Chapter-IV

1,2,3-Triazole, thiazole and benzothiazole derivatives.
Introduction:

Azides are considered as very important compounds due to both, their industrial as well as biological application. P. Grieses effected first time the preparation of an organic azide in 1864. The azide derivatives have been used in rubber vulcanization, polymer cross-linking, dyes, fire cored adhesives, foaming of plastics, pharmaceuticals, pesticides and herbicides. One of the most useful synthetic applications of azide is for the preparation of 1,2,3-triazoles via 1,3-dipolar cycloaddition reactions with substituted acetylene compounds.

The chemistry of 1,2,3-triazoles has received much attention because of their wide range of applications. These triazoles have been used as fungicides, herbicides, light stabilizers, optical brightening agents and corrosive retardants. Moreover, 1,2,3-triazole derivatives show significant antimicrobial, cytostatic, virostatic and anti-inflammatory activities. Derivatives of thiazoles and imidazothiazoles have also possess pronounced biological activities.

In the earlier part of the work we have synthesized some heterocyclic systems containing the 1-phenylpyrazole ring. In view of the importance of the above heterocycles, we have prepared some new 1-phenylpyrazoles coupled the above heterocycles. The biological activity of azides, 1,2,3-triazoles, thiazoles and benzothiazoles are reviewed below.

Biological activity of azides:

Yogadinets et al., have reported the synthesis of 3-azidoacetyl coumarin (I) and 6,8-dichloro-3-azidoacetyl coumarin (II). They reacted with triphenylphosphine to get a heterocyclic system containing phosphorus and nitrogen and screened them for antifungal and antibacterial activities.

\[
\text{I} \quad \text{Cl} \quad \text{II}
\]

Sheri et al., have reported some azido coumarin derivatives (III) and used them as photoaffinity inhibitor for the enzyme NADP(H) dehydrogenase.
Biological activity of 1,2,3-triazoles:

Among the three isomeric triazoles, only the 1,2,4-triazoles are most extensively studied. Only a few 1,2,3-triazoles are reported in the literature.

Honkel and Weygand\textsuperscript{9} have reported the triazole derivatives of type (IV)

\[
\text{C}_{12}\text{H}_{25}-\text{N} = \text{C} = \text{N}\text{CH(OCH}_2\text{H}_3)_2
\]

Miglarese\textsuperscript{10} reported the synthesis of compound (V), which have showed good antifungal activity.

\[
\text{H}_2\text{NOC}-\text{N} = \text{C} = \text{N}\text{COOCH}_3
\]

Sheehan and Robinson\textsuperscript{11} have reported the synthesis and antimicrobial activity of triazole derivatives of the type (VI) and (VII)

\[
\begin{align*}
\text{VI} & \quad \text{H} \\
\text{VII} & \quad \text{CH(OCH}_2\text{H}_3)_2
\end{align*}
\]
Maiorana and associates\textsuperscript{12} reported the triazole derivatives of types (VIII) and (IX) and screened them for antimicrobial activity.

\begin{equation}
\text{VIII} \quad R = \text{C}_6\text{H}_5\text{-NO}_2(4), \text{Ph} \\
\quad R_1 = \text{SO}_2\text{C}_6\text{H}_5, \\
\quad \text{SO}_2\text{C}_6\text{H}_5\text{-NO}_2(4)
\end{equation}

\begin{equation}
\text{IX} \\
\quad H - N - R_1
\end{equation}

1,2,3-Triazole moiety is a substructure of a number of biologically active compounds\textsuperscript{13} and number of its derivatives have found diverse uses in synthetic (Xa) analytical, medicinal, pharmaceutical, agrochemical, dyestuffs, fluroscent whitners (Xb) and photosensitizers (Xc).

\begin{equation}
\text{Xa} \\
\quad \text{Synthetic auxiliary}
\end{equation}

\begin{equation}
\text{Xb} \\
\quad \text{Fluoroscent whitening agent}
\end{equation}

\begin{equation}
\text{Xc} \\
\quad \text{Photosensitizer}
\end{equation}

Aebli \textit{et al.},\textsuperscript{14} have reported the triazolyl styryl triazoles (XI) as fluorescent whiteners.

\begin{equation}
\text{XI} \\
\quad \text{R - } \text{H}_2 - \text{N - Ph}
\end{equation}
Claussen et al.,\textsuperscript{15} have reported the triazole derivatives (XII) as intermediates for
dyes and fluorescent brighteners.

\[
\begin{array}{c}
\text{Ph} \\
\text{H}_2\text{C} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{CH}_3 \\
\end{array}
\]

\textbf{XII}

Horst \textit{et al.},\textsuperscript{16} have reported 3,7-ditriazolocoumarin derivatives (XIII) as optical
brightening agents, scintillators and dyes for lasers.

\[
\begin{array}{c}
\text{H}_2 \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{R} = \text{CH}_3 \\
\text{R}_1 = \text{C}_6\text{H}_5 \\
\end{array}
\]

\textbf{XIII}

\textbf{Biological activity of thiazoles:}

Thiazoles have been possess pronounced biological activity, viz anti-inflammatory, anticancer, antibacterial, antifungal and antiallergic activities.\textsuperscript{5a-c}

Some thiazole derivatives (XIV) and (XV) have been reported\textsuperscript{17} to be anesthetics for aquatic animals and their salts at 100 ppm in fresh or sea water was effective as anesthetics.

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

\textbf{XIV}

\[
\begin{array}{c}
\text{R}_1 \\
\text{N} \\
\text{S} \\
\text{R}_2 \\
\text{R}_3 \\
\text{R}_4 \\
\end{array}
\]

\textbf{XV}

Wododkar \textit{et al.},\textsuperscript{18} have reported 2-amino-4-phenyl-5-arylthiazoles (XVI) which exhibits antibacterial and antifungal activities.

\[
\begin{array}{c}
\text{Ph} \\
\text{N} = \text{N} \\
\text{Ph} \\
\text{N} \\
\text{N} \\
\text{NH}_2 \\
\end{array}
\]

\textbf{XVI}

191
Kazuo and coworkers\textsuperscript{19} have reported thiazole derivatives of type (XVII) and they possess agrochemical biocides have shown 100% control of Nephottettix and Cinticeps at 100 ppm.

\[
\begin{array}{c}
\text{XVII} \\
\begin{array}{c}
\text{R}_1 \\
\text{R}_2 \\
\text{N} \\
\text{S} \\
\text{S(O)}_n\text{R}_1
\end{array}
\end{array}
\]

Jian \textit{et al.},\textsuperscript{20} have reported the preparation of 2,4-Bis-(3-indolyl) thiazoles (XVIII) and tested them for cytotoxic activity against diverse human cancer cell lines and shown significant inhibitory effects in the growth of cancer cell lines.

\[
\begin{array}{c}
\text{XVIII} \\
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{S} \text{CH}_3
\end{array}
\end{array}
\]

Upadhya and associates\textsuperscript{21} have reported the synthesis of 4-(4-thiazolyl) sydnone derivatives (XIX) from our laboratory, which have found to exhibit anti-inflammatory activity.

\[
\begin{array}{c}
\text{XIX} \\
\begin{array}{c}
\text{R} \\
\text{N} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{N}
\end{array}
\end{array}
\]

Badachikar \textit{et al.},\textsuperscript{22a} have reported some thiazole derivatives of sydnone (XX) and (XXI) and screened them for anti-inflammatory, analgesic and antibacterial activity.
Hosamani and coworkers\textsuperscript{22b} have reported the synthesis and antimicrobial activity of 3-aryl-4-[2-(3'-coumarylidene hydrazine)-4-thiazolyl] sydnones (XXII)

\[
\text{XXII}
\]

The synthesis of diamino thiazoles (XXIII) for inhibitory protein kinase was reported by Chu \textit{et al.}\textsuperscript{23} These derivatives are capable of mediating tyrosin kinase signal transduction in order to moderate or inhibit unwanted cell proliferation.

\[
\text{XXIII}
\]

Jachne and associates\textsuperscript{24} have synthesized 8,8a-dihydroindeno[1,2-d] thiazoles (XXIV) for the treatment of obesity and type II diabetes.

\[
\text{XXIV}
\]

**Biological activity of benzothiazoles:**

The synthesis of imidazothiazoles have been receiving attention during recent years as antitumor, anti-inflammatory, cardiotonic and diuretic agents.\textsuperscript{6}

The 5-nitro-2-furyl-subst imidazo heterocyclic compounds (XXV) were screened for biological activity and it has received highest antimicrobial activity, which has nearer to that of Furozolidine.\textsuperscript{25}
Hedgecock et al.\textsuperscript{26} have reported imidazo [2,1-b] benzothiazoles (XXVI) and (XXVII)

\[
\text{XXVI} \quad \text{XXVII}
\]

The synthesis of 3-aryl-4-[6-imidazo(2,1-b)-thiazoles] sydnones (XXVIII) were reported by Tikare et al.\textsuperscript{27} and screened them for antifungal and antibacterial activity.

\[
\text{XXVIII}
\]

Nagarapu et al.\textsuperscript{28} have reported the synthesis of phenylimidazothiazole benzocyclo heptane derivatives (XXIX) as potential anti-inflammatory agents.

\[
\text{XXIX}
\]

In view of above observations we thought of the synthesis of biologically active 1,2,3-triazole, thiazole and imidazothiazoles from the DMAD cycloadduct of sydnones and subject them for the structure-activity relationship studies.
This part of the work, involved the ring conversion of 3-(p-acetyl) phenyl sydnones with DMAD to afford 3-(p-acetyl) phenyl pyrazole-3,4-dicarboxylate (22) the literature method, which is the starting material for the present work. The acetyl group of this compound was converted into the azide keeping the dicarboxylate intact, and then utilized for building different heterocycles.

The compound (22) yielded a crystalline monobromoacetyl derivative (23) on bromination with bromine in chloroform, using 1:1 molar ratio of bromine and with excess of bromine the dibromoacetyl derivative (24) was the major product.

The monobromoacetyl compound was used to construct five membered heterocycles, like 1,2,3-triazoles, thiazoles and benzothiazoles. First the monobromoacetyl cycloadduct of sydnone was converted into azidoacetyl derivative (25) by adding NaN₃ in acetone. The azidoacetyl group of the compound (25) undergoes 1,3-dipolar cycloaddition with dimethylacetylene dicarboxylate (DMAD) to afford 1-[4-(2-pyrazole)-3,4-dicarboxylic acid dimethyl ester (26) which gives tetrahydrazides derivatives(27) on reaction with hydrazine hydrate. On the other hand thiazole derivatives are (28a-b) formed by the addition of thiourea and thioacetamide. The same compounds can be obtained from dibromoacetyl derivative (24) also, as reported in the literature. Finally, the compound (23) when reacted with o-amino phenol yielded the benzothiazole derivatives (29)(Scheme 8).

All the above newly synthesized compounds were confirmed by their IR, H-NMR, C-NMR and mass spectral studies.
Scheme-8
Plausible mechanistic pathway for the cycloaddition to the azide group is shown below. (Scheme-9)

The formation of 1,2,3-triazole is based on the assumption that the attack of nucleophilic nitrogen of the azide (25) on the electrophilic β-carbon of the unsaturated ester (DMAD) (a) is both sterically and electrophilically favoured. Further, it is also based on the assumption that cycloaddition reaction involves conjugate addition of the azide (25) to the Michael acceptor (a), i.e. DMAD, leading to N-C bond formation (25a) which essentially represents the 3+2 approach for the construction of 1,2,3-triazole (26) followed by cyclisation as depicted above. (Scheme 9)

Spectral characterization:

The IR spectrum of the compound (23) (spectrum 38) showed band around 1725,1705 and 1694 cm\(^{-1}\) due to ester and bromoacetyl \(\nu_{C=O}\). The \(^1\)H-NMR spectrum (spectrum 39) showed two singlets at 3.92 and 4.03 \(\delta\) due to methyl protons of two ester groups and the signal at 4.47 \(\delta\) was assigned to the deshielded protons of \(-CO-CH_2-\) group. The aromatic protons resonated as two doublets at 7.92 and 8.16 \(\delta\) and pyrazole ring proton resonated as a singlet at 8.51 \(\delta\).

The IR spectrum of the compound (24) (spectrum 40) exhibited broad band around 1744 and 1722 cm\(^{-1}\) related to \(\nu(C=O)\) of ester and dibromoacetyl groups.
The $^1$H-NMR spectrum (spectrum 41) observed signals at 3.92 and 4.02 $\delta$ were accounted for the methyl protons of ester and singlet at 6.66 $\delta$ was due to proton of -CH-Br$_2$. This signal for the highly deshielded proton as compared to the above carrying single bromine is an evidence for the formation of a dibromo derivative. The two doublets at 7.91 and 8.28 $\delta$ correspond to aromatic protons and the singlet at 8.52 $\delta$ was due to pyrazole proton.

The IR spectrum of compound (25) (spectrum 42) had sharp band at 2109 cm$^{-1}$ due to azide group and bands appeared at 1739 and 1713 cm$^{-1}$ correspond to $\nu_{C=O}$ of two ester groups. The band at 1677 cm$^{-1}$ assigned to azidoacetyl $\nu_{C=O}$ frequencies. The $^1$H-NMR spectrum (spectrum 43) showed signals at 3.92 and 4.03 $\delta$ accountable for methyl protons of ester groups and singlet at 4.60 $\delta$ assigned to $-\text{CH}_2$-$\text{N}_3$. The aromatic protons resonated as two doublets at 7.90 and 8.09 $\delta$ and a singlet at 8.51 $\delta$ was ascribed to pyrazole proton. The $^{13}$C-NMR values of the compound (25) (spectrum 44) have been assigned as following based on the field effects.

The IR spectrum of the compound (26) (spectrum 45) exhibited broad bands at 1694 and 1747 cm$^{-1}$ due to the $\nu_{C=O}$ frequencies. The $^1$H-NMR spectrum (spectrum 46) had four singlets in the region 3.92 - 4.03 $\delta$ (12 H) due to the methyl protons of the esters. The singlet for the $\text{CH}_2-$ protons, which was at 4.60 $\delta$ in the above azide has been shifted downfield to 6.22 $\delta$ and this is an evidence for the formation of an aromatic triazole ring. The signals for aromatic protons were observed as two doublets at 7.96 and 8.16 $\delta$ (2H) and pyrazole ring proton resonated as a singlet at 8.54 $\delta$. The structure of this compound was also evidenced by $^{13}$C-NMR (spectrum 47) and the values are assigned as below.
The mass spectrum of the above compound (spectrum 48) showed molecular ion peak at m/z 485, which is the molecular weight of the compound (Scheme-10).

The IR spectrum of the compound (27) (spectrum 49) exhibited broad band around 3317-3224 cm⁻¹ due to νNH vibrations and band around 1662-1573 cm⁻¹ correspond to the νC=O frequencies. The ¹H-NMR spectrum (spectrum 50) (not resolved due to poor solubility) showed signals at 4.83 δ (8H) assignable to NH₂-protons. The -COCH₃ protons resonated as a singlet at 6.0 δ. The aromatic protons exhibited two doublets at 7.62 and 7.99 δ, while pyrazole ring proton appeared as a singlet at 9.02 δ.
The four NH of hydrazide groups appeared in the deshielded region at 10.35, 11.22, 12.01, and 12.64 δ and disappeared on shaking with D2O.

The IR spectrum (compound 28a) (Spectrum 51) showed bands around 3351-3448 cm⁻¹ due to v NH of thiazole ring and bands at 1698 and 1727 for v C=O frequencies of two ester groups. The ¹H-NMR (spectrum 52) showed two singlets at 3.91 and 4.02 δ for methyl protons of ester groups and another singlet at 5.06 δ was assigned to -NH₂- protons of thiazole. Thiazole ring proton resonated as a singlet at 6.82 δ and two doublets observed at 7.76 and 7.93 δ were related to aromatic protons. The pyrazole ring proton appeared as a singlet at 8.49 δ.

The IR spectrum (compound 28b) (Spectrum 53) showed broad band at 1729 cm⁻¹ was due to two ester v C=O. The ¹H-NMR spectrum (spectrum 54) showed a singlet at 2.33 δ for the methyl protons of thiazole ring and two singlets were observed at 3.91 and 4.02 δ for methyl protons of ester groups, whereas thiazole ring proton resonated as a singlet at 7.27 δ. The two doublets observed around 7.80 and 7.94 δ are due to aromatic protons and pyrazole ring proton resonated as a singlet at 8.44 δ.

The IR spectrum (compound 29) (Spectrum 55) showed band at 1756 and 1712 due to v C=O frequencies of ester groups. The ¹H-NMR spectrum (spectrum 56) exhibited two singlets at 3.93 and 4.05 for methyl protons of ester groups and benzothiazole ring proton was observed at 6.74 δ. The signals around 7.0-7.7 δ are due to the aromatic protons (not well resolved), while the singlet at 8.48 δ was related to pyrazole ring proton.
SPECTRAL DATA

1-[4-(2-Bromo-acetyl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (23)

IR Spectrum
Spectrum 38

3136 cm\(^{-1}\) \(v_{CH}\) of pyrazole ring
1725, 1705 and 1694 cm\(^{-1}\) \(v_{C=O}\) of ester and bromoacetyl groups

\(^1\)H-NMR Spectrum
Spectrum 39

3.92 \(\delta\) (s, 3H)  Methyl protons of C\(_4\) ester
4.03 \(\delta\) (s, 3H)  Methyl protons of C\(_3\) ester
4.47 \(\delta\) (s, 2H)  Protons of C\(_{CH_2}\)Br
7.92 \(\delta\) (d, 2H, J= 6 Hz) and 8.16 \(\delta\) (d, 2H, J= 9 Hz)  Aromatic protons
8.51 \(\delta\) (s, 1H)  Pyrazole ring proton
SPECTRAL DATA

1-[4-(2,2-Dibromo-acetyl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (24)

IR Spectrum:
Spectrum 40

3123 cm⁻¹  \( \nu_{CH} \) of pyrazole ring
1744 and 1722 cm⁻¹  \( \nu_{\text{C=O}} \) of ester and dibromoacetyl group

\(^1\text{H}-\text{NMR Spectrum:}
Spectrum 41

3.92 \( \delta \) (s, 3H)  Methyl protons of C₄ ester
4.02 \( \delta \) (s, 3H)  Methyl protons of C₃ ester
6.66 \( \delta \) (s, 2H)  Protons of –CH-Br₂
7.91 \( \delta \) (d, 2H, \( J=9 \) Hz) and
8.28 \( \delta \) (d, 2H, \( J=6 \) Hz)  Aromatic protons
8.52 \( \delta \) (s, 1H)  Pyrazole ring proton
SPECTRAL DATA

1-[(4-(2-Azido-acetyl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (25)

IR Spectrum:
Spectrum 42
2109 cm\(^{-1}\) Azide group
1739, 1713 and 1677 cm\(^{-1}\) \(\nu_{C=O}\) of ester and azidoacetyl groups

\(^1H\)-NMR Spectrum:
Spectrum 43
3.92 \(\delta\) (s, 3H) Methyl protons of \(\text{C}_4\) ester
4.03 \(\delta\) (s, 3H) Methyl protons of \(\text{C}_3\) ester
4.60 \(\delta\) (s, 2H) Protons of \(-\text{CH}_2\text{-N}_3\)
7.90 \(\delta\) (d, 2H, \(J=9\) Hz) and
8.09 \(\delta\) (d, 2H, \(J=9\) Hz) Aromatic protons
8.51 \(\delta\) (s, 1H) Pyrazole ring proton
SPECTRAL DATA

1-[2-[4-(3,4-Bis-methoxycarbonyl-pyrazol-1-yl)-phenyl]-2-oxo-ethyl]-1H-[1,2,3] triazole-4, 5-dicarboxylic acid dimethyl ester (26)

IR Spectrum:
Spectrum 45
1747 and 1694 cm$^{-1}$  $\nu_{\text{C=O}}$ of ester and COCH$_2$ groups

$^1$H-NMR Spectrum:
Spectrum 46

3.92 δ (s, 3H)  Methyl protons of C$_4$ ester
4.02 δ (s, 3H)  Methyl protons of C$_3$ ester (pyrazole)
3.94 δ (s, 3H)  Methyl protons of C$_4$ ester
4.03 δ (s, 3H)  Methyl protons of C$_3$ ester (triazole)
6.22 δ (s, 2H)  Protons of –CH$_2$–CO-triazole
7.96 δ (d, 2H, J= 9 Hz) and
8.16 δ (d, 2H, J= 9 Hz)  Aromatic protons
8.54 δ (s, 1H)  Pyrazole ring proton

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SPECTRAL DATA

1-{2-[4-(3,4-Bis-hydrazinocarbonyl-pyrazol-1-yl)-phenyl]-2-oxo-ethyl}-1H-
[1,2,3] triazole-4, 5-bis-hydrazide (27)

IR Spectrum
Spectrum 49

3317-3224 cm$^{-1}$ $v_{NH}$ of hydrazides
1662-1573 cm$^{-1}$ (broad) $v_{C=O}$ groups

$^1$H-NMR Spectrum
Spectrum 50

6.0 $\delta$ (s, 2H) Protons of $-\text{CH}_2\text{-CO-}$
4.83 $\delta$ (broad, 8H) Protons of $\text{NH}_2$ groups
7.62 and 7.99 $\delta$ (2d, 4H) Aromatic protons
9.02 $\delta$ (s, 1H) Proton of pyrazole
10.35, 11.22, 12.01 and Four NH protons
12.64$\delta$ (4s, 4H)

205
SPECTRAL DATA

IR Spectrum:
Spectrum 51
3351-3448 cm$^{-1}$
1727 and 1698 cm$^{-1}$

$^1$H-NMR Spectrum:
Spectrum 52
3.91 $\delta$ (s, 3H) Methyl protons of $C_4$ ester
4.02 $\delta$ (s, 3H) Methyl protons of $C_3$ ester
5.06 $\delta$ (s, 2H) NH$_2$ protons of thiazole
6.82 $\delta$ (s, 1H) Proton of thiazole
7.76 $\delta$ (d, 2H, J= 9 Hz) and Aromatic protons
7.93 $\delta$ (d, 2H, J= 9 Hz)
8.49 $\delta$ (s, 1H) Pyrazole ring proton
SPECTRAL DATA

1-[4-(2-Methyl-thiazol-4-yl)-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester (28b)

IR Spectrum:
Spectrum 53

1729 cm\(^{-1}\) (broad) \(\nu_C=O\) of ester groups

\(^1\)H-NMR Spectrum:
Spectrum 54

2.33 (s, 3H) Methyl protons of thiazole ring
3.91 \(\delta\) (s, 3H) Methyl protons of C\(_4\) ester
4.02 \(\delta\) (s, 3H) Methyl protons of C\(_3\) ester
7.27 \(\delta\) (s, 1H) thiazole proton
7.80 \(\delta\) (d, 2H, \(J=9\) Hz) and
7.94 \(\delta\) (d, 2H, \(J=9\) Hz) Aromatic protons
8.44 \(\delta\) (s, 1H) Pyrazole ring proton
SPECTRAL DATA

Dimethyl-1-[4-(imidazo[2,1-b]thiazol-6-yl)-phenyl]-1H-pyrazole-3,4-dicarboxylate (29)

IR Spectrum:
Spectrum 55

1756 and 1712 cm$^{-1}$ $\nu_{\text{C=O}}$ of ester groups

$^1$H-NMR Spectrum:
Spectrum 56

3.93 $\delta$ (s, 3H) Methyl protons of $C_4$ ester
4.05 $\delta$ (s, 3H) Methyl protons of $C_3$ ester
6.74 $\delta$ (s, 1H) Proton of benzothiazole
7.0-7.7 $\delta$ (m, 8H) Aromatic protons
8.48 $\delta$ (s, 1H) Pyrazole ring proton
Spectrum 41 $^1$H-NMR
Solvent  CDCl$_3$
Spectrum 42 IR Spectrum
KBr Pellet
Wavenumbers (cm⁻¹)
Spectrum 45 IR Spectrum
KBr Pellet
Spectrum 46 $^1$H-NMR
Solvent  CDCl$_3$
Spectrum 47 $^{13}$C-NMR
Solvent CDCl$_3$
Spectrum 49 IR Spectrum
KBr Pellet

Wavenumbers (cm⁻¹)

4000 3500 3000 2500 2000 1500 1000
Experimental:

General procedures:

Preparation of 1-[4-(2-bromo-acetyl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (23)

The compound (22) (0.001 mol) was suspended in 30 ml of chloroform and bromine (0.001 mol) in chloroform (10 ml) was added under irradiation of visible light. After 15 minutes, the colour of the bromine bleached. The solvent was removed to dryness and the compound was crystallised from ethanol to give yellow crystals. (Table 36)

Preparation of 1-[4-(2,2-dibromo-acetyl)-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester (24)

To a solution of (22) in 100 ml of chloroform, bromine in chloroform (1:2) ratio was added under the irradiation of visible light. After 15 minutes, the colour of bromine bleached. The solvent was removed to dryness and crystallized from ethanol to get yellow crystals (Table 36).

Preparation of 1-[4-(2-azido-acetyl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (25)

Compound (23) (0.001 mol) was taken in acetone (20 ml), to this sodium azide (0.012 mol) in 3 ml of water was added dropwise with stirring. The stirring was continued for 5 hrs, the separated solid was filtered, washed with water and the white solid was crystallised from ethanol. (Table 36)

Preparation of 1-{2-[4-(3,4-bis-methoxycarbonyl-pyrazol-1-yl)-phenyl]-2-oxo-ethyl}-1H-[1,2,3] triazole-4, 5-dicarboxylic acid dimethyl ester (26)

To a solution of (25) (0.001 mol) in dry xylene (4 ml) dimethylacetylenedicarboxylate (0.001 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 36)
Preparation of 1-{2-[4-(3,4-bis-hydrazinocarbonyl-pyrazol-1-yl)-phenyl]-2-oxo-ethyl}-1H-[1,2,3] triazole-4, 5-bis-hydrazide (27)

To a solution of compound (26) (0.003 mol) in 10 ml of ethanol, hydrazine hydrate (99-100%, 0.006 mol) was added and the reaction mixture refluxed for 5 hours. The white solid separated on cooling was filtered, washed with water and crystallised from ethanol/DMF. (Table 36)

Preparation of 1-[4-(2-amino/methyl thiiazol-4-yl)-phenyl]-1H-pyrazole-3, 4-dicarboxylic acid dimethyl ester (28a-b)

To a solution of compound (23) (0.001 mol) in (20ml) of ethanol was added thiourea / thioamide (0.001 mol) and the reaction mixture was stirred for 3 hours. The precipitate was collected by filtration and dissolved in dilute ethanol (1:1) and the solution was neutralized with sodium hydrogen carbonate. The precipitate was crystallized from ethanol. (Table 36)

These compounds were also prepared from compound (24) by the above procedure.

Preparation of 1-[4-(Benzothiazol-2-yl)-phenyl]-1H-pyrazole-3,4-dicarboxylic acid dimethylester (29)

To a solution of compound (23) (0.001 mol) in (20ml) of ethanol was added o-aminothiophenol (0.001 mol) and the reaction mixture was stirred for 3 hours. The precipitate was collected by filtration and dissolved in dilute ethanol (1:1) and the solution was neutralized with sodium hydrogen carbonate. The precipitate was crystallized from ethanol. (Table 36)
## CHARACTERISATION DATA

**Table 36**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Yield %</th>
<th>M.p. °C</th>
<th>Molecular formula</th>
<th>Elemental Analysis Found (Calculated) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
</tr>
<tr>
<td>23</td>
<td>64</td>
<td>170-172</td>
<td>C₁₅H₁₃BrN₂O₅</td>
<td>47.23</td>
</tr>
<tr>
<td>24</td>
<td>72</td>
<td>167-169</td>
<td>C₁₅H₁₂Br₂N₂O₅</td>
<td>39.12</td>
</tr>
<tr>
<td>25</td>
<td>73</td>
<td>169-171</td>
<td>C₁₅H₁₃N₃O₅</td>
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<tr>
<td>26</td>
<td>67</td>
<td>145-147</td>
<td>C₂₀H₁₉N₅O₉</td>
<td>51.85</td>
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<tr>
<td>27</td>
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<td>165-167</td>
<td>C₁₇H₁₉N₃O₅</td>
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<tr>
<td>28a</td>
<td>67</td>
<td>155-157</td>
<td>C₁₆H₁₄N₄O₄S</td>
<td>53.60</td>
</tr>
<tr>
<td>28b</td>
<td>75</td>
<td>160-162</td>
<td>C₁₇H₁₅N₃O₄S</td>
<td>57.10</td>
</tr>
<tr>
<td>29</td>
<td>68</td>
<td>166-168</td>
<td>C₂₀H₁₇N₃O₄S</td>
<td>60.71</td>
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# ANTIMICROBIAL ACTIVITY

Table 37

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Antibacterial</th>
<th>Antifungal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
<td>Pseudomonas</td>
</tr>
<tr>
<td>23</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>24</td>
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<tr>
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<td>21</td>
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<td>27</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>28a</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
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<table>
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<tr>
<th>Standard</th>
<th>Antibacterial</th>
<th>Antifungal</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Pseudomonas</td>
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<tr>
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<td>Griseofulvin</td>
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<td>-</td>
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References:


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