CHAPTER 2

4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones
Biological Activity of 1,2,4-Triazoles

Triazoles are five membered rings containing three nitrogen atoms. The triazole derivatives are reported to be useful in the field of medicine and agriculture. Though many derivatives of triazoles are reported in the literature, very few 1,2,4-triazolinones are known. Hence, we have surveyed the literature for the 1,2,4-triazole systems in general.

A Japanese patent\(^1\) reported the synthesis of compounds of type (24) and screened for insecticidal and ascaricidal activities.

\[
\text{where, } X=\text{halogen and } Y=\text{alkyl halogen}
\]

Antibacterial and antifungal activities of 4-amino-5-(2'-phenylindol-3'-yl) amino-3-phenoxyethyl-1,2,4-triazole (25) have been studied by S. P. Hiremath et al\(^2\).

\[
\text{(25)}
\]
Ikizlear A.A. et al\textsuperscript{3} synthesised and studied antitumor activity of some 4,5-dihydro-1H-1,2,4-triazole-5-ones (26)

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle] (N1) at (0,0) {N};
\node[draw,shape=circle] (N2) at (0.5,0) {N};
\node[draw,shape=circle] (O) at (1,0) {O};
\node at (0.5,-0.3) {H};
\draw (N1) -- (N2) -- (O);\end{tikzpicture}
\end{center}

(26)

Geslin M. et al\textsuperscript{4} studied 3-amino-1-phenyl-1H-[1,2,4] triazole (27) as antagonists of corticotropic hormone releasing factor.

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle] (N1) at (0,0) {N};
\node[draw,shape=circle] (N2) at (0,0.5) {N};
\node[draw,shape=circle] (NH2) at (0,1) {NH\textsubscript{2}};
\node at (0,1.5) {phenyl};\end{tikzpicture}
\end{center}

(27)

Muller-K-Helmeet et al\textsuperscript{5} prepared sulfonylamino(thio)carbonyl-1,2,4-triazole-5-mes(H) as herbicides (28)

\begin{center}
\begin{tikzpicture}
\node[draw,shape=circle] (N1) at (0,0) {N};
\node[draw,shape=circle] (N2) at (0,0.5) {N};
\node[draw,shape=circle] (Q1) at (0,1) {Q\textsuperscript{1}};
\node[draw,shape=circle] (Q2) at (0,1.5) {Q\textsuperscript{2}};
\node[draw,shape=circle] (O2S) at (0,2) {O\textsubscript{2}S-NH};
\node[draw,shape=circle] (R1) at (0.5,0) {R\textsuperscript{1}};
\node[draw,shape=circle] (R2) at (0.5,0.5) {R\textsuperscript{2}};
\node[draw,shape=circle] (R3) at (0.5,1) {R\textsuperscript{3}};
\node at (0.25,0) {O\textsubscript{2}S-NH};\end{tikzpicture}
\end{center}

(28)

Q\textsuperscript{1}, Q\textsuperscript{2} = O,S  
R\textsuperscript{1} = alkyl, cycloalkyl, alkyl, amino etc.  
R\textsuperscript{2} = alkyl, alkoxy, halo etc.  
R\textsuperscript{1},R\textsuperscript{2} = alkylene  
R\textsuperscript{3} = Ph, substituted Ph, alkyl, heteroaryl.
Yamada N. et al. studied the bleaching activity of 4-alkyl-3-propargyl-1,2,4-1H-triazoles (29).

Cesar J. et al. used 3,5-disubstituted-1,2,4-triazoles for the synthesis of peptidomimetics.

Demirayak S. et al. synthesised and studied the antimicrobial activities of some 3-arylamino-5-[2-(sub-1-imidazolyethyl]-1,2,4-triazole derivatives (30).
Udupi R. H. et al\textsuperscript{9} synthesised and screened for antimicrobial activities of 1,2,4-triazole derivatives containing triazolo-thiadiazole and triazolo-thiadiazolidine ring systems (31) and (32).

\begin{align*}
(31) & \quad (32) \\
\text{R} = (\text{un})\text{substituted Ph}, (\text{aryloxy}) \text{ methyl}, \text{ etc.}
\end{align*}
Purpose of the work

Although most triazoles are readily prepared and stored, expensive starting materials or sensitive intermediates appear to have hindered their industrial synthesis.

The synthetic methods of some amino triazoles reported in the literature are described below

3-Amino-5-aryltri azoles (35) are obtained via N-aryl-N'-aminoguanidines (34) by reduction of N-aryl- N'-nitroguanidines (33) with zinc dust in acetic acid\textsuperscript{10}.

\[
\begin{align*}
\text{H}_2\text{NC} & \quad \text{NCOC}_6\text{H}_4-4\text{—Br} \\
\text{NHNO}_2 & \quad \text{(33)} \\
\text{Zn} & \quad \text{AcOH} \\
& \quad \text{(34)} \\
\text{H}_2\text{N} & \quad \text{NCOC}_6\text{H}_4-4\text{—Br} \\
\text{NHNNH}_2 & \quad \text{(35)}
\end{align*}
\]
In the reaction of 2-methyl-2-thiopseudouera (36) with hydrazides (37) under mild conditions, the intermediate N-(acylamino)guanidines (38) are usually not isolated but undergo cyclization to triazoles11 (39).

\[
\text{H}_2\text{N}^-\text{CH}^-\text{SMe} + \text{CH}_2\text{CONHNH}_2 \xrightarrow{\Delta} \text{H}_2\text{N}^-\text{CH}^-\text{NHNHCOPh}
\]

The interaction of benzylidene hydrazone (40) with thiobenzoylisocynate (41) gave (42) followed by acid hydrolysis of the latter gave 1,3-diphenyl-1,2,4-triazolin-5-one12a*b (43).
The interaction of acetylene (44) with phenyl hydrazine (45) gave (46). Isomerization of (46) in chloroform under mild conditions gave (47).

The synthesis of some hitherto unknown 4-amino-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (19) by a simple method from sydnone has been reported from our laboratory from sydnones. These compounds cannot be obtained by any of the procedures mentioned above.

The search for versatile starting material and development of simple and concise procedures for the preparation of wide variety of heterocyclic compounds is one of the important goals of synthetic organic chemists. It appears that we have made a successful attempt in developing a practical and convenient method for the synthesis of such heterocyclic systems which are inaccessible by alternate method, from a simple compound like sydnone.

Surveying the literature on sydnones in the previous part of thesis, it is apparent that the importance of the sydnone ring is due to its ability to undergo ring transformation to a variety of heterocyclic ring systems. These conversions take place by 1,3-dipolar cycloaddition reactions. In continuation of the ongoing studies in this laboratory on heterocyclic construction mediated by sydnones, it was thought of utilising the
sydnone ring for the synthesis of some more heterocyclic systems, which were accessible with difficulty by routine methods or even inaccessible.

In continuation of our synthetic work on 1,2,4-triazolones we thought of exploring the synthetic scope and reactivity of these oxadiazolinones (18 a-h) towards other nitrogen nucleophiles like phenylhydrazine and amines to obtain more substituted triazolone derivatives. However, oxadiazolinones were found to be unreactive towards phenylhydrazine and aromatic amines. It appears that high basicity of the amines determines the ring opening of oxadiazolinone, because the carbonyl is not of a lactone type but it is a lactam-lactone carbonyl which reduces the susceptibility towards less basic aromatic amines. Hence, we thought of using aliphatic amines amongst which we selected ethanolamine for the preparation of the new triazolone derivatives 4-(2-hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (48 a-h).

This choice would allow us to study the effect of basicity towards ring opening of oxadiazolinones and would also serve our purpose of preparing functionalised triazolones.

Our purpose of preparing these hydroxyethyl derivatives was to utilise them as precursors to introduce long chain alkyl groups, through the chloro derivatives (49). Our attempts to convert the hydroxyethyl compounds (48 a-h) to the corresponding chloro derivatives were unsuccessful. However, these compounds containing the carbonyl and the hydroxy groups would be interesting for the study of hydrogen bonding interactions and also the conformational analysis of the ethylene group side chain.

The mechanism of the reaction may be proposed as following. The initial step is the attack of the nucleophile on the carbonyl carbon leading to the ring fission resulting in the formation of the intermediate (50).
The acetamido carbonyl carbon is then attacked by the –CONH, resulting in the formation of the five membered ring (48).

The reaction was traced by TLC and there was no indication of the existence of the intermediate suggesting that the ring fission and recyclisation by the attack of –CONH- is a simultaneous processes. The hydroxyethyl triazolinones are of great interest as they contain free aliphatic -OH group, which could be utilised for variety of reactions.
4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (48 a-h) were obtained by reaction of 3-aryl-5-methyl-1,3,4-oxadiazolin-2-ones (18 a-h) with ethanolamine in ~ 75% yield. The acetyl derivatives (51 a-h) were obtained by refluxing (48 a-h) in acetic anhydride (Scheme 1).

Scheme 1
Experimental

Preparation of 4-(2-hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (48 a-h)

3-Aryl-5-methyl-1,3,4-oxadiazol-2-ones (0.001 mol) (18 a-h) in excess of ethanolamine were heated in an oil-bath at 155-160 °C for 5-6 hrs. The reaction mixture was then poured into ice-cold water. The resultant solid filtered, washed with water and crystallised from ethanol (Table 1).

Preparation of 4-(2-acetoxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (51 a-h)

4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (0.001 mol.) (26 a-h) in excess of acetic anhydride were heated on an water-bath for 2-3 hrs. The reaction mixture was then poured into ice-cold water. The resultant solid filtered, washed with water and crystallised from ethanol (Table 2).

Spectral Characterisation

The IR spectra of all the compounds (48 a-h) (spectrum 1, compound 48e) showed two broad bands at 3456 and 3363 cm⁻¹ due to νOH and another broad band at 1702 cm⁻¹ for the νC=O. These absorption frequencies indicate the hydrogen bonded interactions between the –OH and C=O groups. However, the band for C=O group does not suggest intramolecular hydrogen bonding. Hence, we may assign the two νOH stretching bands for two types of intermolecular hydrogen bondings between
the two hydroxy groups Fig. 1 and the hydroxy and the carbonyl groups Fig. 2 of the two triazolone moieties.

![Fig. 1](image1.png)

![Fig. 2](image2.png)

$^1$H-NMR

$^1$H-NMR (300 MHz) spectra of all the compounds (48 a-h) (spectrum 2, compound 48e) showed a singlet at $\delta$ 2.36 ppm for the $-\text{CH}_3$ protons of triazolone ring. A broad signal at $\delta$ 2.60 ppm (1H, D$_2$O exchanged) is also suggestive of the intermolecular hydrogen bonded $-\text{OH}$ group. The two distorted triplets at $\delta$ 3.85 and 3.95 ppm were assigned to the methylene protons $-\text{CH}_2a$ and $-\text{CH}_2b$ protons respectively and this pattern is in accordance with literature$^{15}$ of similar type of grouping. This splitting pattern is not clearly of the first order perhaps due to the exchangeable proton on the oxygen, however, these distorted triplets transformed into two clear doublets ($J=5.56$ Hz each) on deuteration. On the basis of this splitting pattern these may be represented as $AA'BB'$. 

48
pattern. Hence, the ethylene group contains magnetically non-equivalent spin systems with two sets of equivalent protons, which can be illustrated by the following Newman and 3D structures Fig. 3 & 4. This conformation with the –CO and –OH far apart rules out intramolecular hydrogen bonding while it can account for two different intermolecular hydrogen bondings. The aromatic protons resonate at 87.3 - 87.9 ppm.

This conformation was also deduced from the \(^1\)H-NOE difference spectrum of a typical compound (48e) (spectrum 3). Upon irradiation of the methyl protons at \(\delta 2.36\)ppm, an enhancement in the methylene triplet at \(\delta 3.85\)ppm was observed which indicated the close proximity of –CH\(_2\) and –CH\(_3\) in space.
The $^{13}$C-NMR spectrum of a typical compound (48e) (spectrum 4) showed the signal for $-\text{CH}_3$ group of triazolone ring at δ12.5 ppm. The signals at δ 45 and δ 60 ppm were assigned to the methylene carbon atoms attached to the $-\text{OH}$ group and the ring respectively. The aromatic carbon atoms showed two intense signals at δ 120 ppm for ($\text{C}_3$' and $\text{C}_5$') and at δ 130 ppm for ($\text{C}_2$' and $\text{C}_6$') and the signals at δ 125 ppm and δ 137 ppm are due to the $\text{C}_1$' and $\text{C}_4$' atoms respectively. The $\text{C}_3$ deshielded by the two nitrogen atoms appears downfield at δ 145 ppm, while the most deshielded carbon atom of $\text{C}=\text{O}$ appeared at δ 154 ppm. The number of $^{13}$C-signals agree with the structure Fig.5.

![Fig 5](image)

The structure of the title compound (48) was unequivocally proved by X-ray study. The ORTEP drawing for the compound (48e) Figure (6), shows that the phenyl group is oriented at an angle of 30.63 (9)° with respect to the plane of the triazole ring. The hydroxylethyl group projects roughly perpendicular to the triazole ring [$\text{C3-N4-C12-C13} = 80.7$ (2)°]. The exocyclic angle N2-C3-O3 [$128.58$ (17)° ] is significantly larger than the normal value of 120°, this may be due to the short contact between atoms H11 of the phenyl ring and O3 (2.54 Å). The hydroxy group forms an intermolecular hydrogen bond with the carbonyl $\text{O}$ atom of an adjacent molecule. This interaction links the molecule into chains.
Crystal structure of 2-(4-chlorophenyl)-4-(2-hydroxyethyl)-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-one(48 e). Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented by circles of arbitrary radii.

Selected geometric parameters (Bond length in Å, Bond angles in degrees)

<table>
<thead>
<tr>
<th>Bond Type</th>
<th>Length</th>
<th>Bond Type</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1-C5</td>
<td>1.296</td>
<td>N4-C5</td>
<td>1.377</td>
</tr>
<tr>
<td>N1-N2</td>
<td>1.401</td>
<td>N4-C3</td>
<td>1.383</td>
</tr>
<tr>
<td>N2-C3</td>
<td>1.370</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5-N1-N2</td>
<td>104.30</td>
<td>N2-C3-N4</td>
<td>103.37</td>
</tr>
<tr>
<td>C3-N2-N1</td>
<td>112.02</td>
<td>N1-C5-C15</td>
<td>124.96</td>
</tr>
<tr>
<td>C5-N4-C3</td>
<td>108.20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 6
The structure of the title compounds was confirmed by its mass spectral analysis. An EIMS spectrum (spectrum 5) of a typical compound (48e) showed the molecular ion peaks at m/z 253 and 255 (isotopic peak for chlorine) in (3:1) which agrees with the molecular weight of the compound. The fragmentation pattern depicted in scheme (2) is as follows

The molecular ion at m/z 253, 255 (61%) looses the side chain \(-\text{CH}_2=\text{CH-OH}\) as a neutral moiety to give the fragment \('A'\) at m/z 209, 211 (64%). The fragment A then looses a unit of 43 as a radical corresponding to \(-\text{HNCO}\) leading to highly unstable fragment B at m/z 166, 168 (13%). The fragment C at m/z 127,129 (100%) which is also the base peak is obtained by the loss of \(-\text{HC}_3\text{N}\) as a neutral moiety. The base peak then looses a unit of 16 as a radical corresponding to \(-\text{NH}_2\) to give the fragment D at m/z 111, 113 (15%).

52
The acetyl derivative \((51 \text{ a-h})\) of the title compounds \((48 \text{ a-h})\) were characterised by the IR spectra (spectrum 6, compound 51e) with the appearance of two \(\nu_{C=O}\) bands one at 1748 cm\(^{-1}\) for the O-acetyl and the other at 1708 cm\(^{-1}\) for the triazolone ring. The \(^1\)H-NMR (300 MHz) spectra (spectrum 7, compound 51e) of all these compounds showed the singlets at \(\delta 2.08\) ppm and \(\delta 2.34\) ppm for the \(-CH_3\) protons of the O-acetyl and \(-CH_3\) protons of the triazolone ring respectively. The two triplets at \(\delta 3.95\) ppm and \(\delta 4.36\) ppm correspond to the \(-CH_2a\) and the deshielded \(-CH_2b\) protons. The signals at \(\delta 7.36\) ppm & \(\delta 7.95\) ppm (2H each, d) were assigned for the aromatic protons.
SPECTRAL DATA

4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones

IR Spectrum
Spectrum 1
3456, 3363 cm\(^{-1}\)
1702 cm\(^{-1}\) \(v_{\text{OH}} \) of ethyl group 
\(v_{\text{C=O}} \) of triazolone ring

\(^1\)H-NMR spectrum
Spectrum 2
2.36 \(\delta \) (s, 3H) \(\text{CH}_3 \) protons of triazolone ring
2.60 \(\delta \) (s, 1H) Proton of hydroxyl group
3.85 \(\delta \) (t, 2H) and 3.95 \(\delta \) (t, 2H) Methylene protons of \((\text{CH}_2a \text{ & CH}_2b)\)
7.37 \(\delta \) (d, 2H) and 7.95 \(\delta \) (d, 2H) Aromatic protons
SPECTRAL DATA

4-(2-Acetoxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones

IR Spectrum
Spectrum 6
1748 cm\(^{-1}\) \(\nu_{\text{C-O}}\) of O-acetyl group
1708 cm\(^{-1}\) \(\nu_{\text{C-O}}\) of triazolone ring

\(^1\)H-NMR spectrum
Spectrum 7
2.08 \(\delta\) (s, 3H) \(\text{CH}_3\) protons of O-acetyl group
2.34 \(\delta\) (s, 3H) \(\text{CH}_3\) protons of triazolone ring
3.95 \(\delta\) (t, 2H) and 4.36 \(\delta\) (t, 2H) Methylene protons of (CH\(_2\)_a & CH\(_2\)_b)
7.36 \(\delta\) (d, 2H) and 7.95 \(\delta\) (d, 2H) Aromatic protons

55
Spectrum 2 $^1$H-NMR
Solvent CDCl$_3$
Spectrum 3 $^1$H-NOE difference
Solvent CD$_2$OD

DIFFERENCE SPECTRUM
X64 TIMES

IRRADIATION ON RESONANCE AT 2.32 ppm

IRRADIATION OFF RESONANCE
Spectrum 5  Mass spectrum
Spectrum 6  IR Spectrum
Method      KBr pellet
Spectrum 7
$^1$H-NMR
Solvent CDCl$_3$
CHARACTERISATION DATA OF COMPOUNDS

Table 1

4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazole-3-ones (48 a-h)

<table>
<thead>
<tr>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>R&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Yield</th>
<th>M.p. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>a</td>
<td>H</td>
<td>H</td>
<td>80</td>
<td>116-118</td>
<td>C&lt;sub&gt;11&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
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<td>(60.30)</td>
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<tr>
<td>b</td>
<td>H</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>78</td>
<td>110-112</td>
<td>C&lt;sub&gt;12&lt;/sub&gt;H&lt;sub&gt;15&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;</td>
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<td>H</td>
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<td>75</td>
<td>106-108</td>
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<tr>
<td>d</td>
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<td>(57.86)</td>
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<td>120-122</td>
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<tr>
<td>f</td>
<td>H</td>
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<td>118-120</td>
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<td>3-Cl</td>
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<td>98-100</td>
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### CHARACTERISATION DATA OF COMPOUNDS

Table 2

4-(2-Acetoxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones (51 a-h)

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<th>R1</th>
<th>R2</th>
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<th>M.p. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated)</th>
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<td>90-92</td>
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<td>C: 59.76 (59.80) H: 5.79 (5.85) N: 16.08 (16.15)</td>
</tr>
<tr>
<td>b</td>
<td>H</td>
<td>78</td>
<td>100-102</td>
<td>C_{14}H_{17}N_{3}O_{3}</td>
<td>C: 61.08 (61.15) H: 6.22 (6.26) N: 15.22 (15.26)</td>
</tr>
<tr>
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<td>H</td>
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<td>94-96</td>
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<td>C: 61.12 (61.15) H: 6.24 (6.26) N: 15.25 (15.26)</td>
</tr>
<tr>
<td>d</td>
<td>H</td>
<td>70</td>
<td>88-90</td>
<td>C_{14}H_{17}N_{3}O_{4}</td>
<td>C: 57.72 (57.80) H: 5.88 (5.94) N: 14.42 (14.48)</td>
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<tr>
<td>e</td>
<td>H</td>
<td>85</td>
<td>110-112</td>
<td>C_{13}H_{14}ClN_{3}O_{3}</td>
<td>C: 52.80 (52.85) H: 4.77 (4.82) N: 14.21 (14.26)</td>
</tr>
<tr>
<td>f</td>
<td>H</td>
<td>80</td>
<td>102-104</td>
<td>C_{13}H_{14}ClN_{3}O_{3}</td>
<td>C: 52.83 (52.85) H: 4.80 (4.82) N: 14.24 (14.26)</td>
</tr>
<tr>
<td>g</td>
<td>H</td>
<td>85</td>
<td>118-120</td>
<td>C_{13}H_{14}BrN_{3}O_{3}</td>
<td>C: 45.90 (46.96) H: 4.15 (4.20) N: 12.35 (12.42)</td>
</tr>
<tr>
<td>h</td>
<td>4-CH_{3}</td>
<td>80</td>
<td>96-98</td>
<td>C_{14}H_{18}ClN_{3}O_{3}</td>
<td>C: 54.29 (54.34) H: 5.21 (5.26) N: 13.57 (13.62)</td>
</tr>
</tbody>
</table>
# ANTIMICROBIAL ACTIVITY

Table 3

4-(2-Hydroxyethyl)-2-aryl-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-ones

<table>
<thead>
<tr>
<th>R₁</th>
<th>R₂</th>
<th>Antibacterial</th>
<th>Antifungal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>B. cirroflagellosus</td>
</tr>
<tr>
<td>H</td>
<td>H</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>H</td>
<td>4-CH₃</td>
<td>12</td>
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<tr>
<td>H</td>
<td>3-CH₃</td>
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<td>10</td>
</tr>
<tr>
<td>H</td>
<td>4-Cl</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>H</td>
<td>3-Cl</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>H</td>
<td>4-Br</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>H</td>
<td>4-OCH₃</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>3-Cl</td>
<td>4-CH₃</td>
<td>12</td>
<td>14</td>
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<table>
<thead>
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<th>Standard</th>
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<th>Antifungal</th>
</tr>
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<tbody>
<tr>
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<td>B. cirroflagellosus</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
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<td>22</td>
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<tr>
<td>Griseofulvin</td>
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## ANTIMICROBIAL ACTIVITY

### Table 4

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<thead>
<tr>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
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<th>Antifungal</th>
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<tbody>
<tr>
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<td>10</td>
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<tr>
<td>H</td>
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<table>
<thead>
<tr>
<th>Standard</th>
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<th>Antifungal</th>
</tr>
</thead>
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<tr>
<td>Griseofulvin</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

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REFERENCES

   (b) Tsuge O. and Kanemase S., Asahi Garasu Kogyo Gisutsu Shoreikai Kenkyu Hokoku, 26, 101 (1975)
