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Design, Synthesis, and Antimicrobial Activity Evaluation of New Developed Compounds via Introducing of 3, 4-Dimethyl Maleimidyl Sulfonamide Moiety

Raghad Naeem Akol* , Ahlam Marouf Al-Azzawi
Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq

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Abstract

The present study focuses on creating and engineering novel compounds based on five established medications: Sulfamethoxazole, Ampicillin, Cefotaxime, Sulfamethazine, and Trimethoprim. The research involves incorporating a biologically active component, specifically the 3,4-dimethyl maleimidyl sulfonamide group, into these drug molecules to produce the target compounds. Many steps were performed on this target; the first one involved a reaction between 3,4-dimethyl maleic anhydride and aniline to produce compound (1) N-phenyl-3,4-dimethyl maleimide which reacts with chlorosulfonic acid in the second step producing compound (2) 4-[N-(3`,4`-dimethyl maleimidyl)phenyl sulfonyl chloride. The third step involved compound (2) reaction with the selected drugs, producing the target-developed compounds (3-7). The newly synthesized compounds were tested for their antibacterial and antifungal activities. Results showed they exhibit high levels of activity against both bacteria and fungi.

Keywords: Drug compounds, 3, 4-dimethyl maleic anhydride, N-phenyl-3, 4 dimethyl maleimide, 3, 4 dimethyl maleimidyl sulfonamide moiety.

تصميم وتحضير وتقدير الفعالية المضادة للمايكروبات لمركبات دوائية مطورة جديدة من خلال ادخال مكونة 4,3 – ثنائي مثيل مالي ايميديل سلفون امايد

رغد نعيم عاكول* ,أحلام معروف العزاوي
جامعة بغداد، كلية العلوم ، قسم الكيمياء ، بغداد ، العراق

الخلاصة

تركز الدراسة الحالية على إنشاء وهندسة مركبات جديدة تعتمد على خمسة أدوية منشأة :السلفاميثاوكسازول ، أمبيسيلين ، سيفوتاكسيم ، سلفاميثازين والتراي ميثوبريم. يتضمن البحث دمج مكونفعال بايولوجيا ، وتحديدا مجموعة 4,3 – ثنائي مثيل مالي ايميديل سلفون أمايد في جزيئات الدواء هذه لإنتاج المركبات المستهدفة. تم تنفيذ عدة خطوات من اجل هذا الهدف تم في الخطوة الأولى تفاعل ثنائي مثيل أنهيدريد الماليك مع الانيلين للحصول على مركب (1) وهو–فنيل– 4,3 – ثنائي مثيل مالي ايمايد والذي تمت مفاعلته مع كلورو حامض السلفونيك في الخطوة الثانية مما انتج المركب (2) وهو N–(3`,4` – ثنائي مثيل مالي ايميديل)] فنيل كلوريد السلفونيل. الخطوة الثالثه تتضمن تفاعل المركب (2) مع الادوية المختارة مما اسفر عن تكوين 4N–]

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*Email: raghad1997na@gmail.com

المركبات الدوائية المطورة المطلوبة وهي. -(4,3 - ثنائي مثيل مالي ايميديل)] فنيل سلفون امايد الدواء (3-
7)N4-] تم اختبار المركبات المصنعة حديثا لفعاليتها المضادة للبكتيريا والفطريات. وأظهرت النتائج أنها
تظهر مستويات عالية من الفعالية ضد كل من البكتيريا والفطريات

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1. Introduction

Medications that contain the sulfonamide functional group are classified as sulfonamides, which are also commonly referred to as sulfa drugs. The earliest synthetic antimicrobial agents are sulfa drugs, which are still widely used today primarily because of their excellent antibacterial action against bacterial infections at a low cost and toxicity [1]. Moreover, sulfonamide derivatives have a wide range of biological activities. As a result, members of this class of pharmacological agents are frequently used in clinics as hypoglycemic, anti-cancer[2], antibacterial, antifungal, anti-inflammatory [3], antimalarial [4, 5], antitumor [6, 7], and antioxidant agents [8]. Cyclic imides represent an important category of compounds characterized by a structure where two amide groups share a common nitrogen atom, forming a ring. This unique arrangement results in a bis-amide linkage within the molecule. They have proven to be helpful building blocks for the production of heterocycles [9] and other natural products[10], they exhibit valuable biological effects including antifungal [11, 12], antibacterial [13-15], anti-cancer[16, 17], anti-inflammatory[18]. Cyclic imides with a para-sulphonamide group have been potential anti-tubercular agents[19]. Besides amoxicillin, cefotaxim[20] is a β-lactam antibiotic with pharmacological activity commonly used to treat a variety of infections [21, 22].

Trimethoprim is a well-known antibacterial agent widely used for urinary and gastrointestinal infections [23, 24], while sulfamethoxazole and sulfamethazine are well-known sulfonamide- containing drugs [25]. According to all the previous facts, besides the urgent need for new active antibiotic drugs that can solve the issue of microorganisms resistant to many drugs, it was necessary to design and create new compounds by introducing both 3,4-dimethyl maleimide and sulfonamide moieties in the molecules of selected drugs including sulfa-drugs, β-lactams and trimethoprim. The presences of these active moieties and drug molecule leads to the formation of new developed compounds that are expected to possess high antibacterial and antifungal activities. The aim of this work is to synthesis a number of cyclic imides namely (3,4-dimethyl maleimides) linked to well-known drug molecules. Thus molecules of the newly synthesized cyclic imides contain three biologically active components namely 3,4-dimethyl maleimides, sulfonamide moiety and drug molecule together and this leading to expect that the presence of these three bioactive components together will supply us with highly biologically active compounds.

2. Experimental Part

1.1. Instrumentation

The melting points of the prepared compounds were determined using a Thomas Hoover device. Their FTIR spectra were analyzed in detail by an FTIR-8400 Fourier Transform Infrared spectrophotometer. The Bruker- 400MHz apparatus was used to record the ^{1}H-NMR and ^{13}C-NMR spectra, with DMSO-d$_6$ acting as the solvent and TMS acting as an internal standard.

2.2. Synthesis

*2.1. N-phenyl 3,4-dimethyl maleimide **1***

Compound **1** was produced via the addition of aniline (0.01mol, 0.911ml) dropwise to the solution of 3,4-dimethyl maleic anhydride (0.01mol, 1.26g) with cooling and stirring in

acetone(15ml)[26].
After two more hours of stirring at room temperature, the mixture was left overnight, followed by recrystallization of the precipitate from ethanol.

2.2. 4-[N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonyl chloride **2**

Chlorosulfonic acid (0.0lmol, 5.25g) was added dropwise to (0.0lmol, 2.01g) of compound 1 with good stirring at 0°C for one hour [27]. After stirring the mixture for an additional six hours at 25°C, it was poured into ice water. The product was then obtained by filtering the mixture, followed by cleaning with cold water and drying. Moreover, it is purified by recrystallization using ethanol.

2.3. 4-[N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonamido Sulfamethoxazole **3**

Sulfamethoxazole (0.01mol,2.53g) was dissolved in (20mL) of dry pyridine then compound **2** (0.01mol, 2.99g) was added gradually while stirring at a temperature under (40°C)[27]. Following the addition, the mixture refluxed for five hours before being stirred and transferred into cold water. The formed precipitate was then filtered, dried, and recrystallized using ethanol.

2.4. 4-[N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonamido ampicilline 4

Compound **4** was synthesized by applying the same procedure as compound **3** except introducing (0.0lmol, 3.49 g) of ampicilline instead of sulfamethoxazole[27]. The solid product that formed was separated from the liquid by filtration. It was then dried to remove any remaining moisture. Finally, the dried solid was purified through recrystallization using dioxane as the solvent.

2.5. 4-[N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonamide cefotaxime **5**

Compound **5** was synthesized by applying the same procedure as compound **3** except introducing (0.01mol, 4.55 g) of cefotaxime instead of sulfamethoxazole[27]. The formed precipitate was then filtered, dried, and recrystallized using acetone.

2.6. 4- [N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonamide sulfamethazine **6**

Compound **6** was synthesized by applying the same procedure as compound **3** except for introducing (0.0lmol, 2.78g) sulfamethazine[27]. The formed precipitate was then filtered, dried, and recrystallized using ethanol.

2.7. Bis [4-(N-(3`,4`-dimethyl maleimidyl) phenyl sulfonamide] trimethoprime **7**

Compound **7** was synthesized via a reaction between (0.02mol, 5.99g) of compound **3** and (0.01mol, 2.90g) of trimethoprime applying the same procedure as compound **3**[27]. The formed precipitate was then filtered, dried, and recrystallized using ethanol.

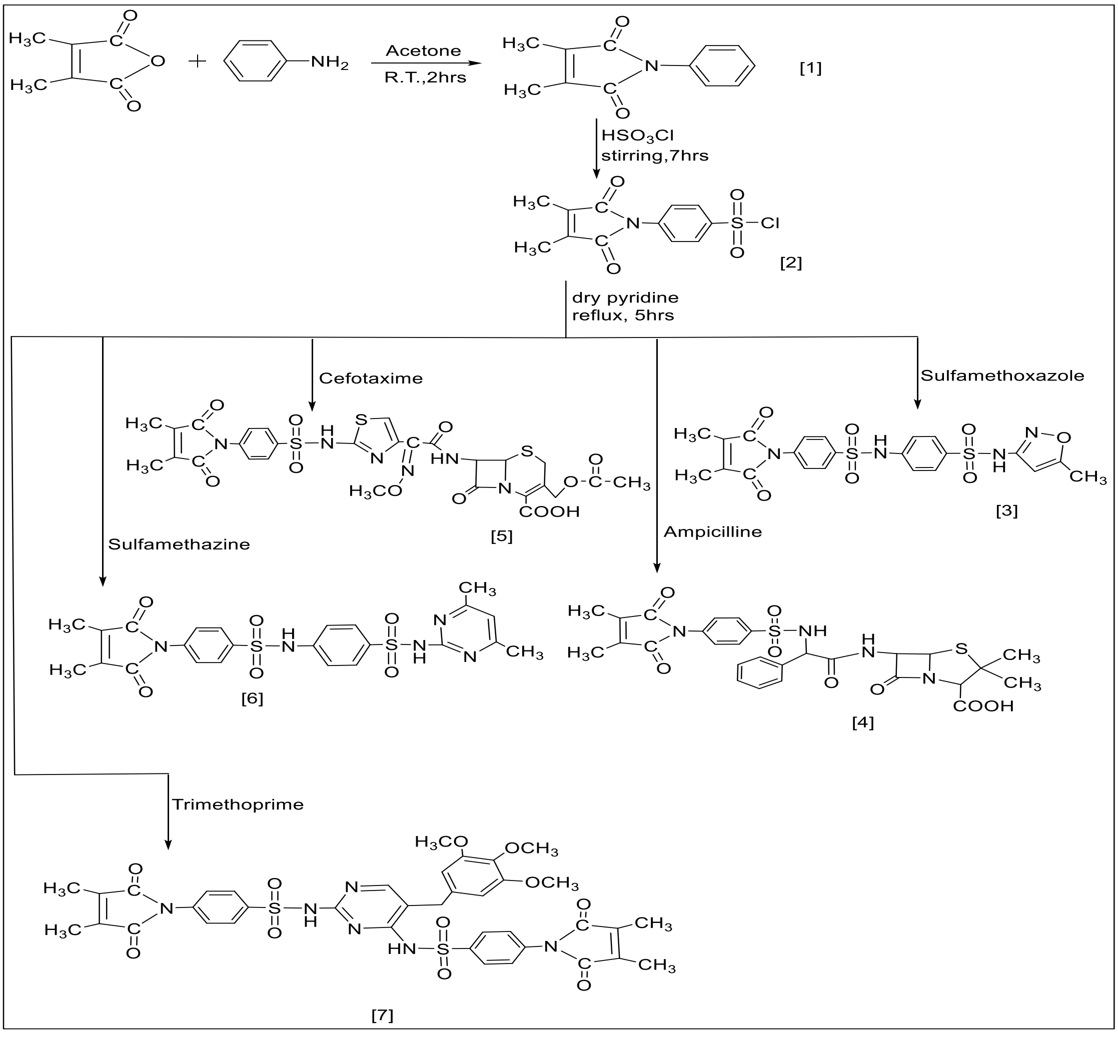
3. Results and Discussion

Multidrug resistance among various bacteria and fungi posed a major problem, necessitating the development of new antibiotic drugs with greater efficacy. Thus, the current research targeted synthesizing and designing newly developed compounds.

This target was made by choosing five well-known drugs, including Sulfamethoxazole, ampicilline, cefotaxime, sulfamethazine, and trimethoprim, then introducing the biologically active components 3,4-dimethyl maleimide and sulfonamide in their molecules producing newly developed compounds. It is expected that the presence of two active moieties beside the initial drug will enhance the biological activity of the newly developed compounds.

The synthetic stages followed in this work are outlined in Scheme 1, which consists of two key steps. The initial step involved a reaction between 3,4-dimethyl maleic anhydride and aniline, generating compound (1), N-phenyl-3,4-dimethylmaleimide. This compound was then subjected to a reaction with chlorosulfonic acid in the second step, producing compound (2), 4-[N-(3,4-dimethylmaleimidyl) phenyl] sulfonyl chloride. The synthetic approach thus entailed a two-step procedure starting from 3,4-dimethyl maleic anhydride, where the first step formed the N-phenyl-3,4-dimethylmaleimide intermediate, which was then further transformed by reaction with chlorosulfonic acid to yield the final target compound. Compound (2) is the key compound in this work from which the desired compounds (3-7) are built by introducing it in reaction with five well-known drugs producing the target compounds .Table (1) includes a list of the physical properties of the prepared compounds (1) and (2), whereas Table (2) includes the physical properties of the developed compounds (3–7).

In order to determine the chemical structures of the produced compounds, FTIR, ^{1}H-NMR, and ^{13}C-NMR spectral data are utilized.



Scheme 1: Synthetic steps for preparation of 4-[N-(3`,4`-dimethyl maleimidyl)] phenyl sulfonamide compounds [3-7]

The FTIR spectra of compound **1** exhibited distinct absorption peaks at (1760), (1701), (1595), and (1394) cm^{-1}, which are owing to asymmetric ʋ (C=O) imide, symmetric ʋ (C=O) imide,
ʋ (C=C) and ʋ (C-N) imide respectively[28].

The FTIR spectra of compound **2** exhibited distinct absorption peaks at (1764), (1710), (1589, 1500), and (1388) cm^{-1}, which can be owing to the asymmetric ʋ (C=O) imide, symmetric
ʋ (C=O) imide, ʋ (C=C), and ʋ (C-N) imide, respectively.
Moreover, the spectra indicated two new peaks of absorption at (1369) and (1176) cm^{-1} due to asymmetric ʋ (SO_2) and symmetric ʋ (SO_2), and this indicates success in the preparation of compound **2**. Besides, the positive result for the sulfur test after the fusion of compound 2 with sodium gave another proof of the successful preparation of compound **2.**
Finally, FTIR spectra of developed compounds **3-7** exhibited absorption peaks at (3330-3101), (1768-1760), (1712-1706), (1598-1535) and (1394-1386) cm^{-1}. These absorption peaks correspond to the ʋ (N-H), asymmetric ʋ (C=O) imide, symmetric ʋ (C=O) imide, ʋ (C=C) and ʋ (C-N) imide respectively[28]. Besides, the spectra also exhibited distinct peaks at (1394-1321) and (1197-1159) cm^{-1}, which can be caused by asymmetric ʋ (SO_2) and symmetric ʋ (SO_2).
Moreover, FTIR spectra of compounds **3**, **5**, **6,** and **7** appear to peaks at (1660-1600) owing to ʋ (C=N).

The FTIR spectrum of compound **4** revealed several distinctive absorption bands. Specifically, a band at (3398) cm^{-1} was attributed to the (O-H) stretching vibration of the carboxyl group. A band at (1760) cm^{-1} corresponded to the (C=O) stretching vibration of the lactam ring. Another band at (1674) cm^{-1} was associated with the (C=O) stretching vibration of the carboxyl group. Lastly, a band at (1664) cm^{-1} was indicative of the (C=O) stretching vibration of the amide group. These spectral features provide structural information about the functional groups present in compound **4**. Other absorption peaks in compound **5** were found at (3429), (1753), (1677), (1635) and (1220, 1128) cm^{-1} which were induced by ʋ (O-H) carboxyl, (1753) cm^{-1} ʋ (C=O) lactam which overlap with ʋ (C=O) ester,
ʋ (C=O) carboxyl, ʋ (C=O) amide and ʋ (C-O) ester receptively.

In compound **7,** FTIR spectrum bands were exhibited at (1128) cm^{-1} and (1033) cm^{-1} owing to asymmetric and symmetric ʋ (C-O) ether. The FTIR spectrums of compounds **1** and **2** are shown in Table 3, and those of compounds **3-7** are shown in Table 4.
^{1}H-NMR and ^{13}C-NMR spectra are also used in this work to prove the chemical structures of the prepared compounds.
Compounds **1** and **2** exhibited ^{1}H-NMR spectra with signals at (δ =1.90-1.95) ppm, which correspond to two CH_3 protons, whereas signals at (δ =7.26-7.69) ppm, which correspond to aromatic protons. ^{13}C-NMR spectra of these compounds showed signals at (δ = 15.8-16.5), (121.07-146.55), and (166.80-170.92) ppm, which refer to methyl, vinylic, aromatic, and (C=O) imide carbons respectively[29].
^{1}H-NMR spectra of compounds **3**, **6**, and **7** showed signals at (δ =1.8-1.93), (6.55-8.07), and (8.30-10.9) ppm, which belong to protons of two CH_3 in imide ring, aromatic protons, and NH protons. Compounds **3** and **6** displayed ^{1}H-NMR spectra with signals at (δ =2.1-2.21) ppm, representing protons of the CH_3 groups in the developed compounds moiety. In contrast, the ^{1}H-NMR spectra of compound **7** showed signals at (δ = 3.53-3.6) ppm corresponding to protons of the benzylic CH_2 group and three CH_3 groups.

The ^{13}C-NMR spectra of compounds **3**, **6**, and **7**, on the other hand, revealed that signals at (δ = 16.5-25.49) ppm correspond to carbons of CH_3 linked to the imide ring, while signals at (δ = 95.75-161.49) ppm correspond to aromatic and vinyl carbons, signals at (δ = 157.87-167.68) ppm correspond to carbons (C=N), and signals at (8=170.21-171.16) ppm correspond to (C=O) imide carbons[29].

^{13}C-NMR spectra of compounds **3** and **6** appear signals at (δ =12.31-12.32) and (23.02-23.46) ppm owing to carbons of CH_3 groups present in developed compounds moiety while ^{13}C-NMR spectrum of compound **7** displayed signals at (δ =32.52) ppm corresponded to benzylic carbon and signals at (δ=56.26, 60.34) ppm belong to carbons of three OCH_3 groups. Tables **5** and **6** provide details on the ^{1}H-NMR and ^{13}C-NMR spectra of the produced compounds.

Table 1: Some physical properties of the prepared compounds **1** and **2**

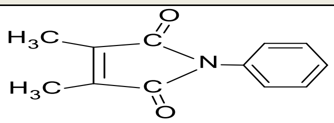
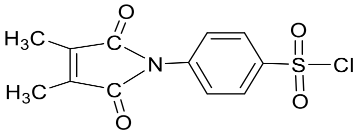
Comp. No.	Compound Structure	Color	Yield %	Melting point °C	Recrystallization Solvent
1		Off white	93	50-52	Ethanol
2		white	81	185-187	Ethanol

Table 2: Some physical properties of the prepared compounds **3-7**

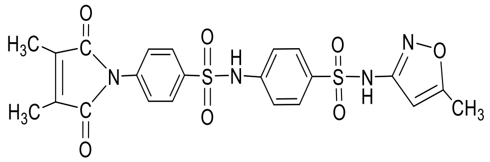
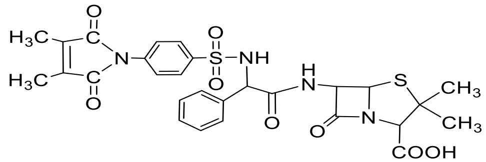
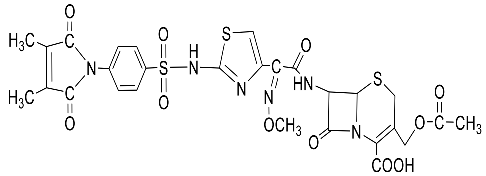
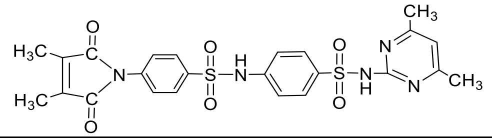
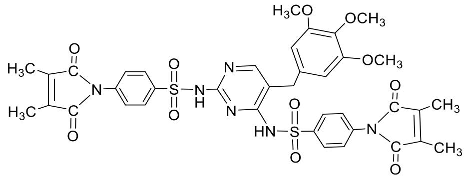
Comp . No.	Compound Structure	Color	Yield %	Melting point °C	Recrystallization Solvent
3		White	77	212-214	Ethanol
4		Yellow	82	140-142	Dioxane
5		Brown	80	160-162	Acetone
6		White	84	188-190	Ethanol
7		Off white	89	200-202	Ethanol

Table 3: Characteristic FT-IR spectral data (υ, cm^{-1}) of compounds **1, 2**

Comp. No.	υ(C-H) Aromatic	υ(C-H) Aliphatic	υ(C=O) Imide	υ(C=C)	υ(C-N) Imide	υ (SO2) asym.	υ (SO2) sym.
1	3049	2989 2923 2850	1760 (asym.) 1701 (sym.)	1595	1394	-	-
2	3062	2989 2921 2850	1764 (asym.) 1710 (sym.)	1589 1500	1388	1369	1176

Table 4: Characteristic FT-IR spectral data (υ, cm^{-1}) of compounds **3-7**

Comp No.	υ(O-H) Carboxyl	υ(N-H) Amide	υ(C-H) Aromatic	υ(C-H) Aliphatic	υ(C=O) Imide	υ(C=O) Carboxyl	υ(C=O) Lactam	υ(C=O) Amid	υ(C=N)	υ(C=C)	υ(C-N) Imide	υ(SO2)	others
3	-	3249 3157	3053	2923 2852	1766 1710	-	-	-	1618	1593	1388	1338 1163	-
4	3398	3240 3136	3068	2968 2918 2856	1760 1708	1674	1760 (overlap)	1664	-	1598	1390	1330 1161	-
5	3429	3137 3101	3072	2920 2830	1706	1677	1753	1635	1600	1535	1394	1394 (overlap) 1197	υ(C=O) ester 1753 (overlap) υ(C-O) ester 1220 1128
6	-	3330 3299 3128	3053	2989 2958 2880	1768 1712	-	-	-	1649 1631	1595	1386	1367 1348 1164	-
7	-	3325 3186 3163	3072	2945 2839	1766 1708	-	-	-	1660 1641	1593	1394	1344 1321 1159	υ(C-O) ether 1128 1033

Table 5: ^{1}H-NMR spectral data (δ, ppm) of compounds (**1-3,6,7**)

Comp. No.	^{1}H-NMR spectral data (δ, ppm)
1	1.95 (6H,2CH$_3$), 7.33-7.49 (5H, Ar-H)
2	1.90(6H, 2CH$_3$), 7.26-7.69 (4H, Ar-H)
3	1.8 (6H,2CH$_3$), 2.1(3H, CH$_3$ in developed compound moiety) 6.0, 6.5(2H, vinylic protons), 7.2-7.90(8H, Ar-H), 8.4-8.5, 10.9 (2H, NH)
6	1.92(6H, 2CH$_3$), 2.15-2.21 (6H, 2CH$_3$ in developed compound moiety), 6.55-8.07 (8H, Ar H protons and proton in hetero ring), 8.76, 10.36 (2H, NH)
7	1.92-1.93 (12H, 4CH$_3$), 3.53-3.60, 3.71 (2H, CH$_2$ benzylic and 9H, 3OCH$_3$), 6.56-8.03 (10H, ArH and proton in hetero ring), 8.30-8.91, 10.43 (2H,NH)

Table 6: ^{13}C-NMR spectral data (δ, ppm) of compounds (**1-3,6,7**)

Comp. No.	^{1}H-NMR spectral data (δ, ppm)
1	15.8(2CH$_3$), 126.60-137.40 (vinyl and Ar-C), 170.92 (C=O).
2	16.71(2CH$_3$), 121.07-146.55 (vinyl and Ar-C), 166.80-170.80 (C=O).
3	12.31-12.32 (CH$_3$ in developed compound moiety), 16.5(2 CH$_3$ imide), 95.75-142.54 (vinyl and Ar-C), 149.83-155.36 (carbons in oxazole ring), 157.87 (C=N), 170.21-170.24 (C=O).
6	16.67 (2CH$_3$ imide), 23.02-23.46 (2CH$_3$ in developed compound moiety), 106.84-156.37 (vinyl and Ar-C), 167.66-167.68 (C=N), 170.47, 171.16(C=O).
7	25.49 (4CH$_3$) 32.52 (benzylic carbon), 56.26, 60.34 (3OCH$_3$), 100.40-161.49 (vinyl, Ar-C), 164.37-166.85 (C=N), 170.36-170.85 (C=O).

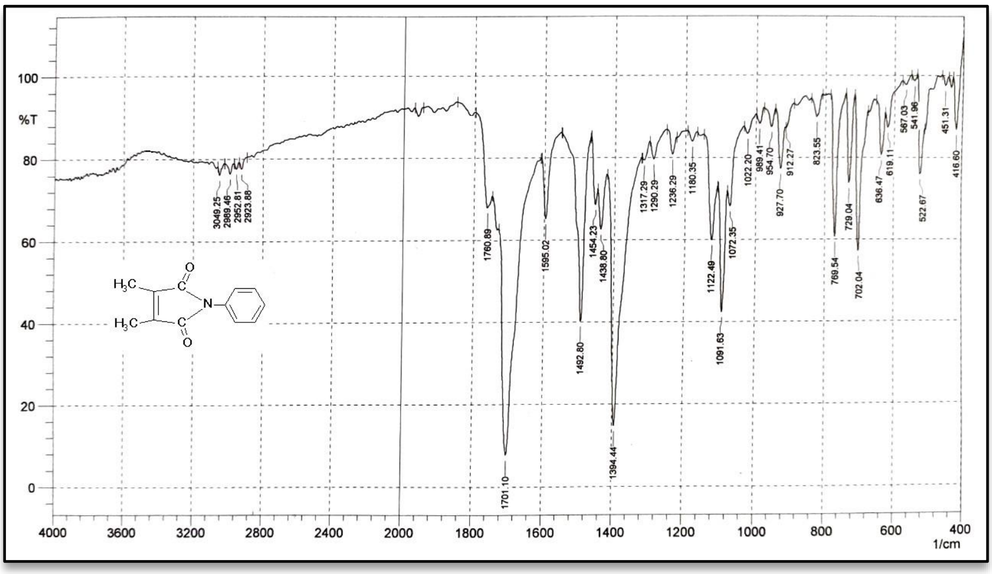


Figure 1 : FT-IR spectrum of compound **1**

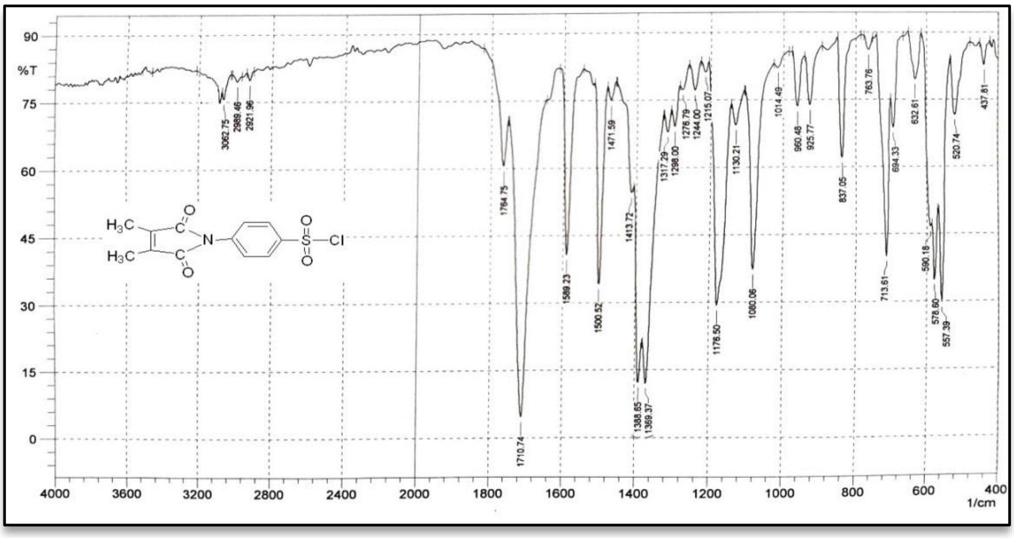


Figure 2: FT-IR spectrum of compound **2**

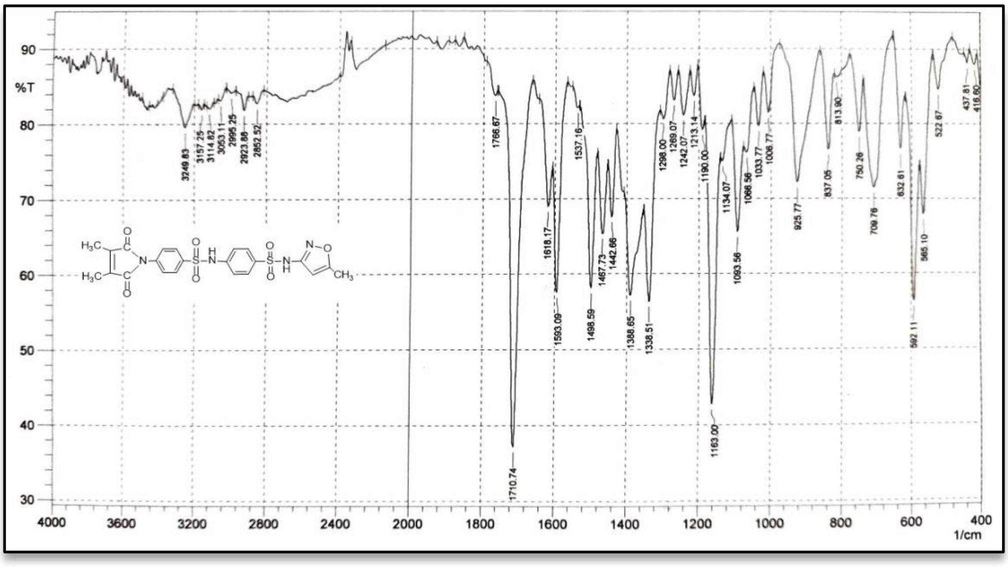
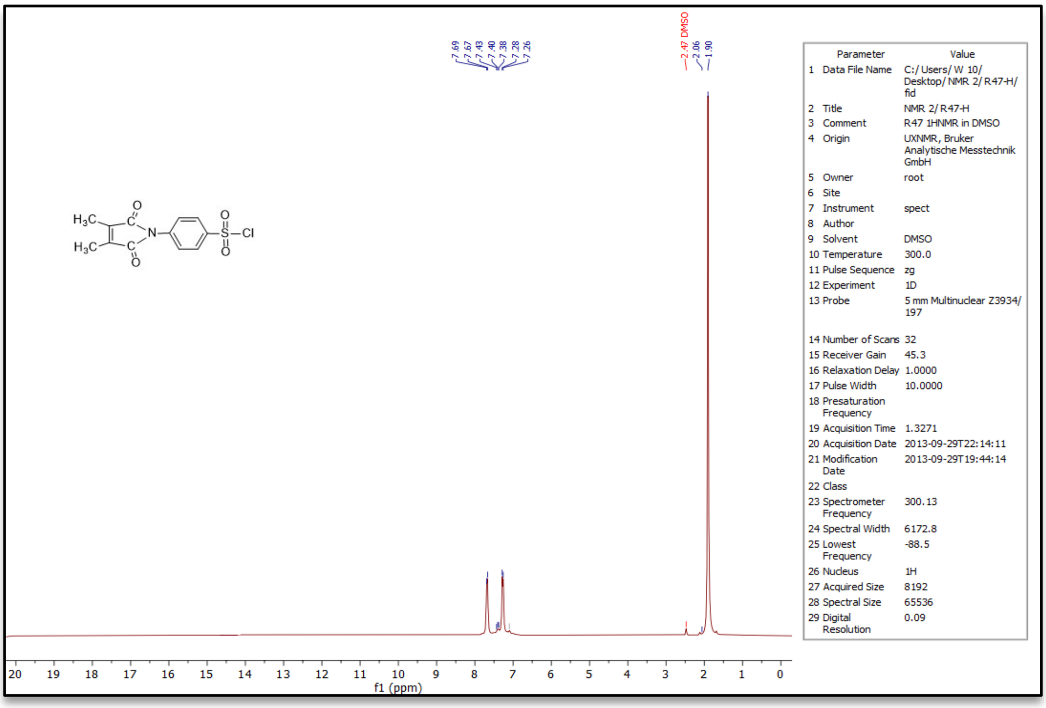


Figure 3 : FT-IR spectrum of compound **3**



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6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
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25	Lowest Frequency	-88.5
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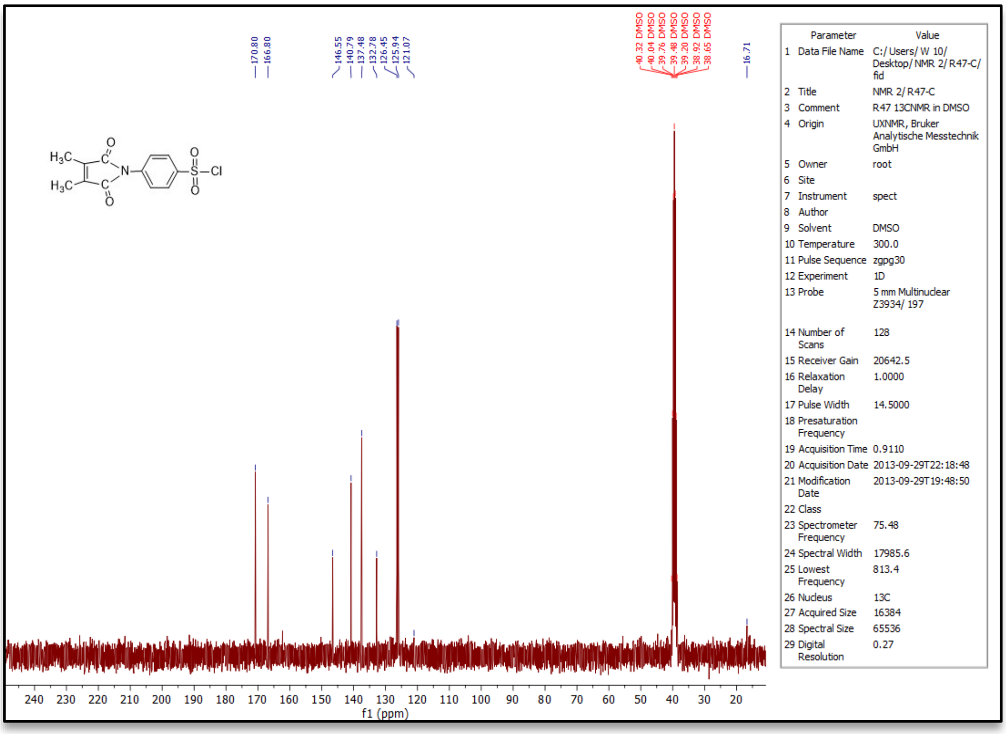
27	Acquired Size	8192
28	Spectral Size	65536
29	Digital Resolution	0.09

Figure 4 : ^{1}H NMR spectrum data of compound **2**



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6	Site	
7	Instrument	spect
8	Author	
9	Solvent	DMSO
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14	Number of Scans	128
15	Receiver Gain	20642.5
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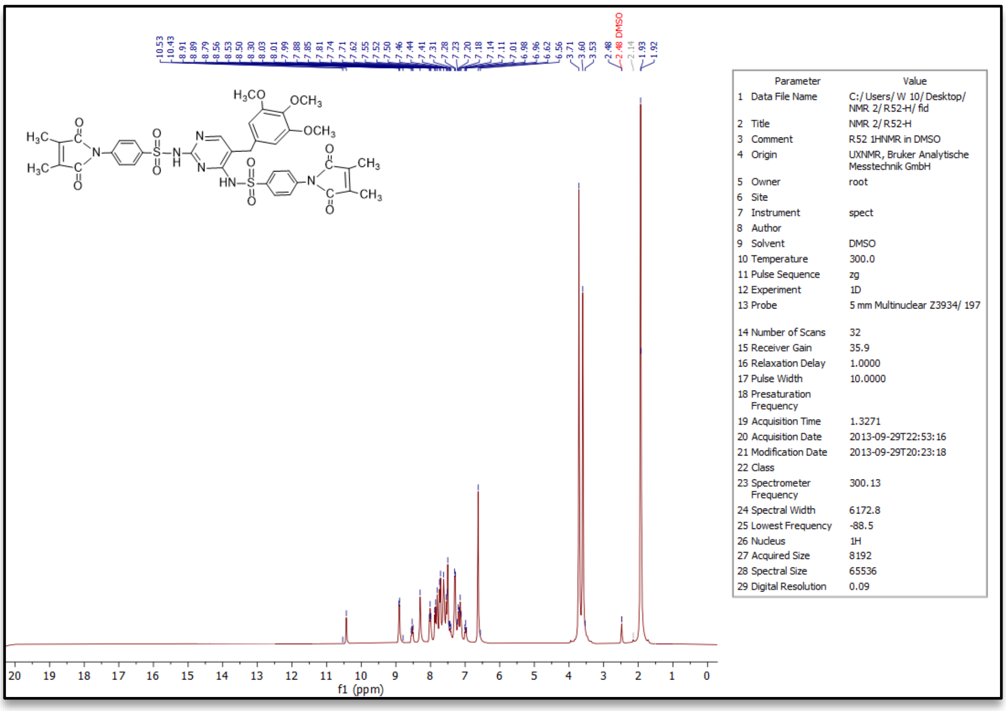
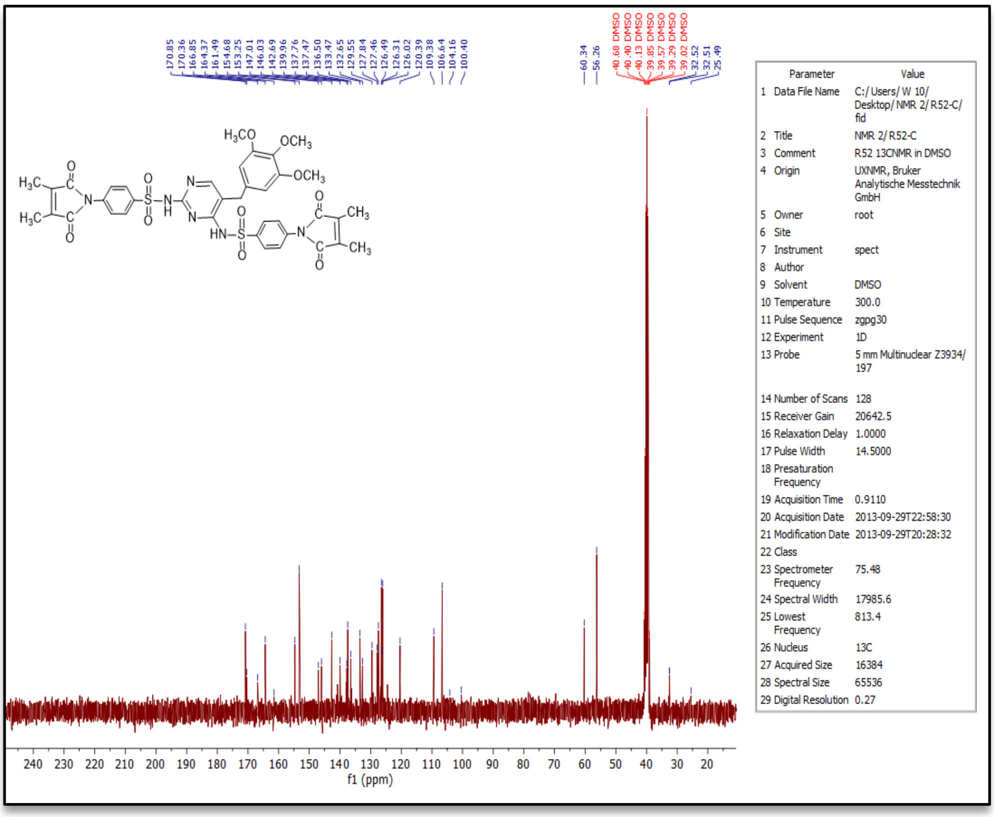
20	Acquisition Date	2013-09-29T22:18:48
21	Modification Date	2013-09-29T19:48:50
22	Class	
23	Spectrometer Frequency	75.48
24	Spectral Width	17985.6
25	Lowest Frequency	813.4
26	Nucleus	13C
27	Acquired Size	16384
28	Spectral Size	65536
29	Digital Resolution	0.27

Figure 5 : ^{13}C NMR spectrum data of compound **2**



Parameter	Value
1 Data File Name	C:/ Users/ W 10/ Desktop/ NMR 2/ R52-H/ fid
2 Title	NMR 2/ R52-H
3 Comment	R52 1HNMR in DMSO
4 Origin	UXNMR, Bruker Analytische Messtechnik GmbH
5 Owner	root
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	DMSO
10 Temperature	300.0
11 Pulse Sequence	zg
12 Experiment	1D
13 Probe	5 mm Multinuclear Z3934/ 197
14 Number of Scans	32
15 Receiver Gain	35.9
16 Relaxation Delay	1.0000
17 Pulse Width	10.0000
18 Presaturation Frequency	
19 Acquisition Time	1.3271
20 Acquisition Date	2013-09-29T22:53:16
21 Modification Date	2013-09-29T20:23:18
22 Class	
23 Spectrometer Frequency	300.13
24 Spectral Width	6172.8
25 Lowest Frequency	-88.5
26 Nucleus	1H
27 Acquired Size	8192
28 Spectral Size	65536
29 Digital Resolution	0.09

Figure 6 : ^{1}H NMR spectrum data of compound **7**



Parameter	Value
1 Data File Name	C:/ Users/ W 10/ Desktop/ NMR 2/ R52-C/ fid
2 Title	NMR 2/ R52-C
3 Comment	R52 13CNMR in DMSO
4 Origin	UXNMR, Bruker Analytische Messtechnik GmbH
5 Owner	root
6 Site	
7 Instrument	spect
8 Author	
9 Solvent	DMSO
10 Temperature	300.0
11 Pulse Sequence	zgpg30
12 Experiment	1D
13 Probe	5 mm Multinuclear Z3934/ 197
14 Number of Scans	128
15 Receiver Gain	20642.5
16 Relaxation Delay	1.0000
17 Pulse Width	14.5000
18 Presaturation Frequency	
19 Acquisition Time	0.9110
20 Acquisition Date	2013-09-29T22:58:30
21 Modification Date	2013-09-29T20:28:32
22 Class	
23 Spectrometer Frequency	75.48
24 Spectral Width	17985.6
25 Lowest Frequency	813.4
26 Nucleus	13C
27 Acquired Size	16384
28 Spectral Size	65536
29 Digital Resolution	0.27

Figure 7 : ^{13}C NMR spectrum data of compound **7**

4. Antimicrobial activity

The newly synthesized compounds were evaluated for both antibacterial and antifungal activities. Antibacterial activity study was performed against *staphylococcus aureas* (gram-positive bacteria) and *E-coli* (gram-negative bacteria) while antifungal activity study was performed against *Candida Albicans* fungi.

Antibacterial activity of reference drugs (Sulfamethoxazole, Ampicillin, Sulfamethazine and Trimethoprim) (against the same bacteria) were evaluated and antifungal activity of Fluconazole against *candida Albicans* fungi was evaluated also and the results are used for comparison.

When comparing the antimicrobial efficacy of the newly synthesized compounds to that of established reference drugs, it became evident that the new compounds [3, 4, 6, 7] possess very high antibacterial activity against *staphylococcus aureus* bacteria, thus it is higher than the initial drugs, as indicated in Table (7) while the same compounds showed moderate activity against

E-Coli. On the other hand compounds [3] and [4] showed good antifungal activity while compound [6] showed high antifungal activity and compound [7] showed very high antifungal activity in comparison with reference drug. All these results are shown in Table (7).

Table 7: Antibacterial and antifungal activities of the tested prepared compounds (**3,4,6,7**) based on the inhibition zone (mm)

No.	**Inhibition zone**		
	Staphylococcus aureus	***Escherichia coli***	***Candida albicans***
3	31	12	16
4	30	13	15
6	23	15	20
7	29	14	33
Sulfamethoxazole	20	17	-
Amoxicillin	21	19	-
Sulfamethazine	19	16	-
Trimethoprim	18	18	-
Fluconazole	0	0	18
DMSO	0	0	0

Conclusion

A multi-step synthetic pathway was employed to synthesize the target compounds. Their resultant FTIR and NMR spectral data corroborated well with anticipated values. Comparison the results of antibacterial and antifungal activity study of the prepared compounds with those of reference drugs indicated clearly that introducing of dimethyl maleimidyl sulfonamido moiety into drug molecules was highly increased their antibacterial activity against *staphylococuss aureas* bacteria and increased their antifungal activity (compounds [6], [7]) against *Candida Albicans* Fungi.

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