Chapter 4

Vilsmeier Haack reaction of substituted 2-acetamidothiazole derivatives
Introduction:

The Vilsmeier-Haack reaction is a mild but efficient method for the formylation of reactive aromatic substrates. Vilsmeier–Haack formylation is done using dimethyl formamide and phosphoryl chloride. It is a mild electrophilic process and proceeds only with activated aromatic systems. The formylating agent, also known as Vilsmeier-Haack reagent, is formed \textit{in situ} from DMF and oxalyl chloride / POCl$_3$.

An electrophilic aromatic substitution leads to \(\alpha\)-chloro amines, which are rapidly hydrolysed during workup to give the aldehyde.
Vilsmeier reaction apart from formylation, also resulted with unexpected cyclisations. Koyama\textsuperscript{1} et al., have reported the formation of very low yields isoquinolines.

Further Paulmier\textsuperscript{2} et al., applied the same method to the corresponding thiophene derivatives giving thienopyridines with better yield than the isoquinolines, but attempts to extend the reaction to 3-acetamidothiophene led to the mixture of 5 products.

Later Meth-Cohn\textsuperscript{3} et al., reported the synthesis of quinolines, thienopyridines and define specific conditions for the formation of 2-chloro or 2-chloro-3-formyl fused pyridines in high yield.

Recently Bruche\textsuperscript{4} et al., reported that on treating 2-Azido-3-phenylamino acrylic acid methyl ester with POCl\textsubscript{3} and N,N-dimethylformamide, observed concomitant N-formylation and 1,5-electrocyclisation, producing 1-(N-aryl-
N-formylamino)1H-tetrazoles, provided that an electron-donating group was present on the aryl ring. In other cases only cyclisation occurs.

\[
\begin{align*}
\text{R} &= \text{Me, Et,} \\
\text{Ar} &= \text{Ph, 2-MeC}_6\text{H}_4, 4-\text{MeC}_6\text{H}_4, 3-\text{MeC}_6\text{H}_4, 3,5-\text{Me}_2\text{C}_6\text{H}_3, 4-\text{NO}_2\text{C}_6\text{H}_4, 2-\text{AcC}_6\text{H}_4
\end{align*}
\]
Presently there are number of drugs used clinically, which are comprised of thiazole moiety, substituted at different positions in association with various other heterocyclic rings. They are mainly used as chemotherapeutic agents such as diuretics and antihistamines. Penicillin, the first antibiotic therapeutically used and vitamin B₁ contain the thiazole moiety.

Recently the structure activity relationship studies have revealed that 2-aminothiazolium salts serves as a new class of Agonist Allosteric Enhancers of A₁ adenosine receptors. Also there are many thiazole containing pharmacologically active compounds reported in the literature viz., B-HT 920-Dopamine Agonist (Park-Davis Pharma), Fanetizole-anti-inflammatory agent (Glaxo-Wellcome Med. Research), PRH-836-EA-antiallergy agent (Boehringer Ingelheim limited), LY 73497: HIV 1 Reverse Transcriptase Inhibitor (Eli Lilly and company).

B-HT 920: Dopamine Agonist

Fanetizole: Anti inflammatory agent

PRH-836-EA: Antiallergy agent

LY73497: HIV-1 Transcriptase Inhibitor

Tetramisole, a broad-spectrum anthelmintic and Niridazole, an schistomicide are clinically used drugs containing the thiazole moiety.
Zolamine is used as an antihistamine and topical local anaesthetic\(^9\) and Clemothiazole is used as hypnotic in the treatment of alcohol withdrawal delirium tremens\(^10\).

Kumita\(^11\) et al., have prepared various thiazole derivatives, which showed excellent insecticidal, fungicidal and medicinal activities.

Anti-inflammatory activity has been reported for some aminoketone derivatives of 2,4-disubstituted thiazoles\(^12\).

Patil\(^13\) et al., have prepared substituted 2-amino-4-carboxy-5-thiazoleacetic acids and their esters, which showed potential anti-inflammatory activity.
A German patent\textsuperscript{14}, has claimed pesticidal activity for the following 2-amino thiazoles.

Fungicidal, antispasmodic and antihistaminic activities have also been reported for the following 2-amino thiazoles\textsuperscript{15}.

Lakhan\textsuperscript{16} \emph{et al.}, reported potential agricultural fungicidal activity for 2-imino-3-(4-arylthiazol-2-yl)-4-thiazolidinones and their 5-arylidene derivatives.

Many other thiazole derivatives have been claimed for various other biological activities like \(\beta_1\)-adrenergic agonist activity\textsuperscript{17}, antiulcer\textsuperscript{18-19}, antibacterial and antifungal\textsuperscript{20-23} and also in the treatment of cardiovascular disorders\textsuperscript{24}.
Purpose of the work:

In continuation of our interest in preparing the thiazole fused diazepinones of pharmacological interest by employing intramolecular transamidation, we wanted to introduce the amine input in the ethoxycarbonyl 2-acetamidothiazole derivatives by carrying out Vilsmeier Haack reaction followed by condensation with hydrazine hydrate.

During the course of this investigation we observed some interesting results, which encouraged us to study the behavior of differently 4-substituted 2-acetamidothiazole derivatives towards the Vilsmeier Haack reaction. Also in view of the pharmacological significance of the amino thiazole derivatives we thought it worthwhile to synthesise different 4-substituted 2-acetamidothiazole derivatives and study their behavior towards Vilsmeier Haack reaction.

Synthetic strategy:

The synthesis of the title compounds involves the following steps:

1. Preparation of various 2-bromoketones.
2. Preparation of Ethyl 2-aminothiazole-4-carboxylate (I).
3. Preparation of Ethyl-[2-(acetylamino)-1,3-thiazol-4-yl]acetate (II).
4. Preparation of N-[(4-alkyl/aryl)-1,3 thiazol-2-yl]acetamides (IVa-g)
5. Preparation of Ethyl 2-(formylamino)-1,3-thiazole-4-carboxylate (III).
6. Preparation of N-[(5-formyl-4-alkyl/aryl)-1,3-thiazol-2-yl]-acetamides (Va-g).
Scheme 4

\[
\begin{align*}
\text{CH}_3\text{COOC}_2\text{H}_5 & \xrightarrow{\text{Br}_2} \text{BrCH}_3\text{COOC}_2\text{H}_5 \xrightarrow{\text{H}_2\text{N}1\text{NH}_2, \text{EtOH, } \Delta} \text{I} \\
\text{I} + \text{H}_2\text{C}-\text{O} & \xrightarrow{\text{Acetic acid}} \text{II} \xrightarrow{\text{VMH}} \text{III} \\
\text{R-COOMe} & \xrightarrow{\text{Br}_2} \text{R-COCH}_2\text{Br} \xrightarrow{\text{H}_2\text{NNH}_2} \text{IV} \xrightarrow{\text{VMH}} \text{V}
\end{align*}
\]

Where a, \(R=\text{CH}_3\text{COOC}_2\text{H}_5\), b, \(R=\text{Ph}\), c, \(R=\text{thienyl}\), d, \(R=5\text{-nitrothienyl}\), e, \(R=4\text{-nitrophenyl}\), f, \(R=\text{CH}_1\), and g, \(R=\text{coumarinyl}\)
Results and Discussion:

A properly substituted thiazole was required for our work for the synthesis of thiazole fused diazepinones. We were interested in preparing thiazole derivatives with a carbonyl residue at C-4 (COOC\(_2\)H\(_5\), CH\(_2\)COOC\(_2\)H\(_5\), coumarinyl etc.) and an amine (NHNH\(_2\)) residue at C-5 as they are the precursors for carrying out the intramolecular transamidation resulting in the formation of thiazolodiazepinones (See Chapter 3). In order to introduce an amine input at C-5 we had to formylate the ethyl 2-acetamidothiazole-4-carboxylate by Vilsmeier Haack reaction which can be further reacted with hydrazine hydrate to have an amine residue to carry out the intramolecular transamidation. But when ethyl 2-acetamido thiazole-4-carboxylate was subjected to Vilsmeier Haack reaction, we found that the product obtained was not 5-formyl derivative but instead deacetylated N-formyl product as established by its analytical and spectral data. The IR spectra of the product showed bands at 1728 (\(\nu\)C=O of ester), 1687 (\(\nu\)C=O of aldehyde) cm\(^{-1}\) and whereas the \(\nu\)C=O of amide (-NHOCH\(_3\)) was absent. The \(^1\)H NMR spectra of the said compound showed the peaks at \(\delta\) 12.59 (br s, 1H, NH), 8.55 (s, 1H, CHO), 8.08 (s, 1H, 5H), 4.28 (q, 2H, CH\(_2\) of ester), 1.29 (t, 3H, CH\(_3\) of ester). There was no peak due to methyl group of acetamido group (-NHOCH\(_3\)). The appearance of C-5 proton indicates that formylation has not taken place at C-5 position where as the aldehydic proton position in the \(^1\)H NMR was a characteristic of N-formylated product which was confirmed by \(^13\)C NMR where two carbonyl carbons at 161.73 (C=O of ester) and 161.03 (C=O of aldehyde) were observed. The acetamido carbonyl carbon was again not observed.
Finally the mass spectra confirmed the N-formylation. There are reports in the literature\textsuperscript{4} where N-formylation has taken place with Vilsmeier Haack reagent.

The formation of N-formylated product followed by deacetylation is explained based on the following mechanism.

These results prompted us to undertake a detail study of Vilsmeier Haack reaction of different 2-acetamido-4-substituted thiazoles. During which we observed that when the thiazole contains 4-substituent other than ethoxycarbonyl group (viz., CH\textsubscript{3}, CH\textsubscript{2}COOEt, Coumarinyl, Ph, etc.,) formylation conveniently takes place at C-5 but only in case of 4-ethoxycarbonyl-2-acetamidothiazole, the N-formylation has taken place. The structures of various formyl derivatives prepared during the present investigation were established by their analytical and spectral data and the results are described in Table 20 and Table 21 respectively. Spectral data of some of the representative compounds are given below.
Spectral data:

*Ethyl 2-(formylamino)-1,3-thiazole-4-carboxylate (III) showed*

\[ \text{UV}(\lambda_{\text{max}}) \varepsilon (\text{L mol}^{-1} \text{ cm}^{-1}) : 274.0 \ (27,272) \text{. (Vide spectrum No. 58).} \]

**IR**

3134-2924 (CH stretching), 1728 (C=O of ester), 1687 (C=O of \(-\text{CHO}\) cm\(^{-1}\)). (Vide spectrum No. 61).

\[^1\text{H} \text{NMR (DMSO-d}_6\) :} \]

\[ \delta 12.59 \ (\text{br s, NH}), \ 8.55 \ (s, 1\text{H, CHO}), \ 8.08 \ (s, 1\text{H, C-5H}), \ 4.28 \ (q, 2\text{H, CH}_2 \text{ of ester}), \ 1.29 \ (t, 3\text{H, CH}_3 \text{ of ester}). \ (\text{Vide spectrum No. 64}). \]

\[^{13}\text{C} \text{NMR (DMSO-d}_6\) :} \]

\[ \delta 161.73 \ (\text{C=O of ester}), \ 161.03 \ (\text{C=O of CHO}), \ 157.30 \ (\text{C-2}), \ 141.89 \ (\text{C-4}), \ 123.94 \ (\text{C-5}), \ 61.48 \ (\text{OCH}_2), \ 14.98 \ (\text{CH}_3). \ (\text{Vide spectrum No. 67}). \]

**Mass**

\[ \text{M}^+ \text{ peak at 200. (Vide spectrum No. 69).} \]

Confirms the product as N-formylated product, but not the C-formylated one.

*N-[(5-formyl-4-phenyl)-1,3-thiazol-2-yl]acetamide (Vb) showed*

\[ \text{UV}(\lambda_{\text{max}}) \varepsilon (\text{L mol}^{-1} \text{ cm}^{-1}) : 276.0 \ (83,892) \text{ and } 361.0 \ (61,521) \text{. (Vide spectrum No. 60).} \]

**IR**

3055 (NH stretching), 3005-2816 (CH Stretching), 1637 (amide carbonyl), 1615 (C=O of \(-\text{CHO}\)). (Vide spectrum No. 63).
$^1$H NMR (CDCl$_3$) : δ 9.82 (s, 1H, CHO), 8.44 (s, 1H, NH), 7.88-7.47 (m, 5H, ArH), 3.17 (s, 3H, -CH$_3$). (Vide spectrum No. 66).

$^{13}$C NMR (CDCl$_3$) : δ 183.9 (C=O of -CHO), 179.8 (C=O of amide), 163.4 (C-2), 157.3 (C-4), 134.1(C-1'), 130.1(C-3'& C-5'), 128.9(C-4'), 128.2(C-2'&C-6') (C-1',2',3',4',5' & 6'corresponds to carbons of phenyl ring), 106.5 (C-5) 35.77 (CH$_3$). (Vide spectrum No. 68).

Mass : M$^+$ peak at 246 and m$^{-1}$+1 peak at 247. (Vide spectrum No. 71).

Confirms the product as C-formylated product at 5-position, but not the N-formylated one. The detailed spectral data of remaining compounds are described in Table 21.

UV spectral data shows that only C-formyl derivatives displayed absorption at longer wavelength compared to N-formyl compound (Vide spectra No. 58, 59 & 60). It is because of extended conjugation in C-formyl derivatives. IR spectra shows the presence of amide carbonyl and aldehydic carbonyl groups in the range of 1640-1625 and 1615-1610 cm$^{-1}$ respectively in C-formylated products but the amide carbonyl band is absent in N-formylated product (Vide spectra No. 61, 62 & 63). These aspects were further confirmed by NMR spectra (Vide spectra No. 64, 65, 66, 67 & 68) and Mass spectra (Vide spectra No. 69, 70 & 71).
Experimental:

1. Preparation of various 2-bromoketones

Preparation of phenacyl bromide, \( p \)-chlorophenacyl bromide, \( p \)-bromophenacyl bromide, \( p \)-nitrophenacyl bromide, 3-bromoacetyl coumarin and ethyl bromopyruvate are described in Chapter I (Page No. 81-83).

i) Preparation of ethyl 4-bromoacetoacetate

To an ice cold solution of ethyl acetoacetate (13.1g, 0.1 mole) in dry ether (25 ml) was added bromine (16.0g, 0.1 mole) dropwise at 0-5°C during the course of 30 minutes, with vigorous stirring. The mixture was kept at room temperature for 24h and added to crushed ice (100g). Aqueous layer was decanted off and the oily product was washed first with aqueous saturated sodium chloride solution and then with water. It was dissolved in ether and the ethereal solution was dried (CaCl\(_2\)). The solvent was removed and the residual oil\(^{25}\) stored after the addition of barium carbonate (0.5g). It was used directly in the next reaction.

ii) Preparation of 2-bromoacetyl thiophene:

To a solution of 2-acetylthiophene (12.6g, 0.1 mole) in dioxane-ether (100 ml 1:2) was added, bromine (16.0g, 0.1 mole) dropwise at 0-5°C, during 1 h at room temperature. It was then poured onto crushed ice (200g). The contents were extracted with ether, ether layer was washed with water and dried (sodium sulphate). Solvent removed and the residual oily product was distilled under reduced pressure to get yellow liquid, 12.0g (58.5%). b.p. 171-74°C / 7 mm, lit.\(^{26}\) b.p. 143-45°C / 3 mm.
Preparation of 5-nitro-2-bromoacetylthiophene:

i) Preparation of 5-nitro-2-acetylthiophene:

A mixture of 2-acetylthiophene (12g) and acetic anhydride (25 ml) was treated with fuming nitric acid (6.5g) dropwise, below 25°C, during 30 minutes. It was then heated at 50°C for 30 minutes, cooled and poured into ice cold water (100 ml). The contents were extracted with ether. The ether layer after washing with sodium bicarbonate solution and water was dried over anhydrous sodium sulphate. Solvent was removed and the crude 5-nitro-2-acetylthiophene was purified by recrystallisation from ether-petroleum ether mixture (1:1), 7.10 g (41%), m.p. 107-108°C lit²⁷ m.p. 108-109°C.

ii) Preparation of 5-nitro-2-bromoacetylthiophene:

A solution of 5-nitro-2-acetylthiophene (8.55g, 0.05 mole) in chloroform (100 ml) was treated, dropwise, with bromine (8.0g, 0.05 mole) during 30 minutes at 20°C. It was further stirred for 18 h at room temperature. The solvent was removed and the residual crude product was purified by crystallisation from chloroform-ether-hexane mixture (1:1:1) to yield yellowish brown crystals, 9.75g (78%), m.p. 103-104°C, lit²⁸ m.p. 104-105°C.

2. Preparation of Ethyl 2-aminothiazole-4-carboxylate (I):

The procedure for the preparation is described in Chapter I (Page No. 83).

3. Preparation of Ethyl-[2-(acetylamino)-1,3-thiazol-4-yl]acetate (II):

To a mixture of ethyl 2-aminothiazole-4-carboxylate (17.2g, 0.1 mole) in acetic acid (50 ml) was added, acetic anhydride (10.2g, 0.1 mole) and pyridine (0.5 ml) slowly with stirring and heated to reflux for 4h. Reaction mixture was
cooled and poured onto crushed ice (300g). The crude acetamido derivative that separated was filtered, washed with ice cold water and dried. It was purified by recrystallisation from aqueous ethanol, colourless crystals, 15.5 g (72.5%), m.p. 208-209°C, lit\(^2\) m.p. 210°C.

4. Preparation of Ethyl 2-(formylamino)-1,3-thiazole-4-carboxylate (III):

Vilsmeier reagent is prepared by adding phosphorous oxychloride (2.5 ml) in dimethyl formamide (7.5 ml) at 0°C. Then Ethyl-[2-(acetylamino)-1,3-thiazol-4-yl]acetate (2.14g, 0.01 mole) was added to the reagent at 0°C. Stirred at room temperature for 2h and further at 60°C for 2h. The reaction mixture was poured into cold sodium carbonate solution (10%) and stirred at 90°C for 2h. After cooling, the solution was extracted with chloroform. The chloroform layer was washed repeatedly with water and dried over anhydrous sodium sulfate. The combined extracts are evaporated to dryness and recrystallised from rectified spirit, Pale yellow needles, m.p. 232-234°C, 1g (50%); Anal.: Found C, 41.75; H, 3.85; N, 13.80 %: C\(_7\)H\(_8\)N\(_2\)O\(_3\)S requires C, 41.99; H, 4.03; N, 13.99 %.

UV(\(\lambda_{\text{max}}\)) \(\varepsilon\) (L mol\(^{-1}\) cm\(^{-1}\)) : 274.0 (27,272). (Vide spectrum No. 58).

IR : 3134-2924 (CH stretching bands), 1728 (C=O of ester), 1687 (C=O of -CHO) cm\(^{-1}\). (Vide spectrum No. 61).

\(^1\)H NMR (DMSO-\(d_6\)) : \(\delta\) 12.59 (br s, NH), 8.55 (s, 1H, CHO), 8.08 (s, 1H, C-5H), 4.28 (q, 2H, CH\(_2\) of ester), 1.29 (t, 3H, CH\(_3\) of ester). (Vide spectrum No. 64).
13C NMR (DMSO-d6) : δ 161.73 (C=O of ester), 161.03 (C=O of CHO),
157.30 (C-2), 141.89 (C-4), 123.94 (C-5),
61.48 (OCH₂), 14.98 (CH₃). (Vide spectrum No. 67).

Mass : M⁺ peak at 200. (Vide spectrum No. 69).

5. Preparation of N-[(4-alkyl/aryl)-1,3-thiazol-2-yl]acetamide (IVa-g):

For the preparation of 4-substituted 2-aminothiazoles and their conversion to corresponding acetyl derivatives (IVa-g) we followed the same procedure as for the preparation of Ethyl-[2-(acetylamino)-1,3-thiazole-4-yl]carboxylate (III). The physicochemical and spectral data of various IVa-g are described in Table 18 and Table 19 respectively.

6. Preparation of N-[(5-formyl-4-alkyl/aryl)-1,3-thiazol-2-yl]acetamides (Va-g):

Vilsmeier-Haack reagent is prepared by adding phosphorous oxychloride (2.5 ml) in dimethyl formamide (7.5 ml) at 0°C. Then N-(4-alkyl/aryl-1,3-thiazol-2-yl)acetamides (IVa-g, 0.01 mole) were added to the reagent at 0°C. Stirred at room temperature for 2h and further at 60°C for 2h. The reaction mixture was poured into cold sodium carbonate solution (20 ml, 10%) and stirred at 90°C for 2h. After cooling, the solution was extracted with chloroform, washed repeatedly with water and dried over anhydrous sodium sulfate. The combined extracts are evaporated to dryness and recrystallised from rectified spirit. The physicochemical and spectral characterization data are described in Table 20 and Table 21 respectively.
Table 18: Physicochemical data of \( \text{N}-[(4\text{-alkyl/aryl})-1,3\text{-thiazol-2-yl}]\)-acetamides (IVa-g):

<table>
<thead>
<tr>
<th>Comp No</th>
<th>R</th>
<th>Yield %</th>
<th>M.P °C</th>
<th>Nature</th>
<th>Molecular formula</th>
<th>Elemental analysis</th>
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<td></td>
<td></td>
<td></td>
<td>Calc %</td>
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<tr>
<td>IVa</td>
<td>CH_2COOC_2H_5</td>
<td>60</td>
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<td>IVb</td>
<td>Phenyl</td>
<td>62</td>
<td>210-12</td>
<td>Pale yellow</td>
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<td>IVc</td>
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<tr>
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<td>IVg</td>
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Table 19: Spectral data of N-[(4-alkyl/aryl)-1,3 thiazol-2-yl]acetamides (IVa-g):

![Chemical Structure]

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>R</th>
<th>UV($\lambda_{max}$) $\varepsilon$ (L mol$^{-1}$ cm$^{-1}$)</th>
<th>IR (KBr)(cm$^{-1}$)</th>
<th>$^1$H NMR (DMSO-d$_6$)(δ)</th>
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<tr>
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<td></td>
<td></td>
<td>$v_{NH}$</td>
<td>$v_{C=O}$</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$v_{NH}$</td>
<td>$v_{C=O}$</td>
</tr>
<tr>
<td>IVa</td>
<td>CH$_3$COOC$_2$H$_5$</td>
<td>275 (54,288)</td>
<td>3173</td>
<td>1731 &amp; 1659</td>
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<tr>
<td>IVb</td>
<td>Phenyl</td>
<td>276 (51,921)</td>
<td>3169</td>
<td>1644</td>
</tr>
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<td>1687</td>
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<td>IVd</td>
<td>5-Nitrothienyl</td>
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<td>3385</td>
<td>1619</td>
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<tr>
<td>IVf</td>
<td>Methyl</td>
<td>277 (37,147)</td>
<td>3170</td>
<td>1660</td>
</tr>
<tr>
<td>IVg</td>
<td>3-Coumarinyl</td>
<td>274 (68,119)</td>
<td>3154</td>
<td>1738 &amp; 1715</td>
</tr>
</tbody>
</table>
Table 20: Physicochemical data of N-[(5-formyl-4-alkyl/aryl)-1,3-thiazol-2-yl]acetamides (Va-g):

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Comp No</th>
<th>R</th>
<th>Yield %</th>
<th>M.P °C</th>
<th>Nature</th>
<th>Molecular formula</th>
<th>Elemental analysis</th>
<th>Calculated %</th>
<th>Found %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Va</td>
<td>CH$_2$COOC$_2$H$_5$</td>
<td>55</td>
<td>230-232</td>
<td>Pale yellow</td>
<td>C$<em>{10}$H$</em>{13}$N$_2$O$_2$S</td>
<td>C: 46.87, H: 4.68, N: 10.93</td>
<td>46.50, 4.44, 10.62</td>
<td></td>
</tr>
<tr>
<td>Vb</td>
<td>Phenyl</td>
<td>52</td>
<td>220-222</td>
<td>Yellow</td>
<td>C$<em>{12}$H$</em>{10}$N$_2$O$_2$S</td>
<td>C: 58.53, H: 4.06, N: 11.38</td>
<td>58.10, 3.68, 11.00</td>
<td></td>
</tr>
<tr>
<td>Vc</td>
<td>Thienyl</td>
<td>55</td>
<td>204-206</td>
<td>Brown</td>
<td>C$<em>{10}$H$</em>{8}$N$_2$O$_2$S$_2$</td>
<td>C: 47.61, H: 3.17, N: 11.11</td>
<td>47.20, 2.80, 10.75</td>
<td></td>
</tr>
<tr>
<td>Vd</td>
<td>5-Nitrothienyl</td>
<td>50</td>
<td>214-216</td>
<td>Yellow</td>
<td>C$<em>{10}$H$</em>{7}$N$_3$O$_4$S$_2$</td>
<td>C: 40.40, H: 2.35, N: 14.14</td>
<td>40.00, 2.04, 14.50</td>
<td></td>
</tr>
<tr>
<td>Ve</td>
<td>4-Nitrophenyl</td>
<td>58</td>
<td>222-224</td>
<td>Yellow</td>
<td>C$<em>{12}$H$</em>{9}$N$_3$O$_4$S</td>
<td>C: 49.48, H: 3.09, N: 14.43</td>
<td>49.10, 3.40, 14.00</td>
<td></td>
</tr>
<tr>
<td>Vf</td>
<td>Methyl</td>
<td>56</td>
<td>232-234</td>
<td>Pale yellow</td>
<td>C$<em>{7}$H$</em>{4}$N$_2$O$_2$S</td>
<td>C: 45.65, H: 4.34, N: 15.21</td>
<td>45.20, 4.00, 14.82</td>
<td></td>
</tr>
<tr>
<td>Vg</td>
<td>3-Coumarinyl</td>
<td>52</td>
<td>210-212</td>
<td>Brown</td>
<td>C$<em>{13}$H$</em>{10}$N$_2$O$_4$S</td>
<td>C: 57.32, H: 3.18, N: 8.91</td>
<td>56.98, 3.50, 8.52</td>
<td></td>
</tr>
</tbody>
</table>

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Table 21: Spectral data of N-[5-formyl-4-alkyl/aryl]-1,3-thiazol-2-yl]-acetamides (Va-g).

<table>
<thead>
<tr>
<th>Comp No</th>
<th>R</th>
<th>UV (λ&lt;sub&gt;max&lt;/sub&gt;) ε (Lmol&lt;sup&gt;-1&lt;/sup&gt; cm&lt;sup&gt;−1&lt;/sup&gt;)</th>
<th>IR</th>
<th>NMR (DMSO-d&lt;sub&gt;6&lt;/sub&gt;) (δ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Va</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;COOC&lt;sub&gt;2&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>275(64,027) &amp; 325(40,745)</td>
<td>3184 1735 (ester) &amp; 1642(-CHO) &amp; 1622 (COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H: 9.60 (s, 1H, CHO), 4.23(q, 2H, CH&lt;sub&gt;2&lt;/sub&gt; of ester), 3.72 (s, 2H, CH&lt;sub&gt;3&lt;/sub&gt; of acetate), 3.18 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;), 0.94(t, 3H, CH&lt;sub&gt;3&lt;/sub&gt; of ester)</td>
</tr>
<tr>
<td>Vb</td>
<td>Phenyl</td>
<td>276(83,892) &amp; 361(61,521)</td>
<td>3055 1637 (-CHO) &amp; 1615(COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H: 9.82 (s, 1H, CHO), 8.44 (s, 1H, NH), 7.88-7.47 (m, 5H, ArH), 3.17 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Vc</td>
<td>Thienyl</td>
<td>276(63,001) &amp; 315(45,819)</td>
<td>3160 1687(-CHO) &amp; 1621(COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H: 10.11 (s, 1H, CHO), 8.41(s, 1H, NH), 7.53-7.13(m, 3H, thienyl H), 2.97 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Vd</td>
<td>5-Nitrothienyl</td>
<td>275(67,521) &amp; 330(47,265)</td>
<td>3120 1619 (-CHO) &amp; 1610(COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H: 10.10 (s, 1H, CHO), 8.42(s, 1H, NH), 8.37-7.85(m, 2H, ArH), 3.18 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Ve</td>
<td>4-Nitrophenyl</td>
<td>277(72,751) &amp; 320(52,910)</td>
<td>3114 1644 (-CHO) &amp; 1611(COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H: 9.80 (s, 1H, CHO), 8.39(s, 1H, NH), 8.12 (d, J=8.5Hz, 2H, ArH), 7.88 (d, J=8.5Hz, 2H, ArH), 3.21 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Vf</td>
<td>Methyl</td>
<td>278(41,823) &amp; 330(29,276)</td>
<td>3160 1665(-CHO) &amp; 1610(COCH&lt;sub&gt;3&lt;/sub&gt;)</td>
<td>1H : 10.00 (s, 1H, CHO), 8.60 (s, 1H, NH), 3.35 (s, 3H, COCH&lt;sub&gt;3&lt;/sub&gt;), 2.25 (s, 3H, CH&lt;sub&gt;3&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Vg</td>
<td>3-Coumarinyl</td>
<td>275(49,964) &amp; 342(17,844)</td>
<td>3098</td>
<td>1731(lactone), 1657(-CHO) &amp; 1628(COCH₃)</td>
</tr>
</tbody>
</table>
Spectrum No. 64

H-NMR

C$_2$H$_5$O 0

0.00 ppm

90° E

65° E

30° E

0° E

-60° E

C$_2$H$_5$O 1
Spectrum No. 68
$^1$H-NMR

$\text{NHC(O)CH}_3$
Molecular weight: 200
Molecular weight: 314
Current Chromatogram(s)
Molecular weight: 246
NHCOCH₃
References:


