHz for $^1$H nuclei and 125.76 MHz for $^{13}$C nuclei. 1D and 2D NMR spectroscopy experiments were obtained by using the pulse programs available from the Bruker library. Details concerning experimental conditions are given in the Figure captions. All NMR measurements were performed under careful temperature regulation by using a Bruker BVT variable temperature unit. Chemical shifts are given in parts per million (ppm) relative to an external reference by using internal capillary (sodium salt of 3-(trimethylsilyl)-2,2,3,3-tetradeuteropropionic acid (98% atom D) in $D_2O$ for $^1$H and $^{13}$C NMR and $H_3PO_4$ in $H_2O$ for $^{31}$P NMR) and calibration was performed by using the signal of the residual signals of the solvent as a secondary reference while taking into account temperature effects. The MALDI-TOF mass spectra were recorded on a MALDI-TOF-TOF Bruker Daltonics Ultraflex II spectrometer in positive reflectron mode by using 2,5-dihydroxybenzoic acid as a matrix and external peptide calibration standard kit (Bruker Daltonics) within a mass range of 750–4200. The acceleration voltage was fixed at 25 keV, the delayed extraction time at 10 ns and the number of laser shots at 200. The samples were dissolved either in $H_2O$, acetone or MeOH and equally mixed with the matrix solution (10 mg mL$^{-1}$ of 2,5-dihydroxybenzoic acid (2,5-DHB) in $H_2O$/0.1% TFA/MeCN, 70:30 (v/v)) and spotted onto a ground-style MALDI target according to the dried droplet method. The UV/Vis experiments were performed by using a Perkin–Elmer Lambda 19 spectrophotometer at ambient temperature (293.15 K) with a 10 mm quartz cell. Gas chromatographic analyses were carried out on a Shimadzu GC-17 A gas chromatograph equipped with a methyl silicone capillary column (30 m × 0.32 mm) and a flame ionisation detector.

**Synthesis of 6$^A$-deoxy-6$^A$-diphenylphosphinyl-2$^A$,2$^B$,2$^C$,2$^D$,2$^E$,2$^F$,2$^G$,3$^A$,3$^B$,-3$^C$,3$^D$,3$^E$,3$^F$,3$^G$,6$^B$,6$^C$,6$^D$,6$^E$,6$^F$,6$^G$-eicosa-*O*-methyl-β-cyclodextrin**: 6$^A$-*O*-(*p*-tolylsulfonyl)-2$^A$,2$^B$,2$^C$,2$^D$,2$^E$,2$^F$,2$^G$,3$^A$,3$^B$,3$^C$,3$^D$,3$^E$,3$^F$,3$^G$,6$^B$,6$^C$,6$^D$,6$^E$,6$^F$,6$^G$-eicosa-*O*-methyl-β-cyclodextrin was obtained in two steps from the native β-cyclodextrin, as previously described in the literature.[25,26] A solution of potassium phosphide ($KPPh_2$) in THF (0.5 M, 6 mL, 3 mmol) was added under an inert atmosphere to a stirred solution of dried 6$^A$-*O*-(*p*-tolylsulfonyl)-2$^A$,2$^B$,2$^C$,2$^D$,2$^E$,2$^F$,2$^G$,3$^A$,3$^B$,3$^C$,3$^D$,3$^E$,3$^F$,3$^G$,6$^B$,6$^C$,6$^D$,6$^E$,6$^F$,6$^G$-eicosa-*O*-methyl-β-cyclodextrin (2.3 g, 1.47 mmol) in dry DMF (15 mL) and freshly distilled THF (20 mL). The reaction mixture was stirred for 18 h at 65 °C under $N_2$, then degassed, deionised (30 mL) $H_2O$ was added. The product was extracted under $N_2$ with degassed EtOAc (4 × 30 mL). After evaporation of most of the solvent, the residual syrup was then purified by column chromatography on silica gel under $N_2$ by using EtOAc as the eluent to give the title product as a white amorphous solid (2.0 g, 85%). $^1$H NMR (500.13 MHz, $D_2O$, 295.15 K, TMSP): $\delta = 7.71$ (t, $^3J(H_c,H_d) = 7.3$ Hz, 1H; $H_d$), 7.69–7.61 (m, 3H; $H_{c'}$, $H_{d'}$), 7.61–7.54 (m, 4H; $H_{b'}$, $H_c$), 7.35 (t, $^3J(H_b,H_c) \approx {}^3J(P,H_b) = 7.3$ Hz, 2H; $H_b$), 5.37 (d, $^3J(H_1,H_2) = 4$ Hz, 1H; $H_1^G$), 5.31–5.28 (m, 2H; $H_1^B$, $H_1^C$), 5.20 (d, $^3J(H_1,H_2) = 3.2$ Hz, 1H; $H_1^F$), 5.17 (d, $^3J(H_1,H_2) = 3.2$ Hz, 1H; $H_1^A$), 5.11 (d, $^3J(H_1,H_2) = 3.5$ Hz, 1H; $H_1^E$), 5.02 (d, $^3J(H_1,H_2) = 3.5$ Hz, 1H; $H_1^D$), 4.38 (dd, $^3J(H_5,H_{6'}) = 4$ Hz, $^2J(H_6,H_{6'}) = 12$ Hz, 1H; $H_6^B$), 4.31–4.23 (m, 1H; $H_5^B$), 4.08 (dd, $^3J(H_5,H_{6'}) = 3.5$ Hz, $^2J(H_6,H_{6'}) = 11$ Hz, 1H; $H_{6'}^C$), 3.98–3.15 (m, 93H; $H_2^{A-G}$, $H_3^{A-F}$, $H_4^{A-G}$, $H_5^A$, $H_5^C$, $H_5^{E-G}$, $H_6^{B-D}$, $H_6^{F-G}$, $H_{6'}^D$, $H_{6'}^{F-G}$, $Me_2^{A-G}$, $Me_3^{A-G}$, $Me_6^{B-G}$), 3.12 (d, $^2J(H_6,H_{6'}) = 11$ Hz, 1H; $H_{6'}^E$), 2.95 (t, $^3J(H_2,H_3) \approx {}^3J(H_3,H_4) = 9.5$ Hz, 1H; $H_3^G$), 2.92–2.86 (m, 1H; $H_5^D$), 2.65 (d, $^2J(H_6,H_{6'}) = 11$ Hz, 1H; $H_6^E$), 2.51 (dd, $^2J(P,H_{6'}) = 5.7$ Hz, $^2J(H_6,H_{6'}) = 13.5$ Hz, 1H; $H_6^A$), 2.22–2.10 ppm (m, 1H, $H_6^A$); $^{13}$C NMR (125.76 MHz, $D_2O$, 295.15 K, TMSP): $\delta = 141.2$ ($C_a$), 139.0 ($C_{a'}$), 135.2 ($C_b$), 134.3 ($C_{b'}$), 132.6 ($C_d$), 132.0 ($C_{d'}$), 131.7 ($C_{c'}$), 131.3 ($C_c$), 100.8 ($C_1^E$), 100.7 ($C_1^D$), 100.6 ($C_1^B$, $C_1^C$, $C_1^F$), 99.5 ($C_1^G$), 98.5 ($C_1^A$), 84.4 ($C_3^A$), 83.7 ($C_3^C$, $C_3^G$), 83.6 ($C_3^D$), 83.2 ($C_2^A$), 83.1 ($C_2^D$ or $C_2^E$, $C_3^F$), 83.0 ($C_4^G$), 82.9 ($C_3^B$), 82.8 ($C_3^E$), 82.7 ($C_2^C$, $C_4^C$), 82.4 ($C_2^D$ or $C_2^E$), 82.3 ($C_2^F$), 82.1 ($C_2^G$), 82.0 ($C_4^F$), 81.8 ($C_2^B$), 81.2 ($C_4^B$), 80.9 ($C_4^E$), 80.5 ($C_4^A$), 78.8 ($C_4^D$), 74.0 ($C_5^G$), 73.6 ($C_5^C$), 73.5 ($C_5^B$), 73.2 ($C_5^F$), 73.0 ($C_6^B$, $C_6^D$), 72.8 ($C_6^G$), 72.6 ($C_5^E$), 71.9 ($C_5^D$), 72.7 ($C_6^C$), 71.5 ($C_6^E$), 71.2 ($C_6^F$), 69.3 ($C_5^A$), 63.9 ($Me_3^G$), 63.5 ($Me_3^C$), 63.3 ($Me_3^B$), 63.2 ($Me_3^F$), 62.4 ($Me_3^E$), 62.0 ($Me_2^G$, $Me_3^D$), 61.4

($Me_2^C$), 61.1 ($Me_6^B$), 61.0 ($Me_3^A$), 60.9 ($Me_6^G$), 60.7 ($Me_6^{C-F}$), 60.4 ($Me_2^D$ or $Me_2^E$), 60.0 ($Me_2^A$), 59.9 ($Me_2^B$), 59.8 ($Me_2^D$ or $Me_2^E$, $Me_2^F$), 33.5 ppm ($C_6^A$); $^{31}P\{^1H\}$ NMR (121.49 MHz, $D_2O$, 293.15 K, TMSP): $\delta = -24.3$ ppm (s); UV/Vis ($H_2O$, 293.15 K): $\lambda_{max}$ ($\log\varepsilon$) = 247 nm (3.79); MALDI-TOF-MS: *m/z* calcd for $[C_{74}H_{119}O_{34}P+H]^+$: 1583.74; found: 1583.64; *m/z* calcd for $[C_{74}H_{119}O_{34}P+Na]^+$: 1605.72; found: 1605.50; *m/z* calcd for $[C_{74}H_{119}O_{34}P+K]^+$: 1621.70; found: 1621.46.

**Determination of the stoichiometry of inclusion complexes by the continuous variation method**: The stoichiometry of CD/ACNa complexes was provided by the continuous variation method (Job's method) by using NMR spectroscopy. A series of samples containing ratios of CD and ACNa that varied from 0 to 1 was prepared, keeping the total concentration of interacting species constant (1 mM). Chemical shift variation of the CD or ACNa was measured for a given molar ratio. The product $\Delta\delta \times c$ ($\Delta\delta$ is the chemical shift variation observed and $c$ is the concentration of the observed compound, that is, CD or ACNa) was plotted as a function of the molar ratio, $r$.

**Determination of the association constant of inclusion complexes**: The evaluation of the host inclusion ability towards the sodium salt of 1-adamantane carboxylic acid (ACNa) was determined by NMR spectroscopy combined with the direct titration method. This method was applied for a fixed concentration of CD (1 mM) and varying concentrations of ACNa.

Assuming a 1:1 stoichiometry, the calculation of the formation constant $K_f$ was developed as follows:

$$K_f = \frac{[CD/ACNa]}{[CD] \times [ACNa]} = \frac{[CD/ACNa]}{([CD]_0 - [CD/ACNa]) \times ([Guest]_0 - [CD/ACNa])}$$

and [CD/ACNa] can be estimated by:

$$[CD/ACNa] = -\frac{1}{2} \times \sqrt{\left(\frac{1}{K_f} + [CD]_0 + [ACNa]_0\right)^2 - 4 \times [CD]_0 \times [ACNa]_0} + \frac{1}{2} \times \left(\frac{1}{K_f} + [CD]_0 + [ACNa]_0\right)$$

For a given value of $K_f$, the [CD/ACNa] concentration was known and thus the chemical shift of the complex can be calculated. An algorithm treatment was then applied to minimise the difference between the experimental and the theoretical values of the spectral characteristics for each concentration of CD. The association constant was determined by computer fitting of the experimental titration curve.

**General procedure for the hydrogenation reaction**: The first step was the preparation of the catalytic solutions under $N_2$ by using standard Schlenk techniques. In a typical experiment, $[Rh(cod)_2]BF_4$ or $[Rh(acac)(CO)_2]$ ($7.55 \times 10^{-3}$ mmol) and phosphane ($1.51 \times 10^{-2}$ mmol) were dissolved in deoxygenated $H_2O$ (12 mL) over 15 min. Then the catalytic aqueous solution was preincubated overnight under a $H_2$ atmosphere in a glass reactor to saturate the solution and to generate the active catalytic species. After this incubation step, 2-methyl-3-buten-2-ol (1.89 mmol) was added to the catalytic solution. The glass reactor was then heated at 60 °C and stirred with a magnetic stirrer, and the link between the glass reactor and the $H_2$ gas burette was established. For kinetic measurements the time corresponding to the desired temperature was considered to be the beginning of the reaction. The reaction medium was sampled during the reaction by GC analyses and $H_2$ consumption.

**General procedure for the hydroformylation reaction**: All catalytic reactions were performed under $N_2$ by using standard Schlenk techniques. All solvents and liquid reagents were degassed with bubbling $N_2$ for 15 min before each use or by performing two freeze–pump–thaw cycles before use. In a typical experiment, $[Rh(acac)(CO)_2]$ ($1.94 \times 10^{-3}$ mmol) and phosphane ($7.76 \times 10^{-3}$ mmol) were dissolved in degassed solvent (6 mL). The resulting aqueous phase and the olefinic-type substrate (0.97 mmol) were added to the 25 mL stainless steel autoclave (Parr) under an atmosphere of $N_2$, then heated at 80 °C. The mechanical stirrer equipped with a multipaddle unit was then started (1500 rpm) and the autoclave was pressurised with $CO/H_2$ (50 bar; 1:1) from a gas reservoir connected to the reactor through a high-pressure regulator valve, which allowed the pressure in the reactor to be kept constant throughout the whole reaction. The reaction medium was sampled after 2 h for GC analyses of the organic phase after decantation. For kinetic measurements, the time corresponding to the addition of $CO/H_2$ was considered to be the beginning of the reaction.

**Determination of the partition coefficient**: The determination of partition coefficient of the cyclodextrin-based phosphane in a heptane/water mixture was determined according to the shake-flask method. Both solvents were mutually saturated before the measurement, which was carried out at a concentration of 0.1 M and for a heptane/water ratio equal to 1:1. The samples were hand-shaken and stirred with a magnetic stirrer for 15 min, then left to equilibrate for 24 h at RT. The amount of PM-β-CD-$PPh_2$ in each phase was determined by UV/Vis spectroscopy. The partition coefficients are mean values for the different experiments. The standard deviation of the partition coefficient was usually around 2% and always less than 5%.

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