Chapter-II

Tetraheterocycles
Introduction:

In the previous chapter we have discussed the preparation of some 2-[4-(5-(aryl)-
4, 5-dihydro-1H-pyrazole-3-yl)-phenyl]-5,6-dihydro-2H-pyrazolo [3,4-d] pyridazine-4,
7-diones and their antimicrobial properties. In this part we thought of preparing the
corresponding N-acetyl pyrazoline derivatives, because N-acetyl pyrazolines have been
reported to exhibit molluscidal activity¹, due to the presence of acetyl group at
1-position and it also increases the stability of pyrazoline derivatives. In an attempt to
prepare the N-acetyl derivatives of the pyrazolo[3,4-d]pyridazines prepared in the
previous chapter, we thought of using the 3-{4-[1-acetyl-5-(4-aryl)-4,5-dihydro-1H-
pyrazol-3-yl]-phenylsydnones (9a-f) as the starting materials, as compounds (3a-j) on
acetylation gave the triacetyl derivatives, which were not useful for further cyclisation to
pyridazines. The compounds (9a-f) on reaction with DMAD followed by reaction with
hydrazine hydrate, afforded the corresponding bis hydrazides (11a-f) with the N-acetyl
pyrazoline ring intact.

Purpose of the work:

However, the compounds (11a-f) on cyclisation to pyridazines with HCl,
hydrolysed the acetyl group also, to afford again the pyrazoline compounds (4) and we
could not obtain the corresponding N-acetyl pyrazoline derivatives. Hence, we thought
of utilizing these bis hydrazide groups to build the pyrrole, pyrazole, oxadiazole-2-
thione, thiadiazole 2-thione and 1,2,4-triazole rings.

We have reviewed the above heterocycles in brief, for their biological properties.

Biological activity of pyrroles:

Pyrrole (I) is a five membered ring system with one nitrogen atom and four
carbon atoms, which occur in, bone oil coal tar and products derived from proteins. It is
one of the most ubiquitous heterocycle in the plant and animal kingdom, because of its
participation as a sub unit of chlorophyll and the haem. Biosynthetically related vitamin
B₁₂ is a tetrapyrrrole, a number of antibiotics are also derived form pyrroles.
Several compounds containing pyrrole nucleus have been used as antitumor\(^2\), analgesics\(^3\), antiinflammatory and antiallergic\(^4\) and photographic emulsion reagents\(^5\). The derivatives of 2,5 dimethyl pyrroles are also known to exhibit antiulcer and hypotensive activities\(^6\).

The 2,5-dimethyl pyrroles (II) were prepared by Lambellin and coworkers\(^7\) and were found to be analgesic, antiphlogistics and antipyretics.

\[ R = \text{Aryl-} \quad \text{CH}_2\text{CH}_2\text{C}_6\text{H}_5, \quad \text{Cyclohexyl, 2-pyridyl} \]
\[ R_1 = \text{CH}_2\text{COOH, CH(CH}_3\text{)}\text{COOH} \]

A German patent described\(^8\) the synthesis of 2,5-dimethyl pyrroles of the type (III) which were used as antihypertensive, antiarrythmics agents and also used as drug for all the treatment of Angina pectoris.

\[ R = \text{-NHCH(CH}_3\text{)}_2, \quad \text{-NHC(CH}_3\text{)}_3, \quad \text{-Morpholino} \]

Vollenberg and Beckamann\(^9\) have prepared several 2,5-dimethyl pyrroles (IV), which exhibited anticholesteremic activity.

\[ \text{IV} \]
Several 2,5-dimethyl pyrrole derivatives (V) were synthesised and reported by Ramalingam et al.,\textsuperscript{10} and some of them are found to be good anti-inflammatory agents. All these pyrrole derivatives bearing 3-pentadecylphenyl (3-PDP) were devoid of toxicity and showed significant anti-inflammatory activity. Similar results were also observed for 1-\(\alpha\)- (3'-pentadecylaryloxy) isobutaramido-2,5-dimethyl pyroles.

\[
\begin{array}{c}
\text{\text{CH}_3} \\
\text{\text{CH}_3} \\
\end{array}
\begin{array}{c}
\text{\text{R}} \\
\text{\text{R}} \\
\end{array}
\begin{array}{c}
\text{\text{R}} \\
\text{\text{R}} \\
\end{array}
\begin{array}{c}
\text{\text{R}}_1 \\
\text{\text{R}}_2 \\
\text{\text{R}}_3 \\
\end{array}
\begin{array}{c}
\text{\text{R}}_4 \\
\text{\text{R}}_5 \\
\end{array}
\begin{array}{c}
\text{\text{R}}_6 \\
\text{\text{R}}_7 \\
\end{array}
\begin{array}{c}
\text{\text{R}}_8 \\
\end{array}
\end{array}
\text{V}
\]

Preparation of novel derivatives of pyrrole 3,4-dicarboxylic acid imide (VI) was reported by Malinka et al.,\textsuperscript{11} and it is used as psychotropic.

Przewosmy and associates\textsuperscript{12} have reported the use of 1,5-dihydropyrrol-2-ones (VII) as painkillers.

Préparation of phenyl pyroles (VIII) and their herbicidal activity was reported by Bettarini et al.,\textsuperscript{13}.
Biological activity of 1,3,4-Oxadiazoles:

Five membered heterocycles with two carbon atoms, two nitrogen atoms and one oxygen atom are called oxadiazoles. Depending upon the orientation of the nitrogen atoms they are classified into 1,2,3, 1,2,4, 1,2,5, and 1,3,4 oxadiazoles (a-d).

The 1,3,4-oxadiazole (d) is thermally stable aromatic nucleus with many uses as biologically active ingredients in medicine, agriculture, as dyestuff and heat resistant polymer etc. The 1,3,4-oxadiazoles also have been shown to possess muscle relaxant, tranquilizing and antitubercular\textsuperscript{14,15}, leprostatic and tuberculostatic\textsuperscript{16}, herbicidal\textsuperscript{17} and antiviral\textsuperscript{18} activities.

Various substituted 1,3,4-oxadiazoles (IX) were prepared by Buguet et al.\textsuperscript{19} and screened them for analgesic, antiinflammatory, anticonvulsant, diuretic and antiulcer activity.

\[ R= \text{Aryl} \]

IX

Ramlngam and associates\textsuperscript{20} have synthesised 2,5-disubstituted-1,3,4-oxadiazoles (X) and evaluated their anti-inflammatory, CNS depressant and anti hypertensive activities.
Recently, Hiremath and coworkers\textsuperscript{21} have prepared several 1,3,4-oxadiazolylindole derivatives (XI) and tested them for their antimicrobial activity.

\begin{equation}
\begin{aligned}
R_1 & = \text{NH}_2, \text{SH}, \\
R_2 & = \text{H}, \text{Cl} \\
R_3 & = \text{H}, \text{CH}_3
\end{aligned}
\end{equation}

Chen et al.,\textsuperscript{22} have showed the fungicidal activity of 2-alkyl-thio-5-pyrazolyl-1,3,4-oxadiazole (XII).

Shrivastav et al.,\textsuperscript{23} have reported the fungitoxicity of 2-amino-[5-(substituted phenoxy) methyl]-1,3,4-oxadiazoles (XIII) against Aspergillus niger and Helminthosporium oryzae.

Krosorskii and coworkers\textsuperscript{24} have synthesised 5-aryl-1,3,4-oxadiazol-2-thiones (XIV) and these are found to be antibacterial activity.
Qian et al.\textsuperscript{25} have reported the insecticidal activity of 2-(2,4-dichloro-5-fluorophenyl 5-(fluorophenoxymethyl)-1,3,4-oxadiazoles (XV)

\[ \text{XV} \]

Sanyal et al.\textsuperscript{26} have synthesised bis 1,3,4-oxadiazoles (XVI) from our laboratory and studied their antimicrobial activity.

\[ \text{XVI} \]

Synthesis and antibacterial activity of the 1,3,4-oxadiazol-2-thione derivatives\textsuperscript{27} (XVII) have been reported.
Biological activity of 1,3,4-thiadiazoles:

The thiadiazole system comprise the 1,2,3-thiadiazoles (XVIII), the 1,2,4-thiadiazoles (XIX), the 1,3,4-thiadiazoles (XX) and 1,2,5-thiadiazoles (XXI).

![](image1)

The 1,3,4-thiadiazoles have found diverse applications as pharmaceuticals, oxidation inhibitors, cyanine dyes and metal complexing agents. A well-known example of 1,3,4-thiadiazole as a chemotherapeutic agent is Acetazolamide (XXII), which acts as a diuretic by inhibiting the enzyme carbonic anhydrase. It is also used for the treatment of epilepsy.

![](image2)

Antiinflammatory and cardiovascular activity of 2-[(4-methyl-2-quinolinyl)methyl]-5-(phenylamino)-1,3,4-thiadiazole were reported by Kidwazi.

Ramachander et al. studied the structure-activity relationship of 4-arylthiosemicarbazones and their cyclised products 2-arylamino-5-aryl-1,3,4-thiadiazoles (XXIII) against mycobacterium tuberculosis.

![](image3)
Chapleo et al. have described a series of 2-aryl-5-hydrazino-1,3,4-thiadiazoles (XXIV) and screened them for both anticonvulsant and antihypertensive properties.

\[
\text{Ar} \quad \begin{array}{c}
\text{N} \\
\text{S} \\
\text{N} \\
\text{N}
\end{array}
\begin{array}{c}
\text{R}_3 \\
\text{R}_2 \\
\text{R}_1
\end{array}
\]

XXIV

Use of 2-substituted-5-(trifluoromethyl)-1,3,4-thiadiazoles (XXV) as amoebicides, fungicides and pesticides were investigated by Reisdorff et al. Santus has reported the synthesis of 5-substituted-2-mercapt-1,3,4-thiadiazoles (XXVI) as potential tuberculostatic drugs.

\[
\begin{array}{c}
\text{F}_3\text{C} \\
\text{N} \\
\text{S} \\
\text{N}
\end{array}
\begin{array}{c}
\text{NHS[O]}_n \text{R}
\end{array}
\]

XXV

Santus has reported the synthesis of 5-substituted-2-mercapt-1,3,4-thiadiazoles (XXVI) as potential tuberculostatic drugs.

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{SH}
\end{array}
\begin{array}{c}
\text{R}
\end{array}
\]

XXVI

Hesegawa et al. have synthesised a large number of 5-(heteroaryl methylthio)-1,3,4-thiadiazole derivatives (XXVII) as possible antiulcer drugs.

\[
\begin{array}{c}
\text{R}_1 \\
\text{SCH}_2 \text{R}_2
\end{array}
\begin{array}{c}
\text{R}_1 = \text{Alkyl, NH}_2, \text{Ph, Pyridyl, Cyclohexyl etc} \\
\text{R}_2 = \text{Ph, Pyridyl, Quinolyl, Thiazolyl etc}
\end{array}
\]

XXVII

Clerici and associates have reported 2-amino-5-sulfanyl-1,3,4-thiadiazoles (XXVIII) to possess very good antidepressant and anxiolytic activity.
Okada et al.,\textsuperscript{35} have prepared N-thiazolyl pyrazole carboxamides (XXIX) and reported insecticidal and ascaricidal activities.

\[
\text{XXIX}
\]

Synthesis and bioactivity of 2-amino-5[(2-chloropyrid)-4-yl]-1,3,4-thiadiazoles (XXX) and these compounds have shown certain plant growth regulating effect as well as fungicidal activity\textsuperscript{36}.

\[
\text{XXX}
\]

**Biological activity of 1,2,4-triazoles:**

Triazoles are five membered heterocycles with three nitrogen and two carbon atoms. There are two possible combinations of these atoms 1H-1,2,4-triazole (XXXIa) and symmetrical triazoles (XXXIb) 4H- 1,2,4-triazoles.
The 3-amino-1,2,4-triazole was the first symmetrical triazole to be manufactured on large scale for use as neutral herbicide and defoliant of cotton. The derivatives of 1,2,4-triazole exhibited wide spectrum of biological activities such as inhibition of cholinesterase interference with mitosis\(^{17}\) and reversible denaturation of serum proteins\(^{28}\).

Several alkyl and aryl derivatives of 1,3,4-triazoles are found to be very active against both bacteria and fungi\(^{19}\).

Madne et al.\(^{40}\) have studied the tuberculostatic activity of triazoles increasing with increase in the magnitude of the total planar surface area of the molecule, whereas decrease in the basicity of amino derivatives of triazoles reduced the tuberculostatic activity. The tuberculostatic activity of triazoles also decreases appreciably when the hydrogen atom of the amino group was replaced by alkyl group.

Burch and Smith reported\(^{41}\) that 5-(5-nitro-2-furyl)-3-alkyl-1,2,4-triazoles (XXXII) exhibited broad antibacterial activity.

\[\text{XXXII}\]

A few 5-mercapto-4-amino-1,2,4-triazoles (XXXIII) displayed bactericidal, herbicidal and diuretic activities\(^{42}\)

\[\text{XXXIII}\]

Synthesis and pharmaceutical activities of 3-aryl-5-mercapto-4-(4-pyridine carbamidino)-4H-1,2,4-triazoles (XXXIV) were reported by Shivodkar and et al.,\(^{43}\) and screened them for antibacterial and antituberculostatic activity.
Dobosz and associates\textsuperscript{44} have reported triazole bis heterocycles of type (XXXV) and studied their effects on CNS activity.

\[
\text{XXXV}
\]

Faming \textit{et al.}\textsuperscript{45} have synthesised triazolyl propanols (XXXVI) as antifungal agents.

\[
\text{XXXVI}
\]

Liu and associates\textsuperscript{46} have reported the synthesis of 1-(1\textsubscript{H}-1,2,4-triazol-1-yl)-3-piperazinopropan-2-ol (XXXVII) as antifungal agents.

\[
\text{XXXVII}
\]

Yamada N \textit{et al.}\textsuperscript{47} have studied the bleaching activity of 4-alkyl-3-propargyl-1, 2,4-1H-triazoles (XXXVIII)

\[
\text{XXXVIII}
\]
Demirayak \textit{S et al.},\textsuperscript{48} have synthesised and studied the antimicrobial activity of some 3-arylamino-5-[2-(sub-l-imidazolylethyl)]-1,2,4-triazole derivatives (XXXIX)

![XXXIX](image)

Literature survey revealed that when one biodynamic heterocyclic system was coupled with another molecule, enhanced biological activity was observed. In view of these reports, under present investigation it was planned to synthesise various tetraheterocycles, wherein biologically interesting N-acetyl pyrazoline and pyrazole moieties have been linked to different heterocycles such as pyrroles, 1,2,4-oxadiazoles, 1,2,4-thiadiazoles and 1,2,4-triazoles with an expectation of obtaining variety of heterocycles, endowed with enhanced biological properties.
Synthetic strategy:

The present investigation involved the 1,3-dipolar cycloaddition reaction of dimethylacetylene dicarboxylate (DMAD) to 3-[p-{5-aryl-2-pyrazolin-3-yl} phenyl] sydnones⁶ (9a-f) in xylene to afford 1-{4-[1-acetyl-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-pyrazole-3,4-dicarboxylic acid dimethyl esters (10a-f). These dicarboxylates when refluxed with hydrazine hydrate (99%) in ethanol gave corresponding bishydrazides (11a-f). These bishydrazides form the key intermediates for the synthesis of the tetraheterocyclic compounds.

The synthesis of the heterocycles was carried out by the known literature procedures. Compounds (11a-f) on reaction with acetylacetone yielded the tetracyclic compounds (12a-f) containing the N-acetylpyrazoline, the pyrazole and the two pyrrole rings, and with acetylacetone the 3,5-dimethylpyrazoles (13a-j) were obtained. (Scheme-5)

The 1,2,4-mercapto-oxadiazoles (14a-f) were synthesized in good yields by refluxing compounds (11a-f) with carbon disulfide in aq-KOH and also in pyridine. The bishydrazides were converted to the bis potassium dithiocarbazates (15a-f), which on cyclisation with glacial acetic acid afforded the 1,2,4-thiadiazole-2-thiones (16a-f), while cyclisation with aq-KOH gave the 1,2,4-mercapto-oxadiazoles (14a-j).

The bis hydrazides (11a-f) on reaction with allyl isothiocyanate gave the allyl thiosemicarbazides (17a-f) which were cyclised with NaOH to the N-1-allyl-1,2,4-triazoles (18a-f). (Scheme-6)
Scheme 6

\[ \text{Reactions and structures as depicted in the diagram.} \]
Spectral Characterization:

The IR spectra of compounds (10a-f) (spectrum 16) showed band at 1743 cm\(^{-1}\) for the ester \(\nu_{\text{C=O}}\) frequencies and another band was observed at 1655 cm\(^{-1}\) due to \(\nu_{\text{C=O}}\) of N-acetyl group. The \(^1\)H-NMR spectra (spectrum 17) showed a singlet at 2.45 \(\delta\) for the methyl protons of the N-acetyl group and two singlets at 3.91 and 4.02 \(\delta\) for the OCH\(_3\) protons. The methylene and methine protons on the pyrazoline ring appeared as unresolved signals at 3.14, 3.80 and 5.55 \(\delta\) respectively. The aromatic protons appeared in the region between 7.18-7.85 \(\delta\) (8H), while the pyrazole ring proton was observed as a singlet at 8.46 \(\delta\).

The IR spectra of compounds (11a-f) (spectrum 18) showed broad peak in the region 3256-3428 cm\(^{-1}\) due to \(\nu_{\text{NH}}\) vibrations of the hydrazide group and a broad band at 1640 cm\(^{-1}\) for the \(\nu_{\text{C=O}}\). The \(^1\)H-NMR spectra (spectrum 19) showed a singlet at 2.46 \(\delta\) for methyl protons of N-acetyl group and three doublet of doublets at 3.23, 3.81, and 5.64 \(\delta\) corresponding to diastereotopic methylene and methine protons of pyrazoline ring. The aromatic protons resonated at 7.35-7.92 \(\delta\) (8H) while pyrazole ring proton was observed at 8.91 \(\delta\). The two singlets at 10.0 \(\delta\) and 12.82 \(\delta\) were assigned to two NH protons of the hydrazide groups, which vanished on D\(_2\)O exchange. The signals for the NH\(_2\) protons appeared at 4.52 \(\delta\).

The IR spectra of compounds (12a-f) (spectrum 20) showed broad band at 3213 cm\(^{-1}\) due to \(\nu_{\text{NH}}\) of amide groups and another band at 1666 cm\(^{-1}\) corresponding to amide and N-acetyl \(\nu_{\text{C=O}}\). The \(^1\)H-NMR spectra (spectrum 21) showed four singlets in the region 2.08-2.18 \(\delta\) for the four-methyl protons on the pyrrole rings, whereas another singlet was observed at 2.43 \(\delta\) for N-acetyl methyl protons. The methylene and methine protons on the pyrazoline ring resonated at 3.11, 3.78 and 5.58 \(\delta\) as doublet of doublets. The two singlets at 5.75 and 5.86 \(\delta\) corresponded to pyrrole ring protons (2H each) and aromatic protons appeared in the range between 7.18-7.90 \(\delta\). The two NH protons resonated as two singlets at 10.29 and 12.20 \(\delta\), which disappeared on D\(_2\)O exchange, while the pyrazole ring proton appeared at 8.91 \(\delta\).

The IR spectra of compounds (13a-f) (spectrum 22) exhibited bands at 1735, 1689 and 1664 cm\(^{-1}\) corresponding to the three \(\nu_{\text{C=O}}\). \(^1\)H-NMR spectra (spectrum 23)
displayed signals at 2.18 and 2.44 δ for protons of four methyl groups (6H each) of dimethyl pyrazole rings and another singlet at 2.24 δ due to methyl protons of N-acetyl group. The pyrazoline protons appeared as the ABX pattern as above. The aromatic protons exhibited their signals in the region 7.33-7.86 δ while the pyrazole ring proton resonated as a singlet at 8.63 δ.

The IR spectra of compounds (14a-f) (spectrum 24) showed a band at 3264 cm\(^{-1}\) due to \(\nu_{\text{NH}}\) stretching vibrations and band at 1640 cm\(^{-1}\) was accounted for \(\nu_{C=O}\) stretching of N-acetyl while a band observed at 1344 cm\(^{-1}\) was for \(\nu_{C=S}\) vibrations. This observation indicates that the compounds (14a-j) exists in the thione form (a) and not in the thiol form (b).

The \(^1\text{H}-\text{NMR}\) spectra of above compounds (spectrum 25) also showed the existence of these compounds in the thione form (a). A broad singlet at 14.61 δ for two protons which disappeared on shaking with D\(_2\)O was assigned to the NH protons of the oxadiazole ring. The SH proton of the thiol form (b) usually appears in the region 4.0 δ. Pyrazole ring proton gave a singlet at 9.34 δ. The peak at 2.33 δ was accounted for methyl protons of N-acetyl group. The ABX pattern is observed for the pyrazoline protons at 3.81 (merged in DMSO), 5.55 δ. The aromatic protons displayed their signals in the region 7.14-8.04 δ.

The IR spectra of compounds (16a-f) (spectrum 26) showed broad band around 3213 cm\(^{-1}\) due to \(\nu_{\text{NH}}\) vibrations of thiadiazole ring and a band at 1651 cm\(^{-1}\) for N-acetyl carbonyl. The presence of band at 1268 cm\(^{-1}\) was due to \(\nu_{C=S}\) vibrations, this indicates that compound exists in thione form and not in thiol form. Further it was
confirmed by its $^1$H-NMR spectrum (spectrum 27), which exhibited a signal at 11.42 $\delta$ (2H) accountable for NH of thiadiazole, which vanished on D$_2$O exchange. The singlet at 9.44 $\delta$ was due to pyrazole ring proton. The methyl protons of N-acetyl group exhibited a singlet at 2.34 $\delta$. The protons pyrazoline ring resonated as above and aromatic protons displayed signals in the range 7.24-8.19 $\delta$.

The IR spectra of compounds (17a-f) (spectrum 28) showed broad band around 3284 cm$^{-1}$ due to $\nu$NH vibrations and all the $\nu$C=O stretching vibrations were observed as a broad band around 1654 cm$^{-1}$ whereas $\nu$C=S gave a band at 1219 cm$^{-1}$. The $^1$H-NMR spectra (spectrum 29) exhibited a very complex splitting pattern. The methyl protons of N-acetyl were observed as a singlet at 2.34 $\delta$. The ABX pattern was observed for the pyrazoline protons. The allylic protons of N-CH$_2$ exhibited a doublet at 4.16 $\delta$ and two triplets around 5.01-5.21 $\delta$ corresponded to C=CH$_2$ protons and another multiplet was seen at 5.62 $\delta$ due to -CH= protons. The signal observed at 8.12 $\delta$ was assigned to (-CS-NH-C-) protons and aromatic protons resonated at 7.24-8.20 $\delta$. The four singlets at 9.60, 9.69, 10.69 and 10.97 $\delta$ were assigned to the four NH protons of side chain and all disappeared on D$_2$O exchange, while pyrazole ring proton appeared as singlet at 9.30 $\delta$.

The IR spectra of triazoles (18a-f) (spectrum 30) showed band at 3400 cm$^{-1}$ due to $\nu$NH vibrations, $\nu$C=N of N-acetyl was observed at 1640 cm$^{-1}$ and band for $\nu$C=S at 1245 cm$^{-1}$. The $^1$H-NMR spectra of above compounds (spectrum 31) showed a singlet at 2.32 $\delta$ for methyl protons of N-acetyl group. The ABX pattern was observed for the pyrazoline protons at 3.94 and 5.53 $\delta$. The signals for N-CH$_2$ protons of triazole appeared as a doublet at 4.61 $\delta$, the protons for C=CH$_2$ were observed in the region 5.01-5.18 $\delta$, while the multiplet around 5.63-6.01 $\delta$ was due to -CH= protons. The aromatic protons appeared in the range of 7.24-8.078. The signal at 14.10 $\delta$ (2H) was attributed to NH protons of triazole which disappeared on D$_2$O exchange. Whereas pyrazole ring proton appeared as a singlet at 9.23 $\delta$. 

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SPECTRAL DATA

1-[(1-Acetyl-5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl)-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester (10b)

IR Spectrum
Spectrum 16

- 3120 cm\(^{-1}\) \(\nu_{CH}\) of pyrazole ring
- 1743 cm\(^{-1}\) \(\nu_{C=O}\) of C\(_4\) and C\(_3\) ester groups
- 1655 cm\(^{-1}\) \(\nu_{C=O}\) of N-acetyl group

\(^1\)H-NMR Spectrum
Spectrum 17

- 2.45 \(\delta\) (s, 3H) Methyl protons of N-acetyl
- 3.91 \(\delta\) (s, 3H) Methyl protons of C\(_4\) ester
- 4.02 \(\delta\) (s, 3H) Methyl protons of C\(_3\) ester
- 3.14 \(\delta\) (dd, 1H) and 3.80 \(\delta\) (dd, 1H) \(\mathrm{CH}_2\) protons (diastereotopic)
- 5.55 \(\delta\) (dd, 1H) Methine proton (C\(_5\))
- 7.18 - 7.85 \(\delta\) (4d, 8H) Aromatic protons
- 8.46 \(\delta\) (s, 1H) Pyrazole proton
1-\{4-[1-Acetyl-5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-pyrazole-3,4-bis-carbohydrazide (11b)

**IR Spectrum:**

**Spectrum 18**

- $3428-3250 \text{ cm}^{-1}$: $\nu_{\text{NH}}$ of CONHNH$_2$ groups
- $3060 \text{ cm}^{-1}$: $\nu_{\text{CH}}$ of pyrazole ring
- $1640 \text{ cm}^{-1}$: $\nu_{\text{C=O}}$ of CONHNH$_2$ and N-acetyl groups

**$^1$H-NMR Spectrum:**

**Spectrum 19**

- $2.46 \delta$ (s, 3H): Methyl protons of N-acetyl
- $3.23 \delta$ (dd, 1H) and $3.81 \delta$ (dd, 1H): CH$_2$ protons (diastereotopic)
- $5.64 \delta$ (dd, 1H): Methine proton
- $7.35 - 7.92 \delta$ (4d, 8H): Aromatic protons
- $8.91 \delta$ (s, 1H): Pyrazole ring proton
- $10.0 \delta$ (s, 1H) and $12.82 \delta$ (s, 1H): Protons of two NH
SPECTRAL DATA

1-{4-[1-Acetyl-5-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-pyrazole-3,4-dicarboxylic acid bis-[(2,5-dimethyl-pyrrol-1-yl)-amide (12b)

IR Spectrum:
Spectrum 20

3213 cm\(^{-1}\) v\(_{NH}\) groups
2922 cm\(^{-1}\) v\(_{CH}\) of pyrazole ring
1666 cm\(^{-1}\) (broad) v\(_{C=O}\) of three amide groups

\(^1\)H-NMR Spectrum:
Spectrum 21

2.08-2.18 \(\delta\) (4s, 6H) Methyl protons of two pyrrole rings
2.43 \(\delta\) (s, 3H) Methyl protons of N-acetyl group
3.11 \(\delta\) (dd, 1H) and 3.78 \(\delta\) (dd, 1H) CH\(_2\) protons (diastereotopic)
5.68 \(\delta\) (dd, 1H) Methine proton
5.75 and 5.86 \(\delta\) (2s, 4H) Protons of two pyrrole ring
7.18 - 7.90 \(\delta\) (4d, 8H) Aromatic protons
8.91 \(\delta\) (s, 1H) Pyrazole proton
10.29 and 12.20 \(\delta\) (2s, 2H) Two NH protons of side chain
SPECTRAL DATA

3,4-Bis-(3,5-dimethyl-1-carbonyl-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl phenyl]-pyrazole (13b)

IR Spectrum:
Spectrum 22

3136 cm\(^{-1}\) \(\nu_{\text{CH}}\) of pyrrole ring
1735 and 1689 cm\(^{-1}\) \(\nu_{\text{C=O}}\) of amide
1664 cm\(^{-1}\) \(\nu_{\text{C=O}}\) of N-acetyl group

\(^1\text{H-NMR Spectrum:}\)
Spectrum 23

2.24 \(\delta\) (s, 3H) Methyl protons of N-acetyl group
2.18 \(\delta\) (s, 6H) and Methyl protons of pyrazole ring
2.44 \(\delta\) (s, 6H)
3.12 \(\delta\) (dd, 1H) (merged) and CH\(_2\) protons (diastereotopic)
3.84 \(\delta\) (dd, 1H)
5.55 \(\delta\) (dd, 1H) Methine proton
7.33-7.86 \(\delta\) (4d, 8H) Aromatic protons
8.63 \(\delta\) (s, 1H) Pyrazole proton
SPECTRAL DATA

3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]- phenyl]pyrazole (14b)

IR Spectrum
Spectrum 24

3264 cm$^{-1}$ $\nu_{\text{NH}}$ of oxadiazole ring
1640 cm$^{-1}$ $\nu_{\text{C=O}}$ of N-acetyl group
1344 cm$^{-1}$ $\nu_{\text{C=S}}$ of oxadiazole

$^1$H-NMR Spectrum
Spectrum 25

2.33 $\delta$ (s, 3H) Methyl protons of N-acetyl group
3.11 $\delta$ (dd, 1H) and 3.81 $\delta$ (dd, 1H) CH$_2$ protons (diastereotopic)
5.55 $\delta$ (dd, 1H) Methine proton (C$_5$)
7.14-8.04 $\delta$ (4d, 8H) Aromatic protons
9.34 $\delta$ (s, 1H) Pyrazole proton (C$_5$)
14.61 $\delta$ (s, 2H) NH proton of oxadiazole

117
3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]-thiadiazole-2-yl)-1-[4-(1-acety1-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl)-phenyl]pyrazole (16b)

**IR Spectrum**

Spectrum 26

- 3213 cm\(^{-1}\) \(v_{NH}\) of thiadiazole ring
- 1651 cm\(^{-1}\) (broad) \(v_{C=O}\) of N-acetyl group
- 1268 cm\(^{-1}\) \(v_{C=S}\) of thiadizole ring

**\(^1\)H-NMR Spectrum**

Spectrum 27

- 2.34 \(\delta\) (s, 3H) Methyl protons of N-acetyl group
- 3.22 \(\delta\) (dd, 1H) and 3.88 \(\delta\) (dd, 1H) CH\(_2\) protons (diastereotopic)
- 5.61 \(\delta\) (dd, 1H) Methine proton
- 7.24-8.19 \(\delta\) (4d, 8H) (\(J=7\) Hz for each doublet) Aromatic protons
- 9.44 \(\delta\) (s, 1H) Pyrazole proton
- 11.42 \(\delta\) (s, 2H) NH proton of thiadiazole
SPECTRAL DATA

3,4-Bis-(N-allyl thiosemicarbazide carbonyl-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl}phenyl]pyrazole (17b)

IR Spectrum
Spectrum 28

3284 cm\(^{-1}\) \(\nu_{\text{NH}}\) of side chain
2918 cm\(^{-1}\) \(\nu_{\text{CH}}\) of pyrazole proton
1654 cm\(^{-1}\) (broad) \(\nu_{\text{C=O}}\) of N-acetyl and side chain
1219 cm\(^{-1}\) \(\nu_{\text{C=S}}\) side chain

\(^1\)H-NMR Spectrum
Spectrum 29

2.34 \(\delta\) (s, 3H)  Methyl protons of N-acetyl group
2.22-3.87 \(\delta\) (dd, 2H)  CH\(_2\) protons (diastereotopic)
5.60 \(\delta\) (ddd, 1H)  Methine proton
4.16 \(\delta\) (d, 4H)  N-CH\(_2\) proton
5.01-5.21 \(\delta\) (d, 4H)  C=CH\(_2\) proton (allyl)
5.62 \(\delta\) (m, 2H)  CH= proton (allyl)
8.12 \(\delta\) (2s, 2H)  NH proton of –CS-NH–
7.24-8.20 \(\delta\) (4d, 8H)  Aromatic protons
9.30 \(\delta\) (s, 1H)  Pyrazole proton
9.60, 9.69, 10.69 and 10.97 \(\delta\)  Four NH protons of thiosemicarbazide chain
(4s, 4H)
SPECTRAL DATA

3,4-Bis-(4-allyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazolo-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chloro phenyl)pyrazole-3-yl]phenyl}pyrazole (18b)

IR Spectrum:
Spectrum 30

3400 cm\(^{-1}\) \(\nu_{\text{NH}}\) of side chain
1640 cm\(^{-1}\) \(\nu_{\text{C=O}}\) of N-acetyl and side chain
1245 cm\(^{-1}\) \(\nu_{\text{C=S}}\) thiosemicarbazide side chain

\(^1\)H-NMR Spectrum
Spectrum 31

2.32 \(\delta\) (s, 3H) Methyl protons of N-acetyl group
3.94 \(\delta\) (dd, 2H) \(\text{CH}_2\) protons (diastereotopic)
5.53 \(\delta\) (dd, 1H) Methine proton (C\(_5\))
4.61 \(\delta\) (2d, 4H) N-\(\text{CH}_2\) proton
5.01-5.18 \(\delta\) (t, 4H) C=\(\text{CH}_2\) proton (allyl)
5.63-6.01 \(\delta\) (m, 2H) CH= proton (allyl)
7.24-8.07 \(\delta\) (2d, 8H) Aromatic protons
9.23 \(\delta\) (s, 1H) Pyrazole proton (C\(_5\))
14.10 \(\delta\) (s, 2H) NH-protons of triazole
Spectrum 17 $^1$H-NMR
Solvent  CDCl$_3$
Spectrum 18 IR Spectrum
KBr Pellet

Wavenumbers (cm⁻¹):

- 3428.76
- 3344.19
- 3300.47
- 3256.76
- 3060.07
- 2918.01
- 2852.45
- 1640.50
- 1599.03
- 1574.13
- 1531.46
- 1459.68
- 1433.16
- 1428.74
- 1387.54
- 1322.37
- 1299.06
- 1286.18
- 1086.18
- 1013.50
- 942.34
- 821.24

% Transmittance vs. Wavenumbers (cm⁻¹):
Spectrum 19 $^1$H-NMR
Solvent  CDCl$_3$
Spectrum 20 IR Spectrum
KBr Pellet

% Transmittance

Wavenumbers (cm⁻¹)

4000
3500
3000
2500
2000
1500
1000

3405.85
3213.35
2927.73
1866.51
1608.59
1531.37
1451.17
1414.24
1323.22
1233.95
1148.41
1086.32
962.67
842.48
755.08

H₃C

H₃C

H₃C

H₃C

N

N

N

N

H

H

H

Cl
Spectrum 21 $^1$H-NMR
Solvent CDCl$_3$
Spectrum 25 'H-NMR
Solvent CDCl₃
Spectrum 27 $^1$H-NMR Solvent DMSO-d$_6$
Experimental:

General procedures:

Preparation of \(1\{-4\{-1\{-acetyl\{-5\{-aryl\}4,5\{-dihydro\{-1\{-H\}pyrazol-3\{-yl\}\}phenyl\}\{-1\{-H\}pyrazole-3,4\{-dicarboxylic\}acid\}dimethyl\}esters\}(10a-f)\)

To a solution of compounds (9a-f) (0.005 mol) in dry xylene (4 ml) dimethylacetylenedicarboxylate (0.005 mol) was added and the reaction mixture heated at 120 °C till the evolution of carbon dioxide ceased (~ 1 hr). The solvent was removed under reduced pressure and the residue triturated with petroleum ether (60 -80 °C). The solid obtained was recrystallised from ethanol (Table 13).

Preparation of \(1\{-4\{-1\{-acetyl\{-5\{-aryl\}4,5\{-dihydro\{-1\{-H\}pyrazol-3\{-yl\}\}phenyl\}\{-1\{-H\}pyrazole-3,4\{-dicarboxylic\}acid\}bis\{-2,5\{-dimethyl\}pyrrol-1\{-yl\}\}amides\}(12\{a-f\})\)

To a suspension of compounds (10a-f) (0.001 mol) in ethanol (15 ml) was added acetonyl acetone (0.002 mol) and glacial acetic acid (0.5 ml) and the reaction mixture heated on a boiling water bath for 6 hrs. The reaction mixture was concentrated to half of its original volume and poured into crushed ice. The separated solid was filtered, washed with water and recrystallised from benzene-pet ether as white compound. (Table 15).

Preparation of \(3,4\{-bis\{-3,5\{-dimethyl\}1\{-carbonyl\}2\{-yl\}\}1\{-4\{-1\{-acetyl\{-4,5\{-dihydro\{-5\{-4\{-chlorophenyl\}pyrazole-3\{-yl\}phenyl\}{pyrazole\}(13a-f)}\)

To a suspension of compounds (11a-f) (0.001 mol) in ethanol (15 ml) was added acetyl acetone (0.002 mol) and glacial acetic acid (0.5 ml) and the reaction mixture...
heated on a boiling water bath for 6 hrs. The reaction mixture was concentrated to half of its original volume and poured into crushed ice. The separated solid was filtered, washed with water, dried and crystallized from benzene-pet ether as white compound. (Table 16).

Preparation of 3,4-bis-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]-phenyl]pyrazole (14a-f)

Method 1

A solution of compound (11a-f) (0.002 mol) in 20 ml of ethanol, KOH (0.46g, 0.008 mol) dissolved in 4 ml water and carbon disulfide (0.46 g, 0.006 mol) were refluxed on a water bath till the evolution of hydrogen sulfide gas ceased (~ 20 hours). The cooled reaction mixture was poured on crushed ice and neutralized with hydrochloric acid. The solid obtained was filtered, washed with water and dried and recrystallisation from dimethylformamide.

Method 2

A solution of compound (11a-f) (0.001 mol) in pyridine (10 ml) was treated with 5 ml of carbon disulfide and the solution stirred at room temperature for 36 hours. The product was isolated as above. (Table 17).

Preparation of 1-{4-[1-acetyl-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-Pyrazole- bis potassium dithiocarbazates (15a-f)

Carbon disulfide (0.5 ml 0.008 mol) was added to a stirred mixture of compound (9a-f) (0.002 mol) and potassium hydroxide (0.004 mol) in 20 ml of dry ethanol. The mixture was stirred for 2 hours at room temperature and diluted with 40 ml of ether. The solid obtained was filtered, washed with ether and dried. (Table 18).

Preparation of 1-{3-[3,4-bis-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-yl]-pyrazol-1-yl]-phenyl}-5-(4-chloro-phenyl)-4,5-dihydro-pyrazol-1-yl]-ethanones (14a-f)

From the above salts (15a-f)

The bis potassium dithiocarbazate (15a-f) (0.002 mol) were suspended in 15 ml ethanol and KOH (0.004 mol) dissolved in 2 ml water and the reaction mixture refluxed
for 20 hours on a heating mantle. The solid obtained after acidification with hydrochloric acid was washed with water and dried and recrystallization from dimethylformamide (Table 17).

**Preparation of 3,4-bis-(5-thioxo-4,5-dihydro-[1,3,4]-thiadiazole-2-yl)-1-[4-(1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]-phenyl]pyrazole (16a-f)**

The bis potassium dithiocarbazate (15a-f) (0.001 mol) in 4 ml of glacial acetic acid were refluxed for 2 hours on a heating mantle. The cooled reaction mixture was poured on crushed ice and the solid separated filtered and recrystallised from glacial acetic acid (Table 19).

**Preparation of 3,4-bis-(N-allyl thiosemicarbazide carbonyl-2-yl)-1-[4-(1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl]phenyl]pyrazole (17a-f)**

To a solution of compound (11a-f) (0.001 mol) in ethanol (15ml) was added allyl isothiocyanate (0.001 mol) with stirring. The mixture was heated under reflux for 4 hrs and part of the solvent was evaporated. The solid separated on cooling to room temperature was filtered, washed with ethanol and recrystallised from ethanol as white compound.(Table 20).

**Preparation of 3,4-bis-(4-allyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazolo-2-yl)-1-[4-(1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl]-phenyl]pyrazole (18a-f)**

Compound (15a-f) (0.001) in sodium hydroxide (4% 10ml) was refluxed for 5 hrs. The reaction mixture after cooling to room temperature was poured into crushed ice and acidified carefully with dil acetic acid. The precipitate thus obtained was filtered, washed with water dried and recrystallised from ethanol as white compound (Table 21).
**CHARACTERISATION DATA**

Table 13

![Chemical structure](image)

1-[(4-[1-AcetyI-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethyl esters (10a-f)

<table>
<thead>
<tr>
<th>R</th>
<th>R(_1)</th>
<th>Yield</th>
<th>M.P. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10a</td>
<td>H</td>
<td>H</td>
<td>60</td>
<td>110-112</td>
<td>C(<em>{24})H(</em>{22})N(_4)O(_5) 64.55 (64.57) C 4.95 (4.97) N 12.58 (12.55)</td>
</tr>
<tr>
<td>10b</td>
<td>H</td>
<td>4-Cl</td>
<td>73</td>
<td>132-134</td>
<td>C(<em>{24})H(</em>{21})ClN(_4)O(_5) 59.91 (59.94) C 4.38 (4.40) N 11.63 (11.65)</td>
</tr>
<tr>
<td>10c</td>
<td>H</td>
<td>4-CH(_3)</td>
<td>68</td>
<td>124-126</td>
<td>C(<em>{25})H(</em>{24})N(_4)O(_5) 65.23 (65.21) C 5.20 (5.25) N 12.14 (12.17)</td>
</tr>
<tr>
<td>10d</td>
<td>H</td>
<td>4-OCH(_3)</td>
<td>75</td>
<td>144-146</td>
<td>C(<em>{25})H(</em>{24})N(_4)O(_6) 63.57 (63.62) C 5.05 (5.08) N 11.73 (11.76)</td>
</tr>
<tr>
<td>10e</td>
<td>H</td>
<td>2-Cl</td>
<td>62</td>
<td>149-151</td>
<td>C(<em>{24})H(</em>{21})ClN(_4)O(_5) 59.91 (59.94) C 4.38 (4.40) N 11.63 (11.65)</td>
</tr>
<tr>
<td>10f</td>
<td>H</td>
<td>4-N(CH(_3))(_2)</td>
<td>70</td>
<td>152-154</td>
<td>C(<em>{25})H(</em>{27})N(_5)O(_5) 63.77 (63.79) C 5.51 (5.56) N 14.33 (14.31)</td>
</tr>
</tbody>
</table>
Table 14

CHARACTERISATION DATA

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R₁</th>
<th>Yield %</th>
<th>M.P. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
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<tr>
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<td>R₁</td>
<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>11a</td>
<td>H</td>
<td>H</td>
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<td>176-178</td>
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<td>4-Cl</td>
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<td>197-199</td>
<td>C₁₂H₁₁ClN₆O₃</td>
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</tr>
<tr>
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<td>H</td>
<td>4-CH₃</td>
<td>68</td>
<td>191-193</td>
<td>C₂₃H₂₄N₆O₃</td>
<td>66.20</td>
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<td>11d</td>
<td>H</td>
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<td>182-184</td>
<td>C₂₃H₂₄N₆O₄</td>
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<td>66.22</td>
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<td>11f</td>
<td>H</td>
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<td>65</td>
<td>195-197</td>
<td>C₂₄H₂₇N₆O₃</td>
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</table>
**CHARACTERISATION DATA**

Table 15

1-[(4-{1-Acetyl-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-pyrazole-3,4-dicarboxylic acid bis-{(2,5-dimethyl-pyrrol-1-yl)-amides (12a-f)

<table>
<thead>
<tr>
<th>R</th>
<th>R₁</th>
<th>Yield %</th>
<th>M.P. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
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<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>12a</td>
<td>H</td>
<td>65</td>
<td>157-159</td>
<td>C₃₄H₃₄N₈O₃</td>
<td>67.73 (67.76)</td>
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<tr>
<td>12b</td>
<td>H</td>
<td>70</td>
<td>142-144</td>
<td>C₃₄H₃₃ClN₈O₃</td>
<td>64.04 (64.09)</td>
</tr>
<tr>
<td>12c</td>
<td>H</td>
<td>58</td>
<td>153-155</td>
<td>C₃₅H₃₆N₈O₃</td>
<td>68.12 (68.16)</td>
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<tr>
<td>12d</td>
<td>H</td>
<td>72</td>
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<td>C₃₅H₃₆N₈O₄</td>
<td>64.40 (64.44)</td>
</tr>
<tr>
<td>12e</td>
<td>H</td>
<td>76</td>
<td>158-160</td>
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<td>64.06 (64.09)</td>
</tr>
<tr>
<td>12f</td>
<td>H</td>
<td>62</td>
<td>151-153</td>
<td>C₃₆H₃₉N₉O₃</td>
<td>66.95 (66.96)</td>
</tr>
</tbody>
</table>
### Characterisation Data

#### 3,4-Bis-(3,5-dimethyl-1-carbonyl-2-yI)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole -3-yl]phenyl]-pyrazole (13a-f)

|   | R  | R<sub>1</sub> | Yield % | M.P. °C | Molecular formula | Elemental Analysis
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>13a</td>
<td>H</td>
<td>H</td>
<td>62</td>
<td>202-204</td>
<td>C&lt;sub&gt;32&lt;/sub&gt;H&lt;sub&gt;30&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C: 66.85 (66.88) H: 5.17 (5.20) N: 19.46 (19.50)</td>
</tr>
<tr>
<td>13b</td>
<td>H</td>
<td>4-Cl</td>
<td>65</td>
<td>213-215</td>
<td>C&lt;sub&gt;33&lt;/sub&gt;H&lt;sub&gt;29&lt;/sub&gt;ClN&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C: 63.06 (63.10) H: 4.82 (4.80) N: 18.37 (18.40)</td>
</tr>
<tr>
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<td>H</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;</td>
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<td>C&lt;sub&gt;33&lt;/sub&gt;H&lt;sub&gt;32&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
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<tr>
<td>13d</td>
<td>H</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>70</td>
<td>210-212</td>
<td>C&lt;sub&gt;33&lt;/sub&gt;H&lt;sub&gt;32&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt;</td>
<td>C: 65.51 (65.55) H: 5.30 (5.33) N: 18.50 (18.53)</td>
</tr>
<tr>
<td>13e</td>
<td>H</td>
<td>2-Cl</td>
<td>63</td>
<td>218-220</td>
<td>C&lt;sub&gt;32&lt;/sub&gt;H&lt;sub&gt;29&lt;/sub&gt;ClN&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C: 63.12 (63.10) H: 4.74 (4.80) N: 18.37 (18.40)</td>
</tr>
<tr>
<td>13f</td>
<td>H</td>
<td>4-N(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>61</td>
<td>207-209</td>
<td>C&lt;sub&gt;34&lt;/sub&gt;H&lt;sub&gt;33&lt;/sub&gt;N&lt;sub&gt;9&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>C: 66.08 (66.11) H: 5.68 (5.71) N: 20.38 (20.41)</td>
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</tbody>
</table>
### 3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-1-[4-(1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl)-phenyl]pyrazole (14a-f)

<table>
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<tr>
<th>R</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Yield %</th>
<th>M.P. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>14a</td>
<td>H</td>
<td>55</td>
<td>209-211</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>54.28 (54.33)</td>
<td>3.38 (3.42)</td>
<td>21.04 (21.12)</td>
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</tr>
<tr>
<td>14b</td>
<td>4-Cl</td>
<td>72</td>
<td>196-198</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>51.06 (51.02)</td>
<td>2.98 (3.03)</td>
<td>19.80 (19.83)</td>
<td></td>
</tr>
<tr>
<td>14c</td>
<td>4-CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>61</td>
<td>194-196</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>55.07 (55.13)</td>
<td>3.64 (3.70)</td>
<td>20.51 (20.58)</td>
<td></td>
</tr>
<tr>
<td>14d</td>
<td>4-OCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>70</td>
<td>205-207</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;H&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;4&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>53.50 (53.56)</td>
<td>3.55 (3.60)</td>
<td>19.93 (19.99)</td>
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</tr>
<tr>
<td>14e</td>
<td>2-Cl</td>
<td>63</td>
<td>201-203</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;N&lt;sub&gt;8&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>51.06 (51.02)</td>
<td>3.00 (3.03)</td>
<td>19.78 (19.83)</td>
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<tr>
<td>14f</td>
<td>4-N(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;</td>
<td>58</td>
<td>198-200</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;H&lt;sub&gt;23&lt;/sub&gt;N&lt;sub&gt;9&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt;</td>
<td>54.39 (54.44)</td>
<td>3.99 (4.04)</td>
<td>21.95 (21.98)</td>
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</table>
CHARACTERISATION DATA

Table 18

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<th>M.P. °C</th>
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<th>Elemental Analysis</th>
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<td>Found (Calculated) (%)</td>
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<td></td>
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<td>15a</td>
<td>H</td>
<td>H</td>
<td>86</td>
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<td>C₂₄H₂₀K₂N₈O₃S₄</td>
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<td>80</td>
<td>142-144</td>
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<td>H</td>
<td>4-CH₃</td>
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1-{4-[1-Acety1-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl]-1H-Pyrazole- bis potassium dithiocarbazates (15a-f)
**CHARACTERISATION DATA**

Table 19

3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]-thiadiazole-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]- phenyl]pyrazole (16a-f)

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<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
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</thead>
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<td></td>
<td></td>
<td>%</td>
<td></td>
<td></td>
<td>C</td>
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<tr>
<td>16a</td>
<td>H</td>
<td>H</td>
<td>65</td>
<td>214-216</td>
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<td>16b</td>
<td>H</td>
<td>4-Cl</td>
<td>70</td>
<td>230-232</td>
<td>C_{24}H_{17}ClN_{4}OS_{4}</td>
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<td>16c</td>
<td>H</td>
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<td>240-242</td>
<td>C_{25}H_{20}N_{8}OS_{4}</td>
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<td>H</td>
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<td>70</td>
<td>234-236</td>
<td>C_{25}H_{20}N_{8}O_{2}S_{4}</td>
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<tr>
<td>16e</td>
<td>H</td>
<td>2-Cl</td>
<td>80</td>
<td>258-260</td>
<td>C_{24}H_{17}ClN_{4}OS_{4}</td>
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<tr>
<td>16f</td>
<td>H</td>
<td>4-N(CH_{3})_{2}</td>
<td>23</td>
<td>200-203</td>
<td>C_{24}H_{23}N_{9}OS_{4}</td>
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</table>
### CHARACTERISATION DATA

Table 20

3,4-Bis-(N-allyl thiosemicarbazide carbonyl-2-yl-)-l-[4-{l-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl]phenyl|pyrazole (17a-f)

<table>
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<th>M.p. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
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<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>17a</td>
<td>H</td>
<td>H</td>
<td>65</td>
<td>214-216</td>
<td>C_{30}H_{32}N_{10}O_{3}S_{2}</td>
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<tr>
<td>17b</td>
<td>H</td>
<td>4-Cl</td>
<td>70</td>
<td>230-232</td>
<td>C_{30}H_{31}ClN_{10}O_{2}S_{2}</td>
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<td>17c</td>
<td>H</td>
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<td>240-242</td>
<td>C_{31}H_{34}N_{10}O_{3}S_{2}</td>
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<td>17d</td>
<td>H</td>
<td>4-OCH_3</td>
<td>70</td>
<td>234-236</td>
<td>C_{31}H_{34}N_{10}O_{4}S_{2}</td>
</tr>
<tr>
<td>17e</td>
<td>H</td>
<td>2-Cl</td>
<td>80</td>
<td>258-260</td>
<td>C_{30}H_{31}ClN_{10}O_{2}S_{2}</td>
</tr>
<tr>
<td>17f</td>
<td>H</td>
<td>4-N(CH_3)_2</td>
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<td>268-270</td>
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</table>
### CHARACTERISATION DATA

#### Table 21

3,4-Bis-(4-allyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazolo-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chloro phenyl)pyrazole-3-yl}-phenyl]pyrazole (18a-f)

<table>
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<tr>
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<th>R</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Yield %</th>
<th>M.p. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Found (Calculated) (%)</td>
</tr>
</tbody>
</table>
|18a| H    | H          | 65      | 214-216 | C<sub>30</sub>H<sub>28</sub>N<sub>10</sub>O<sub>2</sub>S | C  59.15 (59.19)  
|    |      |            |         |         |                   | H  4.60 (4.64)     
|    |      |            |         |         |                   | N  22.97 (23.01)   |
|18b| H    | 4-Cl       | 70      | 230-232 | C<sub>30</sub>H<sub>27</sub>CINO<sub>10</sub>O<sub>2</sub>S | C  55.97 (56.02)  
|    |      |            |         |         |                   | H  4.19 (4.23)     
|    |      |            |         |         |                   | N  21.75 (21.78)   |
|18c| H    | 4-CH<sub>3</sub> | 68    | 240-242 | C<sub>31</sub>H<sub>30</sub>N<sub>10</sub>O<sub>2</sub>S | C  59.75 (59.79)  
|    |      |            |         |         |                   | H  4.82 (4.86)     
|    |      |            |         |         |                   | N  22.44 (22.49)   |
|18d| H    | 4-OCH<sub>3</sub> | 70    | 234-236 | C<sub>31</sub>H<sub>30</sub>N<sub>10</sub>O<sub>2</sub>S<sub>2</sub> | C  59.15 (59.19)  
|    |      |            |         |         |                   | H  4.60 (4.64)     
|    |      |            |         |         |                   | N  22.96 (23.01)   |
|18e| H    | 2-Cl       | 80      | 258-260 | C<sub>30</sub>H<sub>27</sub>CINO<sub>10</sub>O<sub>2</sub>S | C  55.97 (56.02)  
|    |      |            |         |         |                   | H  4.19 (4.23)     
|    |      |            |         |         |                   | N  21.75 (21.78)   |
|18f| H    | 4-N(CH<sub>3</sub>)<sub>2</sub> | 72     | 234-236 | C<sub>32</sub>H<sub>33</sub>N<sub>11</sub>O<sub>2</sub>S | C  59.15 (59.19)  
|    |      |            |         |         |                   | H  4.61 (4.64)     
|    |      |            |         |         |                   | N  22.60 (22.64)   |
### Table 22

1-[4-[1-Acetyl-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethyl esters (10a-f)

<table>
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<th>Compound</th>
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<th>Antibacterial</th>
<th>Antifungal</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td></td>
<td>E. coli</td>
<td>Pseudomonas</td>
</tr>
<tr>
<td>10a</td>
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<tr>
<td>10c</td>
<td>H</td>
<td>4-CH₃</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>10d</td>
<td>H</td>
<td>4-OCH₃</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>10e</td>
<td>H</td>
<td>2-Cl</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>10f</td>
<td>H</td>
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<td>-</td>
<td>10</td>
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<th>Antifungal</th>
</tr>
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</tr>
<tr>
<td>Ciprofloxacin</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Griseofulvin</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
### Table 23

1-[4-[1-Acetyl-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl]-1H-pyrazole-3,4-bis-carboxyhydrazides (11a-f)

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<th>Antifungal</th>
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</tr>
<tr>
<td>11a</td>
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<td>H</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>11b</td>
<td>H</td>
<td>4-Cl</td>
<td>17</td>
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<td>H</td>
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<td>12</td>
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<tr>
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<td>H</td>
<td>4-OCH₃</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>11e</td>
<td>H</td>
<td>2-Cl</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>11f</td>
<td>H</td>
<td>4-N(CH₃)₂</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>17</td>
</tr>
<tr>
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<td>-</td>
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ANTIMICROBIAL ACTIVITY

Table 24

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<td>16</td>
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<td>15</td>
<td>11</td>
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Standard

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</tbody>
</table>

1-{4-[1-AcetyI-5-(aryl)-4,5-dihydro-1H-pyrazol-3-yl]-phenyl}-1H-pyrazole-3,4-dicarboxylic acid bis-{(2,5-dimethyl-pyrrol-1-yl)-amides (12a-f)}
### ANTIMICROBIAL ACTIVITY

**Table 25**

<table>
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<td>4-Cl</td>
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<td>12</td>
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<td>13d</td>
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**3,4-Bis-(3,5-dimethyl-1-carbonyl-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole -3-yl]phenyl]pyrazole (13a-f)**

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<tr>
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</table>

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### ANTIMICROBIAL ACTIVITY

3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]-phenyl]pyrazole (14a-f)

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<td>H</td>
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<td>14f</td>
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**Standard**

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</tr>
<tr>
<td>Ciprofloxacin</td>
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<td>17</td>
</tr>
<tr>
<td>Griseofulvin</td>
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<td>-</td>
</tr>
</tbody>
</table>
Table 27

ANTIMICROBIAL ACTIVITY

3,4-Bis-(5-thioxo-4,5-dihydro-[1,3,4]-thiadiazole-2-yl)-1-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl) pyrazol-3-yl]-phenyl]pyrazole (16a-f)

<table>
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<th>Antifungal</th>
</tr>
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<td></td>
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<td>Pseudomonas</td>
</tr>
<tr>
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<th>Antifungal</th>
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<tr>
<td>Griseofulvin</td>
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### ANTIMICROBIAL ACTIVITY

#### Table 28

3,4-Bis-(N-allyl thiosemicarbazide carbonyl-2-yl-)-l-[4-{1-acetyl-4,5-dihydro-5-(4-chlorophenyl)pyrazole-3-yl}pheny1]pyrazole (17a-f)

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<th>Antifungal</th>
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### ANTIMICROBIAL ACTIVITY

Table 29

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<th>Antifungal</th>
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**Standard**

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3,4-Bis-(4-allyl-5-thioxo-4,5-dihydro-1H-1,2,4-triazolo-2-yl)-1-[4’-{1-acetyl-4,5-dihydro-5-(4-chloro phenyl)pyrazole-3-yl]-phenyl]pyrazole (18a-f)
References:


