Synthesis and Priliminary Evaluation of Antibacterial Activity of a Series of New Phthalimides and Succinimides Linked to Benzothiazole Moiety

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Abstract

A series of new phthalimides and succinimides linked to benzothiazole moiety were synthesized and followed by their antibacterial screenings. Synthesis of the new imides was performed via two steps, the first one involved preparation of a series of N-(substituted benzothiazole-2-yl) phthalamic and succinamic acids via reaction of phthalic anhydride or succinic anhydride with substituted-2-aminobenzothiazoles.

In the secound step the prepared phthalamic and succinamic acids were dehydrated via treatment with acetic anhydride and anhydrous sodium acetate to afford a series of the desirable N-(substituted benzothiazole-2-yl)phthalimides and succinimides. Structures of the prepared compounds were confirmed by spectroscopic methods including FTIR, U.V., ^{1}H-NMR, ^{13}C-NMR spectroscopy and C.H.N analysis.

The synthesized imides were screened for their antibacterial activity against two types of bacteria *Staphylococcus aureus* and *Eschrichia coli.* The new compounds were found to exhibit good to moderate antibacterial activity.

تحضير وتقدير اولي للفعالية ضد البكتريا لسلسة من مركبات الفثال ايمايد والسكسن ايمايد الجديدة المرتبطة بمكونة البنزوثايازول

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مفتاح البحث: حامض الفثالاميك ،حامض السكسناميك، الفثال ايمايد، السكسن ايمايد

الخلاصة:

تم في هذا البحث تحضير سلسلة جديدة من مركبات الفثال ايمايد والسكسن ايمايد الحاوية في تركيبها على مكونة البنزوثايازول. تم تحضير المركبات الجديدة من خلال مرحلتين تم في الاولى تفاعل مركبات 2-امينوبنزوثايازول المعوضة مع كل من انهيدريد الفثاليك وانهيدريد السكسنيك مما اسفر عن تكوين سلسة من حوامض N-(معوض بنزوثايازول-2-يل) فثال آميك وحوامض N-(معوض بنزوثايازول-2-يل) سكسن آميك على التوالي. اما في الخطوة الثانية فقد تم سحب الماء من الحوامض المحضرة باستخدام انهيدريد الخليك وخلات الصوديوم اللامائية كعامل ساحب للماء مما اسفر عن تكوين الايمايدات المطلوبة وهي مركبات N-(معوض بنزوثايازول-2-يل)فثال ايمايد ومركبات N-(معوض بنزوثايازول-2-يل) سكسن ايمايد على التوالي.

تم اثبات تراكيب المركبات المحضرة بالاعتماد على مطيافية الاشعة تحت الحمراء FTIR، الاشعة فوق البنفسجية U.V. والرنين النووي المغناطيسي ^{1}H-NMR و^{13}C-NMR بالاضافة الى تحليل العناصر (C.H.N).

كذلك تمت دراسة الفعالية البايولوجية للايمايدات المحضرة ضد نوعين من البكتريا هما ستافيلوكوكاس اوريس واشريشيا كولي حيث اظهرت نتائج الدراسة بان اغلب الايمايدات المحضرة ذات فعالية بايولوجية جيدة ضد انواع البكتريا المذكورة.

Introduction

Benzothiazoles are bicyclic ring systems with diverse chemical reactivity and a broad spectrum of biological activities including antimicrobial, anticancer, antifungal, antitumor, anti-inflammatory and antilieshmanial activity[1-8]. Some of 2-alkyl and 2-aryl benzothiazoles showed antituberculosis activity while thiazoles substituted with amido group in position (2) were used as herbicides [9].

On the other hand cyclic imides represent important functionality which have been found to maintain significant biological activity[10,11]. Much attention has been paied to various classes of cyclic imides due to their biological properties including antibacterial, antifungal, analgesic and antitumor activities [12-14].

In light of the interesting variety of biological activities seen in cyclic imides and benzothiazoles it was thought of interest to examine the effect of having these two functionalities present simultaneously in one structure.

Based on this notion we thus decided to synthesize new cyclic imides linked to benzothiazole moiety and to test their antibacterial activity.

Experimental

Chemicals were purchased from BDH, Fluka and Merck chemical companies. Melting points were determined on Gallen kamp capillary melting point apparatus and are uncorrected. FTIR spectra were recorded using KBr discs on SHIMADZU FTIR-8400 Fourier transforms Infrared Spectrophotometer. U.V. spectra were recorded on SHIMADZU UV-Visible recording spectrophotometer UV. 1650 and these analyses were performed in Chemistry department, college of Science , Baghdad university.

^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker, Ultrasheild 300 MHz using DMSO-d_6 and $CDCl_3$ as solvents and TMS as internal standard at Al-Albayt University, Jordon.

Elemental analyses were performed on Perkin Elmer 240 element analyzer. Incubator Heraeus D-63450 (Germany) model was used for incubation samples in biological study.

1- Preparation of N-(Substituted benzothiazole-2-yl) phthalamic acids [1-10]

(0.01 mole, 1.48 gm) of phthalic anhydride was dissolved in (20 mL) of dry acetone in a suitable round bottomed flask fitted with dropping funnel which was supplied with (0.01 mol) of substituted-2-amino benzothiazole dissolved in (30 mL) of dry acetone. The solution in dropping funnel was added dropwise to the mixture with stirring and cooling[15,16]. When addition was completed stirring was continued for one hour then the precipitated phthalamic acid was filtered off, washed with diethyl ether and dried. The resulted phthalamic acid was purified by recrystallization from a suitable solvent. Physical properties of the prepared phthalamic acids [1-10] are listed in Table (1).

2- Preparation of N-(Substituted benzothiazole-2-yl) phthalimides [11-20]

A mixture of (0.1 mol) of N-substituted benzothiazole-2-yl)phthalamic acid in (10 mL) of acetic anhydride and (5-10)% by weight of anhydrous sodium acetate was refluxed with stirring for 2 hrs at 75^{o}C. The resulted homogenous solution was cooled to room temperature then poured into excess cold distilled water with vigorous stirring [17]. The obtained precipitate was filtered, washed with distilled water then dried and finally purified by recrystallization from a suitable solvent. Physical properties of the prepared imides [11-20] are listed in Table (2).

3- Preparation of N-(Substituted benzothiazole-2-yl) succinamic acids [21-30]

N- (substituted benzothiazole – 2 – yl) succinamic acids were prepared via reaction of equimolar amounts of succinic anhydride and substituted-2-aminobenzothiazole in dry acetone following the same procedure used in preparation of phthalamic acids [1-10]. The synthesized succinamic acids were purified by recrystallization from a suitable solvents and their physical properties are listed in Table (5).

4- Preparation of N-(Substituted benzothiazole-2-yl) succinimides [31-40]

Synthesis of the titled compounds were performed by dehydration of prepared succinamic acids [21-30] by using acetic anhydride and anhydrous sodium acetate as dehydrating agent following the same procedure used in the preparation of phthalimides [11-20]. Physical properties of the prepared succinimides [31-40] are listed in Table (6).

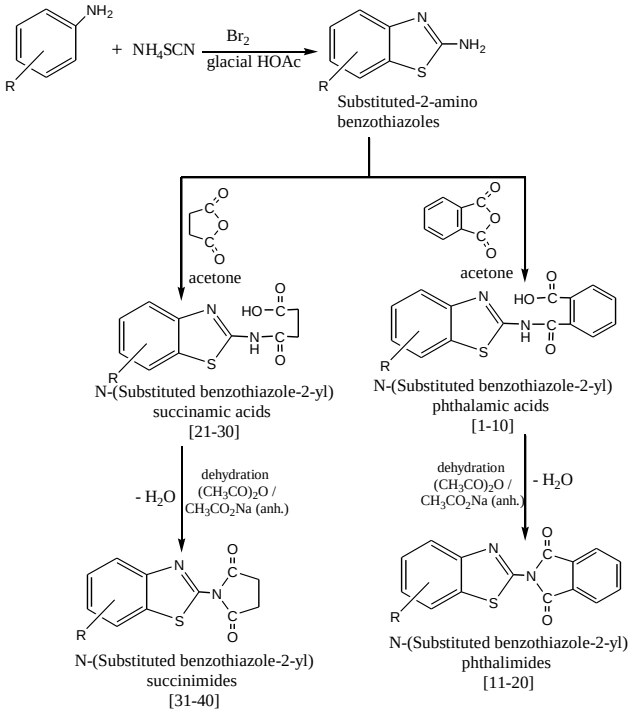
5- Antibacterial Activity

The cup plate method using nutrient agar medium was employed[18,19] in studying the antibacterial activity of the prepared compounds against two types of bacteria, *Staphylococcus aureous* (gram positive) and *Escherichia coli* (Gram negative) respectively using DMF as sample solution. Using a sterilized cork borer cups were scooped out of agar medium contained in a Petri dish which was 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°C for 48hrs. Zones of inhibition produced by each compound was measured in mm and the results are listed in Table (11).

Results and Discussion

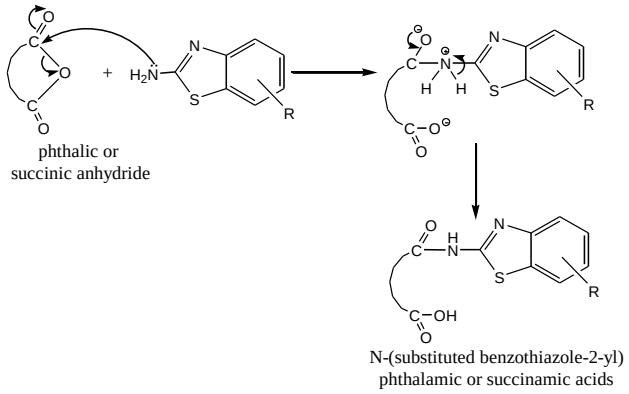
Since both cyclic imides and 2-amino benzothiazoles are biologically active compounds having wide spectrum of biological applications the target of the present work is to synthesize new compounds containing these two biologically active moieties cyclic imide (phthalimide or succinimide) and benzothiazole with expected biological activity.

The plan used in performing this target based on preparation of primary amines already having benzothiazole moiety in their structures thus the first step in this strategy involved preparation of ten 2-aminobenzothiazoles substituted with different substituents by following thiocyanogen method as reported in literatures[20].The prepared 2-aminobenzothiazoles were introduced in reaction with phthalic anhydride and succinic anhydride to produce a series of phthalamic acids and succinamic acids having benzothiazole moiety in their structures. Dehydration of the resulted phthalamic and succinamic acids by using acetic anhydride and anhydrous sodium acetate as dehydrating agent afforded the desirable phthalimides and succinimides. This linear pathway strategy can be summarized in Scheme (1).



Scheme (1)

Synthesis of phthalamic acids and succinamic acids was performed via reaction of equimolar amounts of phthalic anhydride or succinic anhydride with 2-amino benzothiazoles. Mechanism of this reaction involved nucleophilic attack of amino group in primary amine on carbon atom of one carbonyl group in the cyclic anhydride as described in Scheme (2).

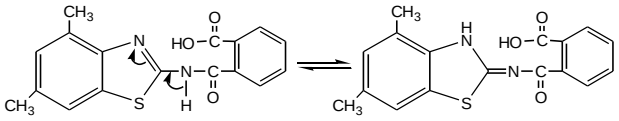


Scheme (2)

The prepared phthalamic and succiniamic acids were colored solids, most of them have sharp melting points and were afforded in good percent yields. Structures of phthalamic acids [1-10] and succinamic acids [21-30] were confirmed by depending on FTIR and U.V. spectral data besides ^{1}H-NMR, ^{13}C-NMR and C.H.N analysis for some of them. FTIR spectra of the prepared phthalamic acids showed many characteristic absorption bands at (3300-3490) cm^{-1}, (3300-3440) cm^{-1}, (1635-1720) cm^{-1} (1558-1666) cm^{-1}, (1645-1590) cm^{-1} and (640-709) cm^{-1} which were attributed to ν(O-H) carboxylic, ν(N-H) amide, ν(C=O) carboxylic, ν(C=O) amide, ν(C=N) thiazole and ν(C-S) thiazole respectively[21]. At the same time FTIR spectra of the prepared succinamic acids showed also many clear absorption bands at (3200-3494) cm^{-1}, (3200-3379) cm^{-1}, (1674-1720) cm^{-1}, (1600-1690) cm^{-1}, (1527-1589) cm^{-1} and (600-704) cm^{-1} which were assigned to ν(O-H) carboxylic, ν(N-H) amide, ν(C=O) carboxylic, ν(C=O) amide, ν(C=N) thiazole and ν(C-S) thiazole respectively.

On the other hand U.V. spectra of phthalamic acids showed clear bands at wavelengths (212-295) nm and (300-364) nm while U.V. spectra of succinamic acids showed clear bands at wavelengths (215-293) nm and (303-335) nm. These absorptions are due to ($\pi\rightarrow\pi^{*}$) and ($n\rightarrow\pi^{*}$) transitions in benzothiazole conjugated system and phthalamic or succinamic acids moieties.

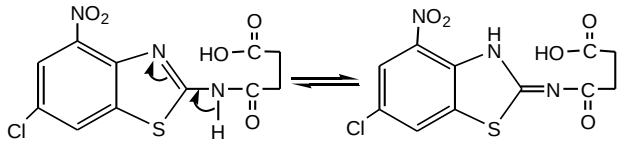
^{1}H-NMR spectrum of phthalamic acid [10] showed clear signals including two singlet signals at (δ = 2.2 and 2.3) ppm belong to CH_3 protons, signals at (δ = 6.8-7.7) ppm due to (N-H) amide proton and aromatic protons and signal at (δ = 12.8) ppm belong to (O-H) carboxylic proton. It is necessary to mention here that there is a tautomerism between amide group and nitrogen atom in thiazole ring as shown in equation below and this caused the appearance of (N-H) amine signal at (δ = 2.5) ppm [17].



^{13}C-NMR spectrum of the same compound [10] showed many clear signals including signals at (18.45) and (21.25) ppm belong to two methyl groups, signals at (118.73-133.34) ppm belong to aromatic ring carbons, signal at (149.65) ppm belong to carbon atom (C=N) in thiazole ring and signals

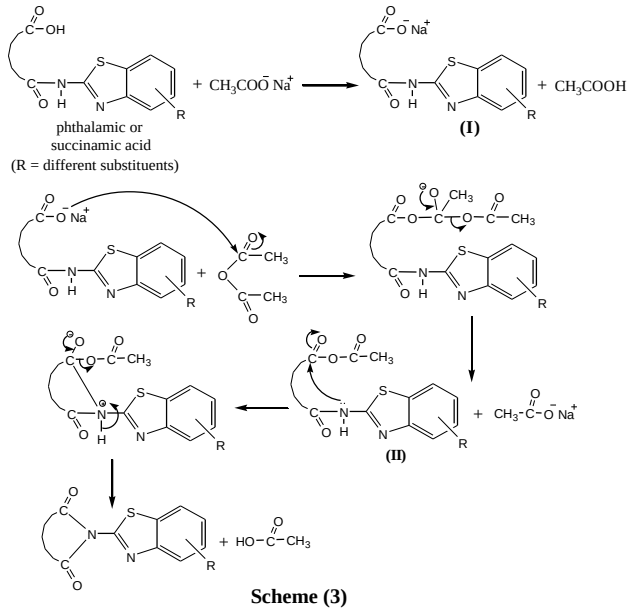
at (165.5) and (168.6-169.1) ppm due to carbonyl carbons of amide group and carboxyl group respectively [23].

Finally ^{1}H-NMR spectrum of compound [29] showed many signals including signals at (δ = 2.2 and 2.5) ppm due to four aliphatic protons, signal at(δ = 6) ppm due to(N-H) amide proton, signal at(δ= 7.9) ppm due to aromatic protons and signal at (δ = 1.25) ppm due to (N-H) amine proton caused by tautomerism.



^{13}C-NMR spectrum of compound [29] showed signal at (33.15) ppm due to aliphatic carbons, signals at (105-113) ppm due to aromatic carbons, signal at (138) ppm belong (C=N) carbon in thiazole ring and signals at (165 and 175.9) ppm belong to carbonyl carbons. The final step in the strategy used in building the desirable cyclic imides involved dehydration of the prepared phthalamic and succinamic acids.

Dehydration was performed by using suitable dehydrating agent acetic anhydride in the presence of anhydrous sodium acetate. Mechanism of this reaction involved abstraction of proton from amic acid by the catalyst sodium acetate producing (phthalamate or sunccinamate ion I) which inturn attacked acetic anhydride producing (phthalamic or succinamic anhydride II) followed by ring closure [24] as described in scheme (3).



Scheme (3)

The prepared phthalimides and succinimides are colored solids, afforded in high percent yields and most of them have sharp melting points. Structures of the prepared phthalimides and succinimides were confirmed by FTIR and U.V. spectral data besides ^{1}HNMR, ^{13}CNMR and C.H.N analysis for some of them. FTIR spectra of all the prepared imides showed disappearance of ν(O-H) carboxylic and ν(N-H) amide absorption bands indicating success of dehydration reaction and imide formation. FTIR spectra of the prepared phthalimides showed clear bands appeared as shoulder at (1740-1780) cm^{-1} due to

asym. ν(C=O) imide while bands due to sym. ν(C=O) imide appeared at (1697-1735) cm^{-1}. Other absorption bands appeared at (1500-1690) cm^{-1}, (1342-1382) cm^{-1}, (1500-1620) cm^{-1} and (648-717) cm^{-1} which were attributed to ν(C=N) thiazole, ν(C-N) imide, ν(C=C) aromatic and ν(C-S) thiazole respectively[20].

U.V. spectra of the new phthalimides showed clear bands at wavelength (225-299) nm and (305-327) nm due to ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transitions in conjugated system of both benzothiazole and phthalimide moieties[23].

^{1}H-NMR spectrum of compound [18] showed clear signals at (δ = 7.5 and 8.1) ppm which belong to two vinylic protons in thiazole ring and aromatic protons, while ^{13}CNMR spectrum of the same compound showed signals at (125.8-131.7) ppm due to aromatic ring carbons, signals at (133.3 and 136.6) ppm were due to two vinylic carbons in thiazole ring, signal at (163.7) ppm due to (C=N) carbon in thiazole ring and signal (169.1) ppm due to two carbonyl carbons in imide ring.

On the other hand FTIR spectra of the prepared succinimdes showed many clear absorption bands at (1690-1745) cm^{-1}, (1570-1690) cm^{-1}, (1512-1610) cm^{-1}, (1336-1384) cm^{-1} and (620-685) cm^{-1} which were assigned to ν(C=O) imide, ν(C=N) thiazole, ν(C=C) aromatic, ν(C-N) imide and ν(C-S) thiazole respectively.

U.V. spectra of the new succinimides showed clear bands at wavelengths (217-293) nm and (305-327) nm due to ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transitions in benzothiazole conjugated system and succinimide moieties.

Finally ^{1}H-NMR spectrum of compound [40] showed many signals including two singlet at (δ = 2.17 and 2.8) ppm for two CH_3 groups protons, signals at (δ = 2.38 and 2.5) ppm belong to four aliphatic protons in succinimide ring and signals at (δ = 7.05-7.7) ppm belong to aromatic protons.

^{13}CNMR spectrum of compound [40] showed also clear signals at (18.25 and 21.45) ppm due to two CH_3 groups and signals at (23.1 and 29.07) ppm due to two aliphatic carbon atoms in succinimide ring. Signals at (119.08-146) ppm were belong to aromatic ring carbons while signal at (156) ppm belong to (C=N) carbon in thiazole ring and signals at (169.6 and 175.6) ppm belong to two carbonyl carbons in succinimide ring. All details of FTIR and U.V. spectra of the prepared amic acids and imides are listed in Tables (3), (4), (7) and (8) respectively while NMR spectral data and C.H.N. analysis for some of the prepared compounds are listed in Tables (9) and (10).

Since the prepared new imides were built from two biologically active components we expected these imides to possess biological activity so the synthesized imides were screened for their antibacterial activity against two types of bacteria *Staphylococcus aureus* and *Escherichia coli*. The test results presented in Table (11) showed that imide (35) is highly active against the two types of bacteria. While imides [16], [19] and [39] showed high activity against *Staphylococcus aureus* and moderate activity against *E. Coli.* Imide [12] is highly active against *E. Coli.* But showed moderate activity against *Staphylococcus aureus.* Compounds [32] and [36] showed moderate activity against the two types of bacteria while compound [15] showed moderate activity against *Staphylococcus aureus* but inactive against *E. Coli.* and compound [17] showed moderate activity against *E. Coli.* and no activity against *Staphylococcus aureus*. Other imides including [14], [18] and [20] showed slight activity against *Staphylococcus aureus* while imides [33], [34] and [40] showed no activity against the tested organisms.

Table (1): Physical properties of the prepared phthalamic acids [1-10]

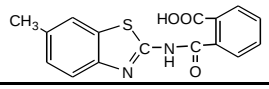
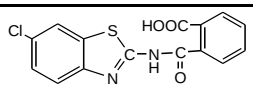
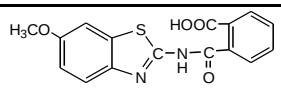
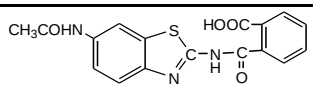
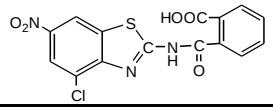
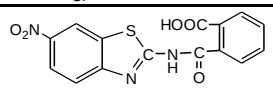
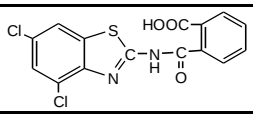
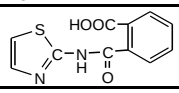
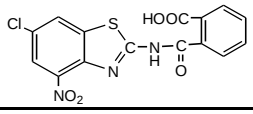
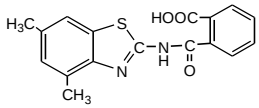
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization solvent
1		White	220 dec.	71	Ethanol
2		Yellow	205-207	80	Methanol
3		Violet	181-183	75	Ethanol
4		Yellowish white	143-145	78	Ethanol
5		Orange	169 dec.	78	Ethanol
6		Deep yellow	184 dec.	83	Methanol
7		Pale yellow	140-142	89	Ethanol
8		Pale pink	147-149	88	Methanol
9		Orange	153 dec.	84	Methanol
10		Brown	174-176	75	Ethanol

Table (2): Physical properties of the prepared phthalimide [11-20]

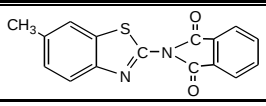
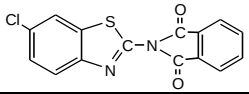
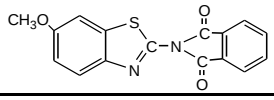
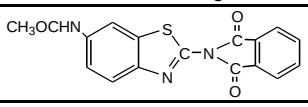
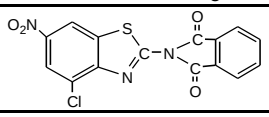
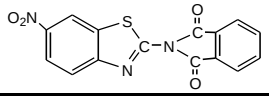
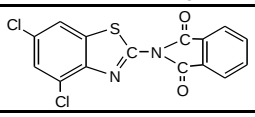
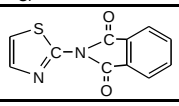
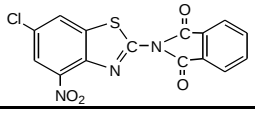
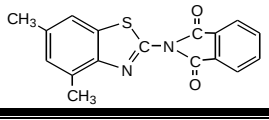
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization solvent
11		Pale yellow	175 dec.	90	Cyclohexane
12		Off white	159-161	95	Cyclohexane
13		Deep violet	122-124	93	Cyclohexane
14		Brown	192 dec.	89	Cyclohexane
15		Orange	86-88	95	Acetone
16		Yellow	179-181	85	Cyclohexane
17		Pale yellow	166 dec.	78	Cyclohexane
18		Pink	126-128	91	Acetone
19		Orange	116-118	80	Cyclohexane
20		Yellow	176 dec.	88	Acetone

Table (3): Spectral data of the prepared phthalamic acids [1-10]

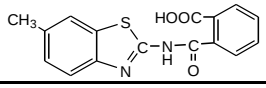
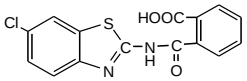
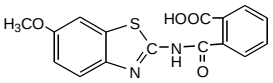
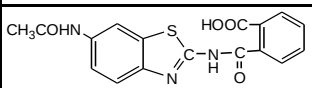
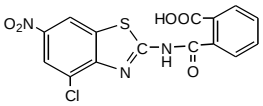
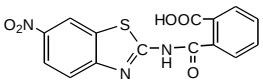
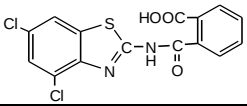
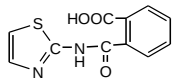
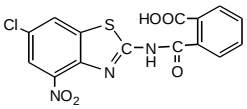
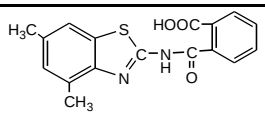
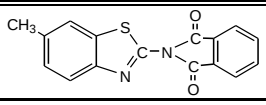
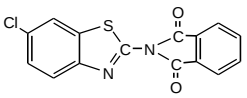
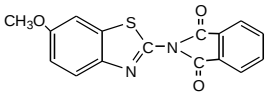
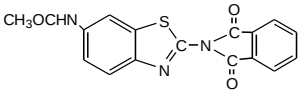
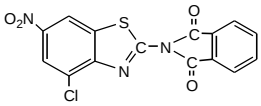
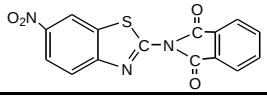
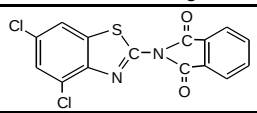
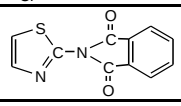
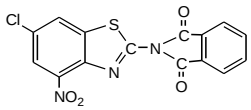
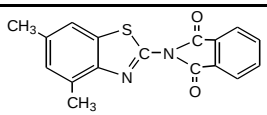
Comp. No.	Compound structure	FTIR spectral data cm^{-1}							U.V. (λ_{max}) nm
		ν(O-H) carboxylic ν(N-H) amide	ν(C=O) carboxyl	ν(C=O) amide	ν(C=N) thiazole	ν(C-S) thiazole	ν(C-H)	Others	
1		3400 3348	1681	1558	1465	709	3155	-	225 300
2		3490 3390	1635	1596	1542	648	3050	**ν(C-Cl)** 1095	242 273
Comp. No.	**Compound structure**	**FTIR spectral data cm^{-1}**							**U.V. (λ_{max}) nm**
		ν(O-H) carboxylic ν(N-H) amide	**ν(C=O) carboxyl**	**ν(C=O) amide**	**ν(C=N) thiazole**	**ν(C-S) thiazole**	**ν(C-H)**	**Others**	
3		3435 3360	1689	1589	1488	678	3016	**ν(C-O-C)** 1280 1141	225 227 267
4		3300	1680	1590	1490	680	3120	-	228 292
5		3480 3360	1695	1630	1590	650	3200	**ν(NO_2)** 1480 1320 **ν(C-Cl)** 1120	212 284 295 364
6		3301	1712	1666	1550	694	3124	**ν(NO_2)** 1504 1342	226 286 334
7		3320	1720	1635	1589	671	2977	**ν(C-Cl)** 1049	218 221
8		3420 3330	1700	1590	1500	670	3000	-	217 224 278
9		3440	1689	1590	1535	671	3078	**ν(NO_2)** 1500 1410 **ν(C-Cl)** 1075	216 227 278
10		3400	1680	1640	1580	640	3000	-	227 279

Table (4): Spectral data of the prepared phthalimide [11-20]

Comp. No.	Compound structure	FTIR spectral data cm^{-1}							U.V. (λ_{max}) nm
		ν(C-H) aromatic	ν(C=O) imide	ν(C=N) thiazole	ν(C-N) imide	ν(C=C) aromatic	ν(C-S) thiazole	Others	
11		3000	1750(sh) 1715	1500	1370	1500	717	-	225 256 308
12		3178	1750(sh) 1689	1604	1373	1566	648	**ν(C-Cl)** 1095	247 282 291 305
13		3062	1840(sh) 1760 1730	1610	1360	1520	715	**ν(C-O-C)** 1255 1120	255 292
Comp. No.	**Compound structure**	**FTIR spectral data cm^{-1}**							**U.V. (λ_{max}) nm**
		ν(C-H) aromatic	**ν(C=O) imide**	**ν(C=N) thiazole**	**ν(C-N) imide**	**ν(C=C) aromatic**	**ν(C-S) thiazole**	**Others**	
14		3178	1780(sh) 1735	1666	1342	1612	678	**ν(N-H)** 3349	287 290 293 298
15		3040	1860(sh) 1766 1700	1590	1350	1540	709	**ν(NO_2)** 1504 1330 **ν(C-Cl)** 1100	292 299
16		3070	1770(sh) 1697	1585	1342	1545	671	**ν(NO_2)** 1519	225 286 327
17		3030	1780(sh) 1718	1650	1382	1587	690	**ν(C-Cl)** 1080	286 307
18		3020	1850(sh) 1770	1690	1360	1600	710	-	253 288 296
19		3100	1780(sh) 1720	1660	1380	1620	710	**ν(NO_2)** 1495 1340 **ν(C-Cl)** 1070	247 249
20		3178	1740(sh) 1697	1650	1375	1570	690	-	249 288

(sh) = shoulder

Table (5): Physical properties of the prepared succinamic acids [21-30]

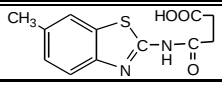
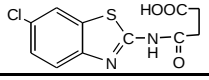
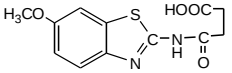
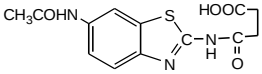
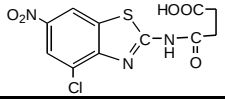
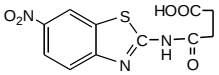
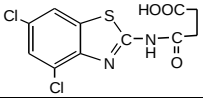
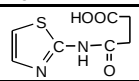
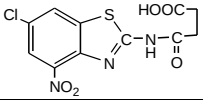
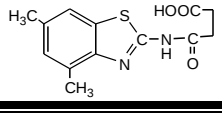
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization solvent
21		White	205 dec.	80	Ethanol
22		Off white	132-134	75	Dioxane
23		Violet	152-154	70	Ethanol
24		Yellowish green	185 dec.	83	Ethanol
25		Orange	102-104	65	Acetone
26		Yellow	193-195	77	Ethanol
27		Off white	158 dec.	85	Dioxane
28		White	159-161	73	Ethanol
29		Deep orange	108-110	81	Acetone
30		Yellow	144-146	76	Methanol

Table (6): Physical properties of the prepared succinimides [31-40]

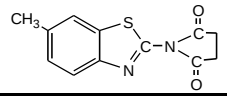
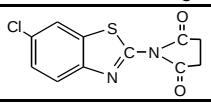
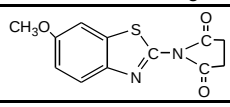
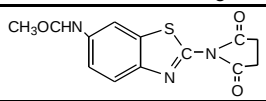
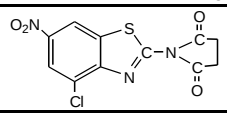
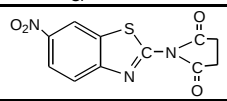
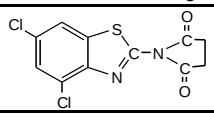
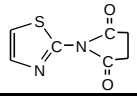
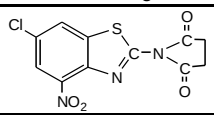
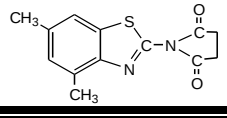
Comp. No.	Compound structure	Color	Melting points °C	Yield %	Recrystallization solvent
31		Off white	186 dec.	91	Cyclochexane
32		White	187-189	93	Cyclochexane
33		Faint violet	164-166	89	Cyclochexane
34		Yellow	163 dec.	87	Acetone
35		Orange	83-85	81	Cyclochexane
36		Deep yellow	170 dec.	75	Acetone
37		Yellow	196 dec.	90	Acetone
38		Redish pink	140-142	93	Acetone
39		Orange	105-107	78	Acetone
40		Faint yellow	193 dec.	95	Cyclochexane

Table (7): Spectral data of the prepared succinamic acids [21-30]

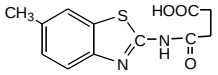
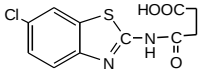
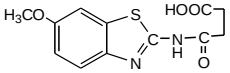
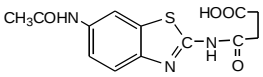
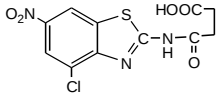
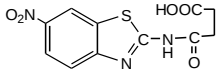
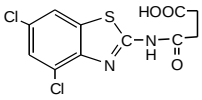
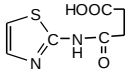
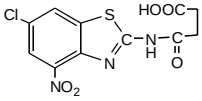
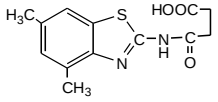
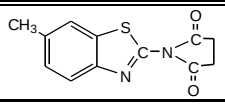
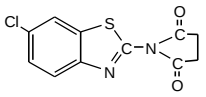
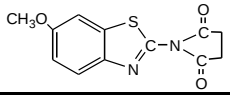
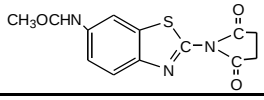
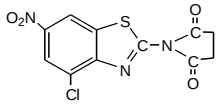
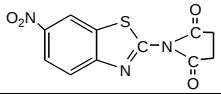
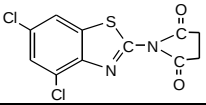
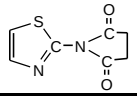
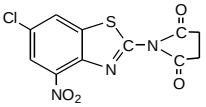
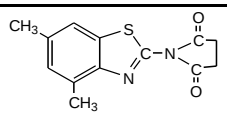
Comp. No.	Compound structure	FTIR spectral data cm^{-1}							U.V. (λ_{max}) nm
		ν(O-H) carboxylic ν(N-H) amide	ν(C=O) carboxyl	ν(C=O) amide	ν(C=N) thiazole	ν(C-S) thiazole	ν(C-H) aromatic	Others	
21		3487 3379	1697	1627	1589	640	3070	-	218 278 306
22		3417 3294	1697	1658	1527	640	3186	**ν(C-Cl)** 1095	222 226 249 303
23		3200	1689	1620	1581	678	3055	**ν(C-O-C)** 1226 1164	216 282 293 308
24		3217	1674	1610	1535	648	3085	-	227 283
25		3494 3379	1697	1627	1589	640	3062	**ν(NO_2)** 1488 1319 **ν(C-H)** 1033	215 310
26		3340	1697	1635	1580	640	3055	**ν(NO_2)** 1496 1326	218 224 319 328 335
27		3440	1680	1600	1540	600	3060	**ν(C-Cl)** 1110	225 270
28		3420 3250	1720	1690	1550	640	-	-	224 239
29		3460 3355	1697	1643	1566	640	3060	**ν(NO_2)** 1504 1340 **ν(C-Cl)** 1033	225 282
30		3300	1690	1630	1535	704	3140	-	233 270

Table (8): Spectral data of the prepared succinimides [31-40]

Comp. No.	Compound structure	FTIR spectral data cm^{-1}							U.V. (λ_{max}) nm
		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	
31		3062	1797(sh) 1728	1589	1550	1342	655		260 315
32		3080	1800(sh) 1720	1590	1550	1340	650	**ν(C-Cl)** 1055	218 237 270 290 305
33		3060	1800(sh) 1728	1604	1560	1342	655	**ν(C-O-C)** 1234 1118	248 291
34		3060	1790(sh) 1697	1627	1589	1342	640	**ν(N-H)** 3320	293
35		3080	1790(sh) 1728	1683	1610	1336	620	**ν(NO_2)** 1463 **ν(C-Cl)** 1100	255 320 327
36		3060	1805(sh) 1720	1570	1512	1342	655	**ν(NO_2)** 1442	314 327
37		3040	1700	1652	1587	1384	685	**ν(C-Cl)** 1080	231 277 306
38		3065	1805(sh) 1745	1690	1565	1360	640	-	217 224 278
39		3080	1710(sh) 1690	1605	1560	1340	650	**ν(NO_2)** 1505 1355 **ν(C-Cl)** 1100	254 308
40		3178	1790(sh) 1728	1650	1560	1375	670	-	249 282

(sh) = shoulder

Table (9): ^{1}H-NMR and ^{13}C-NMR spectral data for some of the prepared compounds

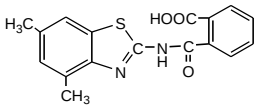
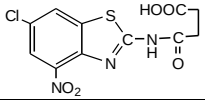
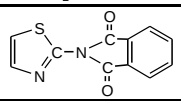
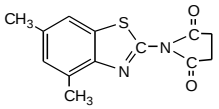
Comp. No.	Compound structure	H-NMR spectra data chemical shifts in ppm	^{13}C-NMR spectra data
10		δ = (2.2 and δ = 2.3), 6H, $2CH_3$ δ = (6.8-7.7), NH, 6H aromatic δ = 12.8 (OH) carboxylic	18.45 and 21.25, $2CH_3$, (118.73-133.34) aromatic ring carbons, 149.65 (C=N), 165.5 and (168.6-169.1) two carbonyl carbons
29		δ = (2.2 and δ = 2.5), 4H aliphatic, δ = 6 (NH), δ = 7.9, 2H aromatic	33.15 two aliphatic carbons, (105-113) aromatic ring carbons, 138 (C=N), (165 and 175.9) two carbonyl carbons
18		δ = 7.5, 2H vinylic, δ = 8.1, 4H aromatic	(125.8-131.7) aromatic ring carbons, (133.3 and 136.6) two vinylic carbons, (163.7) C=N, (169.1) two carbonyl carbons
40		δ = (2.17 and δ = 2.8), 6H, $2CH_3$ δ = (2.38 and δ = 2.5), 4H aliphatic δ = (7.05-7.7), 2H aromatic	18.25 and 21.45 two CH_3, (23.1 and 29.07) two aliphatic carbons, (119.08-146) aromatic carbons, 156 (C=N), (169.6 and 175.6) two carbonyl carbons

Table (10): C.H.N. analysis for some of the prepared compounds

Compd. No.	Calculated			Found		
	%C	%H	%N	%C	%H	%N
4	57.46	3.66	11.83	57.22	3.48	12.04
13	61.93	3.22	9.03	62.10	2.97	9.14
16	57.87	2.25	9.00	58.00	2.11	8.78
22	46.39	3.16	9.84	46.62	3.00	10.03
32	49.53	2.62	10.50	49.27	2.77	10.38
35	42.37	1.92	13.48	42.64	2.12	13.21

Table (11): antibacterial activity of the prepared compounds

Compd. No.	Gram positive *Stapylococcus aureus*	Gram negative *Escherichia coli*
12	++	+++
14	+	+
15	++	-
16	+++	++
17	-	++
18	+	-
19	+++	++
20	+	-
32	++	++
33	-	-
34	-	-
35	+++	+++
36	++	++
39	+++	++
40	-	-

Key symbols: Inactive= (-) inhibition zone < 6mm, Slightly active = (+) inhibition zone 6-9 mm

Moderately active = (++) inhibition zone 9-12mm, Highly active = (+++) inhibition zone > 12 mm

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