Synthesis and preliminary evaluation of antimicrobial activity of new sulfonamido and acetamido cyclic imides linked to benzothiazole moiety

Ahlam Marouf Al-Azzawi* and Ahmed Saadi Hassan **

*Department of Chemistry, College of Science, University of Baghdad
Jadiriya, Baghdad, Iraq
** Health and medical technical college

(K . J . Pharm . Sci)

(Received May 2011 , Accepted Nov. 2011)

Abstract

A new series of citraconimides connected to benzothiazole moiety through sulfonamido group have been prepared by multistep synthesis.In the first step two citraconamic acids N-phenyl and N-benzyl citraconamic acids were prepared via reaction of citraconic anhydride with aniline or benzyl amine. Dehydration of the prepared amic acids by fusion or by treatment with acetic anhydride and anhydrous sodium acetate in the second step afforded N-phenyl and N-benzyl citraconimides which inturn were treated with chloro sulfonic acid in the third step producing 4- (N-citraconimidyl) phenyl sulfonyl chloride and 4-(N-citraconimidyl) benzyl sulfonyl chloride respectively. In the fourth step each one of the two prepared sulfonyl chlorides was introduced in reaction with ten substituted -2-amino benzothizoles producing ten N-(4-(substituted benzothiazole-2-yl) sulfon amido phenyl) citraconimides and ten N-(4-substituted benzothiazole-2-yl)sulfonamido benzyl) citraconimides. Moreover, a series of new phthalimides and succinimides linked to benzothiazole moiety through acetamido group were synthesized via reaction of 2-chloroacetyl amino benzothiazoles with phthalimide and succinimide. Microbiological activities of the prepared imides against four types of bacteria (*Staphylococcus aureus , strepto pyogenes , Escherichia coli and pseudomonas aeuroginosa*) and candida albicans fungi were evaluated and the results showed that the tested compounds have good antibacterial activity.

تحضير وتقدير تمهيدي للفعالية الضدة للمايكروبات لسلفون اميدو واسيت اميدو ايمايدات حلقية جديدة مرتبطة بمكونة البنزوثايازول

*أحلام معروف حسين و**احمد سعدي حسن

* قسم الكيمياء- كلية العوم – جامعة بغداد

** الكلية التقنية الطبية

الخلاصة

تم في هذا البحث تحضير سلسلة من الستراكون ايمايدات الجديدة المرتبطة بمكونة البنزوثايازول من خلال مجموعة السلفون امايد.تم انجاز هذا التحضير بعدة خطوات تضمنت الخطوة الاولى تحضير اثنين من حوامض الستراكون اميك هما N- فنيل و N- بنزيل حامض الستراكون اميك وذلك من تفاعل انهيدريد الستراكونيك مع الانيلين او بنزايل امين.اما في الخطوة الثانية فقد تم سحب الماء من حامضي الستراكون اميك المحضرين باتباع تقنية الصهر او المعاملة مع انهيدريد الخليك بوجود خلات الصوديوم اللامائية كعامل ساحب للماء وبذلك تم الحصول على مركبات N-فنيل وN- بنزايل ستراكون ايمايد وهذه بدورها تمت معاملتها مع حامض كلوروسلفونيك في الخطوة الثالثة للحصول على المركبين 4-(N-ستراكون ايميديل) فنيل كلوريد السلفونيل و 4-(N-ستراكون ايميديل) بنزيل كلوريد السلفونيل على التوالي. اما الخطوة الرابعة فقد تضمنت تفاعل

كلوريدات السلفونيل المحضرة مع مركبات 2-امينو بنزوثايازول المعوضة و بذلك تم الحصول على الايمايدات الجديدة المطلوبة والتي هي N-(4 -معوض بنزوثيازول-2-يل) سلفون اميدوفنيل) ستراكون ايماید و N-(4-معوض بنزوثايازول-2-يل) سلفون اميدو بنزيل) ستراكون ايماید على التوالي. اضافة الى ذلك فقد تضمن البحث تحضير سلسلة من الفثال ايمايدات والسكسن ايمايدات الجديدة المرتبطة بمكونة البنزوثايازول من خلال مجموعة الاسيت امايد. حيث تم التحضير من خلال تفاعل مركبات 2-كلورواستيل امينو بنزوثايازول مع كل من الفثال ايمايد والسكسن ايمايد. تم تقدير الفعالية البايولوجية للايمايدات المحضرة وذلك من خلال دراسة تاثيرها على تثبيط اربعة انواع من البكتريا ونوع واحد من الفطريات وقد اوضحت النتائج بان معظم الايمايدات المحضرة ذات فعالية جيدة ضد انواع البكتريا قيد الدراسة.

Key words : Citraconamic acids, sulfonamido citraconimides, acetamido phthalimides, acetamido succinimides.

Introduction

Cyclic imides are very important functionality which have been found to maintain significant biological activity and represent an important moiety in creation of novel medical materials: A diversity of biological activities [1-3] and pharmaceutical uses have been attributed to them such as anti-inflammatory , antifungal, antibacterial , antitumor, plant growth regulators, analgesic and antispasmodic.

On the otherh and benzothiazoles comprise a class of therapeutic compounds that exert a wide range of biological activities [4-6] i.e, antimicrobial [7,8] , anticancer [9,10] , antifungal [11], antiallergic and antihelmintic [12]. Also a series of potent and selective antitumor agents derived from 2-(4-amino phenyl) benzothiazole was extensively studied and developed during recent years [4] .On the basis of these reports and as a continuation of our research program on benzothiazolyl cyclic imides, we report here the synthesis of new compounds containing the two biologically active moieties cyclic imide and benzothiazole connected together by sulfonamido or acetamido group followed by their antibacterial and antifungal screening.

Experimental

All chemicals employed were purchased from BDH, Merk, Fluka and were used without further purification. Melting points were determined on Thomas Hoover apparatus and were uncorrected. FTIR spectra were recorded on SHIMADZU FTIR- 8400 Fourier Transform Infrared Spectrophotometer as KBr disc.U.V spectra were recorded on SHIMADZU U.V-visible recording spectrophotometer U.V 160.

^{1}-HNMR spectra were recorded on Bruker 300 MHz instrument using DMSO-d_6 , $CDCl_3$ as solvents and TMS as internal reference.

Elemental analysis were performed on perkin Elmer 240 element analyzer.Incubator Hetashi model was used for incubation samples in biological study.

1. Synthesis of N-phenyl citraconamic acid [1]

Citraconamic anhydride (0.01 mol) was dissolved in (30 mL) of diethyl ether then (0.01 mol) of aniline was added to this mixture with stirring and cooling [13] . The resulted ppt. was filtered then purified by recrystallization from dioxane.

Yield 80% , m.p(167-168) ^{0}C, FTIR υ(N-H) amide 3217 cm $^{-1}$, υ (O-H) carboxylic 3286 cm $^{-1}$, υ (C=O) carboxylic 1704 cm $^{-1}$, υ(C=O) amide 1627 cm^{-1} and υ (C=C) vinylic 1550 cm^{-1}.

2. Synthesis of N-phenyl citraconimide [2]

The titled compound was prepared according to literature procedures [14] using fusion technique. The resulted solid was purified by recrystallization

from cyclohexane. Yield 82% , m.p. (71-72) ^{0}C, .υ (C=O) imide 1710 cm^{-1} , υ(C=C) vinylic 1666 cm $^{-1}$and υ(C-N)1434 cm^{-1}.

3. Synthesis of 4-(N-citraconimidyl) phenyl sulfonyl chloride [3]

Chlorosulfonic acid (4 mL) was added drop wise to (0.01 mol) of N- phenyl citraconimide during two hours with stirring and cooling to Zero ^{0}C [15] . Reaction mixture was stirred for another ten hours then poured carefully into cold water with stirring . The obtained ppt. was filtered , dried then recrystallized from benzene. Yield 70%, m.p. (75-76) ^{0}C.

υ(C=O) imide 1704 cm^{-1}, υ(C=C) vinylic 1643 cm^{-1}, υ(SO_2) asym.1396 cm^{-1} and υ(SO_2) sym. 1188 cm^{-1}.

4. Synthesis of N-(4-(N-substituted benzothiazole-2-yl) sulfonamido phenyl) citraconimides [4-13]

The titled compounds were prepared according to literature [16] with some modifications.

Substituted 2- amino benzothiazole (0.01 mol) was dissolved in (30 mL) of dry pyridine then (0.015 mol) of 4-(N- citraconimidyl) phenyl sulfonyl chloride was added in portions with stirring and keeping temperature below 40 ^{0}C . The mixture was refluxed for three hours with continuous stirring then after cooling was poured into excess cold water and the obtained ppt. was filtered , dried and finally purified by recrystallization from a suitable solvent. Physical properties of the prepared compounds [4-13] are listed in Table(1).

5. Synthesis of N-benzyl citraconamic acid [14]

Compound [14] was prepared by following the same procedure used in preparation of compound [1] except using of benzyl amine instead of aniline. The product was purified by recrystallization from dioxane. Yield 83%, m.p. (60-61) ^{0}C. υ (N-H) amide 3271 cm^{-1}, υ(O-H) carboxylic 3355 cm^{-1}, υ(C=O) amide 1627 cm^{-1} and υ (C=C) vinylic 1558 cm^{-1} .

6. Synthesis of N-benzyl citraconimide [15]

Compound [15] was prepared according to literature [17] with minor modifications.

A mixture of (0.01 mol) of N-benzyl citraconamic acid , (30 mL) of acetic anhydride and (5-10) % by weight of anhydrous sodium acetate was refluxed for two hours with stirring . The resulted solution was cooled to R.T before pouring into cold water with stirring and the obtained ppt. was purified by recrystallization from cyclohexane. Yield 70%, m.p. (58-59).

υ(C=O) imide 1704 cm^{-1}, υ (C=C) vinylic 1604 cm^{-1} and υ (C-N) imide 1342 cm^{-1}.

7. Synthesis of 4-(N-citraconimidyl) benzyl sulfonyl chloride [16]

Chlorosulfonic acid (2 mL) was added drop wise to (0.005 mol) of N- benzyl citraconimide dissolved in (20 mL) of chloroform with stirring and cooling then stirring was continued for additional 2 hrs .The resulted mixture was poured into cold water with stirring then the organic layer was extracted with chloroform for three times, washed with water and dried. After evaporation of solvent the resulted product was recrystallized from acetone . Yield 85%, m.p .(109-110)^{0}C.

υ(C=0) imide 1704 cm^{-1}, υ(C=C) vinylic 1635) cm^{-1}, υ (SO_2) asym.1357 cm^{-1} and υ(SO_2) sym. 1134 cm^{-1}..

8. Synthesis of N-(4-(N-substituted benzothiazole -2-yl)sulfonamido benzyl) citraconimides[17-26]

Substituted -2-amino benzothiazole (0.01 mol) was dissolved in (30 mL) of dry pyridine then(0.015 mol) of 4-(N-citraconimidyl) benzyl sulfonyl chloride was added in portions with stirring and keeping temperature below 40 ^{0}C. The mixture was refluxed for 3 hrs. with continuous stirring then after cooling was poured into excess cold water and the resulted organic layer was extracted with chloroform for three times, washed with water and dried. The resulted solid after evaporation of solvent was purified by recrystallization from a suitable solvent.

Physical properties of compounds [17-26] are listed in Table (3).

9. Synthesis of N-(2-acetamido substituted benzo thiazolyl) phthalimides [27-36]

In a suitable round bottomed flask (0.01 mol) of chloroacetamido substituted benzothiazole was dissolved in (25 mL) of absolute ethanol then (0.01 mol) of potassium phthalimide was added gradually with stirring [18]. The resulted mixture was refluxed for six hours with continuous stirring then was cooled and the formed precipitate was filtered , washed with $NaHCO_3$ solution then with distilled water and dried. Finally the product was purified by recrystallization from a suitable solvent.

Physical properties of compounds [27-36] are listed inTable (5).

10. Synthesis of N-(2-acetamido substituted benzothiazolyl) succinimides[37-46]

Compounds [37-46] were prepared by following the same procedure used in preparation of compounds[27-36] except using of potassium succinimide in stead of potassium phthalimide . Purification of the products was performed by recrystallization from a suitable solvent . Physical properties of compounds [37-46]are listed in Table (7).

11. Biological activity

The cup plate method [19] using nutrient agar media was used in studying antibacterial and antifungal activity of the prepared compounds against staphylococcus aureous , strepto pyogenes , Escherichia coli, pseudomonas aeuroginosa and candida albicans fungi.

Each test compound (50 mg) was dissolved in dimethyl formamide (50 mL) which was used as sample solution.Using a sterilized cork cups were scooped out of agar medium contained in a Petri dish which were previously inoculated with the microorganisms. The test compound solution (0.1 mL) was added in the cups and the Petri dishes were subsequently incubated at 37 ^{0}C for 48 hrs. Zones of inhibition by each compound was measured in mm and the results are listed in Tables (11) and (12).

Results and Discussion

Since both cyclic imides and benzothiazoles are very important organic compounds having wide spectrum of biological activities the target of the present work is directed toward synthesis of new compounds containing these two biologically active components with expected biological activity.

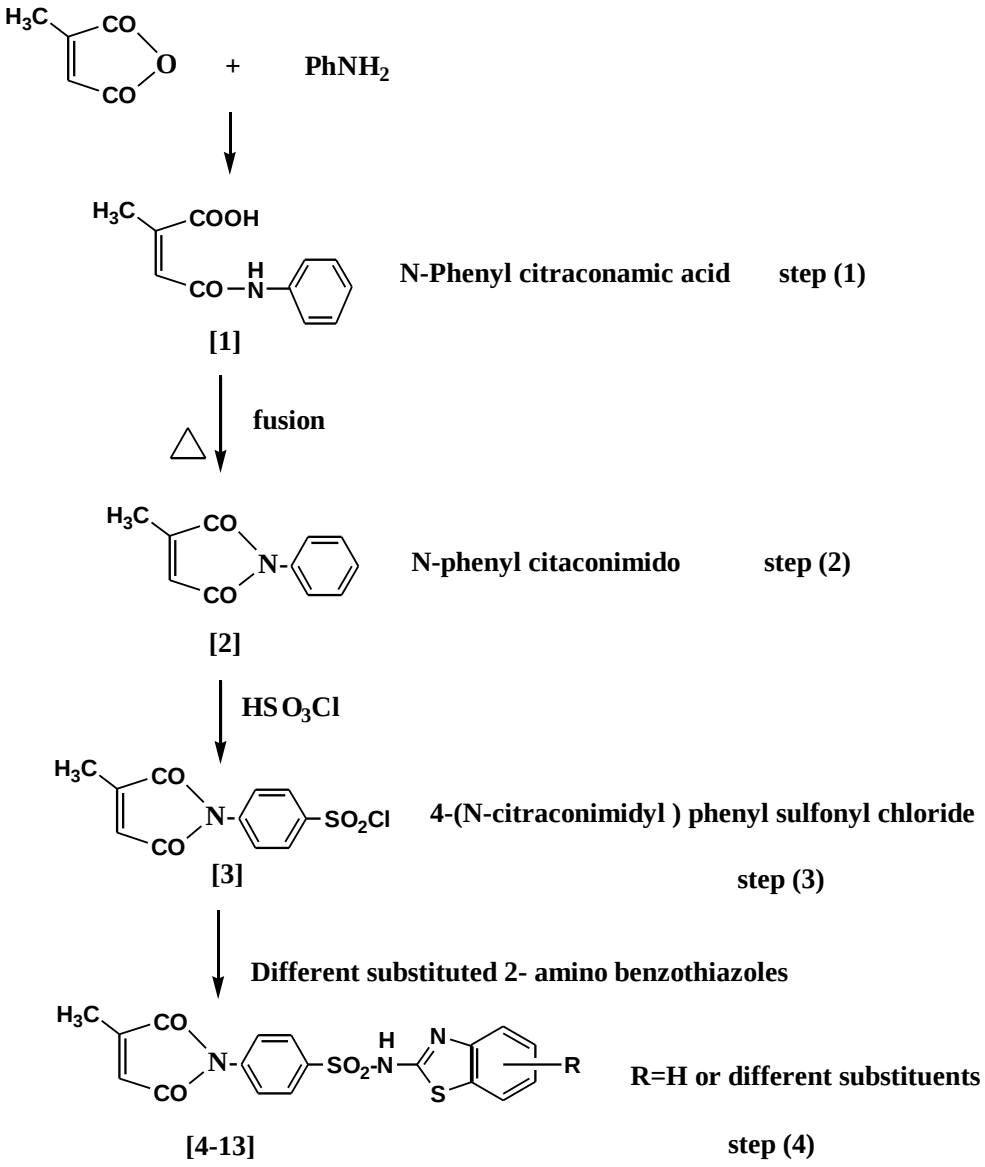
The strategy followed in building the new compounds was based on connecting citraconimide and benzothiazole moieties together by phenyl sulfonamide or benzyl sulfonamide groups thus through this strategy first we built new molecules containing the two desirable active moieties second we introduced the known active sulfonamide group in the new compounds and this may increase the activity of these compounds since sulfonamide drugs

were the first chemotherapeutic agents employed systemically for the prevention and cure of bacterial infection in human beings [20].

The mentioned strategy was performed via many steps the first one involved synthesis of two citraconamic acids N-phenyl and N-benzyl citraconamic acids by reaction of citraconic anhydride with aniline or benzyl amine. These two amic acids were dehydrated in the second step via fusion technique or treatment with acetic anhydride and anhydride and anhydrous sodium acetate producing N-phenyl and N-benzyl citraconimides which inturn on treatment with chloro sulfonic acid in the third step producing citraconimidyl phenyl and citraconimidyl benzyl sulfonyl chlorides.

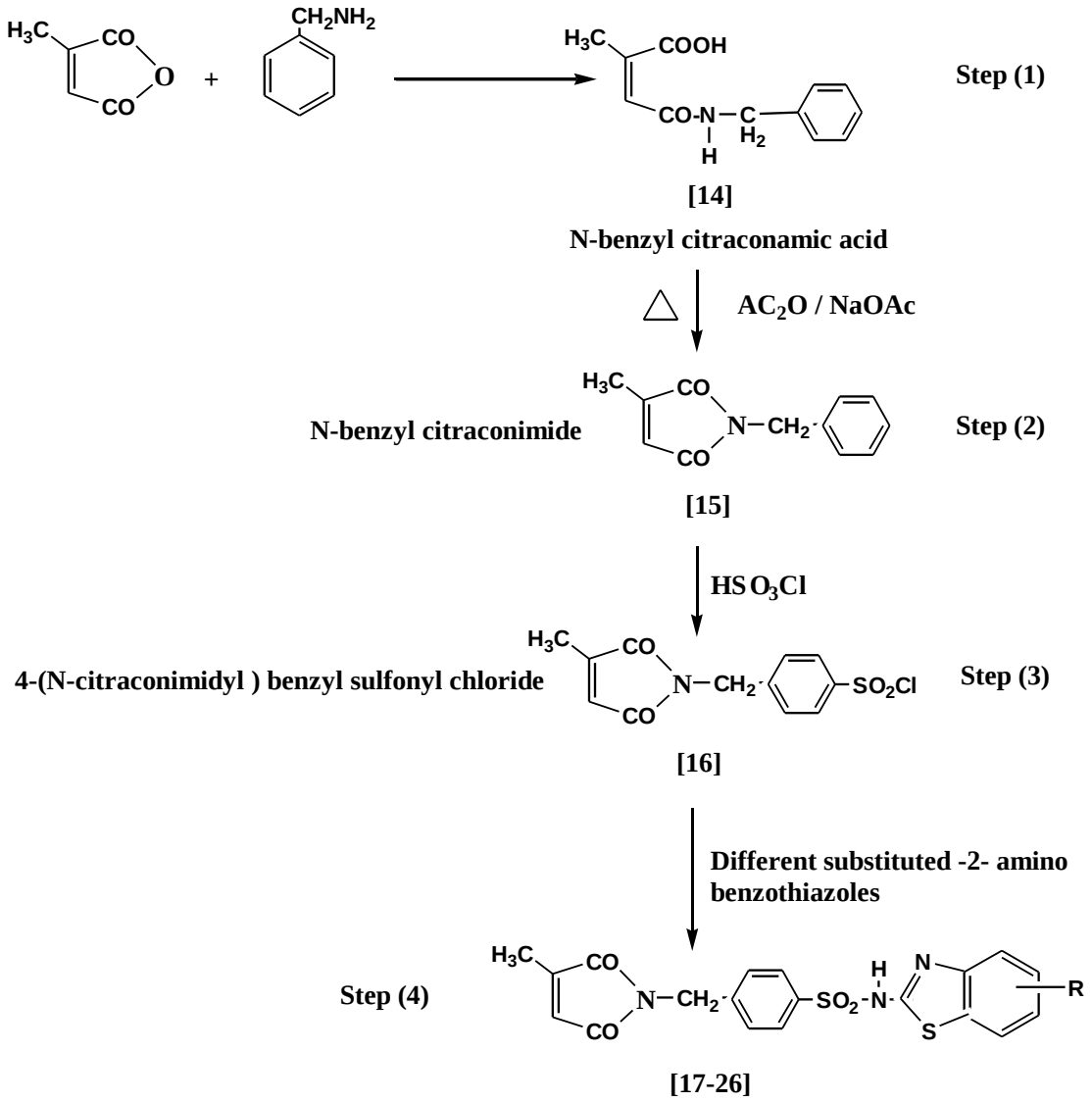
The prepared citraconimidyl sulfonyl chlorides were introduced in reaction with substituted -2-amino benzothiazole in the fourth step producing new ten N-(4-(N-substituted benzothiazole -2-yl) sulfonamido phenyl) citraconimides and new ten N- (4 -(N - substituted benzothiazole -2 - yl) sulfonimido benzyl) citraconimides respectively.

All these steps were summarized in Schemes (1) and (2) while physical properties of compounds [4-13] and [17-26] are listed in Tables (1) and (3).



N-(4-(N-substituted benzothiazole -2-yl) sulfonamido phenyl) citraconimides

Scheme (1)



Scheme (2)

Structures of the prepared compounds were confirmed by FTIR , U.V, H-NMR spectroscopy and C.H.N analysis for some of them.

FTIR spectra of amic acids [1] and [14] showed characteristic absorption bands at (3286-3355) cm-^{1} and (3217-3271) cm^{-1} due to υ (O-H) carboxylic and υ(N-H) amide while these two bands disappeared in FTIR spectra of N-phenyl and N-benzyl citraconimides indicating success of dehydration reaction which lead to cyclization and imide formation.

FTIR spectra of citraconimidyl phenyl sulfonyl chloride [3] and [16] showed appearance of two clear absorption bands at (1357-1396) cm^{-1}and (1134-1188) cm^{-1} which belong to υ (SO_2) asym. and υ(SO_2) sym. respectively [21] .

FTIR spectra of the newly prepared citraconimides [4-13] and [17-26] showed clear absorption bands at

(3340-3463) cm^{-1}, (1635-1713) cm^{-1}, (1310-1405) cm^{-1} and (1105-1180) cm^{-1}which attributed to υ(N-H), υ(C=O) imide , υ(SO_2) asym . and υ(SO_2) sym. respectively. Also bands belong to υ(C=N) and υ(C-S) in thiazole ring appeared at (1411-1575)cm^{-1} and (600-717)cm^{-1}.

U.V spectra of citraconimides [4-13] and [17-26] showed bands at wavelengths (260- 300)nm and (340-399)nm due to ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transitions in the conjugated system of citraconimide ring and substituted benzothiazole ring.Other details of spectral data of the mentioned citraconimides are listed in Tables (2) and (4).On the other hand structures of some of the prepared compounds were confirmed also by ^{1}H-NMR spectra thus ^{1}H-NMR spectra of phenyl citraconimides [4] and [8] showed clear signals in the ranges δ= (2.2-2.5) , (4.9-7.25) and (7.4-8.5) ppm , these signals belong to methyl group protons , vinylic protons , aromatic protons and NH proton respectively. Compound [8] showed also a signal at(δ = 3.4 ppm) belongs to OCH_3 protons.

^{1}H-NMR spectra of benzyl citraconimides [17] ,[20] and [22] showed signals at the ranges δ (2.1-2.49), (3.8-4.6), (4.95-7.1)and (6.45-8.5) ppm which belong to methyl group protons, benzylic protons, vinylic proton, aromatic and NH protons respectively.

Compound [22] showed also two signals at (δ= 2.35 and 2.45) ppm which belong to two methyl groups attached to phenyl ring .

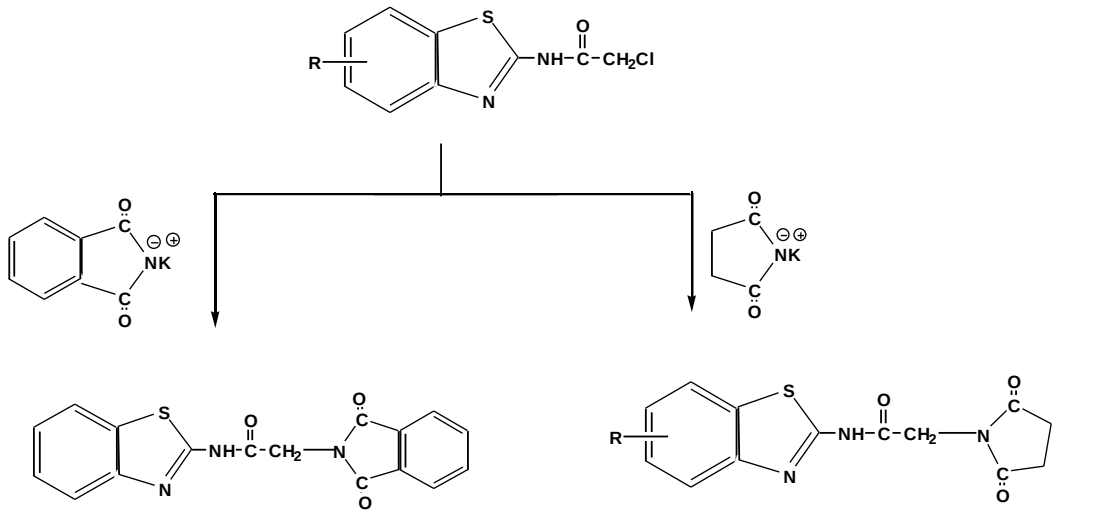
Other details of ^{1}H-NMR spectral data are shown in Table (9).

Our present work involved also synthesis of new phthalimides and succinimides lniked to benzothiazole moiety.

The strategy which followed in building these new imides based on linking between phthalimide or succinimide ring and benzothiazole moiety by acetamido group thus the new acetamido phthalimides and succinimides were prepared by reaction of 2-(2-chloro acetyl amino) substituted benzothiazoles with potassium phthalimide or potassium succinimide according to Gabreil synthesis.

The series of 2-(2-chloro acetyl amino) benzothiazoles used in these syntheses were prepared as reported in literatures [18] while potassium phthalimide and potassium succinimide were prepared via treatment of phthalimide or succinimide with alcoholic KOH.

The linear pathway strategy of these syntheses are summarized in Scheme(3) while physical properties of the prepared phthalimides and succinimdes are listed in Tables (5) and (7).



N-(2-acetamido substituted benzothiazolyl) phthalimides

[27-36]

N-(2-acetamido substituted benzothiazolyl) succinimides

[37-46]

Scheme (3)

Structures of new acetamido phthalimides [27-36] and acetamido succinimides [37-46] are confirmed by FTIR , U.V HNMR spectral data and C.H.N analysis for some of them.

FTIR spectra of these acetamidoimides showed clear absorption bands at the ranges (3201-3438) cm^{-1}, (1640-1743) cm^{-1} due to υ(N-H) amide and υ(C=O) imide and amide.

Other absorption bands appeared at (1566 -1627) cm^{-1}, (1303-1396) cm^{-1} and (617- 648) cm^{-1} which are assigned for υ(C=N) thiazole, υ(C-N) imide and υ(C-S) thiazole respectively.

On the other hand U.V spectra of acetamido imides showed absorptions at wave lengths (240-283) nm and compounds substituted with nitro groups showed other bands at longer wave lengths (332-430) nm. These absorptions are due to ($\pi \rightarrow \pi^*$) and ($n \rightarrow \pi^*$) transitions in benzothiazole and phthalimide or succinimide moieties.

^{1}H-NMR spectrum of compound [33] N-(2-acetamido-6-methoxy benzothiazolyl) phthalimide showed singlet signal at (δ= 4.2) ppm belong to (OCH_3) protons , signal at (δ=4.4)ppm due to (CH_2) protons and signal at (δ= 5.7) ppm due to NH proton. Signals at (δ= 7.3, 7.5,7.7 and 7.9) ppm belong to protons of two aromatic rings.

^{1}H-NMR spectrum of compound [28] N-(2- acetamido-6- methyl benzothiazolyl) phthalimide showed signals at (δ= 2.49)ppm belong to methyl group protons, signal at (.δ= 3.8) ppm belong to (CH_2) protons and signals at (δ= 6.4) ppm and (δ= 7.1-7.9) ppm due to NH proton and aromatic rings protons respectively.

^{1}H-NMR spectrum of compound [43] N-(2-acetamido-6-methoxy benzothiazolyl) succinimide showed signals at (δ= 2.8) ppm belong to (-

CH_2-CH_2-) protons of succinimide ring , signal at (δ= 3.7 and 3.9) ppm due to (CH_2) and (OCH_3) protons.
Signals at (δ= 6.9-7.5) ppm are due to aromatic protons and NH proton.

Microbiological activity

Since the prepared imides in this work are built from known biologically active components they were expected to possess biological activity thus the present work involved also evaluation of antibacterial and antifungal activities for some of the prepared imides against Staphylococcus aureus , Streptococcus pyogenes (*Gram* – positive bacteria) , *Escherichia coli*, *Pseudomonas aeuroginosa* (Gram-negative bacteria) and candida albicans fungi.

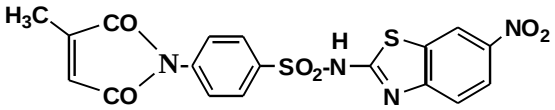
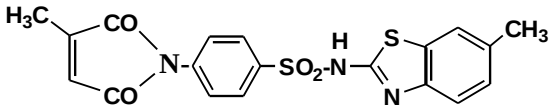
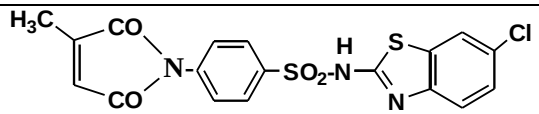
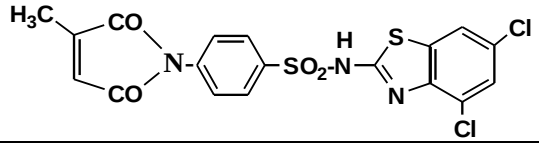
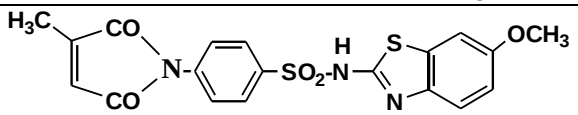
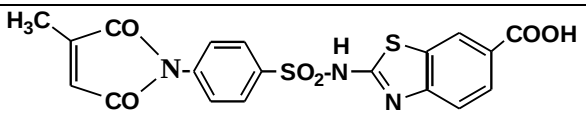
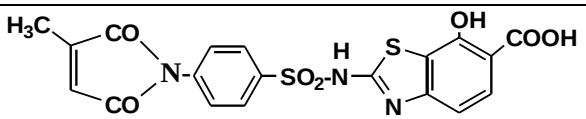
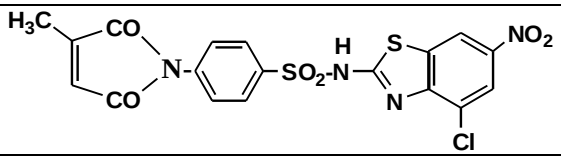
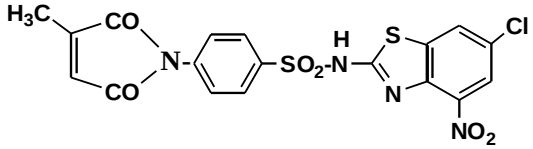
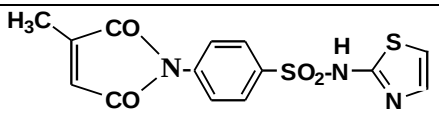
Inhibition zones caused by the tested compounds are determined and the results are listed in Tables (11) and(12). The results indicated that many sulfonoamido phenyl citraconimides posses moderate to high biological activity against (Gram-positive) bacteria and this was due to hydrophilic properties of these compounds and cell wall of Gram positive bacteria , While the prepared sulfonamido benzyl citraconimides have hydrophobic properties and this inturn made these compounds active against Gram- negative bacteria which posses complex lipo poly saccharides in their cell walls . [22]

The results showed also that some of the tested imides (7,8,12,18,21,22) showed weak activity against candida albicans fungi while the other tested compounds showed no activiy against this fungi.

On the other hand acetamido benzothiazolyl phthalimides and succinimides showed different activities against the different types of bacteria and fungi.

Thus compounds (33) and (43) showed high activity against Staphylococcus aureus and Sterptococcus pyogenes bacteria while compounds (29),(31),(34),(42) and (44) showed moderate activity against the same types of bacteria and these mentioned compounds showed weak activity against other types of bacteria and candida fungi. Compound (35) and (45) showed no activity against all the used organisms, compounds (27) and(37) showed no activity against Escherichia coli , Psedomonas ariginosa , candida albicans fungi and weak activity against other types of bacteria. The other treated studied compounds showed weak activity against the studied organisms.

Table (1) Physical properties of compounds [4-13]

Copmd. No.	Compound Structure	Colour	Melting Point ^{0}C	Yield %	Recrystallization solvent
4		Deep Yellow	220-222	70	Acetone
5		Light brown	181-182	65	Ethanol
6		Light Yellow	204-206	77	Hexane
7		Brown	164-166	75	Ethanol
8		Black	244-245	80	Methanol
9		Orange	161-162	88	Hexane
10		Pink	186-188	72	Acetone
11		Deep Yellow	168-169	60	Methanol
12		Light brown	107-108	85	Ethanol
13		Brown	152-154	62	Acetone

Table(2) FTIR and U.V spectral data of the prepared compounds [4-13]

Compd. No.	FTIR spectral data cm^{-1}										U.V (λ max) nm
	υ(C-H) Aromatic	υ(C=C) Aromatic	υ(N-H) Amide	υ(C=O) Imide	υ(C=C) Vinylic	υ(SO_2) Asym.	υ(SO_2) sym.	υ(C=N)	υ(C-S) Thiazole	Others	
4	3075	1490	3340	1650	1600	1330	1126	1527	600	υ(C-NO_2) 848	369 344 394
5	3115	1510	3409	1700	1627	1404	1173	1450	678	-------	283
6	3060	1525	3456	1712	1635	1405	1110	1535	702	υ(C-Cl) 1049	296
7	3090	1465	3450	1712	1635	1388	1150	1536	694	υ(C-Cl) 1100	300
8	3110	1490	3433	1713	1604	1396	1172	1512	694	υ(C-O-C) 1260	281
9	3050	1510	3409	1650	1589	1396	1110	1535	702	υ(C=O) carboxylic 1704	300
10	3100	1502	3450	1635	1542	1365	1160	1458	671	υ(C=O) carboxylic 1625	272 427
11	3075	1560	3425	1635	1566	1340	1126	1504	617	υ(C-Cl) 1126 υ(C-NO2) 840	277 442
12	3125	1540	3456	1690	1635	1350	1157	1504	624	υ(C-Cl) 1160 υ(C-NO2) 894	280 344 422
13	3080	1550	3463	1710	1635	1375	1157	1505	660	-----	300 357

Table (3) Physical properties of the prepared compounds [17-26]

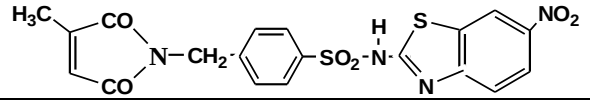
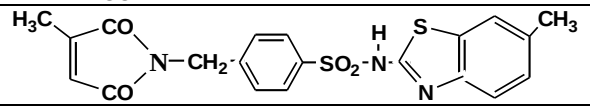
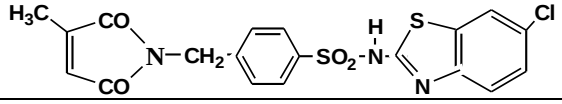
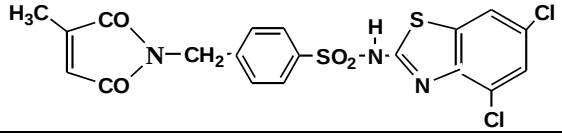
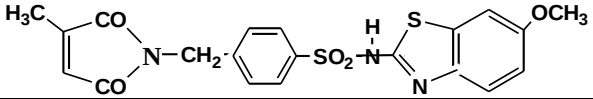
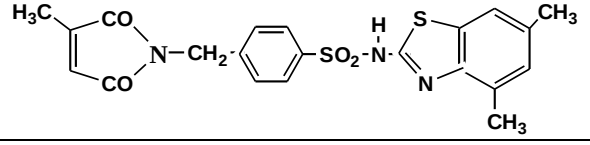
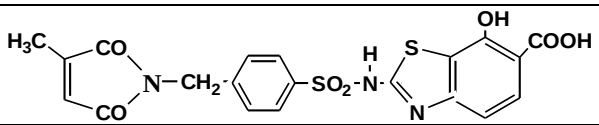
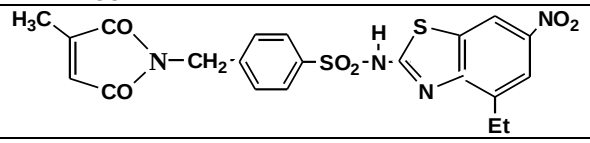
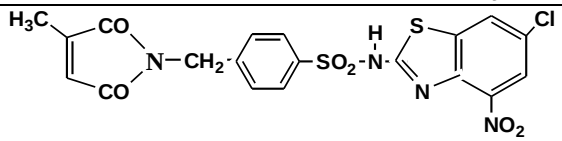
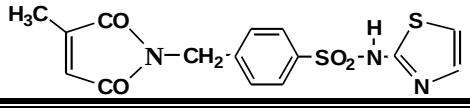
Copmd. No.	Compound Structure	Colour	Melting Point ^{0}C	Yield %	Recrystallization solvent
17		Light Yellow	226-228	77	Acetone
18		White	210-212	70	Ethanol
19		Tan yellow	206-207	65	Hexane
20		White	203-204	82	Acetone
21		Black	193-194	60	Methanol
22		Light Yellow	138-140	85	Ethanol
23		Light Brown	177-178	80	Acetone
24		Light Brown	149-150	71	Acetone
25		Orange	160-162	86	Ethanol
26		Deep Brown	182-184	75	Ethanol

Table (4) FTIR and U.V Spectral data of the prepared compounds [17-26]

Compd. No.	FTIR spectral data cm^{-1}										U.V (λ max) nm
	υ(C-H) Aromatic	υ(C=C) Aromatic	υ(N-H) sulfonamide	υ(C=O) Imide	υ(C=C) Vinylic	υ(SO_2) Asym.	υ(SO_2) sym.	υ(C=N) Thiazole	υ(C-S) Thiazole	Others	
17	3095	1420	3350	1645	1620	1335	1135	1527	625	---	260 340 415
18	3068	1540	3410	1700	1635	1373	1160	1550	671	---	291
19	3125	1520	3456	1635	1535	1335	1180	1442	702	υC-Cl 1095	299
20	3090	1475	3400	1704	1635	1396	1130	1535	717	υC-Cl 1070	260 291
21	3125	1525	3456	1635	1558	1310	1140	1411	617	υC-O-C 1265	260 340 399 461
22	3140	1518	3448	1650	1580	1350	1105	1450	635	-----	294 419
23	3095	1518	3417	1635	1558	1355	1150	1411	624	-----	290 340 418 461
24	3011	1540	3425	1690	1635	1395	1150	1550	617	------	280 350 419 456
25	3150	1602	3417	1704	1620	1390	1152	1550	617	------	280 357 419
26	3050	1520	3456	1705	1635	1360	1140	1575	620	-------	280 340 419

Table (5) Physical properties of the prepared compounds [27-36]

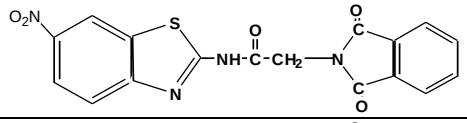
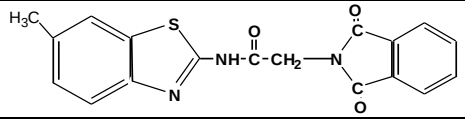
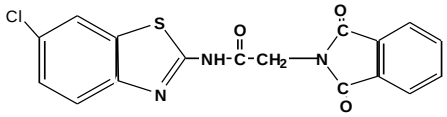
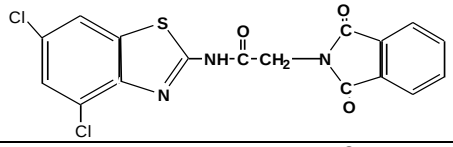
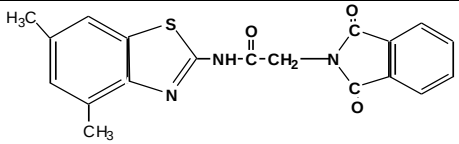
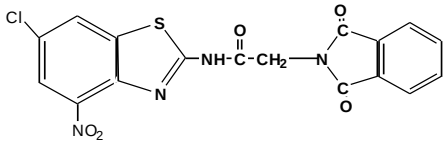
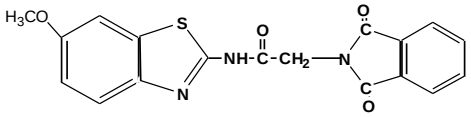
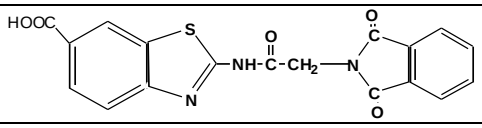
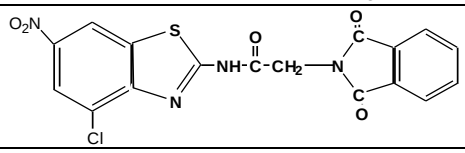
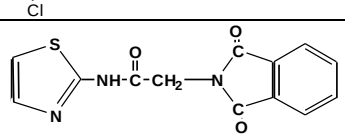
Copmd. No.	Compound Structure	Colour	Melting Point ^{0}C	Yield %	Recrystallization solvent
27		Yellow	166-168	77	Chloroform
28		Light Brown	88-90	80	Cyclohexane
29		Deep Brown	185-186	78	Chloroform
30		Light Yellow	125-126	74	Acetone
31		Yellowish white	120-122	72	Chloroform
32		Gray	170-171	75	Acetone
33		Orange	174-175	88	Chloroform
34		Light Yellow	190-192	70	Chloroform
35		Orange	163-164	90	Acetone
36		Brown	118-120	81	Acetone

Table (6) FTIR and U.V spectral data of the prepared compounds [27-36]

Compd. No.	FTIR spectral data cm^{-1}									
	υ(C-H) Aliphatic	υ(C-H) Aromatic	υ(N-H) Amide	υ(C=O) Imide	υ(C=N) Thaiazole	υ(C=C) Aromatic	υ(C-N)	υ(C-S)	Others	U.V λ (max) nm
27	2830	3100	3409	1720	1610	1589	1380	624	----	245 340 372
28	2890	3132	3409	1712	1610	1589	1373	648	----	249
29	2823	3082	3365	1735	1612	1542	1380	648	υ(C-Cl) 1049	249
30	2792	3070	3385	1740	1620	1580	1310	630	υ(C-Cl) 1100	248
31	2890	3076	3409	1735	1620	1580	1388	632	----	249
32	2900	3050	3355	1735	1600	1560	1388	648	υ(C-Cl) 1049 $\upsilon(NO_2)$ 1504	241 412
33	2832	3112	3294	1730	1604	1581	1380	633	υ(C-O-C) 1218	250
34	2846	3090	3201	1736	1580	1542	1380	648	υ(O-H) 3402 υ(C=O) 1640	283
35	2876	3032	3355	1743	1610	1558	1388	648	υ(C-Cl) 1049 $\upsilon(NO_2)$ 1504	240 416
36	2840	3150	3417	1743	1604	1604	1380	648	----	250 316

Table (7) Physical properties of the prepared compounds [37-46]

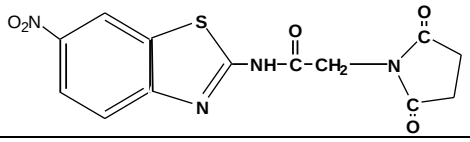
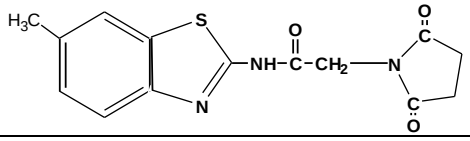
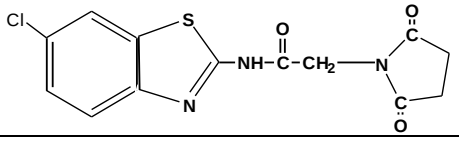
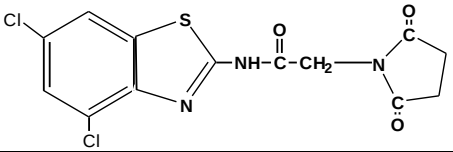
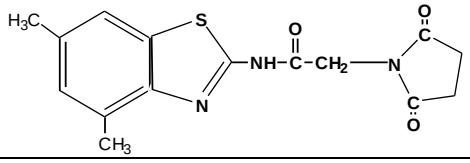
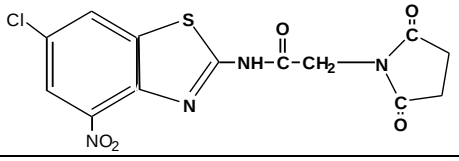
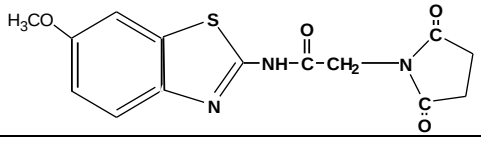
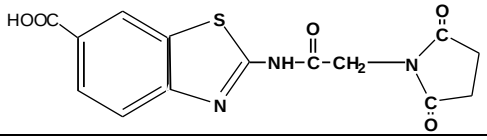
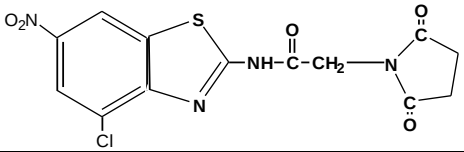
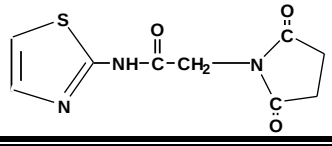
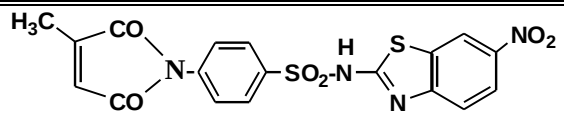
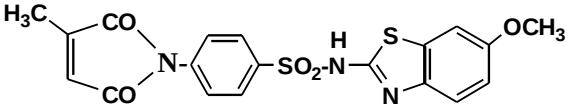
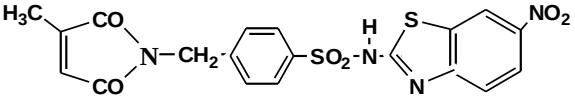
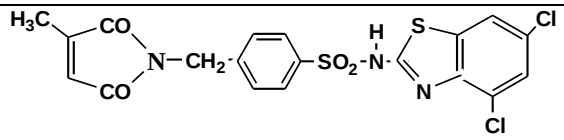
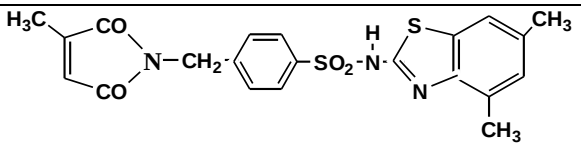
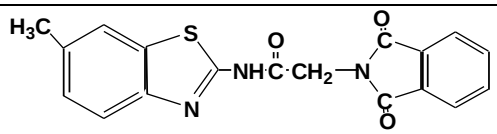
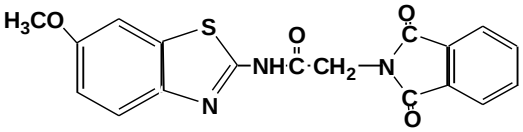
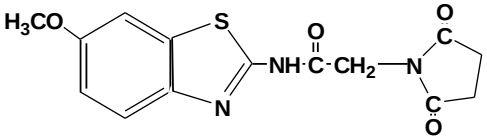
Copmd. No.	Compound Structure	Color	Melting Point ^{0}C	Yield %	Recrystallization solvent
37		Yellow	199-200	90	Chloroform
38		Brown	227-228	70	Cyclohexane
39		Light Yellow	218-220	75	Chloroform
40		Deep Yellow	157-158	76	Acetone
41		Black	148-150	87	Cyclohexane
42		Light brown	160 Dec.	83	Cyclohexane
43		Pall yellow	202 Dec.	78	Chloroform
44		Orange	208-210	80	Acetone
45		Deep Orange	175 Dec.	90	Acetone
46		Brown	140-142	75	Cyclohexane

Table (8) FTIR and U.V spectral data of compounds [37-46]

Compd. No.	FTIR spectral data cm^{-1}							
	υ(C-H) Aromatic	υ(N-H)) Amide	υ(C=O)	υ(C=N) Thiazole	υ(C-N) Imide	υ(C-S) Thiazole	Others	U.V (λ max) nm
37	3130	3440	1704	1612	1388	632	$\upsilon(NO_2)$ 1430	224 332 362
38	3112	3448	1697	1612	1334	640	-----	248
39	3076	3417	1689	1620	1330	632	υ(C-Cl) 1180	244
40	3140	3438	1697	1612	1334	640	----	241 261
41	3095	3417	1640	1620	1342	624	----	252
42	3117	3400	1635	1566	1342	640	$\upsilon(NO_2)$ 1400 υ(C-Cl) 1170	224
43	3112	3417	1704	1627	1350	640	υ(C-O-C) 1195	249
44	3085	3409	1704	1580	1396	640	---	238 266
45	3083	3409	1697	1627	1330	640	$\upsilon(NO_2)$ 1404	246 430
46	3122	3417	1690	1620	1350	617	----	228 264

Table (9) ^{1}H-NMR spectral data for some of the prepared imides

Compd. No.	Compound structure	Chemical shift δ ppm
4		**δ=2.2 CH_3 protons, δ= 4.9 vinylic proton, δ=(7.42-8.5) aromatic ring proton and NH proton.**
8		**δ= 2.5 CH_3 protons, δ=3.4 OCH_3 protons, δ=7.25 vinylic proton, δ= (7.55-7.92)aromatic protons and NH proton.**
17		**δ= 2.1 CH_3 protons, δ=4.04 benzylic protons, δ=6.6 vinylic proton, δ=(6.81-8.5) aromatic protons and NH proton.**
20		**δ=2.49 CH_3 protons, δ=3.8 benzylic protons, δ=7.1 vinylic proton , δ=(7.3-8.5)aromatic protons and NH proton.**
22		**δ=2.05 CH_3 protons, δ=2.35 CH_3 protons, δ=2.45 CH_3 protons, δ= 4.6 benzylic protons, δ=4.95 vinylic proton, δ=(6.45-7.35)aromatic protons and NH proton.**
28		**δ=2.49 CH_3 protons, δ=3.8** protons **(>N-$\underline{CH_2}$-CO-) δ= 6.4 NH , δ=(7.1-7.9) aromatic protons.**
33		**δ= 4.2 OCH_3 protons, δ=4.4** protons, **(>N-$\underline{CH_2}$-CO-) δ= 5.7 NH proton, δ=(7.3-7.9) aromatic ring protons.**
43		**δ=2.8 (-CH_2-CH_2-) protons in imide ring , δ=3.7 (>N-$\underline{CH_2}$-CO-)** protons **δ=3.9 OCH_3 protons, δ= (6.9-7.5) NH and aromatic ring protons.**

Table(10) C.H.N Analysese for some of the prepared Imides

Compd. No.	Calculated			Found		
	% C	%H	% N	% C	% H	% N
5	55.20	3.63	10.16	54.93	3.35	10.41
6	49.82	2.76	9.68	49.70	2.55	9.44
9	51.46	2.93	9.48	51.72	3.11	9.37
12	45.14	2.29	11.70	45.27	2.33	11.50
17	49.78	3.05	12.22	50.02	2.97	12.38
18	56.20	3.98	9.83	56.37	4.12	10.04
23	50.73	3.17	8.87	50.63	3.09	9.00
24	46.29	2.63	11.39	46.35	2.45	11.9
28	61.53	3.70	11.96	61.24	3.95	12.15
30	54.54	2.40	11.22	54.72	2.52	11.44
37	46.70	2.99	16.76	46.97	3.13	17.00
41	56.78	4.73	13.24	56.91	4.94	13.11

Table(11) Antimicrobial activity of some of the prepared compounds

Compd. No.	Gram - positive Bacteria		Gram- negative Becteria		Fungi
	Staphylococcus aureus	Staphylococcus pyogenes	Echerishia coli	Pseudomonas ariginosa	Candida albicans
4	+	+	-	-	-
5	++	++	-	-	-
6	+	+	-	-	-
7	++	++	-	-	+
8	+++	+++	-	-	+
9	++	++	-	-	-
10	++	++	-	-	-
12	++	++	-	-	+
17	-	-	+	+	-
18	-	-	++	++	+
20	-	-	+	+	-
21	-	-	++	++	+
22	-	-	+++	+++	+
23	-	-	+	+	-
25	-	-	+	+	-

Table(12) Antimicrobial activity of some of the prepared compounds

Compd. No.	Gram - positive Bacteria		Gram- negative Becteria		Fungi
	Staphylococcus aureus	Staphylococcus pyogenes	Echerishia coli	Pseudomonas ariginosa	Candida albicans
27	+	+	-	-	-
28	+	+	+	+	+
29	++	++	+	+	+
31	++	++	+	+	+
32	+	+	+	+	+
33	+++	+++	+	+	+
34	++	++	+	+	+
35	-	-	-	-	-
37	+	+	-	-	-
38	+	+	+	+	+
39	+	+	+	+	+
42	++	++	+	+	+
43	+++	+++	+	+	+
44	++	++	+	+	+
45	-	-	-	-	-
46	+	+	+	+	+

Key to symbols : Inactive= (-) inhibition zone < 6 mm
Slightly active =(+) (inhibition zone 6-9 mm)
Moderately active =(++) (hnhibition zone 9-12 mm)
Highly active =(+++) (inhibition zone > 12mm)

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