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# Synthesis and Biological Screening of Some Novel Pyridin-2(1H)-One Derivative

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## ABSTRACT

**Acetone dicarboxylic acid prepared from reaction of citric acid with conc. $H_2SO_4$ .4-(4-chlorophenyl) thiazol-2-amine is prepared by reaction of Thiourea and $I_2$ were triturated and reflux with p-chloroacetophenone. Now, 1-(4-(4-Chlorophenylthiazol-2-yl)-4-(4-Methoxyphenyl)Pyridine-2,6(1H,3H)- dione is prepared by refluxing of 4-(4-chlorophenyl) thiazol-2-amine and 3-(4-Methoxy phenyl) pentanedioic acid in methanol. 5,6-dichloro-1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-Methoxyphenyl) pyridine- 2(1H)-one is prepared by reaction of 1-(4-(4-Chlorophenylthiazol-2-yl)-4-(4-Methoxyphenyl) Pyridine-2,6 (1H,3H)-dioneand phosphorous oxychloride.1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-methoxyphenyl)-5,6-bis(o-/m-/p-Toluidino) pyridine-2(1H)-One is prepared by reaction of 5,6-dichloro-1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-methoxyphenyl) pyridine-2(1H)-One and o-,m-,p-Toluidine. All the title compounds characterised on the basis of their MASS, $^1$H NMR spectroscopic data analysis.**

**Keywords:** Anti-Bacterial activity, Synthesis, Thiazole, Toluidine

## INTRODUCTION

Various 4- substituted phenyl thiazoles exhibited antibacterial and antifungal activity at 2$^{nd}$ position with azetidinones, thiazolidinones andquinazolones.

various 4-(4-substituted phenyl)-5,6-disubstituted-1-(4-substituted phenyl thiazole-2-yl) pyridin- 2(1H) -one and found to have good antibacterial activity.

Therefore our aim is to synthesize & to study the effect of various aromatic amines at 5$^{th}$& 6$^{th}$ position of pyridinone moiety for the antibacterial activity. The structure of the synthesized compounds were elucidated on the basis of their MASS, $^1$H NMR spectroscopic data. These compounds also screened for their antimicrobial activity.

## EXPERIMENTAL

Melting points of all the synthesized compounds were determined in open capillaries and are uncorrected. Thin layer chromatography was performed on microscopic slides (2×7.5cm) coated with Silica-Gel-Gf254 and spots were visualized under UV light and by exposure to iodine vapor. IR spectra of all compounds were recorded in FTIR 8400S Shimadzu Spectrophotometer using KBr. Mass spectra were obtained using 2010EV LCMS Shimadzu instrument. The $^1$H-NMR was recorded on Bruker Advance-II NMR 400 MHz instruments using $CDCl_3$ / DMSO-$d_6$ as solvent and TMS (tetramethylsilane) as internal standard, chemical shifts were expressed as δ values (ppm). All the chemicals use for the synthesis of titled compounds was produced from S.D. Fine Chem. Ltd, Finar Chemical Ltd, and Loba Chemicals. The chemicals were used without further purification.

**[1]. Preparation of 3-(4-methoxyphenyl)-2,3-diene-pentanedioic acid[1][2]**

To the acetone dicarboxylic acid prepared from citric acid (25g) and conc. $H_2SO_4$ (40ml), Anisole (12.2g) was added slowly with stirring, under cold condition. Stirring was continued for a further period of 3 hr and the temperature maintained at 20$^0$C. The contents were poured into 150 ml ice-cold water. The solid obtained was filtered and washed with water till free from acidity. It was then dissolved in saturated solution of sodium bicarbonate and regenerated with dilute. HCl. The solid product was filtered, washed with water and recrystallized from boiling water. Melting point is 168-170 $^0$C.

**[2]. Preparation of 4-(4-chlorophenyl)thiazol-2-amine [1][2]**

Thiourea (30g) and I2 (50g) were triturated and mixed with p-chloroacetophenone (24mL). The mixture was heated on water bath with occasional stirring for 8hr. The obtained solid was triturated with Et2O to remove unreacted acetophenone, washed with aqueous sodium thiosulfate to remove excess iodine and then with water. The crude product was dissolved in hot water, filtered to remove the sulfone, and 4-(4-chlorophenyl)thiazol-2-amine was precipitated by addition of ammonia solution. Crude product was filtered, washed with water, dried and recrystallized from ethanol. Melting point is 144-146 $^0$C.

**[3]. Preparation of 1-(4-(4-Chlorophenylthiazol-2-yl)-4-(4-Methoxyphenyl)Pyridine-2,6(1H,3H)-dione[1][2]**

A mixture of 4-(4-chlorophenyl) thiazol-2-amine (0.01mole) and 3-(4-Methoxy phenyl) pentanedioic acid (0.01mole) was dissolved in methanol and refluxed for 4hrs, then after cooled to room temperature. The solid obtained was filtered and dried. Melting point is 204-206 $^0$C.

**[4]. Preparation of 5,6-dichloro-1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-Methoxyphenyl)pyridine- 2(1H)-one[1][2]**

A mixture of 1-(4-(4-Chlorophenylthiazol-2-yl)-4-(4-Methoxyphenyl)Pyridine-2,6 (1H,3H)-dione(0.01mole) and phosphorous oxychloride (9ml) was refluxed for 1hr and then poured into crushed ice, solid product obtained was filtered, washed with water, dried and recrystallized from ethanol. Melting point is 110-114 $^0$C.

**[5]. Preparation of 1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-methoxyphenyl)-5,6-bis(o-/m-/p-toluidino) pyridine-2(1H)-One [1][2]**

A mixture of 5,6-dichloro-1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-methoxyphenyl) pyridine-2(1H)-One (0.01 Mole) and o-,m-,p- Toluidine was refluxed for 15 hr and distilled to remove excess of amine. The resultant solid was filtered, washed with water and recrystallized from methanol.

**Table- 1. Physicochemical data of the compounds**

| Sr no. | R | Molecular formula | Melting point (˚C) | % yield | *Rf Value |
|---|---|---|---|---|---|
| 5a | -o-Toluidine | $C_{35}H_{29}ClN_4O_2S$ | 92-94 | 58 | 0.30 |
| 5b | -m-Toluidine | $C_{35}H_{29}ClN_4O_2S$ | 68-70 | 63 | 0.35 |
| 5c | -p-Toluidine | $C_{35}H_{29}ClN_4O_2S$ | 54=56 | 60 | 0.32 |

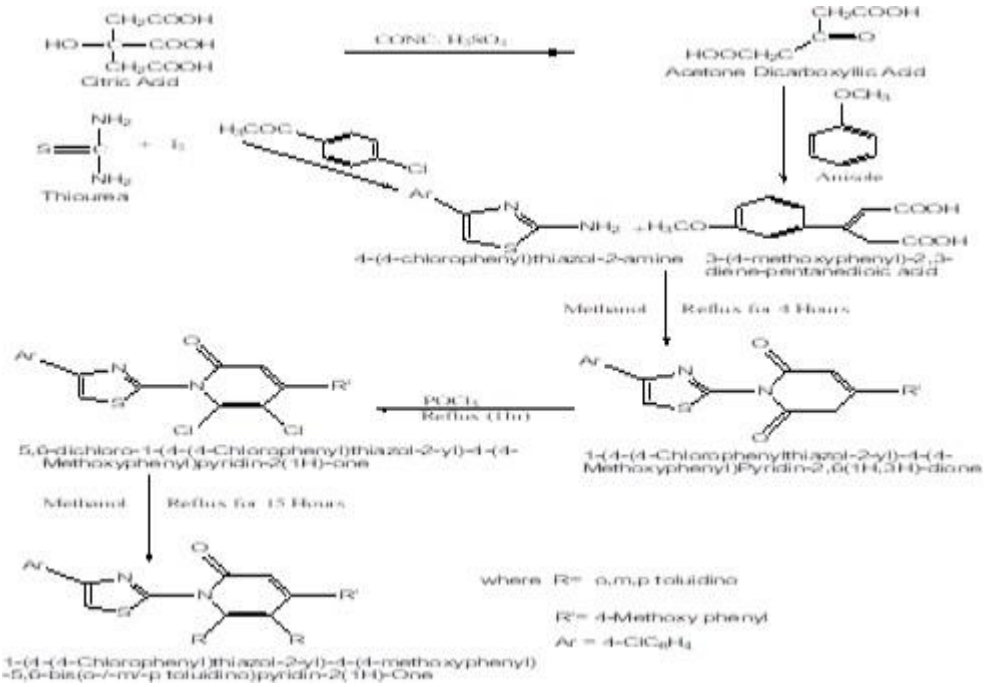
Mobile Phase :Ethyl Acetate- Hexane (2:8)

**Table -2. Spectral data of the compounds**

| Compd. Code | Mol. Wt. (g/mol) | IR (v,cm$^{-1}$) | Mass (m/e) | $^1$H NMR (DMSO-$d_6$, ppm) |
|---|---|---|---|---|
| 5a | 604 | ~C-Cl(1031.83)<br>~C-S (1089.71)<br>~NH(3200-3400)<br>~O-sub(750.26)<br>~P-Sub(833.19) | 605.2($M^{+1}$) | 2.27(s,1H,$CH_3$),6.68-8.1(m,17H,Ar-H,CH-S) |
| 5b | 604 | ~C-Cl (1033.77)<br>~C-S (1089.71)<br>~NH(3200-3400) | 605.2($M^{+1}$) | 2.27(s,1H,$CH_3$),6.68-8.1(m,17H,Ar-H,CH-S) |

| | | | | |
|---|---|---|---|---|
| | | ~m-Sub(760,825) | | |
| 5c | 604 | ~C-Cl(1031.83)<br>~C-S (1089.71)<br>~NH(3200-3400)<br>~P-Sub(833.19) | 605.2($M^{+1}$) | 2.27(s,1H,$CH_3$),6.68-8.1(m,17H,Ar-H,CH-S) |

Scheme for synthesis **1-(4-(4-Chlorophenyl)thiazol-2-yl)-4-(4-methoxyphenyl)-5,6-bis(toluidino)pyridine-2(1H)-One**




## ANTIMICROBIAL

**Activity**

The synrhesized compounds were screened for their in vitro antibacterial activity against Staphylococcus aureus, B. Subtilis, E. coli,by measuring the zone of inhibition in mm. The antibacterial activity was performed by cup plate method at concentration 20µg/ml , 50µg/ml ,60µg/ml and 80µg/ml and reported in Table. Nutrient agar was employed as culture medium and DMF was used as solvent control. Streptomycin and Ampicillin used as standard for antibacterial activity.

**Table. Antibacterial data of compounds[3][4][5]**

| Product Code | Concentration µg/ml | E.coli | S.Aureus | B. Subtilis |
|---|---|---|---|---|
| STD Ampicillin | 20 | 7.1 | 6.2 | 8.2 |
| | 40 | 9.2 | 8.3 | 10.3 |
| | 60 | 12.1 | 10.4 | 11.3 |

| | | | | |
|---|---|---|---|---|
| | 80 | 14.3 | 13.2 | 12.2 |
| STD Streptomycin | 20 | 9.2 | 9.1 | 10.1 |
| | 40 | 11.1 | 10.5 | 11.2 |
| | 60 | 13.2 | 12.3 | 13.3 |
| | 80 | 15.4 | 13.2 | 15.1 |
| 5a | 20 | 3.1 | 2.4 | 2.2 |
| | 40 | 6.2 | 5.5 | 4.1 |
| | 60 | 8.6 | 6.2 | 6.5 |
| | 80 | 10.5 | 10.3 | 7.4 |
| 5b | 20 | 3.4 | 2.2 | 3.3 |
| | 40 | 5.2 | 4.4 | 4.1 |
| | 60 | 6.1 | 7.4 | 5.3 |
| | 80 | 9.5 | 11.1 | 8.2 |
| 5c | 20 | 2.6 | 2.2 | 4.3 |
| | 40 | 6.3 | 4.3 | 6.2 |
| | 60 | 7.4 | 7.6 | 9.1 |
| | 80 | 9.2 | 8.5 | 11.7 |

[a]zone of inhibition in mm

## CONCLUSION

From the antibacterial screening it was observed that all the compounds exhibited activity against all the organisms employed. Looking at the structure activity relationship marked inhibition in bacteria was observed that among the synthesized compounds title compound 5(c) (p-substituted toluidine at the 5$^{th}$ and 6$^{th}$ position of the pyridinone ring ) has shown highest zone of inhibition at b. Subtilis.and title compound 5(a) (o- substituted toluidine at the 5$^{th}$ and 6$^{th}$ position of the pyridinone ring ) shown highest zone of inhibition against S.aureus and E.coli. As we consider all result obtained from antibacterial tests together we can say that entire compounds tested are active towards bacteria.

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