Synthesis, Characterization and Evaluation of Antibacterial Activity of Several New 1,8-naphthalimides Containing Benzothiazole Moiety

Ahlam Marouf Al-Azzawi[*] and Ahmed Sulaiman[**]

[*]Department of Chemistry, College of Science, Baghdad University, Baghdad-Iraq

[**]College of Veterinary Medicine, Al-Anbar University

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Abstract

A series of new 1,8-naphthalimides linked to benzothiazole moiety were synthesized by following two different strategies:

The first one involved direct reaction of equimolar amounts of substituted-2-aminobenzothiazoles with 1,8-naphthalic anhydride in glacial acetic acid under reflux at high temperature for eight hours. The second strategy based on Gabrial synthesis including preparation of unsubstituted-1,8-naphthalimide via refluxing of naphthalic anhydride with ammonium hydroxide at high temperature for six hours then the resulted 1,8-naphthalimide was treated with alcoholic potassium hydroxide to afford naphthalimide potassium salt and this in turn was introduced in the reaction with 2-(2-chloroacetylamino)benzothiazoles (which were prepared via treatment of 2-aminobenzothazoles with chloroacetyl chloride) producing new series of N-(2-acetamido substituted benzothiazole-2-yl)-1,8-naphthalimides.

Structures of the prepared compounds were confirmed by depending on FTIR, ^{1}H-NMR and ^{13}C NMR spectral data which were in agreement with the proposed ones. Finally antibacterial activity of some of the prepared new cyclic imides were evaluated against two types of bacteria and the results showed that the most of the tested imides posses good biological activity against these organisms.

تحضير وتشخيص مع تقدير الفعالية المضادة للبكتريا لعدد من مركبات 8,1- نفثال ايمايد الجديدة المعوضة بمكونة البنزوثايازول

احلام معروف العزاوي واحمد سليمان حمد

الخلاصة

تضمن البحث تحضير سلسلة من الايمايدات الحلقية الجديدة وهي 8,1-نفثال ايمايدات الحاوية في تركيبها على مكونة البنزوثايازول وذلك باتباع طرائق تحضير مختلفة. تضمنت الطريقة الاولى تحضير الايمايدات من خلال التفاعل المباشر بين كميات مولية متساوية من مركبات 2-امينوبنزوثايازول المعوضة بمجاميع مختلفة مع 8,1-انهيدريد النفثاليك في حامض الخليك الثلجي تحت ظروف التصعيد في درجة حرارة عالية لمدة ثمان ساعات.

اما الطريقة الثانية التي اتبعت في تحضير الايمايدات الجديدة فقد تضمنت تحضير 8,1-نفثال ايمايد من خلال تصعيد انهيدريد النفثاليك مع هيدروكسيد الامونيوم في درجات حرارية عالية لمدة ست ساعات بعدها تم معاملة النفثال ايمايد المستحصل مع هيدروكسيد البوتاسيوم الكحولي مما اسفر عن تكوين ملح البوتاسيوم للنفثال ايمايد وهذا بدوره ادخل في تفاعل مع مركبات 2-(2-كلورو استيل امينو) بنزوثايازول والتي سبق تحضيرها من خلال تفاعل مركبات (معوض-2-امينوبنزوثايازول مع كلورو كلوريد الاستيل) مما اسفر عن تكوين سلسلة جديدة من مركبات N-(2-اسيت اميدو ومعوض بنزوثايازول –2-يل)-8,1-نفثال ايمايد.

تم اثبات صحة تراكيب المركبات المحضرة من خلال الاعتماد على مطيافية الاشعة تحت الحمراء والرنين النووي المغناطيسي بنوعية ^{1}HNMR و ^{13}CNMR حيث جاءت نتائجها مطابقة للتراكيب المقترحة. اضافة الى ما تقدم فقد تضمن البحث ايضا دراسة الفعالية البايولوجية للايمايدات المحضرة ضد نوعين من البكتريا حيث اظهرت اغلب الايمايدات المحضرة فعاليه بايولوجية جيدة ضد انواع البكتريا قيد الدراسة.

Introduction

Various substituted benzothiazoles are known to cover a large domain of pharmacological activities serving as antitumor[1,2], antimicrobial[3,4], antihelmintic, anti-inflammatory[5,6] and anticonsulsive agents.

On the other hand naphthalimides first discovered by Brana and coworkers[7,8] are DNA –targeted chemotherapeutic agents acting primairly by attacking DNA at some level (synthesis, replication or processing) thus may naphthalimides have shown high anticancer activity[9,10] against a variety of murine and tumor cells, therefore plenty of naphthalimide based anticancer drugs[11-14] have been synthesized and promising results have been obtained. Also, series of naphthalimides and 4-nitro-1,8-naphthalimides exert pronounced analgesic or antinociceptive effects in mice[15,16] while other N-substituted naphthalimides[15] showed antibacterial and antifungal activities.The therapeutic importance of these rings prompted us to synthesize new compounds by incorporating naphthalimide and benzothiazole moieties in a single molecular framework. The new molecules were expected to possess biological activity.

Experimental

Chemicals used in this work are supplied from BDH and Fluka companies and are used without further purification. Melting points were determined on Gallenkamp capillary melting point apparatus and were uncorrected. FTIR spectra were recorded on SHIMADZU FTIR-8400 Fourier Transform Infrared spectrophotometer using KBr discs. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker 300MHz instrument using DMSO-d_6 as a solvent and TMS as internal reference.

1. Synthesis of N-(Substituted benzothiazole-2-yl)-1,8-naphthalimide [1-13]

The titled compounds were prepared according to literature procedures[15] with some modifications.A mixture of 1,8-naphthalic anhydride (0.01 mole), substituted-2-aminobenzothiazole (0.01 mole) and (50 mL) of glacial acetic acid was refluxed at (140-160)°C for eight hours with stirring.The resulted solution was cooled to room temperature before pouring into cold water and the obtained solid was filtered off, dried then recrystallized from a suitable solvent. Physical properties of compounds [1-13] are listed in Table (1).

2. Synthesis of 2-(2-Chloroacetylamino) substituted benzothiazoles [14-22]

Equimolar amounts of substituted-2-aminobenzothiazoles (0.01 mole) and chloroacetyl chloride (0.01 mole) in chloroform (20 mL) was refluxed in the presence of potassium carbonate (0.01 mole) for four hours with continous stirring[17]. The resulted solid was filtered, washed with 5% $NaHCO_3$ solution and subsequently with distilled water.The crude product was dried and crystallized from a suitable solvent. Physical properties of compounds [14-22] are listed in Table (2).

3. Synthesis of 1,8-Naphthalimide [23]

The titled compound was prepared according to literature[18] with some modifications.

A mixture of (0.01 mole) of 1,8-naphthalic anhydride and (0.01 mole) of concentrated ammonia solution was placed in a suitable round bottomed flask fitted with a wide air condenser. The mixture was refluxed at (160°C)

for four hours then the reflux was continued for two hours at 200°C.
The resulted melt was poured whilst still hot into a porcelain crucible, allowed to cool and solidified. Yield 81%, m.p. = 298-299°C (literature 299-300°C).

4. Synthesis of 1,8-Naphthalimide Potassium Salt [24]

1,8-Naphthalimide (0.01 mole) was dissolved in (25 mL) of absolute ethanol. The resulted clear solution was added to alcoholic potassium hydroxide solution [(0.01 mole) of KOH in (25 mL) of absolute ethanol] with stirring then the obtained precipitate was filtered and dried.

5. Synthesis of N-(2-Acetamido substituted benzothiazole-2-yl)-1,8-Naphthalimides [25-33]

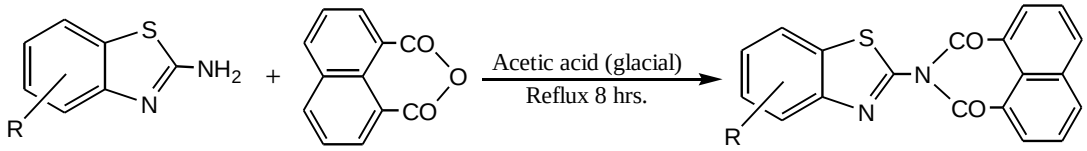
In a suitable round bottomed flask (0.01 mole) of chloro acetyl amino substituted benzothiazole was dissolved in (25 mL) of chloroform, then (0.01 mole) of 1,8-naphthalimide potassium salt was added gradually with stirring. The resulted mixture was refluxed for six hours with continuous stirring then was cooled to room temperature.The formed precipitate was filtered, washed with sodium bicarbonate solution then with distilled water, dried and purified by recrystallization from a suitable solvent.Physical properties of compounds [25-33] are listed in Table (3).

6. Biological Study

The cup plate method using nutrient agar medium was employed in studying he antimicrobial activity of the prepared imides against two types of bacteria, *Stapylococcus aureous* (Gram positive) and *Escherichia coli* (Gram negative) respectively. DMF was used as sample solution and sample size for all the compounds was fixed at (0.1 mL). using a sterilized cork borer cups were scooped out of agar medium contained in a petridish which was previously inoculated with the microorganisms. The test compound solution (0.1 mL) was added, the cups and the petridishes were subsequently incubated at 37°C for 48 hours. Zones of inhibition produced by each compound was measured in mm and the results are listed in Table (7).

Results and Discussion

Since both benzothiazoles and naphthalimides are biologically active components having wide spectrum of medicinal and pharmacological applications, the present work is directed toward synthesis of new compounds containing these two active moieties with expected biological activity.
Two different strategies were followed in performing the target of this work, the first strategy involved synthesis of a series of N-(substituted benzothiazol-2-yl)-1,8-naphthalimides via direct reaction between 1,8-naphthalic anhydride and substituted-2-aminobenzothiazoles in the presence of glacial acetic acid under reflux conditions at high temperature for eight hours. 2-aminobenzothiazoles substituted with different substituents are used here as primary amines which introduced successfully as active nucleophiles attacked carbonyl groups in the cyclic anhydride (1,8-naphthalic anhydride) producing N-(benzothiazol-2-yl)napthalamic acids which intrun introduced directly in dehydration reaction under the influence of glacial acetic acid and heat affording the desirable naphthalimides [1-13].
The starting materials (substituted-2-amino benzothiazoles) used in this work were prepared according to literature via reaction of primary aromatic amines with ammonium thiocyanate and bromine in glacial acetic acid.

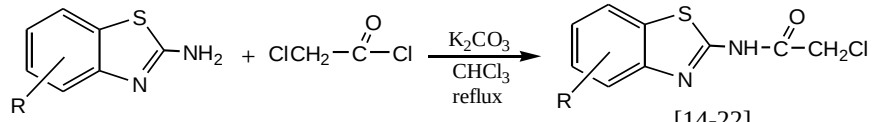


(R=different substitutents)

N-(benzothiazole-2-yl) naphthalimide [1-13]

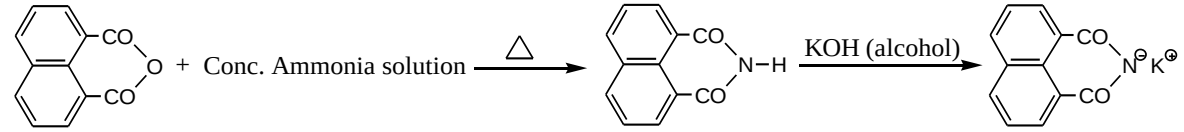
Scheme (1)

On the other hand the second strategy used in this work involved synthesis of new N-(acetamido substituted benzothiazole-2-yl)-1,8-naphthalimide based on Gabrial synthesis. Two components were prepared to perform this strategy the first component (1,8-naphthalimide) was prepared via treatment of naphthalic anhydride with concentrated ammonia solution under reflux at high temperature for six hrs, while the second component 2-(2-chloroacetylamino)benzothiazoles were prepared via treatment of substituted 2-aminobenzothiazoles with chloroacetyl chloride in the presence of K_2CO_3 in chloroform. The reaction between these two components afforded the desirable acetamidobenzothiazolyl-1,8-naphthalimides as described in scheme (2).

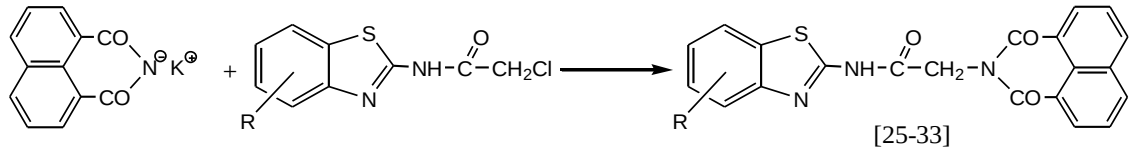


(R=different substitutents)

[14-22]



[23] [24]



[25-33]

Scheme (2)

Structures of the prepared compounds were confirmed by FTIR, ^{1}HNMR and ^{13}CNMR spectra data.

FTIR spectra of naphthalimides [1-13] showed clear absorption bands at (1700-1739) cm^{-1} and (1610-1687) cm^{-1} due to ν(C=O) imide and ν(C=N) in thiazol ring. Other bands appeared at (1550-1600) cm^{-1}, (1320-1360) cm^{-1} and (601-705) cm^{-1} which attributed to ν(C=C) aromatic, ν(C-N) imide and ν(C-S) in thiazole ring respectively[20].

^{1}HNMR spectrum of compound [2] showed clear signals at δ = 2.27 and (7.3-8.5)ppm due to CH_3 and aromatic protons respectively while ^{13}CNMR spectrum of the same compound [2] showed signals at δ = 21.5, (119.5-156), 161.1 and 163.8 ppm due to CH_3, aromatic carbons, C=N and C=O respectively.

^{1}HNMR spectrum of compound [3] showed signals at δ = 3.88 and (7.19-8.56) ppm belong to (OCH_3) and aromatic protons while ^{13}CNMR spectrum of the same compound showed signals at δ = 56.2, (105.5-154.3), 158.2 and 163.8 ppm belong to (OCH_3), aromatic carbons, C=N and C=O respectively.

^{1}HNMR spectrum of compound [8] showed signals at δ = 2.07 and (7.41-8.53) ppm due to two methyl groups and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 15.3 and 18.2 ppm belong to two CH_3 groups and signals at δ = (112-137.8), 139.59 and 163.76 ppm belong to aromatic carbons, C=N and C=O respectively.

^{1}HNMR spectrum of compound [10] showed signals at δ = 2.18, (7.47-8.8) and at 10.3 ppm due to CH_3, aromatic protons and NH (amide) while ^{13}CNMR of this compound showed signals at δ = 24.45, (111.9-146), 155.4, 163.8 and 169.1 ppm belong to CH_3, aromatic carbons, C=N, C=O imide and C=O amide respectively.

Finally ^{1}HNMR spectrum of compound [13] showed signals at δ = (7.92-7.98) and (8.52-8.56) ppm belong to vinylic protons and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 122.4 and 124.6 ppm to vinylic carbons and at δ = (127.8-141.1), 156 and 163.99 ppm due to aromatic carbons, C=N and C=O respectively.

FTIR spectra of 2-(2-chloroacetylamino) benzothiazoles showed clear absorption bands at (3182-3417), (1666-1724), (1581-1662) and (1516-1593) cm^{-1} belong to ν(N-H) amide, ν(C=O) amide, ν(C=N) and ν(C=C) respectively. Other bands appeared at (783-860) and (624-709) cm^{-1} belong to ν(C-Cl) aliphatic and ν(C-S) in thiazole ring respectively.

On the other hand ^{1}HNMR spectrum of compound [14] showed signals at δ = 4.3 and (7.0-8.0) ppm belong to (CH_2) and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 43, (121-149), 158 and 166.3 ppm which belong to (CH_2), aromatic carbons, C=N and C=O respectively.

^{1}HNMR spectrum of compound [15] showed signals at δ = 2.41 and 4.46 and (7.2-7.7) ppm belong to (CH_3), (CH_2) and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 21.45, 42.95, (120.8-146.9), 157 and 166.1 ppm belong to (CH_3), (CH_2), aromatic carbons, C=N and C=O respectively.

^{1}HNMR spectrum of compound [17] showed signals at δ = 3.7, 4.48 and (7.3-8.1) ppm belong to NH, CH_2 and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 42.8, (120.1-159.8), 166.8 and 168.4 ppm belong to (CH_2), aromatic carbons, C=N and C=O respectively.

Finally ^{1}HNMR spectrum of compound [19] showed signals at δ = 4.36 and (7.8-8.2) ppm belong to (CH_2) and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 44, (119.5-143), 145.1 and 166 ppm belong to (CH_2), aromatic carbons, C=N and C=O respectively.

FTIR spectra of acetamidobenzothiazolyl naphthalimides [25-33] showed clear absorption bnads at (3143-3394), (1662-1716), (1631-1693) and (1589-1631) cm^{-1} belong to ν(N-H) amide, ν(C=O) imide, ν(C=O) amide ν(C=N) respectively. Other bands appeared at (1500-1593), (1323-1388) and (636-698) cm^{-1} which belong to ν(C=C), ν(C-N) imide and ν(C-S) thiazole respectively.

On the other side ^{1}HNMR spectrum of compound [25] showed signals at δ = 4.47 and (7.3-8.0) ppm belong to (CH_2) and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 43, (121-131.9), 148.9, 158 and 166.4 ppm belong to (CH_2), aromatic carbons, C=N, C=O imide and C=O amide respectively.

^{1}HNMR spectrum of compound [26] showed signals at δ = 2.41, 4.4 and (7.2-8.4) ppm belong to CH_3, CH_2 and aromatic protons while ^{13}CNMR spectrum of this compound showed signals at δ = 21.4, (120.8-134.8) and 164.6 ppm belong to CH_3, aromatic carbons, C=N and C=O respectively.

Finally ^{1}HNMR spectrum of compound [29] showed signals at δ = 4.47, (6.69-8.4) and 11.7 ppm belong to (CH_2), aromatic protons and NH proton while ^{13}CNMR spectrum of this compound showed signals at δ = 66.3, (120.1-159.8), 164.5, 166.7 and 168.4 ppm belong to (CH_2), aromatic carbons, C=N, C=O imide and C=O amide respectively. Details of FTIR spectral data of the prepared compounds are listed in Tables [4-6].

Biological activity

The prepared compounds were screened for their antibacterial activity against two microorganism including *Staphylococcus aureus* and *E. coli.* The tested compounds showed different biological activities against the studied types of bacteria as shown in Table (7). It was noticeable that biological activity of these compounds depend on nature of substituents in their molecules thus compounds [3,10,27] showed very high activity against E.coli, compounds [1,6,12,25,30] showed high activity against this bacteria while compounds [5,28] showed moderate activity and compounds [2,32] showed no activity against this bacteria.

On the other hand compounds [3,10,12,32] showed high activity against S.aureus while compounds [2,5,27,28,30] showed moderate activity and compounds [1,6,25] showed no activity against this bacteria.

Table (1): Physical properties of benzothiazolyl naphthalimides [1-13]

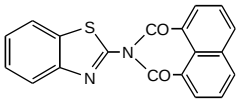
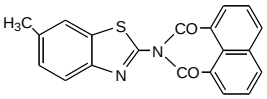
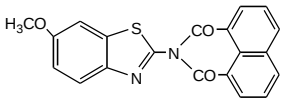
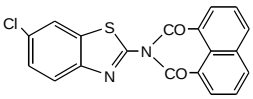
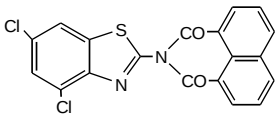
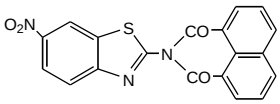
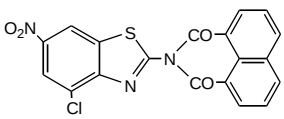
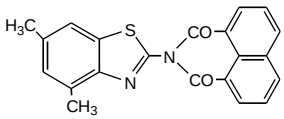
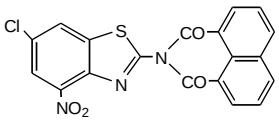
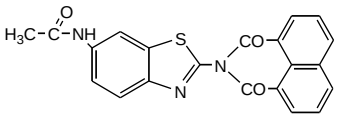
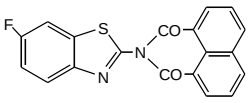
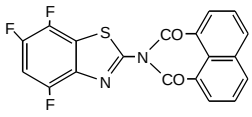
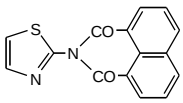
Comp. No.	Compound structure	color	Melting points °C	Yield %	Solvent of Recrystallization
1		Light brown	250 dec.	85	Ethanol
2		Brown	235-237	90	Ethanol
3		Violet	274-276	87	Ethanol
4		Faint yellow	215-216	81	Cyclohexane
5		Yellow	251-253	88	Cyclohexane
6		Yellow	227-229	76	Acetone
7		Greenish yellow	255-256	82	Ethanol/chloroform (1:1)
8		Pink	221-222	91	Ethanol
9		Orange	259-261	78	Ethanol/chloroform (1:1)
10		Dark brown	218-220	90	Ethanol/chloroform (1:1)
11		Off white	231-232	86	Ethanol
12		Faint yellow	277-278	80	Ethanol
13		Brown	287-289	84	Ethanol/chloroform (1:1)

Table (2): Physical properties of 2-(2-chloroacetylamino) benzothiazoles [14-22]

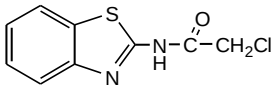
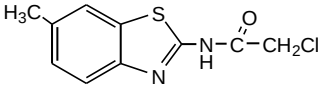
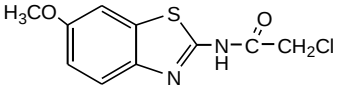
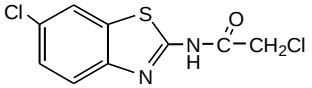
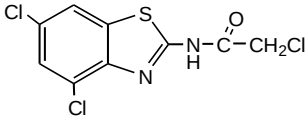
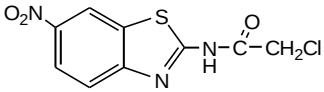
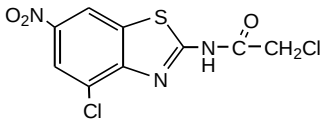
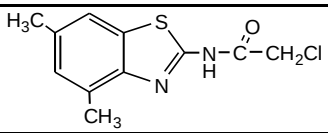
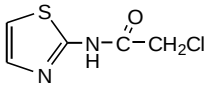
Comp. No.	Compound structure	color	Melting points °C	Yield %	Solvent of Recrystallization
14		Off white	162-164	82	Ethanol
15		White	192-193	90	Cyclohexane
16		Off white	204-205	75	Ethanol
17		Brown	214-216	87	Cyclohexane
18		Pale brown	163-165	91	Cyclohexane
19		Deep yellow	183-185	79	Ethanol
20		Orange	167-168	84	Ethanol
21		Off white	218-220	92	Cyclohexane
22		Light brown	133-135	93	Ethanol

Table (3): Physical properties of acetamido benzothiazolyl naphthalimides [25-33]

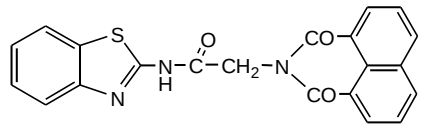
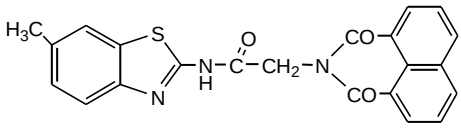
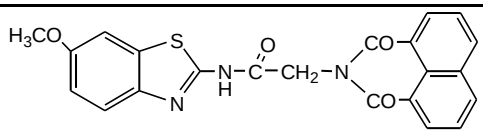
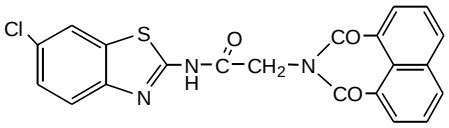
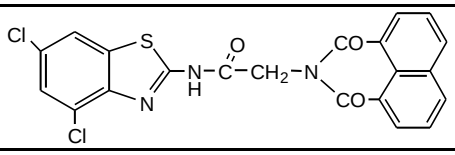
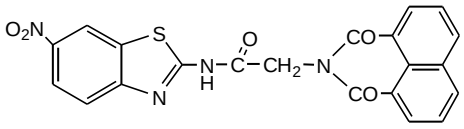
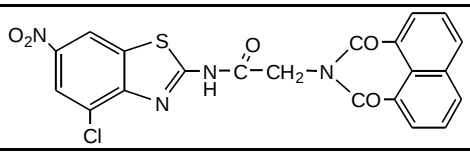
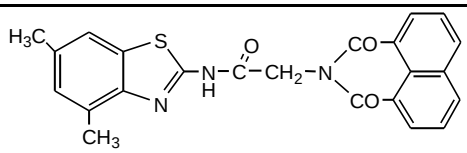
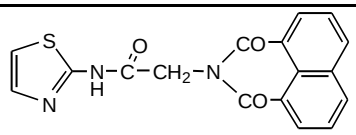
Comp. No.	Compound structure	color	Melting points °C	Yield %	Solvent of Recrystallization
25		Off white	220-221	81	Ethanol
26		Light brown	227-229	85	Chloroform
27		Yellow	> 300	80	Ethanol
28		Faint yellow	284-286	77	Cyclohexane
29		Off white	216-218	74	Cyclohexane
30		Greenish yellow	> 300	83	Ethanol
31		Organge	296-297	78	Ethanol
32		Brown	> 300	82	Chloroform
33		Brown	245-247	75	Ethanol

Table (4): FTIR spectral data of naphthalimides [1-13]

Comp. No.	FTIR spectral data cm^{-1}						
	ν(C-H) aromatic	**ν(C=O) imide**	**ν(C=N) thiazole**	**ν(C=C) aromatic**	**ν(C-N) imide**	**ν(C-S) thiazole**	**others**
1	3066	1716	1685	1585	1346	624	-
2	3050	1735(sh) 1714	1681	1583	1344	700	-
3	3045	1710	1687	1600	1346	610	**ν(C-O-C)** 1260 asym. 1180 sym.
4	3030	1718	1683	1587	1344	705	**ν(C-Cl)** 1100
5	3020	1704	1674	1587	1357	705	**ν(C-Cl)** 1110
6	3070	1728	1610	1581	1360	601	**ν(C-NO_2)** 1496, 1303
7	3058	1739(sh) 1703	1610	1577	1340	660	**ν(C-NO_2)** 1434, 1294 **ν(C-Cl)** 1070
8	3020	1715	1670	1550	1320	690	-
9	3040	1710	1683	1580	1360	670	**ν(C-NO_2)** 1410, 1300 **ν(C-Cl)** 1100
10	3066	1739(sh) 1714	1676	1585	1340	648	**ν(N-H) amide** 3383 **ν(C=O) amide** 1697
11	3058	1735 1700	1685	1577	1355	670	**ν(C-F)** 1215
12	3030	1700	1620	1580	1350	670	**ν(C-F)** 1213
13	3024	1710	1666	1589	1344	610	**ν(C=C) aliph.** 1679

sh=shoulder

Table (5): FTIR spectral data of compounds [14-22]

Comp. No.	FTIR spectral data cm^{-1}						
	ν(N-H) amide	**ν(C=O) amide**	**ν(C=N) thiazole**	**ν(C=C) aromatic**	**ν(C-Cl) aliphatic**	**ν(C-S) thiazole**	**others**
14	3213	1708	1600	1558	813	675	-
15	3417	1724	1643	1581	806	678	-
16	3387	1697	1662	1608	810	705	**ν(C-O-C)** 1219, 1172
17	3182	1670	1600	1539	860	675	**ν(C-Cl)aromatic** 1099
18	3414	1666	1631	1593	852	709	**ν(C-Cl)aromatic** 1068
19	3278	1685	1624	1570	852	686	**ν(C-NO_2)** 1500, 1408
20	3375	1685	1608	1516	783	675	**ν(C-NO_2)** 1446, 1327 **ν(C-Cl)** 1053
21	3240	1670	1581	1535	798	667	-
22	3186	1701	1585	-	810	624	-

Table (6): FTIR spectral data of acetamido benothiazolyl naphthalimides [25-33]

Comp. No.	FTIR spectral data cm^{-1}							
	ν(N-H) amide	**ν(C=O) imide**	**ν(C=O) amide**	**ν(C=N) thiazole**	**ν(C=C) aromatic**	**ν(C-N) imide**	**ν(C-S) thiazole**	**others**
25	3143	1685	1678	1589	1582	1323	690	-
26	3228	1716	1678	1608	1554	1327	690	-
27	3394	1716	1631	1608	1539	1330	636	**ν(C-O-C)** 1261
28	3309	1701	1677	1616	1589	1377	695	**ν(C-Cl)** 1090
29	3267	1678	1643	1624	1589	1388	675	**ν(C-Cl)** 1107
30	3340	1689	1666	1616	1593	1388	686	**ν(C-NO_2)** 1512, 1342
31	3360	1693	1693	1620	1500	1330	698	**ν(C-Cl)** 1045
32	3248	1662	1631	1631	1581	1330	690	-
33	3186	1701	1681	1624	1589	1377	694	-

Table (7): Antibacterial activity for some of the prepared compounds

Comp. No.	Gram positive bacteria	Gram negative bacteria
	Stapylococcus aureus	***Escherichia coli***
1	**_**	**+ + +**
2	**+ +**	**_**
3	**+ + +**	**+ + + +**
5	**+ +**	**+ +**
6	**_**	**+ + +**
10	**+ + +**	**+ + + +**
12	**+ + +**	**+ + +**
25	**_**	**+ + +**
27	**+ +**	**+ + + +**
28	**+ +**	**+ +**
30	**+ +**	**+ + +**
32	**+ + +**	**_**

Key to symbols: inactive = (-) inhibition zone < 6 mm
Slightly active = (+) inhibition zone 6-9 mm
Moderately active (++) inhibition zone 9-12 mm
Highly active = (+++) inhibition zone 13-17 mm
Very high activity = (++++) inhibition zone > 17 mm

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