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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME SUBSTITUTED BENZAZEPINE COMPOUNDS & NEW SUBSTITUTED BIOLOGICAL ACTIVE DERIVATIVE OF BENZENE SULPHONAMIDE

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ABSTRACT

Benzazepine are heterocyclic chemical compound consisting of benzene ring fused to an azepine ring. Benzazepine, ring contain a seven membered aza- heterocyclic ring fused with aromatic unit is involved in research aspired to asses new products that posses interesting biological activities. The aim of this evaluation is to provide an overview of the diverse and important pharmacological activities of benzazepine moiety. The review of show up important of benzazepine derivatives as an anti-fungal, Antimicrobacterial, antihypertensive, Latest efforts ended to various pharmacologically active molecules that contain benzazepine moiety reported.

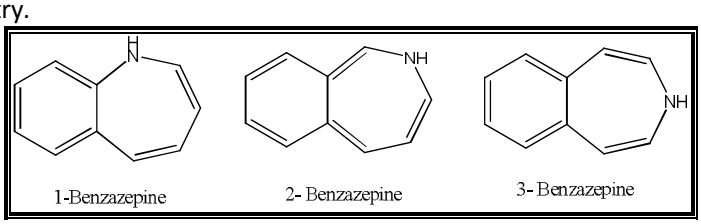
Moreover, sulphonamides of type RSO_2NH_2 (where R may be an aliphatic , aromatic or heterocyclic moiety) make up an important class of drugs , match up to several types of pharmacological agents possessing antibacterial , antiviral and ant carbonic anhydrase , diuretic , protease inhibitor, cyclo-oxygenase and anticancer activities among other. In the present study we have synthesized new analogs of benzazepine and sulphonamides. The structure of these synthesized compounds was confirmed by NMR, IR, Mass and CHN analysis. According to the result of this spectra and analysis were found that in the normal range. These compounds were evaluated for the antibacterial and antifungal.

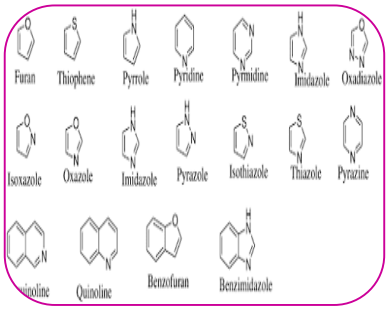
KEYWORDS: *heterocyclic chemical , diverse and important pharmacological activities.*

INTRODUCTION

Drug development has been one of the leading research areas in the field of pharmaceutical industry, as a result the development the new molecules with the help of heterocyclic compound continuous pull toward academic and industrial level. Here attempted trial for prepared newer class of the safer antibacterial and antifungal agent as per necessitate according to time and cost.

The fusion of a benzene ring at different edge of azepine gives rise to three isomeric benzazepine. The benzazepine skeleton has been found to be component of natural product; moreover the derivative of three isomeric benzazepine also made known interest to medicinal chemistry.





The aim of this evaluation is to provide an overview of the diverse and important pharmacological activities of benzazepine moiety. The review of show up important of benzazepine derivatives as antibacterial , anti-fungal, anti-depressant, anti-hypertensive, anti-ischemic and anorectic, anti- histamine agent. Latest efforts ended to various pharmacologically active molecules that contain benzazepine moiety reported.

Sulfonamides are one of the organosulphur compound contain the $–SO_2NH_2$ and $–SO_2NH$ group. As per benzene sulphonamide group contain drugs ready for action inhibit folic acid synthesis in micro-organisms and as a result inhibit multiplication of bacteria but do not kill them but shown activity against the gram positive and gram negative bacteria. Mostly, this sulphonamide derivative is play very important role in the pharmacological activity. It showed it activity as an Antimicrobacterial agent, Moreover, some derivatives also shown the other activity like antifungal, antidepressant.

Here, Sulphonamide and Benzazepine derivatives showed the important role in the pharmaceutical drug chemistry.

RESEARCH METHODOLOGY

My Research approaches include the plan and the procedure for research than duration the steps from broad assumptions to detailed methods of data collection, analysis and interpretation using NMR, IR and mainly thin layer chromatography. The overall decision involves which approach should be used to study a topic.

A research design is the arrangement of conditions for collections and analysis of data in a manner that aims to combined relevance to the research purpose with economy in procedure.

OBJECTIVE

Thesis work based on “Evaluation, synthesis and characterization of novel heterocyclic compounds contain biological activity.

Taking a view, the applicability of heterocyclic compounds, I have undertaken the preparation of heterocycles bearing Sulphonamide and benzazepine nucleus. The placements of a wide variety of substituents of nuclei have been a design in order to evaluate the synthesized products for their pharmacological profile against several of antibacterial, antifungal, and antibiotic. The objective of the proposed research work is as follow:

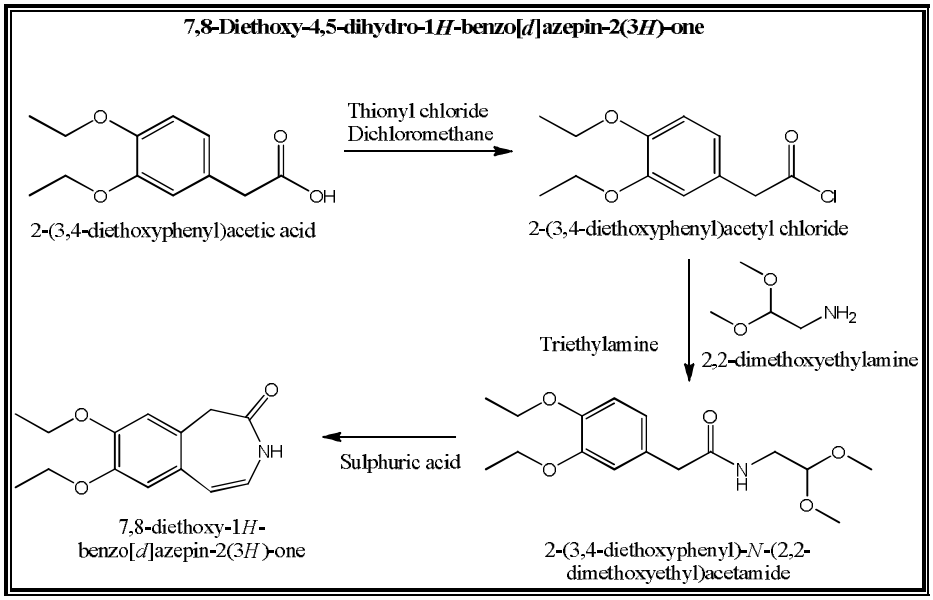
To study on biological active derivative of benzene sulphonamide & new substituted benzazepine compounds.

SCOPE OF STUDY

Research statement of the study is to develop an efficient synthesis route and salt derivatives to isolated class of Antibacterial, antipsychotic, antifungal and therapeutic compounds the unique chemical structure of this series of compound contain Nitrogen, Oxygen and sulpher atom skeleton and their significant activity. The novel structure of the compound makes it a desirable synthetic target, as a successful synthetic route to allow the investigation of related heterocyclic compounds which may show improve research study. Heterocyclic compounds play important role towards the development of drug discovery. The study of biological properties of newly synthesized heterocyclic compounds is the main significance of the proposed research work. The rich activity of heterocyclic compounds in biological systems is important for pharmaceuticals, agricultural, and natural products. Heterocyclic compounds have provided a platform for the rapid exchange of research in the areas of organic, pharmaceutical, analytical, and medicinal chemistry.

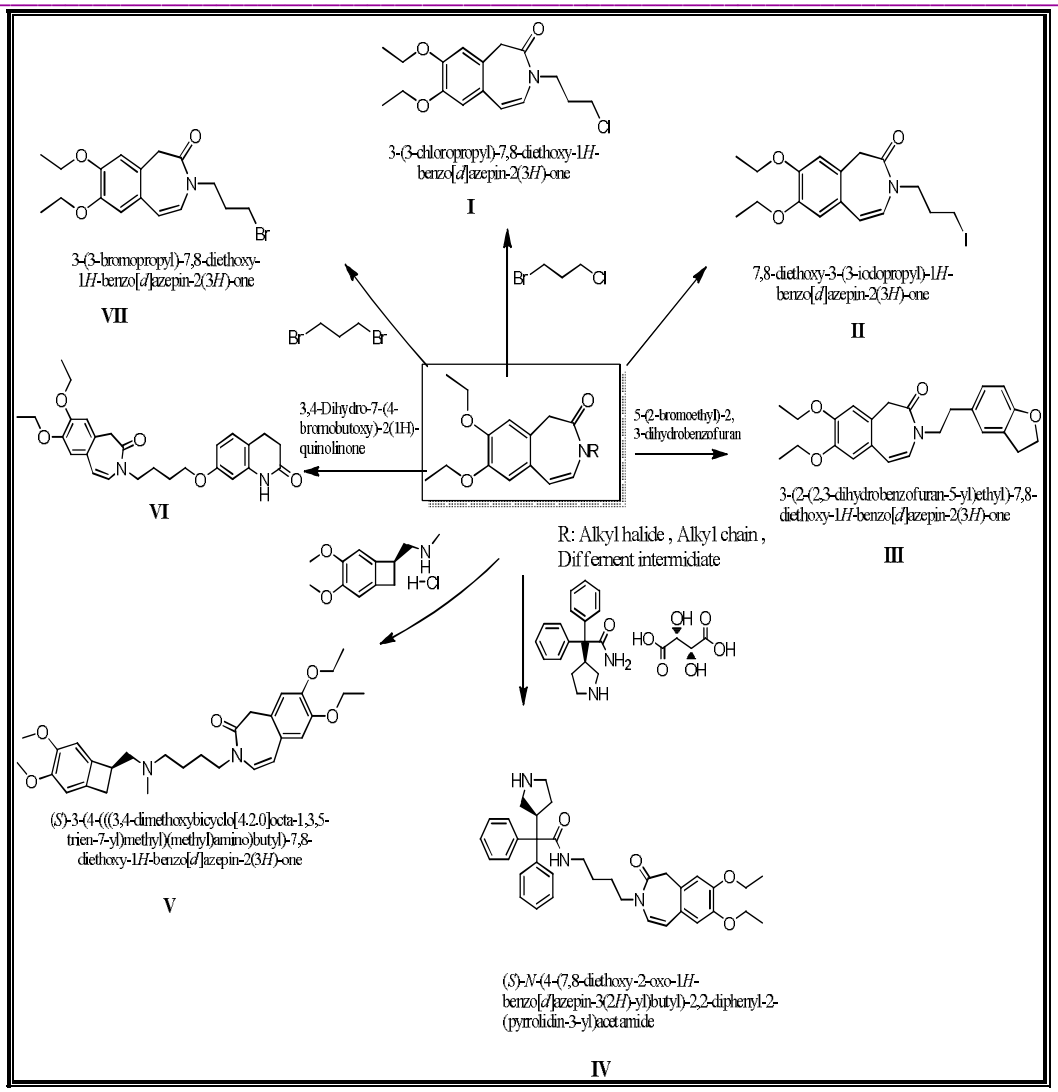
RESULT AND DISCUSSION

Novel benzazepine intermediate prepared as per following route of synthesis for 7, 8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one.



PROCESS

2-(3,4-diethoxyphenyl)acetic acid react in the presence of the Thionyl chloride in dichloromethane solvent at reflux temperature. Further , monitor the reaction mass on TLC, once reaction was complies than distilled the Dichloromethane solvent & isolated the residue.Moreover,2,2-dimethoxyethylamine react with the residue of 2-(3,4-diethoxyphenyl) acetyl chloride in the presence of organic base i.e.triethyamine resultant formation of 2-(3,4-dimethoxyethyl)acetamide. Further this intermediate reaction was conduct with con.sulphuric acid resultant cyclization reaction occur & formation of the desired intermediate. Further this intermediate react with another active intermediate follow on novel compound of benzazepine compounds which shown the biological activity. Using the above intermediate attempted the following novel intermediate of the benzapine. This showed the different biological activity and also possible synthesis in the scale level. further , Moreover, as per above reactions condition with intermediate attempted trial in 7,9-Dimethoxy -1H-benzo[*d*] azepine -2(3H)-one.



Note: prepared different derivative using the benzazepine moiety with condense the heterocyclic compounds (R: Alkyl group, aromatic ring derivatives, Heterocyclic compounds)

Process

a) 3-(3-chloropropyl)-7, 8-diethoxy-1H-benzo[d]azepin-2(3H)-one

This intermediate is prepared using the 7, 8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one in the presence of potassium carbonate and 1-bromo-3-chloropropane in N,N-Dimethylformamide solvent resultant formation of novel compound like 3-(3-chloropropyl)-7,8-diethoxy-1H-benzo[d]azepin-2(3H)-one.

b) 7, 8-diethoxy-3-(3-iodopropyl)-1H-benzo[d]azepin-2(3H)-one

Prepared above compound using the intermediate and inorganic base in N, N-Dimethylformamide resultant formation of the desired compound with good yield and quality. Isolated yield: 90 %.

c)3-(2-(2,3-dihydrobenzofuran-5-yl)ethyl)-7,8-diethoxy-1H-benzo[d]azepin-2(3H)-one

7,8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one react with 5-(2-bromoethyl)-2,3-dihydrobenzofuran in the presence of the inorganic base like potassium carbonate, sodium bicarbonate

using the acetone and N, N-Dimethylformamide solvent follow on the desired product. Material isolated with 80 %.

d)(S)-N-(4-(7,8-diethoxy-2-oxo-1H-benzo[d]azepin-3(2H)-yl)butyl)-2,2-diphenyl-2-(pyrrolidin-3-yl)acetamide

(S)-2,2-diphenyl-2-(pyrrolidin-3-yl)acetamide(2R,3R)-2,3-dihydroxysuccinate heterocyclic compound is conducted reaction with 7, 8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one in the presence of the Dimethyl acetamide solvent and inorganic base at 40-45^{0}C. Monitor the reaction complies on the thin layer chromatography; further isolation conduct with addition of the water and extract in the dichloromethane solvent. Yield of isolated material: 89 %.

e)(S)-3-(4-(((3,4-dimethoxybicyclo[4.2.0]octa-1,3,5-trien-7-yl)methyl)(methyl)amino)butyl)-7,8-diethoxy-1H-benzo[d]azepin-2(3H)-one

(S)-1-(3,4-dimethoxybicyclo[4.2.0]octa-1,3,5-trien-7-yl)-N-methylmethanamine hydrochloride intermediate carry the reaction with prepare above intermediate in the presence of the N,N-Dimethylformamide solvent in the presence of the organic base as Diisoproylamine and also inorganic base as potassium carbonate. Further, add the water drop-wise into the reaction mass at 0-5^{0}C.

Yield: 90 %.

f)7,8-diethoxy-3-(4-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)butyl)-1H-benzo[d]azepin-2(3H)-one

3,4-Dihydro-7-(4-bromobutoxy)-2(1H)-quinolinone compound is conducted the reaction with 7, 8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one resultant isolated desire compound in the presence of the base with different solvent like Dimethyl acetamide , N,N-Dimethylformamide and acetone. Isolated yield: 92%

RESULT

The physical data as well as UV-vis, FT-IR, ^{1}H-NMR and ^{13}C-NMR spectral data confirmed formation of the desired products. All synthesized compounds showed the very good biological activity.

a) 7, 8-diethoxy-4, 5-dihydro-1H-benzo[d]azepin-2(3H)-one (I): yield; 90%, RF: 0.50, IR (KBR cm-1); 1660.12, 2923.56, 1082.34; ^{1}H-NMR (dmso-d_6 δ ppm); 6.84 (d,2H,Ar-H),1.32 (triplet,3H) ,4.09 (m,4H), 3.44 (s, 2H) , 2.81 (t,2H) and 8.03 (s,-NH). ^{13}C-NMR (dmso-d6, δ ppm) 14.8 (-CH_3), 64.9 (-CH_2); 42.6 (-CH_2); 112.9-11.9 (Ar-C), 171.4(-C=O), 146.4, 147.5 (-O-Ar-C).

b) 7,8-diethoxy-3-(3-iodopropyl)-1H-benzo[d]azepin-2(3H)-one (II): yield ; 89% , IR (KBR cm-1); 1660 (-NH-C=O), 2922.4, 3020.32, 1080.32; ^{1}H-NMR (dmso-d_6 ppm); 1.32(t, 3H), 4,09(m,-CH_2) ; 6.85-6.95(d,2H,Ar-H) ; 3.13 (t,-CH_2I) , 3.44 (s,-CH_2) , 4.12(t, -NCH_2)). ^{13}C-NMR (dmso-d6, δ ppm); 14.8 (-CH_3); 64.8 (-CH_2), 169.5 (-N-C=O), 126.6,129,148,1 (-Ar-C).

c)3-(2-(2,3-dihydrobenzofuran-5-yl)ethyl)-7,8-diethoxy-1H-benzo[d]azepin-2(3H)-one : Yield; 80% , IR (KBR cm-1); 1320-1000(-C-O), 3000-2850 (Aromatic ring –CH), 1685 (-NH-C=O), 1375 (-CH_3).^{1}H-NMR (dmso-d_6 ppm);1.32(t,3H),6.85-7.42(d,2H,Ar-H), 4.27(-O-CH_2) ,2.38-3.41(-CH_2).^{13}C-NMR (dmso-d6, δ ppm); 14.8 (-CH_3); 64.6 (-CH_2) ; 109.3-115.3(-Ar-CH) ; 169.5 (-NH-C=O) ,110.0-126.6 (Benzazepine –Ar-CH).

d)(S)-N-(4-(7,8-diethoxy-2-oxo-1H-benzo[d]azepin-3(2H)-yl)butyl)-2,2-diphenyl-2-(pyrrolidin-3-yl)acetamide : yield : 89 %, IR (KBR cm-1) ; 3100-3000 (-Aromatic ring) ; 1685 (-Amide functional group) ; 1320-1000 (-C-O). ^{1}H-NMR (dmso-d_6 ppm); 1.32 (-CH3); 6.18-7.42 (-Ar-CH); .2.97-4.27 (-CH2 of benzofuran methylene group); 2.83-3.41 (-CH_2 methylene group of alkyl chain). ^{13}C-NMR (dmso-d6, δ ppm); 126.2-141.2 (-Ar-CH), 169.5(-C=O), 64.9 (-C-O), 14.8 (-CH_3); 30.3-51.9 (-Pyrrolidin ring methylene group). 56.9 (-C).

e)(S)-3-(4-(((3,4-dimethoxybicyclo[4.2.0]octa-1,3,5-trien-7-l)methyl)(methyl)amino)butyl)-7,8-diethoxy-1H-benzo[d]azepin-2(3H)-one : Yield : 90% , IR (KBR cm-1); 1375(-Methyl group) ; 1690 (-Amide group), 3000-2980 (Aromatic functional group),1089 (-C-O),1400-1500 (Methylene group chain between bicyclic and benzazepine ring). ^{1}H-NMR (δ ppm, dmso-d_6); 6.88-6.92(d, 2H aromatic), 2.77-2.52 (methylene group), 1.76-4.12 (alkyl chain between bicyclic ring and azepine), 3.83 (-OCH_3).^{13}C-NMR (dmso-d6, δ ppm); 109.5-111.8(-Aromatic CH), 44.3 (-NH-CH_3), 126.6-130.5 (Benzazepine aromatic –CH), 56.1 (-O-CH_3) , 169.5 (-N-C=O) , 25.5-60.7 (methylene carbon between bicyclic and benzazepine), 14.8 (-CH_3).

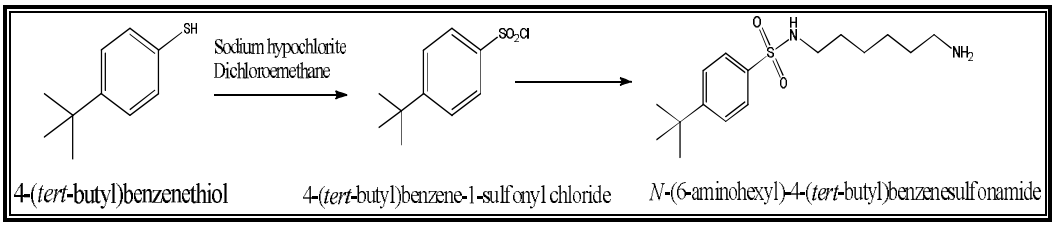
f)7,8-diethoxy-3-(4-((2-oxo-1,2,3,4-tetrahydroquinolin-7-yl)oxy)butyl)-1H-benzo[d]azepin-2(3H)-one ; Yield :92% , IR (KBR cm-1);1690 (NH-C=O) ; 3000-2850 (Alkyl chain between azepine& quinoline ring); 1150-960(-C-O); 3100-2800 (Aromatic ring); ^{1}H-NMR (δ ppm, dmso-d_6) : 8.0 (-NH-C=O) ; 2.49-2.86 ppm (alkyl chain of quinoline ring) ; 6.85-6.95 ppm(Ar-CH, 2d) ; 1.52-4.06 ppm (alkyl chain between quinoline and azepine). ^{13}C-NMR (dmso-d6, δ ppm); 170.1 (-NH-C=O of quinoline ring); 26.3-29.3 (-CH_2 of quinoline); 106.2-128.5 (Aromatic carbon), 169.5 (amide carbon of benzazepine ring); 14.8 (-CH_3); 64.9 (O-CH_2 of benzazepine ring contain aromatic ring alkyl chain), 26.3, 27.1, 68.4 and 48.4 (-CH_2 alkyl chain between quinoline and benzazepine).

RESULT AND DISCUSSION SULPHONAMIDE DERIVATIVES:

According to literature of benzene sulphonamide shown the antibacterial activity, antiviral, antidiabetic and antihypertensive. With the help of the research article ; here prepared the N-(6-aminohexyl)-4-(tert-butyl) benzenesulfonamide intermediate (KSM-01); Moreover , prepared the another intermediate like 3-(2-chloroethyl)-2-methyl-9-(oxiran-2-ylmethoxy)-2H-pyrido[1,2-a]pyrimidin-4(3H)-one (KMS-02) in the presence of the inorganic base and solvent resultant formation of the novel intermediate of sulphonamide derivative follow on shown the biological activity as a Antimicrobacterial. Here following derivative prepared with simple reaction with high yield and quality.

g):4-(tert-butyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide.
h):4-(tert-butyl)-N-(2-chloroethyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido [1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide.
i) N-(2-bromoethyl)-4-(tert-butyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido [1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide.
j) :4-(tert-butyl)-N-(2-iodoethyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide.
k) :tert-butyl (4-(tert-butyl)phenyl)sulfonyl(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)octyl)carbamate.
l):4-(tert-butyl)-N-(3-(9-hydroxy-2-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-3-yl)propyl)benzenesulfonamide.

Scheme:
KSM-01:



Process: N-(6-aminohexyl)-4-(tert-utyl) benzenesulfonamide

Arrange 3N RBF with equipped mechanical stirrer, thermometer, condenser and thermometer pocket. Charge 4- (tert-butyl) benzenethiol in dichloromethane solvent.

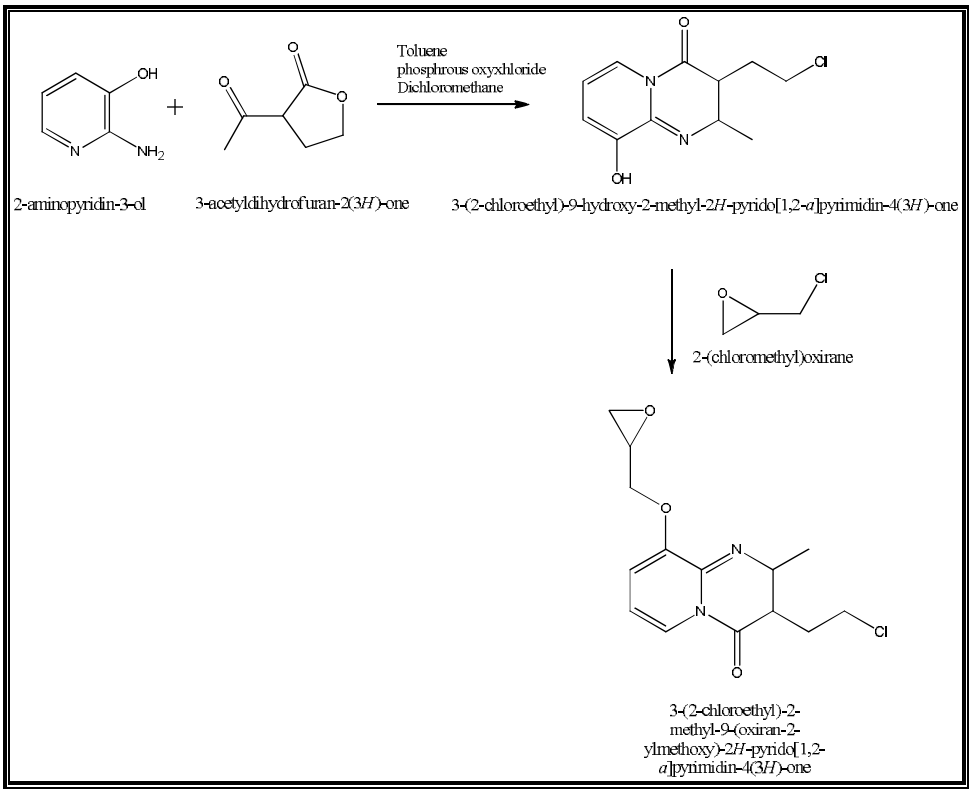
Cool the reaction mass at 0-5^{0}C.Addition of the Sodium hypochlorite (3mmole) solution drop-wise into the reaction mass with maintain the temperature of the reaction mass 0-5^{0}C. Maintain the reaction mass for 3-4 hrs.Charge the water (2 vol) into the reaction mass & Stir the reaction mass. Adjust the PH using the sodium bicarbonate solution. Stirred and the layers separation. Took, Organic layer distil it completed & weight residue. Further the next reaction performed with residue using hexane 1, 6 diamine resultant formation of the N-(6-aminohexyl)-4-(tert-utyl) benzenesulfonamide (KSM-1).

KSM-02:

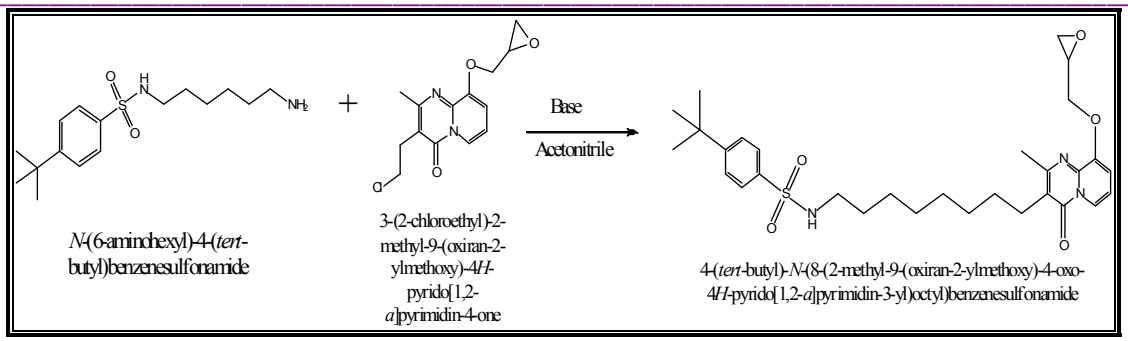
Process:3-(2-chloroethyl)-2-methyl-9-(oxiran-2-ylmethoxy)-2H-pyrido[1,2-a]pyrimidin-4(3H)-one

Arrange 3N RBF with equipped mechanical stirrer, thermometer, condenser and thermometer pocket. Charge the 2- aminopyridin-3-ol react with 3-acetyldihydrofuran -2(3H)-one in toluene solvent with addition of phosphorous oxychloride drop-wise with maintain the temperature of the reaction mass 0-10^{0}C.

Maintain the reaction mass for 4-5 hrs at reflux temperature of toluene solvent. Isolated residue of pyrimidines derivative ; further the reaction was conduct with 2-(Chlromethyl)oxirane in the presence of the base and N,N-Dimethylformamide solvent, follow on isolated the 3-(2-chloroethyl)-2-methyl-9-(oxiran-2-ylmethoxy)-2H-pyrido[1,2-a]pyrimidin-4(3H)-one. **(KSM-02)**.



Prepared the following the desire target molecule using KSM-01 &KSM-02 in the presence of base at room temperature.



Target Molecule process: 4-(tert-butyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide

Charged the 3-(2-chloroethyl)-2-methyl-9-(oxiran-2-ylmethoxy)-2H-pyrido [1,2-a]pyrimidin-4(3H)-one into RBF and Acetonitrile solvent (6 vol) at 20-25 ^{0}C.

Charged another KSM-02 (the N-(6-aminohexyl)-4-(tert-butyl) benzenesulfonamide into RBF. Charge anhydrous Powder Potassium carbonate into the reaction mass at 25-30^{0}C. Maintained the reaction mass at room temperature for overnight. Monitored the reaction using the Thin layer chromatography (Ethylaceate: Cyclohexanol 1:1) ; reaction was monitored on TLC .Cool the reaction mass 10-15 ^{0}C.Addition of the process water (4 vol) slowly into the reaction mass with maintained temperature of the reaction mass. Addition of the process water completed. Stirred the reaction mass for 1-2 hrs.Filter the reaction mass and wash with process water still checked neutral PH using the PH strip. Sucked dry material and Air drying.

RESULT

g)4-(tert-butyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido[1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide : Yield ; 85 %, IR (KBR cm-1); 3000-2840 (aromatic functional) , 1320-1000 (-C-O), 1370-1335 (Sulphonamide), -N 3700-3100 N-H stretching vibration, 2260-2200 (-C=N), 1690 (Amide functional group). ^{1}H-NMR ($CDCl_3$ ppm); 1.35 ppm (Tert –butyl group), 7.74 ppm (-$NHSO_2$), 1.29-3.38 ppm (alkyl chain between sulphonamide and pyrimidine compound), 2.84 (Oxirane –CH_2 group), 7.18-8.94 (Aromatic –CH). ^{13}C-NMR ($CDCl_3$, δ ppm), 31.3(-CH_3), 34.2 (-C) , 125.3-128.0 (Aromatic proton of benzene sulphonamide ring), 29.1, 29,3 ,26.7 , 42.8 alkyl chain of between benzenesulphonamide and pyrimidine), 44.3,52.4 (oxirane methylene group),161.2 (Keto group of pyrimidine).

h)4-(tert-butyl)-N-(2-chloroethyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido [1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide Yield; 87 % , IR (KBR cm-1); 3150-3000(aromatic functional),1350-1000 (-C-O), 1375-1335 (Sulphonamide), -N 3700-3100 N-H stretching vibration, 2260-2205 (-C=N), 1695 (Amide functional group) ; 1400-1550 (Methylene group value of oxirane). ^{1}H-NMR ($CDCl_3$ ppm); 7.74-7.78 (Aromatic –CH), 1.29, 2.41, 1.38, 3.0 ppm (Alkyl chain between pyrimidine and sulphonamide compound), 2, 63-2.84 ppm (Methylene group of oxirane). 2.92 methyl group of pyrimidine. ^{13}C-NMR ($CDCl_3$, δ ppm, 31.3(tert butyl carbon –CH_3), 44.3-52.4 (methylene carbon of Oxirane), 21.7, 26.7, 29.7, 50.0 (methylene carbon between pyrimidine and sulphonamide chain). 125.3, 128.0, 154.4, 143.2 (Aromatic carbon –CH), 161.2 (-NH-C=O).

i)N-(2-bromoethyl)-4-(tert-butyl)-N-(8-(2-methyl-9-(oxiran-2-ylmethoxy)-4-oxo-4H-pyrido [1,2-a]pyrimidin-3-yl)octyl)benzenesulfonamide; Yield : 91% , IR (KBR cm-1); 3170-3005(aromatic functional),1350-1008 (-C-O), 1375-1339 (Sulphonamide),3709-3102 N-H stretching vibration, 2260-2205 (-C=N), 1689 (Amide functional group) ; 1400-1550 (Methylene group value of oxirane). ^{1}H-NMR ($CDCl_3$ ppm); 7.18-8.94 (Aromatic –CH), 1.29, 2.41, 1.38, 3.0 ppm (Alkyl chain between pyrimidine and sulphonamide compound), 3.66, 3.58 (-CH_2-CH_2-Br) 2.63-2.38 ppm (Methylene group of oxirane).2.92 methyl group of pyrimidine. ^{13}C-NMR ($CDCl_3$, δ ppm, 31.3(tert butyl carbon –CH_3), 44.3-52.5 (methylene carbon of Oxirane), 21.7, 26.7, 29.3,

49.8(methylene carbon between pyrimidine and sulphonamide chain). 125.2, 128.5, 154.5, 143.3 (Aromatic carbon –CH), 161.2 (-NH-C=O).

j)4-(tert-butyl)-N-(3-(9-hydroxy-2-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-3-yl)propyl) benzenesulfonamide ; Yield : 93% , IR (KBR cm-1); 3160-3005(aromatic functional),1350-1009 (-C-O), 1365-1339 (Sulphonamide),3609-3102 N-H stretching vibration, 2280-2207 (-C=N), 1679 (Amide functional group) ; 1406-1550 (Methylene group value of oxirane). ^{1}H-NMR ($CDCl_3$ ppm); 7.74-7.78 (Aromatic –CH), 3.38, 1.69, 2.41 ppm (Alkyl chain between pyrimidine and sulphonamide compound), 2.92 methyl group of pyrimidine, 7.74 (-NH-SO_2). ^{13}C-NMR ($CDCl_3$, δ ppm, 31.3(tert butyl carbon –CH_3), 42.5, 26.5 and 18.7 (methylene carbon between pyrimidine and sulphonamide chain). 125.2, 128.5, 152.5, 143.3 (Aromatic carbon –CH), 162.0 (-NH-C=O).

BIOLOGICAL ACTIVITY

The synthesized Benzazepine and Sulphonamide derivatives were screened for their antibacterial and antifungal activity against five gram –negative bacteria (Escherichia coli, aeruginosa, gram positive bacteria (Staphylococcus aures, moreover, three fungal strains (Aspergillus Niger and aspergillus flavus brasiliensis).

Among benzazepine and sulphonamide derivative tested compound a) shown the greater degree activity against aspergillus flavus; moreover the compound b) also shown the activity against aspergillus flavus. Further the compound c) greater activity against the aspergillus Niger. Here similar benzene sulphonamide derivative mainly shown the antibacterial biological activity

Antibacterial and antifungal activity data of compounds

Compound Number	**Antibacterial activity (Zone of inhibition in mm)**				**Antifungal activity**	
	Bacillus sub tilts	**Staphylococcus aureus**	**Escherichia coli**	**Pseudomonas aeruginosa**	**Aspergillus niger**	**Aspergillus flavus**
a)	250	500	500	500	500	1000
b)	250	500	250	500	500	1000
c)	250	1000	500	1000	1000	250
d)	250	500	500	250	500	1000
e)	250	250	1000	1000	250	250
f)	500	1000	500	500	1000	500
g)	1000	250	250	1000		
h)	1000	500	1000	1000		
i)	1000	1000	500	1000		
j)	500	1000	1000	500		
k)						
l)						
Ampicillin	100	100				
Nystain					100	100

Here compound g), h) and i) shown the greater degree activity for bacillus subtiits. Compound i) and j) showed the activity against staphylococcus aureus. Moreover the compound h) and j) represented their activity against the Escherichia coli and compound g), h) and i) shown the activity against pseudomonas aeruginosa. The remaining benzazepine and sulphonamide derivatives group good moderate activity against remaining six bacterial species.

CONCLUSION

We have successfully synthesized a series of novel benzazepine and sulphonamide derivatives in higher yields with adopting simple and straight forward process. The advantage is shorter reaction times with low cost of the staring material and scale activity also feasible. All compounds exhibited antibacterial and antifungal activities.

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