Egypt. J. Chem. **Vol. 65,** No. 2 pp. 29 - 33 (2022)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Synthesis and Studying Antibacterial Activity of New Nitrogen Rich Polymers

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Abstract

New polymers obtained from barbiturates derivatives containing 1,2,3-triazole moiety were prepared via "click" chemistry method. The chemical structures of the polymers synthesized with substituents were identified by some spectroscopic analysis (FTIR, and NMR spectroscopies) besides the thermal stability were confirmed by DSC and TGA techniques. Thermal properties of the copolymers which showed very good thermal stability and high Tg value (260,270 °C). The new copolymers were tested as an antibacterial activity with some types of microorganisms. They showed good antimicrobial activity towards the investigated specific microorganisms (Ec, Pa, Sa).

Keywords: Phenobarbital, 1,2,3-Triazole, Copolymers, Thermal stability, Antimicrobial activity

1. Introduction

Barbituric acid that contains five heteroatoms [three Oxygen and two Nitrogen] commonly known as barbiturates. [1] Many of barbiturates that contain (aryl or 5-alkyl) are utilized as antihypertensive, hypnotic, anticonvulsant drug [2] sedatives, antimicrobial, anesthesia. [3,4] anti-oxidant effects [5] anticancer [6,7] and inhibitors of the α-glucosidase enzyme. [8] Recently 1,2,3-triazole compounds have increased much importance in the field of material science and polymer because of their excellent characteristics such as strong antifouling, anti-microbial nature, medicinal and industrial applications [9,10] for the 1,2,3-triazole derivatives along with simple synthetic procedures and high reaction yield. Before the synthesis of [11] poly-1, 2, 3-triazole appears an elevated solubility, luminescence intensity, and excellent thermal stability. [12,13] Besides, the molecule polymers in poly-1,2,3-triazole derivatives may contain a conjugated system with an aromatic ring, in addition to promoting whiteness and the complementary effect .[14,15] whereas, incorporation of 1,2,3-triazole ring in the polymers is an influential way to upgrade their thermos stabilities, chemical durabilities, [16,17] and antifungal activities, [18,19]. The goal of this study is to prepare and study the thermal properties of new copolymers from barbiturate derivatives containing heterocyclic ring (1,2,3-triazole) by using click chemistry between barbiturate-alkyne and azide-barbiturate monomers and tested their activity as an antibacterial.

2. Experimental Part

All the chemical substances, solvent, and Equipment obtained from some companies are BDH, Fluke, Merck, and Sigma Aldrich besides commercial sources. IR spectra were recorded in Faculty of Science, University of Kufa, Iraq by using a (Bruker ALPHA FT-IR). NMR spectra were determined in University of Mashhad, Iran by using a (Bruker 300 MHz in DMSO-d6 as solvent), DSC was recorded by the thermal analyzer (Perkin-Elmer DSC7, Norwalk, CT). TGA of all copolymers was measured by a thermogravimetric analyzer on (NETZSCH STA 409 PC).

2.1. General Synthetic Method

Barbiturate derivatives which contain alkyl moiety were synthesized according to the past study. [8, 20]

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Receive Date: 07 July 2020, Revise Date: 19 July 2020, Accept Date: 27 July 2020

DOI: 10.21608/EJCHEM.2021.34931.2727

2.2. Preparation of 1,3-bis(2-chloroacetyl)-5-ethyl-5-phenylpyrimidine-2,4,6-(1H,3H,5H)-trione (1) [21]

A solution of Phenobarbital (0.01 mol) in (30 mL) of DMF. Chloro acetyl chloride (0.02 mol) was added with strong stirring. (0.02mol) of tri-ethylamine was added to a mixture. The reaction was stirred and refluxed without heating for (4 hrs.). The solvent (DMF) was evaporated and the precipitate was washed by (5 mL) of water-ether. The result was filtered and crystallized by ethanol. The product pale yellow (80 %), m.p. (174 -176 0C) and Retention factor = (0.64). The TLC was used (benzene: methanol, 4:1). (115). Yield reaction: 90%; m p: 85-87 °C; FTIR, ν cm^{-1}: 3028 (C-Aromantic),2981,2831 (C-Haliph.), 1671 (C=O), 754 (C-Cl), 1H NMR δ ppm: 82.32(q, 4H, CH2 barbituric acid), 0.88(t, 3H, CH3 barbituric acid), 2.9 (s, 2H, O=C--CH2), 7.31-7.44 (m, 4H, Ar-H), 13C-NMR δ ppm: 151,19, 60.26 , 28.97 and 10.16 due to (C=O amide), (CH_2-N_3), (-CH2 barbituric acid) and (-CH3 barbituric acid) respectively and other signals at : 172.57, 139.22, 129.37, 128.48, 126.60, 40.78, 40.50, 40.227, 39.94, 39.67, 39.39, 39.11.

2.3. Preparation of 1,3-bis(2-azidoacetyl)-5-ethyl-5-phenylpyrimidine-2,4,6-(1H,3H,5H)-trione(2) [21]

(0.01mol) of compound (1) and (20mL) of DMF was stirred for (5 min), start addition of sodium azide (0.02 mol) solution in (10 mL) DMF was added . Then reflux for (7 hrs.). The reaction was observed by TLC method. the solvent was eliminated by evaporation and the precipitate was filtered , then dried and washed with distilled water and ether, Yield reaction :85 %, m. p.: 152-154 ^{0}C and R*f* = 0.73, (benzene : methanol, 4:1). FTIR, ν cm^{-1}: 3074(C-Aromantic),2981,2831 (C-Haliph.),2121 (CH_2-N_3), 1661 (C=O), 767 (C-Cl), ^{1}H NMR δ ppm: 82.32(q, 4H, CH_2 barbituric acid), 0.88(t, 3H, CH_3 barbituric acid), 2.9 (s, 2H, O=C-CH_2), 7.31-7.44 (m, 4H, Ar-H), ^{13}C-NMR δ ppm: 151,19, 60.26 , 28.97 and 10.16 due to (C=O amide), (CH_2-N_3), (-CH_2 barbituric acid) and (-CH_3 barbituric acid) respectively and other signals at : 172.57, 139.22, 129.37, 128.48, 126.60, 40.78, 40.50, 40.227, 39.94, 39.67, 39.39, 39.11.

2.4. Synthesis of poly barbiturates [20]

All polymerization procedures were taking place under nitrogen gas. Azide phenobarbital, and alkyl barbiturates mixed in an equivalent number of moles an anticipative 1:1 molar feed ratio dissolved in (10 mL) DMF. Then CuSO4.5H2O (0.01 mmol) and Sodium ascorbate (0.02 mmol) were added. The stirring for 60 hrs at 65 oC, copper salts were washed several times by distilled water and the copolymers products were gained through the precipitation in methanol solvent. The end compounds were washed three times with a copious amount of water and dried on the oven.

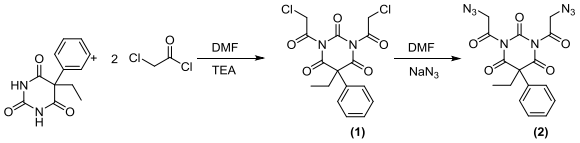
Polymer po1: FTIR, ν cm^{-1}, 1588, 1661, 2862, 2974, 3088; 1H NMR δ: 2.09 ppm (q, J = 7.2, Hz,2H), 1.02 ppm (t, J = 7.2, Hz, 3H), 5.29 ppm (s, 2H, N-COCH2-), 4.52 ppm (s, 2H,-O-CH2-triazole ring), 5.89 ppm (s, 2H, -O-CH2-N-), methylene protons group between triazole and pyrimidine ring), 7.48–7.21 ppm (m, Ar-H), 7.91 ppm (s, 1H proton of triazole ring). ^{13}C NMR δ: 10.50 ppm, 10.53 ppm, 28.74 ppm, 28.76 ppm, 62.05 ppm, 62.14 ppm, 63.66 ppm, 63.71 ppm, 68.57 ppm, 76.65 ppm, 122.88 ppm, 126.31 ppm, 126.31 ppm, 126.34 ppm, 127.25 ppm, 127.28 ppm, 128.58 ppm,128.61 ppm, 137.09 ppm, 137.18 ppm, 143.25 ppm, 153.38 ppm, 153.71 ppm, 169.95 ppm,170.02 ppm.

polymer po2: FTIR, ν cm^{-1}, 1598, 1671, 2874, 2984,3113, 1H NMR δ: 2.02 ppm (q, 2H), 1.03 ppm (t, 3H), 4.61 ppm (s, 2H, -O-CH2-triazole ring), 5.35 ppm (s, 2H, -N-COCH2-),5.91 ppm (s, 2H, -O-CH2-N-, methylene protons group between triazole and pyrimidine ring), 7.57–7.24 ppm (m, Ar-H), 7.87 ppm (s, 1H proton of triazole ring). 13C NMR δ: 10.32 ppm, 10.45 ppm, 29.21 ppm, 29.24 ppm, 61.22 ppm, 61.24 ppm, 62.55 ppm, 63.68 ppm, 69.62 ppm, 78.25 ppm, 123.04 ppm, 126.47 ppm, 127.58 ppm, 129.89 ppm, 138.35 ppm, 143.87 ppm, 155.31 ppm, 155.62 ppm,170.58 ppm, 171.54 ppm.

3.Results and Discussion

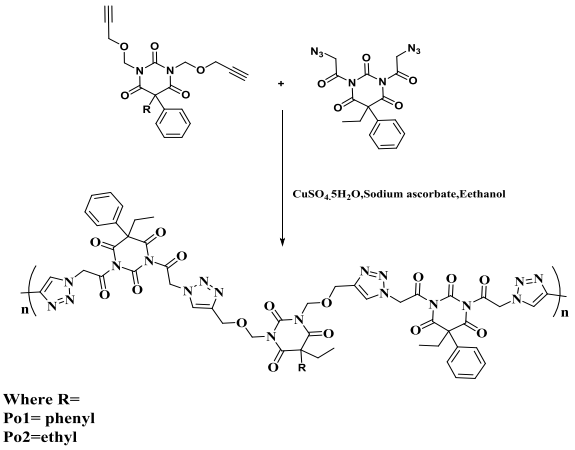
3.1. Chemistry

Barbiturate derivatives prepared because phenobarbital has an active N-H group located at the 1,3-*N*,*N*-positions of the pyrimidine ring. The phenobarbital was reacted with chloroacetyl chloride in DMF as a solvent to produce compound (1) and then with NaN_3 (Scheme 1) Purification of the product from the starting material to improve the isolated yield.



Scheme 1. Synthesis barbiturate derivatives

New polymers po1 and po2 that contain 1,2,3-triazole ring prepared by Cu-catalyzed via [2+3] cycloaddition polymerization method from barbiturate derivatives (Scheme 2).



Scheme 2. Synthesis copolymers

FTIR data: The infrared spectra of (2) compound showed the appearance of a new band at 2121 cm $^{-1}$ assigned to the vibrations of the azide group. This change in absorption bands is good evidence for the formation of compound (2) as well as bands at 1661 cm^{-1} was due to (C=O) groups of the pyrimidine ring. Whereas the stretching vibration peaks of triple bond in C≡C group (2131, 2128 cm^{-1}), C≡C−H (3311, 3281 cm^{-1}), [20], and N_3 (2121 cm^{-1}) disappeared in FTIR spectra of copolymers. This is a good indication to formation the end products from monomers via the Click polymerization reaction. Finally, the stretching absorption of (C−H) aromatic in 1,2,3-triazole and phenyl rings appears in the region 3088−3130 cm^{-1}. [22]

NMR data: Interestingly, different properties were obtained in the ^{1}H and ^{13}C NMR spectra of (po1) and (po2) copolymers. In ^{1}H NMR spectra of synthesized copolymers (po1) and (po2) showed the absence of the alkyne protons at 2.51-2.52 ppm, and showed new signals of methylene protons (-O-CH_2-triazole ring) at 4.52,4.61 ppm, but at 5.29, 5.35 ppm assigned to methylene protons (-N-$COCH_2$-). Also, the chemical shifts of methylene protons (-O-CH_2-N-) appear at 5.89,5.91 ppm. The new signal 7.91,7.87 ppm due to 1,2,3-triazole protons. ^{13}C NMR spectra, of prepared copolymers, showed new signals at 143.25,143.87 ppm due to carbon atoms C-4 and C-5 in 1,2,3-triazole ring.

Thermal data: Thermal features of synthesized copolymers (po1) and (po2) were recorded via (TGA) and (DSC), thermal data was summarized in (Table 1). The heat range that used in thermal degradation of copolymers between 40-700 °C. The values glass-transition temperatures (Tg, 260,270 °C) of the copolymers were showed high morphological stability. Whereas the degradation temperatures (Td) at 430,315 °C of 50%weight loss. The end polymers (po1) and (po2) at higher than 300 °C retained more than 50% of their weights. According to thermal analysis (TGA) and (DSC) that synthesized copolymers have thermal stability compared with many commercial copolymer materials.

Table 1. Thermal Properties

Polymers	Tg C^{o}	Tm C^{o}	Td C^{o}	$T_{50\%}$ C^{o}
Po1	260	450	> 600	430
Po2	270	570	> 600	315

3.2. Antimicrobial activity [23]

All the microorganism's tests were obtained from the microbiology lab of Alsaader hospital (Iraq, Najaf), which included *Escherichia coli* (Es), *Pseudomonas aeruginosa* (Pa), *Staphylococcus aureus* (Sa). The chemicals were weighed and dissolved in dimethylsulfoxide (DMSO) to prepare extract stock solutions of 10 mg/mL. The procedure of evaluation of the antibacterial activity depends on Agar well diffusion method was reported in the previous study [24,25] The results were summarized in Table 2.

Table 2. Antimicrobial activity of polymers

polymers	Ec	Pa	Sa
Po1	8	9	13
Po2	9	12	11
DMSO	7	6	13
Ampicillin	7	6	15

Measurements inhibition zone in diameter (mm): (less than 5 mm: no antimicrobial activity; more than 5 mm: positive antimicrobial activity). *Pa*: *Pseudomonas aeruginosa*; *Ec*: *Escherichia coli*; *Sa*: *Staphylococcus aureus*.

4. Conclusions

The copolymers contain 1,2,3-triazoles ring were synthesized effectively by using a simple procedure called Click chemistry method that depends on polymerization of monomers that contain dipropargyl barbiturates and azide phenobarbital. The copolymer

products have high glass-transition temperatures (Tg) and good thermal stability. On the other hand, the prepared copolymers showed good antimicrobial activity.

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