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Synthesis, characterization and study biological activity of some new pyrimidine and 1,2,3,4-tetrazole derivatives based on sulfadiazine

Abbass F. Abbass , Ezzat H. Zimam*

Department of Chemistry, Faculty of Science, University of Kufa, Iraq

Abstract : New 1,2,3,4-Tetrazole derivatives[S_1a-S_5c]were prepared by 1,3-diolarcyclo addition reaction of compound [2-azido-N-(4-(N-(pyrimidin-2-yl)sulfamoyl)phenyl)acetamide] with Schiff base derivatives[AaS_1-EcS_5], which prepared from a condensation of some aromatic aldehyde with 3- amino acetophenone derivative. The first step include synthesized of chalcone by cliesen –shemidtcondensation of 3-amino acetophenone with (4-Chloro, 2,4-Dichloro,4-Bromo,4-N,N-dimethyl amino and 2-Hydroxy-4-methoxy)benzaldehyde . Then cyclization with urea, thiourea and guanidine to produce pyrimidine derivatives[Aa-Ec], which will use to synthesized Schiff bases derivatives mentioned above . some of the prepared compounds were study biological activity, all the prepared compound werecharacterized bymelting point, FT-IR, H^1 NMR and mass spectroscopy.
Keywords*:* Chalcone, Schiff base, Tetrazole, Sulfadiazine and pyrimidine.

1. Introduction

Sulfadiazine with it's sulfonamide structure consider a useful antibacterial drug. By combining of sulfadiazine with antitumor agent in one compound this will lead to formation new antitumor agent with different activity [1]. Tetrazole are important class of five membered aromatic heterocyclic compound which have a broad spectrum of biological activity in both medicinal and pharmaceutical, such as new antimicrobial and antibacterial agent especially when it possess sulfadiazine as an functional group in the whole structure [2]. Also having anti-fungal, anti-viral, anti-inflammatory [3].

Chalcone are synthesized by base catalyzed Claisen-Schmidt condensation of aromatic aldehyde and ketone followed by dehydration to yield desired product[4].Chalcone are exhibit a wide spectrum of biological activity due to presence of a reactive α,β-unsaturated keto group. Schiff bases are important intermediates for synthesis of some bioactive compounds, which are prepared by the condensation of an primary amine with compound who contain carbonyl compound such as aldehyde or ketone[5]. Furthermore , they are reported to show a variety of interesting biological actions, including antibacterial, antifungal, anticonvulsant, anti-inflammatory and ant tubercular. Pyrimidine derivatives play avital role in many biological processes and in synthesis of many drugs . Many derivatives of pyrimidine have displayed diverse biological activities such as antitumor ,hypnotensive, antiulcer, and anticonvulsant[6].

This research involve synthesis new pyrimidine derivatives mixed with new 1,2,3,4- Tetrazoleand study biological activity of the prepared compounds.

2. Experimental

Melting points were recorded using electro thermal melting point apparatus. FT-IR spectra were recorded using alpha broker Infrared spectrophotometer. H^1 NMR were recorded on bruker spectrometer

operating on (300 MHz) with DMSO-d_6 as solvent. Mass spectrophotometer MAX300-LG. TLC was performed on aluminum plates and coated with layer of silica gel; compounds were detected by iodine vapor.

Preparation methods

Synthesis of chalcone derivatives[A-E] General procedure[7].

An equimolar mixture of 3-aminoacetophenone (0.01mole)and aromatic aldehyde derivatives (4-chloro, 2,4-dichloro, 4-bromo, 4-N,N-dimethylamino and 2-hydroxy-4-methoxybenzaldehyde) (0.01mole) in 20 ml of ethanol was stirred for 2 hrs. in the presence of 40%NaOH. The precipitate was obtained washed well with cold D.W and recrystallized from ethanol. The TLC was used to monitoring reaction progress by using (ethylacetate:n-hexan, 3:1).

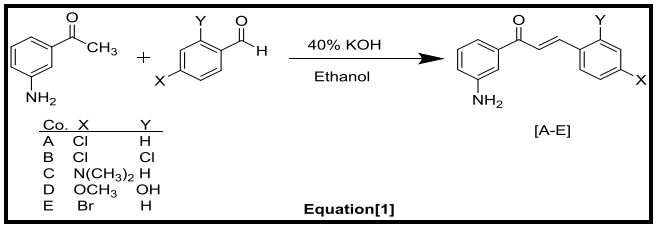


Table (1) Show some physical and chemical properties of compound [A-E]

No.	Molecular formula	M. wt	Yield %	Color	Melting point	R_f
A	$C_{15}H_{12}ClNO$	257.72	80	Yellow	129-131	0.65
B	$C_{15}H_{11}Cl_2NO$	292.16	78	Gray	93-96	0.73
C	$C_{17}H_{18}N_2O$	266.34	90.5	Orange	131-133	0.82
D	$C_{16}H_{15}NO_3$	269.30	75	Red	103-105	0.91
E	$C_{15}H_{12}BrNO$	302.17	79	Pale yellow	133-135	0.67

FT-I.R Spectra (cm^{-1}) **A.** (pri. –N-H str. 3465), (-C=C- str. 1626), (-C=O str. 1664), (-C-H str. 3047 Aromatic), (C-Cl str. 775). **B.** (pri. –N-H str. 3365), (-C=C- str. 1655), (-C=O str. 1671), (-C-H str. 3065 Aromatic), (C-Cl str. 789). **C.** (pri. –N-H str. 3431), (-C=C- str. 1602), (-C=O str. 1641), (-C-H str. 3074 Aromatic, aliphatic 2895,2809). **D**. (pri. –N-H str. 3478), (-C=C- str. 1654), (-C=O str. 1686), (-C-H str. 3066 Aromatic, aliphatic 2827), (-OH str. 3223). **E.** (pri. –N-H str. 3422), (-C=C- str. 1651), (-C=O str. 1682), (-C-H str. 3039 Aromatic), (C-Br str. 1092).

Synthesis of pyrimidine derivatives[Aa-Ee] General procedure[8].

A mixture of chalcone[Aa-Ec] (0.01mole) with urea, thiourea and guanidine (0.01) respectively were prepared in 25ml of absolute ethanol with stirred for 8 hrs.in the presence of 10% KOH. The reaction progress was monitored by TLC , the solvent was partially evaporated and the product was recrystallized from absolute ethanol.

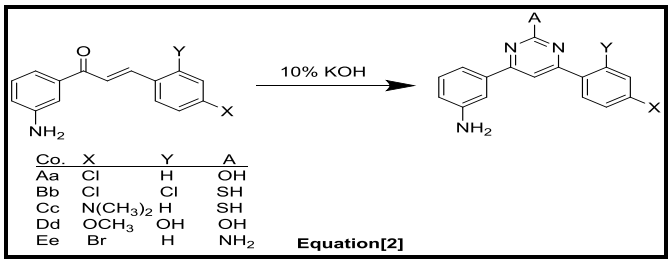


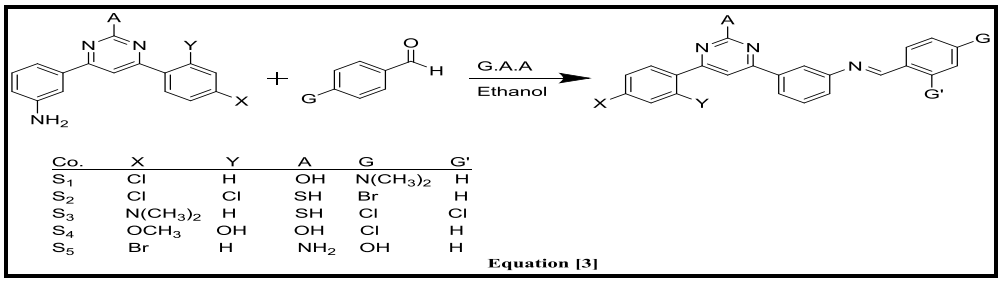
Table (2) Chemical and physical properties for prepared compounds [Aa-Ec].

No.	Molecular formula	M.wt	Yield%	Color	M.P ^{0}C	R_f
Aa	$C_{16}H_{12}ClN_3O$	297.74	75	Blond	255-260	0.67
Bb	$C_{16}H_{11}Cl_2N_3S$	348.25	80	Lemon	275-278	0.85
Cc	$C_{18}H_{18}N_4S$	322.43	75	Orange	245-250	0.68
Dd	$C_{17}H_{15}N_3O_3$	309.33	79	Brown	310-313	0.73
Ee	$C_{16}H_{13}BrN_4$	341.21	62	Fire	217-222	0.80

FT-I.R Spectra (cm^{-1}),**Aa.** (pri. –N-H str. 3435), (HC=N str. Pyrimidine 1564), (-C-H str. Aromatic 3081), (-C=C- str. 1629), (-C-Cl str. 776). **Bb.** (pri. –N-H str. 3462), (HC=N str. Pyrimidine 1596), (-C-H str. Aromatic 3036), (-C=C- str. 1665), (-C-Cl str. 774) , (-S-H str. 2334). **Cc.** (pri. –N-H str. 3423), (HC=N str. Pyrimidine 1578), (-C-H str. Aromatic 3039, aliphatic 2872), (-C=C- str. 1593), (-S-H str. 2649). **Dd.** (pri. –N-H str. 3422), (HC=N str. Pyrimidine 1454), (-C-H str. Aromatic 3099,aliphatic 2828), (-C=C- str. 1582), (-OH str. 3252).**Ee.** (pri. –N-H str. 3338), (HC=N str. Pyrimidine 1393), (-C-H str. Aromatic 3039), (-C=C- str. 1592), (-NH_2 str. 3498).

Synthesis of Schiff base[S_1-S_5] General procedure[9].

(0.001 mole) of some primary amines (Aa,Bb,Cc,Dd and Ee) with (0.001 mole) of different benzaldehyde derivatives dissolved in absolute ethanol and 2 drops of glacial acetic acid were refluxed (2-3 hrs.) at lab. Temp. . The precipitate formed have been washed with diethyl ether and recrystallized from ethanol.



Co.	X	Y	A	G	G'
S_1	Cl	H	OH	$N(CH_3)_2$	H
S_2	Cl	Cl	SH	Br	H
S_3	$N(CH_3)_2$	H	SH	Cl	Cl
S_4	OCH_3	OH	OH	Cl	H
S_5	Br	H	NH_2	OH	H

Equation [3]

Table (3) Some physical and chemical properties of prepared compound

No.	Molecular formula	M.wt	Yield%	Color	M.P ^{0}C	R_f
S_1	$C_{25}H_{21}ClN_4O$	428.92	87	brown	110	0.81
S_2	$C_{25}H_{21}ClN_4O$	479.42	78	Pale yellow	146	0.85
S_3	$C_{25}H_{20}Cl_2N_4S$	479.42	85	Brown	195	0.79
S_4	$C_{24}H_{18}ClN_3O_3$	430.89	88	black	295	0.69
S_5	$C_{23}H_{17}BrN_4O$	445.32	92	Black	290	0.75

FT-IR spectra (cm^{-1}).**S_1**. (Schiff –N=CH str. 1551), (-CH str. Aromatic 3065),(-C=C- str. 1654), (-OH str. 3327), (-C-Cl ben. 830). **S_2**. (Schiff –N=CH str. 1572), (-CH str. Aromatic 3093),(-C=C- str. 1631), (-SH str. 2696), (-C-Cl ben. 766). **S_3**. (Schiff –N=CH str. 1569), (-CH str. Aromatic 3000, Aliphatic 2932),(-C=C- str. 1679), (-SH str. 2781). **S_4**. (Schiff –N=CH str. 1555), (-CH str. Aromatic 3025, Aliphatic 2784),(-C=C- str. 1636), (-OH str. 3278). **S_5**. (Schiff –N=CH str. 1543), (-CH str. Aromatic 3025),(-C=C- str. 1534), (-NH_2 str. 3491).

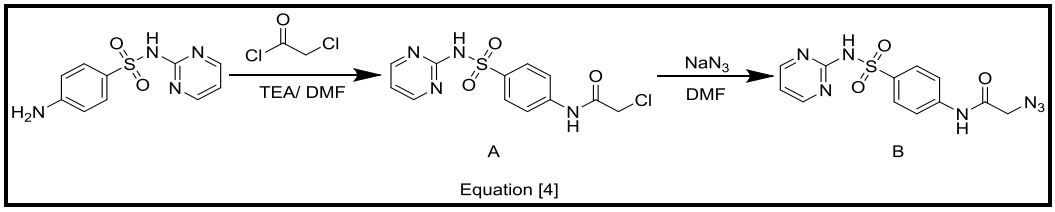
Synthesis of 2-chloro-N-(4-(N-(pyrimidin-2-yl)sulfamoyl)phenyl) acetamid[A][10].

A mixture of sulfadiazine (0.01 mole, 1.2 gm)and triethylamine (1.5ml) in DMF, Chloroacetyl chloride (0.01 mole, 0.7ml) was add drop-wise. The reaction mixture was stirred for (3hrs.).The solvent was evaporated

at the end of reaction, finally the precipitate were dried and recrystallized from ethanol. Yield pale yellow 85%, M.P.(220-222 ^{0}C) R_f (0.65) (ethylacetate: toluene, 4:1).

Synthesis of 2-azido-N-(4-(N-(pyrimidin-2--yl)sulfamoyl)phenyl)acetamide[B][11].

Sodium azide (0.01mole,0.04gm) was add to a solution of 2-chloro-N-(4-(N-(pyrimidin-2-yl)sulfamoyl)phenyl) acetamide (0.01mole,0.4gm) in (10ml) of DMF. The reaction mixture was refluxed at 90 ^{0}C for (7hrs.) with continuous stirring, finally the solvent was evaporated, the brown precipitate was formed and filtered also washing with diethyl ether and recrystallized from ethanol. Yield brown 82%, M.P. (122-125 ^{0}C), R_f (0.5) (ethylacetate: n-hexan, 4;1).



Equation [4]

Synthesis of 1,2,3,4-Tetrazole derivatives[T_1-T_5] General procedure[12].

Appropriate Schiff base (0.01mole) was dissolved in (25ml) of DMF and (0.01 mole) of 2-azido-N-(4-(N-pyrimidin-2-yl-sulfamoyl)phenyl) acetamide was added, the reaction mixture was heated under reflux to 90-95 ^{0}C for (24 hrs.), finally the solvent was partially evaporated and the product were filtered, dried and recrystallized from hot ethanol The TLC was used for monitoring reaction progress (ethyl acetate 3: n-hexan 1).

Table (4) Some physical and chemical properties of prepared compounds

No.	Structural formula	M. wt	Yield%	Color	M.P ^{0}C	R_f
T_1	$C_{37}H_{32}ClN_{11}O_4S$	762.25	78	black	386	0.65
T_2	$C_{35}H_{25}BrCl_2N_{10}O_3S_2$	848.58	81	Dark green	194	0.81
T_3	$C_{37}H_{31}Cl_2N_{11}O_3S_2$	812.75	85	Brown	379	0.79
T_4	$C_{36}H_{29}ClN_{10}O_6S$	765.20	94	Dark brown	282	0.49
T_5	$C_{35}H_{28}BrN_{11}O_4S$	778.65	84	Black	311	0.78

FT-IR spectra (cm^{-1}).**T_1**. (–N=CH str. 1539), (-CH str. Aromatic 3091,3107),(-C=O str. 1675), (-NH str. 3341), (-SO_2 ben. 1364,1330).**T_2**. (–N=CH str. 1578), (-CH str. Aromatic 3038,3076),(-C=O str. 1696), (-NH str. 3354), (-SO_2 ben. 1323,1261).**T_3**. (–N=CH str. 1541), (-CH str. Aromatic 3037,3103),(-C=O str. 1647), (-NH str. 3357), (-SO_2 ben. 1321,1261). **T_4**. (–N=CH str. 1491), (-CH str. Aromatic 3037),(-C=O str. 1681), (-NH str. 3320), (-SO_2 ben. 1325,1260). **T_5**. (–N=CH str. 1539), (-CH str. Aromatic 3034,3095),(-C=O str. 1676), (-NH str. 3340), (-SO_2 ben. 1333,1253).

Test of Biological Activity[13].

The test of biological activity of prepared chemical compounds which includes the following steps:

1. Prepare bacterial suspension from used bacteria (*Streptococcus ssp*. *Staphylococcus arueus,Granulecatella adiacens, proteus mirabilus, prophyromonas gingivalis and Escherichia coli*) and compared with McFarland tube 1.5× 108 cell /ml.
2. Spread bacterial suspension on (Muller Hinton Agar) homogeneously (0.1 ml) to cover the whole medium.
3. Make holes in the paten dish by the cork piercing to diameter 6 mm at concentration used.
4. Prepare dilute solutions (30, 60) mg/ml for each compound at physiological pH (7).
5. Put the prepared concentrated solutions from chemical compounds in holes to know their effectiveness for biological activity.
6. Incubate the paten dish at temperature 37 oC for 24 hours.

7. Measure the diameter of inhibition zone for each disc by the ruler to determine the effectiveness of each compound and compare with the standard limits of sensitivity of the same species of bacteria against antibiotics.

Results and Discussion

Chalcone[A-E] is the starting material of this research were synthesized by by cliesen –shemidt condensation which are characterized by FT-IR where the aliphatic (-C-H) at 2875-2998 cm^{-1} and also aldehyde (-C-H) at 2683-2875 cm^{-1} were disappear and new absorption bands due to stretching vibration of (-C=C-) at 1640-1680 cm^{-1} and conjugation (-C=O) bellow 1700 cm^{-1} were appeared. Compounds[A-E] are cyclized with urea, thiourea and guanidine respectively in a separated reactions to obtain pyrimidine derivatives [Aa-Ee].FT-IR spectrum good evidence to formation these compounds by inspection the changing in the absorption bands the major difference isdisappearing of (-C=O) of the [A-E] compounds and appearing (-N=CH-) of the pyrimidine ring at 1516-1590 cm^{-1}. Schiff bases [S_1-S_5] were synthesized by the condensation of compounds [Aa-Ee] with different aromatic aldehyde like [4-chloro benzaldehyde, 2,4-dichloro benzaldehyde,4-bromo benzaldehyde,4-N,N-dimethylamino benzaldehyde and 2-hydroxy-4-methoxy benzaldehyde] in absolute ethanol with some drops of glacial acetic acid as a catalyst. The FT-IR is used to detect formation of this compound by showing the stretching vibration band of imine group (-N=CH) at 1519-1625 cm^{-1} also the stretching vibration of amine group (-NH_2) are disappeared. Some extra characteristic bands were mentioned in experimental part.The vital compound [B] was synthesized by the reaction of 2-chloro-N-(4-(N-(pyrimidin-2-yl)sulfamoyl)phenyl) acetamid[A] which is prepared first by the reaction of sulfadiazine with chloro acetyl chloride in the presence of tri ethylamine as a catalyst with the DMF as a reaction solvent, with sodium azide in DMF also to formation compound [B]. The first compound which is considered precursors for synthesized of compound [B] was identify by sodium fusion test which isindicate on the presence of the chloride in the product also FT-IR technique indicate on the disappearing of stretching vibration of (-NH_2) group of sulfadiazine at 3358 cm^{-1} and appearance new absorption bands for (-N-H) group of amide at 3379 cm^{-1} also peak at 2995 cm^{-1} due to stretching vibration of (-CH_2), absorption peak at 1685 cm^{-1} attributed to the stretching band of (-C=O). Final important band was at 769 cm^{-1} for bending band of (-C-Cl).The compound[B] was inspected by FT-IR spectrophotometer where presence new absorption peak at 2112 cm^{-1} good evidence to the presence of (-N_3) group also disappearing of (-C-Cl) at 769 cm^{-1} are reasonable proof for synthesized desired compound.1,2,3,4-Tetrazole derivatives were synthesized by reaction of compound [B] with Schiff base derivatives [S_1-S_5] in DMF. This reaction going through [2+3] dipolar cyclo addition where the 1,3-dipolar [B] reacted with dipolarophile [Schiff bases] [S_1-S_5]. These compounds were characterized by FT-IR where the absorption band of (-N_3) in starting material where disappear, Also the reaction progress monitored by TLC (ethyl acetate:n-hexane, 3:1). H^1 NMR and mass spectra were recorded for the prepared compound.

Biological activity

The prepared compounds [T_1, T_2, T_3, T_4 and T_5] were examined for antibacterial activity against *Streptococcus ssp*. (Gram-positive) *and prophyromonas gingivalis*(Gram-negative) by well diffusion method in Mueller-Hinton agar medium. After 24 hours zone of inhibition around each disc. The test results presented in Table (5) showed that [T_2] exhibited slight active against *S. spp.* it was highly active against *Prophy. Gingivals.*

Table (5) Antibacterial activity of some synthesized compounds.

Comp.	Diameter of inhibition zone (mm)	
	Streptococcus spp. (Gram positive bacteria)	*Prophyromonasgingivalis* (Gram negative bacteria)
T_1	-	-
T_2	6	12
T_3	28	22
T_4	30	26
T_5	23	24

Mass spectra data for selected compound

1-[Aa] Figure [1] Chemical Formula: $C_{16}H_{12}ClN_3O$Exact Mass: 297.07M. Wt: 297.74

m/z: 297.07 (100.0%), 299.06 (32.0%), 298.07 (17.3%), 300.07 (5.5%), 299.07 (1.4%), 298.06 (1.1%).

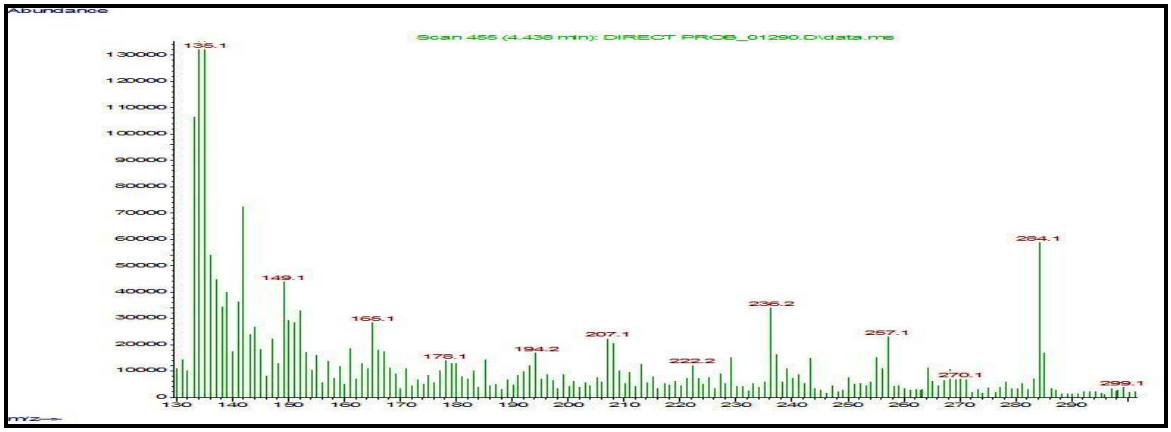


Figure 1: mass spectrum of the compound[Ee]

2-[Bb] Figure [2] Chemical Formula: $C_{16}H_{11}Cl_2N_3S$Exact Mass: 347.01M. Wt: 348.25

m/z: 347.01 (100.0%), 349.00 (63.9%), 348.01 (17.3%), 350.01 (11.1%), 351.00 (10.2%), 349.00 (4.5%), 351.00 (2.9%), 352.00 (1.8%), 349.01 (1.4%), 348.00 (1.1%).

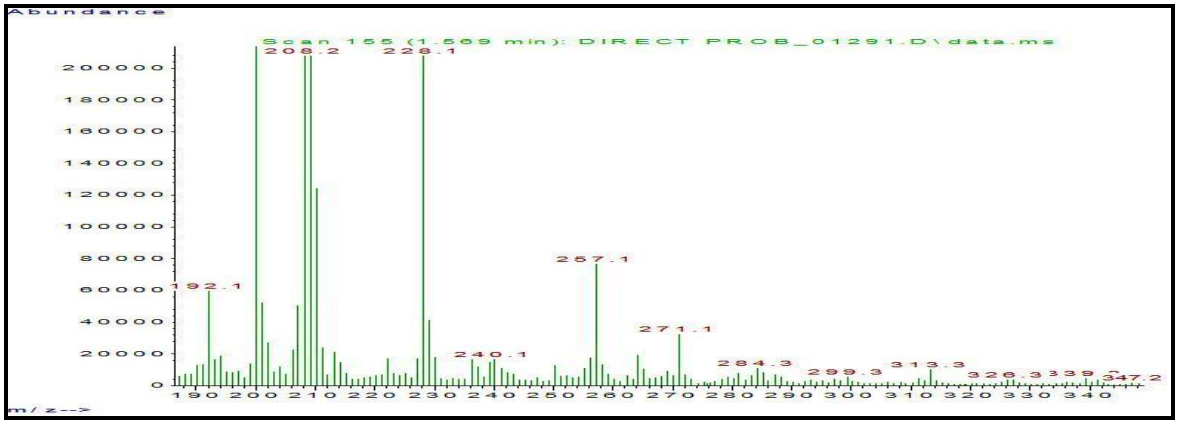


Figure 2: mass spectrum of the compound [Bb]

3-[Ee] Figure [3] Chemical Formula: $C_{16}H_{13}BrN_4$Exact Mass: 340.03M. Wt: 341.21

m/z: 340.03 (100.0%), 342.03 (97.3%), 343.03 (16.8%), 341.04 (16.2%), 341.03 (1.5%), 343.03 (1.4%), 344.04 (1.2%), 341.04 (1.1%), 342.04 (1.1%).

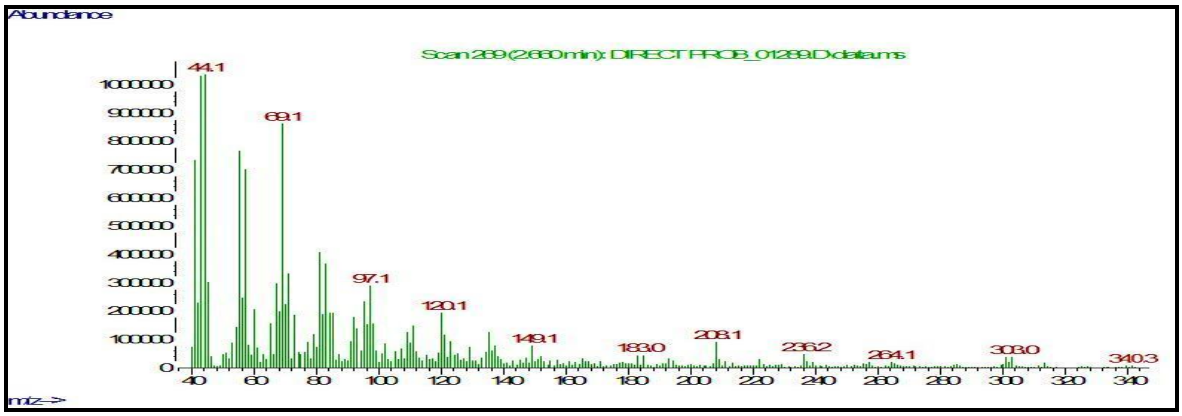


Figure 3: mass spectrum of the compound Aa

4-[S_1]Figure[4] Chemical Formula: $C_{25}H_{21}ClN_4S$Exact Mass: 444.118M. Wt: 444.981

m/z: 444.118 (100.0%), 446.115 (32.0%), 445.121 (27.0%), 447.118 (8.6%), 446.113 (4.5%), 446.124 (2.7%), 445.115 (1.5%), 448.110 (1.4%), 447.117 (1.2%).

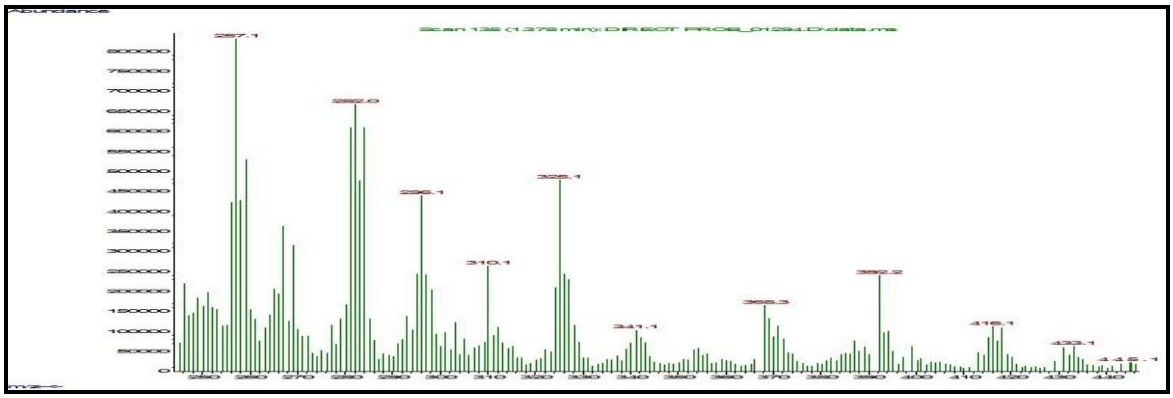


Figure 4: mass spectrum of the compound [S_1]

5-[S_2]Figure[5]Chemical Formula:$C_{25}H_{20}Cl_2N_4S$Exact Mass: 478.079M. Wt. : 479.423

m/z: 478.079 (100.0%), 480.076 (63.9%), 479.082 (27.0%), 481.079 (17.3%), 482.073 (10.2%), 480.074 (4.5%), 482.071 (2.9%), 483.076 (2.8%), 480.085 (2.7%), 482.082 (1.7%), 479.076 (1.5%), 481.078

(1.2%)

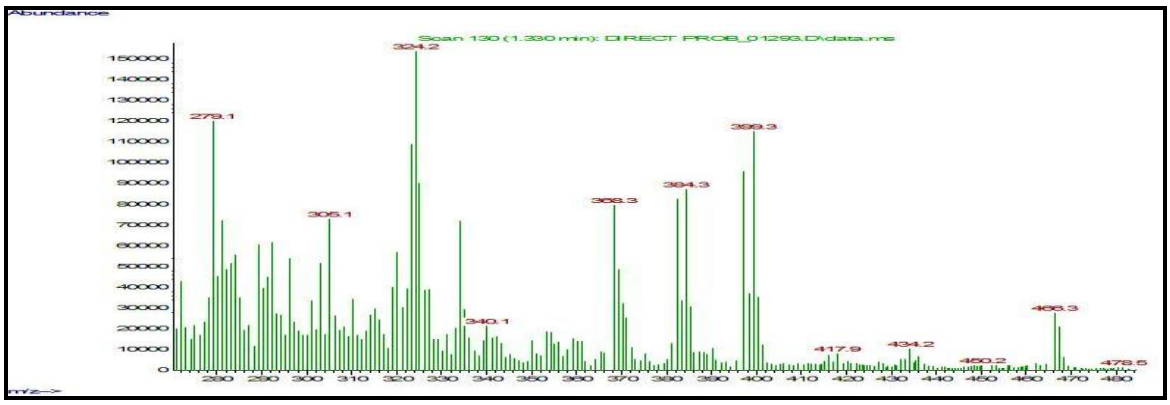


Figure 5: mass spectrum of the compound [S_2]

6-[S_5]Figure[6]Chemical Formula: $C_{23}H_{17}BrN_4O$Exact Mass: 444.059M. Wt.: 445.320

m/z: 444.059 (100.0%), 446.057 (97.3%), 447.060 (24.2%), 445.062 (16.2%), 445.062 (8.7%), 446.065 (2.6%), 448.063 (1.7%), 445.056 (1.5%), 447.054 (1.4%), 448.063 (1.2%)

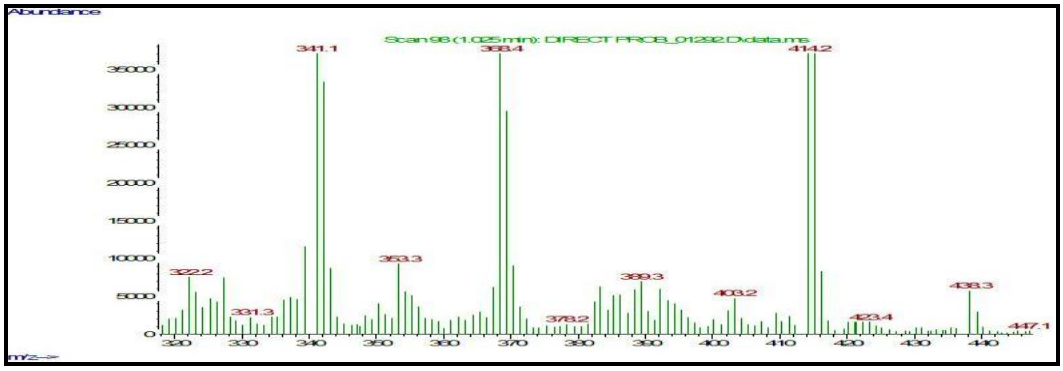


Figure 6: mass spectrum of the compound [S_3]

[1]HNMR Spectra for selected compound

Compound [S_1] Figure [7](DMSO-*d6*) as a solvent:

[(6H), (N-(CH_3)$_2$), 2.895], [(1H), (CH of Imine group), 8.669], [(13H), (Ar-H), 6.809-8.297], [(1H), (-SH), 11.763].

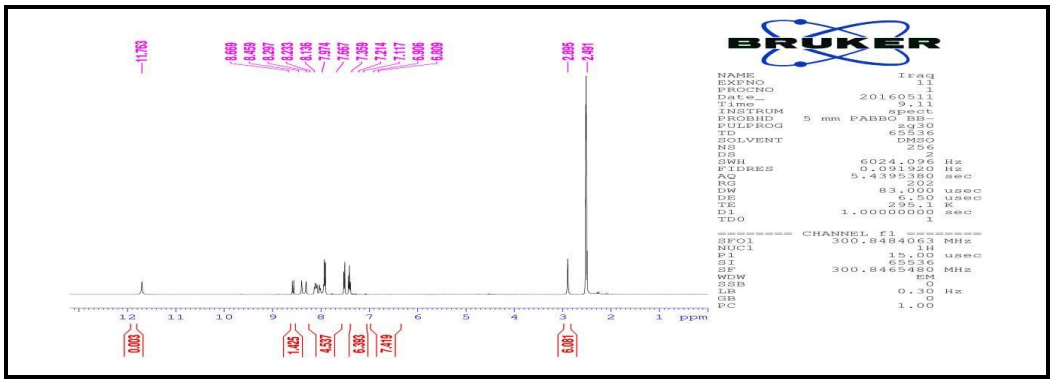


Figure 7: [1]HNMR spectrum of the compound [S_1]

Compound [S_2] Figure [8](DMSO-*d6*) as a solvent:

[(6H), (N-(CH_3)$_2$), 3.425],[(1H), (CH of Imine group), 8.674], [(12H), (Ar-H), 6.697-8.299], [(1H), (-SH), 12.014]

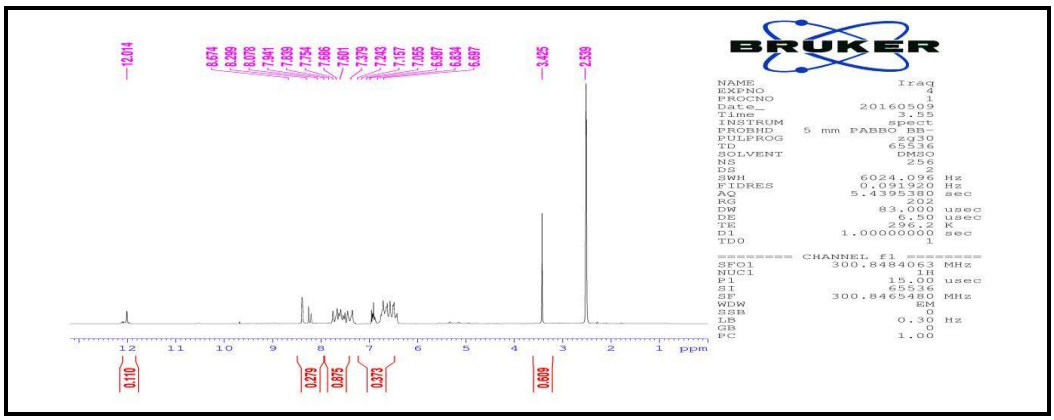


Figure 8: [1]HNMR spectrum of the compound [S_2]

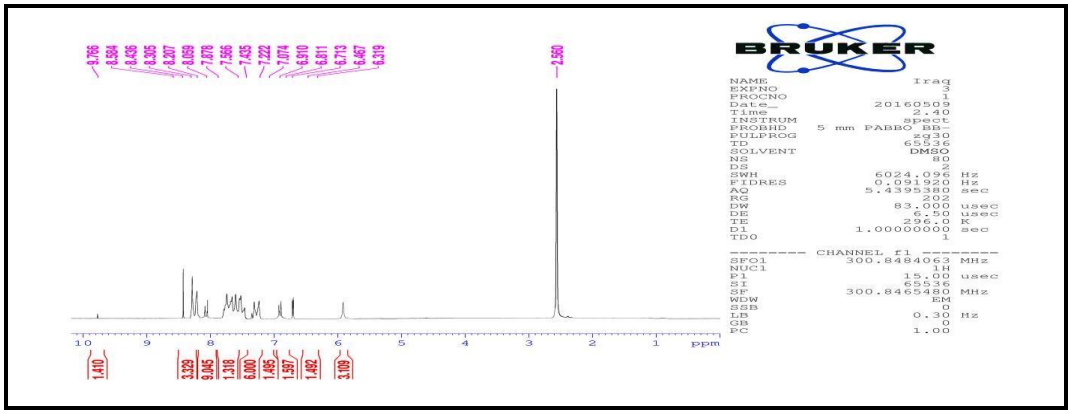


Figure 9: ^{1}HNMR spectrum of the compound [S_3]

Compound [S_3] Figure [9](DMSO-*d6*) as a solvent:

[(1H), (-CH of Imine group), 8.584], [(13H), (Ar-H), 6.467-8.436], [(2H), (-NH_2), 6.319].

Compound [T_1] Figure [10](DMSO-*d6*) as a solvent:

[(6H), (N-(CH_3)$_2$), 2.997], [(2H), (N-CH_2), 3.506], [(1H), (CH of tetrazole ring), 4.883], [(22H), (Ar-H), 6.531-8.382], [(1H), (CO-NH), 9.990], [(1H), (O-H), 10.653].

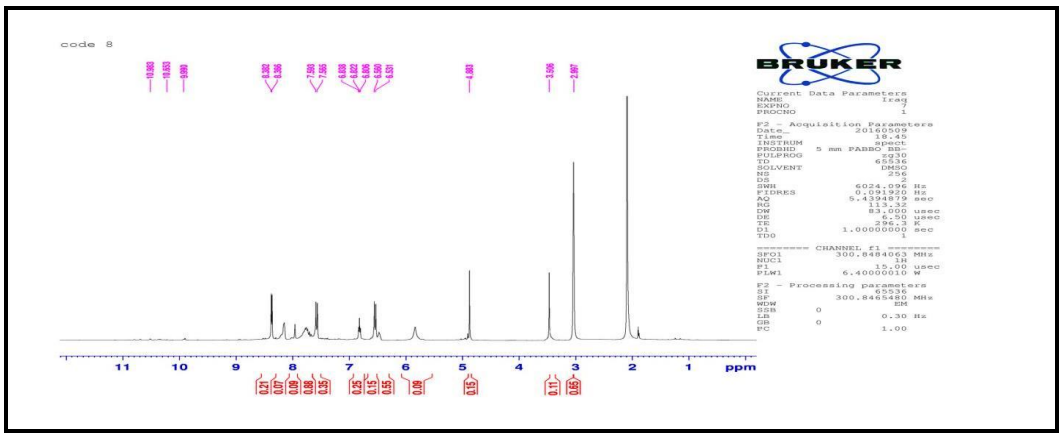


Figure 10: ^{1}HNMR spectrum of the compound [T_1]

Compound [T_2] Figure [11](DMSO-*d6*) as a solvent:

[(2H), (N-CH_2), 3,106], [(1H), (CH of tetrazole ring), 4.560], [(22H), (Ar-H), 6.486-8.524], [(1H), (CO-NH), 10.335], [(1H), (S-H), 12.018].

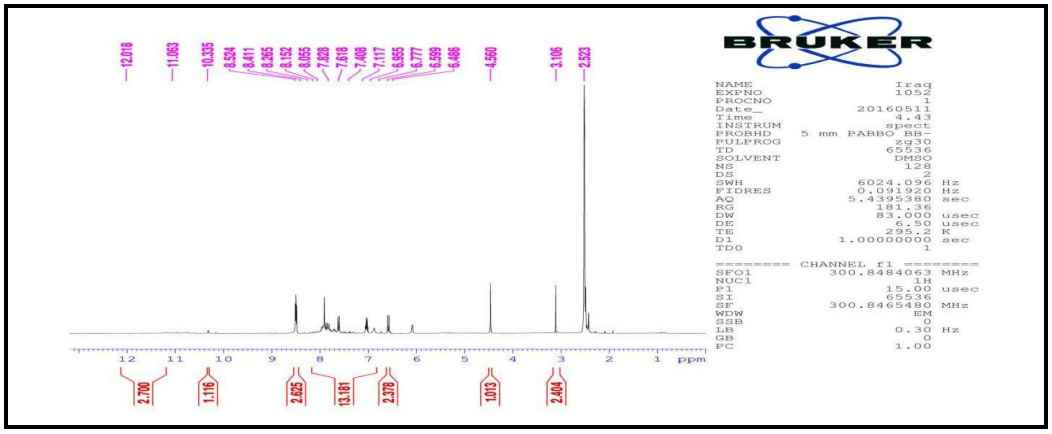


Figure 11: ^{1}HNMR spectrum of the compound [T_2]

Compound [**T_3**] Figure [12] (DMSO-*d6*) as a solvent:

[(6H), (N-(CH_3)$_2$), 3.282], [(2H), (N-CH_2), 3,380], [(1H), (CH of tetrazole ring), 4.389], [(21H), (Ar-H), 6.526-8.499], [(1H), (CO-NH), 10.239], [(1H), (S-H), 11.581].

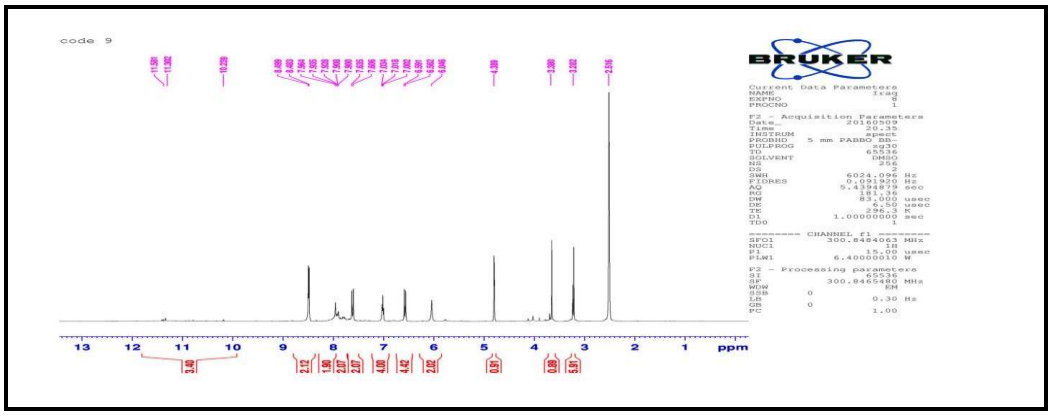


Figure 12: ^{1}HNMR spectrum of the compound [T_3]

Compound [T_4] Figure [13](DMSO-*d6*) as a solvent:

[(3H), (O-(CH_3)), 2.962], [(2H), (N-CH_2), 3,598], [(1H), (CH of tetrazole ring),4.940], [(21H), (Ar-H), 6.564-8.493], [(1H), (CO-NH), 10.236], [(1H), (-OH), 11.149]

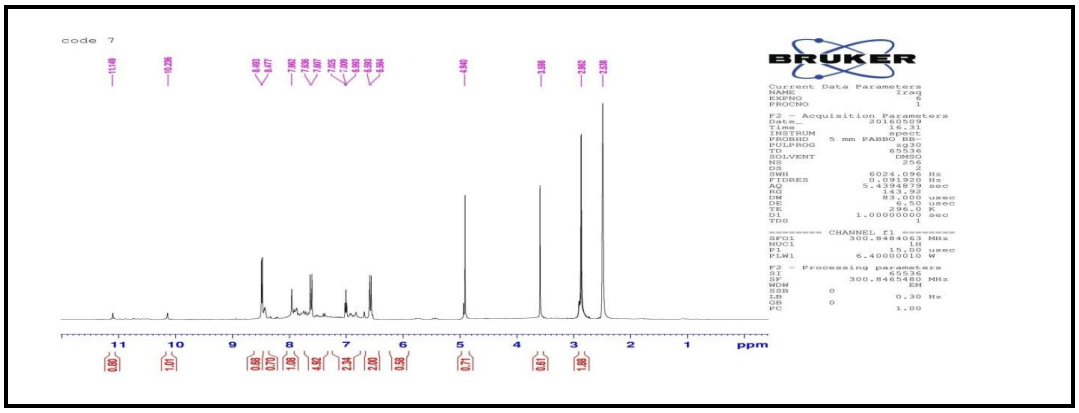


Figure 13: ^{1}HNMR spectrum of the compound [T_4]

Compound [T_5] Figure [14](DMSO-*d6*) as a solvent:

[(2H), (N-CH_2), 3,481], [(1H), (CH of tetrazole ring), 4.755], [(21H), (Ar-H), 6.551-8.605], [(1H), (CO-NH), 10.772], [(2H), (-NH_2), 6.050].

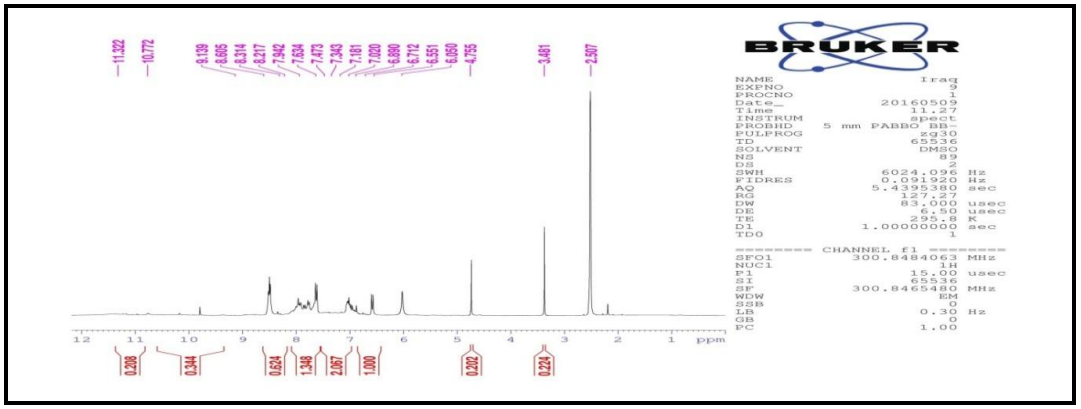
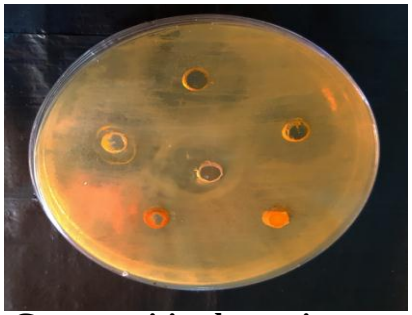
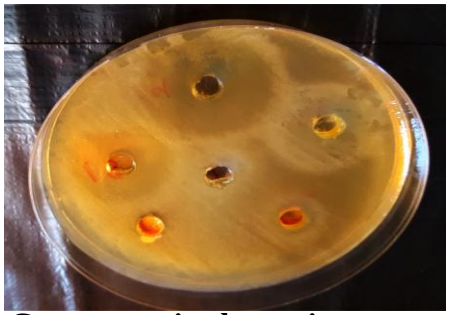


Figure 14: ^{1}HNMR spectrum of the compound [T_5]



Gram positive bacteria



Gram negative bacteria

References

1. N.V. Satheesh Madhav, Shivani Kala, Review on Microparticulate Drug Delivery System, *International Journal of Chem Tech. Research*. 2011, 3-3, 1242-1254.
2. Zhaohua Huang, Genjin Yang, Zhaolianglin, et al ,2-[N1-2- Pyrimidyl- amino benzene sulfonamido] Ethyl 4- Bis(2- chloroethyl) Aminophenyl Butrate: A Potent Antitumor Agent, *Bioorganic and Medicinal Chemistry Letters*, 2001,11, 1099-1103.

3. Xiangping Hu.,Huilin Ch., Huicong Dai and Zhao Zh. ,Synthesis of novel P-ketimine bidentate ferrocenyl ligands with central and planar chirality and comparsion in the catalytic activity between P-ketimine and P-aldimine,*Tetrahedron: Asymmetry* 2003,14: 3415-3421
4. Ahmed Hassen Shntaif , Green Synthesis of Chalcones under microwave Irradiation ,*International Journal of ChemTech. Research*. 2016, 9-02 ,36-39,
5. R. N. Deshmukh and R. V. Dengle, An efficient Synthesis and Characterization of New Bischalcones *International Journal of Chem Tech. Research*,2015,8-3: 1260-1263.
6. Ramchander Merugu, Swetha Garimella, Deepthi Balla and Kalyani Sambaru, Synthesis and Biological Activities of Pyrimidines: A Review , *International Journal of Chem Tech. Research*., 2015, 8-6, 88-93.
7. Ezzat H. Zimam, Synthesis, Characterization and Study Biological activity of some new Sulphadiazine derivatives ,*International journal of chemical and neutral sciences*,2014, 2-4 ,109-115.
8. Bhaskar VH.,Mohite PB.,Pandhare RB., et al, Synthesis and in vitro antimicrobial activity of some novel chalcones containing 5-phenyl tetrazole, *Acta pharm.sci.* ,2010, 52,504.
9. Mohamad Jawad Khubeiz , Synthesis and Spectroscopic Studies on the new Schiff Base Derived from the 1:1 condensation ofIsatinwith Amines and itsEvaluating biological activity *International Journal of ChemTech Research*,2016,9-7: 516-522.
10. Ishwar Bhat K, Sunil Kumar Mishra, Jainey. P. James, et al, Antimicrobial studies of synthesized azetidinone de rivatives from sulfamethoxazole moiety, *Journal of Chem. Pharm. Res.*, 2011, 3-3, 114-118.
11. Alan R. Katritzky, Khalid Widyan and Kostyantyn Kirichenko, Preparation of polyfunctional acyl azides,*Journal of Organic Chemistry*, 2007,72, 5802-5804.
12. Young Soo Gyoung, Jae-Goo Shim and Yoshinori Yamamoto, Regiospecific ,synthesis of 2-allylated-5-substituted tetrazoles via palladium-catalyzed reaction of nitriles, trimethylsilyl azide, and allyl acetates, *TetrahedronLetters*, 2000 ,41, 4193–4196.
13. Ego rove. N. S.,Antibiotics Scientific Approach . *Mir publishers. Moscow*,1985.

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