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Preparation and Characterization of Environmental Functional Poly(Styrene-*Co*-2-[(Diethylamino)Methyl]-4-Formyl-6-Methoxy-Phenyl Acrylate) Copolymers for Amino Acid Post Polymerization

Momen S. A. Abdelaty*

Polymer Lap, Chemistry Department, Faculty of Science (Assiut), Al-Azhar University, Cairo, Egypt
Email: *abdelatymomen@yahoo.com

Abstract

Vanillin was used as renewable resource for preparing new monomer in two stops. The monomer has tertiary amine group which facilitates the pH change and functional aldehyde group that encourages the formation of Schiff base. It was abbreviated by DEAMVA and evaluated using chemical analysis e.g. ^{1}H NMR, ^{13}C NMR and FT IR all data were in logic case. Copolymerization of Styrene with 5 and 15 mol% of DEAMVA has been done by free radical polymerization and AIBN as initiator. The copolymers have been chemically and physically characterized e.g. ^{1}H NMR, FT IR, GPC, and DSC. Post polymerization of poly (styrene-*Co*-DEAMVA) with 15 mol% (III b) was prepared for immobilization of tryptophan and investigated by the same methods used lately. Moreover, the sensitivity of the posted copolymer to pH has also studied by UV-vis. Spectroscopy. Scanning electron microscopy (SEM) was used to study the morphological feature of polymer surface after immobilization of tryptophan.

Keywords

Environmental, Functional, Styrene, Vanillin, Amino Acid,
Post Polymerization

1. Introduction

Environmental pH-responsive polymers are polyelectrolytes that have weak

acidic or basic groups in their structure and either accept or release protons in response to changes in environmental pH. The acidic or basic groups on polyelectrolytes undergo ionization just like acidic or basic groups of mono-acids or mono-basic [1] [2]. By generating the charge along the polymer backbone, the electrostatic repulsion results in an increase in the hydrodynamic volume of the polymer [3] [4]. This transition between tightly coiled and swollen state is influenced by any condition that modify electrostatic repulsion, such as pH, ionic strength, and type of counter ions. The transition from collapsed state to expanded state has been explained by changes in the osmotic pressure exerted by mobile counter ions neutralizing the network charges [2]. Several applications for pH-responsive polymers and hydrogel are especially in the field of biomedicine e.g. Drug delivery systems and Gene carriers [5]-[11].

Several scientists were looking for new alternatives of styrene monomer due to its disadvantages such as, hazardous air pollutants and emitting during metering mixing process and curing; additionally the unreacted styrene continues to be released from composites during life cycle [12]. Renewable resources like (cellulose, starch, natural oil… etc.) have been used as alternative to produce bio-based monomers [13]. The lignin produced from Vanillin becoming relatively easily accessible; still there are only a handful of reports on attempts to utilize vanillin as monomers for bio-based polymer synthesis [14] [15]. Several chemical modifications on vanillin have occurred due to the presence of both aldehyde and hydroxyl active groups [2] [16]. The dimerization and the Polymerization of vanillin through electrochemical reductive with horseradish peroxidase have recently been discussed [17].

Schiff's base has also been played a vital role in the coordination chemistry and was found to be stable under oxidative and reductive conditions [18]. Vanillin was used to prepare Schiff bases [19]. The biological activity of Schiff's base polymers have been widely reported by several authors [20] [21] [22] [23] [24]. The most interested articles used Schiff base as a stimuli-responsive linker in the polymer chain which has been published by Yuan *et al.* [25]. The imine linkage is very sensitive to pH value which is responsible on the responsive feature of the polymer molecule [26] [27]. The formation of complexes with the imine can also be used to demonstrate the pH responsiveness of the linker [28]-[33]. Several publications have reported "click chemistry" as linkers for many bio-based molecules [34] [35] [36]. Here, we synthetized new functional polystyrene polymers by copolymerization with pH-responsive monomer from vanillin as renewable resource. The aldehyde group in the copolymer chain was used for grafting biomolecule by Schiff base click reaction. In future our work will focus on the applications of these kinds of polymers and their gel in the bio-separation for many kinds of biological macromolecule.

2. Experimental

2.1. Material

Acryloyl chloride (98% Merck), (AIBN Acrōs) 2,2'-azobis (isobutyronitrile) was

recrystallized from methanol, styrene (99% Acrōs), vanillin (99% Acrōs), triethylamine (Merck), tryptophan (97% Acrōs). Dichloromethane, toluene, tetrahydrofuran (THF), and diethylether were distilled over potassium hydroxide. Other chemicals were used as received.

2.2. Instruments

Bruker AV 500 spectrometer was used to record ^{1}H and ^{13}C NMR spectra in DMSO d[6] or CDCl$_3$ at 500 MHz and 125 MHz, respectively. Vertex 70 Fourier transform infrared instrument for recording IR spectra. The samples were milled with dry potassium bromide KBr (Merck 99%) and pressed to pellets. The Molecular weights (M) and polydispersity (Đ) were analysed by size exclusion chromatography (SEC). Chloroform was used as eluent (containing of 0.1 vol% triethylamine) with a flow rate of 0.75 mL/min (Jasco 880-PU pump) with a Waters RI-Detector and toluene as internal standard at 30°C. The samples (15 mg/mL) were injected by hand via a 20 μL loop. PSS-SDV columns filled with 5 μm gel particles with a defined porosity of 10^6 Å (guard), 10^5 Å, 10^3 Å and 10^2 Å respectively were used. Molecular weight determination was based on narrow polystyrene standards. UV/vis spectrometer (Perkin Elmer Lambda 45) was used to determine the concentration of amino acid in grafted polymer. The pH of polymer solution was in THF and measured by pH-meter model VWR pH 100. Perkin Elmer Differential Scanning Calorimeter (DSC) Pyris 1 was used for the determination of T_g of solid polymers. The thermogram was recorded at heating and cooling rate of 5°C/min. The morphology of the polymer were examined by Scanning Electron Microscopy (SEM) using a Zeiss NEON 40 instrument (USA); 2 kV (30 μm aperture). Sputter coater is a Bal-Tec SCD 500 with a film thickness monitor QSG 100. We applied approx. 4 nm of gold-palladium (Au:Pd = 80:20).

2.3. Synthesis of Monomer

Synthesis of 2-[(Diethylamino)Methyl]-4-Formyl-6-Methoxy-Phenyl Acrylate (DEMAVA)

Step 1: Synthesis of 3-[(Diethylamino)Methyl)-4-Hydroxy-5-Methoxybenzaldhyde

A mixture of 10 g (0.065 mol) of vanillin, (4-hydroxy-3-methoxybenzaldehyde), 10 g (0.33 mol) of formaldehyde and 10 g of diethylamine (0.136 mol) was dissolved in 150 mL ethanol in 250 mL round bottomed flask fitted with reflux condenser. The mixture was refluxed in oil bath at 90°C - 100°C for 3 h. The mixture allowed cooling to room temperature. The solvent was removed under reduced pressure to collect the product. Yield%: 97%, Physical state: Yellowish white solid.

^{1}H NMR (500 MHz, CDCl$_3$): δ(ppm) = 1.18 (t, 6H, 12-CH$_3$), 1.26 (br., s, 1H, 8-OH), 2.73 (q, 4H, 11-CH$_2$), 3.92 (s, 2H, 9-CH$_2$), 3.94 (s, 3H, 7-CH$_3$), 7.25, 7,34 (dd, 2H, [4]J = 1.6, 3.3⁻-Ar-CH, 10-NH[+]), 9.77 (s, 1H, 1-CHO).

^{13}C-NMR (125 MHz, CDCl$_3$): δ(ppm) = 10.82 (2C, 12-CH$_3$), 46.35 (2C,

11-CH$_2$), 55.85 (1C, 10-CH$_2$), 56.01 (1C, 8-CH3), 109.68 (1C, 4$^-$-Ar-CH), 120.84 (1C, 4-Ar-CH), 125.75 (1C, 5-Ar-C), 127.99 (1C, 3-Ar-CH), 148.65 (1C, 6-Ar-CH), 154.87 (1C,7-Ar-C), 191.65 (1C, 2-C=O).

IR (KBr): ν (cm^{-1}): 2987 (s) (CH$_2$, CH$_3$), 1650 (s) (2-C=O,), 1706 (s) (7-C=O), 820 - 868 (m) (Ar-CH).

Step 2: Synthesis of 2-[(Diethylamino) Methyl]-4-Formyl-6-Methoxyphenyl Acrylate

13.9 g (0.058 mol) of 3-[(diethylamino) methyl)-4-hydroxy-5-methoxybenzaldhyde (I) was dissolved in 200 mL dry CH$_2$Cl$_2$ in two neck flask fitted with argon balloon. During stirring 12.3 g (0.12 mol) of TEA was added. The reaction mixture allowed cooling in ice bath to 0°C - 5°C. After cooling, 5.4 g (0.059 mol) acryloyl chloride was added drop wise. The yellowish suspension was stirred at 5°C for 1 h, and then allowed to stir at RT for 6 h. The precipitate was filtered and solvent was evaporated under reduced pressure. The product was extracted by CH$_2$Cl$_2$ and wash three times with 100 ml dest. water then one time with 0.1 M Na$_2$CO$_3$, and again with 100 mL dest. Water, then product dried with MgSO$_4$ overnight. Yield%: 80%, Physical state: Orange solid.

^{1}H NMR (500 MHz, CDCl$_3$): δ(ppm) = 1.10 (t, 6H, 14-CH$_3$), 2.48 (q, 4H, 13-CH$_2$), 3.51 (s, 2H, 11-CH$_2$), 3.88 (s, 3H, 7-CH$_3$), 6.06 (dd, ^{2}J = 1.3 Hz, ^{3}J = 10.40 Hz, 1H, 10a-CH), 6.37(dd, ^{3}J = 10.40 Hz, ^{3}J = 17.30 Hz, 1H, 9-CH), 6.63 (dd, ^{2}J = 1.3 Hz, ^{3}J = 17.30 Hz, 10b-CH), 7.25, 7.34 (dd, 3H, ^{4}J = 1.6, ^{4}J = 1.9, 3.3$^-$-Ar-CH), 9.77 (s, 1H, 1-CHO).

^{13}C-NMR (125 MHz, CDCl$_3$): δ(ppm) = 10.82 (2C, 12-CH$_3$), 46.35 (2C, 11-CH$_2$), 55.85 (1C, 10-CH$_2$), 56.01 (1C, 8-CH3), 109.68 (1C, 4$^-$-Ar-CH), 120.84 (1C, 4-Ar-CH), 125.75 (1C, 5-Ar-C), 127.99 (1C, 3-Ar-CH), 148.65 (1C, 6-Ar-CH), 154.87 (1C, 7-Ar-C), 191.65 (1C, 2-C=O).

IR (KBr): ν (cm^{-1}): 2987 (s) (CH$_2$, CH$_3$), 1650 (s) (2-C=O,), 1706 (s) (8-C=O), 820 - 868. (m) (Ar-CH).

2.4. Synthesis of Polymer

2.4.1. Synthesis of Poly (Styrene-*Co*-DEAMVA) with 5 and 20 mol% of DEAMVA (II a,b)

A mixture of 5 and 20 mol%, 0.544 g and 1.632 respectively of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate, 4 g (0.038 mol) styrene and 10^{-3} mol% AIBN of the total mole% of monomers was dissolved in 50 mL toluene and added in 100 ml round bottom flask. The reaction mixture was purged in argon for 20 min, and then heated in oil bath at 70°C - 80°C with stirring for 6 h. After cooling at room temperature and also in refrigerator, the polymer was precipitated by solvent evaporation using rotatory evaporator. Polymer was purified by dissolved in THF, and re-precipitated in diethylether to remove the unreacted monomers and impurities. Yield %: 94%, and 86 for 5, and 20 mol% respectively, Physical state: Yellowish white solid.

^{1}H NMR (500 MHz, CDCl$_3$): δ(ppm) = 0.50 - 2.71 (m, 9H, CH, CH$_2$-styrene

repeating unit, 2CH$_3$ DEAMVA), 3.25 - 3.93 (m, 9H, 2CH$_2$, NCH$_2$, OCH$_3$ DEAMVA), 4.60 - 5.13 (m, 3H, CH, CH$_2$-DEAMVA repeating unit), 6.30 - 7.52 (m, 6H, H-Ar), 9.75 - 9.97 (br., 1H, -CHO).

IR (KBr): ν (cm^{-1}): 2990(s) (CH-Aliphatic), 1720-1743 (s) (-C=O), 1134 (s) (-OCH$_3$).

2.4.2. Synthesis of Grafted 20 mol% (III a) Poly (Styrene-*Co*-DEAMVA) with Tryptophan (IV) as a Function of pH

In 50 ml round bottom flasks 1.0 g of 20 mol% P (Styrene-*Co*-DEAMVA) and 1.0 g of (tryptophan) was dissolved in 30 mL THF. The reaction was taken place in different pH solutions (pH4, pH7, pH9, pH10, pH12) by addition of NaOH and HCl. The mixtures were stirred gently for 2 h at room temperature. Solvent was evaporated under reduced pressure. The precipitate was dissolved in THF and re-precipitate in diethylether at −40˚C to remove impurities and unreacted molecules. Physical state: Brownish solid.

^{1}H NMR and IR of Poly (Styrene-*Co*-DEAMVA)-g-Tryptophan at pH12 (IV)

^{1}H NMR (500 MHz, DMSO): δ(ppm) = 0.70 - 1.22 (m, 6H, 2CH$_3$ DEAMVA), 1.30 - 1.65 (m, 1H, CH repeating Styrene), 1.82 - 2.35 (m, 2H, CH$_2$ repeating styrene), 2.80 - 2.90 (m, 2H, 2NCH$_2$ DEAMVA), 3.30 - 3.40 (m, 2H, CH$_2$, DEAMVA), 6.10 - 6.34 (m, 1H, C=CH, tryptophan), 6.80 - 7.85 (m, 9H, H-Ar), 8.5 - 8.6 (br. (s), 1H, CH=N), 9.30 - 9.942 (s) 1H, NH, tryptophan).

IR (KBr): ν (cm^{-1}): 2995(m) (CH-Aliphatic), 1663-1650 (s) (7-C=O), 1570 - 1560 (s) (4-CH=N), 1026-1107 (s) (8-OCH$_3$).

3. Results and Discussion

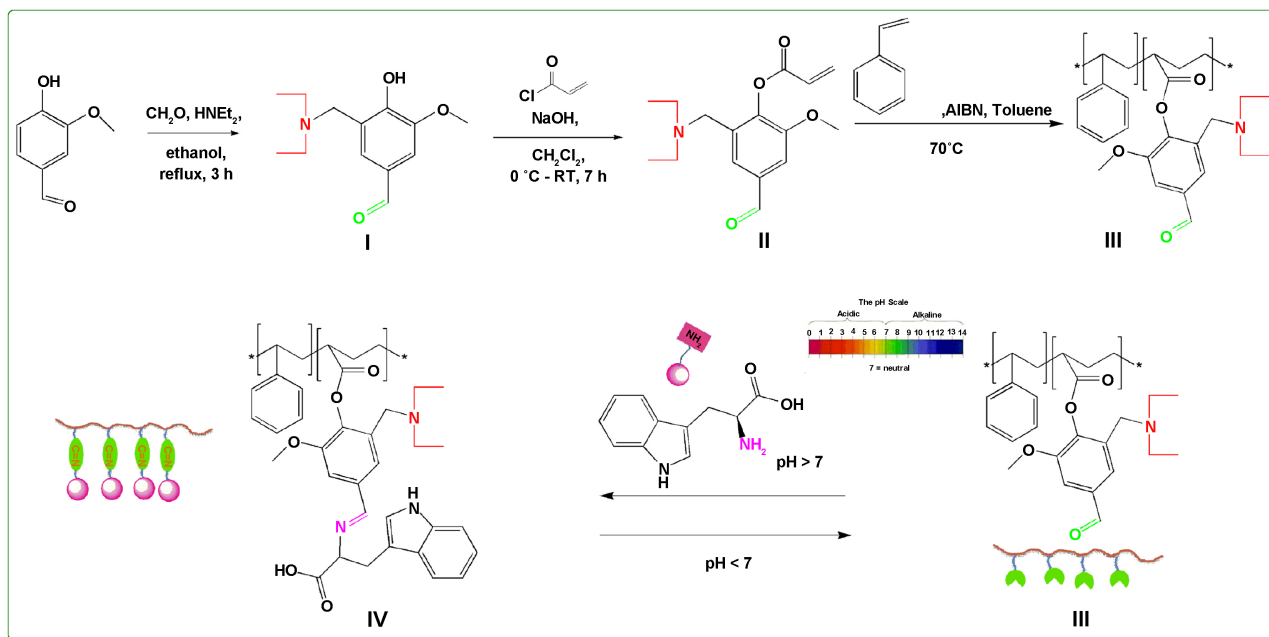### 3.1. Synthesis of Monomer, Copolymers and Grafted Copolymers

Scheme 1 describes the chemical procedure for synthetizing monomer, copolymers and grafted copolymers. Monomer (II) or 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate and abbreviated by (DEAMVA), it was fabricated in two steps reaction. The first step Is the formation of (3-[(diethylamino)methyl]-4-hydroxy-5-methoxy-benzaldehyde) and has been done by the reaction of vanillin with diethylamine and formaldehyde according to Mannich reaction mechanism. In this reaction we did not use any catalysis especially acid catalysis which famous to use in Mannich reaction. The second Step Is the formation of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate (DEMAVA). This was achieved by reaction of compound (I) with acryloyl chloride in the presence TEA to form (II). They have chemically evaluated by ^{1}H NMR and ^{13}C and FT IR in Figure 1, Figure 2 and Figure 5. All data was in logic state and proved the presence of active aldehyde group at 9.97 ppm and 196 ppm.

To improve the functionality of styrene free radical polymerization with 5 and 20 mol% of DEAMVA has been done in the presence of AIBN as initiator as described in Scheme 1. The chemical structure of each polymer was evaluated

**Scheme 1.** Synthesis of DEAMVA, copolymers and grafted polymers with Tryptophan.
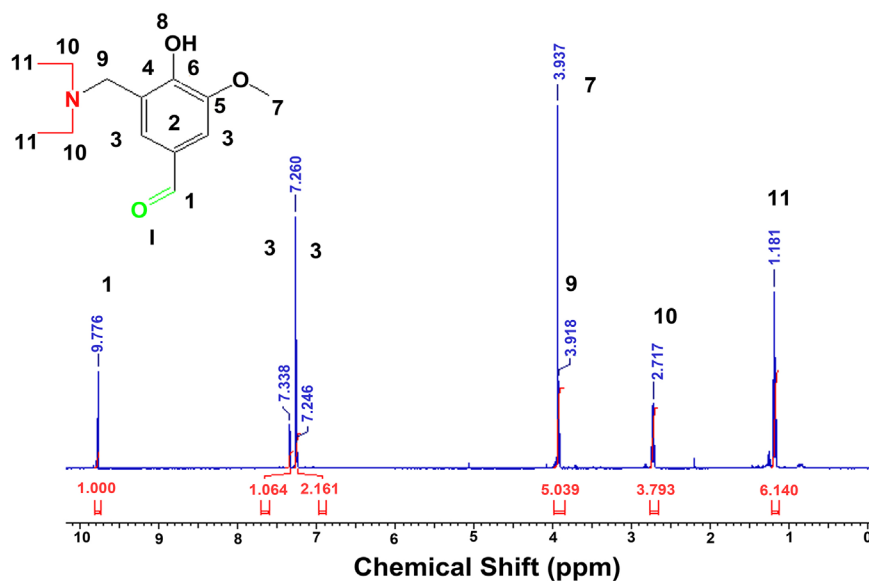
Figure 1. ^{1}HNMR (CDCl$_3$) of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate.

by ^{1}H NMR and FT IR as shown in **Figure 3** and **Figure 5**. The ^{1}HNMR of co-polymers **II a-b** showed specific broad multiples peaks at δ = 0.73 - 1.35 ppm of 2CH$_3$ DEAMVA, at δ = 7.08 - 7.62 ppm of Ar-H of each styrene and DEAMVA, and at δ = 9.94 of H-CHO of DEAMVA monomer. FT IR showed the presence of (C=O stretch) ester at 1745 cm^{-1}. The actually composition of each monomer in the copolymer chain was calculated from ^{1}H NMR spectra by the ratio of the intensity of the signals at 6.66 ppm (for H, Ar-H styrene) with signal at 9.94 ppm (for CHO of DEAMVA) as cleared in **Table 1**.
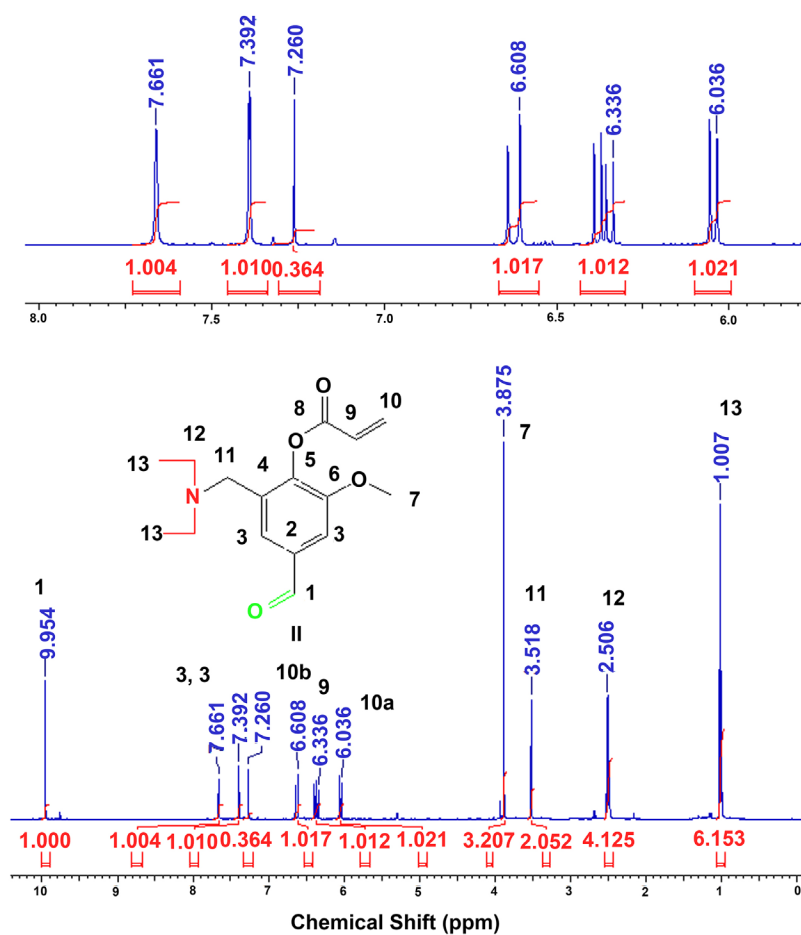
Figure 2. ^{1}H NMR (CDCl$_3$) of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate (DEMAVA).
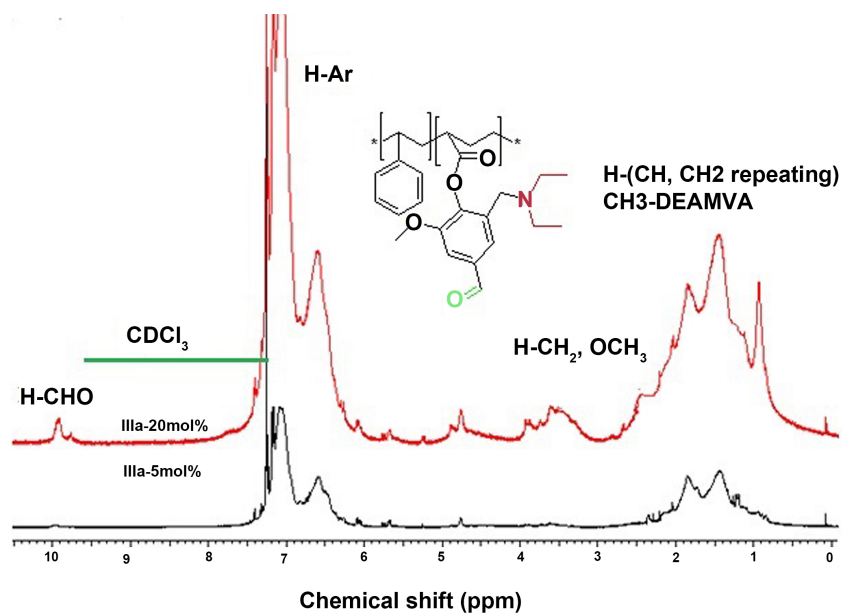
Figure 3. ^{1}H NMR spectra (CDCl$_3$) of P (Styrene-*Co*-DEAMVA) 5, 20 mole ratio of DEAMVA.

Table 1. Yield, composition, conversation, number average molecular weight, polydispersity, and glass temperature of, Poly (Styrene-*Co*-DEAMVA) 5, 20 mole ratio of DEAMVA and grafted Poly (Styrene-*Co*-DEAMVA).

Polymer	Yield (%)	^{1}HNMR DEAMVA (mol%)	Conversion (%)	Mn^a (g/mol)	$Đ^b$	T_g^c (°C)
III a	94	3.35	-	47400	1.98	110
III b	86	15.67	-	18260	2.27	130
IV	78	-	88	16578	2.46	135

^{a}Number average molecular weight, ^{b}Polydispersity, ^{c}Glass transition temperature, ^{d}Lower critical solution temperature.

Functionality with the aldehyde group in the polymer main chain was an interested to make grafting with any amino compound to produce Schiff's base which is familiar by click reaction **Scheme 1**. The grafting process has been done at room temperature in THF at different pH (pH4, pH7, pH9, pH10, pH12). Grafted copolymers were elucidated by ^{1}H NMR and FT IR as shown in **Figure 4** and **Figure 5**. The ^{1}H NMR showed the disappearance of aldehyde signal at 9.74 ppm and formation of imino (HC=N) signal at about 8.5 ppm as shown **Figure 4**. **Figure 5** showed FT IR spectra and proved the presence of (C=N stretch) imine at about 1563 cm^{-1}.

3.2. Polymer Characterization

3.2.1. Molecular Weight

Size exclusion chromatography was used for determination of molecular weight (Mw), number average molecular weight (Mn) and polydispersity (Đ) of polymers using Polystyrene (PS) as standard in CHCl$_3$. **Table 1** has summarized all recorded data for all copolymers. **Figure 6** shows the relation between molecular weight and log M as recoded by GPC and demonstrates one peak, proofing the disappearance of low molecular weight like monomers or impurities.

3.2.2. Conversion of Poly (Styrene-*Co*-DEAMVA) to Poly(Styrene-*Co*-DEAMVA)-g-Tryptophan

The conversion of poly (Styrene-*Co*-DEAMVA) to poly (Styrene-*Co*-DEAMVA)-g-tryptophan through the chemical reaction, absorption has been measured as function with pH at constant time 2 h for each run. The polymer solution has diluted to 10^{-3} W/V for each measurement. **Figure 7** shows the UV.vis. Spectroscopy of grafting reaction between poly(Styrene-*Co*-DEAMVA) with tryptophan. The relation between wavelength and absorbance proofed the disappearance of C=O aldehyde group at 250 - 270 nm and formation of new bond at 340 - 380 nm of C=N imine linkage. The formation of imino linkage has increased with increasing the pH value starting with pH5 which showed about zero absorbance and has been increased gradually till the highest value of absorbance pH12. **Figure 8** shows the relation between pH and absorbance intensity at constant time.
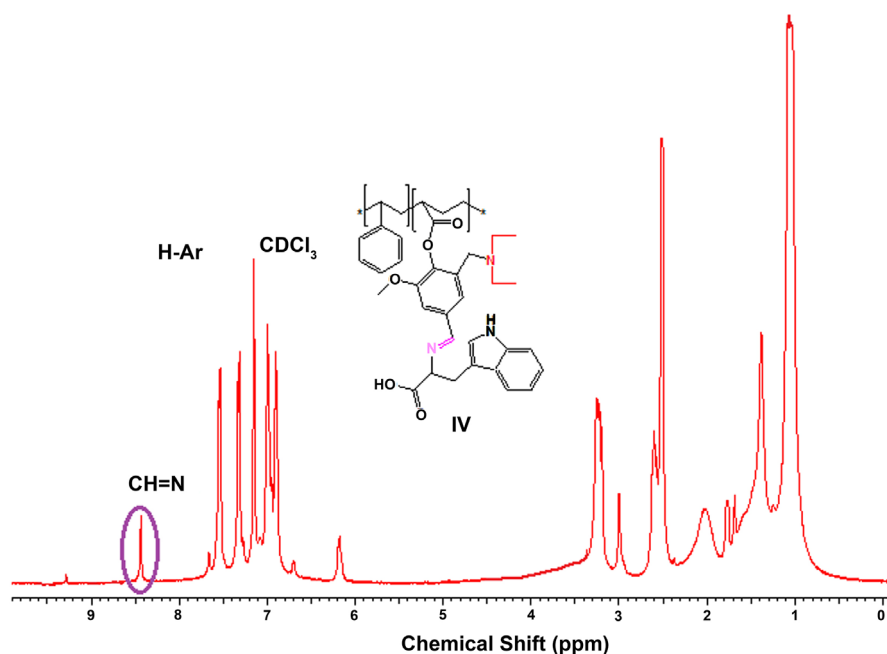
Figure 4. ^{1}H NMR spectra (DMSO) of P (Styrene-*Co*-DEAMVA)-g-Tryptophan.
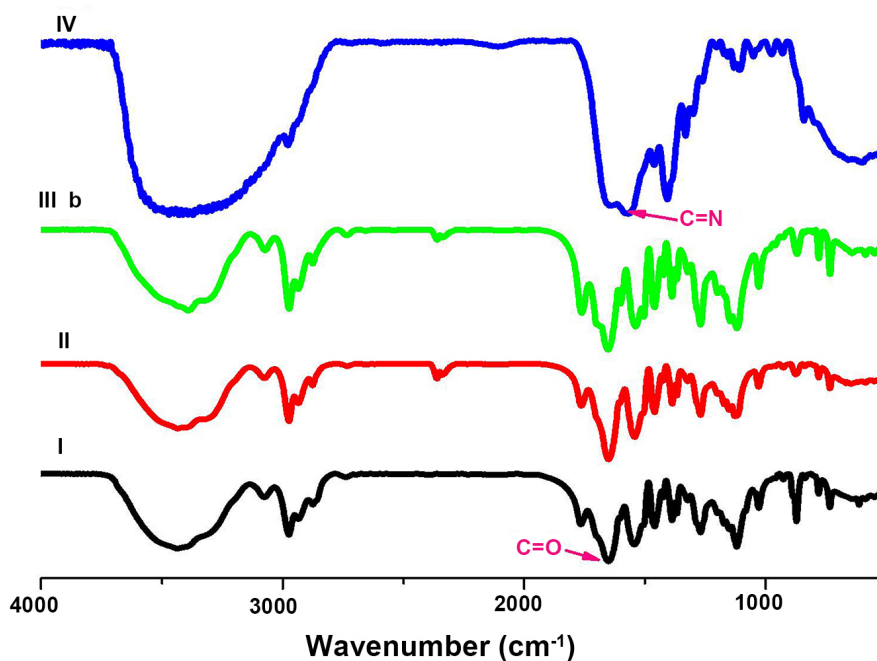

Figure 5. IR spectra KBr for DEAMV (I), DEAMVA (II), Poly (Styrene-*Co*-DEAMVA) (III b) and grafted copolymers IV.

3.2.3. Glass Transition Temperature

The glass transition temperature (T_g) is very important parameters for solid material. It has been recorded by Differential Scanning Calorimeter of dried samples at heating rate 5°C/min as described in experimental part. The T_g was taken as the midpoint inflection. The ($T_g's$) values have been tabulated in **Table 1** for copolymers and grafted copolymers. **Figure 9** showed a single T_g for each
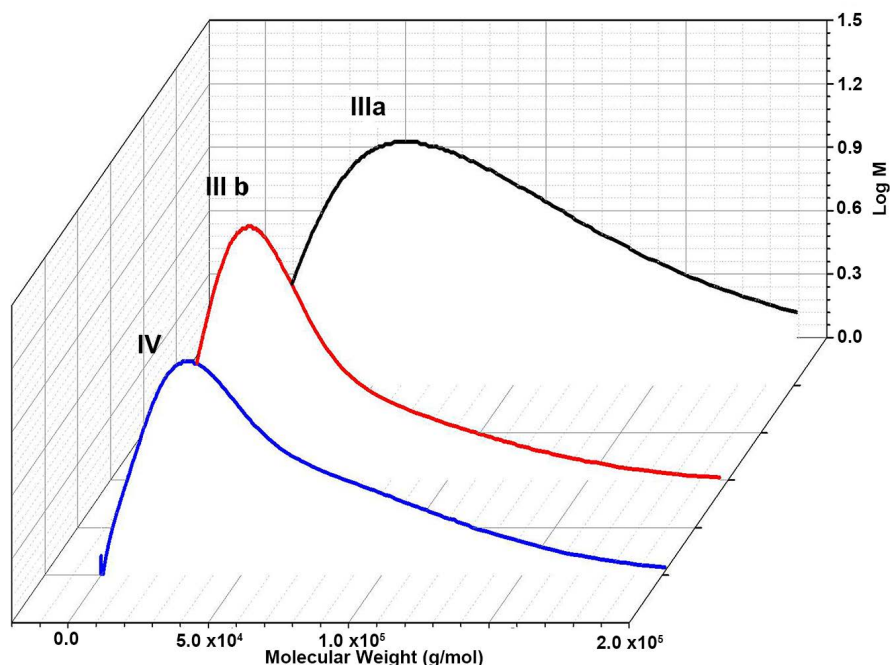
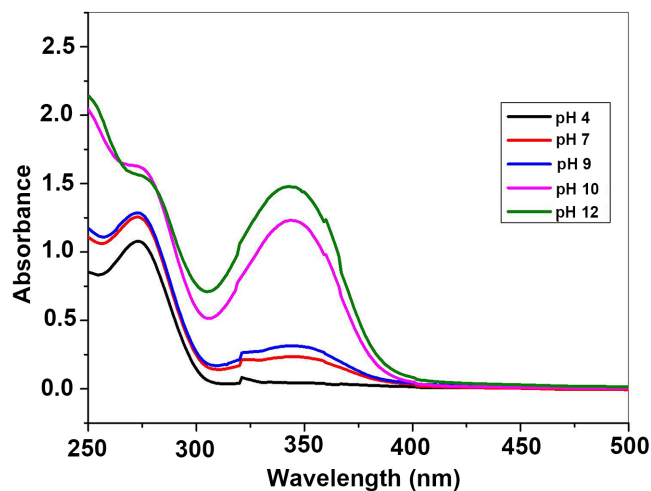**Figure 6.** GPC molecular weight of copolymers.

Figure 7. UV-vis. Spectroscopy for the formation of grafted poly (Styrene-*Co*-DEAMVA)-g-tryptophan as increasing in absorbance from pH5 - pH12.

sample, which indicating the formation of random copolymers [36]. The homo-polystyrene (PS) showed T_g at 100°C [37]. Incorporation of DEAMVA moieties in the copolymers chain with hydrophobic and hydrophilic groups demonstrated in aromatic and tertiary amine respectively resulted in increased T_g, which might be attributed to decrease in the spacing and hence greater interaction between polymer chains leading to lesser flexibility and T_g of the polymer increased [36]. Introducing grafting molecule in copolymer (**IV**) main chain has directly influenced on raising the T_g due to the steric hindrance of aromatic molecule.
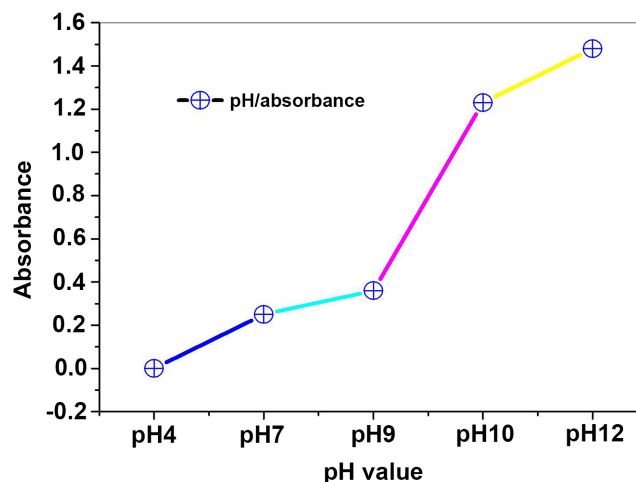
**Figure 8.** Relation between pH values to absorbance.
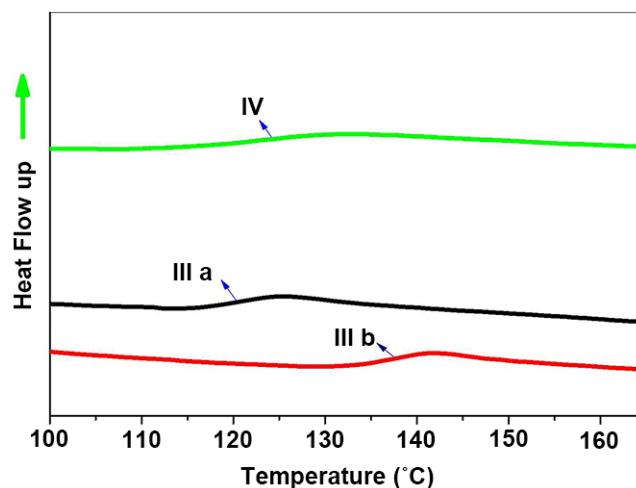
Figure 9. DSC shows the T_g of copolymers and grafted copolymer.

3.2.4. Morphological Feature (SEM)

Figure 10 is the Scanning Electron Microscopy (SEM) image obtained at a magnification of 1000× for grafted copolymer (IV). After grafting the porosity of the grafted polymer surface increases the whole surface looks like waxy with cross-linking referring to the imine linkage and grafting of tryptophan.

4. Conclusion

Here we synthetized new functional polystyrene copolymers. New pH responsive monomer with tertiary amine and aldehyde functional groups were prepared in two steps. Free radical polymerization of styrene with two different mole ratios of DEAMVA was used for synthetizing copolymers. The presence of aldehyde group facilitated the formation of Schiff base with primary amine. Tryptophan was used as biological molecule for immobilization. UV-vis. Spectroscopy was used to detect the immobilization and formation of Schiff base at different pH. We observed the highest absorption at pH12 and lowest at pH4. In
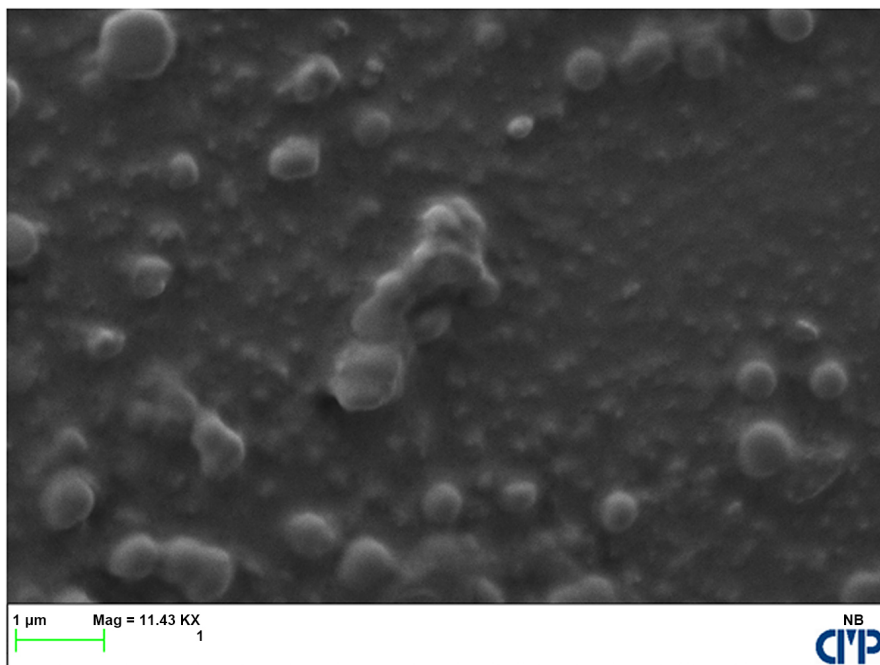
Figure 10. SEM of copolymer IV (grafting) copolymer with tryptophan 1000× magnification.

future, we are looking for using this kind of polymer and its gel in the separation of biomolecules.

Acknowledgements

Conflicts of Interest

The authors declare no conflict of interest.

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Graphical Abstract