Part B

Synthesis

of

Fatty Acid Derivatives
CHAPTER-2

3,5-Disubstituted-

1H-1,2,4-triazoles
2.1 Theoretical

Nitrogen heterocycles of different ring sizes, with different substitution patterns and embedded in various molecular frameworks constitute extremely important structure classes in the search for bioactivity. Despite the large availability of methods to construct nitrogen heterocycles, there is still a strong need to further explore synthetic methods to efficiently synthesize novel heterocyclic structures. This proposal aims at the development of novel methodology for the synthesis of nitrogen heterocyclic structural motifs, containing varied groups.

Many compounds bearing five-membered heterocyclic rings in their structure have an extensive spectrum of pharmacological activities. Among them, 1,2,4-triazole derivatives have attracted considerable interest and can be used as antifungal¹, antibacterial², anti-inflammatory³, antiasthmatic⁴, antidepressant⁵, tuberculotherapeutic⁶, hypoglycemic⁷ and diuretic⁸ activities.

The 1H-1,2,4-triazole compounds are considered interesting heterocycles since they possess important pharmacological activities such as antifungal and antiviral activities. Examples of antifungal drugs⁹, ¹⁰ are fluconazole (i)¹¹, ¹², ICI 153066 (ii)¹³, itraconazole (iii)¹⁴, ravuconazole (iv)¹⁵, voriconazole (v)¹⁶-¹⁸, and posaconazole (vi)¹⁹.
Some 3-amino-1H-1,2,4-triazoles have been used as herbicides and defoliants; meanwhile they were described as catalase inhibitors and blockers for certain ethanol-induced behavior effects. It has been reported that only certain enantiomers of triazoles containing oxazolidine rings (e.g., (vii), 4(R), 5(R)) are active against Candida albicans infections in mice. Ribose N-glycoside (viii) is a broad spectrum antiviral agent containing the 3-aminocarbonyltriazole moiety. It is active against both RNA and DNA virus and is used in an aerosol for lower respiratory tract viral disease as well as in the treatment of influenza, Lassa fever and Hantaan virus. Amidine and guanidine derivatives (ix) (R = H·HCl, Me, CN) exhibiting a broad spectrum of antiviral activity have been prepared.
Some triazole derivatives are considered as angiotensin II receptor antagonists. These compounds, such as (x) and (xi), are used to increase the blood pressure.

In addition, it was reported that compounds having triazole moieties, such as vorozole (xii), letrozole (xiii), and anastrozole (xiv), appeared to be very effective aromatase inhibitors, which in turn prevented breast cancer.

It is known that 1,2,4-triazole moieties interact strongly with heme iron, and aromatic substituents on the triazoles are very effective for interacting with the active site of aromatase.
Morpholine (xv) and N-methyl piperazine (xvi) derivative of 1-aminomethyl-3-substituted-4-[5-(4-methoxy-2-nitrophenyl)-2-furfurylidene]-amino-1,2,4-triazole-5-thiones show potent anticancer activity.\(^{40}\)

\[
\begin{align*}
\text{(xv)} & \quad \text{(xvi)} \\
\end{align*}
\]

The 3-[(4-methylphenoxy)methyl]-4-(N-pyrazin-2'-yl-carboxamido)-5-mercapto-1,2,4-triazoles (xvii) and 3-[(4-methylphenoxy)methyl]-4-(N-pyrazin-2'-yl-carboxamido)-5-hydrazino-1,2,4-triazoles (xviii) are shown to possess anti-inflammatory and analgesic activity.\(^{41}\)

\[
\begin{align*}
\text{(xvii)} & \quad \text{(xviii)} \\
\end{align*}
\]

The various methods for the synthesis of 1,2,4-triazole derivatives are reported by numerous workers. Some of them are discussed here briefly. The reaction of hydrazine or substituted hydrazines with suitable electrophiles is the most common method for the preparation of the triazoles. Examples where hydrazines provide the triazole ring\(^{42-44}\) are described in Scheme 2.1-2.3.
The conversion of a non-triazole ring system into a triazole usually included the substitution of nitrogen for another heteroatom in a five-membered ring, only a few typical examples are illustrated in Scheme 2.4-2.5.
Microwave irradiation has become a widely used method to synthesize many useful organic chemicals rapidly, with good yields and high selectivity\textsuperscript{48-52}. By applying the microwave irradiation method, several 1,2,4-triazole derivatives were recently reported. 3,5-Disubstituted 4-amino-1,2,4-triazoles (xxxi) from the reaction of aromatic nitriles (xxx) with NH\textsubscript{2}NH\textsubscript{2}-2HCl in the presence of NH\textsubscript{2}NH\textsubscript{2}-2H\textsubscript{2}O excess in ethylene glycol under microwave irradiation\textsuperscript{53} (Scheme 2.6).

![Scheme 2.6](image)

An efficient microwave-assisted one-pot and three-component synthesis of substituted 1,2,4-triazoles (xxxv) has been achieved utilizing substituted primary amines\textsuperscript{54} (Scheme 2.7).

![Scheme 2.7](image)

The 1-[(1,5-dialkyl-1\texttextsuperscript{-}1,2,4-triazol-3-yl)] methylthymines (xxxviii)\textsuperscript{55} have been prepared from cycloaddition of the 1-cyanothymine (xxxvi)\textsuperscript{56} with the reactive cumulenes (xxxvii), as potential anti-HIV agents since some acyclic 1,2,4-triazole C-
nucleosides\textsuperscript{57} showed remarkable antiviral properties against HSV-1 and -2 along with other virus (Scheme 2.8).

\begin{center}
\begin{tikzpicture}

\node (n) [draw] at (0,0) {\( \text{xxxvi} \)};
\node (r) [draw] at (2,0) {\( \text{xxxvii} \)};
\node (s) [draw] at (4,0) {\( \text{xxxviii} \)};

\node (o) [draw] at (0,1.5) {\( \text{xxxix} \)};
\node (p) [draw] at (2,1.5) {\( \text{xxxx} \)};

\draw[->] (n) -- (r);
\draw[->] (r) -- (s);
\draw[->] (o) -- (p);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.8}

A series of new 1,2,4-triazoloalkylphthalimides (xl) has been synthesized from cycloaddition of the cyanoalkylphthalimides (alkylmethyl, ethyl, propyl) (xxxix) respectively, with the reactive cumulenes (xxxvii), as promising inhibitors of TNF-\( \alpha \) production\textsuperscript{58} (Scheme 2.9).

\begin{center}
\begin{tikzpicture}

\node (n) [draw] at (0,0) {\( \text{xxxix} \)};
\node (r) [draw] at (2,0) {\( \text{xli} \)};

\draw[->] (n) -- (r);
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.9}

1,2,4-triazole derivatives carrying piperazine residue, (xlii) and (xliv)\textsuperscript{59}, have been synthesized from cycloaddition of (xxxvii) with the 1,4-bis(cyanomethyl) piperazine (xli)\textsuperscript{60} and 1-cyanomethyl-4-methylpiperazine (xliii)\textsuperscript{61}, respectively (Scheme 2.10-2.11).
The short chain, alicyclic and variously substituted aromatic carboxylic acids have been utilized for the synthesis of 1,2,4-triazole derivatives. But 1,2,4-triazoles from long-chain carboxylic acid hydrazides have not been reported earlier. These considerations led to the series of present investigations to synthesize 3,5-disubstituted-1H-1,2,4-triazoles from fatty acid hydrazides.
2.2 Synthesis, Antibacterial and Antifungal Activity of Some Novel 3,5-Disubstituted-1H-1,2,4-triazoles*

The development of new approaches for the synthesis of heterocycles decorated with unique functional groups forms the basis of extensive research activity in synthetic organic chemistry. Justification of much of the chemistry directed to the synthesis of the compounds, possessing nitrogen at the ring fusion is due to the application of compounds having interesting biological properties in the field of medicinal chemistry. The 1,2,4-triazole moiety is a structural element in certain antiasthmatic, antiviral (ribavirin), antifungal (fluconazole), antibacterial, hypotonic (triazolam) drugs. Certain compounds containing 1,2,4-triazole nucleus have been reported to possess bactericidal, antiviral, insecticidal, anticancer, antinflammatory, anticonvulsant properties. Also some triazole derivatives have been synthesized as plant growth regulators.

Owing to its broad spectrum of biological activity the 1,2,4-triazole ring system represents an attractive target to invent new substrates for their synthesis and production of combinatorial libraries. 3,5-Disubstituted-1,2,4-triazoles are found in several pharmacologically active compounds. Recent examples include selective adenosine A2A receptor antagonist and the phosphodiesterase V inhibitor. Previously, 1,2,4-triazoles were synthesized by hydrazides and nitriles either by Pinner reaction and Pellizzari condensation which involve the cyclodehydrative condensation between nitrile and hydrazide. These procedures (Scheme 2.12) path b-d are usually conducted at elevated temperature and involve the activation of nitrile to acylamidrazone intermediate 2 prior to cyclization.

These conventional procedures not only involve high reaction temperature and long reaction time but also result in low yields of product. Herein we are reporting simple and scalable methodology for the one-pot synthesis of 3,5-disubstituted-1H-1,2,4-triazoles.

![Scheme 2.12 Pathways for synthesis of 3,5-disubstituted-1H-1,2,4-triazoles](image)

To the best of our knowledge 3,5-disubstituted-1H-1,2,4-triazoles have not yet been reported from long-chain saturated and olefinic carboxylic acids. The present work is in continuation of study on the synthesis of heterocycles from such acids. Tetrazoles, pyrazolines, tetrazine, spiro [oxathiolane-2, 2'-dihydotetrazoles], aziridines and benzothiazoles have been previously prepared from fatty acids. Cyanoethoxy and morpholine derivatives of hydroxy long-chain acids and fatty esters showed significant antifungal and antibacterial activity. In view of the above mentioned pharmacological applications of 1,2,4-triazoles, the synthesis of this biologically active moiety was successfully carried out bearing long alkyl and alkenyl chain.

### 2.3 Results and discussion

3,5-Disubstituted-1H-1,2,4-triazoles 5a-o were synthesized by the condensation of long-chain saturated and olefinic carboxylic acid hyrazides 3a-e with nitriles 4 in presence of catalytic amount of K₂CO₃ in n-BuOH (Scheme 2.13). The
use of catalytic amount of K$_2$CO$_3$ provided the product in reduced reaction time in appreciable yield.

\[ \text{R}_3\text{CO} + \text{NH-NH}_2 \xrightarrow{\Delta, \text{K}_2\text{CO}_3} \text{3a-e 4a-c 5a-o} \]

a) \( \text{R}_4=\text{R}_5=\text{H} \)

b) \( \text{R}_4=\text{H}, \text{R}_5=\text{OH} \)

c) \( \text{R}_4=\text{R}_5=\text{OH} \)

Scheme 2.13 Synthesis of 3,5-disubstituted-1H-1,2,4-triazoles

As can be seen from Table 2.1 the scope of the reaction using saturated, olefinic (internal and terminal) and hydroxy acid hydrazides was found to be good. The yield of 3,5-disubstituted-1H-1,2,4-triazoles did not depend on the length of chain of acid hydrazide and was found to be appreciable. The synthesized compounds were identified on the basis of elemental analysis, IR, $^1$H NMR, $^{13}$C NMR and mass spectra.
### Table 2.1 3,5-Disubstituted-1H-1,2,4-triazoles

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting from</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a, 4a</td>
<td></td>
<td>H</td>
<td>H</td>
<td>5a</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>3b, 4a</td>
<td></td>
<td>H</td>
<td>H</td>
<td>5b</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>3c, 4a</td>
<td></td>
<td>H</td>
<td>H</td>
<td>5c</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>3d, 4a</td>
<td></td>
<td>H</td>
<td>H</td>
<td>5d</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>3e, 4a</td>
<td></td>
<td>H</td>
<td>H</td>
<td>5e</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>3a, 4b</td>
<td></td>
<td>H</td>
<td>OH</td>
<td>5f</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>3b, 4b</td>
<td></td>
<td>H</td>
<td>OH</td>
<td>5g</td>
<td>88</td>
</tr>
<tr>
<td>8</td>
<td>3c, 4b</td>
<td></td>
<td>H</td>
<td>OH</td>
<td>5h</td>
<td>85</td>
</tr>
<tr>
<td>9</td>
<td>3d, 4b</td>
<td></td>
<td>H</td>
<td>OH</td>
<td>5i</td>
<td>83</td>
</tr>
<tr>
<td>10</td>
<td>3e, 4b</td>
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<td>H</td>
<td>OH</td>
<td>5j</td>
<td>80</td>
</tr>
<tr>
<td>11</td>
<td>3a, 4c</td>
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<td>OH</td>
<td>5k</td>
<td>81</td>
</tr>
<tr>
<td>12</td>
<td>3b, 4c</td>
<td></td>
<td>OH</td>
<td>OH</td>
<td>5l</td>
<td>80</td>
</tr>
<tr>
<td>13</td>
<td>3c, 4c</td>
<td></td>
<td>OH</td>
<td>OH</td>
<td>5m</td>
<td>79</td>
</tr>
<tr>
<td>14</td>
<td>3d, 4c</td>
<td></td>
<td>OH</td>
<td>OH</td>
<td>5n</td>
<td>79</td>
</tr>
<tr>
<td>15</td>
<td>3e, 4c</td>
<td></td>
<td>OH</td>
<td>OH</td>
<td>5o</td>
<td>78</td>
</tr>
</tbody>
</table>

¹H NMR spectrum of 3-(4'-hydroxyphenyl)-5-(dec-9-enyl)-1H-1,2,4-triazole (5g) showed characteristic signals of δ 10.97 of -NH proton, multiplets at δ 7.57-7.53 for four aromatic protons. Methine proton of C-9 showed signals at δ 5.82. C-10 methylene designated as Hₑ and H₂ displayed two distinct δ values when coupled with adjacent C-9 methine protons. Thus, the ¹H NMR spectrum showed two doublet of doublet at δ 5.02 and 4.90 for H₂ and Hₑ protons respectively. A triplet for two hydrogens was observed at δ 2.91 for methylene protons alpha to triazole ring. The structure of 5g was further supported by its mass spectral studies, which showed
molecular ion peak at $m/z$ 299 consistent with its molecular formula $C_{18}H_{25}N_3O$. Base peak appears at $m/z$ 160. Detailed spectra of titled compounds are given in the experimental section.

All the newly synthesized compounds were evaluated \textit{in vitro} against an assortment of two Gram-positive bacteria \textit{Staphylococcus aureus} MSSA 22 and \textit{Bacillus subtilis} ATCC 6051 and two Gram-negative bacteria \textit{Escherichia coli} K 12 and \textit{Salmonella typhimurium} MTCC 98 at a concentration of 100$\mu$g/ml. Chloramphenicol was used as standard drug for the comparison of antibacterial results. Screening results are summarized in Table 2.2.

\begin{table}[h]
\centering
\begin{tabular}{lcccc}
\hline
\textbf{Compound} & \textbf{E.coli} & \textbf{S.typhimurium} & \textbf{B.subtilis} & \textbf{S.aureus} \\
\hline
5a & 14.6±0.61 & 14.6±0.42 & 19.1±0.66 & 15.4±0.51 \\
5b & 14.2±0.64 & 15.3±0.42 & 18.2±0.51 & 15.5±0.50 \\
5c & 13.6±0.53 & 15.6±0.53 & 17.1±0.23 & 16.7±0.31 \\
5d & 13.2±0.53 & 16.5±0.42 & 16.6±0.53 & 15.8±0.60 \\
5e & 13.2±0.50 & 16.3±0.46 & 16.5±0.50 & 16.6±0.53 \\
5f & 16.1±0.98 & 17.1±0.23 & 19.1±0.25 & 16.9±0.83 \\
5g & 15.9±0.36 & 16.7±0.61 & 18.5±0.46 & 16.9±0.34 \\
5h & 15.4±0.61 & 16.2±0.29 & 18.1±0.31 & 17.8±0.72 \\
5i & 13.3±0.75 & 17.1±0.42 & 17.1±0.63 & 18.5±0.42 \\
5j & 13.1±0.65 & 17.4±0.41 & 16.3±0.50 & 18.4±0.53 \\
5k & 16.6±0.59 & 18.2±0.53 & 20.3±0.42 & 20.3±0.46 \\
5l & 16.6±0.60 & 18.5±0.31 & 20.2±0.53 & 20.9±0.90 \\
5m & 15.9±0.65 & 17.1±0.12 & 19.7±0.31 & 21.3±0.64 \\
5n & 14.0±0.91 & 16.7±0.61 & 19.4±0.40 & 22.5±0.50 \\
5o & 14.2±0.53 & 17.2±0.35 & 19.2±0.35 & 22.2±0.81 \\
\hline
\textbf{Chloramphenicol} & 25 & 20 & 24 & 26 \\
\textbf{Control DMSO} & --- & --- & --- & --- \\
\hline
\end{tabular}
\caption{\textit{In vitro antibacterial activity of compounds 5a-o}}
\end{table}

The newly generated compounds 5a-o have exerted significant inhibitory activity against the growth of the test bacterial strains. The data pertaining to Table 2.2 reveal that 5a-o have significant influence on antibacterial profile of \textit{S. typhimurium} and
S. aureus. The synthesized compounds showed good inhibitory results against B. subtilis and E. coli.

In another set of experiments, the above mentioned compounds 5a-o were also examined for antifungal activity. Nystatin was used as standard drug for the comparison of antifungal results. The synthesized compounds showed excellent inhibitory results for Candida albicans IOA-109 and good results against Penicillium sp. (lab isolate) and Helminthosporum oryzae (2537 lab isolate) (Table 2.3).

Table 2.3 In vitro antifungal activity of compounds 5a-o

<table>
<thead>
<tr>
<th>Compound</th>
<th>C.albicans</th>
<th>H.oryzae</th>
<th>A.niger</th>
<th>T.viridae</th>
<th>Penicillium sp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>18.4±0.31</td>
<td>12.3±0.36</td>
<td>15.0±0.25</td>
<td>5.1±0.42</td>
<td>12.5±0.5</td>
</tr>
<tr>
<td>5b</td>
<td>18.1±0.32</td>
<td>12.5±0.50</td>
<td>14.7±0.86</td>
<td>5.4±0.46</td>
<td>12.7±0.61</td>
</tr>
<tr>
<td>5c</td>
<td>18.3±0.55</td>
<td>11.2±0.49</td>
<td>15.1±0.42</td>
<td>5.6±0.60</td>
<td>12.9±0.80</td>
</tr>
<tr>
<td>5d</td>
<td>17.2±0.49</td>
<td>10.7±0.61</td>
<td>14.4±0.40</td>
<td>5.5±0.5</td>
<td>13.2±0.53</td>
</tr>
<tr>
<td>5e</td>
<td>17.2±0.35</td>
<td>10.8±0.71</td>
<td>14.8±0.80</td>
<td>5.4±0.58</td>
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</tr>
<tr>
<td>5f</td>
<td>19.0±0.44</td>
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<td>6.5±0.50</td>
<td>14.6±0.55</td>
</tr>
<tr>
<td>5g</td>
<td>18.9±0.55</td>
<td>13.2±0.46</td>
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<tr>
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<td>15.1±0.55</td>
<td>6.7±0.61</td>
<td>15.2±0.43</td>
</tr>
<tr>
<td>5i</td>
<td>17.6±0.38</td>
<td>14.2±0.47</td>
<td>15.7±0.42</td>
<td>6.8±0.50</td>
<td>15.2±0.58</td>
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<tr>
<td>5j</td>
<td>18.0±0.85</td>
<td>14.2±0.60</td>
<td>15.5±0.50</td>
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</tr>
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<td>5k</td>
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<td>13.6±0.40</td>
<td>16.1±0.40</td>
<td>8.1±0.50</td>
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<td>5m</td>
<td>17.7±0.44</td>
<td>13.9±0.46</td>
<td>15.7±0.80</td>
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<td>5o</td>
<td>17.9±0.57</td>
<td>14.7±0.55</td>
<td>16.0±0.30</td>
<td>9.2±0.62</td>
<td>17.4±0.43</td>
</tr>
<tr>
<td>Nystatin</td>
<td>20</td>
<td>18</td>
<td>18</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Control DMSO</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

All compound showed moderate activity results against Trichoderma viridae (lab isolate) and Aspergillus niger (lab isolate). The data also revealed that 5a-o has produced the marked enhancement in the potency of these analogues as antibacterial and antifungal agents.
2.4 Experimental

Anhydrous conditions were achieved by oven drying flasks and other equipments. Reactions were monitored by TLC on silica gel G. 60-80 mesh silica gel was used for column chromatography. All reagents and solvents were generally used as received from commercial suppliers and when required solvents were dried and distilled before use. Undec-10-enoic, (Z)-octadec-9-enoic and octadecanoic acids and BF₃.OEt₂ were obtained commercially from Fluka Chemicals (Switzerland). The eluent was a mixture of petroleum ether/EtOAc in different proportions for different compounds and visualized under iodine chamber. (9Z, 12R)-12-Hydroxyoctadec-9-enoic (ricinoleic) and (9R, 12Z)-9-hydroxyoctadec-12-enoic (isoricinoleic) acids were isolated from the natural sources i.e. from Ricinus communis and Wrightia tinctoria seed oils respectively. The concentrate of pure hydroxy acids were obtained by Gunstone's partitioning⁸⁸ of freshly prepared fatty acids and further purified by column chromatography. ¹H NMR spectra was recorded in CDCl₃ on a Bruker DRX-400 instrument. The chemical shifts (δ) were measured relative to TMS as an internal standard. Coupling constants (J) are expressed in Hz. Mass spectra were obtained on a Jeol SX-102 (FAB) spectrometer. The molecular ion peak is designated as (M⁺). IR spectra were obtained on Shimadzu 8201 PC FT-IR using KBr pellet with absorption given in cm⁻¹.

General procedure for the preparation of fatty acid hyrazides (3a-e)

The hydrazides of corresponding fatty acids 3a-e were prepared by refluxing the (0.01mmol) methyl esters with hydrazine hydrate (0.02mmol) in MeOH at about 130⁰C for 2 hours⁸⁹. The mixture was then cooled to room temperature. The hydrazide was solidified in solvent. Filtered, washed with water and recrystallized in EtOH. The fatty acid hydrazides 3a-e were characterized by melting points. The spectral details of 3d, 3e is given below.
(9Z, 12R)-12-Hydroxyoctadec-9-enoic acid hydrazide (3d)

Yield 85%; Mp=108-110 °C.

IR (KBr): 3390, 3280, 2960, 2890 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 8.20 (s, 1H, -NH-), 5.46 (m, 2H, -CH=CH-), 4.16 (d, J=6.9 Hz, 2H, -NH₂), 3.88 (m, 1H, -CHOH), 2.88 (t, 2H, J= 7.9 Hz, -CH₂ α to ring), 2.31 (m, 1H, -CHOH), 2.04 (m, 4H, -CH₂=CH-CH₂-), 1.93 (m, 2H, -CH₂ β to ring), 1.33 (br.s, 18H, chain CH₂), 0.86 (3H, dist.t, CH₃).

MS: 309 (M⁺), 175, 87, 73, 59.

Anal: Calcd. for C₁₈H₃₆N₂O₂: C, 69.90; H, 11.65; N, 9.06. Found: C, 69.88; H, 11.62; N, 9.08%.

(9R, 12Z)-9-Hydroxyoctadec-12-enoic acid hydrazide (3e)

Yield 80%; Mp=110-112 °C.

IR (KBr): 3390, 3280, 2960, 2890 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 8.11 (s, 1H, -NH-), 5.39 (m, 2H, -CH=CH-), 4.11 (d, J=6.9 Hz, 2H, -NH₂), 3.76 (m, 1H, -CHOH), 2.90 (t, 2H, J= 7.9 Hz, -CH₂ α to ring), 2.28 (m, 1H, -CHOH), 2.09 (m, 4H, -CH₂=CH-CH₂-), 1.98 (m, 2H, -CH₂ β to ring), 1.31 (br.s, 18H, chain CH₂), 0.86 (3H, dist.t, CH₃).

MS: 309 (M⁺), 199, 87, 73, 59.

Anal: Calcd. for C₁₈H₃₆N₂O₂: C, 69.90; H, 11.65; N, 9.06. Found: C, 69.88; H, 11.62; N, 9.08%.

General procedure for the preparation of 3,5-disubstituted-1H-1,2,4-triazoles from fatty acid hydrazides (5a-o)

A mixture of nitrile 4 (3mmol), acid hydrazide (3a-e) (1mmol) and K₂CO₃ (0.5mmol) in n-BuOH (2ml) was stirred and refluxed at 150°C for 4 hours. The progress of reaction was monitored on TLC. After completion of reaction the solvent was removed under reduced pressure and the compounds were adsorbed on silica gel and purified by column chromatography. All the compounds 5a-o were obtained as
oily liquid. The purity of compounds was ascertained by TLC resolution studies using petroleum ether/EtOAc (4:1, v/v) and few drops of MeOH as mobile phase. For column chromatography (Hexane:EtOAc, v:v) 5a, (99:1); 5b, (99:1); 5c, (98:2); 5d, (95:5); 5e, (95:5); 5f, (98:2); 5g, (98:2); 5h, (96:4); 5i, (95:5); 5j, (95:5); 5k, (98:2); 5l, (97:3); 5m, (95:5); 5n, (94:6); 5o, (94:6).

**Antibacterial activity**

The newly synthesized compounds were screened in vitro against an assortment of two Gram-positive bacteria *Staphylococcus aureus* MSSA 22 and *Bacillus subtilis* ATCC 6051 and two Gram-negative bacteria *Escherichia coli* K12 and *Salmonella typhimurium* MTCC 98. Screening results are summarized in Table 2.2. All the synthesized compounds were dissolved in DMSO. The antibacterial activity of test compounds and standard chloramphenicol was done by filter paper disc method. Media with DMSO was set up as control. All cultures were routinely maintained on NA (nutrient agar) and incubated at 37°C. The inoculums of bacteria were performed by growing the culture in NA broth at 37°C for overnight. The culture was centrifuged at 1000rpm and pellets was resuspended and diluted in sterile NSS to obtain viable count 10^5CFU/ml. 0.1 ml of approximately diluted bacterial culture suspension was spread with the help of spreader on NA plates uniformly. Sterile 8mm discs (Hi-media Pvt. Ltd.) were impregnated with 100μg/ml concentration of the test compounds. Antibiotic disc, chloramphenicol (30μg/disc Hi-Media) was used as control. The disc was placed onto the plate. Each plate had one control disc impregnated with solvent. The plates were then incubated for 24 hours at 37°C. Diameters of the zone of inhibition (mm) were measured and the average diameters for the test samples were calculated in triplicate sets.

**Antifungal activity**

The standard agar disc diffusion method was performed to evaluate the antifungal property of the test compounds and standard nystatin. The newly
synthesized compounds were screened for *Aspergillus niger* (lab isolate), *Candida albicans* IOA-109, *Penicillium* sp. (lab isolate), *Trichoderma viridae* (lab isolate), *Helminthosporum oryzae* (2537 ICAR, Jaipur). The synthesized compounds were dissolved in DMSO. Media with DMSO was set up as control. All cultures were routinely maintained on SDA and incubated at 28°C. Spore formation of filamentous fungi was prepared from 7 day old culture in sterile normal solution (8% NaCl) and approximately diluted to obtain $10^5$CFU/ml. The inoculums of non sporing fungi, *C. albicans* were performed by growing the culture in SD broth at 37°C for overnight. The culture was centrifuged at 1000rpm and pellets was resuspended and diluted in sterile NSS to obtain viable count $10^5$CFU/ml. 0.1 ml of approximately diluted fungal culture suspension was spread with the help of spreader on SDA plates uniformly. Sterile 8mm discs (Hi-media Pvt. Ltd.) were impregnated with test compounds. Antibiotic disc, nystatin (30μg/disc Hi-Media) was used as control. The disc was placed onto the plate. Each plate had one control disc impregnated with solvent. The plates were incubated at 28°C for filamentous fungi for 72 hours or more while for *C. albicans* plates were incubated at 37°C for 18-48 hours. Antifungal activity was determined by measuring the diameters of the inhibition zone (mm) in triplicate sets.

**Spectroscopic data**

3-Phenyl-5-heptadecyl-1H-1,2,4-triazole (5a)

IR (KBr): 3382, 1607, 1123 cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): δ 10.96 (s, 1H, -NH-), 7.69-7.67 (m, 2H, Ar-H), 7.65-7.60 (m, 1H, Ar-H), 7.49-7.42 (m, 2H, Ar-H), 2.96 (t, 2H, $J = 7.6$ Hz -CH$_2$ α to ring), 2.05 (m, 2H, -CH$_2$ β to ring), 1.72 (br.s, 28H, chain CH$_2$), 0.86 (3H, dist.t, CH$_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$): 159.15, 147.91, 133.81, 129.15, 127.35, 32.17, 30.39, 29.91, 28.66, 23.17, 14.84.

MS (m/z, %): (M+1)$^+$ 384 (10.5), M$^+$ 383 (36.1), 354 (25.3), 270 (27.7), 214 (63.8), 186 (16.6), 158 (100).
3,5-Disubstituted 1H-1,2,4-triazoles

**Anal. Calcd.** for C_{25}H_{41}N_{3}: C, 78.29; H, 10.76; N, 10.95. Found: C, 78.85; H, 10.70; N, 10.90%.

3-Phenyl-5-(dec-9-enyl)-1H-1,2,4-triazole (5b)

IR (KBr): 3392, 1594, 1122 cm^{-1}.

\[ ^1H\text{ NMR} \] (400 MHz, CDCl\textsubscript{3}): \delta 10.98 (s, 1H, -NH-), 7.66-7.64 (m, 2H, Ar-H), 7.62-7.58 (m, 1H, Ar-H), 7.49-7.45 (m, 2H, Ar-H), 5.82 (1H, tdd, \( J_{H,H} = 6.6 \) Hz, \( J_{H,H} = 10.2 \) Hz, \( J_{H,H} = 17.1 \) Hz, CH\textsubscript{2}=CH=), 5.02 (1H, dd, \( J_{H,H} = 10.2 \) Hz, \( J_{H,H} = 1.2 \) Hz, \( H_2C=CH-\)), 4.90 (1H, dd, \( J_{H,H} = 17.1 \) Hz, \( J_{H,H} = 1.2 \) Hz, \( H_2C=CH-\)), 3.10 (t, 2H \( J = 7.6 \) Hz, -CH\textsubscript{2} \( \alpha \) to ring), 2.05 (m, 2H, -CH\textsubscript{2}-CH=CH\textsubscript{2}), 1.99 (m, 2H, -CH\textsubscript{2} \( \beta \) to ring), 1.38 (br,s, 10H, chain CH\textsubscript{2}).

\[ ^13C\text{ NMR} \] (100 MHz, CDCl\textsubscript{3}): 158.94, 147.24, 139.82, 133.91, 129.66, 127.63, 114.67, 32.81, 30.85, 29.26, 28.32, 22.97, 14.21.

**MS** (m/z, %): (M+1)\textsuperscript{+} 284 (14.7), M\textsuperscript{+} 283 (10.8), 270 (28.3), 242 (29.9), 228 (11.8), 214 (18.3), 186 (26.2), 144 (100).

**Anal. Calcd.** for C\textsubscript{18}H\textsubscript{25}N\textsubscript{3}: C, 76.29; H, 8.88; N, 14.83. Found: C, 76.75; H, 8.82; N, 14.77%.

3-Phenyl-5-(heptadec-8-enyl)-1H-1,2,4-triazole (5c)

IR (KBr): 3382, 1597, 1133 cm^{-1}.

\[ ^1H\text{ NMR} \] (400 MHz, CDCl\textsubscript{3}): \delta 10.96 (s, 1H, -NH-), 7.67-7.63 (m, 2H, Ar-H), 7.60-7.56 (m, 1H, Ar-H), 7.49-7.44 (m, 2H, Ar-H), 5.34 (m, 2H, -CH=CH-), 2.97 (t, 2H, \( J = 7.6 \) Hz, -CH\textsubscript{2} \( \alpha \) to ring), 2.05 (m, 4H, -CH\textsubscript{2}-CH=CH-CH\textsubscript{2}-), 1.96 (m, 2H, -CH\textsubscript{2} \( \beta \) to ring), 1.73 (br.s, 20H, chain CH\textsubscript{2}), 0.86 (3H, dist.t, CH\textsubscript{3}).

\[ ^13C\text{ NMR} \] (100 MHz, CDCl\textsubscript{3}): 158.22, 146.91, 134.14, 131.15, 129.01, 128.14, 33.81, 30.86, 29.91, 28.63, 22.62, 14.68.

**MS** (m/z, %): (M+1)\textsuperscript{+} 382 (40.5), M\textsuperscript{+} 381 (30.1), 338 (38.3), 310 (27.7), 268 (63.8), 242 (16.6), 158 (100), 144 (10.9).
3,5-Disubstituted-1H-1,2,4-triazoles

**Anal. Calcd.** for C_{25}H_{39}N_{3}: C, 78.70; H, 10.29; N, 11.01. Found: C, 78.28; H, 10.35; N, 11.07%.

3-Phenyl-5-{(8Z, 11R)-11-hydroxyheptadec-8-enyl]-1H-1,2,4-triazole (5d)

IR (KBr): 3386, 1590, 1119 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 10.99 (s, 1H, -NH\(^{-}\)), 7.66-7.64 (m, 2H, Ar-H), 7.60-7.57 (m, 1H, Ar-H), 7.49-7.46 (m, 2H, Ar-H), 3.88 (m, 1H, -CHOH), 3.11 (t, 2H, \(J = 7.6 \text{ Hz}, -\text{CH}_2 \alpha \) to ring), 2.43 (m, 1H, -CHOH), 2.05 (m, 4H, CH\(_2\)-CH=CH-CH\(_2\)), 1.89 (m, 2H, -CH\(_2\) \(\beta \) to ring), 1.73 (br.s, 18H, chain CH\(_2\)), 0.89 (3H, dist.t, CH\(_3\)).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): 157.93, 146.82, 134.05, 131.61, 129.24, 127.95, 67.85, 39.22, 34.62, 31.22, 29.43, 28.72, 27.14, 22.75, 14.91.

**MS** (m/z, %): (M+1)\(^+\) 398 (9.8), M\(^+\) 397 (21.2), 340 (13.2), 312 (13.1), 282 (26.8), 200 (39.9), 186 (100), 172 (30.0).

**Anal. Calcd.** for C_{25}H_{39}N_{3}O: C, 75.53; H, 9.88; N, 10.56. Found: C, 75.01; H, 9.93; N, 10.61%.

3-Phenyl-5-{(8R, 11Z)-8-hydroxyheptadec-11-enyl]-1H-1,2,4-triazole (5e)

IR (KBr): 3387, 1594, 1124 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta \) 10.98 (s, 1H, -NH\(^{-}\)), 7.69-7.65 (m, 2H, Ar-H), 7.62-7.55 (m, 1H, Ar-H), 7.49-7.45 (m, 2H, Ar-H), 3.88 (m, 1H, -CHOH), 3.11 (t, 2H, \(J = 7.6 \text{ Hz}, -\text{CH}_2 \alpha \) to ring), 2.42 (m, 1H, -CHOH), 2.03 (m, 4H, -CH\(_2\)-CH=CH-CH\(_2\)-), 1.98 (m, 2H, -CH\(_2\) \(\beta \) to ring), 1.29 (br.s, 18H, chain CH\(_2\)), 0.88 (3H, dist.t, CH\(_3\)).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): 157.27, 146.81, 134.73, 131.52, 129.57, 127.21, 67.36, 39.17, 34.61, 31.81, 29.14, 28.71, 27.15, 22.51, 14.71.

**MS** (m/z, %): (M+1)\(^+\) 398 (5.8), M\(^+\) 397 (31.2), 368 (33.2), 326 (13.1), 272 (26.1), 228 (19.9), 214 (100), 172 (30.0).

**Anal. Calcd.** for C_{25}H_{39}N_{3}O: C, 75.53; H, 9.88; N, 10.56. Found: C, 75.99; H, 9.82; N, 10.51%.
3-(4'-Hydroxyphenyl)-5-heptadecyl-1H-1,2,4-triazole (5f)

IR (KBr): 3387, 1590, 1132 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta\) 10.97 (s, 1H, -NH\(-\)), 7.57-7.53 (m, 4H, Ar-H), 6.95 (Ar-OH), 2.78 (t, 2H, \(J = 7.6\) Hz, -CH\(_2\) \(\alpha\) to ring), 1.92 (m, 2H, -CH\(_2\) \(\beta\) to ring), 1.23 (br.s, 20H, chain CH\(_2\)), 0.88 (3H, dist.t, CH\(_3\)).

\(^1^3\)C NMR (100 MHz, CDCl\(_3\)) : 159.14, 151.84, 148.76, 138.97, 129.75, 117.33, 32.52, 30.72, 22.82, 21.72, 14.56.

MS (m/z, %): (M+1)\(^+\) 400 (13.8), M\(^+\) 399 (41.6), 286 (16.6), 272 (83.3), 258 (16.6) 188 (8.3), 174 (44.4), 160 (100).

Anal. Calcd. for C\(_{25}\)H\(_{41}\)N\(_3\)O: C, 75.15; H, 10.33; N, 10.51. Found: C, 75.66; H, 10.39; N, 10.45%.

3-(4'-Hydroxyphenyl)-5-(dec-9-enyl)-1H-1,2,4-triazole (5g)

IR (KBr): 3390, 1590, 1129 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) : \(\delta\) 10.97 (s, 1H, -NH\(-\)), 7.57-7.53 (m, 4H, Ar-H), 6.93 (Ar-OH), 5.82 (1H, tdd, \(J_{H-H} = 6.6\) Hz, \(J_{H-CH_2} = 10.2\) Hz, \(J_{H-H_2} = 17.1\) Hz, CH\(_2\)=CH\(-\)), 5.02 (1H, dd, \(J_{H_2-H} = 10.2\) Hz, \(J_{H_2-H_2} = 1.2\) Hz, H\(_2\)=CH\(-\)), 4.90 (1H, dd, \(J_{H_2-H} = 17.1\) Hz, \(J_{H_2=CH_2} = 1.2\) Hz, H\(_2\)=CH\(-\)), 2.91 (t, 2H, \(J = 7.9\) Hz, -CH\(_2\) \(\alpha\) to ring), 2.02 (m, 2H, -CH\(_2\)-CH=CH\(_2\)), 1.93 (m, 2H, -CH\(_2\) \(\beta\) to ring), 1.38 (br.s, 10H, chain CH\(_2\)).

\(^1^3\)C NMR (100 MHz, CDCl\(_3\)) : 158.76, 151.23, 148.15, 139.72, 129.16, 116.27, 114.43, 34.25, 33.76, 29.22, 24.72.

MS (m/z, %): (M+1)\(^+\) 300 (19.9), M\(^+\) 299 (12.3), 272 (12.5), 244 (17.3), 230 (3.9), 216 (2.2), 188 (3.9), 174 (4.2), 160 (100).

Anal. Calcd. for C\(_{18}\)H\(_{25}\)N\(_3\)O: C, 72.22; H, 8.41; N, 14.03. Found: C, 72.74; H, 8.46; N, 14.09%.
3-(4’-Hydroxyphenyl)-5-(heptadec-8-enyl)-1H-1,2,4-triazole (5h)

IR (KBr): 3387, 1594, 1130 cm^-1.

^1H NMR (400 MHz, CDCl3): δ 10.97 (s, 1H, -NH-), 7.57-7.56 (m, 4H, Ar-H), 6.93 (Ar-OH), 5.39 (2H, m, -CH=CH-), 2.79 (t, 2H, J = 5.7 Hz, -CH2 α to ring), 2.02 (m, 4H, -CH2-CH=CH-CH2-), 1.96 (m, 2H, -CH2 β to ring), 1.23 (br.s, 20H, chain CH2), 0.88 (3H, dist.t, CH3).

^13C NMR (100 MHz, CDCl3): 157.73, 151.24, 148.72, 130.82, 129.17, 118.41, 34.27, 31.83, 29.68, 29.19, 27.04, 24.74, 22.56, 14.61.

MS (m/z, %): (M+1)^+ 398 (13.8), M^+ 397 (41.6), 284 (16.6), 258 (16.6) 188 (8.3), 174 (100), 160 (44.4).


3-(4’-Hydroxyphenyl)-5-(8Z, 11R)-n-hydroxyheptadec-8-enyl]-1H-1,2,4-triazole (5i)

IR (KBr): 3390, 1590, 1123 cm^-1.

^1H NMR (400 MHz, CDCl3): δ 10.98 (s, 1H, -NH-), 7.58-7.52 (m, 4H, Ar-H), 6.98 (Ar-OH), 5.46 (m, 2H, -CH=CH-), 3.88 (m, 1H, -CH-OH), 3.44 (t, 2H, J= 7.5 Hz, -CH2 α to ring), 2.31 (m, 1H, -CH-OH), 2.04 (m, 4H, -CH2-CH=CH-CH2-), 1.91 (m, 2H, -CH2 β to ring), 1.33 (br.s, 18H, chain CH2), 0.86 (3H, dist.t, CH3).

^13C NMR (100 MHz, CDCl3): 157.94, 151.62, 148.52, 130.86, 129.36, 118.74, 67.87, 39.26, 34.17, 31.84, 29.63, 28.96, 27.27, 24.72, 22.54, 14.36.

MS (m/z, %): (M+1)^+ 414 (12.2), M^+ 413 (26.1), 370 (75.8), 356 (60.9), 328 (33.4), 202 (69.8), 174 (14.2), 160 (100).

3-(4'-Hydroxyphenyl)-5-{(8R,11Z)-8-hydroxyheptadec-11-enyl}-1H-1,2,4-triazole (5j)

**IR** (KBr): 3379, 1592, 1119 cm⁻¹.

**¹H NMR** (400 MHz, CDCl₃): δ 10.99 (s, 1H, -NH⁻), 7.57-7.53 (m, 4H, Ar-H), 6.93 (Ar-OH), 5.39 (m, 2H, -CH=CH⁻), 3.88 (m, 1H, -CH-OH), 3.23 (t, 2H, J = 6.4 Hz, -CH₂ α to ring), 2.28 (m, 1H, J = 7.2 Hz, -CH-OH), 2.04 (m, 4H, -CH₂-CH=CH-CH₂), 1.89 (m, 2H, -CH₂ β to ring), 1.27 (br.s, 18H, chain CH₂), 0.86 (3H, dist.t, CH₃).

**¹³C NMR** (100 MHz, CDCl₃): 158.94, 151.62, 148.74, 131.11, 129.46, 118.67, 67.36, 39.64, 34.16, 317.8, 29.55, 28.73, 27.22, 24.55, 22.11, 14.42.

**MS** (m/z, %): (M+1)⁺ 414 (12.5), M⁺ 413 (29.1), 342 (51.2), 316 (33.3), 288 (9.8), 188 (100), 174 (18.8), 160 (80.2).

**Anal. Calcd.** for C₂₅H₃₉N₃O₂: C, 72.61; H, 9.49; N, 10.16. Found: C, 72.99; H, 9.43; N, 10.11%.

3-(4',5'-Dihydroxyphenyl)-5-(heptadecyl)-1H-1,2,4-triazole (5k)

**IR** (KBr): 3349, 1592, 1134 cm⁻¹.

**¹H NMR** (400 MHz, CDCl₃): δ 10.97 (s, 1H, -NH⁻), 7.16 (d, 1H, J = 1.6 Hz, Ar-H), 7.07 (d, 1H, J = 2 Hz, Ar-H), 7.03 (d, 1H, J = 2 Hz, Ar-H), 6.89 (Ar-OH), 6.87 (Ar-OH), 2.78 (t, 2H, J = 7.6 Hz, -CH₂ α to ring), 1.92 (m, 2H, -CH₂ β to ring), 1.23 (br.s, 28H, chain CH₂), 0.88 (3H, dist.t, CH₃).

**¹³C NMR** (100 MHz, CDCl₃): 164.57, 145.16, 144.24, 121.92, 115.91, 32.19, 30.38, 28.91, 22.37, 14.50.

**MS** (m/z, %): (M+1)⁺ 416 (17.0), M⁺ 415 (66.0), 356 (10.4), 314 (2.1), 300 (31.2), 208 (19.2), 190 (12.5), 176 (100).

**Anal. Calcd.** for C₂₅H₄₁N₃O₂: C, 72.26; H, 9.93; N, 10.11. Found: C, 72.79; H, 9.99; N, 10.15%.
3-(4',5'-Dihydroxyphenyl)-5-(dec-9-enyl)-1H-1,2,4-triazole (5I)

IR (KBr): 3387, 1596, 1130 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.98 (s, 1H, -NH\(_{-}\)), 7.11 (d, 1H, \(J = 1.6\) Hz, Ar-H), 7.04 (d, 1H, \(J = 2\) Hz, Ar-H), 7.02 (d, 1H, \(J = 2\) Hz, Ar-H), 6.88 (Ar-OH), 6.87 (Ar-OH), 5.82 (1H, t, \(J_{CH}=CH = 6.6\) Hz, \(J_{H-H} = 10.2\) Hz, \(J_{H-H} = 17.1\) Hz, CH\(_2=CH\)), 5.02 (1H, dd, \(J_{H-H} = 10.2\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, \(J_{H-H} = 17.1\) Hz, CH\(_2=CH\)), 3.13 (t, 2H, \(J = 8\) Hz, -CH\(_2\) to ring), 2.02 (m, 2H, -CH\(_2\) to ring), 1.93 (m, 2H, -CH\(_2\) to ring), 1.38 (br.s, 10H, chain CH\(_2\)).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): 164.91, 145.82, 144.85, 139.94, 121.96, 116.72, 114.67, 34.22, 33.79, 29.24, 28.42, 24.21.

MS (m/z, %): (M+1)\(^+\) 316 (25.7), M\(^+\) 315 (23.8), 288 (44.2), 274 (66.6), 243 (17.1), 208 (36.3), 198 (47.6), 176 (100).

Anal. Calcd. for C\(_{18}\)H\(_{25}\)N\(_3\)O\(_2\): C, 68.55; H, 7.98; N, 13.32. Found: C, 68.05; H, 7.93; N, 13.26%.

3-(4',5'-Dihydroxyphenyl)-5-(heptadec-8-enyl)-1H-1,2,4-triazole (5m)

IR (KBr): 3384, 1594, 1127 cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.97 (s, 1H, -NH\(_{-}\)), 7.11 (d, 1H, \(J = 1.6\) Hz, Ar-H), 7.04 (d, 1H, \(J = 2\) Hz, Ar-H), 7.02 (d, 1H, \(J = 2\) Hz, Ar-H), 6.93 (Ar-OH), 6.89 (Ar-OH), 5.34 (m, 2H, -CH\(_2=CH\)), 2.78 (t, 2H, \(J = 7.6\) Hz, -CH\(_2\) to ring), 2.02 (m, 4H, -CH\(_2\) to ring), 1.92 (m, 2H, -CH\(_2\) to ring), 1.23 (br.s, 20H, chain CH\(_2\)), 0.88 (3H, dist.t, CH\(_3\)).

\(^13\)C NMR (100 MHz, CDCl\(_3\)): 163.42, 146.83, 144.84, 131.91, 121.66, 119.83, 33.18, 29.96, 25.69, 22.76, 14.92.

MS (m/z, %): (M+1)\(^+\) 414 (17.0), M\(^+\) 413 (66.0), 356 (10.4), 314 (12.1), 300 (31.2), 208 (19.2), 190 (100), 176 (57.5).

Anal. Calcd. for C\(_{25}\)H\(_{39}\)N\(_3\)O\(_2\): C, 72.61; H, 9.49; N, 10.16. Found: C, 72.06; H, 9.44; N, 10.21%.
3-(4',5'-Dihydroxyphenyl)-5-[(8Z,11R)-11-hydroxyheptadec-8-enyl]-1H-1,2,4-triazole (5n)

IR (KBr): 3386, 1597, 1123 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 10.98 (s, 1H, -NH⁻), 7.13 (d, 1H, J = 1.6 Hz, Ar-H), 7.04 (d, 1H, J = 2 Hz, Ar-H), 7.01 (d, 1H, J = 2 Hz, Ar-H), 6.89 (Ar-OH), 6.86 (Ar-OH), 5.46 (m, 2H, -CH=CH-), 3.88 (m, 1H, -CH-OH), 3.44 (t, 2H, J = 7.5 Hz, -CH₂ α to ring), 2.31 (m, 1H, -CH-OH), 2.04 (m, 4H, -CH₂CH=CH₂), 1.91 (m, 2H, -CH₂ β to ring), 1.33 (br.s, 18H, chain CH₂), 0.86 (3H, dist.t, CH₃).

¹³C NMR (100 MHz, CDCl₃): 163.92, 147.84, 145.15, 131.86, 121.17, 119.23, 68.25, 39.84, 37.25, 33.18, 29.94, 27.6, 24.19, 22.70, 14.35.

MS (m/z, %): (M+1)⁺ 430 (6.6), M⁺ 429 (28.3), 344 (43.3), 260 (13.8), 253 (41.6), 208 (8.3), 190 (47.2), 176 (100).


3-(4',5'-Dihydroxyphenyl)-5-[(8R,11Z)-11-hydroxyheptadec-11-enyl]-1H-1,2,4-triazole (5o)

IR (KBr): 3392, 1600, 1123 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 10.98 (s, 1H, -NH⁻), 7.11 (d, 1H, J = 1.6 Hz, Ar-H), 7.04 (d, 1H, J = 2 Hz, Ar-H), 7.02 (d, 1H, J = 2 Hz, Ar-H), 6.89 (Ar-OH), 6.87 (Ar-OH), 5.39 (m, 2H, -CH=CH-), 3.88 (m, 1H, -CH-OH), 3.23 (t, 2H, J = 6.4 Hz, -CH₂ α to ring), 2.28 (m, 1H, -CH-OH), 2.04 (m, 4H, -CH₂CH=CH₂), 1.89 (m, 2H, -CH₂ β to ring), 1.27 (br.s, 18H, chain CH₂), 0.86 (3H, dist.t, CH₃).

¹³C NMR (100 MHz, CDCl₃): 163.63, 147.55, 145.16, 131.72, 121.26, 119.68, 68.49, 39.80, 37.41, 33.12, 29.5, 27.33, 24.24, 22.47, 14.21.

MS (m/z, %): (M+1)⁺ 430 (55.5), M⁺ 429 (8.3), 372 (55.5), 332 (41.6), 301 (22.2), 280 (13.6), 208 (8.3), 176 (100).

2.5 References


3,5-Disubstituted-1H-1,2,4-triazoles

50. B. L. Heyes, Microwaves Synthesis; Chemistry at the Speed of Light, CEM Publ: Matthews, NC, 2002.
3,5-Disubstituted-1H-1,2,4-triazoles


