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Complete List of Authors:	Armspach, Dominique; Université de Strasbourg, Institut de Chimie UMR 7177 CNRS, Laboratoire de Chimie Inorganique Moléculaire et Catalyse Jouffroy, Matthieu; Université de Strasbourg, Institut de Chimie UMR 7177 CNRS, Laboratoire de Chimie Inorganique Moléculaire et Catalyse Matt, Dominique; Université de Strasbourg, Institut de Chimie UMR 7177 CNRS, Laboratoire de Chimie Inorganique Moléculaire et Catalyse

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Cyclodextrin and Phosphorus (III): a Versatile Combination for Coordination Chemistry and Catalysis

Matthieu Jouffroy,[a] Dominique Armspach,*[a] and Dominique Matt*[a]

Dedicated to Dr. Loïc Toupet on the occasion of his retirement. With our warmest wishes.

With the advent of efficient methods for functionalising cyclodextrins, the synthesis of a variety of cyclodextrin-based P(III) ligands has been made possible. Capable of acting both as first and second coordination sphere ligands towards various transition metals, these compounds have found many applications in homogeneous catalysis. This perspective article describes the different approaches that have been used to covalently associate the ubiquitous P(III) donor atom with a cyclodextrin cavity. In addition, special emphasis is placed on the influence the cyclodextrin receptor has on the coordination and catalytic properties of these cavity-shaped ligands.

[a] Laboratoire de Chimie Inorganique Moléculaire et Catalyse,
Institut de Chimie UMR 7177 CNRS, Université de Strasbourg,
4, rue Blaise Pascal,
67070 Strasbourg cedex (France)
E-mail: d.armspach@unistra.fr; dmatt@unistra.fr

1. Introduction

Since their discovery by Villiers at the end of 19th century,[1] cyclodextrins (CDs) have gathered huge interest among the scientific community.[2] The considerable number of publications related to CDs (no less than 72000 since their discovery) reflects the many applications these naturally-occurring and non toxic cyclic oligosaccharides have found in fields as diverse as drug formulation,[3] analytical chemistry,[4,5] biomimetic chemistry,[6,7] inorganic chemistry,[8] catalysis,[9-14] polymers,[15] artificial sensors,[16] and food industry.[17,18] The commercially available CDs, which are the only ones with well-defined and rigid cavities, are made of six, seven or eight glucopyranose units (α-, β- and γ-CD, respectively).[19] With their α-1,4-linked D-(+)-glucopyranose units rigidly held in the ubiquitous $^4C_1$ chair conformation, these CDs, whether native or chemically modified, adopt a stable conical shape.[20,21] Native CDs comprise primary hydroxyl groups located at the narrow end of the cone called primary hydroxyl face or primary face, and secondary hydroxyl groups at the wider rim called secondary hydroxyl face or secondary face (Fig. 1). Unlike most synthetic cavitands, native CDs behave as water-soluble and chiral host molecules for many lipophilic compounds in aqueous media.[22,23]

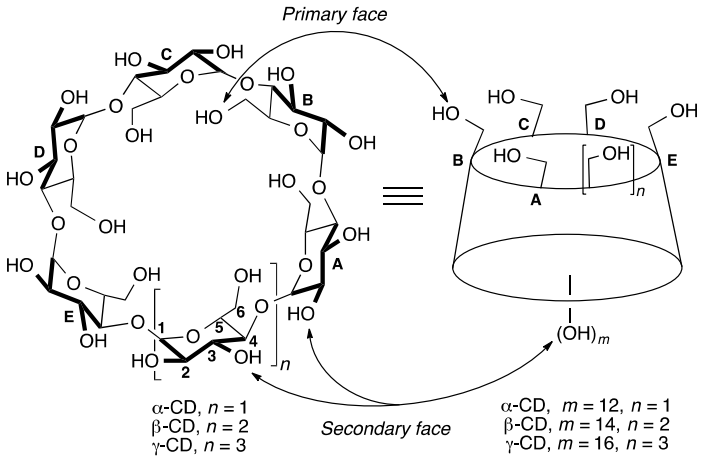
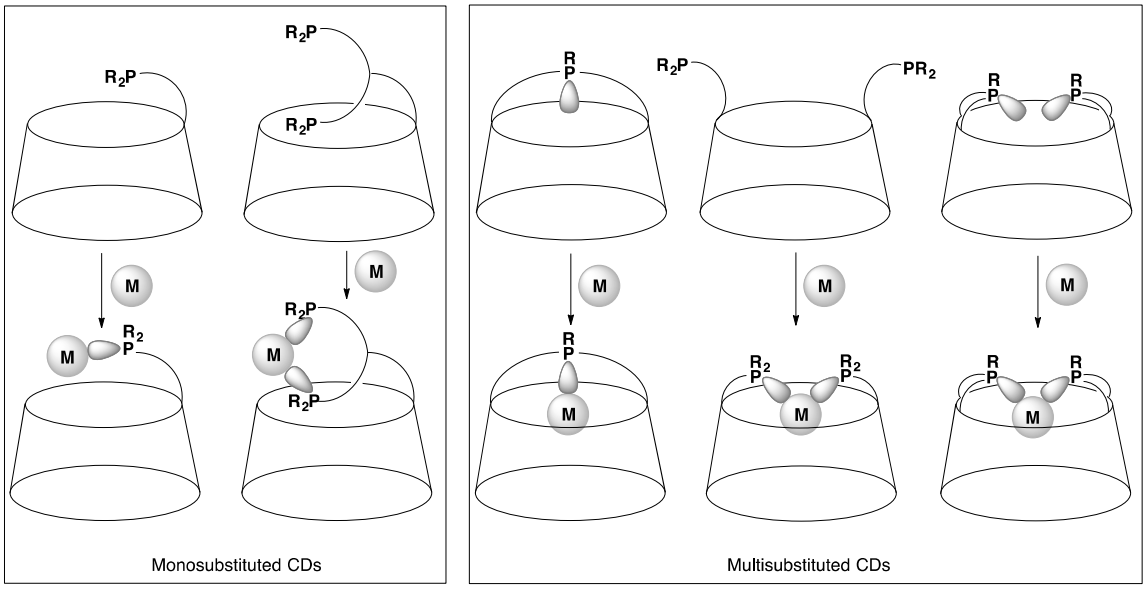


Fig. 1 Two different representations of native CDs. In the left one, the CDs are depicted as seen from the secondary face, with the successive glucose units being designated by letters ranged counterclockwise in alphabetical order.

Because of the possibility of introducing various donor groups at given locations on the macrocyclic structure, the CD skeleton (native or chemically modified) constitutes a versatile preorganisation platform for the synthesis of ligands that can act both as first and

second coordination spheres for transition metals. This particular feature is of prime importance when the stabilisation of unusual metal organic species, notably catalytic ones, is sought.[24-28] Among all coordinating atoms that have been anchored to a CD,[29-31] phosphorus (III) is certainly the one that has generated the most interest in recent years because of its widespread use in catalysis.[32] Thus, numerous CD derivatives bearing appended P(III) ligands have been designed to combine the exceptional host-guest properties of the chiral CDs with the versatile coordination and catalytic properties of the P(III) atom. This perspective article focuses on the synthesis and applications of these hybrid ligands, most notably in coordination and catalytic chemistry. Aqueous organometallic catalysis as well as supramolecular assemblies involving non-covalently bonded CDs and P(III) ligands will not be discussed here as this has already been recently reviewed by Monflier *et al.*.[33,34] The perspective consists of two parts, the first dealing with CDs substituted with a single P(III)-containing unit (Scheme 1, left part), the second concerning multisubstituted CDs (Scheme 1, right part). Special emphasis will be placed on the ability of the CD-P(III) hybrids to stabilise unusual organometallic species, to behave as encapsulating units and to act as supramolecular catalysts. Where possible, comparison between different systems will be made in order to clarify the influence of the CD cavity on the coordination properties of the P(III) atom(s) and the catalytic outcome of reactions. Also, a rapid overview of the various functionalisation methods enabling introduction of the phosphorus moiety on the torus will be given.

In Schemes and Figures fat arrows designate molecular structures recovered from the Cambridge Crystallographic Data Centre (CCDC). For clarity, these do not include counter-ions and solvents nor hydrogen atoms. Carbon atoms are depicted in beige, whilst oxygen, nitrogen, phosphorus, and sulfur atoms are in red, blue, orange and yellow, respectively.



Scheme 1 CD receptors with covalently appended phosphorus(III) units and their metal complexes. Left frame: CDs of which a single anchoring point has been substituted; right frame: multisubstituted CDs.

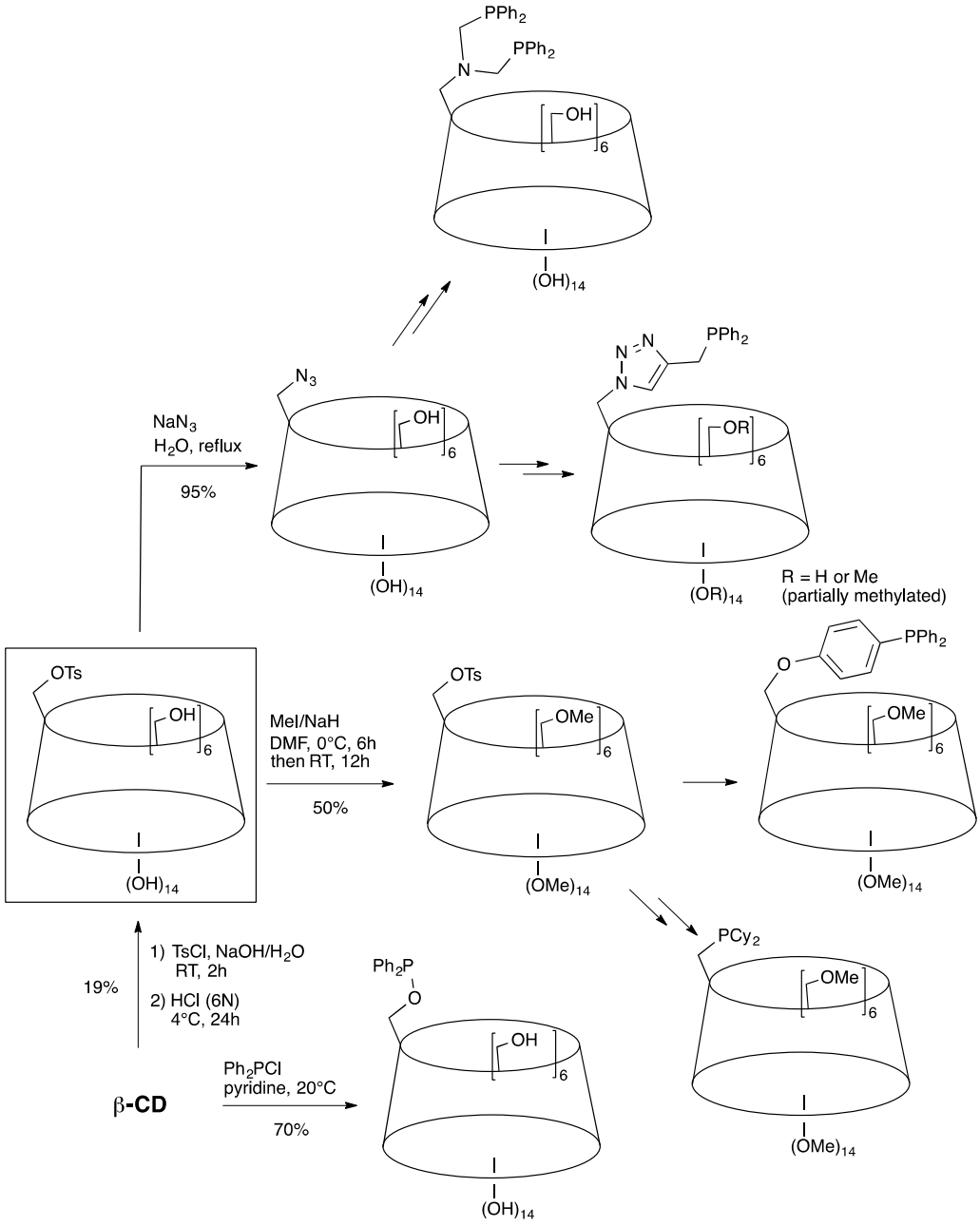
2. Monosubstituted CDs

Several CD platforms have been equipped with coordinating atoms in order to take advantage of the remarkable host-guest properties of CDs for stabilising unusual transition metal complexes or delivering a substrate with a given shape and size to a catalytic centre. Both features could lead to the development of new transition metal catalysts with improved selectivities and activities. Because of the ease with which they can be obtained, both native and modified CDs substituted with a single coordinating fragment, whether monodentate or multidentate, were the first to be studied. This section will start with a brief overview of the methods giving access to monofunctionalised CDs that can be used for grafting a P(III)-containing fragment. Monodentate P(III) ligands will be considered first, before focusing on systems having a dangling chelating fragment, whether homo- or heteromultidentate.

2.1 CD monofunctionalisation

CDs monosubstituted at either the primary or secondary face have become available since the 1990's and a number of these derivatives are now commercially available.[35] In fact, CD monofunctionalisation has been covered as far back as 1998 by D'Souza *et al.* in a special

issue of *Chemical Reviews* dedicated to CDs.[21] A good method for synthesising CDs monosubstituted by a P(III) fragment consists in performing S_N2 reactions on permethylated mono-6-*O*-tosyl-CDs with various P(III) containing nucleophiles, notably phosphides [36] or PR_2-substituted phenolates.[37] Permethylated mono-6-*O*-tosyl-CDs themselves can be obtained straightforwardly by methylating a (non alkylated) mono-6-*O*-tosyl-CD with methyl iodide in the presence of NaH as base (preferred solvent: DMF).[38-40] Note that large quantities of pure mono-6-*O*-tosyl-CD can only be obtained from β-CD,[41] and unsurprisingly, most monosubstituted, P(III)-containing CDs are β-CD derivatives. In some cases, the P(III) fragment was introduced after the tosyl group had been reacted with a nucleophile suitable for further functionalisation (typically sodium azide[42] or amines[43]). Permethylated mono-6-*O*-tosyl-CDs offer more possibilities than their polyhydroxylated counterparts for the introduction of phosphine groups because these derivatives are compatible with strongly basic conditions and are easier to purify. Nevertheless, with weakly basic nucleophiles, the substitution can be performed directly on β-mono-6-*O*-tosyl-CD.[44]

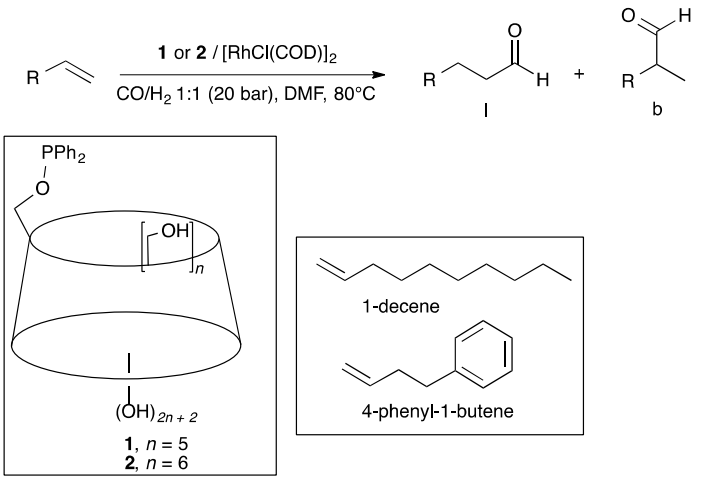


Scheme 2 Typical approaches for anchoring a single P(III)-containing unit on a β-CD platform

On rare occasions, native or partially methylated CDs were reacted with P(III) containing electrophiles (*e.g.* R_2PCl) under basic conditions to generate CDs monosubstituted at either the primary[45] or the secondary face.[46] Scheme 2 summarises the various approaches that have been used for introducing a single P(III)-containing fragment.

2.2 Monodentate ligands

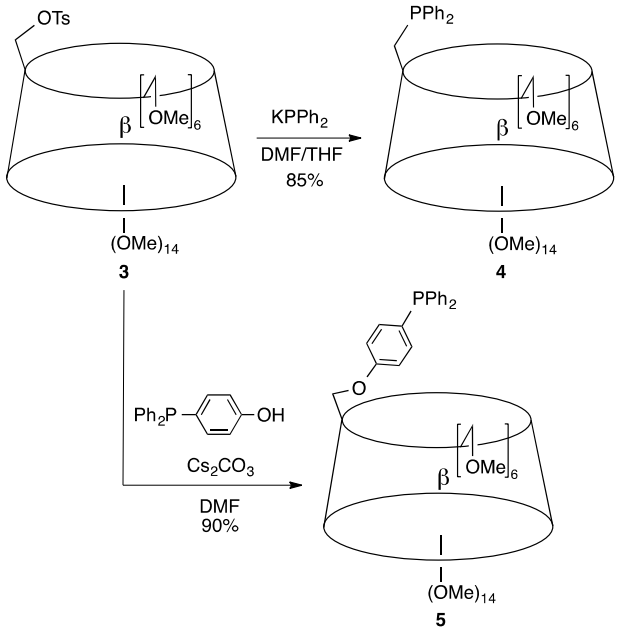
Phosphinites **1** and **2** were synthesised by Ichikawa *et al.* by reacting respectively α- and β-CD with chlorodiphenylphosphine in pyridine. Both ligands were tested in the hydroformylation of mixtures of 1-decene and 4-phenyl-1-butene in DMF (Scheme 3).[45] While **1** showed practically no substrate selectivity (like PPh_3), 4-phenyl-1-butene was hydroformylated 1.7 times faster than 1-decene when using **2**. Contrary to the authors' suggestion, this effect cannot arise from the formation of an inclusion complex between the aromatic substrate and the β-CD cavity, as DMF is known to prevent such non-covalent interactions.[34] Hydroformylation regioselectivities were determined for 1-decene, 4-phenyl-1-butene, 1-octene, and styrene only in the case of ligand **2**. The linear to branched aldehyde selectivities (l/b = 2.8, 2.8, 0.4 and 1.8 for the four above substrates, respectively) are comparable to those obtained with Rh/PPh_3 catalysts.[47-49]



Scheme 3 Ichikawa's phosphinites **1** and **2** and olefins used for substrate-selective hydroformylation studies.

From 2010 onwards, Monflier *et al.* developed a series of phosphines in which the P(III) coordinating unit is covalently linked to a fully methylated β-CD (**4** and **5**) or to the more water-soluble, randomly methylated β-CD (RAME-β-CD) platform (**6**). All of them were tested in metal catalysed reactions (in water or heptane) such as hydrogenation or hydroformylation of olefins.[36] Phosphines **4** and **5** were synthesised by nucleophilic substitution of the tosyl group of **3** with diphenylphosphide and 4-(diphenylphosphino)phenolate, respectively (Scheme 4). Extensive NMR experiments in D_2O proved that one of the phenyl rings of **4** is included in the β-CD cavity, however this being no longer the case in organic solvents. The observed self-inclusion is strong enough to prevent

the formation of a stable inclusion complex in water with 1-adamantanecarboxylate (**ACNa**), known for being an excellent guest molecule for β-CDs. Note that the α-CD analogue of **4** was reported in a PhD thesis, but a possible inclusion of a PPh ring was not considered for this ligand.[50] The catalytic system $[Rh(COD)_2]BF_4$/**4** (COD = 1,5-cyclooctadiene) turned out to be a robust catalyst for hydrogenating the water-soluble olefin 2-methyl-3-buten-2-ol in water. Ligand **4** was also used for the rhodium-catalysed hydroformylation of methyl 4-pentenoate (**S1**, Table 1). Good activities were observed in water (Table 1, entries 1-3), but both chemoselectivity and regioselectivity were in the same range as those observed in heptane (Table 1, entries 4-6). These results are nearly identical to those obtained under the same conditions with the related TPPTS/water (TPPTS = tris(3-sulfophenyl)phosphine trisodium salt) and PPh_3/heptane systems indicating that the presence of the CD cavity has limited impact on the catalytic outcome (Table 1, entries 17 and 20). Entrapment of one of the phenyl rings of **4** makes the formation of inclusion complexes with hydrophobic substrates highly unfavourable, hence the poor selectivity observed.

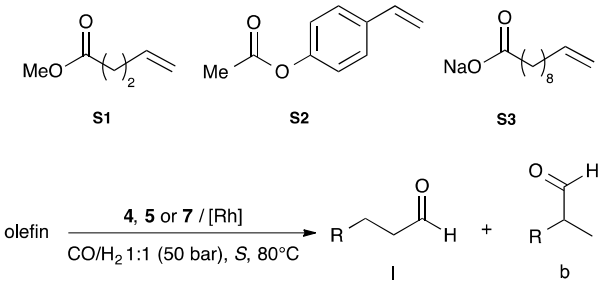


Scheme 4 Synthesis of phosphines **4** and **5**.

Ligand **5** (Scheme 4) was synthesised in order to prevent a similar self-inclusion phenomenon. In this ligand the CD platform is equipped with a longer and more rigid coordinating arm.[37] Unlike **4**, ligand **5** is poorly soluble in water, probably because the hydrophobic PPh_3 unit is here fully exposed to the aqueous outside environment. However,

rhodium complexes of **5** are noticeably more water-soluble than the free ligand. In fact hydrogenation in water of 2-methyl-3-buten-2-ol with **5** was nearly as fast as with **4**.

Table 1 Rhodium-catalysed hydroformylation using **4**, **5** or **7**.[a]



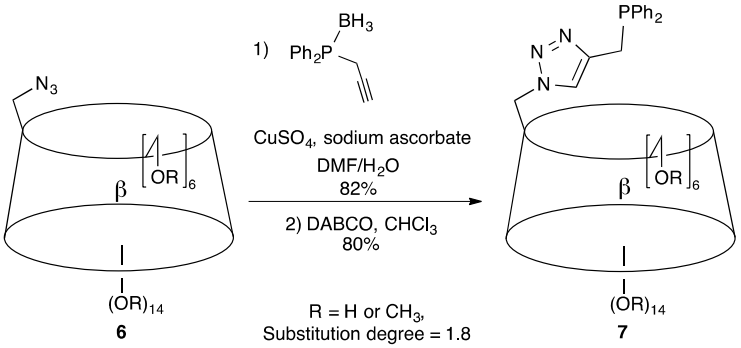
Entry	L	Substrate	Solvent	Competitive Guest (equiv.)[b]	*t* [h]	Conv[c] [%]	l/b[d]	Ref
1	**4**	**S1**	water	-	2	96	1.8	36
2[e]	**4**			-		97	1.8	
3[f]	**4**			-		89	1.7	
4	**4**		heptane	-	2	83	1.2	
5[e]	**4**			-		82	1.2	
6[f]	**4**			-		88	1.2	
7	**5**	**S1**	water	-	2	82	1.1	37
8	**5**			ACNa[g] (0.3)		82	1.1	
9	**5**	**S2**	water	-	2	87	0.1	
10	**5**			ACNa (0.3)		70	0.1	
11	**5**	**S3**	water	-	0.25	99	2.8	
12	**5**			ACNa (1)		80	3.3	
13	**5**			ACNa (9)		32	3.2	
14	**7**	**S1**	water	-	6	99	0.7	42
15	**7**			ACNa (0.3)		99	1.8	
16	**7**			SD[g] (0.3)		98	1.9	
17	TPPTS	**S1**	water	-	2	98	1.8	36
18	TPPTS			ACNa (0.3)		98	1.8	42
19	TPPTS			SD (0.3)		98	1.8	42
20	PPh_3	**S1**	heptane	-	2	98	1.8	36

[a] substrate/rhodium = 500, ligand/rhodium = 4, $P(CO/H_2)$ = 50 bar, (CO/H_2) = 1/1, T = 80 °C. [b] Equivalent of competitive guest added with respect to substrate. [c] Determined by GC using decane as internal standard. [d] l/b aldehyde ratio. [e] Run carried out with

ligand/rhodium = 8. [f] Run carried out with $P(CO/H_2)$ = 25 bar. [g] ACNa and SD stand for sodium adamantylcarboxylate and sodium dodecanoate, respectively.

The three olefins **S1**, **S2** and **S3** were hydroformylated in water with a Rh/**5** catalyst system (Table 1, entries 7-13). Hydroformylation of **S1** and **S2**, which show no affinity for the β-CD cavity, resulted in about the same l/b ratios and conversions as for **4** and TPPTS (Table 1, entries 1 and 17). The presence of competitive CD guests such as sodium dodecyl sulfate (SDS) or 1-adamantanecarboxylate (ACNa) did not alter the catalytic outcome (Table 1, entries 8 and 10, respectively). Conversely, substrate **S3**, which forms an inclusion complex with **5** in water, displayed remarkable activity (TOF up to 1980 h^{-1}) and led to a noticeably higher l/b ratio (2.8) than for the two other olefins (Table 1, entry 11). Because the CD cavity plays an active role in the catalytic process, addition of ACNa reduced dramatically the activity but had no real impact on selectivity (Table 1, entries 12-13).

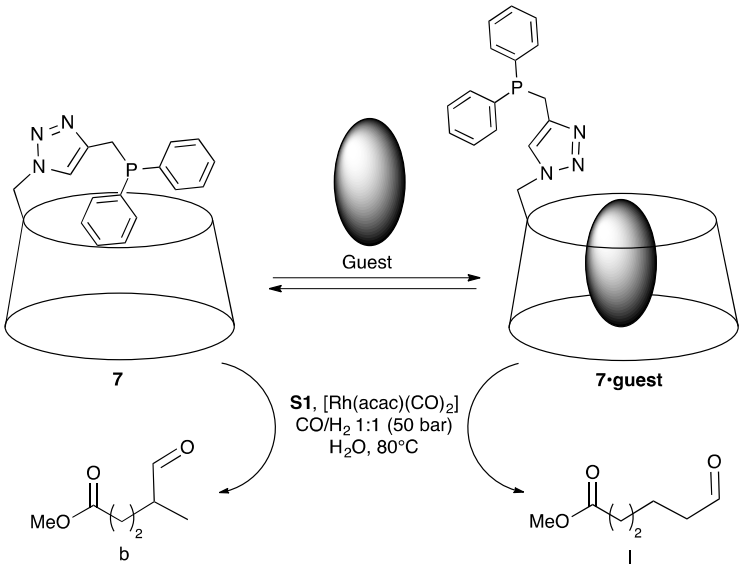
A phosphine with guest-tunable properties (**7**) was obtained by copper catalysed azide-alkyne cycloaddition between borane-protected diphenylpropynylphosphine and 6-mono-azido-RAME-β-CD **6** followed by phosphine deprotection (Scheme 5). While in **4** one of the phenyl rings is firmly held in the CD cavity and cannot be displaced by a competitive guest in water, the buried phenyl group of phosphine **7** can be expelled from the cavity by ACNa.



Scheme 5 Synthesis of **7** via click-chemistry.

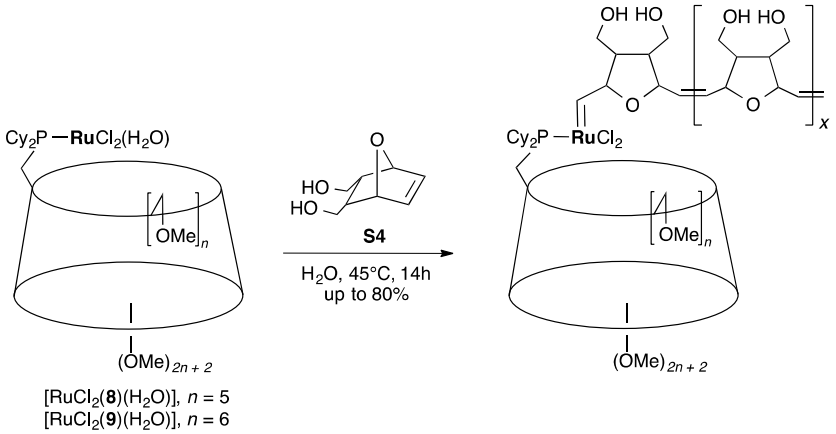
The influence of such a conformational change on the catalytic performance of **7** was assessed by carrying out rhodium-catalysed hydrofomylation reactions in water with olefin **S1**. In the presence of competitive guests (ACNa or sodium dodecanoate (SD)), standard l/b ratios of around 2 were observed (Table 1, entries 15-16 and 17-19) whereas without, the branched product became the major product (Table 1, entry 14). The authors suggest that with a guest molecule included, **7** is bulkier than on its own, a feature which may favour the formation of

the linear regioisomer (Scheme 6).[49] However, steric crowding around the donor atom is probably more severe in the self-included species than in the guest-occupied one. Such a feature is known to be a key factor for promoting the formation of monophosphine complexes at the expense of bis(phosphine) ones. Because singly phosphorus-ligated complexes are known to promote the formation of branched aldehydes, the unusual regioselectivity observed here is probably a direct consequence of a higher than usual proportion of P-monoligated complexes under hydroformylation conditions.



Scheme 6 Guest tuneable conformation of **7** and main hydroformylation products for each case.

Recently, the group of Harada has described the use of the dicyclohexylphosphine complexes [$RuCl_2$(**8**)(H_2O)] and [$RuCl_2$(**9**)(H_2O)] in the ring-opening metathesis polymerisation (ROMP) of the water-soluble diol **S4** in water (Scheme 7).[51] The CD cavity was shown to play an active role in the catalytic reaction as conversions with these complexes (31 and 80 % conversion for [$RuCl_2$(**8**)(H_2O)] and [$RuCl_2$(**9**)(H_2O)], respectively within 14 h at 45°C) were much higher than with CD-free water-soluble analogues. Moreover, CD-guest molecules such as 3-chlorophenol or adamantane inhibit the catalytic reaction to a certain extent, suggesting that supramolecular catalysis is at work in this case. As expected, the best host-molecule for olefin **S4**, namely [$RuCl_2$(**9**)(H_2O)], was more active than its smaller analogue [$RuCl_2$(**8**)(H_2O)]. Note that possible self-inclusion of a P-bound cyclohexyl ring into the macrocycle was not discussed.



Scheme 7 ROMP of olefin **S4** using [$RuCl_2$(**8**)(H_2O)] and [$RuCl_2$(**9**)(H_2O)]. MeO groups of the primary face are probably coordinated to the ruthenium centres.

2.3 Multidentate ligands

The very first CDs bearing appended P(III) ligands were reported independently by the groups of Ito and Reetz in 1993. The group of Ito managed to attach a chiral ferrocenyldiphosphine to the secondary face of a 2,6-permethylated-β-CD (DM-β-CD) by reacting a mesylated derivative of hydroxyethoxy-substituted 1,1'-bis(diphenylphosphino)ferrocene with the fully deprotonated DM-β-CD.[46] Although the resulting ligand (**10**) is practically insoluble in water, the corresponding [$PdCl_2$(**10**)] complex displays high solubility in this medium (Fig. 2). Conductivity measurements showed that [$PdCl_2$(**10**)] assembled in micelle-like aggregates above a given concentration. So far, no catalytic studies involving ligand **10** have been reported.

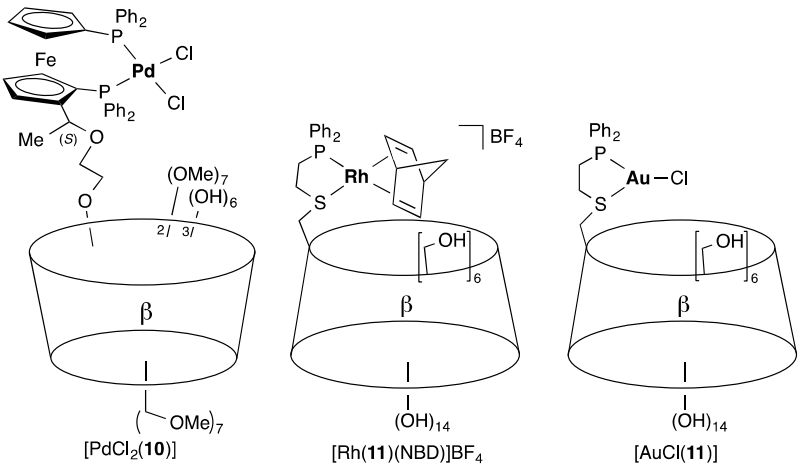


Fig. 2 Complexes of phosphine-functionalised CDs **10** and **11**.

Around the same time, Reetz *et al.* reported the heterobidentate phosphine-thioether ligand **11**, which was synthesised by nucleophilic substitution of β-mono-6-*O*-tosyl-CD by 2-(diphenylphosphino)ethanethiol. Phosphine **11** readily forms the complexes [Rh(**11**)(NBD)]BF_4[44] (NBD = norbornadiene) and [AuCl(**11**)][52] (Fig. 2). Surprisingly, unlike the related cavity-free complex [Rh($Ph_2PCH_2CH_2SMe$)(NBD)]BF_4, [Rh(**11**)(NBD)]BF_4 turned out to be rather ineffective as a hydrogenation catalyst, but no explanation was given for this lack of reactivity.[53,54] A crystal structure reported eight years later showed that the cavity of **11** is able to entrap specifically one of the two phenyl groups by forming a self-inclusion complex in the solid state as for previously mentioned phosphines **4** and **7** (Fig. 3). However, there is no clear evidence for such diastereotopic group recognition in either organic solution or water.[55]

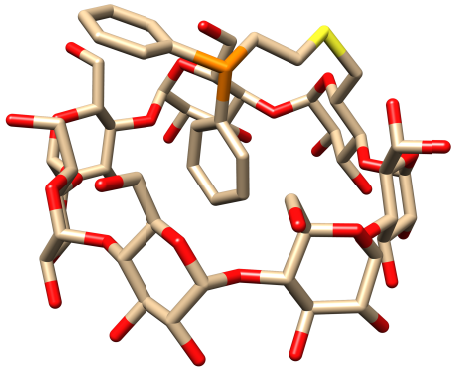
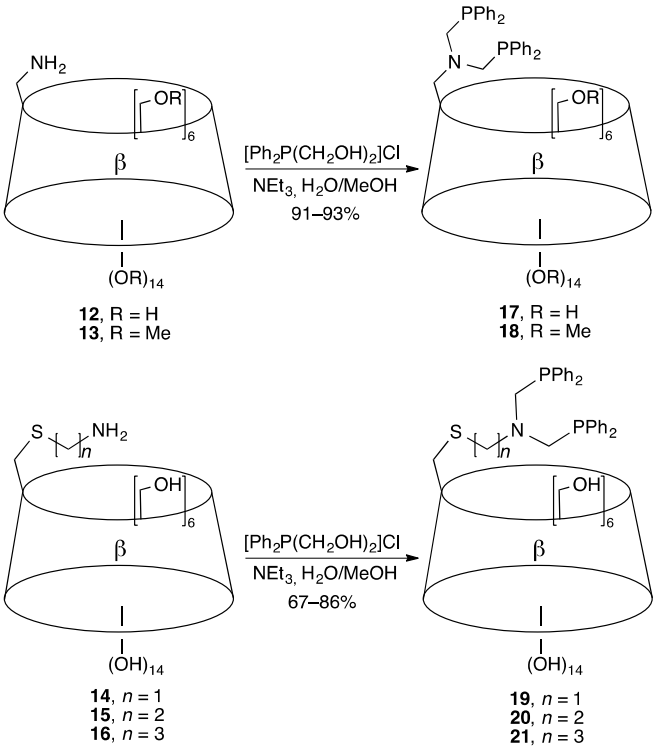


Fig. 3 Molecular structure of phosphine-thioether **11** showing one of the two phenyl groups included in the CD cavity (side view).

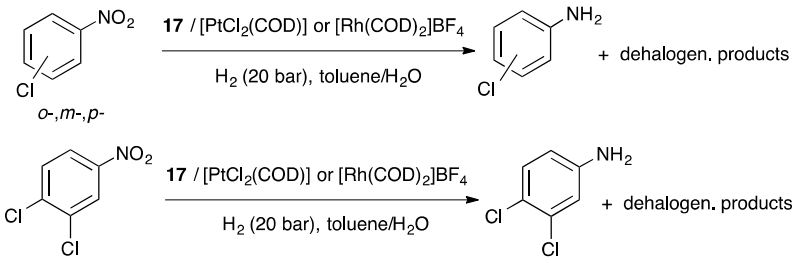
The first ligands combining a chelating diphosphine unit with a CD cavity, namely **17-21**, were reported by Reetz *et al.* These authors proved that metal complexes of these ligands may operate as supramolecular catalysts when used in water-polar organic solvent mixtures.[56,57] Ligands **17-21** were obtained in good yields from 6-monoamino-CDs **12-16**, respectively, in a Mannich-like reaction with [$Ph_2P(CH_2OH)_2$]Cl (Scheme 8). Competitive hydrogenation experiments were carried with catalysts prepared *in situ* from **17-21** and [$Rh(COD)_2$]BF_4.[58,59] For solubility reasons, the reactions were performed in a 30 % DMF-water mixture. The lipophilic olefin 4-phenyl-1-butene was converted up to 6.7 times faster than 1-decene when using **18**, whereas the same reaction with a related CD-free catalyst led to no substrate selectivity. For comparison, a 4-phenyl-1-butene:1-decene substrate selectivity of only 55:45 was observed with the standard Wilkinson catalyst. Preferential substrate inclusion

by the CD cavity, as demonstrated by the decrease in selectivity upon addition of the competitive guest *p*-xylene to the reaction mixture, was invoked to explain this remarkable product distribution.



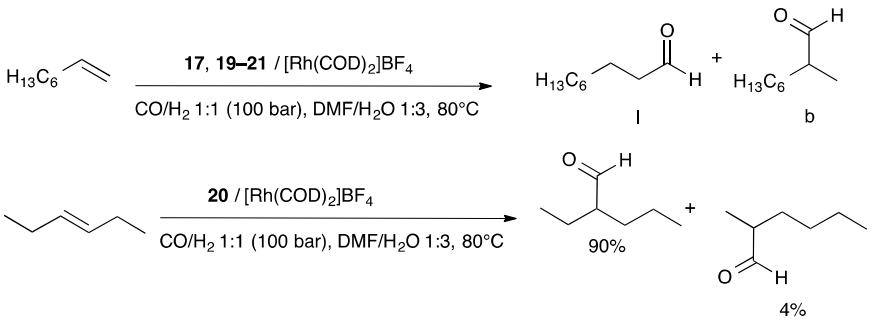
Scheme 8 Synthesis of diphosphines **17**-**21**.

The CD cavity of diphosphine **17** is also responsible for the high chemoselectivity observed in the reduction of halo-nitro aromatic compounds under organic solvent-free biphasic conditions using either $[PtCl_2(COD)]$ or $[Rh(COD)_2]BF_4$ (Scheme 9).[60] Thus, hardly any dehalogenation products were observed with these metal catalysts, which also behave as phase transfer agents (dehalogenation product < 0.5% for the reduction of both 3,4-dichloronitrobenzene and 2-chloronitrobenzene). For comparaison, much lower chemoselectivity was observed when using the water-soluble, cavity-free TPPTS ligand instead (10% decrease in selectivity in the reduction of 4-chloronitrobenzene).



Scheme 9 Chemoselective, metal catalysed reduction of chloronitrobenzenes and 3,4-dichloronitrobenzene.

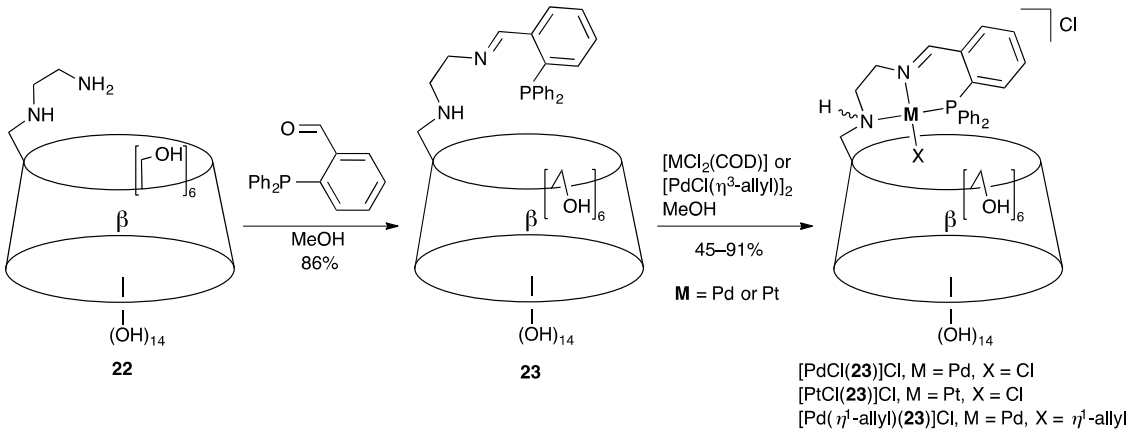
Diphosphines **17** and **19**–**21** were also used in the hydroformylation of 1-octene under biphasic conditions (Scheme 10). Although very robust and remarkably active (150 times more active than the TPPTS catalyst at 80°), the catalysts showed low regioselectivity (l/b = 3.2 vs. 2.8 for the Wilkinson catalyst).[47] The presence of a flexible coordinating arm probably prevents the cavity from having any significant impact on regioselectivity.



Scheme 10 Rhodium-catalysed hydroformylation of 1-octene and (*E*)-3-hexene.

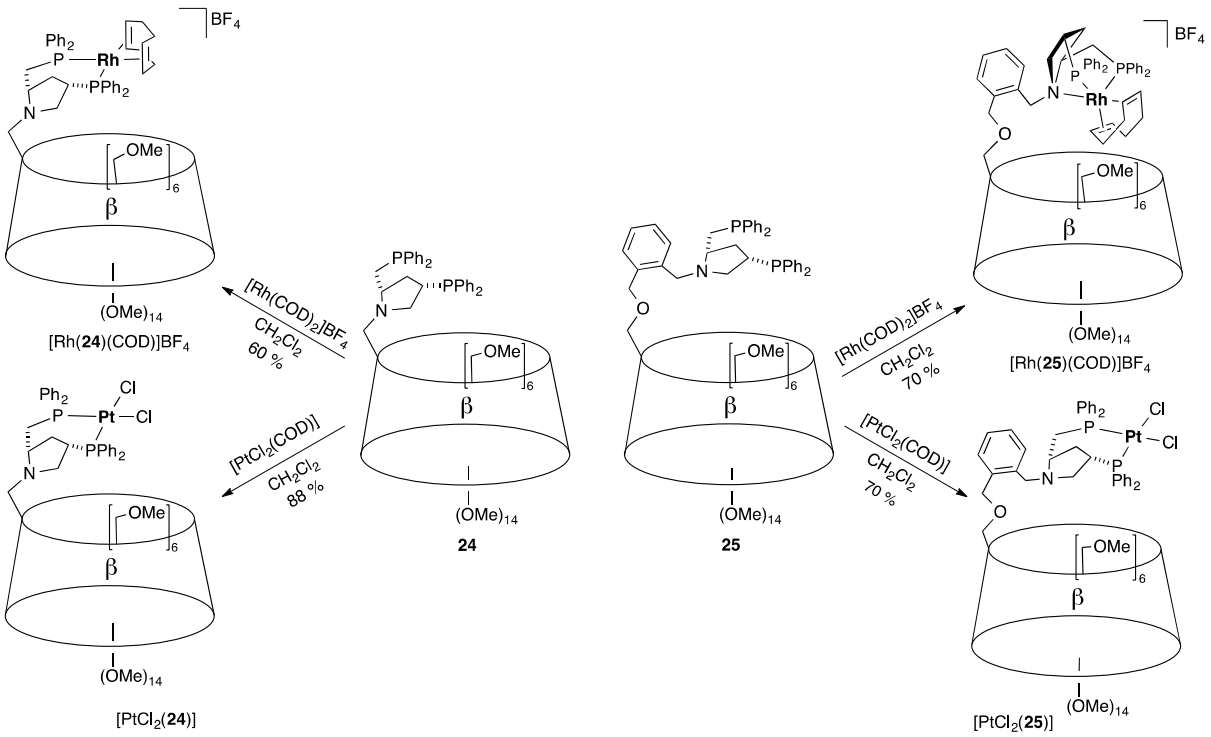
Remarkably, (*E*)-3-hexene could be hydroformylated with **20**/$[Rh(COD)_2]BF_4$ when operating at 60°C under 100 bar CO/H_2 (1:1), giving 2-ethyl-hexanal as the major aldehyde (90%). For comparaison, this internal olefin does not react at all with the standard TPPTS/Rh system.

In 2001, Jia *et al.* reported the synthesis of the *P,N,N′* tridentate ligand **23**, which was obtained by condensation of the diamino-β-CD **22** with 2-(diphenylphosphino)benzaldehyde (Scheme 11). This ligand was used for the preparation of the cationic pincer complexes [PdCl(**23**)]Cl, [PtCl(**23**)]Cl and [Pd(η^1-allyl)(**23**)]Cl.[43] Due to the presence of a stereogenic nitrogen atom, two diastereomers formed upon complexation (1:1 ratio).



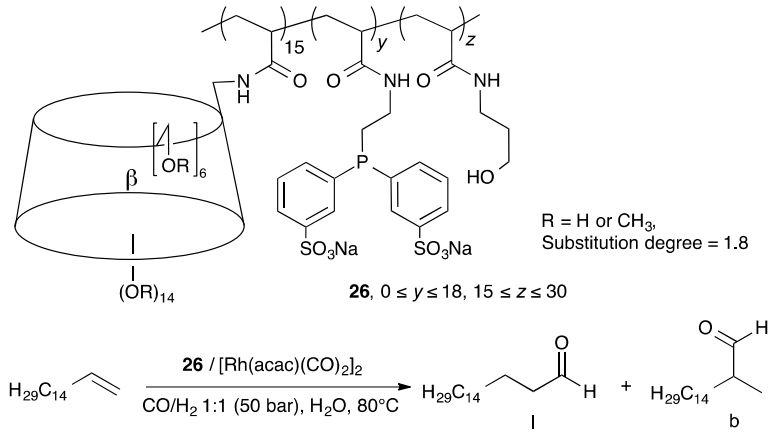
Scheme 11 Synthesis of ligand **23** and pincer complexes thereof.

The chiral (2*S*,4*S*)-(−)-4-(diphenylphosphino)-2-(diphenylphosphinomethyl) pyrrolidine fragment could be attached to a methylated β-CD derivative, leading to diphosphines in which the pyrrolidine is either directly connected to the CD (**24**) or separated from it by an *o*-xylyl spacer (**25**) (Scheme 12). The two phosphines were used for the preparation of the chelate complexes [Rh(**24**)(COD)]BF_4, [$PtCl_2$(**24**)], [Rh(**25**)(COD)]BF_4, and [$PtCl_2$(**25**)].[61] Note that, according to the authors, ligand **25** behaves as a tridentate *P,P',N* ligand in the five-coordinate [Rh(**25**)(COD)]BF_4 complex unlike analogous **24**, which behaves as a chelating diphosphine in [Rh(**24**)(COD)]BF_4. Surprisingly, none of these rhodium complexes have been tested in asymmetric hydrogenation in spite of the potential they represent for this particular reaction.



Scheme 12 Platinum and rhodium complexes obtained from diphosphines **24** and **25**.

Very recently, sulfonated phosphinyl and 6-mono-amino-RAME-β-CD units were successively grafted onto a polymer (polyNAS) to generate water-soluble macromolecules (**26**) that were used as additives in the aqueous Rh-catalysed hydroformylation of the long chain α-olefin 1-hexadecene (Scheme 13).[62] The catalyst activity was shown to be highly dependant of the CD:phosphine ratio. In fact, effective recognition of the substrate by CD receptors to ensure high mass transfer between the substrate-containing organic phase and the catalyst-containing aqueous phase requires the presence of more CD than phosphine units in the polymeric chain to overcome a self-inclusion phenomenon involving the grafted phosphine and CD units.



Scheme 13 Polymers (**26**) equiped with CD units and phosphine moieties and their use in 1-hexadecene hydroformylation.

3. Polysubstituted CDs

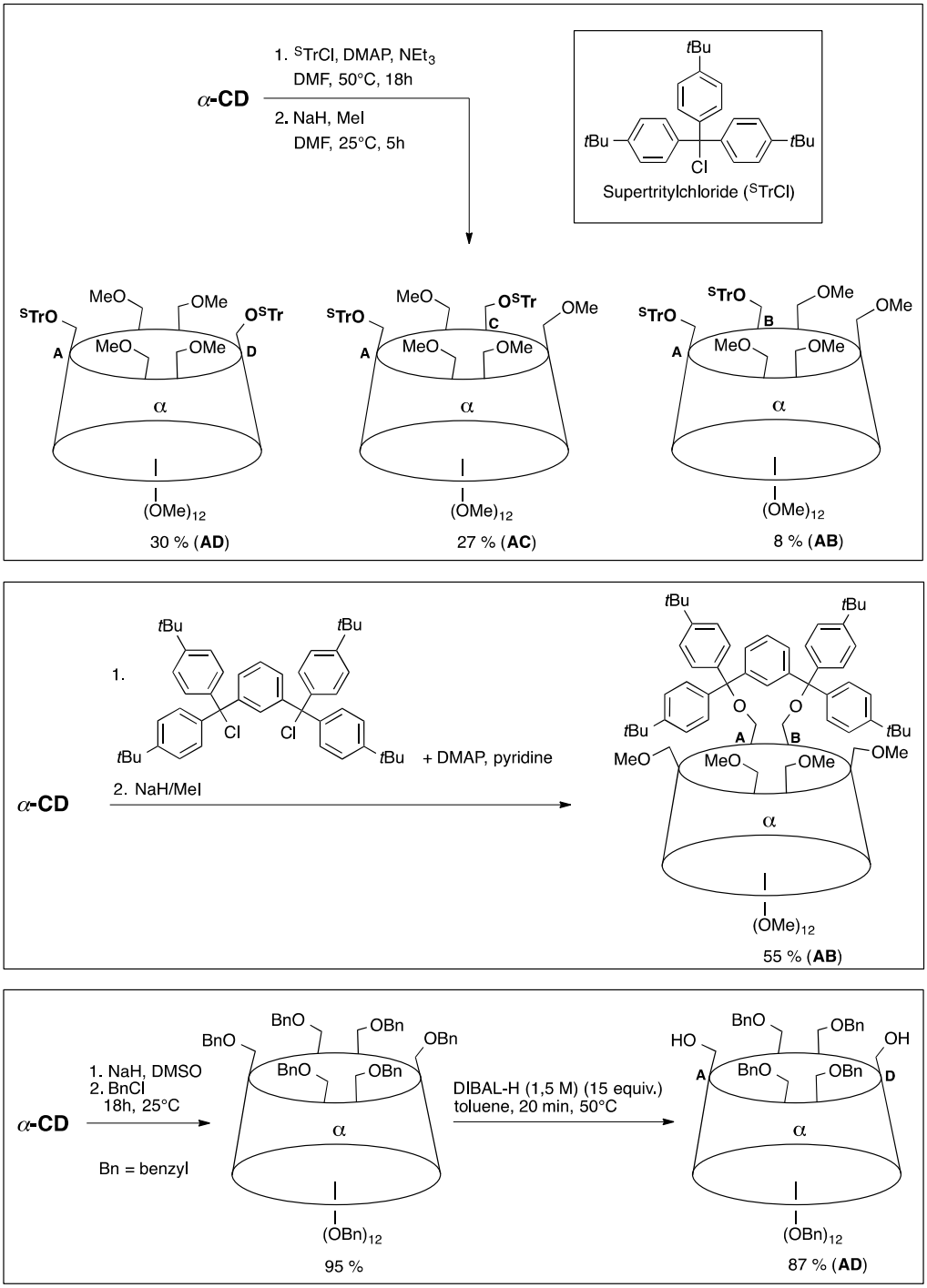
Exact positioning of the metal as close as possible to the CD interior appears to be essential for forcing the metal centre to interact with the CD inner wall, so as to fully exploit the potential CD cavities have in terms of metal protection, chiral induction and hemilabile behaviour. Such a goal can be achieved by creating at least two anchor points on the macrocyclic structure, which can then be used for grafting either pendant or capping P(III) handles. In the former, close proximity between the metal centre and the CD interior is ensured by the propensity of the multidentate ligands to form large chelate rings directly above the cavity, whereas in the latter, it is the inward-pointing nature of the donor atoms that forces the metal centre to stay in close proximity to the CD cavity upon complexation. In the following, all the CD multifunctionalisation methods that have allowed the introduction of one or more P(III) atom onto the CD macrocyle will be detailed. As for section 2, monodentate ligands will be considered next, before dealing with mutidentate systems capable of forming large chelate rings.

3.1 CD multifunctionalisation

Differentiating hydroxyl groups in CDs, which is needed for the selective introduction of various P(III) units onto the macrocycle, has been thoroughly investigated over the last 20 years. Whereas D'Souza *et al.* reported only a handful of moderate yielding methods for accessing multisusbtituted CD derivatives in his review of 1998,[21] many different approaches have been developed since to get hold of gram-scale quantities of CD derivatives, most of them dealing with the introduction of two, three and four identical groups onto the CD primary face. Some of these more modern methods, which have been recently reviewed,[63,64] have allowed to go a step further since access to tri and tetradifferenciated CDs and even penta- and hexadifferenciated ones[65] (*i.e.* CD derivatives bearing three, four, five and six different substituents, respectively) have also become possible. Since no CDs equipped with P(III) units at the secondary face have been so far prepared, only primary face derivatisation will be mentioned in the following. Since 1998, two main strategies have been implemented for achieving effective regioselective multifunctionalisation.

i) The first one is based on the use of sterically hindered protecting groups (trityl and supertrityl), including bridging ones (bis-supertrityl groups), for promoting the formation of given multisubstituted species. After the tritylation step and subsequent alkylation of the residual hydroxyl groups, chromatographic separation of the various alkylated species can be achieved (Scheme 14).[66-70] The protecting trityl groups (and their analogues) are subsequently removed under aqueous acidic conditions. This reaction pathway, dubbed the "long" method, is classical in glycochemistry and allows the synthesis of many multisubstituted CDs, including challenging γ-CD derivatives.[70] In order to introduce P(III) fragments onto the CD platform, the deprotected hydroxyl groups are converted into leaving groups, usually mesyl or the more reactive triflyl groups,[71] before being reacted with nucleophiles, notably phosphides.[72]

ii) The second strategy also relies on steric hindrance but in a reverse sense. Starting from perbenzylated CDs, benzyl groups are surgically removed by adding precise amounts of DIBAL.[73-76] The observed high regioselectivity results from very specific steric interactions between the benzylated primary face and the bulky hydride reagent. Compared to the first one, this method is equally efficient for the α- and β-CD series and affords higher yields of the AD regioisomer. However, it does not allow the synthesis of all isomers, notably A,B-difunctionalised CD derivatives. Remarkably, this method is also effective in the case of persilylated CD derivatives.[77,78] As for the first strategy, the hydroxyl groups are converted to leaving groups before undergoing nucleophilic attack of a reagent containing the appropriate P(III) fragment.[79]

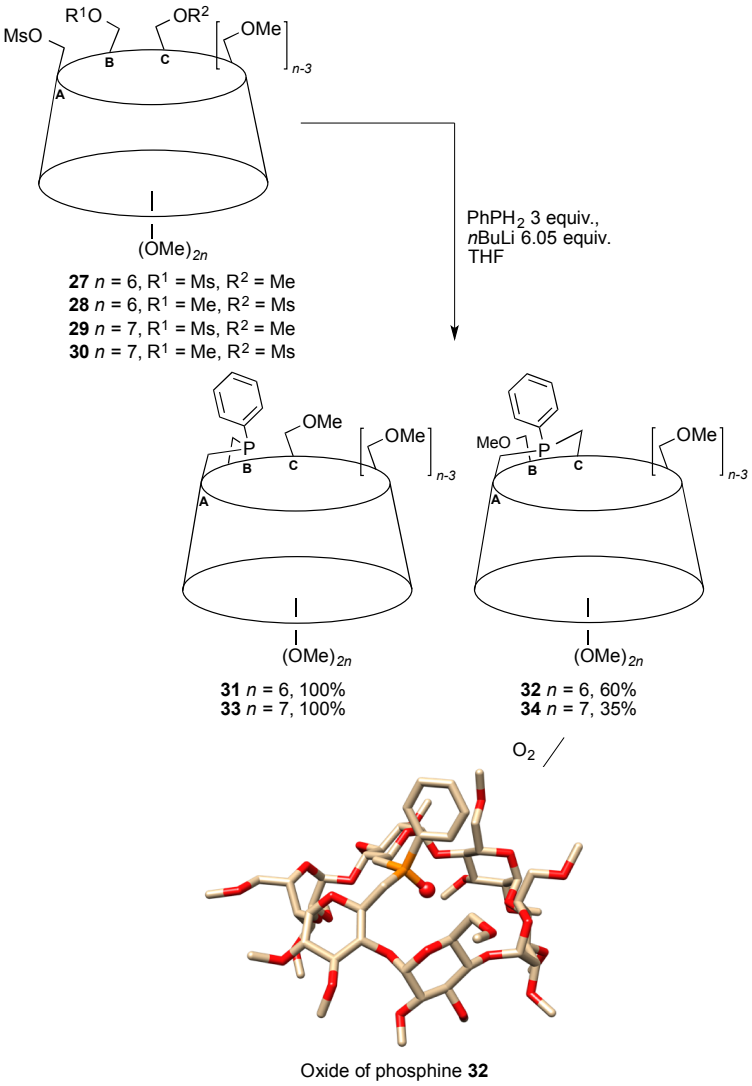


Scheme 14 General strategies for the synthesis of multiply substituted α-CD derivatives suitable for the introduction of P(III)-containing units.

3.2 Monodentate ligands

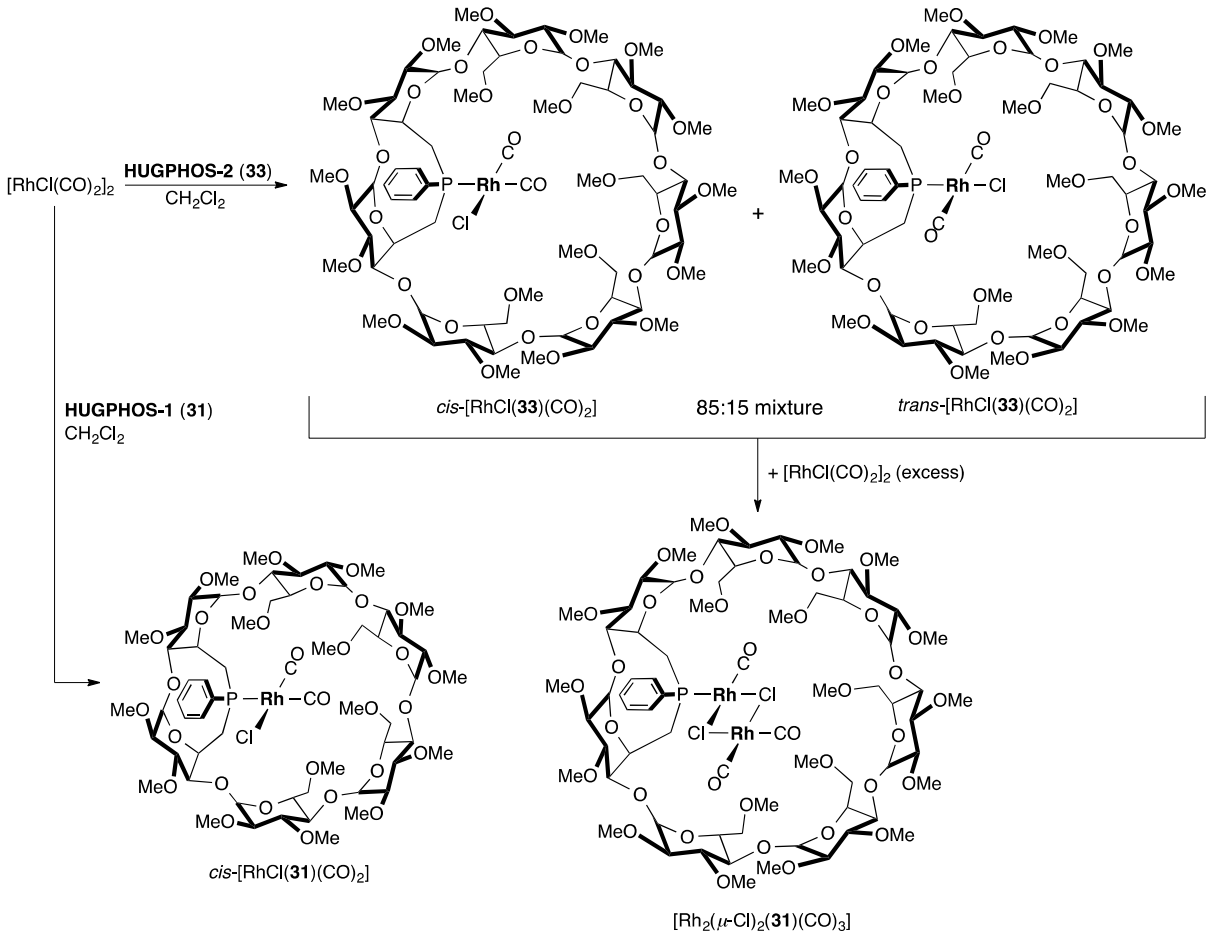
CD derivatives rigidly capped with a coordinating handle have found many applications in various fields of chemistry, most notably enzyme mimicry.[8,80] CDs of this type are expected to maintain the metal centre as close as possible to the cavity entrance for optimal metal

confinement. As far as monodentate ligands are concerned, this is only possible if the lone pair of the coordinating atom is oriented toward the cavity centre. In this respect, the length of the capping unit as well as its rigidity are crucial.[68-70,81-85] In the case of phosphine ligands, Armspach and Matt achieved this goal by bridging two CD glucose units with a single P(III) atom. The first derivatives with a phosphorus lone pair pointing towards the cavity interior (**31**-**34**), were obtained by reaction of dilithium phenylphosphide (Li_2PPh) in THF with dimesylates **27**-**30**, respectively (Scheme 15).[69,86,87] Remarkably, the ring-closure reaction, which does not require high dilution, is 100% stereoselective. Although not as efficient as for **31** and **33**, the cyclisation leading to **32** and **34** remains 100% stereoselective. In the latter two ligands, the presence of a very short "PPh" bridging unit between two *non*-neighbouring glucose moieties induces a strong deformation of the CD torus, as revealed by the unusually wide chemical shift range in which the anomeric protons resonate. This unusual feature was confirmed by a single crystal X-ray diffraction study of the oxide of **32** (Scheme 15), which revealed that glucose unit B has undergone a dramatic conformational change upon capping from the standard $^4C_1$ chair conformation to a $^5S_1$ skew boat one.[88]



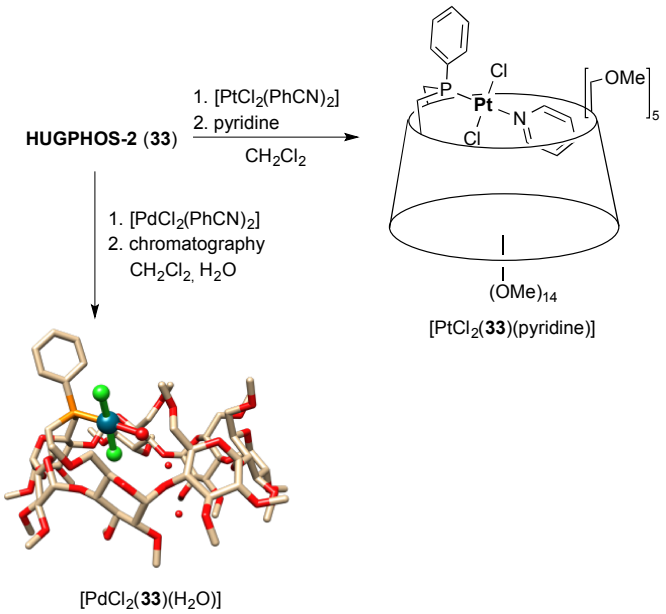
Oxide of phosphine **32**

Scheme 15 Synthesis of capped CDs **31**-**34**.



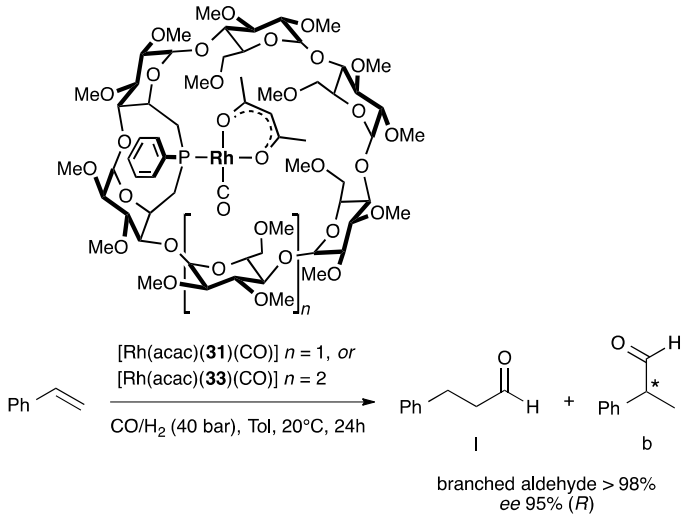
Scheme 16 Monophosphine complexes obtained from the reaction of HUGPHOS ligands **31** and **33** with $[RhCl(CO)_2]$.

As expected, ligands **33** and **34** and their respective α-CD counterparts **31** and **32** form singly P-ligated complexes when opposed to metal complexes such as $[(PdCl(dmba)]_2$ (dmba = *o*-$C_6H_4CH_2NMe_2$) or [AuCl(tht)] (tht = tetrahydrothiophene) and $[RuCl_2(p\text{-cymene})]_2$.[50,86,87,89] Interestingly, owing to the embracing nature of these ligands, the same behaviour was observed with metal complexes which usually promote ML_2 complexes. Thus, mixing an excess of **31** with $[RhCl(CO)_2]_2$ produced only *cis*-[RhCl(**31**)$(CO)_2$] together with unreacted **31**, rather than the expected complex *trans*-[RhCl(**31**)$_2$(CO)] (Scheme 16).[90] Using the larger HUGPHOS-2 ligand (**33**) instead of **31** resulted in the formation of an 85 :15 mixture of the stereoisomeric complexes *cis*-[RhCl(**33**)$(CO)_2$] and *trans*-[RhCl(**33**)$(CO)_2$]. Interestingly, this mixture of mononuclear complexes reacted with a further half equivalent of $[RhCl(CO)_2]_2$ to give the dinuclear complex $[Rh_2(\mu\text{-Cl})_2$(**33**)$(CO)_3]$. Coordination of two metal centres was not observed in the case of **31**, presumably because this cavity is too small.



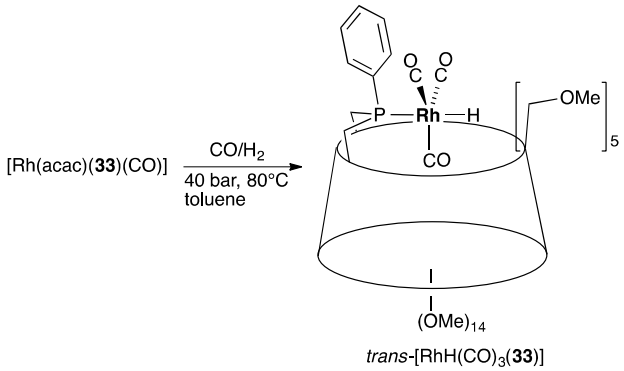
Scheme 17 Monophosphine complexes [$PdCl_2$(**33**)(H_2O)] and [$PtCl_2$(**33**)(pyridine)].

Similarly, reaction of [$PdCl_2(PhCN)_2$] with **33** gave quantitatively the singly P-ligated aquo complex *trans*-[$PdCl_2$(**33**)(H_2O)], the molecular structure of which was determined by a single crystal X-ray diffraction study (Scheme 17). Removal of the water molecule by dehydration resulted in the formation of the chelate complex [$PdCl_2$(**33**-κ^2*P*,*OMe*)] in which one of the primary methoxy groups has replaced the coordinated water molecule. Another singly phosphine-ligated complex, [$PdCl_2$(**33**)(pyridine)], was formed by treating **33** with [$PdCl_2(PhCN)_2$] in the presence of one equivalent of pyridine.



Scheme 18 Asymmetric hydroformylation of styrene using rhodium monophosphine complexes [Rh(acac)(**31**)(CO)] and [Rh(acac)(**33**)(CO)].

While in many metal-catalysed reactions the formation of catalytic intermediates bearing a single phosphine is highly desirable, such a feature is rarely observed under standard catalytic conditions. Indeed, to prevent rapid decomposition of the catalyst, the phosphine/metal ratio is usually kept above one, which in turn promotes the formation of multi-phosphine complexes, even in the presence of bulky phosphines.[91-100] With "embracing" phosphines like **31**–**34**, very robust, air stable Rh(I) complexes ([Rh(acac)(**31**)(CO)] and [Rh(acac)(**33**)(CO)]) were produced. They were used as catalysts for the hydroformylation of styrene and gave equally high branched selectivity and enantioselectivity (98.3 % and 95 % (*R*), respectively) (Scheme 18).[90] Remarkably, no other CD-based catalysts give rise to such an efficient chirality transfer when operating in organic media.[14,71] Furthermore, these catalysts are the first rhodium complexes derived from monodentate phosphines capable of combining high chiral induction with high branched regioselectivity.[101] In situ high-pressure NMR and IR experiments revealed that under hydroformylation conditions the reaction between **33** and [Rh(acac)$(CO)_2$] gave exclusively the mono-phosphine complex *trans*-[RhH$(CO)_3$(**33**)] (Scheme 19).[90] Once formed, this complex induces the selective formation of a key η^3-styrenyl intermediate, which is responsible for the formation of the branched aldehyde, rather than a η^1-styrenyl one.[49] The high chiral induction is a direct consequence of the embracing nature of the ligand.



Scheme 19 Selective formation of complex *trans*-[RhH$(CO)_3$(**33**)] under 40 bar CO/H_2 at 80°C.

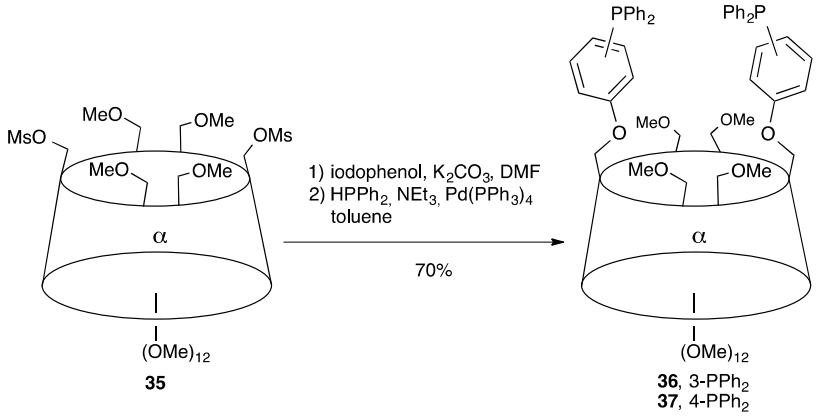
Monophosphines **31** and **33** have also been tested in the palladium-catalysed Mizoroki-Heck coupling of bromoarenes with styrene.[102] Even if the catalysts display activities in the range expected for this type of reaction (up to 81 % conversion after 1h reaction at 130°C with a catalyst loading of 1 mol-%), it is noteworthy to underline the fact

that maximum activity is reached with only one phosphine ligand per metal and not two as usually observed. This again points to an active species consisting of a singly phosphine-ligated complex. Moreover, the authors suggest that the substrate is located outside the cavity during the whole catalytic cycle since the catalyst with the smaller α-CD unit is the most active one.

3.3. Polydentate ligands

3.3.1. Phosphine ligands. The simplest way of bringing a metal centre as close as possible to the CD interior consists in using CDs equipped with two rigid coordinating arms. Upon metal complexation, these podands form large chelate rings in which the metal centre sits above the cavity entrance.[80] Bidentate triarylphosphines **36** and **37** were the first diphosphines of this type to be synthesised.

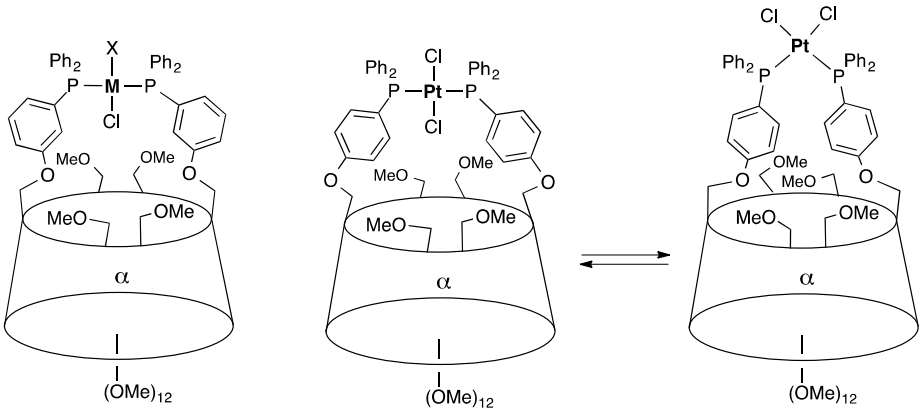
Both were obtained from α-CD using a regioselective difunctionalisation procedure,[66] which allows the convenient introduction of two mesylate leaving groups onto diametrically opposed (A and D) glucose units.[103] Reacting the C_2-symmetric dimesylate **35** with either 3- or 4-iodophenol afforded iodoaryl ether compounds that produced respectively **36** and **37** in 70% overall yields following a palladium-catalysed carbon–phosphorus cross coupling developed by Stelzer (Scheme 20).[104]



Scheme 20 Synthesis of bidentate ligands **36** and **37**.

Despite the large number of bonds separating the P atoms in **36** and **37**, these ligands afforded solely chelate complexes with a number of metal cations, independently of the reagent concentrations. Diphosphine **36** appears to strongly favour *trans*-chelation as exemplified by the exclusive formation of the complexes *trans*-[RhCl(**36**)(CO)] and *trans*-[$PtCl_2$(**36**)] when reacted with $[RhCl(CO)_2]_2$ and $[PtCl_2(PhCN)_2]$, respectively (Scheme 21).

Similarly, the cationic chelate complexes [Au(**36**)]BF_4 and [Ag(**36**)]BF_4, which both display a linear geometry, were the only species formed after metal complexation. In contrast, **37** gives a mixture of the equilibrating chelate complexes *trans*-[$PtCl_2$(**37**)] and *cis*-[$PtCl_2$(**37**)], when treated with [$PtCl_2(PhCN)_2$]. The observed difference of coordination properties between **36** and **37**, which differ from each other only by the aromatic substitution pattern, clearly underlines the fact small structural changes in the CD ligand have a major impact on its coordination mode.

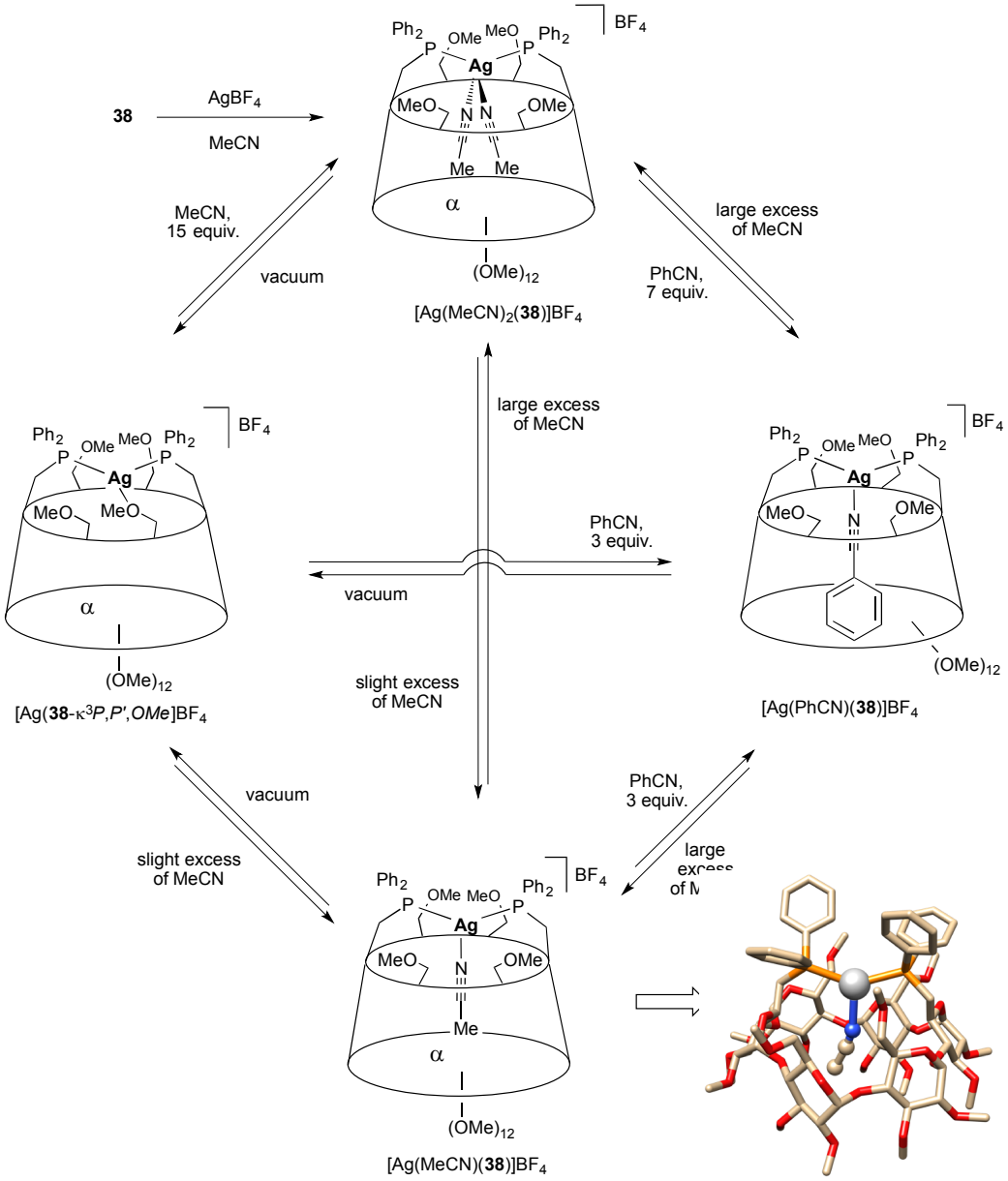


Scheme 21 Coordination chemistry of **36** and **37**.

The complex *trans*-[RhCl(**36**)(CO)] catalyses the hydroformylation of 1-octene in a 6:4 mixture of H_2O and MeOH. The complex being not soluble in pure water, the presence of methanol was needed, this, however, precluding the formation of a strong inclusion complex between the olefin and the CD host. This is in line with the observed linear / branched aldehyde ratio, l/b = 2.3, which is typical of hydroformylation tests carried out in organic media with PPh_3/Rh complexes (See above, Table 1).

In order to maximise the chances of interaction between the first coordination sphere of the metal and the CD walls, very short pendant phosphine groups were grafted onto the CD macrocycle. This was achieved by reacting either the C_2 symmetric dimesylate 6^A,6^D-dimesylate-α-CD **35** or its regioisomer 6^A,6^C-dimesylate-α-CD **28** with an excess of "in situ" prepared $LiPPh_2$ at – 78° in THF.[72] Reaction of **38** with one equivalent of $AgBF_4$ in MeCN led quantitatively to the complex [Ag(**38**)$(MeCN)_2$]BF_4, which comprises two CD-included MeCN ligands (Scheme 22). This complex enabled to study ligand-exchange processes taking place within the cyclodextrin core.[105] Thus, [Ag(**38**)$(MeCN)_2$]BF_4 readily releases one or two acetonitrile molecules depending on the MeCN concentration. Formation of the MeCN-free

complex [Ag(**38**-κ^3*P*,*P*′,*OMe*]BF_4 was achieved by adding acetone, which is known to promote ligand-substitution reactions, prior to evaporation. Replacing acetonitrile with benzonitrile gave only a mononitrile complex, as only one PhCN fits inside the CD cavity (Scheme 22).

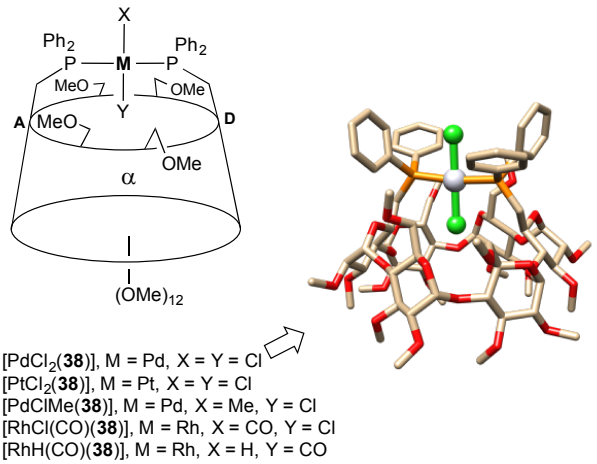


Scheme 22 Diphosphine **38** as probe for nitrile ligand-exchange process.

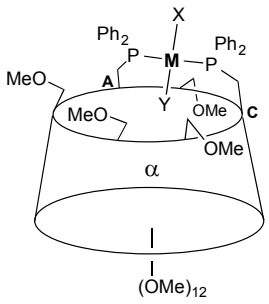
The complex [Ag(**38**-κ^3*P*,*P*′,*OMe*]BF_4 shows fluxional behaviour at the ^{1}H NMR time scale, each of the four primary face methoxy groups being involved alternately in the coordination of the silver cation. Unlike its AD counterpart, [Ag(**39**-κ^3*P*,*P*′,*OMe*]BF_4 (not drawn) displays a sharp ^{1}H NMR spectrum, suggesting non-fluxional ligand behaviour, probably because here the methoxy group of glucose unit B is ideally positioned for

coordination. It is noteworthy that in the case of **39**, only the formation of [Ag(**39**-κ^3*P*,*P*',*OMe*]BF_4, [Ag(**39**)(MeCN)]BF_4 and [Ag(**39**)(PhCN)]BF_4 was observed, but not that of [Ag(**39**)$(MeCN)_2$]BF_4.[72]

In stark contrast with **37**, diphosphines **38** and **39** form exclusively *trans*-chelate complexes with d^8 metal cations rather than *cis*- ones (*trans*-[$PdCl_2$(**38**)], [$PtCl_2$(**38**)], [$PdCl_2$(**39**)], and *trans*-[$PtCl_2$(**39**)]) (Scheme 23). However, small amounts of oligomeric material was also detected in the corresponding reaction mixtures. With their short



[$PdCl_2$(**38**)], M = Pd, X = Y = Cl
[$PtCl_2$(**38**)], M = Pt, X = Y = Cl
[PdClMe(**38**)], M = Pd, X = Me, Y = Cl
[RhCl(CO)(**38**)], M = Rh, X = CO, Y = Cl
[RhH(CO)(**38**)], M = Rh, X = H, Y = CO



[$PdCl_2$(**39**)], M = Pd, X = Y = Cl
[$PtCl_2$(**39**)], M = Pt, X = Y = Cl
[PdClMe(**39**)], M = Pd, X = Me, Y = Cl
[RhCl(CO)(**39**)], M = Rh, X = CO, Y = Cl
[RhH(CO)(**39**)], M = Rh, X = H, Y = CO

Scheme 23 *trans*-spanning behaviour of **38** and **39**.

coordinating arms that force the metal centre to stay close to the CD mouth, diphosphines **38** and **39** behave both as first and second coordination sphere ligands. Indeed, weak C-H•••Cl-M interactions force the M-Cl bond to stay inside the CD cavity in all chlorido complexes derived from **38** and **39**, including those having exogenous ligands different from chloride.[25] Interestingly, chloride substitution with hydride in *trans*-[RhCl(CO)(**38**)] and *trans*-[RhCl(CO)(**39**)] causes the {X–Rh–CO} rod (with X = Cl or H) to rotate about the P•••P axis

and leads to the confinement of the exogenous ligand of highest affinity for the cavity, in this case the CO ligand.

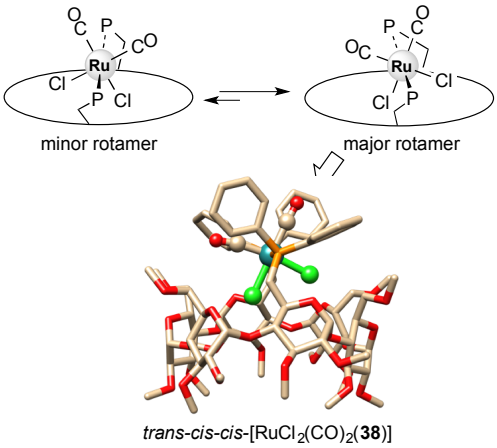
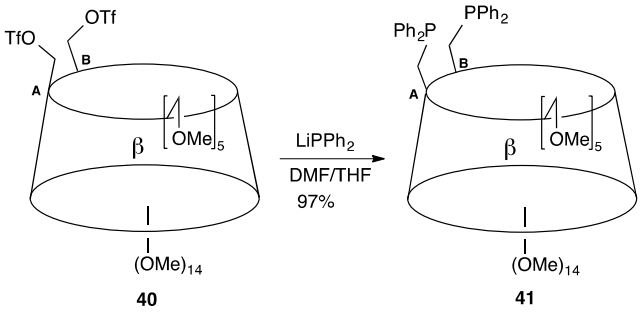


Fig. 4 Equilibrating rotamers of *trans-cis-cis*-[$RuCl_2(CO)_2$(**38**)] with the solid state structure of one of them.

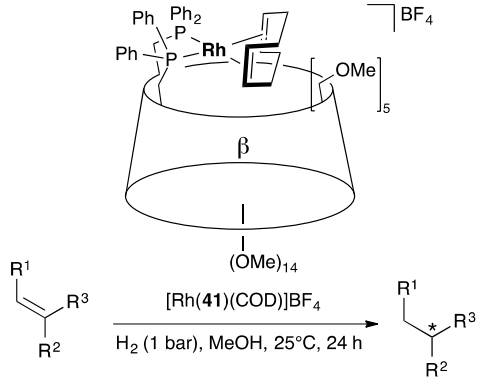
In the case of the octahedral complex *trans-cis-cis*-[$RuCl_2(CO)_2$(**38**)], the cavity captures both chlorido ligands, each competing for the CD central position. This generates an exchange between two rotamers, which correspond to different orientations of the {$Ru(CO)_2Cl_2$} cross (Fig. 4). In solution, this movement is fast at room temperature since both IR and ^{1}H NMR spectra of the complex reflect an apparent C_2-symmetry.[72]



Scheme 24 Synthesis of diphosphine **41** built upon β-CD.

Whereas **38** and **39** give rise solely to *trans*-chelate complexes, the analogous 6^A,6^B-disubstituted CD **41** reported by Jia behaves as an exclusive *cis*-chelator when opposed to [$PtCl_2$(COD)] or [$Rh(COD)_2$]BF_4.[71] Harsher reaction conditions or the use of the better leaving group triflate are required to introduce two PPh_2 units on adjacent glucose units, probably because steric hindrance is more severe in **41** than in **38** and **39** (Scheme 24).

Because of their spatial proximity, the two phosphorus atoms give rise to a strong through-space *J*(P,P) coupling as revealed by a $^{31}P\{^{1}H\}$-$^{31}P\{^{1}H\}$ NMR COSY experiment. Complex [Rh(**41**)(COD)]BF_4 was used in the rhodium-catalysed asymmetric hydrogenation of prochiral α-dehydroamino acids and esters. The highest ee (92%) was observed for the hydrogenation of itaconic acid (Scheme 25). This remarkable study constitutes the first example of metallocyclodextrins giving rise to high chiral induction without the presence of an additional auxiliary chiral group on the CD. The precise location of the metal centre with respect to the CD torus was not determined.[106]

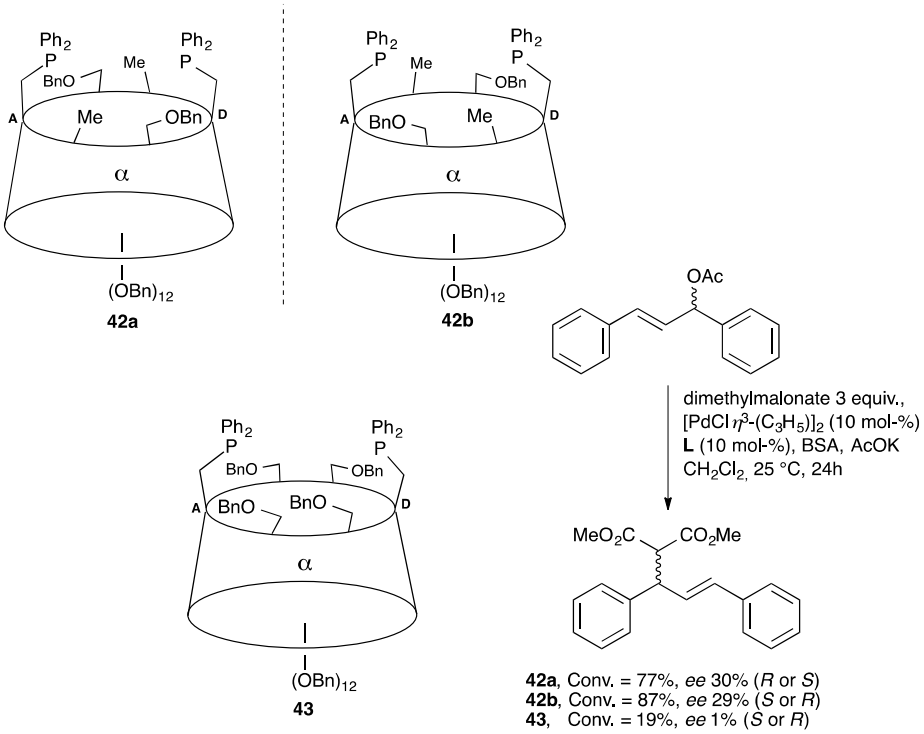


R^1 = Ph, R^2 = COOH, R^3 = NHCOOMe, *ee* 64%
R^1 = Ph, R^2 = COOMe, R^3 = NHCOOMe, *ee* 61%
R^1 = H, R^2 = COOH, R^3 = NHCOMe, *ee* 60%
R^1 = H, R^2 = COOMe, R^3 = NHCOMe, *ee* 78%
R^1 = H, R^2 = COOH, R^3 = CH_2COOH, *ee* 92%
R^1 = H, R^2 = COOMe, R^3 = CH_2COOMe, *ee* 62%

Scheme 25 Rhodium-catalysed asymmetric hydrogenation using [Rh(**41**)(COD)]BF_4.

Introduction of two different substituents on an *achiral* conical cavitand may lower its symmetry and generate *inherent chirality*. This term was used for the first time by Böhmer to describe calixarenes with a non-symmetrical substitution pattern.[107] Strictly speaking, this definition cannot apply to CDs because their numerous stereogenic centres make them chiral molecules anyway. However, two CDs that have “mirror image” substitution patterns can be considered as “pseudo” enantiomers. Sollogoub *et al.* employed this terminology for describing regioisomers **42a** and **42b**, which were prepared from the corresponding benzylated dimesylates (Scheme 26).[108] These were assessed in the palladium-catalysed asymmetric allylic alkylation of 1,3-diphenyl-2-propenyl acetate with dimethylmalonate. As expected for a pair of “pseudo” enantiomers, **42a** and **42b** produced opposite enantioselectivities (*ee* = 30% for both ligands), whereas **43**, with its "achiral substitution pattern", did not induce any selectivity.[109] The “pseudo” enantiomeric complexes [(η^3-PhCH-

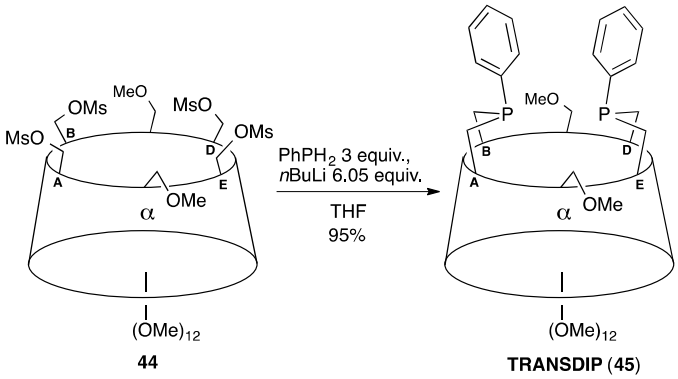
CH-CHPh)Pd(**42a**/**b**)]$^{+}$ were also studied by circular dichroism and gave rise to opposite Cotton effects in the region above 350 nm in keeping with enantiomeric environments around the metal.



Scheme 26 Diphosphines **42a**, **42b** and **43** tested in asymmetric Tsuji-Trost allylic alkylations.

A much more rigid and preorganised diphosphine was prepared by introducing two short phenyl phosphinidene caps on the primary face of an α-CD derivative. Thus, tetramesylate **44**, which can be prepared in gram-scale quantities following a tetrafunctionalisation method devised by Armspach and Matt, reacts with dilithium phenylphosphide (Li_2PPh) in THF to give diphosphine **45**.[67] As for phosphines **31**-**34**, the ring-closure reaction is next to quantitative as well as being 100% diastereoselective (Scheme 27). It is also regiospecific as only adjacent glucose units are being bridged. Unlike phosphines **31**-**34** that readily oxidise in air, **45** is much less prone to oxidation because the two lone pairs, which are spatially close to each other within the CD cavity are shielded from the outside environment. Clear evidence for the inwardly pointing character of the phosphine units came from the existence of through space coupling between the equivalent phosphorus atoms and C-6^{C,F} atoms of non bridged glucose units. Diphosphine **45** was found to be the first authentic *trans*-spanning diphosphine since it forms neither bimetallic complexes nor

polynuclear oligomers upon metal complexation, but only *trans*-chelate complexes when reacted with d^8 and d^{10} cations, unlike many diphosphines that have been sold as such.[110-115]



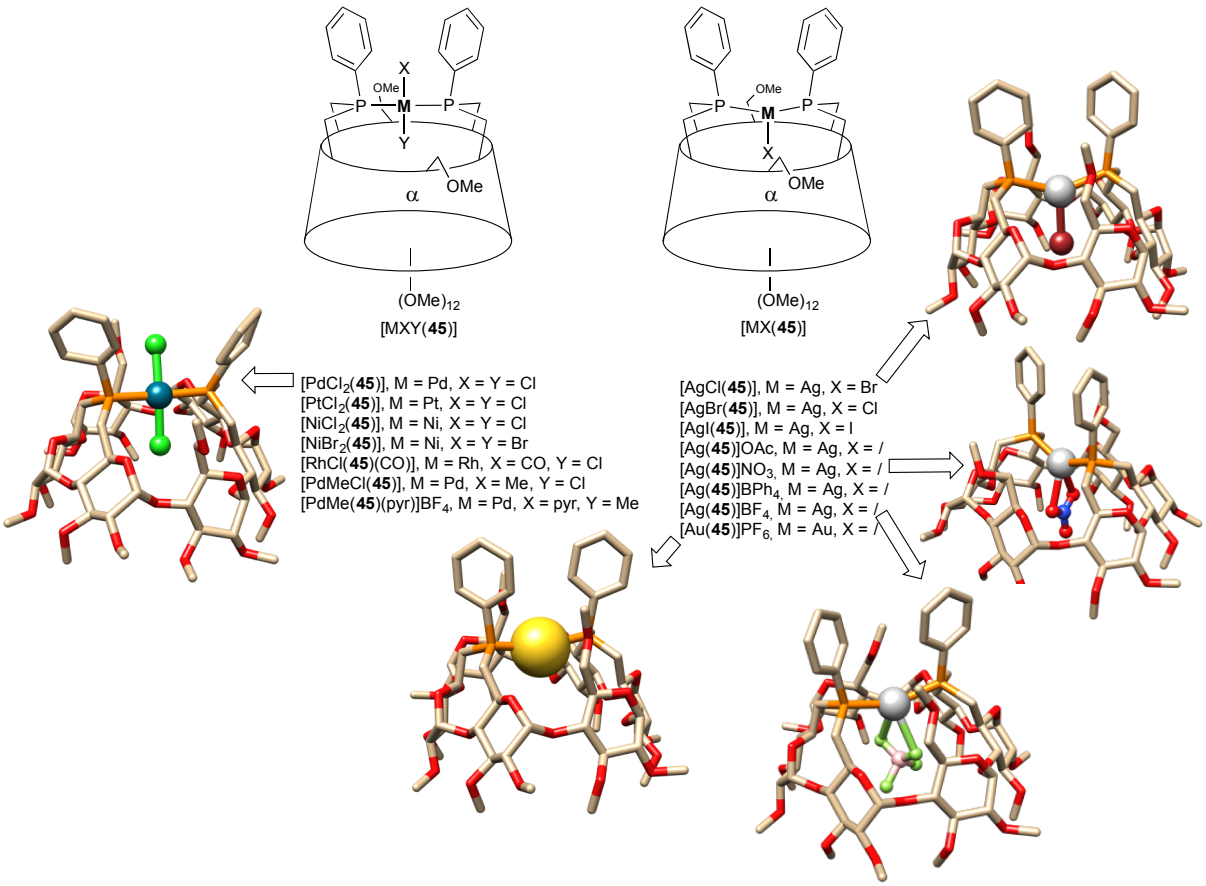
44 **TRANSDIP (45)**

Scheme 27 Synthesis of TRANSDIP (**45**) and formula of TRANSPHOS.

The exclusive *trans*-spanning character of **45** does not only originate from its rigid CD backbone combined with an ideal P...P separation, but also from the inability of the small α-CD cavity to host more than one small exogenous ligand such as chlorido at a time.[116] For example, when reacted with $[PdCl_2(PhCN)_2]$, a *trans*-chelate complex (*trans*-$[PdCl_2$(**45**)]) with a P-M-P angle of about 173° is being formed. When engaged in the unsymmetrical complexes [RhCl(CO)(**45**)] and [PdCl(Me)(**45**)] (Scheme 28), the chlorido ligand is embedded in the CD cavity, exactly as observed in the analogous complexes obtained from **38** and **39** (see above, Scheme 23).[81]

Complex *trans*-[PdMe(**45**)(pyridine)]BF_4 undergoes major conformational changes upon substituting pyridine with chloride, the methyl group moving out of the cavity and the chlorido ligand being captured by the receptor (Scheme 28). While **45** displayed (nearly) perfect *trans*-chelating behaviour towards square planar metal ions, its reaction with AgX moieties resulted in [Ag(**45**)]X complexes (X = Cl, Br, I, OAc, NO_3, BF_4 or BPh_4) in which the silver atom adopts a distorted trigonal or tetrahedral coordination geometry.[27,117] The corresponding P-M-P angles range from 139° for [Ag(**45**)]NO_3 to 152° for [Ag(**45**)]BF_4, as revealed by X-ray diffraction studies. Anions that are compatible with the cavity in terms of size, such as Cl^-, Br^-, NO_3^- and BF_4^- form weak, noncovalent bonds with inner cavity H-5 protons, in addition to coordination bonds with silver. For those that have low affinity for silver such as BF_4^-, the metallocyclodextrin behaves as a true ditopic receptor since here, anion encapsulation is a direct result of the synergistic binding of the anion to both metal

cation and cavity inner wall. Remarkably, the $^{31}P\{^{1}H\}$ NMR chemical shifts of the P(III) atoms are very sensitive to the nature of the included anion.



Scheme 28 Coordination properties of **45** towards late transition metals.

The natural bite angle of diphosphine **45** is likely to be somewhat smaller than 180°, since for complex [Au(**45**)]PF_6,[118] which lacks cavity-interacting exogenous ligands, a slight deviation from linearity was observed in the solid state (P-M-P : 164°). Note that in this complex the two P-Au vectors are directed toward the cavity centre. The important variations in terms of P-M-P angles may originate from the ability or not of the CD torus to act as a second coordination sphere. Depending on the strength of the weak interactions at work,[105] the metal centre sits more or less deeply in the cavity, thus affecting the P-M-P angle (Fig. 5).[27,117]

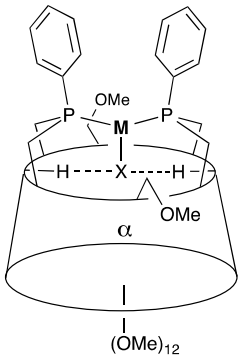
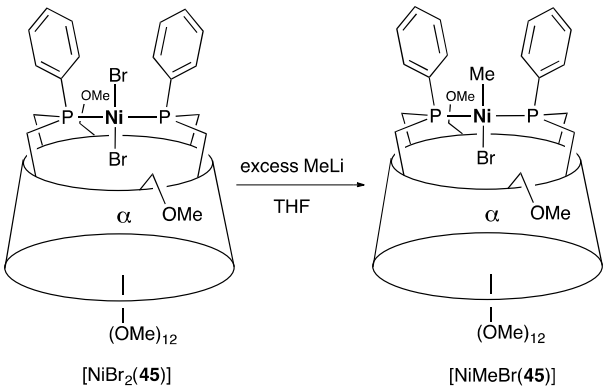


Fig. 5. Noncovalent interactions between an exogenous ligand and some of the inner cavity protons, affecting the P-M-P angle in *trans*-chelate complexes derived from **45**.

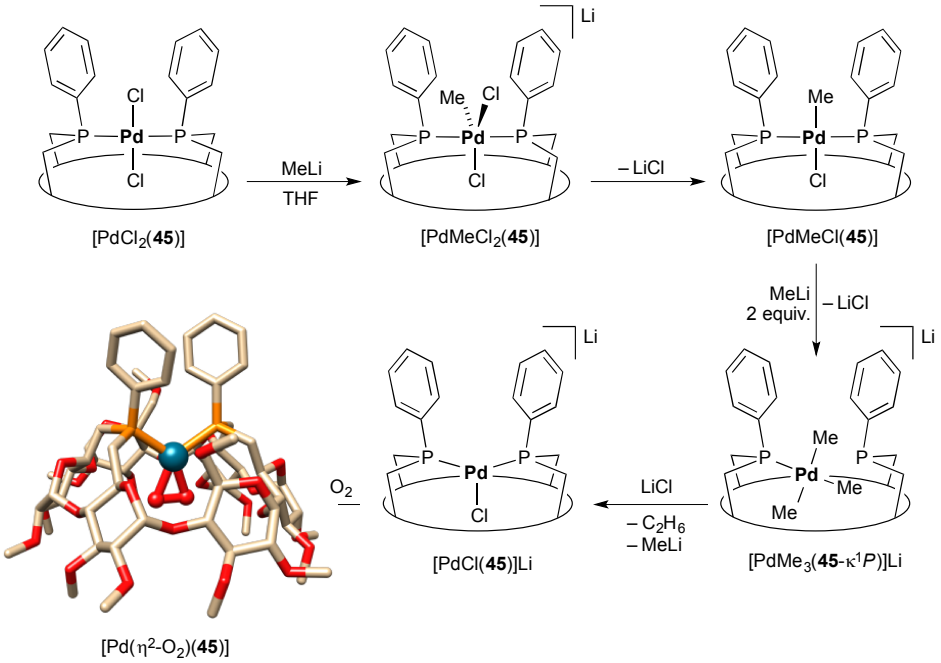
Being a *trans*-spanning ligand, TRANSDIP should not be able to form organometallic complexes capable of mediating the formation of a carbon-carbon bond, since *cis*-coordination of the groups that are being coupled is required.[119,120] To test this hypothesis, the synthesis of Ni and Pd complexes with two metal-methyl units was attempted. Thus, reaction of [$NiBr_2$(**45**)] with MeLi, even in excess, led quantitatively to the exceptionally stable monomethylated complex [NiMeBr(**45**)], but not to the expected dimethyl species,[81] this because the CD provides adequate steric protection against nucleophilic attack by a second MeLi (Scheme 29). In the same vein, reaction of [$PdCl_2$(**45**)] with one equivalent of MeLi resulted in the quantitative formation of the expected monomethylated complex ([PdMeCl(**45**)]). However, when [$PdCl_2$(**45**)] was reacted with *excess* MeLi, a cascade of transormations leading to the production of ethane occurred (Scheme 30)[121] in stark contrast with other *trans*-spanning diphosphines,[111] which give very stable trans chelate dimethylpalladium complexes.[119,122]



[$NiBr_2$(**45**)] [NiMeBr(**45**)]

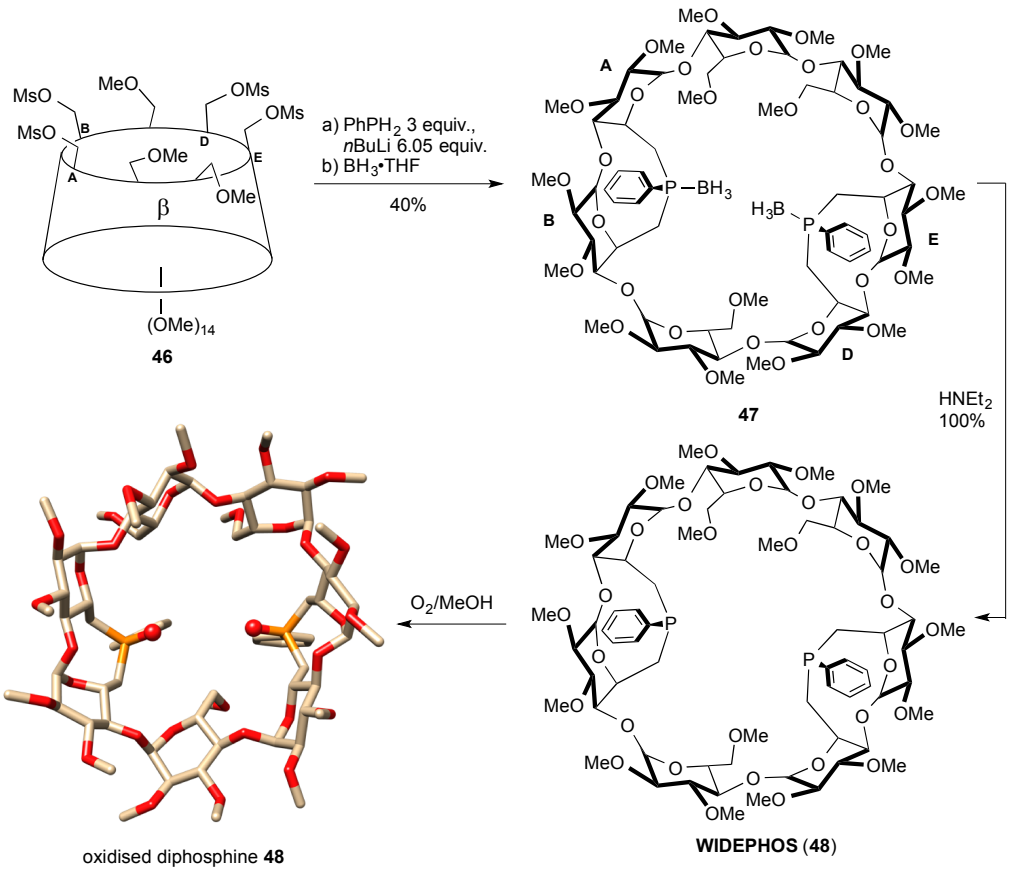
Scheme 29 Alkylation of [$NiBr_2$(**45**)] with excess MeLi.

Once again, the inner cavity protons were used as NMR probes for exploring the different organometallic processes at work.[105] Thanks to a series of low temperature 2D NMR experiments, the mechanisms of the whole set of reactions could be established (Scheme 30). First, addition of one equivalent of MeLi to [$PdCl_2$(**45**)] led quantitatively to [PdMeCl(**45**)] via the trigonal bipyramidal intermediate [$PdMeCl_2$(**45**)], which precipitated out of C_6D_6, allowing its purification and spectroscopic characterisation. Complex [PdMeCl(**45**)] reacted with two extra equivalents of MeLi at –40 °C, to give [$PdMe_3$(**45**-κ^1P)]Li, in which one phosphorus atom is dissociated. Because this transient species has methyl groups that are disposed *cis* to each other, reductive elimination was possible in this case and took place at room temperature to afford ethane, together with the Amatore-Jutand-type[123] Pd^0 complex [PdCl(**45**)]Li with an embedded chlorido ligand.[124] The latter was easily oxidised by air, affording peroxo complex [Pd(η^2-O_2)(**45**)],[125] the molecular structure of which constitutes the first example of a structurally characterised metallo-cavitand containing a {M(η^2-O_2)} unit. The P-M-P angle (111.5°) in [Pd(η^2-O_2)(**45**)] is the smallest for a complex derived from *trans*-chelating **45**. It is however significantly larger than that of the only other reported [Pd(η^2-O_2)(diphos)] chelate complex (104.5°).[126]



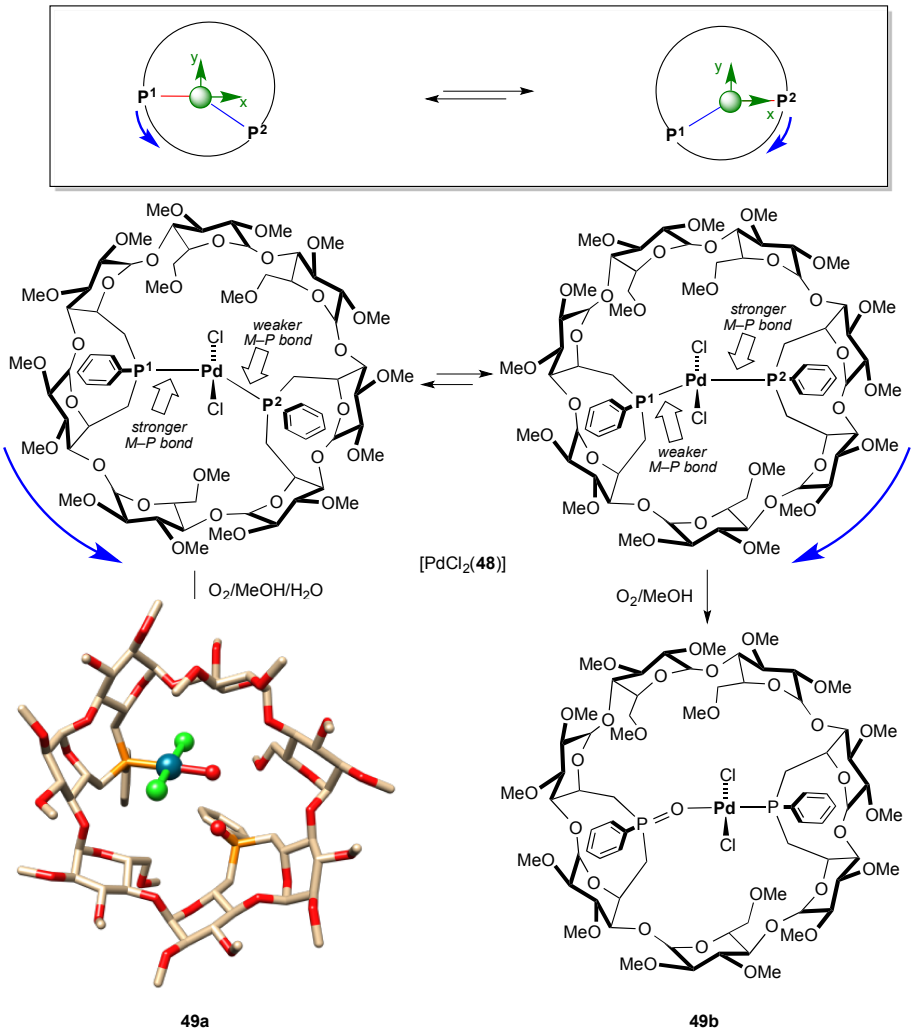
Scheme 30 Reaction pathway leading to the production of ethane from [$PdCl_2$(**45**)] and the formation of peroxo complex [Pd(η^2-O_2)(**45**)].

Unexpectedly, nickel complexes such as [$NiCl_2$(**45**)], [$NiBr_2$(**45**)], [NiMeBr(**45**)] in which ligand **45** acts as a *trans*-chelator, were found to be highly active in α-olefin dimerisation after activation with methylaluminoxane (MAO).[81] In the case of ethylene and for all three catalysts, activity and selectivity to C-4 products lie in the range found for the standard [$NiBr_2(Ph_2PCH_2CH_2PPh_2)$]/MAO system. The TRANSDIP-based catalyst was found to be very robust as it remained active over a prolonged period with a TOF reaching its maximum value after an hour (up to 4.3 x 10^4 mol(C_2H_4)mol(Ni)$^{-1}h^{-1}$). As far as propylene is concerned, the observed activity was about eightfold lower than that of the reference system, probably because of greater crowding about the nickel centre.[127] Since the formation of a C-C bond requires a *cis* arrangement of the metal-bonded alkyl and olefin units undergoing migratory insertion,[119,120] the two phopshorus atoms of TRANSDIP cannot be simultaneously bound to the metal. Possibly, one of the two phosphorus atoms dissociates during the course of the catalytic cycle as described above for the formation of [$PdMe_3(\kappa^1P$-**45**)]Li.[121] However, a mechanism involving a strong distortion of chelated TRANSDIP that brings the two coordinated phosphorus atoms in *cis* position (as proposed initially) cannot be totally excluded.



Scheme 31 Synthesis of WIDEPHOS (**48**) starting from tetramesylate **46**.

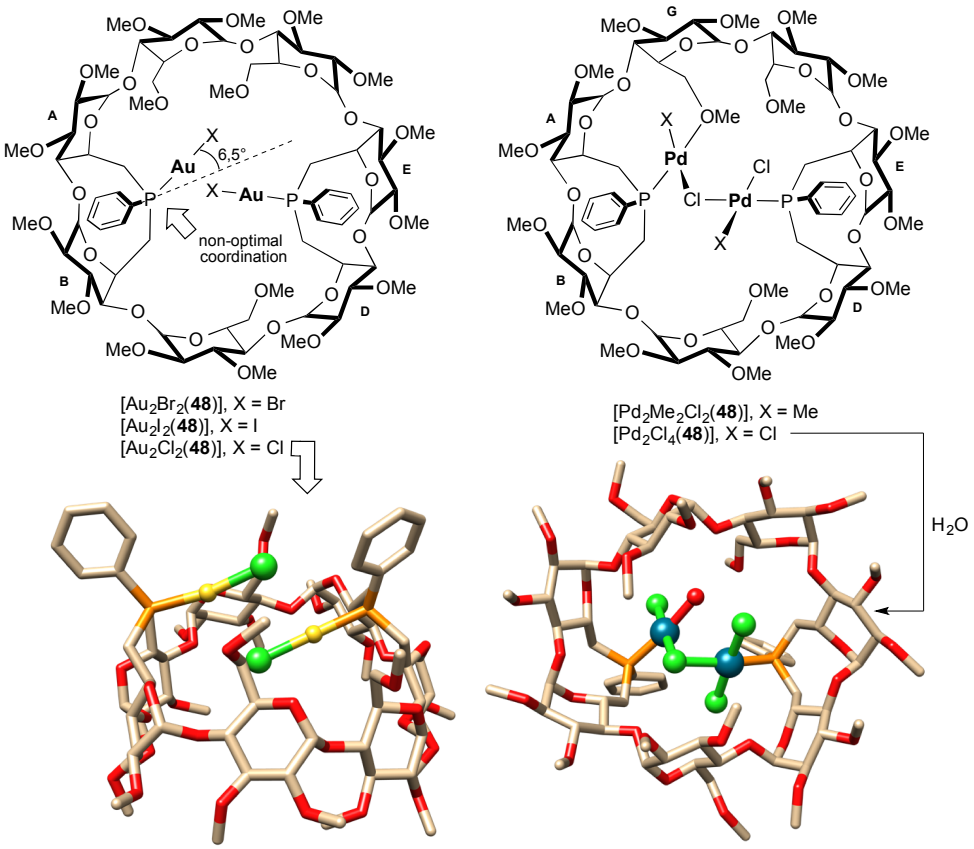
A larger analogue of TRANSDIP, coined WIDEPHOS (**48**), was recently synthesised from β-CD.[69] Similarly to HUGPHOS and TRANSDIP ligands, the synthesis of **48** relies on the regiospecific and 100% stereoselective reaction of adjacent mesylated glucose units of 6^A,6^B,6^D,6^E-tetramesylate β-CD **46** with excess Li_2PPh in THF. In contrast with TRANSDIP, the double-capping reaction is far from being quantitative (40% yield) as significant amounts of elimination products are being formed. For purification purposes, **48** had to be protected with BH_3•THF to afford the non-oxidable phosphine-borane adduct **47**, which after purification could be deprotected with $HNEt_2$ (Scheme 31). Proof that the double-capping reaction had occurred was inferred from an X-ray diffraction study on the oxidised ligand. Unlike TRANSDIP, **48** behaves as an imperfect *trans*-chelator because the P...P separation is rather large (6.91Å) and the two phosphorus lone pairs do not face each other but are at an angle much lower than 180° (151.8° according to the above molecular structure).[28] This means that in all *trans*-chelate complexes of WIDEPHOS, whether square planar ([$PtCl_2$(**48**)], [$PdCl_2$(**48**)] and [RhCl(**48**)(CO)]), or linear ([Au(**48**)]PF_6), overlapping between metal and phosphorus orbitals is not optimal. Such constraints on the metal first coordination sphere manifests itself by a balance wheel-like oscillation of the macrocyclic ligand around the coordinated metal during which the two P lone pairs alternately maximise their overlap with the metal $d_{x^2-y^2}$ orbital. This motion, christened *oschelation*, does not involve any M-P bond dissociation (Scheme 32).[128-133] Unsurprisingly, these complexes are rather unstable and sensitive to oxidation. For example, [$PdCl_2$(**48**)] reacted readily with air in methanol to afford an equimolar mixture of **49a** and **49b**. In each compound, one of the two P atoms underwent dissociation followed by oxidation.



Scheme 32 Balance wheel movement of WIDEPHOS in [$PdCl_2$(**48**)] (view along the CD axis) and mono-oxidised complexes **49a** and **49b**. The green arrows in the frame indicate the orientation of the $d_{x^2-y^2}$ metal orbital involved in the two M–P bonds.

While a genuine *trans*-chelator like TRANSDIP only binds one metal centre at a time, WIDEPHOS is capable of accommodating up to two metal centres.[89] Bimetallic complexes are ubiquitous in catalysis and molecular recognition,[134-139] but the confinement of two metal centres within a molecular cavity,[140-143] as much as diphosphines designed to bring two metal centres close together are a rare occurrence.[111,144-146] Because of the unique location of the two P(III) donor atoms within the rigid macrocyclic framework, the binding of one metal centre strongly influences the coordination behaviour of the second donor atom in dinuclear complexes of WIDEPHOS. For example, one of the two {P-Au-Cl} fragments in [Au_2Cl_2(**48**)] is coordinated in the same way as in the unconstrained monophosphine complex [AuCl(**34**)] while the coordination sphere of the second one is significantly distorted by the

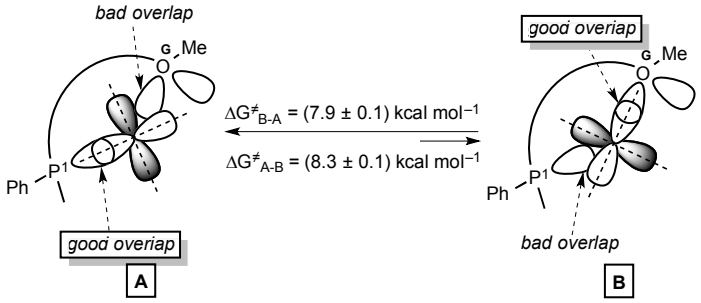
presence of the first metal centre (Scheme 33). The same holds true for other halido complexes such as [Au_2Br_2(**48**)] and [Au_2I_2(**48**)]. The molecular structure of [Au_2Cl_2(**48**)] clearly shows non-optimal coordination of one of the phosphorus atoms (bent P(1)-Au-Cl fragment).



Scheme 33 Dinuclear complexes [Au_2X_2(**48**)] and [$Pd_2X_2Cl_2$(**48**)].

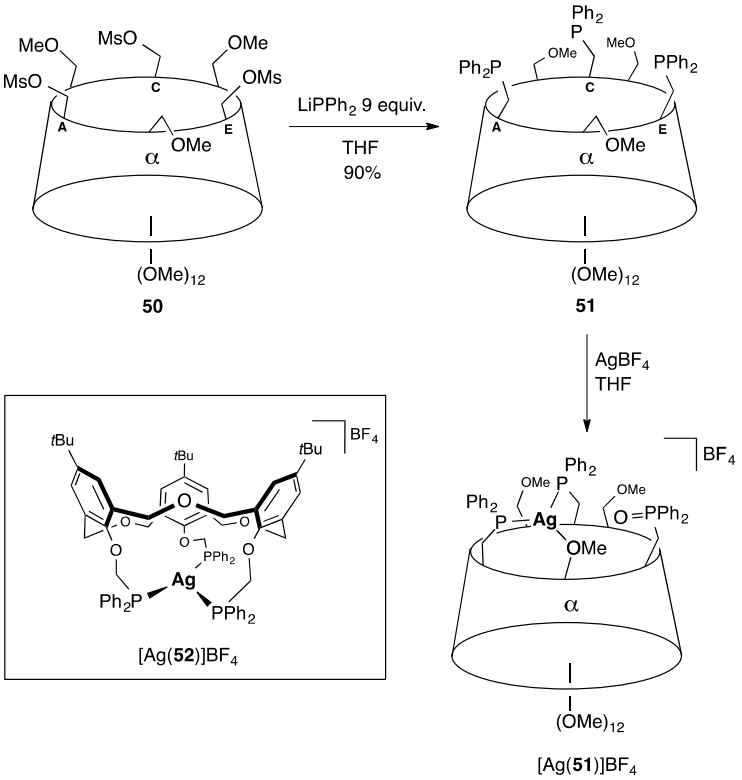
Ligand **48** afforded quantitatively bridged dinuclear palladium (II) complexes ([Pd_2Cl_4(**48**)] and [$Pd_2Me_2Cl_2$(**48**)], respectively) when reacted with two equivalents of [$PdCl_2(PhCN)_2$] or [PdMeCl(COD)] (Scheme 33).[89] Because of its rigidity and the steric crowding generated by the cavity, WIDEPHOS cannot adapt to the flat- or roof-like structures usually expected for a "$Pd_2X_2Cl_2L_2$" motif and instead affords complexes in which two square planar palladium metal centres are linked by a single μ-chlorido bridge. These complexes also display fluxional behaviour as a result of oschelation, but in this case, two different types of donor atoms are involved in the dynamic process, namely the 6^A,6^B-P(III) and the 6-MeO^G atoms. Unlike the mononuclear oschelate complexes mentioned previously, the two equilibrating species (A and B) associated with [Pd_2Cl_4(**48**)] are not present in equal amounts (Scheme 34). Along with monophosphines **31** and **33**, ligand **48** was tested in the palladium-

catalysed Mirozoki-Heck coupling of bromoarenes with styrene. Not surprisingly, the reaction was totally inhibited when using a metal/ligand ratio of 1:1, presumably because of the formation of a non catalytic *trans*-chelate complex. However, when the metal/ligand ratio was raised to 2:1, catalytic activity was restored to a certain extent although this catalytic system is only half as active as the monophosphine-based catalysts. A likely explanation for these results is the formation of a dinuclear active species that is not as active as the mononuclear ones derived from **31** and **33** because of more severe steric crowding.[102]



Scheme 34 Equilibrium between species **A** and **B** taking place in the dinuclear complex $[Pd_2Cl_4(\mathbf{48})]$.

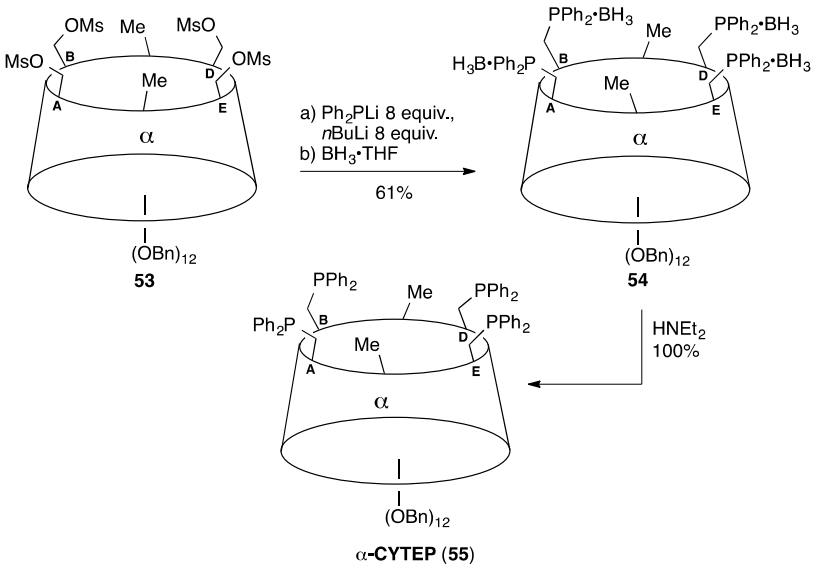
Triphosphine **51** was synthesised by reacting trimesylate **50** with 9 equivalents of $LiPPh_2$ (Scheme 35).[50] This ligand constitutes the first example of a C_3 symmetric triphosphine built on a macrocyclic platform. Unlike the related (C_{3v}-symmetrical) hexahomotrioxa calix[3]arene-based triphosphine **52**,[147] the three phosphorus atoms of which can bind an Ag(I) metal ion simultaneously, **51** acts a P,P,O^{Me} claw toward Ag^+, the remaining phosphorus sidearm being readily oxidised in air. P_3-Tripod-like coordination to Ag(I) is not possible with **51**, as this would result in a highly strained structure. Triphosphine **51** was assessed in the rhodium-catalysed hydroformylation of 1-octene by mixing $[Rh(acac)(CO)_2]$ with one equivalent of **51**. Catalyst activity was low (TOF = 10) and the l/b ratio (2.0) unexceptional.



Scheme 35 Synthesis and coordination properties of triphosphine **51**, and structure of [Ag(**52**)]BF_4.

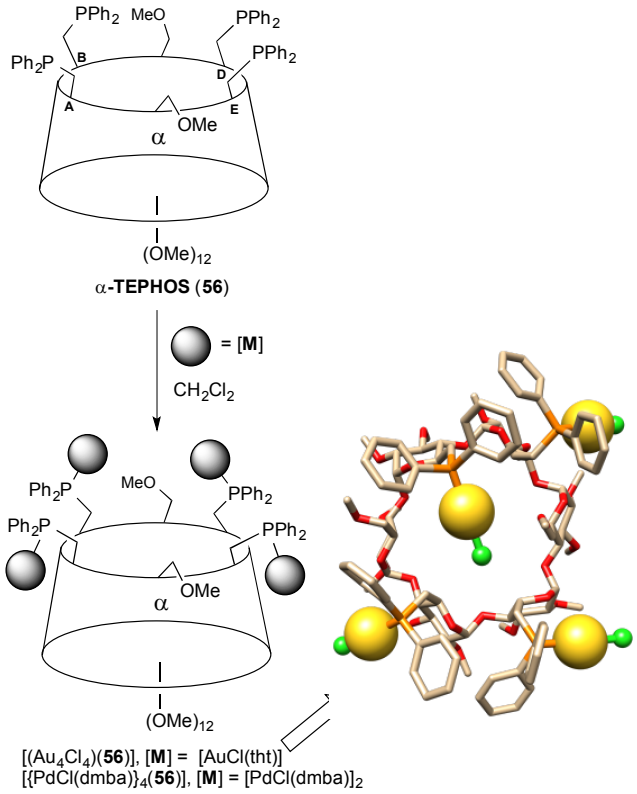
While the use of ligands that promote the formation of singly phosphine ligated complexes are highly beneficial in carbon-carbon bond forming reactions (*vide supra*),[91-100] polyphosphines such as Doucet's and Santelli's TEDICYP, are also known to exhibit exceptional turn-over numbers (TONs) in the same type of reactions, notably in Suzuki-Miyaura coupling.[148,149] These findings prompted Sollogoub *et al.* to design an analogous tetraphosphine built on a benzylated CD platform (ligand **55**, Scheme 36).[76,150,151] This ligand, coined α-CYTEP,[79] was prepared from tetramesylate **53** in a similar way as **51**, except that an additional borane protection/deprotection sequence was needed for purification purposes.[67] Upon reaction with 0.5 equivalent of [Pd(η^3-allyl)Cl]$_2$, **55** gave a fluxional complex in which all P atoms compete for coordination. The catalytic system [Pd(η^3-allyl)Cl]$_2$/**5**□ was tested in Suzuki-Miyaura cross coupling of phenylboronic acid with *p*-bromoacetophenone (Pd/**55** = 1:2; Pd/ArBr = 10^{-3}-10^{-12}; ArBr: 1 mmol; $PhB(OH)_2$: 2 mmol, K_2CO_3: 2 mmol; 120°C). Exceptionally high TON values were obtained when operating at very low Pd/substrate ratios and for prolonged reaction times (14 d, TON = 1.0 ×10^9, Pd/ArBr = 1.10^{-12}). Compared to [PdCl(η^3-allyl)]$_2$, the [Pd(η^3-allyl)Cl]$_2$/**5**□ system led to a 3.4 fold increase of both TOF and

TON. The authors suggest that the unusual life-time and activity of their catalytic system arises from multiple dynamic binding of the metal by the four P(III) donor atoms.



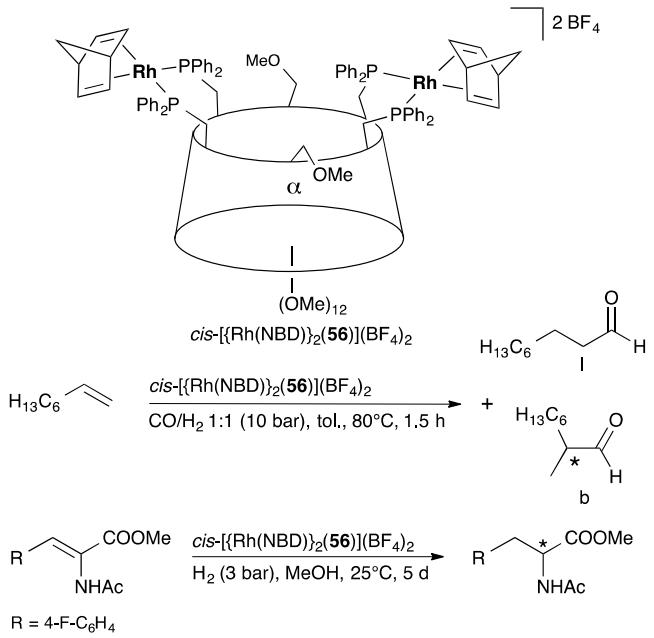
Scheme 36 Synthesis of tetraphosphine **α-CYTEP** (**55**).

A related C_2 symmetric tetraphosphine, namely **56** (α-TEPHOS) was reported a few years earlier (Scheme 37). This ligand forms the tetranuclear complexes [{PdCl(dmba)}$_4$(**56**)] and [(AuCl)$_4$(**56**)] when respectively reacted with 2 equivalents of [(PdCl(dmba)]$_2$ and 4 equivalents of [AuCl(tht)].[152] Interestingly, [(AuCl)$_4$(**56**)] has C_1 symmetry in the solid state, one of the P-Au-Cl rod being included in the CD cavity while the three others are located outside. The observation of an average C_2 symmetry on the NMR time scale at a temperature as low as -80 °C, is consistent with a fast motion in which all four P-Au-Cl units occupy alternatively the centre of the macrocycle.



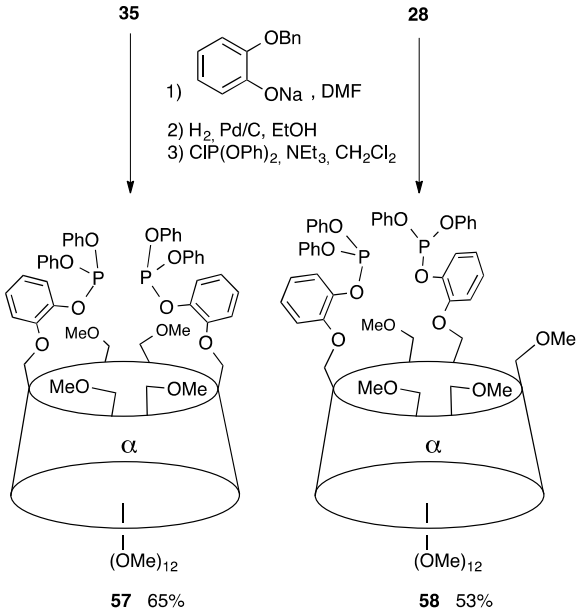
Scheme 37 Coordination chemistry of **α-TEPHOS** (**56**).

Reaction of **56** with $[PtCl_2(COD)]$ afforded a mixture of mononuclear and oligomeric complexes that could not be separated. However, when reacted with cationic $[Rh(NBD)(THF)_2]BF_4$, α-TEPHOS formed a single complex, namely the dinuclear complex *cis*-$[\{Rh(NBD)\}_2(\mathbf{56})](BF_4)_2$ (66% yield). The observed double chelation is regiospecific since only adjacent phosphinated glucose units are being bridged (Scheme 38). *cis*-$[\{Rh(NBD)\}_2(\mathbf{56})](BF_4)_2$ was assessed in the hydroformylation of 1-octene (l/b = 3.2) as well as in the asymmetric hydrogenation of 2-(acetylamino)-3-(4-fluorophenyl)-propenoic methyl ester (25 % *ee),* but the observed selectivities are modest and catalyst activity low as a result of severe steric crowding around the metal centres.



Scheme 38 Hydroformylation of 1-octene and asymmetric hydrogenation of 2-(acetylamino)-3-(4-fluorophenyl)-propenoic methyl ester with *cis*-[{Rh(NBD)}$_2$(**56**)](BF$_4$)$_2$.

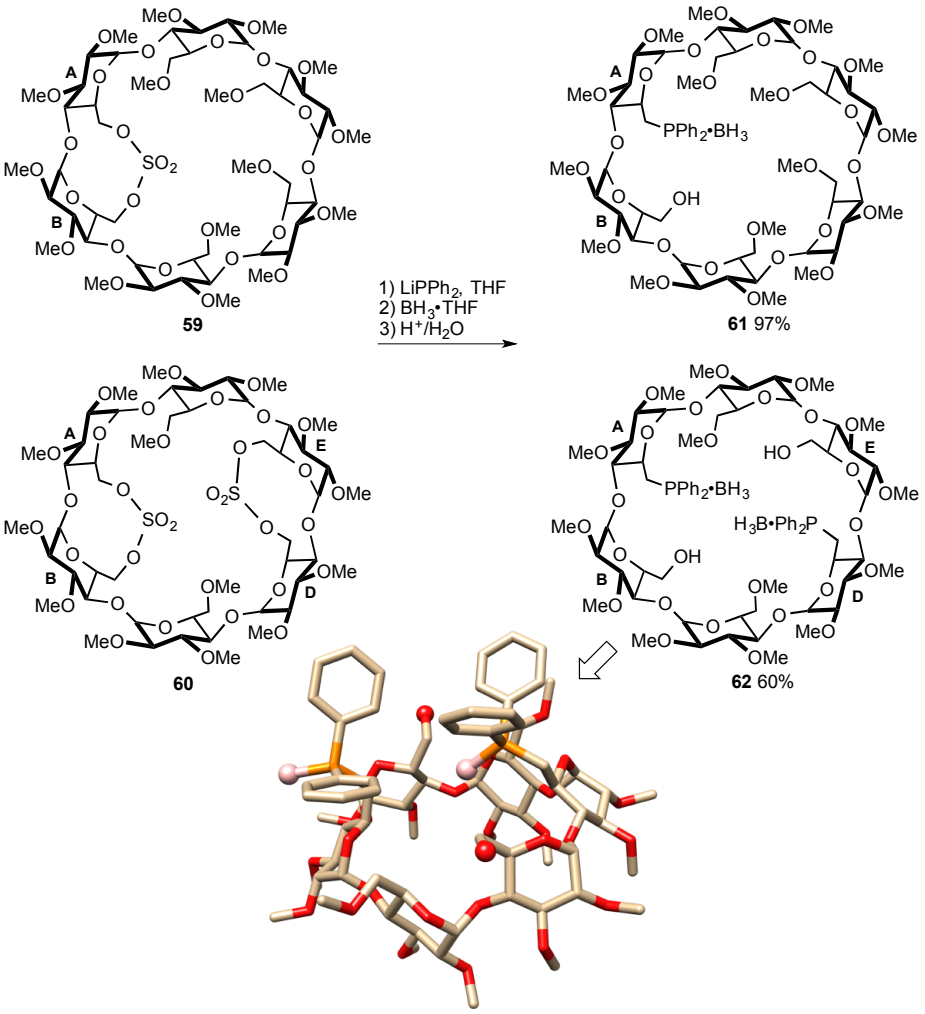
3.3.2. Other P(III) ligands. Like diphosphines **36** and **37**, diphosphites **57** and **58** have their P(III) donor atoms considerably away from the cavity. They constitute the first phosphite-type ligands derived from a CD.[153] Their synthesis involved nucleophilic substitution of dimesylates **35** or **28** with sodium 2-(benzyloxy)phenolate, followed by hydrogenolysis of the resulting benzyl ethers (H_2, Pd/C) and subsequent reaction with chlorodiphenylphosphite (Scheme 39).



Scheme 39 Three-step synthesis of diphosphites **57** and **58**

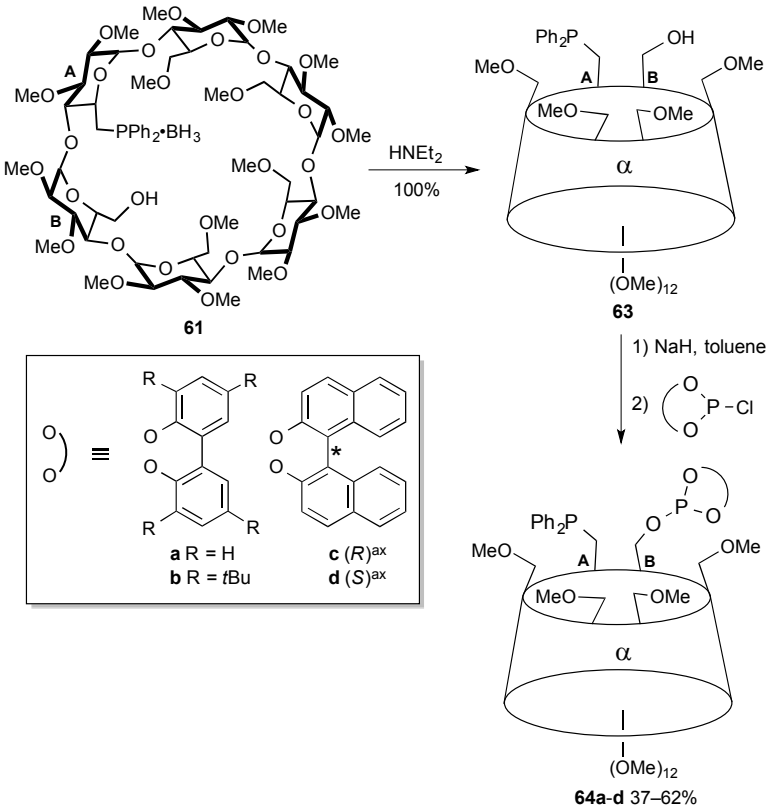
Ligands **57** and **58** form chelate complexes only with highly reactive cationic metal precursors such as $AgBF_4$ or $[Rh(NBD)(THF)_2]BF_4$ and not neutral ones. Metal cations of this type are known to undergo fast coordination by P(III) donor atoms, thereby favouring chelation. The resulting large chelate rings are fairly flexible. The complexes $[Rh(NBD)(\mathbf{57}/\mathbf{58})]BF_4$ were assessed in the metal-catalysed asymmetric hydrogenation of dimethyl itaconate. Surprisingly, only $[Rh(NBD)(\mathbf{58})]BF_4$ was found to be an active hydrogenation catalyst. Despite the flexibility of its large chelate ring, $[Rh(NBD)(\mathbf{58})]BF_4$ gave rise to remarkable enantioselectivity for a catalyst having a CD unit as the only source of chirality (83.6 % *ee*). However, very low activities were measured (17 % conversion after 24 h under 1 bar H_2), reflecting severe steric crowding around the metal. Diphosphites **57** and **58** were also assessed in rhodium-catalysed hydroformylation of 1-octene. Both rates and regioselectivities are comparable to those observed for a related CD-free, bulky diphosphite, indicating that no supramolecular interactions are at work during catalysis.

Opening of sulfato- (**59**) and disulfato-capped (**60**)[69] permethylated CDs with the bulky diphenylphosphide anion at -78°C resulted in the introduction of P(III) atom(s) on specific glucose units (A for **59** and A,D for **60**). After borane protection of the phosphine group(s) and hydrolysis of the pendant sulfate group(s), tridifferenciated phosphine-borane adducts **61** and **62** were formed (Scheme 40).[82]



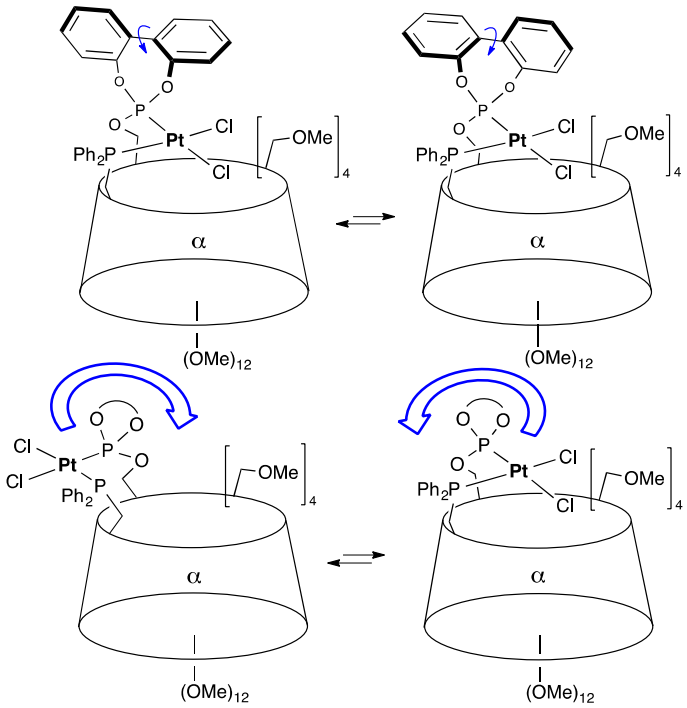
Scheme 40 Regiospecific synthesis of the phosphine-borane adducts **61** and **62**.

The deprotection of **61** with boiling diethylamine afforded hydroxy-phosphine **63**,[106] which is a key starting material for the preparation of hybrid ligands. Thus, deprotonation of **63** with sodium hydride followed by reaction with various diphenylchlorophosphites gave the first phosphine-phosphite ligands (**64**) built on a CD core (Scheme 41).



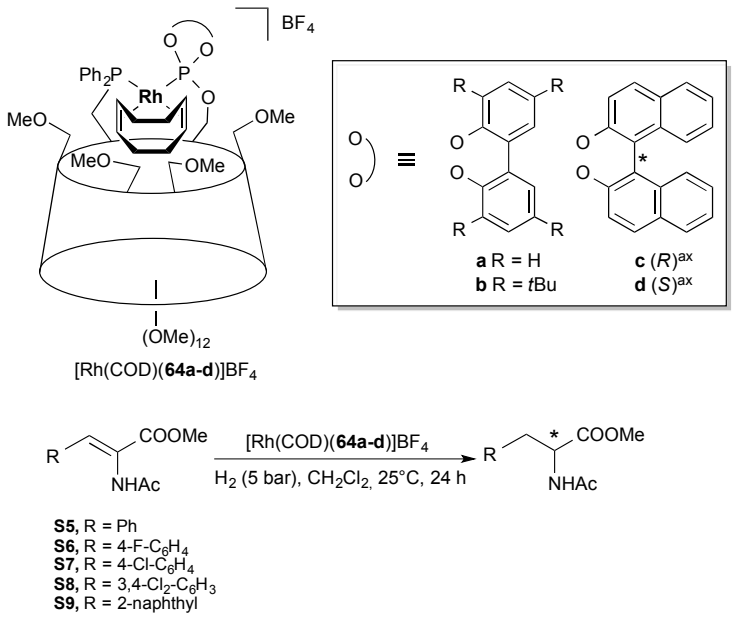
Scheme 41 Synthesis of phosphine-phosphite ligands **64a-d**.

Despite the 10 bonds separating their two donor atoms, these bidentate ligands readily afforded *cis*-chelate complexes when reacted with both neutral $[PtCl_2(PhCN)_2]$ and cationic $[Rh(COD)_2]BF_4$ complexes. Interestingly, complex $[PtCl_2(\mathbf{64a})]$ exhibits fluxional behaviour in solution, the NMR data being consistent with two distinct motions: *i*) a rapid oscillation of the biphenyl rings around the biaryl axis; *ii*) a fan-like movement of the P_2PtCl_2 plane about the $P^A...P^B$ axis (Scheme 42). When atropoisomerisation is blocked as in binaphthyl-containing $[PtCl_2(\mathbf{64c}/\mathbf{64d})]$, only the second motion is observed.



Scheme 42 Movements present in [$PtCl_2$(**64a**)]: *i*) rapid oscillation of the aryl rings in the biphenyl unit (top); *ii*) fan-like movement of the Pt plane (bottom).

Complexes [Rh(COD)(**64a-d**)]BF_4 were assessed in asymmetric hydrogenation of α-dehydroamino esters. This study revealed the dramatic influence of the steric bulk generated by the phosphite moiety on enantioselectivity for all tested substrates (**S5-S9**, Scheme 43). Indeed, the presence of bulky *tert*-butyl groups in **64b** slows down the reaction but is highly beneficial in terms of enantioselectivity. Since chiral groups other than the CD unit are absent from this ligand, only the sugar macrocycle is responsible for the observed chiral induction (60% *ee*). Furthermore, in the case of **64c** and **64d** a clear match/mismatch relationship between the chirality of the torus and the chirality of the binaphtyl substituent was established. While the (*S*)-binaphthyl and CD combination led to a significant *ee* increase, reaching 92% for the bulky naphthyl-containing substrate **S9**, the replacement of the *S*-binaphthyl group with a *R*-binaphthyl one reversed the sense of enantiodiscrimination and resulted in much lower *ee*'s (< 70%) (Scheme 43). Rhodium complex [Rh(COD)(**63b**)]BF_4 was also assessed in asymmetric hydroformylation of styrene, leading to an *ee* of 50% with reasonable TOF values, but without significant modification of the l/b ratio (TOF = 374, l/b = 0.3).



Scheme 43 Rhodium-catalysed asymmetric hydrogenation of prochiral olefins **S5-S9** with phosphine-phosphite comlexes [Rh(COD)(**64a-d**)]BF_4.

4. Conclusion

With their well-defined chiral cavity, CDs decorated with P(III) donor atoms display a rich coordination chemistry that has led to many catalytic applications. The recent development of new methods of CD functionalisation has played a pivotal role in the design and synthesis of a variety of P(III)-functionalised CDs capable of maintaining a coordinated metal centre within or at least close to their hollow, this leading to complexes where the second coordination sphere properties of the sugar macrocycle can be fully expressed and metal confinement achieved. These two features have proved essential for stabilising highly reactive intermediates, for finely controlling the selectivity of numerous catalytic reactions as well as for improving the robustness of the catalysts. When associated with P(III) donor atoms, CDs also constitute effective chiral inductors in metal-catalysed asymmetric reactions, provided their phosphorus atom(s) is(are) rigidly held close to the cavity. Reflecting on the work that has so far been achieved, a delicate balance has to be found in the degree of metal confinement, so that maximum selectivity can been achieved without compromising activity. Ways of combining P(III) atoms with other donor atoms such as nitrogen and sulfur on a CD platform will have to be found in the future to fully exploit the potential cyclodextrins have to offer in homogeneous catalysis.

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Notes and references

1. A. Villiers, *Compt. Rend.*, 1891, **112**, 536-539.
2. J. Szejtli, *Chem. Rev.*, 1998, **98**, 1743-1753.
3. K. Uekama, F. Hirayama and T. Irie, *Chem. Rev.*, 1998, **98**, 2045-2076.
4. J. Mosinger, V. Tomankova, I. Nemcova and J. Zyka, *Anal. Lett.*, 2001, **34**, 1979-2004.
5. L. Szente and J. Szeman, *Anal. Chem.*, 2013, **85**, 8024-8030.
6. R. Breslow and S. D. Dong, *Chem. Rev.*, 1998, **98**, 1997-2011.
7. J. Bjerre, C. Rousseau, L. Marinescu and M. Bols, *Appl. Microbiol. Biotechnol.*, 2008, **81**, 1-11.
8. R. Gramage-Doria, D. Armspach and D. Matt, *Coord. Chem. Rev.*, 2013, **257**, 776-816.
9. J. R. Anderson, E. M. Campi and W. R. Jackson, *Catal. Lett.*, 1991, **9**, 55-58.
10. E. Monflier, G. Fremy, Y. Castanet and A. Mortreux, *Angew. Chem. Int. Ed.*, 1995, **34**, 2269-2271.
11. D. Armspach, D. Matt, F. Peruch and P. Lutz, *Eur. J. Inorg. Chem.*, 2003, 805-809.
12. E. Monflier, *Curr. Org. Chem.*, 2010, **14**, 1265-1265.
13. P. Cintas, G. Cravotto, E. C. Gaudino, L. Orio and L. Boffa, *Catal. Sci. Technol.*, 2012, **2**, 85.
14. M. Guitet, P. L. Zhang, F. Marcelo, C. Tugny, J. Jiménez-Barbero, O. Buriez, C. Amatore, V. Mouries-Mansuy, J. P. Goddard, L. Fensterbank, Y. M. Zhang, S. Roland, M. Ménand and M. Sollogoub, *Angew. Chem. Int. Ed.*, 2013, **52**, 7213-7218.
15. A. Harada, *Supramolecular Polymer Chemistry*, Wiley-VCH, Weinheim, 2012.
16. V. M. Mirsky and A. Yatsimirsky, *Artificial Receptors for Chemical Sensors*, Wiley-VCH, Weinheim, 2011.
17. L. Szente and J. Szejtli, *Trends Food Sci. Tech.*, 2004, **15**, 137-142.
18. G. Cravotto, A. Binello, E. Baranelli, P. Carraro and F. Trotta, *Curr. Nutr. Food Sci.*, 2006, **2**, 343-350.
19. J. L. Atwood, J. E. Davies, D. D. MacNicol, F. Vogtle and J.-M. Lehn, *Cyclodextrins, Comprehensive Supramolecular Chemistry*, Pergamon, Oxford, 1996.
20. W. R. Saenger, J. Jacob, K. Gessler, T. Steiner, D. Hoffmann, H. Sanbe, K. Koizumi, S. M. Smith and T. Takaha, *Chem. Rev.*, 1998, **98**, 1787-1802.
21. A. R. Khan, P. Forgo, K. J. Stine and V. T. D'Souza, *Chem. Rev.*, 1998, **98**, 1977-1996.
22. J. Szejtli, *Cyclodextrins and Their Inclusion Complexes*, Akadémiai Kiadó, Budapest, 1982.
23. H. Dodziuk, *Cyclodextrins and Their Complexes*, Wiley-VCH, Weinheim, 2006.
24. D. R. Alston, A. M. Z. Slawin, J. F. Stoddart and D. J. Williams, *Angew. Chem. Int. Ed.*, 1985, **24**, 786-787.

25. E. Engeldinger, D. Armspach, D. Matt, P. G. Jones and R. Welter, *Angew. Chem. Int. Ed.*, 2002, **41**, 2593-2596.
26. C. Machut, J. Patrigeon, S. Tilloy, H. Bricout, F. Hapiot and E. Monflier, *Angew. Chem. Int. Ed.*, 2007, **46**, 3040-3042.
27. L. Poorters, D. Armspach, D. Matt, L. Toupet and P. G. Jones, *Angew. Chem. Int. Ed.*, 2007, **46**, 2663-2665.
28. R. Gramage-Doria, D. Armspach, D. Matt and L. Toupet, *Angew. Chem. Int. Ed.*, 2011, **50**, 1554-1559.
29. F. Hapiot, S. Tilloy and E. Monflier, *Chem. Rev.*, 2006, **106**, 767-781.
30. F. Bellia, D. La Mendola, C. Pedone, E. Rizzarelli, M. Saviano and G. Vecchio, *Chem. Soc. Rev.*, 2009, **38**, 2756-2781.
31. W. D. Woggon, *Curr. Org. Chem.*, 2010, **14**, 1362-1379.
32. P. W. Atkins, T. L. Overton, J. P. Rourke, M. T. Weller and F. A. Armstrong, *Shriver and Atkins' Inorganic Chemistry, Fifth Edition*, Oxford University Press, Oxford, 2010.
33. F. Hapiot, A. Ponchel, S. Tilloy and E. Monflier, *C. R. Chim.*, 2011, **14**, 149-166.
34. F. Hapiot, H. Bricout, S. Tilloy and E. Monflier, *Eur. J. Inorg. Chem.*, 2012, 1571-1578.
35. Monosubstituted CD derivatives can be purchased from CycloLab Cyclodextrin Research and Development Laboratory Ltd., Budapest, Hungary.
36. C. Machut-Binkowski, F. X. Legrand, N. Azaroual, S. Tilloy and E. Monflier, *Chem. Eur. J.*, 2010, **16**, 10195-10201.
37. F. X. Legrand, N. Six, C. Slomianny, H. Bricout, S. Tilloy and E. Monflier, *Adv. Synth. Catal.*, 2011, **353**, 1325-1334.
38. G. L. Yi, J. S. Bradshaw, B. E. Rossiter, A. Malik, W. B. Li and M. L. Lee, *J. Org. Chem.*, 1993, **58**, 4844-4850.
39. T. Kaneda, T. Fujimoto, J. Goto, K. Asano, Y. Yasufuku, J. H. Jung, C. Hosono and Y. Sakata, *Chem. Lett.*, 2002, 514-515.
40. J. A. Faiz, N. Spencer and Z. Pikramenou, *Org. Biomol. Chem.*, 2005, **3**, 4239-4245.
41. R. C. Petter, J. S. Salek, C. T. Sikorski, G. Kumaravel and F. T. Lin, *J. Am. Chem. Soc.*, 1990, **112**, 3860-3868.
42. D. N. Tran, F. X. Legrand, S. Menuel, H. Bricout, S. Tilloy and E. Monflier, *Chem. Commun.*, 2012, **48**, 753-755.
43. C. L. Yang, Y. K. Cheung, J. Z. Yao, Y. T. Wong and G. C. Jia, *Organometallics*, 2001, **20**, 424-429.
44. M. T. Reetz and J. Rudolph, *Tetrahedron: Asymmetry*, 1993, **4**, 2405-2406.
45. R. M. Deshpande, A. Fukuoka and M. Ichikawa, *Chem. Lett.*, 1999, 13-14.
46. M. Sawamura, K. Kitayama and Y. Ito, *Tetrahedron: Asymmetry*, 1993, **4**, 1829-1832.
47. D. Evans, J. A. Osborn and G. Wilkinson, *J. Chem. Soc. A*, 1968, 3133-3142.
48. G. Wilkinson and C. K. Brown, *J. Chem. Soc. A*, 1970, 2753-2764.
49. P. W. N. M. van Leeuwen and C. Claver, *Rhodium Catalyzed Hydroformylation*, Springer, 2002.
50. E. Engeldinger, Dissertation, Université Louis Pasteur, 2003.
51. Y. Takashima, K. Uramatsu, D. Jomori, A. Harima, M. Otsubo, H. Yamaguchi and A. Harada, *Acs. Macro. Lett.*, 2013, **2**, 384-387.
52. M. T. Reetz, I. D. Kostas and S. R. Waldvogel, *Inorg. Chem. Commun.*, 2002, **5**, 252-254.
53. M. T. Reetz, *Catal. Today*, 1998, **42**, 399-411.
54. J. Rudolph, Dissertation, Universität Bochum, 1995.
55. M. T. Reetz, J. Rudolph and R. Goddard, *Can. J. Chem.*, 2001, **79**, 1806-1811.

56. M. T. Reetz and S. R. Waldvogel, *Angew. Chem. Int. Ed.*, 1997, **36**, 865-867.
57. *German Pat.*, 196 31 322 8, 1996.
58. S. R. Waldvogel, Dissertation, Universität Bochum, 1996.
59. M. T. Reetz, *Top. Catal.*, 1997, **4**, 187-200.
60. M. T. Reetz and C. Frombgen, *Synthesis*, 1999, 1555-1557.
61. C. L. Yang, Y. T. Wong, Z. Y. Li, J. J. Krepinsky and G. C. Jia, *Organometallics*, 2001, **20**, 5220-5224.
62. J. Potier, S. Menuel, D. Mathiron, V. Bonnet, F. Hapiot and E. Monflier, *Beilstein J. Org. Chem.*, 2014, **10**, 2642-2648.
63. M. Sollogoub, *Eur. J. Org. Chem.*, 2009, 1295-1303.
64. M. Sollogoub, *Synlett*, 2013, **24**, 2629-2640.
65. B. Wang, E. Zaborova, S. Guieu, M. Petrillo, M. Guitet, Y. Blériot, M. Ménand, Y. M. Zhang and M. Sollogoub, *Nat. Commun.*, 2014, **5**.
66. D. Armspach and D. Matt, *Carbohydr. Res.*, 1998, **310**, 129-133.
67. L. Poorters, D. Armspach and D. Matt, *Eur. J. Org. Chem.*, 2003, 1377-1381.
68. D. Armspach, L. Poorters, D. Matt, B. Benmerad, F. Balegroune and L. Toupet, *Org. Biomol. Chem.*, 2005, **3**, 2588-2592.
69. R. Gramage-Doria, D. Rodriguez-Lucena, D. Armspach, C. Egloff, M. Jouffroy, D. Matt and L. Toupet, *Chem. Eur. J.*, 2011, **17**, 3911-3921.
70. M. Jouffroy, D. Armspach, D. Matt and L. Toupet, *Org. Biomol. Chem.*, 2013, **11**, 3699-3705.
71. Y. T. Wong, C. Yang, K. C. Ying and G. C. Jia, *Organometallics*, 2002, **21**, 1782-1787.
72. E. Engeldinger, D. Armspach, D. Matt and P. G. Jones, *Chem. Eur. J.*, 2003, **9**, 3091-3105.
73. A. J. Pearce and P. Sinaÿ, *Angew. Chem. Int. Ed.*, 2000, **39**, 3610-3612.
74. W. Wang, A. J. Pearce, Y. M. Zhang and P. Sinaÿ, *Tetrahedron: Asymmetry*, 2001, **12**, 517-523.
75. T. Lecourt, A. Herault, A. J. Pearce, M. Sollogoub and P. Sinaÿ, *Chem. Eur. J.*, 2004, **10**, 2960-2971.
76. O. Bistri, P. Sinaÿ and M. Sollogoub, *Tetrahedron Lett.*, 2005, **46**, 7757-7760.
77. R. Ghosh, P. Zhang, A. X. Wang and C. C. Ling, *Angew. Chem. Int. Ed.*, 2012, **51**, 1548-1552.
78. R. Ghosh, C. Hennigan and C. C. Ling, *Tetrahedron*, 2013, **69**, 5227-5233.
79. E. Zaborova, J. Deschamp, S. Guieu, Y. Blériot, G. Poli, M. Ménand, D. Madec, G. Prestat and M. Sollogoub, *Chem. Commun.*, 2011, **47**, 9206-9208.
80. E. Engeldinger, D. Armspach and D. Matt, *Chem. Rev.*, 2003, **103**, 4147-4173.
81. L. Poorters, D. Armspach, D. Matt, L. Toupet, S. Choua and P. Turek, *Chem. Eur. J.*, 2007, **13**, 9448-9461.
82. M. Jouffroy, R. Gramage-Doria, D. Armspach, D. Matt and L. Toupet, *Chem. Commun.*, 2012, **48**, 6028-6030.
83. M. Jouffroy, D. Armspach, A. Louati, D. Matt and L. Toupet, *Chem. Eur. J.*, 2014, **20**, 2565-2573.
84. D. Armspach, D. Matt and L. Toupet, *Angew. Chem. Int. Ed.*, 2009, **48**, 4555-4558.
85. B. Benmerad, P. Clair, D. Armspach, D. Matt, F. Balegroune and L. Toupet, *Chem. Commun.*, 2006, 2678-2680.
86. E. Engeldinger, L. Poorters, D. Armspach, D. Matt and L. Toupet, *Chem. Commun.*, 2004, 634-635.
87. R. Gramage-Doria, Dissertation, Université de Strasbourg, 2012.
88. D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, 1975, **97**, 1354-1358.

89. R. Gramage-Doria, D. Armspach, D. Matt and L. Toupet, *Dalton Trans.*, 2012, **41**, 8786-8796.
90. M. Jouffroy, R. Gramage-Doria, D. Armspach, D. Semeril, W. Oberhauser, D. Matt and L. Toupet, *Angew. Chem. Int. Ed.*, 2014, **53**, 3937-3940.
91. P. C. J. Kamer and P. W. N. M. van Leeuwen, *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and Synthesis*, Wiley-VCH, Chichester, 2013.
92. U. Christmann and R. Vilar, *Angew. Chem. Int. Ed.*, 2005, **44**, 366-374.
93. T. Fujihara, S. Yoshida, H. Ohta and Y. Tsuji, *Angew. Chem. Int. Ed.*, 2008, **47**, 8310-8314.
94. C. A. Tolman, *Chem. Rev.*, 1977, **77**, 313-348.
95. D. L. Dodds, M. D. K. Boele, G. P. F. van Strijdonck, J. G. de Vries, P. W. N. M. van Leeuwen and P. C. J. Kamer, *Eur. J. Inorg. Chem.*, 2012, 1660-1671.
96. A. F. Littke and G. C. Fu, *J. Am. Chem. Soc.*, 2001, **123**, 6989-7000.
97. D. J. M. Snelders, G. van Koten and R. J. M. K. Gebbink, *J. Am. Chem. Soc.*, 2009, **131**, 11407-11416.
98. A. F. Littke and G. C. Fu, *J. Org. Chem.*, 1999, **64**, 10-11.
99. H. Ohta, M. Tokunaga, Y. Obora, T. Iwai, T. Iwasawa, T. Fujihara and Y. Tsuji, *Org. Lett.*, 2007, **9**, 89-92.
100. T. Iwasawa, T. Komano, A. Tajima, M. Tokunaga, Y. Obora, T. Fujihara and Y. Tsuji, *Organometallics*, 2006, **25**, 4665-4669.
101. R. Franke, D. Selent and A. Börner, *Chem. Rev.*, 2012, **112**, 5675-5732.
102. M. Jouffroy, R. Gramage-Doria, D. Sémeril, D. Armspach, D. Matt, W. Oberhauser and L. Toupet, *Beilstein J. Org. Chem.*, 2014, **10**, 2388-2405.
103. D. Armspach and D. Matt, *Chem. Commun.*, 1999, 1073-1074.
104. O. Herd, A. Hessler, M. Hingst, M. Tepper and O. Stelzer, *J. Organomet. Chem.*, 1996, **522**, 69-76.
105. E. Engeldinger, D. Armspach and D. Matt, *Angew. Chem. Int. Ed.*, 2001, **40**, 2526-2529.
106. M. Jouffroy, D. Sémeril, D. Armspach and D. Matt, *Eur. J. Org. Chem.*, 2013, 6069-6077.
107. V. Böhmer, D. Kraft and M. Tabatabai, *J. Inclusion Phenom. Macrocyclic Chem.*, 1994, **19**, 17-39.
108. S. Guieu, E. Zaborova, Y. Blériot, G. Poli, A. Jutand, D. Madec, G. Prestat and M. Sollogoub, *Angew. Chem. Int. Ed.*, 2010, **49**, 2314-2318.
109. Z. Lu and S. M. Ma, *Angew. Chem. Int. Ed.*, 2008, **47**, 258-297.
110. C. A. Bessel, P. Aggarwal, A. C. Marschilok and K. J. Takeuchi, *Chem. Rev.*, 2001, **101**, 1031-1066.
111. Z. Freixa and P. W. N. M. van Leeuwen, *Coord. Chem. Rev.*, 2008, **252**, 1755-1786.
112. L. Poorters, M. Lejeune, D. Armspach and D. Matt, *Actual. Chim.*, 2009, 15-18.
113. K. Issleib and G. Hohlfeld, *Z. Anorg. Allg. Chem.*, 1961, **312**, 169-179.
114. N. J. Destefano, D. K. Johnson and L. M. Venanzi, *Angew. Chem. Int. Ed.*, 1974, **13**, 133-134.
115. G. Bracher, D. M. Grove, L. M. Venanzi, F. Bachechi, P. Mura and L. Zambonelli, *Helv. Chim. Acta*, 1980, **63**, 2519-2530.
116. D. Armspach and D. Matt, *C. R. Chim.*, 2011, **14**, 135-148.
117. D. Armspach, D. Matt, L. Poorters, R. Gramage-Doria, P. Jones and L. Toupet, *Polyhedron*, 2011, **30**, 573-578.
118. M. C. Blanco, E. J. Fernández, P. G. Jones, A. Laguna, J. M. López-de-Luzuriaga and M. E. Olmos, *Angew. Chem. Int. Ed.*, 1998, **37**, 3042-3043.
119. A. Gillie and J. K. Stille, *J. Am. Chem. Soc.*, 1980, 4933-4941.

120. M. N. Birkholz, Z. Freixa and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2009, **38**, 1099-1118.
121. R. Gramage-Doria, D. Armspach, D. Matt and L. Toupet, *Chem. Eur. J.*, 2012, **18**, 10813-10816.
122. F. Bachechi, L. Zambonelli and L. M. Venanzi, *Helv. Chim. Acta*, 1977, **60**, 2815–2823.
123. E.-i. Negishi, T. Takahashi and K. Akiyoshi, *J. Chem. Soc., Chem. Commun.*, 1986, 1338-1339.
124. S. M. Reid, J. T. Mague and M. J. Fink, *J. Am. Chem. Soc.*, 2001, **123**, 4081-4082.
125. T. Schnetz, M. Roder, F. Rominger and P. Hofmann, *Dalton Trans.*, 2008, 2238-2240.
126. W. Clegg, G. R. Eastham, M. R. J. Elsegood, B. T. Heaton, J. A. Iggo, R. P. Tooze, R. Whyman and S. Zacchini, *J. Chem. Soc., Dalton Trans.*, 2002, 3300-3308.
127. M. Lejeune, D. Sémeril, C. Jeunesse, D. Matt, P. Lutz and L. Toupet, *Adv. Synt. Catal.*, 2006, **348**, 881-886.
128. P. Braunstein, D. Matt, F. Mathey and D. Thavard, *J. Chem. Res. Synop.*, 1978, 232-233.
129. J. C. Jeffrey and T. B. Rauchfuss, *Inorg. Chem.*, 1979, **18**, 2658-2666.
130. A. Bader and E. Lindner, *Coord. Chem. Rev.*, 1991, **108**, 27-110.
131. G. Parkin, *Acc. Chem. Res.*, 1992, **25**, 455-460.
132. P. Comba, A. Hauser, M. Kerscher and H. Pritzkow, *Angew. Chem. Int. Ed.*, 2003, **42**, 4536-4540.
133. T. Hara, T. Yamagata, K. Mashima and Y. Kataoka, *Organometallics*, 2007, **26**, 110-118.
134. M. E. Broussard, B. Juma, S. G. Train, W. J. Peng, S. A. Laneman and G. G. Stanley, *Science*, 1993, **260**, 1784-1788.
135. P. Hofmann, C. Meier, W. Hiller, M. Heckel, J. Riede and M. U. Schmidt, *J. Organomet. Chem.*, 1995, **490**, 51-70.
136. Z. Freixa, P. C. J. Kamer, M. Lutz, A. L. Spek and P. W. N. M. van Leeuwen, *Angew. Chem. Int. Ed.*, 2005, **44**, 4385-4388.
137. T. M. Konrad, J. A. Fuentes, A. M. Z. Slawin and M. L. Clarke, *Angew. Chem. Int. Ed.*, 2010, **49**, 9197-9200.
138. J. M. López-Valbuena, E. C. Escudero-Adan, J. Benet-Buchholz, Z. Freixa and P. W. N. M. van Leeuwen, *Dalton Trans.*, 2010, **39**, 8560-8574.
139. D. Takeuchi, Y. Chiba, S. Takano and K. Osakada, *Angew. Chem. Int. Ed.*, 2013, **52**, 12536-12540.
140. W. Xu, J. J. Vittal and R. J. Puddephatt, *J. Am. Chem. Soc.*, 1993, **115**, 6456-6457.
141. W. Xu, J. J. Vittal and R. J. Puddephatt, *J. Am. Chem. Soc.*, 1995, **117**, 8362-8371.
142. P. Sakhaii, I. Neda, M. Freytag, H. Thonnessen, P. G. Jones and R. Schmutzler, *Z. Anorg. Allg. Chem.*, 2000, **626**, 1246-1254.
143. B. Colasson, N. Le Poul, Y. Le Mest and O. Reinaud, *J. Am. Chem. Soc.*, 2010, **132**, 4393-4398.
144. C. M. Thomas, R. Mafua, B. Therrien, E. Rusanov, H. Stoeckli-Evans and G. Süss-Fink, *Chem. Eur. J.*, 2002, **8**, 3343-3352.
145. V. K. Jain and L. Jain, *Coord. Chem. Rev.*, 2005, **249**, 3075-3197.
146. C. Azerraf, S. Cohen and D. Gelman, *Inorg. Chem.*, 2006, **45**, 7010-7017.
147. C. B. Dieleman, D. Matt, I. Neda, R. Schmutzler, A. Harriman and R. Yaftian, *Chem. Commun.*, 1999, 1911-1912.
148. D. Laurenti, L. Feuerstein, G. Pèpe, H. Doucet and M. Santelli, *J. Org. Chem.*, 2001, **66**, 1633-1637.
149. H. Doucet and M. Santelli, *Synlett*, 2006, 2001-2015.

150. O. Bistri, P. Sinaÿ, J. J. Barbero and M. Sollogoub, *Chem. Eur. J.*, 2007, **13**, 9757-9774.
151. P. Angibeaud and J. P. Utille, *Synthesis*, 1991, 737-738.
152. L. Poorters, D. Armspach, D. Matt and L. Toupet, *Dalton Trans.*, 2007, 3195-3202.
153. E. Engeldinger, D. Armspach, D. Matt, L. Toupet and M. Wesolek, *C. R. Chim.*, 2002, **5**, 359-372.