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Note

Thermodynamic insight into the origin of the inclusion of monosulfonated isomers of triphenylphosphine into the β-cyclodextrin cavity

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Abstract

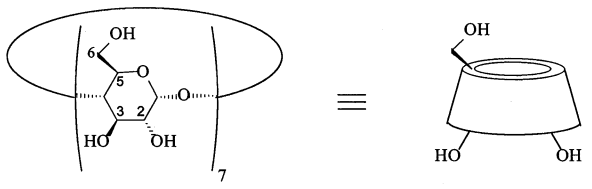
Formation of inclusion complexes between the β-cyclodextrin and the potassium salt of *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphine derivatives was investigated in aqueous solution by NMR spectroscopy. Titration and continuous variation plots obtained from ^{31}P and ^{1}H NMR data indicate the formation of a 1:1 inclusion complex for the three phosphine isomers. T-ROESY NMR experiments show that in all cases a non-sulfonated aromatic ring was included into the hydrophobic cavity of β-cyclodextrin from the secondary hydroxyl groups side. The standard enthalpy and entropy of the inclusion process were estimated from the temperature dependence of the association constant. All inclusion complexes were enthalpy stabilized, but highly entropy destabilized.

Keywords: Inclusion complex; β-Cyclodextrin; Monosulfonated triphenylphosphine; NMR spectroscopy; Enthalpy; Entropy

1. Introduction

In the course of our work on the use of cyclodextrins as mass transfer promotors in aqueous phase organometallic catalysis, we found that β-cyclodextrin (β-CD, Scheme 1) forms inclusion complexes with the water-soluble ligands used to dissolve the catalyst in the aqueous phase.[1,2] So, we have reported that the sodium salt of the *m*-substituted trisulfonated triphenylphosphine [P(*m*-$C_6H_4SO_3Na)_3$][3,4] and the sodium salt of the *m*-substituted monosulfonated triphenylphosphine [P(*m*-$C_6H_4SO_3Na)(C_6H_5)_2$][5] are included into the hydrophobic cavity of the β-CD from the secondary hydroxyl groups side. In these initial studies, no attention was devoted to the complexation thermodynamics and, consequently, the driving forces responsible for the inclusion of these water-soluble phosphines are still unknown.

In order to clarify the mechanism for complexation of sulfonated triphenylphosphines, the formation of the corresponding inclusion complexes of the potassium salt of *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphine derivatives was investigated (Scheme 2). These guests will provide useful information on the possible effect of the position of the sulfonate group on the complexation thermodynamics.



Scheme 1. Schematic representation of the shape of β-CD. Protons H-3 and H-5 are situated inside the host cavity, whereas protons H-1, H-2 and H-4 point outwards.

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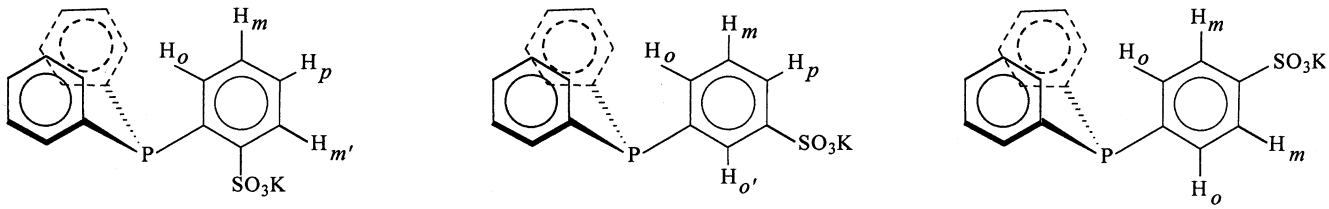

o-TPPMS *m*-TPPMS *p*-TPPMS

Scheme 2. Representation of the potassium salt of the *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphines. Protons of the sulfonated aromatic ring have been annotated (H-*m*, H-*m′*, H-*p*, H-*o′* and H-*o*).

Table 1
Association constant (K_f, M^{-1}) of the potassium salt of the corresponding *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphines with β-CD in water at various temperatures

Phosphine	K_f (298 K)	K_f (308 K)	K_f (318 K)	K_f (328 K)	K_f (338 K)	K_f (348 K)
o-TPPMS	3890 ± 50	2760 ± 30	1480 ± 20	800 ± 10	650 ± 30	410 ± 20
m-TPPMS	7110 ± 890	4770 ± 340	3060 ± 110	2050 ± 70	1550 ± 100	610 ± 40
p-TPPMS	77,300 ± 17720	41,160 ± 6380	26,270 ± 2400	18,000 ± 1800	9520 ± 710	6380 ± 630

Thus, for each inclusion complex, the stoichiometry, binding constant, the thermodynamic parameters ($\Delta H°$, $\Delta S°$) and the orientation of sulfonated triphenylphosphines in the host cavity of β-CD were determined.

2. Results and discussion

The evidence of an inclusion process and the stoichiometry of the inclusion complexes were provided by the continuous variation technique (Job's method).[6,7] For each phosphine, a series of samples containing variable ratios of β-CD and phosphine was prepared keeping the total concentration of species constant. In all cases, the ^{31}P and ^{1}H NMR spectra exhibited chemical shift variations for the phosphorus and protons of the phosphine and for most of the β-CD protons. In particular, the largest differences in the chemical shifts for the β-CD protons are always observed for the protons situated inside the hydrophobic cavity (H-3 and H-5), as expected for inclusion processes.[8] All Job's plots derived from the corresponding ^{1}H and ^{31}P NMR spectra show a maximum at $r = 0.5$ and highly symmetrical shapes, indicative of a 1:1 stoichiometry.[6–9]

The geometry and orientation of the guest molecule in the cavity were determined from two-dimensional T-ROESY experiments.[10] Figs. 1–3 display partial contour plots of the T-ROESY spectra of mixtures of phosphine and β-CD.

The lack of strong interactions between the β-CD protons and the sulfonated aromatic group on the one hand, and the strong dipolar contact observed between the H-5 and H-3 protons of the β-CD and the aromatic protons of the non-sulfonated aromatic ring on the other hand, fully prove that the inclusion occurs by a non-sulfonated aromatic ring for the three phosphines. For *o*-TPPMS and *m*-TPPMS, the weak cross-peaks between some protons of the sulfonated aromatic group (H-*m* and H-*o* for *m*-TPPMS; H-*o*, H-*m*, and H-*p* for *o*-TPPMS) and the H-3 proton suggest that: (i) the inclusion occurs by the secondary ring of the β-CD and that; (ii) the sulfonate group points toward the aqueous phase and remains exposed to the bulk solvent as schematically represented in Figs. 1 and 2. For *p*-TPPMS, the lack of cross-peaks between the H-6 protons of β-CD and guest protons supports that the inclusion of this phosphine also occurs by the secondary side of β-CD.

The stability constant K of each 1:1 inclusion complex at various temperatures was obtained by computer fitting of the phosphorus chemical shift titration curves. It is worth mentioning that whatever the phosphine and the temperature, the chemical shift values increased

Table 2
Thermodynamic parameters for the complexation of the potassium salt of the *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphines with β-CD in water

Phosphine	$\Delta H°$ (kJ mol^{-1})	$\Delta S°$ (J mol^{-1} K^{-1})
o-TPPMS	−39.9 ± 0.8	−65.0 ± 2.5
m-TPPMS	−39.3 ± 3.1	−57.2 ± 4.6
p-TPPMS	−42.5 ± 3.3	−49.1 ± 4.1

linearly up to a 1:1 host–guest molar ratio and leveled off markedly beyond this ratio, confirming the 1:1 stoichiometry obtained by Job's method. All the stability constants evaluated for the inclusion complexes at various temperatures are listed in Table 1.

The data given in Table 1 indicated that the stability of the inclusion complexes varies in the order *p*-TPPMS > *m*-TPPMS > *o*-TPPMS. All values were higher than those previously found for a trisulfonated triphenylphosphine–β-CD inclusion complex (1200 $M^{-1} \pm 120$ at 298 K),[4] indicating a better affinity of β-CD for monosulfonated triphenylphosphines due to their higher hydrophobic character. Surprisingly, the value found for the potassium salt of the *m*-substituted monosulfonated triphenylphosphine was lower than that found for the sodium salt of the corresponding phosphine (12,000 $M^{-1} \pm 700$ at 298 K),[5] suggesting that the counter ion of the sulfonate group could affect the inclusion process.

The thermodynamic parameters for inclusion processes were determined from the temperature dependence of the stability constant K using the van't Hoff relation. As shown in Fig. 4, the van't Hoff plots were apparently linear for the three phosphines within the temperature range considered in our study.

Therefore, changes in the heat capacity were neglected. The enthalpies and entropies were determined

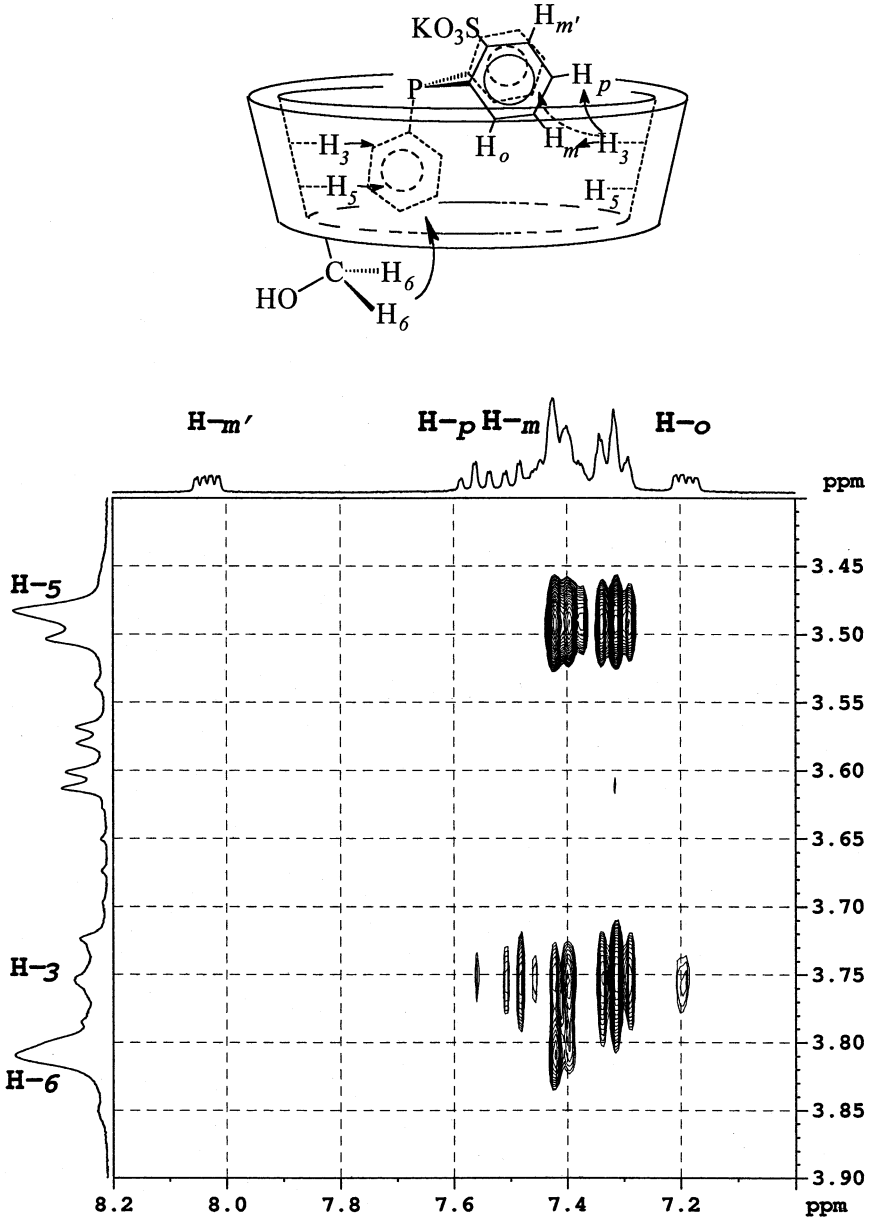

Fig. 1. Partial contour plot of the T-ROESY spectrum of a solution containing β-CD (2 mM) and *o*-TPPMS (8 mM) in D_2O at 298 K with a 300 ms mixing time. The deduced orientation of *o*-TPPMS in the β-CD cavity is also shown.

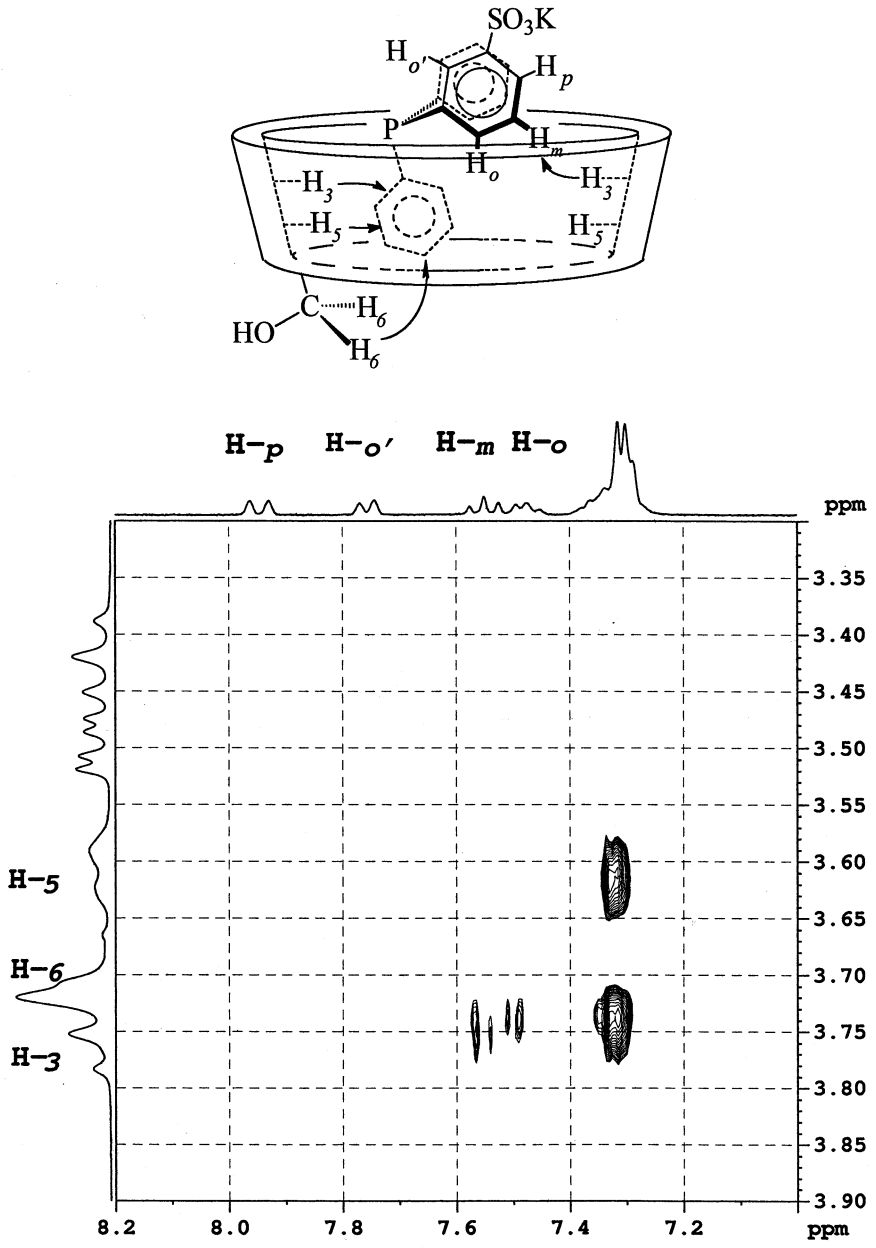

Fig. 2. Partial contour plot of the T-ROESY spectrum of a solution containing β-CD (3 mM) and *m*-TPPMS (6 mM) in D_2O at 298 K with a 300 ms mixing time. The deduced orientation of *m*-TPPMS in the β-CD cavity is also shown.

in the usual manner from the slopes and intercepts of the plots. The results are summarized in Table 2.

In view of the values shown in Table 2, it appears clear that sulfonated phosphine–β-CD inclusion complexes are all enthalpy stabilized and entropy disfavored, showing negative ΔH and ΔS. These negative values indicate that the attractive van der Waals interaction between a non-sulfonated ring of the phosphine and the walls of the CD cavity, rather than the entropically favorable desolvatation, is the major driving force for the inclusion process.[11,12] The fact that the ΔH values are almost identical, within the range of experimental error, may indicate that the three phosphines have the same structural motif included in the β-CD cavity. This is totally consistent with our 2D NMR studies that suggest similar geometries for the inclusion complexes of the *o*-, *m*- and *p*-isomers. The strong negative ΔS is typical of partial complexation of a large guest into the CD cavity. Indeed, when a part of the guest is outside the cavity in contact with the solvent, the positive contribution to ΔS from loss of solvation is minimized, and its loss in rotational and translational degrees lead to negative ΔS.[13,14] The trend observed for the ΔS values, i.e., $\Delta S_o < \Delta S_m < \Delta S_p$, appears to be

consistent with the requirement of a precise orientation of the sulfonate group upon encapsulation which induces decreasing degrees of freedom in the guest and, consequently, negative ΔS. This effect is more important when the sulfonate group is close to the phosphorus atom since less of the possible 'conformers' can fit properly into the cavity.

In conclusion, this work has demonstrated that the potassium salt of *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphine derivatives can bind to β-CD to form a 1:1 inclusion complex. The stability of these inclusion complexes varies in the order *p*-TPPMS > *m*-TPPMS > *o*-TPPMS. Comparison of the relevant ΔS and ΔH values indicates that this trend is entropically derive.

3. Experimental

General methods.—^{1}H and ^{31}P NMR spectra were recorded at 300.13 and 121.49 MHz, respectively, on a Bruker DRX instrument. Chemical shifts are given in

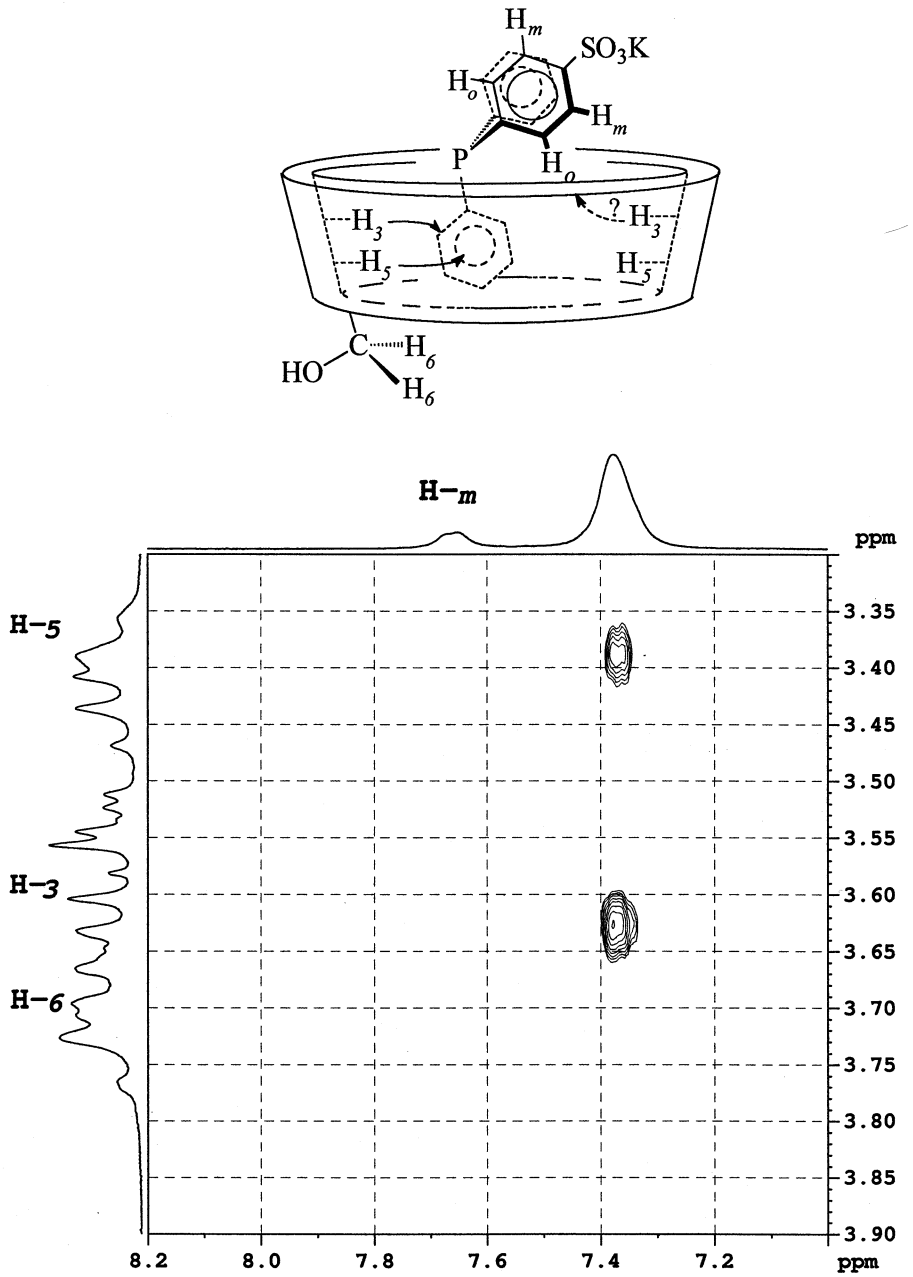

Fig. 3. Partial contour plot of the T-ROESY spectrum of a solution containing β-CD (2 mM) and *p*-TPPMS (8 mM) in D_2O at 298 K with a 300 ms mixing time. The deduced orientation of *p*-TPPMS in the β-CD cavity is also shown.

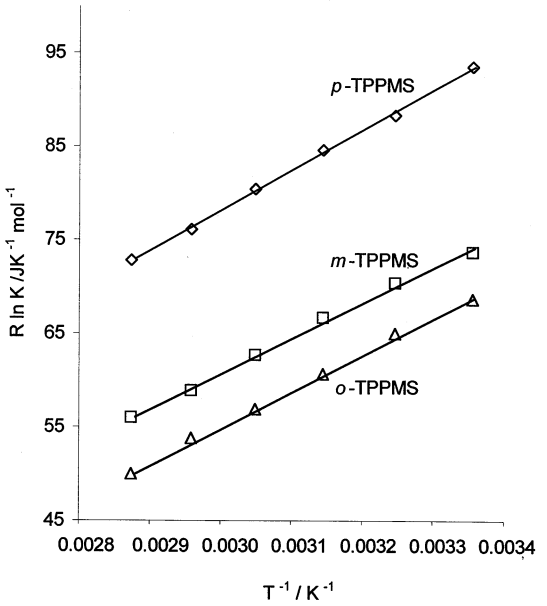

Fig. 4. Van't Hoff plots for the *o*-, *m*-, and *p*-substituted monosulfonated triphenylphosphines.

ppm relative to sodium [D_4]3-(trimethylsilyl)propionate (98% atom D) in D_2O using external reference. The notation used in NMR assignments of the potassium salt of the *o*- and *m*-substituted monosulfonated triphenylphosphines is indicated in Scheme 2. T-ROESY experiments were carried out as previously reported.[5] IRFT spectra were recorded on a Bruker IFS 55 spectrophotometer. Elemental analyses were performed by the Department of Microanalyses at the University of Artois.

Materials.—Deuterium oxide (99.95% isotopic purity) was obtained from E. Merck. β-CD was purchased from Aldrich and carefully dried before use. The potassium salt of *p*-substituted monosulfonated triphenylphosphine (*p*-TPPMS) was synthesized as reported by Wallow et al.[15]

Potassium salt of the m-*substituted monosulfonated triphenylphosphine (*m-*TPPMS).*—It was prepared (yield 10%) by a modification of the literature method for the sodium salt.[16] KOH was used instead of NaOH to neutralize the acidic form of the phosphine, and the potassium salt of the phosphine was recrystallized twice from degassed 1:1 water–EtOH. IRFT (KBr); 1464 (w), 1434 (m), 1092 (s), 787 (m), 746 (m), 739 (m), 726 (w), 674 (m) cm^{-1}; ^{1}H NMR (D_2O): δ 7.42 (um, 10 H, $H_{\text{non-sulfonated ring}}$), 7.51 (m, 2 H, H_m and H_o), 7.71 (d, 1 H, $^3J_{H,H}$ 8.1 Hz, H_p), 7.81 (d, 1 H, $^3J_{P,H}$ 6.9 Hz, $H_{o'}$); ^{13}C{^{1}H} NMR (D_2O): δ 126.4 (s, $C_{H\text{-}p}$), 129.0 (d, $^3J_{P,C}$ 7 Hz, $C_{\text{non-sulfonated ring; C in } \gamma \text{ of P}}$), 129.4 (ud, $C_{H\text{-}m}$), 129.5 (s, $C_{\text{non-sulfonated ring; C in } \delta \text{ of P}}$), 130.5 (d, $^2J_{P,C}$ 24 Hz, $C_{H\text{-}o'}$), 133.9 (d, $^2J_{P,C}$ 19 Hz, $C_{\text{non-sulfonated ring; C in } \beta \text{ of P}}$), 135.8 (d, $^2J_{P,C}$ 14 Hz, $C_{H\text{-}o}$), 136.0 (d, $^1J_{P,C}$ 9 Hz, $C_{\text{non-sulfonated ring; C in } \alpha \text{ of P}}$), 138.3 (d, $^1J_{P,C}$ 12 Hz, $C_{\text{sulfonated ring; C in } \alpha \text{ of P}}$), 143.6 (d, $^3J_{P,C}$ 8 Hz, C_{SO_3K}); ^{31}P{^{1}H} NMR (D_2O, external H_3PO_4): δ −6.65 (s) ppm; Anal. Calcd for $C_{18}H_{14}KO_3PS{\cdot}2\,H_2O$: C, 51.92; H, 4.32. Found: C, 51.79; H, 3.94.

Potassium salt of o-*substituted monosulfonated triphenylphosphine (*o-*TPPMS).*—To a solution of 2 $FC_6H_4SO_3K$ (2.00 g, 9.33 mmol) in dry THF (10 mL) was added 18.6 mL of a 0.5 M solution of Ph_2PK (9.3 mmol) in THF with stirring and the reaction was heated at reflux under N_2 until it became colorless. The reaction mixture was extracted twice with Et_2O (50 mL) and then concentrated to yield a white solid. The residue was recrystallized from degassed 1:1 water–EtOH. Yield 1.17 g (33%). IRFT (KBr); 1455 (w), 1433 (w), 1094 (m), 765 (w), 744 (w), 731 (w), 671 (m), 666 (m), 508 (w) cm^{-1}; ^{1}H NMR (D_2O): δ 6.78 (dd, 1 H, $^3J_{H,H}$ 7.8, $^3J_{P,H}$ 3.9 Hz, H_o), 6.87 (t, 1 H, $^3J_{H,H}$ 8 Hz, H_m), 7.04 (m, 10 H, $H_{\text{non-sulfonated ring}}$), 7.21 (t, 1 H, $^3J_{H,H}$ 7 Hz, H_p), 7.86 (dd, 1 H, $^3J_{H,H}$ 7.5, $^3J_{P,H}$ 3.6 Hz, $H_{m'}$) ppm; ^{13}C{^{1}H} NMR (D_2O): δ 127.6 (d, $^3J_{P,C}$ 5 Hz, $C_{H\text{-}m'}$), 128.9 (d, $^3J_{P,C}$ 6 Hz, $C_{\text{non-sulfonated ring; C in } \gamma \text{ of P}}$), 129.2 (s, $C_{\text{non-sulfonated ring; C in } \delta \text{ of P}}$), 129.9 (s, $C_{H\text{-}p}$), 131.2 (s, $C_{H\text{-}m}$), 133.8 (d, $^2J_{P,C}$ 20 Hz, $C_{\text{non-sulfonated ring; C in } \beta \text{ of P}}$), 134.6 (d, $^1J_{P,C}$ 12 Hz, $C_{\text{sulfonated ring; C in } \alpha \text{ of P}}$), 136.2 (d, $^2J_{P,C}$ 23 Hz, $C_{H\text{-}o}$), 137.3 (d, $^1J_{P,C}$ 10 Hz, $C_{\text{non-sulfonated ring, C in } \alpha \text{ of P}}$), 174.5 (d, $^2J_{P,C}$ 26 Hz, C_{SO_3K}) ppm; ^{31}P{^{1}H} NMR (D_2O, external H_3PO_4): δ −11.91 (s) ppm; Anal. Calcd for $C_{18}H_{14}KO_3PS{\cdot}H_2O$: C, 54.27; H, 4.02. Found: C, 53.84; H, 3.90.

Association constant determination.—The P resonance was chosen for evaluating the association constant on the basis that: (i) the P NMR signal cannot be overlapped by any resonance signals and that; (ii) the P chemical shift difference value between free and bound state of the phosphine ($\Delta\delta_{max}$) is very high (0.758 ppm for the *p*-TPPMS; 1.479 ppm for *m*-TPPMS and 2.848 ppm for the *o*-TPPMS at 298 K). This last point is very important as it has been clearly demonstrated that a low $\Delta\delta_{max}$ value induces significant error on the association constant, and that the corresponding titration has to be discarded on a quantitative point of view.[17,18] The association constants were determined by computer fitting of the P chemical shift titration curves as previously reported.[4] The phosphine concentration was fixed to 3 mM.

Acknowledgements

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