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Synthesis and Antimicrobial Schreening of New 4,5,6,7-Tatra Hydro Benzo Thiophene Derivatives

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Abstract:

A group of derivatives for compounds 2-Amino-3-carboxy-4,5,6,7-tetra hydrobenz -othiophene bearing different heterocyclic moieties such as Schiff bases. B-Lactum, 4-thiazolidinone.1,3-oxazepan. The newly synthesized derivatives have been supported by spectral data FT-IR, H^1-NMR. All the synthesized compounds were screened for their antimicrobial activities against gram-positive and gram-negative bacteria as reference.

Key words: Antimicrobial Activity,2-Azetidinone,3-Oxazepane4-Thiazolidinone, Schiffbases, Tetrazole, Tetra hydrobenzo thiophene.

Introduction:

Heterocyclic chemistry comprises at least half of all organic chemistry research worldw -ide. In particular, hetrocyclic structures form the basis of many pharmaceutical,agrochemical and veterinary products.Cyclohexanone derivatives play an important comounds(1). Many herbicides having cyclohexanone backbone such as tralkoxydim, sethoxydim or clethodimare well known(2,3). In previous work we were synthesis and biological evaluation of tetrahydrobenzo [b].thiophene as anti-cancer agent(4).A large number of tetrabenz othiophene derivatives(5,6,7) have been found to important tools of pharmaceutical activity such as antimicrobial, anti-inflammatory and anti HIV.A number of synthetic compounds such as tetrabenzothiophene(8),thiozoldine(9),tetrazole(10 %),oxazepin(11) have also been play role exploited for antioxidant activity. Schiff bases is nitrogen analog aldehyde or ketone in which the (C=O) group is replaced by a(C=N)group(12). Has the apparent number of apply in many field including medicine, life science and chemical sciences and interesting biological activities, such as antibacterial(13)antifungal(14) anticancer(15)and herbicide activates(16). Furthermore derivatives of Schiff base azelidinone (B-Lactum) ring (17) are class of important compounds in medicinal chemistry and pharmaceutical field the 4-thiazolidenone scaffold is very versatile and has featured in a number of medicinal chemistry(18).

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While the tetrazole is one of organic heterocyclic compounds containing a (5) member di unsaturated ring structure compound of (4) nitrogen atom and one carbon are important role such as antibacterial, antiviral, analgesic ,anti-inflammatory (19).Also oxazepin derivatives is a (7) membered ring that contains two heteroatoms(oxygen & nitrogen)that are available in medicinal chemist and in many pharmaceutical application(11).Also thiadazole and its derivatives are important organic reaction intermediates and they have been widely used as anticonvulsant, antidepressant, analgesic, antiinflammatory, antiplatelet, antimalarial, antiviral, diuredic and muscles relaxant activity(20). In view of these observing we thought that it would be interesting to synthesize the substituted derivative starting from[2-amino-3-carbethoxy-4,5,6,7,tetrahyroben zothiophene] followed by cyclization of Schiff bases lead to compounds with interesting antibacterial profile.

Materials and Methods:

Melting point has been specified in open capillary Electro thermal apparatus and is uncorrected.FT-IR measurement were recorded on shimadzudel Infrered spectra-84005. H^1-NMR spectra were obtained with a Bruker spectrophotometer model ultra-shield at 300MHz in DMSO-d^6solution as a solvent with the TMS as internal reference in this study were reagents grade and they are available from sigma-Aldrich and Fluka companies. Purity of the compounds was checked on silica coated merck-TLC plates using,

chloroform, benzene and a mixture of hexan and ethyle acetate as mobile phase.

Synthesis of compound(1)[ethyl 2-amino-4,5,6,7-tetrahydro-1-benzothiophene-3-sulfinate]: To a mixed of cyclohexanone (0,05mol, 4.9gm), ethyl cyanoactate (0.05mol, 5.65gm) and Sulp –hur (0.05mol,1.6gm)in ethanol(50ml), dipropylamine (0.05mol,5.05gm) was added drop wise with stirring. The reaction was reflux for (10hrs).The residue of solvent was evaporated and the crystals was filtered off solvent off, purification from ethanol yield (95%), m.p(119-121C), FTIR (KBr,νcm^{-1}): 1734 (C=O)of ester,2847-2978 $(CH_2)_{alph}$, 3302-3396(NH_2),698(C-S-C). H^1NMR (300MHz, DSO-d^6, 8,ppm):1.25 (t.3H, $COOCH_2CH_3$, 4.30 (9,2H,$COOCH_2CH_3$) ,5.5(s, 2H, NH_2), (2.01-2.2) (m,4H,CH_2), 1.7(t,2H,CH_2). The physical properties listed in table (1).

Table1. Physical properties of synthesized compound.

Comp. No.	M.P.°C	Yield%	Recry. Solvent	Color	Molecular Formula
1	119-121	95	Ethanol	Brown	$C_{11}H_{15}O_2NS$
2	109-112	85	Ethanol +H_2O	Yellow	$C_{10}H_{14}N_4S_2O$
3	116-118	60	Ethanol+H_2O	Gray	$C_{10}H_{12}N_4S_2$
4	212-214	50	Ethanol	Yellow	$C_{24}H_{20}N_6O_5S_2$
5	230-232	43	Chloroform	Black	$C_{24}H_{20}N_4S_2OCl_2$
6	250-252	69	Benzene	Off white	$C_{24}H_{22}N_{12}S_2O_5$
7	205-208	35	Ethanol	Brown	$C_{24}H_{20}N_6S_4O_7$
8	202-204	40	Ethanol	Black	$C_{24}H_{20}N_4S_4O_3C_{l2}$
9	260-262	70	Chloroform	Off white	$C_{28}H_{20}N_6S_2O_7C_{l2}$
10	270-272	61	Ethanol	White	$C_{32}H_{28}N_6S_2O_{11}$
11	244-246	30	Ethanol	Yellow	$C_{32}H_{28}N_4S_2O_7C_{l2}$.

Synthesis of compound(2)[2-[(2-amino-4,5,6,7-tetrahydro-1-benzothiophen-3-yl) sulfinyl] hydrazinecarbothioamide]: Compound(1)(0.01mo, 2.25gm) and thiosemicarbazide (0.01mol,0.91g) in ethanol (30ml) was reflexed for (7h).The solvent was evaporated under reduced pressure and the viscous mass was poured over ice cold water,filtered and purification to give compound(2). M.P.(109-112°C), yield(85%), FTIR(KBr,νcm^{-1}): 1178(C=S), 1645(C=O), 3402-3356(NH_2),3263 (NH), 2985-2897 $(CH)_{alph}$,^{1}HNMR (300MHz, DMSO-d^6, δppm): 8.70 (m,4H,NHNHCSNH_2), 7.58 (S, 2H, NH_2) 1.75 - 2.72 (m,4H,CH_2), Table(2).

Synthesis of compound (3)[5-(2-amino-4,5,6,7-tetrahydro-1-benzothiophen-3-yl)-1,3,4-thiadiazol-2-amine]: Dissolve of compound(2) (0.002mol,0.5gm) in solution of NaOH (0.0099mol,3.79gm) in distilled water (30ml) at room temperature. The reaction was reflexed for (30 min.) after than kept overnight at (5°C). The solid, thus separated was recrystallized from (ethanol+water) to give compound(3).M.P.(116-118C)(yield=60%),FTIR(KBr,νcm^{-1}) :688(C-S-C),1282(N-N),1448(C-N),1575(C=N),3489-3362(NH_2),^{1}HNMR(300MHz,DMSO-d^6, Sppm): 5.75 (S, 2H , NH_2),(2.01-2.5) (m, 4H, CH_2) ,1.7-1.95(t,2H,CH_2).Table(2)

General method for the synthesis of Schiff bases(4,5): A mixture of compound(2) (0.002mol,0.54g) and (0.004mol) of the (4-chlorobenzaldehyde, 4-nitrobenzaldehyde) was added in absolute ethanol (20ml) refluxing for (10hrs). The mixture was cooled and the precipitate obtained purification from ethanol and chloroform. Table(2)

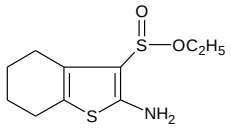
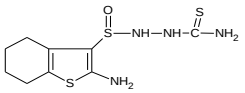
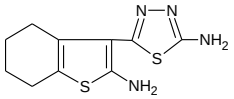
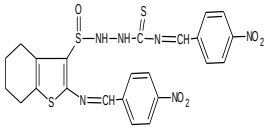
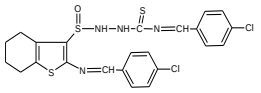
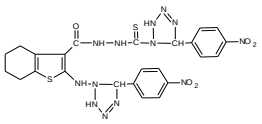
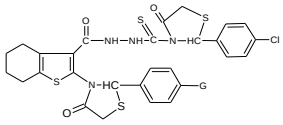
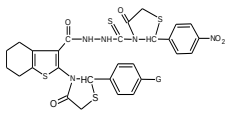
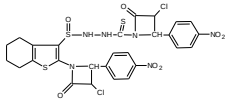
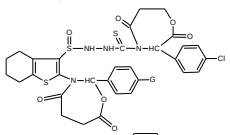
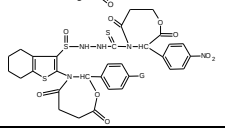
Synthesis of Compound(4): Yield50%,M.P.(212-214)°C,FTIR(KBr,ν,cm^{-1}):3228 (NH), 1687 (C=O) of amide,1579(C=N), 3228(NH),1348, 1523(NO_2), H^1NMR (300MHz,DMSO-d^6 ,ppm): 11.7 (S,1H,NHCO), 8.08-8.61(m,10H,Ar-H,CH=N), 4.4(S,^{1}H,NH), 1.3-1.8(m,2H,CH_2).

Synthesis of Compound(5): Yield43%,M.P(230-232)°C, FTIR3281(NH), 1680(C=O),1591, 1572(C=N), 790(C-Cl), H^1NMR(300MHz,DMSO-d^6S,ppm): 9.91(S,1H,NHCO),5.5(S.1H, NH), 8.37-7.45(m, 20H, Ar-H.CH=N). Table(2)

Synthesis of compound(6): To a stirring of Schiff bases 4(0.001mol,0.5g) with sodium azide (0.002mol,0.13g) and (10ml) tetrahydro furan (THF) was added. reaction was refluxed for (10Hrs.), after that the filtrate was cooled at room temperature the precipitation washed with cold water,purification from benzene,M.P(250-252)°C,Yield69%.FTIR:3360(NH of cyc -lic),3221(NH),1604$(C=C)_{ar}$.,1498(N=N),3055(C-H)$_{ar}$.,2127azidegroup. H^1NMR (300 MHz, DMSO-d^6,Sppm):8.15-8.68(m,8H,Ar-H),4.3(S,1H,NH of tetrazole), 5.8(S,1H,NH), 3.7(S,1H, C-H of tetrazole), 1.3-1.78(m,4H,CH_2), 2.69-2.72 (t,4H,CH_2). Table(2)

General procedure for synthesis of compounds(7,8): A mixture of Schiff bases(4,5) (0.001mol),(0.002mol) of $SHCH_2COOH$ acid was in (10ml)of dry benzene and refluxed in water bath for(4hrs.).The product was treated by 10% sodium bicarbonate to give compounds (7,8) dried and recrystallization from suitable solvent. Table(2)

Table 2. Spectral data of the compounds (1-11).

Comp. No.	Comp. Structure	Characterization bands of FTIR (ATR,νmcm^{-1})					
		C-H)$_{ali.}$	(C-H)$_{arom.}$	(C=O)	(C=N)	(C=C)$_{arom.}$	Other bands cm^{-1}
1		2935-2847	-----	1734 of ester	-----	1572 1593 of thiophene ring	NH_2(3396,3302) C-O(1269) C-S(673,738)
2		2841-2939	-----	1645 of amide	-----	1533 1620 of thiophene ring	NH_2(3402,3356) NH(3298),(3169) C-N(1153) C=S(1178)
3		2966-2827	-----	-----	1575 1525	1448 1514	NH_2(3489,3362) C-S(688,748)
4		2918-2839	3074-3009	1687 of amide	1580 of imine	1446-1523	NH(3228) NO_2(1523,1348) C=S(1207)
5		2982-2806	3049-3097	1680 of amide	1591 1654 of imine	1519 1572	NH(3281) C-Cl(1120) C=S(1209)
6		2949	3055-3003	1672	------	1473 1533 1604	NH(3260) NH(3360)Of tetrazole ring N=N(1498) Azide group (2127) NO_2(1392,1500)
7		2839-2939	3169	1705 of thiazolidine ring 1633of amide	----	1531 1560 1591	(C-S-C) 759,661 NH (3304)
8		2852-2926	3099	1715 of thiazolidine ring 1660 of amide	-----	1599 1562 1525	(C-S-C) 705,690 NH(3286)
9		2854-2976	3010	1722 of B-Lactum 1693 of amide	-----	1568 1595 1637	NO_2(1518,1340) C-Cl(1172) NH(3218)
10		2856-2995	2061-3090	1737 – 1710 of oxazepine ring 1658 of amide	----	1527 1575 1595	NO_2(1336,1514) NH(3263) C-O(1215) C-N(1174)
11		2851	3176	1749,1705 of oxazepine ring 1681 of amide	-----	1525-1635	NH(3215) C-Cl(1172) C-O(1286) C-N(1122)

Synthesis of Compound(7): Yield35%, M.P.(205-208)^{o}C,FTIR(KBr,ν,cm^{-1})1705 (C=O of thiazolidine ring),1681(C=O of amide),3100(C-H)$_{ar.}$,2982-2922(C-H)$_{aliph.}$,709,661(C-S-C), 3307(NH).H^{1}NMR(300,MHz,DMSO-d^{6},Sppm): 7.87-8.21(m,8H$_{Ar}$)5.6(S,1H,NH)9.8(S, 1H, NHCO).1.68-2.74 (m,4H,CH_2),2.75 (S,2H,CH_2) of thiazolidinon ring. Table(2)

Synthesis of Compound (8): Yield40%,m.p(202-204)^{o}C,FTIR(KBr,ν,cm^{-1}): 1715 (C=O of thiazolidine ring),1682(C=O of amide),3098(C-H)aromatic,2900-2899(C-H) aliphatic, 32100 (NH),790(C-Cl). Table(2)

Synthesis of compound(9): To a stirred solution of compound(4)(0.001mol,0.5gm) ,tri methylamine

(0.002mol,0.202gm) in dry dioxin (15ml) chloroacetylchloride (0.002mol,0.226 gm) was added slowely in(0-5)^{o}C the component was then stirred for (6hrs.) after that poured into icewater.The precipitate was filtered and purification from chloroform. Yield 70%, M.P: 260-262^{o}C, FTIR(KBr,ν,cm^{-1}):3200(NH),1722(C=Ogroup,B-Lactam),1693(C=O of amide). H^{1}NMR (300MHz, DMSO-d6,S, ppm): 7.74-8.66(m,8H,Ar-H), 5.0(d,1H,N-CH), 8.89(S,1H, NHCO), 2.2-3.9 (m,4H,CH_2), 1.7(t,2H,CH_2), 4.6(S,H,NH), 5.44(d,1H,CH-Cl) Table(2)

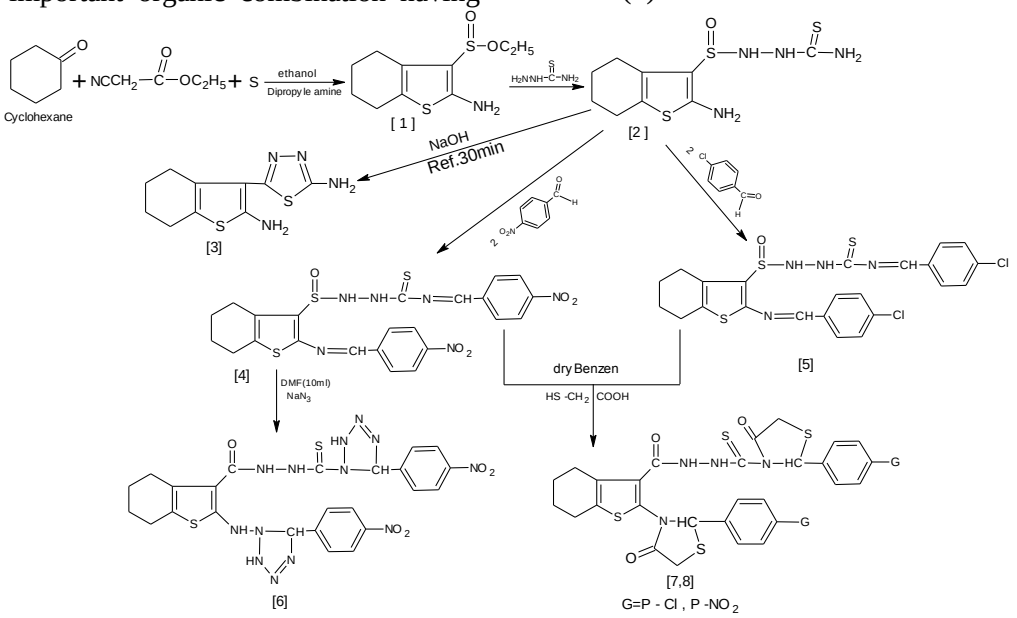
General procedure for the synthesis of compounds(10,11):A mixture of Schiff bases (4,5)(0.001mol)and(0.002mol,0.29gm)of phthalic anhydride was dissolving in(10ml)of dry benzene and refluxed in a water bath for(4hrs.).The product was treated with sodium bicar -bonate to produce compound(10,11)as a solid collected and recrystallized from 95% ethanol.

Synthesis of compound(10): Yield:61%, M.P7.(270-272)^{o}C,FTIR(KBr,ν,cm^{-1}):1737, 1710 (C=O of oxazpine ring),1265(C-O),1174(C-N), (2856(C-H)$_{aliph}$,3090(C–H)ar. H^{1}NMR (300MHz, DMSO-d6, S,pmm):7.13-8.15(m,18H,Ar-H),7.03 (S,1H,C-H of oxazpine ring), 8.85 (S,1H,NHCO), 4.9(S,1H,NH),2.01-2.2(m,4H,CH_2), 1.7 (t,2H,CH_2). Table(2)

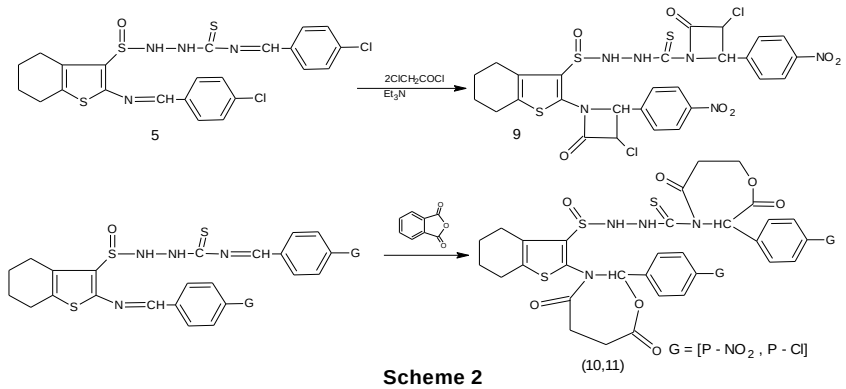
Synthesis of compound(11): Yield:30%, M.P:(244-246)^{o}C.FTIR (KBr, ν,cm^{-1}):1726, 1699 (C=O of oxazpine ring),1233(C-O),1170(C-N),2860(C-H)$_{aliph}$,3100(C-H)$_{ar}$. H^{1}NMR (300MHz, DMSO-d^{6},S,pmm): 7.0-8.4(m, 18H,ArH), 6.93 (S,1H,C-H of oxazpine ring),1.3-1.78 (m, 4H,CH_2), 2.69-2.72(t,4H,CH_2). Table(2)

Results and Discussion:

The scheme 1 and 2 the proof of identify of synthetic sequence used our laboratories to make ready very important organic combination having wide spectrum of biological activities. The target of this work was performed by following different strategic, the synthesis routes used in shown in scheme(1).



Scheme 1



Scheme 2

The derivative(1)2-amino-3-carbethoxy-4,5,6,7-tatrahydrobenzothiophe-ne was synthesized by the react cyclohexanone with ethyl cyanoacetate and sulfur.The structu -re of derivative 1 with clause by presence by IR spectrum of NH_2 group at3302,3396cm^{-1} and carbonyl group(C=O)of ester at1734cm^{-1}.H^1NMR of compound 1 :1.25(t,3H,-CH_3 ester) ,4.30 (9,2H,-CH_2O-)5.5(S,2H,NH_2).The mass spectrum of the derivative1showed the mole -cular ion peak atZ=225(M^+,100%)is in accord with the molecular formula of this compound, $C_{11}H_{15}NS$, (225g/mol)Fig. 1.

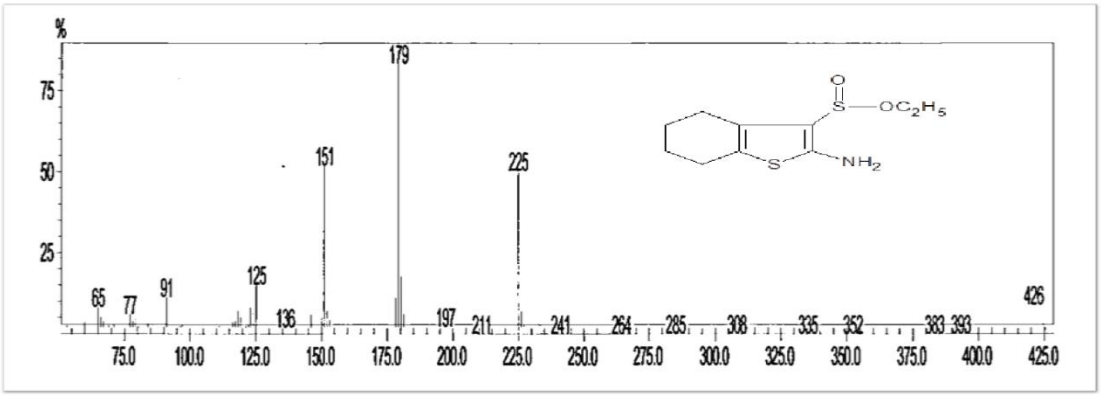


Figure 1. The mass spectrum of compound(1)

When derivative 1 react with thiosemicarbazide gave derivative 2, Fig. 2 the IR spectrum showed disappearance of the(C=O)band of ester at 1734cm^{-1} and appearance of double bands of NH_2 at 3402,3356$cm^{-1}$and(C=O)of amide at 1645cm^{-1}.The ^{1}HNMRof derivative2exhibited signals at 8.70(m,4H,NHNHCSNH_2), 7.58(S,2H,NH_2).

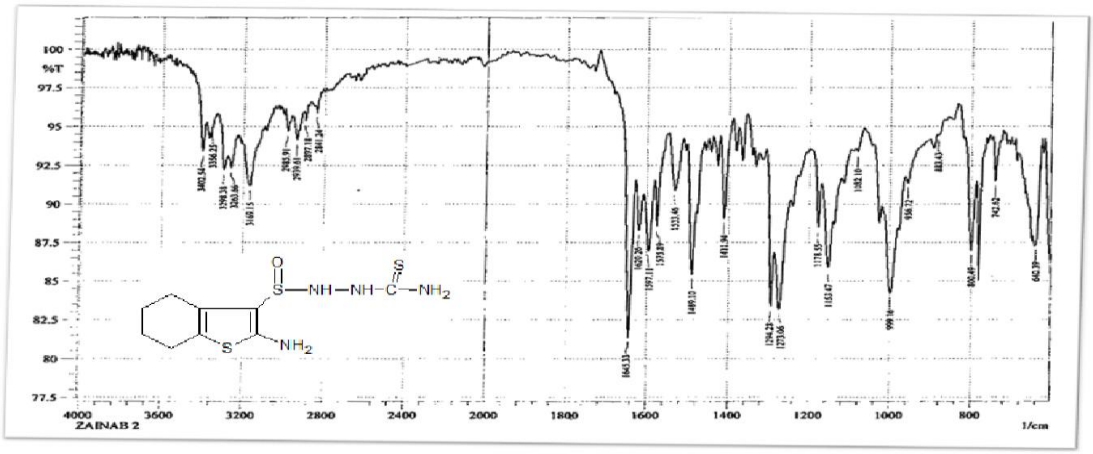


Figure 2. The FTIR spectrum of compound(2)

Reac -tion between derivative2 and NaOH solution afforded thiadazole derivatives 3. The spec -trum of derivative 3 showed the disappearance of absorption bands to (C=O) of amide with appearance of the(C=N)at1575$cm^{-1}$and (N-N)at 1282cm^{-1}. The ^{1}HNMR of compound 3 show -ed singlet signal at5.75ppm for NH_2. Fig. (3)

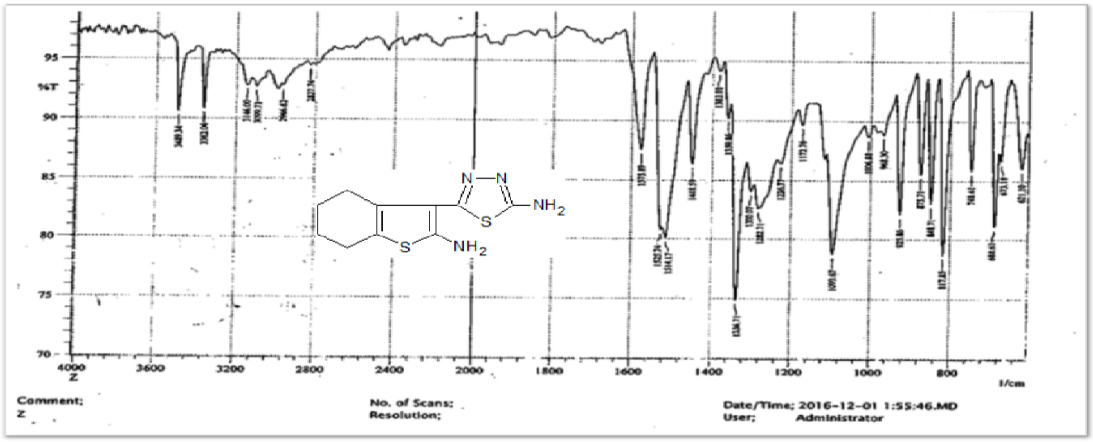


Figure 3. The FTIR spectrum of compound (3)

Fig.4 condensation of derivative 2 with various substituted benzaldehyde in absolute ethanol gave arylidine derivatives 4 & 5.

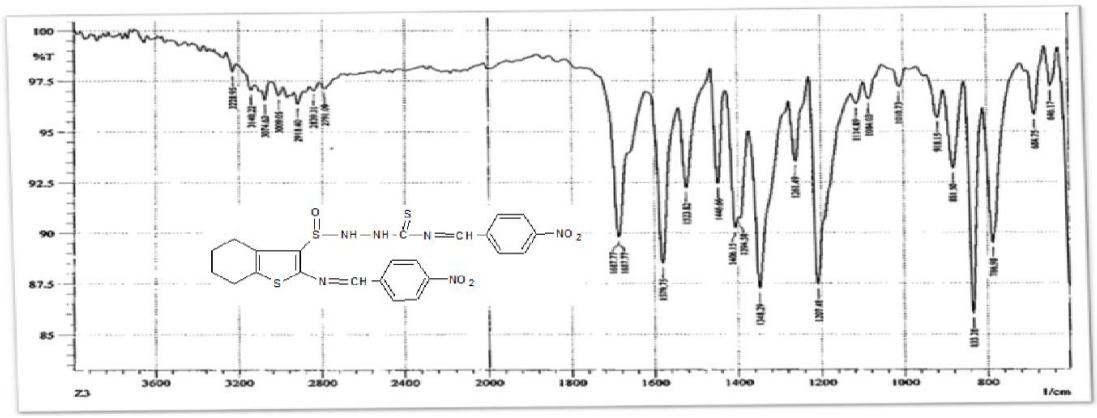


Figure 4. The FTIR spectrum of compound(4).

The creation of these azomethines show that by the presence in the IR spectra of (CH=N)stretching bands at1580-1600cm^{-1} add together the disappearance of NH_2 stretching bands. The H^{1}NMR of compound 5 fig. 5 display singlet signals at 9.91ppm was attributed to NHCO,5.5(S,1H,NH), amultiplet signals at8.37-7.45ppm which belonged to aromatic protons and(N=CH),2.01-2.5 (m.4H,CH_2), 1.7-1.95(t,2H,CH_2)22 fig.4 compound4, Schiff bases were building in water bath at(70-75^{o}C)with NaN_3 in dimethyl furan, to give compound6, IR spectroscopy was used characterize structure of the synthesized compound. The tradition of bands at 1579cm^{-1}, ascribe to(C=N)(imine group) stretching frequency is favor proof for the success of this step. It also, IR spectra for this derivative were appears of a strong band at 2127cm^{-1} characteriza -tion stretching frequency of azide group, bands at 1498cm^{-1} were caused by the cyclic(N=N) stretching of tetrazole circular band.

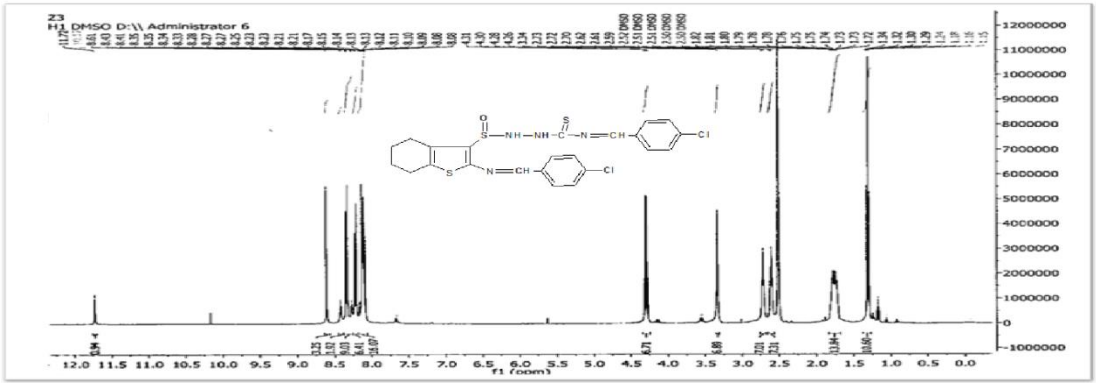


Figure 5. The H^{1}NMR spectrum of compound (5)

Band at (3360cm^{-1}) because of (N-H)group. H^{1}NMR spectrum of compound6 shows the following characteristic, the aromatic ring protons as multiple at8.15-8.68ppm which belonged to aromatic protons and(N-H) proton for tetrazole appeared at 4.3ppm singlet, signal at3.7 ppmdue to the (C-H) proton in tetrazole ring fig 6. Cyclization of derivatives 4 & 5 with thioglycolic acid in the presence of dry Benzene afforded derivatives(7,8). FTIR of compounds shows the arrival of stretching strip of (C=O) group at1705,1715cm^{-1} expected thiazolidine one ring and this was the almost all characteristic evidence for the success of cyclization step. Other typical bands of aromatic system is the showed ofν(C=C)at about(1581cm^{-1}),ν(C-S-C) at 709,661cm^{-1} H^{1}NMR of derivative7 showed singlet signal at(2.75ppm)was attributed to (CH_2)of thiazolidine ring a multiplet broach cast signal at 7.87 &8.21ppmthat has belonged to aromatic protons, singlet signals at 9.8 ppm which was assigned to NHCO,5.6 ppm was characteristic to N-H proton. Fig.7. Handing of derivative4with trimethyl amine and chloroacetyl chloride provide azeti -dinyl compound9.

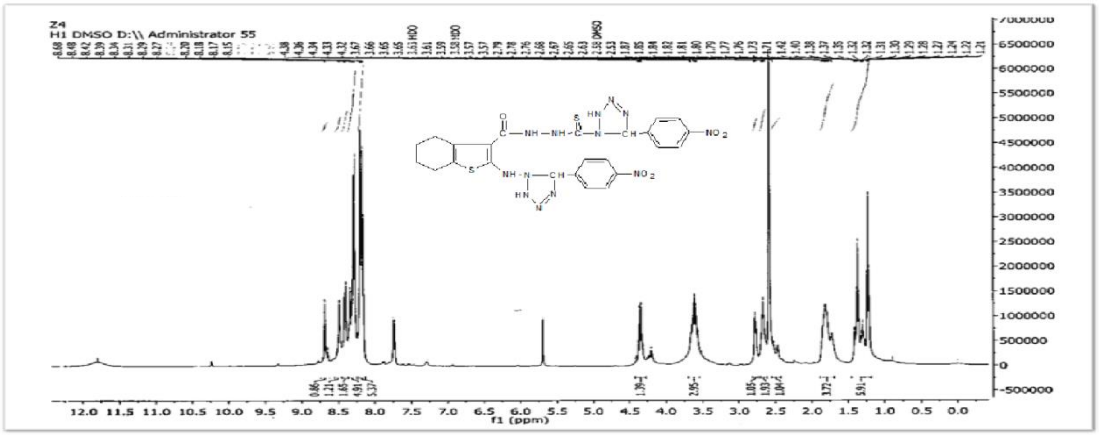


Figure 6. The H^{1}NMR spectrum of compound (6)

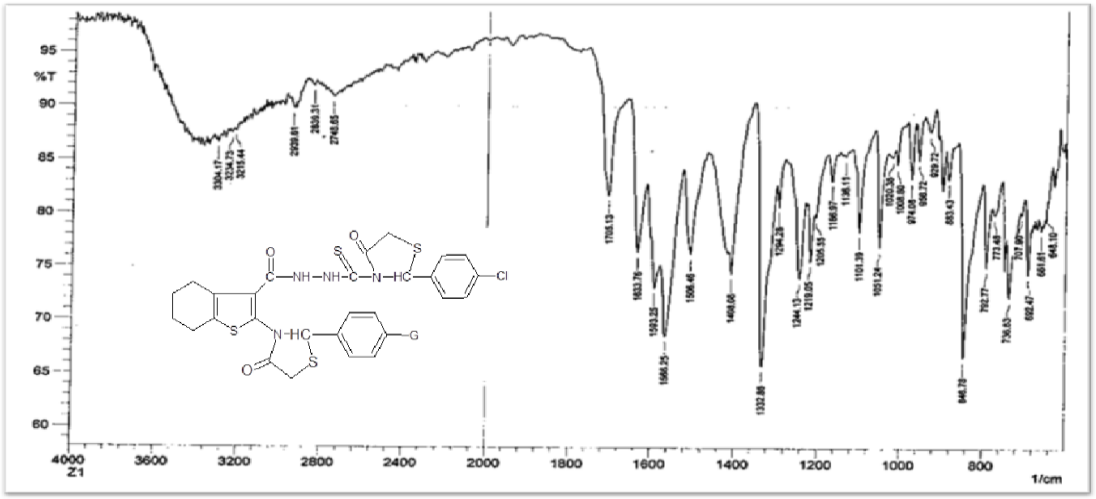


Figure 7. The FTIR spectrum of compound (7)

The structure of compound 9 install by IR spectral data which was display the vanishing band of(CH=N)in the area 1579cm^{-1} united with the looks of absorption band at 1722cm^{-1}(C=O) of B-Lactam). The ^{1}HNMR of derivative 9 make visible signals at (5.0-5.44ppm) due to azetidinyl ring proton, a multiblet signals at 7.74&8.66 due to aromatic protons. Fig.8 .Fig. 9. Schiff bases 4 & 5 react with cyclic anhydrides to give the corresponding addition product.

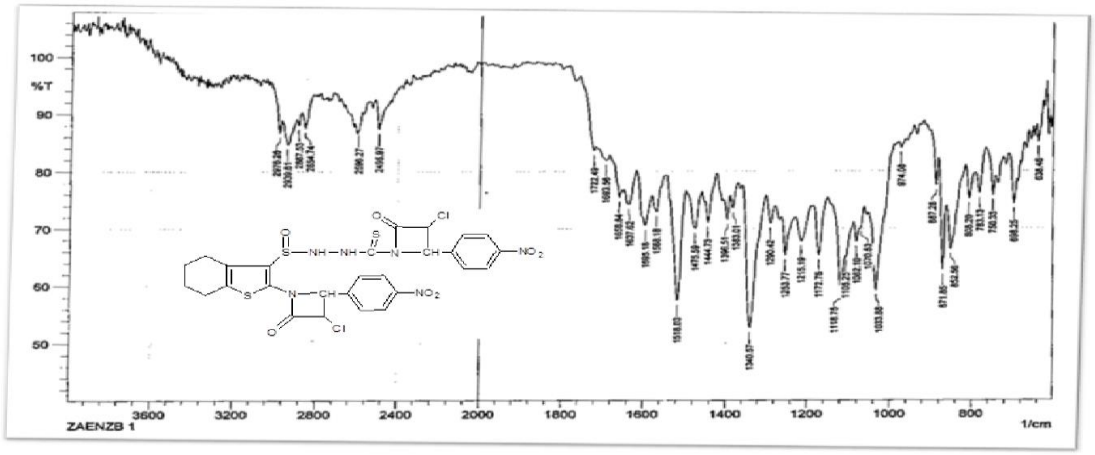


Figure 8. The FTIR spectrum of compound (9)

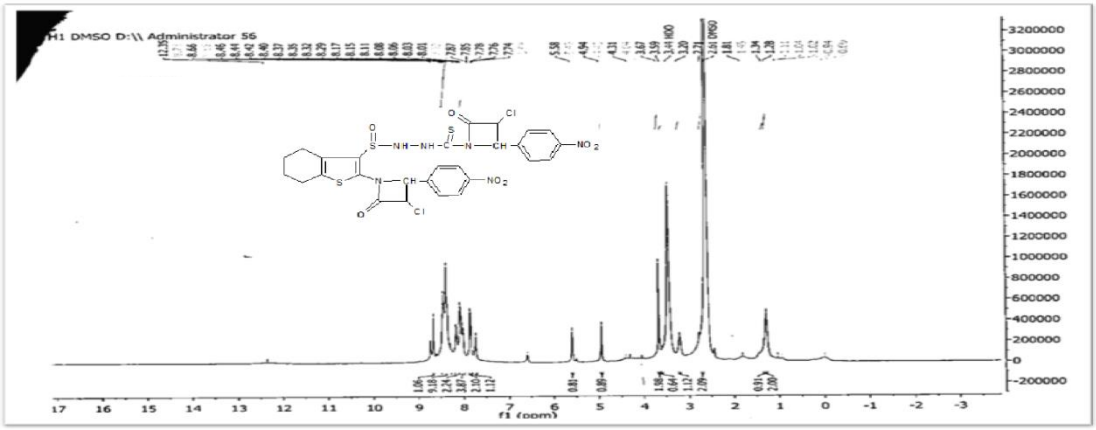


Figure 9. The H^1NMR spectrum of Compound(9).

As a sequence, expected to react with phthalic anhydride to produce oxazepine compounds 10 & 11.The IR spectral of compound point to the looks of (C=O) group band at1737&1726$cm^{-1}$and(C-O) band at (1265cm^{-1}) and (C-N) band at(1174)cm^{-1}.H^1NMR of compound11 showed singlet signals at (6.93ppm)was attributed to C-H proton of oxazpine ring, multiple signals at 7.0-8.4ppm which belonged to aromatic protons. Table2.

2. Antimicrobial Activity:

The antimicrobial activity of the 2-amine-3-cabethoxy-4, 5, 6, 7-tetrahydrobenzothiophene derivatives (2-11) were test by the agar disc-diffusion method against two (G^+) staphylococcus aureus and staphylococcus epidermidisa and two (G-) bacteria E.Coli, Klebsiell as microorganism and fungal strains namely candida albicans. Dimethyl sulfoxide DMSO was used as solvent.

The test was commit at(100μgm/ ml) conc. The bacteria and fungi were carried out in agar and potato dextrose agar medium and these plate were incubated for 24hrs. for bacteria and 48hrs.for fungi at 37°C.

Table 3. Antimicrobial evaluation of compounds.

Synthesized compounds	Inhibition Zone (mm) at 100% μmg/mL				
	Grampositive		Gramnegative		Fungi
	S.aureus	S.epider midis	E.Coli	Klebsiell aspp	C.albican us
2	----	15	23	13	20
3	9	14	18	----	----
4	-----	12	23	----	19
5	18	10	21	10	-----
6	13	10	22	14	15
7	-----	18	21	20	17
8	20	15	18	22	15
9	19	20	23	19	21
10	22	18	11	14	15
11	17	11	12	19	------
Amoxicillin	17	19	16	17	21

Antimicrobial Activity:

In this study it has been used the amoxicilline drugs as standard antibacterial for comparision with the benzothiophene derivatives that is (Schiff base , azetidinone, thiazolidinone and oxazepan). The results of these compounds are summarized in table(3). It could be observed that all the tested compounds were active towards sepidermidis and compounds (7.9.10)show high activity. All the test compounds were active towards saureus except(2,4,7) while compounds (8,10) show high activity, so only compounds (7,8,9,11) were active toward klebiellaspp. On the other hand, All compounds (2-9) has high inhibition toward E.Coli except compounds (10,11) has low inhibition on this kind of bacteria. In addition compounds (2,4,7,9) showed high inhibition candida Fungi.

Conclusion:

The terahydrobenzo thiophene derivatives were prepared and characterization by spectral and four strains of bacteria namely is epidmides S.Aureus as (G+), E.Coli and Klebsiellla SPP as (G-), and it has been comparision with Amoxicillin as caliber drug to reveal the potency of synthesized derivatives. The fungi and bacteria found to be sensitive to all derivatives at lower concentration (100 µmg/mL) but no sensitivity at lower concentration.

Conflicts of Interest: None.

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تحضير واختبار الفعالية البكتيرية لمشتقات 7.6.5.4 – تتراهايدرو بنزوثيوفين الجديدة

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الخلاصة :

مجموعة من مشتقات التتراهيدروبنزوثايوفين تعمل حلقات غير متجانسة مختلفة مثل قواعد شيف،2-ازيتيدينون ، 4-ثيازوليدينون،3،1-اوكسازيبان. وتم الكشف عن بنية المشتقات الجديدة وتفسيرها بواسطه اطياف الاشعة تحت الحمراء والرنين النووي البروتوني ومطيافيه الكتلة. هذه المركبات تم تقييم انشطتها المضادة للميكروبات ضد الغرام الايجابية والسالبة والفطريات باستخدام اجراء التخفيف الجزيئي.

الكلمات المفتاحية : تتراهايدروثايوفين، الفعالية البايولوجية، ثايادايازول، قاعدة شيف، تترازول،2-ازيتيدانون،4-ثايازوليدون،3-اوكسازيين.