A polymer support with controllable solubility in mutually immiscible solvents†

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We report on novel soluble macromolecules displaying rather peculiar solution behaviour, which allows us to gain full control of their partition into three mutually immiscible liquid media: water, dichloromethane and perfluoro(methylcyclohexane); such polymers may be used as soluble supports for reagents or catalysts, yielding supported species whose solubility preference for one out of three liquid phases can be quantitatively and reversibly switched, thereby simplifying separation considerably.

Separation has always been one of the fundamental operations in synthetic chemical technology, since products have to be isolated from residual reagents and/or by-products before being further manipulated or commercially exploited. Separation is also a key issue of many chemical processes involving an expensive homogeneous catalyst, which needs to be recovered and recycled in order to make the whole process economically viable.[1] Today, the need for simple, fast and efficient separation methods is greater then ever,[2] due *inter alia* to the growing concern for the cleanness and efficiency of chemical processes ("green chemistry")[3] and to the problems posed by the purification of compound libraries prepared by combinatorial techniques.[4]

Partition between two different liquid phases is one of the oldest separation techniques. It has been used both to purify reaction products and to recover homogeneous catalysts.[2] The traditional water–organic solvent system has been recently extended by the introduction of other liquid phases, such as fluorous solvents[5] or ionic liquids,[6] which can be made immiscible both with water and with traditional organic solvents. One of the shortcomings of this technique is that the reaction component which has to be isolated should have a considerable preference for one liquid phase as opposed to all other solutes.

We have an ongoing program aimed at the use of microgels as soluble supports for reagents and catalysts.[7–9] Microgels[10] are soluble, intramolecularly cross-linked macromolecules with a globular shape and with a diameter of 10^1–10^2 nm. Microgels can be tailored in order to bear pendant functional groups which can act as anchoring points for homogeneous catalysts,[7] as well as for reactants, reagents or scavenging agents to be used in solution-phase combinatorial synthesis.[11] Furthermore, the functional groups can interact with metal ions or complexes, which are subsequently reduced inside the microgel to yield catalytically active, size-controlled metal nanoclusters.[8,9] Very recently, we have developed microgels based on *N,N*-dimethylacrylamide (DMAA) and have used them in the preparation of Pd and Pt nanoclusters.[9] Such microgels were found to be soluble both in water and in some water-immiscible solvents, most notably in dichloromethane. Given these results, we became interested in studying the partition behaviour of these microgels between two immiscible liquid phases. To this end, we have prepared a suitable microgel by copolymerising DMAA (40 mol%) with dimethylaminoethyl methacrylate (50 mol%) and ethylene dimethacrylate (10 mol%). Treatment of a dichloromethane solution of this microgel with palladium(II) acetate led to anchoring of the metal ions to the polymer-bound trialkylamino groups; subsequent reduction with ethanol led to the formation of microgel-protected Pd nanoclusters (MPdEtOH, 2.4% w/w Pd in the microgel, average nanocluster size 2.2 $\pm$ 0.9 nm as determined by TEM). Similarly, treatment with gold(III) chloride of microgel solutions in water or ethanol followed by spontaneous reduction yielded Au nanoclusters ($MAuH_2O$, 4.2% w/w Au, average nanocluster size 6.4 $\pm$ 3.2 nm, and MAuEtOH, 4.2% w/w Au, average nanocluster size 10.0 $\pm$ 4.4 nm, respectively); in this case the actual reducing agents are probably the polymer-bound trialkylamino groups themselves, which are known to act in a similar way towards less easily reducible metal centers.[12] The microgel-protected metal nanoclusters were conveniently isolated by precipitation and stored in the solid state.

The strong colour of metal nanoclusters (dark brown for Pd, dark red for Au) makes nanocluster-containing microgels ideally suited for monitoring their partition in different solvents. We started by studying a water–dichloromethane biphasic system. We were immediately very surprised to note that, when in contact with the second liquid phase, *the microgels invariably and quantitatively remained in the liquid phase in which they were dissolved first*, no matter which one it was and how long the system was stirred. Transitions could be induced only by changing the pH of the water phase and were easily monitored by following the migration of the nanocluster colour (Fig. 1 top). For example, transition from water to dichloromethane occurred quite abruptly and quantitatively (>99% as judged from ICP-AAS analysis of residual Au in the water phase) when the pH was raised above 10 by adding 1 M aqueous NaOH. Since the pK_a of the ammonium salt of dimethylaminoethyl acetate (a good model of the basic functional groups present in the microgel) is 8.3,[13] the transition pH corresponds to >98% of the amino groups becoming neutral. Conversely, transition from dichloromethane to water was slower but could still be quantitatively induced by lowering the pH below 1 upon addition of 1 M aqueous HCl. Thus, in the broad pH window between 1 and 10 the microgels show the interesting

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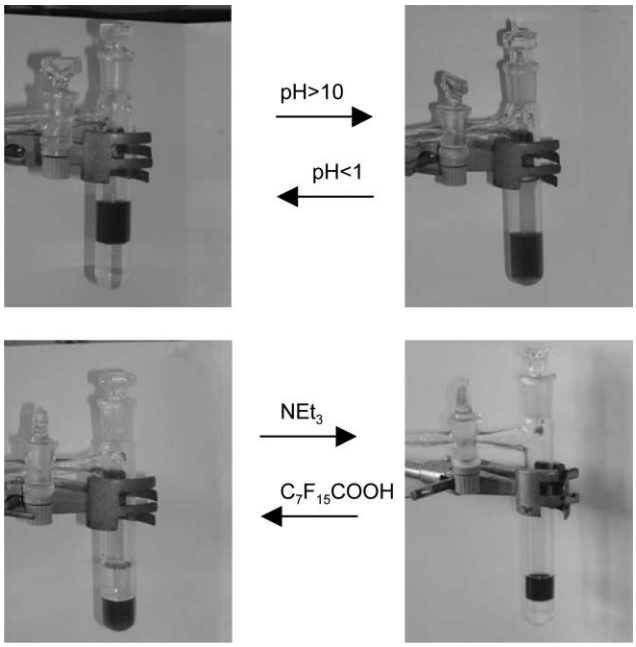

Fig. 1 Partition of sample MAuEtOH (5 mg) in liquid–liquid biphasic systems under different conditions: water–dichloromethane (top, 2 mL of each solvent), dichloromethane–perfluoro(methylcyclohexane) (bottom, 2 mL of each solvent).

property of remaining preferentially soluble in an organic or aqueous phase depending on the phase in which they were dissolved first.

The observed behaviour is the consequence of competitive solvation effects as well as of the acid–base equilibria in which the basic amino groups in the microgel are involved. When the microgels are dissolved in water, the pendant amino groups become partially protonated; consequently, the hydrophilicity of the microgel increases. The microgel becomes organophilic only when almost all ammonium groups in the polymer become neutral. On the other hand, when the microgel is dissolved first in dichloromethane, the amino groups need to become protonated in order for the microgel to migrate into the aqueous phase; however, the solvation of the microgel by dichloromethane efficiently prevents contact between the solvated protons present in the water phase and the amino groups contained in the microgels up to high proton concentrations.

Both transitions occur in the same way independently of the size and of the nature of the metal nanoclusters (Au or Pd). Interestingly, the average size and size distribution of the metal nanoclusters appear to remain unaffected by the solvent change. This is confirmed by UV-visible analysis of the surface plasmon absorption band of Au nanoclusters in sample MAuEtOH. The UV-visible spectrum after extraction of the microgel from water to dichloromethane and the spectrum of a fresh solution of the microgel in dichloromethane turn out to be superimposable: this is a strong indication that no modification of the structure of the gold nanoclusters takes place during extraction.

The position of the absorption peak remains almost constant after the transition from water (525 nm) to dichloromethane (527 nm), despite the increase in solvent refractive index n_D^{20} (from 1.333 to 1.424). It has been reported that for solvent-exposed Au nanoclusters an increase in the solvent refractive index causes a significant red shift of the absorption peak.[14] In the case of our microgel-protected metal nanoclusters, however, the microenvironment around the nanoclusters is not made out of solvent alone, but of solvent-swollen polymeric chains which weakly interact with the nanoclusters through their amino and amide functionalities.[9,15] Consequently, the solvent dependence of the absorption features may be complex and in particular far less marked than in the case of solvent-exposed nanoclusters. Indeed, deviations from this behaviour have already been reported for poly(vinylpyrrolidone)-stabilised nanoclusters.[16]

Reversible microgel transfer has been induced also from dichloromethane to a fluorous phase (Fig. 1 bottom). Microgels are completely extracted into perfluoro(methylcyclohexane) by adding perfluorooctanoic acid (7 equivalents with respect to the microgel-bound amino groups). In this case, an acid–base reaction between the basic amino groups contained in the microgel and the perfluorooctanoic acid additive results in the formation of microgel-anchored trialkylammonium perfluorooctanoate moieties, which impart to the microgel a strong affinity for the fluorous phase.[17] The phase transfer can be reversed by simple addition of triethylamine to the organic–fluorous biphasic system, which cleaves the ammonium moieties liberating the microgel in neutral form.

Again, UV-visible analysis has been conducted in order to assess changes in the surface plasmon absorption of sample MAuEtOH. Comparison with a fresh microgel solution in the fluorous phase is not possible here, since MAuEtOH is not directly dissolved in a perfluoro(methylcyclohexane) solution of perfluorooctanoic acid. In this case, a definite red shift of the absorption band is observed upon moving from dichloromethane (527 nm, $n_D^{20} = 1.424$) to perfluoro(methylcyclohexane) (538 nm, $n_D^{20} = 1.300$), whereas a blue shift was predicted on the basis of simple solvent effects. Such a red shift could be interpreted in terms of aggregation of the Au nanoclusters.[18] However, back extraction of the microgels in dichloromethane restores the original value of the absorption maximum; this indicates that the observed red shift is most probably due to changes in the nature of the microenvironment around the Au nanoclusters (*e.g.* in the local dielectric constant) following protonation of the amine functional groups, and not to aggregation. Remarkably, exactly the same red shift is actually recorded when the microgels are extracted from dichloromethane into water acidified at pH 1.

In conclusion, we have demonstrated that microgels based on DMAA and containing basic functional groups display a unique solution behaviour, on the basis of which we can quantitatively and reversibly switch their solubility in mutually immiscible liquid media. The importance of this finding is related on the one hand to the production of pure, stable, easy to manipulate size-controlled metal nanocluster samples: the possibility to govern the solubility of microgel-stabilised metal nanoclusters greatly facilitates their purification and handling without causing nanocluster aggregation and also without irreversibly modifying the nanocluster surface by *e.g.* covalent capping.[19] On the other hand, the properties of these microgels may open entirely new perspectives for their use as soluble scaffolds for combinatorial solution phase synthesis, as well as for the anchoring of recoverable reagents, scavenging agents or homogeneous catalysts. Extension of the application of our microgels to this broad field is currently underway.

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