



Original Research Article

# Bio-Based Polymers Derived and Modified on *Cis*-1, 3,4, 6-Tetrahydrophthalimide and Its Applications

Muna I. Khalaf\* , Asmaa Mohammed Noori Khaleel

Department of Chemistry, College of Science, University of Baghdad, Iraq

## ARTICLE INFO

## Article history

Submitted 2022-04-26

Revised: 2022-05-15

Accepted: 2022-06-28

Manuscript ID: CHEMM-2205-1546

Checked for Plagiarism: Yes

Language Editor:

Dr. Behrouz Jamalvand

Editor who approved publication:

Dr. Zeinab Arzehgar

DOI:10.22034/CHEMM.2022.344357.1546

## KEYWORDS

Adipoyl chloride

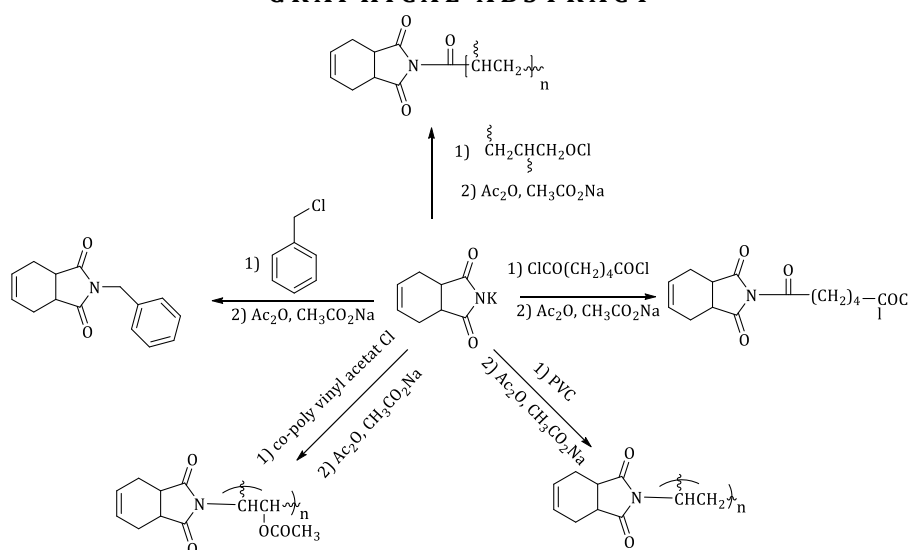
phthalimides substituted

Bio-based polymerization

## ABSTRACT

In the current work, *N*-substituted *cis*-1,3,4,6-tetra hydrophthalimide polymerized derivatives were prepared as bio-based materials. This research was carried out through the following three steps; Firstly, preparing *N*-alkyl *cis*-1,3,4,6-tetra hydrophthalamic acid by reacting of *cis*-1,3,4,6-tetra hydrophthalimide salt with (benzyl chloride, PVC, adipoyl chloride, co-poly vinyl acetate chloride and poly acyloyl chloride) respectively producing, *N*-alkyl tetra hydro phthalimide. Furthermore, the next step includes preparing *N*-creatinyl tetrahydro phthal imide, and followed by the polymerization step of the prepared unsaturated compounds throughutilizing (BPO) as initiator alongside the heating. Several techniques were used to characterize the prepared compounds such as recording the melting points and softening point as well as infrared spectroscopy (FT-IR). However, some of the prepared compounds were characterized by using proton nuclear magnetic resonance <sup>1</sup>HNMR and studied thermally *via* differential scanning calorimetric technique DSC.

## GRAPHICAL ABSTRACT



\* Corresponding author: Muna I. Khalaf

✉ E-mail: [muna.i@sc.uobaghdad.edu.iq](mailto:muna.i@sc.uobaghdad.edu.iq)

© 2022 by SPC (Sami Publishing Company)

## Introduction

Bio-based resins which usually called bio-based polymers are obtained from renewable resources (plants, microorganisms, bacteria, algae, etc.). The synthesis of these materials are carried out either directly or by synthesizing the monomers which undergo polymerization. There are different types of bio-based polymers that are available in the market such as poly-L-lactide, polylactic acid, polyhydroxybuturate, polyhydroxyalkalonates (PHAs), polyamide and polypropylene (PP) which can be obtained from bio-based ethylene which can be acquired through converting thermoplastic materials such as terephthalate, ethanol, polyethylene. Other bio-based resins such as (bio based epoxy epichlorohydrine and polyurethanes with bio-based dyols) which can be obtained partially from glycerol. While the most known applications for bio-based polymers are in the field of packaging, still their uses in other demanding fields are of a great challenge. With taking the following evidences into consideration [1], our plant and the living organisms can take the advantage of using bio-based polymers as they can be used in decreasing the carbon footprint due to the fact that fungi and bacteria (microorganisms) have the ability to degrade these polymers to their constituent monomers and producing CH<sub>4</sub>, CO<sub>2</sub>, and water, therefore, no toxic materials will be generated. Moreover, the bio-based plastics have a wide industrial and daily life applications, in response to increase of the world's population and use of technology [2].

Cyclic imides are one of the pharmacophores which considered to be an important building blocks for synthesizing agrochemicals, drugs, natural products, advanced materials and polymers. Lamprolobine, julocrotine, migrastatin, salfredin C-1, cladoniamide A, and palasimide are some of natural products that possess the imide moiety [3-6]. Imides can be used extensively to synthesize different bio-active natural products [7-13]. For example, the structural feature of phthalimide includes -CO-N(R)-CO- as well as imide ring which unable the compound to be used in terms of biological and pharmaceutical activity [14]. Huge attention has been directed toward phthalimide and its derivatives due to the proven

biological effects that are even better than the known pharmacological molecules, some of the biological effects are; anxiolytic [15], antitumor [16-18], analgesic, antifungal, and antibacterial properties. Therefore, the biological activities of these molecules have been subjected to a lot of biomedical research [19-21].

When it comes to synthesizing phthalimide derivatives, Gabriel synthesis method is considered the main method for that purpose. This method includes N-alkylating the potassium or sodium salt of phthalimide with primary alkyl halide in order to produce the corresponding N-alkyl phthalimide [22, 23]. Most of the secondary alkyl halides cannot be involved in the reaction. In addition, most of the electrically conductive and high strength polymers are containing imide subunits such as polyimide. Kapton is one of the example of these polymers where two imide groups are contained in the repeated unit which derived from aromatic tetra carboxylic. Acids [24-27]. Polyglutarimide represents another example of polyimides which typically derived from ammonia and primary amine and poly methyl methacrylate (PMMA). The rigidity of imide functional groups is influencing the toughness of these materials [28-30]. Aminolysis and cyclization processes of PMMA is carried out at high pressure and temperature.

## Materials and methods

### Chemistry

Electro thermal capillary apparatus was used to determine the melting points of the prepared compounds and the values are uncorrected. Perkin Elmer IR spectrophotometer was used to record the infrared (FT-IR) spectra with (4000-400 cm<sup>-1</sup>) range of wavenumbers utilizing potassium bromide pellets. Moreover, Bruker AC-400F, 400 MHz was used to perform proton (<sup>1</sup>H) nuclear magnetic resonance spectroscopic analysis. Differential Scanning Calorimetry (DSC) was used to study the thermal behavior of the prepared compounds.

### 1-Preparation of *N*-alkyl tetrahydrophthalimide (1-5)

To a solution of tetrahydro phthalimide salt (0.01 mol, 1.48 g) and 25 mL of acetone was added 0.01 mol of benzylchloride (PVC, or adipoyl chloride, or co-poly vinyl acetate chloride or polyacryloyl chloride) respectively [28]. Moreover, for two hours, the stirring was continued at room temperature and then filtrate the resulted precipitate followed by drying and recrystallizing from ethanol. Some physical properties of compound 1-5 are listed in Table 1.

### 2-Synthesis of *N*-creatinyltetrahydrophthal imide [31]

25 mL of a dry acetone and 0.005 mol (0.5 g) of acetic anhydride were placed in a 150 mL two-necked flask which connected to droop funnel and reflux condenser and equipped with magnetic stirrer. By stirring, all the acetic anhydride was dissolved and then 0.005 mol (0.5 g) creatinine solution in 25 mL of acetone was allowed to run through the dropping funnel drop wise for 30 min under cooling range (0-5 °C). The stirring was continued for 2 h under room temperature. Suction filtration was used to separate and filtrate the off-white precipitate. After that, the precipitate was washed with solvent and then dried and recrystallized from ethanol, the 85% yield was obtained pale brown color with m.p. 171-173.

### 3-polymerization of *N*-creatinyltetrahydrophthal imide [31]

5 mL of DMF was used to dissolve 0.3 g of the prepared monomer, and then adding 0.05% weight of dibenzoyl peroxide. Under nitrogen atmosphere, the water bath was covering the polymerization tube in order to be heated to 90 °C for 1 h. The polymer was obtained as a pale yellow with 76% yield and the S.P 115-124 °C as listed in Table 1.

### 4-Polymerization of *N*-creatinyltetrahydrophthal imide acrylonitrile (co-polymerization) [8]

From prepared monomer (0.3 g) and acrylonitrile, where the DMF was used as a solvent as both compounds dissolved in 15 mL of the solvent, and then adding 0.05% weight of dibenzoyl peroxide. Under nitrogen atmosphere, the water bath was covering the polymerization tube in order to be heated to 90 °C for 1.5 h. The co-polymer was obtained as a dark yellow with 55% yield and the S.P 150-162 °C. The some physical properties of compound (6-8) are listed in Table 1.

### Swelling studies

The study of polymer swelling was conducted as follow: the swelling and diffusion parameters was determined by swelling the homo and copolymer in a solution with pH=7 at 37 °C. The swollen matter was removed regularly from the water bath and then superficially dried using filter papers.

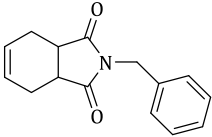
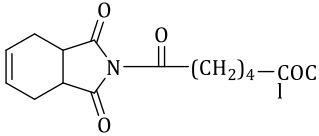
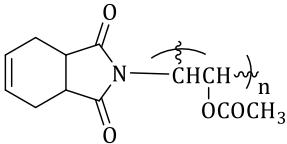
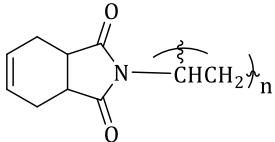
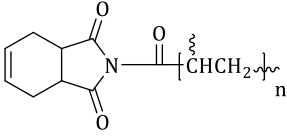
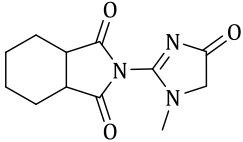
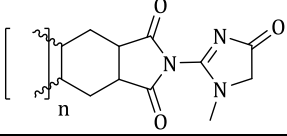
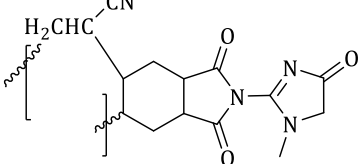
### Differential scanning calorimetry (DSC)

Perkin-Elmer Pyris I analyser was used to record DSC scans at 10 °C/min rate of heating, whereas, the Scanning Calorimetry of (DSC) analysis was differential indium which used as calibration standard. In fact, DSC is considered as a technique for determining the absorbed or released heat quantitatively when a physical or chemical change is occurred to the substance.

### The biological activity [32, 33]

Biological activity of the synthesized compounds was tested, as some of the compounds have shown antimicrobial activities when exposed to gram negative (*E. coli*) as well as gram positive (*Staphylococcus Aurous*). The disc diffusion method was used to study the antimicrobial activities for the synthesized compounds as the bacterial inoculums were spread on nutrient agar. After drying the inoculums, wells of 8 mm diameter were made inside the plate of agar alongside the sterile cork borer. DMSO (10<sup>-3</sup> M) concentration was used as a solvent for the synthesized compounds and the standard compound for antibacterial activity was cephalixin (10<sup>-3</sup> M). The Petri was subjected to incubation at 37 °C for 24 h and the inhibition zone was measured in millimeters.

**Table 1:** Some physical properties of polymers

Compound NO.	Structure	Color	M.P °C	S.P °C	Yield (%)
1		white	114-116	-	72
2		grey	109-112	-	79
3		gold		105-115	72
4		brown	-	140-155	78
5		orange		250-260	82
6		Off white	171-173		85
7		Pale yellow		115-122	76
8		Dark yellow		150-162	55

## Results and Discussions

Gabriel synthesis method was used to synthesize all the prepared compounds, as the reaction steps have been shown in the [Scheme 1](#).

Whereas compounds **6**, **7** and **8** were prepared as shown in the [Scheme 2](#).

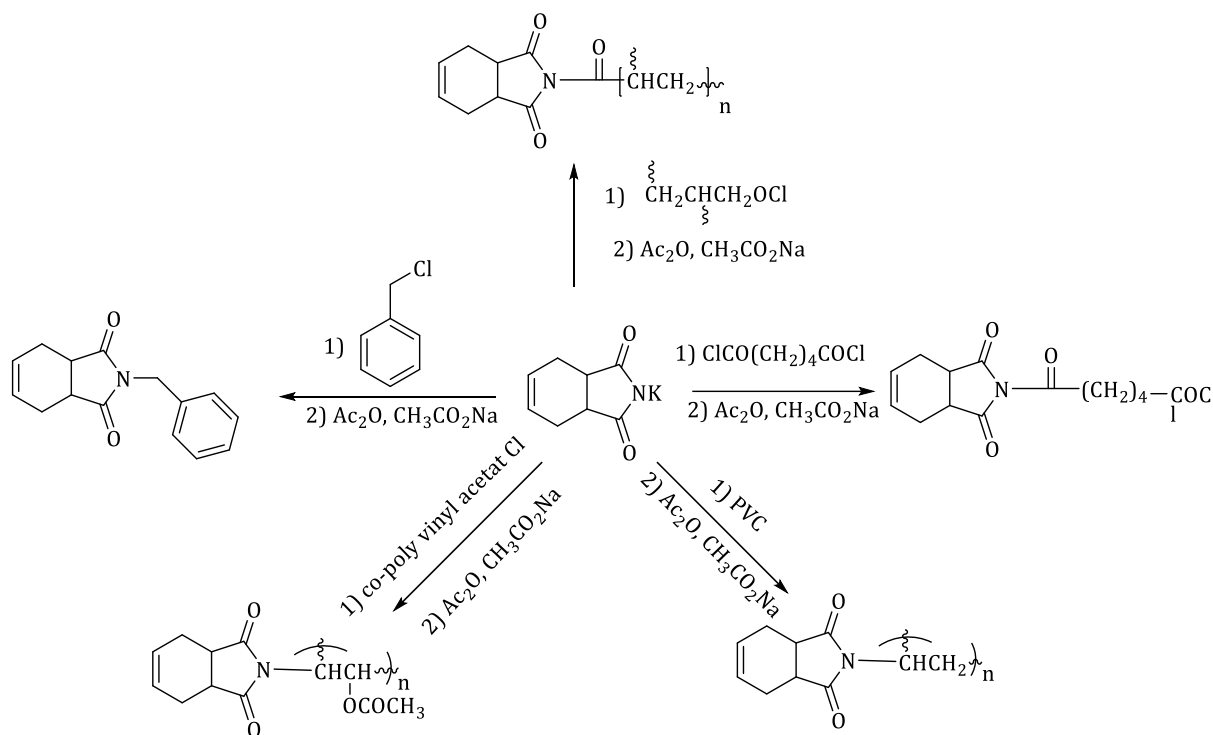
The starting material of the substituted synthetic compounds of *N*-imide was tetrahydrophthalimide and salt's which reacted with halogen atom of compounds at different °C, where compounds **6** and **7** was polymerized with BPO in DMF. All compounds characterized by physical and

chemical properties with FT-IR and <sup>1</sup>H-NMR, <sup>13</sup>C-NMR some of them.

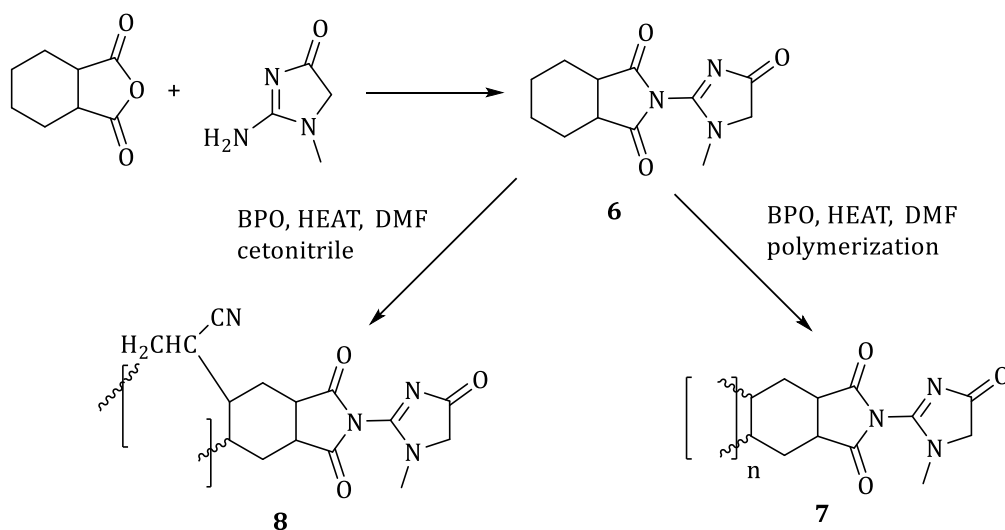
FT-IR showed disappearance of νNH group band at 3203 cm<sup>-1</sup>, whereas a significant absorption at the regions 1770-1780 cm<sup>-1</sup> of νC=O imide group where showed, and bands at 1600-1647 cm<sup>-1</sup> which belongs to νC=C imide, 1883 cm<sup>-1</sup> of ester compound **3**, 1708-1670 cm<sup>-1</sup> of νC=N creatinyl ring, 1327-1370 cm<sup>-1</sup> of νC-N and 1152-1263 cm<sup>-1</sup> contributed to νC-O group. However, some additional absorptions of compounds' functional groups have been listed in the [Table 2](#). <sup>1</sup>H-NMR spectra of compound **3**, **5** and **8** showed signal at

$\delta$ 0.83-0.92 ppm for (s, 5H, CH Polymer),  $\delta$ 3.1 ppm for (s, 3H, CH<sub>3</sub> Ester), and  $\delta$ 5.56 ppm for compound **3** and **5**, while compound **6**, **7** and **8** show  $\delta$ 3.06-3.2 ppm for (s, 3H, NCH<sub>3</sub>),  $\delta$ 4.37-4.42 ppm for (s, 2H, CH<sub>2</sub>, creatinin ring). On the other hand compound **8** show disappearance of signal at

$\delta$ 5.8 ppm due to C=CH with appeared of signal at  $\delta$ 4.08 ppm due to CH<sub>2</sub> creatinin ring. Additional of essential signals for compounds shown in Figures S1, S2 and S3 (Supporting information).



**Scheme 1:** Preparation of compounds 1-5



**Scheme 2:** Preparation of compounds 6-8

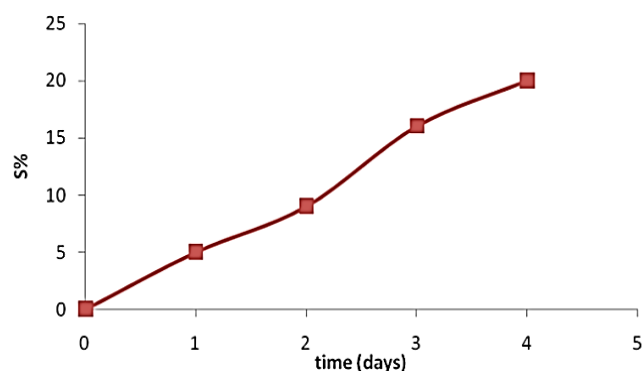
**Table 2:** FT-IR spectral data of the prepared compounds

Compound No.	C-H Olefin or Ar	C-H Aliphatic	C=O Imide	C=C olefin	C-N	C-O	Others
1	3045	2953, 2887	1750	1618	1303	1240	C-C (Ar) 1445, 1567
2	3041	2910, 2888	1774	1620	1325	1267	COCl 1841
3	3015	2920, 2856	1778	1641	1329	1217	CO Ester 1838
4	3012	2902, 2889	1783	1608	1323	1265	-
5	3066	2979, 2887	1769	1606	1348	1230	-
6	3026	2925, 2869	1771	1600	1345	1239	CO cry. Ring 1708
7	3016	2969, 2877	1780	1647	1305	1244	CO cry. Ring 1670
8	3009	2952, 2820	1763	1632	1307	1229	CN 2231

### Study of swelling

The study of dynamic swelling for the polymer includes the following: The polymer was immersed in THF solution at room temperature and with pH=7 in order to determine the swelling and diffusion parameters. The filter paper was used to remove the swollen gels which then weighted and located in the previous bath. Moreover, dynamic swelling study was performed in order to investigate the behavior of time-dependent swelling of the polymer which included in a solution with pH=7. The following equation used to calculate the swelling percentage S%:

$$S\% = \frac{(M_1 - M_0)}{M_0} \times 100 = 109\%$$

**Figure 1:** swelling with several days of polymer 3

Where  $M_0$  represents the dry polymer mass at time=0 which equal to 0.11 g, whereas  $M_1$  represents the swollen mass of polymer 3. At time=t which equal to 0.23 g within 24 h it is worth noting that swelling with several days give parameter as shown in [Figure 1](#).

### Differential scanning calorimetric (DSC)

Polymer 7 showed 72% mass loss in 360 °C ([Figure 2](#)) while polymer 8 showed losing mass in two step one of them at 322 °C in 49% and the other at 594 °C in 47% ([Figure 3](#)). As shown in [Figures 2](#) and [3](#) the TG analysis of this two polymer show thermal stability of polymer 7 seem more than thermal stability of polymer 8 that may be duo to homogenous surface effect.



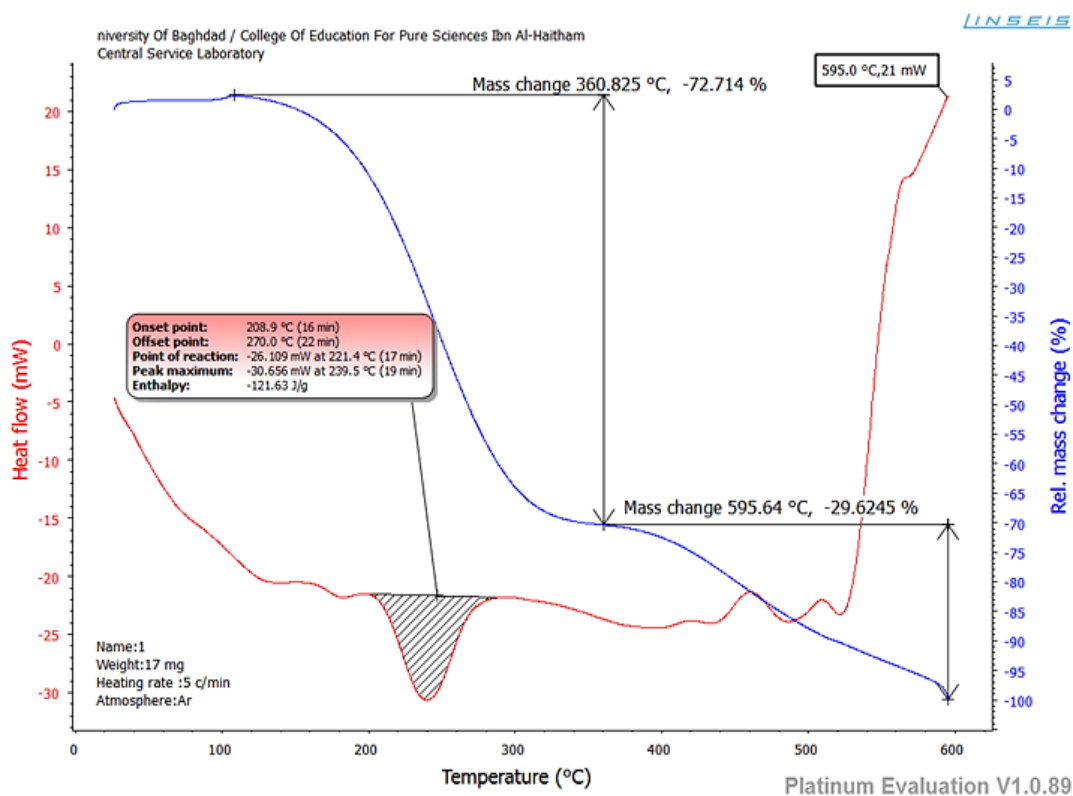


Figure 2: DSC (TG)-analysis of homo creatinyl polymer 7

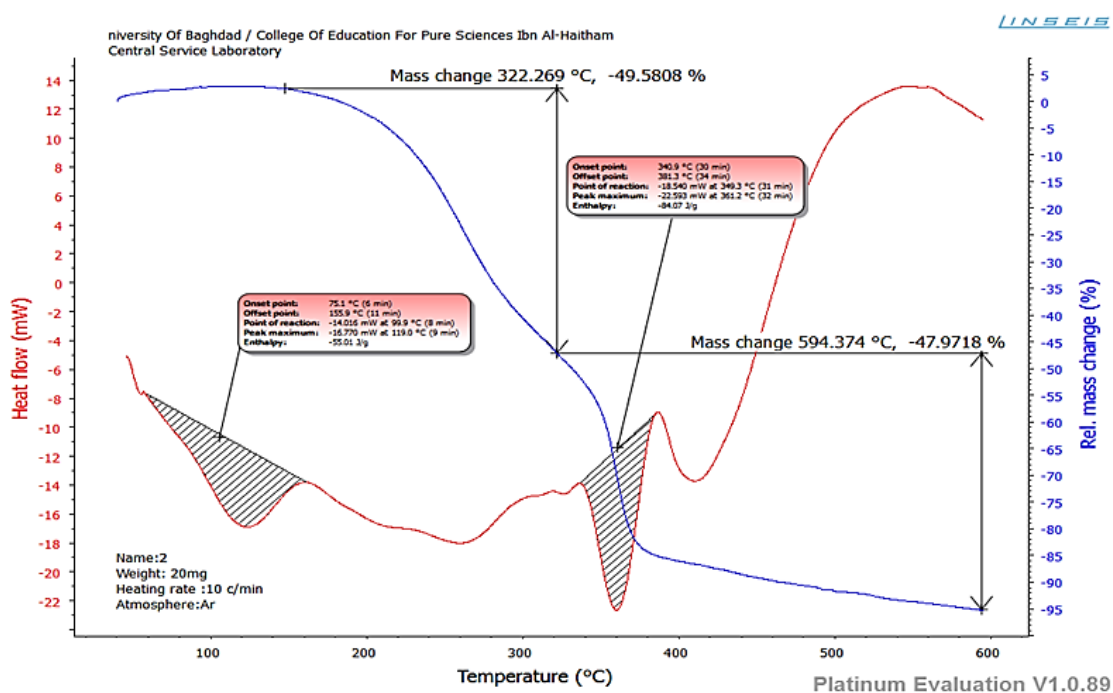


Figure 3: DSC (TG)-analysis of co-acetonitril creatinyl polymer 8

*The biological activity*

Unfortunately, there is no interesting result was found as expected, all compounds show negative

or little more than cephalixin cooperative. This result might contribute to the materials used in examination test which might be expire (Table 3).

**Table 3:** Biological activity of some of the prepared compounds

Compound No.	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>
Standard cephalixin	48	40
3	3	2
4	2	5
5	3	1
6	2	3
7	4	2
8	2	8

Note: Inhibition zone in mm

## Conclusion

The prepared compounds showed thermal stability and good response mass of swollen in one case while giving negative response in the biological activity test.

## Acknowledgments

Funding this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

## Conflict of Interest

We have no conflicts of interest to disclose.

## ORCID

Muna I. Khalaf

<https://orcid.org/0000-0001-6086-153X>

## Supporting Information

Additional supporting information related to this article can be found, in the online version, at DOI: [10.22034/chemm.2022.344357.1546](https://doi.org/10.22034/chemm.2022.344357.1546)

## References

- [1]. Vladan Koncar, 2019, 2.5.2.5 Bio-based resins
- [2]. Akbar M.U., Zia K.M., Nazir A., Iqbal J., Ejaz S.A., Akash M.S.H., Pluronic-based mixed polymeric

- micelles enhance the therapeutic potential of curcumin. *Aaps Pharmscitech*, 2018, **19**:2719 [Crossref], [Google Scholar], [Publisher]
- [3]. Loosley B.C., Andersen R.J., Dake G.R., Total synthesis of cladoniamide G., *Organic letters*, 2013, **15**:1152 [Crossref], [Google Scholar], [Publisher]
- [4]. Kimura T., Kanagaki S., Matsui Y., Imoto M., Watanabe T., Shibasaki M., Synthesis and assignment of the absolute configuration of indenotryptoline bisindole alkaloid BE-54017, *Organic letters*, 2012, **14**:4418 [Crossref], [Google Scholar], [Publisher]
- [5]. Zhang J., Senthilkumar M., Ghosh S.C., Hong S.H., Synthesis of Cyclic Imides from Simple Diols, *Angewandte Chemie International Edition*, 2010, **49**:6391 [Crossref], [Google Scholar], [Publisher]
- [6]. Gaul C., Njardarson J.T., Shan D., Dorn D.C., Wu K.D., Tong W.P., Huang X.Y., Moore M.A.S., Danishefsky S.J., The migrastatin family: discovery of potent cell migration inhibitors by chemical synthesis, *Journal of the American Chemical Society*, 2004, **126**:11326 [Crossref], [Google Scholar], [Publisher].
- [7]. Mostowicz D., Dygas M., Kałuża Z., Heck Cyclization Strategy for Preparation of Erythrinan Alkaloids: Asymmetric Synthesis of Unnatural (-)-Erysotramidine from L-Tartaric Acid, *The Journal of Organic Chemistry*, 2015, **80**:1957 [Crossref], [Google Scholar], [Publisher]
- [8]. Zhang H., Hong L., Kang H., Wang R., Construction of vicinal all-carbon quaternary stereocenters by catalytic asymmetric alkylation reaction of 3-bromooxindoles with 3-substituted indoles: total synthesis of (+)-perophoramidine, *Journal of the American Chemical Society*, Soc. 2013, **135**, 14098. [Crossref], [Google Scholar], [Publisher]



- [9]. Mondal P., Argade N.P., Enantioselective Total Synthesis of Desbromoarborescidines A–C and the Formal Synthesis of (S)-Deplancheine, *The Journal of Organic Chemistry*, 2013, **78**:6802 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [10]. Chiyoda K., Shimokawa J., Fukuyama T., Total syntheses of all the amathaspiramides, *Angewandte Chemie International Edition*, 2012, **51**:2505 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [11]. Deore P.S., Argade N.P., Sonogashira coupling reactions of bromomaleimides: route to alkyne/cis-alkene/alkyl maleimides: synthesis of Luffarin X and Cacospongionolide C., *The Journal of Organic Chemistry*, 2012, **77**:739 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [12]. Jangir R., Argade N.P., A facile synthesis of oxyvicine, *RSC advances*, 2012, **2**:7087 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [13]. Trost M., Osipov M., Dong G., A concise enantioselective synthesis of (–)-ranirestat, *Organic letters*, 2010, **12**:1276 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [14]. Korčušková M., Petruš J., Lepcio P., Kučera F., Jančář J., Novel approaches for functionalization of polypropylene by maleimides, *Polymer*, 2021, **238**:124398 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [15]. Murrell D., Bossaer J.B., Carico R., Harirforoosh S., Cluck D., Isavuconazonium sulfate: a triazole prodrug for invasive fungal infections, *International Journal of Pharmacy Practice*, 2017, **25**:18 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [16]. Rani A., Viljoen A., Johansen M.D., Kremer L., Kumar V., Synthesis, anti-mycobacterial and cytotoxic evaluation of substituted isoindoline-1, 3-dione-4-aminoquinolines coupled via alkyl/amide linkers, *RSC advances*, 2019, **9**:8515 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [17]. Yegorova T., Barnych B., Voitenko Z., Reaction of pyrido [2, 1-a] isoindole with 1, 4-naphthoquinone and study of the product by spectroscopic methods, *French-Ukrainian Journal of Chemistry*, 2016, **4**:33 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [18]. Hassanzadeh F., Rabbani M., Fasihi A., Hakimelahi G.H., Mohajeri M., Synthesis of phthalimide derivatives and evaluation of their anxiolytic activity. *Research in Pharmaceutical Sciences*, 2008, **2**:35 [[Google Scholar](#)], [[Publisher](#)]
- [19]. Hijazi A.K., Taha Z.A., Abuhamad N.J., Al-Momani W.M., Synthesis, and characterization of some Cu (I) complexes having propionitrile and pyridine moieties: An investigation on their antibacterial properties, *Journal of Saudi Chemical Society*, 2021, **25**:101387 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [20]. Beveridge R.E., Hu Y., Gregoire B., Batey R.A., Di-tert-butyl Ethynylimidodicarbonate as a General Synthone for the  $\beta$ -Aminoethylation of Organic Electrophiles: Application to the Formal Synthesis of Pyrrolidinoindoline Alkaloids ( $\pm$ )-CPC-1 and ( $\pm$ )-Alline. *The Journal of Organic Chemistry*, 2020, **85**:8447 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [21]. Mitsunobu O., Gabriel synthesis. *Contemporary Organic Synthesis* 1991, **6**:79 [[Google Scholar](#)]
- [22]. Chen J., Park J., Kirk S.M., Chen H.C., Li X., Lippincott D.J., Melillo B., Smith A.B., Development of an effective scalable enantioselective synthesis of the HIV-1 entry inhibitor BNM-III-170 as the Bis-trifluoroacetate Salt, *Organic Process Research & Development*, 2019, **23**:2464 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [23]. Osby J.O., Martin M.G., Ganem B., "An Exceptionally Mild Deprotection of Phthalimides". *Tetrahedron letters*, 1984, **25**:2093 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [24]. Thanzee F. Yushra, Balaraman Kaluvu About Balaraman Kaluvu, *Angewandte Chemie*, 2020, **132**:21566 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [25]. Zhang Y., Yuan H., Yan W., Chen S., Qiu M., Liao B., Atomic-Oxygen-Durable and Antistatic  $\alpha$ -Al x Ti y O/ $\gamma$ -NiCr Coating on Kapton for Aerospace Applications, *ACS Applied Materials & Interfaces*, 2021, **13**:58179 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [26]. Sharmaa N.K., Gulatia P.K., Diwanb P.K., Kumara S., "Energy loss straggling of 5.486 MeV  $\alpha$ -particles in PP, PET and KAPTON polymeric foils", *Applied Radiation and Isotopes*, 2010, **68**:2252 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [27]. Plummer C.J.G., Kausch H.-H., Tézé L., Halary J.L., Monnerie L., Microdeformation mechanisms

- in methyl methacrylate-glutarimide random copolymers, *Polymer*, 1996, **37**:4299 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [28]. Roussel J., Boutevin B., "Synthesis of polyglutarimides from PMMA, cyclohexylamine and methylamine, 4 - New methods for synthesis of polyglutarimides from ammonium", *Macromolecular Chemistry and Physics*, 2000, **201**:2838 [[Google Scholar](#)]
- [29]. Ali U., Karim K.J.B.A., Buang N.A., "A Review of the Properties and Applications of Poly (Methyl Methacrylate) (PMMA)", *Polymer Reviews*, 2015, **55**:678 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [30]. Azzawi A. Al-Obiadi K.K., *International Journal of Research In Pharmacy and Chemistry*, 2016, **1**:1 [[Google Scholar](#)]
- [31]. Khalaf M.I., Hussein M.K., Synthesis, study and antimicrobial activity of new homo, copolymer maleic anhydride with moiety heterocyclic creatinine, *Journal of Pharmacy and Biological Sciences*, 2017, **12**:29 [[Google Scholar](#)], [[Publisher](#)]
- [32]. Akhileshwari P., Kiran K.R., Sridhar M.A., Sadashiva M.P., Lokanath N.K., Synthesis, crystal structure characterization, Hirshfeld surface analysis, and Quantum chemical computations of Ethyl 5-(thiophene-2-carbonyl) thiazole-4-carboxylate. *Journal of Molecular Structure*, 2021, **1242**:130747 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [33]. Sujit K.M., Sarkar S., Singh V., Pandey R., Agrawal N.K., Trivedi S., Singh K., Gupta G., Rajender S., Genome-wide differential methylation analyses identifies methylation signatures of male infertility. *Human Reproduction*, 2018, **33**:2256 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

#### HOW TO CITE THIS ARTICLE

Muna I. Khalaf, Asmaa Mohammed Noori Khaleel. Bio- Based Polymers Derived and Modified on Cis -1, 3,4, 6-Tetrahydrophthalimide and Its Applications. *Chem. Methodol.*, 2022, 6(9) 710-719

<https://doi.org/10.22034/CHEMM.2022.344357.1546>

URL: [http://www.chemmethod.com/article\\_153210.html](http://www.chemmethod.com/article_153210.html)