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A cyclodextrin dimer as a supramolecular reaction platform for aqueous organometallic catalysis†‡

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A reaction platform based on a cyclodextrin dimer, which is able to simultaneously include a substrate in one cavity and an organometallic catalyst into the other, proved to be highly efficient for aqueous hydroformylation reaction of higher olefins.

In organometallic catalysis processes, the most important goals are to reach high levels of activity and selectivity. Traditionally, the tuning of the ligands is the most widespread solution to increase the catalytic performances of an organometallic complex. Unfortunately, the syntheses of elaborated ligands are often complicated and time consuming. An alternative approach was found in the field of supramolecular catalysis which seeks to produce efficient and selective organometallic complexes by using supramolecular interactions such as hydrogen bonding, coordinative bonding, ion pairing, π–π interactions and the formation of inclusion compounds.[1,2] While numerous supramolecular catalysis processes are described in apolar solvents,[3] the use of aqueous medium is largely less widespread.[4] Indeed, water competes very effectively for binding sites and particularly for hydrogen bonds.[5] However in water, in contrast to organic solvents, the hydrophobic effect can be an advantage when non-covalent substrate binding in a hydrophobic cavity is combined with catalysis. Breslow, one of the pioneers in this field, attached a metal bonding group to β-cyclodextrin (β-CD) to generate an artificial enzyme.[6] In this context, we propose a new concept based on a cyclodextrin dimer acting as a reaction platform, which is able to simultaneously include a substrate in one cavity and an organometallic catalyst into the other (Fig. 1). So, the interaction between the two included entities will be facilitated and thus will lead to a faster substrate transformation. Our approach relies on the self-assembly of a β-CD dimer (CD-dim; Scheme 1) and a water-soluble rhodium phosphane complex produced from a water-soluble phosphane bearing a well-recognized biphenyl moiety[7] (phosphane **1**; Scheme 1). The catalytic performances of this supramolecular catalytic platform were evaluated in aqueous rhodium-catalyzed hydroformylation reaction.

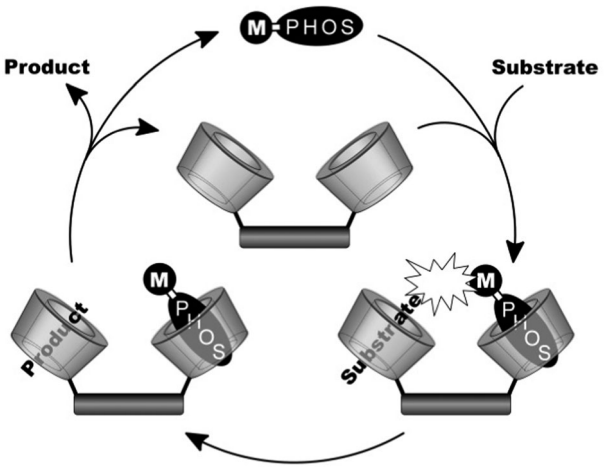

Fig. 1 Cyclodextrin dimer as a supramolecular reaction platform for aqueous organometallic catalysis (M = a transition metal; PHOS = a phosphane).

Treatment of $[Rh(COD)_2^+, BF_4^-]$ with two equivalents of **1** in D_2O produced a limpid yellow solution of $[Rh(COD)(\mathbf{1})_2^+, BF_4^-]$ and its $^{31}P\{^1H\}$ NMR spectrum exhibited a sharp doublet (δ = 25 ppm; $^1J_{Rh,P}$ = 148 Hz). The interaction between CD-dim and $[Rh(COD)(\mathbf{1})_2^+, BF_4^-]$ was studied using NMR spectroscopy measurements (all the data relative to the studies of inclusion complexes are gathered in the ESI‡). In the presence of one equivalent of CD-dim, the $^{31}P\{^1H\}$ NMR signal was not shifted or modified but only a broadening was observed. In parallel, the modifications of the aromatic and CD-dim proton signals observed in the ^1H NMR spectrum indicated that

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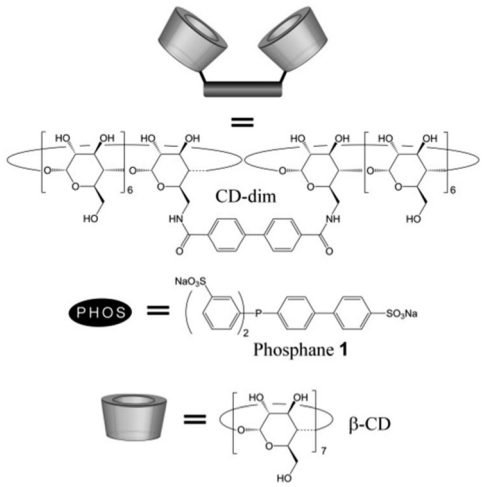
‡ Electronic supplementary information (ESI) available: Synthesis, analytical data and NMR or MALDI spectra. See DOI: 10.1039/c3cc43647k



Scheme 1 Chemical and schematic representation of CD-dim, phosphane **1** and β-CD.

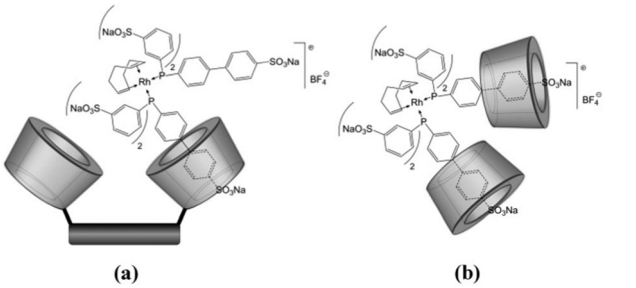


Fig. 3 Schematic representation of the inclusion complexes deducted from NMR experiments: (a) CD-dim : [Rh(COD)(**1**)$_2^+$, BF_4^-] (1 : 1) and (b) β-CD : [Rh(COD)(**1**)$_2^+$, BF_4^-] (2 : 1).

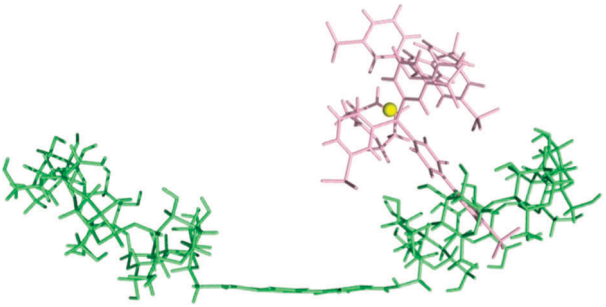


Fig. 4 Molecular dynamic simulation of CD-dim : [Rh(COD)(**1**)$_2^+$, BF_4^-].

the phosphane **1** was included in the CD-dim cavity. All these data unambiguously showed that [Rh(COD)(**1**)$_2^+$, BF_4^-] formed an inclusion complex with CD-dim. For comparison, the same kind of experiments were performed with β-CD showing that [Rh(COD)(**1**)$_2^+$, BF_4^-] also formed an inclusion complex with this CD. The stoichiometry of the supramolecular species between [Rh(COD)(**1**)$_2^+$, BF_4^-] and β-CD or CD-dim was determined by a Job plot analysis of titration experiments (Fig. 2).[8] CD-dim formed a 1 : 1 inclusion complex with [Rh(COD)(**1**)$_2^+$, BF_4^-] whereas β-CD formed a 2 : 1 inclusion complex with this rhodium species. Concerning the geometry of these inclusion complexes, 2D T-ROESY NMR experiments showed that the sulfophenyl moiety of the biphenyl group was included by the secondary face for CD-dim whereas it was included by the primary face for β-CD. Fig. 3a and b show a schematic representation of these two inclusion complexes. This inversion of the inclusion face observed for the β-CD : [Rh(COD)(**1**)$_2^+$, BF_4^-] (2 : 1) structure probably occurred to reduce the steric hindrances around the metallic center. Molecular dynamics simulations of CD-dim : [Rh(COD)(**1**)$_2^+$, BF_4^-] were performed in explicit water (see ESI‡). The structure presented in Fig. 4 corresponds to the most observed inclusion complex during the simulation.[9] The organometallic complex [Rh(COD)(**1**)$_2^+$, BF_4^-] is included in one of the two CD-dim cavities and the free cavity is well oriented and available to include a substrate. So, CD-dim will be able to act as a reaction platform. The catalytic behaviour of the Rh–**1** combination was investigated by a hydroformylation reaction in the absence or presence of CD (β-CD or CD-dim) (see Table 1). 1-Decene was chosen as a highly hydrophobic substrate in order to observe the potential role of the different combinations in the mass transfer.[10] As comparative data, another set of experiments were realized with TPPTS (tris(*m*-sulfonatophenyl)phosphane trisodium salt) as the ligand instead of **1**.[11,12] Indeed, this ligand is very widespread in aqueous organometallic catalytic processes and often used as a reference. The two first experiments were performed without CD and, as expected, gave poor conversions due to the low water-solubility of 1-decene in water (entries 1 and 2). The addition of β-CD or CD-dim modified the chemoselectivity, the regioselectivity and the conversion (entries 3–6). The selectivity in aldehydes was increased in each case with the higher value for the [Rh–**1**–CD-dim] combination (entry 6). For the four combinations, the linear to branched aldehyde ratio

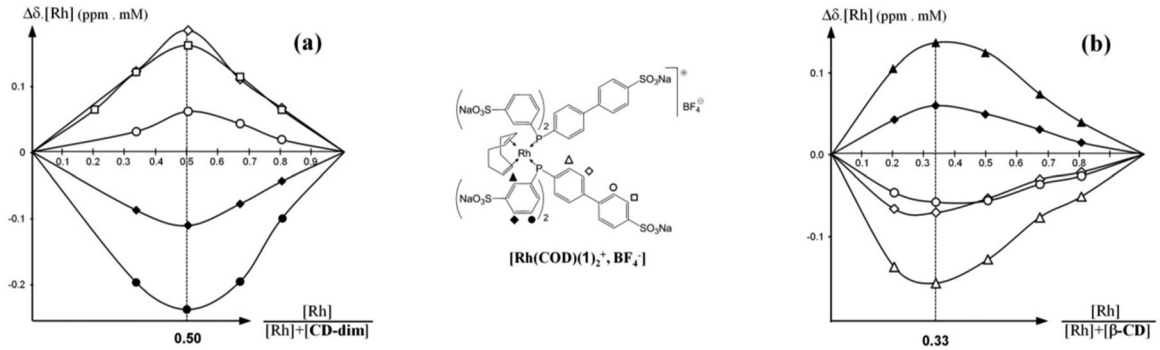
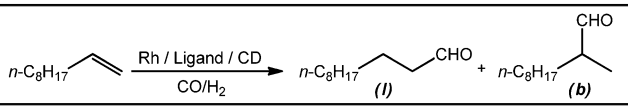


Fig. 2 Job-plot analysis of ^{1}H NMR titration in D_2O of [Rh(COD)(**1**)$_2^+$,BF_4^-] with (a) CD-dim and (b) β-CD.

Table 1 Rhodium-catalyzed hydroformylation of 1-decene in the presence of various ligand–CD couples[a]



Entry	Ligand	CD	C^b (%)	S^c (%)	l/*b*
1	TPPTS	(-)	5	65	2.7
2	**1**	(-)	2	69	3.1
3	TPPTS	β-CD	45	89	1.9
4	**1**	β-CD	40	77	2.2
5	TPPTS	CD-dim	49	78	2.0
6	**1**	CD-dim	99	94	2.1

[a] Experimental conditions: $Rh(acac)(CO)_2$ = 21 μmol (1 eq.), ligand = 105 μmol (5 eq.), CD cavity = 210 μmol (10 eq.), substrate = 10.5 mmol (500 eq.), 6 mL water, 80 °C, 50 bar CO/H_2 (1/1), 1500 rpm, reaction time = 9 h. [b] *C* = 1-decene conversion. [c] *S* = aldehyde selectivity.

(l/*b*) was around 2. This value is classical for hydroformylation experiments performed in the presence of β-CD derivatives.[13] Interestingly, the catalytic activity depended on the ligand–CD combinations. Indeed, the [Rh–TPPTS–β-CD], [Rh–**1**–β-CD] and [Rh–TPPTS–CD-dim] combinations nearly gave the same conversions whereas the conversion was more than two times higher for [Rh–**1**–CD-dim] (compare entries 3, 4 and 5 with entry 6). More precisely, extra-conversions observed with the [Rh–**1**–CD-dim] system were equal to 148%, 120% and 102% compared to the [Rh–**1**–β-CD], [Rh–TPPTS–β-CD] and [Rh–TPPTS–CD-dim] systems, respectively. Actually, the role played by the CD cavity is different in the case of [Rh–**1**–CD-dim] compared to the three other combinations. For the system [Rh–**1**–β-CD], [Rh–TPPTS–β-CD] and [Rh–TPPTS–CD-dim], the three values of conversion were similar and the CD moiety simply acted as a mass transfer agent by forming an inclusion complex with 1-decene.[12] The extra-conversions observed in the case of [Rh–**1**–CD-dim] can be easily explained by the anchoring of both the catalytic species and the substrate on the CD-dim platform by supramolecular interactions. So, 1-decene is in close proximity to the rhodium species facilitating the catalytic act and leading to an extra-conversion. The same experiments were performed with 1-hexadecene as a substrate and the same positive effect was observed. Indeed, extra-conversions with the [Rh–**1**–CD-dim] system compared to the other [Rh–**1**–β-CD], [Rh–TPPTS–β-CD] and [Rh–TPPTS–CD-dim] systems were equal to 96%, 120% and 165%, respectively (see ESI‡).

To summarise, we have elaborated a supramolecular reaction platform based on a CD dimer able to simultaneously host the substrate and the catalyst. Schematically, the catalyst was included inside one cavity while the substrate was included in the other. The proximity between the catalyst and the substrate allowed reaching higher catalytic activities than those reported for classical systems based on CD. We are currently further exploring the scope of this new class of catalyst.

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