Metal-capped α-cyclodextrins: the crowning of the oligosaccharide torus with precious metals

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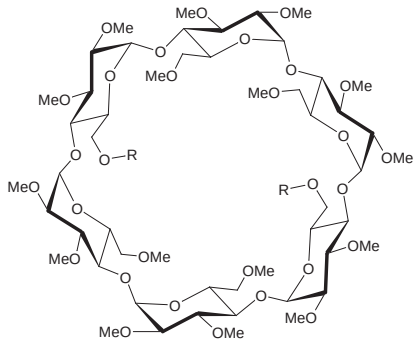
The synthesis of diphosphino α-cyclodextrins (α-CDs) and their capping by transition metals are described; one of the complexes has been tested in biphasic catalytic hydroformylation.

Multidentate ligands preorganised around a macrocyclic platform have attracted much interest in recent years in view of their ability to shape the coordination sphere of metals in a specific manner as well as to provide well defined cavities or clefts.[1] The combination of both features could lead to the development of new metal catalysts with enhanced selectivities and activities. In addition, it may be anticipated that the presence of a bulky cavity will provide protection against undesired side reactions if properly positioned with respect to the metal centre. These issues have, in some respect, been addressed by use of monosubstituted cyclodextrins (CDs) bearing a pendant catalytic site.[2–4] However, until now, no synthetic methodology has been developed for *capping* a CD with a catalytically active transition metal unit. Exact positioning of the metal at the cavity mouth appears to be essential for fully exploiting the intrinsic properties of CDs in terms of water-solubility, chirality and steric crowding. In this preliminary communication, we report on the synthesis of the first C_2-symmetrical diphosphines based on α-CD and describe how these ligands undergo efficient capping of the oligosaccharide torus with catalytically important transition metals.†

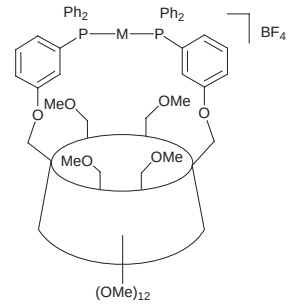


1 R = $C(C_6H_4Bu^t)_3$
2 R = H
3 R = Ms
4a R = 3-C_6H_4I
4b R = 4-C_6H_4I
5a R = 3-$C_6H_4PPh_2$
5b R = 4-$C_6H_4PPh_2$

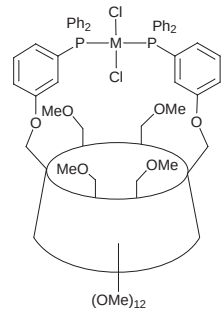
All ligands mentioned here were derived from diol **2** which was obtained in gram-scale quantities and good yield (87%) by acidic cleavage[5] of 6A,6D-di-*O*-tris(*p*-*tert*-butylphenyl)methyl-per-*O*-methyl-α-CD **1**[6] with HBF_4 (34%) in Me_3CN. Diol **2** was converted into dimesylate **3** in 90% yield. Treatment of the latter with 3-iodophenol or 4-iodophenol and K_2CO_3 in DMF afforded respectively di-iodo CDs **4a** and **4b** which on Stelzer's palladium-catalysed cross coupling[7] with diphenylphosphine gave phosphine-based ligands **5a** and **5b** in 69 and 70% overall yields, respectively.

^1H as well as ^{13}C and ^{31}P NMR spectra of diphosphines **5a**† and **5b**† clearly show the presence of the expected twofold molecular symmetry which indicates free rotational motion of the triarylphosphine fragments. For example, the ^{31}P NMR spectrum of either **5a** or **5b** consists of a single singlet respectively at δ −4.5 and −6.8.

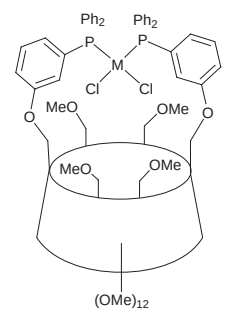
According to CPK‡ models, ligand **5a** possesses the right geometrical features to promote the formation of *trans-P,P*-chelates upon metal complexation. Evidence for the latter was given by studying the coordination of **5a** with metals prone to form linear arrangements. Thus, treatment of **5a** with $AgBF_4$ led to the C_2-symmetric complex P–Ag–P **6**. Likewise, its gold analogue **7** was cleanly obtained by reacting in CH_2Cl_2 the *in situ* prepared complex [Au(thf)(SC_4H_8)]BF_4 (SC_4H_8 = tetrahydrothiophene) with **5a** in high yield. The complex is air stable



6 M = Ag
7 M = Au



8a M = Pt
9a M = Pd



8b M = Pt
9b M = Pd

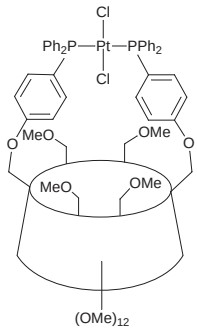
and can be subjected to chromatography on silica gel without noticeable decomposition, an unusual feature for complexes of that type. Similarly, treatment of **5a** with [$PtCl_2(PhCN)_2$] (mixture of *cis* and *trans* isomers) led to the exclusive formation of *trans-P,P*-chelate complex **8a**. However, exposure of a refluxing ethanolic solution of **8a** to sunlight produced after a week a 65:35 equilibrium mixture of **8a** and *cis* chelate **8b**. These compounds could easily be separated by column chromatography without detection of any interconversion during the separation. Molecular-weight determination using vapour phase osmometry (CH_2Cl_2) gave masses of 1890 and 1950 for **8a** and **8b**, respectively [M(calc.) = 1984]. This

Table 1 Selected MS and spectroscopic data for complexes **6**–**11**

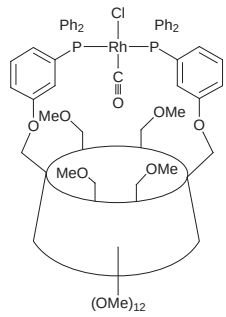
Compound	FAB-MS [*m*/*z* (%)]	$^{31}P\{^{1}H\}$ NMR[a] δ_P (*J*(PM)/Hz)	^{1}H NMR[b] δ_H of MeO-$6^{B,E}$ and MeO-$6^{C,F}$
6	1825 (100), $[M - BF_4]^+$ 1841 (45), $[M - BF_4 + O]^+$	14.2 (495)	2.88, 3.17
7	1913 (100), $[M - BF_4]^+$ 1930 (13), $[M - BF_4 + O]^+$	15.4	3.17, 3.26
8a	1982[d] (20), M^+	21.4 (2642)	3.03, 3.05
8b	1912 (100), $[M - 2Cl]^+$ 1947[d] (75), $[M - Cl]^+$	15.3 (3669)	3.20, 3.29
9a	1859 (50), $[M - Cl]^+$	24.5	3.03, 3.04
9b	1894 (30), M^+	33.5[c]	3.21, 3.26
10a	1947 (75), $[M - Cl]^+$	19.1 (2633)	3.00, 3.16
10b	1982[d] (13), M^+	13.4 (3681)	3.01, 3.10
11	1819 (100), $[M - Cl - CO]^+$ 1847 (15), $[M - Cl]^+$ 1854 (95), $[M - CO]^+$	29.7	3.00, 3.10

[a] In $CDCl_3$ (ext. ref.: H_3PO_4). [b] In $CDCl_3$. [c] The stereochemistry about the palladium centres was assigned empirically according to ref. 8. [d] The monomeric nature of this complex was confirmed by vapour phase osmometry.

clearly demonstrates the monomeric nature of both compounds.§ Moreover, the reaction between ligand **5a** and $[PdCl_2(PhCN)_2]$ (*cis* and *trans* isomers) afforded a rapidly interconverting 80 : 20 equilibrium mixture of *trans*-chelate **9a** and *cis*-chelate **9b** as evidenced by ^{31}P NMR spectroscopy[8] (Table 1). In addition, unlike **5a**, ligand **5b** gave with $[PtCl_2(PhCN)_2]$ both *trans* chelate **10a** and the corresponding *cis* chelate **10b** (not drawn) as a 40 : 60 mixture.¶ Their



10a



11

separation could not be achieved since they interconvert rapidly in solution. Clearly, the phosphine fragments in **5a**, less so in **5b**, are arranged on the cyclodextrin platform so as to favour *trans* chelation. Full evidence for the latter was given by the reaction of $[\{Rh(CO)_2Cl\}_2]$ in dichloromethane with **5a** which quantitatively yielded complex **11**.† The $^{31}P\{^{1}H\}$ NMR spectrum of **11** displays a single doublet [*J*(Rh–P) 127.1 Hz] in agreement with the expected *trans*-P,P stereochemistry.

Complex **11** possesses the essential features known to be important for a hydroformylation catalyst. Indeed, **11** catalyses the conversion of oct-1-ene into the corresponding aldehydes in H_2O–MeOH (conversion and chemoselectivity > 99% after 18 h).‖ Selectivity of linear to branched aldehydes (n : i) is of the order of 70 : 30, which is unexceptional for rhodium(I) bis-(phosphine) complexes. Similarly, the turn-over frequency** (70 h^{-1}) compares well with standard nonionic hydroformylation catalysts. Unfortunately, low water-solubility prevents **11** acting as a supramolecular catalyst as evidenced by the outcome of the catalytic tests which are typical of classical systems both in terms of activity and selectivity. Although **11** is only present in the methanol–water phase in the first place, transfer of the catalyst to the oct-1-ene–aldehydes phase was found to take place during the reaction.

A synthetic methodology has been designed for the preparation of highly preorganised diphosphines based on α-CD. Such ligands promote the formation of chelate complexes in which the P_2 unit rigidly holds a metal centre at the mouth of the cavity. Water-soluble analogues of the aforementioned species are expected to form inclusion complexes in water with substrates that can react catalytically *via* the metal centre. It is hoped that these combined features will improve existing hydroformylation and hydrogenation catalysts both in terms of activity and selectivity.

Notes and references

† Satisfactory elemental analyses have been obtained for all compounds. *Selected data*: for **5a**: ^{1}H NMR ($CDCl_3$): δ 3.21 (s, 6H, C*H*$_3$O-6), 3.22 (s, 6H, C*H*$_3$O-6), 3.47 (s, 6H, C*H*$_3$O), 3.48 (s, 6H, C*H*$_3$O), 3.50 (s, 6H, C*H*$_3$O), 3.64 (s, 6H, C*H*$_3$O), 3.65 (s, 6H, C*H*$_3$O) , 3.66 (s, 6H, C*H*$_3$O), 3.09–4.02 (m, 32H, H-2, H-3, H-4, H-5, H-$6^{B,C,E,F}$), 4.30–4.36 (m, 4H, H-$6^{A,D}$), 4.97 (d, 2H, ^{3}J 3.2 Hz, H-1), 5.01 (d, 2H, ^{3}J 3.2 Hz, H-1), 5.06 (d, 2H, ^{3}J 3.2 Hz, H-1), 6.82 (t, 2H,^{3}J 7.2 Hz, aromatic H), 6.88–7.00 (m, 4H, aromatic H), 7.22–7.33 (m, 22H, aromatic H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 57.87 (×3) (*C*H$_3$O-2), 58.79, 58.93 (*C*H$_3$O-6), 61.72 (×3) (*C*H$_3$O-3), 67.69 (C-$6^{A,D}$), 70.79 and 71.18 (×2) (C-5), 71.25 (×2) (C-$6^{B,C,E,F}$), 81.27 (×3), 82.05 (×3), 82.28, 82.40 and 82.93 (C-2, C-3, C-4), 100.02 (×3) (C-1), 114.65 (s, C_{para}), 120.28 [d, ^{2}J(C,P) 24.8 Hz, C_{ortho}], 126.08 [d, ^{2}J(C,P) 15.3 Hz, C_{ortho}], 128.53 [d, ^{3}J(C,P) 6.7 Hz, C_{meta}], 128.70 (s, C_{para}), 129.45 (d, ^{3}J(C,P) 6.5 Hz, C_{meta}), 133.87 [d, ^{2}J(C,P) 19.6 Hz, C_{ortho}], 137.08 (d, ^{1}J(C,P) 8.5 Hz, aromatic C_{quat}], 138.91 [d, ^{1}J(C,P) 12.0 Hz, aromatic C_{quat}], 158.85 [d, ^{3}J(C,P) 9.9 Hz, C_{meta}]. $^{31}P\{^{1}H\}$ NMR ($CDCl_3$): δ = − 4.5 (s). FAB MS, *m*/*z* (%): 1717 (100) $[M + H]^+$.

For **5b**: $^{31}P\{^{1}H\}$ NMR ($CDCl_3$): δ = − 6.8 (s). FAB MS, *m*/*z* (%): 1739 (100) $[M + Na]^+$.

For **11**: IR (KBr) *ν*/cm^{-1}: 1977m (C≡O). ^{1}H NMR ($CDCl_3$): δ 3.00 (s, 6H, C*H*$_3$O-6), 3.10 (s, 6H, C*H*$_3$O-6), 3.46 (s, 6H, C*H*$_3$O), 3.50 (s, 6H, C*H*$_3$O), 3.51 (s, 6H, C*H*$_3$O), 3.64 (s, 6H, C*H*$_3$O), 3.66 (s, 12H, C*H*$_3$O), 3.08–3.84 (m, 30H, H-2, H-3, H-4, H-$5^{B,C,E,F}$, H-$6^{B,C,E,F}$), 4.19–4.26 (m, 4H, H-6b^{A,D}, H-$5^{A,D}$), 4.65–4.71 (m, 2H, H-6a^{A,D}), 4.99 (d, 2H, ^{3}J 3.2 Hz, H-1), 5.03 (d, 2H, ^{3}J 3.2 Hz, H-1), 5.05 (d, 2H, ^{3}J 3.2 Hz, H-1), 6.98–7.67 (m, 28H, aromatic H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 57.72, 57.79 and 58.08 (CH_3O-2), 58.87 (×2) (CH_3O-6), 61.79 (×3) (CH_3O-3), 68.12 (C-$6^{A,D}$), 69.95 (C-$5^{A,D}$), 70.28 and 70.61 (C-$6^{B,C,E,F}$), 71.30 (×2) (C-$5^{B,C,E,F}$), 81.26, 81.36 (×2), 82.02 (×2), 82.11, 82.18, 82.34 and 83.62 (C-2, C-3, C-4), 99.68 and 99.98 (C-$1^{B,C,E,F}$), 100.77 (C-$1^{A,D}$), 116.04, 122.96, 127.92, 128.12, 132.02, 133.92 and 134.34 (aromatic CH), 129.86, 133.45 and 158.34 (aromatic C_{quat}). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$): δ 29.7 [d, *J*(P,Rh) 127.1 Hz].

‡ CPK stands for Corey-Pauling-Koltun.

§ Mass spectrometry cannot be reliably employed for mass determination for these neutral MCl_2 complexes as peaks due to ion–molecule reactions were detected in the spectra (intensity *ca*. 4% for **8b**).

¶ Vapour phase osmometry measurements (CH_2Cl_2) gave a mass of 1820 for the mixture **10a**/**10b**, thus confirming the monomeric nature of both compounds.

‖ *Conditions*: 40 bar CO–H_2 (1 : 1), 60 °C, H_2O–MeOH (6 : 4), [**11**] = 1.2 × 10^{-3} M, [oct-1-ene] = 0.47 M.

** Turn-over frequency in mol aldehydes formed per mole Rh per hour, averaged over 3.5 h at 60% conversion.

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