

Quantum dot-labelled polymer beads by suspension polymerisation

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CdSe quantum dots with polymerisable ligands have been incorporated into polystyrene beads, via a suspension polymerisation reaction, as a first step towards the optical encoding of solid supports for application in solid phase organic chemistry.

Approaches to synthetic organic chemistry have developed rapidly over recent years with the increased demand for high speed synthesis and screening techniques. Combinatorial techniques, such as 'split and mix' and high-throughput parallel synthesis, are now used routinely. We are concerned in particular with approaches that involve the on-support synthesis and *in situ* screening of large numbers of diverse molecules prepared using split-and-mix techniques. Whilst there has been much success in synthesising libraries of this type, a major problem with this approach is being able to identify exactly which molecule is attached to a particular bead. To this end, a number of innovative deconvolution approaches have been developed to encode individual beads. These include: chemical encoding with molecular tags;¹ organic fluorophores;² fluorescent colloids;³ Raman fingerprints;⁴ and radio frequency transponders.⁵ More recently, Nie *et al.*⁶ have utilised fluorescent inorganic semiconductor quantum dots.

This last approach is most attractive since quantum dots offer significant advantages over conventional fluorescent dyes since they are brighter, more photostable materials with narrow emission bands that can be excited by any wavelength greater than the energy of their lowest transition.⁷ These properties also allow optical barcoding⁶ of polymer supports by combining different colour quantum dots with different intensity levels. However, the approach described to generate the quantum dot encoded materials simply involved embedding the quantum dots into the outer layers of 1–2 μm resin beads then sealing with a final silica layer. Whilst encoded materials of this type appear to be ideal for the optical encoding of biomolecules⁶ the method of quantum dots immobilisation is non-covalent in nature and thus materials generated in this manner would not be suitable for widespread application in solid phase organic synthesis. We thus elected to establish the feasibility of incorporating quantum dots covalently into the polymer matrices of supports of the type used routinely in the solid phase synthesis of combinatorial libraries.

A recent publication by Emrick *et al.*⁸ described an elegant approach to incorporate quantum dots covalently into spin and solution cast polymer films by pre-coating quantum dots with polymerisable ligand **2**. We were intrigued to investigate whether such an approach could be extended to incorporate quantum dots into polymer beads utilising well established suspension polymerisation techniques. We believed that if successful, this new procedure would enable the facile production of many of the bead-types that are available commercially for combinatorial chemistry applications but with the added benefit of quantum dot encoding.

Quantum dots were synthesised from (Li₄)[Cd₁₀Se₄(SPh)₁₆] and hexadecylamine as described previously⁹ to give CdSe core

particles capped with hexadecylamine. Ligand exchange was then performed to displace the hexadecylamine with one of two polymerisable ligands **2** or **5** (Scheme 1).^{8,10†} The structure of each of the ligands is based on the commonly used quantum dot capping agent trioctylphosphine oxide (TOPO) **1**, since TOPO has a good affinity for CdSe quantum dots. Success of ligand exchange was confirmed by ¹H NMR and by observing the increase in solubility of the coated quantum dots in styrene.

Polymerisable ligand **2** was synthesised using the two-step protocol described by Emrick *et al.*^{8,11} and a variation of this route was used to construct ligand **5** (Scheme 1). Specifically, dibutylphosphite **3** was converted into dioctylphosphine oxide **4** by treatment with octylmagnesium bromide followed by an aqueous acid quench. A subsequent sodium hydride mediated alkylation step with 8-bromo-1-octene furnished polymerisable ligand **5** in good yield.‡

To facilitate the generation of a relatively large number of beaded materials, a scaled-down suspension polymerisation procedure (20 ml reaction volume), utilising a Carousel™ reaction station, was used to generate a series of quantum dot-containing polymer beads (Table 1).^{12§} For each of the polymer samples described in Table 1, simple visual inspection indicated that quantum dots had indeed been incorporated successfully. However, in the case of beads produced using ligand **5** the extent of quantum dot incorporation, as evidenced by microanalysis, was very low (Table 1). Thus all subsequent investigations utilised beads constructed using ligand **2**. Each sample was further analysed by i) fluorescent emission fingerprinting (Fig. 1), ii) photoluminescence spectroscopy (Fig. 2) and iii) elemental microanalysis after extended periods of Soxhlet extraction (Table 1).

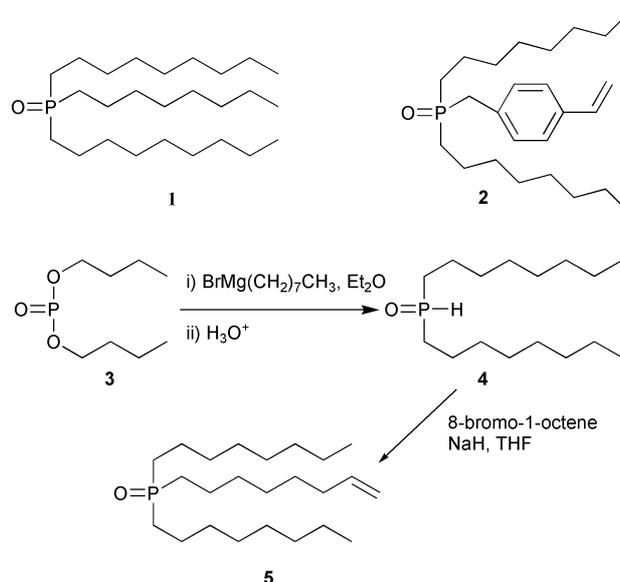
Scheme 1 Synthesis of polymerisable ligand **5**.

Table 1 Compositions of quantum dot-containing beads generated using the small-scale suspension polymerisation procedure

Entry	DVB (mol%)	Mass QD/mg	QD Ligand	Microanalysis (%)		
				C	H	Cd
1	2	6.8	2	90.57	7.70	0.72 ^a
				87.96	7.41	0.67 ^b
				89.69	8.01	0.75 ^c
2	20	6.8	2	87.60	7.50	0.19 ^a
				90.31	8.22	0.17 ^c
3	2	2.7	5	90.84	8.06	<0.01 ^a
4	20	2.7	5	92.06	7.95	<0.01 ^a

^a Before Soxhlet extraction. ^b After Soxhlet extraction with dichloromethane for 4 h. ^c After Soxhlet extraction with dichloromethane for 12 h.

Most importantly, both fluorescent emission fingerprinting and photoluminescence spectroscopy of the polymer beads exhibited strong emissions at approximately 522 nm corresponding directly with the emission observed for the hexadecylamine coated quantum dots prior to ligand exchange (522 nm) (Fig. 1 and 2). Moreover, as Fig. 1 shows, two different regions of the same bead give essentially identical emission spectra indicating that quantum dot incorporation is uniform. In addition, the data in Table 1 show clearly that the amount of cadmium within the beads remains fairly constant, within experimental error, even after prolonged periods of Soxhlet extraction with dichloromethane (entries 1 and 2). This finding

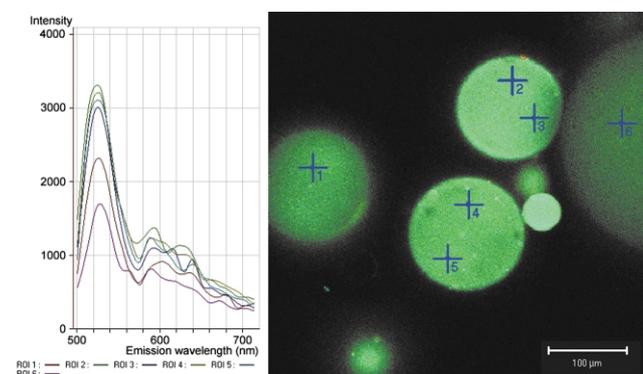


Fig. 1 Fluorescent emission fingerprinting of quantum dot-containing polymer beads.

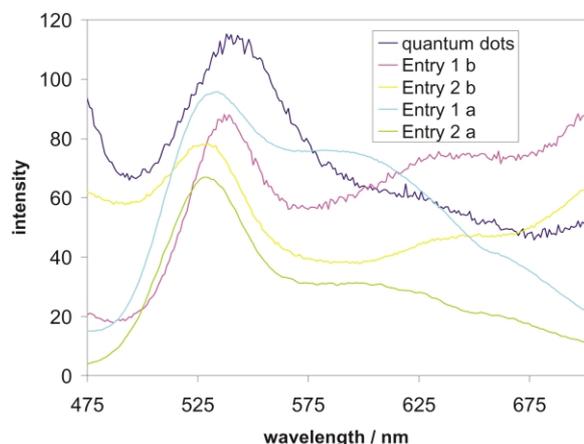


Fig. 2 Photoluminescence spectra of quantum dot-containing polymer beads (excitation wavelength = 380 nm).

indicates that the dots are incorporated into the beads irreversibly, since both the hexadecylamine and ligand **2** coated dots are highly soluble in cold dichloromethane.

In conclusion, we have shown that it is possible to incorporate quantum dots into polystyrene beads by using suspension polymerisation protocols. We are currently extending the protocols described herein to prepare a range of beads with various functional groups and colour/intensities of quantum dots for utilisation in solid phase synthesis. These materials will then be tested for their ability to withstand a wide range of reagents and reaction conditions commonly employed in synthetic organic chemistry.

Notes and references

† Quantum dots, 20 mg, prepared according to a previously published procedure,⁹ were dissolved in 1,4-dioxane, 4 ml, containing a large excess of the polymerisable ligand, 1 mmol. The solution was then stirred for 20 hours at room temperature. Centrifugation and drying resulted in ligand exchanged quantum dots (14 mg for the *p*-vinylbenzylDOPO and 10 mg for *p*-octenylDOPO batches).

‡ Product structures were confirmed by ¹H and ¹³C NMR spectroscopy and APCI mass spectrometry.

§ *Small-scale suspension polymerisation procedure.* Aqueous polyvinyl alcohol (PVA) solution (20 ml, 1% wt/wt, 87–89% hydrolyzed PVA, average MW 85000–146000) was prepared and transferred to the reaction vessel (screw cap boiling tube attached to a N₂/vacuum manifold system) and degassed with N₂ for 20 minutes. A monomer mixture—styrene (10 mmol), divinylbenzene and quantum dots (Table 1)—was prepared and stirred for 5 minutes. AIBN (76 µmol) was added to the monomer mixture then the resultant mixture was stirred for a further 15 minutes with N₂ degassing. The dark orange monomer solution (colour due to the quantum dots) was added to the PVA solution while rapidly stirring with a cross-shaped magnetic stirrer. A two phase system resulted with orange droplets being suspended in the uncoloured aqueous PVA solution. The suspension was stirred at room temperature for 30 minutes before the temperature was increased to 70 °C and stirring was continued for a further 4 hours. The resin beads were then collected over a 38 µm sieve and washed *in situ* with copious amounts of water. The damp beads were then transferred to a sintered funnel and washed with methanol (100 cm³), MeOH/THF, 1/1 (100 cm³), THF (100 cm³), CH₂Cl₂ (100 cm³) and acetone (100 cm³).

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