CHAPTER-1
Synthesis of Fatty Hydrazones
1.1 THEORETICAL

Hydrazones are the class of organic compounds with general formula $R_2C=NNR_2$, which are usually prepared from aldehyde or ketone by replacing $=O$ by $=NNH_2$ (or substituted analogues). Hydrazones have been found to possess diverse pharmacological properties which include antimicrobial\(^1\),\(^2\), antitubercular\(^3\),\(^4\), anticonvulsant\(^5\), antiinflammatory\(^6\) and antiprotozoal\(^7\) activities. Hydrazones are also known as very effective charge transporting compounds. Together with polymer binders hydrazones are used in electrophotographic photoreceptors.\(^8\)-\(^10\) Pyridoxyl isonicotinyl hydrazones and its analogues are proposed chemotherapeutics\(^11\) functioning as iron chelators for treatment of iron loaded diseases.

Development of resistance to existing drugs is a constantly growing phenomenon that has concerned researchers throughout the world and has now reached alarming levels for certain infectious diseases. In view of drug resistance problem, it is important that new drugs inhibit targets different from those of currently used drugs. Antibacterial resistance to drugs can be countered by designing new derivatives.\(^12\) There are two basic approaches to develop new drugs:

(a) Synthesis of analogues, modification or derivatization of existing compounds.

(b) Searching for novel structures that the drug resistant organism has never been presented before.

To pursue this goal, our research efforts are directed to synthesize derivatives of the compounds which are known to have their own biological activities and fatty acids are one such class of compounds. Being the most important and widely distributed constituent of seed oils, fatty acids are extensively studied as they can be of high value for the chemical and pharmaceutical industry.\(^13\),\(^14\) Fatty acid derivatives have been found to be associated with diverse biological activities such as herbicidal,\(^15\) antifeedant,\(^16\) neuroprotective,\(^17\) bactericidal,\(^18\) fungicidal,\(^19\) antioxidant,\(^20\) antimicrobial,\(^19\)-\(^23\) antiparasitic,\(^23\) antifogging,\(^24\) and anti-inflammatory,\(^25\) Thus use of fatty acid substrates as starting materials has become significant because of their own biological activities.
On the basis of these observations, we had the impetus to synthesize a number of hydrazones of fatty acids and subsequently evaluate their *in-vitro* antimicrobial activities (Chapter 6).

A number of methods for synthesis of hydrazones have been reported. The convenient synthesis of hydrazones involves reaction of an aldehyde or ketone with a hydrazide in water by shaking, in alcohol at reflux temperature or by refluxing hydrazide with same aldehyde or ketone.

Yale *et al.* have synthesized different hydrazones from isonicotinohydrazide (1) by different methods. Isobutyraldehyde isonicotinylhydrazone (3) was prepared by shaking compound 1 with freshly distilled isobutyraldehyde (2) in water.

![Chemical structure](attachment:image.png)

Isonicotino-hydrazide (1) on refluxing with excess of acetone (4) gave acetone isonicotinylhydrazone (5).

![Chemical structure](attachment:image.png)

Reaction of 2-furoic acid hydrazide (6) with 4-acetamidobenzaldehyde (7) in aq ethanol gave 4-acetamidobenzaldehyde-2-furoylhydrazone (8). 9-Hendecenal isonicotinylhydrazone (9) was changed to hendecanal isonicotinylhydrazon (10) at 50 Lb of hydrogen in presence of platinum oxide in 95% ethanol.
Ottana et al. synthesized trifluoroacetaldehyde (12a) and 1,1,1 trifluoroacetone isonicotinylhydrazones (12b) by reacting trifluoroacetaldehyde ethylhemiacetal or 1,1,1 trifluoroacetone (11) in ethanol having catalytic amount of 6M HCl with compound 1 and refluxed for 48 hrs.

Hydrazones (14a-f) of dihydrazide of 1,3,4-thiadiazole-2,5-dithioglycolic acid (13) were prepared by reacting it with different aldehydes at 70°C for 1 hr.
Richardson et al.\textsuperscript{11} reported a series of pyridoxyl hydrazones (17a-f) via Schiff base condensation of an aromatic aldehyde, pyridoxal (16), with an acid hydrazide (1, 15a-e) in one step.

<table>
<thead>
<tr>
<th>Compound</th>
<th>$R^1$</th>
<th>$R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>14a</td>
<td>H</td>
<td>CH$_3$</td>
</tr>
<tr>
<td>14b</td>
<td>H</td>
<td>C$_4$H$_3$O</td>
</tr>
<tr>
<td>14c</td>
<td>H</td>
<td>2-HO,3-CH$_3$OC$_6$H$_3$</td>
</tr>
<tr>
<td>14d</td>
<td>H</td>
<td>4-CH$_3$OC$_6$H$_4$</td>
</tr>
<tr>
<td>14e</td>
<td>CH$_3$</td>
<td>3,4-(OCH$_2$O)-C$_6$H$_3$</td>
</tr>
<tr>
<td>14f</td>
<td>CH$_3$</td>
<td>2,4-(OH)$_2$-C$_6$H$_3$</td>
</tr>
</tbody>
</table>

![Diagram of compounds](image-url)
Rutavichyus and Valyulene further reported a series of hydrazones (19a-f) of \( S,S'-(1,3,4\text{-thiadiazole}-2,5\text{-diyl})\text{bis}(2\text{-mercaptopropionic acid}) \text{ dihydrazide (18)}\) by stirring at 70°C with different aldehydes or ketones for 1.5 hr.

\[
\begin{align*}
\text{NH}_2\text{NH} &\quad \text{CH}_3
\end{align*}
\]

\[
\text{18}
\]

\[
\begin{align*}
\text{19a-f} &\quad \text{R}^1\text{R}^2\text{CO}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>( \text{R}^1 )</th>
<th>( \text{R}^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>19a</td>
<td>H</td>
<td>2,3-(OCH\text{3})\text{2-C}_6\text{H}_3</td>
</tr>
<tr>
<td>19b</td>
<td>H</td>
<td>2,4-(OH)\text{2-C}_6\text{H}_3</td>
</tr>
<tr>
<td>19c</td>
<td>H</td>
<td>2-HO,3-CH\text{3-OC}_6\text{H}_3</td>
</tr>
<tr>
<td>19d</td>
<td>H</td>
<td>4-(CH\text{3})\text{2NC}_6\text{H}_4</td>
</tr>
<tr>
<td>19e</td>
<td>C\text{3H}_7</td>
<td>C\text{3H}_7</td>
</tr>
<tr>
<td>19f</td>
<td>CH\text{3}</td>
<td>3,4-(OCH\text{3O}-C\text{6H}_3)</td>
</tr>
</tbody>
</table>
A series of different glass foaming hydrazones (22a,b) were synthesized by reacting N,N-diphenyl hydrazine hydrochloride (21a) or N-methyl-N-phenyl hydrazine hydrochloride (21b) with different substituted carbaldehydes (20a,b) under reflux conditions.\(^{29}\)

Rutavicius and Kuodis\(^{30}\) have further reported hydrazones of [5-(4-pyridyl)-1,3,4-oxadiazol-2-ylthio]acetic acid 4-ethoxy-4-oxo-2-butylidenehydrazide (24a) and [5-(4-pyridyl)-1,3,4-oxadiazol-2-ylthio]acetic acid ethoxymethylidenehydrazide (24b) by refluxing 23 with excess of ethylacetoacetate or ethyl orthoformate at 105-110\(^{\circ}\)C for 2 hrs.
Rollas et al. reported a series of hydrazones of 4-fluorobenzoic acid hydrazide (25) by condensing with different aldehydes (26a-d) in water.

Refluxing 2-hydroxy acetophenone (28) with compound 1 in the presence of glacial acetic acid in ethanolic medium for 9 hrs to give acid hydrazone (29).
Cacic et al.\textsuperscript{2} synthesized hydrazones of (7-hydroxy-2-oxo-2H-chromen-4-yl)-acetic acid hydrazide (30) by reacting with appropriate aromatic aldehyde or with a diketone.

A series of hydrazones of 4-substituted benzoic acid hydrazide (33) were synthesized by reacting with substituted aldehydes in ethanol.\textsuperscript{3}
Siriram et al.\textsuperscript{12} further reported hydrazones (37a-d) of diclofenac acid in moderate yields by carrying out a reaction between diclofenac acid hydrazide (36) and appropriate aldehydes in ethanol by stirring at room temperature for 1 hr.
Ming et al. synthesized trifluoromethyl benzoyl-hydrazone (39) in quantitative yields using diketone-ethyl acetoacetate and trifluoromethyl benzoyl hydrazide (38).

Metwally et al. obtained hydrazones (41a-h) of 2-aryl-quinoline-4-carboxylic acid hydrazide by condensing the acid hydrazides (40) with the appropriate aldehydes in glacial acetic acid under reflux conditions. [X= H, Cl]
Isatin (44a-d) and benzoisatin (44e-h) hydrazones were prepared by carrying out reaction between isatin and benzoisatin with different secondary amine acetic acid hydrazides in ethanol and 3 ml of 12M HCl and boiling the contents for 10 min.\(^{34}\)

Recently Kuodis \textit{et al.}\(^{35}\) reported a series of 2-(5-thioxo-4,5-dihydro-1,3,4-thiadiazole-2-ylthio) aceto hydrazide by reacting with equimolar amount of an aldehyde or ketone in 1,4-dioxane and water by stirring for 3 hrs at 85\(^{\circ}\)C.
### Fatty Hydrazones

![Chemical structure diagram]

<table>
<thead>
<tr>
<th>Compound</th>
<th>R&lt;sup&gt;1&lt;/sup&gt;</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>45a</td>
<td>H</td>
<td>4-CH₃O-C₆H₄</td>
</tr>
<tr>
<td>45b</td>
<td>H</td>
<td>2-HO,5-Br-C₆H₃</td>
</tr>
<tr>
<td>45c</td>
<td>H</td>
<td>2-HO,3-CH₃O-C₆H₃</td>
</tr>
<tr>
<td>45d</td>
<td>CH₃</td>
<td>C₆H₅</td>
</tr>
<tr>
<td>45e</td>
<td>CH₃</td>
<td>4-HO-C₆H₄</td>
</tr>
<tr>
<td>45f</td>
<td>CH₃</td>
<td>2-CH₃O-C₆H₄</td>
</tr>
<tr>
<td>45g, 45h</td>
<td>H / CH₃</td>
<td>2-HO-C₆H₄</td>
</tr>
<tr>
<td>45i, 45j</td>
<td>H / CH₃</td>
<td>2,4-HO-C₆H₃</td>
</tr>
</tbody>
</table>
1.2 RESULTS AND DISCUSSION

The required fatty acid hydrazides were prepared by stirring and refluxing the fatty esters with hydrazine hydrate in ethanol in the presence of air. Absence of peaks for olefinic protons (δ 5.4–4.6) suggest that hydrogenation of double bond of the fatty acid chain has taken place. This indicates that hydrazine hydrate can hydrogenate double bonds in the presence of air. Such findings are already reported in the literature.\(^{36-38}\) The synthetic pathway followed for the synthesis of hydrazones is presented in the Scheme 1.1 to 1.8. Carbonyl group of methyl acetoacetate and acetylacetone has been employed to build the newly synthesized hydrazones from different fatty acid hydrazides.

**Reaction of undecanoic hydrazide (I) with methyl acetoacetate**

Fatty acid hydrazide I and methyl acetoacetate were refluxed in absolute ethanol with a catalytic amount of hydrochloric acid for 3 hrs to afford an oily product which was chromatographed over a column of silica gel using petroleum ether-diethyl ether (98:2 v/v) as an eluent to afford an oily compound V.

\[
\begin{align*}
&\text{CH}_3-(\text{CH}_2)_9-\text{C}-\text{NHNH}_2 + \text{CH}_3-\text{C}-\text{CH}_2-\text{C}-\text{OCH}_3 \\
&\text{Reflex. 3 hrs} \\
&\text{CH}_3-(\text{CH}_2)_9-\text{C}-\text{NHN}=\text{C}-\text{CH}_2-\text{C}-\text{OCH}_3
\end{align*}
\]

Scheme 1.1: Synthesis of methyl 3-(2'-undecanoylhydrazono)butanoate (V)
Structural elucidation of the compound V as methyl 3-(2'-undecanoylhydrazono) butanoate

It was an oily compound which exhibited intensive IR bands at 3210 (NH), 1743 (O=COCH₃), 1660 (O=C-NH), 1449 cm⁻¹ (C=N). The ¹H NMR spectrum of compound V gave diagnostic signals at δ 10.35 (1H, s, NH, exchangeable with D₂O), 3.66 (3H, s, OCH₃), 2.01 (2H, s, CH₂CO₂CH₃), 1.56 (3H, s, N=C-CH₃). In ¹³C NMR characteristic peaks at δ 174.7 and 174.5 (COOCH₃, CONH), 159.2 (C=N) and 25.0 (COCH₃) also supported the structure assigned. The MS spectrum of compound V showed molecular ion peak at m/z 298, an intense peak at 154 in addition to other fragment ions (detailed in experimental section). The structure was further supported by its elemental analysis which was also in good agreement with the calculated values. Based on the above facts compound V was characterized as methyl 3-(2'-undecanoylhydrazono)butanoate

Reaction of octadecanolic hydrazide (II) with methyl acetoacetate

Refluxing octadecanolic hydrazide (II) with methyl acetoacetate in absolute ethanol for 4 hrs in presence of catalytic amount of hydrochloric acid gave a solid product after removing the excess solvent which was crystallized in ethanol to give a white powder.

\[
\begin{align*}
\text{CH}_3-(\text{CH}_2)_6-\text{C} &-\text{NHNNH}_2 \quad \text{CH}_3-\text{C} &-\text{CH}_2-\text{C} &-\text{OCH}_3 \\
\text{II} & & & & \\
\text{Abs. ethanol} & & & & \text{Reflex, 4 hrs} \\
\text{CH}_3-(\text{CH}_2)_6-\text{C} &-\text{NHN}=\text{C} &-\text{CH}_2-\text{C} &-\text{OCH}_3 \\
\text{VI}
\end{align*}
\]

Scheme 1.2: Synthesis of methyl 3-(2'-octadecanoylhydrazono)butanoate (VI)
Structural elucidation of the compound VI as methyl 3-(2'-octadecanoylhydrazono)butanoate

It was a white powder showing IR bands at 3207 (NH), 1736 (O-COCH₃), 1658 (O=C-NH), 1455 cm⁻¹ (C=N). In ¹H NMR diagnostic peaks at δ 10.35 (1H, s, NH, exchangeable with D₂O), 3.66 (3H, s, OCH₃), 1.94 (2H, s, CH₂CO₂CH₃) and 1.59 (3H, s, N=C-CH₃) were observed. In ¹³C NMR characteristic peaks at δ 174.8 and 174.5 (COOCH₃, CONH), 159.1 (C=N) and 25.1 (COCH₃) were found which also supported the structure. The MS spectrum of compound VI showed molecular ion peak at m/z 396, an intense peak at 298 and other fragment ions were also observed (detailed in experimental section). Elemental analysis was also in good agreement with the calculated values. Thus keeping in view the above observations the compound VI was assigned as methyl 3-(2'-octadecanoylhydrazono)butanoate.

Reaction of 12-hydroxyoctadecanoic hydrazide (III) with methyl acetoacetate

A 4 hrs refluxing of 12-hydroxyoctadecanoic hydrazide (III) with methyl acetoacetate in absolute ethanol with a catalytic amount of hydrochloric acid, a solid product was obtained after concentrating and cooling the reaction mixture which was crystallized in ethanol to give an off-white powder.

```
CH₃—(CH₂)₅—CH—(CH₂)₁₀—C—NHNH₂ + CH₃—C—CH₂—C—OCH₃

(III)
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Refux 4 hrs Abs ethanol

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CH₃—(CH₂)₅—CH—(CH₂)₁₀—C—NHN=—C—CH₂—C—OCH₃

(VII)
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Scheme 1.3: Synthesis of methyl 3-[2'-(12-hydroxyoctadecanoylhydrazono)]-butanoate (VII)
Structural elucidation of the compound VII as methyl 3-[2′-(12-hydroxyoctadecanoylhydrazono)]butanoate

An off-white powder giving characteristic IR bands at 3321(OH), 3212 (NH), 1737 (O=COCH₃), 1660 (O=C–NH) and 1458 cm⁻¹ (C=N). The ¹H NMR was more informative in assigning the structure. In addition to the normal fatty acid chain peaks, diagnostic peaks at δ 10.34 (1H, s, NH, exchangeable with D₂O), 3.98 (1H, m, CH-OH), 3.66 (3H, s, OCH₃), 3.58 (1H, br. s, OH, exchangeable with D₂O) 1.91 (2H, s, CH₂CO₂CH₃) and 1.59 (3H, s, N=C–CH₃) were observed. ¹³C NMR spectrum also supported the structure. Peaks at δ 174.44 and 174.40 (COOCH₃, CONH), 159.2 (C=N), 72.1 (CH-OH) and 25.0 (COCH₃) were observed. Molecular ion peak at m/z 412 and an intense peak at 297 were observed. Other fragment ions were also observed (detailed in experimental section). Elemental analysis was also in good agreement with the calculated values. Based on above findings the compound VII was named as methyl 3-[2′-(12-hydroxyoctadecanoylhydrazono)]butanoate.

Reaction of 9-hydroxyoctadecanoic hydrazide (IV) with methyl acetoacetate

Refluxing of 9-hydroxyoctadecanoic hydrazide (IV) with methyl acetoacetate in absolute ethanol for 4 hrs with a catalytic amount of hydrochloric acid and concentrating and cooling the reaction mixture a solid product was obtained which was crystallized in ethanol to give a white powder.

Scheme 1.4: Synthesis of methyl 3-[2′-(9-hydroxyoctadecanoylhydrazono)]-butanoate (VIII)
Structural elucidation of the compound VIII as methyl 3-[2’-(9-hydroxyoctadecanoylhydrazono)]butanoate

Compound VIII was obtained as a white powder giving characteristic IR bands at 3327(OH), 3214 (NH), 1737 (O=COCH₃), 1658 (O=CNH) and 1459 cm⁻¹ (C=N). In ¹H NMR spectrum diagnostic peaks at δ 10.35 (1H, s, NH, exchangeable with D₂O), 4.11 (1H, m, CH-OH), 3.66 (3H, s, OCH₃), 3.58 (1H, br. s, OH, exchangeable with D₂O) 1.91 (2H, s, CH₂CO₂CH₃) and 1.55 (3H, s, N=C-CH₃) were observed. ¹³C NMR spectrum also supported the structure assigned by showing peaks at δ 174.5 and 174.4 (COOCH₃, CONH), 159.2 (C=N), 72.0 (CH-OH) and 25.0 (COCH₃). Molecular ion peak at m/z 412 and an intense peak at 299 were observed. Other fragment ions were also observed (detailed in experimental section). Elemental analysis was also in good agreement with that of calculated values. Based on above facts the compound VIII was characterized as methyl 3-[2’-(9-hydroxyoctadecanoylhydrazono)]butanoate.

Reaction of undecanoic hydrazide (I) with acetylacetone

Undecanoic hydrazide I and acetylacetone in equimolar ratio were refluxed for 4 hrs in absolute ethanol containing few drops of hydrochloric acid as a catalyst. After completion of reaction (monitored by TLC) the reaction mixture was concentrated and cooled to give an oily compound which was chromatographed over a column of silica gel using petroleum ether-diethyl ether (96:4 v/v) as eluent to give an oily compound IX.

\[
\text{CH}_3-(\text{CH}_2)_9-\overset{\text{O}}{\overset{\text{O}}{\text{C}}}-\text{NHNH}_2 + \text{CH}_3-\overset{\text{O}}{\overset{\text{O}}{\text{C}}}-\text{CH}_2-\text{CH}_2-\text{C}-\text{CH}_3
\]

\(\text{(I)}\)

\[
\text{CH}_3-(\text{CH}_2)_9-\overset{\text{O}}{\overset{\text{O}}{\overset{\text{Abs. ethanol}}{\text{Reflex. 4 hrs}}}{\overset{\text{O}}{\text{C}}}}-\text{NHN}==\text{C}-\text{CH}_2-\text{C}-\text{CH}_3
\]

\(\text{(IX)}\)

Scheme 1.5: Synthesis of \(N’\)-(4-oxopentane-2-ylidene)undecanohydrazone (IX)
Structural elucidation of the compound IX as \( N'-(4\text{-oxopentane-2-ylidene})\text{-undecanohydrazide} \)

It was obtained as an oily compound showing intensive IR bands at 3205 (NH), 1721 (C=O) and 1664 cm\(^{-1} \) (O=C-NH) confirming the presence of these functional groups. The \( ^1 \)H NMR data gave characteristic peaks at \( \delta \) 10.33 (1H, s, NH), 2.04 (3H, s, CH\(_3\)), 1.94 (2H, s, CH\(_2\)-COCH\(_3\)) and 1.56 (3H, s, N=C-CH\(_3\)) supporting the structure. In \( ^{13} \)C NMR signals at \( \delta \) 174.4 and 174.3 (COOCH\(_3\) and CONH), 161.3 (C=N) and 29.2 (COCH\(_3\)) were observed. The MS spectrum of compound IX showed molecular ion peak at \( m/z \) 282, an intense peak at 137 besides other fragment ions (detailed in experimental section). The observed elemental analysis data found was in good agreement with that of calculated values. Thus keeping in view the above observations the compound IX was assigned as \( N'-(4\text{-oxopentane-2-ylidene})\text{-undecanohydrazide} \).

Reaction of octadecanoic hydrazide (II) with acetylacetone

Refluxing of octadecanoic hydrazide (II) with acetylacetone in absolute ethanol for 4 hrs with a catalytic amount of hydrochloric acid and removing excess solvent from the reaction mixture gave a solid product which was crystallized in ethanol to give a white crystal.

\[
\text{CH}_3-(\text{CH}_2)_{16}-\text{C}=\text{NHNH}_2 + \text{CH}_3-\text{C}-(\text{CH}_2)\text{COCH}_3 \rightarrow \text{CH}_3-(\text{CH}_2)_{16}-\text{C}-(\text{CH}_2)\text{COCH}_3 \quad \text{(II)}
\]

Scheme 1.6: Synthesis of \( N'-(4\text{-oxopentane-2-ylidene})\text{-octadecanohydrazide} \) (X)
Structural elucidation of the compound X as $N'$-(4-oxopentane-2-ylidene)-octadecanohydrazide

Compound X was obtained as white crystals giving characteristic IR bands at 3207 (NH), 1723 (C=O), 1662 (O=C-NH) and 1443 cm$^{-1}$ (C=N). In $^1$H NMR spectrum diagnostic peaks at $\delta$ 10.33 (1H, s, NH, exchangeable with D$_2$O), 2.04 (3H, s, CH$_3$), 1.94 (2H, s, CH$_2$CO$_2$CH$_3$) and 1.59 (3H, s, N=C-CH$_3$) were observed. $^{13}$C NMR spectrum also supported the structure assigned by showing peaks at $\delta$ 174.38 and 174.36 (COOCH$_3$ and CONH), 161.3 (C=N) and 29.3 (COCH$_3$). Molecular ion peak at $m/z$ 380 and an intense peak at 137 were observed besides other fragment ions (detailed in experimental section). Elemental analysis was also in good agreement with that of calculated values. Based on above facts the compound X was characterized as $N'$-(4-oxopentane-2-ylidene)octadecanohydrazide.

Reaction of 12-hydroxyoctadecanoic hydrazide (III) with acetylacetone

Refluxing 12-hydroxyoctadecanoic hydrazide (III) with acetylacetone in absolute ethanol for 4 hrs in presence of catalytic amount of hydrochloric acid gave a solid product after removing the excess solvent which was crystallized in ethanol to give a off-white powder.

\[
\text{CH}_3-(\text{CH}_2)_5-\text{CH}-(\text{CH}_2)_{10}-\text{C}-\text{NHNH}_2 + \text{CH}_3-\text{C}-\text{CH}_2-\text{C}-\text{CH}_3
\]

\[
\text{CH}_3-(\text{CH}_2)_5-\text{CH}-(\text{CH}_2)_{10}-\text{C}-\text{NHN=C-CH}_2-\text{C}-\text{CH}_3
\]

Scheme 1.7: Synthesis of 12-hydroxy-$N'$-(4-oxopentane-2-ylidene)-octadecanohydrazide (XI)
Structural elucidation of the compound XI as 12-hydroxy-N’-(4-oxopentane-2-ylidene)octadecanohydrazide

It was an off-white powder showing IR bands at 3327 (OH), 3205 (NH), 1719 (O=C–CH₃), 1658 (O=C–NH), 1452 cm⁻¹ (C=N). In ¹H NMR diagnostic peaks at δ 10.35 (1H, s, NH, exchangeable with D₂O), 4.13 (1H, m, CH–OH), 3.58 (1H, br. s, OH, exchangeable with D₂O), 2.04 (3H, s, CH₃), 1.91 (2H, s, CH₂CO₂CH₃) and 1.59 (3H, s, N=C–CH₃) were observed. In ¹³C NMR characteristic peaks at δ 174.36 and 174.34 (COOCH₃, CONH), 161.3 (C=N), 72.1 (CH–OH) and 29.7 (COCH₃) were found which also supported the structure. The MS spectrum of compound XI showed molecular ion peak at m/z 396, an intense peak at 297 and other fragment ions were also observed (detailed in experimental section). Elemental analysis was also in good agreement with the calculated values. Thus keeping in view the above observations the compound XI was assigned as 12-hydroxy-N’-(4-oxopentane-2-ylidene)octadecanohydrazide.

Reaction of 9-hydroxyoctadecanoic hydrazide (IV) with acetylacetone

Refluxing of 9-hydroxyoctadecanoic hydrazide (IV) with acetylacetone in absolute ethanol for 4 hrs with a catalytic amount of HCl and removing the excess solvent from the reaction mixture gave a solid product which was crystallized in ethanol to give a white powder.

CH₃–(CH₂)₈–CH–(CH₂)₇–C–NH₂ + CH₅–C–CH₂–C–CH₃

(IV)

Scheme 1.8: Synthesis of 9-hydroxy-N’-(4-oxopentane-2-ylidene)-octadecanohydrazide.
Structural elucidation of the compound XII as 9-hydroxy-N'-\(4\)-oxopentane-2-ylidene)octadecanohydrazide

Compound XII was obtained as a white powder giving characteristic IR bands at 3325(OH), 3208 (NH), 1724 (\(O=\text{C}−\text{CH}_3\)), 1660 (\(O=\text{C}−\text{NH}\)) and 1455 cm\(^{-1}\) (C=\(\text{N}\)). In \(^1\)H NMR spectrum diagnostic peaks at \(\delta\) 10.35 (1H, s, NH, exchangeable with D\(_2\)O), 4.11 (1H, m, CH-OH), 3.58 (1H, br. s, OH, exchangeable with D\(_2\)O), 2.04 (3H, s, CH\(_3\)), 1.90 (2H, s, CH\(_2\)COCH\(_3\)) and 1.55 (3H, s, N=\(\text{C}−\text{CH}_3\)) were observed. \(^{13}\)C NMR spectrum also supported the structure assigned by showing peaks at \(\delta\) 174.37 and 174.34 (COCH\(_3\), CONH), 161.3 (C=N), 72.0 (CH-OH) and 29.46 (COCH\(_3\)). Molecular ion peak at \(m/z\) 396 and an intense peak at 297 were observed which also supported the structure assigned. Other fragment ions were also observed (detailed in experimental section). Elemental analysis was also in good agreement with that of calculated values. Based on above facts the compound XII was characterized as 9-hydroxy-N'-\(4\)-oxopentane-2-ylidene)octadecanohydrazide.
1.3 EXPERIMENTAL

Undecanoic (purity 98%) and (9Z)-octadec-9-enoic (oleic acid, 97%) acids were purchased from Fluka Chemicals (Buchs, Switzerland) (9Z,12R)-12-Hydroxyoctadec-9-enoic (ricinolic acid, 98%) and (9R,12Z)-9-hydroxyoctadec-12-enoic (isoricinolic acid, 98%) were isolated from Ricinus communis and Wrightia tinctoria seed oils, respectively, following Gunstone's partition procedure. Methyl acetoacetate, acetylacetone and hydrazine hydrate (80%) were purchased from S d FINE-CHEM Ltd (Mumbai, India). Thin layer chromatography was done on glass plates (20 x 5 cm) with a layer of silca gel G (Merck, Mumbai, India, 0.5 mm thickness). Mixture of petroleum ether-diethyl ether-acetic acid (80:20:1, v/v) was used as mobile phase. Column chromatography was carried out on silca gel (Merck, Mumbai, India, 60-120 mesh). IR spectra were obtained on a Shimadzu 8201 PCFT FT-IR spectrometer. ¹H NMR spectra were recorded at 300 MHz and ¹³C NMR spectra were recorded at 75 MHz. The chemical shifts (δ) were measured relative to internal standard TMS. Coupling constants were expressed in Hz. The FAB mass spectra were recorded on a JEOL-SX 102/DA-600 mass spectrometer. Melting points were taken in open capillaries and are uncorrected.

General procedure for the preparation of fatty acid hydrazides

Methyl undec-10-enoate (0.1 mmol) was reacted with hydrazine hydrate (0.25 mmol) while stirring and refluxing in ethanol for 5 hrs. The resulting solution was cooled and poured into crushed ice. The solid thus obtained was filtered and recrystallized from ethanol to afford the corresponding undecanoic hydrazide (I). Similarly, octadecanoic hydrazide (II), 12-hydroxyoctadecanoic hydrazide (III) and 9-hydroxyoctadecanoic hydrazide (IV) were obtained from methyl (9Z)-octadec-9-enoate, methyl (9Z,12R)-12-hydroxyoctadec-9-enoate and methyl (9R,12Z)-9-hydroxyoctadec-12-enoate, respectively.

Undecanoic hydrazide (I). White crystals, yield 80%, m.p. 90–92 °C (lit. 93–94 °C)

IR (KBr, cm⁻¹) 3210–3080 (NH–NH₂), 1660 (O=C–NH)
**Fatty Hydrazones**

\[^1^H\text{NMR} (\text{CDCl}_3) : \delta 8.74 (1\text{H, s, NH}), 3.93 (2\text{H, s, NH}_2), 2.57 (2\text{H, t, } J = 7.8 \text{ Hz, } \text{CH}_2\text{-CONH}), 1.55 (2\text{H, m, CH}_3\text{CH}_2\text{-CO}), 1.24 (14\text{H, br. s, } 7\times \text{CH}_2), 0.87 (3\text{H, deg. t, CH}_3).\]

**Octadecanoic hydrazide (II).** White powder, yield 85%, m.p. 110–112 °C (lit.\(^{36,40}\) m.p. 112–114 °C).

\[\text{IR (KBr, cm}^{-1} : \text{3218–3080 (NH–NH}_2\text{), 1660 (O=C–NH).}\]

\[^1^H\text{NMR} (\text{CDCl}_3) : \delta 8.85 (1\text{H, s, NH}), 3.98 (2\text{H, s, NH}_2), 2.57 (2\text{H, t, } J = 7.8 \text{ Hz, } \text{CH}_2\text{-CONH}), 1.57 (2\text{H, m, CH}_3\text{CH}_2\text{-CO}), 1.25 (28\text{H, br. s, } 14\times \text{CH}_2), 0.87 (3\text{H, deg. t, CH}_3).\]

**12-Hydroxyoctadecanoic hydrazide (III).** White crystals, yield 75%, m.p. 112–114 °C.

\[\text{IR (KBr, cm}^{-1} : \text{3327 (OH), 3278–3095 (NH–NH}_2\text{), 1670 (O=C–NH).}\]

\[^1^H\text{NMR} (\text{CDCl}_3) : \delta 8.70 (1\text{H, s, NH}), 4.11 (1\text{H, m, CH–OH}), 3.90 (2\text{H, s, NH}_2), 3.66 (1\text{H, br. s, OH}), 2.57 (2\text{H, t, } J = 7.8 \text{ Hz, } \text{CH}_2\text{-CONH}), 1.61 (2\text{H, m, CH}_3\text{CH}_2\text{-CO}), 1.27 (26\text{H, br. s, } 13\times \text{CH}_2), 0.88 (3\text{H, deg. t, CH}_3).\]

**9-Hydroxyoctadecanoic hydrazide (IV).** Off-white crystals, yield 70%, m.p. 112–114 °C.

\[\text{IR (KBr, cm}^{-1} : \text{3327 (OH), 3270–3095 (NH–NH}_2\text{), 1669 (O=C–NH).}\]

\[^1^H\text{NMR} (\text{CDCl}_3) : \delta 8.85 (1\text{H, s, NH}), 4.11 (1\text{H, m, CH–OH}), 3.90 (2\text{H, s, NH}_2), 3.66 (1\text{H, br. s, OH}), 2.57 (2\text{H, t, } J = 7.8 \text{ Hz, } \text{CH}_2\text{-CONH}), 1.61 (2\text{H, m, CH}_3\text{CH}_2\text{-CO}), 1.27 (26\text{H, br. s, } 13\times \text{CH}_2), 0.88 (3\text{H, deg. t, CH}_3).\]

**General procedure for the preparation of hydrazones**

Fatty acid hydrazide (0.1 mmol) and methyl acetoacetate (0.1 mmol) were refluxed in absolute ethanol (30 ml) for 3–4 hrs containing a few drops of HCl. The resulting solution was then concentrated and cooled. The solid thus separated was filtered and crystallized from ethanol, except for the oily compound (V), which was
chromatographed on silica gel (60–120 mesh) using petrol ether-diethyl ether (98:2, v/v) as eluent.

Methyl 3-(2'-undecanoylhydrazono)butanoate (V). Oily, yield 86%.

IR (neat, cm⁻¹) : 3210 (NH), 1743 (O=COCH₃), 1660 (O=C–NH), 1449 (C=N).

¹H NMR (CDCl₃) : δ 10.35 (1H, s, NH, exchangeable with D₂O), 3.66 (3H, s, OCH₃), 2.30 (2H, t, J = 7.5 Hz, CH₂–CONH), 2.01 (2H, s, CH₂CO₂CH₃), 1.61 (2H, m, CH₂CH₂CO), 1.56 (3H, s, N=C–CH₃), 1.26 (14H, br. s, 7×CH₂), 0.87 (3H, deg. t, terminal CH₃).

¹³C NMR (CDCl₃) : δ 174.7, 174.5, 159.2, 51.5, 34.2, 31.9, 29.8, 29.7, 29.5, 25 7, 25.0, 22.7, 14.2 (three signals are hidden).

MS (FAB) m/z (%) : 298 (M⁺, 3), 267 (50), 154 (100), 127 (25), 99 (20), 95 (45)

Found: C, 64.18; H, 9.87; N, 9.08 %.

Methyl 3-(2'-octadecanoylhydrazono)butanoate (VI). White powder, yield 78%, m.p. 45 °C.

IR (KBr, cm⁻¹) : 3207 (NH), 1736 (O=COCH₃), 1568 (O=C–NH), 1455 (C=N).

¹H NMR (CDCl₃) : δ 10.35 (1H, s, NH, exchangeable with D₂O), 3.66 (3H, s, OCH₃), 2.30 (2H, t, J = 7.8 Hz, CH₂CONH), 1.94 (2H, s, CH₂CO₂CH₃), 1.61 (2H, m, CH₂CH₂–CO), 1.59 (3H, s, N=C–CH₃), 1.25 (28H, br. s, 14×CH₂), 0.88 (3H, deg. t, terminal CH₃).

¹³C NMR (CDCl₃) : δ 174.8, 174.5, 159.1, 51.6, 34.2, 31.9, 29.8, 29.7, 29.6, 29 5, 29.4, 25.7, 25.1, 22.7, 14.1 (eight signals are hidden).

MS (FAB) m/z (%) : 396 (M⁺, 3), 298 (100), 267 (30), 239 (12), 185 (7), 157 (10), 143 (50), 99 (35).
**Fatty Hydrazones**

Anal  
Calcd for C$_{23}$H$_{44}$O$_3$N$_2$ (395.97): C, 69.65; H, 11.18; N, 7.06.  
Found: C, 69.59; H, 11.02; N, 6.98 %.

**Methyl 3-[2’-(12-hydroxyoctadecanoylhydrazono)]butanoate (VII).**  
Off-white powder, yield 75%, m.p. 47 °C.

IR (KBr, cm$^{-1}$)  
3321 (OH), 3212 (NH), 1737 (O=COCH$_3$), 1660 (O=C-NH), 1458 (C=N).

$^1$H NMR (CDCl$_3$)  
δ 10.34 (1H, s, NH, exchangeable with D$_2$O), 3.98 (1H, m, CH–OH), 3.66 (3H, s, OCH$_3$), 3.58 (1H, br. s, OH, exchangeable with D$_2$O), 2.30 (2H, t, J = 7.5 Hz, CH$_2$CONH), 1.91 (2H, s, CH$_2$CO$_2$CH$_3$), 1.61 (2H, m, CH$_2$CH$_2$–CO), 1.59 (3H, s, N=C–CH$_3$), 1.27 (26H, br. s, 13×CH$_2$), 0.88 (3H, deg. t, terminal CH$_3$).

$^{13}$C NMR (CDCl$_3$)  
δ 174.44, 174.40, 159.2, 72.1, 51.5, 37.6, 34.2, 31.9, 29.8, 29.7, 29.57, 29.55, 29.5, 29.2, 25.7, 25.0, 22.8, 14.2 (five signals are hidden).

MS (FAB) m/z (%)  
412 (M$^+$, 2), 299 (25), 297 (100), 283 (30), 265 (70), 199 (10), 154 (75), 98 (15).

Anal  
Calcd for C$_{23}$H$_{44}$O$_4$N$_2$ (411.96): C, 66.95; H, 10.75; N, 6.79.  
Found: C, 66.91; H, 10.55; N, 6.67 %.

**Methyl 3-[2’-(9-hydroxyoctadecanoylhydrazono)]butanoate (VIII).**  
White powder, yield 75%, m.p. 43 °C.

IR (KBr, cm$^{-1}$)  
3327 (OH), 3214 (NH), 1737 (O=COCH$_3$), 1658 (O=C–NH), 1459 (C=N).

$^1$H NMR (CDCl$_3$)  
δ 10.35 (1H, s, NH, exchangeable with D$_2$O), 4.11 (1H, m, CH–OH), 3.66 (3H, s, OCH$_3$), 3.58 (1H, br. s, OH, exchangeable with D$_2$O), 2.30 (2H, t, J = 7.5 Hz, CH$_2$CONH), 1.91 (2H, s, CH$_2$CO$_2$CH$_3$), 1.61 (2H, m, CH$_2$CH$_2$–CO), 1.55 (3H, s, N=C–CH$_3$), 1.25 (26H, br. s, 13×CH$_2$), 0.88 (3H, deg. t, terminal CH$_3$).
Fatty Hydrazones

$^{13}$C NMR (CDCl$_3$): $\delta$ 174.5, 174.4, 159.2, 72.0, 51.6, 37.6, 37.5, 34.1, 31.9, 29.7, 29.6, 29.53, 29.50, 29.4, 29.2, 25.7, 25.0, 22.7, 14.1 (four signals are hidden).

MS (FAB) $m/z$ (%): 412 ($M^+$, 4), 313 (30), 299 (100), 267 (20), 265 (70), 199 (10), 143 (10), 126 (25), 98 (15).

Anal: Calcd for $C_{23}H_{44}O_4N_2$ (411.96): C, 66.95; H, 10.75; N, 6.79. Found: C, 66.87; H, 10.52; N, 6.63 %.

General procedure for preparation of hydrazides

Fatty acid hydrazide (0.1 mmol) and acetylacetone (0.1 mmol) were refluxed in absolute ethanol (30 ml) for 4 hrs containing a few drops of HCl. The resulting solution was then concentrated and cooled at room temperature. The solid thus separated was filtered and crystallized from ethanol, except for the oily compound (IX), which was chromatographed on silica gel (60–120 mesh) using petrol ether-diethyl ether (96:4, v/v) as eluent.

$N'$-(4-Oxopentane-2-ylidene)undecanohydrazide (IX). Oily, yield 80%.

IR (KBr, cm$^{-1}$): 3205 (NH), 1721 (C=O), 1664 (O=C=NH), 1446 (C=N).

$^1$H NMR (CDCl$_3$): $\delta$ 10.33 (1H, s, NH, exchangeable with D$_2$O), 2.30 (2H, t, $J$ = 7.8 Hz, CH$_2$CONH), 2.04 (3H, s, CH$_3$), 1.94 (2H, s, CH$_2$COCH$_3$), 1.61 (2H, m, CH$_2$CH$_2$CO), 1.56 (3H, s, N=C–CH$_3$), 1.25 (14H, br s, 7×CH$_2$), 0.87 (3H, deg. t, terminal CH$_3$).

$^{13}$C NMR (CDCl$_3$): $\delta$ 174.4, 174.3, 161.3, 74.1, 51.4, 32.0, 29.7, 29.6, 29.4, 29.2, 25.1, 22.8, 14.1 (three signals are hidden).

MS (FAB) $m/z$ (%): 282 ($M^+$, 3), 281 (65), 267 (40), 239 (15), 169 (10), 141 (10), 137 (100).

Anal: Calcd for $C_{16}H_{30}O_2N_2$ (281.98): C, 68.04; H, 10.71; N, 9.92. Found: C, 67.84; H, 10.37; N, 9.71 %.
$N'$-(4-Oxopentane-2-ylidene)octadecanohydrazide (X). White crystals, yield 70%, m.p. 43 °C.

**IR (KBr, cm$^{-1}$)**: 3207 (NH), 1723 (C=O), 1662 (O=C-NH), 1443 (C=N).

$^1$H NMR (CDCl$_3$): $\delta$ 10.33 (1H, s, NH, exchangeable with D$_2$O), 2.30 (2H, t, $J = 7.8$ Hz, CH$_2$CONH), 2.04 (3H, s, CH$_3$), 1.94 (2H, s, CH$_2$COCH$_3$), 1.64 (2H, m, CH$_2$CH$_2$CO), 1.59 (3H, s, N=C-CH$_3$), 1.25 (28H, br s, 14×CH$_2$), 0.88 (3H, deg. t, terminal CH$_3$).

$^{13}$C NMR (CDCl$_3$): $\delta$ 174.38, 174.36, 161.3, 51.4, 34.2, 32.1, 29.8, 29.63, 29.58, 29.52, 29.47, 29.41, 29.3, 25.1, 14.1 (seven signals are hidden).

**MS (FAB) m/z (%)**: 380 (M$^+$, 4), 281 (65), 267 (40), 239 (15), 169 (10), 141 (10), 137 (100).

**Anal**: Calcd for C$_{23}$H$_{44}$O$_2$N$_2$ (379.98): C, 72.58; H, 11.65; N, 7.36. Found: C, 72.51; H, 11.44; N, 7.23 %.

12-Hydroxy-$N'$-(4-oxopentane-2-ylidene)octadecanohydrazide (XI). Off-white powder, yield 70%, m.p. 44 °C.

**IR (KBr, cm$^{-1}$)**: 3327 (OH), 3205 (NH), 1719 (C=O), 1658 (O=C-NH), 1452 (C=N).

$^1$H NMR (CDCl$_3$): $\delta$ 10.35 (1H, s, NH, exchangeable with D$_2$O), 4.13 (1H, m, CH–OH), 3.58 (1H, br. s, OH, exchangeable with D$_2$O), 2.32 (2H, t, $J = 7.5$ Hz, CH$_2$CONH), 2.04 (3H, s, CH$_3$), 1.91 (2H, s, CH$_2$COCH$_3$), 1.64 (2H, m, CH$_2$CH$_2$CO), 1.59 (3H, s, N=C–CH$_3$), 1.25 (26H, br. s, 13×CH$_2$), 0.88 (3H, deg. t, terminal CH$_3$).

$^{13}$C NMR (CDCl$_3$): $\delta$ 174.36, 174.34, 161.3, 72.1, 51.4, 37.6, 37.5, 34.1, 32.0, 29.7, 29.6, 29.5, 29.4, 29.3, 25.1, 22.7, 14.2 (six signals are hidden).
**Fatty Hydrazones**

MS (FAB) m/z (%): 396 (M+, 4), 313 (10), 297 (100), 281 (20), 267 (10), 199 (7), 171 (15), 154 (90), 140 (9), 112 (8), 98 (20).

Anal: Calcd for C_{23}H_{44}O_3N_2 (395.97): C, 69.65; H, 11.18; N, 7.06. Found: C, 69.57; H, 10.98; N, 6.96 %.

9-Hydroxy-N’-(4-oxopentane-2-ylidene)octadecanohydrazide (XII). White powder, yield 75%, m.p. 42 °C.

IR (KBr, cm⁻¹): 3325 (OH), 3208 (NH), 1724 (C=O), 1660 (O=NH), 1455 (C=N).

^1H NMR (CDCl₃): δ 10.35 (1H, s, NH, exchangeable with D₂O), 4.11 (1H, m, CH-OH), 3.58 (1H, br. s, OH, exchangeable with D₂O), 2.30 (2H, t, J = 7.5 Hz, CH₂CONH), 2.04 (3H, s, CH₃), 1.90 (2H, s, CH₂COCH₃), 1.61 (2H, m, CH₂CH₂CO), 1.55 (3H, s, N=C-CH₃), 1.25 (26H, br. s, 13×CH₂), 0.88 (3H, deg. t, terminal CH₃).

^13C NMR (CDCl₃): δ 174.37, 174.34, 161.3, 72.0, 51.4, 37.6, 37.5, 34.2, 32.0, 29.7, 29.63, 29.55, 29.50, 29.46, 29.42, 29.3, 25.0, 22.8, 14.2 (four signals are hidden).

MS (FAB) m/z (%): 396 (M+, 5), 363 (7), 297 (100), 267 (30), 199 (10), 185 (10), 140 (15), 115 (8), 98 (20).

Anal: Calcd for C_{23}H_{44}O_3N_2 (395.97): C, 69.65; H, 11.18; N, 7.06. Found: C, 69.55; H, 10.95; N, 6.92 %

**THESIS**

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1.4 REFERENCES


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