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Formation of Linear Polymers with Pendant Vinyl Groups via Inclusion Complex Mediated Polymerization of Divinyl Monomers

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Cross-linked polymers obtained by simultaneous polymerization/cross-linking of monomers containing multiple double bonds find a wide range of applications, such as ion exchange resins, adsorbents, molecularly imprinted polymers, supports for reagents in organic synthesis, enzyme immobilization, and drug delivery systems. A sequential approach wherein a soluble linear polymer is first synthesized, isolated, condensed with a functional monomer, and then cross-linked offers significant advantages.[1a−c] Soluble linear poly(ethylene glycol dimethacrylate), that is, poly(EGDMA), containing pendant unsaturation could be obtained by esterifying poly(methacrylic acid) with 2-hydroxyethyl methacrylate (HEMA). However, it is not clear if complete conversion could be achieved without cross-linking or homopolymerization of HEMA. There is a need to devise a one-step methodology since recent approaches have led to hyperbranched structures.[2a−c] Cyclodextrins (CD) form host−guest complexes with a variety of organic compounds and polymers.[3a−g] Polyrotaxanes are stabilized by hydrogen bonding between the hydroxyl groups of neighboring CDs and secondary valence interactions between the repeat unit of the polymer and the hydrophobic cavities of CDs.[3a−e] Complexation of anisole with α-CD suppressed the reaction at the *ortho* position and enhanced the *p*/*o* ratio of the chlorinated product from 1.48 to 21.6.[4]

Polymerization of methacrylate and methacrylamide monomers could be carried out in aqueous media as the solubility of monomers was enhanced by complexation with CD.[5] 1,4-Butane diol diacrylate completely penetrated the CD cavity when it formed a complex with dimethyl-β-CD (DM-β-CD), whereas in the case of the 1,4-butane diol dimethacrylate, the CD ring was located at the terminal end of the guest molecule.[6] Polymerization of the diacrylate−CD complex in water resulted in cross-linked polymers containing CD.[6]

In this communication, we report that CDs form a 1:1 inclusion complex (IC) with divinyl monomers, such as EGDMA and ethylene glycol methacrylate 4-vinyl benzoate (EGMAVB). Polymerization of the complex in a medium, in which it is stable and both the complex and the polymer are soluble, leads to a solvent soluble, linear polymer containing a free methacrylate group per repeat unit since the methacrylate group included in the CD cavity does not react with the growing radical chain.

The ICs, EGDMA-β-CD, and EGMAVB-β-CD were obtained by a precipitation method from aqueous solutions of β-CD. EGDMA-DM-β-CD complex was isolated by a solvent evaporation method. The FTIR analysis of the EGDMA-β-CD complex showed the shift in ester carbonyl stretching vibrations from 1720 to 1726 cm^{-1}, which is comparable to that reported by Jeromin and Ritter.[7] The O−H stretching band at 3370 cm^{-1} of β-CD shifted to 3323 cm^{-1} and was narrowed. This shift was attributed to replacement of intramolecular hydrogen bonding in native β-CD by intermolecular hydrogen bonding between the guest molecule and β-CD.[3b−e]

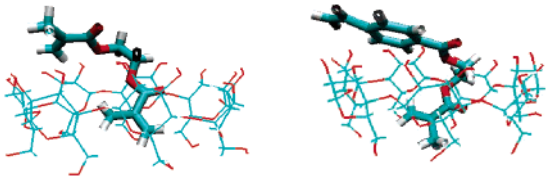

Figure 1. The lowest energy conformation of (a) EGDMA and (b) EGMAVB obtained through molecular dynamics simulations.

The stoichiometry of IC was established by ^{1}H NMR analysis.[3a−d] The peak at δ 4.34 corresponds to four protons of EGDMA (−OCH_2CH_2O−), and the peaks at δ 4.48 and 4.82 correspond to seven protons of β-CD for (−CH_2OH) and (C_1−H), respectively. The integration shows formation of a 1:1 EGDMA-β-CD complex. EGMAVB-β-CD and EGDMA-DM-β-CD also formed 1:1 ICs.

The cross polarization and magic angle spinning (CP/MAS) solid-state ^{13}C NMR spectra of the complexes display well-resolved, single peaks for each carbon of all glucose units. Also, the peaks at ∼78.59 and ∼101 ppm, corresponding to C_1 and C_4, adjacent to a conformationally strained glycosidic linkage, disappeared. These results indicate symmetrical conformation of glycosidic linkage due to inclusion of the EGDMA molecule within the cavity of β-CD.[3a−e] The X-ray diffractograms of EGDMA-β-CD and EGMAVB-β-CD exhibit a cage-type structure.[3a−f] Mass spectral analysis showed that both EGMAVB and EGDMA formed a 1:1 complex with β-CD.[3g]

The conformational analyses of EGDMA and EGMAVB, their complexation with β-CD, and thermodynamics of oligomerization were analyzed by computational studies. The force field and density functional theory, B3LYP/6-31G, calculations indicate that the bent conformation is more stable than the linear one by 3−5 kJ/mol. The complexation of the ligands with β-CD was analyzed by docking, quantum chemical, and molecular dynamics simulations using Autodock 3.0.5,[8] Gaussian 03,[9] and AMBER 8.0[10] programs, respectively. The lowest energy complex, obtained from the Autodock calculation, was taken as the initial structure for MD simulations. TIP3P water models were used as solvent, and equilibration was performed for 500 ps and MD simulation was carried for 2 ns. The MD simulations of EGMAVB complexation with β-CD revealed that the conformation wherein the styrene end is outside the cavity is stable (Figure 1).

Computations were also carried out to ascertain if the monomers could bind to a second β-CD. Docking studies and the subsequent binding energies evaluated at the B3LYP/6-31G level of theory revealed that the complexation of the ligand with the first β-CD has substantial stabilization of the order of 50−100 kJ/mol, while the addition of a second β-CD does not provide substantial stabilization (see Supporting Information). Thus, the observed 1:1

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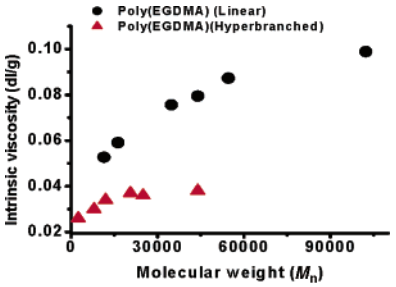

Figure 2. Intrinsic viscosity versus molecular weight for linear and hyperbranched[2a] poly(EGDMA).

complexation and the preferential polymerization at the styrene end of EGMAVB are supported by the computations carried out.

The EGDMA-β-CD complex was polymerized in *N*,*N*′-dimethylformamide (DMF) at 65 °C in the presence of azobisisobutyronitrile (AIBN). FTIR analysis showed that the isolated polymer was free from CD[6] and soluble in solvents, such as DMF, dimethyl sulfoxide (DMSO), chloroform ($CHCl_3$), and tetrahydrofuran (THF). ^{1}H NMR analysis showed that only one of the two unsaturated sites of EGDMA participated in polymerization.

Intrinsic viscosity versus molecular weight plots for two poly(EGDMA)s are shown in Figure 2. The Mark−Houwink−Sakurada exponent for the hyperbranched poly(EGDMA) is 0.14, while the value for the polymer synthesized by us is 0.29. The values of M_w obtained by multi-angel laser light scattering (2.16×10^5) and by gel permeation chromatography (2.46×10^5) are comparable. In contrast, the values differ by an order of magnitude for the branched polymers.[2c] The second virial coefficient (3.5×10^{-4} mol mL/g^2) for poly(EGDMA) of M_w 2.16×10^5 obtained by us is closer to that for linear polystyrene (4.4×10^{-4} mol mL/g^2) of M_w 2.9×10^5 than for the hyperbranched poly(EGDMA) (7.5×10^{-6} mol ml/g^2) of M_w 7.68×10^5.[2c] These results confirm that the polymer obtained by us is linear.

The formation of a soluble, linear polymer in DMF was attributed to the fact that DMF stabilizes the IC.[11] Synthesized poly(EGDMA) is soluble in DMF, and presumably CD encapsulates the methacrylate group even after polymerization. To prove this, the photoinitiator Irgacure was added to the polymer solution, which was then cast into films and exposed to UV irradiation. The film did not cross-link, indicating thereby that the methacrylate group was still included in the CD cavity, which suppressed cyclization and cross-linking reactions.[12] The complex comprising EGDMA and DM-β-CD is soluble in $CHCl_3$ and so is poly(EGDMA). Polymerization of the EGDMA-DM-β-CD complex in $CHCl_3$ resulted in a soluble polymer in which only one double bond of EGDMA reacted during polymerization, and the unreacted double bonds in the cavity of CD appeared as pendant unsaturation. Polymerization of the EGDMA-DM-β-CD complex in water resulted in cross-linked product, as poly(EGDMA) is insoluble in water.[6] During polymerization, DM-β-CD slips off the growing polymer chain, exposing the unsaturated group to the growing radical chain.

Although the IC and the polymer are both soluble in DMSO, the polymerization of the complex in DMSO yielded cross-linked product, as it is rapidly dethreaded in DMSO.[13]

Polymerization of allyl methacrylate in early stages leads to soluble polymers since the allyl group is less reactive and participates in polymerization only during later stages of polymerization.[14] In contrast, the two unsaturated groups in EGMAVB are almost equally reactive. This is evident from the fact that, in the spectrum of EGMAVB polymer prepared at low conversion and in the absence of CD, the peaks at δ 6.69−6.83 (q), 5.92, 5.83 (d), 5.42, and 5.37 (d) are due to the presence of a styrenic double bond, and the peaks at δ 5.59 and 6.15 are due to the methacrylate double bond. The integration shows that 58% of the styrenic double bond reacted, while 42% of the methacrylate double bonds reacted. The ^{1}H NMR analysis of poly(EGMAVB) prepared by the polymerization of the EGMAVB-β-CD complex showed that the peaks at δ 5.59 and 6.15, characteristic of the methacrylate double bond, and that the peaks corresponding to the styrenic double bond disappeared. This proves unequivocally that the methacrylate group included within the CD cavity does not participate in polymerization.

Poly(EGDMA) containing pendant unsaturation was cast into films and cross-linked by both thermal and UV irradiation. FTIR analysis showed no unsaturation, and T_g of the polymer was enhanced from 74 to 93 °C. The polymer solution was suspended in aqueous medium and cross-linked to yield microparticles. Cross-linking below critical concentration leads to nanoparticles in the range of 30−40 nm.

In summary, we have demonstrated that, in the polymerization of divinyl monomers, the double bond included in the CD cavity does not react with the growing radical chain. This results in soluble, linear polymers containing pendant vinyl unsaturations. These can subsequently be cross-linked by UV irradiation to yield films, micro-, and nanoparticles or grafted with hydrophilic monomers.

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Supporting Information Available: Inclusion complexation, polymerization, NMR, FTIR, XRD, MASS, molecular modeling DSC, and GPC data. Complete refs 9 and 10. This material is available free of charge via the Internet at http://pubs.acs.org.

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