Encapsulation of Hydrophilic Pincer−Platinum(II) Complexes in Amphiphilic Hyperbranched Polyglycerol Nanocapsules

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The study of catalytically active dendritic materials has become an attractive subject of intense current interest.[1] Such materials can be obtained either upon attachment of the appropriate catalyst (precursor) at the core or periphery of dendrimers or by the immobilization of metal nanoclusters in dendritic compartments.[2] Unfortunately, the preparation of dendrimers requires multistep syntheses, which limits their large-scale (industrial) application. In contrast, hyperbranched polymers are conveniently prepared on large scales in one-pot procedures via polymerization of AB_m-type monomers.[3] Controlled polymerization of glycidol by anionic ring-opening multibranching polymerization results in the formation of highly hydrophilic hyperbranched polyglycerols.[4] Esterification of a certain fraction (40−60%) of the hydroxyl groups of these hyperbranched polyether polyols with hydrophobic alkyl chains yields amphiphilic molecular nanocapsules with a reverse micelle-type architecture. These low polydispersity ($1.3 < M_w/M_n < 1.5$) amphiphilic molecular nanocapsules are soluble in apolar organic solvents and irreversibly encapsulate various polar, water-soluble dye molecules in their hydrophilic interior by liquid−liquid extraction.[5]

Our interest in the immobilization of homogeneous transition metal catalysts by soluble support systems has motivated us to prepare hydrophilic transition metal complexes which can be encapsulated inside these amphiphilic nanocapsules in a noncovalent manner. Because of their chemical integrity, metal complexes of the pincer ligand (3,5-bis[(dimethylamino)methyl]phenyl anion) have proven to be especially potent candidates for immobilization purposes.[6,7] The introduction of suitable substituents at the para-position of these pincer complexes permits one to tailor their solubility in solvents ranging from apolar to highly polar and protic.[8]

In this communication we report the noncovalent encapsulation of sulfonated pincer−platinum(II) complexes in readily available amphiphilic nanocapsules based on hyperbranched polyglycerol (Scheme 1). The encapsulated platinum(II) complexes have been applied as catalysts in double Michael additions to demonstrate their potential in homogeneous catalysis in continuous membrane reactors. The nanocapsules $P(G_{25}C16_{0.5})$ (**1**) and $P(G_{106}C16_{0.6})$ (**2**), investigated in this study, were synthesized by partial esterification of hyperbranched polyglycerols with molecular weights of $M_n = 2000$ and $M_n = 8000$, respectively.[9] Esterifications were performed with palmitoyl chloride in a mixture of pyridine and toluene,[5a] and the products were characterized by ^1H and ^{13}C NMR spectroscopy, IR spectroscopy and SEC analysis. While nanocapsule **1** possesses a molecular weight of $M_n = 5200$ ($M_w/M_n = 1.2$), with a degree of substitution of 50%, nanocapsule **2** had a molecular weight of $M_n = 23\,500$ ($M_w/M_n = 1.3$) with 60% degree of substitution with palmitoyl tails. Polymers **1** and **2** are completely and homogeneously soluble in apolar solvents such as dichloromethane, chloroform, and toluene. It should be emphasized that the analogous linear polyglycerols after partial esterification (60%) afford chloroform-soluble materials unable to transport polar guest molecules.[10]

The hydrophilic pincer−platinum(II) complexes **3** and **4** (Chart 1) dissolve readily in polar (protic) solvents such as water, methanol, or DMSO. Their solubility in aqueous solvents could be enhanced by the addition of base. These square planar d^8 platinum(II) complexes are air and water stable and were prepared by methods described elsewhere.[8]

Using UV−vis spectroscopy, we monitored the extent to which molecular nanocapsules **1** and **2** were able to encapsulate the platinum complexes **3** (*p*-SO_3H) and **4** (*p*-COOH) by extraction experiments from aqueous solutions (0.5 M NaOH) into dichloromethane solutions. Dichloromethane solutions of the nanocapsules ($c = 5 \times 10^{-5}$ M) were shaken thoroughly with aqueous solutions of the pincer complexes **3** and **4** with various concentrations in the range 10^{-5}−10^{-4} M. The clear organic phase obtained after phase separation was studied by UV−vis spectroscopy. While the sulfonated complex **3** shows very little solubility in neat dichloromethane, it could be extracted from the aqueous phase into dichloromethane solutions of the amphiphilic polyglycerols **1** and **2**. UV−vis spectra from solutions of **3** in the nanocapsules showed two strong bands ($\epsilon_{\pi-\pi^*} \approx 10^4\ M^{-1}\ cm^{-1}$) at 262 and 275 nm. The intensity of these bands increased at higher ratios of [**3**]/[nanocapsule]. Selected UV−vis spectra from the extraction of **3** by nanocapsule **1**, together with the corresponding titration curve, are depicted in Figure 1.

A change in slope of absorbance vs concentration ratio (inflection point) was reached at ratios of 1.5 ([**3**]/[**1**]) and 9.0 ([**3**]/[**2**]), clearly demonstrating the effect of molecular weight on the loading capacity of the amphiphilic hyperbranched polyglycerol. The incorporation behavior of **3** in the molecular nanocapsules is similar to that observed for sulfonated organic dyes.[5] At concentrations above the inflection point, the nanocapsules take up more **3** from the aqueous solution, but clearly by a different mechanism. Clearly different from the sulfonated dyes reported previously,[5a] we explain this tentatively by the aggregation of nanocapsules to form larger micelle-type structures assembled, most probably, around the polar guest, which possesses two polar moieties (SO_3^- and ^-OH) and a Lewis acidic center. It should be pointed out that all our observations to date

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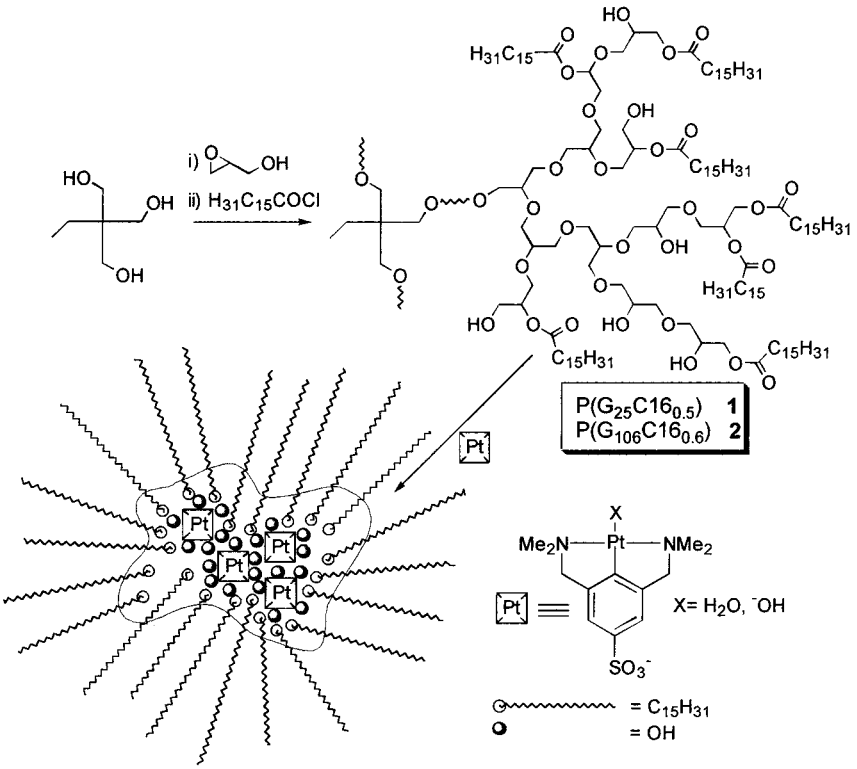
Scheme 1. Molecular Nanocapsule Synthesis, Structure, and Noncovalent Encapsulation of Platinum Pincer Complexes in the Hydrophilic Interior



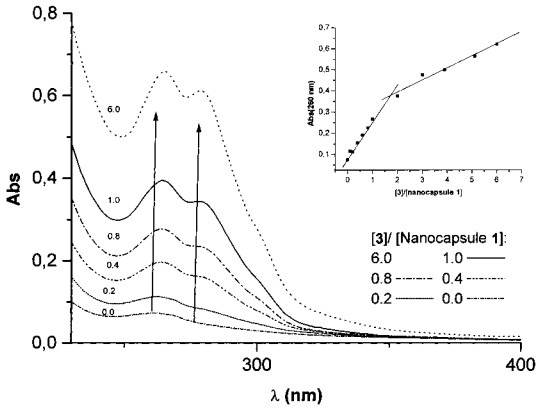
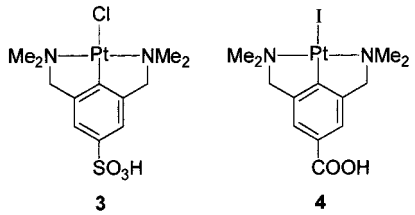


Figure 1. UV/vis spectra and titration curve (inset) of the extractions of **3** by nanocapsule **1** at various ratios of [**3**]/[nanocapsule].

Chart 1. Structures of Pincer Platinum(II) Complexes 3 and 4



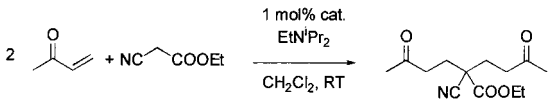
3 **4**

suggest that the unimolecular nature of the solvating nanocapsules depends on the nature of the guest molecule studied. UV−vis analysis of the aqueous phase showed that, at concentrations exceeding the inflection point, **3** is not extracted quantitatively into the organic phase any more.

To perform additional solid-state experiments, loading of **3** into the nanocapsules **1** and **2** on a preparative scale was carried out, using ratios equal to 1.5 and 9, respectively. The resulting yellowish solids were analyzed by ^{1}H, ^{13}C, and ^{195}Pt NMR and SEC chromatography. On the basis of ^{1}H NMR integration, **1** and **2** were found to encapsulate 0.9−1.1 and 3.8−4.1 equiv of **3**, respectively, at the inflection point (1.5 and 9 for [**3**]/**1** and [**3**]/**2** respectively). Calculation of the catalyst loading per polymer has also been achieved from UV−vis experiments by assuming the same extinction coefficient for complex **3** in water and in the amphiphilic structure solubilized in the organic phase. This leads to similar values as determined from NMR integration (calculation error 1−5%).[11] A comparative study via ^{1}H NMR spectroscopy of a saturated solution of **3** in D_2O and a saturated 0.5 M NaOH/D_2O solution shows the presence of two distinct pincer−platinum(II) species in the aqueous phase, as well as in the nanocapsule. This is explained by an equilibrium between the aqua (OH_2 as ancillary ligand) and the hydroxyl ($^-$OH as ancillary ligand) complexes of **3** (in a ratio of 7:3).[12] This finding was confirmed by ^{195}Pt NMR.

The carboxylate platinum(II) pincer **4** is not encapsulated in the hyperbranched nanocapsules. Dichloromethane solutions of **1** and **2** remained unchanged after shaking them with aqueous (0.5 M NaOH) solutions of **4**. UV−vis spectra of the organic phase showed no phase transfer of the complex. Furthermore, the band at 308 nm in the spectrum of **4** in the aqueous phase did not decrease upon repeated extractions with the nanocapsules. Attempts to encapsulate **4** with other counterions, e.g., in 0.5 M KOH and CsOH, were also unsuccessful. It should be noted that the encapsulation behavior observed for the carboxylate pincer complexes is similar to that of carboxylate-substituted organic dye molecules, which have a low affinity for the polyether−polyol interior of the nanocapsules compared to sulfonate substituted dyes.[13]

Table 1. Catalytic Results of the Double Michael Addition, Catalyzed by the Encapsulated Complexes



entry	catalyst	k (10^{-3} h^{-1})	conversion (%, after 40 h)
a	$[Pt(OH_2)NCN]^+BF_4^-$	280	99
b	none	28	38
c	**1**	35	45
d	**2**	29	40
e	**1** + **3**	73	95
f	**2** + **3**	62	81

The isolated loaded nanocapsules **1** + **3** and **2** + **3,** highly soluble in dichloromethane, were loaded with the inflection point concentration, and applied as catalyst in the double Michael addition of methyl vinyl ketone to ethyl cyanoacetate.[14] The Pt loadings determined by ^{1}H NMR integration were used to calculate the amount of catalyst applied in the catalytic reaction. The results of the catalysis experiments are summarized in Table 1.

Amphiphilic polyglycerols P($G_{25}C16_{0.5}$) and P($G_{106}C16_{0.6}$) without encapsulated catalyst do not result in a significant rate enhancement compared to the blank reaction (entries b−d).[15] The loaded nanocapsules **1** + **3** as well as **2** + **3** considerably increased the catalytic activity compared to the blank reaction (entries e and f), albeit the observed activity is lower than observed for the unsubstituted pincer−platinum(II) complex (entry a). This may be due to the fact that the catalysts are shielded from the environment by the core of the nanocapsules, their fatty acid substituents preventing fast exchange of products and substrates. Interactions between the hydroxyl groups of the polyglycerol core and the platinum cation can also render the catalyst less accessible for the coordination of ethyl cyanoacetate. The catalytic activity of **1** + **3** and **2** + **3** supports the finding that **3** is dehalogenated in 0.5 M NaOH, prior to the encapsulation, since the halide platinum(II) pincers are not Lewis acidic and not active in the Michael addition.[16] Due to the size of the nanocapsules, we were able to separate the products from the encapsulated catalysts by dialysis, and recover >97% of the catalytic material.[17] These results shows the suitability of the presented hyperbranched systems as catalyst carriers in continuous membrane reactors.[18]

In conclusion, hydrophilic pincer−platinum(II) complexes have been encapsulated in amphiphilic nanocapsules based on hyperbranched polyglycerols, possessing a reverse micelle-type architecture. The loading of the pincer complexes in the nanocapsules depends on the molecular weight of the hyperbranched polymer as well as on the functionality of the pincer. The incorporated platinum(II) complexes show catalytic activity in a double Michael addition, albeit with decreased activities compared to the free pincer complex. To our knowledge this is the first example of the use of a hyperbranched polymer-based microenvironment for homogeneous catalysis in a noncovalent strategy. The strategy is also promising with respect to the application of catalysts in a membrane reactor setup. Encapsulation of pincer complexes in other molecular nanocapsules with modified core/shell structures is currently under investigation, as well as covalent linking of the pincer complexes to hyperbranched polyglycerols.[19]

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Supporting Information Available: Figures showing UV/vis spectra and titration curves after extractions of **3** by nanocapsules **1** and **2**, in the organic phase as well as in the aqueous phase. This material is available free of charge via the Internet at http://pubs.acs.org.

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(7) Pincer complexes from the nickel triad (Ni, Pd, Pt) are applicable as catalysts in various carbon−carbon coupling reactions, such as the Kharasch addition, the Heck reaction, and aldol condensations.

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(9) (a) Nomenclature for P(G_xCY_z): x = DP_n of polyglycerol; Y = number of carbon atoms of the palmitoyl acid; z = degree of alkyl substitution per hydroxyl group. (b) Partially esterified polyglycerols P($G_{25}C16_{0.5}$) (**1**) and P($G_{106}C16_{0.6}$) (**2**) were prepared as followed: To a pyridine solution (80 mL) of hyperbranched polyglycerol (DP_n = 25; 1.52 g; 20.51 mmol of OH groups) was added dropwise a toluene solution (100 mL) of palmitoyl chloride (3.6 mL; 12 mmol) at 80 °C within 1 h. The mixture was refluxed for 20 h at 130 °C. A stoichiometric amount of $NaHCO_3$ (10.28 mmol; 1.03 g) was added to the cold solution and most of the volatiles were removed in vacuo. Residual pyridine was removed by azeotropic distillation in 100 mL of toluene. The remaining solution was filtered and concentrated in vacuo. The residue was washed several times with ethyl acetate to remove traces of free palmitoyl carboxylic acid and was further purified by dialysis (MWCO 1000) in $CHCl_3$. The polymer was obtained as a white solid. Polymer P($G_{25}C16_{0.5}$) (**1**). Yield: 85%. ^{1}H NMR ($CDCl_3$): 0.81 (t, CH_3), 1.11−1.25 (br, 24H, CH_2), 1.53 (m, $COCH_2CH_2$), 2.24−2.28 (m, CH_2, CH_2CO), 3.44−4.03 (br, 5H, glycerol moiety), 5.04 (br, OH). ^{13}C NMR ($CDCl_3$): 14.08, 22.66, 24.88, 29.16, 29.51, 29.64, 31.90, 34.10, 65.12, 68.65, 69.81, 70.16, 173. IR (NaCl) υ =

1738.43 (C═O), 3441.81 (O−H). α (degree of substitution per hydroxyl group) = 50%; M_n = 5230. Polymer P(G_{106}-$C16_{0.6}$) (**2**). Dried hyperbranched polyglycerol (DP_n = 106; 10 g, 134.95 mmol of OH groups) and palmitoyl chloride (24.54 mL; 80.97 mmol) were reacted following the same procedure as polymer **1**, to give polymer P($G_{106}C16_{0.6}$), **2** as a white solid. Yield: 90%. ^{1}H NMR ($CDCl_3$): 0.84 (t, CH_3), 1.21 (br, 24H, CH_2), 1.57 (m, 2H, CH_2CH_2CO), (m, 2H, CH_2-CO), 2.26−2.3 (m, CH_2, CH_2CO), 3.52−4.07 (br, 5H, glycerol), 5.10 (br, OH). ^{13}C NMR ($CDCl_3$): 14.10, 22.67, 24.94, 29.13, 29.43, 29.66, 31.91, 34.10, 65.12, 68.65, 69.81, 70.16, 173. IR (NaCl) = 1636.76 (C═O), 3388.06 (O−H). α (degree of substitution per hydroxyl group) = 60%; M_n = 23 506; M_w/M_n = 1.3.

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(11) Determination of the encapsulated catalyst **3** in both polymers **1** and **2** was based on ^{1}H NMR spectra recorded in $CDCl_3$ with an acquisition time AQ = 3.6 s/30° pulse. NMe_2 protons ($\delta(CH_3)$ = 3.02 ppm) for catalyst **3** and hydrophobic shell protons ($\delta(CH_3)$ = 0.84 ppm), respectively, were considered for determining the encapsulation equivalents of **3**.

(12) (a) The ^{1}H NMR spectrum of a saturated solution of **3** in D_2O shows, apart from the aromatic and benzylic resonances, a signal for the NMe_2 protons at 2.99 ppm, corresponding to the deprotonated complex **3**. In a saturated 0.5 M NaOH/D_2O solution, this resonance disappears, and two new signals at higher field (2.88 ppm and 2.59 ppm) appear. These shifts correspond to the dehalogenation of **3**, as confirmed by halide abstraction with $AgBF_4$ (b) For pK_a studies on platinum pincer aqua complexes: Schmülling, M.; Grove, G. M.; van Koten, G.; van Eldrik, R.; Veldman, N.; Spek, A. L. *Organometallics* **1996**, *15*, 1384−1391.

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(14) (a) General conditions for the double Michael addition: 1.6 mmol of ethyl cyanoacetate, 4.8 mmol of methyl vinyl ketone, 0.16 mmol of EtN^iPr_2, 1 mol % of catalyst based on Pt, 5 mL of CH_2Cl_2, room temperature. The reaction was followed by ^{1}H NMR, and the products were characterized by ^{1}H NMR and GC−NMR. Lewis acidic palladium(II) and platinum(II) pincer complexes of the type $[M(OH_2)$-$NCN]^+BF_4^-$ can be applied as catalyst in aldol-type reactions. (b) Generally, Pt pincer complexes are not considered to be active catalysts. However, they show some activity in double Michael additions. Their catalytic activity in aldol type reactions is commonly lower than the activity of their Pd analogues. For an overview on the catalytic activity of pincer complexes, see: Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 3750.

(15) Neat dichloromethane, shaken thoroughly with an aqueous solution of **3**, was also not catalytically active in the double Michael addition.

(16) In a control experiment, the encapsulated pincer systems were treated with $AgBF_4$, which is a normal procedure for dehalogenation. The resulting materials did not show significant rate enhancements compared to **1** + **3** and **2** + **3**.

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