Synthesis and characterization of novel 1,8-Naphthalimide derivatives containing 1,3-oxazoles, 1,3-thiazoles, 1,2,4-triazoles as antimicrobial agents

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Abstract

This research include developing new heterocyclic derivatives of 1,8-naphthalimides bearing 1,3-oxazole, 1,3-thiazole and 1,3,4-triazole moieties as the following:

Direct imidation of 1,8-naphthalic anhydride with ethylglycinate in dimethylsulfoxide as solvent under reflux at high temperature for sixteen hours to obtain the *N*-ester-1,8-naphthalimide(1). Then conversion of this ester into (urea, thiourea, semicarbazide, phenylsemicarbazide, thiosemicarbazide and phenylthiosemicarbazide) derivatives through its reaction with (urea, thiourea, semicarbazide, phenylsemicarbazide, thiosemicarbazide and phenylthiosemicarbazide) respectively to give compounds (2,6,10,12,14 and16). Then cyclization of these compounds by using different reagents. The first cyclization of compounds (2 and 6) by using *p*-substituted phenacylbromide to give oxazole derivatives (3-5) and thiazole derivatives (7-9) respectively. Furthermore triazole derivatives were prepared through the second cyclization of compounds (10,12,14 and16) in alkaline media(4N. NaOH) to give compounds (11,13,15 and 17) respectively.

The structure of the newly synthesized compounds was identified by their FTIR, and some of them by ^{1}H-NMR, ^{13}C-NMR spectral data and some physical properties and some specific reactions.

Also new compounds were screened in three concentration for their *in vitro* antimicrobial activity against both Gram (+ve) such as *Staphylococcus aureus, Bacillus* and Gram (-ve) *Escherichia Coli, pseudomonas aeuroginosa* bacteria and against *Candida albicans* fungal and they were found to exhibit good to moderate antimicrobial activities.

Keywords: 1,8-naphthalimides, 1,3-oxazole, 1,3-thiazole and 1,2,4 triazole, synthesis , antimicrobial activity.

Introduction

Naphthalimides, one type of cyclic imides [1] with strong hydrophobicity and desirable large π-conjugated backbone, could easily interact with various active targets in biological system via non-covalent forces such as π–π stacking, and exhibit diverse biological activities including anticancer [2], antibacterial [3], antitrypanosomal[4], analgesic potency [5]. 1,8-Naphthalimides are well-known as broad-spectrum activity against a variety of human solid tumor cells [6]. Several derivatives have reached the phases of clinical trials [7].

The azole moiety is an important structural feature of many biologically active compounds [8]. Various 1,3-oxazole functional group associated biological activities [9],[10] . More thiazole ring system is an important class of compounds in medicinal chemistry [11]. This structure has found applications in drug development. A number of thiazole derivatives have been reported to possess significant and diverse biological activities [12],[13]. Moreover, 1,2,4-triazole and their derivatives have been found to be associated with diverse agricultural, industrial and pharmacological activities [14], [15].

In this connection, the synthesis of 1,8-naphthalimide derivatives containing five membered ring substituent, in particular 1,3-oxazole, 1,3-thiadiazole, and 1,2,4-triazole fragments which could considerably affect biological properties of 1,8-naphthalimide, to develop novel and potent therapeutic agents of synthetic origin, it was decided to synthesize certain these derivatives and evaluate them for their antimicrobial properties

Experimental

Materials and Instruments

Chemicals used in this work are supplied from Merck, Sigma-Aldrich, BDH and Fluka companies and are used without further purification.

Melting points were recorded using digital Stuart Scientific SMP3 melting point apparatus and are uncorrected. FTIR spectra were recorded on SHIMADZU FTIR-8400 Fourier Transform Infrared spectrophotometer using KBr discs in the (500-4000) cm^{-1} spectral range.^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker 300MHz instrument using DMSO-d^6 as a solvent and TMS as internal reference. Thin layer chromatography (TLC) was carried out using Fertigfollen precoated sheets type Polygram Silg, and the plates were developed with iodine vapour. The antimicrobial activity was performed in clinical laboratory department, college of pharmacy, Al-Mustansiriyah University.

Synthesis of *N*-Ethylglycinate-1,8-naphthalimide(1).

(0.005 mol, 1g) of 1,8-Naphthalic anhydride was dissolved in 30 mL dimethyl sulfoxide with stirring and heating. (0.006 mol, 0.837g) ethyl glycinate hydrochloride after neutralized with dilute solution of sodium bicarbonate was added and the mixture was refluxed until TLC showed no 1,8-naphthalic anhydride remained. This reaction was completed in (16 hrs). The mixture was then poured into ice water. The yellow precipitated solid was filtered off and recrystallized from ethanol [16].

Synthesis of (1,8-naphthalimide *N*-yl)aceto-urea(2), thiourea(6), semicarbazide(10), phenylsemicarbazide(12) thiosemicarbazide(14), and phenylthiosemicarbazide (16) respectively:

A mixture of ester (1) (0.0035 mol, 1g) with (urea, thiourea, semicarbazide, phenylsemicarbazide, thiosemicarbazide, and phenylthiosemicarbazide) respectively (0.0035 mol) and sodium acetate (0.0035 mol, 0.31 g) in absolute ethanol (30ml) was refluxed for (10-16 hr). The reaction mixture was filtered and poured on ice water; the precipitate was filtered and recrystallized from suitable solvents to give crystals [17].

Synthesis of (1,8-naphthalimide *N*-yl) acetamido [4-(*p*-substituted phenyl)-1,3-oxazole-2-yl)] (3-5) and (1,8-naphthalimide *N*-yl) acetamido [4-(*p*-substituted phenyl)-1,3-thiazole-2-yl)] (7-9) .

A mixture of compound (2 or 6) (0.0033 mol) with absolute ethanol (20 ml), *p*-substituted phenacyl bromide (0.0033 mol) was refluxed for (12-14 hrs.), cooled and neutralized with ammonium hydroxide solution. The precipitate was filtered off, washed with water, and suitable solvents were used for recrystallization [18].

Synthesis of [(1,8-naphthalimide *N*-yl) methyl]-1,2,4-triazol-3-ol (11), 1,2,4-triazol-1-phenyl-3-ol (13), 1,2,4-triazol-3-thiol (15) and 1,2,4-triazol-1-phenyl-3-thiol (17).

In round bottom flask (0.0032 mol) for compounds [10,12,14 and 16] was refluxed with 20% aqueous sodium hydroxide solution (25ml) for (10-12 hrs.), cooled, poured on to ice water, stirred and neutralized by gradual addition of (1:1) hydrochloric acid. The formed precipitate was filtered and recrystallized from suitable solvents [19].

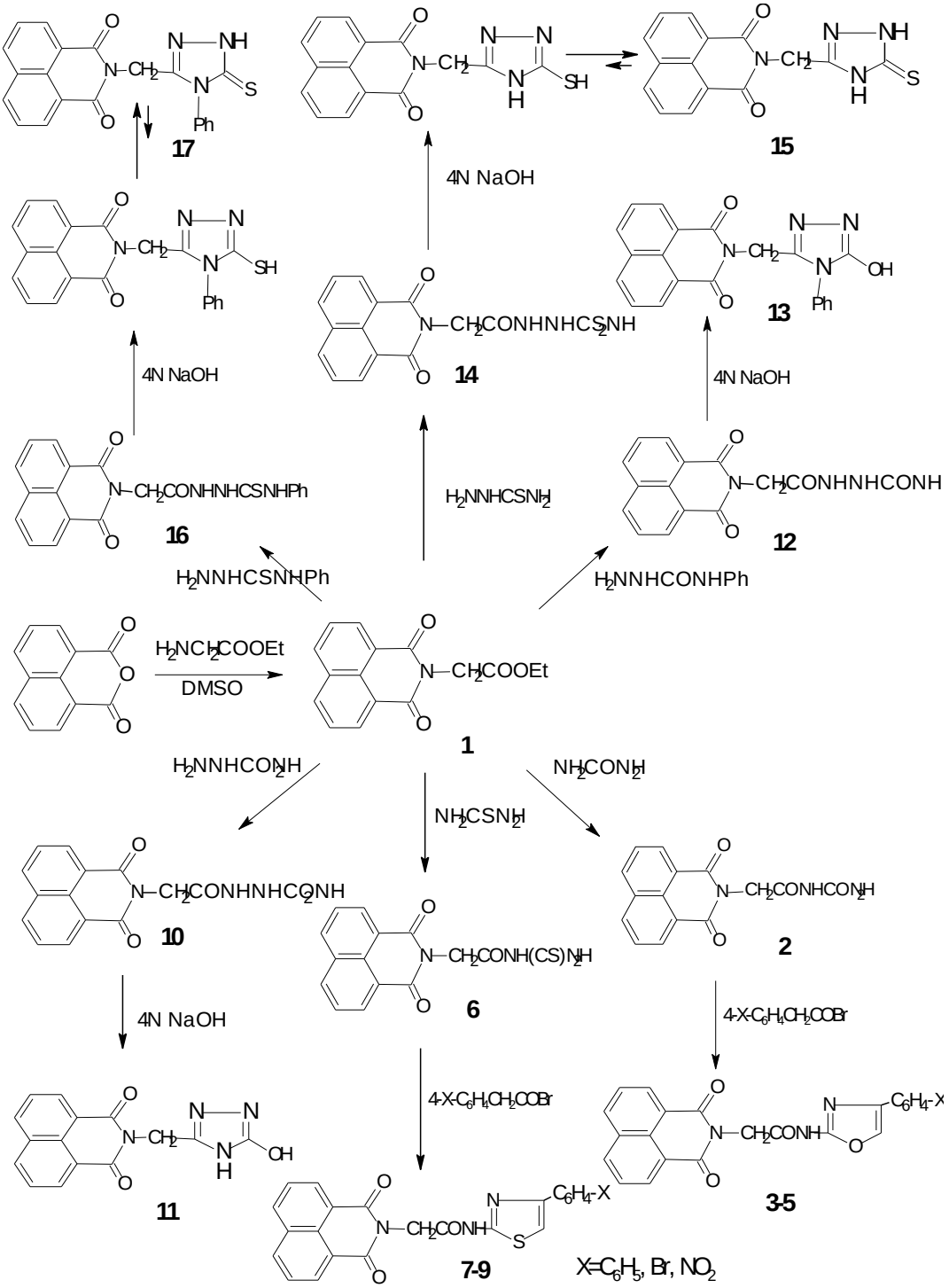
Antimicrobial Activity test

The test compounds were prepared with different concentrations (100, 50, and 25) mg/ml using dimethyl sulfoxide (DMSO) as solvent. The agar well diffusion method was used to determine antimicrobial activity [20]. The culture medium was inoculated with one of tested bacteria or fungi suspended in nutrient broth. Six millimeter diameter wells punched into the agar with fresh bacteria or fungi separately and filled with 100µl of each concentration. DMSO was used as control. The incubation was carried out at 37^{o}C for 4hr. Sulfamethxazole was used as a standard drug. Solvent and growth controls were kept and zones of inhibition were noted. The antibacterial activity was evaluated by measuring the inhibition zone diameter observed are recorded.

Result and Discussion

The synthetic sequences for preparation of series new 1,8-naphthalimides, 1,3-oxazole, 1,3-thiazole, and 1,2,4-triazole is outlined in Scheme (1). Naphthalic anhydride reacts with amines such as liquid ammonia or alkyl amines to form the corresponding

naphthalimides. Therefore, 1,8- naphthalic anhydride have been used as conventional starting material for preparation of 1,8-naphthalimides. Compound (1) were synthesized by condensation of the 1,8-naphthalic anhydride was reacted with ethyl glycinate was carried out in dimethyl sulfoxide media under reflux condition, and the end point of the reaction was examined by thin layer chromatography(TLC). TLC showed the imidation of 1,8-naphthalic anhydride with ethyl glycinate completed at 16 hours. The time required for completion of the imidation reaction for 1,8-naphthalic anhydride with ethyl glycinate is more than for the imidation of 1,8-naphthalic anhydride with alkyl amines [21],[22].



Scheme (1).

This can be attributed to the alkyl amines being more active than the ethyl glycinates in the nucleophilic displacement reaction in which the attacking group is amine. Imidation process of 1,8-naphthalic anhydride with ethyl glycinate as show in the Scheme (1).

Compound (1) was afforded in good yield (76%), having melting point (250-252) ºC Hydroxamic acid test give (+ve) for presence of ester [23]. Physical properties of compound (1) are listed in Table (1). FTIR spectrum showed clear absorption bands at (1774) cm^{-1}, due to υ(C=O) ester, (1701, 1668) cm^{-1} due to υ(C=O) imide. Other absorption bands appeared at (1581) cm^{-1}, (1357) cm^{-1}, and (1211) cm^{-1} due to υ(C=C) aromatic, υ(C–N) imide and υ(C–O–C) ester respectively. ^{1}HNMR spectrum of the same compound (1) showed triplet signal at δ= (1.19-1.27) ppm due to (CH_3) protons, singlet signal at δ= (4.08) ppm belong to (N–$\underline{CH_2}$–CO–) protons, quartate signal at δ= (4.50-4.58) ppm due to (–O–$\underline{CH_2}$–) protons, and signals at δ= (7.04-7.75) ppm due to aromatic protons, Fig.(1). ^{13}CNMR spectrum of this compound (1) showed results were listed in Table (4), Fig.(2).

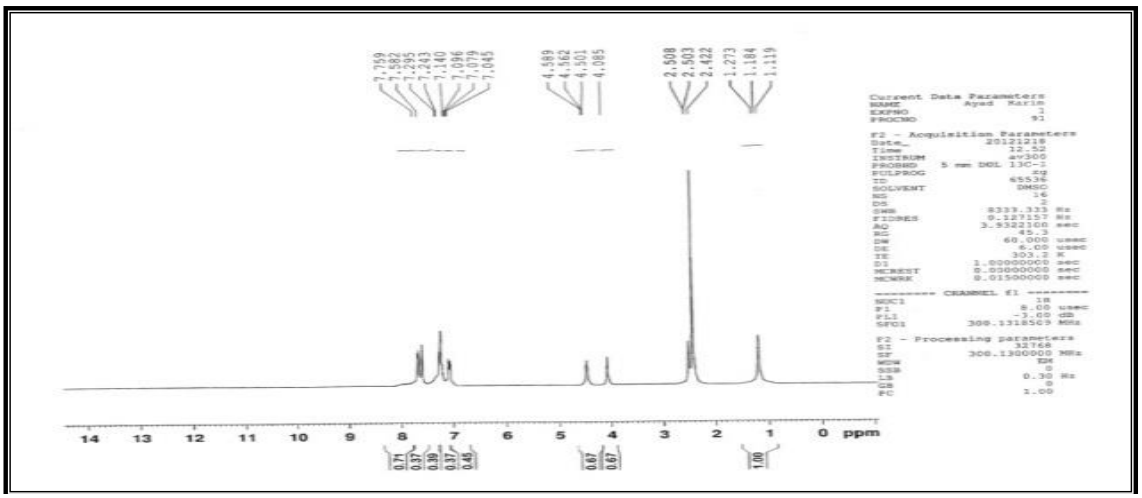


Fig. (1) ^{1}HNMR Spectra for compound (1).

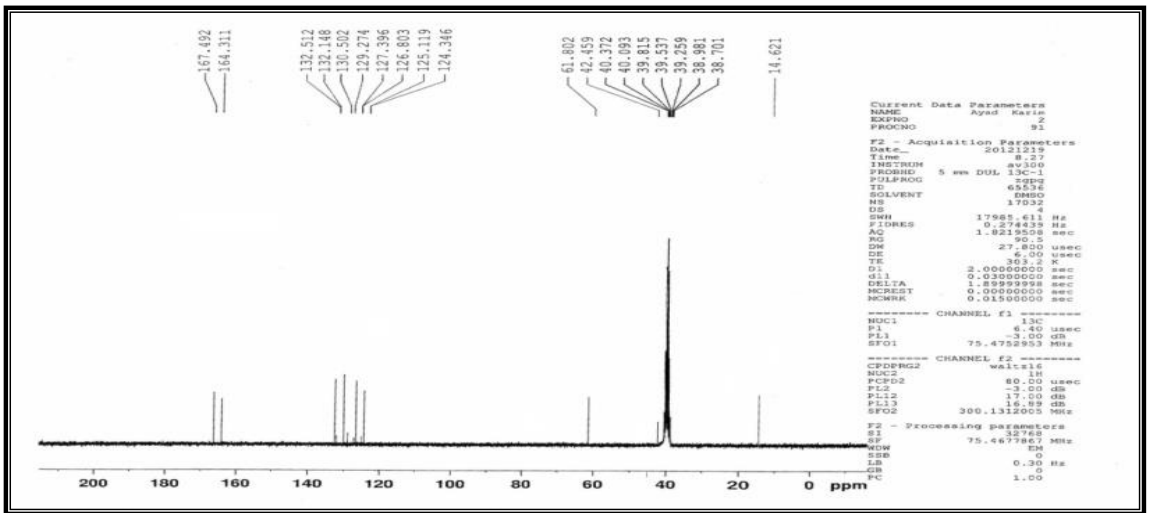


Fig. (2) ^{13}CNMR Spectra for compound (1).

The ester (1) was converted to {urea (2), thiourea (6), semicarbazide (10), phenylsemicarbazide (12), thiosemicarbazide (14) and phenylthiosemicarbazide (16)} derivatives by reaction with (urea, thiourea, semicarbazide, phenylsemicarbazide, thiosemicarbazide and phenylthiosemicarbazide) respectively in absolute ethanol Scheme (1). FTIR spectral date showing the absorption at 3544 cm^{-1} asym. 3498 cm^{-1} sym. for NH_2, 1747 cm^{-1} for C=O amide of compound (2). 3508 cm^{-1} asym. 3430 cm^{-1} sym. for NH_2, 1747 cm^{-1} for C=O amide 1240 cm^{-1} for C=S, of compound (6).

3425 cm^{-1} asym. 3309 cm^{-1} sym. for NH_2 1748 cm^{-1} for C=O amide of compound (10). 3338 cm^{-1} for NH, 1747 cm^{-1} for C=O amide of compound (12). 3416 cm^{-1} asym. 3367 cm^{-1} sym. for NH_2, 1747 cm^{-1} for C=O amide, 1284 cm^{-1} for C=S, of compound (14). 3244 3338 cm^{-1} for NH, 1748 cm^{-1} for C=O amide, 1243 cm^{-1} for C=S, of compound (16). Physical properties of these compounds are listed in Table (1) and Table (2).

Treatment of compound (2) and (6) with *p*-substituted phenacylbromide afford intramolecular cyclization to give the oxazoles (3-5) and thiazoles (7-9).

The FTIR spectrum of compounds (3-5) showed absorption bands between (3464-3427) cm^{-1} for NH, (1747-1748) cm^{-1} for C=O amide, (1705-1666) $cm^{-1}$for C=O imide, (1600-1608) cm^{-1} for C=N, and others 605 cm^{-1} for C-Br (4), (1535 asym. 1431 sym.) cm^{-1} for NO_2 (5) and disappearance the absorption band of (NH_2) group.

^{1}HNMR spectrum of compound [3] showed signal at δ= 4.27 ppm belong to (N–$\underline{CH_2}$–CO–) protons, δ=5.84 ppm (C_5) of oxazole ring proton, δ= (6.85-7.72) ppm aromatic ring protons, δ=8.32 ppm (NH) proton. Figure (3).^{13}CNMR spectrum of this compound (3) showed results were listed in Table (4), Fig.(4).

FTIR spectrum of compound (7-9) showed absorption bands between (3348-3360) cm^{-1} for NH, (1746-1735) cm^{-1} for C=O amide, (1700-1638) cm^{-1} for C=O imide, (1612-1601) cm^{-1} for C=N, and others 613 cm^{-1} for C-Br (8), (1558 asym.1473 sym.) cm^{-1} for NO_2(9) and disappearance the absorption (NH_2 and C=S) groups.

^{1}HNMR spectrum of compound (8) showed results were listed in Table (3) and ^{13}CNMR spectrum of compound (8) showed results were listed in Table (4).

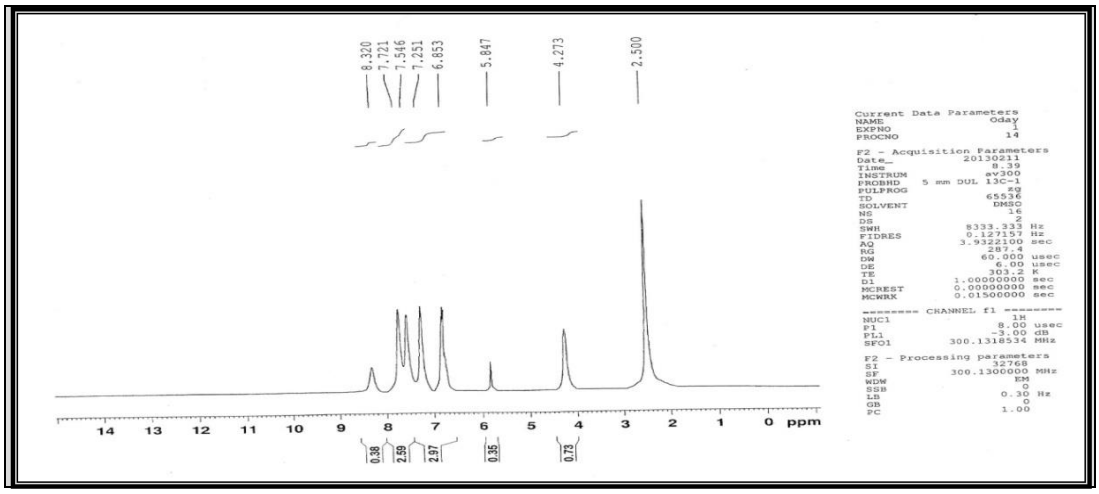


Fig. (3) ^{1}HNMR Spectra for compound (3).

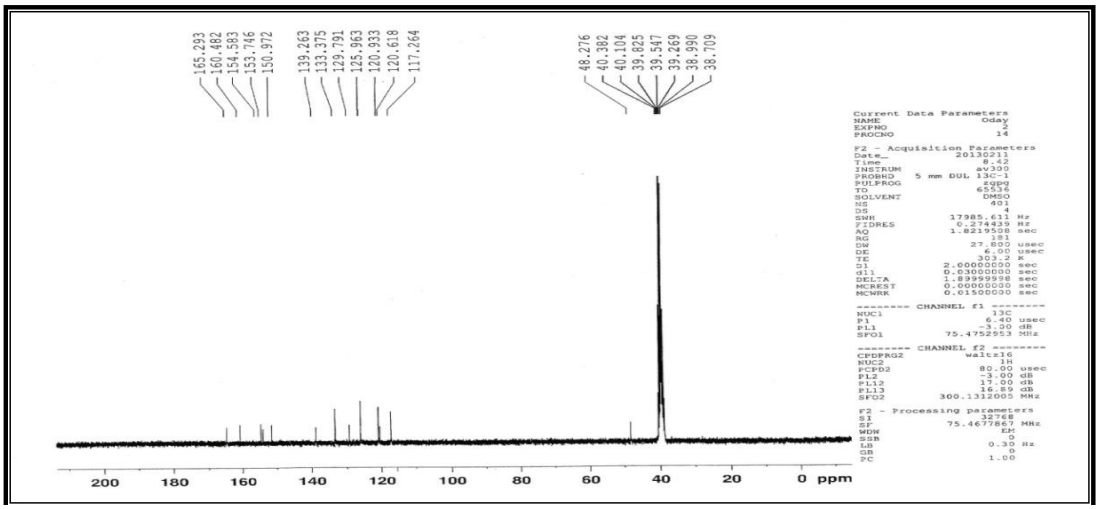


Fig. (4) ^{13}CNMR Spectra for compound (3).

Treatment of compounds (10,12,14 and 16) with (4N.NaOH) solution afford intramolecular cyclization to give the hydroxytriazole (11), Phenylhydroxy-triazole (13), thiotriazole (15) and thiohydroxytriazole (17) were identified from FTIR spectra shows results listed in Table (2). ^{1}HNMR and ^{13}CNMR spectrum of these compounds showed results were listed in Table (3) and (4) respectively.

Table (1)
Physical properties and FTIR spectral data cm^{-1} of compounds (1-9).

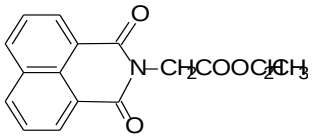
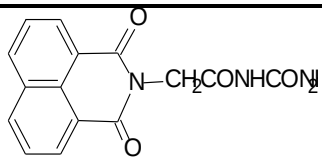
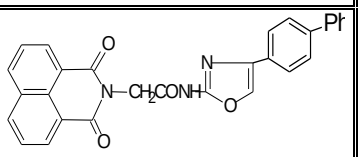
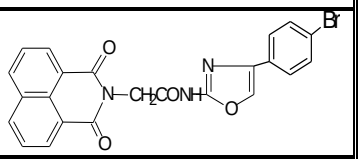
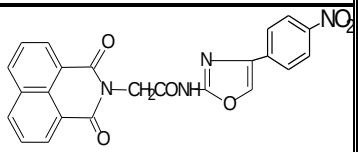
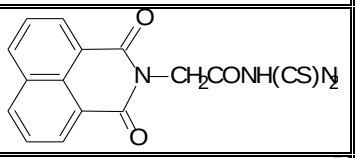
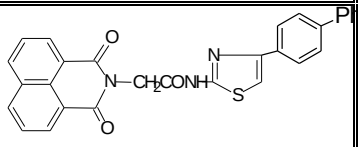
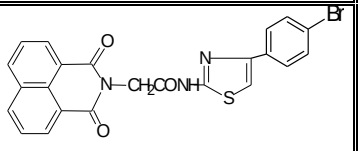
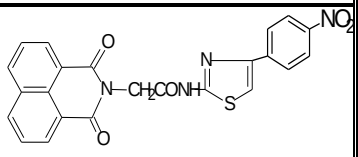
Physical properties					*Major FTIR Absorption cm^{-1}*				
Comp. No.	*Compound structure*	*Color*	*Yield %*	*Melting Point °C*	*ν (NH)*	*ν (C=O) amide*	*ν (C=O) imide*	*ν (C-N) imide*	*Others*
1		**Yellow-green**	**76**	**250-252**	**-**	**-**	**1701 1668**	**1357**	**ν (C=O) ester 1774, ν (C-O-C) ester 1211**
2		**Off white**	**80**	**111–114**	**3414**	**1747**	**1701 1666**	**1384**	**ν (NH_2) Asym.3544, sym.3498**
3		**Dusty**	**71**	**164 -166**	**3464**	**1747**	**1705 1685**	**1384**	**ν (C=N) 1600**
4		**Violet**	**60**	**135 -137**	**3427**	**1747**	**1705 1666**	**1384**	**ν (C=N) 1608, ν (C-Br) 605**
5		**Pale-yellow**	**74**	**153 –155**	**3458**	**1748**	**1705 1666**	**1392**	**ν (C=N) 1608, ν (NO_2) 1535, 1431**
6		**Light brown**	**69**	**194–196**	**3380**	**1747**	**1705 1666**	**1384**	**ν (NH_2) Asym.3508, sym.3430 ν (C=S) 1240**
7		**Brown**	**77**	**202–205**	**3348**	**1735**	**1700 1658**	**1373**	**ν (C=N) 1612**
8		**Brown**	**84**	**187–189**	**3258**	**1746**	**1701 1668**	**1354**	**ν (C=N) 1601, ν (C-Br) 613**
9		**Yellow**	**81**	**179–181**	**3360**	**1742**	**1700 1638**	**1396**	**ν (C=N) 1600 ν (NO_2) 1558,1473**

Table (2)
Physical properties and FTIR spectral data $cm^{-1}$of compounds (10-17).

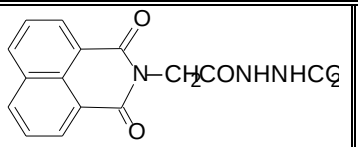
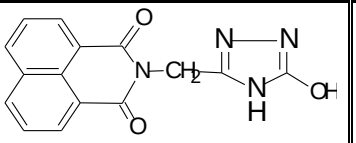
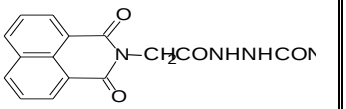
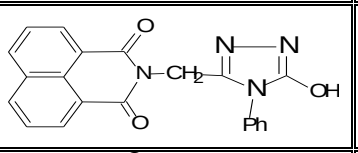
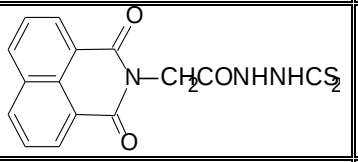
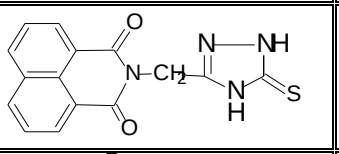
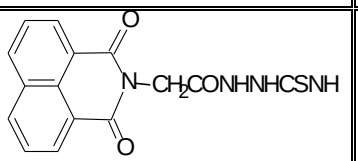
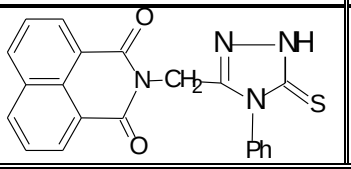
Physical properties					*Major FTIR Absorption cm^{-1}*				
Comp. No.	*Compound structure*	*Color*	*Yield %*	*Melting Point °C*	*ν (NH)*	*ν (C=O) amide*	*ν (C=O) imide*	*ν (C-N) imide*	*Others*
10		**Dusty**	**65**	**151–153**	**3255**	**1748**	**1703 1685**	**1388**	**ν (NH_2) Asym.3425, sym.3309**
11		**White**	**70**	**191–193**	**3541**	**-**	**1705 1666**	**1381**	**ν (OH) 3244 ν (C=N) 1614**
12		**White**	**79**	**170–173**	**3338**	**1747**	**1701 1681**	**1304**	**-**
13		**White**	**76**	**208–210**	**-**	**-**	**1701 1666**	**1357**	**ν (OH) 3260, ν (C=N) 1612**
14		**Pale yellow**	**85**	**180–182**	**3263**	**1747**	**1701 1643**	**1315**	**ν (NH_2) Asym.3416, sym.3367 ν (C=S) 1284**
15		**Off white**	**80**	**197–200**	**3363**	**-**	**1701 1643**	**1319**	**ν (C=N) 1600**
16		**Pale-yellow**	**68**	**175–178**	**3244**	**1748**	**1705 1662**	**1342**	**ν (C=S) 1243**
17		**White**	**71**	**234–237**	**3215**	**-**	**1703 1667**	**1355**	**ν (C=N) 1608**

Table (3)
^{1}HNMR spectral data (δ ppm) for selected compounds.

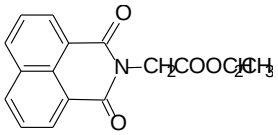
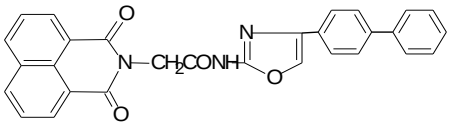
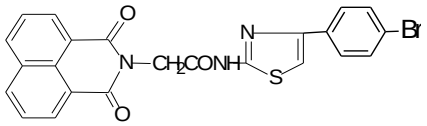
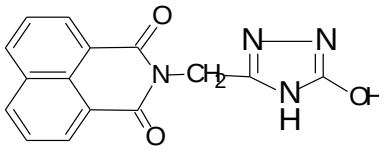
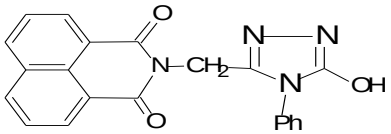
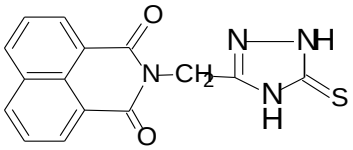
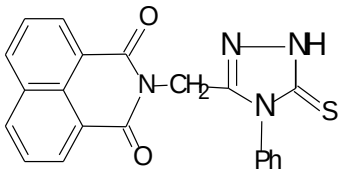
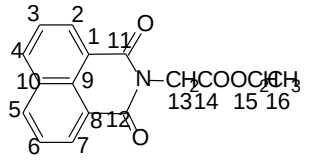
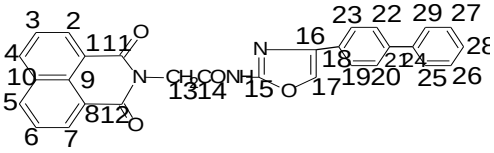
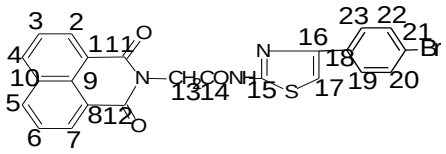
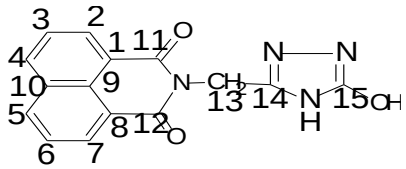
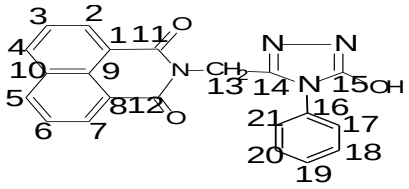
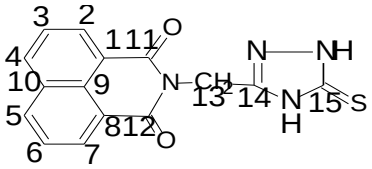
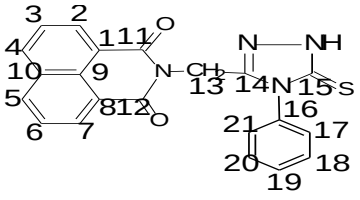
Comp. No.	*Compound structure*	*^{1}HNMR spectral data (δ ppm)*
1		1.27 CH_3protons, 4.08 (N–$\underline{CH_2}$–CO–) protons, 4.50 (–O–$\underline{CH_2}$–) protons, (7.04-7.75) aromatic ring protons.
3		4.27(N–$\underline{CH_2}$–CO–) protons, 5.84 (C5) of oxazole ring proton, (6.85-7.72) aromatic ring protons, 8.32(NH) proton.
8		4.29 (N–$\underline{CH_2}$–CO–) protons, 5.30 (C5) of thiazole ring proton, (6.56-7.99) aromatic ring protons, 8.42(NH) proton.
11		4.56 (N–$\underline{CH_2}$–CO–) protons, 5.64 (OH) proton, (7.06-8.02) aromatic ring protons, 8.27 (NH) proton.
13		4.24 (N–$\underline{CH_2}$–CO–) protons, 5.27 (OH) proton, (6.84-7.95) aromatic ring protons.
15		4.02 (N–$\underline{CH_2}$–CO–) protons, (6.59-7.18) aromatic ring protons, 8.03 (NH) proton.
17		4.05 (N–$\underline{CH_2}$–CO–) protons, (6.54-7.72) aromatic ring protons, 8.32 (NH) proton.

Table (4)
^{13}CNMR spectral data (δ ppm) for selected compounds.

Comp. No.	*Compound structure*	*^{13}CNMR spectral data (δ ppm)*
1		14.62(C_{16}), 42.45(C_{15}), 61.6 (C_{13}), 124.34-132.51(C_1-C_{10}), 164.31(C_{11}, C_{12}), 167.49(C_{14}).
3		48.27(C_{13}), 117.26-139.25(C_1-C_{10}) and (C_{18}-C_{29}), 150.97(C_{16}), 153.74(C_{17}), 154.58(C_{15}), 160.48(C_{11}, C_{12}), 165.29(C_{14}).
8		49.80(C_{13}), 117.53-137.11(C_1-C_{10}) and (C_{18}-C_{23}), 154.91(C_{17}), 158.68(C_{16}), 160.83(C_{15}), 161.19(C_{11},C_{12}), 166.52(C_{14}).
11		46.71(C_{13}), 125.68-131.47(C_1-C_{10}), 151.39(C_{14}), 156.40(C_{15}), 162.66(C_{11},C_{12})
13		44.10(C_{13}), 119.63-133.91(C_1-C_{10}) and (C_{16}-C_{21}), 154.38(C_{14}), 158.02(C_{15}), 163.52(C_{11}, C_{12}).
15		46.13(C_{13}), 124.43-130.86(C_1-C_{10}), 159.91(C_{14}), 161.35(C_{11}, C_{12}), 176.24(C_{15}).
17		48.41(C_{13}), 116.03-131.27(C_1-C_{10}) and (C_{16}-C_{21}), 157.47(C_{14}), 160.29 ($C_{11,}$ C_{12}), 169.83(C_{15}),

Antimicrobial Screening

Selected of some newly synthesized naphthalimides linked to five membered heterocyclic rings were screened *in vitro* for their antibacterial activity against four types of pathogenic bacterial isolates and for antifungal activity against one type of monilia. DMSO as a blank exhibited no antimicrobial activity against any of the tested microorganisms used. The bacterial isolates were more susceptible to the synthesized compounds than isolated fungal. The recorded inhibition zones are summarized in Table (5).

Table (5)
Antimicrobial activity of selected compounds.

	Staphylococcus aureus Concentrations (mg/ml) Inhibition zone diameter (mm)			*Bacillus subtilis* Concentrations (mg/ml) Inhibition zone diameter (mm)			*E. Coli* Concentrations (mg/ml) Inhibition zone diameter (mm)			*Pseudomonas aeuroginosa.* Concentrations (mg/ml) Inhibition zone diameter (mm)			*Candida Albicans* Concentrations (mg/ml) Inhibition zone diameter (mm)		
Comp. No.	*100*	*50*	*25*	*100*	*50*	*25*	*100*	*50*	*25*	*100*	*50*	*25*	*100*	*50*	*25*
3	**20**	**13**	**9**	**18**	**15**	**11**	**25**	**20**	**19**	**14**	**12**	**7**	**10**	**7**	**-**
4	**19**	**15**	**10**	**23**	**19**	**16**	**21**	**18**	**11**	**12**	**9**	**8**	**12**	**-**	**-**
5	**20**	**14**	**8**	**18**	**12**	**8**	**21**	**19**	**14**	**-**	**-**	**-**	**14**	**7**	**-**
7	**22**	**18**	**14**	**18**	**14**	**12**	**26**	**20**	**13**	**17**	**15**	**13**	**15**	**12**	**10**
8	**20**	**16**	**13**	**20**	**16**	**10**	**23**	**17**	**15**	**17**	**16**	**12**	**17**	**12**	**7**
9	**24**	**20**	**17**	**22**	**21**	**15**	**22**	**18**	**15**	**13**	**12**	**10**	**17**	**14**	**11**
11	**18**	**9**	**7**	**13**	**10**	**8**	**14**	**12**	**8**	**15**	**-**	**-**	**19**	**16**	**14**
13	**25**	**21**	**17**	**21**	**20**	**18**	**22**	**15**	**12**	**13**	**-**	**-**	**20**	**17**	**15**
15	**20**	**16**	**8**	**22**	**16**	**14**	**23**	**19**	**18**	**12**	**-**	**-**	**22**	**17**	**14**
17	**22**	**20**	**18**	**20**	**17**	**15**	**19**	**16**	**10**	**15**	**7**	**-**	**21**	**18**	**17**
Sulfamethoxazole (std.)	**32**	**28**	**22**	**34**	**26**	**20**	**31**	**24**	**21**	**29**	**20**	**18**	*****	*****	*****
Clotrimazole (std.)	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	*****	**26**	**24**	**22**

**** = not tested.***
- = no inhibition zone.

We observed some important results from the data of inhibition zone:

Most of the synthesized compounds showed antibacterial and/or antifungal activities. All compounds at concentration (100 mg/ml) were highly active against *Staphylococcus aureus* except (4,11) showed moderate activity.

Most compounds at concentration (100 mg/ml) were highly active against *Bacillus subtilis* whereas (3,5,7,11) showed moderate activity against this microorganism.

All compounds at concentration (100 mg/ml) except (11, 17) showed highly active against *E. Coli*. Gram (-ve) type *Pseudomonas aeuroginosa* showed resistance to compound (5) at all concentrations and to compounds (11, 13, 15, 17) at lower concentrations. Other compounds showed moderate to low activity against this bacterial

isolate. Compounds (11, 13, 15, 17) acts as good antifungal agents towards *Candida Albicans*. While other Compounds show moderate low activity especially at concentrations 50 and 25 (mg/ml). Therefore triazole compounds (11,13,15,17) can be recommended for further studies.

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من هيدروكيد الصوديوم بتركيز (4N) ليعطي المركبات (17,15,13,11) على التوالي. تراكيب المركبات المحضرة الجديدة شخصت من خلال الطرق الطيفية FTIR-,^{1}H NMR و^{13}C-NMR وبعض الخواص الفيزيائية واجراء بعض الكشوفات النوعية حيث كانت النتائج المستحصلة مطابقة للتراكيب المقترحة. المركبات المحضرة اختبرت فعاليتها المضادة للميكروبات بثلاث تراكيز مختلفة خارج جسم الكائن الحي ضد نوعين البكتريا المرضية موجبة الصبغة ونوعين اخرين سالبة الصبغة ونوع من الفطريات وقد اظهرت النتائج فعالية جيدة الى متوسطة ضد انواع الاحياء المجهرية قيد الدراسة.

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الخلاصة

تضمن البحث تحضير مشتقات حلقية غير متجانسة جديدة لـ 8,1- نفثالئميدات التي تحمل معوضات اوكسازول، ثايازول او ترايازول كما يلي :

التفاعل المباشر لـ 8,1- حامض النفثالك اللامائي مع كلايسينات الاثيل في ثنائي مثيل السلفوكسيد كمذيب تحت التصعيد وعند درجة حرارة عالية لمدة ستة عشر ساعة لبنتج N- استر-8,1- نفثالئيميد(1). ثم تم تحويل هذا الاستر الى مشتقات (اليوريا، الثايويوريا، السيميكاربازايد، فينيل سيميكاربازايد، الثايوسيميكاربازايد وفينيل ثايوسيميكاربازايد) وذلك من خلال التفاعل مع (اليوريا، الثايويوريا، السيميكاربازايد، فينيل سيميكاربازايد، الثايوسيميكاربازايد وفينيل ثايوسيميكاربازايد) على التوالي وتم الحصول على المركبات (14,12,10,6,2). بعدها تم حولقة المركبات بأستخدام مختلف الكواشف. الحولقة الاولى للمركبات (6,2) بأستخدام بروميدالفيناسيل المعوض في الموقع بارا اعطى مشتقات الاوكسازول (3-5) ومشتقات الثايازول (7-9) على التوالي. علاوة على ذلك مشتقات الترايازول حضرت من خلال الغلق الحلقي الثاني للمركبات (16,14,12,10) في وسط قاعدي