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Cyclodextrin-based PNN supramolecular assemblies: a new class of pincer-type ligands for aqueous organometallic catalysis

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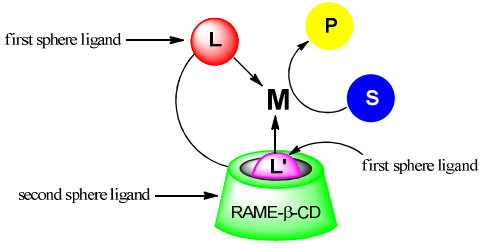
Water-soluble cyclodextrins (CDs) bearing two nitrogen atoms as metal coordinating sites have been synthesized. An appropriate phosphane could be included within their cavity through the primary face to form self-assembled PNN supramolecular edifices. Once the PNN ligands coordinated onto platinum, the resulting complexes proved to be very effective as catalysts in a domino reaction where a Pt-catalyzed reduction of nitrobenzene was followed by a Paal-Knorr pyrrole reaction. In the nitrobenzene reduction, the modified CDs acted both as first- and second-sphere ligands. Contrary to an acyclic glucopyranose-based NN ligand unable to interact with a phosphane ligand, the CD-based PNN ligands proved to stabilize the catalytic species in water by supramolecular means. Interestingly, the product and the water-soluble Pt-catalyst could be recovered in two different phases once the reaction was complete.

Introduction

Growing interest in catalytic organometallic reactions prompts chemists to compete for originality to elaborate new effective catalysts. Among the numerous features determining the catalyst efficiency, the nature of the ligand and its coordination onto an appropriate metal appeared to be of crucial importance. In this context, pincer ligands have attracted much attention during the past fifteen years. Their organometallic complexes are rather rigid resulting in enhanced thermal stability. Moreover, the pincer ligands bulkiness limits side-reactions around the reactive coordination site. When one arm of the ligand is hemilabile, an additional coordination site can even be generated transiently. Though most applications of pincer compounds have been carried out in organic media,[1-4] examples have been reported in the literature on water-soluble pincer ligands. For example, Ryabov et al. reported the first water-soluble imine palladacycle and its application as catalyst for ester hydrolysis.[5] Nájera et al. reported that oxime-derived palladacycles were highly active catalysts for Suzuki-Miyaura coupling of aryl bromides and arylboronic acids or aliphatic boronic acids[6] and could smoothly catalyzed the Suzuki coupling of activated and deactived aryl or heteroaromatic chlorides as well as benzylic chlorides in water.[7] Water-soluble SCS-Pd pincer-assemblies were synthesized by Reinhoudt et al. but no catalytic application was described.[8] Shaughnessy et al. developed imino-NC palladacycles with hydrophilic sulfonic group which were combined with a water-soluble phosphine ligand (*t*-Bu-Amphos). The resulting complex could be efficiently used for eleven reaction cycles for coupling reaction of 4-bromotoluene with phenylboronic acid.[9] More recently, Morales-Morales et al. synthesized three different pincer ligands. Mixtures of these ligands with $PdCl_2$ efficiently catalyzed the Suzuki–Miyaura cross couplings in water.[10] Though some of the pincer ligands described in the literature proved to be effective in aqueous catalysis, their synthesis is mostly tedious and time-consuming. Ten years ago, a simple and faster alternative emerged aiming at designing novel ligands by supramolecular means.[11-13] Many diverse self-assembled ligands have thus been elaborated through hydrogen bonding or coordination chemistry that proved to be effective in various organometallic reactions using organic solvents.[14] Concurrently to the strategies developed in organic media, we demonstrated that the supramolecular approach was applicable to water-soluble bidentate ligands through hydrophobic effects using an appropriate cyclodextrin (CD)/phosphane combination.[15,16,17,18] More precisely, we showed that CDs functionalized on their primary face by nitrogen donor groups could partially include within their cavity a water-soluble sulfonated phosphane to form supramolecular PN ligands. The resulting self-assembled entities were capable of coordinating platinum and rhodium complexes in a κ^2-*P*,*N* coordination mode, the CD simultaneously acting as a first- and second-sphere ligand (Scheme 1).



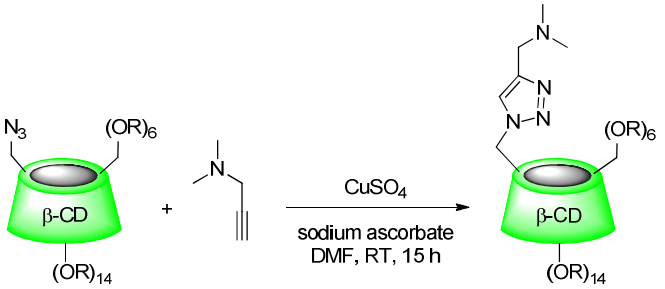
Scheme 1 Conversion of substrate (S) into product (P) using modified CDs as first- and second-sphere ligand in organometallic catalysis.

The obtained Pt- and Rh-complexes showed high turnover frequencies in aqueous Pt-catalyzed hydrogenation of an allylic alcohol and Rh-catalyzed hydroformylation of styrene, respectively.[19] Knowing that self-assembled PN complexes are suitable ligands in supramolecular catalysis, we then explored ways to access supramolecular PNN pincer-type ligands. Herein, we report the synthesis of a water-soluble partially methylated β-CD monosubstituted on its primary face by nitrogen-containing coordinating groups and its ability to form supramolecular PNN ligands when interacting with an appropriate phosphane. The catalytic performance of the synthesized PNN edifice was evaluated in a domino reaction where a Pt-catalyzed reduction of nitrobenzene was followed by a Paal-Knorr pyrrole reaction. The catalytic results clearly demonstrated the remarkable properties of the studied CD-based ligand and validated the approach of supramolecular catalysis in water. A comparison with a glucopyranose-based NN ligand highlighted the catalytic results obtained with the CD-based catalytic system.

Results and discussion

Syntheses of the N,N-coordinating ligands

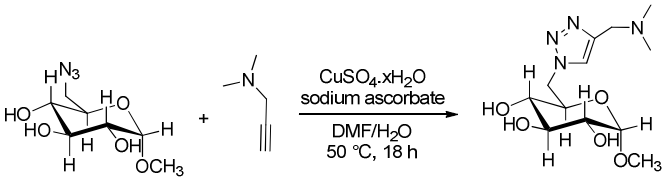
We implemented the synthesis of a water-soluble β-CD-based ligand with specific structural features, namely a cavity to supramolecularly recognize an appropriate phosphane and functionalized sites to coordinate metallic precursors. Due to its adsorption ability at the organic/aqueous interface,[20] the partially methylated β-CD structure was chosen as relevant platform to graft a *N*,*N*-coordinating group on the CD primary face and as suitable host to include a P-ligand within its cavity. The synthesis of the *N*,*N*-coordinating CD-based ligand **1** was carried out as follows (Scheme 2).[21] The partially methylated mono-azido-β-CD[22] and *N*,*N*-dimethyl-2-propyn-1-amine were submitted to a copper-catalyzed azide-alkyne cycloaddition (CuAAC) in DMF at room temperature. Once purified by chromatography, **1** was obtained in 83% yield. The pale yellow powder was characterized by NMR spectroscopy. The ^{1}H NMR spectrum revealed a signal around 8 ppm characteristic of the formation of the triazolyl cycle. A 2D T-ROESY NMR sequence sensitive to dipolar contact showed the CD-substituent to be outside the cavity as no contact could be detected between the *N*,*N*-dimethylaminomethyltriazolyl protons and the inner H-3 and H-5 CD protons (ESI). Ligand **1** was very soluble in water (>500 g/L) and could thus be used as building blocks in the following study.



1

Scheme 2 Synthesis of the *N*,*N*-coordinating CD-based ligand **1** (R = H or CH_3, substitution degree = 1.7).

Concurrently, for comparison purposes, an acyclic glucopyranose-based NN ligand (**2**) was also synthesized by CuAAC in DMF at 50 °C starting from methyl 6-azido-6-deoxy-α-D-glucopyranoside and *N*,*N*-dimethylpropargylamine (Scheme 3). The absence of cavity in **2** should allow understanding the role of the CD cavity in the catalytic system.

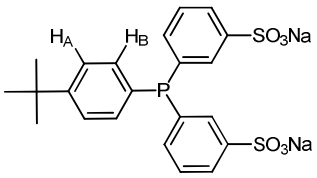


2

Scheme 3 Synthesis of the glucopyranose-based NN ligand **2**.

Cyclodextrin-based PNN supramolecular assembly

Knowing that the *N*,*N*-coordinating substituent was not included within the CD cavity, the latter was then available to host hydrophobic guests. As such, the disodium bis(3-sulfonatophenyl)(4-*tert*-butylphenyl)phosphane [(*p*-*t*BuC_6H_4)P(*m*-$C_6H_4SO_3Na)_2$] (**3**) (Scheme 4) was chosen as potential candidate as previous studies already showed its ability to enter the β-CD cavity through the primary face.[23,24]



Scheme 4 Water-soluble phosphane **3**.

The self-assembling of the PNN supramolecular complex was merely realized by mixing **1** with **3** in water at room temperature. Cross-peaks detected in the T-ROESY spectra were indicative of the inclusion of the *tert*-butylphenyl group of **3** within the hydrophobic cavity of **1** and confirmed the formation of the **3**⊂**1** complex (Figure 1). The **3**⊂**1** association constant was measured by isothermal titration calorimetry (ITC) and was found to be K_a = 63200 M^{-1} at 25 °C and K_a = 41200 M^{-1} at 45 °C. Logically, the K_a value

decreased when increasing the temperature. Compared to the less hindered RAME-β-CD for which a K_a = 250000 M^{-1} was measured, **1** displayed a lower association constant. Indeed, though outside the CD cavity, the *N,N*-dimethylaminomethyltriazolyl substituent probably hampered the recognition process with **3**. However, the high K_a value measured for the **3⊂1** complex ensured the stability of the **3⊂1** complex in water. Note that the enthalpic and entropic stabilization observed at 25 °C (ΔH = -3727 cal.mol^{-1}, -TΔS = -2818 cal.mol^{-1}) became almost exclusively enthalpic at 45 °C (ΔH = -6390 cal.mol^{-1}, -TΔS = -325 cal.mol^{-1}). The negative value of the heat capacity (ΔCp = -133 cal.mol^{-1}.K^{-1}) reflected the desolvation of the phosphane hydrophobic moiety (*tert*-butyl group) during the inclusion process (hydrophobic effects).

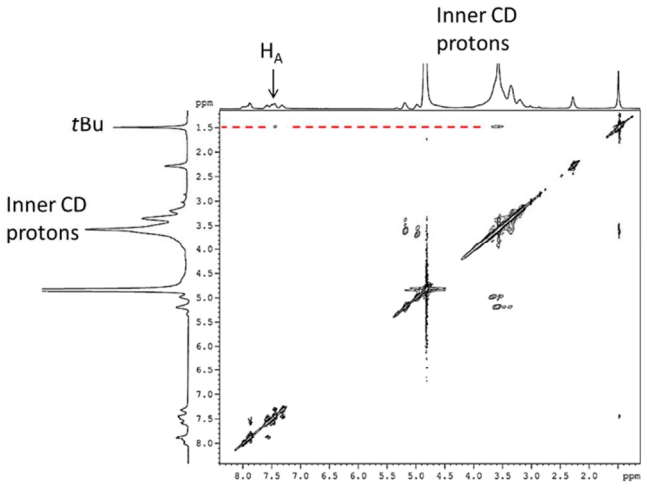


Figure 1 2D T-ROESY NMR spectrum of a stoichiometric mixture of **1** and **3** (10 mM each) at 25 °C in D_2O.

Supramolecular PNN platinum complexes

Once the existence of a **3⊂1** supramolecular complex was established, coordination of the PNN supramolecular edifice onto platinum complexes was readily achievable. Mixing K_2PtCl_4 with **3⊂1** in water at room temperature yielded a mixture of Pt-complexes whose structures have been determined by NMR spectrometry (Figure 2). A ^{31}P NMR spectrum was recorded rapidly on a mixture of **3⊂1** and K_2PtCl_4 in stoichiometric proportions at room temperature (Figure 2a). After 5 min., three distinct signals were detected. To help determining the structure of the respective Pt-complexes, the randomly methylated β-CD (RAME-β-CD, ESI) was used as a non-coordinating host. Actually, as RAME-β-CD could not coordinate the platinum atom, it only acted as a second-sphere ligand resulting in the formation of Pt-complex **4** (Scheme 5).

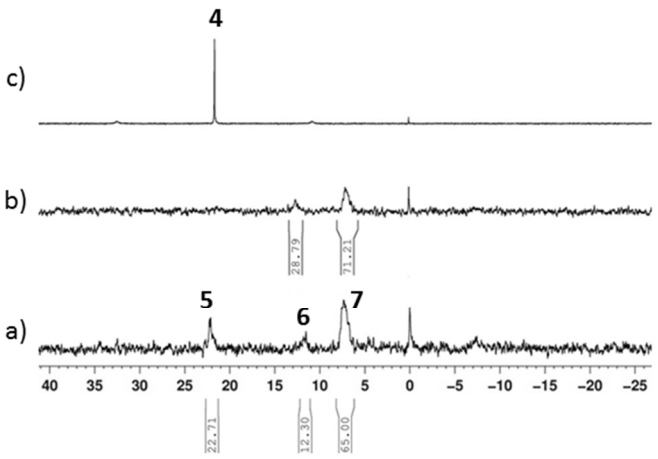
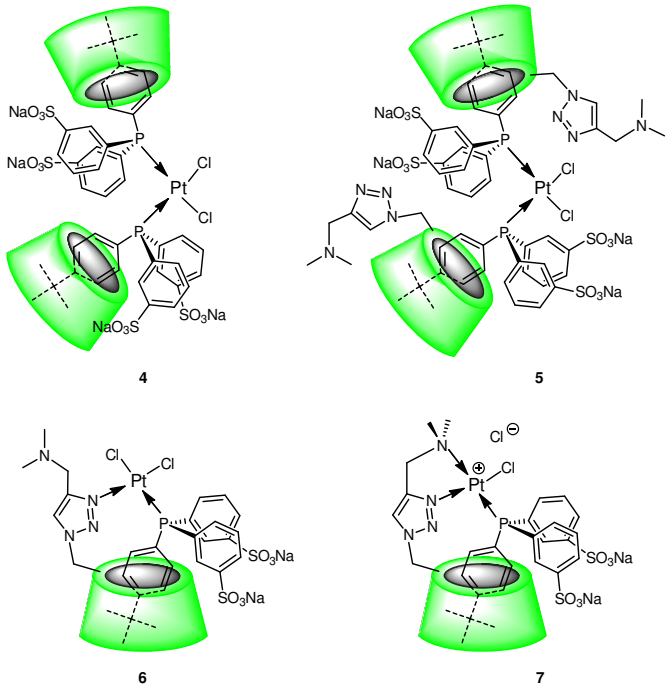


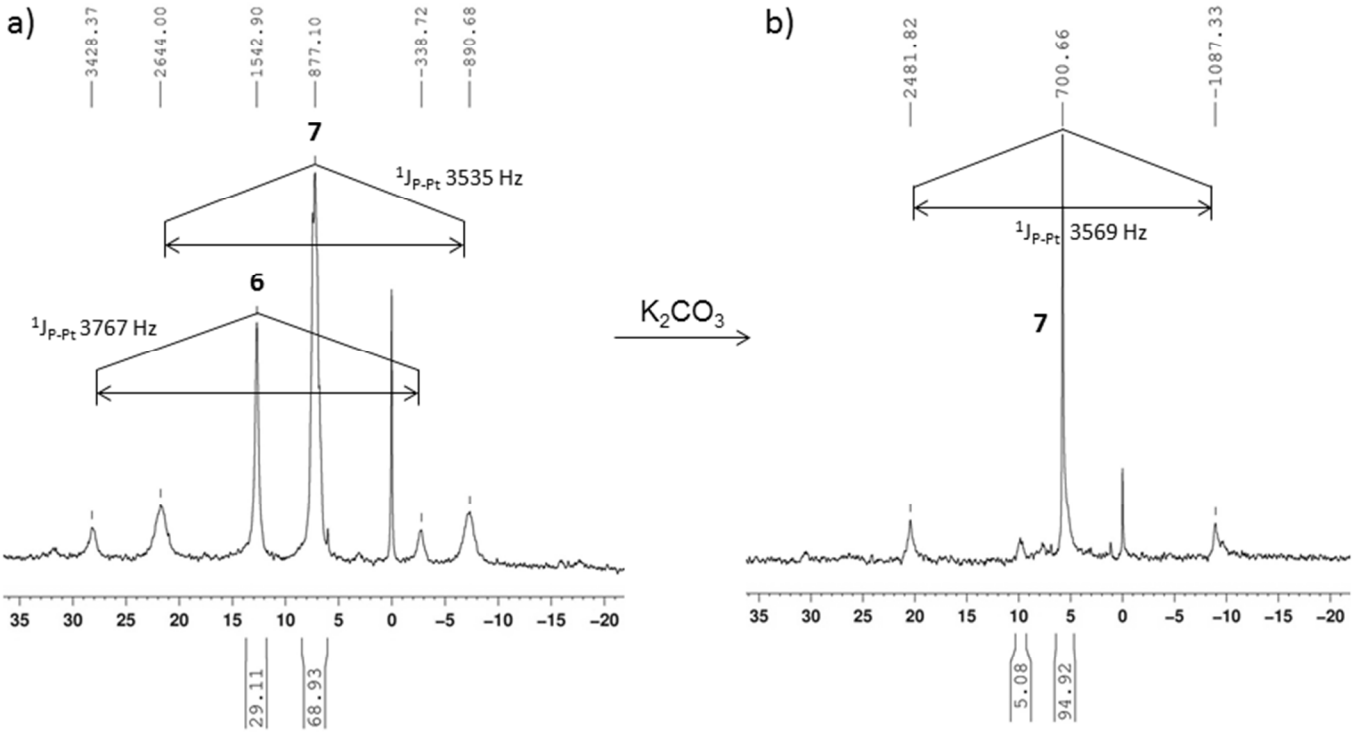
Figure 2 ^{31}P NMR spectrum of RAME-β-CD/**3** and **1/3** couples in the presence of K_2PtCl_4 in water (85% H_3PO_4 external reference). a) **1/3**/K_2PtCl_4 (10 mM each) at 25 °C after 5 min.; b) **1/3**/K_2PtCl_4 (10 mM each) at 70 °C after 15 min.; c) RAME-β-CD/**3**/K_2PtCl_4 (10 mM each) at 25 °C after 5 min.

The closeness of ^{31}P resonances observed for **3** when RAME-β-CD or **1** were used as hosts (compare Figures 2a and 2c) suggested a similar arrangement around the metal giving rise to Pt-complex **5** (Scheme 5). This hypothesis was confirmed by the complete disappearance of the ^{31}P resonance of **5** when heating the solution up to 70 °C (Figure 2b), a temperature at which the nitrogen coordination occurred.[15] Another series of NMR experiments was carried out on longer NMR acquisition times to detect satellite peaks. Well-defined ^{31}P spectra were obtained that allowed us to attribute the other NMR signals. A mixture of **1**, **3** and K_2PtCl_4 heated at 70 °C for 15 min. led to two sets of peaks (Figure 3a). Upon addition of excess K_2CO_3 (5 eq./Pt) at 70 °C, the ^{31}P resonance at 13 ppm was significantly affected (Figure 3b). Indeed, K_2CO_3 acted as a base towards the non-negligible quantity of ammonium protons. The proportion of *N,N*-dimethylamino groups significantly increased and could then coordinate the metal. The concomitant intensity enhancement of the ^{31}P NMR signal at 7 ppm from 69 to 95% and intensity reduction of the ^{31}P NMR signal at 13 ppm from 29 to 5% clearly revealed the coordination of the nitrogen of the *N,N*-dimethylamino group onto Pt. The $^1J_{P\text{-}Pt}$ coupling constants (natural abundance of ^{195}Pt = 33.8%) deduced from their satellite peaks[24] also gave valuable information (Figure 3a). The $^1J_{P\text{-}Pt}$ coupling constant of 3767 Hz was characteristic of a phosphorus and a chloride located *trans* to each other[25] whereas the $^1J_{P\text{-}Pt}$ coupling constant of 3535 Hz was typical of a phosphorus *trans* to a nitrogen.[26] The ^{31}P NMR signal at 13 ppm was then attributed to Pt-complex **6** and that at 7 ppm to Pt-complex **7** (Scheme 5). Note that a slight upfield shift was detected for all the ^{31}P signals upon addition of K_2CO_3 probably due to a salt effect. Accordingly, the aminotriazolyl substituent could coordinate the platinum atom in a κ^1–*N* or κ^2-*N,N*-coordination mode. For both **6** and **7**, the CD derivative **1** could be considered as a first-sphere ligand through the direct nitrogen coordinations onto the platinum atom and as a second-sphere ligand as the CD cavity was occupied by a first-sphere ligand.



Scheme 5 Pt-complexes **4**-**7**.

Figure 3 ^{31}P NMR spectra of **1/3**/K_2PtCl_4 mixtures (10 mM each) in water (recorded at 25 °C). a) after 15 min. at 70 °C; b) after addition of excess K_2CO_3 (5 eq./Pt) at 70 °C.



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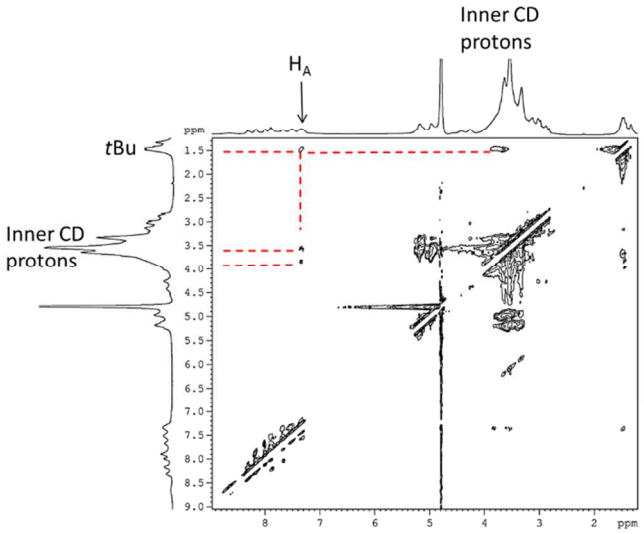


Figure 4. 2D T-ROESY NMR spectrum of a stoichiometric mixture of **3⊂1** and K_2PtCl_4 (10 mM each) at 25 °C in D_2O after 15 min at 70 °C.

6 and **7** thus constituted CD-based PNN Pt-complexes. A stoichiometric mixture of **3⊂1** and K_2PtCl_4 (10 mM each) was heated in D_2O at 70 °C for 15 min to give complexes **6** and **7** and the resulting mixture was analysed by 2D T-ROESY NMR experiments. The 2D T-ROESY spectrum recorded at 25 °C confirmed that the *tert*-butylphenyl group of **3** was still included within the CD cavity of **1** as clearly revealed by cross-peaks connecting *tert*-butyl and the inner CD protons (Figure 4). To confirm that nitrogen and phosphorus atoms were coordinated onto the same Pt center, DOSY experiments have been carried out on each component of the system. DOSY gave access to the diffusion coefficient (D) and hydrodynamic radius.[27-29] The results are gathered in Table 1.

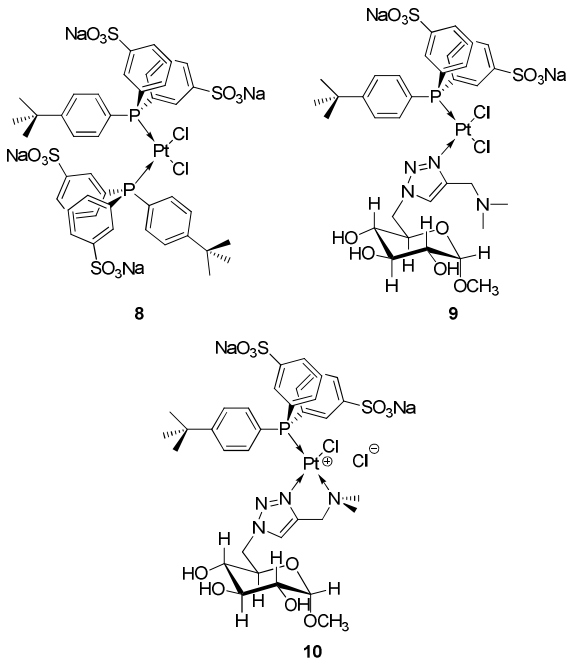
Table 1 Diffusion coefficients and hydrodynamic radius from DOSY experiments.[a]

Component	Log(D)	Diffusion coefficient (D) ($m^2.s^{-1}$)	Hydrodynamic radius (Å)[b]
1	-9.464	$3.436.10^{-10}$	6.2
3	-9.273	$5.334.10^{-10}$	4.0
3⊂1	-9.487	$3.258.10^{-10}$	6.6
4	-9.685	$2.0654.\ 10^{-10}$	10.4
6/7[c]	-9.432	$3.698.10^{-10}$	5.8

[a]) Conditions: D_2O, 25 °C. [b]) calculated from: hydrodynamic radius = $(k_b.T)/(6\pi.\mu.D)$ with k_b the Boltzmann constant, T the temperature and D the diffusion coefficient. [c]) **6/7** were prepared by heating a solution containing a stoichiometric mixture of **3⊂1** and K_2PtCl_4 (10 mM each) at 70 °C for 15 min.

The hydrodynamic radius of **6** and **7** was calculated from ^{1}H DOSY NMR measurements. It was in the same order of magnitude than its constitutive elements. The slight decrease in hydrodynamic radius observed between **6** (or **7**) and **3⊂1** (5.8 Å vs. 6.6 Å, respectively) could be a consequence of the chelate formation, the phosphane ligand **3** being included deeper in the CD cavity upon coordination onto the Pt centre. Logically, the hydrodynamic radius of **4** (10.4 Å) was higher than that measured for **6** (or **7**) as the Pt center in **4** was surrounded by two modified CDs. Note that **5** could not be analyzed by DOSY experiments as its preparation was always accompanied by the formation of **6** and **7**. Also note that attempts to isolate single crystals of Pt-complexes **4**-**7** failed. Pt-complexes derived from **2** were also synthesized following the same experimental procedure for comparison purposes. The chemical shifts and $^1J_{P\text{-}Pt}$ coupling constants detected on the ^{31}P NMR spectra for these Pt-complexes were very similar to those obtained for the **1**-based Pt-complexes **5**, **6** and **7** (Figure 5). Accordingly, these spectroscopic data showed that the **2**-based Pt-complexes (**8**, **9** and **10**) have similar structures than the **1**-based Pt-complexes (Scheme 6).

The results of Table 1 ruled out the existence of polymer Pt-structures in the aqueous solution as far higher hydrodynamic radii would have been obtained in that case.



Scheme 6 Pt-complexes **8**, **9** and **10**.

However, it is worth mentioning that the proportion of **9** and **10** was totally different when compared to their **1**-based counterparts **6** and **7** (compare Fig. 3 and Fig. 5). Moreover, addition of K_2CO_3 was required in that case to convert **9** into **10**. Thus, the inclusion of phosphane **3** into the CD cavity of **1** and the resulting bulkiness around the metal led to a change in the coordination mode. This clearly highlighted that the closeness of the phosphorus and the two nitrogen atoms onto the same CD-based structure of **1** greatly favored a κ^3-*P,N,N* coordination mode onto the platinum center. Accordingly, the synthesis of the above Pt-complexes illustrated a CD-mediated coordination of the P,N ligands onto the metal center. The CD structure played a key role in the coordination process as it pre-organized the coordinating atoms around the metal (template effect).

Domino Pt-catalysed reduction/Paal-Knorr reaction

The rich structural diversity of the above CD-based supramolecular PNN Pt-complexes was exploited in aqueous organometallic catalysis. More precisely, to highlight the potential of **1** and **3** as first- and second-sphere ligands in a PNN arrangement, their behaviour was assessed in an easy-to-implement model reaction, namely a domino Pt-catalysed reduction/Paal-Knorr reaction starting from nitrobenzene (or derivatives) and hexane-2,5-dione as reactants (Scheme 7). The choice of this domino reaction was justified by the formation of amines during the course of the reaction. Their basicity ensured the existence of non-protonated PNN ligands capable of coordinating the Pt-centre in a κ^3-*P,N,N* coordination mode. Nitrobenzene and its derivatives were chosen because of their partial solubility in water and their weak interaction with the CD cavity (by comparison with the strong CD/**3** association constant[17,20]) thus ensuring the stability of the CD/**3** supramolecular complex in catalytic conditions. Without CD or Pt-catalyst, no conversion could be measured (Table 2, entries 1 and 2). The utilization of RAME-β-CD as second-sphere ligand also proved ineffective (Table 1, entry 3). Conversely, using **6** and **7** at room temperature, the Pt-reduction of nitrobenzene was complete within 15 h (Table 2, entry 4). The amino derivative was mainly obtained (78%). The pyrrolyl and pyrrolidinyl products were obtained in 7% and 15%, respectively. Increasing the temperature to 45 °C slightly affect the products proportions in favor of the pyrrolidinyl derivative (Table 2, entry 5). Generally speaking, the domino reaction was more effective at 45 °C than at room temperature once the nitrobenzene was substituted. Nitrobenzene substitution by a chloride in *meta*- and *ortho*-position gave low conversions, even at 45 °C. Conversely, a chloro-substitution in *para*-position positively impacted the formation of pyrrolyl and pyrrolidinyl derivatives (Table 2, entries 10 and 11). Interestingly, the selectivity in pyrrolyl and pyrrolidinyl products could be changed by increasing the temperature from room temperature to 45 °C. Thus, the pyrrolyl product was mainly formed at room temperature (59%) while the pyrrolidinyl product was preferentially obtained (71%) at 45 °C. Nitrobenzene substitution by a bromide or iodide in *para*-position had a deleterious effect on the conversion (Table 2, entries 12-15). The effect of the substituent position on the aromatic cycle was less marked with methyl groups. Indeed, *ortho*-methylated and *para*-methylated nitrobenzenes gave similar results in terms of conversion (Table 2, entries 16, 17, 20 and 21). However, the *ortho*-isomer gave a higher percentage of amino-product (67%) while the *para*-isomer was more readily converted into pyrrolidinyl product (39%). The *meta*-isomer, for its part, remained the less reactive (Table 2, entries 18 and 19). Eventually, the *meta*- and *para*-methoxy nitrobenzenes were readily converted into products even at room temperature (Table 2, entries 22-25). Note that, in that case, higher selectivities in pyrrolidinyl derivatives were obtained at 45 °C than at room temperature (Table 2, compare entries 22-23 and entries 24-25). It should also be emphasized that, contrary to what was described in the literature,[30-32] the Pt-catalyst did not favor the Paal/Knorr reaction. Its efficacy was restricted to the reduction step. Accordingly, the PNN/Pt combination proved to be an effective catalyst to convert various nitroaryl compounds in smooth experimental conditions.

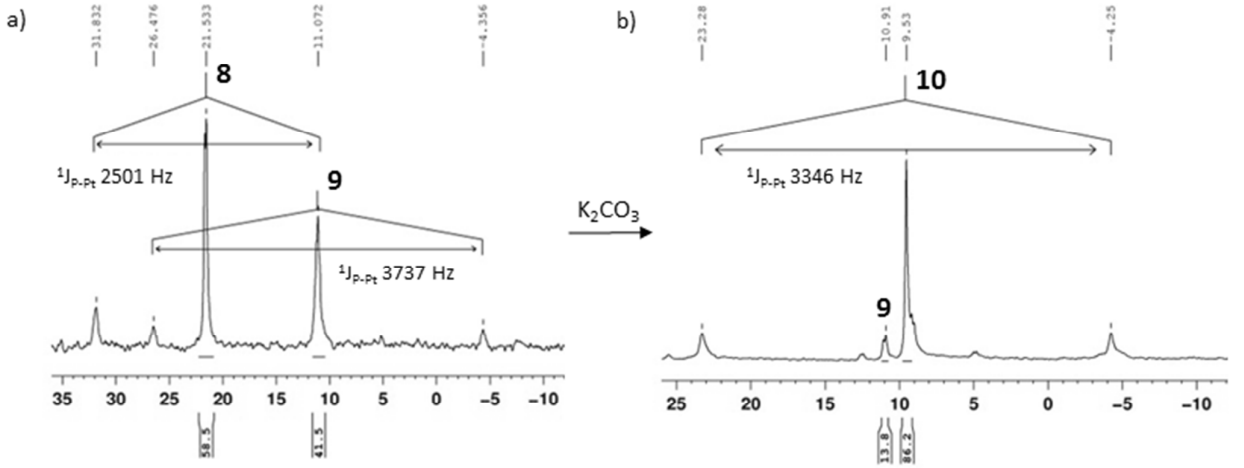
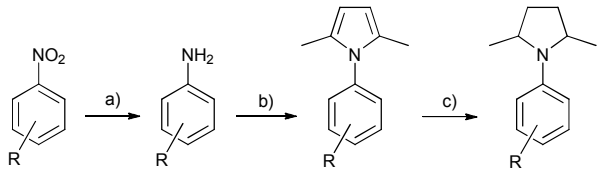


Figure 5 ^{31}P NMR spectra of **2/3**/K_2PtCl_4 mixtures (10 mM each) in water. a) after 15 min. at 70 °C; b) after addition of excess K_2CO_3 (5 eq./Pt) at 70 °C.



Scheme 7 Domino reaction with K_2PtCl_4 as a precursor and **3⊂1** as a supramolecular tridentate ligand. a) Pt-catalyzed reduction; b) Paal-Knorr cyclisation and hexane-2,5-dione; c) Pt-catalyzed hydrogenation.

The main advantage of the current aqueous biphasic process lies in the easy recovery of the product and the catalyst in two separated phases once the reaction was complete. As such, ICP-AES measurements confirmed the absence of Pt-complexes in the organic phase. The reusability of the catalytic system was carried out as follows. Once the organic phase containing the products was removed, the catalytic aqueous phase was filtered on Celite at room temperature (to remove any Pt-particles). Fresh nitrobenzene and hexane-2,5-dione were then added into the catalyst-containing flask and the domino Pt-catalyzed reduction/Paal-Knorr reaction then proceeded under the same experimental conditions as described above. The conversion and selectivity measured for the consecutive runs were identical to those obtained for the initial one (Table 2, run 26-29), indicative of both the robustness of the catalytic system and the absence of Pt-particles in the system. Neither significant loss of catalytic activity nor selectivity could be measured indicative of both the robustness of the catalytic system and the absence of Pt-particles in the system. Note that similar conversion and selectivity were obtained without filtration of the catalytic aqueous phase on Celite (Table 2, entry 30), thus indicating that no loss of Pt-complex (in the form of Pt-particles) took place during the catalytic process. To highlight the above catalytic results, a comparison with the Pt-complexes **9** and **10** was carried out. In catalytic conditions, **9** and **10** were clearly unstable as a colloidal suspension was observed within 15 min (Table 2, entry 31). Thus, though **1** and **2** led to structurally close Pt-complexes, their catalytic behavior appeared to be totally different. Not only did the CD-based PNN Pt-complexes favor the conversion of the nitrobenzene derivatives but they also helped stabilizing the catalytic species in water by supramolecular means. Indeed, the strong interaction existing between **1** and the CD cavity of **3** reinforce the coordination of the weaker coordinating N-ligands onto the metal. This could be assimilated to a supramolecular chelate effect.

Conclusions

PNN pincer-type ligands are readily accessible by supramolecular means. Using the PNN edifice, the first supramolecular water-soluble pincer-type complex was synthesized from a Pt-precursor. The PNN/Pt combination acted as an efficient catalyst in a domino Pt-catalysed reduction/Paal-Knorr reaction. This work demonstrated the ability of the aminotriazolyl-β-CD ligands in forming metal coordination complexes of a rich structural diversity and interesting catalytic properties. Moreover, throughout this study, we demonstrated that the coordination of weak coordinating CD-based N-ligands could be greatly reinforced by supramolecular interactions of the CD cavity which acted as a second-sphere ligand towards an appropriate coordinated phosphane. The advantages of aqueous biphasic catalysis were also revealed, especially the interesting recovery of the products and the water-soluble catalyst in two separated phases at the end of the reaction. Though the current study focused on PNN supramolecular assembly, the concept could be widened to other pincer ligands. As such, extension to other combinations and catalytic reactions is currently investigated.

Experimental

Material and methods

All chemicals were purchased from Acros and Aldrich Chemicals in their highest purity. All solvents were used as supplied without further purification. Distilled water was used in all experiments. Analytical thin-layer chromatography (TLC) was performed on E. Merck aluminum-backed silica gel (Silica Gel F254). Compounds were identified by using UV fluorescence and/or staining with a solution of 10% of sulfuric acid in methanol. NMR spectra were recorded with a Bruker DRX300 spectrometer operating at 300 MHz for ^1H nuclei and at 75.5 MHz for ^{13}C nuclei. D_2O (99.92% isotopic purity) were purchased from Euriso-Top. T-ROESY experiments were preferred to classical ROESY experiments as this sequence provided reliable dipolar cross-peaks with a minimal contribution of scalar transfer. Mixing times for T-ROESY experiments were set at 300 ms. 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 nonphase-sensitive mode after QSINE window processing.

Diffusion coefficients and hydrodynamic radii were calculated from 1H DOSY experiments.

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Table 2 Conversions and yields in the Pt-catalyzed-reduction/Paal-Knorr domino reaction.[a]

Entry	R	T (°C)	Conv. (%)	% nitro derivative	% amino derivative	% pyrrolyl derivative	% pyrrolidinyl derivative
1[b]	H	RT	0	-	-	-	-
2[c]	H	RT	0	-	-	-	-
3[d]	H	RT	0	-	-	-	-
4	H	RT	100	0	78	7	15
5	H	45	100	0	75	2	23
6	Cl (ortho)	RT	0	-	-	-	-
7	Cl (ortho)	45	30	70	30	0	0
8	Cl (meta)	RT	0	-	-	-	-
9	Cl (meta)	45	5	95	5	0	0
10	Cl (para)	RT	100	0	9	59	32
11	Cl (para)	45	100	0	0	29	71
12	Br (para)	RT	35	65	35	0	0
13	Br (para)	45	60	40	11	49	0
14	I (para)	RT	2	98	2	0	0
15	I (para)	45	5	95	5	0	0
16	CH_3 (ortho)	RT	18	82	18	0	0
17	CH_3 (ortho)	45	84	16	67	9	8
18	CH_3 (meta)	RT	19	81	16	3	0
19	CH_3 (meta)	45	25	75	16	7	2
20	CH_3 (para)	RT	35	65	20	7	8
21	CH_3 (para)	45	84	16	29	17	39
22	OCH_3 (meta)	RT	78	22	39	25	14
23	OCH_3 (meta)	45	100	0	0	30	70
24	OCH_3 (para)	RT	69	31	21	2	46
25	OCH_3 (para)	45	100	0	6	9	85
26[e]	H	RT	34	66	26	1	7
27[e,f]	H	RT	31	69	24	1	6
28[e,g]	H	RT	31	69	25	1	5
29[e,h]	H	RT	33	66	27	1	6
30[i]	H	RT	33	65	28	1	6
31[j]	H	RT	< 1	>99	trace	0	0

[a)] Conditions: Preparation of the **6/7** mixture: phosphane **3** (7.10^{-3} mmol), CD-based ligand **1** (7.10^{-3} mmol), K_2PtCl_4 (7.10^{-3} mmol), 3 mL water, 70 °C, 15 min. under N_2. Catalytic experiment: prepared **6/7** mixture, R-nitrobenzene (1.4 mmol), hexane-2,5-dione (1.4 mmol), H_2 pressure = 1 bar, heptane (1.5 mL) ; diethyl ether (1.5 mL), 25 °C, stirring 1000 rpm, 15 h. [b)] without any CD. [c)] without K_2PtCl_4. [d)] with RAME-β-CD. [e)] 4h. [f)] Catalyst recycle test performed using the aqueous catalytic phase recovered from entry 26 filtered on Celite at room temperature. [g)] Catalyst recycle test performed using the aqueous catalytic phase recovered from entry 27 filtered on Celite at room temperature. [h)] Catalyst recycle test performed using the aqueous catalytic phase recovered from entry 28 filtered on Celite at room temperature. [i)] Catalyst recycle test performed using the aqueous catalytic solution recovered from entry 26 without filtration on Celite. [j)] **9/10** mixture in the same catalytic conditions.

Mass spectra were recorded with a MALDI-TOF/TOF Bruker Daltonics Ultraflex II spectrometer in positive reflectron mode with 2,5-DHB as the matrix. ICP-AES measurements have been performed using a ICP-AES Vista-Pro VARIAN spectrometer. The reaction products were analyzed by gas chromatography – mass spectrometry (GC-MS) on a Shimadzu GC-17A using a 5% diphenyl/95% dimethyl siloxane capillary column (60 m length, 0.25 mm diameter) coupled to a Shimadzu GC-MS-QP5000 quadrupole MS. The column temperature was initially kept at 80 °C for 1 min and then raised to 150 °C at 10 °C.min^{-1}.

ITC measurements

An isothermal calorimeter (VP-ITC, MicroCal Inc., USA) was employed for determining the formation constants of the **3⊂1** complex at 298 K and 318 K. The titration protocol was used with a 1425 µL cell and a 300 µL syringe. Each titration experiment was performed three times to assess reproducibility of the results. Degassed aqueous solutions (phosphate buffer, pH = 6.5) were employed for all experiments. A 0.25 mM solution of **3** was titrated by a 2.5 mM solution of **1**. After addition of an initial aliquot of 5 µL, 10 aliquots containing 28 µL of the syringe solution were

delivered (over 28 s for each injection). The corresponding heat flow was recorded as a function of time. The time interval between two consecutive injections was 250 s and stirring speed was 304 rpm for all experiments. In addition, the heat consecutive to dilution was eliminated by performing blank titrations. The areas under the peak following each injection (obtained by integration of the raw signal) were then expressed as the heat effect per mole of added **1**. Binding constants and inclusion enthalpies were finally determined by nonlinear regression analysis of the binding isotherms using a built-in binding model (one set of sites) within MicroCal Origin 7.0 software package (MicroCal, Northampton, MA).

Synthetic procedures

Preparation of randomly methylated 1-(6A-Deoxy-β-D-cyclodextrin)-4-[(dimethylamino)methyl]-1,2,3-triazole (**1**): Randomly methylated mono-6-azido-6^{A}-deoxy-β-D-cyclodextrin (812 mg, 0.6 mmol) and hydrated copper sulfate (175 mg, 0.7 mmol) were added to a solution of *N*,*N*-dimethylpropargylamine (58 mg, 0.7 mmol) in DMF (30 mL). After the subsequent dropwise addition of a freshly prepared solution of sodium ascorbate (277 mg, 1.4 mmol) dissolved in water (3 mL) the solution was stirred for 18 h at room temperature. After evaporation of the solvent the crude product was dissolved in an ammoniac solution (10%) and stirred overnight before being purified by column chromatography on silica gel with water as eluent to give the product as a white powder. Yield: 589 mg, 0.41 mmol, 83%. ^{1}H NMR (300 MHz, D_2O): δ = 8.27 (s, 1 H), 5.19 (m, 4.9 H), 4.98 (m, 50H), 4.44 (m, 2.1 H), 4.13 (m, 3.1 H), 3.98–3.88 (m, 13.1 H), 3.68–3.53 (m, 43.9 H), 3.47–3.29 (m, 17.9 H), 2.82 (s, 6 H) ppm. ^{13}C NMR (75.5 MHz, D_2O): δ = 137.4, 135.2, 112.8, 101.4–99.8, 99.0–97.4, 82.7–81.6, 78.5, 73.4, 73.3, 73.1, 72.6, 72.3, 72.2, 70.9, 70.3, 64.4–59.4, 42.4, 30.2, 20.2, 19.7 ppm. MS: *m/z* (%) = 1433.51 (11.6) (calcd. 1433.57 for $[C_{59}H_{102}N_4O_{34} + Na]^+$), 1447.53 (69.9) (calcd.1447.58 for $[C_{60}H_{104}N_4O_{34} + Na]^+$), 1461.55 (16.1) (calcd. 1461.59 for $[C_{61}H_{106}N_4O_{34} + Na]^+$), 1477.05 (2.3) (calcd. 1475.6 for $[C_{62}H_{108}N_4O_{34} + Na]^+$).

Preparation of Pt-complexes **4**: RAME-β-CD (13.1 mg, 10^{-2} mmol), ligand **3** (5.1 mg, 10^{-2} mmol) and K_2PtCl_4 (4.1 mg, 10^{-2} mmol) were successively dissolved in 1 mL degassed D_2O. The resulting solution was immediately analyzed by NMR. The mixture was then heated at 70 °C for 15 min and cooled down to 25 °C, temperature at which a second set of NMR spectra was collected.

Preparation of Pt-complex **7**: Compound **1** (14.2 mg, 10^{-2} mmol), ligand **3** (5.1 mg, 10^{-2} mmol) and K_2PtCl_4 (4.1 mg, 10^{-2} mmol) were dissolved in 1 mL degassed D_2O. The resulting solution was heated a 70 °C for 15 min and a first set of NMR spectra was collected. After addition of excess K_2CO_3 (6.9 mg, 5.10^{-2} mmol) at 70 °C, the solution was stirred for another 15 min. The solution was cooled down and a second set of NMR spectra was collected.

Preparation of Pt-complexes **10**: Complex **10** was synthesized following the experimental procedure described for **7** from **2** (3.0 mg, 10^{-2} mmol) instead of **1**.

Catalytic experiments

In 3 mL degassed water were consecutively introduced **1** (7.10^{-3} mmol, 10 mg), **3** (7.10^{-3} mmol, 3.7 mg) and K_2PtCl_4 (7.10^{-3} mmol, 3 mg). The mixture was heated at 70 °C for 15 min and then cooled to room temperature. The nitrobenzene derivative (1 mmol) and hexane-2,5-dione (1 mmol, 114 mg) were dissolved in diethyl ether (1.5 mL) and heptane (1.5 mL) and the resulting solution was poured onto the aqueous phase. The mixture was stirred at 800 rpm and maintained at 25 °C or 45 °C for 18 h under 1 bar H_2. Once the reaction was complete, the organic phase was recovered by simple decantation and the aqueous phase was washed with toluene. The organic phases were combined and evaporated. The products were purified by column chromatography over silica gel (conditioned with heptane) using a heptane/acetone (9/1) mixture as eluant. All products were analyzed by GC-MS by comparison with references.

Recycling procedure

After decantation, the recovered catalytic aqueous phase was filtered under nitrogen on Celite which was washed with 0.5 mL degassed water. No Pt particle could be detected on Celite. The filtrate was lyophilized and dissolved in 1 mL degassed water. Fresh substrates were then added and the reaction was restarted.

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Notes and references

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Electronic Supplementary Information (ESI) available: cyclodextrin structure, NMR data. See DOI: 10.1039/b000000x/

1 D. Morales-Morales, C. M. Jensen, (Eds.) The Chemistry of Pincer Compounds, Elsevier, Amsterdam, 2007.
2 The Pincer Ligand: Its Chemistry and Applications (Catalytic Science) (Eds: P. A. Chase, G. Van Koten), Imperial College Press, London, 2012.
3 G. van Koten and R. J. M. Klein Gebbink, Pincers and other hemilabile ligands, *Dalton Trans.*, 2011, **35**, 8713.
4 S. Schneider, J. Meiners and B. Askevold, *Eur. J. Inorg. Chem.*, 2012, 412.
5 E. Y. Bezsoudnova and A. D. Ryabov, *J. Organomet. Chem.*, 2001, **622**, 38.
6 L. Botella and C. Nájera, *J. Organomet. Chem.*, 2002, **663**, 46.
7 L. Botella and C. Nájera, *Angew. Chem. Int. Ed.*, 2002, **41**, 179.
8 H.-J. van Manen, R. H. Fokkens, F. C. J. M. van Veggel and D. N. Reinhoudt, *Eur. J. Org. Chem.*, 2002, 3189.
9 R. Huang and K. H. Shaughnessy, *Organometallics*, 2006, **25**, 4105.
10 C. Crisóstomo-Lucas, R. A. Toscano and D. Morales-Morales, *Tetrahedron Lett*., 2013, **54**, 3116.
11 V. F. Slagt, P. W. N. M. van Leeuwen and J. N. H. Reek, *Chem. Commun.*, 2003, 2474.
12 B. Breit and W. Seiche, *J. Am. Chem. Soc.*, 2003, **125**, 6608.
13 J. M. Takacs, D. S. Reddy, S. A. Moteki, D. Wu and H. Palencia, *J Am Chem Soc.*, 2004, **126**, 4494.
14 M. Raynal, P. Ballester, A. Vidal-Ferrana and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2014, **43**, 1660.
15 C. Machut, J. Patrigeon, S. Tilloy, H. Bricout, F. Hapiot and E. Monflier, *Angew. Chem., Int. Ed.*, 2007, **46**, 3040.

16 J. Patrigeon, F. Hapiot, M. Canipelle, S. Menuel and E. Monflier, *Organometallics*, 2010, **29**, 6668.
17 J. Potier, A. Guerriero, S. Menuel, E. Monflier, M. Peruzzini, F. Hapiot and L. Gonsalvi, *Catal. Commun.*, 2015, **63**, 74.
18 O. Bistri and O. Reinaud, *Org. Biomol. Chem.*, 2015, **13**, 2849.
19 F. Hapiot, H. Bricout, S. Tilloy and E. Monflier, *Eur. J. Inorg. Chem.*, 2012, 1571.
20 H. Bricout, F. Hapiot, A. Ponchel, S. Tilloy and E. Monflier, *Curr. Org. Chem.*, 2010, **14**, 1296.
21 J. Potier, S. Menuel, J. Rousseau, S. Tumkeviciusc, F. Hapiot and E. Monflier, *Appl. Catal. A: Gen.*, 2014, **479**, 1.
22 J. Potier, S. Menuel, D. Fournier, S. Fourmentin, P. Woisel, F. Hapiot and E. Monflier, *ACS Catal.*, 2012, **2**, 1417.
23 L. Caron, M. Canipelle, S. Tilloy, H. Bricout and E. Monflier, *Eur. J. Inorg. Chem.*, 2003, 595.
24 C. Binkowski-Machut, M. Canipelle, H. Bricout, S. Tilloy, F. Hapiot and E. Monflier, *Eur. J. Inorg. Chem.*, 2006, 1611.
25 M. L. Clarke, A. M. Z. Slawin and J. D. Woollins, *Polyhedron*, 2003, **22**, 19.
26 E. W. Ainscough, A. M. Brodie, A. K. Burrell, A. Derwahl, G. B. Jameson and S. K. Taylor, *Polyhedron*, 2004, **23**, 1159.
27 S. Floquet, S. Bentry, J.-F. Lemonnier, M. Henry, M.-A. Delsuc, Y. Prigent, E. Cadot and F. Taulelle, *J. Am. Chem. Soc.*, 2009, **131**, 17254.
28 F. Hapiot, L. Leclercq, N. Azaroual, S. Fourmentin, S. Tilloy and E. Monflier, *Curr. Org. Synth.*, 2008, **5**, 162.
29 N. T. T. Chau, S. Handjani, J. P. Guegan, M. Guerrero, E. Monflier, K. Philippot, A. Denicourt-Nowicki and A. Roucoux, *ChemCatChem*, 2013, **5**, 1497.
30 H. Lee and B. H. Kim, *Tetrahedron*, 2013, **69**, 6698.
31 A. A. Jafari and H. Mahmoudi, *Environ. Chem. Lett.* 2013, **11**, 157.
32 R. Srinivas, B. Thirupathi, J. K. P. Kumar, A. N. Prasad and B. M. Reddy, *Curr. Org. Chem.*, 2012, **16**, 2482.

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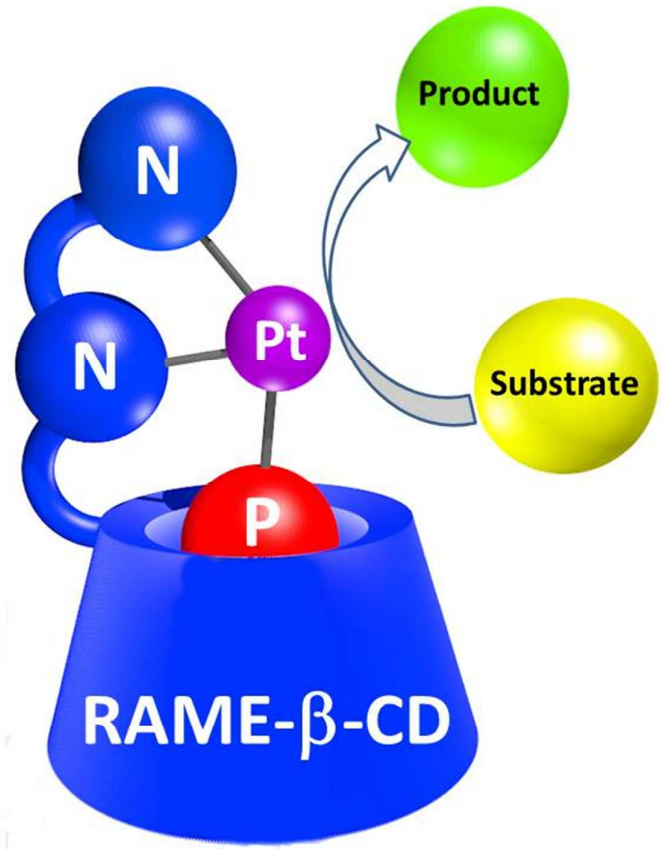

Pt-catalysts stabilized in water by self-assembled PNN supramolecular cyclodextrin-based ligands proved to be effective in a Paal-Knorr pyrrole reaction.