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Synthesis and Characterization of New Phthalimides and Succinimides Substituted with 1,3,4-Oxadiazole Ring

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ABSTRACT

A series of new phthalimides and succinimides connected to 1,3,4-oxadiazole moiety were synthesized via multistep synthesis. The first step involved synthesis of six 5- substituted 2- amino-1,3,4-oxadiazoles by oxidative cyclization of substituted semicarbazones under treatment with bromine and anhydrous sodium acetate in glacial acetic acid.The synthesized 2-amino-1,3,4-oxadiazoles were introduced in reaction with phthalic or succinic anhydride in the second step producing six N - (5-substituted-1,3,4-oxadiazole-2-yl) phthalamic acids and six N-(5-substituted -1,3,4-oxadiazole-2-yl) succinamic acids which in turn were dehydrated in the third step via fusion method or using acetic anhydride and anhydrous sodium acetate as dehydrating agent to afford the desirable N-(5-substituted -1,3,4-oxadiazole -2-yl) phthalimides and N-(5- substituted -1,3,4-oxadiazole -2-yl) succinimides respectively.Structures of the prepared compounds were confirmed by spectroscopic analysis and C.H.N analysis.Some of the synthesized compounds were screened for their antibacterial activity against two microorganisms, staphylococcus aureous (Gram positive) and Escherichia coli (Gram negative) and the results indicated that they exhibit good to moderate antibacterial activity.

Introduction

1,3,4-Oxadiazoles have attracted an interest in medicinal chemistry as ester and amide for a number of biological targets. More over these compounds have also demonstrated a broad spectrum of biological properties in both pharmaceutical and agrochemical fields such as antibacterial, anti – inflammatory, antimitotic, antiarrhythic and anticancer activities (1-6).

They are also applied in agriculture as herbicides, fungicides or insecticides (7,8) .

On the other hand synthetic cyclic imides such as succinimides, glutarimides, phthalimides and related compounds contain an imide ring and a general structure (-CO-N(R)-CO-) that confers ydrophobicity and neutral characteristic and can therefore cross biological membranes in vivo .

A diversity of biological activities and pharmaceutical uses have been attributed to them such as antibacterial, antifungal, antinociceptive, anticonvulsant and antitumor(9-12).

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According to all these facts it was thought worthwhile to synthesize new cyclic imides via incorporating the two biologically active moieties 1,3,4-oxadiazole and phthalimide or succinimide in a single molecular framework.

The obtained new compounds were expected to possess biological activity since they were derived from biologically active components.

Experimental

Chemicals were purchased from Merk and Fluka chemical companies.

Melting points were determined in open capillaries on Thomas Hoover apparatus and were uncorrected. FTIR spectra were recorded using KBr

discs on SHIMADZU FTIR- 8400 Fourier Transform Infrared spectrophotometer. U.V spectra were recorded on SHIMADZU U.V-visible recording spectrophotometer U.V 1650 . 1HNMR and C13NMR spectra were recorded in CDCl3 / DMSO –d6 on a Bruker ultra shield 300 MHz spectrometer using TMS as internal reference . 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. Synthesis of 2-amino-5-substituted -1,3,4-oxadiazoles [1-6]

The titled compounds were prepared according to literatures [(2)]with minor modifications and the required semicarbazones were synthesized via direct reaction between aromatic aldehydes and semicarbazide hydrochloride according to literature procedures [(13)].

A mixture of the prepared semicarbazone (0.01 mol) and sodium acetate (0.01 mol) dissolved in (25 mL)of glacial acetic acid was placed in a suitable round bottomed flask fitted with a dropping funnel which was supplied with (0.01 mol) of bromine dissolved in (8 mL) of glacial acetic acid . Bromine solution was added drop wise with stirring which was continued for two hours . After pouring the mixture in cold water the resulting solid was filtered then purified by recrystallization from a suitable solvent (benzene or dioxane or acetone).

Melting points, colors, and spectral data of the prepared oxadiazoles [1-6] are fitted with properties and data reported in literatures [(14)] .

2. Synthesis of N-(5-substituted-1,3,4-oxadiazole-2-yl)phthalamic acids [7-12]

Phthalic anhydride(0.01 mol) 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-1,3,4-oxadiazole dissolved in (30 mL) of dry acetone [(15)] .

The solution in dropping funnel was added drop wise to the mixture with stirring and cooling, then stirring was continued for additional two hours . The precipitated amic acid was filtered off, then purified by recrystallization from a suitable solvent .

Physical properties of phthalamic acids [7-12] are listed in Table (1).

3. Synthesis of N-(5-substituted -1,3,4-oxadiazole-2-yl) phthalimides [13-18]

The titled compounds were synthesized by dehydration of phthalamic acids either by fusion or by using dehydrating agent as follows:

A- Dehydration by using fusion method

The titled compounds [13-18] were prepared by applying fusion method according to literature [15] via fusion of the prepared phthalamic acids in oil bath for one hour with keeping oil temperature above melting point of the used amic acid by ten degrees.

The obtained solid was purified by recrystallization from a suitable solvent.

B- Dehydration by using acetic anhydride and anhydrous sodium acetate as dehydrating agent

A mixture of (0.1 mol) of N-(5-substituted -1,3,4-oxadiazole-2-yl) phthalamic acid in (10 mL) of acetic anhydride and (5-10) % by weight of anhydrous sodium acetate was refluxed with stirring for two hours [16,17] .

The resulted solution was poured into excess cold water with stirring and the obtained precipitate was filtered then was purified by recrystallization from a suitable solvent.

Physical properties of compounds [13-18] are listed in Table (2).

4. Synthesis of N-(5-substituted-1,3,4-oxadiazole-2-yl) succinamic acids [19-24]

The titled compounds were prepared by following the same procedure used in preparation of compounds [7-12] except using of succinic anhydride instead of phthalic anhydride.

Physical properties of compounds [19-24] are listed in Table (3).

5. Synthesis of N-(5-substituted -1,3,4-oxadiazole-2-yl)succinimides [25-30]

The tilted compounds were prepared by following the same procedures used in preparation of compounds [13-18] except using of N-(5-substituted-1,3,4-oxadiazole-2-yl)succinamic acids instead of N-(5-substituted -1,3,4-oxadiazole -2-yl) phthalamic acids.

Physical properties of compounds [25-30] are listed in Table (4).

6. Biological study

The cup plate method using nutrient agar medium was employed in studying the antibacterial activity of some of the prepared compounds [18,19] against two types of bacteria, staphylococcus aureous (Gram positive) and Escherichia Coli (Gram negative) respectively and DMF was used 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 ^{0}C) for 48 hrs. Zones of inhibition produced by

each compound was measured in mm and the results are listed in Table (12).

Results and discussion

In continuation of our research program directed towards the synthesis of new cyclic imides connected to different heterocycles the target of the present work involved synthesis of a series of new phthalimides and succinimides connected to 5-substituted -1,3,4-oxadiazole ring. We choose 1,3,4-oxadiazole moiety to link with cyclic imides because this moiety belong to a group of heterocycles having wide range of biological interactions and display various biological activities .

Strategy for performing this target involved many steps in the first one a series of 2-amino-5-substituted -1,3,4-oxadiazoles were synthesized through reaction of semicarbazide hydrochloride with different aromatic aldehydes then introducing of the resulted semicarbazones in oxidative cyclization via treatment with bromine and anhydrous sodium acetate in glacial acetic acid. The prepared 2-amino-1,3,4-oxadiazoles were introduced in reaction with phthalic or succinic anhydride in suitable solvent in the second step to obtain a series of N-(5-substituted -1,3,4-oxadiazole-2-yl) phthalamic acids and a series of N-(5-substituted -1,3,4-oxadiazole-2-yl) succinamic acids respectively.

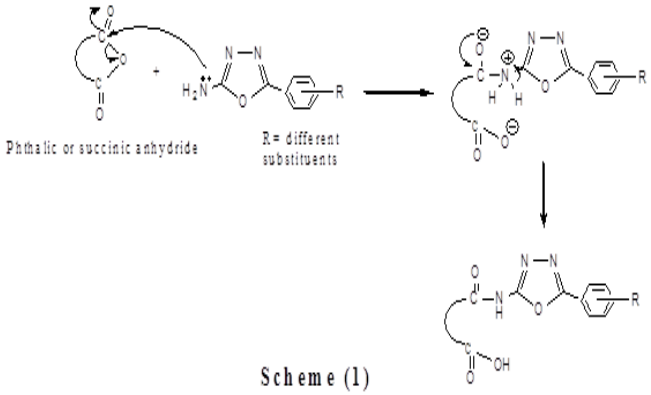
Mechanism of this reaction involved nucleophilic attack of amino group of oxadiazole moiety on carbon atom of one carbonyl group in phthalic or succinic anhydride as shown in scheme (1).

The prepared phthalamic and succinamic acids were white to yellow solids having sharp melting points and were afforded in good yields.

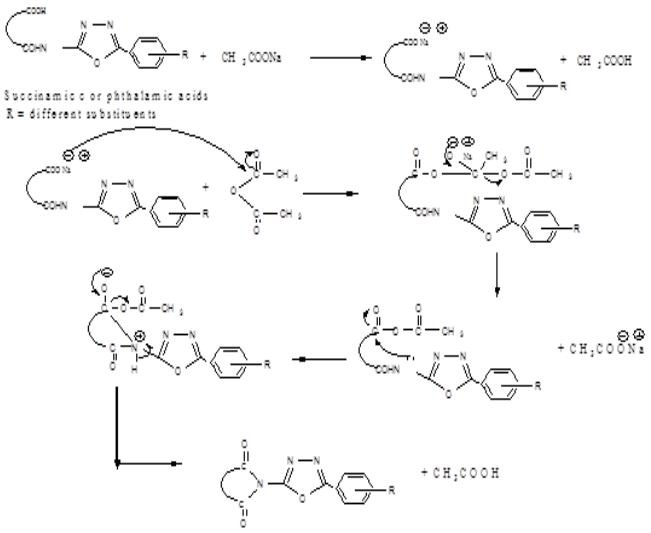
Physical properties of the prepared amic acids are listed in Tables (1) and (3).

The third step of the present work involved dehydration of the prepared oxadiazole phthalamic and succinamic acids by following fusion method or by using acetic anhydride and anhydrous sodium acetate as dehydrating agent to afford the desirable oxadiazole phthalimides and succinimdes.

Anhydrous sodium acetate catalyzed dehydration reaction through abstraction of proton from amic acid as shown in scheme(2).



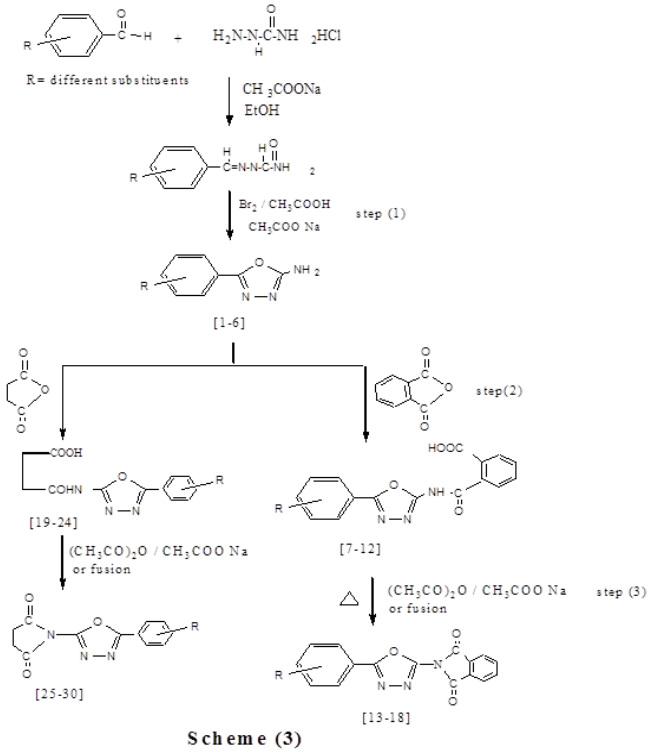
Scheme (1)



Scheme (2)

The prepared oxadiazole phthalimides and succinimides vv were vvcolored solids with sharp melting points and afforded in high percent yields. Physical properties of the prepared phthalimides and succinimidesvv are listed in Tables (2) and (4).

The linear pathway strategy of all these syntheses can be summarized in scheme (3).



Scheme (3)

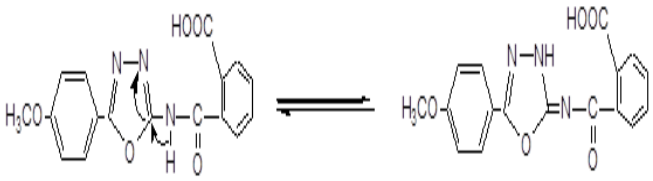
FTIR,U.V, ^{1}H-NMR, and ^{13}C-NMR spectral data were used for confirming structures of the prepared compounds and the obtained spectral data were in full agreement with the proposed structures.

FTIR spectra of the prepared N-(5-substituted-1,3,4- oxadiazole -2-yl) phthalamic acids [7-12]and succinamic acids [19-24] showed many characteristic absorption bands including bands at (3263-3463) cm^{-1} due to υ(O- H) carboxylic and υ (N-H) amide, bands at (1660-1735) cm^{-1} and (1589-1658) cm^{-1} were assigned for υ(C=O) carboxylic and υ(C=O) amide, bands at (1420-1610) cm^{-1} belong to υ (C=N) oxadiazole and υ(C=C)aromatic and finally two bands at(1210-1280) cm^{-1} and (1126-1195) cm^{-1} due to υ(C-O-C) in oxadiazole ring [20,21].

On the other hand U.V spectra of the prepared amic acids [7-12] and [19-24] showed clear absorption bands at wavelengths (211-285) and (300-343) nm. These absorptions were due to ($\pi\rightarrow\pi^{*}$) and ($n\rightarrow\pi^{*}$) transitions in conjugated oxadiazole moiety and attached succinamic or phthalamic acid moiety [20] .

It was noticeable that conjugation of some substituents with conjugated system of acid molecules shifted the absorptions to longer wavelengths.

^{1}H-NMR spectrum of compound [11] showed many signals including signal at (δ=1.3)ppm belong to (N-H) amine proton which was caused by tautomerism with (N-H) amide proton as shown in equation:



Other signals appeared at (δ= 4.2) ppm belong to (OCH_3) protons and at (δ= 7.27-7.69) ppm belong to aromatic ring protons and (N-H) amide proton.

^{13} C-NMR spectrum of the same compound [11] showed signal at (61.59) ppm due to (OCH_3) group, signals at (95.35-133.3) ppm due to aromatic ring carbons, signals at (157.8 and 164.33) ppm belong to two carbon atoms in oxadiazole ring and signals at (168) and (169.1) ppm due to two carbonyl carbons [22] . Also ^{1}H-NMR spectrum of compound [23] showed signal at (δ=1.15) ppm due to (N-H) amine proton which was caused by tautomerism with (N-H) amide, signals at (δ=2.4 and δ=2.5) ppm as two triplet signals belong to four aliphatic ccprotons (-CH_2-CH_2-) in succinamic moiety, signa l at (δ=4.04) ppm due to (OCH_3) protons and signal at (δ=6.48) ppm due to (N-H) amide proton. Signals due to aromatic ring protons appeared at (δ=7.3,7.5,7.7 and 7.8) ppm while signal due to (O-H) carboxylic proton appeared at (δ=10.25) ppm.

^{13} C-NMR spectrum of the same compound [23] showed many signals including signals at (29.15) ppm belong to two aliphatic carbons (-CH_2-CH_2-) in succinamic moiety, signals at (60.37) ppm belong to (OCH_3) group and signals at (124.8-139.66) ppm belong to aromatic ring carbons, signals at (157.4 and 164.32) ppm were due to two carbon atoms in oxadiazole ring while signals at (172.56 and 173.8) ppm were due to two carbonyl groups of amide and carboxyl respectively. On the other hand FTIR spectra of the prepared N-(5-substituted -1,3,4-oxadiazole-2-yl) phthalimides [13-18] and succinimides [25-30] showed disappearance of υ(O-H) carboxylic and υ(N-H) amide absorption bands and this indicate success of dehydration reaction which lead to cyclization and imide formation. Other absorption bands appeared at (1680-1766) cm^{-1}, (1581-1697) cm^{-1}, (1500-1620) cm^{-1} and (1350-1404) cm^{-1} which were attributed to υ(C=O) imide, υ (C=N) oxadiazole, υ(C=C) aromatic and υ (C-N) imide respectively. Moreover two clear absorption bands appeared at (1203-1280) and (1095-1195) cm^{-1} due to υ(C-O-C) in oxadiazole ring .U.V spectra of imides [13-18] and [25-30] showed clear absorptions at wavelengths (210-298) nm and (305-365) nm. These absorptions were due to ($\pi\rightarrow\pi^*$) and ($n\rightarrow\pi^*$) transitions in the conjugated system of oxadiazole moiety and attached phthalimide or succinimide moiety. ^{1}H-NMR spectrum of compound [13] showed signals at (δ= 7.6,7.7,8,8.1) ppm belong to aromatic protons while ^{13} C-NMR spectrum of the same compound [13] showed many signals including signals at (125.8-136.63) ppm due to aromatic ring carbons, signal at (163.68) ppm due to two carbon atoms in

oxadiazole ring and signal at (169.1) ppm belong to two carbonyl carbons in imide ring. ^{1}H-NMR spectrum of compound [14] showed signals at (δ=7.3-7.8) ppm belog to aromatic ring protons of phthalic moiety and phenyl ring linked to oxadiazole ring, ^{13}C-NMR spectrum of the same compound [14] showed signals at (105-135) ppm for aromatic carbons signal at 157 ppm belong to two carbons in oxadiazole ring, signal at 165 ppm belong to two carbonyl carbons in imide ring.

^{1}H-NMR spectrum of compound [17] showed signal at (δ=3.34) ppm which belong to (OCH_3) group protons and signals at (δ=7.3-7.5) ppm belong to aromatic protons.. ^{1}H-NMR spectrum of compound [25] showed clear signals including signals at (δ=2.17 and 2.5) ppm due to four aliphatic protons (-CH_2-CH_2-) in succinimide ring and signals at (δ=7.35-7.9) ppm belong to aromatic ring protons.

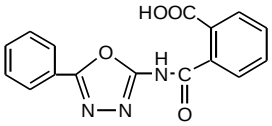
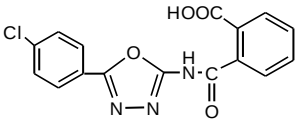
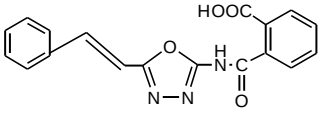
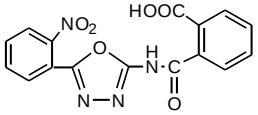
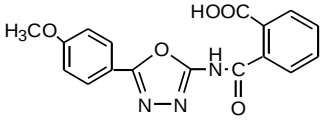
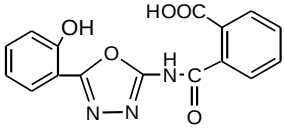
^{13} C-NMR spectrum of the same compound [25] showed many signals including signals at (23.86) ppm belong to (-CH_2-CH_2-)carbons in succinimide ring, signals at (104.62-139.67) ppm due to aromatic ring carbons, signals at (157.18 and 157.89) ppm belong to two carbons in oxadiazole ring and signal at (160.92) ppm due to two carbonyl carbons in succinimide ring. On the other hand ^{1}H-NMR spectrum of compound [28] showed signals at (δ=2.2 and 2.4) ppm belong to four aliphatic protons (-CH_2-CH_2-) in succinimide ring and signals at (δ=7.3-8.1) ppm belong to aromatic protons, while ^{1}H-NMR spectrum of compound [29] showed clear signals at (δ=2.5 and 2.6) ppm due to four aliphatic protons (-CH_2-CH_2-) in succinimide ring, signal at (δ=3.4) ppm due to (OCH_3) protons and signals at (δ=7.3-7.7) ppm belong to aromatic protons. Other details of FTIR, U.V, ^{1}H-NMR and ^{13}C-NMR spectral data of the prepared compounds are listed at Tables (5-10) while C.H.N analysis for some of the prepared compounds are listed in Table (11).

Biological activity

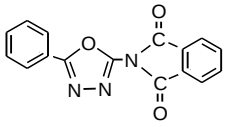
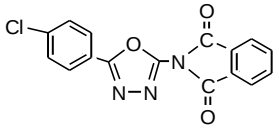
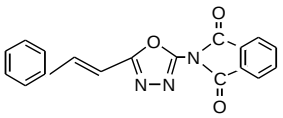
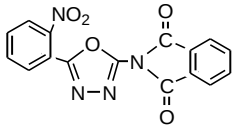
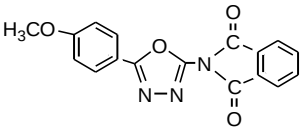
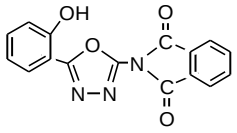
Since the prepared imides in this work were built from two biologically active components (cyclic imide and 1,3,4-oxadiazole) they were expected to possess biological activity, thus studies on the antibacterial activity of synthesized imides have been carried out against two pathogenic organisms including staphylococcus aureous (Gram positive) and Escherichia coli (Gram negative) using cup-plate method. The results of the antibacterial studies are shown in Table (12). It was noticeable that the nature of substituents on imides molecules affected their biological activities against the studied bacteria [(19)]. Thus among the tested imides [13-18] and [25-30] compounds [14,16,26,28] which were substituted with (Cl or NO_2) groups showed high biological activity against Escherichia coli and slight to moderate activity

against staphylococcus aureous .Compounds [17,18,29,30] which were substituted with (OCH_3 and OH) groups showed high biological activity against staphylococcus aureous while they showed no activity against Escherichia coli except compound [18] which showed slight activity against this bacteria. Imides [13,15] showed slight to moderate activity against the two studied bacteria while compounds [25,27] showed slight to moderate activity against Escherichia coli and no activity against staphylococcus aureous .

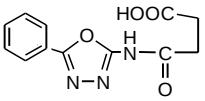
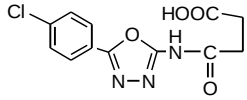
Table (1) Physical properties of the prepared phthalamic acids [7-12]

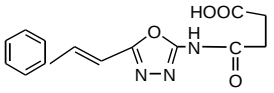
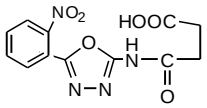
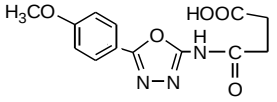
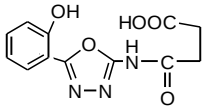
Compd. No	Compound structure	Color	Melting point ^{0}C	Yield %	Recrystallization solvent
7		White	154-156	66	Ethanol
8		Off white	190-192	60	Ethanol
9		Faint ellow	159-161	75	Dioxane
10		Deep ellow	183-185	75	Ethanol
11		White	163-165	73	Dioxane
12		Off white	160-162	70	Methanol

Table(2) Physical properties of the prepared phthalimides[13-18]

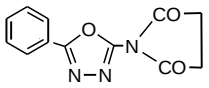
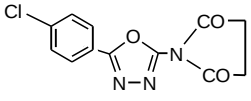
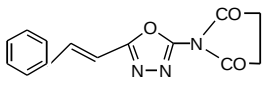
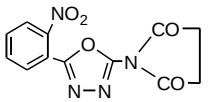
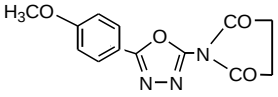
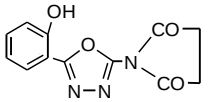
Compd. No	Compound structure	Color	Melting point ^{0}C	Yield %	Recrystallization solvent
13		White	138-140	93	Acetone
١٤		Off white	164-166	92	Acetone
15		Yellow	144-146	٧٥	Cycloexane
16		Brown	154-156	٩٢	Acetone
17		Off white	176-178	82	Cyclohexan e
18		Yellow	183-185	90	Cyclohexan e

Table(3) Physical properties of the prepared succinamic acids [19-24]

Compd. No.	Compound structure	Color	Melting point ^{0}C	Yield %	Recrystallization solvent
19		Off White	128-130	75	Methanol
20		Yellow	148-150	60	Methanol

21		Pale Yellow	155 Decomp.	66	Ethanol
22		Deep Yellow	169-171	70	Ethanol
23		white	168-170	73	Ethanol
24		White	186-188	70	Methanol

Table(4) Physical properties of the prepared succinimides [25-30]

Compd. No.	Compound structure	Color	Melting point ^{0}C	Yieldn %	Recrystallization solvent
25		White	181-183	80	Acetone
26		Pale Yellow	177-179	93	Cyclohexane
27		Yellow	130-132	89	Acetone
28		Yellow	211 Decomp.	88	Acetone
29		Brown	149-151	95	Cyclohexane
30		Off White	165-167	90	Acetone

Table(5) FTIR and U.V spectral data of the prepared phthalamic acids [7-12]

Compd. No.	FTIR spectral data cm^{-1}						u.v (λ max) nm
	υ(O-H) carboxylic υ(N-H) mide	υ(C=O)Carboxyl	υ(C=O)Amide	υ(C=N)and υ(C=C)	υ(C-O-C) Oxadiazole	Others	
7	3263	1674	1589	1490 1440	1280 1134	----	273
8	3420 3300	١٦٦٠	1590	1490 1420	1280 1140	υ(C-Cl) 1080	235 262 308
9	3448	1681	1589	1510 1480	1280 1141	-----	223 313 318
10	3463	١٦٨٩	1589	1527	1280 1134	υ(NO$_2$) 1404 1350	240 285
11	3317	1681	1620	1585 1505	1280 1150	υ(C-OCH$_3$) 1190	236 261 282 300
12	3460 3301	1697	1589	1475 1450	1280 1126	υ(O-H) 3460	222 277 328

Table(6)FTIR and U.V spectral data of the prepared phthalimides [13-18]

Compd. No.	FTIR spectral data cm^{-1}						u.v (λ max) nm
	υ(C=O)nImide	(C=N)	υ(C=C) Aromatic	υ(C-N) Imide	υ(C-O-C) Oxadiazole	Others	
13	1766	1640	1596	1360	1257 1172	----	255 288 298
14	١٧٥٠	1643	1581	1373	1226	υ(C-Cl) 1070	268
15	1689	1581	1500	1404	1280 1141	-----	210 305
16	1766	1697	1596	1350	1257 1172	υ(NO$_2$) 1465 1404	253 288 293

17	1760	1689	1593	1355	1255 1170	υ(C-OCH$_3$) 1110	258 287 296
18	1728	1689	1620	1365	1272 1180	υ(O-H) Phenolic 3471	236 294 365

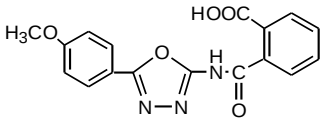
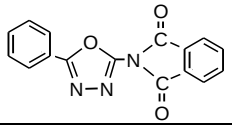
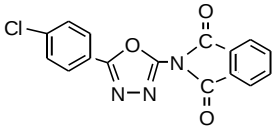
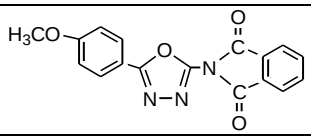
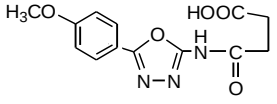
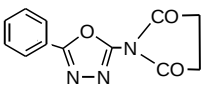
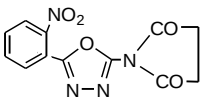
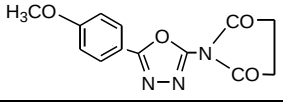
Table (7) FTIR and U.V spectral data of the prepared succinamic acids[19-24]

Compd. No.	FTIR spectral data cm^{-1}						u.v (λ max) nm
	υ(O-H) carboxylic υ(N-H) Amide	υ(C=O) Carboxyl	υ(C=O) Amide	υ(C=N) and υ(C=C) Aromatic	υ(C-O-C) Oxadiazole	Others	
19	3425 3263	1704	1658	1581	١٢٨٠ ١١٨٠	----	273 275 277 279
20	3463 3286	1735	1658	1596	1280 1134	υ(C-Cl) 1049	232 343
21	3425 3325	1710	1620	1580	1210 1172	-----	303 308 312
22	3463 3400	1735	1604	1527	1272 1134	υ(NO$_2$) 1427 1350	211 256 258
23	3448 3278	1728	1658	1610	1249 1180	υ(C-OCH$_3$) 1140	225 228 311
24	3433 3300	1710	1658	1596	1265 1195	υ(O-H) Phenolic 3433	220 275 325

Table(8) FTIR and U.V spectral data of the prepared succinimdes [25-30]

Compd. No.	FTIR spectral data cm^{-1}						u.v (λ max) nm
	υ(C=O) Imide	υ(C=N)	υ(C=C) Aromatic	υ(C-N) Imide	υ(C-O-C) Oxadiazole	Others	
25	1728	1643	1596	1390	1226 1140	----	279
26	١٧٥٨ ١٧٢٨	1635	١٥٨١	1365	1249 1195	υ(C-Cl) 1095	215 220 288
27	1735	1627	١٥٨٠	1373	1280	-----	298 308
28	1740	1682	١٦١٠	1350	1270 1165	υ(NO$_2$) 1517 1430	273 281 328
29	1720 1680	1643	١٦٠٤	1365	1280	υ(C-OCH$_3$) 1249	218 274
30	1758	1689	١٥٨٩	1365	1203 1095	υ(O-H) Phenolic 3433	215 330

Table (9) 1H-NMR spectral data for some of the prepared compounds

Compd. No.	Compound structure	Chemical shifts in ppm
11		δ =1.3(s) NH amine, δ=4.2(s) 3H of OCH$_3$ =(7.27-7.69) (m) 7H aromaticδ
13		δ=(7.6,7.7,8,8.1)9H aromatic
14		δ=(7.3-7.8) (m) 8H aromatic
17		δ=3.34(s) 3H of OCH$_3$, δ=(7.3-7.5) (m)8H aromatic
23		δ=1.15(s) NH amine, δ=2.4(t),2.5(t) 4H of –CH$_2$-CH$_2$-, δ=4.4(s) 3Hof OCH$_3$, δ=6.48 NH amide,δ=(7.3,7.5,7.7,7.8) 4H aromatic, δ=10.25(s) OH carboxyl
25		δ=(2.17,2.5)4H of –CH$_2$-CH$_2$-, δ=(7.35-7.9) 5H aromatic
28		δ=(2.2,2.4) 4H of –CH$_2$-CH$_2$-, δ=(7.3-8.1) 4H aromatic
29		δ=(2.5,2.6) 4H of –CH$_2$-CH$_2$-, δ=3.4(s) 3Hof OCH$_3$, δ=(7.2,-7.7)(m) 4H aromatic

(s)= Singlet, (m)= Multiplet, (t)= Triplet

Table (10) 13C-NMR spectral data for some of the prepared compounds

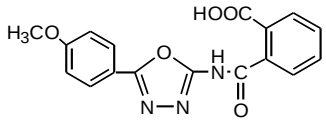
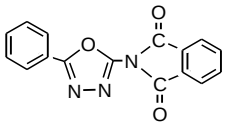
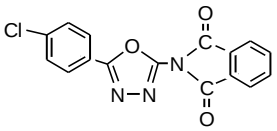
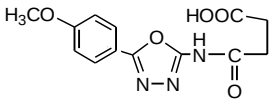
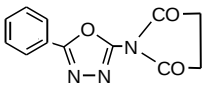
Compd. No.	Compound structure	^{13} C-NMR data (ppm)
11		61.59 OCH_3, (95.35-133.3) aromatic carbons, (157.8,164.33) two carbons in oxadiazole ring, (168,169.1) two carbonyl carbons
13		(125.8-136.63) aromatic carbons, 163.68 two carbons in oxadiazole ring, 169.1 two carbonyl carbons
14		(105-135) aromatic carbons, 157 two carbons in oxadiazole ring, 165 two carbonyl carbons
23		29.15 of two aliphatic carbons (-CH_2-CH_2-), 60.37 OCH_3, (124.8-139.66) aromatic carbons, (157.4,164.32) two carbons in oxadiazole ring, (172.56,173.8) two carbonyl carbons
25		23.86 of two aliphatic carbons (-CH_2-CH_2-), (104.62-139.67) aromatic ring carbons, (157.18,157.89) two carbons in oxadiazole ring, 160.92 two carbonyl carbons

Table (11) C.H.N analysis for some of the prepared compounds

Compd. No.	Calculated			Found		
	C	H	N	C	H	N
9	64.47	3.88	12.53	64.66	4.09	12.33
12	59.07	3.38	12.92	58.83	3.55	13.13
16	57.14	2.38	16.66	56.88	2.43	16.80
18	62.54	2.93	13.68	62.67	2.82	13.91
19	55.17	4.21	16.09	55.39	4.12	16.24
22	47.05	3.26	18.30	47.21	3.18	18.40
26	51.89	2.88	15.13	52.14	3.00	15.06
27	62.45	4.08	15.61	62.27	4.25	15.84

Table (12) Antibacterial activity of compounds [13-18] and [25-30]

Compd. No.	Gram positive bacteria	Gram negative bacteria
	Staphylococcus aureous	Escherichia coli
13	+	+
14	++	+++
15	+	++
16	++	+++
17	+++	-
18	+++	+
25	-	+
26	+	+++
27	-	++
28	+	+++
29	+++	-
30	+++	-

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

References

1. M.D.Mullican, M.W.Wilson, D.T.Connor, C.R.Kostlan, D.J.Schrier and R.D.Dyer, **J. Med. Chem**.36, 1090,1993.
2. K.M.L.Rai and N.Linganna, IL Farmaco, 55, 389, 2000.
3. M.Amir and K.Shika,, Eur.J.Med.Chem., 39,535,2004.
4. A.Almasirad, S.A.Tabatabai,M.Faizi and A.Kebriaeezadeh, Bio org.Med.Chem.Lett., 14, 6057,2004.
5. H.A.Rajapakse, H.Zhu, M.B.Young and B.T.Mott, Tetrahedron Lett, 47,.4827,2006.
6. A.Kudelko and W.Zielinski, Tetrahedron 65,1200, 2009.
7. X.Zheng, Z.Li, Y.Wang, W.Chen,Q.Huang,C.Liu and G.Song, J.Flourine Chem., 123,163,2003.
8. X.J.Zou,L.H.Lai, G.Y.Jin and Z.X.Zhang, J.Agric Food Chem., 50 (13),3757,2002.
9. A.D.Andricopulo, R.A.Yunes, V.C.Filho, R.J.Nunes,J.W.Frazer and E.H.Cordes, Pharmazi, 54 (9), 698,1999.
10. D.S.Stiz,M.M.Souza,V.Golin,R.A.S.Neto, R.Correa, R.J.Nunes, R.A.Yunes and V.C. Filho, Pharmazie, 55(12),942,2000.
11. E.O.Lima,E.F.Queriroz, A.D.Andricopulo, R.J.Nunes, R.A.Yunes and V.C.Filho,, Bol.Soc.Chil.Quim., 44 (2), 185,1999.
12. N.S.Lopez, M.Sortin, A.Escalante,F.decampos and R.Correa,Drug Res., 53, 280,2003.
13. A.I.Vogel, Textbook of practical organic chemistry, 5th Edition Longman 1996.
14. H.K.Yaseen, Msc.Thesis .Chem.Dept.College of Sci.Univ.of Baghdad, 2010.
15. T.Mohammed and I.Abdul Ameer, J.Poly.Sci.,38,3244,2002.
16. T.Mohammed, A.M.Alazzawi and K.K.Al-Obaidi, Journal of Al-Nahrain University, 12(2),1, 2009.
17. D.Fles, R.Vukovic and A.E.Kuzmic, Croat.Chem.Acta., 76(1),.9,2003.

18. A.A.Chavan and N.R.Pai, Molecules, 12, 2467, 2007.
19. A.S.Hassan, Msc.Thesis, Chem.Dept.College of Sci. Univ. of Baghdad, 2009.
20. R.M.Silverstien, G.C.Bassler and T.C.Morill," Spectrometric identification of organic compounds", 4th Edition, John Wiley and Sons, 1981.
21. N.B.Cottup, L.H.Daly and S.E.Wiberley," Introduction to Infrared and Raman Spectroscopy", 2nd Edition, New York and London Academic press 1975.
22. R.J.Abraham and P.Loftus," Proton and 13C-NMR spectroscopy", London:Heyden, 1978.

تحضير وتشخيص مركبات فثال ايمايد و سكسن ايمايد جديدة معوضة بحلقة ٤,٣,١-اوكسادايازول

احلام معروف العزاوي هبه كاظم ياسين

الخلاصة

تضمن البحث تحضير سلسلة من مركبات فثال ايمايد و سكسن ايمايد جديدة مرتبطة بالمكونة ١و٣و٤-اوكسادايازول وذلك من خلال اجراء عدة خطوات تضمنت الخطوة الاولى تحضير ستة من مركبات ٥-معوض-٢-امينو-٤،٣،١-اوكسادايازول وذلك من خلال معاملة مركبات السيميكاربازون مع البروم وخلات الصوديوم اللامائية في حامض الخليك الثلجي اما في الخطوة الثانية فقد تم ادخال مركبات ٢-امينو-٤،٣،١-اوكسادايازول المحضرة في تفاعل مع انهيدريد الفثاليك او انهيدريد السكسنيك وبذلك تم الحصول على ستة من حوامض N-(٥-معوض-٤،٣،١-اوكسادايازول- ٢-يل) فثال اميك وستة من حوامض N-(٥-معوض-٤،٣،١-اوكسادايازول-٢-يل) سكسن اميك،في الخطوة الثالثة تم سحب الماء من حوامض الاميك المحضرة باتباع تقنية الصهر او باستخدام انهيدريد الخليك مع خلات الصوديوم اللامائية كعامل ساحب للماء وبذلك تم الحصول على الايمايدات الجديدة المطلوبة والتي هي N-(٥-معوض-٤،٣،١-اوكسادايازول-٢-يل) فثال ايمايد و N-(٥-معوض-٤،٣،١-اوكسادايازول-٢-يل) سكسن ايمايد على التوالي. تقدير الفعالية البايولوجية للايمايدات المحضرة وذلك من خلال دراسة تاثيرها على تثبيط نوعين من البكتريا هي ستافيلوكوكاس اوريس واشريشيا كولي على التوالي وقد أوضحت النتائج بان معظم الايمايدات المحضرة ذات فعالية جيدة ضد انواع البكتريا قيد الدراسة.