



## **Fabrication and Characterization of Functional pH-Responsive Poly (S-Co-DEAMVA)-g-Tryptophan**

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### **Author's contribution**

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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### **ABSTRACT**

Vanillin was used to synthesize cationic monomers from the amine group with a tertiary amine. It has both an amine and an aldehyde group. For that, it helps graft to form Schiff base with amino acid-like tryptophan. It is abbreviated by {2-[(diethylamino) methyl]-4-formyl-6-methoxyphenyl acrylate} DEAMVA and evaluated by, e.g., <sup>1</sup>H NMR, <sup>13</sup>C NMR, and FT IR results were compared with the chemical structure elevated good agreement. 10 and 25 mol % of vanillin monomer was copolymerized with (S). The copolymers of poly (S-co-DEAMVA) were investigated by <sup>1</sup>H NMR, FTIR, GPC, and DSC. The grafting with tryptophan has also been modified and exposed to the same investigation methods; further, UV/Vis spectroscopy has designated the pH responsiveness. The study aims to improve the general characterization of polystyrene and produce functional pH-responsive polymer for graft biological molecules in the future.

*Keywords: Functional polymer; pH-responsive; styrene; vanillin; tryptophan; grafting modifications.*

### **1. INTRODUCTION**

Responsive polymers are the kind of polymers that change their properties by changing the environment. Among these, pH-responsive

polymers act as polyelectrolytes with the charged positive or negative group according to the amino or carboxylic group in the main chain of the polymer [1,2]. These charges change the electrostatic repulsion between polymer molecule

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and or and solution, producing a change in the hydrodynamically of the polymer volume [3,4]. Numerous applications of pH-responsiveness were unveiled in biotechnology, e.g., Drug delivery systems and Gene carriers [5-11]. Recently, polymer scientists revealed several disadvantages of styrene monomers and their related polymers. They are working hard to find new natural alternatives and have low toxicity, hazardous for the ecological and green environment [12,13]. Vanillin is an important material for producing lignin can be used as bio-based monomers for natural polymers [13-15]. Some modification has preceded the vanillin molecules using aldehyde or hydroxyl groups, which are sometimes used [16]. One of its modifications is dimerization in the electrochemical polymerization process [17].

In the last few decades, many scientists have been searching for green alternatives of styrene monomer due to its disadvantages like hazardous air pollutants and emitting during metering mixing process and curing; moreover, the unreacted styrene continues to be released from composites during the life cycle [12]. The reaction between primary amine and aldehyde to form a Schiff base has been used widely in organic chemistry [18]. It was reacted with vanillin and amines in a recent study [19], variety of biological activities was revealed and recently published [20-25]. The formations of the imine group in the Schiff compounds facilitate the pH responsiveness [27-33]. The reaction to form complex compounds by Schiff base has also been investigated as pH-responsive polymers [34-36]. In our study, we prepared new pH-responsive with copolymerization with styrene. The grafting reaction was done with tryptophan via Schiff base and the formation of imine linkage.

## 2. EXPERIMENTAL

### 2.1 Material

2, 2'azobis (isobutyronitrile) (AIBN, 99%, Sigma-Aldrich), acryloyl chloride (98%, Sigma-Aldrich), vanillin (99%, Sigma-Aldrich), styrene (99% Sigma-Aldrich), tryptophan (97 % Sigma-Aldrich). Other chemicals were used as received.

### 2.2 Instruments

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra in  $\text{CDCl}_3$  or  $\text{DMSO-d}^6$  at 500 MHz and 125 MHz were investigated by Bruker AV 500 spectrometer. Fourier transforms

infrared-FT IR vibrations by Vertex 70. Size exclusion chromatography (SEC) was used to measure the Molecular weights ( $M$ ) and dispersity ( $D$ );  $\text{CDCl}_3$  was used as eluent in 0.1 vol% TEA. Perkin Elmer Lambda 45-UV/vis spectroscopy was used for indicating the imine linkage. Perkin Elmer-differential Scanning Calorimeter (DSC) Pyris-1 has been implemented for the glass transition temperature  $T_g$  of at 5 °C/min.

## 2.3 Preparation of Monomer

### 2.3.1 Preparation of of {2-[(diethylamino)methyl]-4-formyl-6-methoxy-phenyl acrylate (DEMAVA)} [20]

**Step1:** Synthesis of {3-[(diethylamino) methyl]-4-hydroxy-5-methoxybenzaldehyde}[20]

A mixture of 5g (0.032 mol) of vanillic acid or vanillin (4-hydroxy-3-methoxy benzaldehyde), 5g (0.16 mol) of formaldehyde, and 5g of diethylamine (0.054 mol) have been dissolved in 60 ml pure ethanol in a 100 mL round flask fixed with a condenser. The solution was refluxed in an oil bath at 90-130 °C for 4h. Then, they were allowed to cool at room temperature. The solvent was taken off to get the product; yielded %: 96%, Yellowish white solid.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$ (ppm) = 1.18(t, 6H, 12- $\text{CH}_3$ ), 1.26 (br., s, 1H, 8-OH), 2.73 (q, 4H, 11- $\text{CH}_2$ ), 3.92 (s, 2H, 9- $\text{CH}_2$ ), 3.94 (s, 3H, 7- $\text{CH}_3$ ), 7.25, 7.34 (dd, 2H,  $^4J = 1.6, 3.3$ - Ar-CH, 10- $\text{NH}^+$ ), 9.77 (s, 1H, 1-CHO).

$^{13}\text{C}$ -NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$ (ppm) = 10.82 (2C, 12- $\text{CH}_3$ ), 46.35 (2C, 11- $\text{CH}_2$ ), 55.85 (1C, 10- $\text{CH}_2$ ), 56.01 (1C, 8- $\text{CH}_3$ ), 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):  $\nu$  ( $\text{cm}^{-1}$ ): 2987 (s) ( $\text{CH}_2$ ,  $\text{CH}_3$ ), 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 [20]

13.9g (0.058 mol) of 3-[(diethylamino) methyl]-4-hydroxy-5-methoxybenzaldehyde (I) was dissolved in 200 mL dry  $\text{CH}_2\text{Cl}_2$  in two neck flask fitted with an argon balloon. During stirring, 12.3 g (0.12 mol) of TEA was added. The reaction

mixture allowed cooling in an ice bath to 0-5°C. After cooling, 5.4g (0.059 mol) acryloyl chloride was added dropwise. The yellowish suspension was stirred at 5°C for 1h, and then allowed to stir at RT for 6 h. The precipitate was filtered, and the solvent was evaporated under reduced pressure. The product was extracted by CH<sub>2</sub>Cl<sub>2</sub> and washed three times with 100ml distilled water, then with 0.1M Na<sub>2</sub>CO<sub>3</sub>, and again with 100 ml distilled water. Then, the product dried with MgSO<sub>4</sub> overnight. Yield %: 80%, Physical state: Orange solid.

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ(ppm) = 1.10(t, 6H, 14-CH<sub>3</sub>), 2.48 (q, 4H, 13-CH<sub>2</sub>), 3.51 (s, 2H, 11-CH<sub>2</sub>), 3.88 (s, 3H, 7-CH<sub>3</sub>), 6.06 (dd, <sup>2</sup>J = 1.3 Hz, <sup>3</sup>J = 10.40 Hz, 1H, 10a-CH), 6.37(dd, <sup>3</sup>J = 10.40 Hz, <sup>3</sup>J = 17.30 Hz, 1 H, 9-CH), 6.63 (dd, <sup>2</sup>J = 1.3 Hz, <sup>3</sup>J = 17.30 Hz, 10b-CH), 7.25, 7.34 (dd, 3H, <sup>4</sup>J = 1.6, <sup>4</sup>J = 1.9, 3,3'- Ar-CH), 9.77 (s, 1H, 1-CHO).

<sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>): δ(ppm) = 10.82 (2C, 12-CH<sub>3</sub>), 46.35 (2C, 11-CH<sub>2</sub>), 55.85 (1C, 10-CH<sub>2</sub>), 56.01 (1C, 8-CH<sub>3</sub>), 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<sup>-1</sup>): 2987 (s) (CH<sub>2</sub>, CH<sub>3</sub>), 1650 (s) (2-C=O), 1706 (s) (8-C=O), 820- 868. (m) (Ar-CH).

## 2.4 Synthesis of Polymer

### 2.4.1 Preparation of poly (Styrene-co-DEAMVA) with 10 and 25 mol% of DEAMVA (2a)

A mixture of 10 and 25 mol%, 1.088 g, and 2.176 g respectively of 2-[(diethylamino) methyl]-4-formyl-6-methoxyphenyl acrylate, 4g (0.038mol) styrene, and 10<sup>-3</sup> mol% AIBN of the total mole% of monomers was dissolved in 70 ml toluene and then added to 100 ml round bottom flask. Nitrogen was purged, and in an oil bath, was heated at 70-75°C and stirred for 8h. They were precipitated by solvent evaporation, and then the polymer was purified in THF and diethyl ether. The product was yellowish-white solid.

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ (ppm) = 0.53-2.74 (m, 9H, CH, CH<sub>2</sub>- repeating unit, 2CH<sub>3</sub> DEAMVA), 3.27-3.96 (m, 9H, 2CH<sub>2</sub>, -N-(CH<sub>2</sub>)<sub>2</sub>, Ar-OCH<sub>3</sub>), 4.62-5.14 (m, 3H, CH, CH<sub>2</sub>-DEAMVA repeating unit), 6.32-7.53(m, 6H, H-Ar), 9.76-9.98 (br., 1H, Ar-CHO).

IR (KBr): ν (cm<sup>-1</sup>): 2990-3126(s) (CH, CH<sub>2</sub>-Aliphatic), 1722-1746 (s) (Ar-CHO), 1755-1765 (s) (-C=O, ester, 1144 (s) (Ar-OCH<sub>3</sub>).

### 2.4.2 Preparation of 25mol% (2A-25) Poly (Styrene-co-DEAMVA)-graft-tryptophan (2B) as pH-responsiveness

In 50 ml round bottom flasks 1.0 g of 25mol% poly(Styrene-Co-DEAMVA) and 1.0 g of tryptophan has been dissolved in 30 ml THF. The reaction was implemented in different pH solutions, pH 4, pH 7, pH 9, pH 10, and pH 12, by NaOH and HCl. The mixtures were stirred gently for 2 h at room temperature. The solvent was removed under reduced pressure. After that, the residue was dissolved in THF and re-precipitated in diethyl ether at -40 °C to remove impurities and unreacted molecules. Physical state: Brownish solid.

<sup>1</sup>H NMR and IR of poly (Styrene-co-DEAMVA)-post-Tryptophan at pH12 (IV)

<sup>1</sup>H NMR ( ( DMSO d<sub>6</sub>): δ (ppm) = 0.72-1.24(m, 6H, 2CH<sub>3</sub>), 1.30-1.65 (m, 1H, CH repeating unit), 1.84-2.37 (m, 2H, CH<sub>2</sub> repeating unit), 2.82-2.94 (m, 2H, 2-N(CH<sub>2</sub>)<sub>2</sub>, vanillin monomer), 3.30-3.40 (m, 2H, CH<sub>2</sub> vanillin monomer), 6.12-6.36(m, 1H, -C=CH, Try), 6.83-7.87(m, 9H, H-Aromatic), 8.6-8.8 (br. (s), 1H, CH=N, imine), 9.32-9.95 (s) 1H, NH, Try).

IR (KBr): ν (cm<sup>-1</sup>): 2995-3135(m) (CH, CH<sub>2</sub>-Aliphatic), 1723-1745 (s) (-C=O ester), 1665-1654 (s) (-CHO), 1573-1565 (s) (4-CH=N imine), 1036-1117 (s) (Ar-OCH<sub>3</sub>).

## 3. RESULTS AND DISCUSSION

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

Scheme 1 has illustrated The chemical methods of monomer 1B or {2-[(diethylamino) methyl]-4-formyl-6-methoxyphenyl acrylate} abbreviated by (DEAMVA); two steps have been implemented. The preparation of {3-[(diethylamino)methyl]-4-hydroxy-5-methoxy- benzaldehyde} was produced by reacting of vanillic acid or vanillin, diethylamine, and formaldehyde proceeding via Mannich reaction mechanism [1,20] and followed by the preparation of {2-[(diethylamino) methyl]-4-formyl-6-methoxyphenyl acrylate} (DEMAVA), by reacting 1A with acryloyl chloride and TEA to form 1B. They were evaluated by <sup>1</sup>H NMR, <sup>13</sup>C, and FT IR. Data has indicated an agreement

state and confirmed the aldehyde group at 9.97 ppm and 196 ppm, as shown in Figs. 1-3.

Styrene properties have been enhanced by free-radical copolymerization with 10 and 25 mol% of DEAMVA in AIBA, as in scheme 1. Their chemical structures were evaluated by both of  $^1\text{H}$  NMR and FT IR, as shown in Fig 4. The  $^1\text{H}$  NMR of copolymers 1A, 2A exhibited the broad multi-peaks (m) at  $\delta = 0.75\text{-}1.37$  ppm of  $(2\text{CH}_3)$  DEAMVA. Another multi-peaks was proved at  $\delta = 7.08\text{-}7.62$  ppm of Aromatic-H of each styrene and DEAMVA. At  $\delta = 9.96$  for the aldehyde proton H-CHO of DEAMVA. Further, the FT IR detected the functional groups; it illustrated the formation of  $(\text{C}=\text{O}$  stretch) ester at  $1747\text{ cm}^{-1}$ . The accurate concentrations of both monomers in the polymer main chain was obtained from the spectra of the  $^1\text{H}$  NMR from the ratios of the intensity of the peaks at 6.67 ppm (for H, Aromatic-H styrene) with peaks at 9.96 ppm (for -CHO of DEAMVA), all was summarized in Table 1.

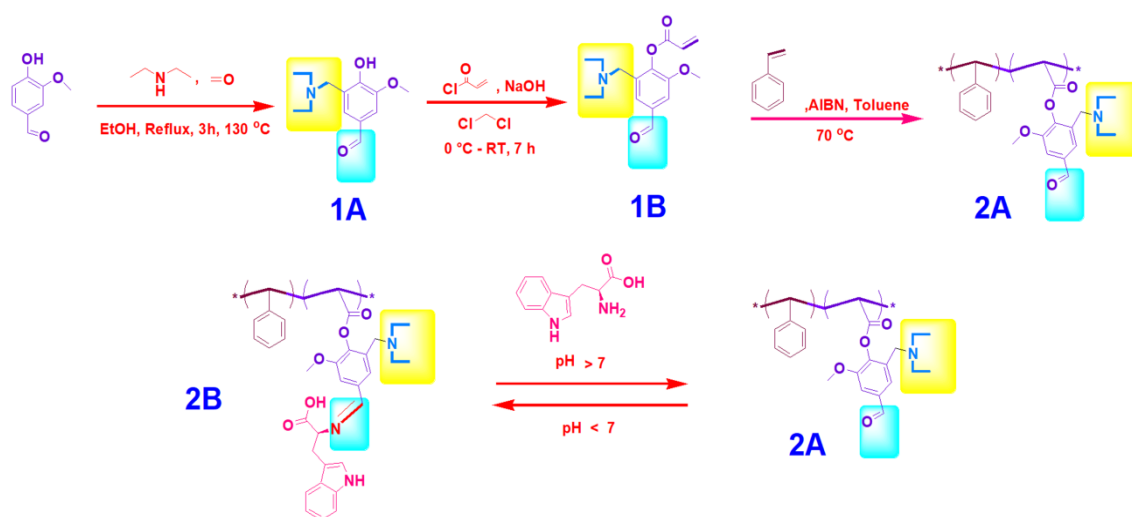
Using the aldehyde group for grafting tryptophan as the formation of Schiff base, The grafting

process was done at RT and in tetrahydrofuran THF as solvent as illustrated in Scheme 1. The reaction has occurred in a variety of pH solutions pH 4, pH 7, pH 9, pH 10, and pH 12. They were investigated via  $^1\text{H}$  NMR and FT IR. FT IR spectra in Fig 4 demonstrated the formation of imine  $(-\text{CH}=\text{N}$  stretch) at about  $1565\text{ cm}^{-1}$ . The aldehyde proton was disappeared, however, the imine  $(-\text{HC}=\text{N})$  was observed at about 8.6 ppm, as in Fig 3.

## 3.2 Polymer Characterization

### 3.2.1 Molecular weight

Gel permeation chromatography GPC is a technique used for measurements of number average molecular weight  $M_n$  and dispersity  $\mathcal{D}$  of copolymers and grafting one. Polystyrene (PS) has been used as a standard in chloroform. All data were summarized in Table 1. Fig. 6 illustrates the relationship between molecular weight and  $\log M$  recorded by the GPC. They exhibited one height peak; they indicated the disappearance of all low molecular weight, e.g., monomers or impurities.



**Scheme 1. Preparation of DEAMVA, copolymers, and graft-Tryptophan**

**Table 1. Yield, composition, conversion, number average molecular weight, dispersity, and glass temperature of, Poly (S-co-DEAMVA) 10, 25 mole ratio of DEAMVA and Poly (S-co-DEAMVA)-graft- Tryptophan**

Polymer number	Product yield (%)	$^1\text{H}$ NMR DEAMVA (mol %)	Conversion (%)	$M_n^a$ (g/mol) $10^4$	$\mathcal{D}^b$	$T_g^c$ (°C)
2A-10	92	6.45	-	45500	1.98	124
2A-25	83	16.67	-	18760	2.06	137
2B	77	-	85	17558	2.48	143

<sup>a</sup> Number average molecular weight; <sup>b</sup> Polydispersity, <sup>c</sup> Glass transition temperature

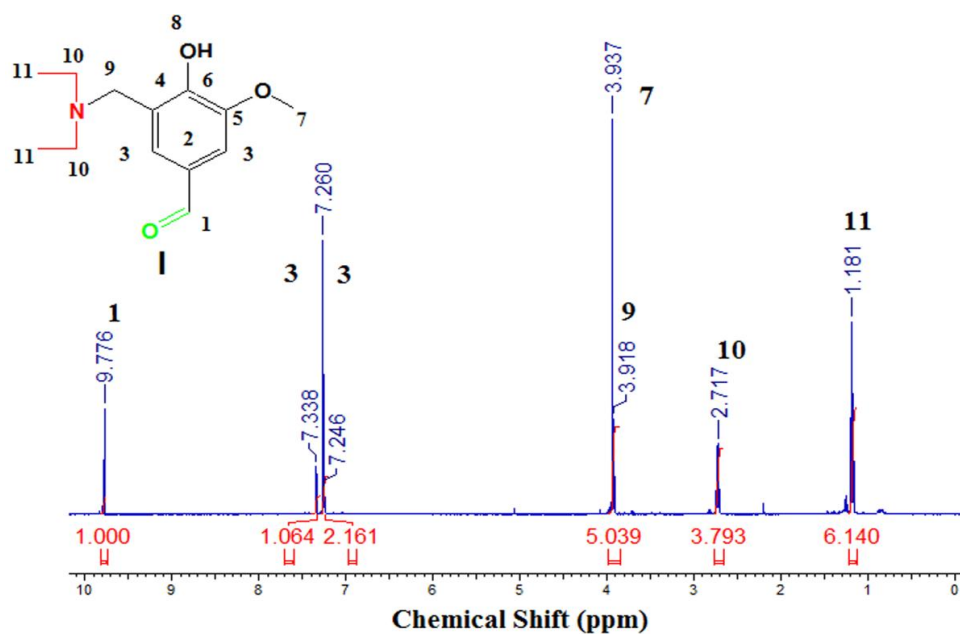


Fig. 1. <sup>1</sup>H NMR (CDCl<sub>3</sub>) of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate

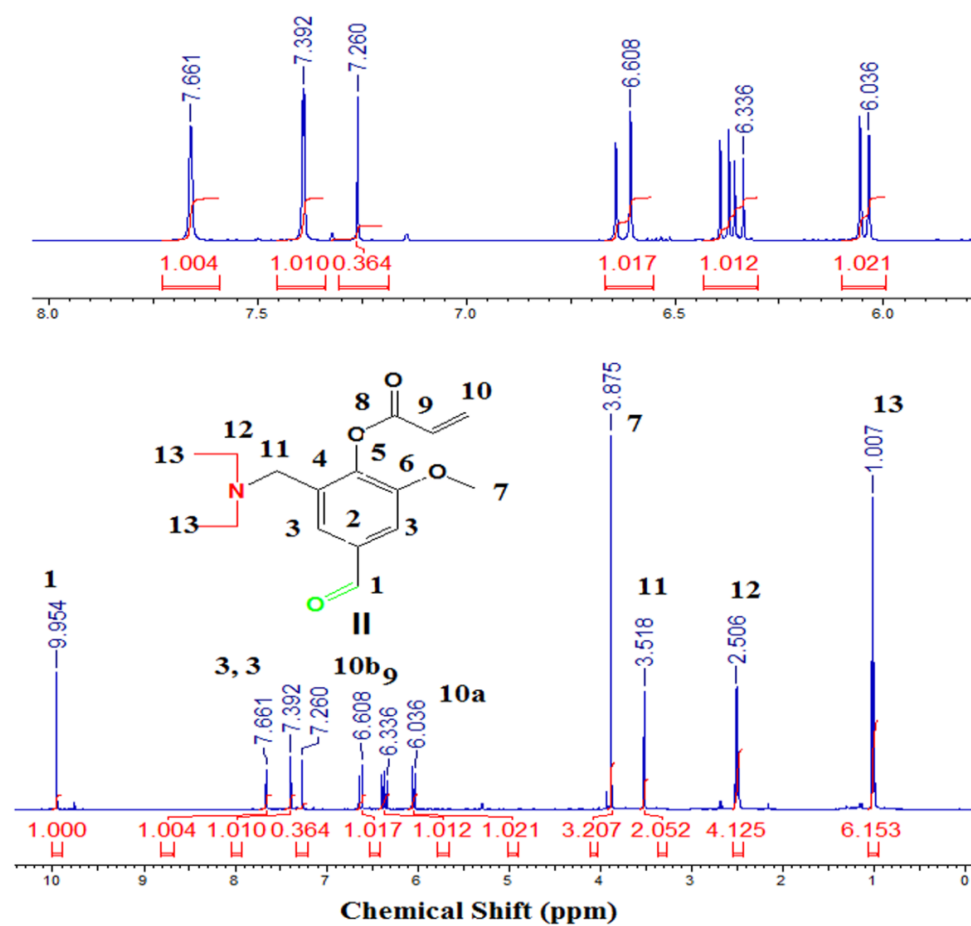


Fig. 2. <sup>1</sup>H NMR (CDCl<sub>3</sub>) of 2-[(diethylamino)methyl]-4-formyl-6-methoxyphenyl acrylate (DEMAVA)

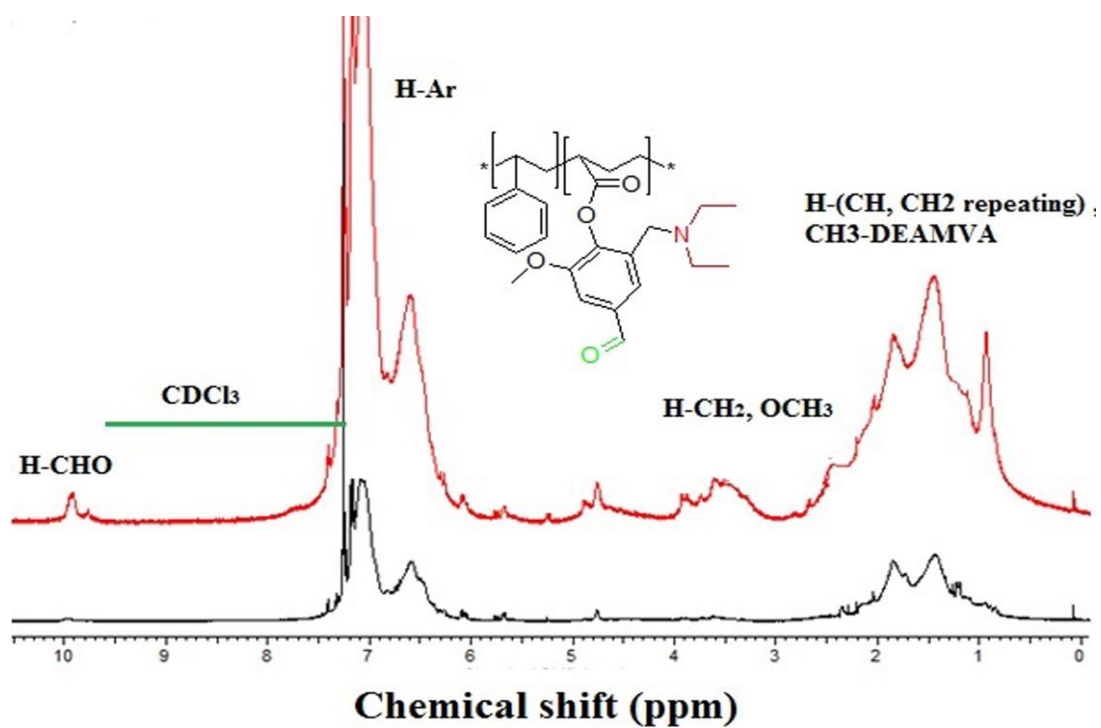


Fig. 3.  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ ) of P(S-co-DEAMVA) 10, 25 mole ratio of DEAMVA

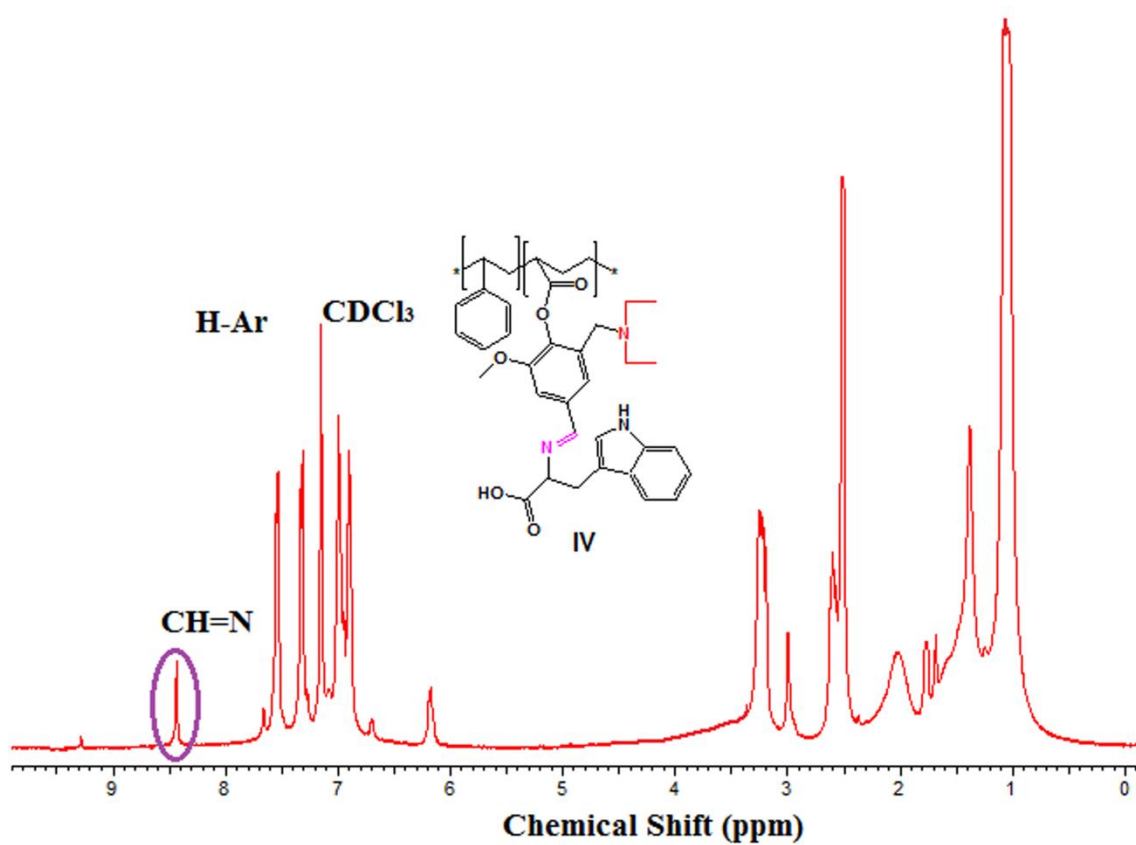


Fig. 4.  $^1\text{H}$  NMR spectra (DMSO) of P(styrene-co-DEAMVA)-g-Tryptophan

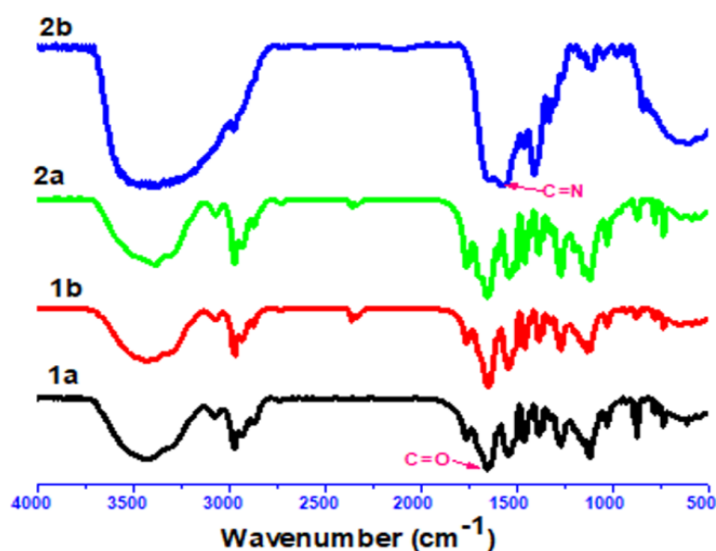


Fig. 5. IR spectra KBr for DEAMV (I), DEAMVA (II), Poly (Styrene-co-DEAMVA) (III b) and grafted copolymers IV

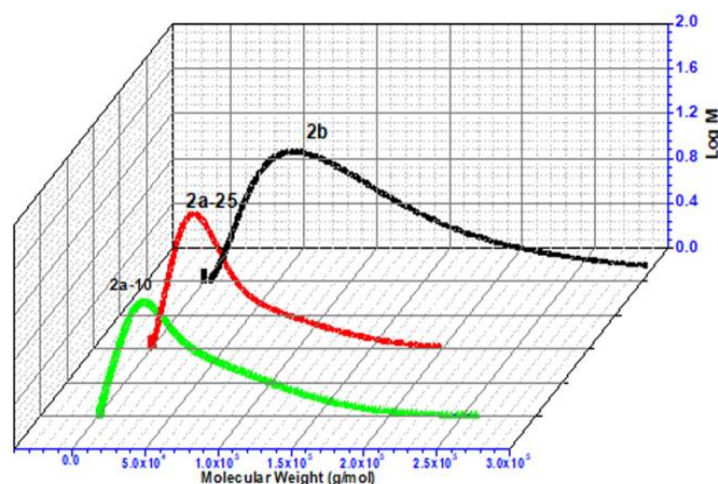


Fig. 6. GPC molecular weight of copolymers

### 3.2.2 Poly (Styrene-Co-DEAMVA)-g-try

The grafting process of poly (Styrene-Co-DEAMVA) to poly (Styrene-Co-DEAMVA)-g-tryptophan has been detected via the pH solutions in two hours for each run and  $10^{-3}$  W/V. the UV/Vis. Spectroscopy of the grafting reaction has been shown in Fig. 7. The disappearance of absorption of the -CHO aldehyde group at 255-275 nm; however, the new functional at 340-380 nm of -CH=N imine linkage has appeared. The intensity of the imine bond was sparked in the higher pH solutions over the highest absorbance in pH 12. The relationships of pH against the absorbance intensity were drawn in Fig. 8.

### 3.2.3 Thermal properties

Differential Scanning Calorimeter measured the thermal properties of copolymer and the grafted one at the heating rate  $5^{\circ}\text{C}/\text{min}$  to detect the glass transition temperature ( $T_g$ ). As shown in Fig. 9, the thermograms were recoded the  $T_g$  at the mid-point inflection; parameters were written in Table 1. Copolymers and graft-try demonstrated a single  $T_g$  to prove the formation of random polymerization [36]. A recent study showed the  $T_g$  of the homo-polystyrene (PS) at  $100^{\circ}\text{C}$  [37]. The copolymerization process of PS with DEAMVA shifted the hydrophobic/hydrophilic interactions represented increased  $T_g$  due to the lower spacing and

increased interaction between polymer chains, producing lesser flexibility and  $T_g$  of the polymer increased [36]. By grafting the tryptophan molecule in copolymer (2B), the  $T_g$  has sparked the steric hindrance of the aromaticity.

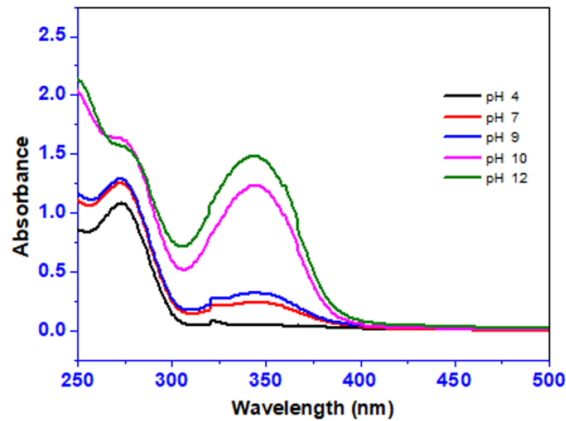


Fig. 7. UV/Vis. Spectroscopy of the grafted poly (Styrene-Co-DEAMVA)-g-try in pH 5-pH 12

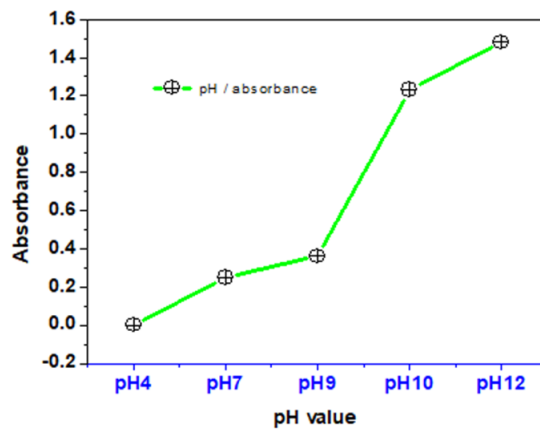


Fig. 8. The relationship of pH against absorbance

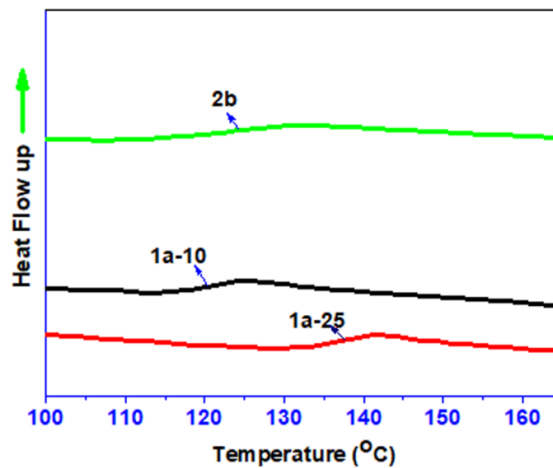


Fig. 9. The diffractogram and the glass transition temperatures  $T_g$  of copolymers and grafted copolymer



#### 4. CONCLUSION

The pH-responsiveness monomer has cationic tertiary amine and aldehyde groups in its main chain; it was prepared in two steps. We prepared functional polystyrene copolymers by free radical polymerization. Styrene was copolymerized with two-mole ratios of DEAMVA. The graft-copolymer has been formed via the reaction of the aldehyde group with tryptophan. The UV/Vis spectroscopy was implemented to record the graft-copolymer formation within the formation of the Schiff base and the absorption in various pH solutions. It was noted that the highest absorption was detected at pH 12; however, the lowest has occurred at pH 4.

#### DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

#### COMPETING INTERESTS

Author has declared that no competing interests exist.

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