Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest

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Received 4 April 2014 ; Accepted 12 June 2014

Abstract

Anew series of chemical compounds derived from 7,8-Dichlorodibenzo [b,d] thiophene-2-carbxylic acid were prepared. Reaction of 7,8-Dichlorodibenzo [b,d] thiophen-2-ethyl ester with hydrazine hydrate yields ,acidhydrazid. Dithiocarbzate prepared by reaction between carbon disulfide and carbahydrazide.4-amino-3-mercapto-1,2,4-triazole Prepared by reaction of thiocarbazate with hydrazine hydrate. Schiff bases prepared by reaction of 4-amino-3- mercapto-1, 2, 4-triazole with different substituted aldehydes. Seven membered ring compounds prepared by reaction of Schiff bases with maleic anhydride. The chemical structures of the products were characterized by (F.T.IR and ^{1}H,^{13}C. NMR), antibacterial activities of some of the prepared compounds were studied against four – kinds of bacterial.

Key Words: synthesis, antibacterial, Derivatives, 1,2,4-triazole, 1,3-oxazenpine, Schiff bases, maleic anhydride.

تحضير مشتقات جديدة من 7, 8 – داي كلورو داي بنزو [b, d] ثايوفين – 2- حامض الكاربوكسليك ذات الفعالية البيولوجية و المهمة صيدلانيا

علي ابراهيم مصطفى

قسم الكيمياء – كلية التربية للعلوم الصرفة – جامعة تكريت, تكريت, العراق

الخلاصة

مجموعة جديدة من المركبات الكيميائية المختلفة المشتقة من 8,7–دايكلورودايفنيل [b,d] ثايوفين -2- حامض الكاربوكسيليك تم تحضيرها من تفاعل 8,7 - دايكلورودايفنيل [b,d] ثايوفين -2- مثيل استر مع الهايدرازين هيدريت قد انتج الكاربوهيدرازايد, وتم تحضير مادة الثايوكاربازيت من تفاعل الكاربون داي سلفايد مع الكاربوهايدرازايد, كما تم تحضير مادة 4- امينو –3مركبتو 4,2,1- ترايازول من تفاعل الثايوكاربازيت مع الهايدرازين هايدرايت .كما تم تحضير قواعد شيف من تفاعل بعض الالديهايدات المعوضة مع 4- امينو -3- مركبتو-4, 2,1-ترايازول ,وكذلك تم تحضير عدد من مركبات الحلقة السباعية من تفاعل قواعد شيف المحضرة من التفاعل الالديهايدات المعوضَة مع 4- امينو-3- مركبتو 4,2,1 ترايازول مع انهدريد حامض الماليك.تم تشخيص المركبات المحضرة باستخدام اطياف الاشعة تحت الحمراء (FTIR) والرنين النووي المغناطيسي [^{1}H, ^{13}C NMR] كما تم دراسة الفعالية المضادة للبكتريا لنماذج منها ضد (اربعة انواع) مختلفة من البكتريا.

الكلمات الدالة: تحضير ،مضاد بكتيري، مشتق، 1,3-oxazepine, 1,2,4- triazole, , قواعد شف, maleic anhydride .

Introduction

Large number of 1, 2, 4-triazole-containing ring system have been incorporated into wide variety of therapeutically interesting drug candidates including anti-inflammatory [1,2] (CNS) stimulants, sedatives, anti-anxiety, antimicrobial agents [2,3], and anti-mitotic activity such as fluconazole, intraconazol, voriconazole [5,6]. Molecular hybridization approach is an emerging structural modification tool to design new molecules with improved pharmacophric properties.1,2,4-triazol-based Mycobacterium tuberculosis inhibitors[7] and synthetic natural product –based tricyclic (carbazol, dibenzo [b,d] thiophene) antimycobacterial agents were

integrated in one molecular platform to prepare various novel 1,2,4-triazol and 1,2,3-triazole hybrids using click chemistry. The results of study provided the potential importance of tubercular hybridization and the development of triazole clubbed dibenzo [b,d] thiophene based lead candidates to treat mycobacterial strains infections [8]. 4-Amino-5-substituted 3-mercapto-1,2,4-traizoles are useful intermediates for the synthesis of various condensed 1,2,4-triazolo derivatives. The most widely utilized method for the preparation of these derivatives depends on the condensation of the carboxylic acid hydrazide with carbon disulphide in ethanolic potassium hydroxide to yield the corresponding potassium-3-acyldithaiocarbazate, which are converted to the corresponding 4-amino -5-substituted-3-mercapto-1,2.4-traiazoles via reaction with hydrazine [9,10]. Alternatively, the cyclization of the 3-acyldithaiocarbzates via heating with aqueous potassium hydroxid yields the corresponding 5-substituted-2-mercapto-1,3,4-oxadiazoles, which yield the corresponding 4-amino-5-substituted -3-mercapto-1,2,4-triazoles upon heating with hydrazine [11]. Literatures were expected to obtain reinforcement of biological activities by means of substitution at different positions of 3-substituted-4-amino-5-mercapto-1,2,4-traiazole derivatives [12.13.14], Schiff bases prepared by reaction of 7,8-Diclorodibenzo [b,d] thiophene-1,2,4-triazole with substituted aldehyde and 1,3-oxazepines prepared also by reaction of Schiff bases with maleic anhydride[15].

Experimental

Instruments

Melting points were determined by using (Electro thermal melting point apparatus). Galen Kamp, and remain uncorrected. The (FTIR) spectra were recorded on (Shimadzu Infrared Spectrophotometer) in KBr discs (δcm^{-1}). Melting points, crystallization solvent of percentage yields are listed in a tables (1 – 6). ^{1}HNMR and ^{13}CNMR spectra (DMSO – d_6) were recorded on university of Al albayt, Jordan.

Materials

Some of chemicals used directly while others were purified to obtain the highest purity. Triazole derivatives (Schiff bases and1, 3- oxazepine) prepared from 7, 8-Dichlorodibenzeo [b, d] thiophene carboxylic acid.

1- Preparation of methyl – 7, 8 – dichlorodibenzo [b, d] thiophene – 2 – carboxylate [16]

(4ml) of 98%sulfuric acid was added drop wise with continues stirring to a solution of 7,8-dichlorodibnzo [b, d] thiophene-2- carboxylic acid (4g,0.025mol) in methanol (40ml),and the mixture was heated under reflux for 3hrs.and cooling .The mixture was poured into crushed ice (125 gm) and the precipitated crystalline was filtered, washed with water, followed by10% sodium hydrogen carbonate solution and finally with water and dried to yield (3.75gm) of methy l-7,8-dichlorodibenzo [b,d] thiophene-2- carboxylate. physical properties are listed in table (1) .

2- Preparation of 7,8-dicholorodibenzo [b,d] thiophene-2- carboxylic acid hydrazaide [16]

A mixture of methyl -7,8–dichlorodibenzo [b,d] thiophene-2-carboxylate (3.0gm, 0.02 mol) and 98% hydazine hydrate(6.0 ml) was heated under reflux with stirring for15 hrs. And cooling, dist. cold water(70ml)was added to the mixture and the separated white crystalline was filtered, washed with cold water ,dried and crystalized from water and dried .physical properties are in table(2).

3- Preparation of potassium N-2-(7,8-dichloro di benzo[b, d] thiophen)di thaiocarbazate [17]

Carbon disulphide (0.8ml, 0.005mol) was added drop wise to a solution of 7,8-dichlorodibenzo [b ,d] thiophene -2-carboxylic acid hydrazide (1.6 gm, o.oo5 mol) and potassium hydroxide (0.4 gm,0.005 mol) in ethanol (10 ml), the mixture was stirred at room temperature for 3hrs. Dry ethyl ether (10 ml) was then added to the mixture and the

precipitated solid was filtered, washed with ether and dried at 65 °C for 1hr. physical properties are listed in table (3).

4- Preparation of 5-(7,8-dichlorodi benzo [b,d]thiophene)4-amino-3-mercapto-1,2,4-triazole *(17)*

A mixture of potassium N-(2-7,8-dichlorodibenzo [b,d] thiophene) dithiocarbazate (0.7 gm ,0,0017 mol) and 98% hydrazinne hydrate (0.5 ml) was heated under reflex till the evolution of hydrogen sulphide completely ceased down (about 1hr). cooling. Water (10 ml) was added the mixture was neutralized with 10% hydrochloric acid and allowed to stand for 3 hrs. The separated crude product was filtered, washed with water, dried and Rcrystallized by ethanol. physical properties are listed in table (4).

5- Preparation of 5-(7, dichlorodibenzo[b, d]thiophen) 4- arylideneamino-3-mercapto-1,2,4-triazoles (Schiff bases) *(17)*

A mixture of a appropriate aromatic aldyhyde (0.0005 mol, 0.53 g m) and 5-(7,8-dichlorodibenzo [b, d] thiophene) -4-amino-3-mercapto-1,2,4-triazole (0.005 mol,0.19 gm)in acetic acid (4 ml) was heated under reflux for 4 hrs. Cooling .The separated solid was filtered, washes with cold ethanol (5ml), dried and Rcrystallized. Physical properties are listed in table (5).

6- Preparation of 1,3-oxazepine derivatives of 5-(7,8-dichlorodibenzo[b,d]thiophene)4-arylidene amino-3-mercapto-1,2,4-riazoles.(Schiff bases) *(14)*

A mixture of (0.0003 mol) Schiff bases which was prepared before in table (5), and(0.0003 mol,0.03 gm) of maleic anhydride, was mixed using, 2 drops of glacial acetic acid by fusion reaction with stirring for (5) minute till the color of fussed materials is fixed ,then let the mixture to cool and clean with ethanol. Dried and recrystallized by ethanol. The physical properties are listed in table(6).

Biological testing:

Antimicrobial activity of the compounds (4, 5, 6, 7, 14, 16, 17, 20) was examined by agar diffusion methanol[18], using four different species i.e. *(Escherichia coli, salmonella typhi, pseudomonas auruginosa, staphylococcus aureus)*. The zone of inhibition was measured in mm [19] and is represented by (-), (+), (++), (+++). Depending upon the diameter, the antimicrobial screening upon data are recorded in table (7). The results indicated that all the assayed compounds have activity against the tested organism, but with different effects of sensitivity using three antibiotics (Amoxicillin, Metheprim, Gentamycin) to compare between the different species activity used (*E. coli, salmonella typhi, pseudomonas auruginosa, staphycococuse aureus).*

Results and discussion

1- FTIR spectral

In this research the starting material is 7,8-Dichlorodibenzo [b, d] thiophen-2-carboxylic acid, from which after esterification 7,8- Dichlorodibenzo [b, d] thiophen-2- carbazide (compound2) and 7,8- Dichlorodibenzo [b, d] dithio carbazate, then the important derivative 7,8- Dichlorodibenzo -2-amino -3-mercapto-1,2,4-triazole is prepared (compound 4).

a. Compound (4) by using FTIR spectral [20, 21] 1,2,4-triazole is identified in which stretching band at (3238 cm^{-1}) for (N-H) and also there is a band at 2586 cm^{-1} for (-SH) group, also strong and obvious band for (-C=N) bond in triazole ring appear in (1525-1608 cm^{-1}) and another sharp and strong band for(-C-N) in triazole ring appear at (1296 cm^{-1}), and middle strong band belong to (-N-N-) in triazole ring at (1045 cm^{-1}) and absorption band at (634 cm^{-1}) for (C – Cl) stretching band. (Figure 1).

b. Compound (6): is prepared as-1,2,4-triazole derivative by Schiff base reaction, by using FTIR spectral to identified the compound, in which stretching band absorption for (-C=N-)

bond at (1525cm^{-1})for Schiff base bond, also absorption band at (2497-2584 cm^{-1}) for band stretching (-SH) as a weak band, also absorption bands in range of(1525-1608 cm^{-1}) for stretching band of (-C=N-) in triazole ring, and another band in range of (1232-1278 cm^{-1}) for (-C-N) band stretching, also absorption bands in a range of(819-1086 cm^{-1}) belong to (-N-N-) bond stretching in triazole ring, and also another bands for benzene ring substitution for example (C – Cl) bond at 696 cm^{-1}, and aband in arrange of (2930-3050 cm-1) for (CH_3) group, and absorption band at (2584 cm^{-1}) for (-SH) stretching band. (Figure 2).

c. Compounds (15): 1,3-oxazepine compounds are prepared by a mixture of Schiff base of 1,2,4-triazole with maleic anhydride in presence of drops of acetic acid by fusion reaction, some compounds prepared are identified by FTIR spectral, compound(15) is example for identification, so that absorption bands appears in (1022 – 1159 cm-1) belong to (C-N) band stretching and another in (1579-1640 cm^{-1}) for (C=O) stretching band, in addition to two absorption bands in a range of (1222-1278 cm-1) and (1579-1600 cm^{-1}) for (C=C) aromatic stretching bond with absorption band in (1222-1278 cm^{-1}) for (C-O) stretching bond, and absorption band at(690 cm^{-1}) for (C-Cl) and absorption band at(2657 cm^{-1}) for (-SH) stretching band. (Figure 3).

2- ^{1}HNMR and ^{13}CNMR spectral

The^{1}HNMR and ^{13}CNMRspectral compounds prepared are studying with using (DMSO-d_6) solvent and TMS (tetra methyl silane) and using standard (δ. ppm).

a. Compound (4): ^{1}HNMR spectral of compound (4) single band of compound observed at (5.53 ppm) with integration corresponds to two protons due two protons of amine group, with wide band (7.3 ppm) due to the protons of the aromatic ring with integration corresponds to five protons, also another single bond at (13.5 ppm) with integration corresponds to one proton for (-SH) group, with appear some humidity of the solvent in a range of (3.4-4.0 ppm). (Figure 5).

^{13}CNMR: 38.72, 39.0, 39.27, 39.55, 39.83, 40.11, 40.39 (dibenzo [b, d] thiophene), 126.72, 128.42, 128.79 (Ar-C), 151.25, 154.29 (triazole C-5 and CH=N),163.2 (Triazole C-3). (Figure 6).

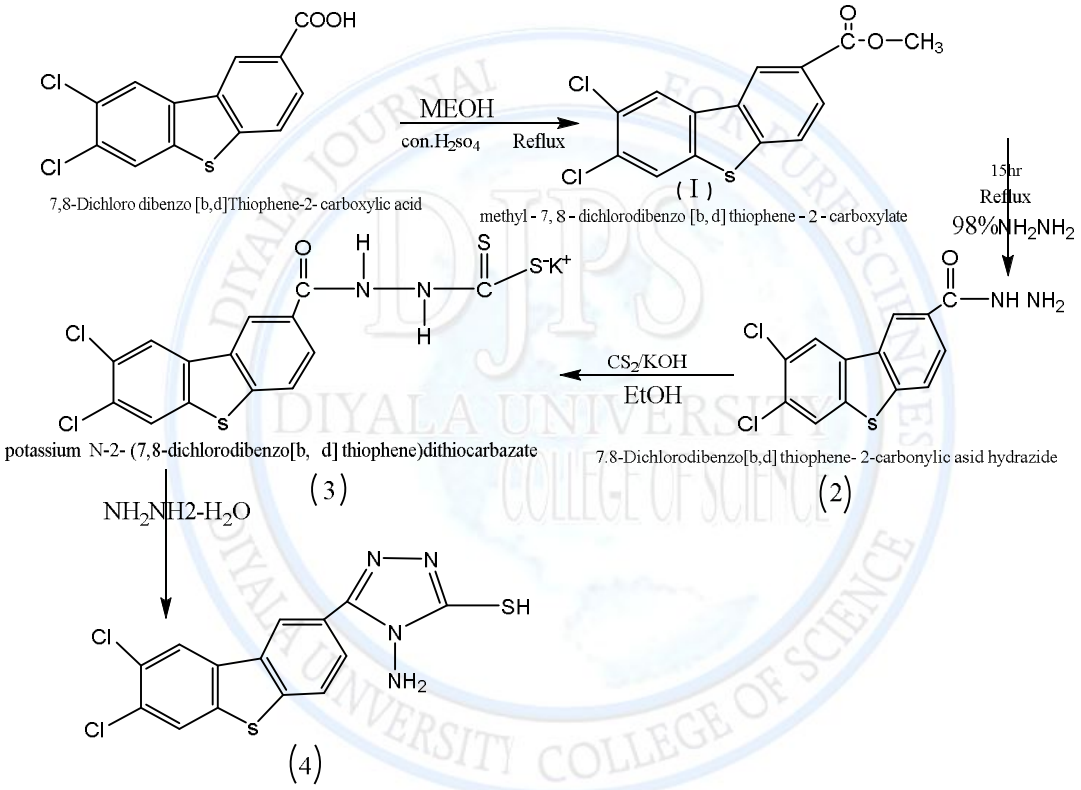
c. Compound (11): ^{1}HNMR spectrum of compound (11) single band unfragment at (10.3 ppm) belong to (-N=C-H-) proton with appearing multiple bands at a range of (7.29-8.15 ppm) related to aromatic protons, in addition to appearing of single band at 13.5 ppm related to (SH) group, and single bands at (3.3-3.8 ppm) to (4.0-4.2 ppm), (5.5 ppm) belongs to (-C-H) group, with appearing some humidity for the solvent in a range (0.8-2.7 ppm). (Figure 9).
^{13}CNMR spectrum of compound (11): 122.4, 126.5, 126.7, 126.8, 128.1, 128.4, 128.49, 128.6 128.79, 128.8, 130.8, 133.97, 134.49, 135.0, 135.4, 148.3 (for benzo thiophenE and benzene), 150.5, 151.2, 159.5 (-1,2,4-triazol C-5 and CH=N), 161.6, 165.9 (Triazole C-3). (Figure 10).

b. Compound (14): ^{1}HNMR spectrum of compound (14) shows single band at (3.2 ppm) with integration corresponds to six protons due to (-N(CH_3)$_2$) group, with appearing another band at (4.0-4.3 ppm) with integration corresponds to two protons of aliphatic bond (HC=CH), and other band inclued multiple bands at a range of (6.5-7,8 ppm) belong to protons of aromatic rings, also there is a singl bond at (7.9 ppm) due to protons of 1,3-oxazepine group (-N-C-O) with integration corresponds to one proton, in addition to appearing another band at (13.46 ppm) with integration corresponds to one proton For (-SH) group (figure). (Figure 11).
^{13}CNMR spectrum of compound (14) 128.4, 128.8, 130.2 for (benzo thiophene), 101.5, 111.5 for (benzene), 41.67, 41.8 for (-CH_3), 154.29 (1,2,4-Triazole C-5 and CH=N), 164.5 (1,2,4-Triazole C-3). (Figure 12).

c. Compound (18): ^{1}HNMR spectrum of compound (18) show double band at (6.1-6.6 ppm) with integration corresponds to two protons due to (-HC=CH-) group with appearing one multiple band in arrange of (7.2-7.7 bppm) belong to protons of aromatic rings, in addition to appearing two singlet bands every one integration corresponds to one proton in a range of (9.5-10.2 ppm) for two hydroxyl groups, and also another single band appear at 13.8 ppm with integration corresponds to one proton for (-SH) group. (Figure 13).

^{13}CNMR spectrum of compound (18) 102.3, 109.79 (benzene), 126.7, 126.8, 128.29, 128.4, 128.7, 129.7, 135.1, 145.6 (benzo thiophene), 149.9, 160.48 (1,2,4-triazole C-5 and CH=N), 163.24 for (1,2,4-Triazole C-3), 164.8 for (carboxyl and –C=C). (Figure 14).

The path ways preparation of the prepared compounds



Scheme (1):

Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest

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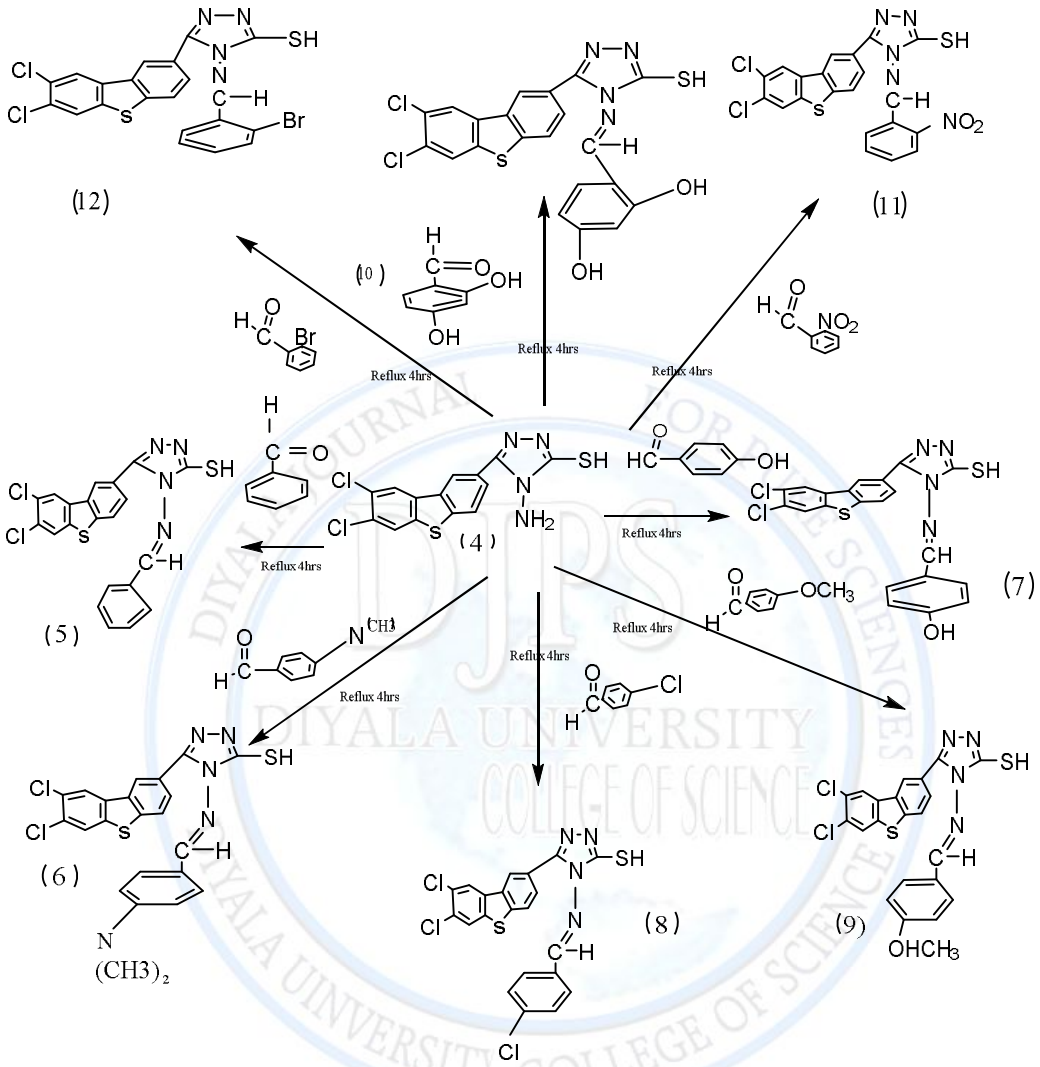
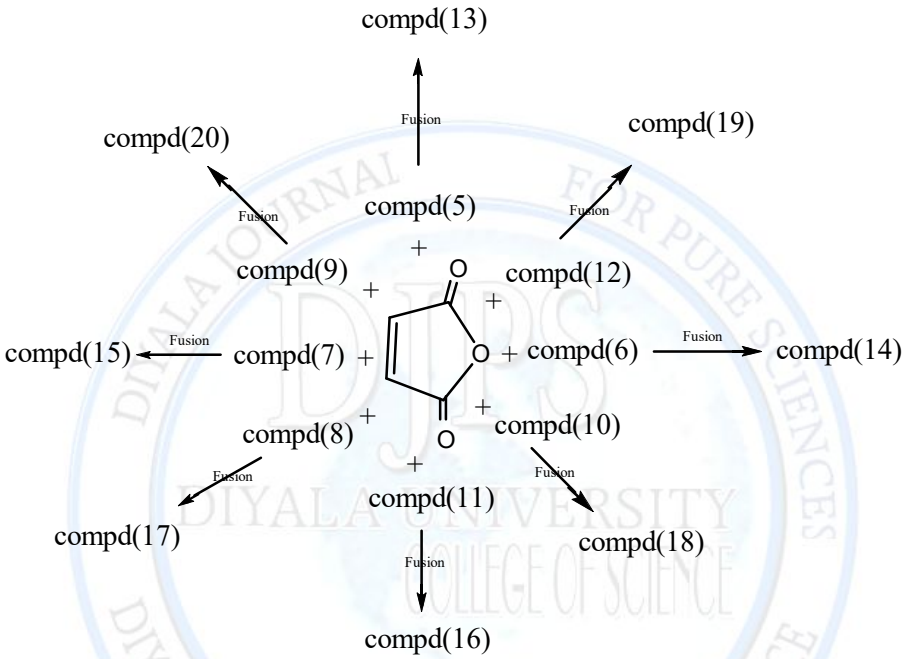


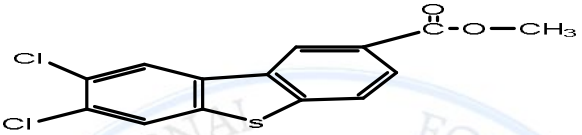
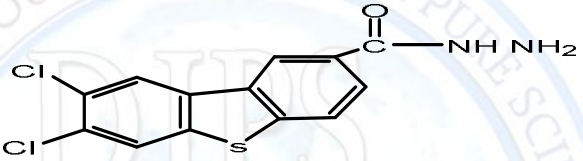
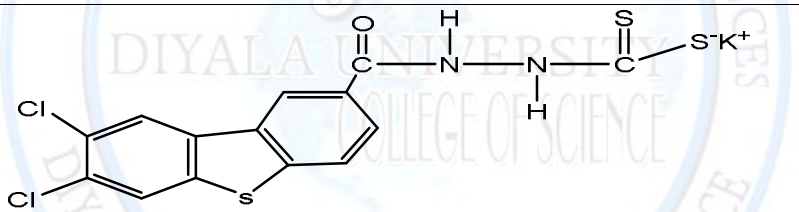
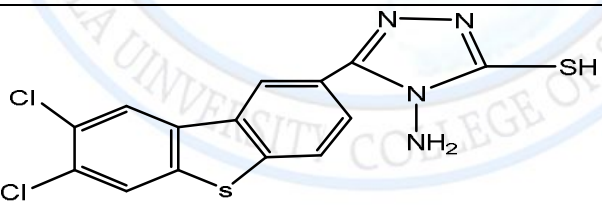
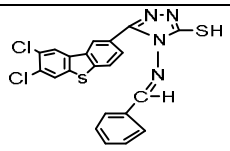
Scheme (2)

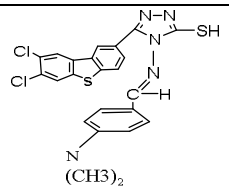
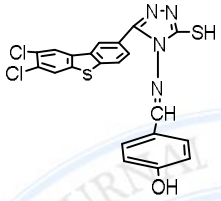
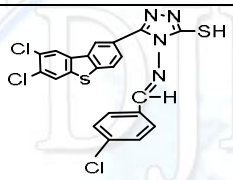
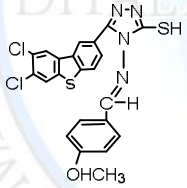
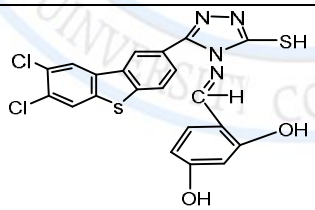
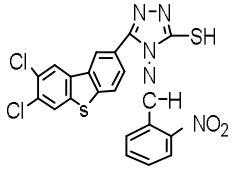
path ways preparation of 5-(7, 8 - dichlorodibenzo [b, d] thiophene)-2-phenyl-4,7-dioxo-4,7-dihydro-1,3-oxazepine derivatives

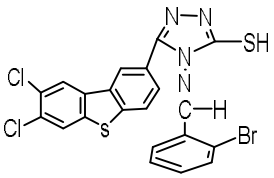
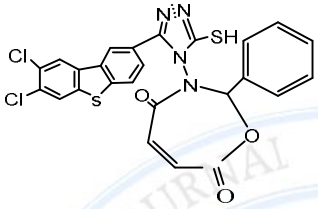
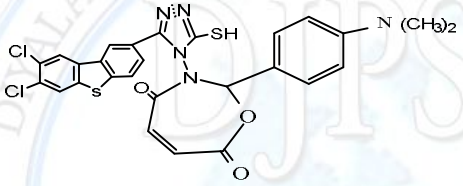
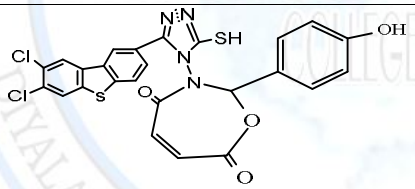
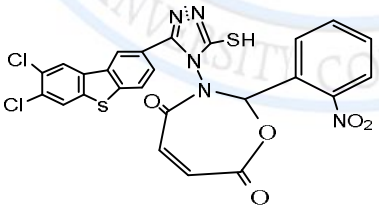


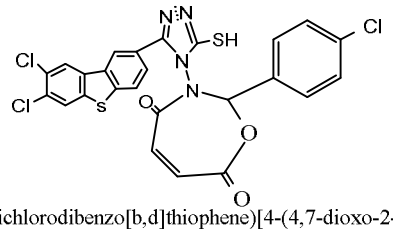
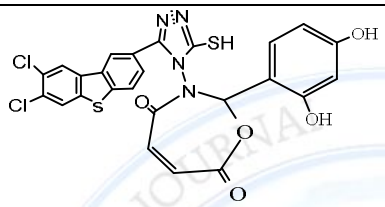
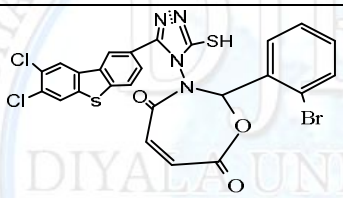
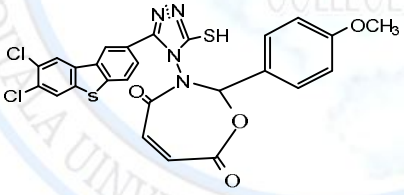
Scheme (3)

The prepared Compounds

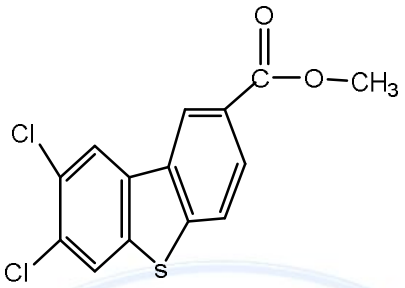
Compd №	Chemical structure
1	 methyl - 7, 8 - dichlorodibenzo [b, d] thiophene - 2 - carboxylate
2	 7.8-Dichlorodibenzo[b,d] thaiophen 2-carbonylic acid hydrazide
3	 potassium N-2-(7,8-dichloro di benzo[b, d] thiophen)di thiocarbazate
4	 5-(7,8-dichlorodibenzo [b,d]thiophene) 4-amino-3-mercapto-1,2,4-triazole
5	 5-(7,8-dichlorodibenzo[b, d]thiophen) 4-(benzylideneamino)-3-mercapto-4H-1,2,4-triazole

6	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[4-(dimethylamine)benzylidne]amino}-3-mercapto-1,2,4-triazole
7	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[4-(hydroxy)benzylidne]amino}-3-mercapto-1,2,4-triazole
8	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[4-(chloro)benzylidne]amino}-3-mercapto-1,2,4-triazole
9	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[4-(meothoxy)benzylidne]amino}-3-mercapto-1,2,4-triazole
10	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[2,4-(dihydroxy)benzylidne]amino}-3-mercapto-1,2,4-triazole
11	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[2-(nitro)benzylidne]amino}-3-mercapto-1,2,4-triazole

12	 5-(7,8 dichlorodibenzo[b, d]thiophene) 4-{[2-(bromo)benzylidne]amino}-3-mercapto-1,2,4-triazole
13	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-phenyl-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
14	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2[4-(dimethylamino)phenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
15	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[4-hydroxyphenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
16	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[2-nitrophenyl]-4,7-dihydro-1,3-oxazepine-3(2H)-yl]

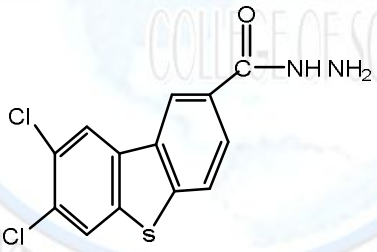
17	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[4-chlorophenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
18	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[2,4-dihydroxyphenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
19	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[2-bromophenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]
20	 5-(7,8-dichlorodibenzo[b,d]thiophene)[4-(4,7-dioxo-2-[4-methoxyphenyl]-4,7-dihydro- 1,3-oxazepine-3(2H)-yl]

Table(1):The physical properties of compound(1)



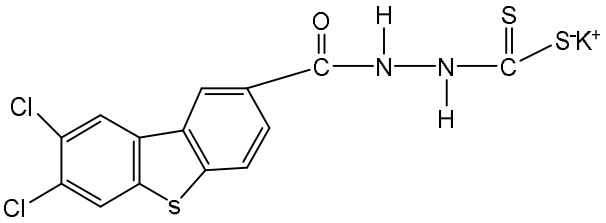
Comp .№	Molecular formula	color	M.P ºc	Yield%	RT	Recryst solvent
1	$C_{14}H_8O_2Cl_2S$	white	76-79	78	3hr	Ethanol

Table(2):The physical properties of compound(2)



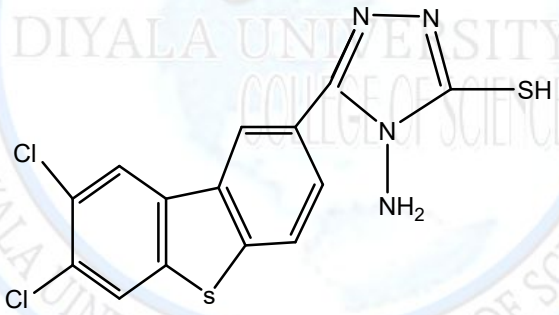
Comp .№	Molecular formula	color	M.P ºC	Yield%	RT	Recryst solvent
2	$C_{13}H_8OCl_2N_2S$	white	116-118	74	15hrs	Ethanol

Table(3):The physical properties of compound(3)



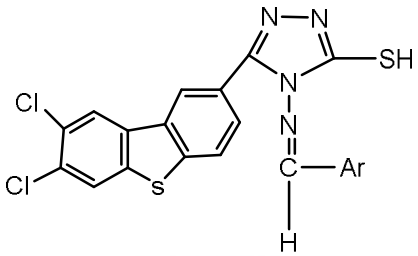
Comp .№	Molecular formula	color	M.P ºC	Yield%	RT	Recryst solvent
3	$C_{14}H_7ON_2S_3Cl_2k$	white	226-227	86	3hrs	Ethanol

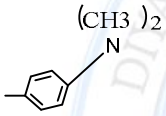
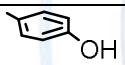
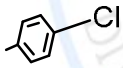
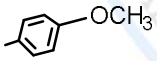
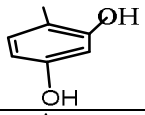
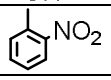
Table(4):The physical properties of compound(4)



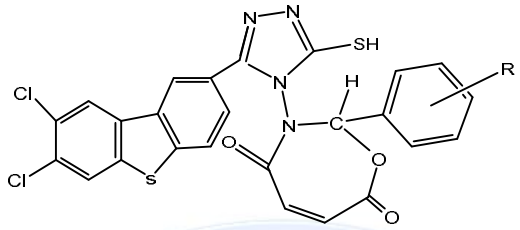
Comp .№	Molecular formula	color	M.P ºC	Yield%	RT	Recryst solvent
4	$C_{14}H_8N_4S_2Cl_2$	white	155-158	71	1hr	Ethanol

Table(5):The physical properties of -1,2,4-triazole shiff base compounds(5-12)



Comp .№	Ar	Molecular formula	Color	M.P ºC	Yield%	RT	Recryst solvent
5		$C_{21}H_{12}N_4Cl_2S_2$	White yellow	178-180	76	5hrs	Ethanol
6		$C_{23}H_{18}N_5Cl_2S_2$	Orange	168-170	66	5hrs	Ethanol
7		$C_{21}H_{13}ON_4Cl_2S_2$	Light metallic	223-224	75	5hrs	Ethanol
8		$C_{21}H_{11}N_4Cl_3S_2$	Light metallic	158-160	58	5hrs	Ethanol
9		$C_{22}H_{14}ON_4Cl_2S_2$	Light yellow	152-155	60	5hrs	Ethanol
10		$C_{21}H_{12}O_2N_4Cl_2S_2$	Light brown	210-212	72	5hrs	Ethanol
11		$C_{21}H_{11}O_2N_4Cl_2S_2$	Pall Yellow	146-148	50	5hrs	Ethanol
12		$C_{21}H_{11}N_4Cl_2S_2Br$	Light metallic	138-140	56	5hrs	Ethanol

Table(6):The physical properties of 7, 8 - dichlorodibenzo [b, d] thiophene-2-phenyl-4,7-dioxo-4,7-dihydro-1,3-oxazepine derivatives compounds (13-20)



Comp .№	R	Molecular formula	Color	M.P	Yield %	Recryst solvent
13	H	$C_{25}H_{14}O_3N_4Cl_2S_2$	White	156-158	61	Ethanol
14	$(CH_3)_2N$	$C_{25}H_{19}O_3N_5Cl_2S_2$	Light orange	160-162	67	Ethanol
15	P-OH	$C_{25}H_{14}O_4N_4Cl_2S_2$	White yellow	198-200	64	Ethanol
16	m-NO_2	$C_{25}H_{13}O_5N_5Cl_2S_2$	Light yellow	159-162	50	Ethanol
17	p-Cl	$C_{25}H_{13}O_3N_4Cl_3S_2$	Melatic	152-154	55	Ethanol
18	o,P-OH	$C_{25}H_{14}O_5N_4Cl_2S_2$	Light green	187-189	63	Ethanol
19	o-Br	$C_{25}H_{13}O_3N_4Cl_2BrS_2$	metalic	190-192	52	Ethanol
20	p-OCH_3	$C_{26}H_{16}O_4N_4Cl_2S_2$	Blacked white	159-162	53	Ethanol

Table(7)Biological testing for some prepared compounds.

Sample №	Concentration Mg/ml	Escherichia coli	Salmonella typhi	Pseudomonas auruginosa	Staphylococcus aureus
4	0.1	++	+	+	++
	0.05	+	-	+	+
5	0.1	+	++	+	+
	0.05	-	+	-	+
6	0.1	++	+	++	+
	0.05	+	-	+	+
7	0.1	++	+	+	+
	0.05	+	-	-	+
14	0.1	++	+	+	++
	0.05	+	+	-	+

16	0.1	+	+	-	-
	0.05	-	_	-	-
17	0.1	++	++	+	++
	0.05	+	-	-	+
20	0.1	++	++	++	++
	0.05	+	-	+	-
Amoxicilin	0.1	+++	+++	+++	+++
	0.05	++	++	++	+
Metheprim	0.1	++	++	+++	+++
	0.05	++	++	++	++
Genta-mycin	0.1	+++	++	+++	+++
	0.05	++	++	++	++

Key symbols;(-) no inhibition (+)=4-7mm,(++)=8-12mm,(+++)=13-25mm

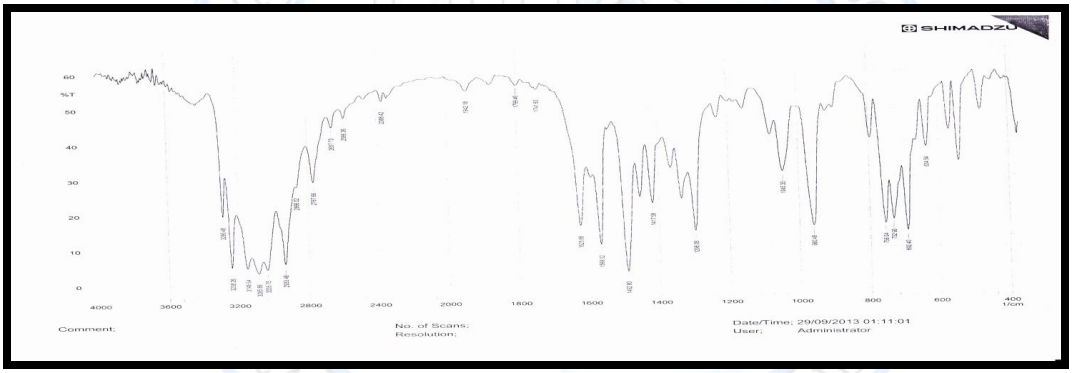


Figure 1: FTIR Compound 4

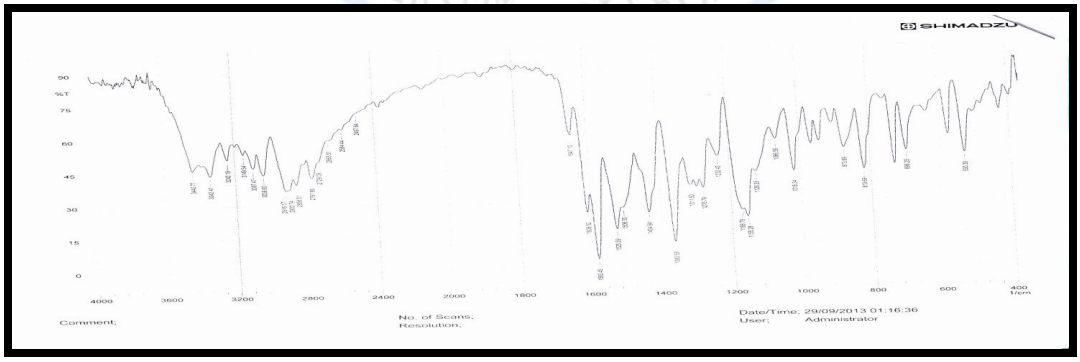


Figure 2: FTIR Compound 6

Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest

Ali .I. Mustafa

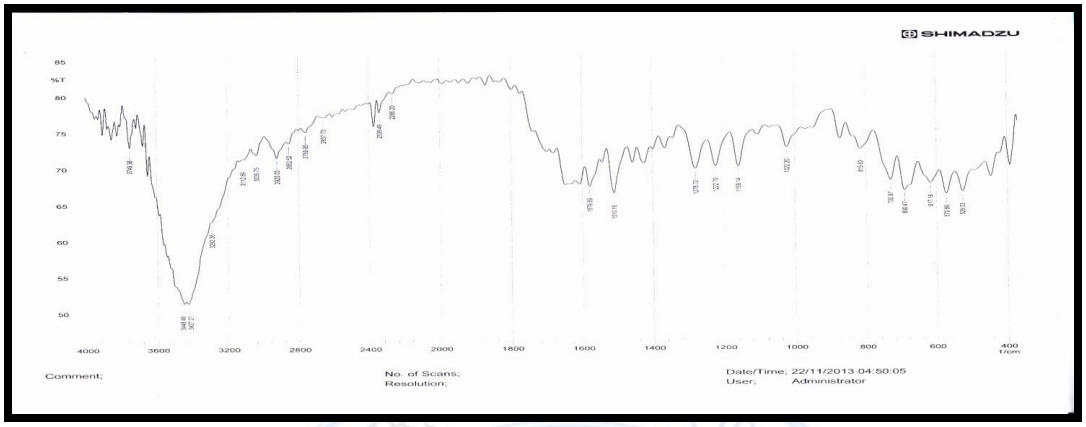


Figure 3: FTIR Compound 15

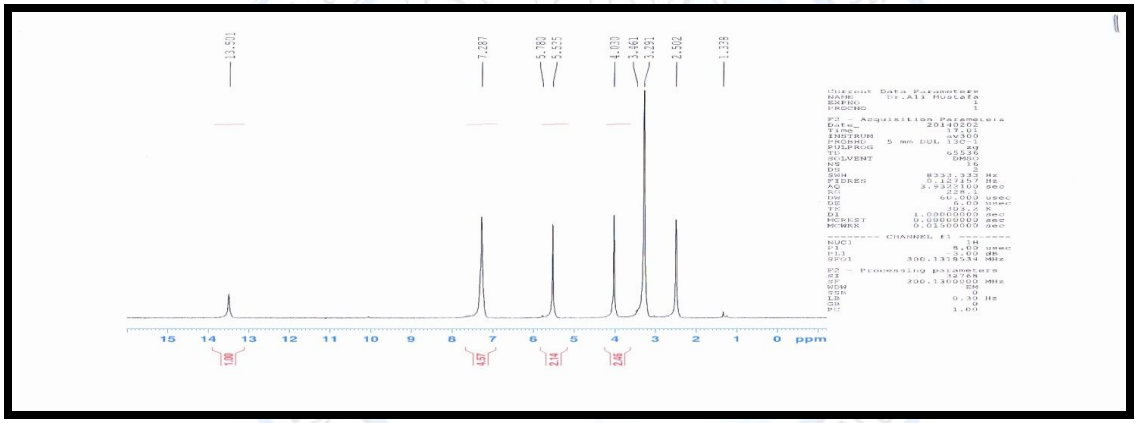


Figure 5: ^{1}HNMR Compound 4

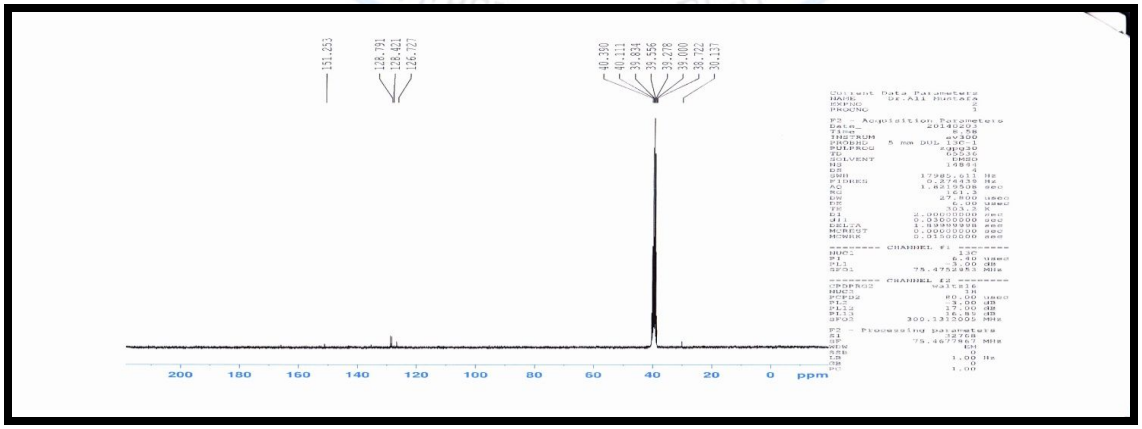


Figure 6: ^{13}CNMR Compound 4

Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest

Ali .I. Mustafa

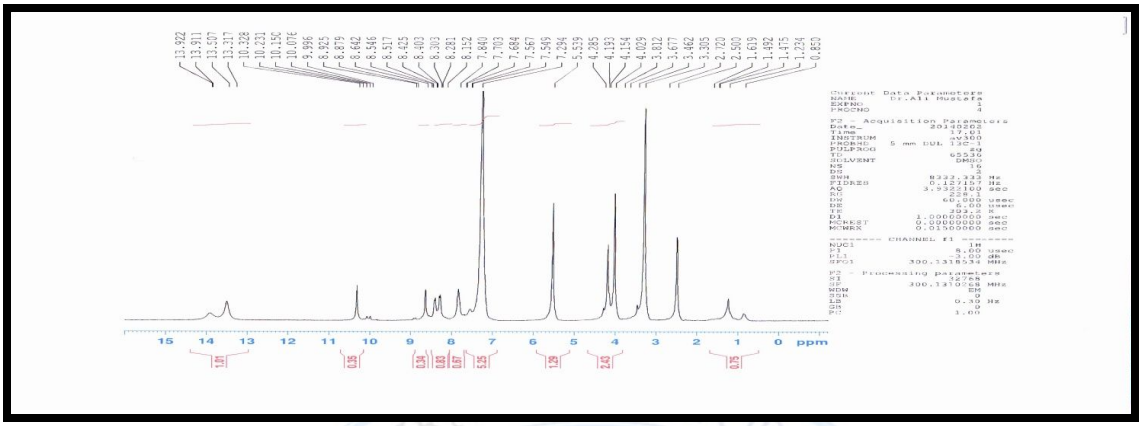


Figure 9: ^{1}HNMR Compound 11

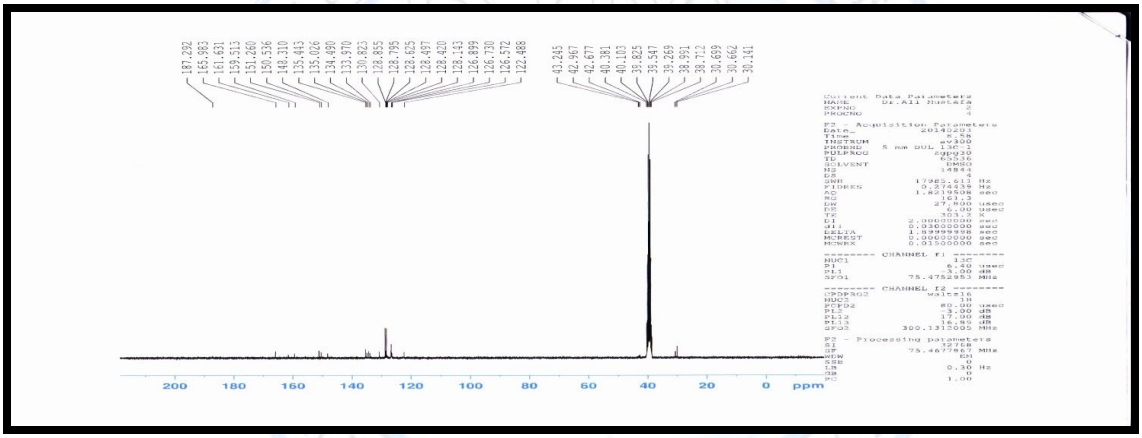


Figure 10: ^{13}CNMR Compound 11

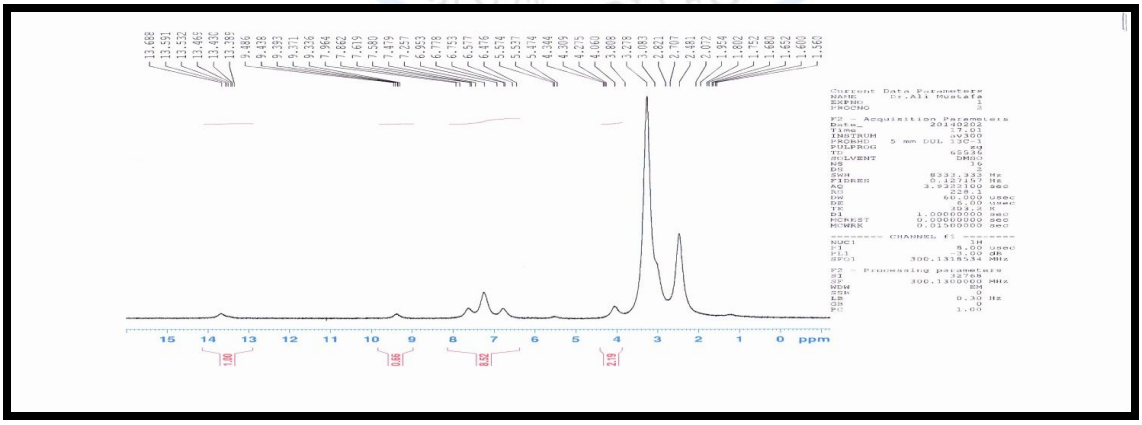


Figure 11: ^{1}HNMR Compound 14

Novel synthesis and antibacterial activities of new derivatives of 7,8-Dichlorodibenzo(b, d)thiophene-2-carboxcyilic acid of pharmaceutical interest

Ali .I. Mustafa

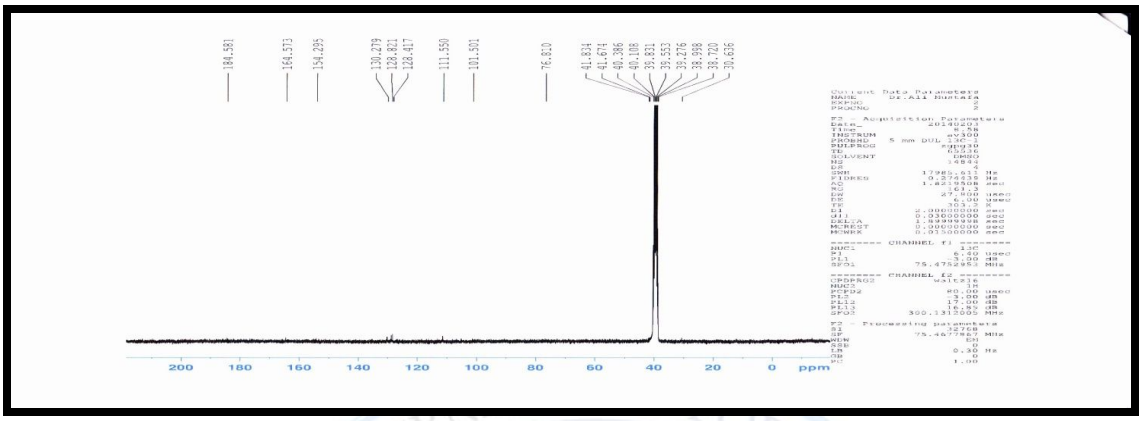


Figure 12: ^{13}CNMR Compound 14

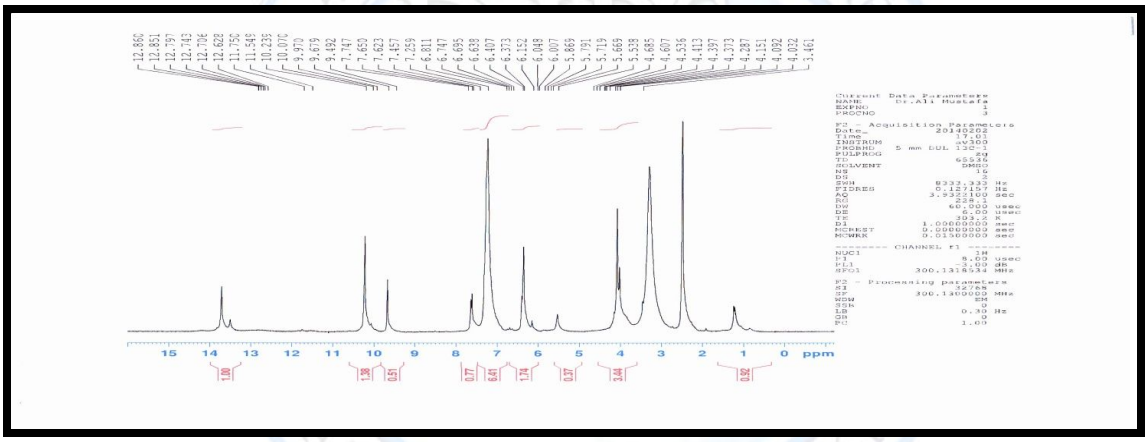


Figure 13: ^{1}HNMR Compound 18

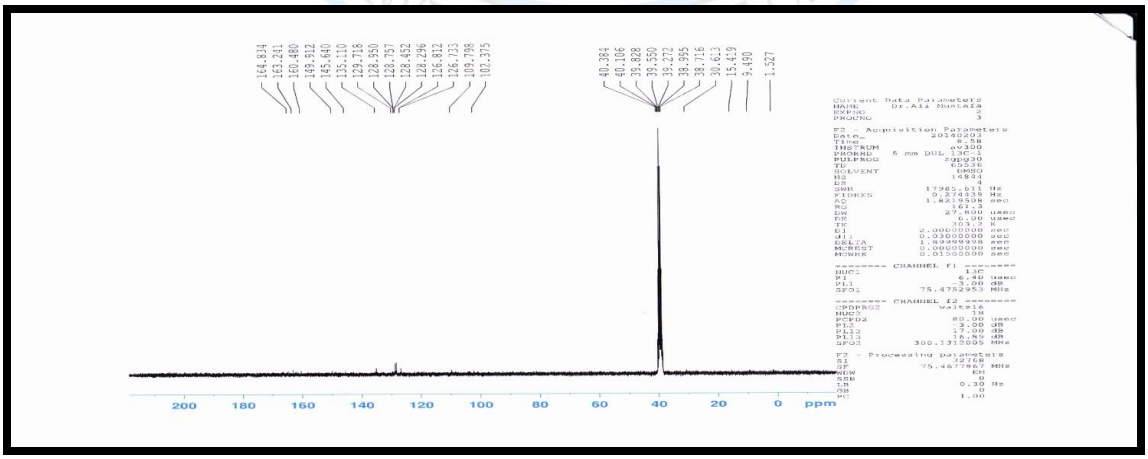


Figure 14: ^{13}CNMR Compound 18

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