Pergamon

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LETTERS

'Tailored' polymers for supported syntheses using boronic acids[†]

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Abstract

A diethanolamine pendant polystyrene polymer was prepared by the copolymerization of diethanolaminomethyl styrene, styrene, and divinylbenzene. The composition of the polymer resins produced agreed with copolymerization starting ratios. The polymer resins readily immobilized phenylboronic acid in THF and released pure phenylboronic acid quantitatively in THF/water/acetic acid.
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Many synthetic systems that attempt to mimic natural systems have employed hydrogen bonding as the main binding force. Such systems have met with great success in non-hydrogen bonding solvents, which are non-competitive with the guest for the binding pocket. Synthetic hydrogen bonding systems may yet evolve and make a successful transition into water. But, if the transition cannot be made, boronic acids may be the answer. Simple boronic acids rapidly and reversibly form cyclic esters with diols albeit in basic aqueous media.[1–3] Boronic acids with a neighboring amine have been used for the recognition and development of sensors for saccharides in neutral aqueous media.[4–12]

To date all the compounds have been prepared using traditional solution phase chemistry. From our experience the reactions are high yielding but the boronic acid product is difficult to isolate and purify. We believe that polymer supported synthesis may offer a solution to the isolation and purification problem.

Polymer supported synthesis requires the immobilization of a substrate on to solid support. Last year, two groups reported the preparation of phenylboronic acid derivatives using diol resins. Hall et al. prepared a modified *N*,*N*-diethanolaminomethyl styrene (DEAM) resin; the

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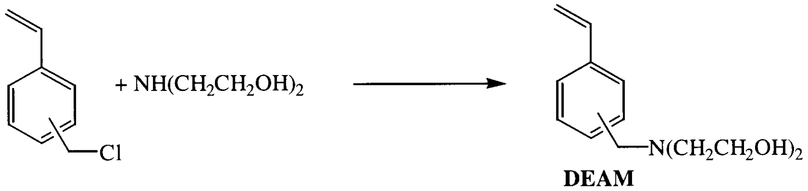
resin was prepared from aminomethylated polystyrene resin and ethylene oxide in a 'high-pressure bottle'.[13,14] Carboni et al. prepared a macroporous support using diol appended styrene-based monomer.[15,16] These polymer resins were useful for preparation of phenylboronic acid derivatives and also for solid state Suzuki coupling reactions.[13–16]

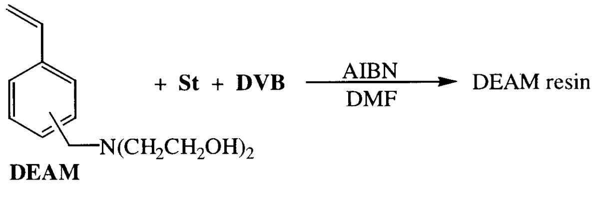
With this research we have developed 'tailor-made' DEAM polymer resins using a much simpler approach to that previously reported.[13,14] Our method requires the preparation of DEAM monomer, and then copolymerization of the DEAM monomer with styrene (St, comonomer) and divinylbenzene (DVB, crosslinker). This method for the preparation of DEAM polymer is very convenient, since we can choose the comonomer and crosslinker, and the copolymerization ratio. We can also choose the method of polymerization (radical polymerization, anion polymerization), polymer type (random, block) and resin types (powder by homogeneous polymerization or beads by heterogeneous polymerization). We believe that the method outlined will be very useful in the preparation of a variety of DEAM polymer resin. With this research we used radical polymerization initiated by AIBN. The DEAM polymer resins formed were evaluated for loading and release of phenylboronic acid.

DEAM monomer was readily prepared according to Scheme 1 from readily available starting materials. The DEAM monomer was prepared from chloromethyl styrene (3- and 4-isomer) and diethanolamine in the presence of potassium carbonate in acetonitrile at room temperature for 20 h under a nitrogen atmosphere. The reaction mixture was purified by column chromatography on silica gel (chloroform/methanol = 30/1 v/v) to give a yellow viscous oil (86%).



Scheme 1. Preparation of DEAM monomer

DEAM resins were prepared using DEAM monomer, St, and DVB, and initiated by AIBN in DMF at 65°C for 24 h under a nitrogen atmosphere (Scheme 2 and Table 1). The DEAM polymer resin was poured into water (to remove DMF), methanol (to remove DEAM monomer) and acetone/methanol (to remove St, DVB and oligomers) the DEAM polymer resin was then dried under vacuum at <70°C for 1 day. These DEAM resins gave a white powder of ca. 60% yield. The DEAM content in these resins was determined by elemental analysis, this result was concordant with the copolymerization-starting ratio (Table 1).



Scheme 2. Copolymerization of DEAM resins

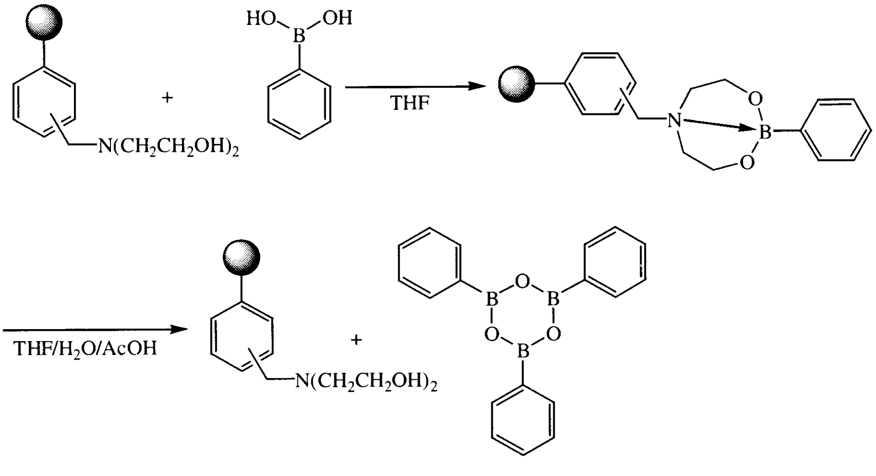
Table 1
Copolymerization of DEAM polymer resins

No.	DEAM/St/DVB (mole ratio)	DEAM content (mmol g^{-1})	Yield (%)	Elemental analysis % Found (calculated)			Recovery of PBA[b]
				C	H	N	%
1	15/70/15	1.19	62	85.17 (85.29)[a]	7.89 (8.04)[a]	1.45 (1.65)[a]	100
2	20/70/10	1.54	62	84.91 (84.87)	8.25 (8.07)	2.08 (2.15)	100
3	12/83/5	0.98	58	87.69 (87.84)	8.02 (7.96)	1.61 (1.37)	97

[a] Calculated including 0.1 mol% H_2O.

[b] Loading was conducted by shaking a slightly excess of DEAM resin (200 mg) with PBA (0.8 equiv.) in dry THF (5.0 ml) at room temperature for 1 h. The release was carried out for all PBA bound DEAM resins in THF/water/acetic acid mixture (90/5/5 volume ratio) (5.0 ml) at room temperature for 1 h.[13]

Phenylboronic acid (PBA) was immobilized on the DEAM polymer resin by stirring in anhydrous THF at room temperature for 1 h. The resin was then filtered, and washed with anhydrous THF. Cleavage of the phenylboronic acid was achieved in THF/acetic acid/water = 90/5/5 at room temperature for 1 h.[13,14] Then resin was filtered, and washed with THF. The solvent was removed, and the residue was dried in vacuo. The purity of the recovered phenylboronic acid anhydride was determined by ^{1}H NMR (in DMSO-d_6) and electrospray mass spectroscopy (M^+ 311) (Scheme 3).



Scheme 3. Loading and release of phenylboronic acid

In conclusion a DEAM polymer resin has been prepared via a new approach using the radical copolymerization of DEAM monomer with St and DVB. The DEAM polymer resins prepared were analyzed using elemental analysis, the results are concordant with the copolymerization-starting ratio. The DEAM polymer resins were loaded with phenylboronic acid, phenylboronic acid was then released from the DEAM polymer resins. The released phenylboronic acid had a high purity. Current work is directed to using the resins as supports for reactions using phenylboronic acid units. We are also optimizing the synthesis of DEAM polymer resins using different comonomers.

We believe that these DEAM polymer resins will be useful in the preparation of phenylboronic acid derivatives and in solid state Suzuki coupling reactions; of course, these DEAM resins will also be used in combinatorial chemistry.

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