Bisphosphine based hetero-capsules for the encapsulation of transition metals†

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Just mixing of solutions of tetracationic diphosphine ligands and tetraanionic calix[4]arene building blocks leads to the formation of supramolecular heterocapsules that coordinate a palladium metal within the cavity of the assembly, giving rise to a new class of potential supramolecular transition metal catalysts.

Supramolecular capsules present an important class of architectures that can reversibly accommodate smaller molecules in their cavities.[1] These capsules consist of two or more building blocks that have a similar size, complementary functional groups and associate *via* multiple non-covalent interactions such as hydrogen bonds, metal–ligand and ionic interactions. A wide variety of homo- and heterocapsules based on functionalized calixarenes, resorcinarenes and other building blocks have been reported.[2] The encapsulation properties of these hosts enable their utilization as nanosized reactor vessels and so far their use has been explored for the stabilization of reactive intermediates, for organic transformations and for catalysis.[3]

Many reactions of interest require well-defined transition metal complexes as catalyst, and the activity and selectivity of these catalysts is determined to a great extent by the ligand associated with the metal. So far only a few supramolecular complexes have been reported in which the catalytic potential of an encapsulated transition metal has been explored. Raymond and Bergman *et al.* have encapsulated iridium-complexes in supramolecular coordination assemblies, which resulted in substrate selectivity (on the basis of size and shape) in the C–H bond activation of aldehydes.[4] We have introduced a templated approach for the encapsulation of ligands and their metal-complexes,[5] in which template-ligands have a bifunctional character in that they coordinate to the active metal center and function as a template for the capsule formation. Such encapsulated rhodium complexes were shown to have unusual reactivity and selectivity in the hydroformylation of 1-octene.

Diphosphine based metal complexes represent an important class of catalysts and we anticipated that hetero-capsules based on functionalized diphosphine ligands and well-known building blocks such as calix[4]arene would provide a new class of easily accessible supramolecular complexes. In this strategy a well-defined transition metal complex is an integrated part of the capsule with the transition metal located inside the capsule, and more importantly, the metal is not involved in the assembly process and is therefore available for the catalytic process. Since the crucial building block, *i.e.* the diphosphine ligand, contains a donor-atom site for metal complexation as well as functional groups for capsule formation, the present strategy comprises a templated approach to metal encapsulation.[5a] In this communication we report the formation and characterization of capsules **1·2** that consist of a tetracationic diphosphine ligand **1a** or a palladium complex thereof (**1b** or **1c**) and a tetraanionic calix[4]arene **2** (Fig. 1).

Diphosphine ligands with a rigid backbone such as the xantphos-type ligands, generally have a concave structure defined by the backbone and the four phenyl-groups. We realized that simple functionalization of these four phenyl-groups would provide a building block that would be of similar size to a functionalized calix[4]arene and should form a supramolecular capsule if the interactions are complementary. Tetrasulfonatocalix[4]arene **2** has already been reported by Timmerman and Crego-Calama *et al.* and forms supramolecular capsules with tetracationic functionalized calix[4]arenes and porphyrins.[6] Protonation of previously reported 4,5-bis[bis(*p*-((diethylamino)-methyl)phenyl)phosphino]-9,9-dimethylxanthene **1** by HCl yields a tetraammonium substituted xantphos-type ligand **1a** (Fig. 1).[7a] Molecular modeling shows that ligand **1a** and calix[4]arene **2** are similar in size and complementary in function and should form capsule **1a·2** *via* multiple ionic interactions (Fig. 1).

Mixing equimolar solutions of **1a** and **2** in water resulted in the precipitation of capsule **1a·2** as a white solid, which was isolated by filtration and appeared to be soluble in methanol and dmso.§ The ^{1}H NMR spectra of **1a·2** in CD_3OD and in dmso-d_6 show significant upfield shifts for the diethylammoniummethyl

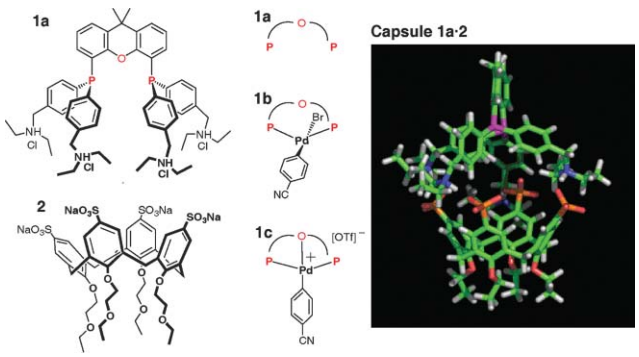

Fig. 1 Molecular structures of **1a**, **1b**, **1c**, and **2** and the structure of capsule **1a·2** obtained by molecular modeling.‡

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substituents, $CH_2NH^+(CH_2CH_3)_2$, with respect to those of **1a** (in CD_3OD: $\Delta\delta(CH_2C\mathbf{H_3})$ = 0.43, $\Delta\delta(C\mathbf{H_2}CH_3)$ = 0.33, $\Delta\delta(C\mathbf{H_2}N)$ = 0.25 ppm) whereas the chemical shifts of the other protons remain relatively unaffected ($\Delta\delta$ less than 0.15 ppm). The upfield shifts are similar to those reported by Corbellini *et al.* and point to partial inclusion of the diethylammoniummethyl substituents inside the hydrophobic cavity of the capsule.[6b] A higher degree of encapsulation of these substituents was observed when the solvent polarity was increased by the addition of D_2O, as was evident from the larger upfield shifts.¶ A single set of proton resonances for the free and bound building blocks was observed in a temperature range of −40 to +50 °C (in CD_3OD), indicating a fast exchange process on the NMR time scale. Due to the fast exchange process the lower symmetry of the capsule compared to the calix[4]arene **2** (C_4v) is not apparent in the ^{1}H NMR spectra.¶[6a] The capsule could also be prepared *in situ* by just mixing methanol (or dmso) solutions of **1a** and **2** in the proper ratio. ^{1}H NMR titrations were carried out in CD_3OD (298 K) providing a stability constant of $K_{\mathbf{1a}\cdot\mathbf{2}} = 6\cdot10^4$ M^{-1} for capsule **1a·2**. The high association constant confirms that the diphosphine ligand **1a** and the tetrasulfonatocalix[4]arene **2** indeed fit well to form a stable capsule. The titration curve fitted to a 1 : 1 binding model is in line with the 1 : 1 stoichiometry of the capsule, and a Job plot analysis of a titration experiment in CD_3OD proved indubitably the 1 : 1 stoichiometry of capsule **1a·2** in solution. The 1D-NOESY spectrum of the heterodimeric capsule **1a·2** in CD_3OD displays significant negative intermolecular NOE contacts between the $NH^+(CH_2C\mathbf{H_3})_2$ protons of **1a** and the aromatic protons of **2**.[8] This illustrates that the aryl-substituents of the diphosphine ligand **1a** and the upper rim of the calix[4]arene **2** are facing one another to form the typical dimeric 1 : 1 capsular structure. The negative NOE enhancement confirms the large size of the capsule. Additional evidence for the formation of capsule **1a·2** was obtained by electrospray ionization mass spectrometry (ESI-MS).[9] The positive-mode ESI-MS spectrum of **1a·2** in CH_3OH shows a prominent monoisotopic ion peak of the capsule at *m/z* 998.3 corresponding to $[\mathbf{1a}\cdot\mathbf{2} + 2Na]^{2+}$. All the capsule's ion peaks correspond to 1 : 1 complexes and no ion peaks for higher aggregates were detected. Moreover, comparison of the measured isotope pattern of **1a·2** with the calculated one confirms the elemental composition and charge state. The assignment of the capsule's ion peaks is in agreement with collision experiments.¶

Encapsulation of a neutral palladium metal inside the supramolecular capsule was achieved by using the neutral palladium complex **1b** [(*trans*-**1a**)Pd(*p*-C_6H_4CN)(Br)] as the complementary building block for **2** (Fig. 1).[7b] The neutral palladium complex **1b** has a distorted square planar geometry with the oxygen atom of the ligand backbone in the apical position.[7c] In spite of the higher rigidity of the palladium complex **1b** compared to the free ligand **1a**, molecular modeling study on capsule **1b·2** illustrates that **1b** and **2** fit well and can form a capsule with the palladium metal located inside the capsule and the *p*-cyanophenyl group of **1b** sticking out of the capsule. This *p*-cyanophenyl group of **1b** is situated above the capsule equator and is not interfering with the assembly process. Indeed, mixing equimolar solutions of **1b** and **2** in water led to the precipitation of capsule **1b·2** as a yellow solid. In contrast to capsule **1a·2**, capsule **1b·2** is only sparingly soluble in methanol and dissolves well only in dmso. The diethylammoniummethyl protons of capsule **1b·2** exhibit high upfield shifts with respect to those of **1b** (in dmso-d_6: $\Delta\delta(CH_2C\mathbf{H_3})$ = 0.41, $\Delta\delta(C\mathbf{H_2}CH_3)$ = 0.27, $\Delta\delta(N\mathbf{H}^+)$ = 1.14 ppm), again pointing to partial inclusion of the alkyl tails. The 1D-NOESY spectrum of **1b·2** in dmso-d_6 shows significant negative intermolecular NOE contacts between the $NH^+(CH_2C\mathbf{H_3})_2$ protons of **1b** and the aromatic protons of **2**, indicating that similar to **1a·2** the upper rim of the calix[4]arene is associated with **1b**. The ESI-MS spectrum of capsule **1b·2** in CH_3OH shows a prominent monoisotopic ion peak of the capsule at *m/z* 719.6 corresponding to $[\mathbf{1b}\cdot\mathbf{2} - Br + 2H]^{3+}$ (Fig. 2). Interestingly, capsule **1b·2** remains stable after Br^- dissociation from the palladium, and the corresponding ionic capsule detected by ESI-MS gives the same ion peaks as the capsule based on the cationic palladium complex **1c** (*vide infra*).

Since many catalytic cycles involve a cationic palladium species as intermediate we were interested in the formation of capsules using the cationic palladium complex **1c** [(*trans*-**1a**)Pd(*p*-C_6H_4CN)]$^+$[CF_3SO_3]$^-$.‡[7c] This cationic palladium complex adopts a square planar geometry with the ligand acting as an η^3 terdentate P,O,P ligand (Fig. 1). Molecular modeling of capsule **1c·2** illustrates that **1c** and **2** fit nicely and that the palladium metal as well as the *p*-cyanophenyl group of **1c** are located inside the capsule. Mixing equimolar solutions of **1c** and **2** in methanol or dmso resulted in clear solutions of capsule **1c·2**.‖ Similar to capsules **1a·2** and **1b·2**, the diethylammoniummethyl substituents of **1c·2** are partly inside the cavity as judged from the upfield shifts observed for these protons in the ^{1}H NMR spectra of **1c·2** (in CD_3OD: $\Delta\delta(CH_2C\mathbf{H_3})$ = 0.58, $\Delta\delta(C\mathbf{H_2}CH_3)$ = 0.39, $\Delta\delta(C\mathbf{H_2}N)$ = 0.17 ppm) (Fig. 3). Again, 1D-NOESY experiments confirm the proposed geometry of the dimeric capsule **1c·2** since significant negative intermolecular NOE contacts between the $NH^+(CH_2C\mathbf{H_3})_2$ protons of **1c** and the aromatic protons of **2** are observed. The ESI-MS spectrum of capsule **1c·2** in CH_3OH shows a prominent monoisotopic ion peak of the capsule at *m/z* 719.7 corresponding to $[\mathbf{1c}\cdot\mathbf{2} - OTf + 2H]^{3+}$. Interestingly, the phosphorus chemical shifts of **1a**, **1b** and **1c** did not exhibit a noteworthy shift upon capsule formation ($\Delta\delta < 0.6$ ppm), indicating that the geometry around the phosphorus atoms did not change upon capsule formation.

^{1}H NMR titration experiments in CD_3OD at 298 K gave an association constant of $K_{\mathbf{1c}\cdot\mathbf{2}} = 6\cdot10^3$ M^{-1} for capsule **1c·2** (1 : 1 binding model), which is ten times lower than the association constant of capsule **1a·2**. A plausible explanation is the poorer complementarity between **1c** and **2**. The more flexible free ligand **1a** can adapt to the favoured geometry to optimize interactions with **2**, whereas the Pd–aryl complex **1c** is too rigid to do so. Additional

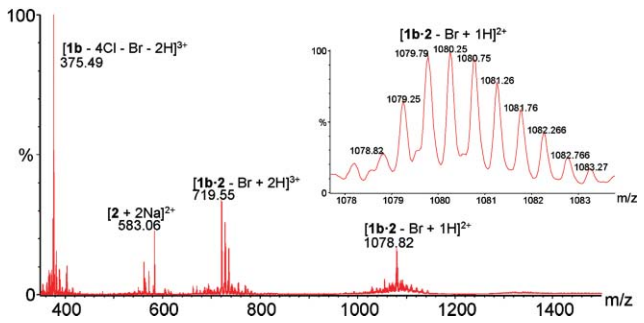

Fig. 2 ESI-MS spectrum of capsule **1b·2** in CH_3OH (inset: measured isotope pattern).

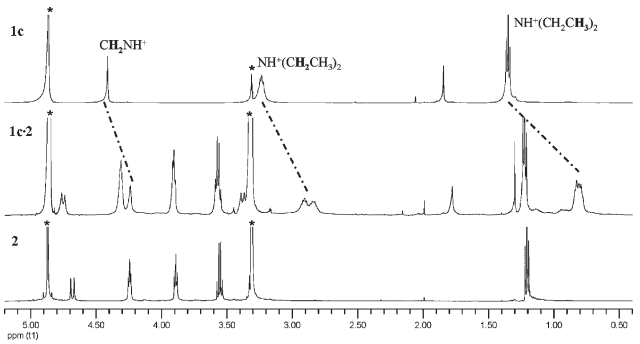

Fig. 3 ^{1}H NMR spectra in CD_3OD. Top: **1c**; Middle: capsule **1c·2** (**1c/2** = 2/3); Bottom: **2**. Asterisks indicate solvent signals.

evidence for this comes from diffusion-ordered NMR spectroscopy (DOSY). The diffusion coefficients D of the three capsules are lower than those of the corresponding free building blocks, confirming the larger size of the capsules (*e.g.* $D_{\mathbf{1c}\cdot\mathbf{2}} = 2.04$ and $D_{\mathbf{1c}} = 3.21\ 10^{-6}$ cm^2 s^{-1}).**[10] More importantly, the diffusion coefficient of capsule **1c·2** is lower than that of capsule **1a·2** ($D_{\mathbf{1c}\cdot\mathbf{2}} = 2.04$ and $D_{\mathbf{1a}\cdot\mathbf{2}} = 2.46\ 10^{-6}$ cm^2 s^{-1}), indicating that **1c·2** is larger than **1a·2**. These results imply that the more rigid Pd-complex **1c** fits less well on the calix[4]arene **2** than the free ligand **1a**, which results in a bigger distance between **1c** and **2** and hence a larger capsule.

Preliminary studies show that the metal center inside the capsule retains its reactivity. Bubbling carbon monoxide through a methanol solution of **1c·2** resulted in a quantitative insertion of CO in the Pd–aryl bond and yielded capsule **1d·2** (**1d** = [(*trans*-**1a**)Pd(C(O)*p*-C_6H_4CN)]$^+$[$CF_3SO_3^-$]).‡[11a,b] The insertion of CO was fast and comparable to the insertion reaction in complex **1c** ($t_{1/2} < 1$ min) as expected for cationic palladium complexes.[11c,d] The proton NMR spectrum of capsule **1d·2** confirms that the capsule remains intact upon CO-insertion. As found for other *trans*-coordinating palladium diphosphine complexes, capsule **1d·2** as well as complex **1d** did not further react with methanol to provide the methanolysis product.[11c]

In summary, we have introduced a simple strategy for the formation of a new type of metallocapsules, which is based on mixing solutions of functionalized diphosphine ligands (and the metal complexes thereof) and calix[4]arenes utilized with complementary groups. In the current example the assembly process is based on ionic interactions; the tetraammonium functionalized diphosphine ligand **1a** or the metal complexes thereof readily associate with the tetraanionic calix[4]arene **2**, forming supramolecular capsules as indicated by ^{1}H-NMR, 1D-NOESY and DOSY experiments, and ESI-MS. Encapsulation of these transition metals opens up new opportunities to control the activity, stability and selectivity of the potential homogeneous catalysts.

Notes and references

‡ The counterions of ligand **1a** in Pd-complexes **1c** and **1d** are $CF_3SO_3^-$ instead of Cl^-.

§ Chloride tests with silver nitrate show the presence of NaCl in the water filtrate and absence in the isolated capsule precipitate.

¶ The observations described for capsule **1a·2** were also found for capsules **1b·2** and **1c·2**.

‖ Compound **1c** is not soluble in water.

** As the free and bound building blocks exchange fast on the NMR timescale, the observed D of the capsules are the weighted average of D of the free and bound building blocks.[10b]

1 (*a*) F. Hof, S. L. Craig, C. Nuckolls and J. Rebek, Jr., *Angew. Chem., Int. Ed.*, 2002, **41**, 1488; (*b*) M. Fujita, K. Umemoto, M. Yoshizawa, N. Fujita, T. Kusukawa and K. Biradha, *Chem. Commun.*, 2001, 509; (*c*) J. Rebek, Jr., *Angew. Chem., Int. Ed.*, 2005, **44**, 2068.

2 (*a*) B. C. Hamann, K. D. Shimizu and J. Rebek, Jr., *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1326; (*b*) S. K. Korner, F. C. Tucci, D. M. Rudkevich, T. Heinz and J. Rebek, Jr., *Chem. Eur. J.*, 2000, **6**, 187; (*c*) A. Shivanyuk and J. Rebek, Jr., *Chem. Commun.*, 2001, 2424; (*d*) F. Fochi, P. Jacopozzi, E. Wegelius, K. Rissanen, P. Cozzini, E. Marastoni, E. Fisicaro, P. Manini, R. Fokkens and E. Dalcanale, *J. Am. Chem. Soc.*, 2001, **123**, 7539; (*e*) N. Takeda, K. Umemoto, K. Yamaguchi and M. Fujita, *Nature*, 1999, **398**, 794; (*f*) M. Scherer, D. L. Caulder, D. W. Johnson and K. N. Raymond, *Angew. Chem., Int. Ed.*, 1999, **38**, 1588; (*g*) S. Ma, D. M. Rudkevich and J. Rebek, Jr., *J. Am. Chem. Soc.*, 1998, **120**, 4977; (*h*) R. Zadmard, M. Junkers, T. Schrader, T. Grawe and A. Kraft, *J. Org. Chem.*, 2003, **68**, 6511; (*i*) R. K. Castellano, B. H. Kim and J. Rebek, Jr., *J. Am. Chem. Soc.*, 1997, **119**, 12671.

3 (*a*) A. Lützen, *Angew. Chem., Int. Ed.*, 2005, **44**, 1000; (*b*) J. Kang, J. Santamaria, G. Hilmersson and J. Rebek, Jr., *J. Am. Chem. Soc.*, 1998, **120**, 7389; (*c*) J. Chen and J. Rebek, Jr., *Org. Lett.*, 2002, **4**, 327; (*d*) M. L. Merlau, M. Del Pilar Mejia, S. T. Nguyen and J. T. Hupp, *Angew. Chem., Int. Ed.*, 2001, **40**, 4239; (*e*) M. Yoshizawa, Y. Takeyama, T. Okano and M. Fujita, *J. Am. Chem. Soc.*, 2003, **125**, 3243; (*f*) M. Ziegler, J. L. Brumaghim and K. N. Raymond, *Angew. Chem., Int. Ed.*, 2000, **39**, 4119.

4 (*a*) D. Fiedler, D. H. Leung, R. G. Bergman and K. N. Raymond, *Acc. Chem. Res.*, 2005, **38**, 349; (*b*) D. H. Leung, D. Fiedler, R. G. Bergman and K. N. Raymond, *Angew. Chem., Int. Ed.*, 2004, **43**, 963.

5 (*a*) A. W. Kleij and J. N. H. Reek, *Chem. Eur. J.*, 2006, DOI: 10.1002/chem.200500875; (*b*) V. F. Slagt, J. N. H. Reek, P. C. J. Kamer and P. W. N. M. Van Leeuwen, *Angew. Chem., Int. Ed.*, 2001, **40**, 4271; (*c*) V. F. Slagt, P. W. N. M. van Leeuwen and J. N. H. Reek, *Angew. Chem., Int. Ed.*, 2003, **42**, 5619; (*d*) V. F. Slagt, P. C. J. Kamer, P. W. N. M. Van Leeuwen and J. N. H. Reek, *J. Am. Chem. Soc.*, 2004, **126**, 1526; (*e*) A. W. Kleij, M. Lutz, A. L. Spek, P. W. N. M. van Leeuwen and J. N. H. Reek, *Chem. Commun.*, 2005, 3661; (*f*) A. W. Kleij, M. Kuil, D. M. Tooke, A. L. Spek and J. N. H. Reek, *Inorg. Chem.*, 2005, **44**, 7696.

6 (*a*) R. Fiammengo, P. Timmerman, J. Huskens, K. Versluis, A. J. R. Heck and D. N. Reinhoudt, *Tetrahedron*, 2002, **58**, 757; (*b*) F. Corbellini, R. Fiammengo, P. Timmerman, M. Crego-Calama, K. Versluis, A. J. R. Heck, I. Luyten and D. N. Reinhoudt, *J. Am. Chem. Soc.*, 2002, **124**, 6569; (*c*) F. Corbellini, R. M. A. Knegtel, P. D. J. Grootenhuis, M. Crego-Calama and D. N. Reinhoudt, *Chem. Eur. J.*, 2005, **11**, 298.

7 (*a*) A. Buhling, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. W. Elgersma, K. Goubitz and J. Fraanje, *Organometallics*, 1997, **16**, 3027; (*b*) R. A. Widenhoefer, H. A. Zhong and S. L. Buchwald, *J. Am. Chem. Soc.*, 1997, **119**, 6787; (*c*) M. A. Zuideveld, B. H. G. Swennenhuis, M. D. K. Boele, Y. Guari, G. P. F. van Strijdonck, J. N. H. Reek, P. C. J. Kamer, K. Goubitz, J. Fraanje, M. Lutz, A. L. Spek and P. W. N. M. van Leeuwen, *J. Chem. Soc., Dalton Trans.*, 2002, 2308; (*d*) P. C. J. Kamer, P. W. N. M. Van Leeuwen and J. N. H. Reek, *Acc. Chem. Res.*, 2001, **34**, 895.

8 (*a*) A. Shivanyuk and J. Rebek, Jr., *J. Am. Chem. Soc.*, 2003, **125**, 3432; (*b*) A. Shivanyuk, M. Saadioui, F. Broda, I. Thondorf, M. O. Vysotsky, K. Rissanen, E. Kolehmainen and V. Boehmer, *Chem. Eur. J.*, 2004, **10**, 2138.

9 (*a*) C. A. Schalley, R. K. Castellano, M. S. Brody, D. M. Rudkevich, G. Siuzdak and J. Rebek, Jr., *J. Am. Chem. Soc.*, 1999, **121**, 4568; (*b*) R. Zadmard, A. Kraft, T. Schrader and U. Linne, *Chem. Eur. J.*, 2004, **10**, 4233.

10 (*a*) Y. Cohen, L. Avram and L. Frish, *Angew. Chem., Int. Ed.*, 2005, **44**, 520; (*b*) O. Mayzel and Y. Cohen, *J. Chem. Soc., Chem. Commun.*, 1994, 1901.

11 (*a*) G. K. Barlow, J. D. Boyle, N. A. Cooley, T. Ghaffar and D. F. Wass, *Organometallics*, 2000, **19**, 140; (*b*) S. J. Dossett, D. F. Wass, M. D. Jones, A. Gillon, A. G. Orpen, J. S. Fleming and P. G. Pringle, *Chem. Commun.*, 2001, 699; (*c*) P. W. N. M. van Leeuwen, M. A. Zuideveld, B. H. G. Swennenhuis, Z. Freixa, P. C. J. Kamer, K. Goubitz, J. Fraanje, M. Lutz and A. L. Spek, *J. Am. Chem. Soc.*, 2003, **125**, 5523; (*d*) G. P. C. M. Dekker, C. J. Elsevier, K. Vrieze and P. W. N. M. van Leeuwen, *Organometallics*, 1992, **11**, 1598.