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RESEARCH ARTICLE

Synthesis of New 2, 4, 5-triphenyl imidazole Derivatives Derived from benzoin and Studying their Biological Activity

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Abstract

In this work a series of new 2, 4, 5-triphenyl imidazole derivatives were synthesized. In the beginning, compound [1] was formed from the reaction of benzoin and benzaldehyde in the presence of ammonia, which was reacted with sodium hydride in DMF to obtain imidazole salt. This salt was reacted with adipoyl chloride to give compound [2]. Acid hydrazide derivative [3] was obtained from the reaction of compound [2] with hydrazine hydrate. After that Shiff bases [4-9] have been synthesized from the reaction of compound [3] with different aromatic aldehydes. These new formed compounds were diagnosed by ^{13}C-NMR, ^{1}H-NMR for some of them (in Ahl-Albate University in Jordan) and FT-IR spectroscopy (In Baghdad University). All of the prepared products have been studied their biological activities toward two kinds of bacteria. These products showed good efficacy to moderate toward bacteria.

Keywords: *Imidazole, Shiffs bases, Biological activity.*

Introduction

Imidazoles is one of the types of heterogeneous ring compounds containing nitrogen and contains a wide area of applications [1].Non-homogeneous ring compounds containing the imidazole system play a major role in chemical processes and pharmaceutical activities. The many compensators of imidazole derivatives are considered a key intermediates to the preparation of many therapeutic agents such as Eprosartan, Omeprazole, Olmesartan ,Pimobendan, Triphenagrel and Losarton [2].

Imidazole derivatives have various activities like herbicides, anti-inflammatory,[3] inhibit of fungicides and antimicrobial activity [4]. Alkylated imidazolium have been used as an ionic liquid [5] providing a process to the Green Chemistry protocol. Imidazole compounds are used in the field of photography as an intrusive compound [6]. Schiff base are produced from the reaction of aromatic aldehydes and aromatic amine in the presence of acid [7]. Schiff bases are intermediate compounds for the preparation of many heterogeneous ring compounds with wide biological applications [8]. They have been used as antiviral, analgesic, plant growth regulator, anti-tubercular, antitumor, and anthelmintic [9, 10].

Material and Method

All reagents were purchased from Aldrich and Merk and used without further purification.

Preparation of 2, 4, 5-triphenyl -1-H-imidazole [1] [11]

Benzaldehyde (0.05 mole) and Benzoin (0.023 mole) in presence of ammonia was refluxed for 4 hours. The separated solid compond was filtered and recrystallized from ethanol.

Preparation of Compound [2] [12]

Compound [I] (0.006 mole) in dimethyl formamide (DMF) (7ml) was cooled to 0°C, and sodium hydride (0.006 mole) was added. The solution was stirred for (30 minutes) then adipoyl chloride (0.006mole) was added drop wise. The mixture was stirred at room temperature for (4 hours). The solvent was evaporated then poured into ice water and filtered. Pale Green powder was obtained then recrystallized from ethanol.

Preparation of Compound [3] [13]

Hydrazine hydrate (0.08 mole) was added to a solution of compound [2] (0.04 mole) in absolute ethanol (10 ml) and was refluxed for 5 hrs. Ethannol was evaporated to give Green product which then crystallized from ethanol. FTIR and physical properties of compounds [1, 2 and 3] are mentioned in Table (1).

Preparation of Shiffs bases [4-9] [14]

A mixture of compound [3] (0.004 mole) (10ml) and few drops of glacial acetic acid in absolute ethanol was slowely added to a solution of aromatic aldehydes (0.004 mole) in (10) ml absolute ethnol and refluxed for (4) hours. The content was poured into crushed ice and the precipitate was filtrated, crystallized with suitable solvent. FTIR and physical properties of compounds [4-9] are mentioned in Table (2).

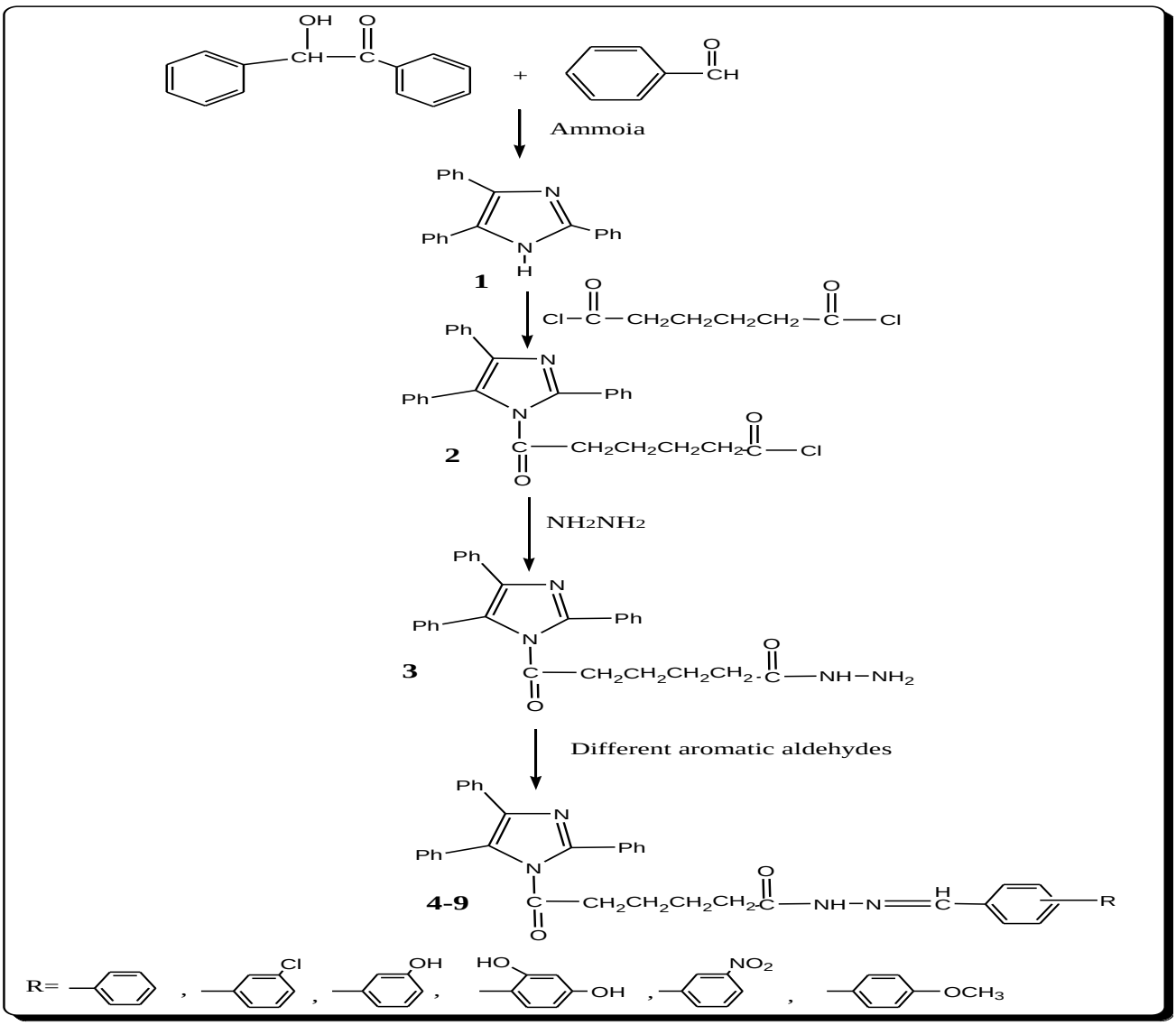
Biological Activity [15]

All of new prepared compounds were tested for their biological activity against Staphylococcus aureus and Escherichia coli in nutrient agar medium. Dimethyl sulfoxide was used as control. The final resulted data of these new compounds and the control are given in Table (5) (Figure 1). Microdilution broth susceptibility method was choiced for the antibacterial evaluation of the compounds and chloramphenicol was candidate as standard antibacterial agent.

Agar dishes were roof inoculated uniformly with 100 µl from both cultures of tasted bacteria. The fattened disks were put in the middle, and the plates kept warm to promot growth at 278 K for 1 h to allow good dispersion and relocated to another machine which kept mixture warm to promot growth at 310 K for 24 hours.

Results and Discussion

In this research new derivatives of 2, 4, 5-trophenyl-1H-imidazole were prepared by the reaction sequences outlined in Scheme (1).



Scheme 1: Synthetic route for prepared compounds [1-9]

Compound [1] was formed from the reaction between benzoin and benzaldehyde in the presence of ammonia .The formation of this compound was indicated by the presence in their IR spectra of (N-H) at (3417cm^{-1}), (C=C) at (1596) cm^{-1}, (C=N) imidazo at (1639) cm^{-1} and (C-H)aromatic at 3062.5 cm^{-1} table [1]. Compound [2] was formed from the reaction between compound [1] and adipoyl chloride. The formation of this compound was indicated by the presence in their FTIR spectra of (C=C) at (1569) cm^{-1}, (C=N) imidazo at (1633) cm^{-1} , (C-H)aromatic at (3030)cm^{-1} , (C=O) at (1677) cm^{-1} , (C-Cl) at (756) cm^{-1} and (C=C) aliphatic at (2850) cm^{-1} table [1].

^{1}HNMR (ppm) of compound [2]: 7-7.5 (m, 15H) aromatic protons, 1.6-2.2 CH_2 group table [3] (Figure 2). ^{13}C-NMR: 127-136 (aromatic carbon), 24-32 (aliphatic carbons). 173 (C=O) table [4] (Figure 3).Reaction between compound [2] and hydrazine hydrate afforded the acid hydrazid derivative [3]. The spectrum showed the appearance of the (C=O) at (1672cm-1), NH at (3544) cm^{-1}, (NH2) asy. At (3463) cm^{-1}, sym. at (3413) cm^{-1}, (C=C) aromatic at 1618 cm^{-1}, (C=N) imidazo at (1637) and (C-H) aromatic at 3029 cm^{-1} table [1] (Figure 8).^{1}HNMR (ppm) of compound [3]: 7-7.9 (15H) aromatic proton, 1.4-2.6 CH_2 group, 3.2 (s,2H,-NH2),and 8.7 (t, NH) table[3](Figure 4). ^{13}C-NMR: 127-131 (aromatic carbon), 20-38 (aliphatic carbon). 170 (C=O), 126 (C-Cl) table [4](Figure 5). FTIR spectrum of Schiff bases [4-9] observed the following bands: (C=N) Schiff bases at (1616-1622) cm$^{-1,}$ (C=C) aromatic at (1569-1579) cm$^{-1,}$ (N-H) at (3330-3429) cm^{-1} and (C=O) at (1670-1704) cm^{-1}. FT-IR spectra of compounds [5, 6, 7, 8 and 9] observed the following bands: (751), (3438), (3440), (1531 asym-1352 sym) and 1100 cm^{-1} belong to (C-Cl), (OH), (OH), (NO_2) and (C-O) respectively. ^{1}HNMR (ppm) of compound [9]: 7-8 (19H) aromatic proton, 1.3CH_2 group, 9(s, NH), 8.6 (s, CH=N), 3.73(s, CH_3) table [3] (Figure 6). ^{13}CNMR: 115-132 (aromatic carbon), 39 (aliphatic carbon). 167 (C=O), 151(CH=N), 56(CH3) table [4] (Figure 7).

Biological Activities

The prepared compounds [1-9] showed various biological activities toward two kinds of bacteria staphylococcus aureus and E. coli. The finding observed that compounds [1, 2, 3, 4,6,7,8 and 9] are inactive against staphylococcus aureus while compounds [5] are very highly active against these bacteria. Compounds [2 and 3] are inactive against E.Coli while compounds [1, 5, 8 and 9] showed moderate activity except compounds [4, 6 and 7] which are very highly active against these bacteria. All these results are shown in Table (5).

Table 1: Physical properties and FT-IR spectral data of compounds [1-3]

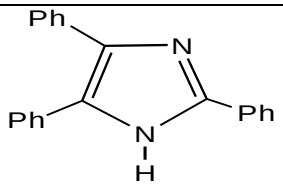
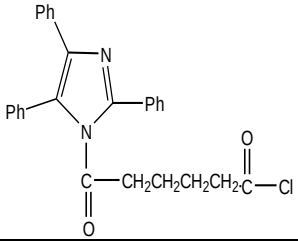
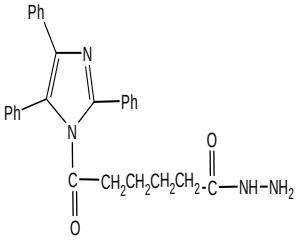
Compd. No.	Compound structure	M.P. 0 C	Yield %	Color	Major FTIR Absorptions Cm-1				
					N-H	C=C aromatic	C=N imidazo	C-H aromatic	others
1		274-278	90	Pale Yellow	3417	1596	1639	3062.5	---
2		94-96	84	Pale Green	----	1569	1633	3030	C=O 1677 C-Cl 756 C=C aliphatic 2850
3		138-140	75	Deep Geen	3544	1618	1637	3029	NH2 3463(asy.) 3413(sym.) C=O 1672

Table 2: Physical properties and FT-IR spectral data of compounds [4-9]

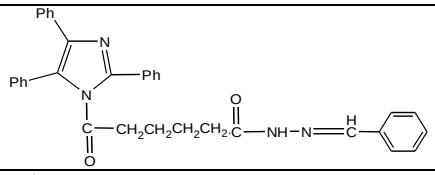
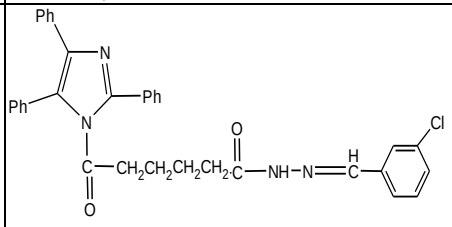
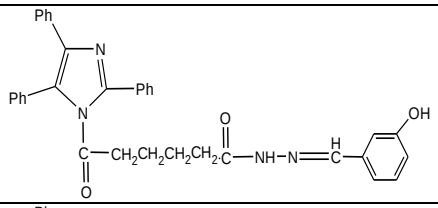
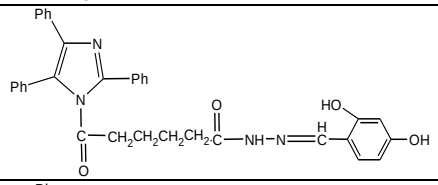
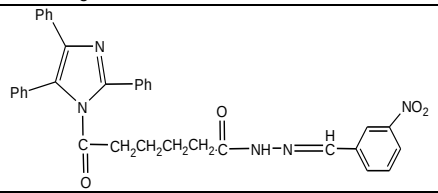
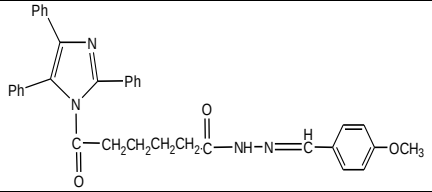
Compd. No.	Compound Structure	M.P. ⁰ C	Yield %	Color	Major FTIR Absorptions Cm^{-1}				
					υC=N shiff bases	υ C=C aromatic	υ N-H	υ C=O	Other
4		Oily	55	Green	1622	1569	3429	1679	---
5		Oily	64	Green	1622	1569	3446	1679	C-Cl 754
6		158-160	69	Brown	1622	1575	3417	1677	OH 3438
7		Oily	72	Yellow	1620	1570	3330	1670	OH 3440
8		Oily	65	Yellow	1616	1579	3388	1704	NO_2 1531asy. 1352 sym
9		Oily	75	Brown	1622	1576	3350	1680	C-O 1100

Table 3: 1H-NMR-spectrum data of compounds [2, 3 and 9]

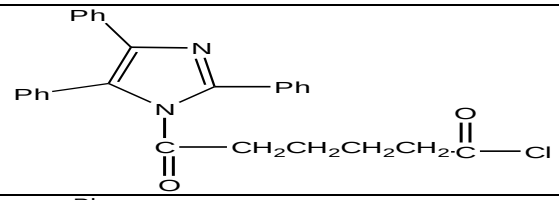
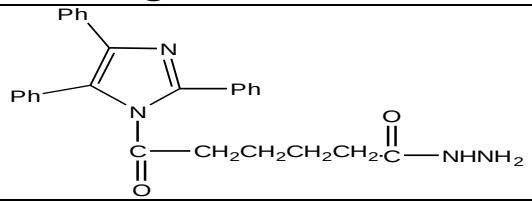
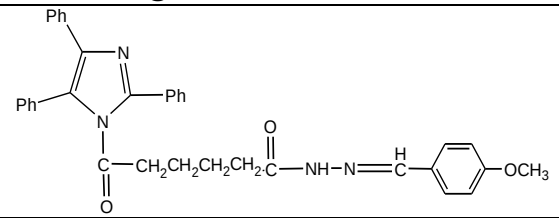
Compound No.	Compound structure	^{1}H-NMR spectral data δ ppm
2		7-7.9 (15H) aromatic protons, 1.6-2.2 CH_2 group
3		7-7.9 (15H) aromatic protons, 1.4-2.6 CH_2 group, 3.2(s,2H,-NH2), 8.7(t, NH)
9		7-8 (19H) aromatic protons, 1.3 CH_2 group, 9 (s, NH),8.6 (s, CH=N) , 3.73(s, CH3)

Table 4: ^{13} C-NMR-spectrum data of compounds [2, 3 and 9]

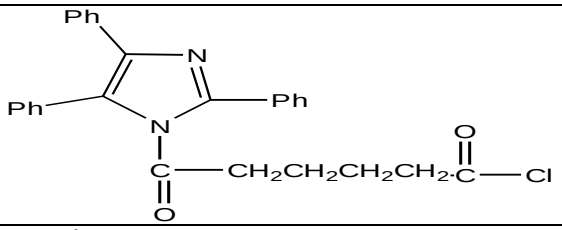
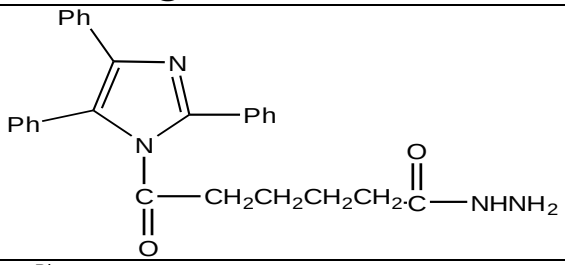
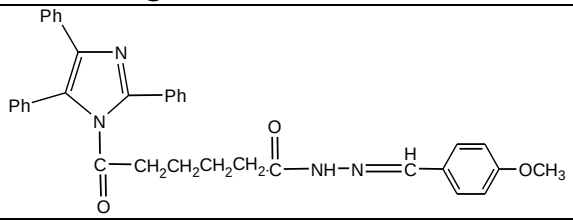
Compound No.	Compound structure	^{13}C-NMR spectral data δ ppm
2		127-136 (aromatic carbons), 24-32 (aliphatic carbon). 173 (C=O), 126 (C-Cl)
3		127-131 (aromatic carbons), 20-38 (aliphatic carbons). 170 (C=O)
9		115 -132 (aromatic carbons), 39 (aliphatic carbons). 167 (C=O), 151(CH=N), 56(CH3)

Table 5: Biological activities of the prepared compounds

Compd. No.	Gram positive bacteria	Gram negative bacteria
	Staph. areus	***E.coli***
1	**----**	**9**
2	**----**	**---**
3	**----**	**----**
4	**----**	**18**
5	**----**	**20**
6	**26**	**14**
7	**-----**	**22**
8	**----**	**26**
9	**-----**	**11**

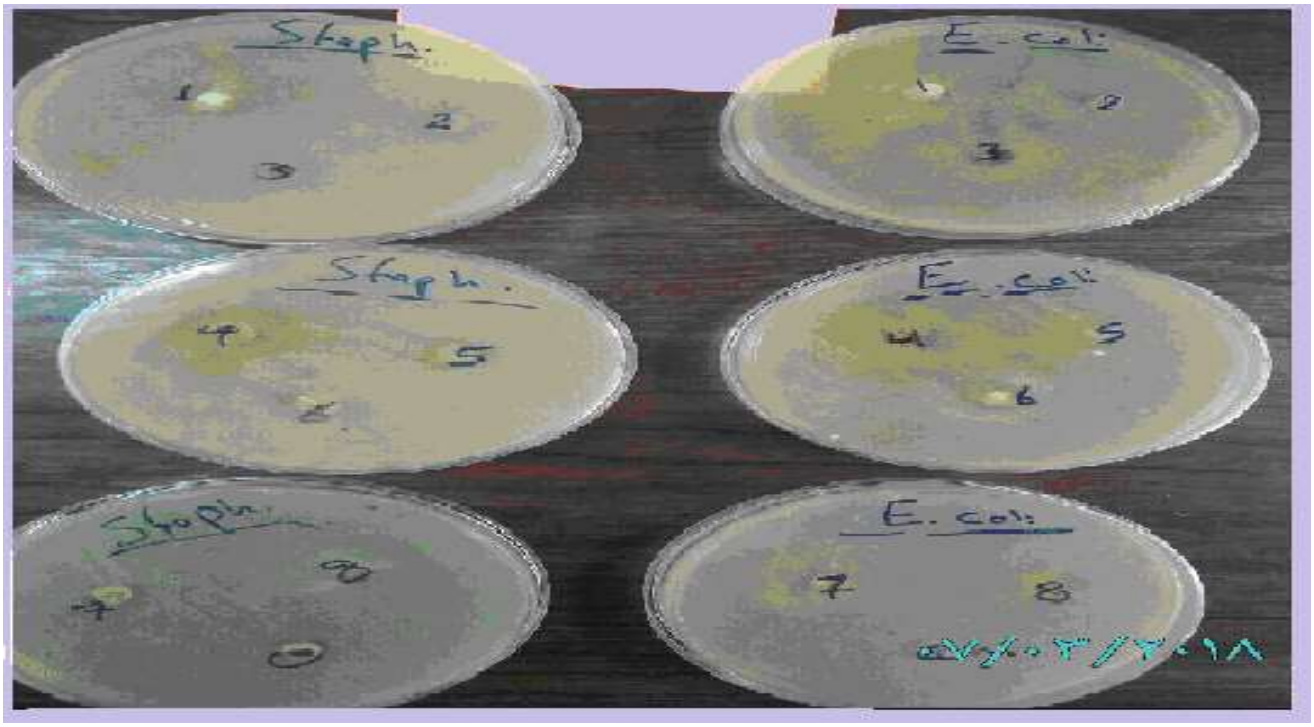


Figure1: Biological activity of the prepared compounds

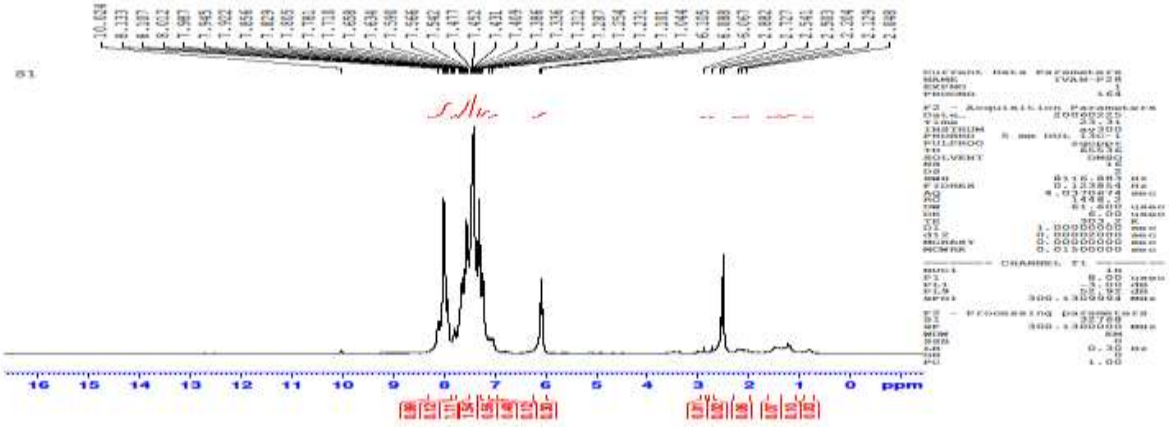


Figure 2: 1HNMR spectrum of compound (2)

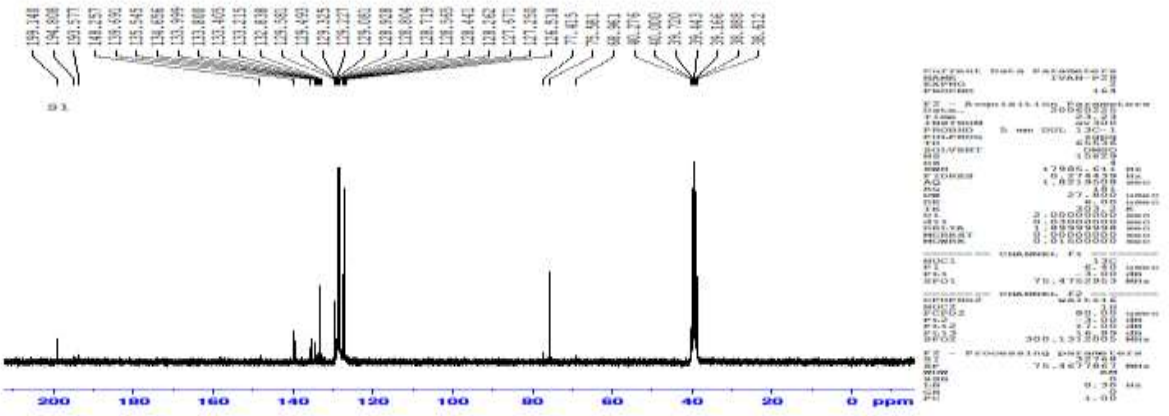


Figure 3: 13C-NMR of compound (2)

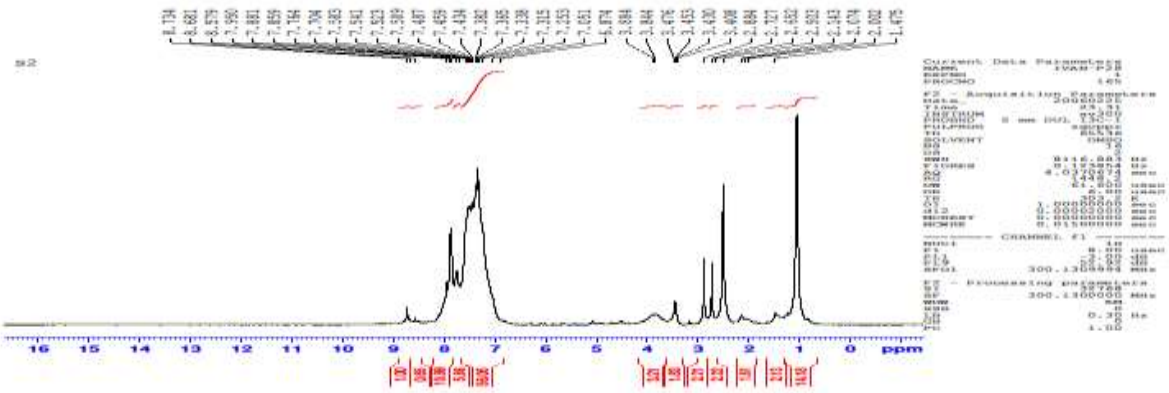


Figure 4: 1HNMR spectrum of compound (3)

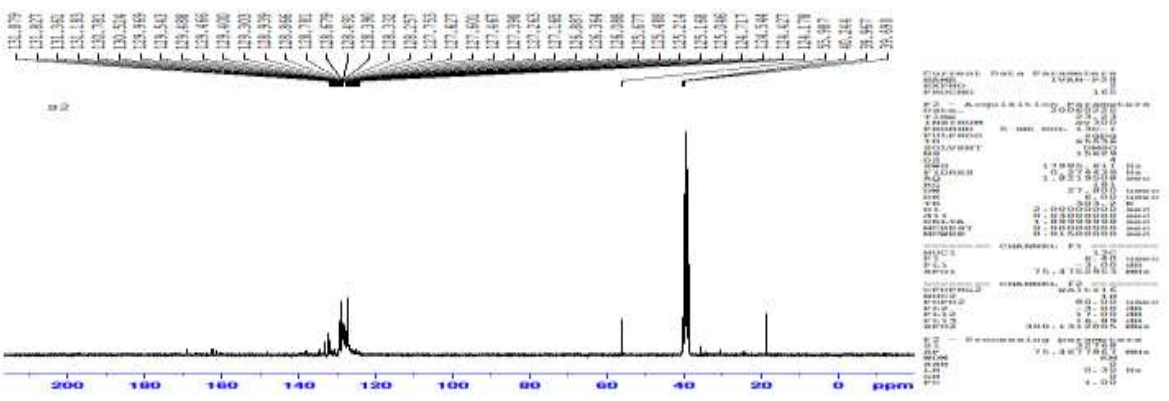


Figure 5: 13C-NMR of compound (3)

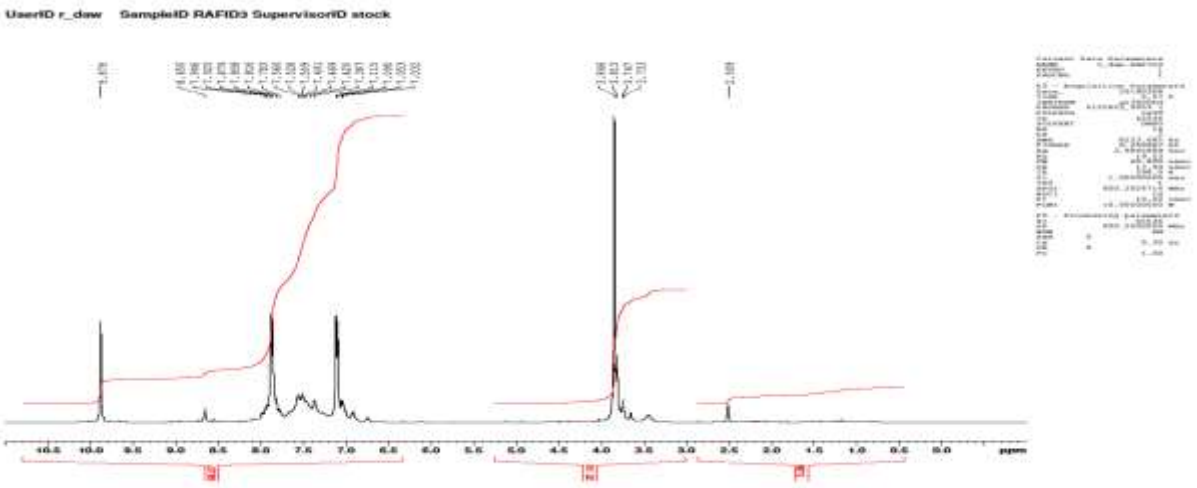


Figure 6: HNMR spectrum of compound (9)

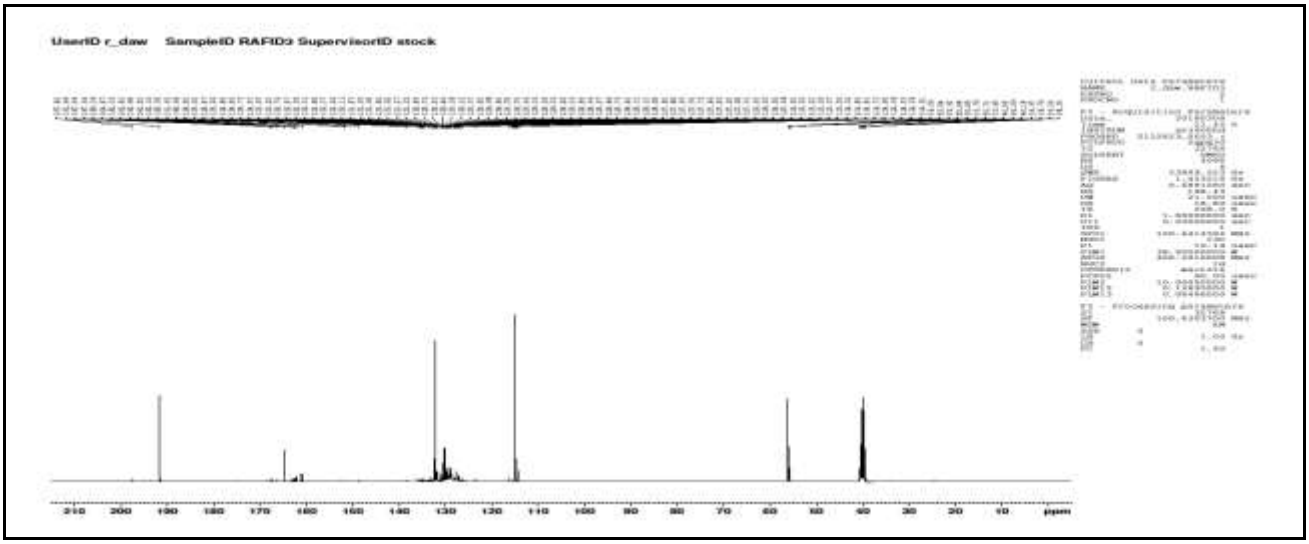


Figure 7: 13C-NMR of compound (9)

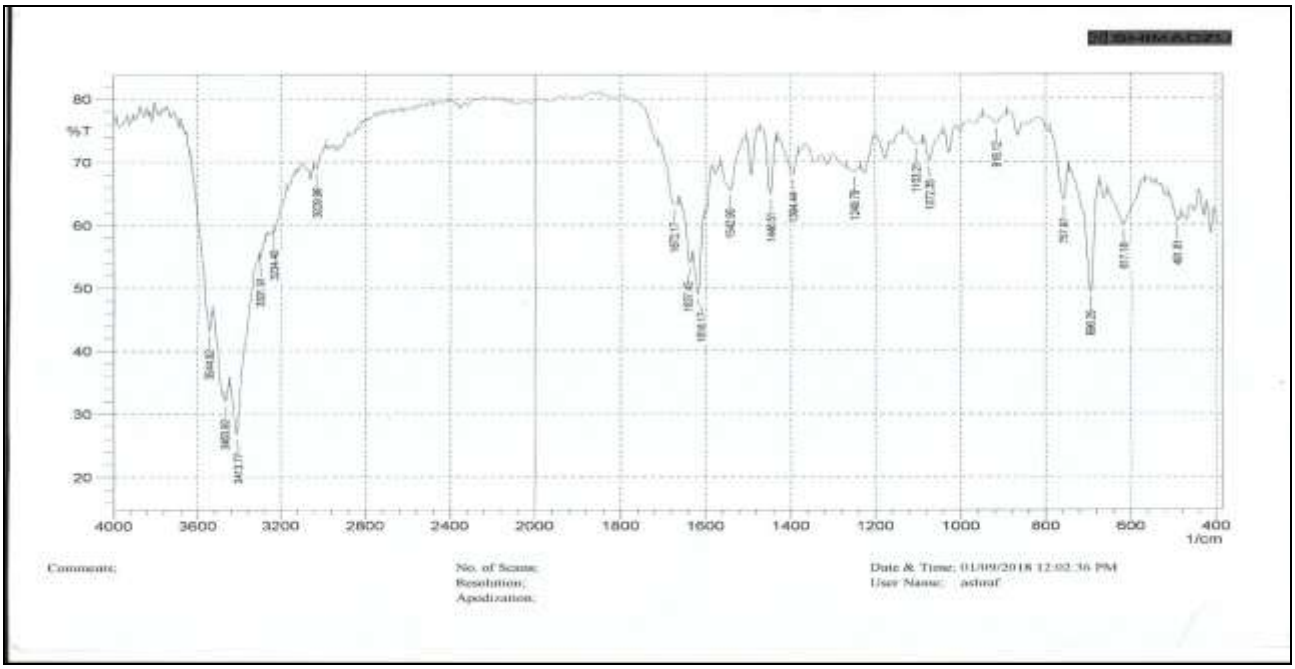


Figure 8: FT-IR of compound [3]

Conclusion

New 2, 4, 5-triphenyl imidazole derivatives were synthesized from benzoin. All of the prepared products have been studied their biological activities toward two kinds of bacteria. These products showed good efficacy to moderate toward these bacteria.

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