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Surface-functionalised nano-beads as novel supports for organic synthesis

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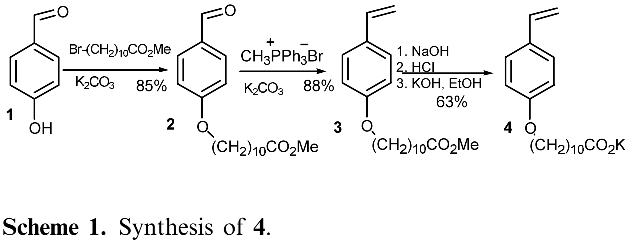
Abstract—A novel polymer support has been prepared in which functional link points are located on the surface of polymer nano-beads; the use of the support has been demonstrated in the syntheses of unsymmetrical porphyrins.

The use of solid-phase supports in organic synthesis is now widely employed.[1] Although inorganic supports such as silica gels and controlled pore glasses[2] are frequently used, organic polymers still comprise the largest class of support materials. Lightly crosslinked, swellable polymers are typically prepared by emulsion polymerisation techniques to give beads in sizes ranging from μm to mm. Such insoluble polymers are convenient for application as supports for synthesis, reagents, scavengers etc. Their efficiency is governed by their ability to swell (allowing access through the polymer matrix) and therefore requires the use of suitable solvents. This limitation is usually accommodated but complications can be envisaged when attempts are made to build up large molecules within the pores of such supports.

In this letter we describe the preparation of a new type of polymeric support based on surface-functionalised nanoparticles. We envisaged that an ideal solid support could comprise small solid particles (ca. 50–300 nm) bearing link points exclusively at the surface. Such supports would be soluble in reaction media but easily isolated by precipitation or SEC. Locating the link points at the surface obviates the problems associated with 'buried' functionality within a porous polymer (heterogeneity of sites, accessibility etc).

We reasoned that such a support could be realised via polymerisation of a microemulsion[3] in which a *polymerisable* sufactant serves as amphiphile and, following polymerisation, as functional link point for solid-phase organic synthesis. We chose a polymerisable carboxylic acid derivative as surfactant to ensure a useful link group would be attached to the final polymer (reasoning that the carboxylic acid could be reduced to provide additional scope). Initial experiments with simple 'surfactants' such as 4-vinylbenzoic acid were unsuccessful and led to the choice of amphiphile **4**.[4] Compound **4** was most conveniently synthesised by the route depicted in Scheme 1.

In a typical procedure polymerisable amphiphile **4** (1.2 g) and CTAB (6.8 g) were used as surfactants to stabilise a styrene/divinylbenzene (10:1, 2.4 g) microemulsion in water (189 mL). The microemulsion was polymerised (AIBN initiation) at 60°C for 7 h to give a transparent solution of the surface-functionalised nanoparticles. Acidification and addition of methanol precipitated the polymer from solution and it was filtered off and washed repeatedly with water to remove CTAB. The resulting polymer was dried under vacuum and characterised by TEM (average bead diameter 317 nm[5]), IR spectroscopy ($\nu_{C=O}$ 1707 cm^{-1}) and titration (loading = 0.89 mmol/g COOH) (Scheme 2).



Scheme 1. Synthesis of **4**.

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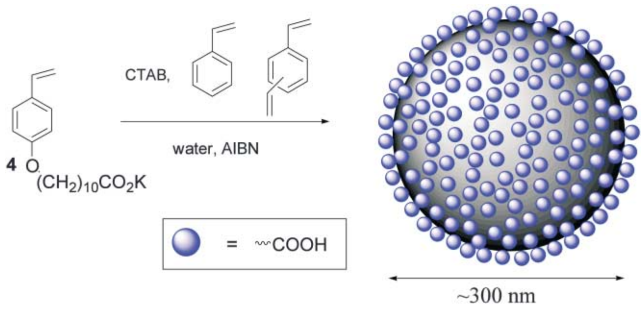

Scheme 2. Preparation of surface-functionalised nanoparticles (see text for details).

The utility of the novel polymer supports was investigated using the syntheses of unsymmetrical porphyrins as model reactions. The synthesis of unsymmetrical porphyrins is generally a difficult process with typical yields ranging from 0.5 to 5%.[6] The synthesis of unsymmetrical tetraarylporphyrins on conventional polymer supports was reported by Leznoff[7] using polymer bound 3- or 4-hydroxybenzaldehyde (Scheme 3) and this reaction was chosen to permit evaluation of the nanoparticulate solid support.

The carboxylic acid functionalised support was treated with oxalyl chloride in CH_2Cl_2 (DMF initiation)[8] and the resulting polymer-bound acid chloride treated with either 3- or 4-hydroxybenzaldehyde and pyridine. Complete conversion to the polymer bound aldehyde-ester was confirmed by IR spectroscopy of the isolated polymer ($\nu_{C=O}$ 1766 and 1705 cm^{-1}). The polymer bound aldehydes were treated with excess pyrrole and *p*-tolylbenzaldhyde in refluxing propionic acid for 1 h.[9] After washing with CH_2Cl_2 the resulting polymers (IR 1765 cm^{-1}) were treated with potassium carbonate in methanol to cleave the bound porphyrins which were isolated (preparative TLC) in yields of 4% (**5**) and 8% (**6**), respectively. It is significant to note that these yields are higher than those reported for their synthesis on conventional solid phase.[7]

In conclusion, surface-functionalised nanoparticles have been prepared and their utility as solid supports has been demonstrated. Their reaction sites are uniformly located at the accessible surface of (selectively) soluble nanoparticles and they could, therefore, offer advantages over their conventional counterparts in challenging applications.

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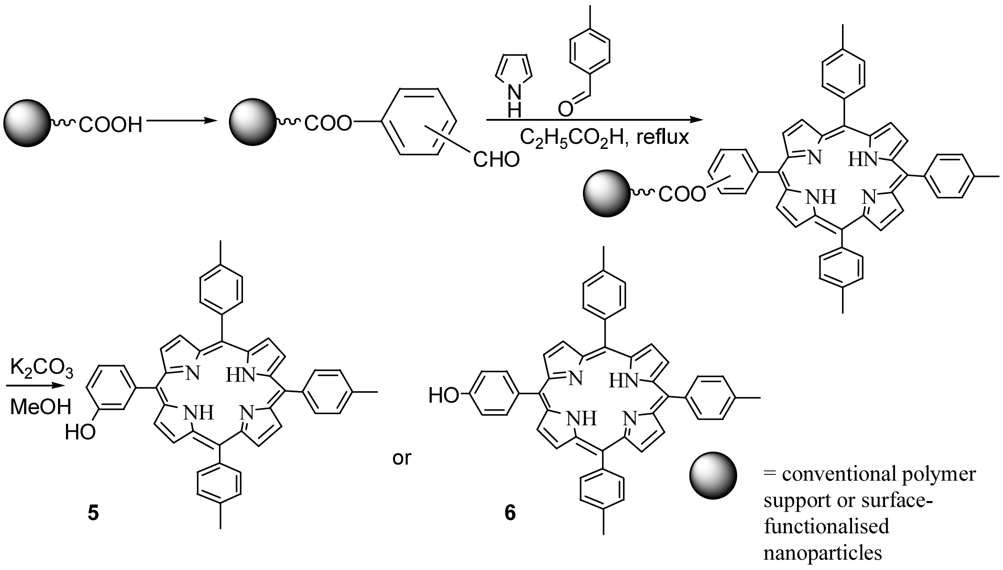

Scheme 3. Polymer supported synthesis of unsymmetrical porphyrins.