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Diastereospecific synthesis of phosphinidene-capped cyclodextrins leading to "introverted" ligands†

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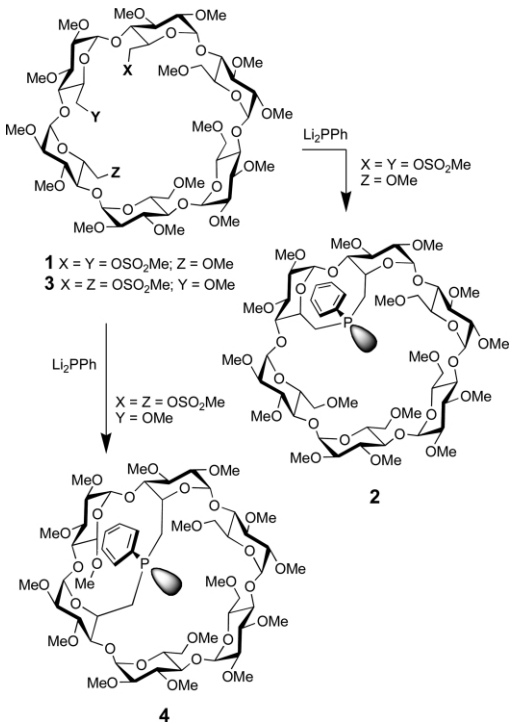
α-Cyclodextrins (α-CDs) containing "PPh" units which cap the primary face of the CD were obtained in high yield by reaction of Li_2PPh with *A*,*B*- or *A*,*C*-dimesylated and *A*,*B*,*D*,*E*-tetramesylated precursors; the resulting phosphines are *diastereomerically* pure and constitute valuable precursors for the synthesis of metallo-cavitands.

Metal-capped cyclodextrins (CDs) constitute useful tools for the study of metal-centred reactions occurring inside a confined environment[1] as well as for the synthesis of supramolecular catalysts suitable for industrial reactions.[2] The construction of such complexes most often relies on the use of CDs bearing several pendant ligands arranged in a manner allowing chelation about one of the two edges. A properly configured podand set is expected to maintain the complexed metal centre near the cavity entrance. In this respect the length of the binding units as well as their rigidity are crucial factors for controlling the position of the metal with respect to the cavity. In the present report we describe the first syntheses of cyclodextrins containing the (very short) "PhP" capping unit. The reported cavity-shaped ligands are characterized by *endo*-oriented donor atoms.

Reaction of Li_2PPh in THF with the *A*,*B*-dimesylated precursor **1** afforded the primary face-capped CD **2**‡ in *ca.* 70% yield (Scheme 1). It is noteworthy that no intermolecular coupling occurred. The ^{31}P NMR spectrum of the resulting phosphine shows a singlet at −16.2 ppm. In the ^1H NMR spectrum, the 6 distinct anomeric signals appear in a narrow range ($\Delta\delta_{max}$ *ca.* 0.1 ppm), indicating that bridge formation does not cause a significant distortion of the CD torus. This situation contrasts with that found in the related *A*,*C*-bridged CD **4** formed in 60% yield from the corresponding dimesylate **3**. In this case the ^1H NMR spectrum reveals a considerable dispersion of the H-1 protons (ranging between 4.66 and 5.69 ppm), in keeping with a marked shape modification. The latter was confirmed by an X-ray diffraction study carried out on the corresponding oxide **5** (*vide infra*). Cyclisation reactions involving the PhP^{2-} dianion and a dimesylated CD precursor are unprecedented, although the synthesis of chiral phosphiranes according to this scheme has been reported recently.[3]

The solid state structure of **5**§ (Fig. 1) reveals discrete supramolecular dimers resulting from inclusion of a single phenyl ring in the neighbouring CD cavity. As expected, the two CDs of dimeric **5** are elliptically distorted, glucose ring B adopting an almost perfect $^5S_1$ skew boat[4] conformation.¶ Interestingly, the observed head-to-tail assembly is not repeated indefinitely, in stark contrast with many other monoarylated CDs which form polymeric chains in the solid state.[5] The most striking feature in each CD unit is the orientation of the P–O bond which points towards the centre of the cavity, the phenyl ring being *exo*-orientated with respect to the CD. Thus, this structural determination also establishes the diastereospecificity of the reaction leading to **4**.

An *endo*-orientation of the phosphorus lone pair was also found in phosphine **2**, as revealed by its reaction with [PdCl(*o*-$C_6H_4NMe_2$]$_2$, which quantitatively produces complex **6**. A 2D ROESY experiment unambiguously showed a spatial proximity between the two diastereotopic NMe groups and three of the



Scheme 1 Syntheses of the capped CDs **2** and **4**.

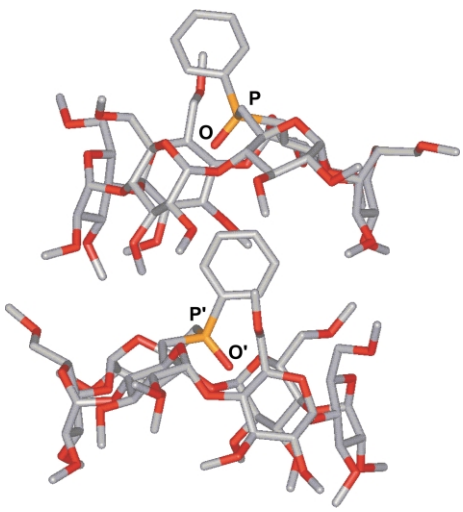


Fig. 1 Supramolecular structure of **5** in the solid state. Bond lengths (Å): P–O 1.488(4), P′–O′ 1.482(4).

† Electronic supplementary information (ESI) available: synthesis and full characterization of all compounds. See http://www.rsc.org/suppdata/cc/b3/b315802k/

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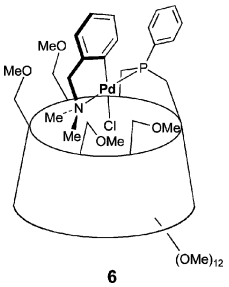
primary methoxy groups. No through-space correlations were detected between CD protons and aromatic ones. These findings clearly indicate that the palladacycle lies above the cavity and its plane roughly parallels that of the CD axis. Furthermore, the significant downfield shift experienced by proton H-5^A (*ca.* 0.6 ppm) on going from free **2** to **6** is fully consistent with encapsulation of the chloride atom within the CD. The "chlorophilic" behaviour of CDs has been documented recently.[6]



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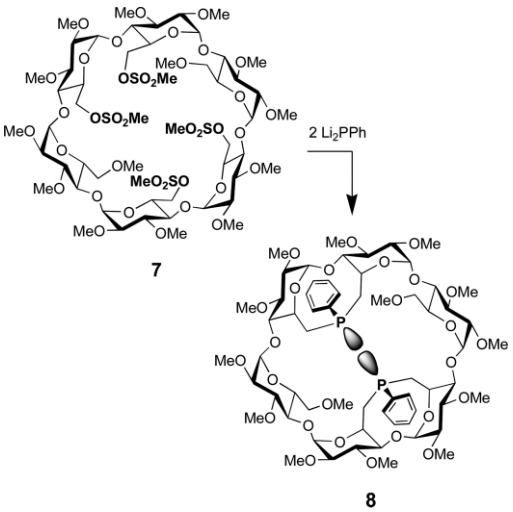
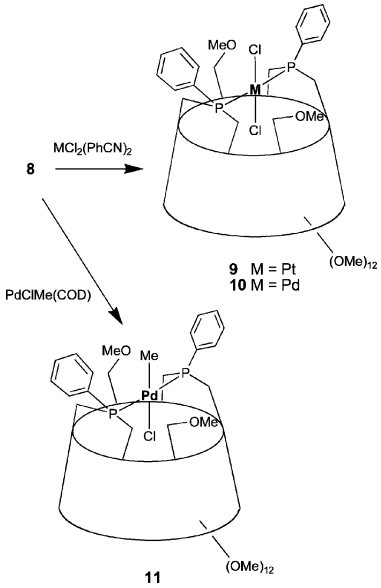
Finally, the aforementioned capping reaction could be extended to the high-yield preparation of a doubly-bridged cyclodextrin, only the second example of this type.[7] Thus, reaction of the *A*,*B*,*D*,*E*-tetramesylate **7** with Li_2PPh in excess afforded the C_2-symmetrical diphosphine **8** (^{31}P: −16.8 ppm) in 90% yield (Scheme 2). Each bridging reaction involves selective substitution of adjacent mesyl groups. As for **2**, there is no indication for an anomalous distortion of the CD core. Ligand **8** is a rare example of a chelating ligand behaving selectively as a *trans*-chelator when bound to d^8-metal ions. For example, its reaction with the complexes $[PtCl_2(PhCN)_2]$, $[PdCl_2(PhCN)_2]$ and [PdClMe(1,5-cyclooctadiene)] afforded quantitatively the complexes **9–11**, respectively (Scheme 3). Again, in each of these complexes one metal–chlorine bond points towards the centre of the cavity, as shown by the presence of downfield-shifted H-5 signals in the corresponding ^{1}H NMR spectra.

In summary, *A*,*B*- or *A*,*C*-dimesylated and *A*,*B*,*D*,*E*-tetramesylated cyclodextrins are valuable synthons for the high yield synthesis of phosphinidene-capped CDs. The coupling reactions with Li_2PPh are not only diastereospecific but also lead to introverted ligands suitable for partial encapsulation of metal–organic fragments.



7 **8**

Scheme 2 Synthesis of diphosphine **8**.



Scheme 3 *trans*-Chelating behaviour of diphosphine **8**.

Notes and references

‡ All compounds were fully characterized on the basis of their spectral data and C–H–N analysis (see ESI). Selected spectroscopic data: **2**: ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = −16.2 (s). **4**: ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = −21.1 (s). **5**: ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$) δ 35.3 (s). **6**: ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = 17.4 (s). **8**: ^{31}P {^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = −16.8 (s). **9**: ^{31}P {^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = −6.5 (s with Pt satellites, $^1J_{Pt,P}$ = 2463 Hz). **10**: ^{31}P {^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = −0.4 (s). **11**: ^{31}P {^{1}H} NMR (121.5 MHz, $CDCl_3$, 25 °C): δ = 3.8 (s). As unambiguously shown by a ROESY experiment, the H atoms of the Pd*Me* group correlate with aromatic protons as well as some H-6 protons.

§ Crystal data for $2C_{58}H_{95}O_{29}P_2{\cdot}CHCl_3{\cdot}1.5C_4H_8O{\cdot}H_2O$ **5**: M = 2800.11, monoclinic, space group $P2_1$, a = 14.8015(1), b = 29.1555(3), c = 17.1807(2) Å, β = 99.330(1)°, U = 7316.2(1) Å^3, Z = 2, T = 110 (1) K, 1706 variables and 18612 reflections with [$I > 2\sigma(I)$], R = 0.078, R_w = 0.189, S_w = 1.012, $\Delta\rho$ < 1.26 e Å^{-3}. The dimer co-crystallized with molecules of chloroform, diethyl ether, and water (ratio: 1:1.5:1). The two molecules of the asymmetric unit have the same absolute configuration. CCDC 219493. See http://www.rsc.org/suppdata/cc/b3/b315802k for crystallographic data in .cif or other electronic format.

¶ All other glucose units are in a typical chair conformation.

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