



# Synthesis and Antimicrobial Screening of new 9,10-dihydro Anthracene-9,10-endo- $\alpha,\beta$ -succinimides Bearing Pharmacologically Active Components

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**Abstract:** This operation five early cyclic imides bearing biologically an effect components were Syntheside. 9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -Succinic anhydride was synthesized then used in the synthesis of target imides. Two nitrogen containing hetero cycles namely pyridine and quinazoline are selected as biologically active components to be used in this work beside two  $\beta$ -lactam antibiotics namely Ampicillin and Cefotaxime in addition to active folic acid. The new cyclic imides were synthesized by two steps in the first one 9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -Succinic anhydride was introduced in reaction with 4-amino pyridine, 1-amino-quinazoline-2-one, Ampicillin and Cefotaxime producing the corresponding N-(drug) or N-(heterocycle)-9,10-dihydro anthracene-9,10-endo- ( $\alpha,\beta$ )-Succinamic acid with acetic anhydride which in turn were dehydrated. In the second step via reaction involving ,acetic anhydride and sodium acetate, anhydrous below reflux conditions producing the target N-(drug) or N-(heterocycle) ,10-dihydro anthracene-(9,10)-endo- $\alpha,\beta$ -Succinimides. N-(folic acid )-9,10-dihydro (anthracene-9,10-endo- $\alpha,\beta$ )-Succinimide was synthesized via direct reaction between folic acid and 9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -Succinic anhydride in glacial acetic acid under reflux. Results of antimicrobial activity evaluation of the newly synthesized imides showed that the new imides exhibit very high antimicrobial activity against the tested bacteria and fungi.

**Key words:** 9, 10-dihydro anthracene-9, 10-endo- $\alpha,\beta$ -Succinic anhydride, Ampicillin, Cefotaxime, cyclic imides.

## Introduction

Cyclic imides are important effect bioactive molecules that have a large scope spectrum of pharmacological activities including antimalarial, anti-inflammatory, antitumor, antiviral and antimicrobial activity (1-5). On the other hand Ampicillin and Cefotaxime are well known pharmacologically active  $\beta$ -lactam antibiotics (6). Folic acid derivatives also represent biologically important compounds (7). Besides nitrogen containing heterocycles like pyridine and quinazoline derivatives are important class of compounds that possess wide

spectrum of various biological activities (8-11). According to all these facts we make scale doing in this work to synthesize new compounds by combination of drug or heterocyclic molecules and 9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -succinimide in a single molecule, thus the resulted new compounds having structural features of both cyclicimide and drug or heterocycle and this would provide new derivatives possessing potent pharmacological activities.

## Experimental

Uncorrected melting points were recorded on Gallenkamp melting point

apparatus. SHIMADZN F.T.I.R-8400 fourier transform Infrared spectrophotometer was used for recording FTIR spectra of the prepared compounds. Bruker ultrasheid 300 MHz apparatus was used for recording  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra using  $\text{DMSO-d}_6$  as solvent and TMS as internal standard. Hetashi model incubator was used for antimicrobial activity evaluation.

### **1-Preparation of N-(Drug)\_9,10-dihydroanthracene-9,10-endo- $\alpha,\beta$ -succinamic acid (2,3)**

Ampicillin or Cefotaxime(0.01mol) was dissolved in 25ml of dry acetone then the resulted solution be additional drop by drop to mixed fluid of 0.01 mol, 2.76g of 9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -succinic anhydride in 25ml of dry acetone with movement and cooling. The resulted mixture was stirred for two hours at room temperature and the result solid was filtered, thirsty and re-crystallized from ethanol (12).

### **2 - Preparation of-(N-(pyridyl-4-yl) or N-(quinazoline-2-one-1-yl)\_9,10-dihydro anthracene-9,10-endo- $\alpha,\beta$ )-succinamic acid (4,5)**

The titled amic acids (4,5) were willing by following the identical procedure used in preparation of amic-acids (2,3) exclud using of 0.01 mol of 4-amino pyridine or 1-amino quinazoline-2-one instead of Ampicillin or Cefotaxime. The obtained amic acids were recrystallized from Dioxane. Physical prop of amic- acids (2-5) are show in (Table 1).

### **3-Preparation of N-(Drug)-9-10-dihydro anthracene-9,10-endo- $\alpha,\beta$ -succinimides (6,7).**

N- Drug - 9,10-dihydro anthracene - 9,10-endo- $\alpha,\beta$ -succinamic acid (2) or (3) (0.01 mol) was dissolved in 20ml of acetic anhydride, then 0.5% of amic acid weight of anhydrous sodium acetate was added and the mixed for 2.5 hrs. There was flow into excess cold water with movement. The mixture was filtered and the collected precipitate was washed with water several times, thirsty and finally recrystallized from acetone (13).

### **4-Preparation of -N-(pyridine-4-yl) or N-(quinazoline-2-one-1-yl)-"9,10" – (dihydro) anthracene-9,10-endo- $\alpha,\beta$ -succinimides (8, 9)**

The imides (8,9) were prepared by following the same procedure used in preparation of imides (6, 7) except using of N-(pyridine-4-yl) or N-(quinazoline-2-one-1-yl)-9,10- dihydro anthracene-9,10-endo-  $\alpha,\beta$ -succinamic acids instead of N-Drug amic acids (2, 3)]. The resulted imides (8, 9) were purified by Recrystallization from Cyclohexane.

### **5-preparation of N-(folic acid)-9, 10-dihydro anthracene-9, 10-endo-( $\alpha, \beta$ )-Succinimide (10, 14).**

The imide (10) was prepared by reflux a mixture of folic acid (0.01mol,4.41g) and (0.01mol,2.76g) of cyclic anhydride (1) in 30 mol of glacial acetic acid for 2hrs. The predicted mixture was flow in ice water with movement and the obtained special properties of filtered, dried and re-crystallized from ethanol .physical prop of the prepared cyclic imides (6, 10) are listed in (Table 2).

### **6-Biological activity evaluation**

Mulerhonton agar was added to one liter of distilled water in suitable conical flask with stirring and heating until

complete dissolving then the flask was Stoppard by cotton and the medium was sterilized in an autoclave for 20 minutes at (121°C) under pressure of 15 bound /inch. The medium was cooled to (45-55)°C then placed in petri dishes about (20 mL) for each one and was left to cool and solidified. The studied bacteria and fungi were placed on the agar surface then by using a antiseptic cork borer cups were cavity out of agar medium contained in a Petri dish and the test compound solution (0.1mL) was added in the cups and the Petri dishes were subsequently incubated at 37°C for 48 hrs(5-7). Ampicillin and

fluconazole were used as reference drugs and DMF as a negative control (Figure 1).

### Results and Discussion

During this work we planned to synthesize new compounds containing two Known pharmacologically active components namely cyclic imides and drug molecules like Ampicillin, Cefotaxime and folic acid or nitrogen containing heterocycles like pyridine and quinazoline.

Table (1): Physical properties of the " prepared amic acids" [2-5]

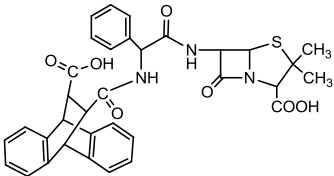
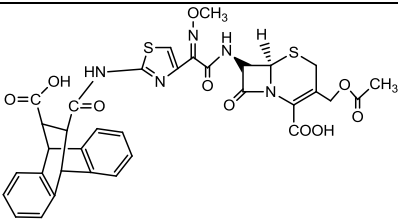
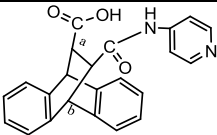
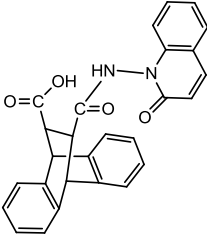
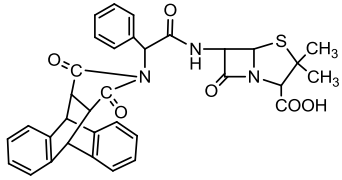
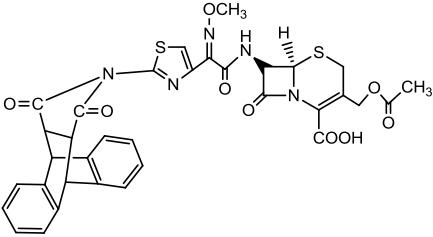
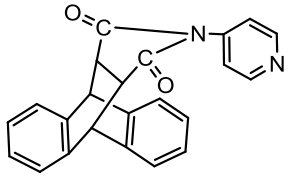
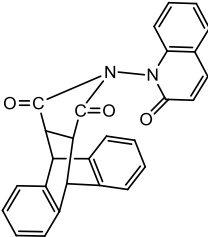
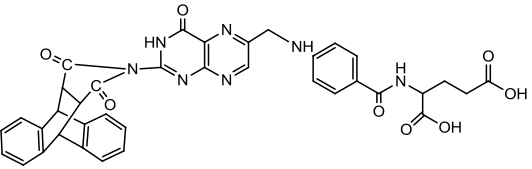
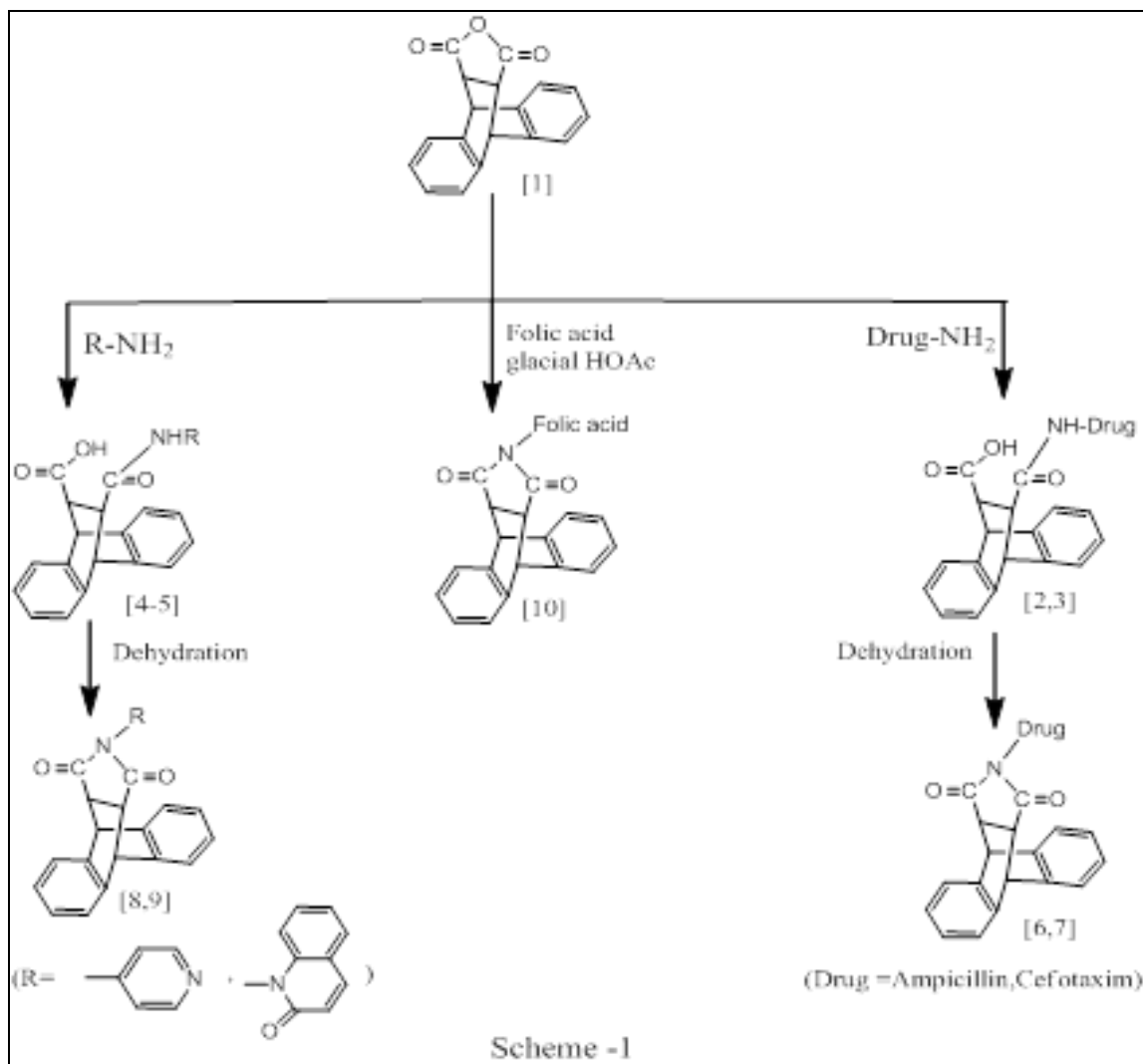
Cop. no.	Comp. structure	Color	"Melting Points" °C	Prod. %	"Recrystallization" Solv.
2		White	286-288	87	ethanol
3		Light gray	296-298	92	Ethanol
4		Faint Yellow	255-257	93	Dioxane
5-		Dark yellow	263-265	81	Dioxane

Table (2): Physical properties of the prepared Imides [6-10]

Cop. no.	"Comp. structure"	Colour	"Melting Points" °C	Yield %	"Recrystallization Solv."
6		Faint Yellow	320dcomp	87	Acetone
7		Faint Brown	318-320	92	Acetone
8		Yellow	308-310	91	Cyclohexane
9		Faint Brown	326-328	93	Cyclohexane
10		Deep Green	340dcomp	88	Dioxane



**Figure (1): Synthesis diagram of the target compounds.**

Synthesis of the target compounds based on the cyclic anhydride 9, 10 - dihydro anthracene-9,10-endo- $\alpha,\beta$  - succinic anhydride[1]. In the first step adduct (1) was prepared according to literature procedure (15) then seconded - step- compound- (1) was led in reaction with drug molecules or heterocyclic amines producing N-(drug) or N-(pyridine) or N-(quinazoline) 9, 10 -dihydro anthracene- 9,10-endo- $\alpha,\beta$  - succinamic acids (2-5). The reaction is proceeded nucleophilic attack of

through Amino group present in drug molecules or heterocyclic amines on carbonyl group in compound (1) leading to ring opening producing amic acids (2-5). Physical prop of amic- acids are listed in (Table 1). Chemical structures of the synthesized amic acids are confirmed on the basis of FTIR,  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectral data ( FTIR Spectra of the prepared amic acids showed clear, absorption bands at  $3269\text{-}3444\text{ cm}^{-1}$  due to- $\nu(\text{O-H})$  carboxyl and  $\nu(\text{N-H})$ -amide soaking up

bands due to,  $\nu$  (C=O) carboxylic,  $\nu$  (C=O)-lactam and  $\nu$  (C=O)-amide" appeared at (1647-1710)  $\text{cm}^{-1}$ , (1689-1690)  $\text{cm}^{-1}$  and (1625-1668)  $\text{cm}^{-1}$  respectively while absorption bands due

to  $\nu$  (C=N),  $\nu$  (C=C) aromatic appeared at (1600-1645)  $\text{cm}^{-1}$  and (1515-1556)  $\text{cm}^{-1}$  (16). All FTIR spectral data of compounds amic acids (2-5) are shown in (Table 3).

Table(3): " FTIR Spectral Data  $\text{cm}^{-1}$  of the "" prepared amic acids[2-5]"

Comp. No.	$\nu$ (O-H) and $\nu$ (N-H)	$\nu$ (C-H) aromatic aliphatic	$\nu$ (C=O) Carboxyl	$\nu$ (C=O) Lactam	$\nu$ (C=O) amide	$\nu$ (C=N)	$\nu$ (C=C) Aromatic	$\nu$ (C-S)	Others
2	3444 3272	3047 2970 2875	1710	1689	1631	-	1539	607	-
3	3400 3320 3280	3049 2902 2835	1700	1690	1668	1645	1541	650	$\nu$ (C=O) ester 1720 $\nu$ (C-O) Ester 1226,1190
4	3434 3353 3301	3076 2987 2852	1647	-	1625	1600	1515	-	$\nu$ (p-sub) 827
5	3430 3350 3269	3045 2987 2890	1700	-	1664 1640	-	1556	-	$\nu$ (C=C) aliphatic 1602

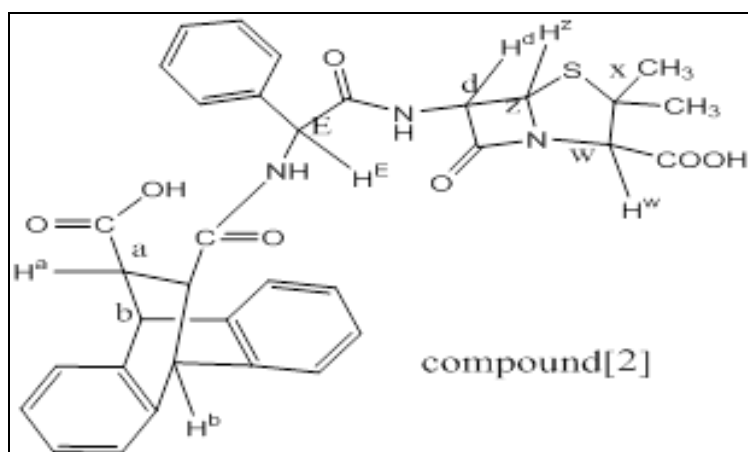


Figure (2): The structure of compound (2).

$^1\text{H}$ NMR- spectrum -of compound (2) (Figure 2) showed sharp signals at ( $\delta=1.7$ ) ppm belong to two ( $\text{CH}_3$ )-protons ,signals at( $\delta=3.1-3.3$ ) ppm and ( $\delta=4.1-4.3$ ) ppm belong to two  $\text{H}^a$  protons and two  $\text{H}^b$  protons respectively. Signals for  $\text{H}^w$  Proton , $\text{H}^z$ , $\text{H}^d$  and  $\text{H}^e$  protons appeared at( $\delta=4.6,4.9,5.3$  and  $6.0$ ) ppm respectively(16). Signals belong to aromatic protons appeared at ( $\delta=7.0-7.41$ ) ppm and Signals belong to ( $\text{NH}$ ) protons and( $\text{OH}$ ) protons appeared at( $\delta=8.1$  and  $11.13$ ) ppm.  $^{13}\text{C}$ NMR spectrum of compound (2) showed signals at ( $\delta=30.12,(42.5-44.5)$  and ( $50.1-55.2$ ) ppm belong to( $\text{CH}_3$ ) carbons, two a carbons and two b carbons respectively. Signals belong to (E,d and x) carbons Appeared at

( $\delta=60.3-65.0$ ) ppm and Signals belong to(z and w) carbons appeared at ( $\delta=74.1$  and  $81.0$ ) ppm. Signals for aromatic carbons appeared at ( $\delta=126-144.3$ ) ppm and signals due to-"( $\text{C}=\text{O}$ ) carboxylic, ( $\text{C}=\text{O}$ ) lactam and ( $\text{C}=\text{O}$ ) amide carbons showed at ( $\delta=171-178.20$ ) ppm  $^1\text{H}$ NMR spectrum of compound [4] (Figure 3) showed signals at ( $\delta=4.21$ ) ppm and ( $\delta=4.4$ ) ppm belong to two ( $\text{H}^a$ ) protons and two ( $\text{H}^b$ ) protons . Signals belong to aromatic protons appeared at ( $\delta=7.06-7.99$ ) ppm while signals belong to ( $\text{NH}$ ) and( $\text{OH}$ ) protons appeared at( $\delta=8.01$ ) ppm and ( $\delta=11.32$ ) ppm respectively.  $^{13}\text{C}$ NMR spectrum of compound (4) showed signals at ( $\delta=42.85$ ) ppm belong to two (a) carbons and two (b) carbons.

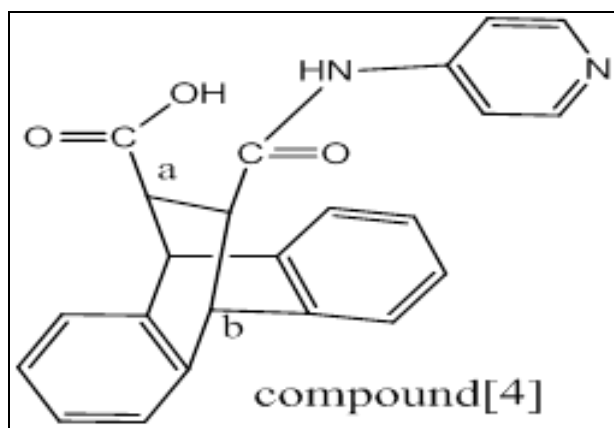


Figure (3): The structure of compound (4).

Signals at ( $\delta=3.0-3.1$ ) ppm and ( $\delta=4.32$ ) ppm belong to two ( $\text{H}^a$ ) protons and two ( $\text{H}^b$ ) protons , Other Signals appeared at ( $\delta=7.11-7.83$ ) ppm,( $8.1$ ) ppm and ( $11.07$ ) ppm which be part of to aromatic protons,( $\text{NH}$ ) and ( $\text{OH}$ ) protons respectively (14).  $^{13}\text{C}$ NMR spectrum of compound (5) showed signals at ( $\delta=42.2-44.1$ ) ppm belong to two (a) carbons and two (b) carbons. Signals for aromatic carbons

appeared at ( $\delta=115.5-140.4$ ) ppm,- while-" signals belong to" ( $\text{C}=\text{O}$ ) amide and ( $\text{C}=\text{O}$ ) carboxyl carbons showed at ( $\delta=165.5-176.4$ ) ppm,(  $166.83$ ) ppm respectively.

Dehydration of amic acids(2-5) afforded the corresponding cyclic imides (6-9). Dehydration reaction was performed by treatment of amic acids (2-5) with acetic anhydride in the

presence of anhydrous sodium acetate under reflux condition. The active response was preceded through intra nucleophilic attack of nitrogen in amide group on electro leading to ring closure with elimination of water molecule producing the target imides. On the other hand imide (10) was prepared via direct reaction between cyclic anhydride (1) and folic acid (under reflux condition in glacial acetic acid) and that means the reaction produced first amic acid which was not isolated but introduced directly in dehydrated active response companioned with ring closure affording the cyclic imid (10). FTIR Spectra of the prepared imides (6-10) showed two clear absorption bands at (1772-1782)  $\text{cm}^{-1}$  and (1701-1724)  $\text{cm}^{-1}$  due to a sym. and sym.  $\nu$  (C=O) imide. Other absorption bands appeared at (1683-1697)  $\text{cm}^{-1}$ , (1672-1674)  $\text{cm}^{-1}$  and (1639-1674)  $\text{cm}^{-1}$  which are attributed to  $\nu$  (C=O) carboxyl,  $\nu$  (C=O) lactam and  $\nu$  (C=O) amide respectively.

While absorption bands due to  $\nu$  (C=N),  $\nu$  (C=C) aromatic and  $\nu$  (C-N) imide appeared at (1604-1649)  $\text{cm}^{-1}$ , (1521-1600)  $\text{cm}^{-1}$  and (1334-1386)  $\text{cm}^{-1}$  respectively<sup>(16)</sup>. List of FTIR spectral data of the prepared imides [6-10] are listed in (Table 4)

<sup>1</sup>H NMR spectrum of compound (7) (Figure 4) showed signal at ( $\delta$ =2.30)

ppm belong to two (CH<sub>3</sub>) protons signals belong to two (H<sup>a</sup>) protons and (-SCH<sub>2</sub>-) protons appeared at ( $\delta$ =3.2) ppm while signals belong to two (H<sup>b</sup>) protons appeared at ( $\delta$ =4.17) ppm. Other signals appeared at ( $\delta$ =3.8, 4.53 and 5.4) ppm are belong to (OCH<sub>3</sub>) protons, (-CH<sub>2</sub>OCO-CH<sub>3</sub>) protons and lactam ring respectively.

Signals belong to aromatic protons and thiazole ring proton appeared at ( $\delta$ =7.20-7.62) ppm and Signals for (NH) and (OH) protons appeared at ( $\delta$ =8.13 and 11.07) ppm respectively. <sup>13</sup>C NMR spectrum of compound (7) showed signals at ( $\delta$ =21.3, 25.2, 42.4 and 45.6) ppm belong to methyl, (-SCH<sub>2</sub>-), two (a) carbons and two (b) carbons respectively. While Signals appeared at ( $\delta$ =55.2, 61.2 and 64.5) ppm are belong to (-CH<sub>2</sub>O-COCH<sub>3</sub>), lactam ring carbons and OCH<sub>3</sub> carbon respectively.

Signals belong to aromatic carbons, thiazole ring carbons, (z) and (w) carbons appeared at ( $\delta$ =121.5-143.1) ppm, signals for (C=N) carbons and (C=O) of carboxyl, amide and lactam carbons appeared at ( $\delta$ =163.2-166.5) ppm and signals belong to (C=O) imide, (C=O) ester carbons appeared at ( $\delta$ =170.1-177.2) ppm.



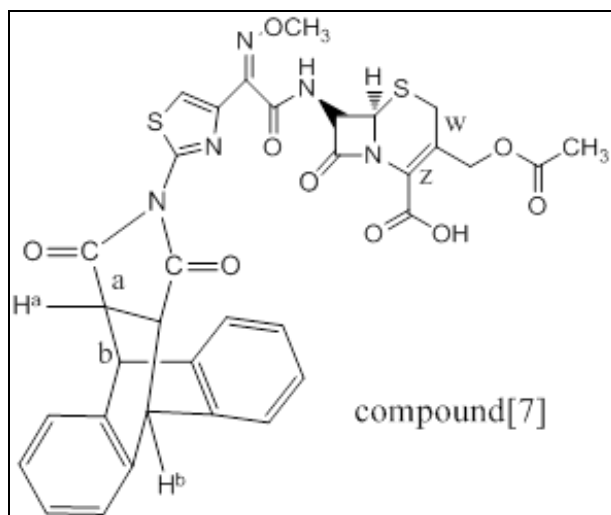


Figure (4): The structure of compound (7).

$^1\text{H NMR}$  spectrum of compound (8) (Figure 5) showed signals at ( $\delta=2.54$  and  $3.33$ ) ppm to two ( $\text{H}^a$ )

protons and two ( $\text{H}^b$ ) protons appeared at ( $\delta=4.17$ ) ppm and signals at ( $\delta=7.67$ - $8.29$ ) ppm belong to aromatic protons.

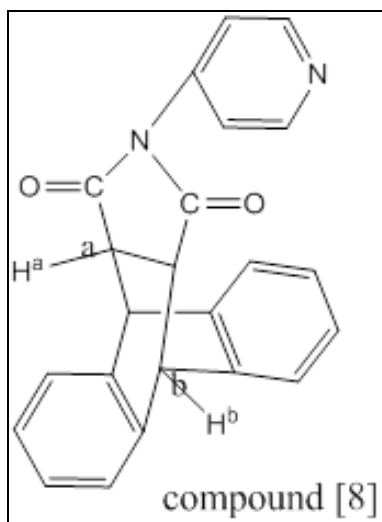


Figure (5): The structure of compound (8).

$^{13}\text{C NMR}$  spectrum of compound (8) appeared signals at ( $\delta=40.5$ ) ppm belong to two (a) carbons and two (b) carbons respectively and signals at ( $\delta=110.51$ - $136.11$ ) ppm are belong to aromatic carbons. Other

signals appeared at ( $\delta=146.31$ ) ppm and ( $\delta=164.31$ ) ppm, which belong to ( $\text{C}=\text{N}$ ) and ( $\text{C}=\text{O}$ ) imide carbons.

$^1\text{H NMR}$  - spectrum of compound (10) (Figure 6) be visible signals at ( $\delta=2.1$ ,  $2.7$ ,  $3.3$  and  $4.3$ ) ppm belong to

two ( $\text{CH}_2^d$ ), ( $\text{CH}_2^w$ ), two ( $\text{H}^a$ ) and two ( $\text{H}^b$ ) protons respectively. Other signals appeared at ( $\delta=4.1, 4.41$  and  $4.62$ ) ppm belong to (NH) amine proton, ( $\text{CH}_2(x)$ ) and ( $\text{CH}(z)$ ) respectively signals for

aromatic protons appeared at ( $\delta=6.9-7.71$ ) ppm, signals for (NH) amide protons appeared at ( $\delta=8.0-8.3$ ) ppm and signals for (OH) protons appeared at ( $\delta=10.8-11.2$ ) ppm.

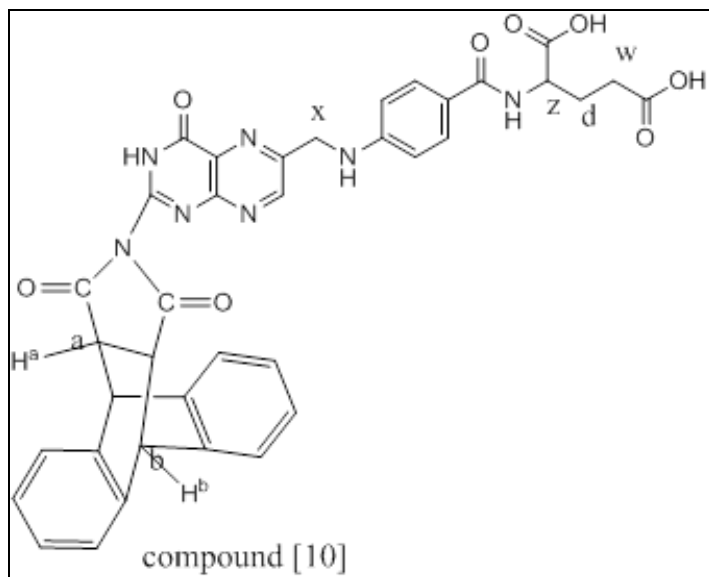


Figure (6): The structure of compound (10).

$^{13}\text{C}$ NMR spectrum of compound (10) showed signals at ( $\delta=27, 31.2, 43.1, 44.5$  and  $48.3$ ) ppm which belong to ( $\text{CH}_2(d)$ ) and ( $\text{CH}(w)$ ), two  $\text{CH}(a)$  two  $\text{CH}(b)$  and  $\text{CH}_2(x)$  carbons respectively (16). Signals for "aromatic carbons appeared" at- ( $\delta= 112.5-141.3$ ) p.p.m, signals- for(  $\text{C}=\text{N}$ ) carbons appeared at ( $\delta=151.2-154.2$ ) ppm and signals for (  $\text{C}=\text{O}$ ) amide", (  $\text{C}=\text{O}$ ) carboxyl and ( $\text{C}=\text{O}$ ) imide carbons shown at ( $\delta=160-165.3$ ) ppm, ( $170.1-176.4$ )ppm and ( $180.1-181.2$ ) ppm respectively.

### Biological Activity

The method cup plate using muller hinton medium agar was [give paid in studying the activity of antimicrobial of the prepared imides against four strains of bacteria and

*candida albicans* fungi .DMf was used as sample solution and the used concentration for all tested compounds was  $100\mu\text{g/mL}$ . Inhibition zone caused by each compound was measured in mm and the results are listed in (Table 5). The results showed that in the new anhydride (1) showed slightly active for gram positive bacteria compounds (2,5,6,7,1 are highly active against *Staphylococcus aureus*, compounds (5, 10) are highly active against *Streptococcus pyogenes*, compounds (8, 9) are highly active against *Klebsiella pneumoniae* and compounds (8, 10) are highly active against *E.coli*. The prepared compounds (3, 8, 9) showed high activity against *Staphylococcus aureus* and *Streptococcus pyogenes*, compounds (5, 9) appeared high activity against *E.coli* and compounds (6, 7, 8)

showed high activity against *Streptococcus pyogenes* and *Klebsiella pneumoniae*. Compounds (3, 10) appeared high activity against *Candida albicans* fungi while the rest imides showed moderate activity against this fungus. On Comparison the obtained

results of the prepared compounds with the results of the standard drugs that they derived from us notice that incorporation of adduct moiety in drug molecule caused enhancement and increase in their antibacterial and antifungal activities.

**Table (4): FTIR Spectral data  $\text{cm}^{-1}$  of the " Prepared Imides "[6-10]**

Comp. No.	Gram-positive bacteria		Gram-negative bacteria		Fungi
	<i>Staphylococcus aureus</i>	<i>Streptococcus pyogenes</i>	<i>klebsiella pneumoniae</i>	<i>Escherichia coli</i>	<i>Candida albicans</i>
1-	+	+	-	-	-
2-	++++	++	+	+	-
3-	+++	++	+	++	+++
4-	++	+	+	-	-
5-	++++	++++	++	+++	+
6-	++++	+++	++	++	++
7-	++++	+++	++	++	+
8-	+++	+++	++++	++++	++
9-	+++	++	++++	+++	++
10-	++++	++++	++++	++++	+++
Ampicillin	+++	++	++	++	-
Cefotaxime	++	++	+++	+++	-
Folic acid	+	+	-	-	-
Fluconazole	-	-	-	-	+++

**Table (5): Antibacterial and antifungal activity of compounds [5-10]**

Comp. No.	v(O-H) and v(N-H)	v(C-H) aromatic aliphatic	v(C=O) Imide	v(C=O) Carboxyl	v(C=O) Lactam	v(C=O) amide	v(C=N)	v(C=C) Aromatic	v(C-N) Imide	Others
6	3365 3340 3292	3062 2964 2869	1772 1705	1695	1672	1656	-	1521	1386	v(C-S) 698
7	3465 3330 3270	3049 2927 2850	1724	1683	1674	1658	1639	1541	1350	v(C=O) ester 1740 v(C-O) Ester 1228,1164 v(C-S) 632
8	-	3085 2958 2850	1774 1708	-	-	-	1649	1600	1334	v(p-sub) 823
9	-	3072 2966 2850	1701	-	-	1674	-	1566	1379	v(C=C) aliphatic 1606
10	3409 3323 3245	3047 2927 2840	1782 1702	1697	-	1639	1604	1570	1338	-

Key of symbols: "slightly active = + =inhibition zone 6-9 mm"

"Moderately active =++=inhibition zone 9-12 mm"

High active =+++ =inhibition zone 13-17 mm" , Highly active =++++ =inhibition zone > -17 mm"

## References:

- Sondhi S.M., Rani R., Roy P. Agarwal S.K. and Saxena A.K. (2009) .Synthesis of N-Substituted cyclic imides and their evaluation for anticancer and anti-inflammatory activities. Bioorg. Med. Chem. Lett., (19),1534-1538.
- Jindal.D.P., Bedi V.,Jit B., Karkra N., Guleria S., Bansal R., Paluszczak A. and Hartmann R.W .(2005). Synthesis and study of some new N-substituted imide derivatives as potential anticancer agents.1L Farmaco,(60),283-290.
- Machado A.L., Lima L.M., Araujo J.X., Fraga C.A.M., Koatz V.L.G. and Barreiro E.J.I , (2005) Synthesis and Anti\_inflammatory Activity of Novel phthalimide derivatives ,structurally related to thalidomide. Bioorg. Med.chem. Lett,(15),1169-1172.
- Malgerzata W.and Katarzyna K.K. (2009) ,Synthesis and anticonvulsant evaluation of some N-substituted phthalimides. Acta poloniae pharm. 66(3), 249-257.
- Miguel F.B., Gema D., Beatriz 5. , Cynthia R., Simmon R. and Teresa B. (2002). Synthesis and Antitumor activity of new dendrite polyamines\_(imide\_DNA\_Intercalator) conjugates : potent Lck inhibitors.Eur .J. Med .chem.,(37),541-551.
- AL\_Azzawi A.M. and Hassan A.S. (2014) . Synthesis and antimicrobial activity study of several new phthalimides linked to drug molecules. Kerbala J. Pharm. Sci. ,(7),85\_93.
- AL\_Obaidi K.K. (2013). Chem.. Department. Ph.D. Thesis ,College of science, Baghdad university.
- Belen, A. , Rosa A. and Rafael, B. (2010), "Triazolo pyridines", the preparation of novel 6,7 \_dihydro [1,2,3] triazole [1,5\_9] pyridines. ARKIVOC, , (iii), 319-327.
- AL\_Azzawi, A.M. and Mehdi S.A. ( 2010). synthesis, characterization and biological activity study of N-substituted maleimides containing

- different heterocycles. Baghdad Sci. J., 7(1), 641-653.
- 10- Fadd A.A., Refat H.M. and Zaki M.M. (2000). Synthesis of some pyridine chromene and thiophene derivatives. *Molecules*,(5),701-709.
  - 11- Hussien H.F.(2008). Msc. Thesis. Chem. Dep. College of sci. AL-Nahrain university.
  - 12- "AL-Azzawi- A.,M. and Al- Hassan A.S"(2014). Synthesis and antimicrobial activity of new succinimides bearing different heterocycles. *Int.J.Res.pharm. chem.*," 4(4),755\_762.
  - 13- "AL\_Azzawi A.M". and" Jassem E.K".,( 2015), synthesis of several new cyclic imides linked to [3-mercapto-5-(4\_tolyl)\_1,2,4-triazole] moiety with anti bacterial activity study. *Kerbala J.Pharm. sci.*,(10),72-84.
  - 14- Hamd A.S.(2012). Ph.D. Thesis. Chem.Department. College of science,Baghdad university.
  - 15- Kavitha K.,Varsha P., Khagga M.,Vangala R.R. and sarbani P, N. (2011). N-(4\_methyl sulfonamide\_3\_phenoxy phenyl)\_9,10\_dihydro\_9,10\_ethanoanthracene\_11,12\_dicarboximide. *Molbank*, ,740-744.
  - 16- Silverstein R.M., Bassler G.C. and Morill T.C. (1981). Spectrometric identification of organic compound, fourth Edition, NewYork.