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Synthesis and characterization of 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*)One as Antibacterial, and Antioxidant Candidates

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A B S T R A C T

A series of all novels 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*) One **5a-5r** poly functionalized derivatives were containing sulfonamide functionality united with 2-Azitidinone (Azitidin-2-one or β-lactam) group which designed and synthesized with moderate to good yield. The starting with 4-acyl-2-pyrazolin-5-one **(APYZ) 1** which condensed with different sulfonamides **2** produced intermediate Schiff bases 4-(arylideneamino)-N-(thiazol-2-yl)benzensulfonamide **3a-r** were cyclization with 2-(4-flourophenyl)chloroacetylchloride (F-CAC) **4** which produced targeted compounds **5a-5r** of 2-Azitidinone versatile group in good yield. The isolated compounds were recognized by spectral and elemental investigation. The compounds **5f, 5l, 5n,** and **5r** showed excellent increased antibacterial activity compared to streptomycin standard drug and **5c, 5f, 5l, 5o,** and **5r** showed moderate to good antioxidant properties with used DPPH radical scavenging assay.

1. Introduction

Over the past few decades, the quick enlargement and investigation of the multidrug-consuming potent fused heterocyclic entities have become the leading and interesting areas for researchers and scientists in the field of advanced medicinal Chemistry. This inducement led us to attempt to expand our criteria for the formation of new synthetic organic moieties and enhancing their biological application.[1-2] Sulfonamides a well-known distinct class of versatile groups has an intensively considered the first drugs used for protective and chemotherapeutic activity against numerous supplementary pharmacological activities, especially as Antibacterial and Antifungal, Cyclooxygenase-2(COX-2), Carbonic anhydrase inhibitors (CAIs), Anti-HIV, Antioxidant, type II diabetes, Anti-malarial, treating male erectile dysfunction, Antituberculosis, etc.[3,4,5,6,5,7,8,9,10] At Present-days a large number of Schiff bases known even as Imine or azomethines synthesized from groups of sulfonamides have received extensive attention as an excellent synthon for various fused ring transformations and examined as various biological action. [11,12,13]

The function of the 2-Azetidinone (β-lactam) framework was recognized as a unique structural synthetic target nucleus and an important contribution in the pharmaceutical research world for the reason that of their most attractive antibacterial drugs globally marketing (above 65%).[14] Since penicillin was found during the 1940s cephalosporin was identified most potent antibiotic including the 2-Azetidinone (β-lactam) motif mainly consumed and prescribed drugs worldwide in 2010 (3). 2-Azetidinon has been the most successive antibiotic having a common structural characteristic ring framework system counting Carbapenems, monobactams, nocardicins, clavulanic acid, tazobactam, sulbactam, these molecules known as **PGPs** (penicillin-binding proteins) or cellular permeability used in bacterial infection as most successful chemotherapeutic agents.[15,16,17,18]Early 90's, mainly the researcher deliberate on the synthesis of β-lactam (azetidin-2-ones) and study their core of the bacterial activity[19]. The most well-known and widely studied method of Staudinger's is extensively employed

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for the preparation of monocyclic 2-azetidinone (β lactams) via ketene-imine cycloaddition.[20] Also alternative synthetic ways have been developed for the formation of azetidine molecular segments which are listed here, (a) Kinugasa reaction a comparatively new approach was proposed for cycloaddition between nitrones with terminal alkyls which catalysed by Cu(I).[21] (b) The unique method to transform 5-nitroisoxazolidines into β-lactam.[22] Recently, our preceding work synthesized compounds **1** has demonstrated that the introduction of the formation of 4-member small fused β-lactam or 2-azitidinone 'N' containing prominent structural hetero ring into sulfonamide derived from Schiff base shown in figure-1 significantly improves zone inhibition as Antibacterial and Anti-fungal efficacy even as higher MIC potency [3]. Some of the reported sulfonamide fused with 2-Azetidinone ring exhibited well antimicrobial activity **Fig. 1** [23-24]

Free radicals such as superoxide (·O_2), alkoxyl(·RO), Nitric oxide (·NO), and Hydroxyl(·OH), are recognized as reactive oxygen species (ROS). They are highly reactive with free single electrons and rapidly bind to nearby molecules also they attack the molecules in adjacent cells therefore damage is unavoidable. Sulfonamide (-RSO_2NH_2) functionality is most useful as an antioxidant that inhibits oxidation, and the action of ROS in the other molecule [25,26,27,28]. Here in we explored and modified our continuing work from the explanations of our previous and some reported derivatives, it would be encouraging to synthesize new series of sulfonamide entities bearing 2-azitidinone, 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*) One **5a-5r.** All Derivatives were investigated for antibacterial activity against gram +ve and gram -ve strains and determined the antioxidant activity by 1,1-dyphenyl-2-picryl-hydrazyl (DPPH) and characterized by elemental analysis and spectral data.

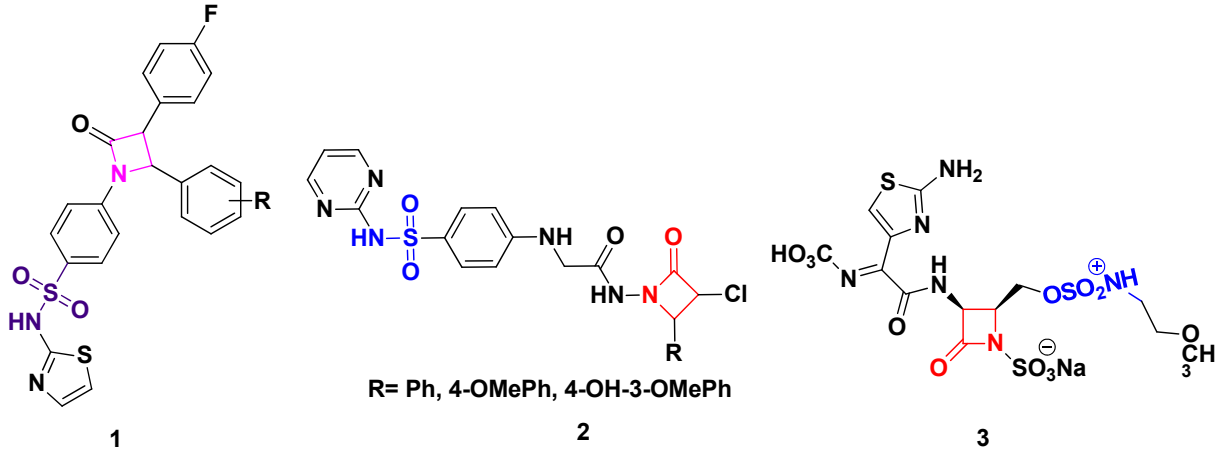


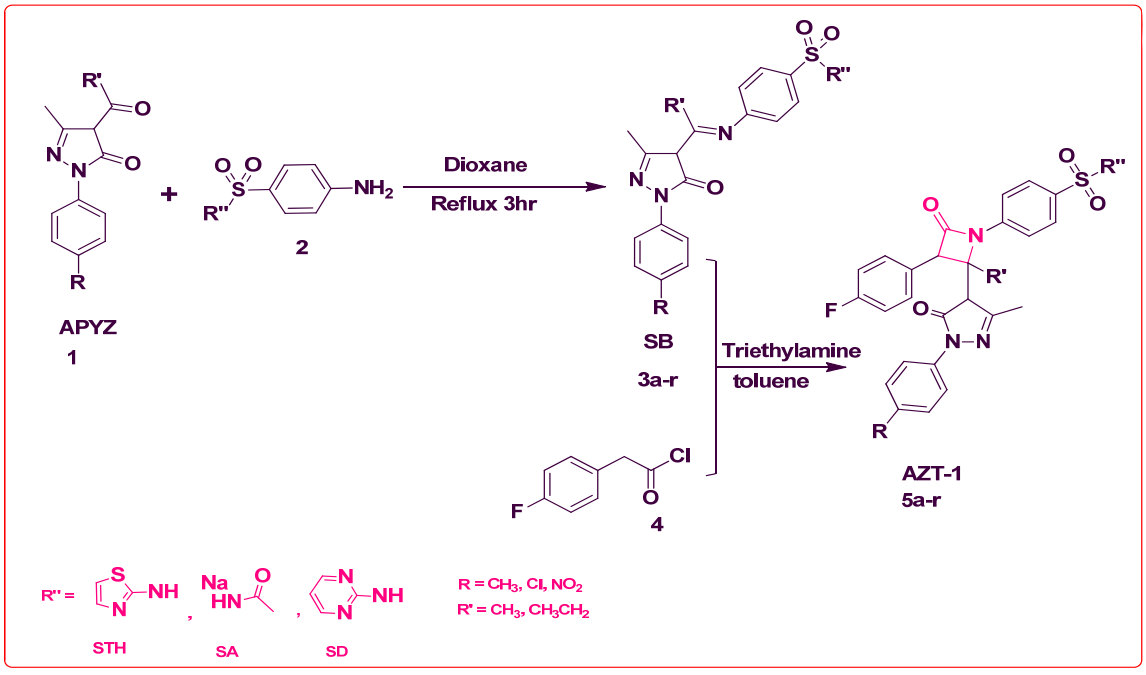
Figure-1 Some of the reported sulfonamide-bearing 2-azetidinone compounds

2. Results and Discussion

2.1 Chemistry

The most widely recognized method of Staudinger's is employed for the preparation of monocyclic 2-azetidinone (β lactams) via ketene-imine cycloaddition. The target sulfonamide Schiff bases **3a-r** intermediate compounds were synthesized via condensation reaction starting from commercial derivatives of the 4-acyl-2-pyrazolin-5-one **(APYZ) 1** and sulfathiazole (**STH**) sulfacetamide sodium **(SA),** sulfadiazine **(SD)**, **2** their synthetic path showed in **Scheme-1**. The Schiff bases following cyclization reaction with 2-(4-fluorophenyl) chloroacetyl chloride (F-CAC) **4** in the presence of triethyl amine (TEA) (0.04 mol) under the cool condition to produce desire 2-azitidinone targeted series of **5a-5r** in a good yield. Based on experimental results, a predictable mechanism for the preparation of final derivatives 2-azitidinone was produced by reaction of 2-(4-fluorophenyl)chloroacetyl chloride (F-CAC) **4** along with ketene-imines [2+2] cycloaddition with triethyl amine (TEA) which is intended to be step by step mechanism through zwitterionic intermediate[29] whereas another competitive route [2+4] pi electron cycloaddition is predominantly one step cycloaddition mechanism.[30]The structure of series target compounds of 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*) One **5a-5r** was confirmed by IR, ^{1}H NMR, ^{13}C NMR, ESI-MS and CHNS elemental analysis.

In IR spectra, the synthesized final sulfonamide-linked 2-azitidinone derivatives gave a broad absorption band at 3340-3317 cm^{-1}, which indicates the appearance of the sulfonyl amino (-NH) group. Furthermore, the characteristic values of C=O stretching that appeared in the region of ~1730 cm^{-1} for the 2-azetidinone ring are affirming of cycloaddition respectively. The sharp stretching peck at ~3029 cm^{-1} represents the vibration of -CH bonds of CH_2 groups. Various absorption bands were detected at the predicted region.



^{1}H NMR (400 MHz, DMSO) the spectra show ~5.16 ppm (CH-Cl) doublet for 2-azetidinone and ~5.04ppm (CH-N) doublet for 2-azetidinone confirming monocyclic ring formation in all derivatives correspondingly. Although different ranges between 12.17-11.10 ppm region chemical shifts showed singlet of -NH hydrogen for sulfonamide as expected. The phenyl ring of hydrogen in all compounds appears chemical shifts in different ranges of ~7.20-8.80 ppm. ^{13}C NMR spectrum (DMSO-d_6) the chemical shifts for all final scaffolds were constant with allocated structures no longer difference was detected. Chemical shifts for the carbon of carbonyl situated at β lactams ring were observed at ~165.0 ppm. While the signals of -NH-linked carbon of sulfonamides (pyrimidine, Thiazole) appeared at ~169-160 ppm. All other carbons ^{13}C signals showed the expected region assigned in the bellowed data section.

2.2 Biological activity

2.2.1 Antibacterial activity

The in vitro agar well diffusion method was used also described in our previous research [5]. Plates of ager well are finished by sterile cork borer (6mm diameter) and inoculated with the bacteria (two Gram-negative MTCC No.8558 Enterobacter aerogens, Escherichia coli MTCC No.1610, and two Gram-positive Micrococcus luteus MTCC No.11948 and Bacillus cereus MTCC No.8558) investigated all solids compounds dissolved in DMSO (because not inhibition) and get a concentration 1000µg/ml was directly encumbered into well of agar plates which inoculated for 37 ºC for 24 hours. The inhibitions region was deliberate where the microorganisms were inhibited after the incubation was finished and were evaluated with standard streptomycin (1000µg/ml). (**Table 1)**

$$\textbf{Activity index}(A.I) = \frac{\textbf{mean of zone of inhibition of derivatives}}{\textbf{zone of inhibition obtained for standard antibiotic drug}}$$

The conc. of the standard drug streptomycin was 1000 µg/ml. **Table 1** all results show that all derivatives of 2-azitidinone **5a-r** were moderate to excellent active against Gram-positive and negative bacteria. The significant results shown for **5f, 5l, 5n,** and **5r** compounds showed increased antibacterial activity compared to standard based depending on the functionality like **NO_2** groups while other compounds showed resultant such as moderate to lower active antibacterial compared to standard, (**Table-1**) However, still the antibacterial activity of synthesized compounds containing 2-azitidinone linked sulfonamide could be considerable.

Table 1. Antibacterial activity of **5a-5r** compounds

Derivatives	*E. aerogens*		*E. coli*		*Micrococcus luteus*		*Bacillus cereus*	
	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)	Mean value for Zone of Inhibition (mm)	Activity Index (A.I.)
5a	28	1.167	27	1.125	19	0.791	34	1.417
5b	27	1.125	27	1.125	30	1.250	24	1.000
5c	34	1.417	34	1.417	30	1.250	26	1.083
5d	22	0.917	22	0.917	22	0.917	30	1.250
5e	25	1.041	28	1.167	28	1.167	22	0.917
5f	36	1.500	34	1.417	36	1.500	30	1.250
5g	15	0.625	17	0.708	29	1.208	15	0.625
5h	22	0.917	22	0.917	29	1.208	19	0.791
5i	29	1.208	27	1.125	25	1.041	24	1.000
5j	22	0.917	20	0.833	16	0.666	14	0.583
5k	34	1.417	28	1.167	22	0.917	24	1.000
5l	36	1.500	22	0.917	34	1.417	34	1.417
5m	24	1.000	24	1.000	26	1.083	19	0.791
5n	36	1.500	30	1.250	24	1.000	36	1.500
5o	34	1.417	28	1.167	29	1.208	29	1.208
5p	22	0.917	23	0.958	28	1.167	34	1.417
5q	21	0.875	24	1.000	30	1.250	30	1.250
5r	36	1.500	28	1.167	34	1.417	34	1.417
Std	24	-	24	-	24	-	24	-

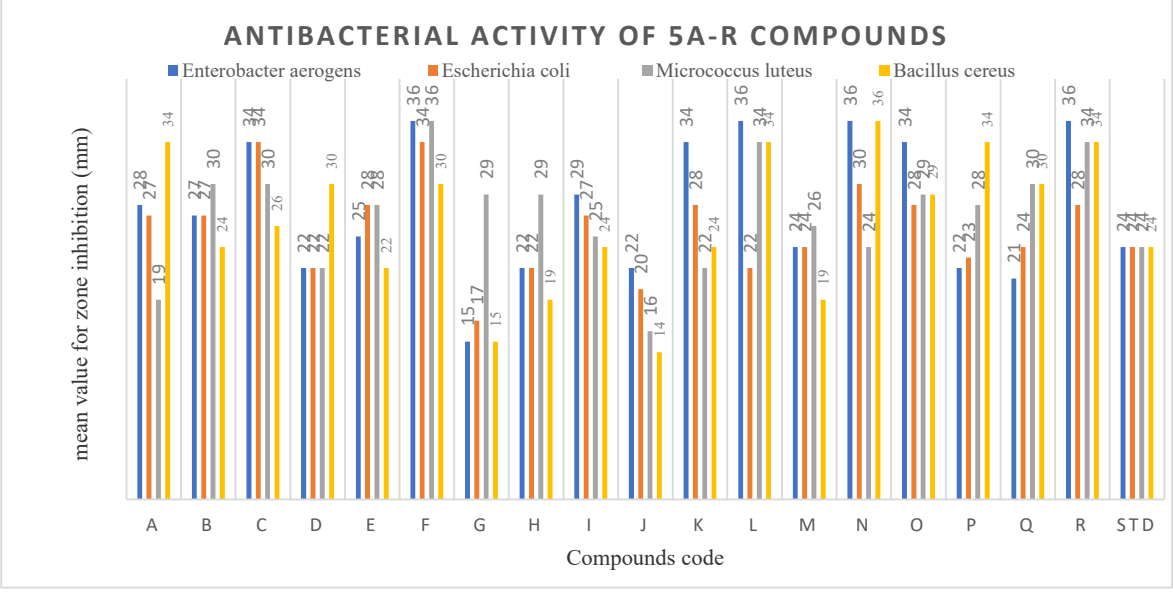


Fig. 2. Zone inhibition antibacterial activity of compounds **5a-5r**

2.2.2 Antioxidant activity

In our previous reported study[5], we have seen that in vitro free radical scavenging antioxidant activity of all the synthesized derivatives **5a-5r** was investigated by 2,2'-diphenyl-1-picrylhydrazyl (DPPH) assay which was calculated by percentage (%) Inhibition As shown in below **Table 2.**

The intense higher value for **5c, 5f, 5l, 5o,** and **5r** compounds indicate the increased value of the scavenging activity of the DPPH radical due to the presence of electro withdrawing Nitro and chloro group which is directly attached to a benzene ring. Also, other derivatives showed good to moderate inhibition.

Table 2. %DPPH radical scavenging activity assay for **5a-5r** compounds

Derivatives	*% DPPH radical scavenging activity assay at various concentrations Mean ± S.E*			
	0.00 µg/ml	**200 µg/ml**	**400 µg/ml**	**600 µg/ml**
5a	0.00	30.25±1.32	54.28±2.05	70.55±3.04
5b	0.00	29.17±1.24	60.22±2.25	68.98±3.32
5c	0.00	40.12±1.22	75.23±2.12	84.25±3.32
5d	0.00	29.35±1.20	61.23±2.22	78.55±3.30
5e	0.00	32.22±1.24	58.84±2.12	75.22±3.01
5f	0.00	38.75±1.24	68.18±2.20	84.82±3.25
5g	0.00	32.15±1.30	57.48±2.09	72.36±3.05
5h	0.00	34.19±1.31	62.33±2.01	71.68±3.22
5i	0.00	30.12±1.22	59.87±2.32	74.22±3.32
5j	0.00	29.35±1.20	61.23±2.22	78.55±3.30
5k	0.00	32.22±1.24	58.84±2.12	75.22±3.01
5l	0.00	38.75±1.24	68.18±2.20	84.82±3.25
5m	0.00	23.00±1.22	47.12±2.19	66.56±3.12
5n	0.00	24.12±1.25	58.25±2.15	70.12±3.32
5o	0.00	38.31±1.32	59.45±2.13	71.25±3.01
5p	0.00	30.12±1.21	60.15±2.12	69.22±3.16
5q	0.00	32.15±1.30	55.78±2.02	71.66±3.01
5r	0.00	39.15±1.23	70.25±2.22	80.25±3.02

According to our preceding report studied[5] The compounds **5a-r** examined for Superoxide anion scavenging activity were analyzed at different concentrations 0.00 µg/ml, 200 µg/ml, 400 µg/ml, and 600 µg/ml which were calculated for IC_{50} values mentioned in below **Table 3.** Compounds **5c, 5i,** and **5o** considered high scavenging activity.

Table 3. Superoxide anion scavenging activity assay for **5a-5r** compounds

Derivatives	*% Superoxide anion scavenging activity assay at various concentrations Mean ± S.E*			
	0.00 µg/ml	**200 µg/ml**	**400 µg/ml**	**600 µg/ml**
5a	0.00	30.21±0.60	59.25±1.48	71.55±1.24
5b	0.00	29.27±0.89	57.63±1.56	72.23±1.29
5c	0.00	36.22±0.72	60.88±1.54	68.44±1.30
5d	0.00	28.55±0.70	60.22±1.50	73.22±1.25
5e	0.00	28.67±0.61	58.22±1.50	71.22±1.26
5f	0.00	30.56±0.55	56.54±1.57	71.22±1.21
5g	0.00	27.45±0.72	53.12±1.55	70.12±1.19
5h	0.00	30.12±0.62	55.40±1.58	65.44±1.21
5i	0.00	35.40±0.72	60.25±1.57	80.41±1.24
5j	0.00	31.99±0.51	52.55±1.51	69.22±1.25
5k	0.00	28.23±0.52	57.23±1.52	68.55±1.27
5l	0.00	34.51±0.55	62.33±1.52	81.45±1.25
5m	0.00	30.22±0.78	54.33±1.53	67.22±1.25
5n	0.00	29.55±0.77	57.58±1.50	73.25±1.20
5o	0.00	38.55±0.60	65.44±1.55	85.24±1.23
5p	0.00	28.30±0.72	58.33±1.56	66.55±1.21
5q	0.00	31.22±0.76	57.22±1.50	67.55±1.22
5r	0.00	33.56±0.77	63.28±1.51	79.56±1.20

3. Conclusions

This current work Including all novel series of 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*) One **5a-5r** which containing sulfonamide functionality combined with 2-Azitidinone (Azitidin-2-one or β-lactam) group were investigated for antibacterial against gram +ve and gram -ve strains, for the examined resulted from **5f, 5l, 5n** and **5r** derivatives showed outstanding potential as antibacterial while **5c, 5f, 5l, 5o** and **5r** (40.12-84.82 µg/ml) for DPPH radical scavenging and **5c, 5i,5o** (38.55-85.24 µg/ml) for superoxide anion scavenging were being maximum influential derivatives.

Acknowledgments

We would honestly feel gratitude to The Sheth M. N. Science College, H.N.G.U., Patan for providing us with laboratory facilities. The authors are also grateful to the 'Center of Excellence' of Saurashtra University for the spectral facility.

4. Experimental

4.1. Materials and Methods

In Synthesis of 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-ox oazitidin-2-yl)-3-methyl-1-(p-tolyl)-1*H*-pyrazol-5(4*H*)One which containing sulfonamide functionality united with 2-Azitidinone (Azitidin-2-one or

β-lactam) group chemical and reagents were used all sulfonamides (sulfa drugs) and 2-(4-fluorophenyl)acetyl chloride, Pyarzoline-1 were acquired from commercial sources (Sigma-Aldrich). 4-acyl-2-pyrazolin-5-one **(APYZ) 1,** and different 1-4 dioxane were purchased from Merck (Germany). Pre-coated aluminum sheets (silica gel 60 $F_{254,}$ Merck) were used as (TLC) thin-layer chromatography, and spots were visualized underneath ultraviolet light. (M.P) The melting point was considered by using a Mel-temp apparatus, and the consequences were uncorrected. Advion expression CMS, USA was used for recorded mass spectra. The compound was analyzed for Carbon, Hydrogen, Nitrogen oxygen and Sulphur and was estimated on CHNS analyzer serial NO.: 15084053. Infra-red spectra were recorded on Shimadzu spectrophotometer in the frequency range 4000-400 cm^{-1} using KBr pallet disc, ^{1}H NMR and ^{13}C NMR spectrum were recorded on Bruker at 400 MHz and 100 MHz in DMSO solution, and chemical shifts were recorded in parts per million (ppm) with TMS at the internal reference.

4.2. General procedure

4.2.1 Synthesis of derivatives of Schiff bases (SB) of (E)-3-methyl-4-(1-((4-(substituted sulfonyl) phenyl)imino)alkyl)-1-(aryl)-1H-pyrazol-5(4H)-one

All compounds of derivatives of Schiff bases were prepared by our earlier method.[3,6] The following concentration among equimolar amounts (1:1) derivatives of the 4-acyl-2-pyrazolin-5-one **(APYZ) 1** (0.1 mol) and sulfathiazole (**STH**), sulfacetamide sodium **(SA),** sulfadiazine **(SD)**, **2** (0.1 mol) in lowest amount amounts of 1,4-dioxane solution. The reaction mixture was refluxed to carry on for three to four hours in an oil bath and then cooled. The solid product was filtrated and washed with some hot1,4-dioxane and then allowed to dry with air and recrystallized from chloroform to get 4-(arylideneamino)-N-(thiazol-2-yl)benzensulfonamide with light pale yellow colored. the reaction was continuously monitored by thin layered chromatography (TLC) using ethyl acetate: hexane (4:7). This subsequent reaction steps of the last product of Schiff bases **3a-r** are shown in **Scheme-1.**

4.2.2 Synthesis of 4(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl) -4-oxoazitidin-2-yl)-3-methyl-1-(p-tolyl)-1H-pyrazol-5(4H)One

The product mixture of Schiff base **3a-r** (0.02 mol) and triethyl amine (TEA) (0.04 mol) was dissolved in toluene (100 ml), cooled close to 5ºC, and stirred. To this well-stirred cooled solution 2,-(4-flurophenyl) chloroacetyl chloride (F-CAC) **4** (0.04 mmol) was added drop by drop within a period of 15 min. The remaining reaction mixture was then stirred for a supplementary 3-4 hrs and kept at room temperature for 48 hrs. The consequential mixture was concentrated, cooled, poured into a beaker of ice-cold water, sieve, and then dried. Reaction was continuously monitored by test of thin layered chromatography (TLC) with using the n-hexane/EtOAc (8:2) thus obtained derivatives of 4-(3-(4-Fluorophenyl)2-methyl-1-(4-(sulfonamidesubtituted)phenyl)-4-oxoazitidin-2-yl)-3-methy l-1-(p-tolyl)-1H-pyrazol-5 (4H) **5a-r** One yellow to light yellow colored.[3,6]

4.3 Physical and Spectral Data

4.3.1 4-(3-(4-Fluorophenyl)2-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazolo-4-yl))-4-oxoa zitidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamdie **5a** Yellow solid, mp 237-239ºC; Anal. Calcd for $C_{31}H_{27}FN_6O_4S$: C, 60.20; H,4.55; F, 3.17, N,14.04; O,10.69; S,5.36%; found C, 60.70; H, 4.52; F, 3.20 N, 14.10; O,10.62, S,5.37%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3315 (NH), 3031 (C-H_{str} saturated hydrocarbon) 1730.01 (C=O_{str} for azitidinone) 1540, 1511,and 1160 (for pyrazolin ring) 1332 Asy., 1180 Syn., (O=S=O), 1598 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.20-2.01 (t 5H, CH_2CH_3) 5.14(d,CH-Cllactam), 5.07(d, CH-Nlactam), 7.30-8.81 (m, aromatic Protons), 12.20 (s, 1H -NH), 11.01 (s,1H -OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.31(C=O,pyrazoline), 166.05(CH-pyrimidine), 165.14(C=O,azi), 159.73(C-F,arC), 157.70(2CH, pyrimidine), 155.8(C-CH,pyrazoline), 139.06(C-N,arC), 136.70(C-CH_3,arC), 135.13(C-,arC), 133(2C-arC), 130.15-129.10(6CH,arC), 126.01(2CH,arC), 121.86(2CH,arC), 115.30(2CH,arC), 61.42(CH,azi), 53.68(C-Pyrozoline), 53.05(CH-azi), 21.60(CH_3,arC), 19.35($2CH_3$); ESI-MS: *m/z* calculated 598.18, found $[M + H]^+$ 597.25

4.3.2 4-(2-(1-(4-Chlorophenyl)3-methyl-5-oxo-4,5-dihydro-1H-pyrazolo-4-yl)-3-(4-flourophen yl)-2-methyl-4-oxoazitidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamdie **5b** Light Yellow solid, mp ~252ºC; Anal. Calcd for $C_{30}H_{24}$ $ClFN_6O_4S$: C, 58.20; H,3.91; Cl, 5.73; F, 3.07; N,13.58; O,10.34; S,5.18%; found C, 58.22; H,3.95; Cl, 5.70; F, 3.11; N,13.60; O,10.30; S,5.16%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3340.2 (NH), 3029 (C-H_{str} saturated hydrocarbon) 1729.33 (C=O_{str} for azitidinone) 1541, 1521, and 1158 (for pyrazoline ring) 1325 Asy., 1178 Syn., (O=S=O), 1590 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.41-2.22 (t 5H, CH_2CH_3) 5.16 (d, CH-Cl_{lactam}), 5.08 (d, CH-N_{lactam}), 7.10-8.71 (m, aromatic Protons), 11.80 (s, 1H -NH), 10.89 (s,1H -OH); ESI-MS: *m/z* calculated 618.13, found $[M + H]^+$ 619.02

4.3.3 4-(3-(4-fluorophenyl)-2-methyl-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihydro-1H-pyra zol-4-yl)-4-oxoazetidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamide **5c** Light Yellow solid, mp ~287ºC; Anal. Calcd for $C_{30}H_{24}FN_7O_6S$: C, 57.20; H, 3.85; F, 3.05; N, 15.60; O, 15.22; S, 5.12%; found C, 57.23; H, 3.84; F, 3.02; N, 15.57; O, 15.25; S, 5.09%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3320.2 (NH), 3040 (C-H_{str} saturated hydrocarbon) 1732.01 (C=O_{str} for azitidinone) 1535, 1491, and 1158 (for pyrazoline ring) 1333 Asy., 1199 Syn., (O=S=O), 1588 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.40-2.25 (t 5H,

CH_2CH_3) 5.17(d, CH-Cl_{lactam}), 5.04(d, CH-N_{lactam}), 7.10-8.58 (m, aromatic Protons), 12.01 (s, 1H -NH), 10.25 (s,1H -OH). ESI-MS: *m/z* calculated 629.15, found $[M + H]^+$ 630.10

4.3.4 4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)-4-oxo azetidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamide **5d** white solid, mp 262-264ºC; Anal. Calcd for $C_{32}H_{29}FN_6O_4S$: C, 62.73; H, 4.77; F, 3.10; N, 13.72; O, 10.45; S, 5.23%; found C, 62.70; H, 4.80; F, 3.12; N, 13.70 O, 10.42; S, 5.25%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3317 (NH), 3032 (C-H_{str} saturated hydrocarbon) 1731 (C=O_{str} for azitidinone) 1542, 1521,and 1165 (for pyrazolin ring) 1334 Asy., 1182 Syn., (O=S=O), 1590 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.10-2.00 (t 5H, CH_2CH_3) 5.17(d,CH-Cl_{lactam}), 5.02(d, CH-N_{lactam}), 7.20-8.78 (m, aromatic Protons), 12.01 (s, 1H -NH), 11.11 (s,1H -OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.55(C=O,pyrazoline), 166.75(CH-pyrimidine), 165.03(C=O,azi), 159.56(C-F,arC), 157.72(2CH, pyrimidine), 155.8(C-CH,pyrazoline), 139.06(C-N,arC), 136.10(C-CH_3,arC), 135.22(C-,arC),133.52(2C-arC), 130.78-129.33(6CH,arC), 126.51(2CH,arC), 121.86(2CH,arC), 115.42(2CH,arC), 61.19(C-C_2H_5,azi), 53.70(C-Pyrozoline), 30.73(CH_2- C_2H_5,azi), 21.52 (CH_3,arC), 19.35($2CH_3$); ESI-MS: *m/z* calculated 612.20, found $[M + H]^+$ 613.01

4.3.5 4-(2-(1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-2-ethyl-3-(4-fluorophenyl)-4-oxoazetidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamide **5e** white solid, mp ~293ºC; Anal. Calcd for $C_{31}H_{26}ClFN_6O_4S$: C, 58.81; H, 4.14; Cl, 5.60; F, 3.00; N, 13.27; O, 10.11; S, 5.06%; found C, 58.80; H, 4.15; Cl, 5.60; F, 3.02; N, 13.30; O, 10.14; S, 5.10%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3325.02 (NH), 3029.33 (C-H_{str} saturated hydrocarbon) 1733.22 (C=O_{str} for azitidinone) 1545, 1522, and 1170 (for pyrazolin ring) 1340 Asy., 1177 Syn., (O=S=O), 1589 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.21-2.15 (t 5H, CH_2CH_3) 5.16 (d, CH-Cl_{lactam}), 5.04 (d, CH-N_{lactam}), 7.01-8.55 (m, aromatic Protons), 12.01 (s, 1H -NH), 10.99 (s,1H -OH). ESI-MS: *m/z* calculated 632.14, found $[M + H]^+$ 633.12

4.3.6 4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihydro-1H-pyrazo l-4-yl)-4-oxoazetidin-1-yl)-N-(pyrimidin-2-yl)benzenesulfonamide **5f** yellow solid, mp >310ºC; Anal. Calcd for $C_{31}H_{26}FN_7O_6S$: C, 57.85; H, 4.07; F, 2.95; N, 15.23; O, 14.91; S, 4.98%; found C, 57.82; H, 4.10; F, 2.96; N, 15.23; O, 14.94; S, 4.99%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3320.15 (NH), 3032.15 (C-H_{str} saturated hydrocarbon) 1734 (C=O_{str} for azitidinone) 1542, 1512 and 1164 (for pyrazoline ring) 1335 Asy., 1182 Syn., (O=S=O), 1582 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.22-2.04 (t 5H, CH_2CH_3) 5.12 (d, CH-Cl_{lactam}), 5.04 (d, CH-N_{lactam}), 6.78-8.88 (m, aromatic Protons), 11.50 (s, 1H -NH), 10.01 (s,1H -OH). ESI-MS: *m/z* calculated 643.16, found $[M + H]^+$ 644.02

4.3.7 4-(3-(4-fluorophenyl)-2-methyl-2-(3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)-4-oxo azetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5g** Yellow solid, mp ~259.1ºC; Anal. Calcd for $C_{30}H_{26}FN_5O_4S_2$: C, 59.69; H, 4.34; F, 3.15; N, 11.60; O, 10.60; S, 10.62%; found C, 59.72; H, 4.31; F, 3.18; N, 11.62; O, 10.60; S, 10.61%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3325 (NH), 3029 (C-H_{str} saturated hydrocarbon) 1730 (C=O_{str} for azitidinone) 1540, 1515,and 1178 (for pyrazolin ring) 1344 Asy., 1178 Syn., (O=S=O), 1578 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.11-2.05 (t 5H, CH_2CH_3) 5.13 (d,CH-Cl_{lactam}), 5.00 (d, CH-N_{lactam}), 7.10-8.65 (m, aromatic Protons), 11.98 (s, 1H -NH), 11.09 (s,1H -OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.45(C=O,pyrazoline), 167.21(C-N,thiazole), 165.46(C=O,azi), 159.40(C-F,arC), 155.05(C-CH,pyrazoline), 140.01(C-N,arC), 137.01(CH-N,thiazole), 136.98(C-arC), 135.25(2C,arC), 134.01(C-CH_3), 129-130.5(6CH,arC), 126.31(2CH,arC), 121.66(2CH,arC), 115.11(2CH ,arC), 114.18(CH-S,thiazole), 60.18(CH,azi), 54.60(C-Pyrozoline), 20.92(CH_3,arC), 19.45($2CH_3$); ESI-MS: *m/z* calculated 603.14, found $[M + H]^+$ 604.44

4.3.8 4-(2-(1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-fluoro phen yl)-2-methyl-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5h** Yellow solid, mp 288-291ºC; Anal. Calcd for $C_{29}H_{23}ClFN_5O_4S_2$: C, 55.81; H, 3.71; Cl, 5.68; F, 3.04; N, 11.22; O, 10.25; S, 10.28%; found C, 55.80; H, 3.73; Cl, 5.65; F, 3.02; N, 11.20; O, 10.25; S, 10.27%; IR (KBr) ($\upsilon_{max,}$ cm^{-1});3343.52 (NH), 3036.04 (C-H_{str} saturated hydrocarbon) 1733.30 (C=O_{str} for azitidinone) 1541, 1489, and 1161 (for pyrazoline ring) 1334 Asy., 1185 Syn., (O=S=O), 1580 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 5.17(d, CH-Cl_{lactam}), 5.07 (d, CH-N_{lactam}), 6.60-8.55 (m, aromatic Protons), 11.79 (s, 1H -NH), 10.00 (s,1H -OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.31(C=O,pyrazoline), 166.09(C-N,thiazole), 161.84(C=O,azi), 158.73(C-F,arC), 156.70(C-CH,pyrazoline), 139.46(C-N,arC), 137.50(CH-N,thiazole), 136.45(C-arC), 135.11(2C,arC), 130.22-129.5(6CH,arC), 125.31(2CH,arC), 121.84(2CH,arC), 116.31(2CH ,arC), 114.99(CH-S,thiazole), 60.39(CH,azi), 54.98(C-Pyrozoline), 20.60(CH_3,arC), 19.35($2CH_3$); ESI-MS: *m/z* calculated 623.09, found $[M + H]^+$ 623.0

4.3.9 4-(3-(4-fluorophenyl)-2-methyl-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihydro-1H-pyraz ol-4-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5i** Yellow solid, mp ~300ºC; Anal. Calcd for $C_{29}H_{23}FN_6O_6S_2$: C, 54.88; H, 3.65; F, 2.99; N, 13.24; O, 15.13; S, 10.10%; found C, 54.86; H, 3.62; F, 2.98; N, 13.21; O, 15.16; S, 10.11%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3360.15 (NH), 3026.01 (C-H_{str} saturated hydrocarbon) 1730.03 (C=O_{str} for azitidinone) 1547, 1520, and 1157 (for pyrazoline ring) 1324 Asy., 1172 Syn., (O=S=O), 1599 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.20-2.09 (t 5H, CH_2CH_3) 5.14 (d, CH-Cl_{lactam}), 5.04 (d, CH-N_{lactam}), 7.01-8.84 (m, aromatic Protons), 12.10 (s, 1H -NH), 10.35 (s,1H -OH)ESI-MS: *m/z* calculated 634.11, found $[M + H]^+$ 635.12

4.3.10 4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazol-4-yl)-4-oxo azetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5j** Light Yellow solid, mp ~280ºC; Anal. Calcd for $C_{31}H_{28}FN_5O_4S_2$: C, 60.28; H, 4.57; F, 3.08; N, 11.34; O, 10.36; S, 10.38%; found C, 60.29; H, 4.58; F, 3.07; N, 11.35; O, 10.34; S, 10.40%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3348 (NH), 3030.12 (C-H_{str} saturated hydrocarbon) 1736.12 (C=O_{str} for azitidinone) 1515, 1454, and 1160 (for pyrazoline

ring) 1337.02 Asy., 1188 Syn., (O=S=O), 1584 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.11-2.15 (t 5H, CH_2CH_3) 5.15 (d, CH-Cl_{lactam}), 5.07 (d, CH-N_{lactam}), 7.10-8.88 (m, aromatic Protons), 12.17 (s, 1H -NH), 11.33 (s,1H -OH). ESI-MS: *m/z* calculated 617.16, found $[M + H]^+$ 618.01

4.3.11 4-(2-(1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-2-ethyl-3-(4-fluoropheny l)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5k** Light Yellow solid, mp >300ºC; Anal. Calcd for $C_{29}H_{23}ClFN_5O_4S_2$: C, 56.46; H, 3.95; Cl, 5.56; F, 2.98; N, 10.97; O, 10.03; S, 10.05%; found C, 56.47; H, 3.94; Cl, 5.58; F, 2.96; N, 10.99; O, 10.01; S, 10.05%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3350.21 (NH), 3029 (C-H_{str} saturated hydrocarbon) 1733 (C=O_{str} for azitidinone) 1489, 1458, and 1164 (for pyrazoline ring) 1336 Asy., 1187 Syn., (O=S=O), 1579 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.29-2.07 (t 5H, CH_2CH_3) 5.17(d, CH-Cl_{lactam}), 5.05(d, CH-N_{lactam}), 7.46-8.98 (m, aromatic Protons), 12.14 (s, 1H -NH), 11.92 (s,1H -OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.86(C=O,pyrazoline), 165.87(C-N,thiazole), 160.73(C=O,azi), 158.89(C-F,arC), 138.44(C-N,arC), 134.51(CH-N,thiazole), 133.05(C-arC), 132.92(2C,arC), 129.97-128.88(6CH,arC), 122.23(2CH,arC), 119.86(2CH,arC), 116.32(2CH ,arC), 112.60(CH-S,thiazole), 60.60(C-C_2H_5,azi), 53.97(C-Pyrozoline), 30.11(CH_2- C_2H_5,azi), 19.33($2CH_3$) ESI-MS: *m/z* calculated 637.10, found $[M + H]^+$ 639.04

4.3.12 4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihydro-1H-pyraz l-4-yl)-4-oxoazetidin-1-yl)-N-(thiazol-2-yl)benzenesulfonamide **5l** Light Yellow solid, mp >308ºC; Anal. Calcd for $C_{30}H_{25}FN_6O_6S_2$: C, 55.55; H, 3.88; F, 2.93; N, 12.96; O, 14.80; S, 9.89%; found C, 55.56; H, 3.87; F, 2.91; N, 12.94; O, 14.82; S, 9.87%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3341.02 (NH), 3030.11 (C-H_{str} saturated hydrocarbon) 1734.01 (C=O_{str} for azitidinone) 1490, 1460, and 1171 (for pyrazoline ring) 1355 Asy., 1178 Syn., (O=S=O), 1571 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.04-2.18(t 5H, CH_2CH_3) 5.19 (d, CH-Cl_{lactam}), 5.01 (d, CH-N_{lactam}), 7.16-8.99 (m, aromatic Protons), 12.14 (s, 1H -NH), 11.55 (s,1H -OH). ESI-MS: *m/z* calculated 648.13, found $[M + H]^+$ 649.06

4.3.13 sodiumacetyl((4-(3-(4-fluorophenyl)-2-methyl-2-(3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyr azol-4-yl)-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5m** White solid, mp 220-222ºC; Anal. Calcd for $C_{29}H_{26}FN_4NaO_5S$: C, 59.58; H, 4.48; F, 3.25; N, 9.58; Na, 3.93; O, 13.68; S, 5.49%; found C, 59.60; H, 4.46; F, 3.24; N, 9.59; Na, 3.92; O, 13.69; S, 5.49%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3342 (NH), 3025 (C-H_{str} saturated hydrocarbon) 1730 (C=O_{str} for azitidinone) 1517, 1439,and 1158 (for pyrazolin ring) 1342 Asy., 1178 Syn., (O=S=O), 1590 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.10-2.10 (t 5H, CH_2CH_3) 5.18 (d,CH-Cl_{lactam}), 5.08 (d, CH-N_{lactam}), 7.30-8.98 (m, aromatic Protons), 12.07 (s, 1H -NH), 11.14 (s,1H -OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.11(C=O,pyrazoline), 171.29 (C=O acetyl), 165.27(C=O,azi), 159.16(C-F,arC), 156.15(C-CH,pyrazoline), 139.77(C-N,arC), 136.23(C-CH_3,arC), 135.32(C-,arC), 130.82-129.12(6CH,arC), 126.49(2CH,arC), 121.73(2CH,arC), 116.19(2CH,arC), 62.04(CH,azi), 53.90(C-Pyrozoline), 53.05(CH-azi), 22.02(CH_3,acetyle), 21.62(CH_3,arC), 19.58($2CH_3$); ESI-MS: *m/z* calculated 584.15, found $[M + H]^+$ 585.11

4.3.14 sodiumacetyl((4-(2-(1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-fluo rophenyl)-2-methyl-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5n** White solid, mp ~269ºC; Anal. Calcd for $C_{28}H_{23}ClFN_4NaO_5S$: C, 55.59; H, 3.83; Cl, 5.86; F, 3.14; N, 9.26; Na, 3.80; O, 13.22; S, 5.30%; found C, 55.60; H, 3.82; Cl, 5.87; F, 3.15; N, 9.27; Na, 3.81; O, 13.20; S, 5.32%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3348.01 (NH), 3033.02 (C-H_{str} saturated hydrocarbon) 1740.12 (C=O_{str} for azitidinone) 1490, 1460 and 1159 (for pyrazolin ring) 1340 Asy., 1179 Syn., (O=S=O), 1581 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.13-2.03 (t 5H, CH_2CH_3) 5.13 (d, CH-Cl_{lactam}), 5.01 (d, CH-N_{lactam}), 7.40-8.82 (m, aromatic Protons), 12.04 (s, 1H -NH), 11.03 (s,1H -OH). ESI-MS: *m/z* calculated 604.10, found $[M + H]^+$ 605.13

4.3.15 sodiumacetyl((4-(3-(4-fluorophenyl)-2-methyl-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihy dro-1H-pyrazol-4-yl)-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5o** Yellow solid, mp ~277ºC; Anal. Calcd for $C_{28}H_{23}FN_5NaO_7S$: C, 54.63; H, 3.77; F, 3.09; N, 11.38; Na, 3.73; O, 18.19; S, 5.21%; found C, 54.62; H, 3.78; F, 3.07; N, 11.40; Na, 3.72; O, 18.19; S, 5.23%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3333 (NH), 3026.15 (C-H_{str} saturated hydrocarbon) 1739 (C=O_{str} for azitidinone) 1498, 1459, and 1169 (for pyrazolin ring) 1350 Asy., 1188 Syn., (O=S=O), 1561 (thiazole ring); ^{1}H NMR (400 MHz, DMSO) δ 3.14-2.08(t 5H, CH_2CH_3) 5.12 (d, CH-Cl_{lactam}), 5.01 (d, CH-N_{lactam}), 7.10-8.90 (m, aromatic Protons), 12.04 (s, 1H -NH), 11.05 (s,1H -OH). ESI-MS: *m/z* calculated 615.12, found $[M + H]^+$ 616.10

4.3.16 sodiumacetyl((4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyra zol-4-yl)-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5p** White solid, mp 277ºC; Anal. Calcd for $C_{30}H_{28}FN_4NaO_5S$: C, 60.19; H, 4.71; F, 3.17; N, 9.36; Na, 3.84; O, 13.36; S, 5.36%; found C, 60.20; H, 4.70; F, 3.19; N, 9.34; Na, 3.86; O, 13.34; S, 5.36%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3344 (NH), 3031 (C-H_{str} saturated hydrocarbon) 1732 (C=O_{str} for azitidinone) 1495, 1456, and 1181 (for pyrazolin ring) 1353 Asy., 1180 Syn., (O=S=O), 1576 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.14-2.10 (t 5H, CH_2CH_3) 5.14 (d, CH-Cl_{lactam}), 5.03 (d, CH-N_{lactam}), 7.01-8.77 (m, aromatic Protons), 12.01 (s, 1H -NH), 11.03 (s,1H -OH). ESI-MS: *m/z* calculated 598.17, found $[M + H]^+$ 599.12

4.3.17 sodiumacetyl((4-(2-(1-(4-chlorophenyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-2-ethyl -3-(4-fluorophenyl)-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5q** White solid, mp ~280ºC; Anal. Calcd for $C_{29}H_{25}ClFN_4NaO_5S$: C, 56.27; H, 4.07; Cl, 5.73; F, 3.07; N, 9.05; Na, 3.71; O, 12.92; S, 5.18%; found C, 56.26; H, 4.08; Cl, 5.72; F, 3.08; N, 9.06; Na, 3.70; O, 12.91; S, 5.19%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3344 (NH), 3031 (C-H_{str} saturated hydrocarbon) 1737 (C=O_{str} for azitidinone) 1480, 1460, and 1154 (for pyrazoline ring) 1340 Asy., 1190 Syn., (O=S=O), 1570 (thiazole ring); ^{1}H NMR (400 MHz,

DMSO) δ 3.13-2.10 (t 5H, CH_2CH_3) 5.16 (d, CH-Cl_{lactam}), 5.04 (d, CH-N_{lactam}), 7.16-8.87 (m, aromatic Protons), 12.14 (s, 1H -NH), 11.12 (s,1H -OH). ESI-MS: *m/z* calculated 618.11, found $[M + H]^+$ 619.10.

4.3.18 sodiumacetyl((4-(2-ethyl-3-(4-fluorophenyl)-2-(3-methyl-1-(4-nitrophenyl)-5-oxo-4,5-dihydro-1 H-pyrazol-4-yl)-4-oxoazetidin-1-yl)phenyl)sulfonyl)amide **5r** Yellow solid, mp >288ºC; Anal. Calcd for $C_{29}H_{25}FN_5NaO_7S$: C, 55.32; H, 4.00; F, 3.02; N, 11.12; Na, 3.65; O, 17.79; S, 5.09%; found C, 55.31; H, 4.01; F, 3.03; N, 11.11; Na, 3.64; O, 17.78; S, 5.09%; IR (KBr) ($\upsilon_{max,}$ cm^{-1}); 3340 (NH), 3023.10 (C-H_{str} saturated hydrocarbon) 1730.01 (C=O_{str} for azitidinone) 1496, 1450,and 1180 (for pyrazolin ring) 1343 Asy., 1182 Syn., (O=S=O), 1580 (thiazole ring);; ^{1}H NMR (400 MHz, DMSO) δ 3.01-2.11 (t 5H, CH_2CH_3) 5.13 (d,CH-Cl_{lactam}), 5.01 (d, CH-N_{lactam}), 7.11-8.56 (m, aromatic Protons), 11.89 (s, 1H -NH), 10.58 (s,1H -OH); ^{13}C NMR (100 MHz, DMSO-d_6) 174.26(C=O,pyrazoline), 171.38 (C=O acetyl), 165.37(C=O,azi), 159.25(C-F,arC), 156.13(C-CH,pyrazoline), 139.15(C-N,arC), 135.32(C-,arC), 130.82-129.26(6CH,arC), 126.49(2CH,arC), 122.01(2CH,arC), 116.15(2CH,arC), 61.04(C-C_2H_5,azi), 54.00(C-Pyrozoline), 31.09(CH_2- C_2H_5,azi), 21.51(CH_3,arC), 19.8($2CH_3$); ESI-MS: *m/z* calculated 629.14, found $[M + H]^+$ 630.02

References

1. Yotphan, S., Sumunnee, L., Beukeaw, D., Buathongjan, C. & Reutrakul, V. **(2016)** Iodine-catalyzed expeditious synthesis of sulfonamides from sulfonyl hydrazides and amines. *Org. Biomol. Chem.* 14, 590–597.

2. Irshad, M. *et al.* **(2016)** Synthesis, biological screening and molecular docking studies of some ethylated sulfonamides having 1,4-Benzodioxane moiety. *Pak. J. Pharm. Sci.* 29, 1913–1925.

3. Variya, H. H., Panchal, V. & Patel, G. R. **(2019)** Synthesis and Biological Evolution of Sulfonamide Fused Azitidinone As Antibacterial and Antifungal Agents. 5, 1–17.

4. Variya, H. H., Panchal, V. & Patel, G. R. **(2019)** Synthesis and Spectral studies of 1,3 benzothiazole-2-thiol conjugated thiosemicarbazide as Antibacterial and Antifungal agents. *Int. J. Res. Advent Technol.* 7, 388–392.

5. Variya, H. H., Panchal, V. & Patel, G. R. **(2019)** Synthesis and characterization of 4-((5-bromo-1h-pyrazolo [3,4-b]pyridin-3-yl)amino)-n-(substituted)benzenesulfonamide as antibacterial, and antioxidant candidates. *Curr. Chem. Lett.* 8, 177–186.

6. Variya, H. H., Panchal, V. & Patel, G. R. **(2020)** Synthesis, anti-tuberculosis and anti-bacterial activities of sulfonamide bearing 4-((2-(5-bromo-1H-pyrazolo[3,4-b]pyridin-1-yl)-2-oxoethyl)amino)-N-(various substitutions)benzenesulfonamide. *Indian J. Chem. - Sect. B Org. Med. Chem.* 59 B, 682–689.

7. Supuran, C. T., Casini, A. & Scozzafava, A. **(2003)** Protease inhibitors of the sulfonamide type: Anticancer, anti-inflammatory, and antiviral agents. *Med. Res. Rev.* 23, 535–558.

8. Garaj, V. *et al.* **(2004)** Carbonic anhydrase inhibitors: synthesis and inhibition of cytosolic/tumor-associated carbonic anhydrase isozymes I, II, and IX with sulfonamides incorporating 1, 2, 4-triazine moieties. *Bioorg. Med. Chem. Lett.* 14, 5427–5433.

9. Supuran, C. T. **(2008)** Carbonic anhydrases: novel therapeutic applications for inhibitors and activators. *Nat. Rev. Drug Discov.* 7, 168.

10. Chen, Z. *et al.* **(2015)** Design, synthesis, biological evaluation and molecular modeling of dihydropyrazole sulfonamide derivatives as potential COX-1/COX-2 inhibitors. *Bioorg. Med. Chem. Lett.* 25, 1947–1951.

11. Ebrahimi, H., Hadi, J. S. & Al-Ansari, H. S. **(2013)** A new series of Schiff bases derived from sulfa drugs and indole-3-carboxaldehyde: Synthesis, characterization, spectral and DFT computational studies. *J. Mol. Struct.* 1039, 37–45.

12. Krátký, M. *et al.* **(2012)** Antimicrobial activity of sulfonamides containing 5-chloro-2- hydroxybenzaldehyde and 5-chloro-2-hydroxybenzoic acid scaffold. *Eur. J. Med. Chem.* 50, 433–440.

13. Vellaiswamy, G. & Ramaswamy, S. **(2014)** Synthesis, spectral characterization and antimicrobial screening of novel Schiff bases from sulfa drugs. *Int. J. Pharm. Pharm. Sci.* 6, 487–491.

14. Elander, R. P. **(2003)** Industrial production of β-lactam antibiotics. *Appl. Microbiol. Biotechnol.* 61, 385–392.

15. Townsend, C. A. **(2016)** Convergent biosynthetic pathways to β-lactam antibiotics. *Curr. Opin. Chem. Biol.* 35, 97–108.

16. Pori, M. *et al.* **(2013)** Azetidinone-retinoid hybrids: Synthesis and differentiative effects. *Eur. J. Med. Chem.* 70, 857–863.

17. Arya, N. *et al.* **(2014)** The chemistry and biological potential of azetidine-2-ones. *Eur. J. Med. Chem.* 74, 619–656.

18. Mehta, P. D., Sengar, N. P. S. & Pathak, A. K. **(2010)** 2-Azetidinone - A new profile of various pharmacological activities. *Eur. J. Med. Chem.* 45, 5541–5560.

19. Vashi, K. & Naik, H. B. **(2004)** Synthesis of Novel Schiff Base and Azetidinone Derivatives and their Antibacterial Activity. *E-Journal Chem.* 1, 272–275.

20. Staudinger, H. **(1907)** Zur Kenntniss der Ketene. Diphenylketen. *Justus Liebigs Ann. Chem.* 356, 51–123.

21. Malig, T. C., Yu, D. & Hein, J. E. **(2018)** A Revised Mechanism for the Kinugasa Reaction. *J. Am. Chem. Soc.* 140, 9167–9173.

22. Jasiński, R. **(2015)** A new mechanistic insight on β-lactam systems formation from 5-nitroisoxazolidines. *RSC Adv.* 5, 50070–50072.

23. Bhat, I. K., Mishra, S. K., James, J. P. & Shastry, C. S. **(2011)** Antimicrobial studies of synthesized azetidinone derivatives from sulfamethoxazole moiety. *J Chem Pharm Res* 3, 114–118.

24. Guanti, G. *et al.* **(1998)** A new class of cis-monobactam derivatives bearing a sulfamoyloxymethyl or an N-alkylsulfamoyloxymethyl group at position 4: synthesis and antibacterial activity. *Farm.* 53, 173–180.

25. Saeedi, M. *et al.* **(2014)** Synthesis and biological investigation of some novel sulfonamide and amide derivatives containing coumarin moieties. *Iran. J. Pharm. Res.* 13, 881–892.

26. Göçer, H., Akincioğlu, A., Öztaşkin, N., Göksu, S. & Gülçin, I. **(2013)** Synthesis, antioxidant, and antiacetylcholinesterase activities of sulfonamide derivatives of dopamine-related compounds. *Arch. Pharm. (Weinheim).* 346, 783–792.

27. Behbehani, G. R., Hossaini Sadr, M., Nabipur, H. & Barzegar, L. **(2013)** A comparative study on the interaction of sulfonamide and nanosulfonamide with human serum albumin. *J. Chem.* 2013,.

28. Husnain, S. *et al.* **(2016)** Evaluation of in vitro antioxidant and thrombolytic studies of some N -acetamide derivatives. 8, 424–431.

29. Jasiński, R. **(2016)** A reexamination of the molecular mechanism of the Diels–Alder reaction between tetrafluoroethene and cyclopentadiene. *React. Kinet. Mech. Catal.* 119, 49–57.

30. Jasiński, R. **(2021)** On the question of stepwise [4+2] cycloaddition reactions and their stereochemical aspects. *Symmetry (Basel).* 13, 1911.