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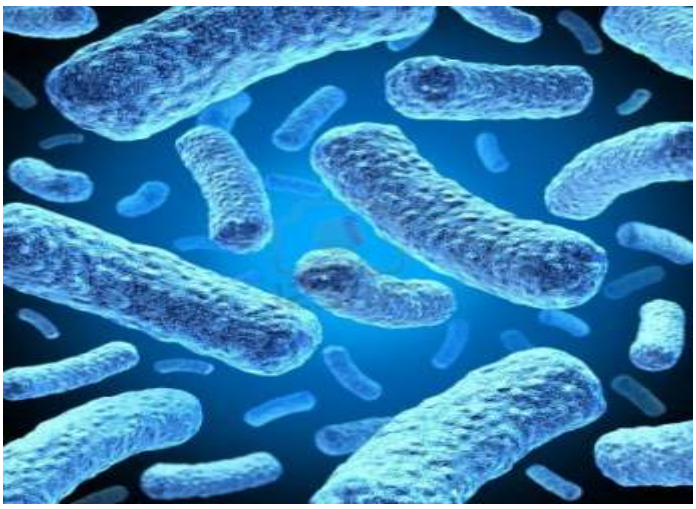
# SYNTHESIS AND ANTITIUBERCULER ACTIVITY OF THIOZOLUDENONE DERIVATIVES

M. S. Salunke
Adv. M. N. Deshmukh Arts, Science and Commerce College, Rajur Tal – Akole
Dist – Ahmednagar.

## ABSTRACT



Now a day there is a worldwide problem of Tuberculosis. Tuberculosis is an infectious disease. Now days there are number of drug present in this era to cure Tuberculosis. According to increase in population there is a need of smart drug. Now a day is a Moiety of choice which possesses many pharmacological properties. Literature survey reveals that 4 - Thiazolidinones and phenolic derivatives show broad spectrum of biological activities. In order to explore the activities associated with above nucleus; we planned the Synthesis of derivatives of Thiazolidinone. The new drug like 2 (Substituted) 3-P acetamindo phenoxy-4 thiazolidinones has anti tubercular property. The most prominent thioglycolic acid compound in nature is Anti tuberculosis, which serves as Anti tubercular activity.

KEYWORDS : *tuberculosis, N atom, Solvent, anti tuberculosis activity, etc.*

## INTRODUCTION –

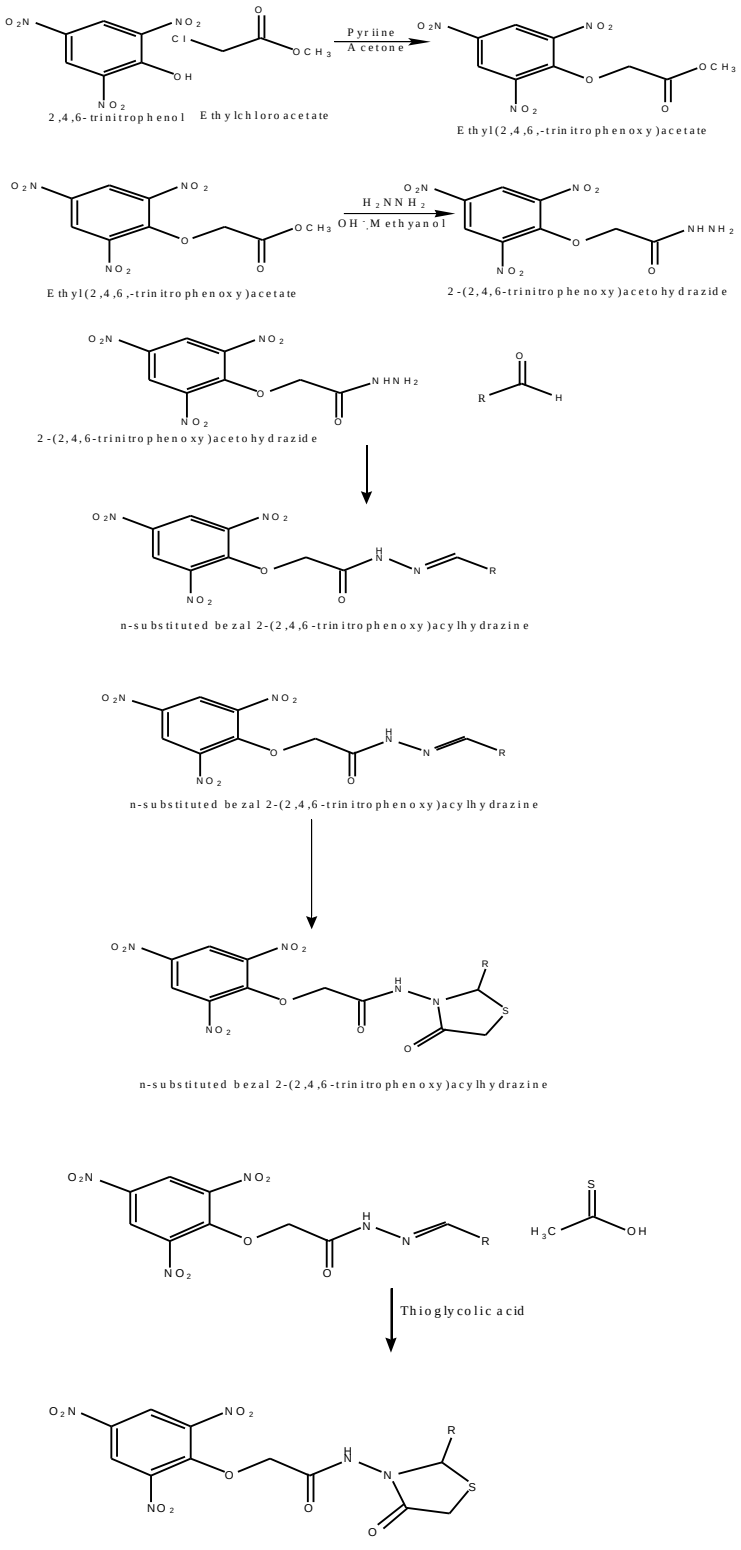
Thiazolidinone compounds have a wide range of biological activities ranging from widely use human and veterinary anthelmintic to anti tubercular activity. A basis for interest in the thiazolidinone ring system as nucleus from which to develop potential chemotherapeutic agent was established in the 1950s when it was found that it was an integral part of the structure of thiazolidinone. .The spectrum of the pharmacological of thiazolidinone has been reviewed by several authors 19-22 along with these different pharmacological properties such as anti ulcer antituberculosis properties have been reported.

## SCOPE –

On the basis of keen interest in anti tuberculosis, Thiazolidinone compounds have a wide range of biological activities ranging from widely use human and veterinary anthelmintic to anti tubercular activity. It has a wide scope in the formation of product like 2 (Substituted) 3-P acetamindo phenoxy-4 thiazolidinones. Though there is a potentially curative treatments have been available in this century, tuberculosis is remains the leading position in the world today. There is a need to take precaution and be aware about the health in the world wide. The treatment of tuberculosis is long and the drug has

numerous side effects. According to increase in population there is a need of smart drug.

## SCHEME –



## EXPERIMENTAL -

The reaction of various substituted phenolic compounds with Ethyl chloro acetate gave substituted phenoxy acetate (1) which was converted to substituted phenoxy acetyl hydrazide (2) by treatment with hydrazine hydrate. The hydrazides (2) were condensed with different aldehydes to obtain Schiff's bases (3). There different Schiff's base (3) were cyclo condensed with thio- glycolic acid to afford corresponding thiazolidinone derivatives (4). The progress of reactions was monitored by TLC (ethyl acetate/ petroleum ether = 1/4). Heat the reaction mixture under reflux for 7 hrs. The solvent was removed by distillation and residue diluted with water (50 ml). The product obtained was washed with $Na_2 CO_3$ and then by water recrystalize the product by pet ether, filtered, dried and M.P. was recorded.

## MATERIALS AND METHODS -

All chemicals were purchased from sigma-Aldrich and used without further purification. All reactions and purity of 4 thiazolidinones and phenolic derivatives were monitored by thin layer chromatography (TLC) using Aluminum plates coated with silica gel (Merck) using 20% ethyl acetate, 80% petroleum ether. Heat the reaction mixture under reflux for 7 hrs. The solvent was removed by distillation and residue diluted with water (50 ml). The product obtained was washed with $Na_2 CO_3$ and then by water recrystalize the product by pet Ether, filtered, dried and M.P. was recorded. Heat the above mixture under reflux for 7 hrs. The reaction is monitored by TLC and Solvent is removed under distillation. Recrystalize the product by pet ether, dried and M.P. was recorded.

## Concept of origin –

Literature survey reveals that 4 - thiazolidinones and phenolic derivatives show broad spectrum of biological activities. In order to explore the activities associated with above nucleus; we planned the Synthesis of derivatives of thiazolidinone.

The reaction of various substituted phenolic compounds with Ethyl chloro acetate gave substituted phenoxy acetate (1) which were converted to substituted phenoxy acetyl hydrazide (2) by treatment with hydrazine hydrate. The hydrazides (2) were condensed with different aldehydes to obtain Schiff's bases (3). There different Schiff's base (3) were cyclo condensed with thio- glycolic acid to afford corresponding thiazolidinone derivatives (4). The structure of the compounds Synthesized in our laboratory were assigned on the basis of elemental analysis.

## Recovery of the product –

The reaction of various substituted phenolic compounds with Ethyl chloro acetate gave substituted phenoxy acetate (1) which was converted to substituted phenoxy acetyl hydrazide (2) by treatment with hydrazine hydrate. The hydrazides (2) were condensed with different aldehydes to obtain Schiff's bases (3). There different Schiff's base (3) were cyclo condensed with thio- glycolic acid to afford corresponding thiazolidinone derivatives (4). The progress of reactions was monitored by TLC (ethyl acetate/ petroleum ether = 1/4). Heat the reaction mixture under reflux for 7 hrs. The solvent was removed by distillation and residue diluted with water (50 ml). The product obtained was washed with $Na_2 CO_3$ and then by water recrystalize the product by pet ether, filtered, dried and M.P. was recorded.

## Analysis by Rf Values Method -

Rf Values of product –N-substituted benzal, P-(2, 4, 6, tri Nitro phenoxy) acyle hydrazines

| Sr.No. | Name of the product | $R_F$ Values of Product |
|---|---|---|
| 1 | benzal,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.58 |
| 2 | O-$NO_2$ Benzaldehyde,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.22 |
| 3 | Vanniline ,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.77 |
| 4 | Anisaldenhyde,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.16 |
| 5 | Cinnamaldehyde P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.20 |
| 6 | P-.Dimenthyl Benzaldedhyde,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 0.62 |

Stage –IV – Rf of Product 2 (Substituted) 3-P acetamindo phenoxy-4-thiazolidinones

| Sr.No | Name of the product | $R_F$ Values of Product |
|---|---|---|
| 1 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of benzaldehyded | 0.27 |
| 2 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of O-$NO_2$ Benzaldehyde, | 0.38 |
| 3 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of Vanniline | 0.42 |
| 4 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of Anisaldenhyde | 0.68 |
| 5 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of Cinnamaldehyde | 0.60 |
| 6 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of Dimenthyl Benzaldedhyde, | 0.70 |
| 7 | 2 (Substituted) 3-P acetamindo phenoxy-4thiazolidinones derivates of Dimenthy Amiono benzaldehyde | 0.72 |

## Analysis by M.P. Method –

M.P.OF Stage- III product –N-substituted benzal ,P-(2, 4, 6, trinito phenoxy) acyle hydrazines

| Sr. No. | Name of the product | %yield | M.P. |
|---|---|---|---|
| 1 | benzal,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 87 | 261 C |
| 2 | O-$NO_2$ Benzaldehyde,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 80 | $201^0$ C |
| 3 | Vanniline ,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 90 | $234^0$ C |
| 4 | Anisaldenhyde,P-(2, 4, 6, trinito phenoxy) acyle hydrazines | 92 | $272^0$ C |
| 5 | Cinnamaldehyde P-(2, 4, 6, trinito phenoxy) acyl hydrazines | 83 | $268^0$ C |
| 6 | P-.Dimenthyl Benzaldedhyde,P-(2, 4, 6, trinito phenoxy) acylel hydrazines | 86 | $234^0$ C |
| 7 | P-Dimenthy Amiono benzaldehydeP-(2, 4, 6, trinito phenoxy) acyle hydrazines | 89 | $252^0$ C |

Stage –IV - M.P. of Product 2 (Substituted) 3-P acetamindo phenoxy-4 thiazolidinones

| Sr.No. | Name of the product | M.P |
|---|---|---|
| 1 | 2 (benzal,P-(2, 4, 6, trinito phenoxy) acyl hydrazines ) 3-P acetamindo phenoxy-4thiazolidinones | 271 $^0$C |
| 2 | 2 (O-$NO_2$ Benzaldehyde,P-(2, 4, 6, trinito phenoxy) acyl hydrazines ) 3-P acetamindo phenoxy-4thiazolidinones | 278 $^0$C |
| 3 | 2 (Vanniline ,P-(2, 4, 6, trinito phenoxy) acyl hydrazines ) 3-P acetamindo phenoxy-4thiazolidinones | 234 $^0$C |
| 4 | 2 (Anisaldenhyde,P-(2, 4, 6, trinito phenoxy) acyl hydrazines ) 3-P acetamindo phenoxy-4thiazolidinones | 272 $^0$C |
| 5 | 2 (,P- Cinnamaldehyde (2, 4, 6, trinito phenoxy) acyl hydrazines ) 3-P acetamindo phenoxy-4thiazolidinones | 252 $^0$C |
| 6 | 2 (P-.Dimenthyl Benzaldedhyde,P-(2, 4, 6, trinito phenoxy) acyl hydrazines) 3-P acetamindo phenoxy-4thiazolidinones | 262 $^0$C |

## RESULT AND DISCUSSION –

### Analysis of Reaction –

Literature survey reveals that 4 - Thiazolidinones and phenolic derivatives show broad spectrum of biological activities. In order to explore the activities associated with above nucleus; we planned the Synthesis of derivatives of Thiazolidinone.

The reaction of various substituted phenolic compounds with Ethylchloroacetate gave substituted phenoxy acetate (1) which was converted to substituted phenoxy acetyl hydrazide (2) by treatment with hydrazine hydrate. The hydrazides (2) were condensed with different aldehydes to obtain Schiff's bases (3). There different Schiff's base (3) were cyclo condensed with thio- glycolic acid to afford corresponding thiazolidinone derivatives (4).

The structure of the compounds Synthesized in our laboratory were assigned on the basis of elemental analysis

### Stage –I

Preparation of (2, 4, 6, Trinitro) Phenoxy Acetate.

A mixture of picric acid (0.1 mole) and Ethyl Chloro acetate (0.1 mole) and pyridine (0.2 mole) was dissolved in Acetone (200 ml) and heated under reflux for 4 hrs, monitored by TLC. The solvent was removed by distillation and residue diluted with water (50 ml). The product obtained was washed with $Na_2CO_3$ and then by water recrystalize the product by pet Ether, filtered, dried and M.P. was recorded.

Picric acid + Ethyl Chloro acetate +( pyridine acetone/4hrs.) $\xrightarrow[\text{Reflux}]{}$ (2, 4,6,Trinitro) Phenoxy Acetate
Product – I

### Stage-II

A mixture (2, 4, 6, Tri nitro) Phenoxy Acetate (50m.m.) and hydrazine hydrate (250m.m.) was dissolved in methanol (250ml). Heat the above mixture under reflux for 7 hrs. The reaction is monitored by TLC and Solvent is removed under distillation. Recrystalize the product by pet Ether, dried and M.P. was recorded.

Product-I + hydrazine hydrate+ (methanol Reflux/7hrs.) $\longrightarrow$ {Substituted Phenoxy acetylhydrazide}
Product–II

### Stage-III

Product –II (2m.m.) is added to various substituted Aldehyde (2m.m.) in presence of 25ml methanol and reflux 4 hrs. Monitored the reaction by TLC for each 30 minutes. Keep the mixture of product overnight, solvent will removing away and product is III is obtained.

Product –II+ vanilline + (methanol / reflux 4hrs.) → Schiff's bases (Product-III A)

### Stage-IV

Take product III (1m.m.) and thio lactic acid (1m.m.) and reflux in oil bath at 1200-125 0c for 4hrs. Reaction is monitored by TLC each 30minites. The product was isolated and washed by 10% Na2 HCO3. The product is recrystalized by Ethanol.

Product –IIIA + Thio glycolic acid + (oil bath-125 0c / reflux 4hrs.) → Thiazolidinone derivatives Product-IV A

### CONCLUSIONS –

In conclusion, this paper describes a convenient and efficient process for Synthesis and Anti Tuberculosis activity of thiozolidinone Derivatives by condensation reaction of Picric acid with Ethyl Chloro Acetate in the presence of Methanol in water. This method offers some advantages in terms of simplicity of performance, using methanol as solvent, low reaction times low cost and it follows along the line of green chemistry. It can conveniently be handled and removed from the reaction mixture. We believe that this procedure is convenient economic and a user-friendly process for the synthesis of substitute 4 thiazolidinones and phenolic derivatives [2 (substituted) 3-P-acetaamido phenoxy-4-thiazolidinones] of biological and medicinal importance.

During the course of the reaction step III more time is required and the process becomes long to take time consumption. The solvent used for recrystalisation are water, as a water is a eco friendly solvent.

In case of the formation of the product in step III the methanol is used as solvent and in the last stage oil bath is used to heat reaction mixture properly.

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