# New Heteroaromatic Polyazomethines Containing Naphthyridine Moieties: Synthesis, Characterization, and Biological Screening

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Received 9 July 2011; accepted 23 October 2011
DOI 10.1002/app.36395
Published online in Wiley Online Library (wileyonlinelibrary.com).

**ABSTRACT:** A new series of heteroaromatic polyazomethines containing 1,8-naphthyridine moieties in the polymer backbone were synthesized with a solution polycondensation technique. A new heteroaromatic monomer containing 1,8-naphthyridine moieties (4-ethoxy-2,7-dicarboxaldehyde-1,8-naphthyridine) was synthesized with an analogous synthetic sequence and confirmed by elemental and spectral data. The resulting polymers were characterized by elemental, spectral analyses, solubility and viscometry measurements. All the synthesized polyazomethines had better solubility in polar aportic solvents. The thermal properties of those polymers were evaluated by thermogravimetric analysis, differential thermogravimetry, and differential thermal analysis measurements and correlated to their structural units. All the polymers had nearly similar maximum polymer decomposition temperatures, which were in the range 557–577°C. A very large difference between the glass transitions (92–222°C) was observed. In addition, with gel permeation chromatography, the molecular weight determination of selected examples of those polymers was evaluated. The values of the average molecular weight for polyazomethines $\mathbf{7_b}$ and $\mathbf{7_c}$ were 34,914 and 24,859, respectively. On the other hand, the biological screening of all of the synthesized polyazomethines was performed in variety of bacteria and fungi. Most of the polyazomethines showed a significant influence against Gram-negative bacteria. The minimum inhibitory concentration of the most active polymers was 0.05 mg/mL. © 2012 Wiley Periodicals, Inc. J Appl Polym Sci 000: 000–000, 2012

**Key words:** biological applications of polymers; heteroatom-containing polymers; polymer synthesis and characterization; thermal properties

## INTRODUCTION

Polyazomethines or polymeric Schiff bases are an interesting class of polymers, which have carbon–nitrogen double-bonded units in the main chain that are capable of protonation and complexation.[1,2] Aromatic polyazomethines have been studied extensively because of their good thermal stability, mechanical strength, nonlinear optical properties, ability to form metal chelates, semiconducting properties, environmental stability, and fiber-forming properties, which are associated mainly with their conjugated backbone and the presence of imine sites.[1,2] These polymers could become materials suitable for use in polymer electronics, especially in view of the recent discovery that the photoluminescence of conjugated polymers containing basic sites in the main chain could be modified by protonic (acid–base) doping.[1–3] A major drawback associated with aromatic polyazomethines is their limited solubility in most common organic solvents.[1–6] Their high melting temperature and insolubility make them intractable for processing by conventional techniques. The efforts devoted toward obtaining soluble and fusible polyazomethines include the introduction of a heteroaromatic moiety, the insertion of a flexible spacer between the main-chain aromatic rings, the introduction of pendant groups, that is, aromatic or alkyl substituents, the insertion of fluorine into the polymer chain, and the introduction of structural irregularities such as kinks, bents, crankshaft-shaped units.[7–15] It is generally recognized that presence of an alkyl chain and ether linkage in the polymer backbone imparts segmental mobility to the polymer, enhances the solubility, and lowers the glass-transition temperature ($T_g$).[16–19] Moreover, polyazomethines as thermostable polymers are interesting candidates for the potential application of such compounds in electronics, optoelectronics, and

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photonics.[20–25] Initial reports have described polyazomethines as insoluble in common solvents and infusible polymers; this would their practical applications and hinder the development of research.[22] Different concepts, such as molecular and supramolecular engineering concepts, are available to reduce the disadvantages of polyazomethines and to promote the appearance of specific properties, such as optoelectronics or mesomorphism.[22] Carbon–nitrogen-bonded units in the main chain of polyazomethines are capable of protonation and complexation. Yang and Jenekhe[26] observed a bathochromic shift of electronic absorption spectra after the complexation of polyazomethines with $GaCl_3$ and diphenyl or di-*m*-cresyl phosphate. The reverse behavior was found by Cho et al.[27] Azomethines are very useful scaffolds for the construction of cyclic compounds via ring closure between the primary amines and aldehydes.[28] Azomethines are also known to have biological activities, such as antitumor[29] and antibacterial[30] activities. They have also been found to have wide application in the areas of dyes and pigments because of their luminescent properties.[31]

1,8-Naphthyridine and its derivatives have been of great interest for many people for the reason that they are potential bidentate ligands and have a broad spectrum of their biological activities.[32–36] In recent years, more and more people have been interested in the development of multifunctional materials.[37–39] In addition, the 1,8-naphthyridine class of molecules has been reported to exhibit potent anti-inflammatory activity.[40,41] 1,8-Naphthyridine derivatives have been assessed for anti-inflammatory and myeloprotective activity with an *in vitro* screening assay based on murine bone marrow derived dendritic cells. The extent of modulation in proinflammatory cytokine and chemokine levels was taken as an indicator of anti-inflammatory and myeloprotective activity. Recently, 1,8-naphthyridine has been exploited in cancer chemotherapy, and one of the molecules, SNS-595, was in its second phase of clinical trials at the time of this writing.[42] Mammalian topoisomerase II is a known target for antitumor agents, such as doxorubicin, etoposide, ellipticine, and amsacrine.[43] 1,8-Naphthyridine derivatives have been found to display moderate cytotoxic activity against murine P388 leukemia when changes were carried out at the N-1 and C-7 positions.[44,45]

This investigation discussed in this article dealt with the synthesis and characterization of new category of heteroaromatic polyazomethines containing naphthyridine moieties in the polymer main chain. The antibacterial activity of the new polymers was tested in the presence of different bacteria and fungi. In addition, other characteristic of these new polymers, such as the thermal stability, solubility, viscometry, and molecular weight, were examined.

## EXPERIMENTAL

### Materials

6-Methyl-2-pyridinamine (Aldrich, Steinheim, Germany), ethyl acetoacetate (Aldrich, 99%, Milwaukee WI 53233 USA), liquid paraffin (El-Nasr Pharmaceutical Chemical Co., Egypt), phosphorus oxychloride (Fluka), ethyl alcohol absolute (El-Nasr Pharmaceutical Chemical), selenium dioxide (Merck, Frankfurt, Germany), magnesium sulfate anhydrous (El-Nasr Pharmaceutical Chemical), dichloromethane (Merck, 99.5%), and sodium hydroxide (El-Nasr Pharmaceutical Chemical) were used without purification. All diamine compounds (Merck and Aldrich) were used without purification. All other reagents were of high purity and were further purified as reported in the literature.[46]

### Methods

#### Monomer syntheses

*2,6-Dimethylpyrido[1,2-a]pyrimidin-4-one (**2**).* Poly(phosphoric acid) (65 g) was added to 6-methyl-2-pyridinamine (10.8 g) and ethyl acetoacetate (14.5 g) and the mixture was heated with stirring at 100°C for 1.25 h. The viscous mixture was cooled and neutralized with a 4*M* sodium hydroxide solution. The solid that separated was filtered, and the filtrate was extracted twice with dichloromethane. The original solid product was dissolved in the combined dichloromethane extracts, and the solution was dried over magnesium sulfate and concentrated to give the crude product (9.5 g, 60%), which was sufficiently pure for the next step. The sample, when recrystallized from light petroleum, had a melting point of 105°C ([literature mp = 105°C[47,48]).

*2,7-Dimethyl-1,8-naphthyridine-4-(1H)-one (**3**).* Liquid paraffin (200 mL) in a 500-mL, round-bottom flask was heated to 350°C on a heating mantle. The solid **2** (10 g) was added in small portions, and the oil was maintained at 350°C for 0.5 h after the addition was complete. To the cooled mixture was added light petroleum (bp 40–60) (200 mL), and the brown solid was filtered and washed with benzene to give the product (7.5 g, 75%, mp = 320°C, literature mp = 320°C[48]).

*4-Chloro-2,7-dimethyl-1,8-naphthyridine (**4**).* A mixture of **3** (8.0 g) in phosphorus oxychloride (25 mL) was heated over the range 90–130°C over 30 min. The solution was then cooled, cautiously poured onto ice, made slightly basic with a 30% sodium hydroxide solution (if the salts separated at this point, they were filtered and washed with chloroform), and extracted three times with chloroform. The dried extracts, over magnesium sulfate, were concentrated, and the brown residue was suction filtered through

silica gel (40 g) with a 1 : 1 dichloromethane/ethyl acetate (500 mL) as an eluent. The evaporation of the solvent gave compound **4** (7.5 g, 85%, mp = 83°C), which was recrystallized from light petroleum (literature mp = 83°C[48]).

*4-Ethoxy-2,7-dimethyl-1,8-naphthyridine (**5**).* Compound **4** (7.68 g) was added in one portion to a freshly prepared sodium ethoxide solution (0.92 g of Na in 50 mL of absolute ethanol) with constant stirring for 0.5 h. The excess solvent was removed by evaporation, and the residue was treated with 1 : 1 water/dichloromethane (200 mL). The dried extracts, over magnesium sulfate, were concentrated near dryness, and the brown residue for compound **5** was precipitated (6.33 g, 78.5%, mp 123°C). This compound was used as it was in the next step without further purification.

IR (KBr, $cm^{-1}$, υ): 1270 (m, O—C), 1580 (m, naphthyridine ring), 2915 (w, CH stretching of aliphatic), 3050 (w, CH stretching of aromatic). $^1$H-NMR ($CDCl_3$, δ): 1.55 (t, 3H, $CH_3$ ethyl), 2.75 (s, 6H, $2CH_3$), 4.30 (q, 2H, $CH_2$ ethyl), 6.70 (s, 1H, Ar—H naphthyridine ring), 7.25 (d, 1H, coupling constant (J), = 8 Hz, Ar—H naphthyridine ring), 8.30 (d, 1H, $J$ = 8 Hz, Ar—H naphthyridine ring).

*4-Ethoxy-2,7-dicarboxaldehyde-1,8-naphthyridine (**6**).* Compound **5** (4 g) was added in one portion to a refluxing mixture of selenium dioxide (9 g) and 1,4-dioxan (300 mL). The heating was continued for 3 h, the mixture was filtered while hot, and the filtrate was concentrated *in vacuo* to 200 mL. Dichloromethane (200 mL) was added, and the solution was extracted with water (2 × 150 mL). The combined organic fractions were dried, and the solvent evaporated to give the new dialdehyde monomer **6** (3.2 g, 70.3%) as a light brown solid (mp 274–276°C) recrystallized from ethanol.

ANAL. Calcd for $C_{12}H_{10}N_2O_3$: C, 62.61%; H, 4.38%; N, 12.17%. Found: C, 61.82%; H, 4.60%; N, 11.77%. IR (KBr, $cm^{-1}$, υ): 1270 (m, O—C), 1585 (m, naphthyridine ring), 1700 (s, CHO), 2920 (w, CH stretching of aliphatic), 3050 (w, CH stretching of aromatic). $^1$H-NMR ($CDCl_3$, δ): 1.67 (t, 3H, $CH_3$ ethyl), 4.50 (q, 2H, $CH_2$ ethyl), 7.55 (s, 1H, Ar—H naphthyridine ring), 8.23 (d, 1H, $J$ = 8 Hz, Ar—H naphthyridine ring), 8.90 (d, 1H, $J$ = 8 Hz, Ar—H naphthyridine ring), 10.29–10.36 (ss, 2H, 2CHO). Mass spectroscopy (MS; $m/z$, %): 229.98 ($M^+$, 100), 231.05 (M + 1, 17.2).

## Polymerization

*General procedures.* In a three-necked flask equipped with a condenser, dry nitrogen inlet, outlet, and dropping funnel, a mixture of (2 × $10^{-3}$ mol) naphthyridine monomer **6** suspended in 20–30 mL of absolute ethanol, and a few drops of piperidine was introduced as a basic catalyst. The different aliphatic and aromatic diamines (2 × $10^{-3}$ mol) dissolved in 15 mL of absolute ethanol were added in a dropwise manner at 25°C during stirring over about 20 min. After the addition was complete, the stirring was continued for 12–15 h at about 80°C; during this time, the viscosity of the solution increased rapidly, and the polymer began to precipitate in the early stages of the reaction. The polymer precipitated was isolated by filtration as a highly brownish solid polymer; it was washed with hot methanol and hot acetone and then dried under reduced pressure (1 mm/Hg) at 80°C for 48 h.

With this general procedure, the following polyazomethines ($\mathbf{7_a}$–$\mathbf{7_e}$) were obtained.

*Polyazomethine $\mathbf{7_a}$.* Polyazomethine $\mathbf{7_a}$ was obtained by the polymerization of monomer **6** (0.46 g) with *p*-phenylenediamine (0.22 g) for 12 h (0.47 g, 77.8%) as a brownish powder.

ANAL. Calcd for $C_{18}H_{14}N_4O$: C, 71.52%; H, 4.64%; N, 18.54%. Found: C, 72.14%; H, 3.89%; N, 17.79%. IR (KBr, $cm^{-1}$, υ): 1265 (m, O—C), 1575 (m, naphthyridine ring). 1600 (s, C=N), 2910 (w, CH stretching of aliphatic), 3030 (w, CH stretching of aromatic). $^1$H-NMR [hexadeuterated dimethyl sulfoxide (DMSO-$d_6$), δ]: 1.60 (t, 3H, $CH_3$ ethyl), 4.50 (q, 2H, $CH_2$ ethyl), 6.78–6.88 (ss, 2H, CH=N), 7.12–7.65 (m, 4H, Ar—H phenyl), 7.85 (s, 1H, Ar—H naphthyridine ring), 8.40 (d, 1H, Ar—H naphthyridine ring), 8.80 (d, 1H, Ar—H naphthyridine ring).

*Polyazomethine $\mathbf{7_b}$.* Polyazomethine $\mathbf{7_b}$ was obtained by the polymerization of monomer **6** (0.46 g) with 4,4′-diaminodiphenyl ether (0.40 g) for 14 h (0.64 g, 81.2%) as a yellowish powder.

ANAL. Calcd for $C_{24}H_{18}N_4O_2$: C, 73.09%; H, 4.57%; N, 14.21%. Found: C, 72.46%; H, 5.08%; N, 13.72%. IR (KBr, $cm^{-1}$, υ): 1270 (m, O—C), 1580 (m, naphthyridine ring). 1600 (s, C=N), 2910 (w, CH stretching of aliphatic), 3030 (w, CH stretching of aromatic). $^1$H-NMR (DMSO-$d_6$, δ): 1.66 (t, 3H, $CH_3$ ethyl), 4.48 (q, 2H, $CH_2$ ethyl), 6.73–6.80 (ss, 2H, CH=N), 7.12–7.52 (m, 8H, Ar—H diphenyl ether), 7.81 (s, 1H, Ar—H naphthyridine ring), 8.46 (d, 1H, Ar—H naphthyridine ring), 8.92 (d, 1H, Ar—H naphthyridine ring).

*Polyazomethine $\mathbf{7_c}$.* Polyazomethine $\mathbf{7_c}$ was obtained by the polymerization of monomer **6** (0.46 g) with 4,4′-diaminodiphenyl sulfone (0.50 g) for 14 h (0.72 g, 81.4%) as a yellowish powder.

ANAL. Calcd for $C_{24}H_{18}N_4SO_3$: C, 65.16%; H, 4.07;% N, 12.67%. Found: C, 64.39%; H, 4.64%; N, 11.93%. IR (KBr, $cm^{-1}$, υ): 1270 (m, O—C), 1125–1340 (s, $SO_2$), 1565 (m, naphthyridine ring), 1600 (s, C=N), 2890 (w, CH stretching of aliphatic), 3030 (w, CH stretching of aromatic). $^1$H-NMR (DMSO-$d_6$, δ): 1.53 (t, 3H, $CH_3$ ethyl), 4.49 (q, 2H, $CH_2$ ethyl), 6.66–6.82 (ss, 2H, CH=N), 7.31–7.66 (m, 8H, Ar—H diphenyl sulfone), 7.92 (s, 1H, Ar—H naphthyridine

ring), 8.37 (d, 1H, Ar—H naphthyridine ring), 8.90 (d, 1H, Ar—H naphthyridine ring).

*Polyazomethine* $7_d$. Polyazomethine $\mathbf{7_d}$ was obtained by the polymerization of monomer **6** (0.46 g) with 1,3-dianimopropane (0.15 g) for 15 h (0.41 g, 76.5%) as a reddish powder.

ANAL. Calcd for $C_{15}H_{16}N_4O$: C, 67.16%; H, 5.97%; N, 20.90%. Found: C, 67.61%; H, 6.37%; N, 20.12%. IR (KBr, $cm^{-1}$, υ): 1260 (m, O—C), 1570 (m, naphthyridine ring), 1610 (s, C=N), 2915 (s, CH stretching of aliphatic). $^1$H-NMR (DMSO-$d_6$, δ): 1.35 (t, 4H, $2CH_2$), 1.50 (t, 3H, $CH_3$ ethyl), 1.60 (m, 2H, $CH_2$), 4.38 (q, 2H, $CH_2$ ethyl), 6.85–710 (ss, 2H, CH=N), 7.82 (s, 1H, Ar—H naphthyridine ring), 8.32 (d, 1H, Ar—H naphthyridine ring), 8.70 (d, 1H, Ar—H naphthyridine ring).

*Polyazomethine* $7_e$. Polyazomethine $\mathbf{7_e}$ was obtained by the polymerization of monomer **6** (0.46 g) with 1,12-dianimododecane (0.40 g) for 15 h (0.58 g, 73.6%) as a reddish powder.

ANAL. Calcd for $C_{24}H_{34}N_4O$: C, 73.09%; H, 8.63%; N, 14.21%. Found: C, 72.73%; H, 8.23%; N, 13.65%. IR (KBr, $cm^{-1}$, υ): 1260 (m, O—C), 1575 (m, naphthyridine ring), 1610 (s, C=N), 2910 (s, CH stretching of aliphatic). $^1$H-NMR (DMSO-$d_6$, δ): 1.30 (m, 16H, $8CH_2$), 1.47 (t, 3H, $CH_3$ ethyl), 1.58 (m, 8H, $4CH_2$), 4.45 (q, 2H, $CH_2$ ethyl), 6.90–7.10 (ss, 2H, CH=N), 7.75 (s, 1H, Ar—H naphthyridine ring), 8.38 (d, 1H, Ar—H naphthyridine ring), 8.85 (d, 1H, Ar—H naphthyridine ring).

## Measurements

All melting points reported for the monomer or the model compounds were uncorrected and were determined on a Gallenkamp melting-point apparatus with a digital thermometer type MFB-595-010M London, UK. Elemental analyses were performed by the Mikrolabor of the Laboratorium für Organische Chemie, ETH Zürich, Switzerland. The samples were dried rigorously *in vacuo* before analysis to remove strongly adhering solvent molecules. IR spectra were recorded on an IR-470 infrared spectrophotometer (Shimadzu) with the KBr pellet technique. The $^1$H-NMR spectra were recorded on a GNM-LA 400-MHz NMR spectrophotometer, Jeol Ltd. Japan and on a Bruker (AM 200) 200-MHz spectrometer, brucker Peoria, USA and chemical shifts were reported as δ values (parts per million) relative to the internal reference at room temperature (RT) in $CDCl_3$ or DMSO with Tetramethylsilane (TMS) as the internal reference. Mass spectra were recorded on a JEOL JMS600 mass spectrometer and with high-resolution matrix-assisted laser desorption/ionization (MALDI)–time of flight (TOF)–MS, DIT–MALDI–TOF–MS, and DCTB–MALDI–TOF–MS analysis performed by the MS service of the Laboratorium für Organische Chemie at ETH Zürich, Switzerland.

## Characterization techniques

*Viscosity measurements.* The inherent viscosities ($\eta_{inh}$'s) of the polymer solutions (0.5 g/100 mL) in DMSO were measured at 25°C with an Ubbelohde suspended-level viscometer with the help of a Gallenkamp controlled-temperature viscometer bath Cannon Instrument Company, State College USA. $\eta_{inh}$ is defined as

$$\eta_{inh} = [2.3 \log(\eta/\eta_o)]/C$$

where $C$ is the solution concentration and has a value of 0.5 g/100 mL and $\eta/\eta_o$ is the relative viscosity (or viscosity ratio).

*Solubility.* The solubility characteristics of the polymers were tested with the same solvents under the same conditions: 50 mg of polymer in 1 mL of solvent at RT. Solubility measurement was determined for powdery samples in excess solvent, including concentrated sulfuric acid, methylene chloride, hexane, dimethylacetamide (DMA), tetrahydrofuran (THF), dimethylformamide (DMF), and dimethyl sulfoxide (DMSO).

*Thermal analyses.* Thermogravimetric analysis (TGA), differential thermogravimetric (DTG), and differential thermal analysis (DTA) measurements were carried out in air with a TA 2000 thermal analyzer, Thermo Fisher Scientific Inc. Suwanee, USA and a Shimadzu DTG-60, Shimadzu Corporation Analytical & Measuring Instruments Devision- Kyoto, Japan at a heating rate of 10°C/min in air.

*Molecular weight determination.* The molecular weight of a selected example of the newly synthesized polyazomethines was determined by gel permeation chromatography (GPC; Agilent Technologies, Germany). This was a G-1362A with 100–104–105 Å Altrastyragel columns connected in series. THF was used as the eluent with a flow rate of 1 mL/min. Commercially available linear poly(methyl methacrylate) and polystyrene standards were used to calibrate the columns. The GPC apparatus was run under the following conditions: flow rate = 2.000 mL/min, injection volume = 100.000 μL, and sample concentration = 1.000 g/L.

*Biological screening.* Antimicrobial screening of the synthesized polyazomethines $\mathbf{7_a}$–$\mathbf{7_e}$ was performed against different organisms (fungal and bacterial species) according to the following methods.

### *Antifungal screening*

Organisms. Five pathogenic, phytopathogenic, or food-poisoning fungal species were used in this study: *Aspergillus flavus*, *Aspergillus niger*, *Fausarium*

*oxysporum*, *Candida albicans*, and *Geotrichum candidum*.

Materials and method[49,50]. A spore suspension in sterile water was prepared from 2-to-5-days-old culture of the test fungi growing on potato dextrose agar or sabouraud agar media. The final spore concentration was $5 \times 10^5$ spores/mL. About 15 mL of the growth medium was introduced onto a sterilized Petri dish 9 cm in diameter and inoculated with 1 mL of the spore suspension. The plate was shaken gently to homogenize the inoculum. The antifungal activity of the polymers was tested by the standard agar disc diffusion method as follows: Sterile 5-mm filter paper discs (Whatman) were impregnated with solutions of the test polymers and dermatin (0.1 or 0.05 mg/mL in DMSO). In addition, other discs were impregnated with the solvent (DMSO) and served as controls. The impregnated discs were then dried for 1 h and placed in the center of each plate. The seeded plates were incubated at 30 ± 2°C for 6 days. The radii of the inhibition zones (in millimeters) were measured at successive intervals during the incubation period. Triplicate sets were applied for each treatment, and the results are given in Table V (shown later).

***Antibacterial screening***

Organisms. Five bacterial species representing both Gram-positive and Gram-negative strains were used to test the antibacterial activities of the target polyazomethines: *Serratia marcescens*, *Escherichia coli*, and *Pseudomonas aeruginosa* were the representative Gram-negative strains, and *Bacillus cereus* and *Micrococcus luteus* were the representative Gram-positive strains.

Materials and method[49,50]. A cell suspension of each bacterial strain was prepared from 48-h-old cultures grown on nutrient agar in sterilized water. One milliliter of the cell suspension was added to a Petri dish (9 cm in diameter); we then poured 15 mL of NA onto the plate. The plate was shaken gently to homogenize the inoculum. Sterile 5-mm filter paper discs (Whatman) were impregnated with solutions of the tested polymer and ampicillin solution as a reference drug (0.1 and 0.05 mg/mL in DMSO as a negative control). In addition, other discs were impregnated with the solvent (DMSO) as a control. The impregnated discs were then dried for 1 h and placed in the center of each plate. The seeded plates were incubated at 33 ± 2°C for 36–48 h. The radii of inhibition zones (millimeter) of the triplicate sets were measured, and the results are given later in Table V.

## RESULTS AND DISCUSSION

Our target in this work was to synthesize new polyazomethines containing heteroaromatic naphthyridine moieties in the polymer backbones. We selected

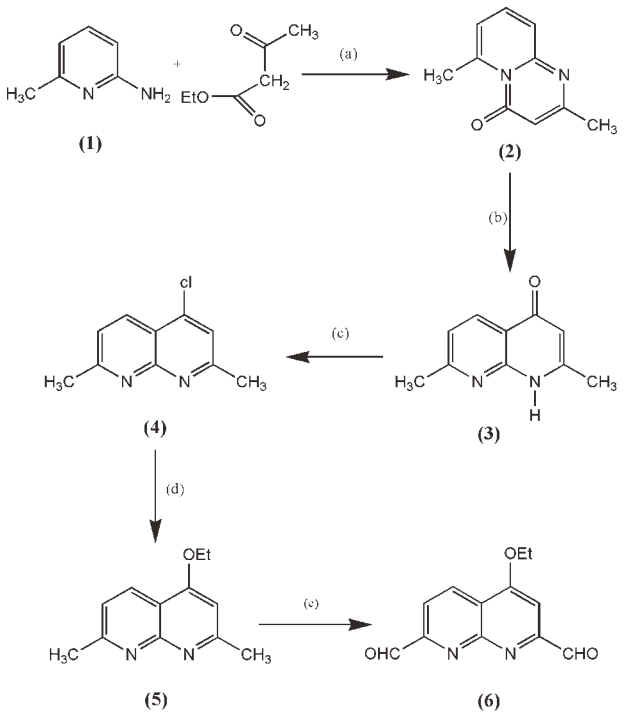


**Figure 1** Synthesis of monomer **6:** (a) Polyphosphoric acid (PPA) , heating at 100°C; (b) paraffin oil, 15 min; (c) $POCl_3$; (d) absolute ethanol/sodium metal; and (e) $SeO_2$/dioxane.

heterocyclic ring in the main chain and designed ethyl side chain as pendent group of the synthetic polymers to impart certain properties to the polymers. Among different heterocyclic rings, the advantages of using a naphthyridine nucleus and its alkyl side chain include better solubility and biological screening properties.[51–54] The new polymers necessitated the synthesis of a new monomer.

### Monomer syntheses

For an analogous synthetic sequence, it was necessary to obtain a substantial amount of **4**. This compound was prepared previously by Chandler et al.[48] with 6-methyl-2-pyridinamine as a starting compound in good yield, and isolation of the product was easy, as described in the following: In the condensation reaction between 6-methyl-2-pyridinamine and ethyl acetoacetate with poly(phosphoric acid), ring formation occurred on the ring nitrogen of the pyridine to give **2**.[47] This kinetically favored product was then thermally isomerized at 350°C to the desired ring system **3**. The reaction of **3** with phosphorus oxychloride gave the chloronaphthyridine **4**. Although this was a multistep procedure, there was the decided advantage that all steps were experimentally straightforward and could be run on any desired scale. Our new monomer required the synthesis of a new premonomer **5** by the interaction of

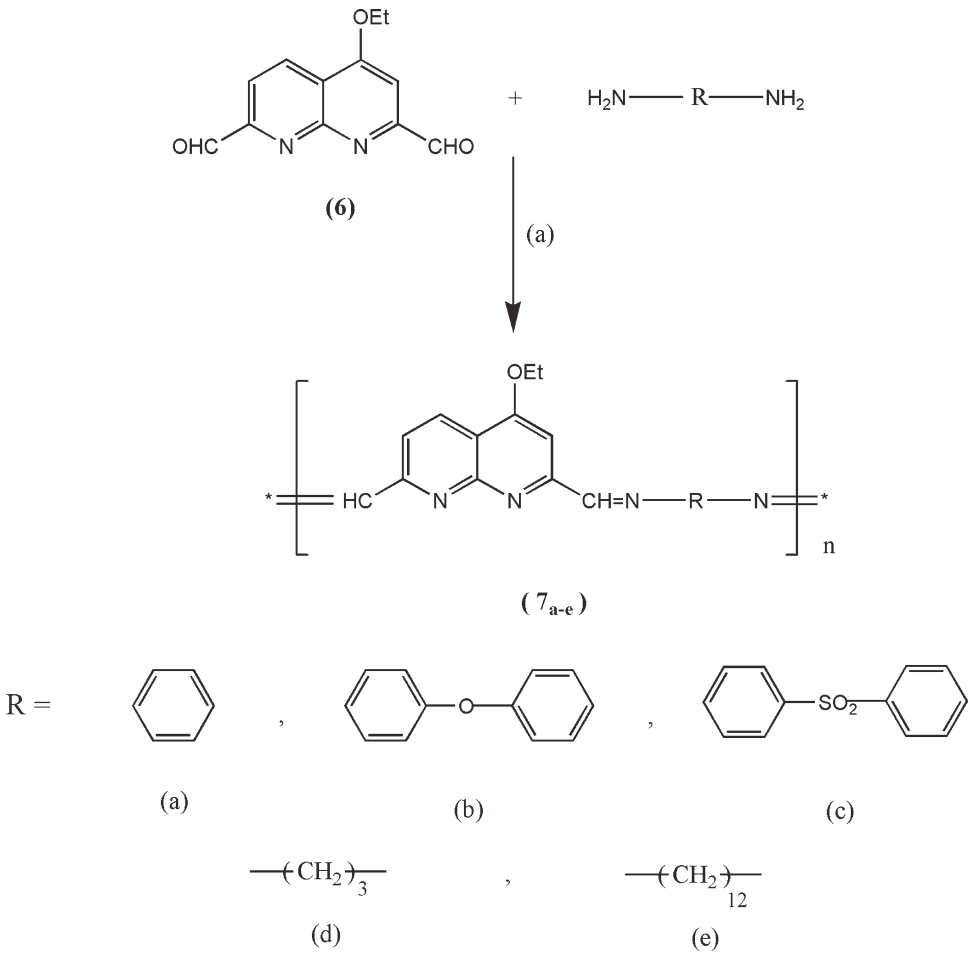


**Figure 2** Syntheses of polyazomethines $7_a$–$7_e$: (a) solution polycondensation, absolute ethanol, piperidine, and reflux.

compound **4** with a freshly prepared sodium ethoxide solution. The oxidation of **5** to our targeted monomer **6** with selenium dioxide in dioxan was achieved in good yield, as described in Figure 1. The introduction of ethoxy group as a side chain to the new naphthyridine-based monomer **6** was very important to increase the solubility behavior for the desired polymers as one of the most important characteristics reported in the literature and as previously mentioned in the introduction. The structure of the new dialdehyde monomer was confirmed by elemental and spectral analyses, as discussed in the Experimental section.

## Polymer syntheses

A new series of polyazomethines containing naphthyridine as heteroaromatic moieties in the polymer main chains were synthesized with a solution polycondensation technique by the interaction of the dialdehyde monomer **6** with different aliphatic and aromatic diamines, including: *p*-phenylenediamine, 4,4′-diaminodiphenyl ether, 4,4′-diaminodiphenyl sulfone, 1,3-diaminopropane, and 1,12-dianimododecane. The polymerization occurred in absolute ethanol in the presence of few drops of piperidine as a basic catalyst under a nitrogen atmosphere, as illustrated in Figure 2. The structure of those new polymers was confirmed by elemental and spectral analyses, as discussed in the Experimental section.

## Polymer characterization

The resulting polymers were characterized by their solubility and by viscometry measurements. Moreover, the thermal properties of those polymers were evaluated by TGA, DTG, and DTA. In addition, the GPC molecular weight determination of the selected examples of those polymers was evaluated.

The solubility characteristics of the resulting polyazomethines $7_a$–$7_e$ were tested as described in the Experimental part; the solubility behavior for those polymers are given in Table I. As we mentioned before, most previously prepared polyazomethines have not been nicely soluble in most common organic solvents.[1–6] Our efforts devoted toward obtaining soluble polyazomethines included the introduction of a naphthyridine nucleus as a

**TABLE I**
**Solubility Characteristics of Polyazomethines $7_a$–$7_e$**

| Polymer code | DMSO | DMF | THF | DMA | Hexane | $CH_2Cl_2$ | Concentrated $H_2SO_4$ | $\eta_{inh}$ (dL/g)[a] |
|---|---|---|---|---|---|---|---|---|
| $7_a$ | ++ | ++ | ++ | − | − | − | ++ | 0.94 |
| $7_b$ | ++ | ++ | ++ | − | − | − | ++ | 1.23 |
| $7_c$ | ++ | ++ | ++ | +− | +0 | +0 | ++ | 1.03 |
| $7_d$ | ++ | ++ | ++ | +0 | +0 | +0 | ++ | 0.78 |
| $7_e$ | ++ | ++ | ++ | +− | +0 | +0 | ++ | 1.29 |

++, Soluble at RT; +−, soluble on heating, +0, partially soluble on heating; −, insoluble.
[a] The $\eta_{inh}$ values were determined in DMSO at 25°C.

heteroaromatic moiety and the insertion of flexible aliphatic spacers in the polymer main chain, which appeared clearly in polymers $7_d$ and $7_e$, and moreover, the introduction of ethoxy side chains as alkyl oxy substituents or as pendant groups. As we mentioned, from the data presented in Table I, all the synthesized polyazomethines had better solubility than that observed in our previous polyazomethine series.[55] All the polymers were soluble in concentrated sulfuric acid as protonic solvents and had a yellow to red color. In polar aportic solvents, such as DMSO, DMF, and THF, we found that the polyazomethines were completely soluble at RT. In DMA, polymers $7_c$ and $7_e$ were soluble on heating, and polymer $7_d$ was partially soluble on heating. Polymers $7_a$ and $7_b$ were completely insoluble. On the other hand, the majority of the polymers were partially soluble on heating in hexane and methylene chloride, except polymers $7_a$ and $7_b$, which were completely insoluble in the same solvents. It can be clarified from that description that the order of higher solubility for all the synthesized polyazomethines was as follows: $7_e$ and $7_c > 7_d > 7_a$ and $7_b$ (this was clear in DMA and methylene chloride). Moreover, polymers based on the flexible aliphatic chains $(CH_2)_3$ and $(CH_2)_{12}$ had slightly more solubility than other polymers containing aromatic moieties; this may have been due to the higher flexibility of oligomethylene and polymethylene spacers.[56] On the other hand, polyazomethines with aromatic substituents $7_a$–$7_c$ are less soluble in most organic solvents, including chloroform, dichloromethane, pyridine, *m*-cresol, and so on.[57]

The thermal behavior of polyazomethines $7_a$–$7_c$ and $7_e$ was evaluated by TGA, DTG, and DTA at a heating rate of 10°C/min in the presence of an air atmosphere. The thermogravimetric (TG) curves showed a small weight loss in the range 1–2% starting at 75°C up to 110°C; this may have been due to the loss of moisture and entrapped solvents. Table II gives the temperatures for various weight loss percentages. The thermographs of all of the polymers had the same pattern of decomposition. It is noteworthy that the decomposition of polyazomethines is a three-step process. The first stage is between 173 and 230°C. The second and the third stages of degradation of those polymers usually overlap and occur between 339 and 557°C. The rate of degradation in the second and third stages is somewhat faster than in the first stage. The first degradation step involves the scission of azomethine groups, the scission of many bonds with the liberation of free shorter chains, depending on the nature of these polymers. The expected nature of decomposition in the second and the third overlapped degradation steps involved the cleavage of ether side chain, random scission of the free linear chains into smaller fragments, in addition to the formation of char as an end product. This observation was in agreement with observations reported in the literature.[58] The initial decomposition temperature (IDT)[59] corresponded to the temperature at which the initial degradation could occur. The IDTs of all of the prepared polymers appeared at the temperatures for 10% weight loss percentages ($T_{10}$), which was considered at the same time the polymers decomposition temperatures;[60,61] it occurred in the range 212–330°C. Therefore, the data in Table II indicate that the thermal stabilities of polyazomethines $7_a$–$7_c$ and $7_e$ (at 10%) were in the order: $7_b > 7_a$ and $7_c > 7_e$. The maximum polymer degradation temperature ($PDT_{max}$) corresponded to the temperature at which the maximum rate of weight loss occurred. $PDT_{max}$ for polyazomethines $7_a$–$7_c$ and $7_e$ are given in Table III. It was clear that all the polymers had similar $PDT_{max}$ values, which appeared in the range 557–577°C. On comparing the temperatures for 40% weight loss percentages ($T_{40}$) and temperatures for 50% weight

**TABLE II**
**Thermal Properties of Polyazomethines 7a, 7b, 7c, and 7e**

| Polymer code | Temperature (°C) for various percentage decompositions[a] | | | | |
|---|---|---|---|---|---|
| | 10% | 20% | 30% | 40% | 50% |
| $7_a$ | 246 | 423 | 490 | 524 | 542 |
| $7_b$ | 330 | 424 | 453 | 478 | 499 |
| $7_c$ | 246 | 407 | 446 | 478 | 496 |
| $7_e$ | 212 | 312 | 430 | 450 | 467 |

[a] The values were determined by TGA at heating rate of 10°C/min.

**TABLE III**
**$T_g$ and $PDT_{max}$ Rates for Polyazomethines $7_a$, $7_b$, $7_c$, and $7_e$**

| Polymer code | $T_g$ (°C)[a] | $PDT_{max}$[b] |
|---|---|---|
| $7_a$ | 222 | ~ 569 |
| $7_b$ | 199 | ~ 564 |
| $7_c$ | 285 | ~ 577 |
| $7_e$ | 92 | ~ 557 |

[a] Determined from the DTA curves.
[b] Determined from the derivative of the TG curves.

loss percentages ($T_{50}$) values, we found that polymer **$7_e$** was less stable than the other polymers. This may have been due to the higher flexibility of such polymers, which was related to the aliphatic spacer $(CH_2)_{12}$ in the polymer main chain. The $T_{50}$ value is one of the main criteria for determining the relative thermal stability of a polymer. An examination of the data showed that the $T_{50}$ values of the polyazomethines were in the range 467–542°C; this indicated good thermal stability. The resulting polymers were similar to previously prepared polyazomethines containing methoxy substituents, which presented high thermal stabilities.[62] The *final decomposition temperature* corresponds to the temperature at which the rate of degradation that may occur is nearly completed. It could be clarified from the TG curves that the final decomposition temperature for all polymers was near 549–563°C. This indicated that the synthesized polymers had a somewhat high thermal stability, that is, over 500°C. The weight residue of the polyazomethines when heated to 750°C in air was in the range 2–3%.

The $T_g$ values of polyazomethines **$7_a$–$7_c$** and **$7_e$** were evaluated by DTA. These $T_g$ values are given in Table III. It is interesting to note that in contrast with the fact that polyazomethines are high-$T_g$ materials, the polymers synthesized in this study exhibited glass transitions in the range 92–222°C. The literature data for polyazomethines include melting transitions above 400°C.[56] The large depression in the $T_g$ values resulted from the presence of pendant ethoxy chains. The ethoxy side chain acted as a bound solvent or internal plasticizer for the polymer backbone. A longer aliphatic side chain as a pendant group should be better for obtaining the lower expected $T_g$. Similar observations have been reported for polyazomethines containing alkoxy side chains.[16,63,64] A comparison of the $T_g$ values of polyazomethines derived from the aromatic substituent **$7_a$–$7_c$** and those of polyazomethines derived from the aliphatic substituents **$7_d$** and **$7_e$** indicated that the former had higher $T_g$'s (222, 199, and 285°C, respectively) than the aliphatic-based polyazomethines (92°C). This could have been due to the rigid *p*-phenylene, diphenyl ether, and diphenyl sulfone linkages present in the aromatic-based polyazomethines. A very large difference between the glass transition (92–222°C) and IDT (212–246°C) was observed. This offered the polyazomethines a wide processing window.

GPC is a form of chromatography that is widely used for molecular weight determination. The molecular weight determination of the selected examples, polyazomethines **$7_b$** and **$7_c$**, was done with GPC (Agilent Technologies), as mentioned in the Experimental section. The value of the molecular weight was computed by means of a computer program. The values of average molecular weight for selected examples of the synthesized polyazomethines are listed in Table IV. Polymer **$7_b$** showed a weight-average average molecular weight ($M_w$) of 34,914, which was due to repeating $P_w \approx 89$ units and PDI = 1.09. Moreover, polymer **$7_c$** showed an $M_w$ of 24,859 ($P_w \sim 56$ and PDI = 1.23; see Supporting Information, Figs. S1 and S2). Furthermore, the $\eta_{inh}$ values of the polyazomethines were measured in DMSO at 25°C with an Ubbelohde suspended-level viscometer with the help of a Gallenkamp temperature-controlled viscometer bath. In fact, there was a good correlation between the $\eta_{inh}$ values and the average molecular weigh of such polymers. Therefore, polymers with high viscosities should have had a high molecular weight; this was apparent from the selected $P_w$ values. As shown in Table I, all the resulting polyazomethines had $\eta_{inh}$ values, in the range 0.78–1.29 dL/g. Polymer **$7_e$** had a high viscosity (1.29 dL/g), and this may have been due to the high molecular weight of the polymer. The $\eta_{inh}$ of polymer **$7_d$** was 0.78 dL/g; this may have been due to the low molecular weight of this polymer. The nearly similar $\eta_{inh}$ values for all polymers were due to their expected similar average molecular weights. According to the previous results, the GPC data was in agreement with the results obtained from the viscosity measurements. Higher molecular weight polymers were generally difficult to obtain; this may have been due to the growing of macromolecular chains precipitating out of the solution during polycondensation.

**TABLE IV**
**Molecular Weights of Polyazomethines $7_b$ and $7_c$**

| Polymer code | Molecular formula | GPC[a] | | | |
|---|---|---|---|---|---|
| | | $M_n$ | $M_w$ | $P_w$ | PDI |
| **$7_b$** | $(C_{24}H_{18}N_4O_2)_n$ | 32,000 | 34,914 | ~ 89 | 1.09 |
| **$7_c$** | $(C_{24}H_{18}N_4O_3S)_n$ | 20,217 | 24,859 | ~ 56 | 1.23 |

$M_n$, number-average molecular weight.
[a] All GPC measurements were performed at 40°C in DMF with polystyrene as a standard.

**TABLE V**
**Antimicrobial Screening of Polyazomethines $7_a$–$7_e$**

| | MIC (mg/mL)/Inhibition zone (mm) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $7_a$ | | $7_b$ | | $7_c$ | | $7_d$ | $7_e$ | Reference drug[a] | |
| Organism | 0.1 | 0.05 | 0.1 | 0.05 | 0.1 | 0.05 | 0.1 | 0.1 | 0.1 | 0.05 |
| Bacteria | | | | | | | | | | |
| *S. marcescens* (negative) | 6 | 0 | 20 | 14 | 20 | 16 | 0 | 9 | 24 | 21 |
| *E. coli* (negative) | 4 | 2 | 6 | 5 | 8 | 4 | 0 | 2 | 12 | 10 |
| *P. aeruginosa* (negative) | 5 | 0 | 17 | 14 | 22 | 17 | 0 | 0 | 29 | 25 |
| *B. cereus* (positive) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 25 | 20 |
| *M. luteus* (positive) | 0 | 0 | 0 | 0 | 12 | 10 | 0 | 0 | 35 | 32 |
| Fungi | | | | | | | | | | |
| *A. flavus* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *A. niger* | 0 | 0 | 28 | 22 | 17 | 15 | 0 | 0 | 40 | 32 |
| *F. oxysporum* | 0 | 0 | 14 | 8 | 10 | 7 | 0 | 0 | 22 | 16 |
| *C. albicans* | 0 | 0 | 0 | 0 | 14 | 9 | 0 | 0 | 25 | 18 |
| *G. candidum* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 35 | 30 |

[a] Reference drug: antibacterial (ampicillin) and antifungal (dermatin).

## Biological screening

The antimicrobial screening of all the synthesized polyazomethines $7_a$–$7_e$ was performed with the standard agar diffusion method, as described in the Experimental section[49,50] and as reported in the literature[65,66] against different organisms (fungal and bacterial species). The tested polymers were screened for their antifungal and antibacterial activities *in vitro* in comparison to dermatin (an antifungal) and ampicillin (an antibacterial). The results are cited in Table V and expressed as the inhibition zone in millimeters. As shown in Table V, the majority of the tested polymers showed a moderated antibacterial activity against the representative Gram-negative bacteria, except polymer $7_d$, which had no significant influence. Polymers $7_b$ and $7_c$ showed strong antibacterial activity against the same type of bacteria compared with the controlled values. Polymer $7_b$ had strong antibacterial activity against *S. marcescens* (20/24) at a higher concentration (0.1 mg/mL). Moreover, polymer $7_c$ showed strong antibacterial activity against *S. marcescens, E. coli*, and *P. aeruginosa* (20/24, 8/12, and 22/29, respectively), whereas none of the synthesized polymers had considerable antibacterial activity against the Gram-positive bacteria, except polymer $7_c$, which showed a slight effect on both lower and higher concentrations of *M. luteus* (10/32 and 12/35, respectively). When we compared the aromatic-based polyazomethines $7_a$–$7_c$ and the aliphatic-based polyazomethines $7_d$ and $7_e$, we found that the former polymers had a higher influence than the latter against the representative Gram-negative bacteria.

On the other hand, all of the tested polyazomethines showed no significant influence against the selected fungi species, except polymers $7_b$ and $7_c$. A strong antifungal influence against *A. niger* and *F. oxysporum* for polymer $7_b$ was found compared with the controlled values, which started at 22/32

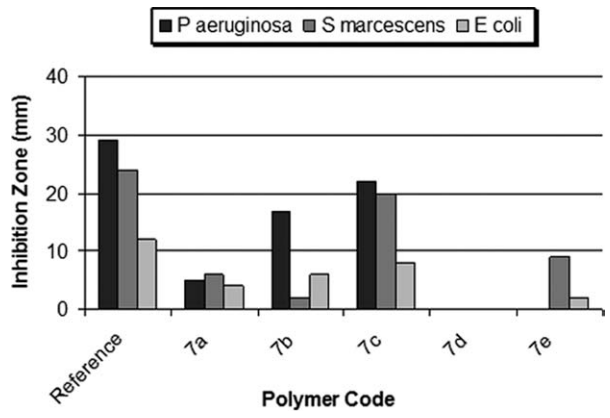


**Figure 3** Effects of polyazomethines $7_a$–$7_e$ on the growth of Gram-negative bacteria.

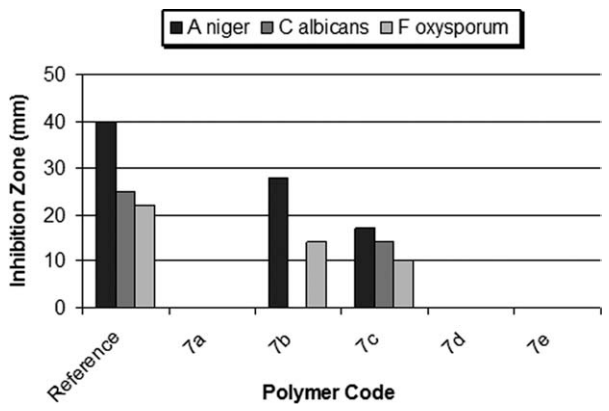


**Figure 4** Effect of the polyazomethines on the growth of fungi.

and 8/16, respectively, for the lower concentration (0.05 mg/mL) and ranged up to 28/40 and 14/22, respectively, for the higher concentration (0.1 mg/mL). Moreover, polymer $\mathbf{7_c}$ showed considerable antifungal activity against the same type of fungi at the lower concentration only (15/32 and 7/16, respectively) and showed a slight effect on the higher concentrations (17/40 and 10/22, respectively). In addition, only polymer $\mathbf{7_c}$ had antifungal activity against *C. albicans*, and it had a considerable effect. From the previous data, we found that the synthesized heteroaromatic polyazomethines showed moderated antibacterial activity against the representative Gram-negative bacteria compared to those against Gram-positive bacteria and antifungal species. The *minimum inhibitory concentration* (MIC) is defined as the lowest concentration where no visible turbidity is observed in the test tube (bacteriostatic concentration). MIC of the most active polymers was 0.05 mg/mL. Lower concentrations showed no significant influence versus the standard antifungal and antibacterial agents.

Figures 3 and 4 provide a comparative account of the effect of the polyazomethines $\mathbf{7_a}$–$\mathbf{7_e}$ on the growth of Gram-negative bacteria (*P. aeruginosa*, *S. marcescens*, and *E. coli*) and the fungal species (*A. niger*, *C. albicans*, and *F. oxysporum*), respectively. These data indicate that the polyazomethines significantly inhibited the growth of microorganisms (c.f. Fig. 3). Figure 4 shows no significant inhibition on the growth of the representative fungi. More particularly, it can be clarified from these figures that the control culture (without the polymer sample) generally exhibited maximum growth. On the other hand, the polymer samples showed different growth according to variation in the polymer structures. The synthesized polyazomethines showed results similar to those reported previously by Di Braccio et al.[53] for 1,8-naphthyridine derivatives.

## CONCLUSIONS

New heteroaromatic polyazomethines $\mathbf{7_a}$–$\mathbf{7_e}$ containing 1,8-naphthyridine moieties were synthesized with a solution polycondensation technique by the interaction of monomer **6** with different aliphatic and aromatic diamines. The resulting polymers were characterized by elemental and spectral analyses and by solubility and viscosity measurements. The order of higher solubility for all the synthesized polyazomethines was as follows: $\mathbf{7_e}$ and $\mathbf{7_c} > \mathbf{7_d} > \mathbf{7_a}$ and $\mathbf{7_b}$. Polymer $\mathbf{7_e}$ showed low significant temperatures of degradation at the $T_{40}$ and $T_{50}$ values; this may have been due to the lower thermal stability of that polymer compared to those of the other polymers. The IDTs of all of the prepared polymers were in the range 212–330°C. The aromatic-based polyazomethines had a higher $T_g$ values compared to the aliphatic-based polyazomethines. The resulting polyazomethines showed moderated antibacterial activity against the representative Gram-negative bacteria compared to the Gram-positive bacteria and antifungal species.

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