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Preparation and Characterization of some new Benzothiazole-Heterocyclic Derivatives

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Abstract

In this work new different hetero cyclic derivatives were synthesized that which including β-Lactam, teterazole and also thiazole rings.The starting material is 2-amino-6-methoxy-Benzothiazole. All these reactions follow by (TLC) and Measurement melting points for some of these derivatives. The compounds identified by FT-IR and some of them by 1H-NMR and 13C-NMR spectra., The prepared benzothiazole derivatives in this study gave good results through appearance of new bands and disapearance of other bands in formatted compounds that gave first data to formation benzothiazole derivative , while second technique represented by resonance spectra that gave also good results for formatted benzothiazole derivative.m in addition to flowing of all reactions by paper chromatography.

Keywords: Thiazole , Microwave, β-Lactam, Tetrazole , Azetidinone.

1.Introduction

The Thiazole ring, a five membered heterocyclic unit with sulfur and nitrogen at(1, 3) positions, is found in natural products such as a component of the vitamin thiamine (B1)[(1)]. Thiazole ring and it Derivatives are planar and aromatic(pi-electron) delocalization and more aromaticity[(2-4)]than oxazole ring . A number of thiazole derivatives were synthesized by the Hantzsch thiazole synthesis, along with other methods[(5,6)] . Thiazole derivatives have attracted the interest of medicinal chemists due to group of their biological activities including anti-fungal, anti-bacterial, anti-HIV, anti-hypertension, anti-inflammatory, anti-cancer, anti-convulsive and anti-depressant [7–13].

β-lactam (also known 2-Azetidinone) are four-membered cyclic amide derived from 3-amino-propanoic acid[(14,15)]. The parent heterocyclic ring of azetidinone is azetidine that is a four member heterocyclic ring system with (N) as hetero atom . 2-Azetidinone includes a carbonyl group on the second position which is one of the most common heterocyclic rings found in many antibiotics[(16)]. β-lactam is named as such, because (N) atom is attached to the β- carbon atom relative to the carbonyl group. The(N)atom in this ring chemically is reactive in nature and also is responsible for the antimicrobial activity[(17,18)]. Tetrazoles contains a five-member ring consisting of four nitrogen atoms, one carbon, two hydrogen atoms, and an electron-rich planar structural features and poly-nitrogen [(19,20)]. Tetrazole rings are an important organic compounds category of nitrogen-rich heterocyclic, showing the wide range of applications in various fields like drug development, organic synthesis, material science, and chemistry coordination [(21)]. Through non-covalent reactions, Tetrazole can interact with many enzymes and receptors in living organisms to demonstrate broad biological properties like anti-bacterial[(22)] anticancer[(23)] antifungal[(24)] anti-inflammatory[(25)] anti-malarial[(26)] anti-tubercular[(27)] antihypertensive activities[(28)] analgesic[(29,30)] and anti-viral [(31,32)]. the synthesis by assisted Microwave is a branch of green chemistry. The application of this branch in organic, organometallic and coordination chemistry continues to develop at striking pace. Microwave-irradiated reactions under solvent free or less solvent conditions are catchy offering reduced pollution, low cost and offer high yields together with simplicity in processing and handling. The salient features of microwave approach are shorter reaction times, simple reaction conditions and enhancements in yields[(33-34)].

Materials and Methods:

Chemistry

All chemicals were of highest purity and supplied by Fluka and Merck -company.

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Measurements of the melting points were recorded by using electro thermal 9300," melting point engineering LTD , U.K". (T.L.C)Thin layer chromatography was performed on silica gel and spots were visualized by Iodine vapors." FT-IR" spectra, Fourier transform infrared shimadzu (8400) using potassium bromide (KBr pellets) and the values are expressed in cm^{-1}, 1H-NMR & 13C-NMR-spectra in (ppm) unit were operating in *DMSO -d6* as solvent using (**Agilent Varian 500 MHz**)-Tehran university /Iran.

General procedure for synthesis of Schiff bases derivatives (Y,N)by Microwave irradaition[35]:

(Y) [4- ((6-methoxybenzo[d]thiazol-2-ylimino)methyl)phenol].

(N) [6-methoxy -N-(4-nitrobenzylidene)benzo[d]thiazol-2-amine].

A mixture of aromatic aldehydes (0.001 mol) (0.122 gm of p-hydroxy benzaldehyde and 0.15 gm of p-Nitro benzaldehyde) respectively with 2-amino-6-methoxy benzothiazole (0.18gm,0.001 mol) in absolute Ethanol (1 mL)and 2 drops of glacial acetic acid were added in ceramic crucible. The contents were subjected to microwave irradiation at 120 W about 6 min. for (Y) ,7 min. for (N). Progress of the reaction was monitored by TLC. After the completion of the reaction, solid product was obtained in reaction mixture which re crystallized with absolute Ethanol. re crystallization provides the title compounds as solid crystals.

(Y) yellow,M.F= $C_{15}H_{12}N_2O_2S$, M.Wt.= 284, M.P °C=234-236, R_f =0.95 (Benzene 2.5 ml : EtOH2.5 ml) ,Yield =59 %.

(N) Orange ,M.F= $C_{15}H_{11}N_3O_3S$, M. Wt.= 313, M.P °C=246-248, R_f =0.8 (Benzene 4 ml : EtOH 1 ml), Yield =73.43 %.

Traditional method for synthesis of Schiff base derivative(Z)[36].

(Z) 2-(6-methoxybenzo[d]thiazol-2-ylimino)-1,2-diphenylethanol

(0.001 mol, 0.21gm) of Benzoin(ketone) was dissolved in absolute Ethanol about (25 ml) in the presence 3drops of glacial acetic acid then added 2-Amino-6-methoxy-Benzothiazole (0.001 mol,0.18 gm) . The reaction mixture was refluxed at (78 ^{0}C)with stirring for 24 hour. The progress of the reaction was followed by TLC by using (Benz: EtOH,) as mobile phase. After the completion the mixture was re-crystallized from absolute Ethanol.

(Z) Earthy ,M.F= $C_{22}H_{18}N_2O_2S$, M. Wt.= 374, M.P °C=108-110, R_f =0.85 (Chloroform 4 ml: MeOH 1 ml) ,Yield =70 %.

General procedure for synthesis of β- Lactam derivatives (LY,LN,LZ)[37].

(LY) [3-chloro-4-(4-hydroxyphenyl)-1-(6-methoxybenzo[d]thiazol-2-yl)azetidin-2-one].

(LN) [3-chloro-1-(6-methoxybenzo[d]thiazol-2-yl)-4-(4-nitrophenyl)azetidin-2-one].

(LZ) [**3-chloro-4-(hydroxy(phenyl)methyl)-1-(6-methoxybenzo[d]thiazol-2-yl)-4-phenylazetidin-2-one].**

To a mixture of Schiff base (Y,N,Z) (0.001 mol)(0.28, 0.31, 0.374) gm Respectively in dioxane (30ml)and Et_3N (0.35 ml, 0.0025mole), chloro acetyl chloride (0.2 ml, 0.0025 mol) was added drop-wise at(5-10 ^{o}C)for each reaction . The reaction mixture was stirred for (24 hrs.) at room temperature ,then poured into crushed ice to dissolve The salt(Et_3N^+ HCl) tri ethyl amine hydrochloride. The mixture was extracted by using chloroform($CHCl_3$) ,then the solvent was evaporated and the yield was re-crystallized from absolute ethanol. the reaction was monitored by (T.L.C).

(LY) Brown ,M.F= $C_{17}H_{13}ClN_2O_3S$, M. Wt.= 360, M.P °C=oil, R_f =0.85 (Benzene 2.5 ml : EtOH 2.5 ml) ,Yield =57.7 %.

(LN) Red Brown,M.F= $C_{17}H_{12}ClN_3O_4S$, M. Wt.= 389, M.P °C=Decom.285, R_f =0.65 (Benzene 3 ml : MeOH 2 ml) ,Yield =50 %.

(LZ) Light Earthy , M.F= $C_{24}H_{19}ClN_2O_3S$, M. Wt.= 450.5, M.P °C=102-104, R_f =0.7 (Chloroform 4ml: EtOH 1 ml) ,Yield =90.4 %.

synthesis of N-Chloroacetamide derivative(C) [38].

[2-chloro-N-(6-methoxybenzo[d]thiazol-2-yl)acetamide].

An equivalent moles (0.01mole,1.8gm) of 2-Amino-6-methoxy-Benzothiazole and tri ethyl amine (1gm ,0.01mol) in DMF, then(1.13gm, 0.01mol)from chloro acetyl chloride was added drop-wise. The reaction mixture was stirred for(5 hrs.) at room temp. The progress of the reaction was monitored by T.L.C. at the end of the reaction; the solvent was evaporated. The precipitate obtained was washed with distilled water ,filtered and re-crystallized from abs. ethanol. The product has been confirmed to be formed by the sodium fusion process where the test was positive by forming a white precipitate when adding a solution of ($AgNO_3$).

(C) Dark Earthy , M.F= $C_{10}H_9ClN_2O_2S$, M. Wt.= 256.5, M.P °C=77-79, R_f =0.8 (Benzene 3ml: EtOH 2ml) ,Yield =72.5 %.

synthesis of Azide derivative(C1)[39] by Microwave irradaition:

(C1) [2-azido-N-(6-methoxybenzo[d]thiazol-2-yl)acetamide].

An equivalent moles(1.3gm,0.005 mol.) from N-chloro acetamide derivative(C) and Sodium Azide (0.33gm,0.005mol) with (2ml) DMF were added in ceramic crucible. The contents were subjected to microwave irradiation at 120 W about 26 min. Progress of the reaction was monitored by TLC. After the completion of the reaction, solid product was obtained which re crystallized with absolute Ethanol.

(C1) Earthy , M.F= $C_{10}H_9N_5O_2S$, M. Wt.= 263, M.P °C=123-125, R_f =0.9 (Benzene 3ml: EtOH 2ml) ,Yield =71 %.

synthesis of Thiazole ring derivative(C3)[40] by Microwave irradaition:

(C3) [N^5-(6-methoxybenzo[d]thiazol-2-yl)thiazole-2,5-diamine]

An equivalent moles(0.26gm, 0.001mol) from N-chloro acetamide derivative(C) and Thio urea (0.076gm, 0.001mol) with (2ml) absolute Ethanol were added in ceramic crucible. The contents were subjected to microwave irradiation at 120 W about 15 min. Progress of the reaction was monitored by TLC. After the completion of the reaction, solid product was obtained which re crystallized with absolute Ethanol.

(C3) Light Brown , M.F= $C_{11}H_{10}N_4OS_2$, M. Wt.= 278, M.P °C=Oil, R_f =0.8 (Chloroform 2ml : MeOH 3ml) ,Yield =76.4 %.

steps of synthesis Tetrazole Derivative (T1):

synthesis of Schiff bases derivative (Sh)by Microwave irradaition:

(SH) (4-((pyrimidin-2-ylimino)methyl)phenol):

A mixture of 4-Hydroxy Benzaldehyde (0.61gm, 0.005 mol) with 2-amino Pyrimidine (0.5 gm,0.005 mol) in absolute Ethanol (1 mL)and 2 drops of glacial acetic acid were added in ceramic crucible. The contents were subjected to microwave irradiation at 120 W about 53 min. Progress of the reaction was monitored by TLC. After the completion of the reaction, solid product was obtained in reaction mixture which re crystallized with absolute Ethanol.

(SH) yellow , M.F= $C_{11}H_9N_3O$, M. Wt.= 199, M.P °C=78-80 , R_f =0.8 (Chloroform 2.5ml : MeOH 2.5ml) ,Yield =66.8 %.

synthesis of Tetrazole Derivative (T1)[41]:

(T1)[2-(5-(4-hydroxyphenyl)-1-(pyrimidin-2-yl)-1H-tetrazol-2(5H)-yl)-N-(6-methoxy benzo[d]thiazol-2-yl) acetamide].

(0.2gm ,0.001mole) of Schiff base (SH) was dissolved in(25 mL) of DMF and to that (0.26gm ,0.001mole) of Azide derivative (C1)was added and the resultant reaction mixture was refluxed to (90)°C for (7 hrs.) The solvent was partially evaporated. Finally, the contents were filtered, dried and recrystallized from absolute ethanol.

(T1) Brown , M.F= $C_{21}H_{18}N_8O_3S$, M. Wt.= 462, M.P °C=110-112, R_f =0.8 (Benzene 3ml: MeOH 2ml) ,Yield =77 %.

synthesis of Tetrazole Derivative (T2)[42] :

(T2)[2,2'-(1,1'-(1,4-phenylene)bis(5-thioxo-1H-tetrazole-2,1(5H)-diyl))bis(N-(6-methoxybenzo[d]thiazol-2-yl)acetamide)].

(0.53gm ,0.002mole) of Azide derivative (C1)was dissolved in(25 mL) of DMF and to that (0.19gm ,0.001mole) of p-phenylene di isothiocyanate was added and the resultant reaction mixture was refluxed to (90)°C for (10 hrs.) The solvent was partially evaporated. Finally, the contents were filtered, dried and recrystallized from absolute ethanol.

(T2) Light Brown , M.F= $C_{28}H_{22}N_{12}O_4S_4$, M. Wt.= 718, M.P °C=81-83, R_f =0.8 (Benzene 2.5ml: MeOH 2.5ml) ,Yield =73 %.

Results and Discussion:

2-Amino-6-methoxybenzothiazole is starting material for synthesis of different hetero cyclic derivatives in many lines. The first line included preparation of β-Lactam derivatives .In this line many Schiff bases were prepared from2-Amino-6-methoxybenzothiazole with two aromatic aldehydes that which (p-hydroxy benzaldehyde and p-nitro benzaldehyde)(Y,N) respectively by Microwave irradiation by Very small quantities of the reactants and the solvent, the other Shiff base was prepared from the same aromatic amine with the Keton (Benzoin)by The reflux process to the boiling point of the solvent absolute EtOH, It lasted for a long time, unlike the microwave method, Which took a few minutes **Scheme(1)**. All Shiff bases characterized by FT-IR Spectra **Figures(1,2,3)** Where it is observed disappearing two bands of aromatic amine at (3388-3294)Cm^{-1} and appearing the imine group bands at(1600.9,1666.5 and 1672) Cm^{-1} for (Y,N and Z) respectively , also appearance the absorption bands for (OH) in Y and Z at (3415.9,3388) Cm^{-1} respectively. Schiff Base (Y) also confirmed by 1H-NMR and 13C-NMR **Figures(4,5)**. 1H-NMR spectrum (ppm)(DMSO-*d6*) for (Y)characteristic signals at ppm: (S, 1H,OH)10.83,(S,1H,CH=N- ,) 8.82,(S ,3H ,OCH_3) 3.67 ,(m,5H for benzene rings) (6.40-7.35). 13C-NMR spectrum for (Y)characteristic signals at ppm: C (S-C=N in Thiazole ring) 166.53 , C (-C-OH in phenyl ring)162.79, C (-CH=N)154.18, C (Aromatic

rings)(121.60-138.21), C(OCH_3) 55.21These signals are confirm to the formation of Schiff Base (Y).
From these Shiff bases have been prepared β-Lactam derivatives(LY, LN, LZ) by a mechanism [2+2] cyclo addition Which is known as Staudinger Reaction Via addition Chloro acetyl chloride in the presence of Tri ethyl amine as base catalyst at (5-10) ^oC [43]. β-Lactam derivatives characterized by FT-IR Spectra **Figures(6,7,8)** via disappearing absorption bands for imine groups and appearance the absorption bands duo to carbonyl lactam ring at(1730,1732 , 1710)for (LY, LN, LZ) Cm^{-1} respectively. in an acyclic amide the carbonyl group has stretching vibration about (1735-1755)cm in the case of monocyclic lactams. this indicates that the carbonyl group in four membered ring behaves like" ester" group[44]. also appearance the absorption bands for (OH)group in LY and LZ at (3414,3415.9) Cm^{-1} respectively.` β-Lactam(LY) confirmed by ^{1}H-NMR and ^{13}C-NMR **Figures(9,10)**. 1H-NMR spectrum (ppm)(DMSO-*d6*) for (LY)characteristic signals at ppm: (S, 1H,OH)10.26, (S ,3H ,OCH_3) 3.67,(*d, J=5 Hz*,1H,CH-N Lactam ring)(4.35), (*d, J=5Hz* ,1H,CH-Cl Lactam ring)(9.35)[45] ,(m,5H for benzene rings) (7.60-8.01). 13C-NMR spectrum for (LY)characteristic signals at ppm: C (-C=O in Lactam ring) 178.95 , C (-C-OH in phenyl ring)163.67, C (-C-S-N inThiazole ring)166.53, C (Aromatic rings)(112.57-142.74),C(-CH-Cl) 54.27,C(OCH_3) 47.27 These signals are confirm to the formation of (LY).

2-Amino-6-methoxybenzothiazole was converted to chloro acetamide derivative by reaction it with chloro acetyl chloride in DMF as solvent and Tri ethyl amine (Et_3N) as base catalyst with stirring at laboratory temperature to give Chloroacetamide derivative(C), **equation(1).**

The derivative(C) was confirmed by FT-IR spectrum figure (11) through disappearing the absorption bands for primary amine in starting material and appearing the carbonyl amide band at 1728.29 Cm^{-1} This value is high Attributed to the link Chloride atom, which are characterized as strong electron-withdrawing group Close to the carbonyl amide group. The band of NH amide showed at 3421.72 Cm^{-1} In addition to strong absorption band at 792.74 Cm^{-1} due to C-Cl bond. the band of aliphatic C-H showed at (2972.31-2941.44) Cm^{-1}. The derivative(C) also was confirmed by ^{1}H-NMR and ^{13}C-NMR **Figures(12,13)**. ^{1}H-NMR spectrum (ppm)(DMSO-*d6*) for (C)characteristic signals at ppm: (S, 1H,NH)10. 67, (S ,3H ,OCH_3) 3.57,(2H,CH_2-Cl)(4.33), (m,3H for benzene ring) (7.11-8.18). ^{13}C-NMR spectrum for (C)characteristic signals at ppm: C (-C=O in Chloro acet amide) 170.34 , C (S-C-N in Thiazole ring)162.53, C (Aromatic ring)(112.59-138.64),C(-CH_2-Cl) 44.28,C(OCH_3) 55.77 These signals are confirms the formation of (C) derivative.

From the derivative (C) prepared the Thiazole ring derivative (C3) by reaction it with Thio urea via microwave irradiation with 2ml of absolute ethanol **equation(2).**
The derivative(C3) was confirmed by FT-IR spectrum figure (14) through disappearing the absorption band for Carbonyl chloro acetamide in the derivative (C) and appearing the absorption bands for primary aromatic amine and group NH between thiazole ring and benzothiazole at (3415.93-3259.70),3176.76 Cm^{-1} respectively. The band of (C=N) endo cyclic for Thiazole ring showed at 1653.72 Cm^{-1} ,while The band of (C=N) endo cyclic for Thiazole in benzothiazole appeared at 1602.85 Cm^{-1} . the band of aliphatic C-H showed at (2978.09-2943.37) Cm^{-1}.

Also from the derivative (C) was prepared Azide derivative (C1) by the reaction of (C) with Sodium Azide in 2 ml DMF via microwave irradiation **equation(3).**

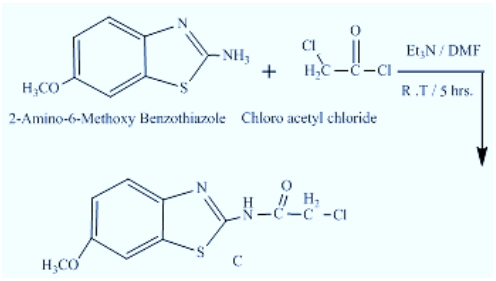
The derivative(C1) Was confirmed by FT-IR spectrum figure (15) through decrease the stretching vibration for amide carbonyl from 1728.29 Cm^{-1} to 1674 Cm^{-1} , appearing the sharp absorption band for Azide group at 2125.56 Cm^{-1} and appearing the absorption band for aromatic NH amide group at 3446.79 Cm^{-1} . The band of (C=N) endo cyclic for Thiazole ring in benzothiazole appeared at 1637.56 Cm^{-1}. By^{1}H-NMR spectrum figure (16) The derivative(C1) Was confirmed through signals at ppm: (S, 1H,NH)10. 56, (S ,3H ,OCH_3) 3.69,(S, 2H,CH_2-N_3)(2.29), (m,3H for benzene ring) (6.72-8.03). ^{13}C-NMR spectrum figure (17) for (C1)characteristic signals at ppm: C (-C=O amide) 171.72 , C (S-C-N in Thiazole ring)162.16, C (Aromatic ring)(112.59-143.24),C(-CH_2-N_3) 52.70,C(OCH_3) 55.21 These signals are confirms the formation of the derivative (C1).

The Schiff base(SH)was prepared from 4-Hydroxy Benzaldehyde with 2-amino Pyrimidine in absolute Ethanol (1 mL)and 2 drops of glacial acetic acid as catalyst via microwave irradiation at 120 W about 53 min **equation(4).**.
The Schiff base(SH)was identified by FT-IR spectrum figure (18) Where it is observed disappearing two bands of aromatic amine and appearing the imine group band at 1680 Cm^{-1}, also appearance the absorption bands for (OH) 3323.35 Cm^{-1}, (C=N) endocyclic in Pyrimidine ring at 1589.34 ,finally the absorption band for aromatic (C=C)was appeared at (1566.20- 1512.19) Cm^{-1}.

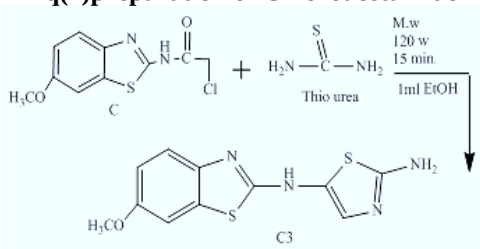
Tetrazole compounds are a five membered ring heterocycle [tetrazole derivatives (T1,T2) were one of known ways to prepare tetrazole derivatives is by (3+2) cycloaddition reaction between compound (C1) and Schiff base (SH) [47] for (T1) the other derivative(T2) was prepared from comp. (CI) with p-phenylene di isothiocyanate in DMF as solvent and the reflux at 90 °C **equation 5** .

The suggested mechanism (3+2) cyclo addition show in **Scheme (2).**

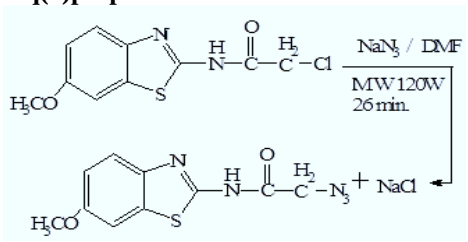
These derivatives were characterized by FT-IR spectra figures(19,20) respectively through disappearance of the Azide band in C1 at 2125 Cm^{-1} and appearance the bands at (1598.99,1608.63) Cm^{-1} due to N=N endo cyclic in Tetrazole derivatives (T1,T2),in addition to the bands for carbonyl amide that which appeared at(1668.43,1658.78) Cm^{-1} , the bands of NH amide are appeared at (3348.42, 3296.35) Cm^{-1} and the band at 3383.14 Cm^{-1} in T1 due to hydroxyl group . The bands of (C=N) endo cyclic in each derivative are appeared at(1543.05,1539.20) Cm^{-1} respectively.



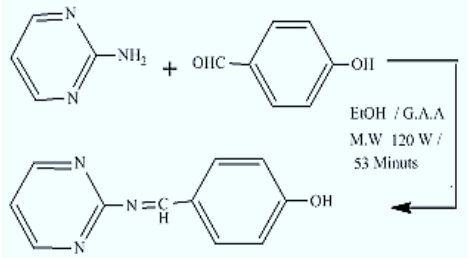
Eq(1)preparation of Chloroacetamide



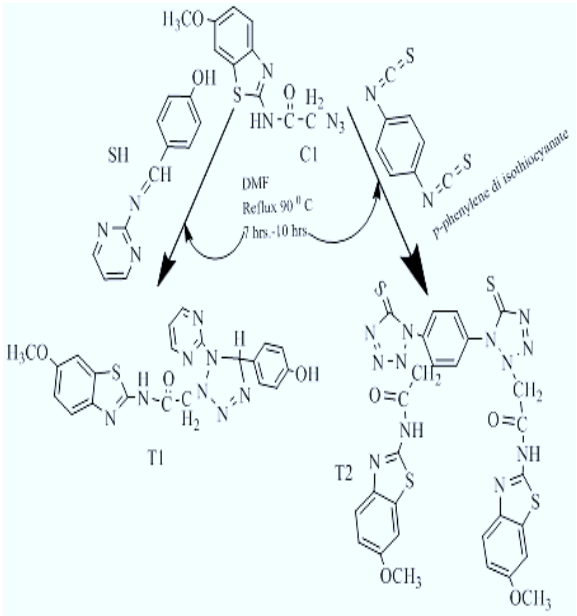
Eq(2)preparation of Thiazole derivative



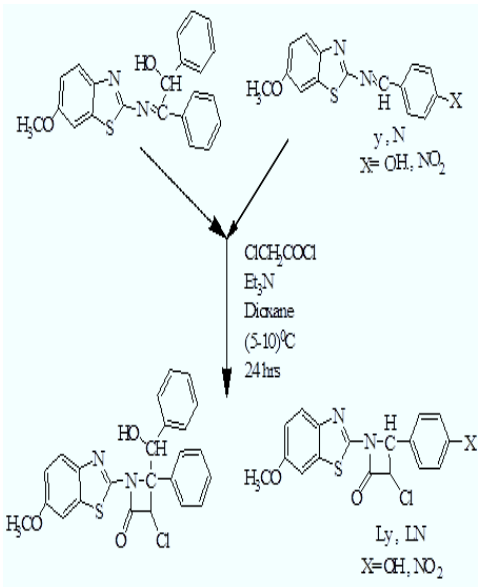
Eq.(3)preparation of Azide derivative(C1)



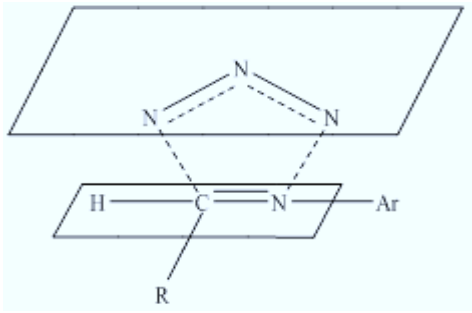
Eq.(4):preparation of Schiff base(SH)



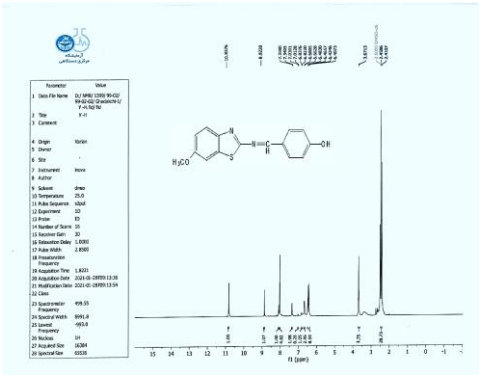
Eq.(5) preparation of Tetrazole Derivative



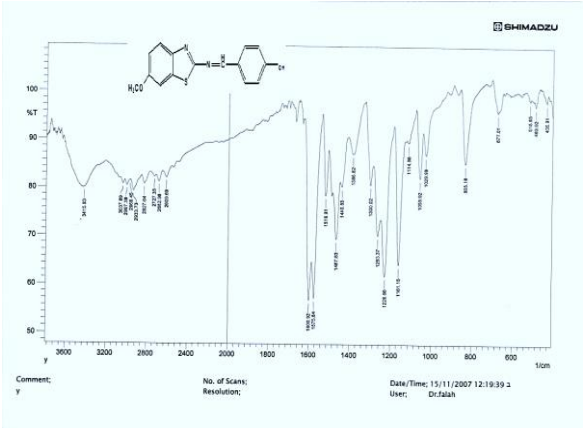
Scheme(1)preparation of β-Lactam derivatives



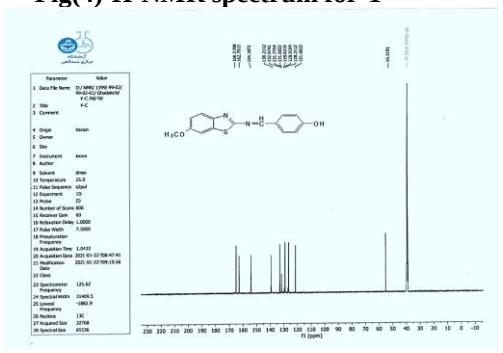
Scheme(2):mechanism(3+2)cyclo addition



Fig(4)^{1}H-NMR spectrum for Y



Fig(1)FT-IR spectrum for Y



Fig(5)^{13}C-NMR spectrum for Y

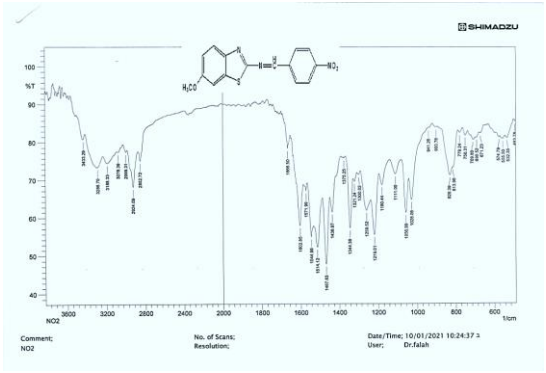
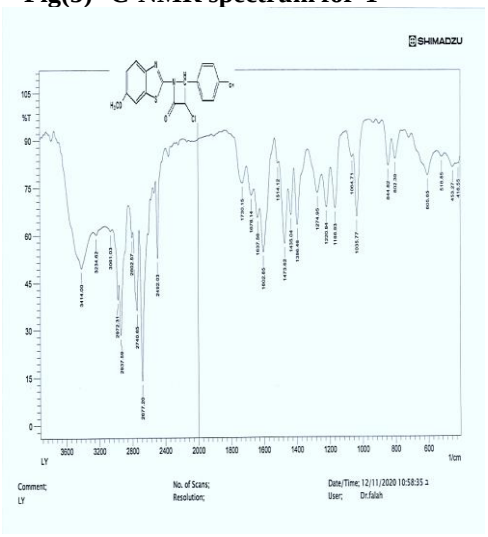
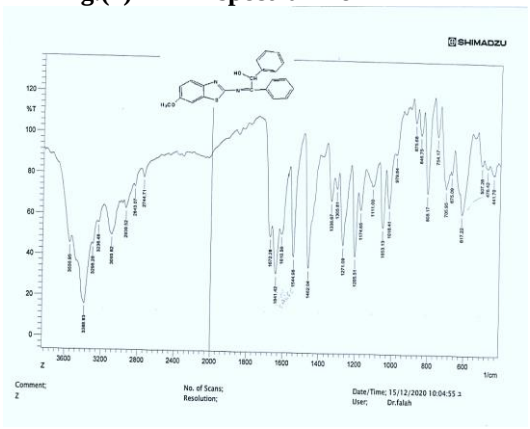


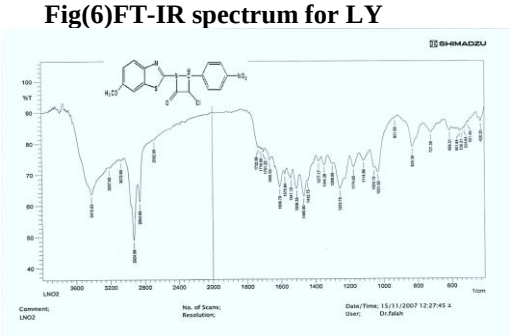
Fig.(2) FT-IR spectrum for N



Fig(6)FT-IR spectrum for LY



Fig(3) FT-IR spectrum for Z



Fig(7)FT-IR spectrum for LN

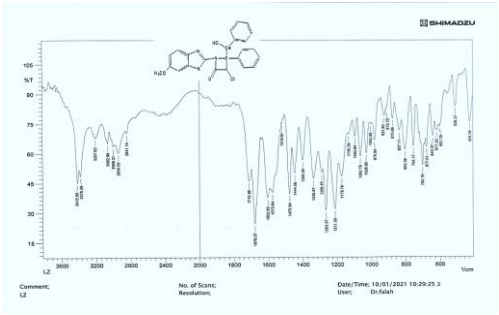
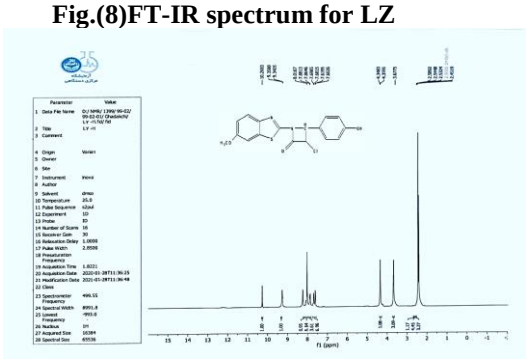
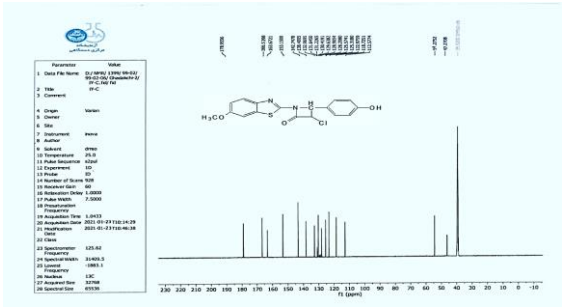


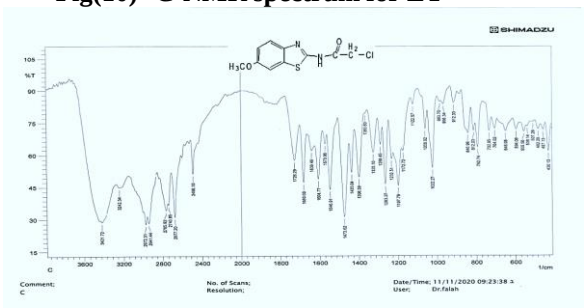
Fig.(8)FT-IR spectrum for LZ



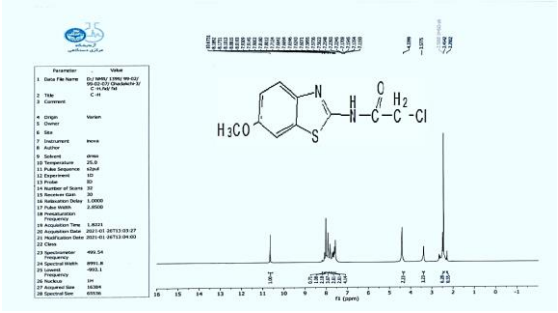
Fig(9)^{1}H-NMR spectrum for LY



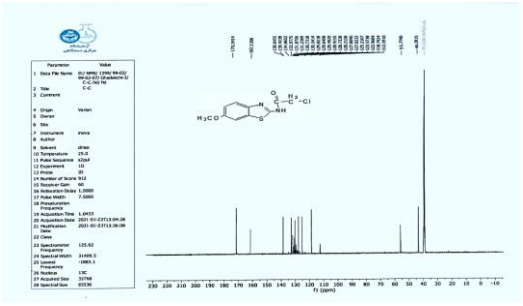
Fig(10)^{13}C-NMR spectrum for LY



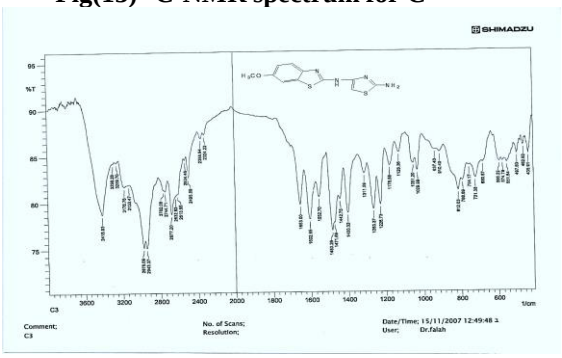
Fig(11)FT-IR spectrum for C



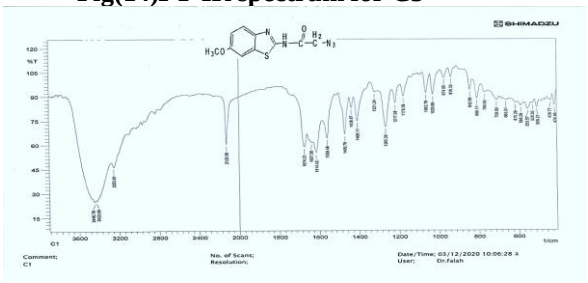
Fig(12)^{1}H-NMR spectrum for C



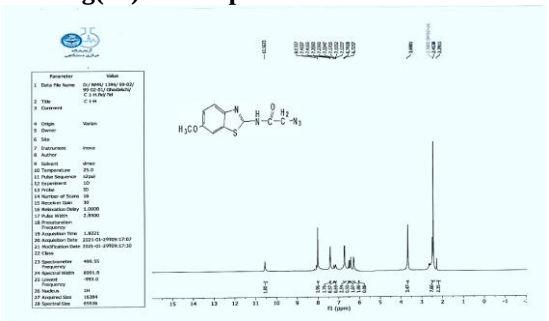
Fig(13)^{13}C-NMR spectrum for C



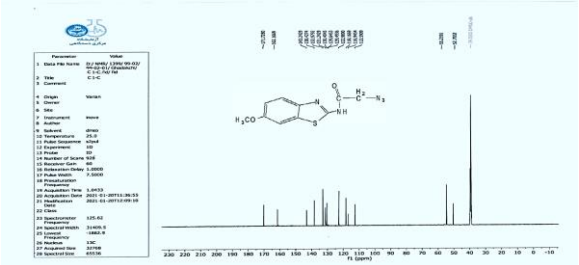
Fig(14)FT-IR spectrum for C3



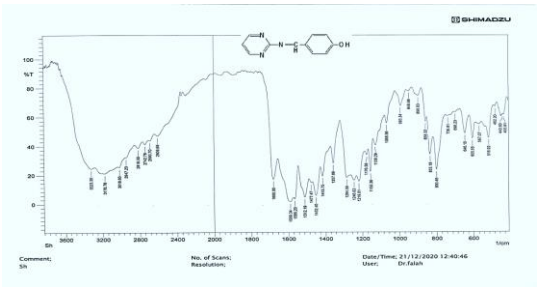
Fig(15)FT-IR spectrum for C1



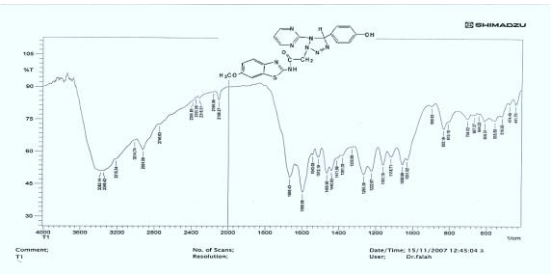
Fig(16)^{1}H-NMR spectrum for C1



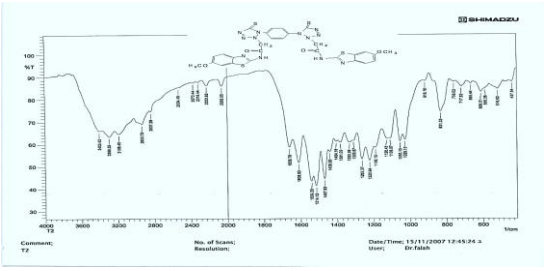
Fig(17)^{13}C-NMR spectrum for C1



Fig(18)FT-IR spectrum for Shiff base (SH)



Fig(19)FT-IR spectrum for(T1)



Fig(20)FT-IR spectrum for(T2)

CONCLUSION

In this study we are reported synthesis of different heterocyclic derivatives four and five membered rings .some of these derivatives are prepared via, Staudinger Reaction [2+2]cyclo addition and the other via [3+2]cycloaddition in addition to the Thiazole ring derivative . These derivatives were found to be stable at room temperature due to the aromaticity .one of The β-Lactam derivatives is oily. These derivatives confirmed from spectral data analysis; FTIR, 1H-NMR and 13C-NMR.

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References

1- Debasis Das, Papiya Sikdar, Moumita Bairagi," Recent developments of 2-aminothiazoles in medicinal chemistry" *European Journal of Medicinal Chemistry*, Volume 109, 15 February 2016, Pages 89-98.

2- Verma A., Saraf S.K." 4-Thiazolidinone—A biologically active scaffold". ***Eur. J. Med.*** Chem.2008;43:897–905. doi: 10.1016/j.ejmech.2007.

3- Lesyk R.B., Zimenkovsky B.S., Kaminskyy D.V., Kryshchyshyn A.P., Havrylyuk D.Y., Atamanyuk D.V., Subtel'na I.Y., Khylyuk D.V. "Thiazolidinonemotif in anticancer drug discovery. Experience of DH LNMU medicinal chemistry scientific group".Biopolym.Cell.2011;27:107–117. doi: 10.7124/bc.000089.

4- Nagham Mahmood Aljamali, Manar Ghyath AbdAlmutalib Almosawy,Ahmed Adnan Abdul Hussein, Nour Alhuda Abdul Abbas Bahar,Rajaa Abdul Ameer Ghafil&Noorhan Ali Hamza," REVIEW ONCHEMICAL-BIOLOGICAL APPLICATIONS OF THIAZOLEDERIVATIVES", Forefront Journal of Engineering &TechnologyVolume 2, Issue 3, Mar 2020, 9-22.

5- Lagoja, C. Pannecouque, G. Griffioen, S. Wera, V. M. Rojasdelaparra and A. V. Aerschot, Substituted 2-aminothiazoles are exceptional inhibitors of neuronal degeneration in tau-driven models of Alzheimer's disease, Eur. J. Med. Chem. 43 (2011) 386–392; https://doi.org/org/10.1016/j.ejps.2011.05.014

6- S. Kamila, K. Mendoza and E. R. Biehl, Microwave-assisted Hantzsch thiazole synthesis of N-phenyl-4-(6-phenylimidazo[2,1-b]thiazol-5-yl)thiazol-2-amines from the reaction of 2-chloro-1-(6-phenylimidazo[2,1-b]thiazol-5-yl)ethanones and thioureas, Tetrahedron Lett. 53 (2012) 4921–4924; https://doi.org/10.1016/j.tetlet.2012.06.116.

7- Dos Santos TA, da Silva AC, Silva EB, Gomes PA, Espíndola JW, Cardoso MV, Moreira DR, Leite AC, Pereira VR. Antitumor and immunomodulatory activities of thiosemicarbazones and 1,3-Thiazoles in Jurkat and HT-29 cells. Biomed Pharmacother.2016;82:555–60.

8- Ulusoy N, Kiraz M, Kucukbasmaci O. New 6-(4-Bromophenyl)-imidazo[2,1-b]thiazole Deriva-

tives: Synthesis and Antimicrobial Activity. Monats Chem. 2002; 133(10):1305–5.

9- Al-Saadi MS, Faidallah HM, Rostom SA. Synthesis and biological evaluation of some 2,4,5-trisubsti-tuted thiazole derivatives as potential antimicrobial and anticancer agents. Arch Pharm (Weinheim).2008;341(7):424–34.

10- N. S. Finiuk , V. P. Hreniuh, Yu. V. Ostapiuk, V. S. Matiychuk, D. A. Frolov, M. D. Obushak, R. S. Stoika, A. M. Babsky," Antineoplastic activity of novel thiazole derivatives" Biopolymers and Cell. 2017. Vol. 33. N 2. P 135–146.

11- Rehse K, Baselt T. New 2-amino-thiazole-4-acetami des with antiplatelet activity. Arch Pharm (Wein-heim). 2008;341(10):645–54.

12- Karade HN, Acharya BN, Sathe M, Kaushik MP.Design, synthesis, and antimalarial evaluation of thiazole-derived amino acids Med Chem Res. 2008, 17(1):19–29.

13- Nour E. A. Abdel-Sattar, Abeer M. El-Naggar, and M. S. A. Abdel-Mottaleb," Novel Thiazole Derivatives of Medicinal Potential:Synthesis and Modeling", Journal of Chemistry, Volume 2017, Article ID 4102796, 11 pages

14- Fred. van der Steen and Gerard van Koten ,"Syntheses of 3-Amino-2-azetidinones: A Literature Survey",*Tetrahidron*41(36), Pp. 7503-7524.(1991).

15- R. Deshmukh , A. Kumar Jha , A. Singh Thakur and P.SudhirKumar.,"SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME THIAZOLE COMPOUNDS CONTAINING AND AZETIDINONES AND THIAZOLIDINONES DERIVATIVES",*World Journal of Pharmaceutical research*,3(2), (2014).

16- A.A.Ashokrao, "Synthesis And Biological Activities Of Some Substituted Azetidinones" (dissertation), Rajiv Gandhi University of health sciences, Karnataka, 23,(2006).

17- P. ShankarMishra, Himanshu,S.K.Gupta andRakhiMishra.,"Synthesis, Characterization and Free Radical Scavenging Activity of 2-Azetidinone Derivatives"*International Journal of PharmTech Research*,8(7), pp 39-45,(2015).

18- D. Chandra, P. S. Mishra, Dr. S. K. Gupta and Ritu.,"Synthesis, Characterizationand Antimicrobial Activity of 2-Azetidinon Derivatives",*WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES* ,Vol. 3, 860-868 (2014).

19- H. Z. Zhang, L. L. Gan, H. Wang, C. H. Zhou. "New progress in azole compounds as antimicrobial agents. Mini-Rev"*Med. Chem.* 17, 122-166,(2017).

20- N. Kaushik, N. Kumar, A. Kumar, U. K. Singh. "Tetrazole: Synthesis and biological activity"*Immun., Endoc. & Metab. Agents in Med. Chem.* 18, 1-19,(2018).

21- Witten berger S. J, A New Journal for Organic Synthesis," RECENT DEVELOPMENTS IN TETRAZOLE CHEMISTRY. A REVIEW",(1994) ,26(5), 499-531.

22- T. Elavarasan, D. Sivakumar, M. Gopalakrishnan. "Tetrazole-ciproflocavin hybrids as antibacterial and anti-fungal agents"*J. Pharm. Res.* 12, 749-757,(2018).

23- R. Romagnoli, P. G. Baraldi, M. K. Salvador, D. Preti, M. A. Tabrizi, A. Brancale, X. H. Fu, J. Li, S. Z. Zhang, E. Hamel, R. Bortolozzi, G. Basso, G. Viola. "Synthesis and evaluation of 1,5-disubstituted tetrazoles as rigid analogues of combretatin A-4 with potent antiproliferative and antitumor activity"*J. Med. Chem.* 55, 475-488,(2012).

24- A. R. Qian, Y. Z. Zheng, R. L. Wang, J. H. Wei, Y. M. Cui, X. F. Cao, Y. S. Yang. "Design, synthesis, and structure-activity relationship studies of novel tetrazole antifungal agents with potent activity, broad antifungal spectrum and high selectivity"*Bioorg. Med. Chem. Lett* 28,344-350,(2018).

25- P. F. Lamie, J. N. Philoppes, A. A. Azouz, N. M. Safwat. "Novel tetrazole and cyanamide derivatives as inhibitors of cyclooxygenase-2 enzyme: Design, synthesis, anti-inflammatory evaluation, ulcerogenic liability and docking study"*J. Enzym. Inhib. Med. Chem.* 32, 805-820,(2017).

26- M. Tukulula, R. K. Sharma, M. Meurillon, A. Mahajan, K. Naran, D. Warner, J. Huang, B. Mekonnen, K. Chibale. "Synthesis and Antiplasmodial and Antimycobacterial Evaluation of New Nitroimidazole and Nitroimidazooxazine Derivatives"*ACS Med. Chem. Lett.* 4, 128-131,(2013).

27- Q. C. Ren, S. Zhang, C. Gao, Z. Xu, J. W. Ding, L. Huang, L. S. Feng. "Recent development of tetrazole derivatives as anti-tubercular

agents"*World Notes on Antibiotics* 38, 238-240,(2017).

28- Bijeta M., Suvodip M., Gyan Chandra P., Pranab G., *Tetrahedron Lett.*, 59, 1385–1389,(2018).

29- Lee K. H., Park C.E., Min K. H., Shin Y. J., Chung C. M., Kim H. H., Yoon H. J., Kim W., Ryu E. J., Shin Y. J., Nam H.S., Cho J.W., Lee H. Y., *Bioorg. Med. Chem. Lett.*,20,5567-5571,(2010).

30- Zhan P., Li Z., Liu X., De Clercq E., ***Med. Chem***., 9,1014-1023,(2016).

31- K. S. Yeung, Z. Qiu, Z. Yang, C. J. D'Arienzo, M. R. Browning, S. Hansel, X. S. Huang, B. J. Eggers, K. Riccardi, P. F. Lin, N. A. Meanwell, J. F. Kadow. "Inhibitors of HIV-1 attachment. Part 9: An assessment of oral prodrug approaches to improve the plasma exposure of a tetrazole-containing derivative"*Bioorg. Med. Chem. Lett.* 23, 209-212,(2013).

32- R. Arulmozhi, N. Abirami, K. P. Helen. A "Pharmacological expedition of tetrazole compounds towards medical filed-An overview"*Int. J. Sci. Rev. Res.* 46, 110-114,(2017).

33- Sharma, K., Singh, R., Fahmi, N., Singh, R.V." Microwave assisted synthesis, characterization and biological evaluation of palladium and platinum complexes with azomethines", 2010. *Spectrochimica. Acta* part A. 75(1), 422-427.

34- Sun, Y., Machala, M.L., Castellano, F.N." Controlled microwave synthesis of Ru^{II} synthons and chromophores relevant to solar energy conversion", 2010. *Inorg. Chim. Acta* ,Vol.363(1), 283-287.

IN PHARMACY AND CHEMISTRY (IJRPC), 2(1) (2012).

41-KhitamT. A. Al-Sultani, Suaad M. H. Al-Majidi, Oday H. R. Al-Jeilawi," Synthesis, Identification and Evaluation Biological Activity for Some New Triazole, Triazolineand Tetrazoline Derivatives From 2-Mercapto-3-phenyl-4(3H)Quinazolinone"***Iraqi Journal of Science,*** Vol. 57, No.1B, pp: 295-308,(2016).

42- Robert J. Deeth, Kieran C. Molloy, Mary F. Mahon and Sophie Whittaker," Organotin mediated cycloaddition reactions: a re-investigation of the reaction between organotin azides and iso thiocyanates", *Journal of Organometallic Chemistry,* 430 (1992) 25-35.

35- Sunita Bhagat, Nutan Sharma, and Tejpal Singh Chundawat," Synthesis of Some Salicylaldehyde-Based Schiff Bases in Aqueous Media", *Journal of Chemistry* , 2013, Article ID 909217, 4 pages.

36- B.T. VhanaleN.J. DeshmukhA.T. Shinde," Synthesis, characterization, spectroscopic studies and biological evaluationof Schiff bases derived from 1–hydroxy-2-acetonapthanone", ***Heliyon*** 5 (2019) e027743.

37- Radhiyah A. Khdur and Ezzat H. Zimam;" Synthesis and Characterization of some new β-Lactam Derivatives from Azo Sulphadiazine and its Biological Evaluation as Anticancer", ***Orient. J. Chem***., Vol. 34(1), 371-380 (2017).

38- Radhiyah A. Khdur and Ezzat H. Zimam." Synthesis, Characterization and study Biological Screening of Some new Azetidinone Derivatives From Azo- Sulphadiazene" ***Pak. J. Biotechnol***. Vol. 15 (1) 201-217 (2018) .

39- MOHAMMED AARJANE, SIHAM SLASSI, BOUCHRA TAZI, MOHAMED MAOULOUA and AMINA AMINE," Novel series of acridone-1,2,3-triazole derivatives: microwave-assisted synthesis, DFT study and anti bacterial activities", ***J. Chem. Sci.*** (2019) 131:85.

40- V. S. Kamble1, B.M. Habade1, G. K. Patil and Y. Agasimundin "Synthesisand Evaluationof 4-(1-Benzofuran-2- yl)-1,3-Oxazole-2-Amine andits Derivatives", ***INTERNATIONAL JOURNAL OF RESEARCH***

43- H. Hamza Salman,M. Abdul-Jaleel ,M. Ali and A. Ahmed Albader.,"Synthesis, Characterization of New Azetidinone Derivatives and Evaluation of Their Antimicrobial Activity" , ***Misan Journal of Academic studies***,(2014),24.

44- K.Anusha , Y. Pradeep Kumar, M.Vara Prasad, V. Baktamarkandeyaraju, C.Gopinath.,"A review on 2-Azetedinones" ,***Journal of Global Trends in Pharmaceutical Sciences,JGTPS***, (2015) ,6(1): 2388 – 2402.

45- Demirbas A, Sahin D, Demirbas N, Karaoglu SA. Synthesis of some new 1,3,4-thiadiazol-2-ylmethyl-1,2,4-triazole derivatives and investigation of their antimicrobial activities. Eur J Med Chem . 2009; 44:2896–2903. doi: 10.1016/j .ejmech.2008.12.005. .

46- Nagham Mahmood Aljamali., 2015. Synthesis and Chemical Identification of Macro Compounds of (Thiazol and Imidazol)".,Research J. Pharm. and Tech, 8,1, 78-84., DOI: 10.5958/0974-360X.2015.00016.5.

47- Rajaa Abdul Ameer Ghafil, Nour A Alrazzakb, Nagham Mahmood Aljamali., Synthesis of Triazole Derivatives *via* Multi Components Reaction and Studying of (Organic Characterization, Chromatographic Behavior, Chem-Physical Properties)., Egypt. J. Chem. Vol. 63, No. 11, pp. 4163 - 4174 (2020). DOI: 10.21608/EJCHEM.2020.23541.2399 .

48- Ammar .A . Al-sultani,"Synthesis of new Schiff Bases Derived from 3-Acetylindol",***Diala , Jour.*** **(2009) ,**Volume , 36.

49- Madhusudana Reddy Muthukur Bhoje Gowdand Mohamed Afzal Pasha, ***J. Chem. Sci.,*** Vol. 123, 1, p.75-79,**(2011).**