# SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL N-SUBSTITUTEDPHENYL-4-(3',4'-METHYLENEDIOXYPHENYL)-3-CHLORO-2-AZETIDINONE DERIVATIVES

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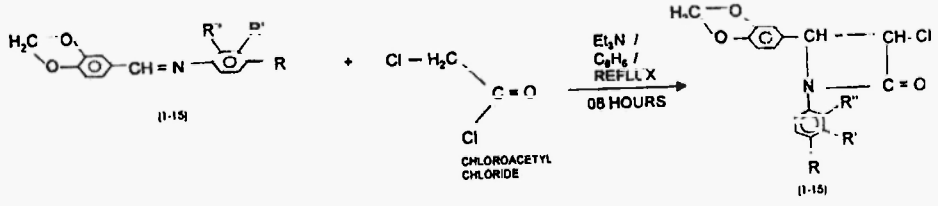
**Abstract**: Among the wide variety of heterocycles, that have been explored for developing pharmaceutical important molecules,2-azetidinones have also played an important role in medicinal chemistry .Led by this observation and to study pharmacological profile, the synthesis of novel 2-azetidinones have been undertaken .The substituted anilines when refluxed with aromatic aldehyde 3,4-methylenedioxybenzaldehyde (piperonal) yielded the Schiff's bases which on cyclocondensation with chloroacetyl chloride in presence of trimethyl amine in benzene yielded 2-azetidinones (Scheme-1). The structures of these compounds have been assessed on the basis of spectral and elemental data. The compound were also evaluated for their antimicrobial activities. The minimum inhibitory concentration (MIC) values are obtained by serial dilution method.




Scheme-1

## Introduction

Azetidinones have been known to exhibit interesting biological activities like anti-inflammatory, sedative, hypotonic and anticonvulsant[1].Azetidinones possesses antimicrobial activity[2] and found to be potential antimicrobial agent[3].Azetidinones have also shown wide range of pharmaceutical activities[4-7].Azetidinones and its corresponding derivatives have been synthesized by number of workers[8-11].The powerful antibiotic activity shown by monocyclic β- lactum of azetidinones[12,13].The azetidinones were tested against test organisms like Staphylococcus aureus, Bacillus megatherium, Bacillus subtillus, Proteus vulgaris (Table-2). Escherichia coli, Pseudomonas aeruginosa etc. Minimum Inhibitory Concentration (MIC) in μg/ml calculated by serial dilution methods[14-18].

The present study deals with the synthesis and biological evaluation of some novel N-substituted phenyl-4-(3',4'-methylenedioxyphenyl)-3-chloro-2-azetidinone derivatives. 1-(3,4-methylenedioxyphenylidine)substituted aniline were prepared by known method[19].

**Experimental: Preparation of N-chloro phenyl -4-(3',4'-methylenedioxyphenyl)-3-chloro-2-azetidinone ( IIh) :**

A mixture of 3,4-methylenedioxyphenylidine-4'-chloro aniline ( 0.01 mol ) and chloroacetyl chloride ( 0.01 mol ) in presence of 2 ml of triethylamine in 20 ml of benzene was refluxed for 08 hours .It was then cooled. The solvent

was evaporated on hot water bath, a sticky mass was then obtained .The solid mass was triturated with petroleum ether .The resulting solid was crystallized from ethanol yielded compound IIh.

MF - $C_{16}H_{11}O_3NCl_2$, MW - 336, M.P. - 148 $^0$C , Yield - 72 %

Similarly, the other derivatives of 2-azetidinones were also prepared by the same method and listed in Table-1.

**Spectral Data of Compound IIh :**

**IR (KBr): vmax** – 3288 $cm^{-1}$ ( -OH str.),2953 $cm^{-1}$(-CH str.),2677 $cm^{-1}$(-CH2 str.),1708$cm^{-1}$(C=O of β- lactum str.),1605$cm^{-1}$(C=N str.),1172$cm^{-1}$(C-N).

**NMR :** δ 2.47 ( s,2H,-$CH_2$) , 6.12 ( dd ,1H , -$CHH_A$) , 6.3( dd , 1H , -$CHH_B$) , 7-8.5 ( m, 5H , Ar-H ).

**Table-1**: Physical characterisation data of synthesised compounds.

| S.No. | Compound | Mol.Formula | Mol.Wt. | M.P.( $^0$C ) | % Yield | % N Found (Cal.) | %Cl (Cal.) |
|---|---|---|---|---|---|---|---|
| 01 | IIa | $C_{16}H_{12}O_3NCl$ | 301.5 | 276 | 70 | 4.69(4.64) | 11.77 |
| 02 | IIb | $C_{16}H_{11}O_5N_2Cl$ | 346.5 | 132 | 68 | 8.09(8.08) | 10.24 |
| 03 | IIc | $C_{16}H_{11}O_5N_2Cl$ | 346.5 | 98 | 77 | 8.10(8.08) | 10.24 |
| 04 | IId | $C_{16}H_{11}O_5N_2Cl$ | 346.5 | 42 | 65 | 8.09(8.08) | 10.24 |
| 05 | IIe | $C_{17}H_{14}O_3NCl$ | 315.5 | 107 | 78 | 4.48(4.44) | 11.25 |
| 06 | IIf | $C_{17}H_{14}O_3NCl$ | 315.5 | 89 | 70 | 4.47(4.44) | 11.25 |
| 07 | IIg | $C_{17}H_{14}O_3NCl$ | 315.5 | 67 | 72 | 4.49(4.44) | 11.25 |
| 08 | IIh | $C_{16}H_{11}O_3NCl_2$ | 336 | 148 | 70 | 4.19(4.17) | 21.13 |
| 09 | Iii | $C_{16}H_{11}O_3NCl_2$ | 336 | 115 | 68 | 4.20(4.17) | 21.13 |
| 10 | IIj | $C_{16}H_{11}O_3NCl_2$ | 336 | 98 | 73 | 4.21(4.17) | 21.13 |
| 11 | IIk | $C_{16}H_{12}O_4NCl$ | 317.5 | 168 | 80 | 4.45(4.41) | 11.18 |
| 12 | IIl | $C_{16}H_{12}O_4NCl$ | 317.5 | 137 | 78 | 4.47(4.41) | 11.18 |
| 13 | IIm | $C_{16}H_{12}O_4NCl$ | 317.5 | 112 | 74 | 4.46(4.41) | 11.18 |
| 14 | IIn | $C_{17}H_{12}O_5NCl$ | 345.5 | 229 | 70 | 4.08(4.05) | 10.27 |
| 15 | IIo | $C_{16}H_{12}O_3NCl$ | 331.5 | 95 | 80 | 4.27(4.22) | 10.70 |

**Table-2**: Antimicrobial activities of 2-azetidinone derivatives (mic in μg/ml).

| S.No. | Compound | Gram +ve Bacteria | | | Gram – ve Bacteria | | |
|---|---|---|---|---|---|---|---|
| | | Staphylococcus Aureus | Bacillus Megatherium | Bacillus subtillis | Porteus Vulgaris | Escherichia coli | Pseudomonas Aeruginosa |
| 01 | IIa | 25 | 25 | 25 | 25 | 25 | 25 |
| 02 | IIb | 100 | 50 | 100 | 50 | 100 | 25 |
| 03 | IIc | 200 | 50 | 50 | 25 | 100 | 25 |
| 04 | IId | 100 | 50 | 200 | 50 | 200 | 50 |
| 05 | IIe | 25 | 25 | 25 | 25 | 25 | 25 |
| 06 | IIf | 100 | 50 | 100 | 50 | 100 | 25 |
| 07 | IIg | 100 | 50 | 200 | 50 | 200 | 50 |
| 08 | IIh | 50 | 50 | 25 | 100 | 50 | 50 |
| 09 | IIi | 50 | 50 | 25 | 100 | 50 | 50 |
| 10 | IIj | 50 | 25 | 25 | 25 | 50 | 50 |
| 11 | IIk | 25 | 25 | 12.5 | 25 | 25 | 12.5 |
| 12 | III | 3 | 3 | 3 | 3 | >3 | 3 |
| 13 | IIm | >3 | >3 | >3 | >3 | >3 | >3 |
| 14 | IIn | 50 | 25 | 25 | 25 | 50 | 25 |
| 15 | IIo | 12.5 | 25 | 50 | 50 | 25 | 25 |
| 16 | Chlorom-phenicol | 12.5 | 3.0 | 3.0 | 12.5 | 6.0 | 12.5 |

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