Covalent adhesion; organic reactivity at a solid–solid interface through an inter-bead Diels–Alder reaction†

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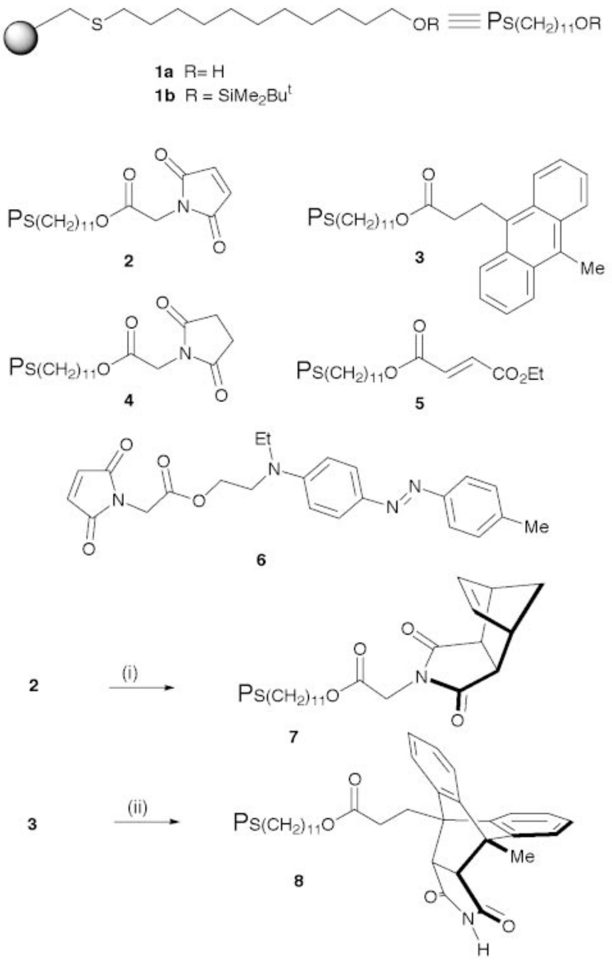
Polystyrene resin beads carrying respectively maleimide and anthracene groups attached to extended side-chains adhere to one another in a manner consistent with an inter-bead cycloaddition reaction.

We reported earlier on the synthesis of modified polymers based on cross-linked polystyrene where *ca.* 60% of the arene rings bore a long alkyl side-chain possessing terminal functionality.[1] The quality of ^{13}C NMR spectra observed for the solvent-swollen polymer and in particular the high degree of mobility deduced from the ^{13}C T_1 relaxation times indicated a fluid-like polymer where the functional groups were readily accessible. In addition, their effective concentration is in the 2–2.5 mM region. This led us to consider the possibility for reaction at the interface between two polymers of this type, each carrying a different reactive entity. There are interesting precedents for employing an intermolecular Diels–Alder reaction as a probe for the reaction environment, or immobilisation;[2] the reaction is a formal addition to give a single product, and it is relatively insensitive to solvent polarity.[3]

Synthesis of the desired polymers was accomplished according to Scheme 1. For the dienophilic component, the maleimide functionality was introduced in a one-step sequence whereby the alcohol **1a** was reacted with *N*-(chlorocarbonylmethyl)maleimide, giving **2**.[4] First attempts at forming a polymer-linked diene involved attachment of chlorodimethylcyclopentadienylsilane[5] (in the expectation of forming a regiochemically defined product) but were not quantitative. A more successful approach involved reaction of alcohol **1a** with 9-(2-chlorocarbonylethyl)-10-methylanthracene[6] from which resin **3** was obtained. For control experiments, the saturated succinimide **4** and fumarate ester **5** were synthesised using related methods. A staining procedure was adapted by synthesis of the dienophilic dye **6** prepared from Disperse Red 1 which was shown to selectively stain the resin diene **3** bright red[7] (1% solution, 1 h, THF), and to leave the dienophilic resin **2** unaffected under the same conditions. It was confirmed by ^{13}C NMR that the desired polymers had been synthesised without significant side-reactions and also that the staining procedure introduced an insignificant number of additional linkages into resin **3**. It were further confirmed by ^{13}C NMR that diene resin **3** reacted with maleimide to form the adduct **8** and dienophile resin **2** reacted with cyclopentadiene to form the adduct **7**. Both cycloadditions were complete by ^{13}C NMR. Since there is a rapid intermolecular Diels–Alder reaction between maleimide and 9,10-dimethylanthracene,[8] these polymer-bound entities provided a suitable test for investigation of interfacial reactivity.

Solvent effects on the aggregation of resin beads were explored first. Alcohol **1a** and its silyl ether **1b** were suspended in a range of solvents; the former aggregated in toluene or cyclohexane, the latter in ethanol (weakly) or DMF, indicating the inverse relationship between functional group polarity and disposition to aggregation in a given solvent. Further experiments demonstrated that all the resins **2**, **3** and **5** possessing unsaturated chains were aggregated in cyclohexane and fully dispersed in DMF. On this basis a protocol for the desired inter-bead Diels–Alder reaction was established. Approximately equal quantities of stained resin **3** and resin **2** were briefly sonicated together and then stood in toluene or cyclohexane. After 20 h there was considerable aggregation which persisted on transfer to suspension in DMF. On standing longer the degree of aggregation increased after the same treatment, and after an extended period agglomeration was observed.

Two more quantitative approaches were then attempted. Samples of resins **2** and **3** were mixed by sonication as before, centrifuged together for a defined period (0–75 min, 6500 rpm), suspended in the minimum quantity of DMF (centrifugation was not necessary in order to observe the described phenomena, but shortened the timescale). After completion the suspension was transferred to water on a microscope slide, causing considerable dispersal of aggregates, and observed by microscopy. The following observations were made, facilitated by the staining of the diene with maleimide **6** before reaction.



Scheme 1 *Reagents*: (i) neat cyclopentadiene, rt, 3 d; (ii) xs. maleimide, C_7H_8, rt, 6 d.

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† A colour version of Fig. 1 is available as supplementary data from the RSC web site, see http://www.rsc.org/suppdata/cc/1999/1507/

Table 1 Analysis of bead–bead contacts after centrifugation in DMF and resuspension in water

	No. of beads		No. of contacts							
t/min	Diene **3**	Dienophile **2**	**3**–**3**	**2**–**2**	**2**–**3**	Total beads	No. in aggregation	Total contacts[a]	Statistical **2**–**3**	Actual **2**–**3**
0	213	445	43	54	96	658	273	193	0.438	0.497
30	700	1051	77	109	449	1751	780	635	0.480	0.707
75	703	1119	233	155	832	1822	1006	1220	0.487	0.682

[a] Includes single and multiple contacts.

(a) The extent of aggregation and the average size of aggregates increased with time; without mechanical intrusion the proportion of **2**:**3** (heterotopic) contacts was significantly higher than statistical, the proportion of **2**:**2** and **3**:**3** (homotopic) contacts likewise significantly lower than statistical expectation. Results are recorded in Table 1.

(b) When either resins **2** or **3** was subjected to the same treatment separately, no aggregation phenomena were observed.

(c) The nature of the interface was distinct for **2**:**3** contacts when compared to **2**:**2** or **3**:**3** contacts. For the latter, the point of contact was not defined, so that two or three beads made visible rolling movements, the stable state of most trimers being triangular. In contrast, association between beads **2** and **3** occurred at a fixed point and the interaction was stable (Fig. 1). Alternating linear tetramers were observed, but rarely higher states of linear aggregation. These aggregates could move freely maintaining their inter-bead vectors. By carrying out the staining procedure *after* inter-bead reaction, it was verified that heterotopic interactions (**2**:**3**) were uniquely responsible for the distinctive stable linear trimers and tetramers.

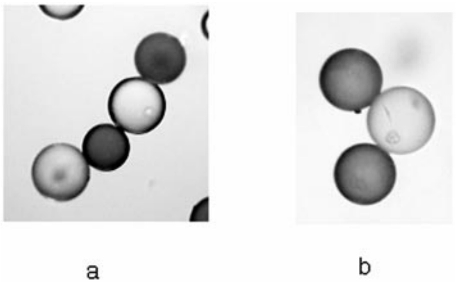


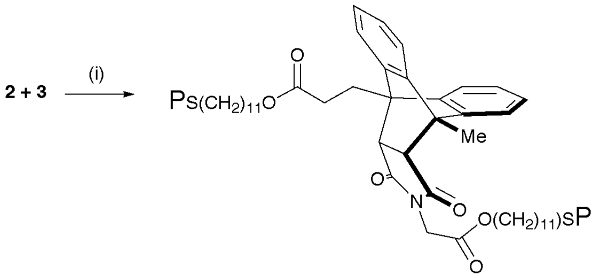
Fig. 1 Reaction of diene beads **3**, stained with Disperse Red to 1% of accessible functionality (dark spheres), with dienophile **2** in DMF (light spheres). Aggregates were located by microscopy after dispersal in water.

(d) Aggregates were not observed in control experiments involving the succinimide-capped resin **4** together with resin **3**, where complete dispersal to individual beads was observed on transfer to a polar medium.

(e) Aggregates formed in DMF were not broken down by exposure to maleimide (1 M in DMF, 20 min).

Although these aggregates were robust enough to be mechanically manipulated, their fragility is evident from the loss of adhesion after evaporation of all solvent DMF and attendant shrinkage of the beads.

Although the definitive explanation must await further studies at the nanochemical level, these experiments are best interpreted through the operation of a cycloaddition reaction occurring between diene and dienophile on separate beads, in the manner of Scheme 2. The beads remain undistorted, so that the extent of reaction is small. For a hard contact of a pair of beads 10^5 nm diameter in a solvent (DMF) of molecular volume 0.13 nm^3, the contact area is 7500 nm^3, with respectively 7×10^3 diene and 8×10^3 dienophile moieties in the surface segment. With long alkyl chains attached to an spatially irregular polymer backbone the surface of the bead will be rough at molecular dimensions, permitting reaction over a greater surface area than this. Since the activation free energy of the retro-Diels–Alder reaction is about 190 kJ mol^{-1},[10] each cycloaddition provides an interparticle bond of strength 3×10^{-19} J. Many bonding events are likely to be necessary to overcome shear forces.



Scheme 2 Suspend in DMF, sonicate 1–2 min, centrifuge 0–75 min, 5000 rpm.

There are few precedents for a well-defined reacting system with the components confined to different surfaces. A reasonable analogy can be made with the work of Sasaki and Maeda,[11] who studied peptide–peptide interactions with one component bound to magnetic polystyrene beads and the other bound to 5 μm controlled pore glass beads. Recent work of Whitesides and co-workers has been concerned with surface adhesion of micromachined objects through controlled hydrophobic or hydrophilic character of surfaces.[12] Our aims are to develop these present observations and define the scope and limitations of solid–solid interfacial chemistry.

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