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Synthesis and Spectral Characterization of Pyrimidine Based 2-Azetidinones

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ABSTRACT: In this study we report the synthesis of a series of 2-Azetidinones from N-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl)pyrimidin-2- yl)-1-(aryl) methanimine. A mixture of N-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl)pyrimidin-2-yl)-1-(aryl) methanimine and triethyl amine was reacted with chloroacetyl chloride in 1,4-dioxane. The N-(4-(5-bromothiophen-2-yl)-6-(4 -chlorophenyl) pyrimidin-2- yl)-1-(aryl) methanimine was prepared from reaction of 4-(5-bromothiophene-2-yl)-6-(4-chloropheneyl)pyrimidin-2-amine with aromatic aldehydes in ethanol in presence of catalytic acetic acid. All newly synthesized compounds were characterized on the basis of ^{1}H NMR, IR, and MASS spectral data.

KEYWORDS: 2-Azetidinones, Schiff bases Pyrimidine, Spectral Characterization

INTRODUCTION

In organic chemistry almost 50% study is on heterocyclic compounds, because heterocyclic structures are the framework on which number of developed and developing products are in various fields like agrochemical, medicinal and veterinary chemistry [1-2]. Pyrimidine among the known heterocyclic compounds is associating with number of pharmacological activities [3]. Pyrimidine shows anticancer [4-5], Antibacterial [6-8], antiviral [9-10] and antifungal [11].

2-azetidinone is a very well investigated four membered cyclic lactams has been known as an important building block for the synthesis of large number of heterocyclic compounds. The β-lactam based heterocyclic compounds penicillin, cephalosporins, carumonam, thienamycin, aztreonam and the nocardicin are still the most important antibiotics used in medicine. 2-Azetidinones are of great importance due to their wide pharmacological spectrum especially as antimicrobial [12-14], anticancer [15-17], anti-convulsant [18], antioxidant [19] and antidepressant [20]. In view of above properties of, we propose the synthesis of heterocyclic framework containing pyrimidine and 2-azetidinone moieties.

EXPERIMENTAL

All Chemicals used for the synthesis of the said compounds were of analytical grade and were procured from SDFCL. Melting points were determined in open capillary tube and are uncorrected. The progress and purity of compounds was checked by thin-layer chromatography using with F-252 silica gel precoated aluminium plates using petroleum ether-ethyl acetate (9:2) as a developing solvent and spots were visualised by exposing the plates in iodine vapours. Infrared spectra were recorded on Shimadzu spectrophotometer using KBr pellets technique (λ_{max} in cm^{-1}). ^{1}H Nuclear magnetic resonance spectra were recorded on BRUKER ADVANCE (400 FT- NMR) spectrophotometer using dimethyl sulfoxide (DMSO- d_6) as a solvent and tetramethyl silane as internal reference (chemical shifts, δ in ppm). Mass spectra were observed on Waters UPLC- TQC Mass Spectrometer.

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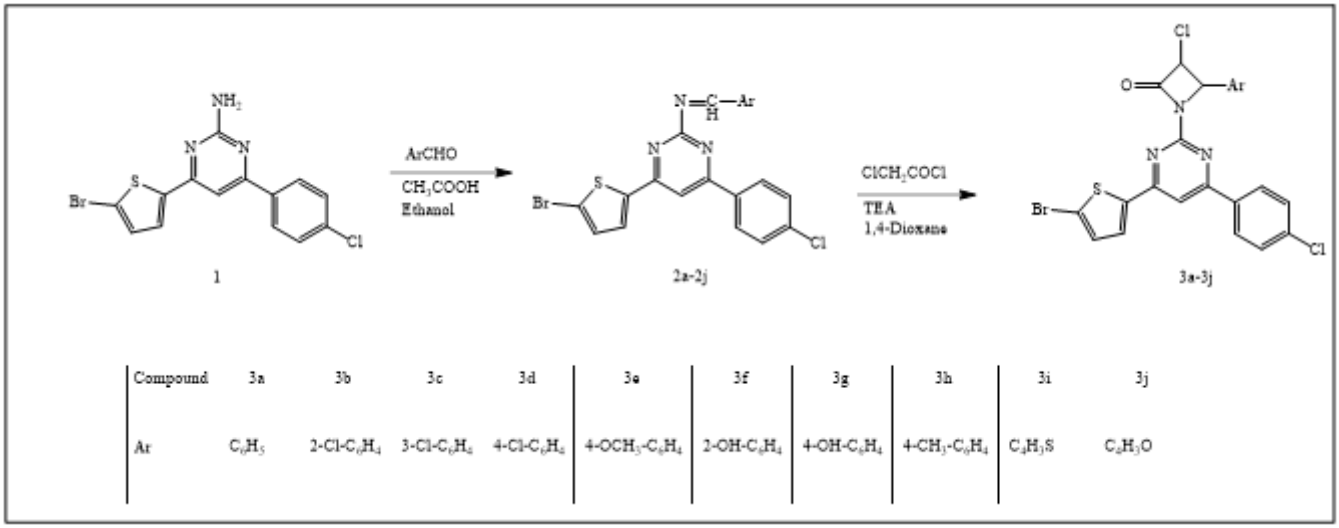

Scheme

General procedure for the synthesis of 1-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl) pyrimidin-2-yl)-3-chloro-4-(aryl)azetidin-2-one:

A mixture of N-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl)pyrimidin-2-yl)-1-(aryl) methanimine (2a - 2j). (0.01 mol) and triethylamine (TEA) (0.01 mol) was dissolved in 40 ml 1,4-dioxane, cooled and stirred at 0 – 5^{O}C. To this well-stirred cooled solution chloroacetyl chloride (0.01 mol) was added drop wise within a period of half hour. The reaction mixture was then stirred for 5 hours, the white precipitate of amine hydrochloride was filtered off. The filtrate was then refluxed for 8 to 15 hours. The reaction mixture then cooled and poured into ice-cold water. The resulting solid was filtered, washed with water and purified by reacrystallization from ethanol/ dioxane.

Table No. 1. Analytical Data of compounds (3a-3j)

Sr. No.	Compound	Ar	Molecular Formula	Colour	Melting point in ^{0}C	% Yield
1	3a	C_6H_5	$C_{23}H_{14}BrCl_2N_3OS$	Pale yellow	168	62
2	3b	2-Cl-C_6H_4	$C_{23}H_{13}BrCl_3N_3OS$	Yellow	156	59
3	3c	3-Cl-C_6H_4	$C_{23}H_{13}BrCl_3N_3OS$	Brown	153	54
4	3d	4-Cl-C_6H_4	$C_{23}H_{13}BrCl_3N_3OS$	Brown	148	58
5	3e	4-OCH_3-C_6H_4	$C_{24}H_{16}BrCl_2N_3O_2S$	Yellow	162	61
6	3f	2-OH-C_6H_4	$C_{23}H_{14}BrCl_2N_3O_2S$	Pale yellow	153	50
7	3g	4-OH-C_6H_4	$C_{23}H_{14}BrCl_2N_3O_2S$	Brown	147	52
8	3h	4-CH_3-C_6H_4	$C_{24}H_{16}BrCl_2N_3OS$	Yellow	165	60
9	3i	C_4H_3S	$C_{21}H_{12}BrCl_2N_3OS_2$	Yellow	159	64
10	3j	C_4H_3O	$C_{21}H_{12}BrCl_2N_3O_2S$	Dark brown	139	60

Spectral analysis of 3a

IR (KBr) cm^{-1} :1681 (C=O), 1558(C=N), 1419 (C=C), 3093 (C—H), 678 (C—Br); ^{1}H NMR: δ 8.2 ppm (s, 1H, C—H pyrimidine), δ 3.2 (d, 1H, H—C—N), δ 4.4 (d, 1H H—C—Cl), δ 7.0-8.2 (m, 11H, Ar—H); Mass: m/z = 532 (M+)

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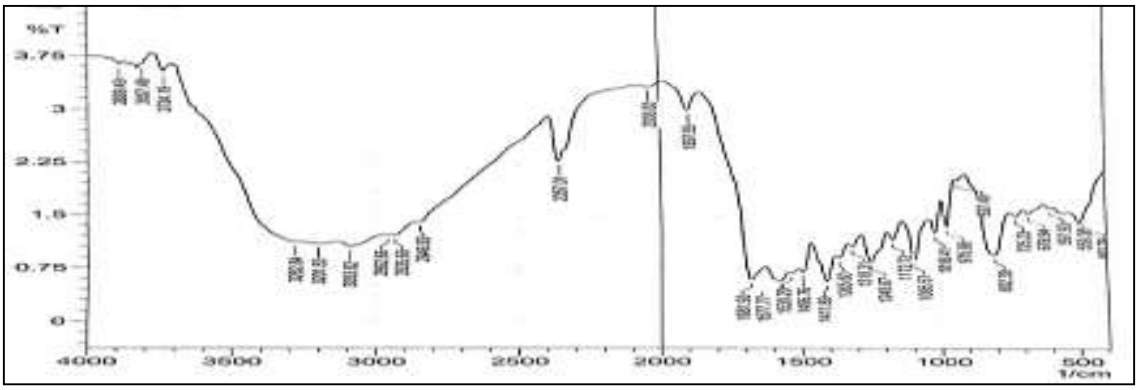

Figure No. 1. IR Spectra of compound3a

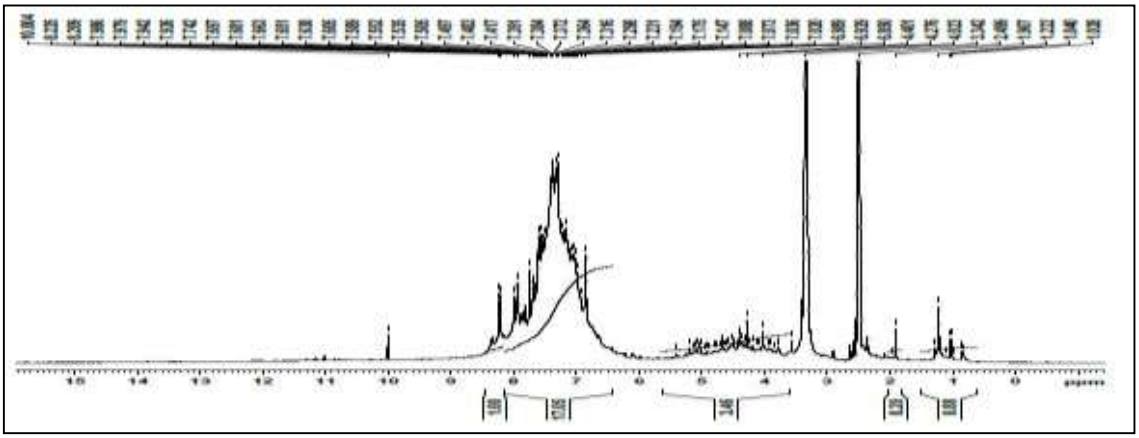

Figure No. 2. ^{1}H NMR Spectra of Compound 3a

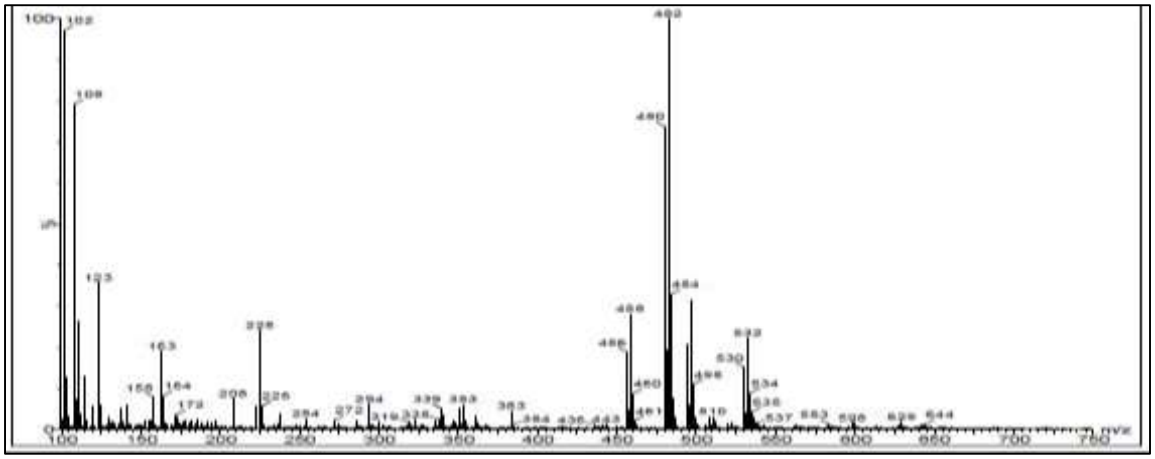

Figure No. 3. Mass Spectra of Compound 3a

RESULTS AND DISCUSSION

Synthesis of title compounds, 3a-3j was accomplished in accordance with the synthetic route as depicted in scheme. Synthesis of 4-(5-bromothiophene-2-yl)-6-(4-chloropheneyl)pyrimidin-2-amine was carried out by the reported method and published in our previous work (Manohare, 2019). Schiff bases, N-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl) pyrimidin-2-yl)-1-(aryl)methanimine (2a-2j) were prepared by condensing 4-(5-bromothiophene-2-yl)-6-(4-chloropheneyl)pyrimidin-2-amine with different aromatic aldehydes in presence of catalytic amount of acetic acid in ethanol. The prepared Schiff bases then subjected

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to react with triethylamine (TEA) and chloroacetyl chloride in 1,4-dioxane to form 1-(4-(5-bromothiophen-2-yl)-6-(4-chlorophenyl)pyrimidin-2-yl)-3-chloro-4-(aryl)azetidin-2-one.

All newly synthesized compounds were purified by recrystallization and structures were established on the basis of IR, ^{1}H NMR and Mass spectroscopy data. Spectral data of all the synthesized compounds are in full agreement with the proposed structures. In IR spectra a strong absorption band at 1681 cm^{-1} due to C=O stretching vibration, absorption bands at 1558 cm^{-1} and at 1419 cm^{-1} are for C=N stretching and C=C stretching vibrations respectively, a absorption band at 3093 cm^{-1} for C—H stretching vibration and a band at 678 cm^{-1} is observed for C—Br. The ^{1}H NMR spectrum shows a sharp singlet at δ 8.2 ppm for C—H (pyrimidine), a characteristic doublet at δ 3.2 ppm observed for H—C—N, a doublet at δ 4.4 ppm appeared for H—C—Cl (azetidinone) and aromatic protons showed multiplate at δ 7.0-8.2 ppm. The m/z values obtained from Mass spectra for the characterized 2-azetidinones are in good agreement with the molecular weights.

CONCLUSION

A new series of 2-azetidinones containing Pyrimidine moiety from Schiff bases was prepared and the structures of synthesized compounds were confirmed on the basis of spectroscopy data. Spectral data of compounds and proposed structures are in full agreement.

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