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Research Article

NOVEL SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL SCHIFF BASE DERIVED QUINOLIN AND THEIR β-LACTUM DERIVETIVES

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ABSTRACT

Objective: The unique chemotherapeutic properties of β–lactam antibiotics continue to attract the attention of the chemical community. One important application of the β-lactam moiety in synthesis involves the production of natural and non-natural α-amino acids. Methods: A study on the structural activity and a series of oxa-azetidin-1-yl quinoline 3-carbaldehide starting from 4-Amino acetanilide **1** on condensation with aromatic aldehyde (2a-j) yield N-(4-(4/-methoxybenzylideneamino) phenyl) acetamide **(3a-J),** which on reaction with dimethyl formamide in presence of $POCl_3$ formed 6-(4/- methoxybenzylideneamino) 2-chloroquinoline-3-carbaldehyde (**4a-J)**. On the treatment of there Schiff base derived quinoline with acetyl chloride and triethyl amine in DMF furnish the respective 2-chloro-6-(2/-(4/-methoxyphenyl) 4- oxaazetidin-1-yl) quinoline-3-carbaldehyde (**5a-J**).

Results: The structure of the compounds has been confirmed by IR, ^{1}HNMR and Elemental analysis.

Conclusion: These newly synthesized compounds has been screened against bacteria and fungus.

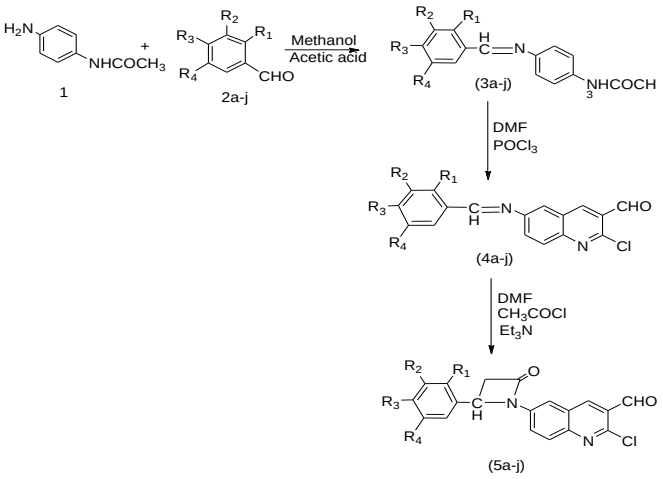
Keywords: Azetidinone, Schiff Base, 2-chloroquinoline, Biological Evaluation.

INTRODUCTION

Azetidin-2-one (β-lactam) a four membered cyclic amide is a partial structure of many biologically important antibiotics. The unique structural and chemotherapeutic properties of the β–lactam antibiotics continue to attract the attention of the synthetic community as they present a variety of synthetic challenges, containing antibiotic including carbapenems, rendering them ineffective[1]. After discover the β-lactum four membered ring (2-azetidinone system) is a unit of antibiotics of penicillin and cephalosporin type the most widely employed family of antimicrobial agents to date accounting for 50% of the world's total antibiotics market[2,3]. In the mid 1970s, a new class of β-lactum antibiotics characterized by a single monocyclic structure called monobactams, were discovered and some of them, of nature origin, have already been isolated and identified[4]. It has been use as chiral building blocks in organic synthesis and also used as synthons in the preparation of various heterocyclic compounds of biological significance. Because of this general trend of β-lactum use, the search for clinically useful β-lactum that are antibiotics or have medically important properties motivated to synthetic organic and medicinal chemist to design new functionalized 2-azetidinones, apart from there clinical use as antibacterial agents[5]. Number of N-substituted and unsubstituted β-lactum derivatives have been reported to show antimalarial activity[6], anti-Bacillus agent[7], anti-MRSA[8], Antitubercular activity[9], Anti-inflammatory activity[10] and anticancer activity[11], anit-oxidant activity [12]. Recently discovered antitumor monocyclic and bicyclic β-lactum system[13] in general are in a good agreement with the phenomenon of azetidin-2-one pharmacophore inexhaustible pharmacological potential due to specific ability of its numerous derivatives to inhibit not only bacterial trans peptidase but also mammalian serin and cystein proteases. β-lactum compound really are "evergreen" bioactive molecule[14]. 2-Azetidinone is antibiotics are the most commonly prescribed medicines for treating bacterial diseases. Among this monocyclic- β-lactum is a kind of new compound which is not only structurally simple for easy of synthesis, but also has a special feature in the biological activity.

Schiff base possess antituberior and anticancer activity[15]. Heterocyclic compounds containing quinoline nuclei have been shown to possess significant pharmacological activity such as anti-inflammatory, antifungal, antidepressant and anti-HIV infection[16]. Chloroquinoline has been evaluated for their blood schizontocidal activity and reversal of chloroquine resistance activity[17], antimalarial and antiviral activity[18].

Reaction Scheme



MATERIAL AND METHOD

All the recorded melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded with FT-IR perkin-Elmer Rx-I instrument using nujol. ^{1}H NMR spectra were recorded on 400 MHz. Bruker AC-300 F instrument with using TMS as internal standard and deuterio-Chloroform as solvent and Mass spectra were recorded on VG.70 S instrument at SAIF Chandigarh. The purity of compound was checked by TLC using silica gel G.

General Method for Preparation of Schiff bases (3a-j)

Preparation of *N*-(4-(4/-methoxybenzylideneamino) phenyl) acetamide 3a

The mixture of 4-amine acetanilide 1 (0.1m) and 4-methaoxy benzaldehyde (0.1m) was dissolved in methanol (30 mL), these solution was acidified by adding glacial acetic acid (2-3 drops) and reflux for 5h. The excess of solvent was removed under reduced pressure. The resulting compound **3a** was washed with solvent ether, dried and crystallized from ethanol.

Comp. No. 3a. Yield 85%, m.p. 153^0 C; IR (KBr) cm^{-1}: 3300-3200 (N-H str.), 1690 (C=O amide), 1600 (CH=N str.), 3110 ($COCH_3$). ^{1}H NMR ($CDCl_3$): δ : 2.1 (s, 3H, $COCH_3$), 3.8 (s, 3H, OCH_3), 6.9-7.8 (m, 8H, Ar-H) ppm. MS (m/z) 268 (M^+). Anal. Calcd. for $C_{16}H_{16}O_2N_2$: C, 71.39; H, 6.25; N, 10.10. Found: C, 71.62; H, 6.01; N, 10.44.

Similarly below the other compounds **(3b-j)** were synthesized (there analytical data are recorded in **table-II**)

Comp. No. 3c. *N*-(4-(4/-hydroxybenzylideneamino) phenyl) acetamide

Yield, 83%, m.p. 209^{0}c; IR (KBr) cm^{-1}: 3360-3230 (N-H str.), 3250-3140 (OH), 1665 (C=O amide), 1632 (CH=N str.), 3125 ($COCH_3$). ^{1}H NMR: δ: 2.3 (s, 3H, $COCH_3$), 10.6 (s, 1H, OH), 6.9-7.9 (m, 8H Ar-H) ppm. MS (m/z) 254 (M^+). Anal.Calcd. for $C_{15}H_{14}O_2N_2$: C, 70.42; H, 5.71; N,11.57. Found: C, 70.85; H, 5.55; N, 11.02.

Comp. No. 3d. *N*-(4-(dimethylamino) benzylideneamino) phenyl) acetamide

Yield 84%, m.p. 206^{0}c; IR (KBr) cm^{-1}: 3360-3230 (N-H str.), 2920-2850 (-CH_3), 1632 (C=O amide), 1625 (CH=N str.), 3145 ($COCH_3$). ^{1}H NMR : δ: 2.2 (s, 3H, $COCH_3$), 2.4 (s, 3H, CH_3), 6.8-8.1 (m, 8H, Ar-H) ppm. MS (m/z) 281 (M^+). Anal. Calcd. for $C_{17}H_{19}ON_2$: C, 72.79; H, 6.58; N,14.59. Found: C, 72.57; H, 6.81; N, 14.94.

Comp. No. 3e. *N*-(4-(2-chlorobenzylideneamino) phenyl) acetamide

Yield 77%, m.p. 109^{0}c; IR (KBr) cm^{-1}: 3230-3140 (N-H str.), 1675 (C=O amide), 1632 (CH=N str.), 3132 ($COCH_3$). ^{1}H NMR : δ: 2.3 (s, 3H, $COCH_3$), 6.7-8.3 (m, 8H, Ar-H) ppm. MS (m/z) 272 (M^+). Anal.Calcd. for $C_{15}H_{13}ON_2Cl$: C, 66.42; H,4.53; N,10.63. Found: C, 66.06; H, 4.80; N, 10.27.

Comp. No. 3f. *N*-(4-(3-nitrobenzylideneamino) phenyl) acetamide

Yield 84%, m.p. 173 ^{0}c; IR (KBr) cm^{-1}: 3330-3168 (NH), 1665 (C=O amide), 1520-1350-(NO_2), 1642 (CH=N), 3152 ($COCH_3$). ^{1}H NMR :(δ) 2.5 (s, 3H, $COCH_3$), 6.8-8.3 (m, 8H, Ar-H) ppm. MS (m/z) 283 (M^+). Anal.Calcd. for $C_{15}H_{13}O_3N_3$: C, 63.44; H,4.39;N,14.50. Found: C, 63.60; H, 4.63; N, 14.83.

Comp. No. 3h. *N*-(4-(benzylideneamino) phenyl) acetamide

Yield 81%, m.p. 130 ^{0}c; IR (KBr) cm^{-1}: 3232 ($COCH_3$), 1665 (C=O amide), 1662 (CH=N str.). ^{1}H NMR: δ: 2.3 (s, 3H, $COCH_3$), 6.8-8.3 (m, 9H, Ar-H) ppm. MS (m/z) 272 (M^+). Anal.Calcd. for $C_{15}H_{14}ON_2$: C, 74.48; H, 5.60; N,11.31. Found: C, 74.61; H, 5.92; N, 11.76.

Comp. No. 3i. *N*-(4-(4-hydroxy-3-methylbenzylideneamino) phenyl) acetamide

Yield 83%, m.p. 221^{0}c; IR (KBr) cm^{-1}: 3354-3250 (N-H str.), 3250-3140 (OH str.), 2932-2843 (-CH_3), 1685 (C=O amide), 1635 (CH=N str.), 3185 ($COCH_3$). ^{1}H NMR : δ: 2.3 (s, 3H, CH_3), 2.7 (s, 3H, $COCH_3$), 11.4 (s, 1H, OH), 6.6-7.9 (m,7H, Ar-H) ppm. MS (m/z) 268 (M^+). Anal.Calcd. for $C_{16}H_{16}O_2N_2$: C,71.39; H, 6.55; N, 10.60. Found: C, 71.62; H, 6.01; N, 10.44.

Comp. No. 3j. *N*-(4-(3, 4, 5-trimethoxybenzylideneamino) phenyl) acetamide

Yield 79%, m.p. 130 ^{0}C; IR (KBr) cm^{-1}: 3244-3143 (N-H str.), 2955-2840 (CH_3), 1655 (C=O amide), 1635 (CH=N str.), 3085 ($COCH_3$). ^{1}H NMR : δ: 2.5 (s, 3H, $COCH_3$), 3.54 (s, 9H, OCH_3), 6.8-7.9 (m 6 Ar-H) ppm. MS (m/z) 328 (M^+). Anal.Calcd. for $C_{18}H_{20}O_4N_2$: C, 65.61; H, 6.31; N, 8.31. Found: C, 65.84; H, 6.14; N, 8.53.

General Method for Preparation of substituted 2-chloroquinoline-3-carbaldehyde (4a-j)

Preparation of 6-(4-methoxybenzylideneamino) 2-chloroquinoline-3-carbaldehyde 4a

To the ice-cold dimethyl formamide (0.3 m), phosphoric chloride (0.7 m) was added drop wise with constant stirring and after one hour in this mixture added *N*-(4-(4-methoxybenzylideneamino) phenyl) acetamide (0.1 m) **3a** was added slowly with constant stirring. The reaction mixture was heated 17 h at 90^{0}C. The reaction was monitor by TLC, after completion the reaction mixture poured in ice cold water. and crystallized from ethyl acetated and methanol (1:1).

Comp. No. 4a. Yield 75%, m.p. 234 ^{0}C. IR (KBr) cm^{-1}: 2745 (CH str. of CHO), 1740 (C=O) CHO, 1665 (OCH_3), 1635 (CH=N str.), 720 (C-Cl). ^{1}H NMR: δ: 3.8 (s, 3H, OCH_3), 6.8-7.7 (m, 8H, Ar-H), 9.7 (s, 1H, CHO) ppm. MS (m/z) 324 (M^+). Anal.Calcd. for $C_{18}H_{13}O_2N_2Cl$: C, 66.30; H, 4.27; N, 8.47; Cl, 10.48. Found: C, 66.57; H, 4.03; N, 8.63; Cl, 10.92.

Similarly other compounds **(4b-j)** were synthesized (there analytical data are recorded in table-**III**)

Comp. No. 4c. 6-(4-hydroxybenzylideneamino) -2-chloroquinoline-3-carbaldehyde

Yield 73%, m.p.184 ^{0}C; IR (KBr) cm^{-1}: 3230-3140 (OH str.), 2765 (CH str. of CHO), 1710 (C=O) CHO, 1626 (CH=N str.), 764 (C-Cl). ^{1}H NMR: δ: 3.7 (s, 3H, OCH_3), 6.52-8.43 (m, 8H, Ar-H), 9.9 (s, 1H, CHO) 10.8 (s, 1H, OH), ppm. MS (m/z) 310 (M^+). Anal.Calcd. for $C_{17}H_{11}O_2N_2Cl$: C, 65.25; H, 3.31; N, 9.77; Cl, 11.69. Found: C, 65.71; H, 3.57; N, 9.02; Cl, 11.41.

Comp. No. 4d. 6-(4-(dimethylamino) benzylideneamino) -2-chloroquinoline-3-carbaldehyde

Yield 74%, m.p. 240 ^{0}C; IR (KBr) cm^{-1}: 2932-2843 (CH_3 str.), 2730 (CH str. of CHO), 1735 (C=O) CHO, 1646 (CH=N str.), 735 (C-Cl). ^{1}H NMR: δ: 2.5 (s, 6H, CH_3), 6.73-8.63 (m, 8H, Ar-H), 9.7 (s, 1H, CHO) ppm. MS (m/z) 338 (M^+). Anal.Calcd. for $C_{19}H_{16}ON_3Cl$: C, 67.32; H, 4.49, N, 12.20; Cl, 10.17. Found: C, 67.56; H, 4.77; N, 12.44; Cl, 10.50.

Comp. No. 4e. 6-(2-chlorobenzylideneamino) -2-chloroquinoline-3-carbaldehyde

Yield 67%, m.p.122 ^{0}C. IR (KBr) cm^{-1}: 2740 (CH str. of CHO), 1735 (C=O) CHO, 1663 (CH=N str.), 769 (C-Cl).^{1}H NMR : δ: 6.4-8.7 (m, 8H, Ar-H), 10.2 (s, 1H, CHO) ppm. MS (m/z) 329 (M^+). Anal.Calcd. for $C_{17}H_{10}ON_2Cl_2$: C, 62.37; H, 3.40; N, 8.28; Cl, 21.20. Found: C, 62.03; H, 3.06; N, 8.51; Cl, 21.54.

Comp. No. 4f. (6-(3-nitrobenzylideneamino) -2-chloroquinoline-3-carbaldehyde

Yield 74%, m.p. 215 ^{0}C; IR (KBr) cm^{-1}: 2755 (CH str. of CHO), 1735 (C=O) CHO, 1663 (CH=N str.), 1510-1350 (-NO_2 str.), 769 (C-Cl). ^{1}H NMR: δ: 6.4-8.7 (m, 8H, Ar-H), 10.2 (s,1H, CHO) ppm. MS (m/z) 339 (M^+). Anal.Calcd. for $C_{17}H_{10}O_3N_3Cl$: C, 60.38; H, 2.43; N, 12.15; Cl, 10.67. Found: C, 60.10; H, 2.97; N, 12.37; Cl, 10.44.

Comp. No. 4h. 6-(benzylideneamino) -2-chloroquinoline-3-carbaldehyde

Yield 79%, m.p. 229 ^{0}C. IR (KBr) cm^{-1}: 2735 (CH str. of CHO), 1775 (C=O) CHO, 1644 (CH=N str.), 756 (C-Cl). ^{1}H NMR: δ: 6.8-8.9 (m, 9H. Ar-H), 9.7 (s, 1H, CHO) ppm. MS (m/z) 295 (M^+). Anal. Calcd. for

$C_{18}H_{13}O_2N_2Cl$: C, 62.27; H, 3.63 N, 8.28; Cl, 21.30. Found: C, 62.03; H, 3.06; N, 8.51; Cl, 21.54.

Comp. No. 4i. 6-(4-hydroxy-3-methylbenzylideneamino)-2-chloroquinoline-3-carbaldehyde

Yield 73 %, ,m.p. 128 ^{0}C; IR (KBr) cm^{-1}: 3190-3175 (OH str.), 2985-2885 (CH_3 str.), 2735 (CH str. of CHO), 1730 (C=O) CHO, 1663 (CH=N str.), 769 (C-Cl). ^{1}H NMR: δ: 2.5 (s, 3H, CH_3), 11.3 (s, 1H, OH), 6.4-8.7 (m, 7H, Ar-H), 10.2 (s, 1H, CHO) ppm. MS (m/z) 324 (M^+). Anal.Calcd. for $C_{18}H_{13}O_2N_2Cl$: C, 66.30 H, 4.27; N, 8.47; Cl, 10.48.Found: C, 66.57; H, 4.03; N, 8.63; Cl, 10.92.

Comp. No. 4j. 6-(3,4,5-trimethoxybenzylideneamino)-2-chloroquinoline-3-carbaldehyde.

Yield 79 %, m.p. 221^{0}C; IR (KBr) cm^{-1}: 2720 (CH str. of CHO), 1765 (C=O) CHO, 1625 (CH=N str.), 745 (C-Cl). ^{1}H NMR: δ: 3.8 (s, 3H, OCH_3), 7.1-8.2 (m, 6H, Ar-H), 9.8 (s, 1H, CHO) ppm. MS (m/z) 385 (M^+). Anal.Calcd. for $C_{21}H_{18}O_4NCl$: C, 62.11; H, 4.23; N, 7.81; Cl, 9.47. Found: C, 62.42; H, 4.45; N, 7.21; Cl, 9.21.

General Method for Preparation of β-lactam (5a-j)

Preparation of 2-chloro-6-(2-(4-methoxyphenyl)4-oxaazetidin-1-yl) quinoline-3-carbaldehyde 5a

To 6-(4-methoxybenzylideneamino) 2-chloroquinoline-3-carbaldehyde **4a** (0.01m) dissolved in DMF (8 ml), was added acetyl chloride (0.01m) and triethyl amine (0.01 m). This reaction mixture was refluxed for 5 h. The completion of reaction mixture was monitored by TLC. The reaction mixture was cooled to room temperature which was then diluted with dioxane (10mL) and poured in ice cold water to get compound **5a**, crystallized from ethanol.

Comp. No. 5a. Yield 68%, m.p. 160 ^{0}C; IR (KBr) cm^{-1}: 2755 (CH str. of CHO), 1760 (C=O) monocyclic β-lactam, 1720 (C=O) CHO, 720 (C-Cl). ^{1}H NMR: δ: 3.8 (s, 3H, OCH_3), 3.66-3.68 (d, 1H, CH_2-CH), 4.82-4.84 (t, 2H, CH_2-CH), 6.8-7.83 (m, 8H, Ar-H), 9.6 (s, 1H, CHO)ppm. MS (m/z): 366.33, 337.26(M^+), 308.26(M+1), 292.24(M+2), 162.63, 130.43(M+2), 128.78, 101.32(M+2), 91.72. Anal. Calcd for $C_{20}H_{15}O_3N_2Cl$: C, 65.20; H, 4.62; N, 7.87; Cl, 9.32. Found: C, 65.49; H, 4.12; N, 7.64; Cl, 9.67.

The other entire compounds **(5b-j)** were prepared by similar procedure. (There analytical data are recorded in table-**IV**)

Comp. No. 5c. 2-chloro-6-(2-(4-hydroxylphynyl)-4-oxoazetidin-1-yl) quinoline-3-carbaldehyde

Yield 65%, m.p. 196 ^{0}C; IR (KBr) cm^{-1}: 3265-3140 (OH str.), 2725 (CH str. of CHO), 1735 (C=O) monocyclic β-lactam, 1710 (C=O) CHO, 745 (C-Cl). ^{1}H NMR: δ: 4.12-4.13 (d, 1H, CH_2-CH), 4.82-4.85 (t, 2H, CH_2-CH), 6.72-8.83 (m, 8H, Ar-H), 10.8 (s, 1H, OH), 9.6 (s, 1H, CHO) ppm. MS (m/z): 352.77. Anal.Calcd for $C_{19}H_{13}O_3N_2Cl$: C, 64.26 ; H,3.31; N,7.67; Cl,10.43. Found: C, 64.69; H, 3.71; N, 7.94; Cl, 10.05.

Comp. No. 5d. 2-chloro-6-(2-(4-dimethylamino))-4-oxoazetidin-1-yl) quinoline-3-carbaldehyde

Yield 64%, m.p. 145 ^{0}C; IR (KBr) cm^{-1}: 3032-2943 (CH_3 str.), 2765 (CH str. of CHO), 1720 (C=O) monocyclic β-lactam, 1695 (C=O) CHO, 725 (C-Cl). ^{1}H NMR: δ: 2.45 (s, 6H, CH_3), 4.01-4.02 (d, 1H, CH_2-CH), 5.10-5.12 (t, 2H, CH_2-CH), 6.8-7.95 (m 8H Ar-H), 9.75 s 1H (CHO) ppm. MS (m/z): 379.84. Anal.Calcd for $C_{21}H_{18}O_2N_3Cl$: C, 66.78; H, 4.53; N, 11.45 Cl, 9.01. Found: C, 66.40; H, 4.74; N, 11.06; Cl, 9.33.

Comp. No. 5e. 2-chloro-6-(2-(2-chlorophenyl) -4-oxoazetidin-1-yl) quinoline-3-carbaldehyde

Yield 67%, m.p. 242^{0}C; IR (KBr) cm^{-1}: 2755 (CH str. of CHO), 1735 (C=O) monocyclic β-lactam, 1695 (C=O) CHO, 775 (C-Cl). ^{1}H NMR: δ: 3.63-364 (d, 1H, CH_2-CH), 4.72-4.73 (t, 2H, CH_2-CH), 6.9-8.1 (m, 8H, Ar-H), 9.8 s 1H (CHO) ppm. MS (m/z): 371.22. Anal.Calcd for $C_{19}H_{12}O_2N_2Cl_2$: C, 61.62; H, 3.70; N, 7.78; Cl, 19.37. Found: C, 61.47; H, 3.26; N, 7.55; Cl, 19.10.

Comp. No. 5f. 2-chloro-6-(2-(3-nitrophenyl) -4-oxoazetidin-1-yl) quinoline-3-carbaldehyde

Yield 64%, m.p. 157 ^{0}C; IR (KBr) cm^{-1}: 2745 (CH str. of CHO), 1740 (C=O) monocyclic β-lactam, 1705 (C=O) CHO, 1535-1380 (NO_2 str.), 755 (C-Cl). ^{1}H NMR: δ: 3.82-3.83 (d, 1H, CH_2-CH), 4.82-4.86 (t, 2H, CH_2-CH), 6.9-8.4 (m, 8H, Ar-H), 9.6 (s, 1H, CHO) ppm. MS (m/z): 381.77. Anal.Calcd for $C_{19}H_{12}O_4N_3Cl$: C, 59.41; H, 3.53; N, 11.46 Cl, 9.56. Found: C, 59.78; H, 3.17; N, 11.01; Cl, 9.29.

Comp. No. 5h. 2-chloro-6-(2-oxo-4-phenylazetidin-1-yl) quinoline-3-carbaldehyde

Yield 71%, m.p. 210 ^{0}C; IR (KBr) cm^{-1}: 2750 (CH str. of CHO), 1755 (C=O) monocyclic β-lactam, 1725 (C=O) CHO, 735 (C-Cl). ^{1}H NMR: δ: 3.43-3.44 (d, 1H, CH_2-CH), 4.73-4.75 (t, 2H, CH_2-CH), 6.9-8.0 (m, 9H, Ar-H), 9.8 (s, 1H, CHO) ppm. MS (m/z): 366.77. Anal.Calcd for $C_{19}H_{13}O_2N_2Cl$: C, 67.11; H, 3.43; N, 8.81; Cl,10.23. Found: C, 67.76; H, 3.89; N, 8.32; Cl, 10.53.

Comp. No. 5i. 2-chloro-6-(2-(4-hydroxymethlphynyl)-4-oxoazetidin-1-yl) quinoline-3- carbaldehyde

Yield 73%, m.p. 152 ^{0}C; IR (KBr) cm^{-1}: 3290-3165 (OH str.), 2885-2755 (CH_3 str.), 2730 (CH str. of CHO), 1745 (C=O) monocyclic β-lactam, 1715 (C=O) CHO, 750 (C-Cl). ^{1}H NMR: δ: 2.32 s CH_3, 11.3 (OH), 4.12-4.13 (d, 1H, CH_2-CH), 4.82-4.85 (t, 2H, CH_2-CH), 6.9-8.2 (m, 7H, Ar-H), 9.7 s 1H (CHO) ppm. MS (m/z): 366.8. Anal.Calcd for $C_{20}H_{15}O_3N_2Cl$: C, 65.86; H, 4.60; N, 7.42; Cl, 9.32. Found: C, 65.49; H, 4.12; N, 7.64; Cl, 9.67.

Comp. No. 5j. 2-chloro-6-(2-(3,4,5-trimethoxyphenyl)-4-oxoazetidin -1-yl) quinoline-3- carbaldehyde

Yield 69%, m.p. 205^{0}C; IR (KBr) cm^{-1}: 2745 (CH st CHO), 1765 (C=0) monocyclic β-lactam, 1735 (C=0) CHO, 745 (C-Cl). ^{1}HNMR: (δ) 3.8 s 9H (OCH_3), 3.96-3.97 (d, 1H, CH_2-CH), 4.71-7.72 (t, 2H, CH_2-CH), 6.8-8.1 (m, 6H, Ar-H), 9.9 (s, 1H, CHO) ppm. MS (m/z): 411.82. Anal.Calcd for $C_{23}H_{20}O_3NCl$: C, 61.21; H, 4.13; N, 6.81; Cl, 8.65. Found: C, 61.90; H, 4.49; N, 6.56; Cl, 8.31.

Biological Assay

Antimicrobial activity

All the compounds (**4a-j** and **5a-j**) were evaluated *in-vitro* for antifungal and antibacterial activity by using standard cup plate diffusion method[19] against *bacteria like Escherischia.coli*, *Staphylococcus aureus and* fungi like *Aspergillus niger*. All the compounds along with standard for bacteria Erythromycin and fungi Glesofloxzine were used at a concentration of 100ug/ml in DMF as a solvent control and nutrient agar were used as culture method. After incubation of 24h for bacteria and 48 h for fungus at 370c, the zone of inhibition was measured in mm.

Structural activity relationship:

The biological result **(Table-I)** for compound **4a-j** and **5a-j** showed that the substitution pattern on 4-possition of 2-Chloroquinoline Schiff base and oxa-azetidin-1-yl quinoline- 3-carbaldehyde moiety appear to be vital for better activity.

The synthesized compound **4a-j** exhibit promising activity, in this compounds 4a-c and **4i-j** shows moderate to good activity against E.Coli, same in case of **4a**, **4d-e** and **4h** was observed against S.Aureus. While against A. Niger compounds like **4c** and **4g-j** shows moderate activity.

Cyclization of compound **4a-j** in there corresponding azetidinone **5a-j** enhanced the antimicrobial activity. Compounds **5e** and **5i** are less active than corresponding compounds like **5a-d**, **5-h** and **5j**. The compounds **5a**, **5d** and **5j** shows maximum zone of inhibition compare with the 5b-c and 5e-i in S. Aureus. Similarly for fungi stain compounds **5c**, **5g** and **5j** shows higher activity than **5a-b**, **5d-f** and **5h-i** in A. Niger. All these results was compare against standard drugs like Erythromycin for bacteria and Glesofloxzine for fungi. Besides this, the conversion of compounds **4a-j** into respective oxa-azetidine-yl quinoline 3-carbaldehyde (**5a-j**) has remarkable changes on there antibacterial and antifungal activity. It is clear from the results that azetidinones possessing maximum biological activity than Schiff bases quinoline.

It is important to note from the biological data that compound 4b, 4e, 4i and 5c-d, 5g having chloro, methyl, hydroxy and dimethyl amine group as a substituent shows maximum antibacterial and

antifungal activity. Compound **4b** and **5c** has better activity against *E. coli* but in *S. aureus* 4b is high activity than 5c having hydroxy group and 5d is a better activity than 4e having *n-dimethyl amine* substitution. Interesting the other compounds is displayed better significant activity against the bacteria and fungi with the help of functionalized substituted phenyl ring.

Table I: Antibacterial and antifungal activity of the synthesized compounds.

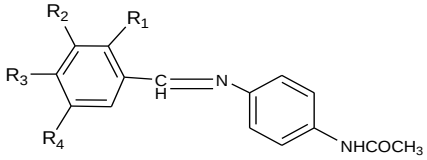
Compound	Bacterial growth inhibition (diameter in mm)		Fungal growth inhibition (diameter in mm)
	Escherichia coli	*Staphylococcus aureus*	*Aspergillus niger*
4a	16	18	13
4b	18	16	12
4c	16	16	14
4d	15	17	13
4e	14	19	10
4f	15	10	9
4g	15	15	14
4h	14	17	14
4i	16	16	15
4j	16	16	14
5a	18	20	16
5b	18	19	17
5c	19	18	19
5d	18	21	16
5e	16	19	17
5f	18	17	16
5g	17	19	20
5h	18	17	16
5i	16	18	18
5j	18	20	19
Erythromycin	20	24	-
Glesofloxzine	-	-	22

*100ug/ml – Drug concentration.

RESULT AND DISCUSSION

The chemical synthesis initiated with reaction of 4-Amine acetanilide **1** reacts with aromatic aldehyde **(2a-j)** yield *N*-(4-(4-methoxybenzylideneamino) phenyl) acetamide **3a**. The reaction of Schiff base acetamide **(3a-j)** was carried out at 80-90 ^{0}C for 17 h, using the Vilsmeier Haack reagent derived from phosphorus oxychloride-dimethyl formamide in *situ.* The analytical spectroscopic data confirmed the product as 6-(4-methoxybenzylideneamino) 2-chloroquinoline-3-carbaldehyde **4a**. The Vilsmeier Haack reagents are usually applied for the formulation of aromatic and heteroaromatic compounds. These are the chloromethyleniminium species responsible for the formulation. As in our reaction the chloromethyleniminium species obtained in *situ* from phosphorus oxychloride-Dimethyl formamide reacts with the active methyl group of *N*-(4-(4-methoxybenzylideneamino) phenyl) acetamide **3a,** these reaction yields product 2-chloroquinoline **4a**.

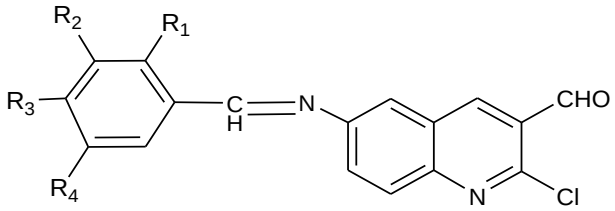
The reaction yielded a mixture of product 2-chloroquinoline **4a.** On the treatment of these Schiff base derived quinoline with acetyl chloride and triethyl amine in DMF furnish the respective 2-chloro-6-(2-(4-methoxyphenyl) 4- oxaazetidin-1-yl) quinoline-3-carbaldehyde (**5a-J) (Table-IV)**. The structures of all the newly β-lactum derivatives were confirmed on the basis of spectral and analytical data.



(3a-j)

Table II: Characterization data of compound 3a-j

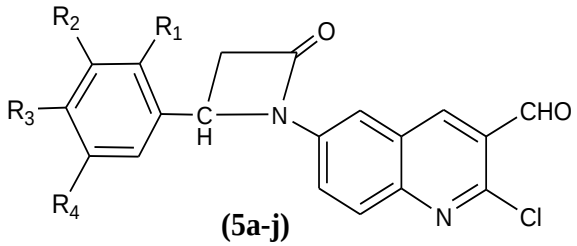
Product	R_1	R_2	R_3	R_4	Mol. Formula	M.p (^{0}C)	Yield %	% found(Calcd) C	H	N
3a	H	H	*p*-OCH_3	H	$C_{16}H_{16}O_2N_2$	153	85	71.62 (71.39)	71.62 (6.25)	71.62 (10.10)
3b	H	H	*H*	H	$C_{16}H_{16}O_2N_2$	61	78	71.62 (71.39)	6.01 (6.25)	10.44 (10.10)
3c	H	H	*P*-OH	H	$C_{15}H_{14}O_2N_2$	209	83	70.85 (70.42)	5.55 (5.71)	11.02 (11.57)
3d	H	H	*p*-$N(CH_3)_2$	H	$C_{17}H_{19}ON_2$	206	84	72.57 (72.79)	6.81 (6.58)	14.94 (14.59)
3e	*o*-Cl	H	H	H	$C_{15}H_{13}ON_2Cl$	109	77	66.06 (66.42)	4.80 (4.53)	10.27 (10.63)
3f	H	*m*-NO_2	H	H	$C_{15}H_{13}O_3N_3$	173	84	63.60 (63.44)	4.63 (4.39)	14.83 (14.50)
3g	H	m-Cl	H	H	$C_{15}H_{13}ON_2Cl$	143	79	66.06 (66.42)	4.80 (4.53)	10.27 (10.63)
3h	H	H	H	H	$C_{15}H_{14}ON_2$	130	81	74.61 (74.48)	5.92 (5.60)	11.76 (11.31)
3i	H	*m*-CH_3	*p*-OH	H	$C_{16}H_{16}O_2N_2$	221	83	71.62 (71.39)	6.01 (6.55)	10.44 (10.60)
3j	H	*m*-OCH_3	*m*- OCH_3	*m*- OCH_3	$C_{18}H_{20}O_4N_2$	130	79	65.84 (65.61)	6.14 (6.31)	8.53 (8.31)



(4a-j)

Table III: Characterization data of compound 4a-j

Product	R_1	R_2	R_3	R_4	Mol. Formula	M.p (^{0}C)	Yield %	% found(Calcd) C	H	N	Cl
4a	H	H	*p*-OCH_3	H	$C_{18}H_{13}O_2N_2Cl$	234	75	66.57 (66.30)	4.03 (4.27)	8.63 (8.47)	10.92 (10.48)
4b	H	H	*H*	H	$C_{18}H_{13}O_2N_2Cl$	232	78	66.57 (66.20)	4.03 (4.37)	8.63 (8.47)	10.92 (10.68)
4c	H	H	*P*-OH	H	$C_{17}H_{11}O_2N_2Cl$	184	73	65.71 (65.25)	3.57 (3.31)	9.02 (9.77)	11.41 (11.69)
4d	H	H	*p*-$N(CH_3)_2$	H	$C_{19}H_{16}ON_3Cl$	240	74	67.56 (67.32)	4.77 (4.49)	12.44 (12.20)	10.50 (10.17)
4e	*o*-Cl	H	H	H	$C_{17}H_{10}ON_2Cl_2$	122	67	62.03 (62.37)	3.06 (3.40)	8.51 (8.28)	21.54 (21.20)
4f	H	*m*-NO_2	H	H	$C_{17}H_{10}O_3N_3Cl$	215	74	60.10 (60.38)	2.97 (2.43)	12.37 (12.15)	10.44 (10.67)
4g	H	m-Cl	H	H	$C_{17}H_{10}ON_2Cl_2$	229	79	62.03 (62.27)	3.06 (3.63)	8.51 (8.28)	21.54 (21.30)
4h	H	H	H	H	$C_{17}H_{11}ON_2Cl$	210	71	69.28 (69.15)	3.76 (3.21)	9.50 (9.81)	12.03 (12.38)
4i	H	*m*-CH_3	*p*-OH	H	$C_{18}H_{13}O_2N_2Cl$	128	73	66.57 (66.30)	4.03 (4.27)	8.63 (8.47)	10.92 (10.48)
4j	H	*m*-OCH_3	*m*- OCH_3	*m*-OCH_3	$C_{21}H_{18}O_4NCl$	221	79	62.42 (62.11)	4.45 (4.23)	7.21 (7.81)	9.21 (9.47)



(5a-j)

Table IV: Characterization data of compound 5a-j

Product	R_1	R_2	R_3	R_4	Mol. Formula	M.p (^{0}C)	Yield %	% found(Calcd) C	H	N	Cl
4a	H	H	*p*-OCH_3	H	$C_{20}H_{15}O_3N_2Cl$	160	68	65.49 (65.20)	4.12 (4.62)	7.64 (7.87)	9.67 (9.32)
4b	H	H	*H*	H	$C_{20}H_{15}O_3N_2Cl$	209	71	65.49 (65.20)	4.12 (4.62)	7.64 (7.87)	9.67 (9.32)
4c	H	H	*P*-OH	H	$C_{19}H_{13}O_3N_2Cl$	196	65	64.69 (64.26)	3.71 (3.31)	7.94 (7.67)	10.05 (10.43)
4d	H	H	*p*-$N(CH_3)_2$	H	$C_{21}H_{18}O_2N_3Cl$	145	64	66.40 (66.78)	4.74 (4.53)	11.06 (11.45)	9.33 (9.01)
4e	*o*-Cl	H	H	H	$C_{19}H_{12}O_2N_2Cl_2$	242	67	61.47 (61.62)	3.26 (3.70)	7.55 (7.78)	19.10 (19.37)
4f	H	*m*-NO_2	H	H	$C_{19}H_{12}O_4N_3Cl$	157	64	59.78 (59.41)	3.17 (3.53)	11.01 (11.46)	9.29 (9.56)
4g	H	m-Cl	H	H	$C_{19}H_{12}O_2N_2Cl_2$	168	69	61.47 (61.62)	3.26 (3.70)	7.55 (7.78)	19.10 (19.37)
4h	H	H	H	H	$C_{19}H_{13}O_2N_2Cl$	210	71	67.76 (67.11)	3.89 (3.43)	8.32 (8.81)	10.53 (10.23)
4i	H	*m*-CH_3	*p*-OH	H	$C_{20}H_{15}O_3N_2Cl$	152	73	65.49 (65.86)	4.12 (4.60)	7.64 (7.42)	9.67 (9.32)
4j	H	*m*-OCH_3	*m*- OCH_3	*m*-OCH_3	$C_{23}H_{20}O_3NCl$	205	69	61.90 (61.21)	4.49 (4.13)	6.56 (6.81)	8.31 (8.65)

CONCLUSION

The Schiff bases were found to exhibit moderate activity against bacterial species. On the contrary all the Beta-lactam derivatives exhibited varied activity against different bacteria. The less active Schiff bases became active after cyclization, respectively. These studies may serve as a basis for the chemical modifications directed towards the development of a new class of antibacterial agents.

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