4. Chemistry:

General:

All the chemicals and solvents used were purchased from standard chemical suppliers. Melting points were determined on a Toshniwal capillary melting point apparatus and are uncorrected. Thin layer chromatography was carried out on silica gel pre coated plates (Merck 60F₂₅₄) and the spots were visualized under UV lamp (254 or 366 nm) and/or iodine vapor. The absorption spectra are recorded on Shimadzu UV/Vis spectrometer UV 1800. IR spectra were recorded on FTIR-8300 Shimadzu using KBr pellets. ¹H NMR was recorded at 400 MHz (Brucker), CDCl₃ as solvent. Mass spectrum was recorded on LC-MS-2010A Shimadzu, Japan (ESI, Mobile phase: Methanol: water, 90:10). NMR and Mass spectra were obtained for final compounds and were consistent with assigned structures.

Materials and Methods

4.1. Thiazolidin-4-one derivatives with mercaptoacetic acid (p-Chlorophenoxyacetic acid derivatives):

Part- I: Procedure for the preparation of p-Chlorophenoxyacetic acid

p-Chlorophenol (6.5g, 0.05 mol) and monochloroacetic acid (4.75g, 0.05 mol) were taken in a 500 ml beaker. A solution of sodium hydroxide (4.5g, 0.112 mol) in 25 ml of water was added slowly with stirring, considerable heat being generated during the reaction. The reaction mixture was heated on a wire gauge until most of the liquid evaporated. The residue was treated with 150 ml of water, cooled and filtered. The clear solution was acidified with dilute hydrochloric acid and the precipitated product was filtered. The crude product was re-crystallized from distilled water. Yield = 9.3 g (98%); Melting point= 156-157 °C.

Reaction:
Part- II: Procedure for the preparation of Ethyl p-Chlorophenoxyacetate

p-Chlorophenoxyacetic acid (22g, 0.12 mol) was dissolved in ethanol (50 ml). Concentrated sulphuric acid (10 ml) was added and refluxed for 3 hours. The solution was cooled and poured into crushed ice. Sodium bicarbonate was added to remove the excess acid and extracted with ether. The ether extract was dried over sodium sulphate. The ether layer was evaporated to get a thick concentrated ester. Yield = 21g (83%)

Reaction:

\[
\begin{array}{c}
\text{Cl} \quad \begin{array}{c}
\text{O} \\
\text{C} \\
\text{H}_2 \text{COOH}
\end{array} \\
\text{Cl} \quad \begin{array}{c}
\text{O} \\
\text{C} \\
\text{H}_2 \text{COOC}_2\text{H}_5
\end{array}
\end{array}
\]

Part- III: Procedure for the preparation of p-Chlorophenoxyacetic acid hydrazide

Ethyl p-chlorophenoxyacetate (21.5g, 0.1mol) was taken in 100 ml round bottomed flask and 5.2 ml of 99% hydrazine hydrate (0.1mol) and ethanol (30 ml) were added and refluxed for half an hour. Ethanol was removed under reduced pressure and then poured into a beaker containing ice cubes. The solid separated was filtered and re-crystallized from ethanol. Yield = 17 g (85 %), Melting point =159 ºC.

Reaction:

\[
\begin{array}{c}
\text{Cl} \quad \begin{array}{c}
\text{O} \\
\text{C} \\
\text{H}_2 \text{COOC}_2\text{H}_5
\end{array} \\
\text{Cl} \quad \begin{array}{c}
\text{O} \\
\text{C} \\
\text{H}_2 \text{CONHNH}_2
\end{array}
\end{array}
\]
4.1. a: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 1; ANI -TGA)

4.1. a. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-((4-methoxybenzylidene) acetohydrazide

p - Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. To this, anisaldehyde (1.36g, 0.01mol) was added after dissolving in 20 ml methanol. A few drops of glacial acetic acid were added and refluxed for 15 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 2.55 g (80%), Melting point=189-190 ºC.

Reaction:

\[
\text{Cl-OCH}_2\text{CONHNH}_2 + \text{OHC-OCH}_3
\]

\[
\text{Cl-OCH}_2\text{CONHNH}_2 + \text{OHC-OCH}_3 \rightarrow 2-(4\text{-Chlorophenoxy})-\text{N'}-(4\text{-methoxybenzylidene})\text{acetohydrazide}
\]
4.1. a. 2. Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)acetamide (ANI -TGA)

The method of Sriram et al., (2005) was followed. To a stirred solution of 2-(4-Chlorophenoxy)-N'-(4-methoxybenzylidene)acetohydrazide in 50 ml dry toluene (3.19 g, 0.01 mol), 2.0 ml (98%) of mercaptoacetic acid was added. The mixture was irradiated in an unmodified domestic microwave oven (KenStar, model no. OM 20 DGQ) at power setting of 80% with 3 minutes/cycle for 16 minutes. The toluene in the reaction mixture after 16 minutes was removed under vacuum. The yellow solid was treated with saturated solution of sodium bicarbonate to remove the unreacted mercaptoacetic acid. The crude thiazolidin-4-one was filtered and washed with water and dried. Repeated recrystallization of the crude product from methanol gave colorless fine crystals. **Yield** = 1.7 g (53%); **Melting point** = 118-120 °C; **λ**<sub>max</sub> in methanol-280 nm; **IR** (KBr); 3446 (-NH), 3030 (Ar ,C-H, Str), 2916, 1703 and 1662 (-C=O of −CH₂CO- and -CONH), 1595 (C=C, Str), 1280 (-OCH₃), 1238 (C-O Str), 1170, 1074 (C-Cl), 950, 823, 763 & 669 (C-S-C) cm⁻¹ respectively; **¹HNMR** (CDCl₃): δ = 3.85 (t, 3H, CH₃), 3.88 (s, 2H, CH₂), 4.65 (s, 2H, CO-CH₂-O), 5.9 (S, 1H, CH), 6.9 - 7.0 (m, 4H, aromatic), 7.3 - 7.8 (m, 4H, aromatic), 8.6 (br s, 1H, NH) ppm; **Mass spectrum**: MS (ESI) = m/z 393, 353 (M-Cl)

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R&lt;sub&gt;f&lt;/sub&gt; values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.86</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
\text{Cl} & \quad \text{O} & \quad \text{CH}_2 & \quad \text{C} & \quad \text{NH} & \quad \text{N} \equiv \text{CH} & \quad \text{Cl} \\
\text{Cl} & \quad \text{O} & \quad \text{CH}_2 & \quad \text{C} & \quad \text{NH} & \quad \text{N} \equiv \text{CH} & \quad \text{Cl}
\end{align*}
\]

2-(4-Chlorophenoxy)-N\(^{-}\)(4-methoxybenzylidene)acetohydrazide

\[
\begin{align*}
\text{Cl} & \quad \text{O} & \quad \text{CH}_2 & \quad \text{C} & \quad \text{NH} & \quad \text{N} \equiv \text{CH} & \quad \text{S} & \quad \text{O} & \quad \text{Cl} \\
\text{Cl} & \quad \text{O} & \quad \text{CH}_2 & \quad \text{C} & \quad \text{NH} & \quad \text{N} \equiv \text{CH} & \quad \text{S} & \quad \text{O} & \quad \text{Cl}
\end{align*}
\]

2-(4-Chlorophenoxy)-N\(^{-}\)(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)acetamide (ANI-TGA)
IR Spectrum of ANI - TGA

Chemistry

TZDMW27
Mass Spectrum of ANI- TGA

Mol. Wt = 393

MS Spectrum

Line#: 1  R.Time: 0.719(Scan#: 44) Negative
MassPeaks: 287  BasePeak: 367.15(8687705)
RawMode: Single 0.719(44)
BG Mode: Peak Start 0.460(28)
$^1$H NMR Spectrum of ANI-TGA
4.1. b: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 2; PCB -TGA):

4.1.b. 1: Procedure for the preparation of N’-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetohydrazide:

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. p-chlorobenzaldehyde (1.4g, 0.01 mol) was dissolved in methanol (20ml) in a separate beaker. Aldehyde solution were added slowly to hydrazide solution present in a round bottomed flask. A few drops of glacial acetic acid were added and refluxed for 20 minutes. The resultant solid was filtered under vacuum. The Schiff’s’ base was recrystallized with chloroform. Yield = 2.90 g (90%), Melting point=184-185 ºC.

Reaction:

![Reaction structure](image)

$N'$-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetohydrazide
4.1. b. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide (PCB-TGA)

The method of Surrey (1949) was followed. N’-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetohydrazide (3.22g, 0.01 mol) and mercapto acetic acid (2 ml, 98%) were taken in dry benzene (30 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol in cold condition gave a colorless solid. **Yield** = 3 g (76%); **Melting point** = 126-127 ºC; $\lambda_{\text{max}}$ in methanol-280 nm; **IR (KBr)**; 3450 (-NH), 3059 (Ar, C-H, Str), 2989, 1710 and 1678 (-CO- of –CH$_2$CO- & -CONH), 1591 (C=C, Str), 1236 (C-O, Str), 1172, 1060 (C-Cl), 962,833,763 & 671 (C-S-C) cm$^{-1}$, respectively; **$^1$HNMR (CDCl$_3$)**; $\delta$ = 3.70 - 3.85 (s, 2H, CH$_2$), 4.47 - 4.62 (s, 2H, CO-CH$_2$-O), 5.9 (s, 1H, CH), 6.7 - 7.2 (m, 4H, aromatic), 7.36 (m, 4H, aromatic), 8.0 (br s, 1H, NH) ppm; **Mass spectrum: MS (ESI)** = m/z 397, 321(M-2Cl).

**Table-2: TLC profile of PCB -TGA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R$_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.69</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.75</td>
</tr>
</tbody>
</table>
Reaction:

\[ \text{N’-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetohydrazide} \]

\[ \rightarrow \]

\[ \text{2-(4-Chlorophenoxy)-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide (PCB -TGA)} \]
IR Spectrum of PCB - TGA

\[
\begin{align*}
\text{Cl} & \quad \text{O} \quad \text{C} \\
\text{H}_2 & \quad \text{O} \quad \text{NH} \quad \text{N} \\
& \quad \text{Cl} \quad \text{S} \\
\end{align*}
\]
Mass Spectrum of PCB - TGA

Mol. Wt = 397

MS Spectrum

Line#:1  R.Time:0.492(Scan#:30) Negative
MassPeaks:164  BasePeak:395.15(4285463)
RawMode:Single 0.492(30)
BG Mode:Peak Start 0.310(19)
$^{1}H$ NMR Spectrum of PCB -TGA
4.1. c: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 3; OCB- TGA)

4.1. c. 1: Procedure for the preparation of N’-(2-Chlorobenzylidene)-2-(4-chlorophenoxy) acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. o-chlorobenzaldehyde (1.4g, 0.01 mol) was dissolved in methanol (20ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. A few drops of glacial acetic acid were added refluxed for 20 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized with chloroform. Yield = 2.90 g (90%), Melting point = 171-173 °C.

Reaction:

\[
\text{Cl}_2\text{C}_\text{O}\text{CH}_2\text{CONHNH}_2 + \text{OHC} \rightarrow \text{Cl}_2\text{C}_\text{O}\text{CH}_2\text{CONHNH}_2 + \text{N'}-(2-\text{Chlorobenzylidene})-2-(4-\text{chlorophenoxy})\text{acetohydrazide}
\]
4.1. c. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide (OCB-TGA)

The method of Surrey (1949) was followed. N’-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetoxydrazide (3.22 g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (30 ml) in 100 ml RB flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 30 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol to give a colorless solid. Yield = 3.6 g (91%); Melting point=141-142 ºC; λ_max in methanol-279 nm; IR (KBr); 3244 (-NH), 3064 (Ar, C-H, Str), 2987, 1719 and 1684 (-CO of CH2CO & -CONH), 1589 (C=C, Str), 1240 (C-O, Str), 1095, 1055 (C-Cl), 958, 825, 758 & 669 (C-S-C) cm\(^{-1}\), respectively; \(^1\)HNMR (CDCl\(_3\)): δ=3.72 - 3.85 (s, 2H, CH\(_2\)), 4.5 - 4.6 (s, 2H, COCH\(_2\)O), 6.4 (s, 1H, CH), 6.73 - 7.19 (m, 4H, aromatic), 7.30-7.47(m, 4H, Ar), 8.03 (brs, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 397, 325 (M-2Cl); 254 (M-C\(_6\)H\(_4\)OCl).

Table-3: TLC profile of OCB -TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.80</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Reaction:

\[
N'-(2-\text{Chlorobenzylidene})-2-(4-\text{chlorophenoxy})\text{acetohydrazide} \rightarrow
\]

\[
2-(4-\text{Chlorophenoxy})-N-(2-(2-\text{chlorophenyl})-4-\text{oxothiazolidin-3-yl})\text{acetamide (OCB-TGA)}
\]
IR spectrum of OCB- TGA

\[
\text{Cl}\text{-}O\text{-}CH}_2\text{-}C\text{-}\overset{\text{O}}{\text{NH}}\text{-}\overset{\text{N}}{\text{CH}}\text{-S}\text{-O}\text{-Cl}
\]

- 3743.96
- 3435.34
- 3244.38
- 2987.84
- 2362.88
- 1718.63
- 1683.91
- 1589.40
- 1489.10
- 1438.94
- 1386.86
- 1307.78
- 1282.71
- 1240.27
- 1170.83
- 1095.60
- 1055.10
- 958.65
- 902.72
- 825.56
- 758.05
- 669.32
- 613.38
- 576.74
- 501.51

OCBTZD-1
Mass Spectrum of OCB - TGA

Mol. Wt = 397

MS Spectrum

Line#: 1  R.Time: 0.687(Scan#: 42) Negative
MassPeaks: 301  BasePeak: 367.15(5665126)
RawMode: Single 0.687(42)
BG Mode: Peak Start 0.477(29)
$^1$H NMR Spectrum of OCB - TGA
4.1. d: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 4; BHT- TGA)

4.1. d. 1: Procedure for the preparation of 3, 5-di-tert-butyl-4-hydroxybenzaldehyde

The method of Inagaki et.al, (2003) was followed. 2,6-di-tert-butyl-4-methylphenol (14.4g, 0.065 mol) was dissolved in DMSO (250 ml) and 48% HBr (2.7 ml, 033 mol) was added at 23 ºC. The mixture was heated at 100 ºC for 3 hours. After being cooled to 23 ºC, the reaction was quenched with water. The product was extracted with chloroform and organic layer was washed with water twice, followed by brine. The organic layer was dried and evaporated. The final product was recrystallized from methanol. Yield = 7.46 g (55%) and Melting point=186-187 ºC. The product was also characterized with IR data (-C=O, 1668 cm\(^{-1}\)).

Reaction:

\[
\text{HO CHOHO CH}_3 \quad \text{3,5-di-tert-butyl-4-hydroxybenzaldehyde}
\]

\[
\text{HO CH}_3 \quad \text{2,6-di-tert-butyl-4-methylphenol}
\]

4.1. d. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N’-(3, 5-di-tert-butyl-4-hydroxybenzylidene)acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in a 250 ml round bottomed flask. 3, 5-di-tert-butyl-4-hydroxybenzaldehyde (2.34g, 0.01 mol) was dissolved in methanol (80ml) in a separate beaker by heating. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. A few drops of glacial acetic acid were added and refluxed for 10 minutes. The resulting solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 3.0 g (72%), Melting point = 248 - 250 ºC.
Reaction:

\[
\begin{align*}
\text{Cl-OCH}_2\text{CONHNH}_2 + \text{OHC-CH}_2\text{OH} \rightarrow \\
\text{Cl-O-CH}_2\text{C-NH-N=CH-CH}_2\text{OH}
\end{align*}
\]

2-(4-Chlorophenoxy)-N'-(3,5-di-tert-butyl-4-hydroxybenzylidene)acetohydrazide
4.1. d. 3: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3, 5-di-tert-butyl-4-hydroxyphenyl)-4-oxothiazolidin-3-yl)acetamide (BHT- TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(3, 5-di-tert-butyl-4-hydroxybenzylidene)acetohydrazide (4.17 g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (60 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 31 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol afforded white solid. Yield = 3.7 g (75%), Melting point = 192-193 ºC; λ$_{max}$ in methanol-278 nm; IR (KBr): 3620 (-OH, Str), 3327 (-NH), 3064 (Ar, C-H, Str), 2056, 1726, & 1685 (-C=O of –CONH & -CH$_2$-C=O), 1595 (C=C, Str), 1246 (C-O, Str), 1155, 1058 (C-Cl), 1008, 889, 833, & 675 (C-S-C) cm$^{-1}$, respectively. $^1$HNMR (CDCl$_3$): δ = 1.49 (m, 18H, (CH$_3$)$_n$), 3.70 - 3.85 (s, 2H, CH$_2$), 4.45 - 4.60 (s, 2H, COCH$_2$O), 5.40 (s, 1H, -OH), 5.90 (s, 1H, CH), 6.90 (m, 2H, aromatic), 7.2 (m, 4H, aromatic), 7.9 (br s, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 491,171(M- C$_8$H$_6$O$_2$Cl$^-$)

Table-4: TLC profile of BHT- TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R$_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.87</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.79</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-(3,5-di-tert-butyl-4-hydroxybenzylidene)acetoxydrazide

\[ \text{2-(4-Chlorophenoxy)-N-(2-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-oxothiazolidin-3-yl)acetamide (BHT-TGA)} \]
IR Spectrum of BHT - TGA

![Chemical Structure of BHT]

![Infrared Spectrum Graph]

**Chemistry**
Mass Spectrum of BHT- TGA

Mol. Wt = 491

Line#:1 R.Time:0.714(Scan#:43) Negative
MassPeaks:391 BasePeak:489.35(11040135)
RawMode:Single 0.714(43)
BG Mode:Peak Start 0.427(26)
$^1$H NMR Spectrum of BHT - TGA
4.1. e: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(2-nitrophenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 5; ONB- TGA)

4.1. e. 1: Procedure for the preparation of 2-(4-chlorophenoxy)-N'-(2-nitrobenzylidene) acetohydrazide:

p-Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in ethanol (30 ml) in 100 ml round bottomed flask. 2-nitrobenzaldehyde (1.51g, 0.01mol) was dissolved in methanol (40ml) in a separate beaker by heating. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resulting solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 2.0 g (80%), Melting point=163-164 ºC.

Reaction:
4.1. e. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(2-nitrophenyl)-4-oxothiazolidin-3-yl)acetamide (ONB -TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'-(2-nitrobenzylidene)acetohydrazide (3.33g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (60 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 30 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a colorless solid. The recrystallized product was again purified by column chromatography by using silica gel as the stationary phase and acetone as eluting solvent. **Yield = 3.25 g (80%)**.

**Melting point** = 159-160 °C; \( \lambda_{\text{max}} \) in methanol-258 nm; **IR (KBr)**: 3427 (-NH), 3072 (Ar, C-H, Str), 2914, 1722 & 1680 (-C=O of –CONH & -CH₂-C=O), 1597 (C=C, Str) 1521 & 1386 (N-O, Str), 1242 (C-O, Str), 1170, 1063 (C-Cl), 825, 790 & 667(C-S-C) cm⁻¹, respectively ; **¹HNMR** (CDCl₃): \( \delta = 3.77 \) (s, 2H, CH₂), 4.53 (s, 2H, COCH₂O), 6.4 (s, 1H, CH), 6.73 - 7.19 (m, 4H, aromatic), 7.5 - 8.0 (m, 4H, aromatic), 8.18 (br s, 1H, NH) ppm; **Mass spectrum: MS (ESI):** = m/z 408, 127 (M- C₆H₄O Cl⁻), 92 (M-C₆H₄O⁻)

### Table-5: TLC profile of ONB- TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.79</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.61</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
\text{Cl} & \text{O} \text{CH}_2 \text{C} \text{NH} \text{N} = \text{CH} \text{O}_2 \text{N} \\
\text{Cl} & \text{O} \text{CH}_2 \text{C} \text{NH} \text{N} \text{CH} \text{O}_2 \text{N} \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N’-(2-nitrobenzylidene)acetohydrazide

\[
\begin{align*}
\text{Cl} & \text{O} \text{CH}_2 \text{C} \text{NH} \text{N} \text{CH} \text{O}_2 \text{N} \\
\text{Cl} & \text{O} \text{CH}_2 \text{C} \text{NH} \text{N} \text{CH} \text{O}_2 \text{N} \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N-(2-(2-nitrophenyl)-4-oxothiazolidin-3-yl)acetamide (ONB-TGA)
IR Spectrum of ONB - TGA

Chemistry
Mass Spectrum of ONB - TGA

Mol. Wt = 408

MS Spectrum

Line#: 1  R.Time: 0.707 (Scan#: 43) Negative
MassPeaks: 288  BasePeak: 406.15 (10951276)
RawMode: Single 0.707 (43)
BG Mode: Peak Start 0.427 (26)
$^1$H NMR Spectrum of ONB- TGA

![Chemical Structure]

**Chemistry**
4.1. f: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(4-oxo-2-(thiophen-2-yl)thiazolidin-3-yl)acetamide (Compound No. 6; T2C- TGA)

4.1. f. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(thiophen-2-ylmethylene)acetohydrazide:

p- Chlorophenixyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask thiophen-2-carbaldehyde (1.12g, 0.01 mol) was dissolved in methanol (20ml) in a separate beaker by heating. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. Few drops of glacial acetic acid were added. The mixture was refluxed for 10 minutes. The resultant solid was filtered under vacuum. The Schiff base was recrystallized with methanol. Yield 1.8 g (60%), melting point=194-196 °C.

Reaction:

\[
\text{Cl-OCH}_2\text{CONHNH}_2 + \text{OHC-s} \rightarrow \text{Cl-OCH}_2\text{C-NO-HN-N=CH-s}
\]

2-(4-Chlorophenoxy)-N'-(thiophen-2-ylmethylene)acetohydrazide
4.1.f.2: Procedure for the preparation of 2-(4-chlorophenoxy)-N-(4-oxo-2-(thiophen-2-yl)thiazolidin-3-yl)acetamide: (T$_2$C- TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'(thiophen-2-ylmethylene)acetohydrazide (2.95g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a pale brown colored solid. **Yield** = 2.75 g (75%), **Melting point** = 118-120 ºC; $\lambda_{\text{max}}$ in methanol-327 nm; **IR (KBr)**: 3437 (-NH), 3030 (Ar, C-H Str), 2908, 1716 & 1678 (-C=O of –CONH & -CH$_2$-C=O), 1604 (C=C, Str), 1236 (C-O, Str), 1182 (C-Cl), 1047, 945, 823 (S-C, Str), 765 & 665 (S-S-C) cm$^{-1}$, respectively; **$^1$HNMR (CDCl$_3$)**: δ = 3.20 - 3.30 (s, 2H, CH$_2$), 4.65 (s, 2H, COCH$_2$-O), 6.9 (s, 1H, CH), 7.06 - 7.16 (m, 3H, Thiophen), 7.30 - 7.46 (m, 4H, aromatic), 8.75 (br s, 1H, NH) ppm; **Mass spectrum: MS(ESI)** = m/z 369, 222 (M-C$_7$H$_8$OCl$^-$).

**Table-6: TLC profile of T$_2$C -TGA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.83</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.63</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-(thiophen-2-ylmethylene)acetohydrazide

2-(4-Chlorophenoxy)-N-(4-oxo-2-(thiophen-2-yl)thiazolidin-3-yl)acetamide (T₂C⁻ TGA)
IR Spectrum of T₂C - TGA
Mass Spectrum of $T_2C\cdot TGA$

Mol. Wt = 369

MS Spectrum

Line#: 1  R.Time: 0.555(Scan#: 34)  Negative
MassPeaks: 261  BasePeak: 367.20(4804956)
RawMode: Single 0.555(34)
BG Mode: Peak Start 0.277(17)
$^1$H NMR Spectrum of T$_2$C- TGA
4.1. g: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(4-oxo-2-p-tolythiazolidin-3-yl)acetamide (Compound No. 7; PMB -TGA)

4.1. g. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(4-methylbenzylidene) acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask; p-methylbenzaldehyde (1.2g, 0.01mol) was also dissolved in methanol (20ml) in a separate beaker by heating. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 05 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 2.70 g (89%), Melting point = 200-210 ºC.

Reaction:

\[
\begin{align*}
\text{Cl} & \quad \text{OCH}_2\text{CONHNH}_2 + \quad \text{OHC} & \quad \text{CH}_3 \\
\downarrow & \downarrow & \downarrow \\
\text{Cl} & \quad \text{O} & \quad \text{CH}_2 & \quad \text{C} & \quad \text{NH} & \quad \text{N=CH} & \quad \text{CH}_3 \\
& \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow \\
2-(4-\text{Chlorophenoxy})-\text{N}’-(4-\text{methylbenzylidene})\text{acetohydrazide}
\end{align*}
\]
4.1. g. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(4-oxo-2-p-tolyl thiazolidin-3-yl)acetamide (PMB-TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'- (4-methylbenzylidene)acetohydrazide (3.0 g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (60 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 32 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. The dried product was recrystallized from methanol to give a colorless solid. The recrystallized product was again purified by column chromatography by using silica gel as the stationary phase and acetone as eluting solvent. **Yield = 1.9 g (50%)**, **Melting point = 104-106 ºC; λmax in methanol-279 nm; IR (KBr): 3217 (–NH), 2989, 1722 & 1676 (-C=O of –CONH & -CH2-CO), 1589 (C=C, Str) 1292 (-CH3), 1238 (C-O, Str), 1220, 1170, 1060 (C-Cl), 962, 821, 740 & 667 (C=S-C) cm⁻¹, respectively; ¹HNMR (CDCl₃): δ = 3.70 - 3.85 (s, 2H, CH₂), 4.32 - 4.56 (s, 2H, COCH₂O), 5.90 (s, 1H, CH), 6.65 - 7.25 (m, 8H, Aromatic), 8.05 (br s, 1H, NH) ppm; **Mass spectrum: MS (ESI) = m/z 377 (M⁺); 379 (M+2), 237 (M-C₇H₆OCl)***.

Table-7: TLC profile of PMB -TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.86</td>
</tr>
<tr>
<td>02</td>
<td>Acetonitrile : acetone : methanol (40:10:50)</td>
<td>0.80</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-(4-methylbenzyldene)acetohydrazide

2-(4-Chlorophenoxy)-N-(4-oxo-2-p-tolylthiazolidin-3-yl)acetamide (PMB -TGA)
IR Spectrum of PMB-TGA

![IR Spectrum Graph](image-url)
Mass Spectrum of PMB - TGA

Mol. Wt = 377

MS Spectrum

Line#: 1  R.Time: 0.559(Scan#: 34) Positive
MassPeaks: 195  BasePeak: 377.10 (1798239)
RawMode: Single 0.559(34)
BG Mode: Peak Start 0.377(23)
$^1$H NMR Spectrum of PMB - TGA

![Chemical Structure](image)

**IISc-NRC**

**NAME** 14_VasanthaRaju_11
**EXPNO** 10
**PROCNO** 1
**Date** 20090514
**Time** 21:30
**INSTRUM** spect
**PROBND** 5 mm PABBO NS-
**PULPROG** zg30
**TD** 65536
**SOLVENT** CDCl3
**NS** 16
**DS** 2
**SWR** 8223.685 Hz
**FIDRES** 0.125483 Hz
**AQ** 3.9846387 sec
**BG** 203
**DW** 60.800 us
**DE** 6.50 us
**TE** 298.0 K
**DI** 1.00000000 sec
**TD0** 1

**CHANNEL f1 =======**
**NUCl** 1H
**FL** 14.10 us
**FL1** -3.00 dB
**FL1W** 13.48193649 W
**SPO1** 400.2324716 MH;
**XI** 12768
**SF** 400.2300205 MH;
**WDW** 80
**SBB** 0
**LB** 0.30 Hz
**GB** 0
**PC** 1.00

[Image of NMR Spectrum]
4.1. h: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 8; PFB- TGA)

4.1. h. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N’-(4-fluorobenzylidene)acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask p-fluorobenzaldehyde (1.24g, 0.01mol) was dissolved in methanol (20ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized with methanol. Yield = 2.80 g (91%), Melting point = 181-182 ºC.

Reaction:

\[
\begin{align*}
\text{Cl-OCH}_2\text{CONH}_2 + \text{OHC-F} & \rightarrow \\
\text{Cl-OCH}_2\text{C-CH}_2\text{CONH-N=CH-F} & \rightarrow \\
2-(4\text{-Chlorophenoxy})-N'-(4\text{-fluorobenzylidene})\text{acetohydrazide}
\end{align*}
\]
4.1. h. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)acetamide (PFB -TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'- (4-fluorobenzylidene)acetohydrazide (3.07 g, 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (60 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield = 2.0 g (52%), Melting point = 116-118 °C; \( \lambda_{max} \) in methanol=281 nm;**

**IR (KBr):** 3209 (-NH), 2922, 1710 & 1708 (-C=O of –CH₂CO- & -CONH), 1599 (C=C, Str), 1230 (C-O, Str), 1163 (C-F), 1070 (C-Cl), 1008, 829, 752 & 671(C-S-C) cm⁻¹ , respectively; **¹HNMR (CDCl₃):** \( \delta = 3.70 - 3.85 \) (s, 2H, CH₂), 4.50 - 4.60 (s, 2H, CO-CH₂-O), 5.9 (s, 1H, CH), 6.70 - 7.85 (m, 8H, Aromatic), 7.95 (br s, 1H, NH) ppm; **Mass spectrum: MS(ESI) = m/z 381, 341 (M-Cl').**

### Table-8: TLC profile of PFB -TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>Rf values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.86</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.77</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{array}{c}
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} = \text{CH} - \text{F} \\
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{S} - \text{O} - \text{F} \\
\end{array}
\]

2-(4-Chlorophenoxy)-N'-(4-fluorobenzylidene)acetohydrazide

\[
\begin{array}{c}
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} = \text{CH} - \text{F} \\
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{S} - \text{O} - \text{F} \\
\end{array}
\]

2-(4-Chlorophenoxy)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)acetamide (PFB- TGA)
IR Spectrum of PFB - TGA

Chemistry
Mass Spectrum of PFB-TGA

\[
\text{Cl} \quad \text{O} \quad \text{CH}_2 \quad \text{O} \quad \text{NH} \quad \text{N} \quad \text{CH} \quad \text{S} \quad \text{O} \quad \text{F}
\]

Mol. Wt = 381

MS Spectrum

Line#: 1  R.Time: 0.539(Scan#: 33) Negative
MassPeaks: 209  BasePeak: 379.20(3280516)
RawMode: Single 0.539(33)
BG Mode: Peak Start 0.343(21)
$^1$H NMR Spectrum of PFB-TGA

Chemistry
4.1. i: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,4-dimethoxyphenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 9; VERA -TGA)

4.1. i. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N’-(3, 4-dimethoxy benzylidene)acetohydrazide:

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask veratraldehyde (3,4-Dimethoxybenzaldehyde) (1.66g, 0.01 mol) was dissolved in methanol (10ml) in a separate beaker by heating. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 10 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 3.4 g (97%), Melting point = 195-196 ºC.

Reaction:

\[
\begin{align*}
\text{Cl-OCH}_2\text{CONHNH}_2 + \text{OHC-OCH}_3 \\
\text{Cl-OCH}_2\text{C-NH-N=CH-OCH}_3 \\
\text{2-(4-Chlorophenoxy)-N’-(3,4-dimethoxybenzylidene)acetohydrazide}
\end{align*}
\]
4.1. i. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3, 4-dimethoxy phenyl)-4-oxothiazolidin-3-yl)acetamide (VERA -TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(3,4-dimethoxybenzylidene)acetohydrazide (3.07g , 0.01 mol) and mercaptoacetic acid (2 ml, 98%) were taken in dry benzene (150 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. Yield = 3.0 g (71%); Melting point = 156-158 °C; λ_max in methanol-279 nm; IR (KBr): 3448 (-NH), 3026 (Ar, C-H, Str), 2974, 1703 & 1662 (-C=O of -CONH & –CH₂-C=O), 1593 (C=C, Str), 1236 (C-O, Str), 1072 (C-Cl), 950, 821, 796 & 669 (C-S-C) cm⁻¹ respectively; ¹HNMR (CDCl₃): δ = 3.70 - 3.85 (s, 2H, CH₂), 3.88 (t, 6H, (OCH₃)₂), 4.49 - 4.59 (s, 2H, CH₂), 5.89 (s, 1H, CH), 6.68 - 7.20 (m, 8H, Aromatic), 8.00 (br s, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 423, 383 (M-Cl⁻), 294 (M-C₆H₄OCI⁻).

Table-9: TLC profile of VERA- TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.86</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
&\text{Cl} - \overset{\text{O}}{\text{O}} - \overset{\text{CH}_2}{\text{C}} - \overset{\text{NH}}{\overset{\text{N} = \text{CH}}{\text{N}}} - \overset{\text{S}}{\overset{\text{O}}{\text{O}} \text{CH}_3} \\
\rightarrow& \\
&\text{Cl} - \overset{\text{O}}{\text{O}} - \overset{\text{CH}_2}{\text{C}} - \overset{\text{NH}}{\overset{\text{N}}{\overset{\text{CH}}{\text{N}}}} - \overset{\text{O}}{\overset{\text{C}}{\overset{\text{H}_3}{\text{OCH}_3}}} \\
&\text{2-(4-Chlorophenoxy)-N-(2-(3,4-dimethoxyphenyl)-4-oxothiazolidin-3-yl)acetamide} \\
&\text{(VERA-TGA)}
\end{align*}
\]
IR Spectrum of VERA-TGA

Chemistry
Mass Spectrum of VERA - TGA

Mol. Wt = 423

MS Spectrum

Line#: 1  R.Time: 0.535(Scan#: 32) Negative
MassPeaks: 248  BasePeak: 421.20(5249453)
RawMode: Single 0.535(32)
BG Mode: Peak Start 0.327(20)
$^{1}H$ NMR Spectrum of VERA-TGA

![NMR Spectrum Image]

VERA TGA
4.1. j: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(furan-2-yl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 10; FURAL-TGA)

4.1. j. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(furan-2-ylmethylene) acetohydrazide

p-Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask furan-2-carbaldehyde (0.96g, 0.01 mol) was dissolved in methanol (10ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 2.65 g (95%), Melting point = 166-167 ºC.

**Reaction:**

\[
\text{Cl} \quad \text{OCH}_2\text{CONHNH}_2 \quad + \quad \text{OHC} \quad \text{O} \quad \text{C} \quad \text{N} \quad \text{N} \quad \text{H} \quad \text{C}
\]

\[
\text{Cl} \quad \text{O} \quad \text{CH}_2\text{C} \quad \text{NH} \quad \text{N} \quad \text{N} \quad \text{H} \quad \text{C} \quad \text{O} \quad \text{C} \quad \text{NH} \quad \text{N} \quad \text{H} \quad \text{C}
\]

2-(4-Chlorophenoxy)-N’-(furan-2-ylmethylene)acetohydrazide
4.1. j. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(furan-2-yl)-4-oxothiazolidin-3-yl)acetamide (FURAL -TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'-(furan-2-ylmethylene)acetohydrazide (2.78g, 0.01 mol) and mercaptoacetic acid (2.3 ml, 98%) were taken in dry benzene (120 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33hrs). The mixture was cooled and solvent was evaporated *in vacuo*. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. The crude product was recrystallized from methanol. The recrystallized solid was again purified with alumina neutral as stationary phase and acetone: methanol (10:90) as the mobile phase. **Yield** = 2.3 g (66%), **Melting point** = 128-129 °C; \( \lambda_{\text{max}} \) in methanol-279 nm; **IR (KBr)**: 3429 (-NH), 3053 (Ar, C-H, Str), 2978, 1708 & 1668 (-C=O of -CONH & –CH2-C=O), 1589 (C=C, Str), 1236 (C-O, Str), 1103 (ether linkage, C-O-C), 1068(C-Cl), 933, 827, 744 & 669 (C-S-C) cm\(^{-1}\), respectively; **\(^1\)HNMR (CDCl\(_3\))**: \( \delta = 3.70 - 3.82 \) (s, 2H, CH\(_2\)), 4.52 - 4.64 (s, 2H, CO- CH\(_2\)-O), 5.97 (s, 1H, CH), 6.78 - 6.90 (m, 3H, Furan), 7.23 - 7.42 (m, 4H, aromatic), 8.13 (br s, 1H, NH) ppm; **Mass spectrum: MS (ESI)** = m/z 353, 223 (M-C\(_7\)H\(_6\)OCl\(^-\)).

### Table-10: TLC profile of FURAL -TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.63</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.65</td>
</tr>
</tbody>
</table>
Chemistry

Reaction:

\[
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - N \equiv H - \text{C} - \text{O} - \text{F}\]

2-(4-Chlorophenoxy)-N'-(furan-2-ylmethylene)acetohydrazide

\[
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} - \text{C} - \text{O} - \text{S} - \text{O} - \text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} - \text{C} - \text{O} - \text{F}\]

2-(4-Chlorophenoxy)-N-(2-(furan-2-yl)-4-oxothiazolidin-3-yl)acetamide (FURAL-TGA)
IR Spectrum of FURAL- TGA

![IR Spectrum of FURAL- TGA](image)
Mass Spectrum of FURAL - TGA

Mol. Wt = 353

MS Spectrum

Line# 1  R.Time: 0.540(Scan#:33)  Negative
MassPeaks: 145  BasePeak: 351.15(1213672)
RawMode: Single 0.540(33)
BG Mode: Peak Start 0.310(19)
\(^1\)H NMR Spectrum of FURAL- TGA

![Chemical Structure]

**Parameters:**
- **NAME:** 14_VasanthaRaju_11
- **EXPNO:** 1
- **PROCNO:** 1
- **Date:** 20090514
- **Time:** 17.38
- **INSTRUM:** spect
- **PROBHD:** 5 mm PARBO BB-
- **PULPROG:** zg30
- **TD:** 65536
- **SOLVENT:** CDC13
- **NS:** 16
- **DS:** 2
- **SNH:** 8233.6 Hz
- **FIDRES:** 0.125483 Hz
- **AQ:** 3.9846387 sec
- **DG:** 203
- **DM:** 60.888 us
- **DE:** 6.50 us
- **TS:** 298.0 K
- **D1:** 1.0000000 sec
- **TDO:** 1

**CHANNEL F1:**
- **NHC1:** 1H
- **P1:** 14.10 us
- **P11:** -3.00 dB
- **PL1W:** 13.48193645 W
- **SPO1:** 400.2384716 MHz
- **SI:** 32768
- **ST:** 400.2300200 MHz
- **MDW:** EM
- **SSB:** 0
- **Ls:** 0.30 Hz
- **GS:** 0
- **PC:** 1.00
4. 1. k: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(4-oxo-2-(4-(trifluoro methyl)phenyl)thiazolidin-3-yl)acetamide: (Compound No. 11; TRIFLU- TGA)

4. 1. k. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-((trifluoro methyl)benzylidene)acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask α, α, α-trifluoro p-tolualdehyde (1.74g, 0.01 mol) was dissolved in methanol (20ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The solution was left over night. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 2.75 g (77%), Melting point = 152-154 ºC.

Reaction:

\[
\text{Cl} \text{OCH}_2 \text{CONHNH}_2 + \text{OHC} \overset{\text{F}}{\text{F}} \overset{\text{F}}{\text{F}} \text{C} \overset{\text{Cl}}{\text{O}} \text{CH}_2 \text{CONHNH}_2 \rightarrow \text{Cl} \text{OCH}_2 \text{C} \overset{\text{NH}}{\text{N}} \overset{\text{F}}{\text{F}} \overset{\text{C}}{\text{F}} \text{O} \]

2-(4-chlorophenoxy)-N'-((trifluoromethyl)benzylidene)acetohydrazide
4.1. k. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)acetamide: (TRIFLU- TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'(4-(trifluoromethyl)benzylidene)acetohydrazide (3.57g, 0.01 mol) and mercaptoacetic acid (2.4 ml, 98%) were taken in dry benzene (90 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 48hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. Yield = 3.5 g (81%), Melting point = 140-141 °C; \( \lambda_{\text{max}} \) in methanol-283 nm; IR (KBr); 3275 (-NH), 3090 (Ar, C-H, Str), 2937, 1735 & 1716(-C=O of -CONH & –CH$_2$-O), 1595 (C=C, Str), 1228 (C-O, Str), 1163 (C-F, Sym), 1055(C-Cl), 960, 850 & 666 (C-S-C) cm$^{-1}$, respectively; $^1$HNMR (CDCl$_3$): \( \delta = 3.72 - 3.89 \) (s, 2H, CH$_2$), 4.50 - 4.70 (s, 2H, CO-CH$_2$-O), 5.95 (s, 1H, CH) 6.70 - 7.86 (m, 8H, Aromatic), 8.00 (br s, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 431, 391(M-Cl).

Table-11: TLC profile of TRIFLU- TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.83</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-((trifluoromethyl)benzyldene)acetohydrazide

\[ \text{Cl} \quad \overset{\text{O}}{\text{O}} \quad \underset{\text{CH}_2}{\text{C}} \quad \overset{\text{O}}{\text{NH}} \quad \overset{\text{N} = \text{CH}}{\text{C}} \quad \overset{\text{F}}{\text{F}} \quad \overset{\text{F}}{\text{F}} \]

2-(4-Chlorophenoxy)-N-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)acetamide

\( \text{TRIFLU- TGA} \)
IR Spectrum of TRIFLU- TGA
Mass Spectrum of TRIFLU-TGA

Mol. Wt. = 431

MS Spectrum

Line#: 1  R.Time: 0.551(Scan#: 33) Negative
MassPeaks: 361  BasePeak: 429.25(7561613)
RawMode: Single 0.551(33)
BG Mode: Peak Start 0.327(20)
$^{1}$H NMR spectrum of TRIFLU-TGA
4.1.1: Procedure for the preparation of N-(2-(4-Bromophenyl)-4-oxothiazolidin-3-yl)-2-(4-chlorophenoxy)acetamide: (Compound No. 12; PBB- TGA)

4.1.1.1: Procedure for the preparation of N’-(4-Bromobenzylidene)-2-(4-chlorophenoxy)acetohydrazide:

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed p-Bromobenzaldehyde (1.85g, 0.01mol) was dissolved in methanol (20ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 15 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 3.5 g (95%), Melting point=195-196 ºC.

**Reaction:**

![Reaction equation](image)
4.1.1.2: Procedure for the preparation of N-(2-(4-Bromophenyl)-4-oxothiazolidin-3-yl)-2-(4-chlorophenoxy)acetamide: (PBB- TGA)

The method of Surrey (1949) was followed. N'-(4-Bromobenzylidene)-2-(4-chlorophenoxy)acetohydrazide (3.67g, 0.01 mol) and mercaptoacetic acid (2.5 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropically distillation of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield = 4.1 g (92%), Melting point=141-143 °C; $\lambda_{\text{max}}$ in methanol-278 nm; IR (KBr): 3448 (-NH), 3051 (Ar, C-H, Str), 2982, 1714 & 1674 (-C=O of–CH$_2$-C=O & -CONH) 1587 (C=C, Str), 1230 (C-O, Str), 1176, 1058 (C-Cl), 964, 829 & 673 (C-S-C) cm$^{-1}$, respectively; $^1$HNMR (CDCl$_3$): $\delta = 3.05 - 3.26$ (s, 2H, CH$_2$), 3.78 - 3.95 (s, 2H, -CH$_2$-CO), 5.64( s, 1H, CH), 6.11 - 6.72 (m, 4H, Aromatic), 6.87 - 7.15 (m, 4H, Aromatic), 7.84 (br s, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 442, 363 (M-Br), 404 (M-Cl), 312 (M-C$_6$H$_4$OCl)).

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.73</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.80</td>
</tr>
</tbody>
</table>
Reaction:

\[ \text{Cl-} \quad \text{O-} \quad \text{CH}_2 \quad \text{C-} \quad \text{NH} \quad \text{N=CH} \quad \text{Br} \]

\[ N'-(4-\text{Bromobenzylidene})-2-(4-\text{chlorophenoxy})\text{acetohydrazide} \]

\[ \downarrow \]

\[ \text{Cl-} \quad \text{O-} \quad \text{CH}_2 \quad \text{C-} \quad \text{NH} \quad \text{S} \quad \text{N} \quad \text{CH} \quad \text{Br} \]

\[ N-(2-(4-\text{Bromophenyl})-4-\text{oxothiazolidin}-3-\text{yl})-2-(4-\text{chlorophenoxy})\text{acetamide} (\text{PBB-TGA}) \]
Mass Spectrum of PBB - TGA

\[ \text{Mol. Wt.} = 442 \]

MS Spectrum

Line# 1 R.Time: 0.555 (Scan#: 34) Negative
MassPeaks: 248 BasePeak: 441.10 (3334944)
RawMode: Single 0.555 (34)
BG Mode: Peak Start 0.327 (20)
$^1$H NMR Spectrum of PBB-TGA
4.1. m: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,4-dichlorophenyl)-4-oxothiazolidin-3-yl)acetamide (Compound No. 13; DCL - TGA)

4.1. m. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N’-(3, 4-dichlorobenzylidene)acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed 3,4-dichlorobenzaldehyde (1.75g, 0.01 mol) was dissolved in methanol (25ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. To this a few drops of glacial acetic acid were added and refluxed for 15 minutes. The resultant solid was filtered under vacuum. The Schiff’s base was recrystallized from methanol. Yield = 3.0 g (84%), Melting point=179-181 °C.

Reaction:

\[
\text{Cl}-\text{OCH}_2\text{CONHNH}_2 + \text{OHC-Cl}
\]

\[
\begin{array}{c}
\text{Cl} \\
\text{O} \\
\text{C} \\
\text{H}_2 \\
\text{N}
\end{array} \quad \text{Cl}
\]

\[
\begin{array}{c}
\text{Cl} \\
\text{O} \\
\text{C} \\
\text{H}_2 \\
\text{N}
\end{array} \quad \text{N} = \text{C} \\
\text{Cl} \\
\text{Cl}
\]

2-(4-Chlorophenoxy)-N’-(3,4-dichlorobenzylidene)acetohydrazide
4.1. m. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,4-dichlorophenyl)-4-oxothiazolidin-3-yl)acetamide: (DCL - TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(3,4-dichlorobenzylidene)acetohydrazide (3.58 g, 0.01 mol) and mercaptoacetic acid (2.5 ml, 98%) were taken in dry benzene (130 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 48 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The thick oily mass was kept overnight in dilute sodium bicarbonate solution for solidification. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. Yield = 4.0 g (92%), Melting point=142-143 °C; $\lambda_{\text{max}}$ in methanol-279 nm; IR (KBr): 3228 (-NH), 3022 (Ar, C-H, Str), 2914, 1730 & 1687 (-C=O of–CH$_2$-C=O & -CONH), 1585 (C=C, Str), 1481, 1369, 1219 (C-O, Str), 1130, 1060 (C-Cl), 960, 823, 758 & 667 (C-S-C) cm$^{-1}$, respectively; $^1$HNMR (CDCl$_3$): $\delta = 3.11$ - 3.29 (s, 2H, -CH$_2$), 3.88 - 4.05 (s, 2H, -CH$_2$-CO), 5.64 (s, 1H, CH), 6.39 - 6.82 (m, 3H, Aromatic), 6.88 - 7.33 (m, 4H, Aromatic), 8.52 (br s, 1H, NH) ppm; Mass spectrum: MS (ESI) = m/z 432, 261 (M-C$_8$H$_9$O$_2$Cl$^-$).

Table-13: TLC profile of DCL- TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (35:65)</td>
<td>0.78</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.83</td>
</tr>
</tbody>
</table>
Reaction:

\[
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} = \text{CH} - \text{Cl}
\]

2-(4-Chlorophenoxy)-N'-(3,4-dichlorobenzylidene)acetohydrazide

\[
\text{Cl} - \text{O} - \text{CH}_2 - \text{C} - \text{NH} - \text{N} - \text{CH} - \text{S} - \text{O} - \text{Cl} - \text{Cl}
\]

2-(4-Chlorophenoxy)-N-(2-(3,4-dichlorophenyl)-4-oxothiazolidin-3-yl)acetamide

(DCL-TGA)
IR Spectrum of DCL- TGA

![IR Spectrum Diagram]

**Chemistry**

93
Mass Spectrum of DCL-TGA

Mol. Wt. = 432

MS Spectrum

Line#:1  R.Time:0.575(Scan#:35) Negative
MassPeaks:311  BasePeak:431.15(3661757)
RawMode:Single 0.575(35)
BG Mode:Peak Start 0.327(20)
$^1$H NMR Spectrum of DCL- TGA
4.2. Thiazolidin- 4-one derivatives of Clofibric acid

Part- I: Procedure for the preparation of Ethyl 2-(4-chlorophenoxy)-2-methylpropanoate:

2-(4-Chlorophenoxy)-2-methylpropanoic acid (12.84g, 0.06mol) was dissolved in ethanol (25 ml). Concentrated sulphuric acid (5 ml) was added and refluxed for 3 hours. The solution was cooled and poured into crushed ice. Sodium bicarbonate was added to remove the excess acid and extracted with ether. The ether extract was dried over sodium sulphate. The ether layer was evaporated to get a thick concentrated ester. Yield = 13.2g (90%)

Reaction:
Part- II: Procedure for the preparation of 2-(4-Chlorophenoxy)-2-methylpropanehydrazide

Ethyl 2-(4-chlorophenoxy)-2-methylpropanoate (24.3g, 0.1mol) was taken in 100 ml round bottomed flask and 5.2 ml of 99% hydrazine hydrate (0.1mol) and ethanol (30 ml) were added and refluxed for six hours. Ethanol was removed under reduced pressure and then poured into a beaker containing ice cubes. The hydrazide was extracted with solvent ether and ether was evaporated to get the oily liquid of hydrazide and dried over sodium sulphate. Yield = 12 g (53%).

Reaction:
4. 2. a: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide: (Compound No. 14; CLOANI-TGA)

4.2. a. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(4-methoxybenzylidene)-2-methylpropanehydrazide:

2-(4-Chlorophenoxy)-2-methylpropanehydrazide (2.3g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. To this, anisaldehyde (1.36g, 0.01mol) was added after dissolving in 20 ml methanol. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant mass was concentrated under vacuum. The crude Schiff’s base was recrystallized from methanol. Yield = 3.3 g (95%), Melting point = 194 - 196 °C.

Reaction:

\[
\begin{align*}
\text{Cl} & - \text{O} - \text{C} - \text{CONHNH}_2 + \text{OHC} - \text{OCH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 & \quad \text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & - \text{O} - \text{C} - \text{C} - \text{NH} - \text{N} = \text{CH} - \text{OCH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 & \quad \text{O} & \quad \text{O} & \quad \text{OCH}_3 \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N'-(4-methoxybenzylidene)-2-methylpropanehydrazide
4. 2. a. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide (CLOANI- TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(4-methoxybenzylidene)-2-methylpropanehydrazide (3.47 g, 0.01 mol) and mercaptoacetic acid (2.0 ml, 98%) were taken in dry benzene (30 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The thick oily mass was kept overnight in dilute sodium bicarbonate solution for solidification. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a crystalline solid. Yield = 2.5 g (60%), Melting point = 142-143 °C; λ_{max} in methanol-235 nm; IR (KBr): 3281 (-NH), 3080 (Ar, C-H, Str), 2892, 1710 & 1680 (-C=O of-CH_{2}-C=O & -CONH), 1612 (C=C, Str), 1251 (C-O, Str), 1143, 1095 (C-Cl), 848, 817, 709 & 663 (C-S-C) cm^{-1}, respectively; ^{1}HNMR (CDCl_{3}): δ = 1.37 (t, 3H, -CH_{3}), 1.47 (t, 3H, -CH_{3}), 3.66 - 3.70 (t, 2H, OCH_{3}), 3.80 - 3.84 (s, 2H, CH_{2}), 5.90 (s, 1H, CH), 6.75-7.35 (m, 8H, Aromatic), 8.17(br s, 1H, -NH) ppm; Mass spectrum: MS (ESI) = m/z 421 293, (M-C_{6}H_{4}OCl), 312 (M-C_{7}H_{7}O') .

Table-14: TLC profile of CLOANI -TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Methanol: acetone (60:40)</td>
<td>0.78</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
\text{Cl} & \quad \text{O} \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{O} \\
\text{Cl} & \quad \text{O} \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{O} \\
\text{Cl} & \quad \text{O} \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{O}
\end{align*}
\]

2-(4-Chlorophenoxy)-N′-(4-methoxybenzylidene)-2-methylpropanehydrazide

\[
\begin{align*}
\text{Cl} & \quad \text{O} \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{O} \\
\text{Cl} & \quad \text{O} \quad \text{C} \quad \text{C} \quad \text{O} \quad \text{N} \quad \text{H} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{O}
\end{align*}
\]

2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide (CLOANI-TGA)
IR Spectrum of CLOANI- TGA

Chemistry
Mass Spectrum of CLOANI- TGA

mol. Wt. = 421

MS Spectrum

Line#: 1 R.Time: 0.621(Scan#: 38) Negative
MassPeaks: 414 BasePeak: 419.25(7990694)
RawMode: Single 0.621(38)
BG Mode: Peak Start 0.327(20)
$^1$H NMR Spectrum of CLOANI- TGA
4. 2. b: Procedure for the preparation of 2-(4-Chlorophenoxy)-2-methyl-N-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)propanamide (Compound No. 15; CLOTRIFLU-TGA)

4. 2. b. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-2-methyl-N'-(4-(trifluoromethyl)benzylidene)propanehydrazide

2-(4-Chlorophenoxy)-2-methylpropanehydrazide (2.3g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. To this, 4-(trifluoromethyl)benzaldehyde (1.74g, 0.01 mol) was added after dissolving in 10 ml methanol. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant mass was concentrated under vacuum. The crude Schiff’s base was purified from methanol. Yield = 3.0 g (78%), Melting point = 134 - 136 °C.

Reaction:

\[
\text{Cl}_2\text{C}_6\text{H}_4\text{O} - \text{C} - \text{CONHNH}_2 + \text{OHC}_6\text{H}_4\text{CH}_3\text{F}_3\text{F}^2 \\
\downarrow \\
\text{Cl}_2\text{C}_6\text{H}_4\text{O} - \text{C} - \text{C} - \text{NH} - \text{N} = \text{CH} - \text{C}_6\text{H}_4\text{CH}_3\text{F}_3\text{F}^2 \\
\]

2-(4-Chlorophenoxy)-2-methyl-N'-(4-(trifluoromethyl)benzylidene)propanehydrazide
4. 2. b. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-2-methyl-N-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)propanamide (CLOTRIFLU-TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-2-methyl-N’-(4-(trifluoromethyl)benzylidene)propanehydrazide (3.85 g, 0.01 mol) and mercaptoacetic acid (2.0 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 32 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield = 4.0 g (87%)**, **Melting point = 159-160 °C; \( \lambda_{\text{max}} \)** in methanol-272 nm; **IR (KBr):** 3279 (-NH), 3082 (Ar, C-H, Str), 2995, 1716 & 1689(-C=O of–CH\(_2\)-C=O & -CONH), 1587 (C=C, Str), 1228 (C-O, Str), 1158 (C-F, Sym), 1068 (C-Cl), 817, 758 & 667 (C-S-C) cm\(^{-1}\), respectively; \(^1\)HNMR (CDCl\(_3\)): \( \delta = 1.37 \) (t, 3H, -CH\(_3\)), 1.46 (t, 3H, -CH\(_3\)), 3.72 - 3.87 (s, 2H, CH\(_2\)), 5.90 (s, 1H, CH), 6.79 - 7.65 (m, 8H, Aromatic), 8.14 (br s, 1H, -NH) ppm; **Mass spectrum:** MS (ESI) = m/z 459, 312 (M-C\(_7\)H\(_4\)F\(_3\)), 420(M-CI\(^-\)).

**Table-15: TLC profile of CLOTRIFLU -TGA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>( R_f ) values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.82</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.51</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
\text{2-(4-Chlorophenoxy)-2-methyl-N'-(4-(trifluoromethyl)benzylidene)propanehydrazide} \\
\text{\downarrow} \\
\text{2-(4-Chlorophenoxy)-2-methyl-N-(4-oxo-2-(4-(trifluoromethyl)phenyl)thiazolidin-3-yl)propanamide} \\
\text{(CLOTRIFLU-TGA)}
\end{align*}
\]
IR Spectrum of CLOTRIFLU- TGA

[Chemical structure image]

[Graph with IR spectrum data]
Mass Spectrum of CLOTRIFLU- TGA

Mol. Wt. = 459

Line#1  R.Time:0.541(Scan#:33) Negative
MassPeaks:259  BasePeak:457.20(11004471)
RawMode:Single 0.541(33)
BG Mode:Peak Start 0.310(19)
$^1$H NMR Spectrum of CLOTRIFLU-TGA
4.2. c: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide (Compound No. 16; CLOPFB - TGA)

4.2. c. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(4-fluorobenzylidene)-2-methylpropanehydrazide:

2-(4-Chlorophenoxy)-2-methylpropanehydrazide (2.3g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. To this, 4-Fluorobenzaldehyde (1.24g, 0.01 mol) was added after dissolving in 10 ml methanol. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant mass was concentrated under vacuum. The crude Schiff’s base was recrystallized from methanol. Yield = 3.1 g (92%), Melting point = 196-198 ºC.

Reaction:

\[
\text{ClOC} \overset{\text{CONHNH}_2}{\longrightarrow} + \text{OHC} \overset{\text{F}}{\longrightarrow} \rightarrow \text{ClOC} \overset{\text{CONHN} \equiv \text{CH}}{\longrightarrow} \overset{\text{F}}{\longrightarrow}
\]

2-(4-Chlorophenoxy)-N’-(4-fluorobenzylidene)-2-methylpropanehydrazide
4.2. c. 2.: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide (CLOPFB-TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'-(4-fluorobenzylidene)-2-methylpropanehydrazide (3.35 g, 0.01 mol) and mercaptoacetic acid (2.0 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. Yield = 3.5 g (86%), Melting point = 130-132 °C; $\lambda_{\text{max}}$ in methanol-271 nm; IR (KBr): 3250 (-NH), 3043 (Ar, C-H, Str), 2985, 1726 & 1674 (-C=O of-CH$_2$C=O & -CONH), 1599 (C=C, Str), 1228 (C-O, Str), 1157 (C-F), 1085 (C-Cl), 937, 850 & 648 (C-S-C) cm$^{-1}$, respectively; $^1$HNMR (CDCl$_3$): $\delta = 1.37$ (t, 3H, -CH$_3$), 1.47 (t, 3H, -CH$_3$), 3.67 - 3.85 (s, 2H, CH$_2$), 5.90 (s, 1H, CH), 6.77 - 7.43 (m, 8H, Aromatic), 8.10 (br s, 1H, -NH) ppm; Mass spectrum: MS (ESI) = m/z 409, 286 (M-C$_6$H$_4$OCl$^-$), 249 (C$_6$H$_4$OCl$^-$-Cl).

Table-16: TLC profile of CLOPFB-TGA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R$_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.78</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.42</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-(4-fluorobenzylidene)-2-methylpropanehydrazide

\[\text{CL O P F B - T G A}\]
IR Spectrum of CLOPFB - TGA:

![Chemical Structure](image)

![Graph of IR Spectrum and TGA](image)
Mass Spectrum of CLOPFB- TGA

Mol. Wt. = 409
$^1$H NMR Spectrum of CLOPFB- TGA
4. 2. d: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-oxythiazolidin-3-yl)-2-methylpropanamide (Compound No. 17; CLOBHT-TGA)

4.2. d. 1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(3,5-di-tert-butyl-4-hydroxybenzylidene)-2-methylpropanehydrazide:

2-(4-Chlorophenoxy)-2-methylpropanehydrazide (2.3g, 0.01mol) was dissolved in methanol (30 ml) in 250 ml round bottomed flask. To this, 3,5-di-tert-butyl-4-hydroxybenzaldehyde (2.34g, 0.01 mol) was added after dissolving in 100 ml hot methanol. To this a few drops of glacial acetic acid were added and refluxed for 45 minutes. The resultant mass was concentrated under vacuum. The crude Schiff’s base was recrystallized from methanol. Yield = 4.0 g (90%), Melting point = 234-236 ºC.

Reaction:

\[
\begin{align*}
\text{Cl} & \quad \text{O} & \quad \text{C} & \quad \text{CONHNH}_2 & \quad + & \quad \text{OHC} & \quad \text{OH} \\
& & & \text{CH}_3 & & & \quad \text{OH} \\
\downarrow & & \text{OH} & \text{CH}_3 & \text{O} & \text{C} & \text{CONHNH}_2 \quad \text{N} & \quad \text{N} & \quad \text{CH} & \quad \text{OH} \\
\text{Cl} & \quad \text{O} & \quad \text{C} & \quad \text{C} & \quad \text{CONHNH}_2 & \quad + & \quad \text{OHC} & \quad \text{OH} \\
& & & \text{CH}_3 & & & \quad \text{OH} \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N'-(3,5-di-tert-butyl-4-hydroxybenzylidene)-2-methylpropanehydrazide
4. 2. d. 2.: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide (CLOBHT-TGA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(3,5-di-tert-butyl-4-hydroxybenzylidene)-2-methylpropane hydrazide (4.45 g, 0.01 mol) and mercaptoacetic acid (3.0 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 34 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted mercaptoacetic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield** = 2.5 g (48%), **Melting point** = 220-221 °C; $\lambda_{max}$ in methanol-237 nm; **IR (KBr)**: 3636 (-OH), 3543 (-NH), 3001 (Ar, C-H, Str), 2955, 1740 & 1697 (-C=O of –CH$_2$-C=O & -CONH), 1600 (C=C, Str), 1236 (C-O, Str), 1209, 1024 (C-Cl), 887, 773 & 626 (C-S-C) cm$^{-1}$, respectively; **$^1$HNMR (CDCl$_3$)**: $\delta$ = 1.21 - 1.28 (s, 6H, (CH$_3$)$_2$), 1.42 (s, 18H, (CH$_3$)$_6$), 3.06 - 3.44 (s, 2H, s -CH$_2$-CO-), 4.54 (s, 1H, -OH), 5.03 -5.17(s, 2H, Aromatic), 6.23 (s, 1H, CH), 7.45 - 7.57 (m, 4H, Ar’) ppm, respectively ; **Mass spectrum**: MS (ESI) = m/z 518, 321 (M- C$_{10}$H$_{11}$O$_2$Cl).

**Table-17: TLC profile of CLOBHT- TGA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>$R_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Methanol : acetone (60:40)</td>
<td>0.82</td>
</tr>
<tr>
<td>02</td>
<td>Ethyl acetate: petroleum ether (60:80): methanol (20:75:05)</td>
<td>0.63</td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-{(3,5-di-tert-butyl-4-hydroxybenzylidene)-2-methylpropanehydrazide} 

2-(4-Chlorophenoxy)-N-{(2-(3,5-di-tert-butyl-4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-2-methylpropanamide} 

(CLOBHT- TGA)
IR Spectrum of CLOBHT- TGA:
Mass Spectrum of CLOBHT-TGA:

Mol. Wt. = 518

Line#: 1  R.Time: 0.528(Scan#: 32) Negative
MassPeaks: 749  BasePeak: 611.45(3893445)
RawMode: Single 0.528(32)
BG Mode: Peak Start 0.343(21)
$^1$H NMR Spectrum of CLOBHT-TGA
4.3. Thiazolidin-4-one derivatives of p-Chlorophenoxyacetic acid from Thiolactic acid

4.3. a: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-5-methyl-4-oxothiazolidin-3-yl)acetamide (Compound No. 18; ANI- TLA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N’-(4-methoxybenzylidene)acetohydrazide (3.19 g, 0.01 mol) and thiolactic acid (2.0 ml, 98%) were taken in dry benzene (30 ml) in 50 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 36 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any un reacted thiolactic acid. The thick oily mass was kept overnight in dilute sodium bicarbonate solution for solidification. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield = 3.0 g (75%)**, **Melting point =**114-115 °C; $\lambda_{\text{max}}$ in methanol-277 nm; IR (KBr): 3281 (-NH), 2935, 1735 & 1683 (-C=O of–CH$_2$-C=O & -CONH), 1587(C=C, Str), 1383 (-CH$_3$), 1244 (C-O, Str), 1165, 1064 (C-Cl), 964, 821,744 & 636(C-S-C) cm$^{-1}$ respectively; $^1$HNMR (CDCl$_3$): $\delta = 3.23 - 3.24$ (s, 3H, -CH$_3$), 3.63 - 3.97 (s, 3H, -CH$_2$-CH$_3$), 5.94 (s, 1H, -CH), 6.12 - 6.66 (m, 4H,Ar), 6.84 - 7.15 (m, 4H, Ar’), 8.15 (br s, 1H, -NH) ppm; **Mass spectrum**: MS (ESI) = m/z 407, 368 (M-Cl), 285 (M-C$_6$H$_4$OCl$^-$).

Table-18: TLC profile of ANI- TLA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R$_f$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate : methanol</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>(20 : 80)</td>
<td></td>
</tr>
<tr>
<td>02</td>
<td>Methanol: acetone</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>(60 : 40)</td>
<td></td>
</tr>
</tbody>
</table>
Reaction:

2-(4-Chlorophenoxy)-N'-((4-methoxybenzylidene)acetohydrazide

\[ \text{2-(4-Chlorophenoxy)-N'}-(4-methoxybenzylidene)acetohydrazide \]

2-(4-Chlorophenoxy)-N-(2-(4-methoxyphenyl)-5-methyl-4-oxothiazolidin-3-yl)acetamide

(ANI- TLA)
Mass Spectrum of ANI- TLA

Mol. Wt. = 407
$^1$H NMR spectrum of ANI- TLA
4. 3. b: Procedure for the preparation 2-(4-Chlorophenoxy)-N-(2-(4-chlorophenyl)-5-methyl-4-oxothiazolidin-3-yl)acetamide (Compound No. 19; PCB -TLA)

The method of Surrey (1949) was followed. N’-(4-Chlorobenzylidene)-2-(4-chlorophenoxy)acetohydrazide (3.22 g, 0.01 mol) and thiolactic acid (1.5 ml, 98%) were taken in dry benzene (30 ml) in 100 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted thiolactic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol in cold condition (2 – 8°C) gave a white solid. Yield = 3.2 g (76%), Melting point = 156-157 ºC; λ_max in methanol-279 nm; IR (KBr): 3279(-NH), 3057 (Ar, C-H, Str), 2980, 1726 & 1693 (-C=O of–CH₂-C=O & -CONH), 1585 (C=C, Str), 1383 (-CH₃), 1205 (-C-O, Str), 1168, 1070 (C-Cl), 962, 773 & 636 (C-S-C) cm⁻¹ respectively; HNMR (CDCl₃): δ =1.37 - 1.55 (s, 3H, -CH₃), 3.75 - 3.92 (s, 2H, -CH₂-), 5.69 (s, 1H, -CH), 6.09 - 6.77 (m, 4H,Ar), 6.85 - 7.03 (m, 4H, Ar'), 7.66 (br s, 1H, -NH) ppm; Mass spectrum: MS (ESI) = m/z 411, 339 (M-2Cl).

Table-19: TLC profile of PCB -TLA

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.63</td>
</tr>
<tr>
<td>02</td>
<td>Methanol : acetone (60 : 40)</td>
<td>0.72</td>
</tr>
</tbody>
</table>
Reaction:

$N'-(4$-Chlorobenzylidene)$-2-(4$-chlorophenoxy$)$acetohydrazide$

$\rightarrow$

$2-(4$-Chlorophenoxy$)$-$N$(2-(4-chlorophenyl)$-5$-methyl$)-4$-oxothiazolidin$-3$-yl$)$acetamide

(\textbf{PCB- TLA})
Mass Spectrum of PCB- TLA

Mol. Wt. = 411

MS Spectrum

Line#:1 R.Time:0.550(Scan#:33) Negative
MassPeaks:255 BasePeak:409.15(5293367)
RawMode:Single 0.550(33)
BG Mode:Peak Start 0.327(20)
\(^1\)H NMR Spectrum of PCB- TLA
4.3. c: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(2-(3,4-dichlorophenyl)-5-methyl-4-oxothiazolidin-3-yl)acetamide: (Compound No. 20; DCL - TLA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'-(3,4-dichlorobenzylidene)acetohydrazide (3.56 g, 0.01 mol) and thiolactic acid (1.5 ml, 98%) were taken in dry benzene (80 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 36 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted thiolactic acid. The thick oily mass was kept overnight in dilute sodium bicarbonate solution for solidification. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol gave a white solid. **Yield = 3.8.0 g (85%), Melting point =159-161 °C; λ\text{max} in methanol-278 nm; IR (KBr): 3277 (-NH), 3050(Ar, C-H, Str), 2980, 1726 & 1695 (-C=O of–CH₂-C=O & -CONH), 1585 (C=C, Str), 1490, 1378 (-CH₃), 1217 (-C-O, Str), 1126, 1060 (C-Cl), 966, 821, 738 & 638(C-S-C) cm⁻¹ respectively; HNMR (CDCl₃): δ = 1.34 - 1.53 (s, 3H, -CH₃), 3.67 ( 1H, -CH – CH₃), 3.79 -3.90 (s, 2H, -CH₂-), 5.68 (s, 1H, -CH), 6.61 - 6.95 (m, 3H,Ar), 7.16 - 7.25 (m, 4H, Ar’), 8.36(br s, 1H, -NH) ppm; Mass spectrum: MS (ESI) = m/z 448 (M+2),339 (M-Cl).**

**Table-20: TLC profile of DCL- TLA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>Rₕ values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.75</td>
</tr>
<tr>
<td>02</td>
<td>Methanol : acetone (60 : 40)</td>
<td>0.84</td>
</tr>
</tbody>
</table>
Reaction:

\[
\begin{align*}
\text{2-(4-Chlorophenoxy)-N'-(3,4-dichlorobenzylidene)acetohydrazide} & \quad \rightarrow \quad \text{2-(4-Chlorophenoxy)-N-(2-(3,4-dichlorophenyl)-5-methyl-4-oxothiazolidin-3-yl)acetamide (DCL-TLA)} \\
\end{align*}
\]
IR Spectrum of DCL - TLA
Mass Spectrum of DCL- TLA

Mol. Wt. = 444

MS Spectrum

Line# 1  R.Time: 0.570(Scan#: 35) Negative  MassPeaks: 299  BasePeak: 443.10(2703276)  RawMode: Single 0.570(35)  BG Mode: Peak Start 0.327(20)
$^1$H NMR Spectrum of DCL- TLA

![NMR Spectrum Image]
4.3. d: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(5-methyl-4-oxo-2-(pyridin-2-yl)thiazolidin-3-yl)acetamide: (Compound No. 21; PY- TLA)

4.3. d.1: Procedure for the preparation of 2-(4-Chlorophenoxy)-N'-(pyridin-2-ylmethylene) acetohydrazide

p- Chlorophenoxyacetic acid hydrazide (2.0g, 0.01mol) was dissolved in methanol (30 ml) in 100 ml round bottomed flask. Pyridine 2-aldehyde (picolinaldehyde) (1.07g, 0.01 mol) was dissolved in methanol (10ml) in a separate beaker. Aldehyde solution was added slowly to hydrazide solution present in round bottomed flask. A few drops of glacial acetic acid were added. The mixture was refluxed for 45 minutes. The resultant solid was filtered under vacuum. The Schiff base was recrystallized with methanol. Yield = 1.50 g (52%), Melting point=179-180 °C.

Reaction:

![Reaction diagram]

2-(4-Chlorophenoxy)-N'-(pyridin-2-ylmethylene)acetohydrazide
4.3. d. 2: Procedure for the preparation of 2-(4-Chlorophenoxy)-N-(5-methyl-4-oxo-2-(pyridin-2-yl)thiazolidin-3-yl)acetamide (PY- TLA)

The method of Surrey (1949) was followed. 2-(4-Chlorophenoxy)-N'-(pyridin-2-ylmethylene)acetohydrazide (2.90 g, 0.01 mol) and thiolactic acid (2 ml, 98%) were taken in dry benzene (75 ml) in 250 ml R B flask fitted with Dean-Stark water separator and reflux condenser. A fresh quantity of dry benzene (20 ml) was added in order to replenish the flask after azeotropic removal of water. The reaction was stopped when the distillate was free from turbidity and also monitored by TLC (reaction time; 33 hrs). The mixture was cooled and solvent was evaporated in vacuo. A saturated solution of sodium bicarbonate was poured into the flask and stirred well to neutralize any unreacted thiolactic acid. The solid that separated was filtered, washed and dried. Repeated recrystallization of the crude product from methanol in cold condition (2 – 8°C) gave a white solid. **Yield = 2.8 g (74%), Melting point=139-140 ºC; λ_max in methanal-263 nm; IR (KBr): 3159 (-NH), 2966, 1732 & 1691(-C=O of -CH₂-C=O & -CONH) 1587 (C=C, Str), 1496 (C=N), 1342 (-CH₃), 1238 (-C-O, Str), 1180, 1060 (C-Cl), 997, 829, 754 & 661 (C-S-C) cm⁻¹ respectively; ¹HNMR (CDCl₃): δ = 1.42 - 1.45 (s, 3H, -CH₃), 3.76 - 3.89 (s, 2H, -CH₂), 6.10 (s, 1H, -CH), 6.14 – 6.52 (m, 4H, Pyridine), 6.68 - 6.90 (m, 4H,Ar), 8.45(br s, 1H, -NH) ppm; Mass spectrum: MS (ESI) = m/z 378, 208 (M-C₈H₈O₂Cl⁻).**

**Table-21: TLC profile of PY- TLA**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Solvent system</th>
<th>R_f values</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Ethyl acetate: methanol (20:80)</td>
<td>0.80</td>
</tr>
<tr>
<td>02</td>
<td>Methanol : acetone (60 : 40)</td>
<td>0.68</td>
</tr>
</tbody>
</table>
Chemistry

Reaction:

\[
\begin{align*}
&\text{Cl} \quad \text{O} \quad \text{H}_2\text{C} \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} = \text{CH} \\
\text{Cl} \quad \text{O} \quad \text{CH}_2 \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} \quad \text{CH} \quad \text{S} \\
\end{align*}
\]

\[
\begin{align*}
&\text{Cl} \quad \text{O} \quad \text{H}_2\text{C} \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} = \text{CH} \\
\text{Cl} \quad \text{O} \quad \text{CH}_2 \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} \quad \text{CH} \quad \text{S} \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N’-(pyridin-2-ylmethylene)acetohydrazide

\[
\begin{align*}
&\text{Cl} \quad \text{O} \quad \text{H}_2\text{C} \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} = \text{CH} \\
\text{Cl} \quad \text{O} \quad \text{CH}_2 \quad \text{C} \quad \text{O} \quad \text{NH} \quad \text{N} \quad \text{CH} \quad \text{S} \\
\end{align*}
\]

2-(4-Chlorophenoxy)-N-(5-methyl-4-oxo-2-(pyridin-2-yl)thiazolidin-3-yl)acetamide (**PY-TLA**)
IR Spectrum of PY- TLA

Chemistry
Mass Spectrum of PY- TLA

Mol. Wt. = 378

MS Spectrum

Line#: 1  R.Time: 0.553 (Scan#: 34) Negative
MassPeaks: 271  BasePeak: 376.15 (8162719)
RawMode: Single 0.553 (34)
BG Mode: Peak Start 0.327 (20)
$^1H$ NMR Spectrum of PY- TLA