

Pt(IV) Complexes with Polystyrene-bound Schiff Bases as Antimicrobial Agent: Synthesis and Characterization

Dilek Nartop, Nursen Sari, and Hatice Ögütçü

Abstract—Novel polystyrene-bound Schiff bases and their Pt(IV) complexes have been prepared from condensation reaction of polystyrene-A-NH₂ with 2-hydroxybenzaldehyde and 5-fluoro-3-bromo-2-hydroxybenzaldehyde. The structures of Pt(IV) complexes with polystyrene including Schiff bases have been determined by elemental analyses, magnetic susceptibility, IR, ¹H-NMR, UV-vis, TG/DTA and AAS. The antibacterial and antifungal activities of the synthesized compounds have been studied by the well-diffusion method against some selected microorganisms: (*Bacillus cereus* spp., *Listeria monocytogenes* 4b, *Micrococcus luteus*, *Staphylococcus aureus*, *Staphylococcus epidermis*, *Brucella abortus*, *Escherichia coli*, *Pseudomonas putida* spp., *Shigella dysenteria* type 10, *Salmonella typhi* H).

Keywords—Polymer-bound Schiff bases, polystyrene-A-NH₂, Pt(IV) complexes, biological activity.

I. INTRODUCTION

THE studies on complexation polymeric-Schiff base with various metal ions are important due to some potential properties such as high catalytic activity, ion selectivity, heat resistance, conductivity, thermal stability [1]-[4]. Polymers have wide applications for the synthesis of drugs as antimutagen and antibacterial. Therefore, there is considerable interest in the synthesis and characterization of these compounds. However, drug resistances against antibacterial agents may pose a problem in their use for medical purpose. The problem could be overcome by the preparation of metal complexes, using a process of chelation with the coordination of transition metal ions. It is well known that N and O atoms play a key role in the coordination of metals. Polymer-attached Schiff bases and metal complexes can be used antimicrobial polymers which are candidates for polymeric drugs due to their high biological activity [5].

Polymer-metal complexes are prepared by chemical reaction of polymeric ligands with metal ions, which have four

or six coordinate bonding sites. Pt(IV) complexes are typical example of these type polymer containing Schiff bases. Pt(IV) complexes are widely used as platinum-based anticancer drugs due to their biological activity and reduced toxicity [6]-[7].

Here in, to evaluation their antibacterial effects, novel modified polymers synthesized with condensation reaction of the polystyrene-A-NH₂ with 2-hydroxybenzaldehyde and 5-fluoro-3-bromo-2-hydroxybenzaldehyde (Fig. 1). The results of biological activity show that the synthesized modified polymers may be used in medicinal chemistry.

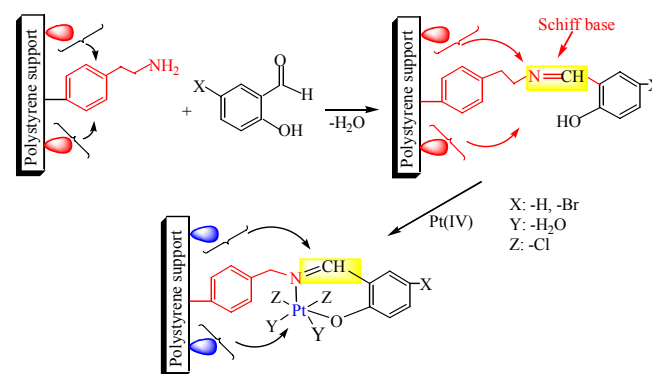


Fig. 1 Synthesis rotation of Pt(IV) complexes with polystyrene-bound Schiff bases

II. MATERIALS AND METHODS

A. Chemicals

All the chemicals were purchased from Sigma-Aldrich Company and used without further purification.

B. Apparatus for Characterization

The elemental analyses were determined on a Leco CHNS-932 analyzer. IR spectras were recorded on a Mattson-5000 FT-IR instrument in KBr pellets. ¹H-NMR spectra were taken on a Bruker Spectrospin Avance DPX-400 MHz instrument using TMS standard and DMSO-d₆ as solvent. UV-vis spectra were recorded on a Unicam-UV2-100 spectrophotometer with dimethylformamid (DMF). TG/DTA analysis was carried out by Setaram-simultaneous model thermal analyzer under nitrogen atmosphere the temperature range of 25-900°C at a heating rate of 10°C min⁻¹. Metal contents were obtained with a Philips PU 9285 instrument. Magnetic susceptibility measurements were taken at room temperature with MK-1 model Gouy balance of Christison Scientific Equipment Ltd.

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C. Synthesis of Polymer-Bound Schiff Bases (PS-Sch)

The polymeric-Schiff bases (PS-Sch) were synthesized by reacting of polystyrene-A-NH₂ (PS) (1g, 0.8–1.2mmol/g –NH₂ loaded, 1% cross-linked with divinylbenzene) in hot DMF (15mL) with 1.0mmol 2-hydroxybenzaldehyde/5-fluoro-3-bromo-2-hydroxybenzaldehyde in DMF (10mL) (Fig. 1). Aldehyde solutions were slowly added by the drop wise on amine solutions while stirring through 30min. The mixture was stirred under a reflux for 3h at 70°C. After refluxing, the product was cooled at the room temperature and washed by adding acetone. Finally, yellow crude product was filtered and dried in the oven and kept with desiccator over anhydrous CaCl₂.

D. Synthesis of Polymer-bound Schiff Base Complexes (PS-Sch-Pt)

The polymeric-Schiff base complexes (PS-Sch-Pt) were synthesized by reacting of polystyrene-A-NH₂ (PS) (1g, 0.8–1.2mmol/g–NH₂ loaded, 1%cross-linked with divinylbenzene) in hot DMF (15mL) with 1.0mmol 2-hydroxybenzaldehyde/5-fluoro-3-bromo-2-hydroxybenzaldehyde in DMF (10mL). The reaction mixture was boiled and stirred under a reflux condenser ca. 3h, at 70°C. Following this stage, PtCl₄ metal salt was added upon the mixture in about 15 minute and mixing process stirred ca. 3h (Fig. 1). After reflux stage, the product was cooled at the room temperature and washed by using acetone. Eventually, brown color product was filtered and dried in the oven and kept with desiccator over anhydrous CaCl₂.

E. Antimicrobial Evaluation

The antimicrobial investigation of polymer-bound Schiff bases and their Pt(IV) complexes were screened against *Staphylococcus aureus* (ATCC 25923), *Listeria monocytogenes* 4b (ATCC 19115), *Staphylococcus epidermidis* (ATCC 12228), *Micrococcus luteus* (ATCC 93419), *Bacillus cereus* (RSKK 863) as gram (+) bacteria; *Shigella dysenteria* type 7 (NCTC 9363), *Escherichia coli* (ATCC 1230), *Salmonella typhi* H (NCTC 901.8394), *Brucella abortus* (RSKK 03026), *Pseudomonas putida* spp. as gram (-) bacteria and *Candida albicans* (Y-1200-NIH) as yeast.

The control of antibacterial and antifungal activity of synthesized polymers were performed using the well-diffusion method [8]. In this scene, DMF was used as a control solvent and it was not found active as biological against all microorganism. The modified polymers were kept dry at room temperature and were dissolved in DMF (0.15g/mL). 1% (v/v) of 24 broth culture containing 10⁶CFU/mL was placed in sterile petri dishes. Mueller-Hinton Agar (15mL) was used to culture the test bacteria and it was kept ca 45°C. The molten nutrient agar was added into Petri-dishes and allowed to solidify. Then, 6mm diameter holes were punched using a sterile cork borer and were completely filled with the test solutions. The plates were incubated at 37°C for 24h. After incubation process, the mean value was obtained for all holes

and it was used to calculate the zone of growth inhibition each samples against the test microorganism.

TABLE I
ANALYTICAL DATA AND SOME PHYSICAL PROPERTIES OF STUDIED POLYMERS

Symbol Chem.Form. (n:6-9, b:1) ^a	M _w / M _{n,NMR} , HI, Color, μ _{eff}	Elemental Analysis Found (Calcd.) %			
		C	H	N	Pt
PS-Sch _H [(C ₈ H ₈) _n (C ₁₇ H ₁₆ NO) _b] (n:6, b:1)	874/725 1.2, yellow, -	89.24 (88.31)	7.32 (6.75)	1.60 (1.95)	-
PS-Sch _{Br} [(C ₈ H ₈) _n (C ₁₇ H ₁₅ NOBr) _b] (n:6, b:1)	953/845 1.1, yellow, -	81.85 (82.70)	6.61 (6.49)	1.47 (1.86)	-
PS-Sch _H -Pt [(C ₈ H ₈) _n (C ₁₇ H ₁₉ NO ₃ Cl ₂ Pt) _b] (n:9, b:1)	1487 -, brown, dia.	71.82 (71.11)	6.12 (5.68)	0.94 (1.56)	13.21 (12.43)
PS-Sch _{Br} -Pt [(C ₈ H ₈) _n (C ₁₇ H ₁₉ NO ₃ Br ₂ Cl ₂ Pt) _b] (n:7, b:1)	1439 -, brown, dia.	60.88 (61.85)	5.21 (5.98)	0.97 (1.30)	13.55 (12.97)

^aM_w : number average molecular weight (measurements are according to elemental analyses), M_{n,NMR} : number average molecular weight calculated from ¹H-NMR.

TABLE II
IMPORTANT SOME SPECTRAL DATA OF STUDIED POLYMERS

Symbol	IR		UV-vis	
	v(OH), v(CH) _{arom/aliph}	v(CH=N) v(C=C)	v(M-O) v(M-N)	n→π* _(imine) , π→π* _(arom. ring) , CT, d→d
PS-Sch _H	3420 3017/2923	1637 1632	- -	318(227), 220(157) - 288(206)
PS-Sch _{Br}	3424 3015/2926	1631 1640	- -	320(232), 223(162) - 281(204), -
PS-Sch _H -Pt	- 3025/2926	1643 1633	519 439	327(252), 333(256) 219(168) - 290(223) *339(242), *377(269)
PS-Sch _{Br} -Pt	- 3012/2931	1639 1628	528 447	322(252), 329(257) 226(177) - 294(230) *345(250), *370(268)

*CT: Charge transfer transition

III. RESULTS AND DISCUSSION

A. Characterization Studies

The elemental analyses, the average molecular weights (M_w, M_{n,NMR}) polydispersity index (HI) results and some physical properties of all modified polymers were given in Table I. The weight average molecular weight (M_w) was suggested from elemental analyses and the number average weight (M_{n,NMR}) was suggested from ¹H-NMR spectra. The elemental analyses can be considered compatible with the chemical formulas. In the same time, deviations from these values should be considered due to the different chain lengths of polymers [9].

B. IR Spectra of Polymer-Anchored Schiff Bases and their Pt(IV) complexes

The characteristic IR spectras of all synthesized polymers are given in Table II. In the IR spectrum of PS-Sch_H and PS-Sch_{Br} ligands were observed characteristic bands at 1637 and 1636cm⁻¹, respectively, were assigned to v(CH=N). This observation were evaluated the condensation of amine and carbonyl groups [10]. The IR spectra of PS-Sch_H-Pt and PS-

Sch_{Br}-Pt complexes showed two imine bands in 1640cm⁻¹ and 1643cm⁻¹; 1639cm⁻¹ and 1641cm⁻¹, respectively. Furthermore, the ν(M-O) and ν(M-N) frequencies were determined in the 465-542 and 469-539 cm⁻¹, respectively, for PS-Sch_H-Pt and PS-Sch_{Br}-Pt. This observation indicated that the coordination of metal ion with pair of electrons on the nitrogen atom in imine groups [11].

TABLE III
¹H-NMR CHEMICAL SHIFT AND TG/DTA RESULTS OF STUDIED POLYMERS

Symbol	TGA		DTA			¹ H-NMR OH, CH=N H _(Arom.) H _(Aliph.)
	T _i	T _{1/2}	T _f	R.M (%)	End. Temp. 1. 2. 3.	
PS-Sch _H	361	410	450	8	105 174 408	10.15(s), 7.91(s) 6.18 - 7.05(m) 0.86 - 2.15(m)
PS-Sch _{Br}	370	417	458	9	100 165 410	10.21(s), 7.80(s) 6.00 - 7.12(m) 0.95 - 2.21(m)
PS-Sch _H -Pt	379	425	469	10	115 178 418	-, 7.90(s) 6.13 - 7.19(m) 0.90 - 2.20(m)
PS-Sch _{Br} -Pt	388	429	474	11	112 171 422	-, 7.89(s) 6.11 - 7.10(m) 0.84 - 2.19(m)

*R.M; Residue mass T_i: Temperature of initial degradation.
T_(1/2): Temperature of half degradation. T_f : Temperature of finally degradation
(s) singlet, (m) multiplet

The characteristic bands belonging to ν(CH)_{arom.}, ν(CH)_{aliph.} and ν(C=C) were obtained in the range 3012-3025, 2923-2931 and 1618-1640 cm⁻¹ respectively, for all modified polymers. The ν(CH) bands were also observed at 3420 and 3424cm⁻¹ for PS-Sch_H and PS-Sch_{Br}, Schiff bases, respectively.

C. ¹H-NMR Spectra of Polymer-Anchored Schiff Bases

¹H-NMR spectral data of synthesized polymers are presented in Table II. According to the integral values in ¹H-NMR spectrum, the structure of each polymer unit was suggested [9]. In the ¹H-NMR spectra, four signals were observed at 7.91, 7.80, 7.90 and 7.89ppm which were assigned to CH=N groups for synthesized PS-Sch_H, PS-Sch_{Br}, PS-Sch_H-Pt and PS-Sch_{Br}-Pt, respectively, and these signals were taken as value of polymeric-Schiff bases integration. Following this, the peak heights (one unit) were compared with the total peak heights of the -CH-CH₂ signals in modified polymers. Finally, the number of repeated unit determined as the ratio of -CH=N/-CH-CH₂ constitute 1/6 for PS-Sch_H and PS-Sch_{Br} ligands, 1/12 for PS-Sch_H-Pt complex and 1/14 for PS-Sch_{Br}-Pt complex, respectively. Additionally, the peaks were revealed in the regions 6.00-7.19ppm and 0.84-2.20ppm which were attributed to aromatic protons and aliphatic protons, respectively, for all modified polymers. The OH protons were disappeared for the spectrum of PS-Sch_H-Pt and PS-Sch_{Br}-Pt complexes while these protons were observed at 10.15 ppm and 10.21ppm for the ligands of PS-Sch_H and PS-Sch_{Br}. This observation could be considered as the coordination between metal ions and the oxygen atoms.

D. UV-Vis Spectra of Polymer-Anchored Schiff Bases and Their Pt(IV) Complexes

The results of electronic spectrum of the synthesized polymers are given in Table II. The absorption bands were determined in 318-333nm regions which were assigned to n→π* transitions of the imine for all modified polymers. Similarly, for these polymers the bands were observed in the region 219-294nm which were attributed to π→π* transitions of the aromatic ring [9]. In the spectra, two bands were exhibited at 339nm and 377nm for diamagnetic PS-Sch_H-Pt complex, at 345nm and 373nm for diamagnetic PS-Sch_{Br}-Pt complex. These bands were assigned to the forbidden transitions ¹A_{1g} → ³T_{1g} and ¹A_{1g} → ³T_{2g} for octahedral geometry around Pt(IV) ion [12].

E. TG/DTA Analysis of Polymer-Anchored Schiff Bases and Their Pt(IV) Complexes

The finding of thermal analysis of the synthesized polymers complexes are demonstrated in Table IV.

All of these compounds were exhibited a one-step weight in the range of 361-474°C. The initial decomposition were determined at 361 and 370°C, respectively, PS-Sch_H and PS-Sch_{Br} ligands. This observation indicate that the ligand of PS-Sch_{Br} more stable. Correspondingly, the initial decomposition were obtained at 379°C for PS-Sch_H-Pt complex and 388°C for PS-Sch_{Br}-Pt complex. Also, this result show that PS-Sch_H-Pt complex has high stable as thermal.

Additionally, all temperature change are above 100°C in the TGA curves. This case indicate that Pt(IV) metal complexes haven't got cristal water [8].

Three endothermic peaks were determined from the DTA thermograms of all synthesized polymers. The endothermic curves were found in between 100 and 410°C for PS-Sch_H and PS-Sch_{Br} ligands. Likethis, these peaks were observed in between 115 and 422°C for PS-Sch_H-Pt and PS-Sch_{Br}-Pt complexes.

TABLE IV
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF STUDIED POLYMERS

Microorganisms	PS-Sch _H	PS-Sch _{Br}	PS-Sch _H -Pt	PS-Sch _{Br} -Pt
<i>B. cereus</i>	12	16	12	18
<i>L. monocytogenes 4b</i>	-	-	-	-
<i>M. luteus</i>	-	-	11	-
<i>S. aureus</i>	-	15	-	13
<i>S. epidermis</i>	11	12	13	-
<i>Br. abortus</i>	20	18	15	17
<i>E. coli</i>	-	-	11	12
<i>P. putida</i>	-	11	12	11
<i>Sh. dys.typ 7</i>	15	12	12	-
<i>E.aerogenes</i>	-	-	12	-
<i>C. albicans</i>	17	17	22	-

Control (DMF) not zone, Diameter of zone of inhibition (mm)

F. Magnetic Properties of Polymer-Anchored Schiff Base Pt(IV) Complexes

The results of magnetic susceptibility of PS-Sch_H-Pt and PS-Sch_{Br}-Pt were determined as diamagnetic. According to this observation, it could be suggested that these coordination polymers were octahedral geometry.

G. Biological Activity Investigation Polymer-Anchored Schiff Bases and Their Pt(IV) Complexes

The antimicrobial activity results of the synthesized polymers are shown in Table IV. The antibacterial and antifungal activities of the polymeric-Schiff bases and their Pt(IV) complexes were investigated against *Staphylococcus aureus* (ATCC 25923), *Listeria monocytogenes* 4b (ATCC 19115), *Staphylococcus epidermidis* (ATCC 12228), *Micrococcs luteus* (ATCC 93419), *Bacillus cereus* (RSKK 863), *Shigella dysenteria* type 7 (NCTC 9363), *Escherichia coli* (ATCC 1230), *Salmonella typhi* H (NCTC 901.8394), *Brucella abortus* (RSKK 03026), *Pseudomonas putida* sp. and *Candida albicans* (Y-1200-NIH) in DMF solvent as a control material.

All modified polymers exhibited a moderate activity against selected microorganisms except *L. monocytogenes* 4b. The highest antibacterial activity of synthesized compounds determined against *Br. abortus* which is bacterial disease for humans and livestock [13]. PS-ScbBr-Pt complex did not exhibit any zone of inhibition while three modified polymers showed a strong antifungal activity on the yeast of *C. albicans* which is caused some infections for people and animals [14]. The PS-SchBr ligand showed more strong activity than PS-SchH ligand against all test bacteria. Similarly, the antimicrobial activity of PS-SchH-Pt complex was found higher than PS-SchBr-Pt complex.

After evaluating from the results of microbiological activity, we can say that the synthesized polymers may be used as antimicrobial agents.

H. Conclusion

The scope of this study, new polystyrene-anchored Schiff bases with Pt(IV) complexes were prepared and characterized by spectroscopic methods. At the same time, these modified polymers were screened against some bacterial strains to investigate their antimicrobial properties and were found to have antibacterial and antifungal effect. To sum up, it can be concluded that the synthesized polymers may have been an importance in biomedical domains as polymeric-agents.

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