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Synthesis , characterization and biological activity study of N-substituted sulfonamido maleimides substituted with different heterocycles

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Abstract:

Eighteen new cyclic imides (maleimides) conncted to benzothiazole moiety through sulfonamide group were synthesized via multistep synthesis.The first step involved preparation of two maleamic acids N-phenylmaleamic acid and N-benzylmaleamic acid via reaction of maleic anhydride with aniline or benzyl amine.Dehydration of the prepared amic acids by treatment with acetic anhydride and anhydrous sodium acetate in the second step afforded N-phenylmaleimide and N-benzyl maleimide which in turn were treated with chlorosulfonic acid in the third step to afford 4-(N-maleimidyl) phenyl sulfonyl chloride and 4-(N-maleimidyl) benzyl sulfonyl chloride respectively.In the Fourth step of this work each one of the two prepared maleimidyl sulfonyl chlorides was introduced in reaction with nine substituted-2-amino benzothiazole compounds producing nine N-(4-(N-substituted benzothiazole -2-yl) sulfonamido phenyl) maleimides and nine N-(4-(N-substituted benzothiazole-2-yl)snlfonamido benzyl) maleimides.More over another new six sulfonamide phenyl and benzyl maleimides substituted with other heterocycles (pyridine and phenazone)were prepared via reaction of 4-(N-maleimidyl) phenyl and benzyl sulfonyl chlorides with heterocyclic amines including (2-amino pyridine,4-amino-pyridine,4-aminophenazone). Microbiological activity of the prepared compounds against two typs of bacteria(staphylococcus aureus and klebsiella pneumonia) and (candida albicans) fungi were evaluated and the results showed that these compounds have good antibacterial and good antifungal activities.

Keywords: Synthesis, sulfonamido maleimides , different heterocycles

Introduction:

Cyclic imides and their derivatives have found to be an important moiety in creation of novel medical materials.In view of their broad spectrum of biological applications numerous derivatives containing such moiety have been extensively studied and many of these compounds have proved to be active as antibacterial agents antifungal agents [(1)], plant growth[(2)] regulators, insecticides[(3)] and some of them are used in therapeutic of different diseases. On the other hand heterocyclic compounds in general comprise a class of organic compounds that exert a wide range of biological activities .Among five-membered heterocycles fused with benzene ring,benzothiazoles and its derivatives are of particular interest since great variety of these compounds display various biological activities ,antiviral[(4)], antimicrobial[(5)], antifungal[(6)],anticancer [(7)]and antihelmintic[(8)]. According to the mentioned facts it was thought worth while to synthesize new compounds via introducing the two biologically active moieties cyclic imide (maleimide) and benzothiazole or other heterocycles in a single molecular frame work followed by their antimicrobial screening.

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Material and Methods:

The chemicals used in this work were from BDH and Fluka and used without further purification .Melting points were determined on Gallenkamp capillary melting point apparatus and were un corrected. FTlR spectra were recorded using KBr discs on SHIMADZU FTIR-8400 Fourier Transform Infrared spectrophotometer. U.V spectra were recorded using SHlMADZU UV-visible recording spectrophotometer U.V 160. H-NMR spectra were recorded on near magnetic resonance Bruker, ultrasheild 300 MHz in Jorden using tetra methyl silane as internal standard,DMSO-d_6 and $CDCl_3$ as solvents.Incubator Heraeus D-63450(Germany) model was used for incubation samples in biological study.

1-Synthesis of N-phenyl maleamic acid [1]

Maleic anhydride (0.0l mol) was dissolved in (30 ml) of diethyl ether in a suitable round bottomed flask then (0.0l mol) of aniline was added dropwise with stirring and cooling [9-12] .The mixture was stirred for one hour then the resulted precipitate was filtered then purified by recrystallization from ethanol.Yield % 95 and m.p. (195-196) °C.

2- Synthesis of N- phenyl maleimide [2]

A mixture of (0.05 mol) of N-phenyl maleamic acid in (50 mL) of acetic anhydride and (5-10) % by weight of anhydrous sodium acetate [13] was refluxed with stirring for two hours.The resulted homogenous solution was cooled to room temperature then poured into excess cold water with vigorous stirring . The obtained precipitate was filtered, washed with water and finally purified by recrystallization from cyclohexane.Yield% 82 and m.p. (80-81) °C.

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

The titled compound was prepared by following literature procedures [14] with some modifications:(0.0l mol) of N-phenyl maleimide was placed in asuitable round bottomed flask fitted with dropping funnel which was charged with (4 ml)of chloro sulfonic acid. Chloro sulfonic acid was added dropwise during two hours with continous stirring and cooling to zero °C.Reaction mixture was stirred for another ten hours then poured carefully into cold water with stirring .The obtained precipitate was filtered,washed with cold water then was recrystalized from methanol.Yield %75, m.p. (120-121) °C.Physical properties of compounds [1,2,3] are listed in Table(1).

4-Synthesis of N-(4-(N-substituted benzothiazole-2-yl)sulfonamido phenyl)maleimides [4-12]

(0.0l mol) of substituted 2-amino benzothiazole was dissolved in (30 ml) of dry pyridine then (0.0l mol) 0f 4-(N- maleimidyl)phenyl sulfonyl chloride was added in portions with stirring and keeping temperature below 40°C [15]. The resulted mixture was refluxed for three hours with stirring then was cooled to room temperature before pouring into (100 ml) of cold water The obtained precipitate was filtered,washed with water then was recrystallized from a suitable solvent.Physical properties of the prepared compounds [4-12] are listed in Table(2).

5-Synthesisof N-(4-sulfonamido phenyl)maleimides substituted with different heterocycles [13-15] [16]

In a suitable round bottomed flask (0.0l mol) of heterocyclic amine (2-amino pyridine or 4-amino pyridine or 4-amino phenazone) was dissolved in (10 ml) of DMF then (3ml) of

triethyl amine was added followed by (0.01 mol) of 4-(N-maleimidyl) phenyl sulfonyl chloride then the mixture was refluxed for two hours with stirring .The resulted mixture was cooled to room temperature then fillered and the filtrate was poured into crushed ice with stirring. The formed precipitate was filtered,washed with water then purified by recrystallization from suitable solvent. Physical properties of compounds [13-15] are listed in Table (3)

6-Synthesis of N-Benzyl maleamic acid [16]

The titled acid was prepared by following the same procedure used in preparation of N-phenyl maleamic acid except using of benzylamine instead of aniline. The product was purified by recrystallization from methanol.Yield% 81,m.p.(128-129) °C.

7-Synthesis of N-benzyl malemide [17]

The titled compound was prepared by following the same procedure used in the preparation of N-phenyl maleimide except using of N-benzylmaleamic acid instead of N -phenyl maleamic acid .The final product was purified by recystallization from cyclohexane.Yield % 62,m.p.(61-63) °C.

8-Synthesis of 4-(N-maleimidyl) Benzyl sulfonyl chloride[18]

N-Benzyl maleimide (0.005 mol) was dissolved in (12 ml) of chloroform then (2 ml) of chlorosulfonic acid was added dropwise with stirring and cooling to Zere °C. The resulted mixture was stirred for additional two hours before pouring in crushed ice with stirring .the organic layer was extracted with chloroform for three times then washed with distilled water, dried and left until evaporation of solvent. The obtained oil was recrystallized from ethanol.Yield %71 ,m.p.(200 Dec.) °C. Physical properties of compounds [16,17,18] are listed in Table(7).

9-Synthesis of N- (4-(N-substituted benzothiazole-2-yl)sulfonamido benzyl maleimides [19-27]

The titled compounds were prepared by following the same procedure used in the preparations of compounds [4-12] except using of 4-(N-maleimidyl)benzyl sulfonyl chloride instead of 4-(N-maleimidyl) phenyl sulfonyl chloride. The products were purified by recrystallization from a suitable solvent. Physical properties of compounds [19-27] are listed in Table (8) .

10- Synthesis of N-(4-sulfonamido benzyl) maleimides substituted with different heteroycles [28-30]

The titled compounds were prepared by following the same procedure used in the preparation of compounds [13-15] except using of 4-(N-maleimidyl)benzyl sulfonyl chloride instead of 4-(N-maleimidyl) phenyl sulfonyl chloride. The products were recrystallized from a suitable solvent, physial properties of compounds [28-30] are listed in Table (9).

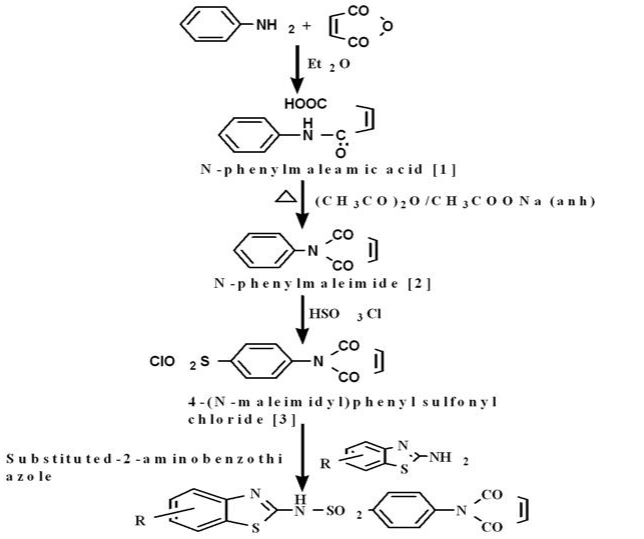
11-Microbiological Tests

Nutrient agar was added to (1L) of distilled water in suitable conical flask with stirring and heating until complete dissolving then the flask was stoppered 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 placed in petridishs about (20 ml) for each one and was left to cool and solidified. The studied bacteria and fungi were placed on the nutrient agar surface using the loop and by streaking processor then the discs saturated with tested compound

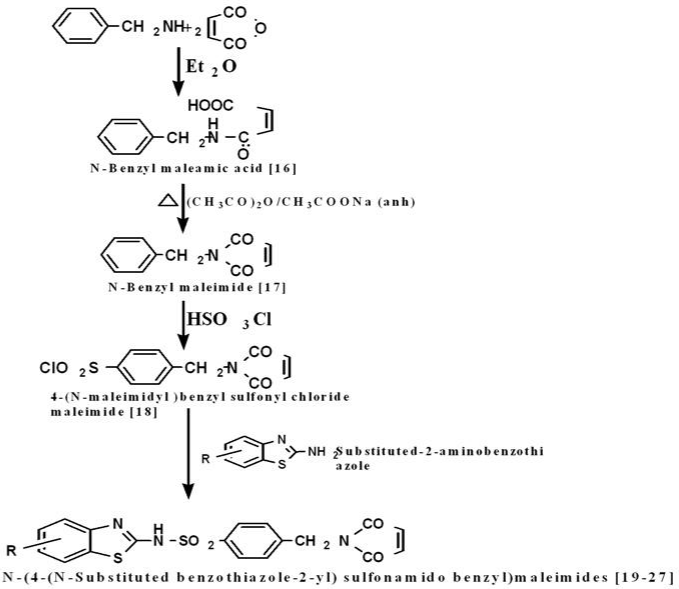
solutions. The samples were incubated for 24 hrs.at 37 °C. [17]

Results and discussion

Since both maleimides and 2-amino benzothiazoles are biologically active components the aim of the present work is synthesis of new compounds containing these two active moieties with expected biological activity. The strategy which was followed in building the new compounds was based on connecting between maleimide and benzothiazole moieties by phenyl sulfonamide or benzyl sulfonamide group thus through this strategy first we built new compounds containing the two mentioned active moieties second we Introduced the known active sulfonamide group in the synthesized new compounds and this may increase the activity of these compounds .The new strategy was performed via many steps the first step involved synthesis of two maleamic acids namly N-phenyl maleamic and N-benzyl maleamic acids via reaction of maleic anhydride with aniline or benzyl amine. These two maleamic acids were treated with acetic anhydride and anhydrous sodium acetate in the second step to afford the corresponding N-phenyl and N-benzyl maleimides which in turn were treated with chloro sulfonic acid producing maleimidyl phenyl and maleimidyl benzyl sulfonyl chlorides in the third step.The prepared maleimidyl sulfonyl chlorides were introduced in reaction with 2-amino benzothiazole compounds in the fourth step producing new nine N-(4-(N-substituted benzothiazole-2-yl) sulfonamido phenyl maleimides and new nine N- (4- (N - substituted benzothiazole - 2- yl) sulfonamido benzyl maleimides respectively. All these steps were summarized in schemes (1) and (2) and physical properties of all the mentioned compounds are listed in tables (1),(2),(7) and (8).



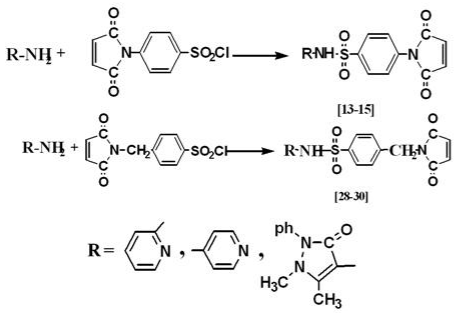
Scheme (1)



Scheme (2)

Structure of the prepared new compounds were confirmed by FTIR and U.V spectroscopy . FTIR spectra of the prepared amic acids [1] and [16] showed absorption bands at (3200 – 3280) cm^{-1} due to υ(O–H) carboxylic and υ (N – H) amide while these bands were disappeared in FTIR spectra of N–phenyl and N-benzyl maleimides indicating success of dehydration reaction which lead to imide formation .On the other hand FTIR spectra of maleimidyl phenyl and benzyl sulfonyl chlorides [3] and [18] showed two characteristic absorption bands at (1380) cm^{-1} and (1175) cm^{-1} which were assigned to asym υ (SO_2) and sym υ (SO_2) respectively [18] .FTIR spectra of the prepared (benzothiazole–2–yl)sulfonamido phenyl maleimides [4-12] and (benzothiazole-2-yl) sulfonamido benzyl maleimides [19-27] showed characteristic absorption bands at (3309-3456) cm^{-1} , (1695-1720) cm^{-1} , (1325 – 1396)cm^{-1} , (1140- 1180)cm^{-1} (1470 – 1596)cm^{-1} and (617-694)cm^{-1} which were attributed to υ (N-H) sulfonamide , υ (C=O) imide , asym υ (SO_2) , sym υ (SO_2) , υ (C=N) and υ (C-S) in thiazole ring respectively .On the other hand U.V spectra of the prepared imides [4-12] and [19-27] showed clear absorptions at wave lengths (273-415) nm and (259-420) nm due to ($\pi \rightarrow \pi^*$) and ($n \rightarrow \pi^*$) transitions in the conjugated system of maleimide ring and substituted benzothiazole rings .Other details of FTIR and U.V spectral data of the prepared mentioned compounds are listed in Tables (4,5,10,11) .On the other hand structures of some compounds were confirmed also by H-NMR spectra thus H-NMR spectrum of 4-(N-maleimidyl) phenyl sulfonyl chloride [3] showed singlet signal at δ=7.2 ppm belong to two vinylic protons in maleimide ring and four multiplet signals at δ=(7.5 , 7.7 , 8, 8.3) ppm belong to aromatic protons.H-NMR spectrum of compound [6] N-(4-(N-4,

6- dimethyl benzothiazole-2-yl) sulfonamido phenyl maleimide showed many signals including two singlet signals at δ =2 and 2.2 ppm belong to two methyl groups protons , signal at δ=6.5 ppm belong to two vinylic protons in maleimide ring and signals at δ=7.3-7.6 ppm belong to aromatic protons and NH proton .Also H-NMR spectrum of compound [19] N-(4-(N-benzothiazole –2-yl) sulfonamido benzyl) maleimide showed singlet signal at δ=3.65 ppm which was assigned to benzylic protons , singlet signal at δ=6.25 ppm belong to two vinylic protons in maleimide ring , two signals at δ=7.25 and 7.65 ppm belong to aromatic protons and signal at δ=9.3 ppm belong to NH proton . The second part in this work involved preparation of new maleimides connected to hetero rings through phenyl and benzyl sulfonamide group .Synthesis of these compounds was performed via reaction of the prepared maleimidyl phenyl and benzyl sufonyl chlorides [3] and [18] with three heterocyclic amines including 2-amino pyridine, 4-amino pyridine and 4-amino phenazone as described in scheme (3).



Scheme (3)

Physical properties of compounds [13 – 15] and [28 – 30] are listed in Tables(3) and(9). Structure of compounds [13 -15] and [28 – 30] were confirmed by FTIR and U.V spectroscopy .FTIR spectra of these compounds showed clear absorption bands at (3180–3433)cm $^{-1}$, (1704 – 1712)cm^{-1} and (1620 – 1670)cm^{-1} due to υ (N –H) amide , υ (C=O) imide and υ (C=C) vinylic respectively .The spectra showed also two clear absorption bands at (1319 – 1396)cm^{-1} and (1157- 1172)cm^{-1} which were attributed to stretching vibrations of asym (SO_2) and sym (SO_2).On the other hand U.V spectra of compounds [13 – 15] and [28 – 30] showed clear bands at wave lengths (268-300)nm due to ($\pi\rightarrow\pi^*$)and ($n\rightarrow\pi^*$) transitions in the conjugated system of maleimide ring and heterocyclic rings .Other details of FTIR and U.V spectral data of these compounds are listed in Tables (6) and (12) .

Microbiological activity

The prepared new imides in this work were expected to possess biological activity since their structures contained benzothiazole , maleimide and sulfonamide moieties and all these moieties are known biologically active components , thus the last part in this work involved evaluation of antimicrobial activity of the prepared imides against staphylococcus aureus (Gram positive) bacteria , klebsiella pneumonia (Gram negative) bacteria and candida albicans fungi.Inhibition zones caused by the various prepared compounds were determined and the results are listed in Table (13) .The results showed that biological activity of the studied compounds depend on nature of substituents in their molecules thus compounds [6] , [7] and [8] showed high biological activity due to the presence of (Cl) and electron releasing substituents (CH_3)and (OCH_3) respectively [16] .Results at Table (13) indicated that many benzothiazol-2-yl sulfonamido phenyl maleimides possess moderate to high biological activity against Gram-positive bacteria and this was

due to the hydrophilic properties of these compounds and cell wall of Gram - positive bacteria .On the other hand the molecules of the prepared benzothiazole-2-yl sulfonamido benzyl maleimides have hydrophobic properties and this in turn made these compounds active against Gram-negative bacteria which possess complex lipo polysaccharides in their cell walls.Finally both phenyl and benzyl sulfonamido maleimides substituted with other hetero cyclic rings showed moderate activity against the two types of bacteria while most of them were not active against candida albicans fungi.Compounds [4-12] showed different biological activity against candida albicans thus compounds [6,7,8] showed high biological activity while the other showed moderate or weak activity. compounds [19-27] also showed different biological activites against canddida fungi thus compounds [22,23,26] showed high biological activity while compounds [21,24,26,27] showed no activity against this fungi .

Table (1): Physical properties of the prepared compounds[1], [2], [3]

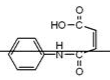
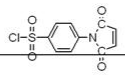
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Rescrystallization solvent
1		White	195-196	95	Ethanol
2		Faint yellow	80-81	82	Cyclohexane
3		white	120-121	75	Methanol

Table (2): Physical properties of benzothiazole sulfonamido phenyl maleimides [4-12]

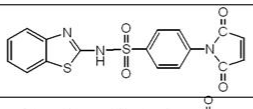
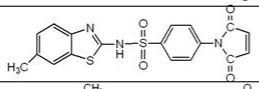
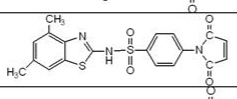
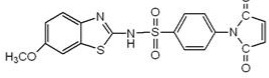
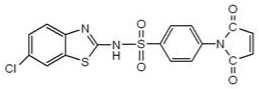
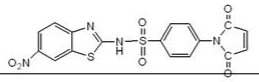
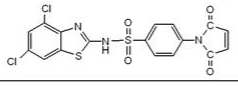
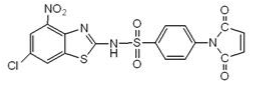
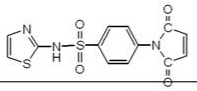
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Rescrystallization solvent
4		Brown	240 Dec.	70	Acetone
5		Brown	> 320	77	Acetone
6		Brown	> 320	65	Acetone
7		Brown	> 320	62	Ethanol
8		Brown	170-172	57	Ethanol
9		Yellow	Yellow	310 Dec.	Acetone
10		White	White	228-229	Ethanol
11		Deep yellow	Deep yellow	240 Dec.	Acetone
12		Redish brown	Redish brown	220 Dec.	Ethanol

Table (3):Physical properties of sulfonamido phenyl maleimides with different heterocycles [13-15]

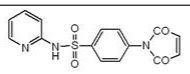
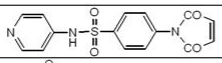
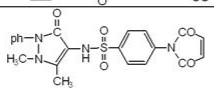
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Recystallization solvent
13		Off white	272 Dec.	67	Ethanol
14		Off white	264 Dec.	72	Acetone
15		Deep brown	220 Dec.	64	Acetone

Table (4): FTIR and UV spectral data of [1], [2], [3]

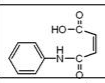
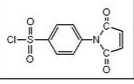
Comp. No.	Comp. structure	IR Absorption data (cm^{-1})							U.V data λ_{max} (nm) in ethanol
		ν(O-H) carboxylic	ν(N-H) amide	ν(C=O) carboxylic	ν(C=O) amide	ν(C=C) vinylic	ν(C=C) aromatic	ν(C-H) aromatic	
1		3255	3255	1704	1640	1590	1530	3070	235 250 300
2		ν(C=O) Imide		ν(C=C) vinylic		ν(C-N)		ν(C=C) aromatic	300
		1712		1589		1396		1504	
3		ν(C=O) Imide	ν(C=C) vinylic	Asym. $\nu(SO_2)$		sym. $\nu(SO_2)$		ν(C-N)	247
		1720	1589	1380		1175		1296	

Table (5): FTIR and UV spectral data of benzothiazole sulfonamide maleimides [4-12]

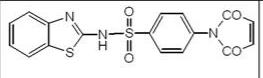
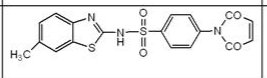
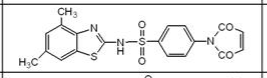
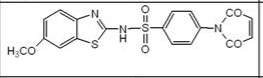
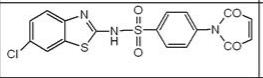
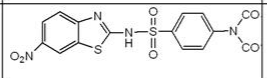
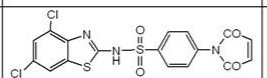
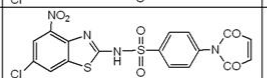
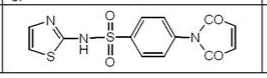
Comp. No.	Compound structure	IR Absorption data (cm^{-1})									U.V λ_{max} (nm) in ethanol
		ν(N-H) sulfonamide	ν(C=O) Imide	ν(C=C) vinylic	$\nu(SO_2)$ asym	$\nu(SO_2)$ sym	ν(C-N) Imide	ν(C=N) Thiazole	ν(C-S) Thiazole	others	
4		3309	1720	1589	1380	1172	1311	1542	663	-	300
5		3309	1712	1600	1380	1172	1319	1510		-	317, 290, 273
6		3417	1712	1643	1373	1164	1319	1542	617	-	292
7		3433	1712	1643	1388	1180	1315	1596	678	-	276
8		3417	1712	1643	1388	1180	1319	1596	663	1126 C-Cl	273
9		3363	1712	1650	1326	1180	1302	1504	670	848 C-NO_2	382
10		3456	1712	1635	1388	1140	1319	1535	678	1090 C-Cl	312
11		3417	1705	1627	1325	1157	1315	1496	693	894 C-NO_2	317, 415
12		3340	1712	1600	1357	1180	1390	1542	663	-	304

Table (6): FTIR and UV spectral data of sulfonamido phenyl maleimide with different heterocycles [13-15]

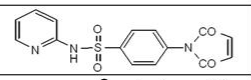
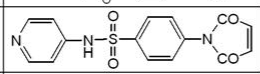
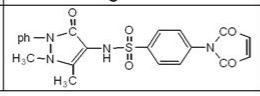
Comp. No.	Comp. structure	IR Absorption data (cm^{-1})							U.V data λ_{max} (nm) in ethanol
		ν(N-H) Sulfonamide	ν(C=O Imide	ν(C=C) vinylic	ν(C=N)	$\nu(SO_2)$ asym	$\nu(SO_2)$ sym	ν(C-S)	
13		3186	1712	1620	1596	1388	1164	655	300
14		3180	1712	1650	1504	1380	1172	655	275
15		3250	1712	1643	-	1380	1164	671	280

Table (7): physical properties of [16] ,[17], [18]

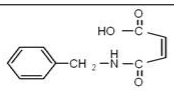
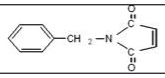
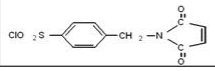
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Recystallization solvent
16		White	128-129	81	Methanol
17		Yellow	61-63	62	Cyclohexane
18		Off white	200 Dec.	71	ethanol

Table (8): physical properties of benzothiazole sulfonamido benzyl maleimides [19-27]

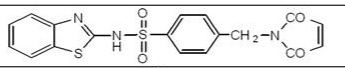
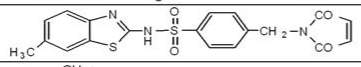
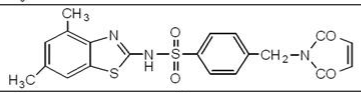
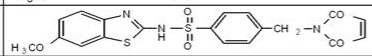
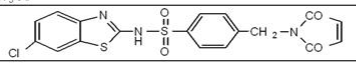
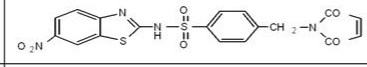
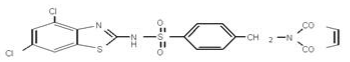
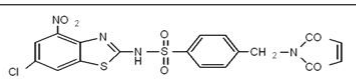
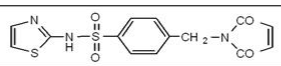
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Recystallization solvent
19		Off white	192-194	82	Acetone
20		Brown	200 Dec.	70	Acetone
21		Yellow	140-142	65	Ethanol
22		Brown	310 Dec.	62	Ethanol
23		Faint brown	278-279	55	Ethanol
24		Yellow	290 Dec.	50	Acetone
25		Faint yellow	234-235	60	Ethanol
26		Deep yellow	210 Dec.	53	Acetone
27		Brown	190 Dec.	77	Ethanol

Table (9): physical properties of sulfonamido benzyl maleimides with different heterocycles [28-30]

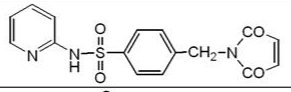
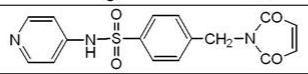
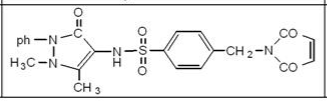
Comp. No.	Compound structure	Color	Melting point °C	Yield %	Recystallization solvent
28		Off white	280 Dec.	70	Ethanol
29		Brown	204-205	75	Ethanol
30		Faint brown	228 Dec.	65	Acetone

Table (10): FTIR and UV spectral data of [16] ,[17], [18]

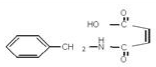
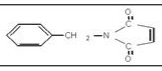
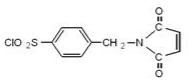
Comp. No.	Comp. structure	IR Absorption data (cm^{-1})							U.V data λ_{max} (nm) in ethanol
		ν(O-H) carboxylic	ν(N-H) amide	ν(C=O) carboxylic	ν(C=O) amide	ν(C=C) vinylic	ν(C=C) aromatic	ν(C-H) aromatic	
16		3400	3280	1697	1620	1573	1542	3070	249
		ν(C=O) Imide		ν(C=C) vinylic		ν(C-N)		ν(C=C) aromatic	
17		1704		1540		1342		1504	245
		ν(C=O) Imide	ν(C=C) vinylic	asym. ν(SO_2)		sym. ν(SO_2)	ν(C-N)	ν(C=C) aromatic	
18		1704	1627	1380		1172	1290	1520	221

Table (11): FTIR and UV spectral data of benzothiazole sulfonamido benzyl maleimides [19-27]

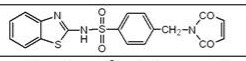
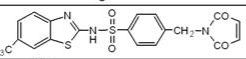
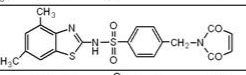
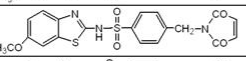
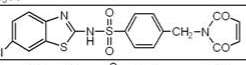
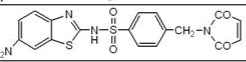
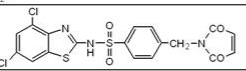
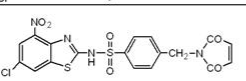
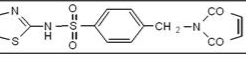
Comp. No.	Compound structure	IR Absorption data (cm^{-1})									U.V λ_{max}(nm) in ethanol
		ν(N-H) sulfonamide	ν(C=O) Imide	ν(C=C) vinylic	ν(C=N) Thiazole	ν(SO_2) asym	ν(SO_2) sym	ν(C-N) Imide	ν(C-S) Thiazole	others	
19		3409	1704	1643	1535	1396	1180	1342	686	-	259
20		3309	1704	1643	1535	1396	1180	1342	680	-	273
21		3400	1704	1643	1535	1396	1172	1342	686	-	274
22		3417	1704	1643	1488	1396	1180	1342	686	1218 C-O-C	281
23		3417	1704	1643	1470	1396	1180	1342	666	1025 C-Cl	272
24		3402	1704	1627	1512	1334	1180	1226	686	848 C-NO_2	274
25		3456	1712	1635	1535	1375	1172	1319	694	1110 C-Cl	259, 388
26		3400	1695	1627	1504	1375	1150	1226	686	1050 C-Cl 894 C-NO_2	312
27		3355	1704	1620	1550	1396	1180	1342	694	-	320, 420

Table (12): FTIR and UV spectral data of sulfonamido benzyl maleimides with different heterocycles[28-30]

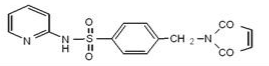
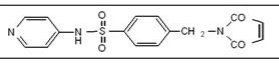
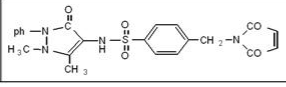
Comp. No.	Comp. structure	IR Absorption data (cm^{-1})						U.V data λ_{max} (nm) in ethanol	Others
		ν(N-H) Sulfonamide	ν(C=O) Imide	ν(C=C) vinylic	$\nu(SO_2)$ asym	$\nu(SO_2)$ sym	ν(C-S)		
28		3409	1704	1627	1396	1172	694	268	-------
29		3409	1704	1670	1319	1157	694	272	------
30		3433	1704	1643	1396	1172	686	275	νC=O Phenazone 1700

Table (13): Microbiological activities of compounds [4-15]and [19-30]

Comp. No.	*Staphylococcus aureus*	*Klebsiella pneumoniae*	Zone of Inhibition in (mm)	Comp. No	*Staphylococcus aureus*	*Klebsiella pneumoniae*	*Candida albicans fungi*
4	10	5	5	19	5	7	5
5	10	5	7	20	8	9	9
6	17	15	10	21	5	7	R
7	15	3	15	22	10	25	15
8	12	17	17	23	10	23	19
9	R	R	3	24	R	R	R
10	5	R	3	25	R	R	R
11	7	5	3	26	5	13	12
12	R	R	9	27	R	R	R
13	8	4	R	28	3	7	5
14	15	9	R	29	12	10	R
15	5	10	3	30	R	R	R

Key to symbols : R= Resistant, Inhibition zone < 6 mm = Inactive, Inhibition zone 6-9 mm = Slightly active, Inhibition zone 9-12 mm = Moderately active, Inhibition zone > 12 mm = Highly active

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تخليق،تشخيص ودراسة الفعالية البايولوجية لمركبات N – معوض سلفون اميدو مالي ايماید معوضة بحلقات غير متجانسة مختلفة

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الخلاصة:
تضمن البحث تحضير ثمانية عشر من الايمايدات الحلقية (المالي ايمايدات) الجديدة المرتبطة مع حلقات البنزوثايازول عبر مجموعة السلفون اماید وذلك من خلال اجراء عدة خطوات .
تضمنت الخطوة الاولى تحضير اثنين من حوامض المالي آميك هما N- فنيل مالي آميك وN - بنزيل مالي آميك وذلك من خلال تفاعل انهيدريد الماليك مع الانيلين او امين البنزيل .
اما في الخطوة الثانية فقد تم سحب الماء من حامضي الاميك المحضرين وذلك بمعاملتهما مع انهيدريد الماليك وخلات الصوديوم اللامائية وبذلك تم الحصول على N-فنيل مالي ايماید و N - بنزيل مالي ايماید واللذان تمت معاملتهما لاحقا في الخطوة الثالثة مع حامض كلوريد السلفونيك وبذلك تم الحصول على المركبين 4 – (N-مالي ايميديل) فنيل كلوريد السلفونيل و 4 -(N – مالي ايميديل) بنزيل كلوريد السلفونيل على التوالي .
اما في الخطوة الرابعة فقد تم ادخال المركبين الناتجين من الخطوة الثالثة في تفاعل مع تسعة من مركبات 2-أمينوبنزوثايازول المعوضة وبذلك تم الحصول على تسعة من مركبات N–(4-(N-معوض بنزوثايازول -2- يل) سلفون اميدو فنيل) مالي ايماید وتسعة من مركبات N–(4-(N - معوض بنزوثايازول -2- يل) سلفون اميدو بنزيل) مالي ايماید .
اضافة الى ذلك فقد تضمن البحث تحضير ستة من مركبات سلفون اميدو فنيل وبنزيل مالي ايماید معوضة بحلقات غير متجانسة اخرى هي حلقتي (البريدين والفينازون)وذلك من خلال تفاعل مالي ايميديل فنيل كلوريد السلفونيل ومالي ايميديل بنزيل كلوريد السلفونيل مع امينات حلقية غير متجانسة هي على التوالي (2-امينوبريدين, 4-امينوبريدين و 4- امينو فينازون).
تمت دراسة الفعالية المايكروبايولوجية لبعض المركبات المحضرة ضد نوعين من البكتريا هما (ستافيلوكوكاس اوريس) و(كليبسلا نيومونيا) وضد احد انواع الفطريات وهو (كانديدا البكانس) وقد اظهرت المركبات قيد الدراسة فعالية بايولوجية جيدة ضد الاحياء المجهرية المدروسة.