WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.990
Volume 4, Issue 11, 1762-1775. Research Article ISSN 2277– 7105

A FACILE SYNTHESIS OF BIO ACTIVE 2-AZETIDINONES DERIVATIVES AND THEIR PHARMACOLOGICAL ACTIVITY

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Article Received on
13 Sept 2015,

Revised on 05 Oct 2015,
Accepted on 27 Oct 2015,

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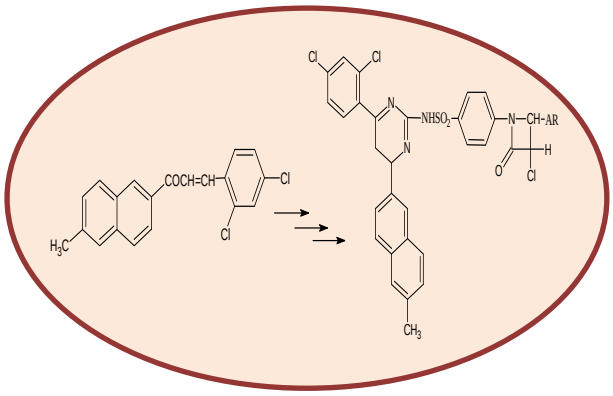
ABSTRACT

An expeditious method for preparation of azetidine-2-ones 7(a-h) are an important class of heterocycles, having potential biological importance due to their unique features. The process of convert of imine (Schiffs base) to azetidine (β-lactam) through an intermediate of monochloro acetyl chloride is important synthetic method for preparation of azetidine-2-ones. The structures of the synthesized compounds were confirmed by IR, ^{1}H-NMR, ^{13}C NMR and Mass spectral studies. The compounds were screened for their antimicrobial activity against Bacillus subtilis, Staphylococcus aureus, Esherichia coli and Pseudomonas aeruginosa was determined by disc diffusion technique. All the synthesized compounds exhibited promising antimicrobial activity against the studied set of microorganisms. However, the activity was less than that of standard drugs used in this study.



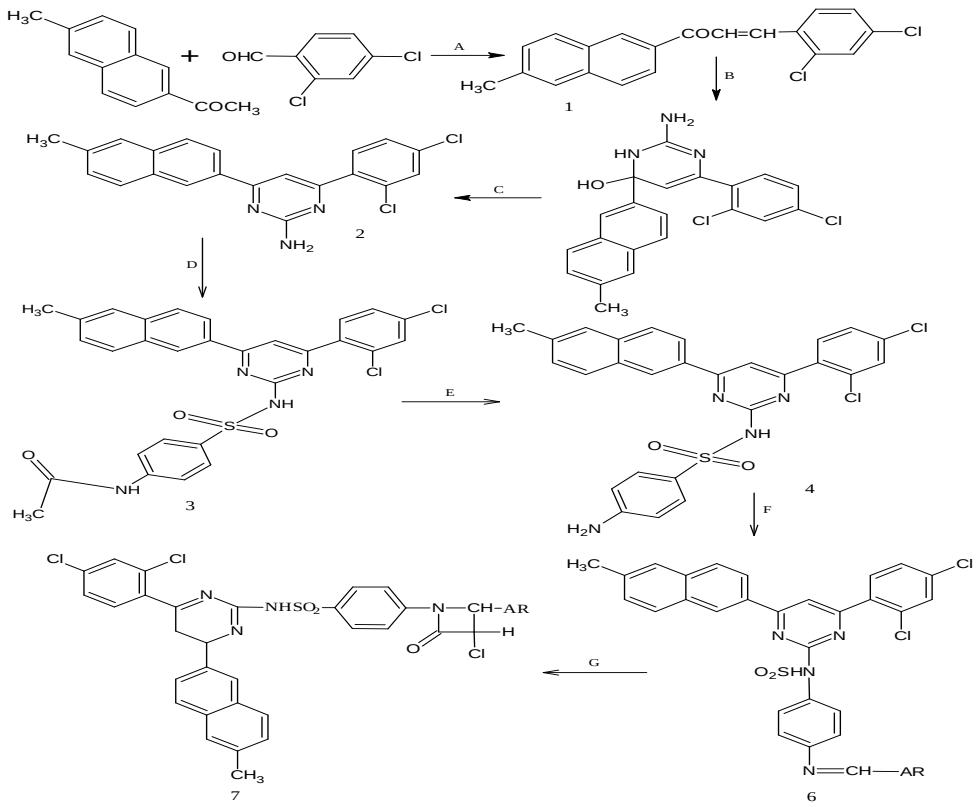
KEYWORDS: 2-Aminobenzothiazole, azetidinones, Schiff base, antibacterial activity.

INTRODUCTION

The β-lactam heterocycles are still the most prescribed antibiotics used in medicine. They are considered as an important contribution of science to humanity.[1] The most widely used antibiotics such as the penicillins, cephalosporins, carumonam, aztreonam, thienamycine and the nocardicins all contain β-lactam rings.[2] The long-term use of β-lactam antibiotics exerts selective pressure on bacteria and permits the proliferation of resistant organisms.[3] Azetidinones, which are part of the antibiotic structure, are known to exhibit interesting biological activities.[4] The β-lactams also serve as synthons for many biologically important classes of organic compounds.[5] 2-azetidinone derivative possess wide therapeutic activity like antifungal.[6] anticonvulsant.[7] antitumour.[8] cholesterol absorption inhibitior.[9] enzyme inhibition activities.[10,11] A large number of 3-chloro monocyclic β-lactams possess powerful antibacterial,antimicrobial, anti-inflammatory, anticonvulsant and antitubercular activity.[12-16] They also functionas enzyme inhibitors and are effective on the central nervous system.[17] N-Substituted-3-chloro-2-Azetidinones as Potential Anticonvulsant Agents.[18]

MATERIALS AND METHODS

Materials: All the chemicals and solvents were obtained from E-Merck and S.D. Fine India (AR grade) and were used without further purification. Thin Layer Chromatography was performed on aluminium sheet of silica gel 60F 254, E-Merk, Germany using iodine as visualizing agent. Melting points were determined in open capillary tubes on Mel-Temp apparatus and are uncorrected. The IR Spectra were recorded as KBr pellets on Perkin-Elmer 1000 units, instruments. All ^{1}H and ^{13}C-NMR spectra were recorded on a Varian XL-300 spectrometer operating at 400MHz for ^{1}H -NMR and 75 MHz for ^{13}C-NMR. The compounds were dissolved in DMSO-d6 and Chemical shifts were referenced to TMS (^{1}H and ^{13}C-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system.Elemental analysis was recorded on a Carlo Erba 1108 elemental Analyzer, Central Drug Research Institute, Lucknow, India.



Reaction Scheme

Reaction reagent and condition

A= 40% KOH, OH^- E= Hydrolysis

B= Guinidine Hydrochloride, F= Different Aldehyde (5a-h)

C= $-H_2O$, $-H_2$ G= $CLCOCH_2CL$, TEA/ 1,4-Dioxane, -HCL

D= P-Acetyl-aminobenzenesolphonyl chloride and pyridine

METHODOLOGY

Synthesis of 3-(2,4-dichlorophenyl)-1-(6-methylnaphthalen-2-yl)prop-2-en-1-one (1)

To a well stirred solution of 2,4-dichloro benzaldehyde (0.01 mole) and 1-(6-methylnaphthalen-2-yl)ethanone (0.01 mole) in ethanol (35 ml), 40% KOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol.

Synthesis of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (2)

A mixture of Chalcone (0.01 mole) in 25 ml of absolute alcohol, add Guanidine Hydrochloride (0.015 mole) and sodium hydroxide (0.045 mole in 2 ml of water) was

refluxed in water bath at temp 80-90°c for 8 hr. The reaction mixture was poured into ice. The product was isolated and crystallized from ethanol.

Synthesis of N-(4-(N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)sulfamoyl)phenyl)acetamide (3)

The derivative was prepared by reactions of amino pyrimidine (2) (0.01 mole) with P-Acetylamino-benzenesulfonyl chloride (0.012 mole) in dry pyridine (30 ml) was heated to 70-75°C on a water bath for 5 hr. the cold reaction mixture was acidified with dil. hydrochloric acid. The solid that separated was filtered, washed several times with hot water, dried and crystallized from proper solvent.

4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

N-(4-(N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)sulfamoyl)phenyl)acetamide (3) was hydrolysed by refluxing 0.5-1.0 molar solution containing 3.5 equivalents of sodium hydroxide for two hours. After this period, the mixture was cooled to room temperature and neutralized with concentrated HCl pH by approximately 6.0. The mixture was cooled in the ice bath until the total precipitation of the product, the filtered vacuum, washed with small volume of water ice and purification by recrystallization from ethanol to give white product.

Synthesis of 4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6 a-h)

The various Schiff bases (6a-h) of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4) have been prepared in the similar manner. The procedure is as follow.

A mixture of equimolar amount (0.01 mole) of of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4) and the Substituted Benzaldehydes **(5)** in absolute ethanol (70 ml) and piperidine (0.5 ml) was refluxed for 10 hr in a water bath. The reaction mixture was concentrated, cooled and poured into ice cold water the solid obtained was filtered and Recrystallized from absolute ethanol to give white Schiff base.

Synthesis of 4-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (7a-h).

A mixture of Schiff base (6 a-h) (0.002 mole) and triethyl amine (TEA) (0.004 mole) was dissolved in 1,4-dioxane (50 ml), cooled, and stirred. To this well-stirred cooled solution chloroacetyl chloride (0.004 mole) was added drop wise within a period of 40 minutes. The reaction mixture was then stirred for an additional 5 hours and left at room temperature for 48 hours. The resultant mixture was concentrated, cooled, poured into ice-cold water, and then air-dried. The product thus obtained was purified by column chromatography over silica gel using 30% ethyl acetate: 70% benzene as eluent. Recrystallization from ether/n-hexane gave 2-azetidinone (7a-h), which were obtained in 60-65% yield. The analytical and spectral data of compounds (7a-h) are described.

RESULTS AND DISCUSSION

SPECTRAL STUDIES

IR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

Sulfa Pyrimidine is a heterocyclic compound. It is an aromatic compound thus it provides the IR frequencies. The bands due to pyrimidine are at 3220-3440 cm^{-1} and 1610-1640cm^{-1} corresponds to N-H (str.) and C=N groups. The peak at 1630cm^{-1} is indicative of C=N, 1600 cm^{-1} due to C=C cm^{-1}, and 1310 cm^{-1} and 1150 cm^{-1} diagnostic for the presence of the sulphonamido group(-SO2NH-) also The corresponding N-H in plane and out of plane bending vibrations occurs at 1630 and 699 cm^{-1} respectively.

NMR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

The signal at 4.0 ppm is responsible for N-H proton of pyrimidine $–SO_2NH-$, signal at 6.35 ppm is responsible for $-NH_2$ proton, and multiple signals between 6.15-7.8 ppm are responsible for aromatic proton. While signal at 2.30 due to two $–CH_3$ on benzene ring.

CMR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

The signals at 101.7 (C_5), 162.5 (C_4), 165.4 (C_6) and 169.3 (C_2) ppm are responsible for pyrimidine multiple signals between 114-140 ppm are responsible for aromatic segments. While signal at 18.8 and 19.1 are due to two $–CH_3$.

Finally the structure of compound conform by LC-MS compound (4) shows peak of (m/Z) at 534.07 which consistent with the calculated molecular weight of Compound (4) i.e. 534.07.

Spectral Studies of compound 6a-6h

4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 6a

Yield: 60%, MP 193^{0}C, Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N-, 1315-1375 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.5 multiplet, aromatic+ CH of CH=N protons + H of Pyrimdine + H of SO_2NH +), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134- Ar-Cl, 160- CH=N, 162-169- pyrimidine.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-methoxybenzylideneamino)benzenesulfonamide 6b

Yield: 61%, MP 197^{0}C**,** Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO_2-, 3250-3330 -NH- of -SO_2NH-, 1200- Ar-O-alkyl, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic+ CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 163-C-O, 56 - CH_3

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-hydroxybenzylideneamino)benzenesulfonamide 6c

Yield: 60%, MP 199^{0}C**,** Infrared Spectral Features around cm^{-1} 3370-OH, 3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375-SO_2-, 3250-3330 -NH-of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic + CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 163 -C-O.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-hydroxybenzylideneamino)benzenesulfonamide 6d

Yield: 62%, MP 191^{0}C, Infrared Spectral Features around cm^{-1} 3370-OH, 3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375-SO_2-, 3250-3330-NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic + CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 163 -C-O.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-methylbenzylideneamino)benzenesulfonamide 6e

Yield: 62%, MP 193^{0}C**,** Infrared Spectral Features around cm^{-1} 2950, 1370 - CH_3, 3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO_2- ,3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic+ CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 2.34 (3H, singlet, CH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 21-CH_3.

4-(benzo[d][1,3]dioxol-5-ylmethyleneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 6f

Yield: 60%, MP 201^{0}C, Infrared Spectral Features around cm^{-1}2920, 2850 - CH_2-, 1450, 3030, 1500, Aromatic C-H stretching, 1600–1640 -CH=N-, 1315-1365 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 6.07 (2H, singlet, -O-CH_2-O-), ^{13}CMR spectral Features (δ Ppm) 101.2 -CH_2-O-, 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 21-CH_3.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(3-hydroxy-4-methoxybenzylideneamino)benzenesulfonamide 6g

Yield: 57%, MP 199^{0}C**,** Infrared Spectral Features around cm^{-1} 3370 -OH, 2950,1370 -CH_3, 3030,1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 3.83 (3H, singlet, -O-CH_3) 5.35 (1H, Singlet, -OH), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 -pyrimidine, 149-151 -C - O, 56-OCH_3.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(3,4-diethoxybenzylideneamino)benzenesulfonamide 6h

Yield: 60%, MP 190^{0}C**,** Infrared Spectral Features around cm^{-1} 2950,2820, -CH_2-, 1450,3030,1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic+ CH of CH=N protons + H of Pyrimdine + H of SO_2NH) 4.0 (4H, quartet, 2CH_2) 1.33 (6H, triplet, 2CH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 149-151 -C-O.

Spectral Studies of Compound 7a -7h

4-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7a

Yield: 64%, MP 199-99^{0}C**,** Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N,1315-1375 -SO_2-, 3250-3330-NH- of -SO_2NH-, 1697 C=O of β-lactum, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 135.6- Ar-Cl, 160 -CH=N, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2 -C=O.

4-(3-chloro-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7b

Yield: 60%, MP 191-92^{0}C, Infrared Spectral Features around cm^{-1}3030, 1600, Aromatic C-H stretching , 1600-1641 -CH=N,1315-1375 - SO_2-, 3250-3330 -NH- of -SO_2NH-, 1697 C=O of β-lactum, 1200 Aryl-alkyl ether, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 3.83 (3H, singlet, OCH_3) ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2 -C=O, 158-159 -C-O, 56 CH_3.

4-(3-chloro-2-(4-hydroxyphenyl)-4-oxoazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7c

Yield: 55%, MP 189-90^{0}C**,** Infrared Spectral Features around cm^{-1}3370, 3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N, 1315-1375-SO_2-, 3250-3330-NH- of -SO_2NH-, 1697 C=O of β-lactum, 3200,2600 -OH Phenolic (broad) 1200 Aryl-alkyl ether, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 3.36 (H of OH), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2-C=O,119 -C-O-H.

4-(3-chloro-2-(2-hydroxyphenyl)-4-oxoazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7d

Yield: 59%, MP 185-86^{0}C**,** Infrared Spectral Features around cm^{-1}3370, 3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N, 1315-1375-SO_2-, 3250-3330 -NH- of -SO_2NH-, 1697 C=O of β-lactum, 3200,2600 -OH Phenolic (broad), PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH),

5.44 (1H of C_3H of β-lactam), 3.36 (Hof OH), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2 -C=O,119 -C-O-H.

4-(3-chloro-2-oxo-4-p-tolylazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7e

Yield: 60%, MP 199-96^{0}C, Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N, 1315-1375 -SO_2 - ,3250-3330 -NH- of -SO_2NH-, 1697 C=O of β-lactum, 2950, 1370 -CH_3, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 2.34 (3H, singlet, CH_3), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2 -C=O, 21.30 CH_3.

4-(2-(benzo[d][1,3]dioxol-5-yl)-3-chloro-4-oxoazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7f

Yield: 61%, MP 188-89^{0}C, Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641-CH=N, 1697 C=O of β-lactum, 2950, 1370 -CH_3, 1315-1365 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 5.8 (2H of O-CH_2-O), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene,163-169- pyrimidine, 143,48,156 β-lactum, 162.2 -C=O, 165 C of CO, 91 O-CH_2-O.

4-(3-chloro-2-(4-hydroxy-3-methoxyphenyl)-4-oxoazetidin-1-yl)-N-(4-(2,4 dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7g

Yield: 62%, MP 191-92^{0}C, Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N, 1697 C=O of β-lactum, 3200-2600 –OH phenolic Broad, 1200 Ar-O-alkyl,2950, 1370 -CH_3, 1315-1365 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 3.36 (1H of OH), 4.3(3H, s, -OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene,163-169- pyrimidine, 143,48,156 β-lactum, 162.2- C=O, 56 -O-CH_3.

4-(3-chloro-2-(3,4-diethoxyphenyl)-4-oxoazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7h

Yield: 60%, MP 199-00^{0}C**,** Infrared Spectral Features around cm^{-1}3030, 1500, Aromatic C-H stretching , 1600-1641 -CH=N, 1697 C=O of β-lactum, 3200-2600 –OH phenolic Broad,

1200 aryl-alkyl ether, 2920, 2850, 1450 -CH_2-, 2950, 1370 –CH_3-, 1315-1365 -SO_2-, 3250-3330 -NH- of -SO_2NH-, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimdine + C4H of β-lactum + H of SO_2NH), 5.44 (1H of C_3H of β-lactam), 3.36 (1H of OH), 4.3(3H, s, -OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 163-169- pyrimidine, 143,48,156 β-lactum, 162.2- C=O, 56- O-CH_3, 135- C-O.

MICROBIAL ACTIVITY

The compounds tested for antimicrobial activity are listed in table 4, 5 and 6 show the size of zone of inhibition of bacterial growth procedure by test compounds for broad range of antimicrobial activity inhibiting growth of Gram-positive bacterial strains B. Subtillis and S. Aureus, and Gram-negative bacterial strains E. Coli and Ps. Aeruginosa.

Table.1: The benzaldehyde derivatives (5a-h) used for Schiff bases formation of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

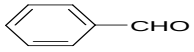
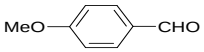
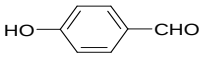
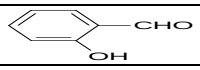
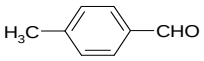
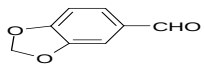
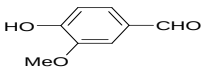
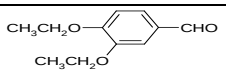
No.	Benzaldehyde derivative	Structure
5a	Benzaldehyde	
5b	4-Methoxy benzaldehyde	
5c	4-Hydroxy benzaldehyde	
5d	2-Hydroxy benzaldehyde	
5e	4-Methyl benzaldehyde	
5f	3,4-Methylenedioxy benzaldehyde (i.e. Veretral)	
5g	4-Hydroxy-3-methoxy benzaldehyde	
5h	3,4-Diethoxy benzaldehyde	

Table.2: Physical characterisation constant of 4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6 a-h)

Com. No	Molecular Formula	-Ar	Molecular Weight	Elemental analysis, Cal/Found			
				%C	%H	%N	%S
6a	$C_{34}H_{24}Cl_2N_4O_2S$	Phenyl	622.10 gm/mole	65.49 65.19	3.88 3.57	8.99 8.89	5.14 5.10
6b	$C_{35}H_{26}Cl_2N_4O_3S$	4-Methoxy phenyl	652.11 gm/mole	64.32 64.12	4.01 3.92	8.57 8.51	4.91 4.86
6c	$C_{34}H_{24}Cl_2N_4O_3S$	4-Hydroxy phenyl	638.09 gm/mole	63.85 63.55	3.78 3.65	8.76 8.56	5.01 5.00
6d	$C_{34}H_{24}Cl_2N_4O_3S$	2-Hydroxy phenyl	638.09	63.85	3.78	8.76	5.01

			gm/mole	63.55	3.65	8.56	5.00
6e	$C_{34}H_{26}Cl_2N_4O_2S$	4-Methyl phenyl	636.12 gm/mole	63.93 63.73	4.11 4.01	8.89 8.79	5.03 5.00
6f	$C_{35}H_{24}Cl_2N_4O_4S$	3,4-Methylenedioxy phenyl	666.09 gm/mole	62.97 62.81	3.62 3.55	8.39 8.32	4.80 4.70
6g	$C_{35}H_{26}Cl_2N_4O_4S$	4-Hydroxy-3-methoxy phenyl	668.11 gm/mole	62.78 62.68	3.91 3.76	8.37 8.30	4.79 4.73
6h	$C_{38}H_{32}Cl_2N_4O_4S$	3,4-Diethoxy phenyl	710.19 gm/mole	64.13 64.00	4.53 4.48	7.87 7.81	4.51 4.44

Table. 3: Physical characterisation constant of 4- (3-chloro-2-oxo-4-phenylazetidin-1-yl)-N-4-(2,4-dichlorophenyl)-6-(6 methylnaphthalen-2-yl) pyrimidin-2-yl) benzenesulfonamide (7a-h)

Com. No	Molecular Formula	-Ar	Molecular Weight	Elemental analysis, Cal/Found			
				%C	%H	%N	%S
7a	$C_{38}H_{25}Cl_3N_4O_3S$	Methylbenzene	698.07 gm/mole	61.77 61.51	3.60 3.52	8.00 7.93	4.58 4.50
7b	$C_{37}H_{27}Cl_3N_4O_4S$	1-Methoxy-4-methylbenzene	728.08 gm/mole	60.83 60.70	3.73 3.53	7.67 7.62	4.39 4.31
7c	$C_{36}H_{25}Cl_3N_4O_4S$	4-Methylphenol	714.07 gm/mole	60.39 60.19	3.52 3.36	7.82 7.80	4.48 4.40
7d	$C_{36}H_{25}Cl_3N_4O_4S$	2-Methylphenol	714.07 gm/mole	60.39 60.15	3.52 3.36	7.82 7.83	4.48 4.39
7e	$C_{37}H_{27}Cl_3N_4O_3S$	1,4-Dimethylbenzene	712.09 gm/mole	62.24 62.04	3.81 3.65	7.85 7.80	4.49 4.42
7f	$C_{37}H_{25}Cl_3N_4O_5S$	5-Methyl-1,3-benzodioxole	742.17 gm/mole	59.73 59.59	3.39 3.30	7.53 7.44	4.31 4.22
7g	$C_{37}H_{27}Cl_3N_4O_5S$	2-Methoxy-4-methylphenol	744.08 gm/mole	59.57 59.38	3.65 3.60	7.51 7.41	4.30 4.27
7h	$C_{40}H_{33}Cl_3N_4O_5S$	1,2- Diethxy-4-methylbenzene	786.12 gm/mole	60.96 60.82	4.22 4.18	7.11 7.01	4.07 4.00

Table. 4: Antimicrobial activity of Standards and Solvent (DMF)

No.	Name of compound	Zone of inhibition (in mm)			
		Gram positive		Gram negative	
		B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa
1	DMF	8	5	6	7
2	Ampicillin	15	12	20	20
3	Tetracyclin	21	22	15	18
4	Gentamycin	20	19	18	22
5	Chloramphenicol	21	23	17	24

Table. 5: Antimicrobial activity of 4-(arylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6a-h)

Compound (Designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa
6a	12	13	08	12
6b	10	12	10	10
6c	14	14	15	10
6d	10	10	08	09
6e	06	16	12	20
6f	13	11	10	14
6g	21	19	14	16
6h	14	14	18	17

Table.6: Antimicrobial activity of 4-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (7a-h).

Compound (designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa
7a	08	07	15	07
7b	10	10	14	10
7c	16	14	10	19
7d	15	19	22	14
7e	08	09	10	04
7f	20	13	08	13
7g	09	09	10	13
7h	08	16	12	13

CONCLUSIONS

In conclusion, a new series of compound 6(a-h) and 7(a–h) were synthesized, compounds screened for their spectral study and biological study. The investigation of antimicrobial activities data revealed that the compounds **(**7c**), (**7d**),** (7f), **(**7g**)** and **(**7h**),** displayed excellent activity, the compounds(7a), (7b) and (7e) showed moderate activity and rested compounds showed less activity compared with standard drugs.

ACKNOWLEDGEMENTS

We heartily thankful to Department of Chemistry for providing elemental analysis and also thankful to Head, CDRI, Lucknow for providing spectral data for the compounds.

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