STUDIES ON THE SYNTHESIS AND REACTIVITY OF 1,2,3-TRIAZOLE-DIAZONIUM SALTS AND RELATED COMPOUNDS

by

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To My Wife and Parents
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Summary

The subject matter of this thesis concerns the synthesis, structure and reactions of 1H-1,2,3-triazole-diazonium salts and related compounds.

The preparation of some simple aminotriazoles is described. It is shown that these aminotriazoles condense smoothly with β-dicarbonyl compounds, to form the corresponding 1,2,3-triazolo[1,5-a]pyrimidines. In addition, variable temperature ¹H n.m.r. studies of some 1,2,3-triazolo[1,5-a] pyrimidines have demonstrated the existence of diazoalkylidene-1,2,3-triazole tautomerism in these compounds. Investigations of the synthesis of 1,5-diaminotriazoles and their condensation reactions with simple α-dicarbonyl compounds are also described.

The diazotisation reactions of some aminotriazoles have been investigated and simple nucleophilic displacement reactions of the resulting 1H-1,2,3-triazole-diazonium salts demonstrated. In addition, the photochemical transformations of 4-phenyl-1H-1,2,3-triazole-5-diazonium betaine in various solvents has been shown to occur, with extrusion of nitrogen, forming products derived from phenylcyanocarbene.

The bifunctional reactivity of a variety of 4-substituted 1H-1,2,3-triazole-5-diazonium salts is illustrated by their condensation with a series of simple and novel active methylene components, providing synthetic routes to new 1,2,3-triazolo[5,1-c]-1,2,4-triazine derivatives. The structures of such fused triazolotriazines, and their hydrazone precursors, have been established by physical methods and chemical transformations.
The formation of 1,2,3-triazolo[5,1-c]-1,2,4-triazines, by reductive condensation reactions of some 4-substituted 5-diazo-1H-1,2,3-triazoles, has been demonstrated. Further studies on the nucleophilic displacement reactions of 3-benzene-sulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazines, with simple nucleophiles, has resulted in the formation of benzylidene products explicable in terms of a new type of Dimroth rearrangement.
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The Synthesis and Reactivity of 5-Diazo-1H-1,2,3-triazoles

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Chapter 1

A Review of the Synthesis and Reactivity of
Five-membered Heterocyclic Diazoc Compounds
and Diazonium Salts
Scheme 1

\[ \text{ArNH}_2 + 2\text{HNO}_2 \rightarrow \text{ArN}^+\text{N}=\text{O} + \text{H}_2\text{O} + \text{NO}_2 \] (4)

\[ \text{HX} \uparrow \]

\[ \text{ArN}^-\text{N}=\text{O} \quad \Leftrightarrow \quad \text{ArN}^-\text{N}=\text{O} \quad \text{H}^+ \downarrow \text{H}^+ \] (5)

\[ \text{ArN}=\text{N} \quad \downarrow \text{OH} \]

\[ \text{ArN}^+\text{N}=\text{O} \] (6)

\[ \text{ArN}^+\text{N}=\text{N} \quad \text{X} \] (7)

\[ \text{ArN}^-\text{N}=\text{N} \quad \text{X} \] (8)
1.1 Synthesis of Five-membered Heterocyclic Diazo Compounds and Diazonium Salts

1.1.1 Preparation from Amines

The diazotisation reactions of five-membered heterocyclic amines have not been as extensively studied as those of their benzenoid counterparts. Aromatic diazo compounds have been known since 1858, when Griess\(^1\)first diazotised picramic acid. However it was some forty years later, in 1899, that the first heterocyclic diazo compound was reported by Bamberger\(^2\), who isolated 3-diazoindiazole (3) by diazotising 3-aminoindazole (1) followed by treatment of the resulting diazonium salt (2) with base\(^2,3\).

The diazotisation of aromatic and heteroaromatic primary amines is most commonly achieved using nitrous acid generated in situ in aqueous solution from sodium nitrite and mineral acid, and is considered to involve the mechanism shown in scheme 1. The first step, which is slow and rate determining, involves N-nitrosation of the free amine (4) (rather than the amine salt) to form the primary nitrosoamine (6).
Scheme 2

R-NH₂ → R--N≡N X⁻

HNO₂
HX

RN'R HX R'NR

H
H

(11) (12)

(13)

R

a) H

b) Ph

(14) (15)

Scheme 2
The subsequent isomerisation to the \( \text{N-hydroxy-azo} \) compound \([(6) \xrightarrow{\text{N}} (7)]\) and subsequent attack by acid to form the diazonium salt \([(7) \xrightarrow{\text{N}} (8)]\) are fast. If the diazonium salt produced contains an acidic proton, subsequent treatment with base can lead to the corresponding diazo compound as in the formation of diazo-oxides from phenol diazonium salts \([(9) \rightarrow (10)]\).

\[
\begin{align*}
&\text{(9)} \\
&\begin{array}{c}
\text{O} \\
\text{R} \\
\text{N} \equiv \text{N} \text{X}^{-}
\end{array} \\
&\begin{array}{c}
\text{B}^{-} \\
\text{R} \\
\text{N} \equiv \text{N}
\end{array} \\
&\begin{array}{c}
\text{O}^{-} \\
\text{R} \\
\text{N} \equiv \text{N}
\end{array}
\end{align*}
\]

Treatment of \( \text{C-substituted 3-aminopyrroles (11)} \) with sodium nitrite in strong or weak acid affords the pyrrole-3-diazonium salts (12), which can be isolated as relatively stable crystalline solids\(^4\), but readily lose a proton, even in dilute acid, to give the corresponding stable 3-diazo pyrroles (13)\(^5\). \( \text{N-substituted pyrrole-3-diazonium salts (15)} \) are also readily formed by treatment of \( \text{N-substituted 3-aminopyrroles (14)} \) with sodium nitrite in hydrochloric acid\(^6\)-\(^8\), and can be isolated as relatively stable solids\(^6\)-\(^8\).
Scheme 3
Few reports have appeared in the literature concerning the preparation of diazonium salts from aminofurans and aminothiophens. 3-Amino-2-methylfuran (16a) and 3-amino-2,5-dimethylfuran (16b), when treated with sodium nitrite in the presence of sulphuric acid, give stable solutions which are considered to contain the diazonium salts (17a and b), although neither have been isolated. 2-Aminothiophen has been successfully diazotised in the form of a double salt [(C₄H₃S-NH₂.HCl)₂-SnCl₄] by Putokin and Yakovlev, using sodium nitrite in 10% hydrochloric acid solution, although the salt was obtained only in solution and not isolated in solid form. However, Paulmier has shown that 2-substituted aminothiophens (18) and 2-substituted aminoselenophens (19) can be directly diazotised using sodium nitrite in aqueous hydrochloric acid to give stable solutions of the corresponding diazonium salts, though again no attempt was made to isolate these in solid form. More recently, the diazotisation of 3-aminothiophen-2-carboxamides (20) with sodium nitrite in concentrated hydrochloric acid has been reported to give the thieno-1,2,3-triazines (22), probably by cyclisation of the diazonium
Scheme 4
salts (21)\textsuperscript{15}. A similar reaction was observed with the 4-carboxamide derivatives, and with the 2,4-dicarboxamide derivatives, condensation of the diazo group with the 2-carboxamide group was preferred\textsuperscript{15}. The conversion of 3-amino-1H-pyrazoles (23) and 4-amino-1H-pyrazoles (27) into the corresponding stable crystalline diazonium salts (24) and (28)\textsuperscript{4}, appears to require strongly acidic conditions, and is usually accomplished using sodium nitrite in hydrochloric or phosphoric acids, (scheme 4)\textsuperscript{16-22}. In contrast the diazotisation of 3-amino-1H-pyrazole (23) using sodium nitrite in acetic acid affords diazoaminopyrazoles of type (26)\textsuperscript{16,17}. Deprotonation of the pyrazolediazonium salts (24) and (28) by treatment with base affords the relatively stable diazopyrazoles (25) and (29)\textsuperscript{4,16,21,22}, although the 3-diazopyrazoles (25) are noticeably less stable than the 4-diazo isomers (29)\textsuperscript{4}. Simple 2- and 4-aminoimidazoles are readily diazotised to give stable solutions of diazonium salts which have not been isolated, although it is reported that the diazotisation of aminoimidazoles containing electron withdrawing groups yields stable diazo-compounds directly\textsuperscript{9}. For example, treatment of 2-amino-4,5-dicyano-1H-imidazole (30) with sodium nitrite in hydrochloric acid results in the formation of the diazo compound (31)\textsuperscript{23}. Similarly, diazotisation of 5-aminoimidazole-4-carboxamide (32) under the same conditions gives the diazoimidazole (33) which readily cyclises on standing to give 2-azohypoxanthine (34) (scheme 5)\textsuperscript{24}. It has
Scheme 5
been reported recently that the diazotisation of methyl 5-amino-1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)imidazole-4-carboxylate (35) with sodium nitrite in the presence of nitric acid yields methyl 1-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-2-oxo-Δ^4-imidazoline-4-carboxylate (36).

\[
\begin{align*}
(35) & \quad \xrightarrow{\text{N\textsuperscript{3}C\textsuperscript{2}}} \quad (36)
\end{align*}
\]

\[R = 2,3,5\text{-tri-O-acetyl-β-D-ribofuranosyl}\]

This unusual rearrangement probably occurs via nitrosation at the 2-position, followed by attack by a water molecule. Few reports concerning the preparation of diazonium salts from aminooxazoles appear in the literature. For example, diazotisation of 2-aminobenzoxazole (37) with sodium nitrite in dilute hydrochloric acid has been reported, but the products were not isolated. The solution instead was treated with concentrated hydrochloric acid to form the
chloro derivative and coupled with β-naphthol to give the corresponding azo dye (see later)\textsuperscript{26}. Both these reactions indicate the presence of the diazonium salt (38).

2-Aminothiazoles and 2-aminobenzothiazoles are readily diazotised to diazonium salts using sodium nitrite in strong oxyacids such as phosphoric, sulphuric or nitric acids, although only dediazoniation products are isolated\textsuperscript{27-29}. For example diazotisation of the amine (39) in concentrated hydrochloric acid affords 2-chlorothiazole, via the diazonium salt (40)\textsuperscript{28}, (see later).

Treatment of 5-aminoisoxazoles with sodium nitrite and mineral acids readily affords the corresponding diazonium salts, but these salts are unstable and have not been isolated\textsuperscript{30}.
5-Amino-4-ethoxycarbonyl-3-methylisoxazole (41) when diazotised with concentrated hydrochloric acid gives the diazonium salt (42), which then rapidly decomposes to the chloro derivative (43).

Isothiazole-3-diazonium salts (44) are also readily generated from the parent amines by the action of sodium nitrite in the presence concentrated mineral acids, but these salts, as in the case of their isoxazole analogues...
\[
\begin{align*}
\text{R} & \quad \text{X} \\
a) \text{Me} & \quad \text{NO}_3 \\
b) \text{H} & \quad \text{NO}_3 \\
c) \text{Me} & \quad \text{Cl} \\
d) \text{H} & \quad \text{Cl}
\end{align*}
\]

\[
\begin{align*}
\text{x}^- \\
a) \text{Cl} \\
b) \text{BF}_4
\end{align*}
\]
have not been isolated, dediazoniation products being obtained\textsuperscript{31}.

A wide range of amino-1,2,4-triazoles have been diazotised with sodium nitrite in strong acids (hydrochloric, tetrafluoroboric, perchloric or nitric acids) to give the expected diazonium salts (chlorides, tetrafluoroborates, perchlorates or nitrates)\textsuperscript{32-40}. The stability of these diazonium salts appears to depend markedly on the nature of the anion (X) and on the position the diazonium group occupies. For example, 5-methyl-1,2,4-triazole-3-diazonium nitrate (45a) and 1,2,4-triazole-3-diazonium nitrate (45b) are quite stable in solution\textsuperscript{34}, and couple readily with \(\beta\)-naphthol, and can be isolated as gold chloride salts\textsuperscript{34}. However, the corresponding 1,2,4-triazole-3-diazonium chlorides (45c and d) are unstable in solution, even at 0\textdegree, and decompose rapidly to the chlorotriazoles\textsuperscript{34}. On the other hand, 3-phenyl-1,2,4-triazole-5-diazonium chloride (46a) is much more stable and can be isolated as a relatively stable solid\textsuperscript{33}. The observation that the 3-diazonium nitrates (45a and b) are more stable than the corresponding 3-diazonium chlorides (45c and d) is unusual. Generally, diazonium nitrates are the least stable diazonium salts and are usually only obtained in solution. Diazonium chlorides however, are normally relatively stable compounds, and can sometimes be isolated as stable solids. Diazonium fluoroborates are the most stable diazonium salts as is illustrated by 3-phenyl-1,2,4-triazole-5-diazonium fluoroborate (46b), which can be isolated as a high melting crystalline solid\textsuperscript{33}.
Diazotisation of 3-amino-1,2,4-thiadiazoles (47) with sodium nitrite in the presence of hydrochloric acid affords the corresponding diazonium salts (48)\textsuperscript{41-44}, which are reported to be unstable\textsuperscript{44}. However, the diazotisation of 5-amino-1,2,4-thiadiazoles (49) and 5-amino-1,3,4-thiadiazoles (50) using sodium nitrite affords diazonium salts (51) and (52) which are relatively stable in solution\textsuperscript{44}.
Scheme 6

a) H
b) Me
Diazotisation of 5-aminotetrazole (53a) with sodium nitrite in hydrochloric \(^9\) or nitric \(^45\) acids readily yields solutions of the explosively unstable diazonium salt (54) which on treatment with base affords a solution which probably contains the diazotetrazole (55) \(^4\). If however, the diazotisation of 2-methyl-5-aminotetrazole (53b) is carried out with sodium nitrite in dilute nitric acid, the diazoamino compound (56) is obtained \(^46\), thus paralleling the result observed with 3-amino-1H-pyrazoles (23) (see earlier). Shevlin \(^47\) has recently isolated tetrazole-5-diazonium chloride \([(54) X = Cl]\) as a crystalline solid by treating 5-aminotetrazole (53a) with isoamyl nitrite in tetrahydrofuran containing hydrogen chloride, although the salt is reported to be extremely unstable, even at low temperature \(^47\).

Five-membered heterocyclic amines are also readily converted into the corresponding diazonium salts using nitrosylsulphuric acid as the reagent. Thus, treatment of a range of 1-substituted 2-amino-4,5-diphenylimidazoles (57) with nitrosylsulphuric acid (prepared \textit{in situ}) yields the corresponding 2-diazonium salts (58) \(^48\). Although, 1-N-phenyl-
2-aminoimidazoles (59) when treated with nitrosylsulphuric acid in phosphoric acid yield imidazo[2,1-c]-1,2,4-triazines (61) by subsequent intramolecular coupling\textsuperscript{49}.

\[
\text{H}_2\text{N} - \text{N} - \text{H}
\]
\[
\text{Ph} - \text{N} - \text{N} - \text{R}
\]
\[
\text{R} \quad \text{R}
\]
\[
\text{H}_2\text{N} - \text{N} - \text{N}
\]
\[
\text{Ph} - \text{N} - \text{N} - \text{R}
\]
\[
\text{R} \quad \text{R}
\]
\[
\text{N} - \text{N} - \text{N}
\]
\[
\text{Ph} - \text{N} - \text{N} - \text{R}
\]
\[
\text{R} \quad \text{R}
\]

Diazotisation of the hydrochlorides of 2-aminoselenazole (62a) and 2-amino-5-phenylselenazole (62b) with nitrosyl-sulphuric acid in a mixture of concentrated sulphuric and phosphoric acids has been attempted\textsuperscript{50}, and although the products were not isolated, it is reported that the diazonium salts (63a and b) were formed in solution\textsuperscript{50}.

\[
\text{H} - \text{N} - \text{N} - \text{Se}
\]
\[
\text{NH}_2
\]
\[
\text{N} - \text{N} - \text{Se}
\]
\[
\text{N} - \text{N} - \text{HSO}_4^-
\]
Recently, Goerdeler and Roegler\textsuperscript{31} have reported that the diazonium salts [(44), $X = \text{BF}_4$], (64) and (65) can be isolated as stable crystalline solids from the diazotisation of 3-, 4-, and 5-aminoisothiazoles using nitrosyltetrafluoroborate in a mixture of acetic acid and propionic acid.
1.1.2 Preparation from Nitrosoamines

When aromatic primary amines are treated with nitrite ion in the presence of strong or weak acids, diazonium salts are usually formed. However, in the case of some aromatic primary amines the reaction appears to stop at the nitrosoamine stage and further treatment of the latter is necessary to obtain the diazonium salt.

The conditions of diazotisation are thought to play a vital role in determining whether the product is a nitrosoamine or a diazonium salt. Generally diazotisation in strong acids tends to favour the formation of a diazonium salt, and nitrosoamine formation predominates in dilute acid solution.

In theory, primary nitrosoamines can exist in two tautomeric forms [equation (i); (67) ⇌ (68)] and in addition the N-hydroxy-azo tautomer (68) can exhibit syn-anti isomerism [equation (ii); (68a) ⇌ (68b)]. Due to their instability nitrosamines derived from carbocyclic compounds have, to date, not been successfully isolated. However, extensive and controversial studies of the effect of pH on the equilibrium between the syn and anti isomers have been carried out in solution, and it now seems generally accepted that the syn and anti isomers are both present in solution, and that the diazonium salts arise from the syn N-hydroxy-azo form.
Scheme 7
The diazotisation of heterocyclic primary amines (71) is considered to occur by a similar mechanism (see scheme 7). However, the isolation of primary nitrosoamines in some instances suggests a stopping of the sequence at some point prior to the formation of the diazonium salt (75). A likely stopping point is at the syn N-hydroxy-azo isomer (73b), by stabilisation, through an intramolecular hydrogen bond, as shown in scheme 7. The presence of electron withdrawing substituents or rings could also stabilise the nitrosoamine, probably by resonance. However, strong acid, by protonating not only the nitrosoamine moiety, but also
the cyclic \(-\overset{1}{\mathrm{C}}=\overset{1}{\mathrm{N}}-\) lone pair, prevents stabilisation, and therefore favours diazonium salt formation, as was mentioned earlier.\(^9\) The presence of labile ring protons also appears to favour diazonium salt formation. This is borne out by the fact that very few heterocyclic primary amines with labile ring protons show a tendency to form nitrosoamines.\(^9\)

The isolation of stable primary nitrosoamines by the diazotisation of certain five membered heterocyclic amines provides strong evidence for the existence of such compounds as intermediates in the diazotisation process as generalised in scheme 1.

In the literature, there appears to be some confusion regarding the names of intermediates in the diazotisation mechanism. Butler\(^9\) and Zollinger\(^64\) both refer to compounds such as (73a) and (73b) as diazohydroxides. However, strictly speaking these species should be termed \(\text{N}-\text{hydroxyazo}\) derivatives. Whereas compounds of type (74) should be called diazohydroxides.

Diazotisation of 2-aminothiazoles (76) with sodium nitrite in dilute hydrochloric acid is reported to give unstable compounds, thought to be \(\text{N}-\text{hydroxy-azo}\) compounds (77)\(^28,65\), which however are readily converted, in the presence of hydrochloric acid, into the corresponding chlorothiazoles (78)\(^28\).
Wieland, in 1903, reported that the diazotisation of 3-phenyl-4-aminoisoxazole (79a) gave an unstable compound considered to be the N-hydroxy-azo derivative (80a). The diazotisation of 5-methyl-4-amino-3-phenylisoxazole (79b) has also been reported to afford the hydroxy-azo compound (80b). However, acidification of (80b), in an attempt to...
Scheme 8
obtain the diazonium salt resulted in the isolation of dediazoniation products \(^{67}\) (see later). When 5-aminoisothiazoles (81) are treated with sodium nitrite in dilute sulphuric acid, phosphoric acid, or formic acid, the stable nitrosoamines (82) are obtained\(^{31}\). Further treatment of these nitrosoamines with boron trifluoride etherate affords the stable 5-diazonium fluoroborates (64)\(^{31}\), whose direct formation has already been discussed (see page 12).

Diazotisation of \(N\)-substituted-3-amino-1,2,4-triazoles (83) with sodium nitrite in dilute hydrochloric acid leads to the formation of the stable primary nitrosoamines (84)\(^{68}\), although the attempted conversion of these compounds into the corresponding diazonium salts by treatment with acid has not been reported. The behaviour of \(N\)-substituted-3-amino-1,2,4-triazoles thus contrasts with that of the \(N\)-unsubstituted cases (see earlier) in that reaction stops at an earlier stage. However, the diaminotriazol (85), when diazotised with sodium nitrite in dilute hydrochloric acid, is reported to give the nitrosoamine (86)\(^{69,70}\).
Treatment of the nitrosoamine (86) with concentrated hydrochloric acid readily affords the diazonium salt (87)\textsuperscript{69,70}.

Diazotisation of N-substituted-3-amino-1,2,4-triazoles, when the N-substituent is itself reactive, does not lead to the isolation of primary nitrosoamines. Thus, when the N-substituent is an amino group, as in the triazole derivative (88), N-deamination occurs together with normal diazotisation of the C-amino group, and the product is a diazonium salt of the type (46)\textsuperscript{71,72} (see before).

\[
\begin{align*}
\text{(88)} & \quad \text{(46)}
\end{align*}
\]

Diazotisation of 5-amino-1,3,4-oxadiazoles (89) with sodium nitrite in dilute hydrochloric acid is also reported to afford nitrosoamines (90)\textsuperscript{73-75}. However treatment of the nitrosoamines with strong acid in an attempt to obtain the diazonium salts, results in the formation of de diazoniation products\textsuperscript{73-75} (see later).

\[
\begin{align*}
\text{(89)} & \quad \text{(90)}
\end{align*}
\]
Scheme 9
Diazotisation of 5-amino-1,2,4-thiadiazoles (49), 5-amino-1,3,4-thiadiazoles (50) and 5-amino-1,2,3-thiadiazoles (91) with sodium nitrite, in the presence of dilute sulphuric or hydrochloric acids, yields the stable primary nitrosoamines [(92)-(94)]\textsuperscript{73,76-78}. Subsequent treatment of the nitrosoamines (92) with concentrated acid readily affords the diazonium salts of the type (51)\textsuperscript{41}. However, similar treatment of the nitrosoamines (93) and (94) resulted in the formation of dediazonation products\textsuperscript{73,78}.

When the labile ring proton of an aminotetrazole is replaced by an aryl or alkyl substituent, diazotisation with sodium nitrite in the presence of dilute hydrochloric acid parallels that of N-substituted-amino-1,2,4-triazoles (see earlier) and primary nitrosoamines are obtained\textsuperscript{73,74-79}. Thus, diazotisation of 2-methyl-5-aminotetrazole (53b), for example, under these conditions leads to the formation of the nitrosoamine (95).

\[
\begin{align*}
\text{(53b)} & \quad \rightarrow \\
\text{(95)}
\end{align*}
\]
Scheme 10
1.1.3 Preparation by Direct Introduction of the Diazonium Group

Many aromatic diazonium compounds cannot be prepared by orthodox diazotisation procedures due to the instability of the starting amine. However, in such cases the required diazonium compound can often be prepared by the direct introduction of the diazonium group into a suitable non-aminated precursor. Tedder et al.22,80-82 have shown that a wide variety of aromatic nuclei (96) can be converted directly into diazonium derivatives (98) by preliminary nitrosation and subsequent further conversion of the nitroso intermediate (97) in situ. The mechanism of this reaction is outlined in scheme 1083. The initial step is the formation of the nitroso derivative (97), which is then converted, on further reaction with nitrous acid, to the radical (99). Reaction of the radical (99) with a further molecule of nitrous acid affords the nitroso-nitrite ester (100) which rearranges to the nitrate ester (101). Further rearrangement of (101) gives the diazonium nitrate (98).

Treatment of 2,3,5-triphenylpyrrole (102) with nitrous acid affords the stable 3-diazopyrrole (13b) obtained before5, which on treatment with strong acid gives the diazonium salt (12b)4. This method has also been applied to the preparation
of 2-diazopyrroles (104)\textsuperscript{84}, representing the first reported synthesis\textsuperscript{4}, and moreover in view of the instability of 2-aminopyrroles the only viable route to this class of compound\textsuperscript{4}. Thus the attempted reaction of 2-aminopyrroles with nitrous acid leads to their decomposition\textsuperscript{85}. The 2-diazopyrroles (104) prepared by the treatment of pyrroles (103) with
nitrous acid, are less stable and more reactive than the 3-diazopyrroles (13) prepared as discussed before (see p. 2)\textsuperscript{84}. Treatment of the diazo-compounds (104) with strong acid affords the stable diazonium salts (105)\textsuperscript{4}.

Direct introduction of a diazonium group has also been applied to the synthesis of diazopyrazoles\textsuperscript{86}. 5-Methylpyrazole (106a) and 5-phenylpyrazole (106b) for example, have been successfully converted into the corresponding diazonium salts (28a) and (28b), obtained previously by conventional diazotisation procedures\textsuperscript{22,86}.

\begin{center}
\begin{tikzpicture}

\node at (0,0) {\textbf{(106)}};
\node at (2,0) {\textbf{(28)}};

\node at (-0.5,-0.5) {$R$};
\node at (0.5,-0.5) {$H$};
\node at (1.5,-0.5) {$H$};

\node at (-1.5,-1) {$R$};
\node at (-0.5,-1) {$\text{Me}$};
\node at (0.5,-1) {$\text{Ph}$};

\node at (1.5,-1) {$\text{X}^-$};
\node at (2.5,-1) {$\text{N=}$};
\node at (3,-1) {$\text{N}$};
\node at (3.5,-1) {$\text{H}$};

\end{tikzpicture}
\end{center}

\textbf{1.2 Reactions of Five-membered Heterocyclic Diazo Compounds and Diazonium Salts}

The reactions of aromatic diazo compounds and diazonium salts can be divided into two main classes: those in which the nitrogen atoms are replaced during the reaction, and those where they are retained in the product.
1.2.1 Reactions Involving Loss of Nitrogen

(Dediazoniation Reactions)

Reactions of diazonium compounds involving loss of nitrogen are now collectively referred to as dediazoniation reactions. Processes of this type can occur by two fundamentally different pathways, either heterolytic or homolytic. In the case of arenediazonium ions, nitrogen can be replaced by a variety of nucleophiles, including nucleophilic solvents, and the nature of the nucleophile, the reaction solvent and the reaction conditions, markedly influence the outcome of dediazoniation. It is these dediazoniation reactions which make diazo compounds important as intermediates in the preparation of numerous substituted aromatic products. The scope and mechanism of dediazoniation reactions have been extensively investigated by Horner and Stöhr, De Tar and Kosuge, and in particular Burnett et al., who found that numerous arenediazonium ions decomposed in methanol under nitrogen to afford the corresponding hydrocarbon as the predominant product in a radical hydro-dediazoniation process [equation (iii)].

\[ \text{Ar}^+ \text{N}=\text{N} + \text{CH}_3\text{OH} \xrightarrow{N_2} \text{ArH} + \text{CH}_2\text{O} + \text{H}^+ + N_2 \]  

\[ \text{Ar}^+ \text{N}=\text{N} + \text{CH}_3\text{OH} \xrightarrow{O_2} \text{ArOCH}_3 + N_2 + \text{H}^+ \]
\[ \text{Scheme 11} \]
\[ \text{Scheme 12} \]
In the presence of oxygen however, methoxy-dediazoniation was found to take place, via a heterolytic pathway [equation (iv)], giving the ether as the major product. Similar observations were made by Zollinger and coworkers\textsuperscript{92} who showed that when dimethyl sulphoxide was used as solvent reaction of benzenediazonium ion (107) with nitrobenzene resulted in meta-phenylation to afford 3-nitrobiphenyl (108). However, reaction of the p-nitrobenzenediazonium salt (109) with nitrobenzene under the same conditions resulted in the formation of ortho and para substituted products (110). These results indicate an electrophilic aromatic substitution in the former case and a radical process in the latter\textsuperscript{92} (cf. scheme 11).

The two pathways followed in the dediazoniation reactions of aromatic substrates can be generalised as shown in scheme 12. In the case of heterolytic dediazoniations the diazonium ion (111) is able to reversibly form the cation (112)\textsuperscript{93,94} which then reacts further with a suitable nucleophile to afford the desired product (113). In homolytic dediazoniations the nucleophile is suggested to attack the \( \beta \)-nitrogen of the diazonium group affording an azo-intermediate (114) which fragments to a hydrocarbon radical (115). Further reaction of the latter with a nucleophilic reagent then affords the observed product [Scheme 12: \( (115) \rightarrow (116) \rightarrow (117) \)]\textsuperscript{62}.

As a prelude to the detailed discussion of dediazoniation reactions of five-membered heterocyclic diazonium compounds, dediazoniation reactions of aromatic diazonium salts in general will be briefly discussed.
Replacement of an arenediazonium group by hydroxyl occurs in most cases simply by warming an aqueous solution of an arenediazonium salt, the product being a phenol [equation (v)]. The intermediate in this type of reaction is an aryl cation which then reacts rapidly with water to give the observed product.

The uncatalysed reactions of arenediazonium salts with halogens to afford aryl halides have been known for some considerable time but, except in special cases\textsuperscript{95}, such displacements occur only in good yield in the case of iodine. The reaction of arenediazonium salts with iodine to give iodoarenes is considered to involve a diazonium tri-iodide intermediate [equation (vi)].
Scheme 13
Scheme 14

(121) \[ \text{ArN}_\equiv\text{N}^+ \text{X}^- \quad \xrightarrow{\text{Cu}^\text{I}X} \quad \left[ \text{ArN}_\equiv\text{N}.\text{Cu}^\text{I}X_2^- \right] \]

(122) \[ \text{ArX} \quad \text{Cu}^\text{I}X \quad \text{Ar}^+ \quad \text{Cu}^\text{II}X_2 \]

(123) \[ \text{ArX} \quad \text{Cu}^\text{I}X \quad \text{Ar}^+ \quad \text{Cu}^\text{II}X_2 \]

(124)
Buchmann and Hamilton report that chloride replacement in 2-ethoxyquinoline-4-diazonium chloride (119) [formed in situ from the amine (118)] to give 4-chloro-2-ethoxyquinoline (120) occurs in good yield, but generally catalysts are required to promote such diazonium displacements in arenediazonium salts.

Reactions which involve the use of copper halides as catalysts to promote halide substitution in arenediazonium salts are termed Sandmeyer reactions. Conversely such displacements in which copper metal is used as the catalyst are called Gattermann reactions, although it is now considered that there is very little mechanistic distinction between the two. The mechanism now generally accepted for the Sandmeyer reaction is outlined in scheme 14. Initially an intermediate complex (122) is formed between the diazonium salt (121) and the copper (I) halide. Subsequent breakdown of the complex, probably by a process involving aryl radicals, gives rise to the aryl halide, [scheme 14: (122) → (123) → (124)]. It is also well established that other nucleophiles can be introduced via Sandmayer or Gattermann type copper-catalysed reactions. Cyanide ion is readily introduced in the form of cuprous cyanide. Nitro groups can also be introduced by treatment of the diazonium salt with solutions of nitrites using copper or copper oxide as catalyst. This type of reaction is referred to as the nitro-Sandmeyer reaction but it appears to be confined to those diazonium salts containing electron attracting groups, such as 2,4,6-tribromobenzenediazonium sulphate.
Scheme 15

\[ \text{ArN}=\text{N} + \text{N}_3^- \rightarrow \text{ArN}^+\text{N}^- \text{N}^+\text{N}^- \]

\[ \text{ArN}=\text{N} = \text{N} + \text{N}_2 \]

\[ \text{Ar}-\text{N}^+\text{N}^- = \text{N} + \text{N}_2 \]

\[ \text{Ar}-\text{N} = \text{N} + \text{N}_2 \]

\[ \text{ArN}=\text{N}^- \]
Although the Sandmeyer or Gattermann reactions are important for the formation of aryl chlorides and bromides, they are not suitable for the preparation of aryl fluorides. However, Balz and Schiemann have shown that the thermal decomposition of arenediazonium fluoroborates gives aryl fluorides (127) in excellent yield. This process (the Baltz-Schiemann reaction) involves the initial formation of stable arenediazonium fluoroborate salts (126).

\[
\begin{align*}
\text{ArNH}_2 & \quad \rightarrow \quad \text{ArN}=N\text{BF}_4^- \\
(125) & \quad \rightarrow \quad (126) \\
\Delta & \quad \rightarrow \quad \text{ArF} + \text{BF}_3 + \text{N}_2 \\
(127)
\end{align*}
\]

Treatment of arenediazonium salt solutions with sodium azide results in the formation of aryl azides (scheme 15). The initial step in such reactions is believed to be the formation of a diazo-azide intermediate (129) which is suggested to cyclise to give the aryl pentazole (130) before breakdown to the aryl azide (131). It has been shown by isotopic labelling that only one of the nitrogen atoms in the attacking azide ion is incorporated into the azide product, the other two coming from the diazonium group.

When an arenediazonium salt solution is stirred with a liquid aromatic hydrocarbon in the presence of a slight excess of base, nitrogen is eliminated and a biaryl product results. This type of diazonium replacement is termed the
Gomberg-Bachmann reaction. The diazonium salt employed in such reactions appears to influence the reaction mechanism as described earlier (page 24). Thus, when unsymmetrical salts are used, a mixture of isomeric products is obtained, whereas, symmetrical salts lead to the formation of a single product. The reaction is however useful for the preparation of biaryls not readily accessible by other routes.

Heating a solution of an arenediazonium salt in methanol or ethanol usually results in the formation of two products, the hydrocarbon and the ether, but as mentioned before [page 23, equation (iii) and (iv)] the reaction conditions appear to play a vital role in determining which product predominates. The reductive deamination of diazonium salts in alcoholic solution is a well known process. Cowdrey and Davies have suggested that reactions of this type involve the oxidation of the alcohol as exemplified by equation (vii).

\[
\text{ArN=N} + \text{C}_2\text{H}_5\text{OH} \rightarrow \text{ArH} + \text{CH}_3\text{CHO} + \text{N}_2 + \text{H}^+ \quad (\text{vii})
\]

The reaction of diazonium salts with certain reducing agents, (particularly hypophosphorous acid) results in the displacement of the diazonium group by hydrogen. The use of copper, copper oxide, alkaline formaldehyde and sodium stannite as reducing agents all give similar results.
It is suggested that in some cases such reactions involve the initial formation of an unstable aryldi-imine which rapidly loses nitrogen to give the hydrocarbon product. In the case of hypophosphorous acid however, an aryldi-imine is considered to be the intermediate.

\[
\begin{align*}
\text{ArN} = \text{N} \quad \text{X} & \rightarrow \text{ArN} = \text{NH} \\
& \rightarrow \text{ArH} + \text{N}_2
\end{align*}
\]

Arenediazonium salts can be decomposed photochemically with the loss of nitrogen to afford products the nature of which depends on the particular conditions employed. For example, the irradiation of arenediazonium salts in aqueous solution results in the formation of phenols and nitrogen, thus paralleling the action of heat, and suggesting an aryl cation mechanism (see before, page 25). In alcoholic solution the photochemical decomposition of arenediazonium salts results in the replacement of the diazoniurn group by hydrogen, probably via a radical intermediate, also paralleling the earlier observation of the thermal decomposition of diazonium salts in methanol, (page 23).

The pyrazolediazonium salts are reported to undergo normal dediazioniation reactions. For example replacement of the diazoniurn group by hydrogen occurs readily when such salts are treated in solution with copper powder or copper-potassium hydroxide, the products being the deaminated pyrroles.
Scheme 16

(135) \[ \text{R} \text{O}^+ \text{N} \equiv \text{N} \text{BF}_4^- \] \[ \longrightarrow \]

(137) \[ \text{R} \text{O} \text{H} \]

(136)
\[ \text{Scheme 17} \]
Scheme 18
Replacement of nitrogen by hydrogen or cyanide could not be achieved with aqueous solutions of furan-3-diazonium salts\textsuperscript{10,112}. However, the 2-diazonium fluoroborate (135) underwent hydrolysis to the corresponding phenol (136), and displacement by hydrogen in the presence of methanol and copper to give the furan (137)\textsuperscript{113} (scheme 16). Recently Paulmier\textsuperscript{13,14} has reported the displacement of the diazonium group from 2-substituted thiophen-3-diazonium salts (138a) and 2-substituted selenophen-3-diazonium salts (138b) by azide ion to afford the corresponding azide derivatives (139a) and (139b). However, in the case of the 2-nitrothiophen-3-diazonium salts and the 2-nitro-selenophen-3-diazonium salts, cyclisation can occur to give the corresponding N-oxides (140a) and (140b)\textsuperscript{13,14}.

Pyrazole-3-diazonium salts (24) undergo normal dediazoniation reactions\textsuperscript{114-116} (scheme 18). The Sandmeyer reaction yields 3-halogenopyrazoles (141) and heating the pyrazole-3-diazonium fluoroborates with alkali fluorides affords the corresponding 3-fluoropyrazoles (142)\textsuperscript{114}. It has been reported\textsuperscript{117} recently that when 4-diazo-3,5-dimethylpyrazole (143) is heated in benzene, 4-phenyl-3,5-
Scheme 19
dimethylpyrazole (144), 3,5-dimethylpyrazole (145) and biphenyl are produced in a free radical process (the Gomberg-Bachmann reaction). The photolytic dediazoniation reactions of diazopyrazoles in various solvents have also been reported. Thus, photolysis of 4-diazo-3-benzoyl-5-phenylpyrazole (146) and 3-diazo-5-benzoyl-4-phenylpyrazole (147) in benzene results in the evolution of nitrogen, and in both cases, the product is 3-benzoyl-4,5-diphenylpyrazole (148). More recently, 3,4-disubstituted-5-
Scheme 20
\[
\text{Scheme 21}
\]
diazopyrazoles have been shown to form azirines and insertion products when subjected to photolytic dediazoniation. For example, thermolysis or photolysis of 3-diazo-4-methyl-5-phenylpyrazole (149) affords 2-cyano-2-methyl-3-phenyl-2H-azirine (152). However, photolysis of (149) in cyclohexane leads to insertion, and 3-cyclohexyl-4-methyl-5-phenylpyrazole (154) is the product.

Imidazolediazonium salts are also reported to undergo dediazoniation reactions. For example, imidazole-2-diazonium fluoroborates react with sodium nitrite in the presence of copper powder (the nitro-Sandmeyer reaction) to afford 2-nitroimidazoles, some of which are useful pharmaceutical agents. The diazodicyanoimidazole (31) is reported to undergo the Gomberg-Bachmann reaction when heated with benzene, the product being the 2-phenylimidazole (155) (scheme 21). Similarly, 2-cyclohexyl-4,5-dicyanoimidazole (156) is obtained (scheme 21) by the thermolysis of (31) in refluxing cyclohexane. Pyrolysis of the diazo-imidazole (31) in halobenzenes however, affords a mixture of products [(157)-(159)] (scheme 21) in varying yields. The ylid (158a) is not obtained, and (158b) easily forms the haloimidazole (159b) when heated. However (158c) and (158d) are stable, and (158d) is the primary product formed on pyrolysis of the imidazole (31) in iodobenzene.

Irradiation (scheme 22) of the imidazole-2-diazonium tetrafluoroborates (160) and the imidazole-4-diazonium tetrafluoroborates (161) in tetrafluoroboric acid solution is
Scheme 22

R

a) CH₂CH₂NH₂

b) CH₂CHCOOH

\[ \text{BF}_4^- \text{N}^+ \text{N} \equiv \text{N} \text{BF}_4^- \quad \rightarrow \quad \text{F} \text{N} \equiv \text{N} \text{BF}_4^- \]

\[ \text{BF}_4^- \text{N}^+ \text{N} \equiv \text{N} \equiv \text{N} \quad \rightarrow \quad \text{F} \text{N} \equiv \text{N} \equiv \text{N} \]

\[ \text{CH}_2 \text{CH}_2 \text{NH}_2 \]

\[ \text{CH}_2 \text{CHCOOH} \]

\[ \text{NH}_2 \]
Scheme 23
Scheme 24
reported to yield the corresponding 2- and 4-
fluoroimidazole derivatives (162) and (163), the first
fluoroimidazoles to be prepared. These, in turn, are
useful synthetic precursors of fluorohistamine and fluoro-
histidine derivatives (163a and 163b), which are
important pharmacologically. Photochemical dediazoniation
reactions provide the only simple route to fluoroimidazole
derivatives. The more orthodox thermal decomposition
(Balz-Schiemann reaction) of imidazole-diazonium fluoroborates
results either in no reaction or in the formation of intract-
able tars.

Photochemical dediazoniation (scheme 23) of the diazo-
imidazole (165) (which was obtained from the diazonium
fluoroborate (164) by treatment with mild base in
ethanol and benzene affords the phenylimidazole (166) and
the imidazole (167). Attempted synthesis of the 4-
fluoroimidazole-5-carboxamide (169) from the corresponding
diazocompound (33) was thwarted by the cyclisation of (33)
to the 2-azohypoxanthine (34) (see earlier, page 4) which
was more rapid than photodediazoniation. However, the
fluoroimidazole (169) was eventually obtained via the ester
(165), which was converted back to the amide after phote-
dediazoniation.

Benzoxazole-2-diazonium salts of the type (38) are
reported to undergo orthodox Sandmeyer reactions in
solution. Benzoxazole-2-diazonium chloride (38) for
example readily affords the chloro derivative (170) on
treatment with concentrated hydrochloric acid. Normal
Scheme 25

(40) → (171)
Dediazoniation reactions of thiazolediazonium salts also occur\textsuperscript{125} in concentrated hydrochloric acid. Thus, the diazonium salt (40) reacts rapidly with hydrochloric acid to give the 2-chlorothiazole (171)\textsuperscript{28,126}. A wide range of dediazoniation reactions have been accomplished with thiazole-2-diazonium tetrafluoroborates, allowing the introduction of substituents such as Br, I, F and N\textsubscript{3} at the 2-position\textsuperscript{127,128}. However, introduction of the azido substituent can lead, by cyclisation of the azidothiazole (172), to thiazolo[3,2-d]tetrazoles (173)\textsuperscript{127}. 

\[
\begin{align*}
\text{(38)} & \quad \rightarrow \quad \text{(170)} \\
\text{(172)} & \quad \rightarrow \quad \text{(173)}
\end{align*}
\]
The nitro-Sandmeyer reaction of thiazole-2-diazonium salts provides a general method for the synthesis of 2-nitrothiazole derivatives of potential pharmaceutical value. Thus, treatment of solutions of the thiazole-2-diazonium salts (174) with powdered copper affords the corresponding 2-nitrothiazoles (175) accompanied, in some cases, by the products of hydrodediazoniation, namely deaminated thiazoles (176). Attempted Sandmeyer reactions with selenazole-2-diazonium salts have been largely unsuccessful. Thus, treatment of aqueous solutions of the selenazole-2-diazonium salts (63a) and (63b) with cuprous chloride resulted in the formation of decomposition products rather than the desired 2-chloroselenazoles (177a) and (177b). Similarly, attempts to obtain the free
selenazoles by hydrodediazoniation of the diazonium salts (63a) and (63b) was also unsuccessful\textsuperscript{50}.

The preparation of a solution of the isoxazole-5-diazonium salt (42) in hydrochloric acid is followed by its rapid reaction with chloride ion to afford the corresponding 5-chloro derivative (43)\textsuperscript{133}. In contrast, under similar conditions, the isoxazole-5-diazonium salts (178) undergo degradation to yield the alkene (179)\textsuperscript{134}. 
Scheme 26
It has been reported\textsuperscript{67} that treatment, in situ, of the diazonium products (80b) of 4-amino-5-methyl-3-phenylisoxazole (79b) with concentrated hydrochloric acid gives the corresponding 4-chloroderivative (180), or if heated directly, the 4-hydroxyisoxazole (181). More recently,\textsuperscript{135} dediazoniation reactions of 3,4-dimethylisoxazole-5-diazonium salts (178) have been reported. For example substituents such as H, I and alkyl have been introduced at the 5-position to afford the corresponding substituted isoxazoles.
The isothiazole diazonium fluoroborates [(44), (64) and (65)] are also reported to undergo dediazonation reactions. For example, isothiazole-4-diazonium fluoroborate (65) undergoes the normal Sandmeyer reaction with cuprous chloride in the presence of hydrochloric acid to afford 4-chloroisothiazole (183) in good yield. Similarly, other isothiazole diazonium salts undergo dediazonation reactions, to afford the corresponding substituted isothiazoles.

Dediazoniation reactions are readily undergone by a wide range of 5-substituted-1,2,4-triazole-3-diazonium salts. Thus, azido and hydro dediazoniations for example both occur readily to afford the expected 3-azido-1,2,4-triazoles (184a) and deaminated 1,2,4-triazoles (184b) respectively. Similarly, 1,2,4-triazole-5-diazonium salts undergo smooth nitro-dediazoniations in the presence of sodium nitrite to afford 5-nitro-1,2,4-triazoles (186) in good yield (scheme 27).
Scheme 28
Scheme 27
R = aryl

Scheme 29
The diazonium salts (188) produced (scheme 28) by diazotisation of 4-\(\text{N}\)-substituted-3-amino-1,2,4-triazoles (187) in concentrated hydrochloric acid are rapidly converted into 3-chloro-1,2,4-triazoles (189)\(^68\). However, the course of such dediazoniation reactions appears to be markedly dependent on the \(\text{pH}\) of the acidic medium\(^68\).

Heating solutions of the diazonium salts (190) derived from 5-amino-2-aryl-1,3,4-oxadiazoles (89) in the presence of benzene results in the formation of the corresponding diaryloxadiazoles (191) (Gomberg-Bachmann reaction)\(^73\).

1,2,4-Thiadiazole-5-diazonium salts (51) also readily undergo dediazoniation reactions. Substitution of the diazonium group by a variety of substituents (\(Y\)) affords the corresponding 5-substituted-1,2,4-thiadiazoles (192)\(^27,41,76\).
1,2,4-Thiadiazole-3-diazonium salts have also been reported to readily undergo dediazoniation reactions. For example, heating the diazonium fluoroborates (193) results in their smooth conversion into the 3-fluoro-1,2,4-thiadiazoles (194). However, Sandmeyer reactions of the diazonium salts of type (193) are best carried out \textit{in situ}. 1,3,4-Thiadiazole-5-diazonium salts (52) likewise undergo dediazoniation reactions, affording the corresponding 5-substituted products (195).
Scheme 30

*(R = aryl)*
Tetrazole-5-diazonium chloride (196) undergoes substitution by hydrogen in the presence of hypophosphorous acid to afford the tetrazole (197)\textsuperscript{139}. Controlled thermolysis of the diazonium salt (196) is reported to afford atomic carbon\textsuperscript{47,140}. However, when a solution of the diazonium salt (196) is heated in the presence of aromatic hydrocarbons, a Gomberg-Bachmann reaction occurs, affording 5-aryltetrazoles (198)\textsuperscript{73}.

1.2.2 Reactions Involving Retention of Nitrogen

(Reactions Involving Retention of Nitrogen)

The second general class of reactions in which diazonium salts take part are those where the two nitrogen atoms are retained in the product. There are two important reactions of this type which are undergone by the majority of aromatic diazonium salts, namely reduction to hydrazine derivatives, and coupling with electron rich aromatic rings such as phenols and arylamines. This latter type of process is extremely important in the chemical dyestuffs industry since it provides the principal route to azo-dyes.
The arenediazonium group can be reduced to a mono-substituted hydrazine using a variety of reducing agents, under different conditions (equation viii). Commonly potassium or sodium sulphite is the reducing agent of choice, although in some cases zinc dust in combination with acetic acid, or sodium hydrogen sulphite are better reagents. Sulphur dioxide or triphenylphosphine have also been employed as reducing agents for the reduction of arenediazonium salts to aryl hydrazines.\textsuperscript{141,142}

In arenediazonium coupling reactions the diazonium cation $\text{[ArN=N]}$ behaves as a weak electrophilic reagent, being able to attack nucleii having enhanced nucleophilic reactivity. Primary and secondary aliphatic amines couple with arenediazonium salts through the nitrogen of the amine, affording a diazoamino compound (199), although in some instances the process can occur twice, and a bisdiazoamino compound (200) results.

\[
\text{ArN=N + RNH}_2 \rightarrow \text{ArN=NNNH}_2 \quad \text{(vi)}
\]

\[
\text{ArN=N + RNH}_2 \rightarrow \text{ArN=N=NNHR} \quad \text{(199)}
\]

\[
\text{R}
\]

\[
\text{ArN=N-N-N=NR} \quad \text{(200)}
\]
Primary and secondary aromatic amines likewise couple with arenediazonium salts in weak acid solution to form the corresponding diazoamino compounds, although depending on the conditions coupling with the aromatic nucleus can occur to give a C-azo compound. Where coupling with the aromatic nucleus occurs, the azo group enters para or ortho to the amino group, although the former usually predominates. Tertiary arylamines for example couple readily to form predominantly p-azo compounds (N-azo compounds cannot be formed in this case).

Phenols and phenolic ethers also couple with arene-diazonium salts to form either O-azo compounds or p-hydroxyazo compounds, the latter being the usual products.

1,3-Diketones and α-ketonic esters couple very readily with arenediazonium salts to yield hydrazones (201) (the so-called Japp-Klingemann reaction)\textsuperscript{143,144}. In some cases, reactive hydrocarbons may couple with diazonium salts, but usually this only occurs when the diazonium compound itself is highly reactive.

\[
\text{ArN}^+\text{N}^\equiv\text{N} + \text{CH}_2(\text{COR})_2 \rightarrow \text{ArN}=\text{N} \overset{\text{H}}{\text{C}}(\text{COR})_2
\]

(201)
Scheme 31
Scheme 32
1H-Pyrrole-3-diazonium salts are too weakly reactive to couple with phenols. In aqueous alkali, which is necessary to generate the phenolate anions required for coupling, the 1H-pyrrole-3-diazonium salts of type (12) form the insoluble diazopyrroles (13) which will not react with phenolate anions. However, coupling does occur when the diazo compounds (13) are heated with β-naphthol, the azo compounds (202) being the products formed. There are however conflicting and contradictory reports of the coupling ability of N-phenyl-pyrrole-3-diazonium salts (15). The most recent report indicates that these salts do undergo normal coupling reactions, to give azo derivatives (203). 2-Diazoypyroles (104), which are more reactive than their 3-diazo counterparts, also readily form the corresponding azo compounds (204) with β-naphthol (scheme 32).

Furan-3-diazonium salts of type (17) couple readily with β-naphthol to afford azo compounds (205). Thiophendiazonium salts also undergo coupling reactions with β-naphthol, leading to the formation of many azo dyes in the thiophen series. Thiophen-2-diazonium salts (206) for example react with β-naphthol to afford the azo compound (207).
Scheme 33
Scheme 34
Pyrazole-3-diazonium salts, pyrazole-4-diazonium salts and the corresponding diazo compounds are reported to undergo normal coupling reactions. For example, coupling of the pyrazole-3-diazonium salts (24) [or the corresponding diazo compounds (25)] with β-naphthol yields pyrazolotriazines (209) by an intramolecular condensation reaction (scheme 33). β-Keto acids or esters also couple with pyrazolediazonium salts giving products which cyclise spontaneously to pyrazolotriazines of type (211). Pyrazole-4-diazonium salts (28) [and the 4-diazopyrazoles (29)] have been coupled with many active methylene compounds, affording the corresponding hydrazones (212) (scheme 35).

Imidazolediazonium salts and diazo compounds couple readily with phenols and amines. 5-Diazoimidazole-4-carboxamide (33) for example has been reported to react readily with active methylene compounds of the type (213) to afford the corresponding hydrazones (214). More recently, 5-diazoimidazole-4-carboxamide (33) has also been reported to couple with hydrazine and certain thio compounds.
Substituted thiazolediazonium salts are reported to undergo normal coupling reactions with aromatic hydrocarbons and phenols\(^\text{27}\). For example, the thiazole-2-diazonium salts (174) react readily with trimethylbenzene to afford azo compounds of the type (215)\(^\text{27}\).

Diazonium salts obtained by the \textit{in situ} diazotisation of aminoselenazoles (62), when treated with \(\beta\)-naphthol give rise to strongly coloured solutions. Although the products of these reactions were not isolated, the highly coloured solutions suggest the presence of the corresponding azo compounds (216)\(^\text{50}\).
A wide range of phenols and aromatic hydrocarbons have been reported to react with 3,4-dimethylisoxazole-5-diazonium salts (178), in the presence of dilute alkali, to afford the azo compounds (217)\textsuperscript{151}. Isothiazole diazonium fluoroborates
\[(221) \rightarrow (222) \rightarrow (223)\]

*Scheme 36*
also readily undergo coupling reactions. For example, the diazonium fluoroborates (64) react readily with β-naphthol to yield the azo compounds (218). Other isothiazole diazonium salts, generated in solution, are also reported to undergo normal coupling reactions with phenols to afford similar azo compounds.

Many 1H-1,2,4-triazole diazonium salts have been coupled with phenols and amines to form the corresponding azo compounds in high yield. For example, the triazole diazonium salt (185) couples readily with N,N-dialkylanilines (219) giving the azo compounds (220). 1H-1,2,4-Triazole-5-diazonium nitrates (221) have recently been shown to couple with a wide variety of active methylene compounds. The hydrazones (222) so formed can then be cyclised to 1,2,4-triazolotriazines (223) (scheme 36).
Scheme 37
Scheme 38
Nitrosoamines (84) obtained by the diazotisation of N-substituted amino-1,2,4-triazoles (83) are readily reduced to hydrazines of type (224) by zinc dust\(^68\). The nitrosoamines (83) are also reported to couple with N,N-dimethylaniline to afford the azo compounds (225)\(^68\).

Nitrosoamines (92) obtained by the diazotisation of 5-amino-1,2,4-thiadiazoles (49) have been shown to form the corresponding azo compounds (226) with β-naphthol\(^76\). Primary nitrosoamines (94) obtained from 5-amino-1,2,3-thiadiazoles (91) also exhibit diazo coupling reactions with β-naphthol to afford the corresponding azo compounds (227)\(^78\).

Reduction of the tetrazolediazonium salt (54) or the nitrosoamine (229) with stannous chloride readily yields the hydrazine (228)\(^73,155\). More recently the coupling of tetrazole-5-diazonium salts (54) with phenols and other aromatic systems have been reported, to afford the corresponding azo derivatives of type (230)\(^152\).
The synthesis of new 1,2,3-triazoles and their diazonium salts, and the reactions of these and related 1,2,3-triazole-diazonium salts constitute the subject material of the following thesis.
Chapter 2

The Synthesis and Carbonyl Condensation
Reactions of 5-Amino-1H-1,2,3-triazoles
and 1,5-Diamino-1,2,3-triazoles
$\text{Me}$ $\text{N} = \text{N}$ $\text{Me}$

$\text{Me}$ $\text{N} = \text{N}$ $\text{Me}$

(231) $\rightleftharpoons$ (232)

$\text{Me}$ $\text{N} = \text{N}$ $\text{Me}$

(233)

$R^1$

a) Ph

b) CONH$_2$

Scheme 39
2.1 The Synthesis and β-Dicarbonyl Condensation Reactions of 5-Amino-1H-1,2,3-triazoles

2.1.1 Introduction

The 1,2,3-triazolo [1,5-a]pyrimidine ring system (231) has recently been shown to undergo the Dimroth type rearrangement, [(231) ⇌ (232) ⇌ (233)], involving the as yet unobserved diazo structure (232) as an intermediate or transition state. Thus, variable temperature $^1$H n.m.r. studies with the 1,2,3-triazolo [1,5-a]pyrimidines (231a and 231b) have shown that on heating, the two discrete methyl signals present in their $^1$H n.m.r. spectra collapse in each case to a single peak. These results may be interpreted in two possible ways. Either the structures (231) and (233) are in rapid equilibrium at elevated temperatures thus resulting in the averaging of the methyl signals on the n.m.r. time scale, or the bicyclic structure (231) is converted, at elevated temperature, entirely into the open-chain diazo form (232) in which the methyl groups are equivalent. In either case the existence of diazoalkylideneimine-1,2,3-triazole tautomerism [(231) ⇌ (232)] is implied. Moreover, it was also found that the triazolopyrimidine-3-carboxamide (231b) underwent the described spectral changes at lower temperature than the 3-phenyltriazolopyrimidine (231a). This observation is consistent with the stabilising effect on the diazo tautomer (232), compared with the fused structure (231), of an electron withdrawing substituent at C-3 in the 1,2,3-triazole ring. A similar stabilising effect on the diazo tautomer (232) should be exerted by electron withdrawing substituents.
Scheme 40
in the pyrimidine ring. Consequently, by a suitable choice of electron withdrawing substituents in the triazole and pyrimidine moieties of a 1,2,3-triazolo [1,5-a]pyrimidine, it should be possible to enhance the stability of the diazo tautomer (232) to the extent that it becomes of comparable or even greater stability than the ring closed form (231) at room temperature. It was therefore decided to synthesise a series of suitable 1,2,3-triazolo [1,5-a]pyrimidines with a view to studying the temperature variance of their $^1$H n.m.r. spectra and hopefully to observe, for the first time, stable diazo tautomers of the type (232).

To date, the methods used to synthesise 1,2,3-triazolo [1,5-a]pyrimidine derivatives of the type (236) have been based on acid or base catalysed condensation reactions of 1H-amino-1,2,3-triazoles (234) with $\delta$-dicarbonyl compounds (235) (scheme 40). Reactions of this type are analogous to the syntheses of 1,2,4-triazolo[1,5-a]pyrimidines (238) from amino-1,2,4-triazoles (237) (scheme 40). However, the synthesis of 1,2,4-triazolo[1,5-a]pyrimidines containing the desired electron withdrawing substituents is more straightforward than that of their 1,2,3-triazolo counterparts. As outlined above, a general synthetic approach to 1,2,3- and 1,2,4-triazolo [1,5-a]pyrimidines is to utilise the bifunctionality of amino-NH-1,2,3- and 1,2,4-triazoles. However, it is more difficult to obtain amino-NH-1,2,3-triazoles containing electron withdrawing substituents, than to obtain the analogous amino-NH-1,2,4-triazoles. The difficulty in synthesising 1,2,3-triazolo[1,5-a]pyrimidines of the type (236) with the desired
Scheme 41
Scheme 42
substituents at C-3 is thus closely related to problems associated with the preparation of amino-1H-1,2,3-triazoles.

Most of the important methods for the formation of NH-1,2,3-triazoles involve the use of azides. Hydrazoic acid and sodium azide add readily to acetylenes of type (239) containing electron withdrawing groups, probably by nucleophilic addition to the triple bond, followed by 1,5-dipolar cyclisation to afford the observed NH-1,2,3-triazole (241) product (scheme 41). Similarly, olefins (242) containing an electron withdrawing substituent (X) form NH-1,2,3-triazoles when reacted with organic azides or sodium azide, the group (X) being lost in the course of reaction. Phosphonium salts of type (243) also react with sodium azide in aqueous solution to afford the NH-1,2,3-triazoles (241) in high yield.

Debenzylation of 1-benzyl-1,2,3-triazoles (which are readily available by the condensation of benzyl azide with active methylene compounds), either oxidatively or under reducing conditions, is a well established method for the synthesis of NH-1,2,3-triazoles.

Ring closure (scheme 42) of α-diazo-imines (245) followed by spontaneous deacylation of the intermediate N-acyl-1,2,3-triazole (246) produced is also a useful method for the preparation of NH-1,2,3-triazoles. The requisite α-diazo-imines (245) are usually prepared in situ by the condensation of α-diazoketones (244) with amines, or by diazo transfer reactions (see later) of suitable active methylene compounds.
The reactions described above are all well established methods for the preparation of 1H-1,2,3-triazoles but are not readily applicable to the synthesis of 5-amino-1H-1,2,3-triazoles containing electron withdrawing 4-substituents required in the present studies. For example, the application of the azide-acetylene method (see before) would require synthetically unavailable amino-acetylenes substituted by electron withdrawing groups \((X = \text{acyl}, \text{nitro}, \text{benzene-sulphonyl})\) of the type \((247)\). Likewise, although the

\[
X-C≡C-NH_2
\]

\((247)\)

preparation of 5-amino-1-benzyl-1,2,3-triazoles containing electron withdrawing C-4 substituents would present no particular synthetic problem, the final reductive debenzylation to the \(NH\)-1,2,3-triazole would tend to result in undesirable side reactions of the C-4 substituent.

In the present section, studies of a new route to 5-amino-1H-1,2,3-triazoles, as well as further examples of the synthesis and thermal Dimroth rearrangement of 1,2,3-triazolo[1,5-a]pyrimidines, are described.

2.1.2 The Synthesis of 4-Substituted 5-Amino-1H-1,2,3-triazoles

Previous studies in this department\(^{160}\) have shown that the presence of the electron withdrawing carboxamide substituent at C-3 in the 1,2,3-triazolo[1,5-a]pyrimidines \((231b)\) lowers the activation energy for the Dimroth type rearrangement
Scheme 43

R

a) $\text{SO}_2\text{Ph}$
b) $\text{COPh}$
c) $\text{CN}$
Scheme 44
Scheme 45
In relation to this observation it was of interest to synthesise 1,2,3-triazolo[1,5-a]pyrimidines bearing other electron withdrawing groups at C-3 in the hope of demonstrating a decrease in activation energy for the Dimroth process with increasing electron withdrawal in the C-3 substituent. To this end it was necessary to synthesise the 5-amino-1H-1,2,3-triazoles (249a-c) as suitable precursors for the 1,2,3-triazolo[1,5-a]pyrimidines of type (236) required for such an investigation.

The synthesis of 5-amino-4-cyano-1H-1,2,3-triazole (249c) has been reported by various workers, and was prepared in the present studies by debenzylation of the readily available 1-benzyl-4-cyano-1,2,3-triazole (248c) using sodium in liquid ammonia. 5-Amino-4-benzene-sulphonyl-1H-1,2,3-triazole (249a) and 5-amino-4-benzoyl-1H-1,2,3-triazole (249b) on the other hand were unknown and as mentioned earlier (cf. page 54) cannot be prepared by debenzylation of the corresponding 1-benzyltriazoles (248a and b) due to sensitivity of the C-4 substituent (benzenesulphonyl or benzoyl) in (248) to reduction. Alternative syntheses of (248a and b) therefore had to be sought.

The extensive investigations of Regitz have shown that toluene-p-sulphonyl azide reacts in the presence of base with certain active methylene compounds of the type (250) to afford the corresponding diazo compounds (253) (scheme 44). When the active methylene component also incorporates an imine function [e.g. (254)] ring closure of the initially formed diazo intermediate (255) occurs to afford a 1,2,3-triazole derivative (256) (scheme 45).
\[ \text{R-CH}_2\text{C} \equiv \text{NH} \xrightarrow{\text{TSO}_2\text{N}_3} \text{N} \equiv \text{N} \equiv \text{R} \]

\( R \)

a) \( \text{SO}_2\text{Ph} \)

b) \( \text{COPh} \)

Scheme 46
Scheme 47

(249)  \[
\text{NH}_2 \quad \text{NH}_2
\]

(260)  \[
\text{NH}_2 \quad \text{NH}_2
\]

\[\text{R} \quad \text{SO}_2 \text{Ph}
\]

\[\text{R} \quad \text{COPh}
\]
Processes of the type shown in schemes 44 and 45 are termed diazo-transfer reactions, since the toluene-p-sulphonyl azide transfers a diazo group to the active methylene compound. The strength of the base needed to catalyse such reactions is dependant on the acidity of the methylene protons. Application of the diazo-transfer process to the acetamidines (257a and b) represents a potential route to the triazoles (249a and b) required for study.

Nitriles of type (258) are known to add ethanol in the presence of hydrogen chloride to afford imidate hydrochlorides (259) readily convertible by reaction with ammonia into the corresponding amidine hydrochlorides (260). Thus, treatment of benzenesulphonylacetonitrile (258a) with ethanolic hydrogen chloride afforded the known ethyl benzenesulphonylacetimidate hydrochloride (259a) in good yield. The i.r., $^1$H n.m.r. and mass spectral data for the compound (259a) were all consistent with the acetimidate hydrochloride structure, but correct analytical data could not be obtained for this compound. Shaking the acetimidate hydrochloride (259a) with ammonia gas at room temperature readily afforded benzenesulphonylacetamidine hydrochloride (260a) in good yield. The structure of the product (260a) is readily supported by combustion analysis and i.r., $^1$H n.m.r. and mass spectral data.

When a cooled ethanolic suspension of the acetamidine hydrochloride (260a) was treated with toluene-p-sulphonyl azide in the presence of ethanolic sodium ethoxide, 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a) was obtained in moderate yield. Attempts to synthesis the triazole (249a) from the acetamidine hydrochloride (260a) using triethylamine
\[
\begin{align*}
\text{MeCO-} & \text{N} = \text{N} \quad \text{(261)} \\
\text{62.79} & \\
\text{MeCO-} & \text{N} = \text{N} \\
\text{62.87} & \\
\text{MeCO-} & \text{N} = \text{N} \\
\text{62.77} & \\
\end{align*}
\]
as the base resulted in only a poor recovery of the desired product (249a). Similar attempts using piperidine as the base yielded toluene-p-sulphonamide as the only identifiable product.

In accord with the assigned structure, the benzenesulphonyltriazole (249a) showed acidic properties. It dissolved readily in dilute aqueous alkali and was recovered from the solution unchanged on acidification. Moreover, in accord with its NH-1,2,3-triazole structure (249a) it was converted in acetic anhydride under mild conditions into an N-acetyl product showing characteristically high i.r. carbonyl absorption. However, the presence of two sharp methyl singlets at δ 2.70 and δ 2.63 in the ratio of roughly 3:1 indicated the presence of a mixture of two monoacetylated species. The possibility that the product was a diacetyl derivative can be readily excluded on the basis of analytical and mass spectral data. It is reported that the 1H n.m.r. signals due to the methyl protons of the N(1)-acetyl groups in the compounds (261) and (262) resonate further downfield than signals due to the acetyl methyl protons in the isomeric structures (263) and (264). On this basis it is tentatively suggested that the product of the acetylation of the aminotriazole (249a) is in fact a mixture of the N(1)- and N(2)- monoacetyl derivatives (265) and (266), the former predominating.
Scheme 48
The mechanism of formation of (249a) is probably that outlined in scheme 48. Reaction of ethoxide ion with the amidine hydrochloride (260a) affords the free amidine (257a) which is readily converted to its anion (267). Further reaction with toluene-p-sulphonyl azide followed by rearrangement of the intermediate readily affords the desired product (249a).

It was expected that the benzenesulphonyl substituent at C-4 in the triazole (249a) might be amenable to nucleophilic displacement, thus opening up synthetic routes to a variety of 4-substituted 5-amino-1H-1,2,3-triazoles. However, the triazole (249a) was recovered unchanged after heating under reflux in ethanolic sodium ethoxide.

Treatment of benzoylacetonitrile (258b) with ethanol in the presence of hydrogen chloride afforded the known \textsuperscript{171} ethyl benzoylacetic acid hydrochloride (259b). However, attempted transformation of the acetimidate hydrochloride (259b) into the corresponding acetamidine hydrochloride (260b), employing the conditions successful for the conversion of ethyl benzenesulphonylacetimidate hydrochloride (259a) into

\[ \text{Ac-N} = \text{N} = \text{N} \text{SO}_2\text{Ph} \]

(265)

\[ \text{Ac-N} = \text{N} = \text{N} \text{SO}_2\text{Ph} \]

(266)
benzenesulphonylacetamidine hydrochloride (260a) were continually frustrated by the formation of ethyl benzoylacetimidate (271). Treatment of an ethanolic solution of ethyl benzoylacetimidate (271) with liquid ammonia at room temperature resulted largely in recovery of the starting material, while heating an aqueous ethanolic solution of ethyl benzoylacetimidate (271) under reflux with ammonium chloride produced a similar result. Roth and Smith have reported the successful reaction of ethyl benzoylacetimidate hydrochloride (259b) with ammonia to give the desired amidine (257b), but attempts to repeat the work of these authors simply afforded the free imidate (271). These failures to synthesise the benzoylamidine (257b), or its hydrochloride (260b), precluded its conversion into the desired 5-amino-4-benzoyl-1H-1,2,3-triazole (249b) and
hence, unfortunately 1,2,3-triazolo[1,5-a]pyrimidines having a benzoyl group at C-3.

2.1.3 Condensation Reactions of 5-Amino-1H-1,2,3-triazoles with β-Dicarbonyl Compounds

It has been shown,\textsuperscript{156-158} that reaction of aminotriazoles of the type (234) with β-dicarbonyl compounds of type (235) in the presence of base affords the 1,2,3-triazolo[1,5-a]pyrimidine ring system (236) (scheme 40). In an attempt to obtain the 1,2,3-triazolo[1,5-a]pyrimidines (272a-g) the condensation of the aminotriazoles (249a and c) with acetylacetone, benzoylacetone, ethoxymethyleneacetylacetone and ethyl ethoxymethyleneacetoacetate in the presence of piperidine was investigated.

5-Amino-3-cyano-1H-1,2,3-triazole (249c) condensed smoothly with acetylacetone in the presence of piperidine to afford the sole product 3-cyano-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272a). The structure assigned to this compound is based on \textsuperscript{1}H n.m.r., i.r. and mass spectral data and combustion analysis. The presence of the diazostructure (273a) and hence the equilibrium \{[(272a) \xrightleftharpoons{} (273a)]\}, either in the solid state or in solution at room temperature is excluded by the lack of significant i.r. absorption above 1600 cm\(^{-1}\), and by the presence of \textsuperscript{1}H n.m.r. signals, attributable to two non-equivalent methyl groups in the condensation product. The \textsuperscript{1}H n.m.r. spectrum in a solution of \textsuperscript{2}H\textsubscript{6} dimethyl sulfoxide showed a one proton singlet at 6.97 p.p.m. due to H(6), and a poorly resolved three proton
Scheme 49

R

a) $\text{SO}_2\text{Ph}$

c) $\text{CN}$

\[
\begin{array}{ccc}
R^1 & R^2 & R^3 \\
a) & \text{CN} & \text{Me} & \text{H} \\
b) & \text{SO}_2\text{Ph} & \text{Me} & \text{H} \\
c) & \text{CN} & \text{Ph} & \text{H} \\
d) & \text{SO}_2\text{Ph} & \text{Ph} & \text{H} \\
e) & \text{CN} & \text{H} & \text{COMe} \\
f) & \text{CN} & \text{H} & \text{CO}_2\text{Et} \\
g) & \text{SO}_2\text{Ph} & \text{H} & \text{COMe}
\end{array}
\]

(273)
doublet at 2.90 p.p.m. and a sharp three proton singlet at 2.68 p.p.m., due to the two methyl groups. On expansion of the spectrum in \(^{2}H_6\) dimethyl sulphoxide to 250 Hz, the singlet at 6.97 p.p.m. became a poorly resolved quartet, and the signal at 2.90 p.p.m. was resolved into a well defined doublet. The signal at 2.68 p.p.m. remained unsplit. The assignment of the doublet at 2.90 p.p.m. to Me(7) and that at 2.68 p.p.m. to Me(5) is based on the expectation that owing to bond fixation in the structure (272a), the splitting associated with the benzylic type Me(7)-H(6) coupling will be larger than that due to Me(5)-H(6) coupling.\(^{173,174}\) The absorption of the C(7) methyl protons would in addition be shifted downfield, relative to those of the C(5) methyl group. The enhanced deshielding of the protons of a methyl group adjacent to the bridgehead nitrogen atom in the triazolo[4,3-a]pyrimidine ring system has been demonstrated.\(^{173}\)

Acetylacetone also condensed readily with 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a) in the presence of piperidine to give a single product assigned the 3-benzenesulphonyl-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine structure (272b) on the basis of its elemental analysis and spectral properties. In particular, the lack of NH-absorption in the i.r. spectrum indicated a condensed structure and proton resonances at \(\delta\) 7.29 and at \(\delta\) 2.82 and \(\delta\) 2.67 in \(^{2}H_6\) dimethyl sulphone can be assigned to H(6) and the C(7) and C(5) methyl groups respectively by comparison with the triazolopyrimidine (272a).
Scheme 50

R = CN and SO₂Ph
The formation of the triazolopyrimidines (272a and b) can be explained by two mechanistic pathways (scheme 50). Condensation with acetylacetone could occur at the primary amino function to afford an intermediate of the type (274) or at the ring nitrogen to give the intermediate (275). Subsequent dehydrative cyclisation of either of the two intermediates (274) or (275) would lead to the product obtained (272). Though there is no evidence to exclude the alternative pathway, initial condensation with the primary amino centre appears the more likely. 156

Condensation of the aminotriazoles (249a and c) with benzoylacetonate also occurred smoothly on heating under reflux in ethanol in the presence of piperidine, to afford the triazolopyrimidines (272 c and d). The structures assigned to these products are based on elemental analysis and i.r. and mass spectral data, and on the assumption that the most reactive methyl carbonyl group of benzoylacetonate will condense preferentially with the primary amino group of the amino-1,2,3-triazoles (249a and b). 156 However, the verification of this assumption by means of 1H n.m.r. data could not be achieved due to the insolubility of the products (272c and d) in solvents (\([\text{H}_6\]) dimethyl sulfoxide; deuteriochloroform; \([\text{H}_6\]) acetone or diphenyl ether) suitable for measuring their 1H n.m.r. spectra.

The attempted condensation of 5-amino-4-cyano-1H-1,2,3-triazole (249c) with ethoxymethyleneacetylacetone in the presence of piperidine to give the triazolopyrimidine (272e) resulted in the formation of dark intractable solids, which were shown by t.l.c. examination to be multicomponent mixtures. Similarly, the attempted synthesis of the triazolopyrimidine
Scheme 51

\[
R = \text{CN and } \text{SO}_2\text{Ph}
\]
(272f) by piperidine catalysed condensation of ethyl ethoxymethyleneacetoacetate with the aminotriazole (249c) also resulted in the isolation of intractable tars. The attempted synthesis of the triazolo[1,5-a]pyrimidine derivative (272g) by the condensation of ethoxymethyleneacetylacetone with the 4-benzenesulphonyl-1,2,3-triazole (249a) in the presence of piperidine also resulted in the formation of intractable tars.

2.1.4 Variable Temperature $^1$H n.m.r. Studies of Diazoalkylideneamine/1,2,3-Triazole Tautomerism in 1,2,3-Triazolo[1,5-a]pyrimidines

As mentioned earlier (Chapter 2.1.1), triazolopyrimidines have been shown to undergo Dimroth rearrangement. Variable temperature $^1$H n.m.r. studies have also demonstrated that 5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine-3-carboxamide (231b) undergoes this transformation at lower temperatures and with lower activation energy than 5,7-dimethyl-3-phenyl-1,2,3-triazolo[1,5-a]pyrimidine (231a) supporting the view that an electron withdrawing substituent at C(3) helps to stabilise structures of type (232) relative to (231) and (233). The successful synthesis of the triazolopyrimidines (272a and b) prompted further investigation by variable temperature $^1$H n.m.r. of their potential Dimroth rearrangement. Thus, if the electron withdrawing effect of the C(3) substituent has a significant influence on the ease of Dimroth rearrangement $[(272) \xrightarrow{\text{Dimroth}} (273) \xrightarrow{\text{Dimroth}} (276) \xrightarrow{\text{Dimroth}} (277)]$ then C(3) cyano and benzene-sulphonyl groups being more electron withdrawing than a carboxamide group should promote rearrangement at even lower temperatures and with lower activation energies.
Figures 1-5: The Variable Temperature $^1$H n.m.r. Spectrum of the Me(5) and Me(7) Absorptions in 3-Cyano-5,7-dimethyl-
1,2,3-triazolo[1,5-a]pyrimidine (272a)

1. $28^\circ$

2. $95^\circ$

3. $106^\circ$

4. $117^\circ$

5. $130^\circ$

coalesced Me-7/Me-5

Me-7/Me-5
When the change in $^1$H n.m.r. absorption of 3-cyano-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272a) in [$^2$H$_6$] dimethyl sulphoxide with temperature was examined it was found that as the temperature was raised the Me(5) and Me(7) signals gradually coalesced (see figures 1-5). At room temperature ($28^\circ$) the doublet attributable to the Me(7) protons and the sharp singlet due to Me(5) are clearly seen (figure 1). Raising the temperature to $95^\circ$ (figure 2) results in the transformation of the Me(7) doublet and the Me(5) singlet into two broad singlets. Further elevation of the temperature results in the gradual coalescence of the two broad singlets, until at $117^\circ$, the appearance of a single broad absorption due to the coalesced Me(7) and Me(5) signals is seen (figures 3 and 4). Increasing the temperature still further (figure 5) results in the appearance of a single singlet due to the fully coalesced methyl signals. The spectrum reverted back to a spectrum identical with the original when cooled to room temperature ($28^\circ$). The $^1$H n.m.r. absorption of 3-benzene-sulphonyl-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272b) in [$^2$H$_6$] dimethyl sulphoxide showed similar temperature dependent effects, although the coalescence occurred at slightly lower temperature ($115^\circ$) for (272b) than for (272a) ($117^\circ$). The temperature dependence of the $^1$H n.m.r. absorption of the triazolopyrimidines (272a and b) may be attributed to the reversible Dimroth rearrangement [scheme 51; (272) ⇌ (273) ⇌ (276) ⇌ (277); $R = \text{CN or SO}_2\text{Ph}$] which averages the methyl absorption on the n.m.r. time scale.

The free energies of activation ($\Delta G^*$) for the reversible Dimroth rearrangements of the triazolopyrimidines (272a and b) were calculated from the observed coalescence temperatures.
(115° and 117°) using the equation outlined below.\textsuperscript{175,176} The

\[ \Delta G^* = 4.59 T_C [9.97 + \log_{10} \frac{T_C}{\delta}] \]

\( T_C \) - coalescence temperature (°K)
\( \delta \) - average chemical shift (Hz)

calculated values of \( \Delta G^* \) for (272a) and (272b) are 76.1 kJ mol\(^{-1}\) and 75.7 kJ mol\(^{-1}\) respectively, and are surprisingly very similar to that reported\textsuperscript{160} for the triazolopyrimidine carboxamide (231b) (ca. 76 kJ mol\(^{-1}\)), despite the greater electron withdrawal of the C(3) cyano and benzenesulphonyl groups in (272a and b). These results indicate that although an electron withdrawing substituent at C(3) (e.g. CONH\(_2\)) in a triazolopyrimidine decreases the free energy of activation (\( \Delta G^* \)) for the reversible Dimroth rearrangement when compared to a C(3) substituent in a triazolopyrimidine which is not electron withdrawing (e.g. Ph),\textsuperscript{160} the actual difference in the electron-withdrawing power of any particular substituent (e.g. CONH\(_2\); CN or SO\(_2\)Ph) appears to have little effect on the activation energy of the reversible Dimroth rearrangement of such triazolopyrimidines [(231b), (272a and b)].

The insolubility of the phenyl substituted triazolopyrimidines (272c and d) in both \(^2\)H\(_6\) dimethyl sulphoxide and diphenyl ether precluded investigations into their thermally induced Dimroth rearrangement.
2.1.5 Experimental

(For general experimental procedures, see Appendix).

The Preparation of 5-Amino-1-benzyl-4-cyano-1,2,3-triazole (248c)

5-Amino-1-benzyl-4-cyano-1,2,3-triazole (248c) m.p. 170-172° (lit.,\textsuperscript{168b} 180-182°) was prepared in 94% yield as described in the literature,\textsuperscript{168b} and was used without further purification.

5-Amino-4-cyano-1H-1,2,3-triazole (249c)

A vigorously stirred suspension of 5-amino-1-benzyl-4-cyano-1,2,3-triazole (248c) (48.0 g) in liquid ammonia (ca. 1000 ml) was treated continuously with small pieces of sodium (total 13.8 g). After ca. 0.75 h the suspension became dark inky blue and stirring was continued for a further 0.5 h, when the reaction was considered to be complete. Ammonium chloride was then added to discharge any remaining blue colour and the ammonia was allowed to evaporate overnight.

The residue obtained was treated with water (200 ml), filtered, washed with methylene chloride and acidified with concentrated aqueous hydrochloric acid. Evaporation and extraction of the residue obtained with boiling ethyl acetate afforded 5-amino-4-cyano-1H-1,2,3-triazole (249c) (13.39 g) (51%) m.p. 223-226° (lit.,\textsuperscript{168a} 226-228°), which was used without further purification.
Ethyl Benzenesulphonylacetimidate Hydrochloride (259a)

Ethyl benzenesulphonylacetimidate hydrochloride (259a) was prepared in 92% yield as described in the literature, as colourless plates m.p. 117-118° (from ethanol), $\nu_{\text{max}}$ 2720 br, 2690 br, and 2630 br (NH$_2$), 1665 (C=N), and 1570 br (NH def.) cm$^{-1}$, $\delta$[(CD$_3$)$_2$SO] 8.00-7.54 (5H, m, ArH), 7.39 br (1H, s, NH), 6.90 br (1H, s, NH), 4.59 (2H, s, CH$_2$), 4.01 (2H, q, J 7Hz, CH$_2$) and 1.05 (3H, t, J 7Hz, CH$_3$).

*Found:* C, 44.4; H, 5.1; N, 5.2%; M$^+$-HCl, 227

$\text{C}_{10}\text{H}_{14}\text{ClNO}_3\text{S}$ requires: C, 45.5; H, 5.1; N, 5.3%; M, 263.5

Benzenesulphonylacetamide Hydrochloride (260a)

Ethyl benzenesulphonylacetimidate hydrochloride (259a) (39.60 g, 0.15 mol) was added in one portion to 0.15 M ethanolic ammonia (90.0 ml) and the resulting suspension was shaken at room temperature for 2 h. The solid was collected and combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the residue obtained with ether to afford benzenesulphonylacetamidine hydrochloride (260a) (total 33.48 g) (95%) m.p. 253-255° as colourless needles (from glacial acetic acid), $\nu_{\text{max}}$ 3420 br, and 3150 br (NH), 1700 br (C=N) and 1620 and 1580 (NH def.) cm$^{-1}$, $\delta$[(CD$_3$)$_2$SO] 9.08 br (4H, s, NH), 8.00-7.56 (5H, m, ArH), and 4.58 (2H, s, CH$_2$).

*Found:* C, 40.7; H, 4.5; N, 11.6%; M$^+$-HCl, 198.

$\text{C}_8\text{H}_{11}\text{ClNO}_2\text{S}$ requires: C, 40.9; H, 4.7; N, 11.9%; M, 234.5.

Evaporation of the ether mother liquor afforded a negligible quantity of yellow gum.
5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a)

(a) A suspension of benzenesulphonylacetamidine hydrochloride (260a) (23.50 g, 0.10 mol) in absolute ethanol (150 ml) was treated dropwise with stirring at 0° (ice-salt bath) with a solution of sodium (6.90 g) in absolute ethanol (150 ml), followed by a solution of toluene-p-sulphonyl azide (19.70 g, 0.10 mol) in absolute ethanol (25.0 ml), such that the temperature never exceeded 0°. Stirring was continued at 0° for 2 h and the mixture (containing solid) was evaporated. The residue obtained was treated with water (250 ml) and extracted with methylene chloride to afford a dark oil (5.20 g) which was shown by comparison (i.r. spectrum and t.l.c. in methylene chloride over silica) with an authentic sample to consist mainly of toluene-p-sulphonyl azide.

Acidification of the basic aqueous mother liquor with concentrated aqueous hydrochloric acid and crystallisation of the resulting solid (17.50 g) afforded 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a) (10.87 g) (46%) as buff plates m.p. 203-204° (from ethanol-light petroleum), v_{max} 3450, 3310 br, and 3220 w (NH) and 1640 (NH def.) cm^{-1}.

Found: C, 43.0; H, 3.7; N, 24.9%; M^+ 224.
C_{8}H_{8}N_{4}O_{2}S requires: C, 42.9; H, 3.6; N, 25.0%; M, 224.

Evaporation of the ethanol-light petroleum mother liquor and trituration of the resulting residue with toluene afforded a solid which was combined with a second crop obtained by extraction of the aqueous mother liquor with methylene chloride to give toluene-p-sulphonamide (total 6.94 g) (41%) m.p. 121-126° identical (m.p. and i.r. spectrum) to an authentic sample. Evaporation of the toluene mother liquor afforded a negligible quantity of dark oil.
Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

(b) A suspension of benzenesulphonylacetamidine hydrochloride (260a) (2.35 g, 0.01 mol) in absolute ethanol (15.0 ml) was treated dropwise, with stirring at 0°C (ice-salt bath) with a solution of triethylamine (2.75 g, 0.022 mol) in absolute ethanol (5.0 ml) followed by a solution of toluene-p-sulphonyl azide (4.50 g, 0.022 mol) in absolute ethanol (5.0 ml), such that the temperature never exceeded 0°C. Stirring was continued at 0°C for 2h, and the mixture was filtered to remove starting material (0.20 g) m.p. 249-253°C, which was identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Evaporation of the ethanol filtrate and treatment of the resulting red oil with water and methylene chloride afforded the insoluble 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a) (0.70 g) (31%) m.p. 198-201°C which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Evaporation of the methylene chloride extract, treatment of the resulting semi-solid with aqueous 2M sodium hydroxide and extraction with methylene chloride afforded toluene-p-sulphonyl azide (1.08 g) which was identified by comparison (i.r. spectrum) with an authentic sample.

Neutralisation of the basic aqueous extract with aqueous 2M hydrochloric acid afforded a solid, which was combined with a second crop obtained by extracting the neutral aqueous mother liquor with methylene chloride, to give toluene-p-sulphonamide (total 0.67 g) (39%) m.p. 123-127°C identical (m.p. and i.r. spectrum) with an authentic sample.
(c) Benzenesulphonylacetamidine hydrochloride (260a) 
(0.94 g, 0.004 mol) and piperidine (0.90 g, 0.012 mol) were stirred in super-dry ethanol (30.0 ml) at 00 (ice-salt bath) for 10 min and then treated dropwise with stirring with a solution of toluene-p-sulphonyl azide (1.75 g, 0.008 mol) in super-dry ethanol (10.0 ml). The mixture was stirred at 00 for 2h, then evaporated and the residue obtained was treated with aqueous 2M sodium hydroxide and extracted with methylene chloride to afford an unidentified solid (0.03 g) m.p. > 300° (decomp.) having an ill-defined i.r. spectrum.

Acidification of the basic aqueous layer with aqueous 2M hydrochloric acid afforded toluene-p-sulphonamide (0.48 g) (70%) m.p. 122-126° which was identical (m.p. and i.r. spectrum) to an authentic sample.

The triazole (249a) was readily soluble in aqueous 2M sodium hydroxide, and was regenerated, unchanged, on acidification with aqueous 2M hydrochloric acid.

The Acetylation of 5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a)

5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a) 
(0.22 g, 0.001 mol) was heated at 100° with acetic anhydride (0.30 ml) until the solid just dissolved. The solution was cooled and allowed to stand at room temperature for 20 min. then diluted with ether to afford a mixture of 1-acetyl-5-amino-4-benzenesulphonyl-1,2,3-triazole (265) and 2-acetyl-5-amino-4-benzenesulphonyl-1,2,3-triazole (266) (0.19 g) (71%) m.p. 110-112° as colourless plates (from toluene), ν_max. 3455 and
3290 br (NH) and 1755 (CO) cm\(^{-1}\), \(\delta[(CD_3)_2SO]\) 8.20-7.88
(5H, m, ArH), 7.82-7.56 (5H, m, ArH), 7.35 br (2H, s, NH),
6.52 br (2H, s, NH), 2.70 (3H, s, CH\(_3\)) and 2.63 (3H, s, CH\(_3\)),
in the ratio ca. 3:1 as estimated from the integrated ratio
of the methyl signals in the \(^1\)H n.m.r. spectrum.

**Found:** C, 45.4; H, 3.8; N, 20.9%; M\(^+\), 266.
**C\(_{10}\)H\(_{10}\)N\(_4\)O\(_3\)S requires:** C, 45.1; H, 3.8; N, 21.1%; M, 266.

Evaporation of the ether mother liquor afforded a
negligible quantity of dark oil.

The Attempted Reaction of 5-Amino-4-benzenesulphonyl-1H-
1,2,3-triazole (249a) with Ethanolic Sodium Ethoxide

5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (249a)
(0.45 g, 0.002 mol) dissolved in warm super-dry ethanol
(15.0 ml) was treated dropwise with a solution of sodium
(0.092 g) in super-dry ethanol (6.0 ml) and the mixture was
heated under reflux for 0.5 h. The solution was cooled and
the insoluble solid was collected and washed with aqueous 2M
hydrochloric acid to afford unreacted starting material (0.38 g)
m.p. 199-202\(^\circ\) which was identified by comparison (m.p. and i.r.
spectrum) with an authentic sample. Extraction of the acidic
aqueous mother liquor with methylene chloride gave no material.

Evaporation of the ethanol mother liquor, treatment of the
residue with water, and extraction with methylene chloride or
acidification of the aqueous layer with aqueous 2M hydrochloric
acid and extraction with methylene chloride gave no further
material.
Ethyl Benzoylacetimidate Hydrochloride (259b)

Ethyl benzoylacetimidate hydrochloride (259b) prepared in 82% yield as described in the literature\textsuperscript{171} had m.p. 138-141° (lit.,\textsuperscript{171} 140°), and was used without further purification.

The Attempted Preparation of Benzoylacetamidine Hydrochloride (260b)

(a) Ethyl benzoylacetimidate hydrochloride (259b) (4.56 g, 0.02 mol) was added in one portion to 0.02 M ethanolic ammonia (20.0 ml) and the mixture was shaken at room temperature for 2 h, then left in a refrigerator overnight. The insoluble ammonium chloride was collected (1.38 g) and the ethanol mother liquor was evaporated to afford a red gum (2.53 g) which partially solidified on scratching, and was identical (i.r. spectrum) to authentic ethyl benzoyacetimidate (271) obtained later.

Treatment of a solution of the red gum (1.35 g) in dry ether (20.0 ml) with dry hydrogen chloride afforded the hydrochloride (259b) (0.62 g) m.p. 135-139° which was identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

(b) Ethyl benzoylacetimidate (271) (1.91 g, 0.01 mol) dissolved in absolute ethanol (20.0 ml) was treated with liquid ammonia (ca. 3.5 ml) and the reaction vessel was tightly stoppered and left at room temperature for 24 h. The solution obtained was evaporated and the resulting gum was triturated with ether to yield unreacted ethyl benzoylacetimidate (271) (1.34 g) m.p. 80-86° which was identical (m.p. and i.r. spectrum) to an authentic sample. Evaporation of the ether mother liquor gave a negligible quantity of gum.
(c) Ethyl benzoylacetimidate (271) (3.82 g, 0.02 mol) was heated under reflux with ammonium chloride (2.16 g) in 70% aqueous ethanol (30.0 ml) for 4 h. The solution obtained was cooled and evaporated and the residue obtained was treated with water to afford the starting material (271) (3.30 g) m.p. 82-88° which was identified by comparison (m.p. and i.r. spectrum) with an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride afforded a negligible quantity of gum.

The Attempted Preparation of Benzoylacetamidine (257b)

The method described by Roth and Smith was followed, but the only product isolated was ethyl benzoylacetimidate (271) (53%) m.p. 80-86° which was identical (m.p. and i.r. spectrum) to an authentic sample.

The Synthesis of Some 3-Cyano-1,2,3-triazolo[1,5-a]pyrimidines

The triazole (249c) (0.004 mol) and acetylacetone, benzoylacetone, ethoxymethyleneacetylacetone or ethyl ethoxymethyleneacetooacetate (0.004 mol) were heated under reflux with piperidine (0.2 ml) in ethanol (20.0 ml) for 24 h. The reaction mixtures were allowed to cool.

(i) Acetylacetone afforded a solution which when evaporated and the gum obtained treated with ether gave 3-cyano-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272a) (55%) m.p. 130-131° as buff plates (from ethanol-light petroleum), νmax. 2240 (CN) cm⁻¹, δ[(CD₃)₂SO] 6.97 (1H, s, H-6), 2.90 (3H, d, J1 Hz, Me-7) and 2.68 (3H, s, Me-5).
Found:  C,55.5;  H,4.0;  N,40.4%;  M⁺,173

\[ \text{C}_8\text{H}_7\text{N}_5 \text{ requires: C,55.5; H,4.0; N,40.5%; M, 173.} \]

Evaporation of the ether mother liquor, treatment of the gum with aqueous 2M hydrochloric acid and extraction with methylene chloride afforded a gum (0.44 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(ii) Benzoylacetone gave a solid which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the resulting semi-solid with methanol to afford 3-cyano-5-methyl-7-phenyl-1,2,3-triazolo[1,5-a]pyrimidine (272c) (47%) m.p. 194-196°C as buff plates (from glacial acetic acid), \( \nu_{\text{max.}} \) 2230 (CN) cm⁻¹.

Found:  C,66.2;  H,3.8;  N,29.7%;  M⁺,235

\[ \text{C}_{13}\text{H}_9\text{N}_5 \text{ requires: C,66.4; H,3.8; N,29.4%; M,235.} \]

Evaporation of the methanol mother liquor, treatment of the gum obtained with aqueous 2M hydrochloric acid, and extraction with methylene chloride afforded a yellow gum (0.11 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(iii) Ethoxymethyleneacetylacetone yielded a dark solid (0.12 g) m.p. > 300°C (decomp.) whose i.r. spectrum was ill-defined and which defied crystallisation, and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
Evaporation of the ethanol mother liquor and treatment of the residue obtained with aqueous 2M sulphuric acid afforded a dark intractable solid (0.18 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Extraction of the acidic aqueous mother liquor with methylene chloride afforded a small quantity of unidentified gum (0.04 g). Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

(iv) Ethyl ethoxymethyleneacetoacetate gave a solution which when evaporated and the residue obtained treated with aqueous 2M hydrochloric acid and extracted with methylene chloride afforded a red gum (0.19 g) shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

The Synthesis of Some 3-Benzenesulphonyl-1,2,3-triazolo[1,5-a]pyrimidines

The triazole (249a) (0.002 mol) and acetylacetone, benzoylaceton or ethoxymethyleneacetylacetone (0.002 mol) were heated under reflux with piperidine (0.1 ml) in ethanol (20.0 ml) for 24 h.
(i) Acetylacetone gave a solution which when cooled and evaporated and the residue obtained triturated with ether to afford 3-benzenesulphonyl-5,7-dimethyl-1,2,3-triazolo[1,5-a] pyrimidine (272b) (90%) m.p. 189-190° as colourless needles (from ethanol), δ[(CD₃)₂SO] 8.12-7.96 (2H, m, ArH), 7.70-7.50 (3H, m, ArH), 7.29 (1H, s, H-6), 2.82 (3H, d, J 1Hz, Me-7), and 2.67 (3H, s, Me-5).

Found: C, 54.2; H, 4.2; N, 19.3%; M⁺, 288.

C₁₃H₁₂N₄O₂S requires: C, 54.2; H, 4.2; N, 19.1%; M, 288.

Evaporation of the ether mother liquor, treatment of the gum obtained with aqueous 2M hydrochloric acid, and extraction with methylene chloride gave a red oil (0.09g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(ii) Benzoylacetone gave a solution which when cooled afforded 3-benzenesulphonyl-5-methyl-7-phenyl-1,2,3-triazolo[1,5-a] pyrimidine (272d) (33%) m.p. 226-228° as colourless plates (from dimethylformamide).

Found: C, 61.6; H, 4.1; N, 16.2%; M⁺, 350

C₁₈H₁₄N₄O₂S requires: C, 61.7; H, 4.0; N, 16.0%; M, 350.

Evaporation of the ethanol mother liquor, treatment of the gum obtained with aqueous 2M hydrochloric acid, and extraction with methylene chloride afforded a yellow gum (0.39 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
(iii) Ethoxymethyleneacetylacetone gave a solution which when hot filtered afforded a dark intractable solid (0.21 g) m.p. > 300° (decomp.) having an ill-defined i.r. spectrum and shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Evaporation of the ethanol filtrate, treatment of the dark residue with aqueous 2M sulphuric acid, and extraction with methylene chloride yielded a dark gum (0.41 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

The Variable Temperature $^1$H n.m.r. Study of Some 1,2,3-Triazolo[1,5-a]pyrimidines

The $^1$H n.m.r. spectra in $[^2]$H$_6$] dimethyl sulphoxide of:
(a) 3-Cyano-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272a),
(b) 3-Benzensulphonyl-5,7-dimethyl-1,2,3-triazolo[1,5-a] pyrimidine (272b),
were measured at 28°, and thereafter at various intervals, using sweep width 250 Hz. Extracts of the results are collected in tables 1 and 2, including the calculated activation energy values ($\Delta G^*$) for each of the two pyrimidines (272a) and (272b), using the equation described in the text (cf. Chapter 2.1.4).
In each case the \([^{2}H_{6}]\) dimethyl sulphoxide solution was allowed to cool after reaching a temperature of 130° and the spectrum retaken at 28° was shown to be identical with the original (measured at 28°).
Table 1
The variable temperature $^1$H n.m.r. spectrum of 3-cyano-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272a), over a range which includes the Me-5 and Me-7 signals

<table>
<thead>
<tr>
<th>Temperature ($^{\circ}$C)</th>
<th>Me-5 (Hz)</th>
<th>Coalesced Me-5/Me-7</th>
<th>Me-7 (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>268.2</td>
<td></td>
<td>289.6$^b$</td>
</tr>
<tr>
<td>95</td>
<td>266.5$^c$</td>
<td></td>
<td>288.5$^c$</td>
</tr>
<tr>
<td>106</td>
<td>267.1$^c$</td>
<td></td>
<td>286.8$^c$</td>
</tr>
<tr>
<td>117$^d$</td>
<td></td>
<td>276.0$^c$</td>
<td></td>
</tr>
<tr>
<td>130</td>
<td></td>
<td>276.0$^c$</td>
<td></td>
</tr>
</tbody>
</table>

$\Delta G^* = 76.1$ kJ mol$^{-1}$

$^a$ All signals, measured in Hz from silicone oil as external standard at the temperature stated, were sharp singlets unless otherwise specified.

$^b$ Doublet (J, 1Hz)

$^c$ Broad singlet

$^d$ Temperature of coalescence.
Table 2
The variable temperature $^1$H n.m.r. spectrum of 3-benzenesulphonyl-5,7-dimethyl-1,2,3-triazolo[1,5-a]pyrimidine (272b), over a range which includes the Me-5 and Me-7 signals

<table>
<thead>
<tr>
<th>Temperature ($^\circ$C)</th>
<th>Temperature of coalescence</th>
<th>Signals$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Me-5</td>
<td>Coalesced Me-5/Me-7</td>
</tr>
<tr>
<td>28</td>
<td>268.2</td>
<td>282.0$^b$</td>
</tr>
<tr>
<td>64</td>
<td>266.5</td>
<td>281.2$^b$</td>
</tr>
<tr>
<td>86</td>
<td>265.8$^c$</td>
<td>281.2$^b$</td>
</tr>
<tr>
<td>115$^d$</td>
<td></td>
<td>271.5$^c$</td>
</tr>
<tr>
<td>130</td>
<td></td>
<td>271.5$^c$</td>
</tr>
</tbody>
</table>

$\Delta G^* = 75.7$ kJ mol$^{-1}$

$^a$ All signals, measured in Hz from silicone oil as external standard at the temperature stated, were sharp singlets unless otherwise specified.

$^b$ Doublet (J, 1Hz)

$^c$ Broad singlet

$^d$ Temperature of coalescence
Scheme 52
Scheme 53
2.2 The Synthesis and α-Dicarbonyl Condensation Reactions of 1,5-Diamino-1,2,3-triazoles

2.2.1 Introduction

As shown in scheme 52, the 1,2,3-triazolo[5,1-c]-1,2,4-triazine ring system (278) can undergo potential reversible Dimroth rearrangement [(278) ⇋ (279) ⇋ (280) ⇋ (281)] to the 1,2,3-triazolo[1,5-b]-1,2,4-triazine ring system (281). The possibility of such rearrangement, therefore raises the question as to which of the two possible isomers [(278) or (281)] is obtained in a given instance. This question can best be answered by X-ray structure analysis of single products or, if both possible isomers can be synthesised unambiguously, by comparison of their respective spectral and chemical properties. The synthetic approach to the problem of the reversible interconversion of the 1,2,3-triazolo[5,1-c]-1,2,4-triazine and 1,2,3-triazolo[1,5-b]-1,2,4-triazine ring systems is the subject of the present section.

Compounds of type (284) have been reported as the products of the coupling reactions of 1H-1,2,3-triazole-5-diazonium salts (282) with active methylene compounds, followed by cyclisation of the resulting hydrazones (283). The triazolotriazines (284) so formed have been shown to react with phenylhydrazine to afford the azo compounds (287) whose structures were established by unambiguous synthesis. Since for structural reasons the corresponding [1,5-b] isomers (286) cannot form azo products of the type (287), formation of the latter is consistent with the products of the diazo coupling reactions having the 1,2,3-triazolo[5,1-c]-1,2,4-triazine
Scheme 54
structure (284). The possibility that the products of the diazo coupling reactions are $1,2,3$-triazolo[1,5-b]-1,2,4-triazines (286) and undergo rearrangement [(286) $\xrightarrow{\rightleftharpoons}$ (285) $\xrightarrow{\rightleftharpoons}$ (284)] to their $1,2,3$-triazolo[5,1-c]-1,2,4-triazine isomers (284) prior to reaction with phenylhydrazine cannot be ruled out, but is considered unlikely under the conditions used both in the coupling reactions and in the condensations with phenylhydrazine. The unambiguous synthesis of derivatives of the $1,2,3$-triazolo[1,5-b]-1,2,4-triazine ring system (281) has as yet not been reported.

The synthesis of $1,2,3$-triazolo[1,5-b]-1,2,4-triazine derivatives may be achieved by utilising the bifunctionality of $1,5$-diamino-$1,2,3$-triazoles of type (288). Thus, condensation of such $1,2,3$-triazole derivatives with $\alpha$-dicarbonyl compounds should afford triazolotriazines of the desired configuration [scheme 54; (288) + (289)$\rightleftharpoons$(281)]. Processes of this type are analogous to the many reported condensation reactions of N-amino-C-amino 1,2,4-triazoles. For example, 3,4-diamino-1,2,4-triazoles (290) condense very readily with benzil to afford the 1,2,4-triazolo-[4,3-b]-1,2,4-triazines (291). Therefore, as in the synthesis of triazolopyrimidines (see earlier), the synthesis of $1,2,3$-triazolo[1,5-b]-1,2,4-triazines (281) is closely related to the problems associated with the preparation of suitable $1,2,3$-triazole precursors (i.e. $1,5$-diamino-1,2,3-triazoles).
Scheme 55
A number of synthetic routes to N-amino-1,2,3-triazoles have been reported in the literature. The most common method involves the oxidative cyclisation of the bis hydrazones of \( \alpha \)-dicarbonyl compounds. It has been shown by a number of workers that bis-arylhydrazones of the type (292) are oxidised by mercury (II) oxide in the presence of iodine to afford the so-called triazolylisoimides (293) which can be readily hydrolysed with mineral acids to the corresponding N-amino-1,2,3-triazoles (294). Similarly, Alexandrou and Adamopoulas have demonstrated the formation of ureido-triazoles (297) by reaction of bis-semicarbazones (296) with lead tetraacetate. Acidic hydrolysis of the ureidotriazoles (297) readily affords the N-amino-1,2,3-triazoles (294).

An adaptation of these reactions has recently been reported by Hauptmann et al. Oxidation of the bis hydrazines (295) with manganese dioxide affords the N-amino-1,2,3-triazoles (294) directly.

Direct amination of the 1,2,3-triazole nucleus to afford N-amino-1,2,3-triazoles has also been demonstrated by some workers. The use of hydroxylamine-O-mesitylene sulphate as the reagent in such transformations has been shown to convert NH-1,2,3-triazoles (298) into the corresponding N-amino derivatives (299).
Scheme 56
have reported the similar conversion of benzotriazoles (300) into the 1-aminobenzotriazoles (301) using hydroxylamine-0-sulphonic acid,\textsuperscript{197} the 2-aminobenzotriazole also being obtained as a by-product.\textsuperscript{190,191} N-Aminobenzotriazoles of type (301) can also be obtained by series of reactions starting with ortho-nitroaniline derivatives (302).\textsuperscript{190-192} Diazotisation of the aniline (302) and reaction with diethyl malonate or ethyl cyanoacetate affords hydrazones (303) which on reduction with hydrogen and palladium charcoal afford amines (304) convertible by diazotisation into N-aminated triazoles (305). Subsequent acidic hydrolysis affords the N-amino-1,2,3-triazoles (301).

The preparation of 1,5-diamino-1,2,3-triazoles (288) however, has yet to be reported. The only example\textsuperscript{198} of a diaminotriazole of type (288) has been obtained in this department by an adaptation of the diazo transfer reaction used in the synthesis of the novel 4-benzenesulphonyl-1H-1,2,3-triazole (249a) (see earlier).

The following study was therefore undertaken with a view to extending this type of reaction to provide a general synthesis of 1,5-diamino-1,2,3-triazoles for use as starting materials for the synthesis of 1,2,3-triazolo[1,5-b]-1,2,4-triazine derivatives.

2.2.2 The Synthesis of 1,5-Diamino-1,2,3-triazoles

The acetamidrazone hydrochloride (306) has been shown to react with toluene-p-sulphonyl azide in the presence of base to afford the 1,5-diaminotriazole (307).\textsuperscript{198} As extensions
R

a) $\text{SO}_2\text{Ph}$

b) $\text{COPh}$
Scheme 57
of this type of reaction the synthesis of the 1,5-diaminotriazoles (308a) and (308b) was undertaken.

Treatment of an ethereal solution of ethyl benzene-sulphonylacetic acid hydrochloride (259a) (obtained as described earlier) with gaseous ammonia afforded ethyl benzene-sulphonylacetic acid (309) as a low melting solid, whose elemental analysis and i.r. and mass spectra are in full agreement with the proposed structure. However, the $^1$H n.m.r. absorption of (309) in deuteriochloroform shows the presence of more than one species and is consistent with the presence of both tautomeric forms (309) and (312).

This interpretation finds analogy in the literature. It has been reported$^{199,200}$ that imidates of the type (313), containing a cyano group, exhibit such tautomerism $^{[(313) \xrightarrow{\text{t}} (314)]}$ in dimethyl sulfoxide. It is also suggested$^{199,200}$

that the nature of the solvent and temperature determine the relative proportion of the two tautomeric forms (313) and (314) present.

Treatment of ethyl benzenesulphonylacetimidate (309) with formylhydrazine readily afforded 1-formylbenzenesulphonylacetamidrazone (310) in quantitative yield. The structure assigned to (310) is based on spectral evidence and elemental analysis. The i.r. spectrum showed an absorption band at 1660 cm\(^{-1}\) attributable to the C=N stretching vibration, characteristic of amidrazones. A signal at \(\delta 9.95\) in the \(^1H\) n.m.r. spectrum of (310) is assigned to the formyl proton and is split into a doublet due to coupling with the adjacent NH group, which also appears as a doublet at \(\delta 8.01\). Treatment of formylamidrazones with hydrogen chloride are known to give amidrazone hydrochlorides. 1-Formylbenzenesulphonylacetamidrazone (310) when treated in this fashion readily afforded the corresponding benzenesulphonylacetamidrazone hydrochloride (311) whose elemental analysis and spectral data corresponded to the assigned structure. The amidrazone hydrochloride (311) afforded 4-benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a) as the sole product when
Scheme 58
reacted with toluene-p-sulphonyl azide in the presence of piperidine. The moderate yield obtained in this reaction step could not be improved by employing different bases. The use of sodium ethoxide and triethylamine for example both resulted in the isolation of unresolvable multicomponent oils or gums.

Reaction of the amidrazone hydrochloride (311) with toluene-p-sulphonyl azide could in principle result in ring closure of the presumed diazo intermediate (315) to the isomeric hydrazone structure (317) [scheme 58; (315) ⇄ (316) → (317)], which might also result from subsequent Dimroth rearrangement [scheme 58; (315) → (308a) ⇄ (317)] of the initially formed 1,5-diamino-triazole (308a).

However, the hydrazine structure (317) for the product of the reaction of amidrazone hydrochloride (311) with toluene-p-sulphonyl azide could be readily excluded on the basis of its behaviour with nitrous acid. It has been shown that 3,4-diamino-1,2,4-triazoles of the type (88) undergo N-deamination when diazotised in acid solution affording the corresponding 1,2,4-triazole diazonium salts.

\[
\begin{align*}
\text{H}_2\text{N} & - \text{N} \equiv \text{N} \\
\text{NH}_2 & \\
\text{Ph} & \\
\text{(88)} & \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & - \text{N} \equiv \text{N} \\
\text{HNO}_2 & \\
\text{HX} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{N} & - \text{N} \equiv \text{N} \\
\text{NH}_2 & \\
\text{Ph} & \\
\text{(88)} & \\
\end{align*}
\]

\[
\begin{align*}
\text{N} & - \text{N} \equiv \text{N} \text{X}^- \\
\text{H}_2\text{N} & - \text{N} \equiv \text{N} \\
\text{NH}_2 & \\
\text{Ph} & \\
\text{N} & - \text{N} \equiv \text{N} \text{X}^- \\
\text{H}_2\text{N} & - \text{N} \equiv \text{N} \\
\text{NH}_2 & \\
\text{Ph} & \\
\text{(46)} & \\
\end{align*}
\]
Scheme 59

(308a)

(318)

(319)

(320)
(46) (see Chapter 1). In an analogous reaction, it was shown that consistent with its 1,5-diamino-1,2,3-triazole structure (308a), the product of the reaction of the amidrazone hydrochloride (311) with toluene-p-sulphonyl azide reacted with nitrous acid followed by sodium acetate to afford the diazonium betaine (319), identical with a sample obtained later (see Chapter 3). This result excludes the hydrazine structure (317) which would have reacted with nitrous acid to afford the corresponding azide (320) prepared later (see Chapter 3).

The reaction of the amidrazone hydrochloride (311) with toluene-p-sulphonyl azide in the presence of piperidine to afford the 1,5-diamino-1,2,3-triazole (308a) can be rationalised by the mechanism shown in scheme 60 which is closely akin to that postulated for the reaction of toluene-p-sulphonyl azide with amidine hydrochlorides to afford 5-amino-1H-1,2,3-triazoles (see scheme 48). As in these reactions the species attacked is probably the free amidrazone.

The successful synthesis of the diaminotriazole (308a) prompted an analogous investigation into the synthesis of 4-benzoyl-1,5-diamino-1,2,3-triazole (308b). As has been demonstrated (see earlier) ethyl benzoylaceticamide hydrochloride (259b) is readily converted into the known ethyl benzoylaceticamide (271) by the action of ammonia under a variety of conditions. However, on attempted reaction with formylhydrazine using conditions successful for the conversion of ethyl benzenesulphonylacetimidate (309) into the formylacetamidrazone (310), ethyl
Scheme 60
Scheme 61
benzoylacacetimidate (271) afforded only an unidentified solid (A) whose i.r. and mass spectra and combustion analysis did not suggest a plausible structure. Further investigation into the synthesis of the diaminotriazole (308b) was therefore curtailed by the inability to isolate the corresponding formylacetamidrazozone derivative.

2.2.3 The Condensation Reactions of 1,5-Diamino-1,2,3-triazoles with α-Dicarbonyl Compounds

By direct analogy with 3,4-diamino-1,2,4-triazoles (290), 1,5-diamino-1,2,3-triazoles (288) should condense with α-dicarbonyl compounds to afford the corresponding 1,2,3-triazolo[1,5-b]-1,2,4-triazines (281).

In practice, condensation of 4-benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a) with biacetyl in the presence of a catalytic amount of glacial acetic acid afforded a single product, whose m.p., mixed m.p. and i.r., $^1$H n.m.r. and mass spectra were identical to 3-benzenesulphonyl-6,7-dimethyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (325a) obtained later (see Chapter 3). A similar result was obtained when
Scheme 62

(308a) 

(317) 

(327) 

(328) 

(326) 

(325) 

\[ R^1 \quad R^2 \]

a) Me  Me

b) H  Me
the diaminotriazole (308a) was condensed, under identical conditions, with methylglyoxal the product being 3-benzene-sulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (325b), identical in all respects to a sample obtained later. Evidence is presented in Chapter 3 which supports the 1,2,3-triazolo[5,1-c]-1,2,4-triazine structures (325a) and (325b) as opposed to the anticipated 1,2,3-triazolo[1,5-b]-1,2,4-triazine structures (326a) and (326b) for these products. Since conclusive evidence has been obtained for the 1,5-diamino configuration (308a) for the starting triazole, it follows that Dimroth rearrangement must have occurred either prior to, or after condensation (see scheme 62). Rearrangement of the triazole (308a) to the hydrazine (317) could occur before condensation with the dicarbonyl compound [(308a) ⇔ (317) ⇔ (328) ⇔ (325)]. Alternatively rearrangement may take place after condensation, but prior to cyclisation [(308a) → (327) ⇔ (328) ⇔ (?25)]. Finally, the [1,5-b] structure could rearrange to the [5,1-c] isomer (325) after initial cyclisation [(326) ⇔ (325)]. At the present time the available evidence still does not allow a choice between these various possibilities, and further work will have to be undertaken to resolve the problem.
2.2.4 Experimental

(For general experimental procedures, see Appendix).

The Preparation of the Acetimidate Hydrochlorides (259a) and (259b)

Ethyl benzenesulphonylacetimidate hydrochloride (259a) and ethyl benzoylacetimidate hydrochloride (259b) were prepared as described earlier (cf. pages 67 and 72 respectively).

Ethyl Benzenesulphonylacetimidate (309)

A suspension of ethyl benzenesulphonylacetimidate hydrochloride (259a) (7.13 g, 0.027 mol) in dry ether (50.0 ml) was cooled to -20°C, stirred and treated with a stream of ammonia gas for 1.5 h. The insoluble ammonium chloride (1.47 g) was filtered off and the ether filtrate was evaporated to afford ethyl benzenesulphonylacetimidate (309) as a low melting solid (6.11 g) (100%) which formed colourless plates m.p. 48-49°C (from light petroleum), \( \nu_{\text{max}} \) 3290 br (NH), 1750 (C=N), and 1650 br and 1580 (NH def.) cm\(^{-1}\), \( \delta[\text{CDCl}_3] \) 8.00-7.40 (m, ArH), 4.13 (s, CH), 4.11 (s, CH), 4.08 (s, CH\(_2\)) 4.00 (dq, J 9Hz, overlapping CH\(_2\)) and 1.09 (dt, J 9Hz, overlapping CH\(_3\)).

Found: C, 53.2; H, 5.8; N, 5.9%; M\(^+\), 227

C\(_{10}\)H\(_{13}\)NO\(_3\)S requires: C, 52.9; H, 5.7; N, 6.2%; M\(^+\), 227.
1-Formylbenzenesulphonylacetamidrazone (310)

A solution of ethyl benzenesulphonylacetimidate (309) (4.54 g, 0.02 mol) in super-dry ethanol (10.0 ml) was added in one portion at 0°C (ice-salt bath) to a stirred solution of formylhydrazine (1.20 g, 0.02 mol) in super-dry ethanol (20.0 ml). The resulting solution was left in the refrigerator overnight and the solid which precipitated was collected and combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the resulting oil with ethyl acetate to afford 1-formylbenzenesulphonylacetamidrazone (310) (total 4.80 g) (100%) as colourless plates m.p. 167-168°C (from ethanol), $\nu_{\text{max}}$ 3440, 3345 br and 3200 br (NH), 1685 (CO), 1660 (C=NH), and 1630 and 1545 br (NH def.) cm$^{-1}$, $\delta$[(CD$_3$)$_2$SO] 9.95 (1H, d, $J$ 10Hz, CHO), 8.01 (1H, d, $J$ 10Hz, NH), 7.94-7.48 (5H, m, ArH), 6.20 (2H, s, NH) and 4.09 (2H, d, $J$ 5Hz, CH$_2$).

Found: C, 44.7; H, 4.6; N, 17.2%; $M^+$ 241

C$_9$H$_{11}$N$_3$O$_3$S requires: C, 44.8; H, 4.6; N, 17.4%; $M$, 241.

Evaporation of the ethyl acetate mother liquor afforded a small quantity of an unidentified yellow oil (0.09 g).

Benzenesulphonylacetamidrazone Hydrochloride (311)

1-Formylbenzenesulphonylacetamidrazone (310) (26.51 g, 0.11 mol) was added to 1.5 M ethereal hydrogen chloride (250 ml) and the solution obtained was stirred vigorously at room temperature for 17 h. The solid (31.70 g) which precipitated was collected and heated under reflux in
absolute ethanol (300 ml) for 1 h to afford on cooling a solid which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the resulting semi-solid with ether to afford benzenesulphonylacetamidrazone hydrochloride (311) (total 25.72 g) (94%) m.p. 204-206° as colourless needles (from ethanol-glacial acetic acid), \( \nu_{\text{max.}} \) 3375 and 3345 (NH), 2430 br (\( \tilde{\text{N}}\text{H}_2 \)) and 1710, 1640, and 1580 (NH def.) cm\(^{-1}\), \( \delta[(\text{CD}_3)_2\text{SO}] \) 8.92 br (2H, s, NH), 8.06-7.90 (2H, m, ArH), 7.84-7.54 (3H, m, ArH) and 4.61 (2H, s, CH\(_2\)).

**Found:** C, 38.4; H, 4.7; N, 16.6%; \( M^+\text{HCl} \), 213.

**C\(_8\)H\(_7\)C\(_9\)N\(_5\)O\(_2\)S requires:** C, 38.4; H, 4.8; N, 16.8%; M, 249.5.

Evaporation of the ether mother liquor afforded a negligible quantity of gum.

**4-Benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a)**

(a) A solution of benzenesulphonylacetamidrazone hydrochloride (311) (2.50 g, 0.01 mol) and piperidine (1.87 g, 0.022 mol) in super-dry ethanol (40.0 ml) was stirred and treated with stirring at 0° (ice-salt bath) with a solution of toluene-p-sulphonyl azide (4.50 g, 0.022 mol) in super-dry ethanol (10.0 ml). Stirring was continued at 0° for 2 h and the mixture was then evaporated. Treatment of the resulting gum with water and chloroform afforded an insoluble solid which was combined with a second crop obtained by evaporating the chloroform extract and triturating the resulting oil with ether to give 4-benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a)
(total 0.85 g) (35%) as colourless needles m.p. 239-240° (from water), ν max. 3460, 3340 and 3280 br (NH), and 1655 br and 1605 br (NH def.) cm⁻¹.

Found: C, 40.5; H, 3.7; N, 28.9%; M⁺, 239
C₈H₉N₅O₂S requires: C, 40.2; H, 3.8; N, 29.3%; M, 239.

Evaporation of the ether mother liquor afforded a red oil (3.31 g) which was shown by t.l.c. in methylene chloride over silica to be a unresolvable multicomponent mixture.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride afforded a negligible quantity of gum.

(b) A solution of benzenesulphonylacetamidrazone hydrochloride (311) (1.00 g, 0.004 mol) and triethylamine (1.21 g, 0.012 mol) in absolute ethanol (15.0 ml) was stirred and treated at 0° (ice-salt bath) with a solution of toluene-p-sulphonyl azide (0.79 g, 0.004 mol) in absolute ethanol (5.0 ml). Stirring was continued at 0° for 3 h, and the solution was then filtered to remove a negligible amount of black tar, and evaporated. The residue obtained was treated with aqueous 2M sodium hydroxide (15.0 ml) and extracted with methylene chloride to afford a red oil (0.81 g), which was shown by t.l.c. in methylene chloride over silica to consist of four unresolvable components.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride gave no further material.

(c) A solution of benzenesulphonylacetamidrazone hydrochloride (311) (10.00 g, 0.04 mol) in absolute ethanol (80.0 ml) was treated dropwise at 0° (ice-salt bath) with stirring with a solution of sodium (1.84 g) in absolute ethanol
(96.0 ml), followed by a solution of toluene-p-sulphonyl azide (7.88 g, 0.04 mol) in absolute ethanol (32.0 ml) and stirring was continued in the melting ice-bath for 2h. The solid which had precipitated was collected (2.71 g) and dissolved in water (20.0 ml). Extraction of the resulting aqueous solution with methylene chloride afforded a negligible quantity of yellow gum. Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride gave no material.

Evaporation of the ethanol mother liquor, treatment of the residue with water (100 ml) and extraction with methylene chloride afforded an oil (4.72 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride gave no further material.

The Diazotisation and Subsequent Reaction of 4-Benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a) with Sodium Acetate

A solution of 4-benzenesulphonyl-1,5-diamino-1,2,3-triazole (308a) (0.24 g, 0.001 mol) in concentrated nitric acid (d 1.42, 0.5 ml) and water (2.5 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.30 g) in water (2.0 ml). The mixture was stirred at 0°C for 3h and then treated dropwise with a solution of sodium acetate (0.53 g) in water (2.0 ml). Stirring was continued in the melting ice-bath for 2h and the precipitated solid was collected and washed with water to afford 4-benzene-sulphonyl-1H-1,2,3-triazole-5-diazonium betaine (319) (0.20 g)
(85%) m.p. 144-152° which was identical (m.p. and i.r. spectrum) to a sample obtained later.

Extraction of the combined aqueous filtrate and washings with methylene chloride gave no further material.

**Ethyl Benzoylacetimidate (271)**

Ethyl benzoylacetimidate hydrochloride (259b) (43.32 g, 0.19 mol) was added in one portion at 0° (ice-salt bath) to a saturated solution of ethanolic ammonia (200 ml) and the resulting suspension was left stoppered at room temperature for 3 days. The insoluble ammonium chloride was filtered off and the ethanol filtrate was evaporated. Treatment of the residue with ether afforded ethyl benzoylacetimidate (271) (23.10 g) (53%) m.p. 85-90° (lit., 171 89°) which was used without further purification.

Evaporation of the ether mother liquor afforded a dark oil (0.12 g) which was discarded.

**The Attempted Reaction of Ethyl Benzoylacetimidate (271) with Formylhydrazine**

Ethyl benzoylacetimidate (271) (4.78 g, 0.025 mol) in absolute ethanol (20.0 ml) was treated in one portion with swirling with a solution of formylhydrazine (1.50 g, 0.025 mol) in absolute ethanol (10.0 ml) and the mixture was left in a refrigerator overnight. Evaporation of the resulting solution and trituration of the residue with ether afforded a solid (A) (3.60 g) m.p. 158-159° as colourless plates (from ethanol-light petroleum), \( \nu_{\text{max.}} \) 3250 br, 1675 br, and 1620 cm\(^{-1}\).
Found: C, 59.6; H, 5.6; N, 17.3%; $M^+$ 187.

Evaporation of the ether mother liquor afforded a gum (0.83 g) which was shown by t.l.c. in ethyl acetate over silica to consist of an unresolvable mixture of four components.

The Condensation Reactions of 4-Benzencesulphonyl-1,5-diamino-1,2,3-triazole (308a) with α-Dicarbonyl Compounds

The triazole (308a) (0.002 mol) and biacetyl or methylglyoxal-dimethylacetal (0.002 mol) were heated under reflux with glacial acetic acid (2.5 ml) in methanol (20.0 ml) for 5 h. The reaction mixtures were cooled, evaporated and treated with ethanol.

(i) Biacetyl afforded 3-benzenesulphonyl-6,7-dimethyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (325a) (24%) as cream plates m.p. 146-147° (from ethanol-light petroleum), which was identical (m.p., mixed m.p. i.r., $^1$H n.m.r. and mass spectra) to a sample obtained later.

(ii) Methylglyoxal-dimethylacetal afforded 3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (325b) (47%) as buff needles m.p. 216-217° (from glacial acetic acid) which was identical (m.p., mixed m.p. i.r., $^1$H n.m.r. and mass spectra) to a sample obtained later.

Evaporation of the ethanol mother liquor afforded a dark gum (0.20 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(iii) Methylglyoxal-dimethylacetal afforded 3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (325b) (47%) as buff needles m.p. 216-217° (from glacial acetic acid) which was identical (m.p., mixed m.p. i.r., $^1$H n.m.r. and mass spectra) to a sample obtained later.

Evaporation of the ethanol mother liquor afforded a red oil (0.22 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
Chapter 3

The Synthesis and Reactivity of 5-Diazo-1H-1,2,3-triazoles
Scheme 63
Scheme 64
3.1 The Synthesis and Nucleophilic Displacement Reactions of Some 1H-1,2,3-Triazole-5-diazonium Salts

3.1.1 Introduction

1H-1,2,3-Triazolediazonium salts are of interest as sources of a variety of 1H-1,2,3-triazole derivatives and as precursors of certain reactive intermediates. As has already been mentioned (Chapter 1), arenediazonium salts are important synthetic intermediates in the benzene series because of their ready preparation from virtually any primary aromatic amine and because of the wide range of nucleophilic displacement reactions which they undergo (see scheme 63). If similar displacement reactions could be applied to 1H-1,2,3-triazolediazonium salts, they would provide valuable routes to otherwise inaccessible 1H-1,2,3-triazole derivatives. Scheme 64 summarises the various possibilities. For example, synthetically useful 5-nitro-1H-1,2,3-triazoles which cannot be prepared by direct nitration might be made available by nucleophilic displacement of the diazonium group in a 1H-1,2,3-triazole-5-diazonium salt by nitrite ion [Scheme 64; (337)\[\rightarrow\](338)]. Also, successful substitution by cyanide, azide, or thiocyanate ion would lead to cyano-, azido-, and thiocyano-1H-1,2,3-triazoles [Scheme (64); (337)\[\rightarrow\](339), (340) or (341)], useful synthetic intermediates which would be difficult to obtain by other means. In addition, substitution of the diazonium group in a 1H-1,2,3-triazole-5-diazonium salt by halide ion would yield 5-halogeno-1H-1,2,3-triazoles [Scheme (64); (337)\[\rightarrow\](342), X = F, Cl, Br, I] which might in turn be useful as stable intermediates for the synthesis (by nucleophilic
Scheme 65
Scheme 66
Scheme 67
displacement) of other 1H-1,2,3-triazole derivatives [Scheme (64); (342) → (339), (340) or (341)].

As well as being potentially reactive towards nucleophilic displacement, it might be expected from their structures that 1H-1,2,3-triazole diazonium salts should undergo thermal or photochemical extrusion of nitrogen and thus act as relatively stable precursors of cyanocarbenes [Scheme 65; (343) → (347)]. It is well known that the 1,2,3-triazole ring system (348) is susceptible to photochemical extrusion of nitrogen (Scheme 66). The intermediate produced by loss of nitrogen from a 1,2,3-triazole (348) can be written as an imino-carbene (349), as a zwitterion (350), or as a diradical (351). The subsequent reactions of the intermediate which have been observed, include a photochemical Wolff rearrangement [suggesting an intermediate singlet carbene structure (349)], ring closure involving the R¹ substituent, and ring closure to a 1H-azirine followed by rearrangement to a 2H-azirine. The latter reaction appears to be a more favourable process than a Wolff rearrangement, since no ketenimines are formed in this case. Boyer and Selvarajan have investigated the photolysis of 1H-1,2,3-triazoles of type (352), and have demonstrated that the substituent R plays a key role in the efficiency of the reaction. Photolysis of 4-phenyl-1H-1,2,3-triazole (352, R=H) occurs slowly in methanol to give phenylacetetonitrile (359) and methoxyphenylacetetonitrile (360) (Scheme 67). However, 5-bromo-4-phenyl-1H-1,2,3-triazole (352, R=Br) reacts considerably faster under the
same conditions to give the same two products (359) and (360). The mechanism suggested for these reactions is that outlined in scheme 67. The first, and rate determining step of the reaction, is loss of the substituent R (Br or H) in (352), to afford the radical species (353). Abstraction of hydrogen then occurs to give the diradical (354), which can rearrange to either the azide (355) or the diazo species (356). Loss of nitrogen from the latter then follows to give the carbene (358) which reacts further with the solvent to afford the products (359) and (360). Burgess and Sanchez have also reported the photolysis of triazolefulvenes of the type (361) and (362), from which they obtained numerous products, attributable to a carbene intermediate.

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{C} & \quad \text{Ph} \\
\text{N} & \quad \text{N} \\
\text{Ph} & \quad \text{Ph} \\
\end{align*}
\]

(361)  

(362)

The photochemical reactions of arenediazonium salts have been well documented, and Kirk and Cohen have recently reported the photochemical reactions of imidazolidiazonium fluoroborates (see Chapter 1). In contrast, the photochemistry of 1H-1,2,3-triazolediazonium salts have not been investigated.

The preparation of diazonium salts, derived from amino-1,2,3-triazoles, has not been so extensively investigated as those obtained from amino-1,2,4-triazoles. However, the
\[
\begin{align*}
&\text{(363)} \\
&\text{(364)} \\
&\text{(365)}
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
a) & \quad \text{Ph} \quad \text{Ph} \\
b) & \quad \text{PhCH}_2 \quad \text{Ph} \\
c) & \quad \text{PhCH}_2 \quad \text{CONH}_2 \\
d) & \quad \text{Ph} \quad \text{CO}_2\text{Me}
\end{align*}
\]

Scheme 68
\[
\begin{align*}
\text{R} & \\
\text{a)} & \text{CONH}_2 \\
\text{b)} & \text{Ph}
\end{align*}
\]
diazotisation of the N-substituted 5-amino-1,2,3-triazoles (363 a-d) has been studied in concentrated hydrochloric and hydrobromic acids in the presence of sodium nitrite.\(^{208}\) The products obtained from these reactions were the corresponding halo compounds (365 a-d, \(X = \text{Cl or Br}\)) indicating the formation of the diazonium salts (364 a-d, \(X = \text{Cl or Br}\)) in solution. It is widely known that more stable diazonium salts are formed with oxy-acids (e.g. \(\text{HNO}_3\) and \(\text{H}_2\text{SO}_4\)) than with halogen acids (e.g. \(\text{HCl}\) and \(\text{HBr}\)). This is because the counter ion in the former case is not as good a nucleophile (i.e. \(\text{NO}_3^-\), \(\text{SO}_4^{2-}\)) as in the latter (i.e. \(\text{Cl}^-\), \(\text{Br}^-\)). Consequently, there is less risk of nucleophilic displacement of the diazonium group by such counter ions (i.e. \(\text{NO}_3^-\) or \(\text{SO}_4^{2-}\)), and thus less chance of the halo compounds (365 a-d) being formed. However, an attempt to obtain the diazonium salt (364 a, \(X = \text{NO}_3\)) by reaction of the amine (363a) in nitric acid in the presence of sodium nitrite, afforded only a multicomponent oil.\(^{178}\) Diazotisation of the aminotriazole (363a) in fluoroboric acid on the other hand, gave a fairly stable crystalline solid, whose spectral properties are in accord with its being the diazonium fluoroborate (364a, \(X = \text{BF}_4\)).\(^{178}\) Diazotisation of the amine (366a) using sodium nitrite in acetic acid has been reported to give the diazonium betaine (367), which is unstable and readily cyclises to 2,8-diazohypoxanthine (368).\(^{24}\) Recently however, the triazole diazonium salts (369 a and b) have been isolated as stable crystalline solids\(^{178,208}\) formed by treatment of the corresponding amines (366a and b) with amyl nitrite in the presence
Scheme 70
Scheme 72

(376) → (378)

(377)

Scheme 72
of hydrogen chloride. Regitz et al\textsuperscript{166,209} have reported the preparation of the diazonium betaine (372) and the diazonium salt (373) by reaction of the respective N-tosylamine (370) and the N-H amine (371) with nitrous acid.

Nucleophilic displacement reactions of N-substituted 1,2,3-triazole diazonium salts by halide ions have been achieved \textit{in situ} (cf. page 101).\textsuperscript{178,208} The ease of these reactions contrasts with the relative difficulty of converting benzenediazonium salts into aryl halides, such substitution reactions normally requiring the presence of a copper catalyst (see Chapter 1). The direct halogenation reactions of the 1,2,3-triazole diazonium salts (364) probably involve the formal substitution of the diazonium cation by halide ion. Such a process may occur by way of a resonance stabilised intermediate of the type \([(374)\leftrightarrow(375)]\), obtained by nucleophilic attack of the halide ion (X) on the diazonium salt (364) (Scheme 71). Formation of the stabilised intermediate \([(374)\leftrightarrow(375)]\) probably accounts for the ready displacement of the 1,2,3-triazole diazonium cations compared with their benzene counterparts, which cannot form such stabilised intermediates. The attempted synthesis of the fluoro-1,2,3-triazole (377) from the corresponding diazonium fluoroborate (376) by the Schiemann procedure however, was unsuccessful, only the deaminated triazole (378) being obtained.\textsuperscript{178}

In contrast to the N-substituted 1,2,3-triazole diazonium salts, few nucleophilic displacement reactions have been reported for 1H-1,2,3-triazole-5-diazonium salts. However, Shealy and O'Dell\textsuperscript{210} have reported the synthesis of
PhCH$_2$-N$\equiv$N$\equiv$N$\equiv$N=N-NH$_2$  \hspace{1cm} \rightarrow \hspace{1cm} $\text{HN-}$ \text{f-L k NH}_2$

R

a) Ph  
b) CONH$_2$  
c) CN  
d) SO$_2$Ph

\[
\begin{align*}
\text{HN} & \text{f-L k NH}_2\\
\text{R} & \text{NEN X}^- 
\end{align*}
\]

R  \hspace{1cm} X

a) Ph  \hspace{1cm} Cl  
b) CONH$_2$  \hspace{1cm} Cl  
c) CN  \hspace{1cm} Cl  
d) SO$_2$Ph  \hspace{1cm} Cl  
e) CONH$_2$  \hspace{1cm} NO$_3$  
f) CN  \hspace{1cm} NO$_3$  
g) SO$_2$Ph  \hspace{1cm} NO$_3$  
h) SO$_2$Ph  \hspace{1cm} BF$_4$

Scheme 73
\[ \text{(383)} \]
\[ \text{(385)} \]

- \( R \)
  - a) Ph
  - b) CONH_2
  - c) CN
  - d) SO_2 Ph

\[ \text{(387)} \]
5-iodo-1,2,3-triazole-4-carboxamide (379) from the diazonium betaine (367) by treatment with iodine and potassium iodide.

\[
\begin{align*}
\text{(367)} & \quad \text{CONH}_2 \\
\rightarrow & \\
\text{(379)} & \quad \text{CONH}_2 \\
\end{align*}
\]

The following studies were undertaken in an attempt to synthesise new 1H-1,2,3-triazole-diazonium derivatives, and to investigate the displacement reactions of these and related compounds.

3.1.2 The Synthesis of Some 4-Substituted-1H-1,2,3-triazole-5-diazonium Salts

As mentioned previously, work in this department has shown\textsuperscript{178,211} that the 4-substituted 5-amino-1H-1,2,3-triazoles (381a and b) [obtained by debenzylation of the respective N-benzyl-1,2,3-triazoles (380a and b)\textsuperscript{157,167} using sodium and liquid ammonia] can be diazotised by treatment with amyl nitrite in the presence of hydrogen chloride to give the corresponding stable diazonium chlorides (382a and b).

Treatment of a solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) with a saturated aqueous solution of sodium carbonate afforded a crystalline solid whose elemental analysis and spectral properties are in accord with the diazonium betaine structure (383a). The betaine (383a) is
reasonably stable when stored at 0\(^\circ\) in a dark container. The conversion of the diazonium salt (382a) into the betaine (383a) is analogous to transformations undergone by other five-membered heterocyclic diazonium salts (see Chapter 1). 1H-Pyrrolediazonium salts for example readily undergo deprotonation, even in dilute acid to afford the corresponding betaines. Reaction of 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (382 b) however, using the same conditions which proved successful for the conversion of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) into the 4-phenyl-1,2,3-triazole-5-diazonium betaine (383a), afforded only a solid, which was judged to be inorganic. Shealy et al.\(^{24}\) have reported the synthesis of the betaine (383b), which they obtained directly by diazotisation of 5-amino-1H-1,2,3-triazole-4-carboxamide (381b) in a weakly acidic medium (i.e. aqueous acetic acid). Treatment of the amine (381b) under these conditions however, resulted only in the isolation of a negligible quantity of a solid, and a red oil, shown by t.l.c. to be a multicomponent mixture. The attempted reaction of the diazonium nitrate (382e), [prepared \textit{in situ} by reaction of the amine (381b) with sodium nitrite in concentrated nitric acid] with an aqueous solution of sodium acetate afforded a solid, having properties essentially identical to 1,2,3-triazolo-[4,5-d]-1,2,3-triazin-7(6H)-one (384) reported by Shealy et al.\(^{24}\)
In an attempt to obtain the cyano substituted diazonium salt (382c), a methanol solution of the known amine (381c) was treated with amyl nitrite in the presence of hydrogen chloride. This resulted in the isolation of an unidentified solid which defied crystallisation, and whose spectral properties did not suggest any plausible structure. Treatment of this solid with aqueous sodium acetate, in an attempt to observe possible diazonium betaine formation, resulted in the isolation of a second solid, which likewise could not be characterised, and whose i.r. spectrum was ill-defined and did not suggest a readily assignable structure. Alternative treatment of a solution of the amine (381c) in glacial acetic acid with amyl nitrite and hydrogen chloride afforded a solid whose i.r. spectrum and explosive character suggested it to be the required diazonium salt (382c). However, treatment of this solid with an aqueous solution of sodium carbonate, in an attempt to form the diazonium betaine (383c) afforded an amorphous solid which showed an ill-defined i.r. spectrum, and could not be crystallised. In a further attempt to isolate the cyano substituted
diazonium betaine (383c), the amine (381c) was diazotised with sodium nitrite in nitric acid and the resulting solution of the diazonium nitrate (382f) was then neutralised with sodium acetate. However, no identifiable material was isolated by this procedure.

The diazotisation of 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (381d) (prepared as described in Chapter 2) using amyl nitrite and hydrogen chloride, under conditions identical to those which had proved successful for the preparation of the diazonium salts (382a and b), resulted in the isolation of a solid whose elemental analysis and spectral properties were consistent with its being the diazonium betaine (383d), and not the expected diazonium chloride (382d). The betaine (383d) readily formed a soluble sodium salt with aqueous sodium hydroxide and aqueous sodium carbonate, but was unaffected when treated with aqueous sodium hydrogen carbonate. In an attempt to protonate the betaine (383d) to form the diazonium chloride (382d), its solution in dioxan was treated with hydrogen chloride. This treatment resulted in the formation of a small quantity of an unidentified solid, and a yellow gum which was shown by t.l.c. examination to be a multicomponent mixture. Likewise, treatment of 4-benzenesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (383d) with fluoroboric acid in an attempt to isolate the diazonium fluoroborate (382h), resulted only in a low recovery of the starting material. Diazotisation of the amine (381d) with sodium nitrite in nitric acid, followed by neutralisation of the solution of the presumed
diazonium nitrate (382g) with sodium acetate also resulted in the formation of the diazonium betaine (383d) in good yield.

3.1.3 Nucleophilic Displacement Reactions of Some
4-Substituted-1H-1,2,3-triazole-5-diazonium Salts

Aromatic diazonium salts readily undergo nucleophilic displacement reactions as has already been described (see Chapter 1). However, few nucleophilic displacement reactions of 1H-1,2,3-triazolediazonium salts have been reported. As previously stated (Chapter 3.1.1), work in this department\(^{178,208}\) has demonstrated that nucleophilic displacement reactions of N-substituted-1,2,3-triazole-5-diazonium salts occur during their attempted preparation. It was shown that these reactions occurred in the absence of copper catalysts, which are usually required for similar reactions with benzenediazonium salts. As a follow up to this work, it was decided to investigate the uncatalysed nucleophilic displacement reactions of the diazonium salts (382a, b, f and g) and the diazonium betaine (383d). As noted before, the diazonium salts (382a) and (382b) were readily to hand as reasonably stable solids, whereas it was proposed to prepare and study the diazonium nitrates (382f) and (382g) in nitric acid solution.

Treatment of a solution of the diazonium salt (382a) in aqueous dioxan with a solution of sodium azide in aqueous dioxan resulted in the isolation of 5-azido-4-phenyl-1H-1,2,3-triazole (385a) in excellent yield. However, the
Scheme 74
attempted conversion of the 4-carbamoyl-1H-1,2,3-triazole-5-
diazonium chloride (382b) into the corresponding azide (385b)
under conditions successful for the phenyl-substituted
diazonium salt gave no identifiable product. The azide
(385a) was also obtained in much lower yield from the reaction
of the diazonium salt (382a) with sodium azide when ethanol
was used as the co-solvent. When a solution of the diazonium
nitrate (382g) was treated with an aqueous solution of sodium
azide, 5-azido-4-benzenesulphonyl-1H-1,2,3-triazole (385d)
was obtained in quantitative yield. The reaction of 4-
benzenesulphonyl-1,2,3-triazole-5-diazonium betaine (383d)
with an aqueous solution of sodium azide also readily afforded
the azidotriazole (385d) in excellent yield. Treatment of
the diazonium nitrate (382f) under identical conditions
however, resulted in only a moderate yield of the corresponding
azide (385c). The azides (385a, c and d) all gave elemental
analysis and spectral data consistent with the assigned
structures (385a, c and d). The question arises as to the
mechanism involved in the transformations of the diazonium
compounds (382a, f and g) and (383d) into the corresponding
azido-1,2,3-triazoles. By analogy with the mechanism accepted
for the reaction of benzenediazonium salts with azide ion to give
azidobenzene derivatives (cf. chapter 1) it is assumed
in the present reactions that the initial formation and
decomposition of a 1,2,3-triazolylpentazole intermediate
(386) is involved (scheme 74).
Scheme 75
The successful preparation of the azidotriazoles (385a, c and d) prompted further investigations on the reactions of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) with other nucleophilic reagents. This particular diazonium salt was chosen because of its stability in the solid state, hence allowing its study in isolation, using a variety of different reaction conditions. In an attempt to introduce the thiocyanosubstituent into the 1,2,3-triazole ring, the diazonium salt (382a) was reacted with an aqueous ethanolic solution of sodium thiocyanate. However, the sole product, isolated in moderate yield, from this reaction, was the known deaminated triazole (387). The reductive deamination of diazonium salts in alcoholic solution is a well known process. Replacement of a diazonium group in a 1,2,3-triazole by hydrogen has previously been observed by Thiele and Schleussner in their studies of the diazotisation of 5-amino-4-hydroxy-2-phenyl-1,2,3-triazole (388). They observed that warming a solution of the diazonium salt (389) derived from (388), with copper powder, resulted in its deamination to (390). In an attempt to avoid the dediazoniation of the diazonium salt (382a) by hydrogen, which apparently occurs in an aqueous alcoholic medium, the reaction of the salt (382a) with sodium thiocyanate in aqueous dioxan was investigated. However, this procedure resulted in the formation of a red oil whose t.l.c. showed it to be an unresolvable multicomponent mixture.

Reaction of the diazonium salt (382a) with sodium cyanide in aqueous ethanolic solution resulted in the formation of an amorphous brown solid which had an ill-defined i.r. spectrum and from which no identifiable material could be obtained.
The attempted reaction of the diazonium salt (382a) with iodide ion in aqueous methanolic solution also resulted in deamination to give 4-phenyl-1H-1,2,3-triazole (387). On the other hand, the attempted replacement of the diazonium group in the salt (382a) by nitrite ion using sodium nitrite in aqueous ethanol led to the formation of the diazonium betaine (383a). The reason for the different course of this reaction compared with the deamination observed in other cases (see before), is not clear. One possibility is that in the case of aqueous ethanolic sodium nitrite the solution is basic enough (due to some hydrolysis of the sodium nitrite to sodium hydroxide) to permit deprotonation to the betaine (383a) which is then stable to further dediazoniation.

Having failed to replace the diazonium group in the salt (382a) by simple nucleophiles in the absence of copper catalysts, an attempt was made to demonstrate a copper catalysed nucleophilic displacement with the salt (382a). However, the reaction of the latter with cuprous chloride failed to effect its conversion into the chloro-1,2,3-triazole, no identifiable material being recovered from this reaction.

3.1.4 Photochemical Transformations of 5-Diazo-1H-1,2,3-triazole Betaines

1H-1,2,3-Triazoles, when subjected to photochemical irradiation, have been shown to undergo homolytic ring scission involving the loss of molecular nitrogen. 206 1H-1,2,3-Triazolediazenium compounds should also possess
this same ability. Thus, 4-phenyl-1H-1,2,3-triazole-5-diazonium betaine (383a) was irradiated in dry benzene in a medium pressure photochemical reactor, under an atmosphere of dry nitrogen. These conditions afforded a red oil, chromatography of which gave a solid whose elemental analysis and $^1$H n.m.r. i.r. and mass spectra were all in accord with the known\textsuperscript{214} 7-cyano-7-phenylnorcaradiene (392). Further evidence for this structure was obtained by the unambiguous synthesis of (392). Ciganek\textsuperscript{214} reports that thermolysis of phenylcyanodiazomethane (391) in benzene affords the norcaradiene (392). Preparation of phenylcyanodiazomethane (391) by the method outlined by Breslow and Yaun,\textsuperscript{215} followed by thermolysis in benzene afforded an oil. Chromatography of the oil gave the norcaradiene (392), identical in all respects (m.p., mixed m.p. and i.r. spectrum) to the product obtained by the photolysis of the betaine (383a) in benzene. The norcaradiene (392) is reported\textsuperscript{214} to be in equilibrium with the cycloheptatriene (394), but the structure (392) predominates at room temperature.\textsuperscript{214}

Chromatography of the original red oil also gave a solid which contained an absorption band at 2220 cm$^{-1}$ in its i.r. spectrum, and whose elemental analysis and mass spectrum were in accord with the molecular formula C$_{22}$H$_{16}$N$_2$. This product is tentatively assigned the structure (393). Supporting $^1$H n.m.r. evidence for the structure (393) could not be obtained due to the insolubility of the compound even in [\textsuperscript{2}H$_6$] dimethyl sulfoxide. The proposal of the structure (393) is based on work by Regitz\textsuperscript{216} and his co-workers. They
Scheme 77
\[ \begin{align*}
\text{Me} \quad \begin{array}{c}
\text{N} \equiv \text{N} \\
\downarrow \\
\text{Me} - \text{C} - \text{OMe}
\end{array} \\
\text{(400)}
\end{align*} \]

\[ \begin{align*}
\text{(401)} & \quad \text{(402)} & \quad \text{(403)} \\
\text{Me} & \quad \text{Me} & \quad \text{Me}
\end{align*} \]

Scheme 78
Scheme 79
observed that the photolysis of diazomethane derivatives of
the type (396) in benzene readily affords the noncaradienes
(398) and the 3,8-diaryl-3,8-bis-tricyclo[5.1.0.0.2.4]
oct-5-enes (399). It has also been reported\(^{217}\) that
thermolysis of methyl diazoacetate (400) in benzene yields
the expected norcaradiene (401), as well as the two adducts
(402) and (403). The tentative assignment of structure
(393) to the photolysis product of the diazonium betaine
(383a) is therefore based on these reports. However, it is
equally probable that (393) exists as, or is in equilibrium
with, the cyclooctatriene (395), formed by valence isomeris-
ation of (393).

The question arises as to the mechanism involved in
the photolysis of the betaine (383a) in benzene. Clearly,
Ciganek's results\(^ {214}\) are consistent with the intermediate
formation of phenylcyanocarbene, and the isolation of the
norcaradiene (392) from the photolysis of 4-phenyl-1,2,3-
triazole-5-diazonium betaine (383a) also strongly suggests
the intermediate formation of the same carbene. This
proposal is supported by the work of Boyer and Selvarajan.\(^ {206}\)
These workers report that photolysis of 1H-1,2,3-triazoles
results in products derived by further reaction of carbene
intermediates. Formation of the norcaradiene (392) from
the betaine (383a) is thus suggested to involve the
mechanism outlined in Scheme 79. Loss of nitrogen to form
the diradical (404) is followed by ring opening to the diazo
structure (405). Loss of a second molecule of nitrogen
then affords the carbene (406), which readily inserts into
the benzene solvent to give the norcaradine (392).
Scheme 80
The formation of (393) is explained by further insertion of phenylcyanocarbene into the norcaradiene (392), (cf. Scheme 79). Further evidence for the formation of a carbene intermediate in the photolytic decomposition of the betaine (383a) is provided by its photolysis in acetonitrile. The isolation of the known\textsuperscript{218} 9,10-dicyanophenanthrene (411) in this reaction can be explained by dimerisation of phenylcyanocarbene to afford the stilbene (407), which is known\textsuperscript{218,219} to undergo photocyclisation to (411), (cf. Scheme 80).

In an attempt to obtain further information on the mode of photolytic breakdown of the diazonium betaine (383a), its photolysis in other solvents was investigated. Photolysis in acetone gave an unidentified oil (B) whose elemental analysis and mass spectrum indicated the molecular formula C\textsubscript{14}H\textsubscript{16}NO\textsubscript{2}. The i.r. spectrum of the oil (B) showed absorption at 2230 and 1725 cm\textsuperscript{-1}, consistent with the presence of a cyano and a carbonyl group respectively. Examination of the \textsuperscript{1}H n.m.r. spectrum of the oil (B) showed a singlet at \(\delta\) 7.44 p.p.m., attributable to equivalent aromatic protons. Singlets at \(\delta\) 1.71, 1.58, 1.04 and 0.78 p.p.m., and a poorly resolved doublet at \(\delta\) 1.64 p.p.m. were also present. The attempted preparation of a hydrazine derivative by reaction of the oil (B) with hydrazine afforded only a dark yellow oil, shown by t.l.c. examination to be an unresolvable multicomponent mixture. Lack of time prevented a more detailed study of the oil (B), whose structure must await the outcome of further investigations.
Scheme 81
Photolysis of the betaine (383a) in ethanol solution resulted in the isolation of 4-phenyl-1H-1,2,3-triazole (387). This product is readily explained by abstraction of hydrogen from the ethanol solvent by intermediate (404) [postulated earlier in Scheme 79] to afford the triazole (387) (see Scheme 81). Further photolysis of (387) is conceivable, but according to Boyer and Selvarajan, photolytic breakdown of 4-phenyl-1H-1,2,3-triazole (387) is very slow, thus accounting for its isolation in the present work. The attempted thermolysis of the betaine (383a) in ethanol resulted in the recovery of the unreacted starting material, indicating that the formation of (387) is the result of a photochemical, rather than a thermal process.
3.1.5 Experimental

(For general experimental procedures, see Appendix).

The Preparation of the 5-Amino-1H-1,2,3-triazoles (381 a-d)

5-Amino-4-phenyl-1H-1,2,3-triazole (381a) was prepared (yield 76%) by the method of Tennant and Sutherland\(^{157}\) and had m.p. 103-107\(^\circ\) (lit., 167, 125\(^\circ\)).

5-Amino-1H-1,2,3-triazole-4-carboxamide (381b) was prepared by the method of Hoover and Day\(^{167}\) in 80% yield, m.p. 218-221\(^\circ\) (lit., 167, 225\(^\circ\)).

5-Amino-4-cyano-1H-1,2,3-triazole (381c) and 5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (381d) were prepared as described earlier (cf. pages 66 and 68 respectively).

The Preparation of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (382a), and 4-Carbamoyl-1H-1,2,3-triazole-5-diazonium Chloride (382b)

4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) was prepared (yield 79%) by the method of Mackie and Tennant\(^{211}\) and was used without further purification.

4-Carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (382b) was prepared (yield 84%) by the method of Tennant and Vevers\(^{178}\) and was used without further purification.

4-Cyano-1H-1,2,3-triazole-5-diazonium Chloride (382c)

(a) A solution of 5-amino-4-cyano-1H-1,2,3-triazole (381c) (1.10 g, 0.01 mol) in methanol (25.0 ml) was cooled to 0\(^\circ\) (ice-salt bath) saturated with dry hydrogen chloride
and treated, dropwise with stirring at 0° with amyl nitrite (2.40 g, 0.012 mol). The mixture was stirred at 0° for 1.5h, and the amorphous solid which had precipitated was collected (1.11g) m.p. 170-194° (decomp.). This solid left a residue when burnt, showed an ill-defined i.r. spectrum, and could not be crystallised. When treated with aqueous sodium acetate it afforded a yellow solid (0.89 g) m.p. 129-151° (decomp.) which likewise showed an ill-defined i.r. spectrum, and could not be crystallised.

(b) A solution of the aminotriazole (381c) (1.10 g, 0.01 mol) in glacial acetic acid (30.0 ml) was cooled to 0° (ice-salt bath), saturated with dry hydrogen chloride and treated dropwise with stirring at 0° with amyl nitrite (2.40 g, 0.012 mol). The mixture was stirred at 0° for 1h then filtered to afford 4-cyano-1H-1,2,3-triazole-5-diazonium chloride (382c) (0.62 g) (40%) m.p.100-105° (explosive decomp.) as a cream powder, v_max. 3310 br and 3130 br (NH), 2250 br (CN, $\equiv$N) and 1820 br ($\equiv$N) cm⁻¹.

Dilution of the acetic acid filtrate with ether afforded unreacted amine (381c) (0.09 g) m.p. 210-220° (decomp.) which was identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether-acetic acid mother liquor gave a dark gum (1.11 g) which was shown by t.l.c. in ethyl acetate over alumina to be an unresolvable multicomponent mixture.
The Attempted Preparation of 4-Benzencesulphonyl-1H-1,2,3-triazole-5-diazonium Fluoroborate (382h)

The diazonium betaine (383d) (0.23 g, 0.001 mol) in glacial acetic acid (10.0 ml) was treated with swirling with a solution of 40% w/v fluoroboric acid (0.5 ml) and the resulting solution was allowed to stand at room temperature for 24 h. The solution was then diluted with ether to afford unreacted starting material (0.03 g) m.p. 155-159° which was identical (m.p. and i.r. spectrum) to an authentic sample.

The ether-acetic acid mother liquor was extracted with methylene chloride and after washing with saturated aqueous sodium hydrogen carbonate and water was evaporated to afford a negligible quantity of gum.

Acidification of the combined aqueous washings with aqueous 2M hydrochloric acid and extraction with methylene chloride afforded a negligible quantity of an oil.

The Attempted Preparation of 4-Benzencesulphonyl-1H-1,2,3-triazole-5-diazonium Chloride (382d)

The diazonium betaine (383d) (0.23 g, 0.001 mol) in freshly distilled dioxan (30.0 ml) was saturated (ca. 15 mins) at 0° (ice-salt bath) with dry hydrogen chloride. The resulting solution was evaporated and the residue was triturated with ethyl acetate to afford a small quantity of an unidentified solid (0.07 g) m.p. 135-143°.

Evaporation of the ethyl acetate mother liquor gave a yellow gum (0.18 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
A suspension of 4-phenyl-1H-1,2,3-triazole-5-diazoium chloride (382a) (2.66 g, 0.012 mol) in chloroform (40.0 ml) was cooled to 0° (ice-salt bath) and treated dropwise with stirring with a saturated solution of aqueous sodium carbonate (40.0 ml). The mixture was stirred in the melting ice-bath for 10 min. and the chloroform layer was then separated and evaporated to afford 4-phenyl-1H-1,2,3-triazole-5-diazoium betaine (383a) (1.99 g) (97%) m.p. 131-132° as yellow needles (from ethanol), ν_max. 2180 br (N≡N) cm⁻¹.

Found: C, 56.0; H, 3.1; N, 41.2%; M⁺, 171
C₈H₅N₅ requires: C, 56.1; H, 2.9; N, 40.9%; M, 171

The Attempted Preparation of 4-Carbamoyl-1H-1,2,3-triazole-5-diazoium Betaine (383b)

(a) The method described by Shealy et al.²⁴ was carried out as follows. A solution of the aminotriazole (381b) (1.0 g) in water (7.0 ml) was added to 70% v/v aqueous acetic acid (43.0 ml), cooled to 5° (ice-salt bath) and treated dropwise with stirring with amyl nitrite (1.3 ml). Stirring was continued in the melting ice-bath overnight.

Evaporation of the resulting solution and trituration of the red oil with methanol afforded a small quantity of unidentified solid (0.03 g) m.p. 215-220°.

Evaporation of the methanol mother liquor gave a red oil (0.44 g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multi-component mixture.
(b) 4-Carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (382b) (0.36 g, 0.002 mol) in chloroform (10.0 ml) was cooled to 0° (ice-salt bath) and treated dropwise with stirring with a saturated solution of aqueous sodium carbonate (10.0 ml). The mixture was stirred in the melting ice-bath for 10 min. and the chloroform layer was separated and evaporated to afford a negligible quantity of solid.

Concentration of the aqueous mother liquor gave only inorganic material.

(c) A suspension of 5-amino-1H-1,2,3-triazole-4-carboxamide (381b) (1.27 g, 0.01 mol) in concentrated aqueous nitric acid (d, 1.42, 5.0 ml) and water (15.0 ml) was cooled to 0° (ice-salt bath) and treated dropwise with stirring with a solution of sodium nitrite (2.5 g) in water (10.0 ml). The resulting solution was stirred at 0° for 15 min. and then treated at 0° with stirring with a solution of sodium acetate (2.5 g) in water (15.0 ml). The mixture was stirred in the melting ice-bath for 2 h, washed with chloroform and neutralised with aqueous 2M sodium hydroxide to afford a solid. This was combined with a second crop which separated from the neutral aqueous mother liquor on standing at room temperature to give 1,2,3-triazolo[4,5-d]-1,2,3-triazin-7(6H)-one (384) (total 0.68 g) (49%) m.p. 222° (explosive decomp.) (lit.,24 270° explosive decomp.).

Extraction of the aqueous mother liquor with chloroform gave no further material.
The Attempted Preparation of 4-Cyano-1H-1,2,3-triazole-5-diazonium Betaine (383c)

(a) A suspension of 4-cyano-1H-1,2,3-triazole-5-diazonium chloride (382c) (0.47 g, 0.003 mol) in methylene chloride (10.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a saturated aqueous solution of sodium carbonate (10.0 ml) and stirring was continued at 0°C for 15 min. Evaporation of the methylene chloride layer gave no material.

The basic aqueous layer was neutralised with glacial acetic acid to afford an amorphous solid (0.46 g) m.p. 220-226°C (decomp.) which showed an ill-defined i.r. spectrum and could not be characterised.

Extraction of the neutral aqueous mother liquor with methylene chloride gave no further material.

(b) A solution of 5-amino-4-cyano-1H-1,2,3-triazole (381c) (0.55 g, 0.005 mol) in concentrated nitric acid (d 1.42, 0.5 ml) and water (1.5 ml) was cooled to 0°C (ice-salt bath) and treated dropwise with stirring at 0°C with a solution of sodium nitrite (0.3 g) in water (3.5 ml). The mixture was stirred at 0°C for 15 min. and then treated with stirring at 0°C with a solution of sodium acetate (0.53 g) in water (1.3 ml). The mixture was stirred in the melting ice-bath for 2 h and then extracted with methylene chloride to afford a negligible quantity of gum.

Neutralisation of the basic aqueous mother liquor with glacial acetic acid and extraction with methylene chloride gave no material.
Evaporation of the neutral aqueous mother liquor and extraction of the residue with boiling ethyl acetate gave no further material.

4-Benzencesulphonyl-1H-1,2,3-triazole-5-diazonium Betaine (383d)

(a) A suspension of 5-amino-4-benzencesulphonyl-1H-1,2,3-triazole (381d) (3.14 g, 0.014 mol) in concentrated nitric acid (d 1.42, 7.5 ml) and water (20.0 ml) was cooled to 0°C (ice-salt bath) and treated dropwise with stirring at 0°C with a solution of sodium nitrite (3.5 g) in water (15.0 ml). The mixture was stirred at 0°C for 15 min. and then treated with stirring at 0°C with a solution of sodium acetate (3.5 g) in water (20.0 ml). The mixture was stirred in the melting ice-bath for 2h and the precipitated solid was collected and washed with water to afford 4-benzencesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (383d) (3.26 g) (99%) m.p. 158-159°C as colourless plates (from glacial acetic acid), νmax. 2230 (N=N) cm⁻¹.

Found: C, 41.0; H, 2.1; N, 29.5%; M⁺, 235.

C₈H₅N₅O₂S requires: C, 40.9; H, 2.1; N, 29.8%; M, 235.

(b) 5-Amino-4-benzencesulphonyl-1H-1,2,3-triazole (381d) (0.90 g, 0.004 mol) in Analar methanol (20.0 ml) was saturated at 0°C (ice-salt bath) with dry hydrogen chloride, then treated dropwise with stirring at 0°C with amyl nitrite (0.63 g, 0.005 mol). Stirring was continued in the melting ice-bath for 2h and the solid which precipitated was collected and combined with a second crop obtained by concentrating the methanol mother liquor to afford 4-benzencesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (393d) (total 0.67 g) (71%)
m.p. 156-158° which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Evaporation of the methanol mother liquor afforded a small quantity of gummy semi-solid (0.06 g) which was discarded.

The betaine (383d) was readily soluble in aqueous 2M sodium hydroxide and aqueous sodium carbonate, but was insoluble in aqueous sodium hydrogen carbonate.

The Preparation of some 5-Azido-1H-1,2,3-triazoles

(a) A solution of the diazonium salts (382a) or (382b) (0.002 mol) in freshly distilled dioxan (10.0 ml) and water (10.0 ml) was added dropwise with stirring to a solution of sodium azide (0.26 g, 0.004 mol) in freshly distilled dioxan (5.0 ml) and water (2.5 ml) at 0° (ice-salt bath). Stirring was continued in the melting ice-bath for 0.5 h. The mixture was then evaporated and the residue treated with water, and any insoluble solid collected.

(i) 5-Azido-4-phenyl-1H-1,2,3-triazole (385a) (91%) formed colourless needles m.p. 129-130° (from benzene); $\nu_{\text{max}}$ 3140 br (NH) and 2140 (N==T) cm$^{-1}$.

Found: C, 50.9; H, 3.2; N, 44.1%; $M^+$, 186.

$C_8H_6N_6$ requires: C, 51.6; H, 3.2; N, 45.2%; M, 186.

(ii) 4-Carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (382b) gave a solution which yielded no material on extraction with chloroform.

Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with chloroform likewise gave no material.
(b) A solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) (0.42 g, 0.002 mol) in ethanol (10.0 ml) and water (10.0 ml) was added dropwise with stirring at 0°C (ice-salt bath) to a solution of sodium azide (0.26 g, 0.004 mol) in ethanol (5.0 ml) and water (2.5 ml). Stirring was continued in the melting ice-bath for 0.5 h and the solution was then heated at 100°C for 0.5 h. The mixture was cooled and evaporated and the residue was treated with water to afford 5-azido-4-phenyl-1H-1,2,3-triazole (385a) (0.14 g) (38%) m.p. 127-128°C which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Extraction of the aqueous mother liquor with chloroform gave no further material.

(c) A suspension of the aminotriazoles (381c) or (381d) (0.005 mol) in concentrated nitric acid (d 1.42, 0.5 ml) and water (1.5 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.3 g) in water (1.5 ml). The mixture was stirred at 0°C for 15 min. and then treated dropwise at 0°C with a solution of sodium azide (0.65 g, 0.01 mol) in water (5.0 ml). Stirring was continued in the melting ice-bath for 0.5 h, and any solid deposited was collected.

(i) 5-Amino-4-cyano-1H-1,2,3-triazole (381c) gave a solution which when extracted with chloroform afforded 5-azido-4-cyano-1H-1,2,3-triazole (385c) (30%) as colourless needles m.p. 133-134°C (from toluene), νₘₐₓ. 2250 (CN) and 2160 (N≡N=N) cm⁻¹.
Found: C, 26.9; H, 0.8; N, 72.1%; M⁺, 135
C₃H₇N₇ requires: C, 26.7; H, 0.7; N, 72.6%; M, 135.

(ii) 5-Azido-4-benzenesulphonyl-1H-1,2,3-triazole (385d)
(100%) formed cream plates m.p. 139-140° (from toluene),
νmax. 3250 br (NH) and 2140 (N=N=N) cm⁻¹.

Found: C, 38.7; H, 2.4; N, 32.9%; M⁺, 250.
C₈H₆N₆O₂S requires: C, 38.5; H, 2.5; N, 33.6%; M, 250.

(d) A solution of the diazonium betaine (383d) (0.45 g, 0.002 mol) in ethanol (50.0 ml) and water (10.0 ml) was
treated dropwise at room temperature with vigorous stirring
with a solution of sodium azide (0.26 g, 0.004 mol) in water
(10.0 ml). The mixture was stirred at room temperature for
0.5 h then concentrated to remove the ethanol and acidified
with aqueous 2M hydrochloric acid to afford 5-azido-4-benzenesulphonyl-1H-1,2,3-triazole (385d) (0.40 g) (80%) m.p. 136-139°
which was identical (m.p. and i.r. spectrum) to a sample
obtained in (c) before.

The Attempted Nucleophilic Displacement Reactions of 4-Phenyl-
1H-1,2,3-triazole-5-diazonium Chloride (382a)

(a) A solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium
chloride (382a) (0.42 g, 0.002 mol) in ethanol (10.0 ml) and
water (10.0 ml) was added dropwise with stirring at 0° (ice-
salt bath) to a solution of sodium thiocyanate, sodium nitrite
or sodium cyanide (0.004 mol) in ethanol (5.0 ml) and water
(2.5 ml). Stirring was continued in the melting ice-bath
for 0.5 h, and any solid deposited was collected.
(i) Reaction with sodium thiocyanate gave a solution which when concentrated to remove the ethanol and extracted with chloroform afforded 4-phenyl-1\(\text{H}\)-1,2,3-triazole (387) (59\%) m.p. 144-145° (lit., \(\text{mp}^\text{2}12\) 143-145°).

(ii) Reaction with sodium nitrite gave a solution which when concentrated to remove the ethanol afforded a solid. This was combined with a second crop obtained by extracting the aqueous mother liquor with methylene chloride and triturating the gummy semi-solid with ethyl acetate-light petroleum to afford 4-phenyl-1\(\text{H}\)-1,2,3-triazole-5-diazonium betaine (383a) (76\%) m.p. 128-131° which was identical (m.p. and i.r. spectrum) to a sample obtained before.

(iii) Reaction with sodium cyanide afforded an amorphous brown solid, which was combined with two further crops, obtained by concentrating the aqueous ethanol mother liquor and extracting the aqueous solution with chloroform and by acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid (total 0.15 g) m.p. 180-195° (decomp.), i.r. spectrum ill-defined. The attempted crystallisation of the amorphous brown solid from a variety of solvents was unsuccessful and it was shown by t.l.c. in methylene chloride over silica to be an unresolvable mixture of four components.

Neutralisation of the acidic aqueous mother liquor with aqueous 2M sodium hydroxide and extraction with methylene chloride afforded only a negligible quantity of gum.

(b) A solution of the diazonium salt (382a) (0.42 g, 0.002 mol) in distilled dioxan (10.0 ml) and water (10.0 ml) was added dropwise with stirring at 0° (ice-salt bath) to a
solution of sodium thiocyanate (0.32 g, 0.004 mol) in distilled dioxan (5.0 ml) and water (2.5 ml) and stirring was continued in the melting ice-bath for 0.5 h. The solution obtained was evaporated and the gummy residue was treated with water and extracted with chloroform to afford a red oil (0.39 g) which partially solidified on standing and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multi-component mixture.

(c) A solution of the diazonium salt (382a) (0.77 g, 0.0037 mol) in methanol (20.0 ml) and water (10.0 ml) was cooled to 0°C (ice-salt bath) and treated dropwise with vigorous stirring with a solution of sodium iodide (0.70 g, 0.0047 mol) in water (15.0 ml). After the initial vigorous effervescence had ceased, the resulting red solution was heated at 100°C for 0.5 h, then cooled and extracted with ether to give a gum. Trituration of the gum with benzene afforded 4-phenyl-1H-1,2,3-triazole (387) (0.17 g) (32%) m.p. 140-143°C which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before. Evaporation of the benzene mother liquor gave no further material.

Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with chloroform likewise gave no material.

(d) A solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (382a) (0.16 g, 0.0008 mol) in aqueous 6M hydrochloric acid (5.0 ml) was added dropwise with stirring at 0°C (ice-salt bath) to a freshly prepared solution of cuprous chloride (0.002 mol) in 6M aqueous hydrochloric acid (1.1 ml). The solution obtained was then allowed to reach room temperature and then heated at 60°C for 15 min. cooled and left at room temperature for 20 h. Extraction of the
mixture directly or after neutralisation with 2M aqueous sodium hydroxide and solid sodium acetate gave no identifiable material.

The Photolysis of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Betaine (383a) in Benzene

4-Phenyl-1H-1,2,3-triazole-5-diazonium betaine (383a) (1.20 g, 0.007 mol) was irradiated in dry benzene (200 ml) at room temperature under dry nitrogen for 24 h using a Hanovia medium pressure photochemical reactor. The resulting red solution was evaporated and the red oil obtained (1.50 g) was chromatographed over alumina.

Elution with light petroleum afforded a small quantity of yellow gum (0.04 g). Further elution with light petroleum-toluene (3:1) gave 7-cyano-7-phenyl-norcaradiene (392) (0.38 g) (28%) m.p. 134-136°C (lit., 214°C 135-137°C) as yellow plates (from ethanol), νmax. 2240 (C=Н) cm⁻¹, δ[CDCl₃] 7.42-7.32 (5H, m, ArH), 6.54-6.16 (4H, m, CH) and 3.56-3.44 (2H, m, CH).

Found: C, 86.5; H, 5.8; N, 7.2%; M⁺, 193

C₁₄H₁₁N requires: C, 87.0; H, 5.7; N, 7.3%; M, 193.

Subsequent elution with toluene afforded 3,8-dicyano-3,8-diphenyltricyclo[5.1.0.0²,4]oct-5-ene (393) (0.12 g) (6%) m.p. 284-285°C as orange plates (from dimethylformamide), νmax. 2220 (C=Н) cm⁻¹.

Found: C, 85.6; H, 5.1; N, 9.1%; M⁺, 308

C₂₂H₁₆N₂ requires: C, 85.7; H, 5.2; N, 9.1%; M, 308.

Subsequent elution with toluene-methylene chloride (3:1) yielded a red oil (0.22 g) which was shown by t.l.c. in light petroleum-methylene chloride (9:1) over silica to
contain at least three unresolvable components. Final elution with ethanol gave a yellow gum (0.10 g) which was shown by t.l.c. in methylene chloride over silica to contain at least two unresolvable components.

**Phenylcyanodiazomethane (391)**

Phenylcyanodiazomethane (391), $\nu_{\text{max}}$ 2220 (C≡N) and 2080 (N≡N) cm$^{-1}$ was prepared in 53% yield by the method described by Breslow and Yuan, and was used immediately without further purification.

**The Thermolysis of Phenylcyanodiazomethane (391) in Benzene**

A freshly prepared solution of phenylcyanodiazomethane (391) (2.26 g, 0.016 mol) in dry benzene (200 ml) was heated under reflux for 1 h. The solution was cooled and evaporated and the gum obtained (1.30 g) was chromatographed over alumina. Elution with light petroleum-toluene (3:1) afforded a yellow oil (0.07 g) which was shown by t.l.c. in methylene chloride over silica to consist of three unresolvable components. Further elution with toluene afforded a yellow gum (0.25 g) which was triturated with ethanol to give 7-cyano-7-phenyl-norcaradiene (392) (0.22 g) (7%) m.p. 129-134$^\circ$ (lit., 135-137$^\circ$) which was identical (m.p., mixed m.p. and i.r. spectrum) to a sample obtained before. Evaporation of the ethanol mother liquor afforded a negligible quantity of gum.

Further elution with toluene afforded a dark yellow oil (0.35 g) which was shown by t.l.c. in methylene chloride over silica to consist of three unresolvable components.
Subsequent elution with methylene chloride yielded a yellow oil (0.43 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Final elution with methylene chloride-ethanol (3:1) gave a yellow gum (0.11 g) which was shown by t.l.c. in methylene chloride over silica to consist of at least two unresolvable components.

The Photolysis of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Betaine (383a) in Ethanol

A solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium betaine (383a) (1.36 g, 0.008 mol) in absolute ethanol (200 ml) was irradiated for 24 h as in benzene solution (see earlier). Evaporation of the solution and trituration of the resulting semi-solid with light petroleum afforded 4-phenyl-1H-1,2,3-triazole (387) (0.42 g) (36%) m.p. 139-144° which was identical (m.p. and i.r. spectrum) to a sample obtained before.

Evaporation of the light petroleum mother liquor afforded a yellow oil (0.78 g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multicomponent mixture.

The Attempted Thermolysis of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Betaine (383a) in Ethanol

A solution of the diazonium betaine (383a) (0.17 g, 0.001 mol) in absolute ethanol (200 ml) was left at room temperature for 24 h. The resulting solution was evaporated to afford unchanged starting material (0.17 g) m.p. 129-132° which was identical (m.p. and i.r. spectrum) to an authentic sample.
The Photolysis of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Betaine (383a) in Acetonitrile

A solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium betaine (383a) (0.86 g, 0.005 mol) in dry, freshly distilled acetonitrile (200 ml) was irradiated for 24 h as for the solution in benzene (see earlier). Evaporation of the solution and trituration of the resulting red gum with ether afforded 9,10-dicyanophenanthrene (411) (0.12 g) (11%) as buff needles m.p. 289-290\(^\circ\) (lit., 218-285\(^\circ\)) (from ethyl acetate-ethanol), \(v_{\text{max}}\) 2220 (C=EN) cm\(^{-1}\).

Found: M\(^+\), 228.070457 (error < 8 p.p.m.).

C\(_{16}\)H\(_{8}\)N\(_2\) requires: M, 228.068745.

Evaporation of the ether mother liquor gave a dark gum (0.59 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

The Photolysis of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Betaine (383a) in Acetone

A solution of the betaine (383a) (0.86 g, 0.005 mol) in Analar acetone (200 ml) was irradiated for 24 h as for the solution in benzene (see earlier). Evaporation of the solution yielded a yellow oil (B) (0.61 g) b.p. 125-129\(^\circ\)/0.8 mm Hg, \(v_{\text{max}}\) 2230 (C=N) and 1725 (CO) cm\(^{-1}\), \(\delta[(\text{CD}_3)_2\text{SO}]\) 7.44 (s, ArH), 1.71 (s), 1.64 (d), 1.58 (s), 1.04 (s) and 0.78 (s).

Found: C, 72.1; H, 6.6; N, 7.1%; M\(^+\), 216.

C\(_{13}\)H\(_{14}\)NO\(_2\) requires: C, 72.2; H, 6.5; N, 6.5%, M, 216.

The distillation residue (0.30 g) was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.
The Attempted Reaction of the Oil (B) with Hydrazine

A solution of the oil (B) (0.43 g) in methanol (10.0 ml) was heated under reflux with a solution of 85% v/v hydrazine hydrate (0.5 ml) for 1.5 h. The solution was cooled and evaporated and the residue was treated with water (5.0 ml) and neutralised by the dropwise addition of glacial acetic acid. Extraction with methylene chloride afforded a dark yellow oil (0.31 g), shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
$\text{Ar}^- \text{N} \equiv \text{N} X^- + \text{COR} \overset{\text{CH}_2}{\rightarrow} \text{ArNHN} \equiv \text{COR}$

(412) \hspace{1cm} (413) \hspace{1cm} (414)

$R^2$

a) COMe
b) COPh
c) CO$_2$Et
d) CN

Scheme 82
Scheme 83
Scheme 84
3.2 The Coupling Reactions of 4-Substituted-5-diazo-1H-1,2,3-triazoles with Active Methylene Compounds

3.2.1 Introduction

Aromatic diazonium salts are able to couple with many types of active methylene compounds (see Chapter 1). Their ability to couple with β-dicarbonyl related compounds has been reviewed by Parmerter.\textsuperscript{220} Typical examples of such reactions are summarised in Scheme 82. The products in all cases are the expected hydrazones (414 a-d). Recently the related coupling reactions of benzenediazonium salts (412) with benzenesulphonylacetophenone (415), to afford the expected hydrazones (416) in good yield, have also been described.\textsuperscript{221}

Arenediazonium salts have also been reported to couple with phosphonium ylids.\textsuperscript{222,223} Thus, Markl\textsuperscript{222} has described the coupling reactions of arenediazonium salts with phosphoranes of the type (418), to form phosphonium salts (419), (which can be isolated in some cases) which on treatment with base afford the phosphoranes (420). Kamashima and Inamoto\textsuperscript{223} have also recently reported the coupling reactions of the betaine (421) with phosphinimines of the type (422) to give the corresponding benzotriazinones (423).

It is also known\textsuperscript{224} that arenediazonium salts will couple with thiocyanomethylene compounds (425) to afford thiadiazolines of the type (428) (Scheme 84). The mechanism proposed for these reactions (cf. Scheme 84) involves the initial formation of the hydrazone (427) and its subsequent
Scheme 85
Scheme 86
Scheme 87
Scheme 88

\[
\begin{align*}
&\text{N}=\text{N} \\
&\text{N}=\text{N} \\
&\text{N}=\text{N} \\
\end{align*}
\]

\[
\begin{align*}
&\text{N=NNX}^+ \quad \text{COR} \\
&\text{CH}_2 \quad \text{PPh}_3 \times^- \\
&\text{PhP}^+ \\
\end{align*}
\]

\[
\begin{align*}
&\text{ROC=NNNH} \\
&\text{Ph}_3\text{P}^+ \times^- \\
\end{align*}
\]

\[
\begin{align*}
&\text{R} \quad \text{N=NN} \\
&\text{N=NN} \\
&\text{N=NN} \\
\end{align*}
\]

\[
\begin{align*}
&\text{R} \quad \text{N=NN} \\
&\text{Ph}_3\text{P}^+ \times^- \\
\end{align*}
\]
cyclisation via the thiocyanato group [(427)→(428)].

Diazonium coupling reactions of the type shown in Scheme 84 represent the only method for the synthesis of thiadiazolines of structure (428). 224

The coupling of arenediazonium salts with naphthols and phenols is well documented, notably as a method for the synthesis of azo dyestuffs, and these reactions have already been discussed in Chapter 1. Such reactions are however, illustrated by the transformations [(429)→(430)] and [(429)→(431)] shown in Scheme 85.

The coupling reactions of arenediazonium salts, shown in Schemes 82-85, should also be applicable to heterocyclic diazonium salts, and in particular to the 1H-1,2,3-triazole-diazonium salts under investigation in the present work. The application of such coupling reactions to 1H-1,2,3-triazolatediazonium salts should lead to hydrazone intermediates, capable of undergoing cyclisation to a variety of interesting bridgehead fused 1,2,3-triazole products (cf. Schemes 86-90). Thus, coupling with β-dicarbonyl compounds might lead eventually to 1,2,3-triazolo[5,1-c]-1,2,3-triazines [Scheme 86; (432) + (433)→(434)→(435)]. The use of a benzenesulphonylmethylene compound as the coupling component should afford, after cyclisation of the hydrazone intermediates, triazolotriazines having a 6-benzenesulphonyl group capable of further modification (e.g. by nucleophilic displacement) (cf. Scheme 87). Correspondingly the use of a phosphorane as coupling component (Scheme 88) might ultimately yield interesting phosphonium salts (441) of the triazolotriazine series. The use of thiocyanomethylene compounds in such coupling reactions would provide a method
Scheme 89
Scheme 90
Scheme 91
Scheme 92
Scheme 93
\[
\begin{align*}
\text{(460)} & \quad \begin{array}{c}
\text{HN} - N - N - N \\
\text{N} & \text{N} \\
& \text{X}^{-}
\end{array} + \begin{array}{c}
\text{O} \\
\text{H} \\
\text{N} - N
\end{array} \\
\text{(461)} & \quad \begin{array}{c}
\text{N} & \text{N} \\
\text{HO} \\
\text{N} & \text{N}
\end{array} \\
\rightarrow & \quad \begin{array}{c}
\text{N} & \text{N} \\
\text{HO} \\
\text{N} & \text{N}
\end{array} \\
\text{(462)} & \quad \begin{array}{c}
\text{N} & \text{N} \\
\text{HO} \\
\text{OH}
\end{array}
\end{align*}
\]

Scheme 94
for the synthesis of 6-thiocyanotriazolotriazine derivatives
(Scheme 89; (444)). Similarly, triazolonaphthotriazines
(Scheme 90; (447)) would be the expected end-products of
initial coupling of a 1H-1,2,3-triazole diazonium salt with
β-naphthol.

Transformations of the types shown in Schemes 86-90
find analogy in the reactions undergone by 1H-pyrazole-,
1H-imidazole-, 1H-1,2,4-triazole- and 1H-tetrazolediazonium
salts. For example, coupling of ethyl cyanoacetate (449)
with 1H-pyrazole-3-diazonium salts of type (448) readily
affords the hydrazone (450), which is easily cyclised (in
acidic media) to the pyrazolo-1,2,4-triazine (451).\textsuperscript{146}
The 1H-imidazole-4-diazonium salts (452) readily couple with
active methylene compounds, such as acetylacetone, to afford
hydrazones of the type (454) (Scheme 92).\textsuperscript{147} However, it
is reported by Stanovnik et al,\textsuperscript{147} that such hydrazones defy
cyclisation to the corresponding imidazolotriazines (455).

Many examples of the coupling reactions of 1H-1,2,4-
triazolediazonium salts with active methylene compounds
have been reported. Benzoylacetone, for example, couples
with 1H-1,2,4-triazole-5-diazonium nitrate (456) in the
presence of sodium acetate, to give the hydrazone (458) which
is readily cyclised to the corresponding triazolotriazine
(459).\textsuperscript{153} 1H-Tetrazolediazonium salts (460) are known
to couple with phenols to afford azo compounds such as
(462),\textsuperscript{152} but subsequent cyclisation to the corresponding
tetrazolotriazine (463) was not reported.\textsuperscript{152}
Scheme 95
R
a) CN
b) COPh

Scheme 96
In contrast, the literature contains few reports of the coupling reactions of 1H-1,2,3-triazole-diazonium salts with active methylene compounds or with phenols. Work in this department has however, shown \(^{177,178}\) that the 4-substituted 1H-1,2,3-triazole-5-diazonium salts (464; \(R = \text{Ph or CONH}_2\)) couple readily with active methylene compounds to give hyrazones of type (466) which can be readily cyclised to the corresponding 1,2,3-triazolo[5,1-c]-1,2,4-triazine derivatives (467) (cf. Scheme 95).

It has also been reported \(^{166,209}\) recently that 4-cyano-1H-1,2,3-triazole-5-diazonium salts (468a) and 4-benzoyl-1H-1,2,3-triazole-5-diazonium salts (468b) couple very readily with 8-naphthol, to afford the corresponding azo compounds (469 a and b), though no attempt was made to cyclise these compounds to the triazolonaphthotriazine derivatives (470 a and b) (Scheme 96).

The objectives of the following studies therefore, were to investigate the coupling reactions of 1H-1,2,3-triazole-5-diazonium salts with a variety of coupling components, in particular active methylene compounds and phenols, and to study the cyclisation of the resulting hydrazone products to 1,2,3-triazolo-1,2,4-triazines of novel structure (cf. Schemes 86-90).
\[
\begin{align*}
\text{(471)} & \\
\text{(472)} & \\
\text{(473)} & \\
\end{align*}
\]

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 & \quad \text{R}^3 \\
a) & \text{COMe} & \text{COMe} & \text{H} \\
b) & \text{COMe} & \text{COMe} & \text{Ac} \\
c) & \text{COMe} & \text{COPh} & \text{H} \\
d) & \text{COMe} & \text{COPh} & \text{Ac} \\
e) & \text{COMe} & \text{CO}_2\text{Et} & \text{H} \\
f) & \text{COMe} & \text{CO}_2\text{Et} & \text{Ac} \\
g) & \text{COPh} & \text{COPh} & \text{H} \\
h) & \text{COPh} & \text{COPh} & \text{Ac} \\
i) & \text{COPh} & \text{CO}_2\text{Et} & \text{H} \\
j) & \text{COPh} & \text{CO}_2\text{Et} & \text{Ac} \\
k) & \text{COPh} & \text{CN} & \text{H} \\
l) & \text{CO}_2\text{Et} & \text{CO}_2\text{Et} & \text{H} \\
m) & \text{CO}_2\text{Et} & \text{CO}_2\text{Et} & \text{Ac} \\
n) & \text{CO}_2\text{Et} & \text{CN} & \text{H} \\
o) & \text{CO}_2\text{Et} & \text{CN} & \text{Ac} \\
p) & \text{CN} & \text{CN} & \text{H} \\
q) & \text{CN} & \text{CONH}_2 & \text{H} \\
a) & \text{NH}_2 \\
b) & \text{NO}_3^{-} \\
\end{align*}
\]
\[
\begin{align*}
(474) \\
(475) \\
(476) \\
(477)
\end{align*}
\]

<table>
<thead>
<tr>
<th>( R^1 )</th>
<th>( R^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>COMe</td>
</tr>
<tr>
<td>Me</td>
<td>COPh</td>
</tr>
<tr>
<td>Me</td>
<td>CO(_2)Et</td>
</tr>
<tr>
<td>Ph</td>
<td>COPh</td>
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<tr>
<td>Ph</td>
<td>CO(_2)Et</td>
</tr>
<tr>
<td>NH(_2)</td>
<td>COPh</td>
</tr>
<tr>
<td>NH(_2)</td>
<td>CO(_2)Et</td>
</tr>
<tr>
<td>NH(_2)</td>
<td>CN</td>
</tr>
<tr>
<td>NH(_2)</td>
<td>CONH(_2)</td>
</tr>
</tbody>
</table>

\( a \) Ph \\
\( b \) OEt
3.2.2 The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with β-Dicarbonyl Compounds and Related Substrates

As stated earlier in Chapter 1, the ability of diazonium salts to couple with suitably activated methylene compounds has long been known. However, few examples have been reported utilizing such diazo coupling reactions to form fused heterocyclic compounds, particularly those containing a 1,2,3-triazole nucleus. Work in this department¹⁷⁷,¹⁷⁸ has shown that coupling of 1,2,3-triazole-diazonium salts with β-dicarbonyl and related compounds leads to the formation of hydrazones, which are readily cyclised to the corresponding triazolotriazine derivatives (cf. Chapter 3.2.1). By analogy with this work, the coupling reactions of new 1,2,3-triazole-5-diazonium salts with β-dicarbonyl and related compounds have now been investigated.

When a cooled suspension of the diazonium betaine (471) in ethanol was treated with an ethanolic solution of acetylacetone and triethylamine, the hydrazone (473a) was isolated. Acetylacetone also coupled with the betaine (471) and the diazonium nitrate (472b), (which was prepared in situ), in aqueous ethanolic sodium carbonate to form the hydrazone (473a). However, attempted coupling of the diazonium nitrate (472b) with acetylacetone in aqueous ethanolic sodium acetate, resulted only in the recovery of unreacted diazonium betaine (471). The hydrazone (473a) gave i.r. and mass spectral data consistent with the assigned structure, though difficulty was encountered in obtaining correct analytical data for (473a). The hydrazone (473a) was
Scheme 97
soluble on brief treatment with aqueous sodium hydroxide solution and was regenerated, unchanged, from its alkaline solution on acidification with aqueous hydrochloric acid. This behaviour is consistent with the presence of an acidic triazole NH-group. It has been shown\textsuperscript{158} that acetylation of 1H-1,2,3-triazolylhydrazones results in the formation of N-acetyl derivatives, which exhibit characteristic signals between $\delta$ 2.85 and 2.60 p.p.m. in their $^1$H n.m.r. spectra, due to the protons of the acetyl methyl group, and a band at 1790–1740 cm\textsuperscript{-1} in their i.r. spectra due to the acetyl carbonyl absorption. Correspondingly, acetylation of the hydrazone (473a) was accomplished smoothly by brief treatment with warm acetic anhydride, giving the N-acetyl derivative (473b) which showed characteristically high carbonyl absorption in its i.r. spectrum. However, the multiplicity of the signals in its $^1$H n.m.r. spectrum indicated the presence of more than one species. The $^1$H n.m.r. spectrum of (473b) contained two three proton singlets at $\delta$ 2.83 and 2.66 p.p.m. attributable to the presence of two N-acetyl groups. Two three proton singlets at $\delta$ 2.36 and 2.19 p.p.m. and a six proton singlet at $\delta$ 1.87 p.p.m., due to the presence of four acetyl carbonyl groups, were also observed. The possibility that the product was a diacetyl derivative can be readily excluded on the basis of analytical and mass spectral data. The multiplicity observed in the $^1$H n.m.r. spectrum of (473b) can be accounted for by the possible existence of hydrogen bonded structures of the type (478a) in equilibrium with non-bonded structures of type (478b). However, as well as hydrogen bonded structures being responsible for the
Scheme 98
Scheme 99
Scheme 100
Scheme 101
observed multiplicity, another explanation is possible. N-
Unsubstituted 1,2,3-triazoles are generally written as in
structure (479; R¹=H). However, the tautomeric structures
(480; R¹=H) and (481; R¹=H) are equally likely. Correspond-
ingly, the acetyl derivatives (480; R¹=Ac) and (481; R¹=Ac)
may be formed as well as (479; R¹=Ac). Thus the ¹H n.m.r.
spectrum of (473b) may be explained in terms of the formation
of two isomeric mono-N-acetyl derivatives.

The mechanism of formation of the hydrazone (473a) can
be explained by Scheme 99.

Heating the hydrazone (473a) under reflux in ethanol, caused
its smooth cyclisation to a product whose elemental analysis
and i.r., ¹H n.m.r. and mass spectra were consistent with its
being either the triazolo[5,1-c]-1,2,4-triazine (474a) or the
triazolo[1,5-b]-1,2,4-triazine (475). The formation of the
isomer (475) is possible because of the Dimroth rearrangement
of (474a) after initial cyclisation (cf. Scheme 100).

Work carried out in this department has shown conclusively
that triazolo[5,1-c]-1,2,4-triazines of the type (474a) react
with phenylhydrazine to afford the azo compounds of type
(492), whose structures were established by unambiguous
synthesis. Since, for structural reasons, the corresponding
[1,5-b] isomers (e.g. 475) cannot form azo structures of the
type (492), formation of the latter is consistent with the
products of the cyclisation of the hydrazones of type (473),
having the 1,2,3-triazolo[5,1-c]-1,2,4-triazine structure
(474). The possibility that the products of such cyclisation
reactions are 1,2,3-triazolo[1,5-b]-1,2,4-triazines
(e.g. 475) which then undergo rearrangement to their 1,2,3-
Scheme 102
triazolo[5,1-c]-1,2,4-triazine isomers (e.g. 474), prior to condensation with phenylhydrazine, cannot be ruled out, but it is considered unlikely under the conditions used, both in the cyclisation reactions and in the condensations with phenylhydrazine. Thus, reaction of the triazolotriazine (474a) with phenylhydrazine afforded a product whose i.r., $^1$H n.m.r. and mass spectra and elemental analysis were consistent with the azo structure (492). This result confirms the presence of the triazolo[5,1-c]-1,2,4-triazine nucleus (474) rather than the corresponding triazolo[1,5-b]-1,2,4-triazine isomer (475).

The mechanism involved in the cyclisation of the hydrazone (473a) to the triazolo[5,1-c]-1,2,4-triazine (474a) is outlined in Scheme 102. Cyclisation of the hydrazone (473a) in ethanol is explained by thermal elimination of water [e.g. (493) → (494) → (495)]. Whereas, cyclisation of the hydrazone (473a) in acetic acid involves initial protonation of the carbonyl group of the hydrazone (473a). Subsequent cyclisation to the triazine then follows, [e.g. (493) ⇌ (496) → (497) → (495)].

Treatment of a cooled ethanolic suspension of the betaine (471) with an ethanolic solution of benzoylaceton and triethylamine, readily afforded the hydrazone (473c), as indicated by its i.r. spectrum. The hydrazone (473c) was readily soluble in aqueous sodium hydroxide and was regenerated, unchanged, from its alkaline solution on acidification with aqueous hydrochloric acid. Such behaviour is consistent with the presence of an acidic triazole NH-group. Attempted crystallisation of the
hydrazone (473c) however, from a variety of solvents, resulted only in its ready cyclisation to the corresponding triazolotriazine (474b) (see later). Brief treatment of the hydrazone (473c) with acetic anhydride in an attempt to convert the hydrazone into its corresponding N-acetyl derivative (473d) however, resulted only in a large recovery of the unchanged starting material. Prolonged treatment with acetic anhydride gave a tar which was shown by t.l.c. examination to be a multicomponent mixture.

As mentioned earlier, the hydrazone (473c) is readily cyclised to the triazolotriazine (474b) on attempted crystallisation. Consequently, the hydrazone was smoothly converted into the triazolotriazine (474b) when heated under reflux in glacial acetic acid. The product obtained from such treatment gave i.r., $^1$H n.m.r. and mass spectra and elemental analysis consistent with the assigned structure (474b). The possible existence of the isomer (476) can be ruled out, based on the expectation that cyclisation will occur via the most reactive of the two ketonic groups (i.e. MeCO-). In addition, the structure (476) would exhibit a higher carbonyl absorption in its i.r. spectrum, and a different methyl signal in the $^1$H n.m.r. spectrum, would also be observed.

The triazolotriazine (474b) is considered to have the [5,1-c] structure, as opposed to the [1,5-b] structure by analogy with the triazolotriazine (474a).
Ethyl acetoacetate coupled with the betaine (471) in the presence of triethylamine to form a product whose i.r. spectrum was consistent with its being the hydrazone (473e). This product was soluble on brief treatment with aqueous sodium hydroxide and was regenerated unchanged on acidification with aqueous hydrochloric acid, indicating the presence of a free triazole NH group. However, attempted crystallisation of the hydrazone (473e) from a variety of solvents, always resulted in the formation of red gums which could not be characterised further. In an endeavour to establish the hydrazone structure (473e) its conversion into the corresponding N-acetyl derivative (473f), by gentle warming with acetic anhydride was attempted. However, such treatment resulted in the recovery of unchanged starting material, and a gum (shown by t.l.c. examination to be an unresolvable multicomponent mixture).

When the hydrazone (473e) was heated under reflux in either ethanol or glacial acetic acid, in an attempt to effect its cyclisation to the triazolotriazine (474c), dark intractable gums were obtained. Examination of the gums, by t.l.c., showed them in both cases to be unresolvable multicomponent mixtures.

When an ethanolic solution of dibenzoylmethane and triethylamine was introduced to a cooled ethanolic suspension of the betaine (471), the product isolated was the triethylamine salt of the hydrazone (473g), as indicated by its elemental analysis and its i.r. and $^1$H n.m.r. spectra. However, brief treatment with aqueous hydrochloric acid readily liberated the free hydrazone (473g). The
The hydrazone (473g) had correct elemental analysis, and showed i.r. and mass spectra consistent with the structure (473g). The presence of a free triazole NH-group was also readily demonstrated by the formation of a water soluble sodium salt which was reconverted into the unchanged hydrazone (473g) on acidification with aqueous hydrochloric acid.

Acetylation of the hydrazone (473g) (or its triethylamine salt) was accomplished smoothly by brief treatment with warm acetic anhydride. The N-acetyltriazolylhydrazone (473h) so formed gave the expected elemental analysis and mass spectrum, and showed $^1$H n.m.r. and i.r. spectra consistent with the presence of a triazole ring N-acetyl group (see before).

When the hydrazone (473g) was heated under reflux in glacial acetic acid, the triazolotriazine (474d) was obtained. Similar treatment of the triethylamine salt of the hydrazone (473g) also gave the triazolotriazine (474d) in good yield. The triazolotriazine (474d) gave elemental analysis, and i.r. and mass spectra consistent with the cyclic structure (474d). The mechanism involved in the formation of the triazolotriazine (474d) is directly analogous to that postulated for the triazolotriazine (474a) (see Scheme 102).

The hydrazone (473i) was obtained as its triethylamine salt when an ethanolic solution of ethyl benzoylacetate and triethylamine was introduced to a cooled ethanolic suspension of the betaine (471). The triethylamine salt of the hydrazone (473i) showed correct elemental analysis and i.r. and $^1$H n.m.r. spectra. Brief treatment of the triethylamine salt with aqueous hydrochloric acid afforded the free hydrazone as indicated by its i.r., $^1$H n.m.r. and mass spectra and
combustion analysis. Consistent with its assigned structure, the hydrazone (473i) was soluble in aqueous sodium hydroxide and was regenerated, unchanged on acidification with aqueous hydrochloric acid. Also, the triethylamine salt of the hydrazone (473i) afforded the N-acetyl derivative (473j) on brief treatment with warm acetic anhydride.

The hydrazone (473i) was readily cyclised to the corresponding triazolotriazine (474e) when heated under reflux in glacial acetic acid. The structure of the triazolotriazine (474e) was supported by its i.r., $^1$H n.m.r. and mass spectra and by analytical data. The possibility of cyclisation occurring to form the lactam structure (477a) is therefore ruled out. This is however, to be expected, since cyclisation should occur via the more reactive keto group, rather than through the less reactive ester group.

When the betaine (471) was coupled with benzoylacetonitrile in the presence of triethylamine, a product was isolated whose properties are consistent with its being 7-amino-3-benzene-sulphonyl-6-benzoyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474f), rather than the expected, isomeric hydrazone (473k). Although no confirmation of this structure is possible on the basis of elemental analysis or $^1$H n.m.r. or mass spectral evidence, absorptions at 3400 and 3280 br. cm$^{-1}$ in the i.r. spectrum of (474f), attributable to a primary amino group, and the absence of any band assignable to a cyano group, rules out the open chain structure (473k) and supports the cyclic structure (474f). In addition, the high m.p. of the product and the fact that crystallisation was achieved using a polar solvent (dimethylformamide) also lend support
Scheme 103
to the cyclic structure. This is so because the high m.p. and solvent behaviour of the product is not consistent with that expected of a hydrazone. Generally, hydrazones are fairly low m.p. solids and are usually crystallised from non-polar solvents, (e.g. ethyl acetate). Insolubility of the crude solid, obtained from the coupling reaction of the betaine (471) with benzoylacetonitrile, in aqueous sodium hydroxide, also discounts cyclisation of the hydrazone (473k) to (474f) during its crystallisation. Cyclisation of the hydrazone (473k) occurs via the cyano group, as opposed to the benzoyl group, since only a simple addition reaction is involved (cf. Scheme 103).

When diethylmalonate was coupled with the betaine (471) in the presence of triethylamine, the triethylamine salt of the hydrazone (473l) was isolated as indicated by its elemental analysis and \(^1\)H n.m.r. spectrum. Brief treatment of the triethylamine salt with aqueous hydrochloric acid afforded the free hydrazone (473l) as its monohydrate. The i.r. spectrum and elemental analysis were consistent with the monohydrate structure, although the mass spectrum gave the correct parent ion peak for the hydrazone (473l), due to loss of water in the probe. Consistent with its assigned structure, the hydrazone (473l) was soluble in aqueous sodium hydroxide, and was regenerated, unchanged, from its alkaline solution on acidification with aqueous hydrochloric acid. However, brief treatment of the hydrazone (473l) with warm acetic anhydride, in an attempt to form the corresponding N-acetyl derivative (473m), only resulted in a large recovery of unchanged starting material. Attempted acetylation of the triethylamine salt of the hydrazone (473l),
using conditions successful for the acetylation of the triethylamine salt of the hydrazone (473i) (see earlier) was also unsuccessful. The result of this reaction was the isolation of a dark gum which could not be characterised.

Attempted cyclisation of the hydrazone (473l) to the corresponding lactam (477b) was unsuccessful. Heating the hydrazone (473l) under reflux in either glacial acetic acid or ethanolic sodium acetate resulted in the recovery of unchanged starting material in each case. In a further attempt to cyclise the hydrazone (473l), its triethylamine salt was heated under reflux in glacial acetic acid. However, these conditions also proved unsuccessful and resulted in the formation of a dark intractable gum, which could not be characterised.

When an ethanolic solution of ethyl cyanoacetate was added to a cooled suspension of the betaine (471), or the diazonium nitrate (472b) (prepared in situ), in the presence of triethylamine or sodium carbonate the hydrazone (473n) was isolated. This product gave elemental analysis and showed spectroscopic properties consistent with its assigned structure. The hydrazone (473n) also readily formed a soluble sodium salt on brief treatment with aqueous sodium hydroxide from which the free hydrazone (473n) was liberated by acidification with aqueous hydrochloric acid. Treatment of the hydrazone (473n) with warm acetic anhydride resulted in the formation of the corresponding N-acetyl derivative (473o) whose structure is supported by elemental analysis and i.r., $^1$H n.m.r. and mass spectral data.
The hydrazone (473n) was heated under reflux in ethanol in an attempt to effect its conversion into the corresponding triazolotriazine (474g). However, it was largely unchanged by this treatment and underwent conversion into the triazolotriazine (474g) in only low yield. The triazolotriazine (474g) gave i.r., $^1$H n.m.r. and mass spectra and elemental analysis consistent with its assigned structure. Cyclisation of the hydrazone (473n) involves addition across the cyano group as in the case of the hydrazone (473k) (cf. Scheme 103).

When the betaine (471) was coupled with malononitrile in the presence of triethylamine, a product whose properties are consistent with the triazolotriazine structure (474h) was obtained. By analogy with the triazolotriazine (474f) (see before), the presence of absorptions at 3480 and 3300 cm$^{-1}$ in the i.r. spectrum of (474h), and its high m.p., lend support to the cyclic structure (474h), as opposed to the hydrazone formulation (473p) for this product. However, although a correct parent ion peak in the mass spectrum of (474h) was observed, accurate analytical data could not be obtained.

In an attempt to gain more information about the triazolotriazine (474h), its reactions with polyphosphoric acid and acetic anhydride were investigated. The reaction with polyphosphoric acid was designed to hydrolyse the cyano group present to an amide function, in the hope of obtaining a derivative, which might handle more easily. However, reaction of the triazolotriazine (474h) with polyphosphoric acid gave no identifiable product. Similarly, attempted acetylation of the triazolotriazine (474h) by reaction with warm acetic anhydride, in the hope of synthesising an acetyl derivative, resulted only in the recovery of unchanged starting material.
(501)

\[ \text{R} \]

a) \( \text{NH}_2 \)

b) \( \frac{\text{N} \equiv \text{N}}{\text{NO}_3} \)

(502)

\[ \begin{array}{cccc}
\text{R}^1 & \text{R}^2 & \text{R}^3 \\
\text{a)} & \text{Me} & \text{COMe} & \text{H} \\
\text{b)} & \text{Me} & \text{COMe} & \text{Ac} \\
\text{c)} & \text{Me} & \text{COPh} & \text{H} \\
\text{d)} & \text{Me} & \text{COPh} & \text{Ac} \\
\text{e)} & \text{Me} & \text{CO}_2\text{Et} & \text{H} \\
\text{f)} & \text{Me} & \text{CO}_2\text{Et} & \text{Ac} \\
\text{g)} & \text{Ph} & \text{COPh} & \text{H} \\
\text{h)} & \text{Ph} & \text{CO}_2\text{Et} & \text{H} \\
\text{i)} & \text{Ph} & \text{CN} & \text{H} \\
\text{j)} & \text{Ph} & \text{CN} & \text{Ac} \\
\text{k)} & \text{OEt} & \text{CO}_2\text{Et} & \text{H} \\
\text{l)} & \text{OEt} & \text{CN} & \text{H}
\end{array} \]
\[
\begin{array}{c|c}
R^1 & R^2 \\
\hline
\text{a)} & \text{Me} \\
\text{b)} & \text{Me} \\
\text{c)} & \text{Me} \\
\text{d)} & \text{Ph} \\
\text{e)} & \text{Ph} \\
\text{f)} & \text{NH}_2 \\
\text{g)} & \text{NH}_2 \\
\text{h)} & \text{NH}_2 \\
\text{i)} & \text{NH}_2 \\
\end{array}
\]
When the betaine (471) was coupled with cyanoacetamide in the presence of triethylamine, in an attempt to isolate the hydrazone (473g) or the triazolotriazine (474i), an amorphous solid was obtained. This solid had an ill-defined i.r. spectrum, and readily decomposed to tars on attempted crystallisation from a variety of solvents.

The successful coupling reactions of the betaine (471) with active methylene compounds just described, prompted the study of the similar coupling reactions of 4-cyano-1H-1,2,3-triazole-5-diazonium nitrate (501b). When a fresh solution of the diazonium nitrate (501b) [prepared in situ by diazotisation of the corresponding amine (501a)] was treated with a solution of acetylacetone in the presence of sodium acetate, the hydrazone (502a) was obtained. The hydrazone (502a) showed i.r. and mass spectra consistent with the assigned structure, but correct analytical data could not be obtained. However, consistent with the presence of a free NH-group, the hydrazone (502a) formed a soluble sodium salt which on acidification was reconverted into the free hydrazone (502a). Also treatment of the hydrazone (502a) with warm acetic anhydride afforded a product, whose elemental analysis and spectroscopic properties are consistent (see earlier) with the N-acetyl structure (502b). The mechanism of formation of the hydrazone (502a) can be explained by analogy with the corresponding benzenesulphonyl hydrazone (473a) (see earlier). However, it is difficult to detect whether deprotonation of the diazonium salt (501b) occurs prior to coupling with acetylacetone in this case. If this does occur, then the acidity of the aqueous ethanolic medium
must be sufficient to allow final protonation, since no acidification is required to isolate the hydrazone (502a).

When the hydrazone (502a) was heated under reflux in ethanol, the corresponding triazolotriazine (503a) was obtained in good yield. This product gave elemental analysis and i.r., $^1$H n.m.r. and mass spectra consistent with the assigned structure. The alternative [1,5-b] structure can be ruled out by analogy with the triazolotriazine (474a) (see earlier). Because of the conditions used to cyclise the hydrazone (502a) to the triazolotriazine (503a), it is reasonable to suggest that its mechanism of formation is also similar to that postulated for the triazolotriazine (474a) (cf. Scheme 102).

When an aqueous ethanolic solution of benzoylaceton and sodium acetate was introduced to a cooled solution of the diazonium nitrate (501b), the expected hydrazone (502c) was also accompanied by the triazolotriazine derivative (503b) (see later). The triazolotriazine (503b) was also isolated when crystallisation of the hydrazone (502c) was attempted from a variety of solvents. However, consistent with its assigned structure, the hydrazone (502c) was soluble on brief treatment with aqueous sodium hydroxide, and was regenerated, unchanged, on acidification with aqueous hydrochloric acid. Also, treatment of the hydrazone (502c) with warm acetic anhydride, readily afforded the corresponding N-acetyl derivative (502d) whose elemental analysis and i.r. and mass spectra were in accord with the assigned structure. However, the $^1$H n.m.r. spectrum of (502d) showed multiple absorption consistent with the presence of more than one
species. This multiplicity can be explained by analogy with the N-acetyl derivative (473b) (see earlier) as due to the presence of a mixture of ring mono N-acetyl derivatives. The possibility of a diacetyl derivative being present is ruled out on the basis of elemental analysis and mass spectral data.

When the hydrazone (502c) was heated under reflux in ethanol, the corresponding triazolotriazine (503b) was obtained. This compound gave analytical and spectroscopic data consistent with its assigned structure. The mechanism of the cyclisation of the hydrazone (502c) to the triazolotriazine (503b) is presumed to be analogous to that leading to the 3-benzenesulphonyltriazolotriazine (474b) (see before).

The diazonium nitrate (501b) coupled readily with ethyl acetoacetate in the presence of sodium acetate, to afford the hydrazone (502e), which had an i.r. spectrum consistent with its structure, but could not be crystallised from a variety of solvents. The presence of a free triazole NH-group in the hydrazone (502e) was readily demonstrated by its solubility in aqueous sodium hydroxide. However, an attempt to prepare the N-acetyl derivative (502f) by warming the hydrazone (502e) in warm acetic anhydride was unsuccessful, no identifiable material being obtained.

In an attempt to obtain the corresponding triazolotriazine (503c), the hydrazone (502e) was heated under reflux in ethanol. However, this treatment resulted in the recovery of unreacted starting material, and a dark intractable gum. In a further attempt to effect its cyclisation to the triazolotriazine (503c), the hydrazone (502e) was heated
Scheme 104

(505) \[ \begin{align*}
&\text{HNN=CN} \\
&\text{HNN=} \text{COR} \\
&\text{HNN=} \text{CO}_{2}\text{Et}
\end{align*} \]

(506) \[ \begin{align*}
&\text{HNN=CN} \\
&\text{HNN=} \text{CO}_{2}\text{Et} \\
&\text{HNN=} \text{COR}
\end{align*} \]
under reflux in glacial acetic acid. These conditions also proved unsuccessful, no identifiable material being isolated.

When an aqueous ethanolic solution of dibenzoylmethane and sodium acetate were introduced into a cooled aqueous solution of the diazonium nitrate (501b), the hydrazone (502g) was obtained. This product gave an elemental analysis and i.r. spectrum consistent with its assigned structure. However, it showed a parent ion peak in its mass spectrum at \((M^+ - H_2O)\), indicating cyclisation to the corresponding triazolotriazine in the probe. The hydrazone (502g) readily formed a soluble sodium salt in aqueous sodium hydroxide, from which it was regenerated, unchanged, on acidification with aqueous hydrochloric acid. However, when the hydrazone (502g) was heated under reflux in glacial acetic acid in an attempt to effect its conversion into the triazolotriazine (503d), no identifiable material was obtained.

When the diazonium nitrate (501b) was coupled with ethyl benzoylacetate in the presence of sodium acetate, the hydrazone (502h) was obtained in excellent yield. This compound gave correct analytical and i.r. and mass spectral data, but its \(^1\)H n.m.r. spectrum indicated the presence of more than one species. The multiplicity of signals in the \(^1\)H n.m.r. spectrum of the hydrazone (502h), may be explained in terms of geometrical isomerism, due to hindered rotation about the carbon-nitrogen double bond. This would result in the possible existence of two geometrically isomeric structures (505) and (506), which would be expected to show different chemical shifts for the protons of the ester group.
Consistent with the presence of a free triazole NH-group the hydrazone (502h) formed a soluble sodium salt in aqueous sodium hydroxide. However, heating the hydrazone (502h) under reflux in acetic acid, in an attempt to effect its cyclisation into the corresponding triazolotriazine (503e) was unsuccessful. These conditions resulted only in the formation of a dark intractable tar, from which no identifiable material could be obtained.

The hydrazone (502i) was formed when an ethanolic solution of benzoylacetonitrile and sodium acetate was introduced into a cooled aqueous solution of the diazonium nitrate (501b). The hydrazone (502i) showed i.r. absorption consistent with its assigned structure, but on attempted crystallisation from a variety of solvents cyclised to the triazolotriazine (503f). Formation of a soluble sodium salt in aqueous sodium hydroxide, however, showed the presence of a free triazole NH-group in the hydrazone (502i). Correspondingly, treatment of the hydrazone (502i) with warm acetic anhydride afforded the expected N-acetyl derivative (502j), as indicated by its i.r., $^1$H n.m.r. and mass spectra and its elemental analysis.

When the hydrazone (502i) was heated under reflux in glacial acetic acid, it was smoothly converted into the corresponding triazolotriazine (503f). The structure assigned to this product is supported by i.r. and exact mass spectral data. The presence of absorption bands at 3430 and 3400 cm$^{-1}$ in the i.r. spectrum of (503f), attributable to a primary amino group support cyclisation via the cyano group, as in the formation of the triazolotriazine (474f) (see earlier).
When the diazonium nitrate (50lb) was coupled with diethyl malonate in the presence of sodium acetate, the hydrazone (502k) was obtained, as indicated by its elemental analysis and i.r., $^1$H n.m.r. and mass spectra. Consistent with its assigned structure, the hydrazone (502k) formed a soluble sodium salt in aqueous sodium hydroxide. However, heating the hydrazone (502k) under reflux in glacial acetic acid in an attempt to effect its conversion into the corresponding triazolotriazine (504) was unsuccessful. Attempted cyclisation under these conditions gave only an intractable gum, shown by t.l.c. to be a multicomponent mixture, from which no identifiable material could be obtained.

When an aqueous ethanolic solution of ethyl cyanoacetate and sodium acetate was introduced into a cooled aqueous solution of the diazonium nitrate (501b), the expected hydrazone (502l) was isolated as well as the isomeric triazolotriazine (503g) (see later). The hydrazone (502l) gave an elemental analysis and showed i.r. and mass spectra consistent with its structure. However, examination of the $^1$H n.m.r. spectrum of (502l) revealed the presence of more than one species. As with the hydrazone (502h) (see before) the multiplicity of the signals in the $^1$H n.m.r. spectrum of (502l) can be explained by the presence of geometrical isomers due to hindered rotation around the carbon-nitrogen double bond. The hydrazone (502l) was soluble in aqueous sodium hydroxide, and was regenerated, unchanged, by acidification with aqueous hydrochloric acid. Such behaviour indicates the presence of a free triazole NH-group in (502l).
When the hydrazone (5029) was heated under reflux in glacial acetic acid, the triazolotriazine (503g) was obtained in excellent yield. This product analysed correctly and showed i.r., $^1$H n.m.r. and mass spectral absorption in accord with its assigned structure. Absorption bands at 3430, 3340 and 3250 cm$^{-1}$ in its i.r. spectrum (assignable to a primary amino group), and peaks at $\delta$ 4.46 and 1.38 p.p.m. in its $^1$H n.m.r. spectrum (due to an ester group) support cyclisation via the cyano group [cf. the cyclisation to the triazolotriazine (474g) described earlier].

Malononitrile coupled readily with the diazonium nitrate (501b) in the presence of sodium acetate, to afford the triazolotriazine (503h) as its hemihydrate, as indicated by its i.r. spectrum and elemental analysis. Although no confirmation of the cyclic structure (503h) is possible on the basis of elemental analysis or mass spectral data, the high m.p. and presence of absorption bands in the i.r. spectrum of (503h), attributable to a primary amino group, support the cyclic structure. In addition, the triazolotriazine (503h) was insoluble in aqueous sodium hydroxide, indicating the absence of a free triazole NH-group.

Cyanoacetamide, when coupled with the diazonium nitrate (501b), in the presence of sodium acetate, afforded a solid whose i.r. and mass spectra are consistent with it being the triazolotriazine (503i). However, analytical data consistent with this structure could not be obtained. The triazolotriazine (503i) was found to be insoluble in aqueous sodium hydroxide, indicating the absence of a free triazole NH-group, and thus supporting the presence of a cyclic structure.
\[ R^1 \]
\begin{align*}
a) & \text{ Ph} \\
 b) & \text{ CONH}_2
\end{align*}

\[ R - \text{CH}_2\text{SO}_2\text{Ph} \]

\[ R \]
\begin{align*}
a) & \text{ COMe} \\
b) & \text{ COPh} \\
c) & \text{ CN}
\end{align*}
\[
\begin{array}{c}
\text{(510)} \\
\begin{array}{c}
R^1 \quad R^2 \quad R^3 \\
a) \text{Ph} \quad \text{COMe} \quad \text{H} \\
b) \text{Ph} \quad \text{COMe} \quad \text{Ac} \\
c) \text{Ph} \quad \text{COPh} \quad \text{H} \\
d) \text{Ph} \quad \text{COPh} \quad \text{Ac} \\
e) \text{Ph} \quad \text{CN} \quad \text{H} \\
f) \text{CONH}_2 \quad \text{COPh} \quad \text{H} \\
g) \text{CONH}_2 \quad \text{COPh} \quad \text{Ac} \\
h) \text{CONH}_2 \quad \text{CN} \quad \text{H} \\
i) \text{SO}_2 \text{Ph} \quad \text{COMe} \quad \text{H} \\
\end{array}
\end{array}
\]

\[
\begin{array}{c}
\text{(511)} \\
\begin{array}{c}
R^1 \quad R^2 \\
a) \text{Ph} \quad \text{Me} \\
b) \text{Ph} \quad \text{Ph} \\
c) \text{Ph} \quad \text{NH}_2 \\
d) \text{CONH}_2 \quad \text{Ph} \\
e) \text{CONH}_2 \quad \text{NH}_2 \\
f) \text{SO}_2 \text{Ph} \quad \text{Me}
\end{array}
\end{array}
\]
The successful synthesis of derivatives of the 1,2,3-triazolo[5,1-c]-1,2,4-triazine ring system using coupling reactions of 1H-1,2,3-triazole-5-diazonium compounds with simple active methylene compounds (cf. Chapter 3.2.2), prompted further studies of such reactions using other types of active methylene compounds. In particular, it was considered of interest to investigate the coupling reactions of 1H-1,2,3-triazole-5-diazonium salts with benzenesulphonylmethylene derivatives, since the hydrazone products of these reactions should be capable of cyclisation to 6-benzenesulphonyl derivatives of 1,2,3-triazolo[5,1-c]-1,2,4-triazines. The latter compounds would be of synthetic interest since it might be expected that the 6-benzenesulphonyl group should undergo nucleophilic displacement with a variety of reagents thus providing methods for the synthesis of 1,2,3-triazolo[5,1-c]-1,2,4-triazines functionalised at C(6). This proposal finds analogy in the literature. It is reported that substituents at the 6-position in 1,2,4-triazines show appreciable reactivity in nucleophilic displacement reactions. For example, a bromo substituent at C(6) in a 1,2,4-triazine, is easily displaced by chloride ion, secondary amines, hydrazine or thiols affording the corresponding 5-substituted 1,2,4-triazine. In addition, the sulphonyl group (SO₂R) is known to be a good leaving group, and is considered to be as easily replaced as a halogen substituent (e.g. Cl or Br) in nucleophilic displacement reactions. With this ultimate aim in mind, the coupling
reactions of the diazonium chlorides (507a) and (507b) and the diazonium betaine (508) with the benzenesulphonylmethylene compounds (509a-c) was investigated.

When the diazonium chloride (507a) was coupled with benzenesulphonylacetone (509a), the hydrazone (510a) was obtained in good yield. This product had an i.r. spectrum consistent with its assigned structure, but attempted crystallisation from a variety of solvents always resulted in its ready cyclisation to the triazolotriazine (511a) (see later). However, the hydrazone (510a) reacted with aqueous sodium hydroxide to form a water soluble sodium salt, the acidification of which regenerated the unchanged hydrazone (510a). This behaviour is consistent with the presence of a free triazole NH-group in the molecule. Furthermore, brief treatment of the hydrazone (510a) with acetic anhydride effected its smooth conversion into the corresponding N-acetyl derivative (510b), as demonstrated by its i.r., $^1$H n.m.r. and mass spectra and combustion analysis. However, a small quantity of the triazolotriazine (511a) was also isolated from this reaction.

When the hydrazone (510a) was heated under reflux in either ethanol or aqueous ethanolic sodium acetate, the triazolotriazine (511a) was obtained, as demonstrated by its elemental analysis and $^1$H n.m.r. and mass spectra. The absence of any significant bands above 1600 cm$^{-1}$ in the i.r. spectrum of (511a) is also consistent with the triazolotriazine structure. The question arises as to the mechanism involved in the formation of the hydrazone (510a) [and the corresponding triazolotriazine (511a)]. The probable course
is outlined in Scheme 105. A route exists for coupling of the active methylene compound with the diazonium salt (512), or the betaine (513) [the latter being formed by deprotonation of the diazonium salt (512) prior to the coupling reaction (512)\rightarrow (513)] to form the hydrazone (514). Cyclisation of the hydrazone (514), by loss of water, then occurs to afford the triazolotriazine (516) [Scheme 105; (514)\rightarrow (515)\rightarrow (516)].

When an aqueous solution of the diazonium chloride (507a) was added dropwise to a cooled aqueous ethanolic suspension of benzenesulphonylacetophenone (509b) and sodium acetate, the hydrazone (510c) was obtained in good yield. The hydrazone (510c) gave correct analytical and spectroscopic data and, consistent with its assigned structure, formed a soluble sodium salt on treatment with aqueous sodium hydroxide. Also, brief treatment of the hydrazone (510c) with warm acetic anhydride, readily afforded the corresponding N-acetyl derivative (510d), as indicated by its elemental analysis and i.r., $^1$H n.m.r. and mass spectra.

When the hydrazone (510c) was heated under reflux in ethanol, the corresponding triazolotriazine (511b) was obtained. Surprisingly, heating the hydrazone (510c) under reflux with aqueous ethanolic sodium acetate, in an attempt to effect its conversion into the triazolotriazine (511b), gave only a low recovery of starting material. Similarly, the hydrazone (510c) was largely unchanged when briefly heated under reflux in glacial acetic acid, only a small quantity of the triazolotriazine (511b) being obtained. The spectroscopic properties and combustion analysis of the triazolotriazine were consistent with its assigned structure.
\[ (517) \]

\[ \text{Scheme 106} \]
When benzenesulphonylacetonitrile (509c) was coupled with the diazonium chloride (507a), in the presence of sodium acetate, the triazolotriazine (511c) was obtained. Although no confirmation of this structure is possible on the basis of \(^1\)H n.m.r. and mass spectral or analytical data, the high m.p. supports the cyclic structure (511c) rather than that of the hydrazone (510e) (cf. page 144). In addition, the i.r. spectrum of (511c) contained bands at 3420 and 3330 cm\(^{-1}\), attributable to the presence of a primary amino group, but lacked absorption in the region expected for a cyano group. The insolubility of the crude material obtained from the coupling reaction, in aqueous sodium hydroxide, further confirms the presence of the cyclic structure (511c). Formation of the triazolotriazine (511c) demonstrates (as in other cases - cf. Scheme 106) preferential cyclisation via the cyano group.

The successful reactions of the diazonium chloride (507a) with the benzenesulphonylmethylene compounds (509a-c), prompted the investigation of the coupling reactions of the diazonium chloride (507b) and the diazonium betaine (508) with the same substrates.

Thus, when an aqueous ethanolic solution of the diazonium chloride (507b) was added to a cooled aqueous ethanolic suspension of benzenesulphonylacetophenone (509b) and sodium acetate, the expected hydrazone (510f) was obtained. This product had an i.r. spectrum consistent with its assigned structure, but on attempted crystallisation it underwent smooth conversion into the triazolotriazine (511d). The hydrazone (510f) did however, form a soluble sodium salt in
aqueous sodium hydroxide, and was regenerated, unchanged, from its alkaline solution on acification with aqueous hydrochloric acid. Treatment of the hydrazone (510f) with warm acetic anhydride also resulted in its smooth conversion into the N-acetyl derivative (510g) in quantitative yield. The combustion analysis and i.r. $^1$H n.m.r., and mass spectra of the latter were consistent with the assigned structure (see earlier, Chapter 3.2.2).

The hydrazone (510f) was converted easily into the triazolotriazine (511d) by heating its ethanolic solution under reflux, but this reaction also resulted in a large recovery of unchanged starting material. The elemental analysis of the triazolotriazine (511d) and its i.r. and mass spectral data were in accord with the assigned structure.

When the diazonium chloride (507b) was coupled with benzene-sulphonylacetonitrile (509c) in the presence of sodium acetate, the product obtained was the triazolotriazine (511e) as indicated by its analytical and spectroscopic data. The isomeric hydrazone structure (510h) for this product is excluded by its insolubility in aqueous sodium hydroxide, indicating the absence of a free triazole NH-group. The formation of the triazolotriazine (511e) can be explained by a mechanism analogous to that outlined for the triazolotriazine (511c) (see earlier).

The hydrazone (510i) was obtained when the diazonium betaine (508) was coupled with benzenesulphonylacetonitrile (509a) in the presence of sodium acetate. Although this compound had an i.r. spectrum consistent with the assigned structure, attempted crystallisation resulted in its ready cyclisation to the triazolotriazine (511f). However, its
$R^1$ $R^2$

a) Me OEt  
b) Me OMe  
c) Me OH  
d) Me $N_3$  
e) Me $\text{NH$_2$NH}_2$  
f) $\text{NH}_2$ OMe  
g) $\text{NH}_2$ $\text{NH$_2$NH}_2$  
h) $\text{NH}_2$ $N_3$
Scheme 107
solubility in aqueous sodium hydroxide and its regeneration unchanged, on acification with aqueous hydrochloric acid, is consistent with the presence of a free triazole NH-group and hence of the hydrazone structure (510i).

The hydrazone (510i) was smoothly converted into the triazolotriazine (511f), when heated under reflux in glacial acetic acid. This product gave $^1$H n.m.r. and mass spectra and an elemental analysis consistent with its assigned structure. The absence of any significant bands above 1600 cm$^{-1}$ in the i.r. spectrum of (511f), also indicated the presence of the triazolotriazine ring system.

As mentioned earlier, the benzenesulphonyl group at C-6 in a triazolotriazine ring should be amenable to nucleophilic displacement. To investigate this possibility, 6-benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) was heated under reflux with a solution of ethanolic sodium ethoxide. The major product of this reaction was the corresponding ether (521a), which was accompanied by a small quantity of the phenol (521c) (see later). The elemental analysis and spectral properties of the compound (521a) were fully consistent with its assigned structure. The question arises as to the mechanism involved in the displacement of the 6-benzenesulphonyl group in the triazolotriazine (511a) by ethoxide ion. It is known that the displacement of substituents from a triazine ring usually occurs via an addition-elimination reaction. The probable course of the reaction of (511a) with ethoxide ion is thus probably that outlined in Scheme 107. The isolation of the hydroxytriazolotriazine (521c) as a minor product in
the reaction of (511a) with ethoxide ion, can be explained by competing reaction of the triazolotriazine (511a) with a small amount of sodium hydroxide present as impurity in the reaction mixture and formed by the reaction of traces of water, present in the ethanol solvent, with the sodium ethoxide.

The successful formation of the ethyl ether (521a) prompted the investigation of the similar formation of the methyl ether (521b). This was accomplished by heating the triazolotriazine (511a) under reflux in methanolic sodium methoxide. As in the reaction of the triazolotriazine (511a) with sodium ethoxide (see earlier), the methyl ether (521b) was accompanied by a small quantity of 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) whose formation can be explained as in the sodium ethoxide promoted reaction (see before). The structure of the methyl ether (521b) was readily supported by its i.r., $^1$H n.m.r. and mass spectra and by its combustion analysis.

As has already been explained, formation of the phenol (521c) as a by-product in the reactions of the triazolotriazine (511a) with sodium ethoxide and sodium methoxide, can be attributed to the presence of small quantities of sodium hydroxide in each case. This origin for the phenol (521c) was readily demonstrated by its formation in good yield by heating the triazolotriazine (511a) under reflux in aqueous sodium hydroxide. The phenol (521c) gave an elemental analysis and spectroscopic data consistent with its assigned structure.
Scheme 108
Scheme 109
When the triazolotriazine (511a) was heated under reflux with sodium azide in aqueous dioxan, the corresponding azide (521d) was obtained. This product was identified by the presence of an absorption band at 2130 cm\(^{-1}\) in its i.r. spectrum, consistent with the presence of an azido group. However, its attempted crystallisation from a variety of solvents resulted in decomposition to complex mixtures.

Heating the triazolotriazine (511a) under reflux with hydrazine hydrate, gave the expected hydrazine derivative (521e) as its hemi-hydrate, as indicated by its elemental analysis and i.r. spectrum. The hydrazine (521e) also gave \(^1\)H n.m.r. and mass spectral data consistent with its assigned structure.

In an attempt to displace the benzenesulphonyl group at C(6) in the triazolotriazine (511a) by hydrogen, the triazolotriazine (511a) was heated under reflux with sodium borohydride in aqueous dioxan. The product isolated from this reaction gave an elemental analysis and spectroscopic data consistent with its being 7-methyl-3-phenyl-4,5,6,7-tetrahydro-1,2,3-triazolo[5,1-c]-1,2,4-triazine (525). The structure assigned to (525), is further supported by the formation of the triazolotriazine (526) (obtained independently as described later in Chapter 3.2.4) when (525) was oxidised with manganese dioxide. The mechanism of the formation of (525) probably involves initial displacement of the benzenesulphonyl group by hydride ion to form the triazolotriazine (526) as an intermediate (Scheme 109). Further reduction of (526), by sodium borohydride, then occurs to form the product (525). The proposal that the triazolotriazine (526) is an intermediate in the suggested mechanism,
is supported by the reaction of (526) with sodium borohydride to afford the tetrahydrotriazolotriazine (525) obtained before.

When the triazolotriazine (511a) was heated under reflux with piperidine in ethanol, the ethyl ether (521a) obtained before, was isolated in excellent yield. None of the expected piperidine substituted product could be detected. However, it is widely known\textsuperscript{227} that basic reagents can interact with alcohols to form alkoxide ions, and thus alcoholysis is a possible side reaction whenever nucleophilic substitution is conducted in an alcoholic solvent. In some cases this is only a minor reaction, but it can sometimes be the major.\textsuperscript{227} For example, displacement of fluorine from p-fluoronitrobenzene by phenoxide ion in methanol results in a significant quantity of the p-methoxynitrobenzene.\textsuperscript{228} Similarly, nucleophilic substitution reactions of some substituted 2,4-dinitrobenzene derivatives by piperidine in methanol also result in the formation of the corresponding methyl ether.\textsuperscript{229} However, Cowell and Chapman\textsuperscript{230} report no observation of alcoholysis in their work on the substitution reactions of pyrimidines and dinitrobenzenes with 3- and 4-picoline. It is therefore suggested\textsuperscript{229} that the appearance of alcoholysis in some cases, and not others, indicates a dependance on the nucleophilic reactivity of the two reagents (alcohol and base). It is therefore tentatively suggested in the present studies that the formation of the ether (521a) in the attempted reaction of the triazolotriazine (511a) with piperidine, occurs by reaction of (511a) with ethoxide ion. Consideration of equation (i) shows that ethoxide ion can be obtained by
reaction of piperidine (B) with the ethanol solvent. It is however, somewhat surprising that no product was isolated due to reaction of (511a) with piperidine, particularly since piperidine is apparently a strong enough base to promote ethoxide formation from ethanol.

In an attempt to curtail the formation of the ether (521a), the triazolotriazine (511a) was heated under reflux with piperidine in dioxan. However, this resulted in the recovery of a small quantity of unchanged starting material, accompanied by a moderate yield of the phenol (521c). The isolation of the phenol (521c) can be explained by consideration of equation (ii). The presence of a small quantity of water in the dioxan solvent results in the formation of hydroxide ion, which subsequently displaces the benzene-sulphonyl group to afford the phenol (521c).

The triazolotriazine (511a) was heated under reflux with sodium cyanide in aqueous ethanol, in an attempt to introduce a cyano group at the C(6) position in the triazine ring. However, the ethyl ether (521a) and the phenol (521c) were the only products isolated from this reaction.
The formation of these two products [(521a) and (521c)] is not surprising and can be explained by hydrolysis of the sodium cyanide to sodium hydroxide which can function directly as the nucleophile or can deprotonate the ethanol solvent to ethoxide ion which can in turn displace the benzenesulphonyl group with formation of the ether (521a). In an attempt to suppress the formation of the ether (521a) and the phenol (521c) the triazolotriazine (511a) was heated under reflux with sodium cyanide in aqueous dioxan. However, these conditions only resulted in the formation of the phenol (521c), obtained before.

When the triazolotriazine (511a) was heated under reflux with potassium cyanate in aqueous dioxan, the phenol (521c) was isolated in good yield. The formation of the phenol (521c) in this reaction is again consistent with the presence of hydroxide ion generated by the hydrolysis of potassium cyanate by the water present.

In an attempt to introduce a thiocyano group at C(6) in the triazine ring, the triazolotriazine (511a) was heated under reflux with sodium thiocyanate in aqueous dioxan. However, in this case only unreacted starting material was recovered. A similar result was obtained when the triazolotriazine (511a) was heated under reflux with sodium acetate in aqueous ethanol.

A high yield of the phenol (521c) was recovered as the only product when the triazolotriazine (511a) was heated under reflux with diethylamine in dioxan. As explained before, the small quantity of water associated with the dioxan solvent is converted, by diethylamine, into hydroxide ion [cf. equation (ii)], which then reacts with (511a) to
afford the phenol (521c).

When the triazolotriazine (511a) was heated under reflux with triethylamine in dioxan, a quantitative recovery of unchanged starting material was obtained.

The successful nucleophilic displacement of the 6-benzenesulphonyl group in the triazolotriazine (511a), prompted an analogous investigation into the displacement reactions of the 6-benzenesulphonyl group in the triazolotriazine (511c). It was hoped that if suitable substituents could be introduced at the 6-position of (511c), then fused systems of the type (528) could be synthesised. When the aminotriazolotriazine (511c) was heated under reflux with

\[
\begin{array}{c}
\text{Y} \\
\text{X} \\
\text{N} \\
\text{N} \\
\text{N} \\
\text{N} \\
\end{array}
\]

(528)

methanolic sodium methoxide, the corresponding ether (521f) was obtained, in good yield. This product gave an elemental analysis and i.r., \(^1\text{H}\) n.m.r. and mass spectra consistent with its assigned structure. In contrast to the similar reaction of 6-benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]1,2,4-triazine (511a), (see before) none of the corresponding phenol was obtained in the reaction of (511c) with methanolic sodium methoxide.

The hydrazine derivative (521g) was obtained in virtually quantitative yield when the triazolotriazine (511c) was heated
under reflux with hydrazine hydrate. The structure of the hydrazine derivative (521g) is supported by its combustion analysis and by i.r. and mass spectral data. Further evidence in support of the structure of the hydrazine derivative (521g) was obtained by its diazotisation with nitrous acid. The product isolated from this reaction had an absorption band at 2100 cm⁻¹ in its i.r. spectrum, consistent with its being the corresponding azide (521h). However, attempted crystallisation of this compound from a variety of solvents always resulted in its ready decomposition to dark intractable mixtures.

In an attempt to utilise the bifunctionality of the hydrazine derivative (521g), for the synthesis of the azo-pteridine ring system (529), its reaction with acetic anhydride was investigated. Brief treatment of (521g) with acetic anhydride resulted in the recovery of unchanged starting material. However, when the hydrazine (521g) was heated under reflux in acetic anhydride for a prolonged period, only a dark oil, shown by t.l.c. examination to be a multi-component mixture, was isolated. A similar result was obtained when the hydrazine (521g) was heated under reflux with formic acid, in a further attempt to synthesise the ring system (529). Only a dark intractable solid, which could not be characterised was recovered from this reaction.
\[
\text{Ph}_3\text{P}^+\text{CHCOR}_2^+ + \text{RN}_3^3 \rightarrow \text{N}^3_3 \text{N} \quad (531)
\]

\[
\text{Ph}_3\text{P}^+\text{CHCOR}_2^+ + \text{RN}_3^3 \rightarrow \text{N}^3_3 \text{N} \quad (532)
\]

\[
\text{Ph}_3\text{P}^+\text{CH}=\text{CHCOR} X^- \rightarrow \text{N}^3_3 \text{N} \quad (533)
\]

\[
\text{Ph}_3\text{P}^+\text{CH}=\text{CHCOR} X^- \rightarrow \text{N}^3_3 \text{N} \quad (534)
\]

Scheme 110
3.2.4 The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Methylene phosphonium Salts and Related Compounds

Organophosphorus substrates have been used extensively for the preparation of many compounds since Wittig's observation that the carbon-phosphorus double bond of phosphorus ylids, reacts with the carbon-oxygen double bond of carbonyl compounds to afford olefins. Zbiral, amongst others, has recently reviewed the uses of certain phosphorus containing compounds for the synthesis of numerous heterocyclic nuclei. In particular, there have been many reports of the synthesis of the 1,2,3-triazole ring system by this method. Examples of these reactions are outlined in Scheme 110. Acylyphosphonium salts of the type (530), afford a wide variety of 1,2,3-triazoles of type (532), by their reaction with certain azides (531). Similarly, azide ion reacts with alkenylphosphonium salts to afford the 1,2,3-triazoles (534)

\[ \text{Scheme 110; (533)\rightarrow (534)} \]

However, despite their many uses in organic synthesis, organophosphorus compounds have not been used to synthesise fused heterocyclic ring systems.

Aryldiazonium salts have been reported to react with phosphorus containing active methylene compounds (cf. Chapter 3.2.1). However, the coupling reactions of heterocyclic diazonium salts with methylene phosphonium salts has not been reported before. The use of phosphorus containing substrates as coupling components may ultimately lead to interesting fused heterocyclic ring systems, by cyclisation of the initially formed hydrazone intermediates. Consequently, the reactions of the 1H-1,2,3-triazole-5-diazonium salts (534 a,b and d) and the betaine (536) with the methylene-phosphonium salts (537 a-d) were investigated.
\[ \text{HN} \]
\[ \text{N} \]
\[ \text{R}^1 \]
\[ \text{R}^2 \]
\[ \text{HN} \]
\[ \text{N} \]
\[ \text{R}^1 \]
\[ \text{R}^2 \]
\[ \text{R}^1 \]
\[ \text{R}^2 \]
\[ \text{a)} \text{Ph} \quad \text{N}_2^+ \text{Cl}^- \]
\[ \text{b)} \text{CONH}_2 \quad \text{N}_2^+ \text{Cl}^- \]
\[ \text{c)} \text{CN} \quad \text{NH}_2^- \]
\[ \text{d)} \text{CN} \quad \text{N}_2\text{NO}_3^- \]

\[ \text{Ph}_3^+ \text{P=CHCOR}^2 \text{X}^- \]
\[ \text{Ph}_3^+ \text{P=CHCOMe} \]

\[ (535) \]

\[ (536) \]

\[ (537) \]

\[ (538) \]
(539)

\[
R^1 \quad R^2 \quad R^3
\]

a) Ph  Me  H
b) Ph  Ph  H
c) Ph  Ph  Me
d) Ph  Me  Ph
e) CONH_2  Ph  H
f) SO_2Ph  Ph  H
g) CN  Ph  H

(540)
When an aqueous ethanolic solution of the diazonium chloride (535a) was introduced into a cooled suspension of acetonyltriphosphorylphosphonium chloride (537a) and sodium acetate, a solid whose properties are consistent with 7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539a) was obtained. The triazolotriazine (539a) was also obtained by the reaction of the phosphorane (538) with the diazonium chloride (535a) in the absence of sodium acetate. Further evidence for the proposed structure of (539a) was obtained by its reaction with glacial acetic acid. Prolonged heating under reflux of the triazolotriazine (539a) in glacial acetic acid resulted in the ready scission of the triazole ring to give the α-acetoxyethyltriazine (540), which was isolated as a red oil. The structure assigned to (540) follows from its i.r. and $^1$H n.m.r. spectra. A band at 1740 cm$^{-1}$ in the i.r. spectrum of (540) is assignable to the carbonyl group. Similarly, a singlet at $\delta$ 6.88 p.p.m. in the $^1$H n.m.r. spectrum of (540) is attributable to a benzylic proton. Furthermore, two three proton singlets at $\delta$ 2.55 and 2.24 p.p.m. are assignable to the protons of the ring and acetoxy methyl substituents. However, an attempt to characterise the α-acetoxytriazine (540) directly, by its oxidation with chromic acid, was unsuccessful, no identifiable material being obtained from this reaction. The acid-catalysed scission of fused 1,2,3-triazoles containing a non-electron withdrawing substituent at C-3 finds analogy in the literature. The mechanism involved in such reactions is probably that outlined in Scheme III.
Scheme 112
Scheme 113
Scheme 114

\[
\text{Ph}_3\text{P}=\text{CHCOR} \quad \xrightarrow{\text{Ph}_3\text{P}-\text{CHCOR}} \quad \text{Ph}_3\text{P}=\text{CHCOR} \\
\downarrow \quad \downarrow \\
\text{R-N-NEN} \quad \xrightarrow{\text{R-N-NEN}} \\
\text{Ph}_3\text{P} \quad \text{Ph}_3\text{P}
\]

\[
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R} \\
\downarrow \quad \downarrow \\
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R}
\]

\[
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R} \\
\downarrow \quad \downarrow \\
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R}
\]

\[
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R} \\
\downarrow \quad \downarrow \\
\text{Ph}_3\text{P}=\text{O} \\
\text{N-N-R}
\]
The question now arises as to the mechanism involved in the formation of the triazolotriazine (539a). The proposed mechanism is outlined in Scheme 112. The phosphonium salt (546) is probably converted into the phosphorane (547) in the basic reaction medium (sodium acetate), and it is the ylid form of the phosphorane which then couples with the diazonium salt to form (549) [this proposal readily finds support from the ability of the phosphorane (538) to couple with the diazonium salt (535a) in the absence of sodium acetate (see before)]. Cyclisation of the intermediate (549), followed by extrusion of triphenylphosphine oxide, then follows to afford the triazolotriazine (552).

As mentioned earlier, organophosphorus compounds have been used to synthesise 1,2,3-triazole ring systems [cf. Scheme 110]. The mechanism proposed in the literature for these reactions is via a 1,3-cycloaddition mechanism, outlined in Scheme 113. The phosphorane, in its enol-betaine form (551), reacts with the azide to form the intermediate (555), which then loses triphenylphosphine oxide to give the observed product [(555)→(556)→(557)]. However, an alternative course is possible for these reactions, analogous to the unambiguous mechanism proposed for the synthesis of the triazolotriazine (539a) as outlined in Scheme 112. If it is the ylid form of the phosphorane (559) which reacts with the azide moiety, then the mechanism can be written as in Scheme 114. Further reaction of the intermediate (560) so formed, would then give [(561)→(562)] which can readily lose triphenylphosphine oxide to afford the product (563). Thus, the synthesis of 1,2,3-triazoles from phosphorus compounds (described in the literature as cyclo-
addition reactions) can also be assigned a mechanism analogous to that described in Scheme 112 for the formation of the triazolotriazine (539a).

When the diazonium chloride (535a) was introduced into a cooled suspension of phenacyltriphenylphosphonium bromide (537b) in the presence of sodium acetate, the triazolotriazine (539b) was obtained in excellent yield. The triazolotriazine (539b) gave $^1$H n.m.r. and mass spectra and elemental analysis consistent with its assigned structure. The absence of any significant bands above 1600 cm$^{-1}$ in the i.r. spectrum of (539b) also supports the proposed structure.

The triazolotriazine (539c) was obtained only in very poor yield when the diazonium chloride (535a) was coupled with 1-methylphenacyltriphenylphosphonium bromide (537c), in the presence of sodium acetate. Its i.r. and mass spectra and elemental analysis were consistent with the proposed structure. However, no $^1$H n.m.r. spectrum of (539c) could be obtained due to its insolubility in [2$^2$H$_6$] dimethyl sulphoxide. An attempt to obtain the corresponding triazolotriazine isomer (539d) by the reaction of the diazonium salt (535a) with the phosphonium salt (537d) was unsuccessful. Only unreacted phosphonium salt (537d) accompanied by an unresolvable multicomponent gum, were obtained. In a further attempt to isolate the triazolotriazine (539d), the diazonium salt (535a) was coupled with the phosphonium salt (537d) in the presence of sodium hydroxide. However, these conditions resulted only in the formation of multicomponent gums, accompanied by a trace
amount of triphenylphosphine oxide. The failure of the phosphonium salts (537c and 537d) to couple satisfactorily with the diazonium salt (535a) can be explained by steric hindrance. The presence of the methyl and phenyl groups at the α-carbon in the phosphonium salts (537c) and (537d) will clearly hinder the approach to the diazonium salt, thus resulting in little or no reaction.

When the diazonium chloride (535a) was coupled with 3-triphenylphosphoranylidene-1-phenylmaleimide (564) in the presence of sodium acetate in aqueous ethanol, a large quantity of unchanged phosphorane (564) was recovered. Further work up of the reaction mother liquor resulted in the isolation of the known \(^{212}\) 4-phenyl-1H-1,2,3-triazole (566) obtained before. The formation of the triazole (566) is explained in terms of the reductive deamination of the diazonium salt (535a), which readily occurs in alcoholic solvents (cf. Chapter 3.1). Similarly, no reaction occurred when an attempt was made to couple the diazonium salt (535a) with 2-triphenylphosphoranylidene-1,2,3,4-tetrahydronaphthalene-1,4-dione (565) in the presence of sodium acetate. The unchanged phosphorane (565) from this attempted reaction was accompanied by an unresolvable multicomponent oil, which could not be separated. The inability of the phosphoranes (564) and (565) to couple with the diazonium salt (535a) is somewhat surprising, particularly since they are reported to behave as normal phosphoranes by readily undergoing normal Wittig type reactions.\(^{239-242}\)
The successful reactions of the phosphonium salts (537 a,b and c) with the diazonium chloride (535a) prompted investigations into the coupling reactions of the diazonium salts (535b and d) and the diazonium betaine (536) with the phosphonium bromide (537b). Thus, when a cooled suspension of phenacyltriphenylphosphonium bromide (537b) and sodium acetate was treated with 3-carbamoyl 1H-1,2,3-triazole-5-diazonium chloride (535b), the triazolotriazine (539e) was obtained, but only in poor yield. Further work up of the reaction mother liquor resulted in a large recovery of unchanged phosphonium salt (537b). The spectroscopic properties and elemental analysis of the triazolotriazine (539e) were consistent with the assigned structure.

The expected triazolotriazine (539f) was accompanied by triethylamine hydrobromide when the diazonium betaine (536) was coupled with the phosphorane (537b) in the presence of triethylamine. The triazolotriazine (539f) gave the expected elemental analysis and $^1$H n.m.r. and mass spectral data, and consistent with its condensed cyclic structure it showed no absorption bands above 1600 cm$^{-1}$ in its i.r. spectrum.

When an aqueous solution of the diazonium nitrate (535d) [prepared in situ by diazotisation of the corresponding amine (535c) with nitrous acid] was added to an aqueous ethanolic suspension of the phosphonium salt (537b) and sodium acetate, a large quantity of the unchanged salt (537b) was recovered. Further work up of the reaction mother liquor afforded a yellow oil, which was shown by t.l.c. to be an unresolvable multicomponent mixture.
Scheme 115
The ability of methylene phosphonium salts to couple with 1,2,4-triazole-5-diazonium salts is also readily demonstrated. When a freshly prepared solution of the diazonium nitrate (567b) [prepared in situ from the corresponding amine (567a)] was introduced into a suspension of the phosphonium salt (537b) and sodium acetate the 1,2,4-triazolo[5,1-c]-1,2,4-triazine (568) was obtained. The elemental analysis and spectral properties of the triazolotriazine (568) were consistent with its assigned structure.

The successful synthesis of the triazolotriazines (539 a-c, e, f) prompted an investigation into the coupling reactions of 3-phenyl-1H-1,2,3-triazole-5-diazonium chloride (535a) with the arsonium, sulphonium and ammonium salts (569 a-c). Thus, when a solution of the diazonium chloride (535a) was introduced into a cooled suspension of the arsonium salt (569a) and sodium acetate, the triazolotriazine (539b), obtained before, was isolated. The mechanism of formation of the triazolotriazine (539b) under these conditions is probably analogous to that postulated in Scheme 112 earlier (i.e. extrusion of triphenyl arsonium oxide). In contrast, however, the coupling of the diazonium chloride (535a) with the sulphonium salt (569b) in the presence of sodium acetate under identical conditions, resulted only in the formation of a multicomponent gum which yielded no characterisable product.

When the diazonium chloride (535a) was coupled with the ammonium salt (569c) an amorphous solid was recovered. The solid showed a peak at 1675 cm\(^{-1}\) in its i.r. spectrum, attributable to the presence of a carbonyl group. However, attempted crystallisation of the amorphous solid from a
(570)

(571)

R-CH₂SCN

(572)

(573)

(574)
variety of solvents resulted in its rapid decomposition to dark gums, which could not be further characterised.

3.2.5 The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Thiocyanomethylene Compounds

A wide variety of aliphatic substrates containing an activated methylene group are known to react with heterocyclic diazonium salts and diazo compounds, to form the corresponding hydrazones, as already discussed in Chapter 1. In contrast, the coupling reactions of heterocyclic diazonium salts with methylene compounds activated by a thiocyano group, have not been reported. Indeed, only one example of the coupling of a thiocyanomethylene component with aryl-diazonium salts appears in the literature (cf. Chapter 3.2.1).

The coupling reactions of 1,2,3-triazolatediazonium compounds with simple thiocyanate-containing substrates have now been demonstrated.

When the diazonium chloride (570a) was coupled with the thiocyanomethylene compound (572a) in the presence of sodium acetate, 5-benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ^4-1,3,4-thiadiazoline (573a) was isolated in quantitative yield. The assignment of a thiadiazoline structure to this product as opposed to a simple hydrazone structure has been confirmed by spectral and chemical methods. The thiadiazoline (573a) showed an absorption band at 3300 cm\(^{-1}\) in its i.r. spectrum, due to the presence of a free NH-group, but lacked any peak attributable to a free SCN substituent. Furthermore, the coupling product did not change when heated under reflux in ethanol, ethanolic sodium acetate or glacial acetic acid.
Scheme 116

R
a) Ac
b) NO
This failure to effect any change in the product (573a) under these standard cyclisation conditions strongly suggests that it already exists in a cyclic form. The triazolotriazine structure (574) is readily ruled out by i.r. spectral data, absorption at 1640 cm\(^{-1}\) in the i.r. spectrum of (573a) indicating the presence of a benzoyl carbonyl group. The formation of the thiadiazoline (573a) finds direct analogy in the literature. Shawali and Abdelhamid\(^{224}\) report the isolation of thiadiazoline products from the coupling of aryl diazonium salts with thiocyanomethylene substrates.

Further evidence for the thiadiazoline structure (573a) is provided by reaction with acetic anhydride. When the thiadiazoline (573a) was heated briefly with acetic anhydride, the diacetyl derivative (573b) was obtained in moderate yield. The spectral properties of this product were fully consistent with the assigned structure. However, correct analytical figures could not be obtained. The diacetyl derivative (573b) was also obtained when the thiadiazoline (573a) was subjected to prolonged heating under reflux in acetic anhydride, and when heated under reflux in aqueous ethanol, it gave a product which crystallised as a solvate from toluene and showed spectral properties in accord with its formulation as the monoacetyl derivative (573c). The presence of the acetylimino substituent in (573c) is readily supported by the presence in its i.r. spectrum of a carbonyl band at 1645 cm\(^{-1}\). Shawali and Abdelhamid\(^{224}\) report that acetylation of the thiadiazoline (575) affords the corresponding N-acetyl derivative (576a). The acetyl derivative (576a) shows an absorption band at 1640 cm\(^{-1}\).
in its i.r. spectrum, attributable to the imino N-acetyl group. Furthermore, it has been shown conclusively that a 1,2,3-triazole ring N-acetyl group gives rise to absorption in the i.r. spectrum at between 1790-1740 cm⁻¹. When the monoacetyl derivative (573c) was briefly warmed in acetic anhydride, the diacetyl derivative (573b) obtained before was isolated.

In a further attempt to provide conclusive evidence for the structure of the thiadiazoline (573a), it was subjected to acidic and basic hydrolysis as well as reaction with nitrous acid, hydrazine and hydroxylamine. When the thiadiazoline (573a) was heated under reflux with sulphuric acid, it was recovered unchanged as its sulphate salt which gave the free thiadiazoline by treatment with saturated aqueous sodium hydrogen carbonate. Hydrolysis of the thiadiazoline (573a) in aqueous sodium hydroxide afforded an amorphous solid, which showed an ill-defined i.r. spectrum and could not be characterised. Further work up of the reaction mother liquor afforded a moderate yield of benzoic acid. When the thiadiazoline (573a) was heated under reflux with hydrazine, no identifiable material was obtained. Similarly, its attempted reaction with hydroxylamine, gave only an intractable gum, shown by t.l.c. to be a multicomponent mixture. However, when the thiadiazoline (573a) was diazotised with sodium nitrite in the presence of acetic acid, 5-benzoyl-2-nitrosoimino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573d) was obtained, as indicated by its elemental analysis and spectral properties. This result parallels that
Scheme 117
described by Shawali and Abdelhamid,\textsuperscript{224} who observed that similar treatment of the thiadiazoline (575) afforded the corresponding nitrosoimine (576b). An attempt to characterise the nitrosoimine (573d) further by reduction with sulphur dioxide was unsuccessful. The product from this reaction was an unidentified solid (C), whose i.r. and mass spectra and elemental analysis did not suggest any plausible structure. However, when the nitrosoimine (573d) was warmed briefly with acetic anhydride, in an attempt to obtain its N-acetyl derivative, the diacetyl derivative (573b), obtained before, was isolated in good yield.

The mechanism proposed for the formation of the thiadiazoline (573a) is outlined in Scheme 117 and is directly analogous to that described by Shawali and Abdelhamid.\textsuperscript{224} Formation of the hydrazone (579) is followed by cyclisation, via the thiocyanate group, to afford the product. [Scheme 117; (577) + (578)\rightarrow(579)\rightarrow(580)].

When the diazonium chloride (570a) was coupled with acetonylthiocyanate (572b) in the presence of sodium acetate, the corresponding thiadiazoline (573e) was obtained. The combustion analysis and spectral properties of this product were consistent with its assigned structure. In addition, the thiadiazoline (573e) was recovered unchanged, when heated under reflux in ethanol and ethanolic sodium acetate supporting its cyclic structure [cf. the thiadiazoline (573a)]. The thiadiazoline (573e) also formed the corresponding diacetyl derivative (573f) on brief treatment with acetic anhydride. The monoacetyl derivative (573g) was
readily isolated when the diacetyl derivative (573f) was heated under reflux in aqueous ethanol.

Cyanomethylenethiocyanate (572c) was readily available as a yellow oil, prepared by reaction of potassium thiocyanate with chloroacetonitrile. Despite the fact that the compound (572c) is reported in the literature as a solid, m.p. 96-98° the oil obtained in the present studies showed properties consistent with its formulation as (572c). However, when the diazonium salt (570a) was introduced into a cooled solution of the thiocyanate (572c) and sodium acetate, a dark amorphous solid (which could not be characterised) was isolated, accompanied by a gum, shown by t.l.c. to be a multicomponent mixture. Similarly, when the diazonium chloride (570a) was coupled with ethyl thiocyanoacetate (572d), no identifiable material was obtained.

The successful synthesis of the thiadiazolines (573a) and (573e) prompted a further investigation into the coupling reactions of phenacylthiocyanate (572a) with the diazo compounds (570b), (570d) and (571). Thus, when a solution of phenacylthiocyanate (572a) and sodium acetate was added to a cooled suspension of the diazonium betaine (571), the corresponding thiadiazoline (573h) was obtained. Similarly when the diazonium nitrate (570d) [prepared in situ from the corresponding amine (570c)] was coupled with the thiocyano compound (572a), in the presence of sodium acetate, the thiadiazoline (573i) was also obtained. This compound crystallised from glacial acetic acid as the acetic acid solvate.
\[
\text{Scheme 118}
\]
When 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (570b) was coupled with phenacylthiocyanate (572a), in the presence of sodium acetate, a product was isolated whose spectral properties and elemental analysis are consistent with its being 5-benzoyl-3H-1,2,3-triazolo[4,5-d]-1,3,4-thiadiazolo[2,3-b]pyrimidin-8-one (584) as opposed to the expected thiadiazoline (582). Further work up of the mother liquor from this reaction gave an unidentified solid (D) whose i.r. spectrum showed the presence of an NH-substituent and a carbonyl group, and whose elemental analysis and mass spectrum indicated the formula C_{19}H_{14}N_{6}O_{2}S. However, no plausible structure could be assigned to the solid (D), and lack of time prevented its further investigation.

The formation of the product (584) can be explained in terms of the tentative mechanism outlined in Scheme 118. Coupling of the diazonium salt (570b) with phenacylthiocyanate (572a) occurs to afford the thiadiazoline (582), by cyclisation of the intermediate hydrazone (581) (cf. Scheme 117 before). Cyclisation of the thiadiazoline (582), via the amide substituent, can then occur to give (583). Final loss of ammonia then gives rise to the observed product (584).

3.2.6 The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Naphthols and Phenols

The coupling of aryldiazonium salts with naphthols and phenols is very well documented in the literature, as already outlined earlier in Chapter 1. Numerous heterocyclic
Scheme 119

a) CN
b) COPh
diazonium compounds have also been reported to couple with naphthols and phenols, to afford the corresponding azo compounds (cf. Chapter 1). However, although the coupling reactions of NH-pyrazole, NH-imidazole, NH-1,2,4-triazole and NH-tetrazolediazonium salts with phenols and naphthols have been reported, the formation of fused six-membered ring systems, by cyclisation of the so formed azo products, has not been exploited to any extent. Reimlinger and his co-workers have observed, however, that 3-diazopyrazole (585) when reacted with alkaline β-naphthol afforded the naphthopyrazolotriazine (586), via an intramolecular cyclisation (Scheme 119). The coupling of 1H-1,2,3-triazolediazonium salts with β-naphthol has also been demonstrated. Regitz et al. have reported the formation of the azo compounds (588a and 588b) by coupling the diazonium salts (587a and 587b) with β-naphthol. However, as with other heterocyclic azo compounds formed in this way, no attempt was made to synthesise the corresponding naphthotriazolotriazines (589a and 589b). The aim of the following work was therefore to exploit the coupling reactions of other 1H-1,2,3-triazolediazonium salts with naphthols and phenols, in an attempt to gain synthetic access to the 1,2,3-triazolonaphtho-1,2,4-triazine and 1,2,3-triazolobenzo-1,2,4-triazine ring systems.

When an aqueous ethanolic solution of the diazonium salt (590a) was added to a cooled ethanolic solution of β-naphthol containing aqueous sodium hydroxide, the azo compound (592a) was obtained in quantitative yield. The azo compound (592a) gave correct analytical and i.r. and mass spectral data. Its $^1$H n.m.r. spectrum (see figure 6) showed


(590)

\[
\begin{align*}
R^1 & \quad R^2 \\
\text{a)} & \quad \text{Ph} & \quad \text{N}^2+\text{Cl}^- \\
\text{b)} & \quad \text{CONH}_2 & \quad \text{N}_2^+\text{Cl}^- \\
\text{c)} & \quad \text{CN} & \quad \text{NH}_2^- \\
\text{d)} & \quad \text{CN} & \quad \text{N}_2\text{NO}_3^- \\
\end{align*}
\]

(593)

\[
\begin{align*}
R & \\
\text{a)} & \quad \text{Ph} \\
\text{b)} & \quad \text{CONH}_2 \\
\text{c)} & \quad \text{CN} \\
\text{d)} & \quad \text{SO}_2\text{Ph} \\
\end{align*}
\]
Figure 6

The $^1$H n.m.r. Spectrum of 1-(4-phenyl-1H-1,2,3-triazol-5-yl)azo-2-napthol (592a) in $[^2H_6]$ Dimethyl Sulphoxide

(592a)
a single proton multiplet at δ 8.64-8.46 p.p.m., assigned to H-8, and two single proton doublets at δ 8.09 and 7.20 p.p.m., due to H-3 and H-4 respectively. The three proton multiplet at δ 7.98-7.82 p.p.m. is assigned to H-7 and the two ortho protons of the 4-phenyl group (see figure 6). The five proton multiplet at δ 7.74-7.38 p.p.m. is assigned to the protons at H-5 and H-6 and to the remaining meta and para protons of the phenyl group at C(4). These assignments are based on the expectation that the ortho protons in the C(4) phenyl group will be shifted downfield, due to the deshielding effect of the triazole ring. The azo compound (592a) was soluble on brief treatment with aqueous sodium hydroxide, and was regenerated, unchanged from its alkaline solution, by acidification with aqueous hydrochloric acid. This behaviour is consistent with the acidity of the proton at N-1 on the triazole ring. The presence of a free triazole N-H proton in (592a) was further demonstrated by its reaction with acetic anhydride. Thus, acetylation of the azo compound (592a) was accomplished smoothly by brief treatment with warm acetic anhydride to afford the corresponding N-acetyl derivative (592b) whose elemental analysis and spectral properties are consistent with the assigned structure (see before).

When the azo compound (592a) was heated under reflux in either glacial acetic acid or ethanolic sodium acetate, it underwent smooth conversion into the corresponding triazolonaphthotriazine (593a). However, in the case of glacial acetic acid, the triazolonaphthotriazine (593a) was accompanied
by a moderate yield of the naphthotriazine (598a), formed by acid scission of the triazole ring in (593a) (see later). The triazolonaphthotriazine (593a) gave an elemental analysis and mass spectrum consistent with its structure. The lack of any absorption above 1600 cm\(^{-1}\) in the i.r. spectrum of (593a) also supports the cyclic structure. However, no confirmation of this by an \(^1\)H n.m.r. spectrum could be obtained, due to the insolubility of (593a) in \([\text{\textsuperscript{2}}\text{H}_6]\) dimethyl sulphoxide and \([\text{\textsuperscript{2}}\text{H}_6]\) acetone.

The successful synthesis of the triazolonaphthotriazine (593a) prompted an investigation into the coupling reactions of other triazolodiazonium compounds with \(\beta\)-naphthol. Thus, when 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (590b) was coupled with \(\beta\)-naphthol in the presence of aqueous sodium hydroxide, a solid was recovered which when crystallised afforded the triazolonaphthotriazine (593b) (see later). The presence of a free triazole NH-group in the crude solid obtained from the coupling of (590b) with \(\beta\)-naphthol was readily demonstrated by its formation on treatment with aqueous sodium hydroxide, of a water soluble sodium salt, from which it could be recovered, unchanged, by acidification with aqueous hydrochloric acid. This behaviour is consistent with the product of the coupling of (590b) with \(\beta\)-naphthol being the azo compound (592c). However, an attempt to form the \(\text{N}\)-acetyl derivative (592d), by treatment of the azo compound (592c) with warm acetic anhydride, was unsuccessful. This treatment resulted only in the ready cyclisation of (592c) to the triazolonaphthotriazine (593b) obtained before. Correspondingly, the
triazolonaphthotriazine (593b) was obtained in excellent yield, when the azo compound (592c) was heated under reflux in glacial acetic acid. The triazolonaphthotriazine (593b) gave a correct elemental analysis and showed i.r. and mass spectra consistent with its structure. However, as with the triazolonaphthotriazine (593a) the confirmation of this structure by $^1$H n.m.r. could not be achieved due to the insolubility of (593b) in $[^2H_6]$ dimethyl sulfoxide.

When a cooled aqueous solution of the diazonium nitrate (590d) [prepared in situ from the corresponding amine (590c)] was treated with an aqueous ethanolic solution of β-naphthol and aqueous sodium hydroxide, the azo compound (592e) reported by Regitz et al.\textsuperscript{209} was obtained in excellent yield. The combustion analysis and i.r. and mass spectra of the azo compound (592e) were consistent with its assigned structure. The $^1$H n.m.r. spectrum of (592e) showed a similar pattern to that of the azo compound (592a) described before (cf. figure 6). In accord with its NH-triazole structure the azo compound (592e) also formed a soluble sodium salt when treated with aqueous sodium hydroxide, and was recovered, unchanged from its alkaline solution, on acidification with aqueous hydrochloric acid. However, when the azo compound (592e) was heated under reflux in acetic acid in an attempt to effect its conversion into the corresponding cyclic structure (593c), only a small recovery of starting material was obtained. Further work up of the reaction mother liquor afforded a red gum which could not be characterised.
\[ R \]
\[ \text{a) } H \]
\[ \text{b) } Ac \]
When the diazonium betaine (591) was coupled with β-naphthol in the presence of sodium hydroxide, the product obtained had spectral and chemical properties consistent with the azo structure (592f). When it was heated under reflux in glacial acetic acid, it was smoothly converted into the corresponding triazolonaphthotriazine (593d) in excellent yield. The i.r. and mass spectral properties and combustion analysis of this product were fully in accord with its assigned structure. However, as with the triazolonaphthotriazines (593a and 593b), no confirmation of the structure (593d) by $^1$H n.m.r. could be achieved, due to the insolubility of (593d) in $[^2H_6]$ dimethyl sulfoxide.

The successful synthesis of the triazolonaphthotriazines (593a,b and d) prompted an analogous investigation into the coupling reactions of the diazonium chloride (590a) with various phenols, in an attempt to gain access to the corresponding 1,2,3-triazolobenzo-1,2,4-triazines. Thus, when a solution of the diazonium salt (590a) was introduced into a cooled solution of p-cresol and aqueous sodium hydroxide, the corresponding azo compound (594a) was obtained in excellent yield. In accord with its assigned structure, the azo compound (594a) was smoothly converted into the corresponding N-acetyl derivative (594b) by treatment with warm acetic anhydride. Unfortunately the attempted cyclisation of the azo compound (594a), by heating under reflux in acetic acid, was unsuccessful, the unchanged starting material being recovered in high yield. A similar result was obtained when cyclisation of (594a) to the triazolobenzotriazine (595) was attempted by heating under reflux in ethanolic sodium acetate.
When an aqueous ethanolic solution of the diazonium chloride (590a) was introduced into a cooled ethanolic solution of 5-methyluracil and aqueous sodium hydroxide, a solid was obtained whose i.r. spectrum and m.p. were identical to the known 212 4-phenyl-1H-1,2,3-triazole (596) obtained before (see Chapter 3.1). The isolation of the triazole (596) from this reaction is readily explained by dediazoniation of the salt (590a). The dediazoniation of 1,2,3-triazole diazonium salts has been reported in the literature, 95,213 and has also been encountered before in the present work (cf. Chapter 3.1). The triazole (596) was also obtained when an aqueous ethanolic solution of the diazonium salt (590a) was reacted with a cooled ethanolic solution of pyrimidin-4(1H)-one or hydroquinone, containing aqueous sodium hydroxide. When an aqueous ethanolic solution of the diazonium chloride (590a) was introduced into a cooled ethanolic solution of p-nitrophenol and aqueous sodium hydroxide, the deaminated triazole (596) was accompanied by a large amount of unchanged p-nitrophenol.

Heterocyclic scission, involving the loss of molecular nitrogen, of numerous fused 1,2,3-triazole derivatives has been demonstrated by many workers. Thus, the 1,2,3-triazolo[1,5-a]pyrimidine156,157,238, 1,2,3-triazolo[1,5-a]quinazoline234,235, 1,2,3-triazolo[5,1-c]-1,2,4-benzotriazine236,237 and 1,2,3-triazolo[1,5-a]pyridine233 ring systems all undergo decomposition in acidic media, involving loss of molecular nitrogen from the triazole moiety, to afford the corresponding pyrimidine, quinazoline, benzotriazine and pyridine derivatives. However, a noteworthy observation concerning acid-catalysed scission of this type is the unwillingness156,157,233,234 of
$R$

a) O.Ac

b) OH
fused triazoles of type (597) to undergo cleavage, with subsequent loss of nitrogen, when the substituent at C-3 is electron-withdrawing. Consequently, the successful synthesis of the 1,2,3-triazanaphthotriazine (593a) prompted an investigation into its susceptibility to acid catalysed triazole scission. Thus, when the triazolonaphthotriazine (593a) was heated under reflux in glacial acetic acid, unchanged starting material (593a) was accompanied by the acetoxy compound (598a). The naphthotriazine derivative (598a) gave a correct elemental analysis and mass spectrum. The presence of an absorption band at 1745 cm\(^{-1}\) in the i.r. spectrum of (598a), attributable to the presence of an acetoxy group, and a one proton singlet at \(\delta 7.22\) p.p.m. in its \(^1\)H n.m.r. spectrum, due to a benzylic proton, are also consistent with the assigned structure (598a). Furthermore, when the \(\alpha\)-acetoxybenzylnaphthotriazine (598a) was heated under reflux in ethanol containing aqueous sodium carbonate, the \(\alpha\)-hydroxy derivative (598b) was obtained in good yield. Evidence for the structure of this product was provided by its reaction with chromium trioxide. When (598b) was heated under reflux with chromium trioxide in glacial acetic acid, the ketone (599) was obtained in good yield. The product (599)
Scheme 120
showed spectral properties, consistent with the assigned structure.

When the triazolonaphthotriazine (593a) was heated under reflux in glacial acetic acid with aqueous sulphuric acid, the α-hydroxy derivative (598b) obtained before, was isolated in good yield.

The probable mechanism involved in the acid catalysed scission reactions of the triazolonaphthotriazine (593a) is outlined in Scheme 120. The first step involves protonation of (600) to afford the intermediate [(601)←→(602)]. Rearrangement of the resulting tautomer (603) then occurs, to give the diazonium salt (604). Breakdown of(604) then follows, resulting in the formation of the α-acetoxy derivative [Scheme 120; (605)←→(606)].
The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with β-Dicarbonyl Compounds

The Preparation of the 5-Amino-1H-1,2,3-triazoles (472a) and (501a)
5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (472a) and 5-amino-4-cyano-1H-1,2,3-triazole (501a) were prepared as described previously in Chapter 2 (cf. pages 68 and 66 respectively).

The Preparation of the Diazonium Betaine (471)
4-Benzensulphonyl-1H-1,2,3-triazole-5-diazonium betaine (471) was prepared as described earlier (page 121).

Coupling Reactions of 4-Benzensulphonyl-5-diazonium Betaine (471) with β-Dicarbonyl Compounds
(a) A suspension of the diazonium betaine (471) (0.002 mol) in absolute ethanol (5.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of the active methylene compounds (see below) (0.002 mol) and triethylamine (0.3 ml, 0.0022 mol) in absolute ethanol (10.0 ml). Stirring was continued in the melting ice-bath for 2h, and any solid which precipitated was collected.
(i) Acetylacetone gave a solution which was evaporated and the residue obtained treated with water and acidified with aqueous 2M hydrochloric acid. Extraction with methylene
chloride and trituration of the yellow gum obtained, with ether-light petroleum afforded pentane-2,3,4-trione-3-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473a) (72%) as colourless plates m.p. 133-135°C (from toluene-light petroleum), $\nu_{\text{max}}$. 3300 br (NH), 1695 (CO), and 1590(NH def.) cm$^{-1}$.

Found: C, 48.0; H, 4.0; N, 19.7%; M, 335

C$_{13}$H$_{13}$N$_{5}$O$_{4}$S requires: C, 46.6; H, 3.9; N, 20.9%; M, 335.

Evaporation of the ether-light petroleum mother liquor gave no material. Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave only a negligible quantity of an oil.

(ii) Ethyl cyanoacetate gave a solution which when evaporated, treated with water, acidified with aqueous 2M hydrochloric acid and extracted with methylene chloride gave a gum which was tritutated with ether to afford ethyl cyanoglyoxalate-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473n) (95%) as pale yellow plates m.p. 176-177°C (from ethanol-water), $\nu_{\text{max}}$. 3235 br (NH), 2230 (C=N), 1720 (C=O), and 1630 br (NH def.) cm$^{-1}$, $\delta[(\text{CD}_3)_2\text{SO}]$ 8.10-7.86 (2H,m,ArH), 7.82-7.52 (3H,m,ArH), 4.40(2H, q, J 7Hz, CH$_2$) and 1.35 (3H, t, J 7Hz, CH$_3$).

Found: C, 45.0; H, 3.4; N, 24.1%; M$^+$, 348.

C$_{13}$H$_{12}$N$_{6}$O$_{4}$S requires: C, 44.8; H, 3.4; N, 24.1%; M, 348.

Evaporation of the ether mother liquor afforded a negligible quantity of gum.

(iii) Benzoylacetonone gave a solution which when evaporated, treated with water and acidified with aqueous 2M hydrochloric acid afforded 1-phenylbutane-1,2,3-trione-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473c) (68%) m.p. 160-170°C, $\nu_{\text{max}}$. 3470 br and 3280 (NH) and 1660 (CO) cm$^{-1}$, which when
crystallised from a variety of solvents was cyclised to 3-benzenesulphonyl-6-benzoyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474b) m.p. 209-210°, identical (m.p. and i.r. spectrum) to a sample obtained later.

Extraction of the aqueous mother liquor with methylene chloride gave no further material.

(iv) Dibenzoylmethane afforded 1,3-diphenylpropane-1,2,3-trione-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473g) as the triethylamine salt (63%) as yellow plates m.p. 119-120° (from ethanol), $\nu_{\text{max}}$, 2640 br ($\text{NH}$) and 1640 sh (C=O) cm$^{-1}$, $\delta[(\text{CD}_3)_2\text{SO}]$ 8.20-7.80 (4H, m, ArH), 7.74-7.40 (11H, m, ArH), 3.02 (6H, q, J 8Hz, CH$_2$) and 1.12 (9H, t, J 8Hz, CH$_3$).

**Found:** C, 62.0; H, 5.7; N, 14.9%
**C$_{29}$H$_{32}$N$_6$O$_4$S requires:** C, 62.1; H, 5.7; N, 15.0%

Treatment of the triethylamine salt with aqueous 2M hydrochloric acid liberated the free hydrazine (61%) which formed cream plates m.p. 203-205° (from toluene), $\nu_{\text{max}}$, 3400 br (NH) and 1640sh (C=O) cm$^{-1}$.

**Found:** C, 60.4; H, 3.9; N, 15.0%; $M^+$, 459.
**C$_{23}$H$_{17}$N$_5$O$_4$S requires:** C, 60.1; H, 3.7; N, 15.3%; $M$, 459.

Evaporation of the ethanol mother liquor, treatment of the residue with water and acidification with aqueous 2M hydrochloric acid and extraction with methylene chloride afforded a red gum (0.11 g) which was shown by t.l.c. in methylene chloride over silica to be three unresolvable components.

(v) Diethyl malonate gave a solution which when evaporated and the residue triturated with ether afforded diethyl mesoxalate-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473k)
as the triethylamine salt (59%) which formed orange plates m.p. 122-124° (from ethyl acetate), \( \nu_{\text{max}} \). 3165 br (NH), 2650 br and 2460 br (\( \sim \text{N=H} \)) and 1750 and 1680 (C=O) cm\(^{-1}\), 
\( \delta[\text{CDCl}_3] \) 7.92-7.76 (2H, m, ArH), 7.66-7.50 (3H, m, ArH), 4.27 (4H, dq, J 6.5Hz, overlapping CH\(_2\) ), 3.10 (6H, q, J 7.5Hz, CH\(_2\) ), 1.27 (6H, dt, J 6.5Hz, overlapping CH\(_3\) ), and 1.16 (9H, t, J 7.5Hz, CH\(_3\) ).

\[ \text{Found: C, 51.1; H, 6.5; N, 17.0\%; C}_{21}\text{H}_{32}\text{N}_{6}\text{O}_{6}\text{S requires: C, 50.8; H, 6.5; N, 16.9\%;} \]

Treatment of the triethylamine salt with aqueous 2M hydrochloric acid liberated the free hydrazone (473%) (49%) as its monohydrate buff plates m.p. 88-89° (from toluene), \( \nu_{\text{max}} \). 3410 br (OH), 3165 br (NH), and 1700 and 1680 (C=O) cm\(^{-1}\), 
\( \delta[\text{CDCl}_3] \) 8.14-7.98 (2H, m, ArH), 7.80 br (2H, s, NH), 7.66-7.40 (3H, m, ArH), 4.40 (4H, dq, J 6.5Hz, overlapping CH\(_2\) ) and 1.36 (6H, dt, J 6.5Hz, overlapping CH\(_3\) ).

\[ \text{Found: C, 43.8; H, 4.6; N, 17.0\%; M}^+, 395 \]

\[ \text{C}_{15}\text{H}_{19}\text{N}_{6}\text{O}_{6}\text{S.H}_{2}\text{O requires : C, 43.6; H, 4.6; N, 16.9\%; M, 395} \]

Evaporation of the ether mother liquor afforded a negligible quantity of gum.

(vi) Ethyl benzoylacetate gave a solution which when evaporated and the gum triturated with ether afforded ethyl 2-benzoyl-glyoxylate-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl) hydrazone (473i) as the triethylamine salt (70%) which formed yellow needles m.p. 140-141° (from ethanol), \( \nu_{\text{max}} \). 3160 br (NH), 2660 (\( \sim \text{N=H} \)) and 1680 and 1660 (C=O) cm\(^{-1}\).

\[ \text{Found: C, 57.1; H, 6.1; N, 16.1\%; C}_{25}\text{H}_{32}\text{N}_{6}\text{O}_{5}\text{S requires: C, 56.8; H, 6.1; N, 15.9\%;} \]
Treatment of the triethylamine salt with aqueous 2M hydrochloric acid liberated the free hydrazone (473i) (67%) as pale yellow plates m.p. 134-136° (from toluene-light petroleum), \( v_{\text{max}} \) 3200 br (NH) and 1690 and 1665 (CO) cm\(^{-1}\), \( \delta(\text{CD}_3)_2\text{SO} \) 7.80-7.60 (4H, m, ArH), 7.44-7.26 (6H, m, ArH), 4.04 (2H, q, J 7Hz, CH\(_2\)) and 1.01 (3H, t, J 7Hz, CH\(_3\)).

Found: C,53.5; H,4.0; N,16.5%; M\(^+\), 427  
\( \text{C}_{19}\text{H}_{17}\text{N}_{5}\text{O}_{5}\text{S} \) requires: C,53.4; H,4.0; N,16.4%; M\(^+\), 427.

Evaporation of the ether mother liquor afforded a negligible quantity of gum.

(vii) Ethyl acetoacetate gave a solution which was evaporated, treated with water and acidified with aqueous 2M sulphuric acid. Extraction with methylene chloride and trituration of the resulting gum with ether-light petroleum afforded ethyl 2,3-dioxobutyrate-2-(4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473e) (47%) m.p. 126-129°, \( v_{\text{max}} \) 3390 br and 3175 br (NH) and 1725 sh (C=O) cm\(^{-1}\). Attempted purification of the hydrazone (473e) by crystallisation from a variety of solvents resulted in the formation of dark red gums which could not be characterised.

Evaporation of the trituration mother liquor afforded a negligible quantity of yellow gum.

Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

(viii) Benzoylacetonitrile gave a solid which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the gum with ethanol to afford 7-amino-3-benzenesulphonyl-6-benzoyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474f) (36%) as yellow needles m.p. 237-238°
(from dimethylformamide), $v_{\text{max}}$ 3400 and 3280 br (NH) and 1660 (C=O) cm$^{-1}$.

**Found:** C, 54.1; H, 3.2; N, 22.3%; $M^+$, 380

$\text{C}_{17}\text{H}_{12}\text{N}_{6}\text{O}_{3}\text{S}$ **requires:** C, 53.7; H, 3.2; N, 22.1%; $M$, 380.

Evaporation of the ethanol mother liquor afforded a dark gum (0.38 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

The crude triazolotriazine (474f) was insoluble in aqueous 2M sodium hydroxide.

(ix) Malononitrile afforded 7-amino-3-benzenesulphonyl-

sulphonyl-6-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine

(474h) (86%) as orange plates m.p. 251-252$^\circ$ (from glacial acetic acid), $v_{\text{max}}$ 3480 and 3300 (NH), 2210w (CN), and 1645 br (NH def.) cm$^{-1}$.

**Found:** C, 44.7; H, 3.7; N, 26.9%; $M^+$, 301

$\text{C}_{11}\text{H}_{7}\text{N}_{7}\text{O}_{2}\text{S}$ **requires:** C, 43.9; H, 2.3; N, 32.6%; $M$, 301.

Evaporation of the ethanol mother liquor afforded a dark red oil (0.09 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

The triazolotriazine (474h) was insoluble in aqueous 2M sodium hydroxide.

(x) Cyanoacetamide gave a solution which was evaporated, treated with water, and extracted with methylene chloride. Evaporation of the methylene chloride extract and trituration of the gum obtained with ether afforded an amorphous dark solid (0.34 g) m.p. 88-104$^\circ$ (decomp.) which showed an ill-defined i.r. spectrum and on attempted crystallisation from
a variety of solvents decomposed to a dark tar.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded only a small quantity (0.03 g) of an unidentified solid.

The hydrazones (473 a,c,e,g,i,i, and n) were all soluble in aqueous 2M sodium hydroxide, and were regenerated, unchanged on acidification with aqueous 2M hydrochloric acid.

(b) A suspension of the diazonium betaine (471) (0.47 g, 0.002 mol) in ethanol (5.0 ml) and water (5.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of acetylacetone (0.20 g, 0.002 mol) and sodium carbonate (0.32 g) in ethanol (5.0 ml) and water (5.0 ml). Stirring was continued in the melting ice bath for 2h and the red solution was then concentrated to remove the ethanol and extracted with chloroform to afford a negligible quantity of oil. The aqueous mother liquor was acidified with aqueous 2M hydrochloric acid and extracted with methylene chloride to give a gum which was trituated with ethyl acetate - light petroleum to give pentane-2,3,4-trione-3-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473a) (0.36 g)(54%) m.p. 130-134°C which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Evaporation of the trituration mother liquor gave no further material.
Coupling Reactions of the 1H-1,2,3-Triazole-5-diazonium Nitrates (472b) and (501b) with β-Dicarbonyl Compounds.

(A) A suspension of the aminotriazoles (472a) or (501a) (0.015 mol) in concentrated aqueous nitric acid (d 1.42, 1.5 ml) and water (3.5 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.9 g) in water (4.0 ml). Stirring was continued for 15 min. and the solution was then treated dropwise at 0°C with a solution of the active methylene compounds (see below) (0.015 mol) and anhydrous sodium acetate (1.6 g) in ethanol (10.0 ml) and water (6.0 ml). The mixture was stirred in the melting ice-bath for 2 h and any solid product deposited was collected. The filtrate was worked up as described for the individual reactions below.

(a) (i) Acetylacetone when coupled with the diazonium nitrate (501b) as described in (A) afforded pentane-2,3,4-trione-3-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502a) (67%) as yellow needles m.p. 128-131°C (from toluene-ethyl acetate), \( \nu_{\text{max}} \) 3530 and 3430 (NH), 2240 (C\(=\)N), and 1685 (C=O) cm\(^{-1}\).

\[
\text{Found: C, 42.5; H, 3.9; N, 37.9%; M, 220;}
\]

\[
\text{要求: C, 43.6; H, 3.6; N, 38.2%; M, 220.}
\]

Neutralisation of the acidic aqueous mother liquor with solid sodium acetate and extraction with chloroform gave no further material.
(ii) 4-Benzenesulphonyl-1H-1,2,3-triazole-5-diazonium nitrate (472b) when coupled with acetylacetone as described in (A) afforded 4-benzenesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (471) (98%) m.p. 154-157° which was identical (m.p. and i.r. spectrum) to a sample obtained before.

(b) Ethyl cyanoacetate afforded ethyl cyanoglyoxalate-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502k) (29%) as pale yellow plates m.p. 164-166° (from toluene), $\nu_{\text{max}}$ 3200 br (NH), 2260 and 2230 (C=\(\equiv\)N), and 1710 (C=O) cm$^{-1}$, \(\delta[(\text{CD}_3)_2\text{SO}]\) 9.30 br (1H, s, NH), 8.32 br (1H, s, NH), 4.40 (4H, dq, J 7Hz, overlapping CH$_2$) and 1.36 (6H, dt, J 7Hz, overlapping CH$_3$).

**Found:** C, 41.7; H, 3.0; N, 41.5%; M$^+$, 233

C$_8$H$_7$N$_7$O$_2$ requires: C, 41.2; H, 3.0; N, 42.1%; M, 233.

On standing at room temperature the mother liquor slowly deposited ethyl 7-amino-3-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine-6-carboxylate (503g) (34%) m.p. 201-204° which was identical (m.p. and i.r. spectrum) to a sample obtained later.

Concentration of the mother liquor to remove the ethanol and extraction with methylene chloride afforded a yellow gum (0.31 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(c) Benzoylacetonone afforded a solid which was washed with aqueous 2M sodium hydroxide and combined with a second crop obtained by concentrating the mother liquor to remove the ethanol, extracting with methylene chloride and triturating the gum obtained with ethyl acetate - ether to afford 6-benzoyl-3-cyano-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-
triazine (503b) (18%) m.p. 153-154° which was identical (m.p. and i.r. spectrum) to a sample obtained later.

Evaporation of the trituration mother liquor afforded a red gum (0.93 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Neutralisation of the original acidic aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no material.

The basic aqueous washings were acidified with aqueous 2M hydrochloric acid to afford 1-phenylbutane-1,2,3-trione-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502c) (30%) m.p. 88-93°, v_max. 3320 and 3250 w (NH), 2240 (C≡N) and 1670 and 1650 (C=O) cm^{-1}, which was converted on attempted crystallisation from a variety of solvents into the triazolotriazine (503b) m.p. 151-154° obtained later.

Extraction of the acidic aqueous mother liquor with methylene chloride gave no further material.

(d) Dibenzoylmethane gave a solid which was washed with aqueous 2M sodium hydroxide leaving dibenzoylmethane (49%) insoluble, m.p. 74-79° identical (m.p. and i.r. spectrum) to an authentic sample.

Acidification of the red basic aqueous mother liquor afforded 1,3-diphenylpropane-1,2,3-trione-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502g) (60%) m.p. 148-150° as yellow plates (from ethanol-water), v_max. 3300 br (NH), 2250 (CN), and 1670 (CO) cm^{-1}.
Found: C, 63.0; H, 3.7; N, 23.9%; M$^+$-H$_2$O, 326.

$C_{18}H_{12}N_6O_2$ requires: C, 62.8; H, 3.5; N, 24.4%; M, 344.

Concentration of the ethanol-water mother liquor and extraction with methylene chloride afforded only a negligible quantity of gum.

(e) Diethyl malonate gave a solution which when concentrated, extracted with methylene chloride and the gummy semi-solid triturated with light petroleum afforded diethyl mesoxalate-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502k) (27%) as colourless plates m.p. 130-131$^\circ$ (from toluene), $\nu_{max}$ 3310 and 3180 br (NH), 2240 (C≡N), and 1730 sh (CO) cm$^{-1}$, $\delta$[CDCl$_3$] 4.40 (4H, dq, J 8Hz, overlapping CH$_2$) and 1.37 (6H, dt, J 8Hz, overlapping CH$_3$).

Found: C, 43.4; H, 4.2; N, 29.7%; M$^+$, 280

$C_{10}H_{12}N_6O_4$ requires: C, 42.9; H, 4.3; N, 30.0%; M, 280.

Evaporation of the light petroleum mother liquor afforded only a negligible quantity of gum.

(f) Ethyl benzoylacacetate afforded ethyl 2-benzoylglyoxylate-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502h) (91%) as buff plates m.p. 127-129$^\circ$ (from ethanol-water), $\nu_{max}$ 3350 br and 3160 br (NH), 2230 (C≡N), and 1710 and 1665 (CO) cm$^{-1}$ $\delta$[CD$_3$]$_2$SO] 7.60-7.28 (1OH, m, ArH), 4.10 (4H, dq, J 8Hz, overlapping CH$_2$), and 1.15 (6H, dt, J 8Hz, overlapping CH$_3$).

Found: C, 53.9; H, 3.8; N, 26.5%; M$^+$, 312.

$C_{14}H_{12}N_6O_3$ requires: C, 53.8; H, 3.8; N, 26.9%; M, 312.

Concentration of the ethanol-water mother liquor and extraction with methylene chloride afforded only a negligible quantity of gum.
(g) Ethyl acetoacetate afforded ethyl 2,3-dioxobutyrate-2-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502e) (70%) m.p. 129-139°, $\nu_{\text{max}}$ 3410 br and 3195 br (NH), 2240 (C≡N), and 11730 br (CO) cm$^{-1}$, which on attempted crystallisation from a variety of solvents resulted in the formation of red intractable oils, from which no identifiable material could be obtained.

The ethanol-water mother liquor was concentrated to remove the ethanol and extracted with methylene chloride to afford a red oil (0.72 g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.

(h) Benzoylacetonitrile afforded phenylglyoxalonitrile-1-(4-cyano-1H-1,2,3-triazol-5-yl)hydrazone (502i) (64%) m.p. 115-120°, $\nu_{\text{max}}$ 3650 and 3450 br (NH), 2240 and 2220 (C≡N) and 1630 (C=O) cm$^{-1}$, which was converted on attempted crystallisation from a variety of solvents into 7-amino-6-benzoyl-3-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine (503f) m.p. 206-210° obtained later.

Concentration of the ethanol-water mother liquor and extraction with methylene chloride afforded only a negligible quantity of gum.

(i) Malononitrile afforded a solid which was combined with a second crop obtained by concentrating the ethanol-water mother liquor to afford 7-amino-3,6-dicyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine (503h) (92%) as the hemihydrate, which formed yellow needles m.p. >320° (decomp.) (from glacial acetic acid-water), $\nu_{\text{max}}$ 3620 (OH), 3560, 3330 and 3280 (NH) and 2240 (C≡N) cm$^{-1}$. 
Found: C,37.0; H,1.7; N,57.4%; M⁺186.
\[ C_6H_2N_8\cdot\frac{1}{2}H_2O \] requires: C,36.9; H,1.5; N,57.4%; M,186.

The triazolotriazine (503h) was insoluble in aqueous 2M sodium hydroxide.

(j) Cyanoacetamide afforded 7-amino-3-cyano-1,2,3-triazolo
[5,1-c]-1,2,4-triazine-6-carboxamide (503i) (52%) as yellow plates m.p. >320°C (decomp.) (from glacial acetic acid),
\( \nu_{\text{max.}} \) 3370 br and 3150 br (NH), 2240 (C≡N), and 1680 br (C=O) cm⁻¹.

Found: C,32.7; H,2.6; N,47.4%; M⁺,204.
\[ C_6H_4N_8O \] requires: C,35.3; H,2.0; N,54.9%; M,204.

Concentration of the mother liquor and extraction with methylene chloride afforded a negligible quantity of gum.

Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no material. Evaporation of the aqueous mother liquor and soxhlet extraction with boiling ethyl acetate afforded only a small quantity of an unidentified semi-solid (0.06 g).

The triazolotriazine (503i) was insoluble in aqueous 2M sodium hydroxide.

All of the hydrazones (502a,c,e,g-i,k,l) were soluble in aqueous 2M sodium hydroxide and were regenerated, unchanged, on acidification with aqueous 2M hydrochloric acid.

(B) A suspension of 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (472a) (0.45g, 0.002 mol) in concentrated aqueous nitric acid (d 1.42, 1.0 ml) and water (3.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.50 g) in water (2.0 ml). Stirring was continued for 15 min at 0°C and the
solution was then treated dropwise at 0° with a solution of either acetylacetone or ethyl cyanoacetate (0.002 mol) and sodium carbonate (2.80 g) in ethanol (5.0 ml) and water (5.0 ml). The mixture was stirred in the melting ice-bath for 2h and then concentrated to remove the ethanol, acidified with aqueous 2M hydrochloric acid and extracted with methylene chloride. Evaporation of the methylene chloride extract and trituration of the gum with ether or ethyl acetate gave the hydrazones (473a) and (473n).

(a) Acetylacetone afforded pentane-2,3,4-trione-3-(4-benzene-sulphonyl-1H-1,2,3-triazol-5-yl)hydrazon (473a) (48%) m.p. 129-133° which was identical (m.p. and i.r. spectrum) to a sample obtained before.

Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no further material.

(b) Ethyl cyanoacetate afforded ethyl cyanoglyoxalate-2-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473n) (62%) m.p. 171-174° which was identical (m.p. and i.r. spectrum) to a sample obtained before.

Acetylation of the 1H-1,2,3-Triazol-5-yl Hydrazones (473a,c,e,g,i,l,n) and (502 a,c,e,i)

(a) The hydrazones (473a,c,e,g,i,l,n) and (502a,c,e,i) (0.001 mol) were heated at 100° with acetic anhydride (0.4 ml) until the solid just dissolved (1-2 min). In each case the reaction mixture was allowed to cool, left at room temperature for 20 min., and diluted with ether to give the corresponding monoacetyl derivatives.
(i) Pentane-2,3,4-trione-3-(1-acetyl-4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473b) (83%) formed yellow plates m.p. 124-126°C (from toluene-light petroleum), \( \nu_{\text{max}} \) 1775 and 1690 (C=O) cm\(^{-1} \), 6[(CD\(_3\))\(_2\)SO] 8.10-7.94 (4H, m, ArH), 7.74-7.52 (6H, m, ArH), 2.83 (3H, s, CH\(_3\)) 2.66 (3H, s, CH\(_3\)), 2.36 (3H, s, CH\(_3\)) 2.19 (3H, s, CH\(_3\)) and 1.87 (6H, s, CH\(_3\)).

Found: C, 47.9; H, 3.9; N, 18.5%; M\(^{+}\), 377.

\( \text{C}_{15}\text{H}_{15}\text{N}_{5}\text{O}_{5}\)S requires: C, 47.7; H, 4.0; N, 18.6%; M, 377.

(ii) Ethyl cyanoglyoxylate-2-(1-acetyl-4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473o) (92%) formed colourless plates m.p. 153-154°C (from toluene-light petroleum), \( \nu_{\text{max}} \) 2220 (CN), 1780 sh, and 1700 (C=O) cm\(^{-1} \), 6[(CD\(_3\))\(_2\)SO]
8.31-7.99 (4H, m, ArH), 7.76-7.44 (6H, m, ArH) 4.41 (2H, q, J 7Hz, CH\(_2\)), 2.71 (3H, s, CH\(_3\)) and 1.33 (3H, t, J 7Hz, CH\(_3\)).

Found: C, 46.6; H, 3.6; N, 21.2%; M\(^{+}\), 390.

\( \text{C}_{15}\text{H}_{14}\text{N}_{6}\text{O}_{5}\)S requires: C, 46.2; H, 3.6; N, 21.5%; M, 390.

(iii) The hydrazone (473c) gave unreacted starting material (93%) m.p. 162-168°C which was identical (m.p. and i.r. spectrum) to an authentic sample.

(iv) 1,3-Diphenylpropane-1,2,3-trione-2-(1-acetyl-4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473h) (46%) formed colourless plates m.p. 175-176°C (from toluene), \( \nu_{\text{max}} \) 3300 w (NH) and 1790 and 1665 (C=O) cm\(^{-1} \), 6[CDCl\(_3\)] 8.20-7.94 (4H, m, ArH) 7.74-7.20 (11H, m, ArH) and 2.61 (3H, s, CH\(_3\)).

Found: C, 60.1; H, 3.8; N, 13.9%; M\(^{+}\), 501.

\( \text{C}_{25}\text{H}_{19}\text{N}_{5}\text{O}_{5}\)S requires: C, 59.9; H, 3.8; N, 14.0%; M, 501.

Evaporation of the ether mother liquor gave a dark gum (0.09g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.
(v) The hydrazone (473f) afforded unchanged starting material (68%) m.p. 121-124° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor gave a small amount (0.06 g) of an unidentified gum.

(vi) The hydrazone (473e) gave unreacted starting material (45%) m.p. 124-127° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor afforded a red gum (0.09 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(vii) Pentane-2,3,4-trione-3-(1-acetyl-4-cyano-1,2,3-triazol-5-yl)hydrazone (502b) (27%) formed yellow plates m.p. 108-109° (from toluene-light petroleum), \( \nu_{\text{max}} \) 3220 (NH), 2240 w (C≡N) and 1780 sh and 1670 sh (C=O) cm\(^{-1}\). \( \delta[^{3}CDCl_{3}] \)

2.81 (3H, s, CH\(_{3}\)), 2.16 (3H, s, CH\(_{3}\)) and 1.92 (3H, s, CH\(_{3}\)).

Found: C, 45.5; H, 3.9; N, 31.9%; M\(^{+}\), 262

C\(_{10}\)H\(_{10}\)N\(_{6}\)O\(_{3}\) requires: C, 45.8; H, 3.8; N, 32.1%; M, 262.

Evaporation of the ether mother liquor afforded a red oil (0.44 g) which was shown by t.l.c. in ethyl acetate over alumina to contain four unresolvable components.

(viii) 1-Phenylbutane-1,2,3-trione-2-(1-acetyl-4-cyano-1,2,3-triazol-5-yl)hydrazone (502d) (74%) formed colourless needles m.p. 129-130° (from toluene), \( \nu_{\text{max}} \) 3230 (NH), 2250 (C≡N), and 1760 and 1670 br (C=O) cm\(^{-1}\), \( \delta[^{3}CDCl_{3}] \) 7.98-7.84 (2H, m, ArH), 7.74-7.34 (8H, m, ArH), 2.78 (3H, s, CH\(_{3}\)), 2.76 (3H, s, CH\(_{3}\)), 2.65 (3H, s, CH\(_{3}\)) and 2.54 (3H, s, CH\(_{3}\)).
Found: C, 55.7; H, 3.7; N, 25.9%; M+324
C₁₅H₁₂N₆O₃ requires: C, 55.6; H, 3.7; N, 25.9%; M, 324.

(ix) The hydrazone (502e) gave a dark gum (0.23 g) which could not be obtained solid, and which was shown by t.i.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Phenylglyoxalonitrile-1-(1-acetyl-4-cyano-1,2,3-triazol-5-yl)hydrazone (502j) (78%) formed yellow plates m.p. 154-156° (from toluene), νₐₘₚₓₙ. 3190 br (NH), 2250 w and 2230 w (C≡N), and 1790 and 1660 (C=O) cm⁻¹, δ[(CD₃)₂SO] 8.12-7.91 (2H, m, ArH), 7.58-7.42 (3H, m, ArH) and 2.77 (3H, s, CH₃).

Found: C, 54.9; H, 3.0; N, 32.2%; M⁺307.
C₁₄H₉N₇O₂ requires: C, 54.7; H, 2.9; N, 31.9%; M, 307.

(b) 1-Phenylbutane-1,2,3-trione-2-(4-benzesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473c) (0.40 g, 0.001 mol) was heated at 100° with acetic anhydride (0.9 ml) for 0.5 h. The dark solution obtained was cooled, left at room temperature for 20 min. and then evaporated to afford a dark tar (0.21 g), which could not be solidified and was shown by t.i.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(c) The triethylamine salts of the hydrazones (473g,i, and l) (0.0007 mol) were heated at 100° with acetic anhydride (0.1 ml) until the solid just dissolved, (1-2 min.). In each case the reaction mixture was allowed to cool and stand at room temperature before being diluted with ether.
(i) 1,3-Diphenylpropane-1,2,3-trione-2-(1-acetyl-4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473h) obtained in 55% yield had m.p. 175-176°C and was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Evaporation of the ether mother liquor afforded a dark gum (0.09 g) which was shown by t.l.c. in ethyl acetate over silica to consist of four unresolvable components.

(ii) When the triethylamine salt of the hydrazone (473i) was heated with acetic anhydride as described in (c), a dark gum (0.43 g) was obtained which could not be obtained solid and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(iii) Ethyl 2-benzoylglyoxylate-2-(1-acetyl-4-benzenesulphonyl-1,2,3-triazol-5-yl)hydrazone (473j) (90%) formed pale yellow plates m.p. 167-169°C (from toluene-light petroleum), \( \nu_{\text{max.}} 1775, 1710, \) and 1665 (C=O) cm\(^{-1}\), \( \delta[\text{CDCl}_3] 8.20-7.94 (4H, m, ArH), 7.74-7.44 (6H, m, ArH), 4.44 (2H, q, J 8Hz, CH\(_2\)), 2.70 (3H, s, CH\(_3\)), \) and \( 1.32 (3H, t, J 8Hz, CH\(_3\)). \)

Found: C, 54.1; H, 4.2; N, 15.0%; M\(^+\) 469.

\( \text{C}_{21}\text{H}_{19}\text{N}_5\text{O}_6\text{S} \) requires: C, 53.7; H, 4.1; N, 14.9%; M, 469.

The Cyclisation of the 1H-1,2,3-Triazol-5-ylhydrazones (473a,e,n) and (502a,c,e) in Boiling Ethanol

The hydrazones (473a,e,n) and (502a,c,e) (0.001 mol) were heated under reflux in ethanol (15.0 ml) for 0.5 h. The reaction mixture was cooled, and any solid product deposited was collected. The filtrate was worked up as described for the individual reactions below.
The hydrazone (473a) gave a solid which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the gum with ethanol, to afford 6-acetyl-3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474a) (79%) as buff needles m.p. 173-174° (from ethanol-glacial acetic acid), $\nu_{\text{max}}$ 1710 (C=O) cm$^{-1}$, $\delta$ [CDCl$_3$] 8.34-8.14 (2H, m, ArH), 7.96-7.74 (3H, m, ArH), 3.05 (3H, s, CH$_3$), and 2.88 (3H, s, CH$_3$).

**Found:** C, 49.3; H, 3.5; N, 21.9%; M$^+$, 317.

$\text{C}_{13}\text{H}_{12}\text{N}_6\text{O}_3\text{S}$ requires: C, 49.2; H, 3.5; N, 22.1%; M, 317.

Ethyl 7-amino-3-benzenesulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-6-carboxylate (474g) (16%) formed yellow needles m.p. 202-203° (from ethanol-glacial acetic acid), $\nu_{\text{max}}$ 3380 w and 3290 w (NH) and 1725 (CO) cm$^{-1}$, $\delta$ [(CD$_3$)$_2$SO] 9.30 br (1H, s, NH), 8.26 br (1H, s, NH), 8.06-7.92 (2H, m, ArH), 7.74-7.54 (3H, m, ArH), 4.43 (2H, q, J 8Hz, CH$_2$), and 1.36 (3H, t, J 8Hz, CH$_3$).

**Found:** C, 45.2; H, 3.4; N, 24.2%; M$^+$, 348

$\text{C}_{13}\text{H}_{12}\text{N}_6\text{O}_4\text{S}$ requires: C, 44.8; H, 3.4; N, 24.18%; M, 348.

Evaporation of the ethanol mother liquor and trituration of the resulting gum with ether gave the starting hydrazone (473n) (44%) m.p. 172-175° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor afforded a yellow gum (0.14 g) which was shown by t.l.c. in ethyl acetate over silica to consist of four unresolvable components.

(c) The hydrazone (473e) yielded a dark solution which was evaporated to give a dark gum (0.21 g). This could not be obtained solid, and was shown by t.l.c. in methylene chloride over silica to be a multicomponent mixture.
(d) The hydrazone (502a) gave a solid which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the resulting gum with ether, to afford 6-acetyl-3-cyano-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (503a) (85%) as colourless needles m.p. 131-132° (from ethanol), ν max. 2230 (C=\text{N}) and 1730 (C=0) cm⁻¹, δ[\text{CDCl}_3] 3.02 (3H, s, CH₃) and 2.86 (3H, s, CH₃).

Found: C,47.3; H,3.0; N,40.9%; M⁺, 202
C₈H₆N₅O requires: C,47.5; H,3.0; N,41.6%; M, 202.

(e) The hydrazone (502c) gave a dark solution which when evaporated, and triturated with water afforded 6-benzoyl-3-cyano-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (503b) (45%) as buff plates m.p. 153-154° (from glacial acetic acid-water), ν max. 2250 (C=\text{N}) and 1675 (C=0) cm⁻¹, δ[(\text{CD}_3)₂\text{SO}] 8.20-8.02 (2H, m, ArH), 7.92-7.50 (3H, m, ArH) and 2.76 (3H, s, CH₃).

Found: C,58.2; H,3.0; N,31.1%; M⁺, 264.
C₁₃H₆N₅O requires: C,59.1; H,3.0; N,31.8%; M, 264.

Extraction of the aqueous mother liquor with methylene chloride afforded only a negligible quantity of gum.

(f) The hydrazone (502e) gave a solution which when evaporated and triturated with ether afforded unreacted starting material (32%) m.p. 131-136° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor afforded a dark gum (0.34 g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.
Cyclisation of the 1H-1,2,3-Triazol-5-ylhydrazones (473 c,e,g,i,2,) and (502 e,g-i,k,l,) in Hot Acetic Acid

(a) The hydrazones (473 c,e,g,i,2,) and (502 e,g-i,k,l,) (0.001 mol) were heated under reflux in glacial acetic acid (15.0 ml) for 0.5 h. The resulting solution was cooled and any solid product deposited was collected. The filtrate was worked up as described for the individual reaction below.

(i) 3-Benzencesulphonyl-6-benzoyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474b) (42%) formed pale yellow plates m.p. 209-210° (from glacial acetic acid-water), \( \nu_{\text{max}} \) 1675 (C=O) cm\(^{-1}\), \( \delta[(\text{CD}_3)_2\text{SO}] \) 8.20-8.04 (4H, m, ArH), 7.84-7.50 (6H, m, ArH) and 2.78 (3H, s, CH\(_3\)).

\[
\text{Found: C,57.0; H,3.5; N,18.5%; M}^+, 379. \\
\text{C}_{18}\text{H}_{13}\text{N}_5\text{O}_3\text{S} \text{requires: C,57.0; H,3.4; N,18.5%; M, 379.}
\]

Evaporation of the acetic acid mother liquor afforded a yellow oil (0.11 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(ii) 3-Benzencesulphonyl-6-benzoyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474d) (88%) formed yellow needles m.p. 213-214° (from glacial acetic acid), \( \nu_{\text{max}} \) 1690 (C=O) cm\(^{-1}\).

\[
\text{Found: C,62.6; H,3.5; N,15.8%; M}^+, 441 \\
\text{C}_{23}\text{H}_{15}\text{N}_5\text{O}_3\text{S} \text{requires: C,62.6; H,3.5; N,15.9%; M, 441.}
\]

(iii) The hydrazone (473l) gave a dark solution which when evaporated, and the gum triturated with ether afforded unchanged starting material (80%) m.p. 88-90° identical (m.p. and i.r. spectrum) to an authentic sample.
(iv) The hydrazone (473i) afforded a dark solution which was evaporated and the oil triturated with ether to give ethyl 3-benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-6-carboxylate (474e) (46%) as colourless plates m.p. 184-185° (from glacial acetic acid), $\nu_{\text{max}}$ 1740 (C=O) cm$^{-1}$, $\delta$ [(CD$_3$)$_2$SO] 8.16-8.00 (2H, m, ArH), 7.80-7.52 (8H, m, ArH), 4.36 (2H, q, J 8Hz, CH$_2$) and 1.17 (3H, t, J 8Hz, CH$_3$).

Found: C,55.3; H,3.7; N,17.1%; M$^+$,409.

C$_{19}$H$_{15}$N$_5$O$_4$S requires: C,55.7; H,3.7; N,17.1%; M, 409.

Evaporation of the ether mother liquor and trituration of the gum obtained with ether-ethyl acetate afforded the starting hydrazone (473i) (7%) m.p. 133-136° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the trituration mother liquor gave a yellow gum (0.20 g) which was shown by t.l.c. in ethyl acetate over silica to consist of four unresolvable components.

(v) The hydrazone (473e) afforded a solution which when evaporated gave a dark gum (0.29 g). This could not be obtained solid and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(vi) the hydrazone (502i) gave a dark solution which was evaporated and triturated with ethanol to afford ethyl 7-amino-3-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine-6-carboxylate (503g) (94%) as bright yellow plates m.p. 204-205° (from ethanol), $\nu_{\text{max}}$ 3430, 3340 and 3250 (NH), 2250 (C=N), and 1715 br (C=O) cm$^{-1}$, $\delta$ [(CD$_3$)$_2$SO] 9.22 br (1H, s, NH), 8.32 br (1H, s, NH), 4.46 (2H, q, J 8Hz, CH$_2$) and 1.38 (3H, t, J 8Hz, CH$_3$).
(vii) The hydrazone (502g) gave a solution which when evaporated afforded a brown gum (0.26 g). This could not be obtained solid and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(viii) The hydrazone (502k) afforded a dark solution when evaporated gave a dark tar (0.26 g) shown by t.l.c. in methylene chloride over silica to be a multicomponent mixture.

(ix) When the hydrazone (502h) was heated under reflux in acetic acid as described in (a) the result was a dark solution, which when evaporated and triturated with ether gave an orange solid. This decomposed to a tar on attempted collection.

(x) The hydrazone (502e) afforded a dark solution which on evaporation gave a dark oil (0.21 g) shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent gum.

(xi) The hydrazone (502i) gave a solution which when evaporated and triturated with ether-ethyl acetate afforded 7-amino-6-benzoyl-3-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine (503f) (87%) as yellow plates m.p. 209-211° (from ethanol-water), $v_{max}$ 3430 and 3400 w (NH), 2260 (C=N), and 1670 cm$^{-1}$

Found: $M^+$, 265.071555 (error < 2 p.p.m.)

$C_{12}H_7N_7O_2$ requires: $M$, 265.071204.
(b) The triethylamine salts of the hydrazones (473g) and (473l) (0.0008 mol) were heated under reflux in glacial acetic acid (10.0 ml) for 0.5h. The resulting solution was cooled and any solid deposited was collected. The filtrate was worked up as described for the individual reactions below.

(i) 3-Benzenesulphonyl-6-benzoyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474d) (90%) had m.p. 213-214° and was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

(ii) The triethylamine salt of the hydrazone (473l) afforded a dark solution which when evaporated gave a dark gum (0.41g). This could not be obtained solid and was shown by t.l.c. in methylene chloride over silica to be a multicomponent mixture from which no identifiable material could be obtained.

The Attempted Cyclisation of Diethyl Mesoxalate-2-(4-benzene-sulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (473l) using Aqueous Ethanolic Sodium Acetate

The hydrazone (473l) (0.80g, 0.002 mol) was heated under reflux with aqueous 2M sodium acetate solution (5.0 ml)
in ethanol (15.0 ml) for 1.5h. The solution was cooled and evaporated and the gummy residue was treated with water to afford the starting hydrazone (473l) (0.51 g) (64%) m.p. 122-124° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride gave no material. Acidification of the aqueous mother liquor with concentrated aqueous hydrochloric acid and extraction with methylene chloride afforded a yellow
gum (0.10g) which was shown by t.l.c. in methylene chloride over silica to consist of four unresolvable components.

The Reaction of 6-Acetyl-3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474a) with Phenylhydrazine

6-Acetyl-3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474a) (0.32g, 0.001 mol) was heated under reflux with freshly distilled phenylhydrazine (0.11g, 0.001 mol) in Analar methanol (15.0 ml) for 3h. The cooled solution deposited a solid which was combined with a second crop obtained by evaporating the methanol mother liquor and triturating the red gum with ether to afford the pyrazole derivative (492) (total 0.36 g) (89%) as yellow plates m.p. 194-195° (from ethanol-water). \( \nu_{max} \) 3265 br (NH) cm\(^{-1}\), \( \delta[(CD_3)_2SO] \) 8.08-7.88 (2H, m, ArH), 7.76-7.42 (8H, m, ArH), 2.59 (3H, s, CH\(_3\)) and 2.45 (3H, s, CH\(_3\)).

Found: C,55.8; H,4.2; N,23.8%; M\(^+\),407.

C\(_{19}\)H\(_{17}\)N\(_7\)O\(_2\)S requires: C,56.0; H,4.2; N,24.1%; M, 407.

Evaporation of the ether mother liquor afforded only a small quantity of an unidentified red gum (0.04 g).

The Attempted Reaction of 7-Amino-3-benzenesulphonyl-6-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474h) with Polyphosphoric Acid

The triazolotriazine (474h) (0.30 g, 0.001 mol) was heated at 80° with polyphosphoric acid (ca. 4.0 ml) for 2h. The mixture was cooled and treated with ice-water and extracted with methylene chloride to afford only a negligible quantity of green gum.
Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with methylene chloride afforded only a negligible quantity of gum.

The Attempted Reaction of 7-Amino-3-benzenesulphonyl-6-cyano-1,2,3-triazolo[5,1-c]-1,2,4-triazine (474h) with Acetic Anhydride

The triazolotriazine (474h) (0.30 g, 0.001 mol) was heated with acetic anhydride (1.0 ml) at 100°C for 5 min. The resulting mixture was cooled and left at room temperature for 20 min. Trituration of the resulting semi-solid with ether afforded starting material (0.28 g) (93%) m.p. 248-251°C, which was identical (m.p. and i.r. spectrum) to an authentic sample.

The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Benzenesulphonylmethylene Compounds

The Preparation of the Diazonium Chlorides (507a) and (507b) and the Diazonium Betaine (508).

4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (507a) and 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (507b) were prepared as described earlier (cf. page 115). 4-Benzensulphonyl-1H-1,2,3-triazole-5-diazonium betaine (508) was prepared as described on page 121.
Preparation of the Benzenesulphonylmethylene Compounds

Benzenesulphonylacetone\(^{169}\) (509a) m.p. 54-56\(^{\circ}\) (lit., 55-58\(^{\circ}\)) (yield 86%), benzenesulphonylacetophenone\(^{245}\) (509b) m.p. 89-91\(^{\circ}\) (lit., 245 96\(^{\circ}\)) (yield 100%), and benzenesulphonylacetonitrile\(^{169}\) (509c) m.p. 109-112\(^{\circ}\) (lit., 169 114\(^{\circ}\)) (yield 77%) were all prepared as described in the literature, and were used without further purification.

Coupling Reactions of the 1H-1,2,3-Triazole-5-diazonium Chlorides (507a) and (507b), and the 1H-1,2,3-Triazole-5-diazonium Betaine (508) with the Benzenesulphonylmethylene Compounds (509a), (509b) and (509c).

(a) A solution of the diazonium salts (507a) or (507b) (0.0065 mol) in ethanol (25.0 ml) and water (25.0 ml) was added dropwise with stirring over 15 min. at 0\(^{\circ}\) (ice-salt bath) to a suspension of the benzenesulphonylmethylene compounds (509a), (509b) or (509c) (0.007 mol) and anhydrous sodium acetate (0.8 g) in ethanol (5.0 ml) and water (2.0 ml). Stirring was continued for 2h in the melting ice-bath and the resulting solids were collected and washed with water.

(i) 1-Benzenesulphonylpropane-1,2-dione-1-(4-phenyl-1H-1,2,3-triazol-5-yl)hydrazone (510a) (95%) had m.p. 218-222\(^{\circ}\), \(\nu_{\text{max}}\) 3345 and 3120 br (NH) and 1650 (C=O) cm\(^{-1}\), and was converted on attempted crystallisation into 6-benzensulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) m.p. 222-224\(^{\circ}\) identical (m.p. and i.r. spectrum) to an authentic sample, obtained later.
(ii) 1-Benzene sulphonyl-2-phenylethane-1,2-dione-1-(4-phenyl-1H-1,2,3-triazol-5-yl)hydrazone (510c) (84%) formed yellow needles m.p. 180-182° (from toluene), $\nu_{\text{max.}}$ 3460 and 3120 w (NH) and 1660 w (C=O) cm$^{-1}$.  
Found: C, 61.9; H, 4.2; N, 15.4%; M$^+$, 431.

C$_{22}$H$_{17}$N$_5$O$_3$S requires: C, 61.3; H, 3.9; N, 16.2%; M, 431.

(iii) 7-Amino-6-benzene sulphonyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511c) (92%) formed red needles m.p. 204-205° (from glacial acetic acid), $\nu_{\text{max.}}$ 3420 and 3330 (NH) cm$^{-1}$.  
Found: C, 54.1; H, 3.4; N, 24.0%; M$^+$, 352.

C$_{16}$H$_{12}$N$_6$O$_2$S requires: C, 54.5; H, 3.4; N, 23.9%; M, 352.

The triazolotriazine (511c) was insoluble in aqueous 2M sodium hydroxide.

(iv) 1-Benzene sulphonyl-2-phenylethane-1,2-dione-1-(4-carbamoyl-1H-1,2,3-triazol-5-yl)hydrazone (510f) (94%) had m.p. 184-186°, $\nu_{\text{max.}}$ 3400 br, 3260 w and 3140 w (NH) and 1660 br (C=O) cm$^{-1}$, and was converted on attempted crystallisation into 6-benzene sulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-3-carboxamide (511d) m.p. 231-233° identical (m.p. and i.r. spectrum) to a sample obtained later.

(v) 7-Amino-6-benzene sulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-3-carboxamide (511e) (92%) formed yellow plates m.p. 282-284° (decomp.) (from dimethylformamide), $\nu_{\text{max.}}$ 3410 and 3120 br (NH) and 1675 (C=O) cm$^{-1}$.  
Found: C, 41.2; H, 3.4; N, 29.8%; M$^+$, 319.

C$_{11}$H$_9$N$_7$O$_3$S requires: C, 41.4; H, 2.8; N, 30.7%; M, 319.
The triazolotriazine (511e) was insoluble in aqueous 2M sodium hydroxide.

(b) To a suspension of the diazonium betaine (508) (0.47 g, 0.002 mol) in ethanol (10.0 ml) and water (5.0 ml) at 0°C (ice-salt bath) was added dropwise with stirring a solution of benzenesulphonylaceton (509a) (0.40 g, 0.002 mol) and anhydrous sodium acetate (0.25 g) in ethanol (20.0 ml) and water (5.0 ml). Stirring was continued for 2h in the melting ice-bath and the solid deposited was collected and combined with a second crop, obtained by concentrating the mother liquor to remove the ethanol, and acidifying the aqueous solution with aqueous 2M sulphuric acid, to afford 1-benzenesulphonylpropane-1,2-dione-1-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)hydrazone (510i) (total 0.56g) (65%) m.p. 120-123°C. ν <sub>max</sub> 3400 br and 3170 br (NH) and 1625 (C=O) cm<sup>-1</sup>. The hydrazone (510i) was converted on attempted crystallisation into 3,6-dibenzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511f) m.p. 221-223°C, identical (m.p. and i.r. spectrum) to a sample obtained later.

In each case, the hydrazones (510a), (510c), (510f), and (510i) were soluble in aqueous 2M sodium hydroxide and were regenerated, unchanged, on acidification with aqueous 2M hydrochloridic acid.

Acetylation of the Hydrazones (510a,c and f)

The hydrazones (510a,c and f) (0.002 mol) were heated with acetic anhydride (2.5 ml) at 100°C for 3 min. The reaction mixtures were then allowed to cool and stand at room temperature for 20 min.
(i) The hydrazone (510a) afforded 6-benzenesulphonyl-7-
methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a)  
(14%) m.p. 220-224°C identical (m.p. and i.r. spectrum) to a  
sample obtained later. Evaporation of the acetic anhydride  
mother liquor and trituration of the resulting gum with  
ether afforded 1-benzenesulphonylpropane-1,2-dione-1-(1-acetyl-
4-phenyl-1,2,3-triazol-5-yl)hydrazone (510b) (28%) as yellow  
plates m.p. 146-148°C (from benzene-light petroleum), ν_max.  
1755 and 1650 (C=O) cm⁻¹, δ[(CD₃)₂SO] 8.60-7.56 (10H, m, ArH),  
2.79 (3H, s, CH₃) and 2.30 (3H, s, CH₃).

Found: C,55.8; H,4.2; N,17.0%; M⁺,411.  
C₁₉H₁₆N₅O₄S requires: C,55.5; H,4.1; N,17.0%; M, 411.  
Evaporation of the ether mother liquor gave a red gum  
(0.07 g) which was shown by t.l.c. in chloroform over  
silica to consist of three unresolvable components.

(ii) The hydrazone (510c) gave a gummy semi-solid which  
when triturated with ether afforded 1-benzenesulphonyl-2-
phenylethane-1,2-dione-1-(1-acetyl-4-phenyl-1,2,3-triazol-
5-yl)hydrazone (510d) (49%) as yellow plates m.p. 180-181°C  
(from toluene), ν_max. 1745 and 1635 (C=O) cm⁻¹, δ[CDCl₃]  
8.27-7.10 (15H, m, ArH) and 2.80 (3H, s, CH₃).

Found: C,60.8; H,4.0; N,14.5%; M⁺, 473.  
C₂₄H₁₉N₅O₄S requires: C,60.9; H,4.0; N,14.8%; M, 473.  
Evaporation of the ether mother liquor yielded a dark  
gum (0.16 g) which was shown by t.l.c. in chloroform over  
silica to consist of four unresolvable components.
(iii) The hydrazone (510f) gave a gummy semi-solid which when triturated with ether afforded 1-benzenesulphonyl-2-phenylethane 1,2-dione-1-(1-acetyl-4-carbamoyl-1,2,3-triazol-5-yl) hydrazone (510g) (100%) as colourless plates m.p. 171-173° (from ethanol-glacial acetic acid), $\nu_{\text{max.}}$ 3380, 3305 br and 3195 br (NH), 1770, 1690 and 1655 (C=O) cm$^{-1}$ $\delta$(CDCl$_3$), 8.52 br (1H, s, NH), 8.20-8.08 (2H, m, NH), 7.98-7.26 (10H, m, ArH) and 2.68 (3H, s, CH$_3$).

Found: C, 51.9; H, 3.6; N, 19.2%; M, 440.

C$_{19}$H$_{16}$N$_{6}$O$_5$S requires: C, 51.8; H, 3.6; N, 19.1%; M, 440.

The Cyclisation of the Hydrazones (510a,c,f and i)

(a) The hydrazones (510a,c, and f) 0.004 mol) were heated under reflux in ethanol (50.0 ml) for 24h [15 min. in the case of the hydrazone (510a)]. The solutions were cooled and the deposited solid products collected. The filtrate was worked up as described for the individual reactions below.

(i) 6-Benzene sulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) (86%) had m.p. 222-224° as orange needles (from glacial acetic acid), $\delta$(CD$_3$)$_2$SO) 8.34-7.20 (1OH, m, ArH) and 2.99 (3H, s, CH$_3$).

Found: C, 58.1; H, 3.8; N, 20.2%; M$^+$, 351.

C$_{17}$H$_{13}$N$_{5}$O$_2$S requires: C, 58.1; H, 3.7; N, 19.9%; M, 351.

(ii) The hydrazone (510c) afforded a solid, which was combined with a second crop obtained by evaporating the ethanol mother liquor and triturating the gum with ether to afford 6-benzenesulphonyl-3,7-diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511b) (55%) as orange plates m.p. 220-221° (from glacial acetic acid).
C\textsubscript{22}H\textsubscript{15}N\textsubscript{5}O\textsubscript{2}S \textit{requires}: C,63.9; H,3.6; N,17.0%; M, 413.

Evaporation of the ether mother liquor afforded a red gum (0.56g) which was shown by t.l.c. in chloroform over silica to consist of four unresolvable components.

(iii) 6-Benzensulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-3-carboxamide (511d) (35%) had m.p. 231-233° as yellow plates (from ethanol-glacial acetic acid), \(v\text{max.} \ 3440\text{ br and }3120\text{ br (NH) and }1675\text{ br (C=O) cm}^{-1}.

\textit{Found}: C,53.8; H,3.2; N,22.0%; M\textsuperscript{+},380.

C\textsubscript{17}H\textsubscript{12}N\textsubscript{6}O\textsubscript{3}S \textit{requires}: C,53.7; H,3.2; N,22.1%; M, 380.

Evaporation of the ethanol mother liquor and trituration of the resulting gum with ether afforded the starting hydrazone (510f) (62%) m.p. 176-180° (decomp.) identical (m.p. and i.r. spectrum) to an authentic sample.

(b) The hydrazones (510a) and (510c) (0.001 mol) were heated under reflux with aqueous 2M sodium acetate (5.0 ml) in ethanol (10.0 ml) for 1h. The reaction mixtures were cooled and any solid product deposited was collected and washed with water. The filtrates were worked up as described for the individual reactions below.

(i) The hydrazone (510a) gave a solid which was combined with a second crop obtained by concentrating the mother liquor to afford 6-benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo [5,1-c]-1,2,4-triazine (511a) (48%) m.p. 222-224° which was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.
Extraction of the aqueous mother liquor with chloroform afforded only a negligible amount of yellow gum. Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with chloroform gave no further material.

(ii) The hydrazone (510c) gave a solution which when concentrated and extracted with chloroform afforded a red oil. This was triturated with ether to give the unchanged hydrazone (510c) (24%) m.p. 179-182° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor yielded a dark gum (0.24g) which was shown by t.l.c. in chloroform over silica to consist of four unresolvable components.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with chloroform gave no further material.

(c) The hydrazones (510c) and (510i) (0.001 mol) were heated under reflux in glacial acetic acid (10.0 ml) for 0.5 h. In each case the solution was cooled and the solid product which deposited was collected. The filtrate was worked up as described for the individual reactions.

(i) 6-Benzensulphonyl-3,7-diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511b) (9%) had m.p. 218-221° and was identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Evaporation of the acetic acid mother liquor and trituration of the gum with ether afforded unchanged hydrazone (510c) (44%) m.p. 179-182° identical (m.p. and i.r. spectrum) to an authentic sample.
Evaporation of the ether mother liquor afforded a red gum (0.04 g) which was shown by t.l.c. in chloroform over silica to consist of three unresolvable components.

(ii) 3,6-Dibenzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511f) (55%) formed pale green plates m.p. 219-220° (from dimethylformamide-water), δ([CD₃]₂SO) 8.14-7.52 (10H, m, ArH) and 2.98 (3H, s, CH₃).

Found: C, 48.8; H, 3.2; N, 16.8%; M⁺, 415
C₁₇H₁₃N₅O₄S₂ requires: C, 49.2; H, 3.1; N, 16.9%; M, 415.

Evaporation of the acetic acid mother liquor afforded a small quantity of gum (0.09 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multi-component mixture.

The Reaction of the 1,2,3-Triazolo[5,1-c]-1,2,4-triazines (511a) and (511c) with Methanolic Sodium Methoxide

Solutions of the triazolotriazines (511a) and (511c) (0.001 mol) in hot methanol (25.0 ml) were treated with a solution of sodium (0.184g) in methanol (6.0 ml) and the mixtures were heated under reflux for 0.5h. In each case the reaction mixture was cooled and evaporated and the residue treated with water and the insoluble product was collected.

(a) 6-Methoxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521b) (75%) formed yellow plates m.p.225-226° from glacial acetic acid), δ([CD₃]₂SO) 8.36-8.18 (2H, m, ArH), 7.66-7.50 (3H, m, ArH) 4.22 (3H, s, CH₃), and 2.58 (3H, s, CH₃).

Found: C, 59.5; H, 4.5; N, 29.0%; M⁺, 241.
C₁₂H₁₁N₅O requires: C, 59.8; H, 4.5; N, 29.0%; M, 241.
Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (13%) m.p. 178-181° which was identical (m.p. and i.r. spectrum) to a sample obtained later.

(b) 7-Amino-6-methoxy-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521f) (83%) formed yellow needles m.p. 222-223° (from ethanol), ν_max. 3410 and 3310 (NH) cm⁻¹, δ[(CD₃)₂SO] 8.26-8.10 (2H, m, ArH), 7.52-7.20 (3H, m, ArH) and 4.13 (3H, s, CH₃).

Found: C, 54.4; H, 4.3; N, 35.3%; M⁺, 242.

C₁₁H₁₀N₆O requires: C, 54.6; H, 4.1; N, 34.7%; M, 242.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded a negligible quantity of an unidentified solid (0.03 g) m.p. 170-175°.

6-Ethoxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521a)

A solution of 6-benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) (0.35 g, 0.001 mol) in hot absolute ethanol (25.0 ml) was treated with a solution of sodium (0.046 g) in absolute ethanol (3.0 ml) and the mixture was heated under reflux for 0.5 h. The red solution was cooled and the solid was collected and combined with a second crop obtained by evaporating the mother liquor and treating the residue with water to afford 6-ethoxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521a) (total 0.15g) (67%) as pale yellow plates m.p. 198-199° (from glacial acetic acid) δ[CDCｌ₃] 8.42-8.24 (2H, m, ArH), 7.60-7.20 (3H, m, ArH), 4.57 (2H, q, J 6Hz, CH₂), 2.63 (3H, s, CH₃) and 1.55 (3H, t, J 6Hz, CH₃).
Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (0.06 g) (26%) m.p. 177-180º, which was identical (m.p. and i.r. spectrum) to a sample obtained later.

6-Hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c).

A suspension of the triazolotriazine (511a) (0.25 g, 0.0007 mol) in aqueous 2M sodium hydroxide (15.0 ml) was heated under reflux for 0.5 h. The solution obtained was cooled and the solid was collected and washed with aqueous 2M hydrochloric acid to afford 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (0.14 g) (87%) as pale yellow plates m.p. 179-181º (from ethyl acetate-light petroleum), \( \nu_{\text{max.}} \) 3350 br (OH) cm\(^{-1} \), \( \delta[(\text{CD}_3)_2\text{SO}] \) 8.26-8.10 (2H, m, ArH), 7.60-7.20 (3H, m, ArH) and 2.51 (3H, s, CH\(_3\)).

Acidification of the basic aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with chloroform gave no further material.

The Attempted Reaction of 6-Benzensulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Sodium Cyanide

(a) A solution of the triazolotriazine (511a) (0.35 g,
0.001 mol) in hot ethanol (20.0 ml) was treated with a solution of sodium cyanide (0.20 g, 0.004 mol) in water (5.0 ml) and the mixture was heated under reflux for 0.5 h. The red solution was cooled and the solid was collected to afford 6-ethoxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521a) (0.10 g) (39%) m.p. 195-199° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Concentration of the mother liquor and treatment of the residue with water afforded 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (0.06 g) (26%) m.p. 177-180° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with chloroform gave no more material.

(b) A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with a solution of sodium cyanide (0.20 g, 0.004 mol) in water (5.0 ml) and the solution was heated under reflux for 0.5 h. The dark solution was cooled and evaporated, and the residue was treated with water. The solid obtained (0.19 g) was washed with aqueous 2M hydrochloric acid and combined with a second crop obtained by acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid to give 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (total 0.16 g) (70%) m.p. 178-181° identical (m.p. and i.r. spectrum) to a sample obtained before.

Extraction of the combined acidic aqueous mother liquor and washings with chloroform gave no further material.
The Attempted Reaction of 6-Benznesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Sodium Thiocyanate

A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with a solution of sodium thiocyanate (0.32 g, 0.004 mol) in water (5.0 ml) and the solution was heated under reflux for 0.5 h. The solution was cooled and evaporated and the residue obtained was treated with water to afford unreacted triazolotriazine (511a) (0.26 g) m.p. 220-224° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with chloroform, before or after acidification with aqueous 2M hydrochloric acid, gave no further material.

The Attempted Reaction of 6-Benznesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Potassium Cyanate

A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was mixed with a solution of potassium cyanate (0.32 g, 0.004 mol) in water (5.0 ml) and the solution was heated under reflux for 0.5 h. The solution obtained was cooled and evaporated and the residue was treated with a little water. The solid obtained was washed with aqueous 2M hydrochloric acid to afford 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (0.18 g) (79%) m.p. 174-179° identical (m.p. and i.r. spectrum) to an authentic sample.
Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with chloroform gave no further material.

6-Azido-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521d)

A solution of the triazolotriazine (511a) (0.70 g, 0.002 mol) in dioxan (40.0 ml) was treated with a solution of sodium azide (0.52 g, 0.008 mol) in water (10.0 ml) and the mixture was heated under reflux for 0.5h. The dark solution was cooled and evaporated and the residue was treated with water. Extraction of the aqueous mother liquor with chloroform gave only an amount of gum (0.06 g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multicomponent mixture.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded 6-azido-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521d) (0.20 g) (42%) m.p. > 300° (decomp.), $\nu_{\text{max}}$ 2130 (-N=N=N=) cm$^{-1}$, whose attempted purification by crystallisation from a variety of solvents resulted in decomposition to complex mixtures.

Extraction of the acidic aqueous mother liquor with chloroform gave no further material.

The Attempted Reaction of 6-Benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Ethanolic Sodium Acetate.

The triazolotriazine (511a) (0.70 g, 0.002 mol) was heated under reflux with aqueous 2M sodium acetate (5.0 ml) in ethanol (10.0 ml) for 1h. The solution was cooled and the
solid was collected to afford unchanged triazolotriazine (511a) (0.61 g) m.p. 220-224° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Concentration of the mother liquor, treatment of the residue with water and extraction with chloroform gave only a negligible quantity of gum.

7-Methyl-3-phenyl-4,5,6,7-tetrahydro-1,2,3-triazolo[5,1-c]-1,2,4-triazine (525)

A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with a solution of sodium borohydride (0.15 g, 0.004 mol) in water (5.0 ml) and the mixture was heated under reflux for 0.5 h. The solution was cooled and evaporated, and the residue was treated with a little water to afford 7-methyl-3-phenyl-4,5,6,7-tetrahydro-1,2,3-triazolo[5,1-c]-1,2,4-triazine (525) (0.20 g) (93%) m.p. 180-181° as colourless plates (from ethyl acetate), ν_max. 3330 br and 3130 br (NH) cm^{-1}, δ[(CD_3)_2 SO] 7.80-7.64 (2H, m, ArH), 7.50-7.06 (4H, m, ArH and NH), 6.55 (1H, d, J 2Hz, NH), 3.60-3.18 (1H, m, H-7), 2.94-2.64 (2H, m, H-6 and H-6') and 1.19 (3H d, J 6Hz, Me-7).

Found: C, 61.1; H, 6.0; N, 32.5%; M^+, 215.

C_{11}H_{13}N_5 requires: C, 61.4; H, 6.1; N, 32.6%; M, 215.

Extraction of the aqueous mother liquor with chloroform before or after acidification with aqueous 2M hydrochloric acid gave no further material.
7-Methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (526)

The tetrahydrotriazolotriazine (525) (0.22 g, 0.001 mol) in Analar acetone (10.0 ml) was heated under reflux with manganese dioxide (1.32 g) for 1.5 h. The suspension was hot filtered and the filtrate was evaporated to give a gummy red solid which was triturated with ethyl acetate to afford 7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (526) (0.08 g) (38%) m.p. 251-253\( ^\circ \) identical (m.p. and i.r. spectrum) to a sample obtained later.

Evaporation of the ethyl acetate mother liquor afforded a red gum (0.11 g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multicomponent mixture.

The Reduction of 7-Methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (526) using Sodium Borohydride

The triazolotriazine (526) (0.84 g, 0.004 mol) in 1,4-dioxan (90.0 ml) was heated under reflux with a solution of sodium borohydride (0.66 g, 0.016 mol) in water (30.0 ml) for 0.5 h. The solution was cooled and evaporated and the residue was treated with water to afford 7-methyl-3-phenyl-4,5,6,7-tetrahydro-1,2,3-triazolo[5,1-c]-1,2,4-triazine (525) (0.80 g) (93%) m.p. 179-181\( ^\circ \), which was identical (m.p. and i.r. spectrum) to a sample obtained before.

Extraction of the aqueous mother liquor with methylene chloride gave no further material.

The Attempted Reaction of 6-Benzencesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Diethylamine

A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with diethylamine (5.0 ml)
and the solution was heated under reflux for 0.5 h. The solution obtained was cooled and evaporated and the oily residue was treated with water to give a solid which was combined with a second crop obtained by acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid to afford 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (total 0.21 g) (92%) m.p. 173-177° identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of 6-Benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Triethylamine

A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with triethylamine (5.0 ml) and the solution was heated under reflux for 0.5 h. The solution was cooled and evaporated and the residue was treated with water to afford unreacted triazolotriazine (511a) (0.35 g) m.p. 219-223° which was identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of 6-Benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (511a) with Piperidine

(a) A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in hot ethanol (25.0 ml) was treated with piperidine (0.34 g, 0.004 mol) and the reaction mixture was heated under reflux for 0.5 h. The red solution was cooled and the solid was collected and combined with a second crop obtained by evaporating the mother liquor and treating the gummy solid with water to afford 6-ethoxy-7-methyl-3-phenyl-1,2,3-triazolo
[5,1-c]-1,2,4-triazine (521a) (total 0.24 g) (94%) m.p. 195-199° and was identical (m.p. and i.r. spectrum) to an authentic sample.

(b) A solution of the triazolotriazine (511a) (0.35 g, 0.001 mol) in dioxan (20.0 ml) was treated with piperidine (0.35 g, 0.004 mol) and the solution heated under reflux for 0.5 h. The solution obtained was cooled and evaporated and the tar was triturated with ethyl acetate-light petroleum to afford unreacted triazolotriazine (511a) (0.06 g) m.p. 217-221° which was identical (m.p. and i.r. spectrum) to an authentic sample. Evaporation of the organic mother liquor and trituration of the red gum with water afforded 6-hydroxy-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (521c) (0.10 g) (44%) m.p. 177-180° which was identical (m.p. and i.r. spectrum) to an authentic sample. Extraction of the aqueous mother liquor with chloroform gave a negligible quantity of gum.

The Reaction of the 1,2,3-Triazolo[5,1-c]-1,2,4-triazines (511a) and (511c) with Hydrazine

Solutions of the triazolotriazines (511a) and (511c) (0.004 mol) were heated under reflux with 100% hydrazine hydrate (0.80 g, 0.016 mol) in dioxan (75.0 ml) for 0.5 h. In each case the resulting solution was cooled and the deposited product was collected. The filtrate was worked up as described for the individual reactions below.

(i) The triazolotriazine (511a) gave a solid which was combined with a second crop obtained by evaporating the dioxan mother liquor and subjecting the gum (1.12 g) to dry column chromatography in ether over alumina to afford 6-hydrazino-7-
methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (52le) (66%) as its hemi-hydrate, which formed pale yellow plates m.p. 220-222° (from ethanol), \( \nu_{\text{max}} \) 3400 br (OH), 3265, 3170 br, and 3120 (NH) and 1670 (NH def.), cm\(^{-1}\) \( \delta [\text{CD}_3]_2\text{SO} \) 8.26-8.12 (2H, m, ArH), 7.58-7.20 (3H, m, ArH) and 2.49 (3H, s, CH\(_3\)).

Found: C, 52.5; H, 4.6; N, 38.3%; M\(^+\), 241

\( \text{C}_{11}\text{H}_{11}\text{N}_7\cdot\frac{1}{2}\text{H}_2\text{O} \) requires: C, 52.8; H, 4.8; N, 39.2%; M, 241.

(ii) The triazolotriazine (511c) gave a solid which was combined with a second crop obtained by evaporating the dioxan mother liquor and treating the residue with water to afford 7-amino-6-hydrazino-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (52lg) (98%) as dark yellow plates m.p. 253-255° (decomp.) (from dimethylformamide-water), \( \nu_{\text{max}} \) 3470 br, 3360 br, 3275 br and 3165 br (NH) and 1660 (NH def.) cm\(^{-1}\).

Found: C, 49.5; H, 4.3; N, 46.5%; M\(^+\), 242.

\( \text{C}_{10}\text{H}_{10}\text{N}_8 \) requires: C, 49.9; H, 4.1; N, 46.7%; M, 242.

7-Amino-6-azido-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (52lh)

A suspension of the hydrazinotriazolotriazine (52lg) (0.48 g, 0.002 mol) in concentrated aqueous nitric acid (d 1.42, 0.4 ml) and water (1.5 ml) was treated dropwise with stirring at 0° (ice-salt bath) with a solution of sodium nitrite (0.12 g) in water (4.0 ml). The suspension was stirred at 0° for 15 min. and the solid was collected and washed with water to afford 7-amino-6-azido-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (52lh) (0.41 g) (82%) m.p. 204-210°
(decomp.), \( \nu_{\text{max}} \) 3350 br and 3290 br (NH) and 2100 
\( (N=N=N) \) cm\(^{-1}\), which decomposed on attempted crystallisation 
from a variety of solvents.

The Attempted Reaction of 7-Amino-6-hydrazino-3-phenyl-
1,2,3-triazolo[5,1-c]-1,2,4-triazine (521g) with Acetic
Anhydride

(a) The hydrazinotriazolotriazine (521g) (0.24 g, 
0.001 mol) was heated at 100\(^\circ\) with acetic anhydride (0.75 ml) 
for 5 min. The mixture was allowed to cool and the residue 
was treated with ether to afford unchanged starting material 
(0.23 g) m.p. 245-250\(^\circ\) (decomp.) which was identical (m.p. and 
i.r. spectrum) to an authentic sample.

(b) The hydrazinotriazolotriazine (521g) (0.24 g, 0.001 
mol) was heated under reflux in acetic anhydride (5.0 ml) 
for 3h. The dark mixture was cooled and evaporated to afford 
a dark oil (0.16 g) which could not be obtained solid, and 
was shown by t.l.c. in methylene chloride over silica to be 
an unresolvable multicomponent mixture.

The Attempted Reaction of 7-Amino-6-hydrazino-3-phenyl-1,2,3-
triazolo[5,1-c]-1,2,4-triazine (521g) with Formic Acid

The hydrazinotriazolotriazine (521g) (0.24 g, 0.001 mol) 
was heated under reflux in 99\% formic acid (5.0 ml) for 3h. 
The dark mixture was cooled evaporated, and the dark residue 
treated with water and extracted with methylene chloride. 
Evaporation of the methylene chloride mother liquor afforded 
a dark intractable solid (0.14 g), which was shown by t.l.c. 
in methylene chloride over silica to be an unresolvable 
multicomponent mixture.
The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Methylene phosphonium Salts and Related Compounds

The Preparation of 5-Amino-4-cyano-1H-1,2,3-triazole (535c)

5-Amino-4-cyano-1H-1,2,3-triazole (535c) was prepared as described earlier in Chapter 2 (cf. page 66).

The Preparation of the Diazonium Chlorides (535a) and (535b) and the Diazonium Betaine (536)

4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (535a) and 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (535b) were prepared as described earlier (cf. page 115).

4-Benzencesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (536) was prepared as described on page 121.

The Preparation of the Phosphonium Salts (537 a-d) and the Phosphoranes (538), (564) and (565)

The phosphonium salts (537 a-d) and the phosphoranes (538), (564) and (565) were all prepared as described in the literature, and were used without further purification.

(a) Phenacyltriphenylphosphonium bromide\(^{246}\) (537b) (yield 91%) had m.p. 268-271\(^{\circ}\) (lit.,\(^{246}\) 269-271\(^{\circ}\)).

(b) Acetonyltriphenylphosphonium chloride\(^{247}\) (537a) (yield 54%) had m.p. 244-246\(^{\circ}\) (lit.,\(^{247}\) 252\(^{\circ}\)).

(c) Acetonyltriphenylphosphorane\(^{247}\) (538) (yield 98%) had m.p. 198-206\(^{\circ}\) (lit.,\(^{247}\) 199-202\(^{\circ}\)).

(d) 1-Methylphenacyltriphenylphosphonium bromide\(^{248}\) (537c) (yield 53%) had m.p. 242-243\(^{\circ}\) (lit.,\(^{248}\) 246\(^{\circ}\)).
(e) 1-Phenylacetonyltriphenylyphosphonium bromide \(249\) (537d)
yield 34%) had m.p. 224-226\(^\circ\) (lit., \(249\) 271\(^\circ\)).

(f) 3-Triphenylphosphoranylidene-1-phenylmaleimide \(239\) (564)
yield 58%) had m.p. 172-173\(^\circ\) (lit., \(239\) 175-178\(^\circ\)).

(g) 2-Triphenylphosphoranylidene-1,2,3,4-tetrahydropthalene-1,4-dione \(242\) (565) (33%) had m.p. 160-165\(^\circ\) (lit., \(242\) 166-169\(^\circ\)).

Phenacyltrimethylammonium Bromide (569c)

Phenacyltrimethylammonium bromide (569c) was prepared in
84% yield as described in the literature \(250\) and had m.p.
203-207\(^\circ\) (lit., \(250\) 206\(^\circ\)).

Diphenylphenacylsulphonium Fluoroborate (569b)

Diphenylphenacylsulphonium fluoroborate (569b) was
prepared in 30% yield as described in the literature \(251\) and
had m.p. 149-154\(^\circ\) (lit., \(251\) 160\(^\circ\)).

Phenacyltriphenyl arsonium Bromide (569a)

Phenacyltriphenyl arsonium bromide (569a) was prepared in
43% yield as described in the literature \(252\) and had m.p.
177-179\(^\circ\) (lit., \(252\) 186\(^\circ\)).

The Coupling Reactions of 4-Phenyl-1H-1,2,3-triazole-5-diazonium
Chloride (535a) with Acytltriphenylphosphonium Salts

(a) To mixtures of the phosphonium salts (537 a-d)
(0.007 mol) and anhydrous sodium acetate (0.8 g) in ethanol
(5.0 ml) and water (5.0 ml) was added dropwise with stirring
at 0\(^\circ\) (ice-salt bath) a fresh solution of 4-phenyl-1H-1,2,3-
triazole-5-diazonium chloride (535a) (1.39g, 0.0067 mol) in
ethanol (25.0 ml) and water (25.0 ml). Stirring was continued at room temperature for 2h, and any solid product deposited was collected. The filtrate was worked up as described for the individual reactions below.

(i) 7-Methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539a) (86%) formed yellow needles m.p. 251-253 °C (from glacial acetic acid), δ[(CD₃)₂SO] 9.08 (1H, s, H-6), 8.68-8.54 (2H, m, ArH), 7.92-7.70 (3H, m, ArH), and 3.05 (3H, s, CH₃).

Found: C, 62.5; H, 4.4; N, 33.8%; M⁺, 211.
C₁₁H₆N₅ requires: C, 62.6; H, 4.3; N, 33.2%; M, 211.

(ii) 3,7-Diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539b) (96%) formed orange plates m.p. 234-235 °C (from glacial acetic acid), δ[(CD₃)₂SO] 9.55 (1H, s, H-6), 8.50-8.34 (4H, m, ArH) and 7.76-7.42 (6H, m, ArH).

Found: C, 70.1; H, 3.9; N, 25.6%; M⁺, 273.
C₁₆H₁₁N₅ requires: C, 70.3; H, 4.0; N, 25.6%; M, 273.

(iii) 3,7-Diphenyl-6-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539c) (6%) formed yellow needles m.p. 215-216 °C (from glacial acetic acid-water).

Found: C, 71.0; H, 4.7; N, 24.5%; M⁺, 287.
C₁₇H₁₃N₅ requires: C, 71.1; H, 4.5; N, 24.4%; M, 287.

Concentration of the mother liquor and extraction with methylene chloride gave a gum which was triturated with ethyl acetate to afford unreacted phosphonium salt (537c) (45%) m.p. 229-238 °C identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ethyl acetate mother liquor afforded a red gum (0.36 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
(iv) The phosphonium salt (537d) gave a solid which was combined with a second crop obtained by concentrating the mother liquor, extracting with methylene chloride and triturating the resulting gum with ether-ethyl acetate, to afford unreacted phosphonium salt (537d) (46\%) m.p. 209-217° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the trituration mother liquor gave a red gum (1.13 g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multicomponent mixture.

(b) A suspension of the phosphonium salt (537d) (1.90 g, 0.004 mol) in aqueous 2M sodium hydroxide (5.0 ml) and ethanol (5.0 ml) was treated dropwise with stirring over 15 min. at 0° (ice-salt bath) with a solution of the diazonium chloride (535a) (0.70 g, 0.0034 mol) in ethanol (12.5 ml) and water (12.5 ml). Stirring was continued at room temperature for 2h and the solution was concentrated and extracted with chloroform to afford a red oil (2.09 g). Dry column chromatography of the oil in ethyl acetate over alumina afforded a gum (0.10 g), which was shown by t.l.c. in methylene chloride over silica to contain at least four unresolvable components, and a gummy semi-solid. This was triturated with methanol to give a dark amorphous solid (0.22 g) m.p. 214-231° (decomp.) which defied crystallisation and was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Evaporation of the methanol mother liquor afforded a red gum (0.66 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Neutralisation of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with chloroform yielded
triphenylphosphine oxide (0.13 g) (12%) m.p. 146-147° which was identical (m.p. and i.r. spectrum) to an authentic sample.

The Coupling Reactions of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (535a) with the Phosphoranes (538), (564) and (565).

(a) A suspension of acetonylidenetriphenylphosphorane (538) (0.64 g, 0.002 mol) in ethanol (2.5 ml) and water (2.5 ml) was treated dropwise with stirring at 0° (ice-salt bath) over 15 min. with a solution of the diazonium salt (535a) (0.35 g, 0.0017 mol) in ethanol (6.0 ml) and water (6.0 ml). Stirring was continued at room temperature for 2h and the precipitated solid was collected and combined with a second crop obtained by concentrating the mother liquor extracting with methylene chloride, and triturating the resulting red gum with ethanol to afford 7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539a) (total 0.31 g) (74%) m.p. 244-249° identical (m.p. and i.r. spectrum) to a sample obtained before.

(b) A suspension of the phosphoranes (564) or (565) (0.005 mol) and sodium acetate (0.50 g) in ethanol (5.0 ml) and water (5.0 ml) was treated dropwise with stirring over 15 min. at 0° (ice-salt bath) with a solution of the diazonium salt (535a) (0.83 g, 0.004 mol) in ethanol (12.5 ml) and water (12.5 ml). Stirring was continued at room temperature for 2h and the precipitated solid was collected. The filtrate was worked up as described for the individual reactions below.
(i) 3-Triphenylphosphoranylidene-1-phenylmaleimide (564) gave unreacted phosphorane (564) (91%) m.p. 169-172° which was identical (m.p. and i.r. spectrum) to an authentic sample. Concentration of the mother liquor and extraction with chloroform gave a semi-solid which was triturated with toluene to afford 4-phenyl-1H-1,2,3-triazole (566) (33%) m.p. 141-144° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the toluene mother liquor afforded a red gum (0.20 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(ii) 2-Triphenylphosphoranylidene-1,2,3,4-tetrahydronaphthalene-1,4-dione (565) gave unchanged phosphorane (565) (74%) m.p. 154-159° identical (m.p. and i.r. spectrum) to an authentic sample.

Concentration of the mother liquor and extraction with chloroform afforded a dark oil (0.57 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

7-Phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine-6-carboxamide (539e)

A suspension of phenacyltriphenylphosphonium bromide (537b) (1.84 g, 0.004 mol) and anhydrous sodium acetate (0.40g) in ethanol (5.0 ml) and water (5.0 ml) was treated dropwise with stirring over 15 min. at 0° (ice-salt bath) with a solution of the diazonium chloride (535b) (0.70 g, 0.004 mol) in ethanol (12.5 ml) and water (12.5 ml). Stirring was continued at room temperature for 2h and the precipitated solid was collected to afford 7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-
triazine-6-carboxamide (539e) (0.23 g) (24%) as green needles
m.p. 251-253° (from ethanol-glacial acetic acid), $\nu_{\text{max}}$. 3350 and
3250 (NH) and 1650 (C=O) cm$^{-1}$, $\delta$[CDCl$_3$] 8.46-8.32 (2H, m, ArH),
8.24 (1H, s, H-6) and 7.60-7.38 (3H, m, ArH).

Found: C, 54.7; H, 3.4; N, 34.6%; M$^+$, 240

C$_{11}$H$_8$N$_6$O requires: C, 55.0; H, 3.3; N, 35.0%; M, 240.

Concentration of the aqueous ethanol mother liquor and
extraction with methylene chloride gave a yellow gum which was
triturated with ether to afford the unreacted phosphonium salt
(537b) (1.51 g) m.p. 254-259° identical (m.p. and i.r. spectrum)
to an authentic sample.

Evaporation of the ether mother liquor yielded only a
negligible quantity of gum.

3-Benzensulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine
(539f)

A suspension of phenacyltriphenylphosphonium bromide
(537b) (0.94 g, 0.002 mol) and triethylamine (0.3 ml,
0.0022 mol) in dimethylformamide (7.5 ml) was treated dropwise
with stirring at 0° (ice-salt bath) with a freshly prepared
solution of 4-benzenesulphonyl-1H-1,2,3-triazole-5-diazonium
betaine (536) (0.47 g, 0.002 mol) in dimethylformamide
(2.0 ml). Stirring was continued in the melting ice-bath
for 2h and the precipitated solid was collected to afford
triethylamine hydrobromide (0.15 g) (41%) as colourless
needles m.p. 256-257° (from ethanol-light petroleum) (lit., 253
248°).

Found: C, 40.1; H, 8.8; N, 7.7%

C$_{6}$H$_{16}$N Br requires: C, 39.6; H, 8.8; N, 7.7%.
Dilution of the mother liquor with water (10.0 ml) afforded 3-benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539f) (0.48 g) (71%) as pale green plates m.p. 214-215° (from glacial acetic acid), δ(CD₃)₂SO 9.64 (1H, s, H-6), 8.46-8.26 (2H, m, ArH), 8.18-7.98 (2H, m, ArH) and 7.76-7.50 (6H, m, ArH).

Found: C, 56.7; H, 3.3; N, 21.0%; M⁺, 337
C₁₆H₁₁N₅O₂S requires: C, 57.0; H, 3.3; N, 20.8%; M, 337.

Extraction of the aqueous dimethylformamide mother liquor with methylene chloride gave a brown oil (0.12 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

The Attempted Reaction of 4-Cyano-1H-1,2,3-triazole-5-diazonium Nitrate (535d) with Phenacyltriphenylphosphonium Bromide (537b)

A suspension of 5-amino-4-cyano-1H-1,2,3-triazole (535c) (1.26 g, 0.015 mol) in concentrated aqueous nitric acid (d 1.42, 1.5 ml) and water (3.5 ml) was treated dropwise with stirring at 0° (ice-salt bath) with a solution of sodium nitrite (0.9 g) in water (4.0 ml). The solution was stirred at 0° for 15 min. then added, dropwise with stirring at 0° (ice-salt bath) to a suspension of phenacyltriphenylphosphonium bromide (537b) (6.93 g, 0.015 mol) and anhydrous sodium acetate (1.6 g) in water (10.0 ml) and ethanol (20.0 ml). Stirring was continued in the melting ice-bath for 2 h and the mixture (containing a gummy semi-solid) was then extracted with methylene chloride to give a gum which was triturated with methanol-ether to afford the unreacted phosphonium salt (537b) (4.48 g) m.p. 251-259° identical (m.p. and i.r. spectrum) to an authentic sample.
Evaporation of the mother liquor gave a yellow oil (0.69g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.

7-Phenyl-1,2,4-triazolo[5,1-c]-1,2,4-triazine (568)

A solution of 3-amino-1H-1,2,4-triazole (567a) (0.42g, 0.005 mol) in concentrated nitric acid (d 1.42, 0.5 ml) and water (1.5 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.30 g) in water (3.5 ml). Stirring was continued at 0°C for 15 min. and the solution was then added dropwise with stirring at 0°C (ice-salt bath) to a suspension of phenacyltriphenylphosphonium bromide (537b) (2.31 g, 0.005 mol) and anhydrous sodium acetate (0.53 g) in water (1.3 ml) and ethanol (12.0 ml). Stirring was continued in the melting ice-bath for 2h and the precipitated solid was collected to afford 7-phenyl-1,2,4-triazolo[5,1-c]-1,2,4-triazine (568) (0.14 g) (14%) as pale yellow plates m.p. 180-182°C (from ethanol), δ[(CD₃)$_2$SO] 9.71 (1H, s, H-6), 9.05 (1H, s, H-2), 8.52-8.34 (2H, m, ArH) and 7.94-7.50 (3H, m, ArH).

Found: C, 61.3; H, 3.6; N, 35.2%; M$^+$, 197.

C$_{10}$H$_7$N$_5$ requires: C, 60.9; H, 3.6; N, 35.5%; M, 197.

Concentration of the aqueous ethanol mother liquor and extraction with methylene chloride gave an orange gum which was triturated with light petroleum to afford the unreacted phosphonium salt (537b) (0.71g) m.p. 254-261°C identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the light-petroleum mother liquor afforded a red gum (1.18 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.
Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride gave no further material.

The Attempted Reaction of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (535a) with Phenacyltrimethylammonium Bromide (569c)

A solution of phenacyltrimethylammonium bromide (569c) (0.52 g, 0.002 mol) and anhydrous sodium acetate (0.40 g) in ethanol (10.0 ml) and water (10.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of the diazonium salt (535a) (0.42 g, 0.002 mol) in ethanol (10.0 ml) and water (10.0 ml). Stirring was continued at room temperature for 2h and the solution was concentrated and extracted with methylene chloride to give a semi-solid which was triturated with ether to afford an amorphous solid (0.44 g) m.p. 66-74°C (decomp.), \( \nu_{\text{max}} \) 1675 (C=O) cm\(^{-1}\), which on attempted crystallisation from a variety of solvents resulted in the formation of dark intractable gums which defied characterisation.

The Attempted Reaction of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (535a) with Diphenylphenacylsulphonium Fluoroborate (569b)

A suspension of diphenylphenacylsulphonium fluoroborate (569b) (1.46 g, 0.004 mol) and anhydrous sodium acetate (0.80 g) in ethanol (8.0 ml) and water (4.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (535a) (0.83 g, 0.004 mol) in ethanol (12.5 ml) and water (12.5 ml). Stirring was continued at room temperature for 2h and the
mixture (containing an oil) was concentrated to remove the ethanol and extracted with methylene chloride to afford a dark oil (1.40 g) which was shown by t.l.c. in ether over alumina to be an unresolvable multicomponent mixture. Wet column chromatography of the gum over alumina afforded gums which were shown by t.l.c. in methylene chloride over alumina to be unresolvable mixtures.

The Reaction of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (535a) with Phenacyltriphénylarsonium Bromide (569a)

A suspension of phenacyltriphénylarsonium bromide (569a) (1.10 g, 0.002 mol) and anhydrous sodium acetate (0.4 g) in ethanol (4.0 ml) and water (2.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of 4-phenyl-1H-1,2,3-triazole-5-diazonium chloride (535a) (0.42 g, 0.002 mol) in ethanol (7.0 ml) and water (7.0 ml). Stirring was continued at room temperature for 2h and the precipitated solid was collected to afford 3,7-diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (539b) (0.40 g) (73%) m.p. 230-234°C which was identical (m.p. and i.r. spectrum) to a sample obtained before.

Concentration of the mother liquor and extraction with methylene chloride gave a red oil which was triturated with ether to afford the unreacted arsonium salt (569a) (0.27 g) m.p. 169-174°C identical (m.p. and i.r. spectrum) to an authentic sample.
Evaporation of the ether mother liquor afforded a red gum (0.08 g) which was shown by t.l.c. in chloroform over silica to contain at least three unresolvable components.

3-(α-Acetoxybenzyl)-5-methyl-1,2,4-triazine (540)

The triazolotriazine (539a) (0.42 g, 0.002 mol) was heated under reflux in glacial acetic acid (20.0 ml) for 65 h. The dark solution was evaporated and the dark semi-solid obtained was triturated with ether to give the starting triazolotriazine, (539a) (0.05 g) m.p. 246-251° which was identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor afforded a red oil whose i.r. and ¹H n.m.r. spectra were consistent with its being 3-(α-acetoxybenzyl)-5-methyl-1,2,4-triazine (540) (0.36 g) (74%), ν max. 1740 br (C=O) cm⁻¹, δ(CDCl₃) 8.98 (1H, s, H-6), 7.68-7.50 (2H, m, ArH), 7.42-7.24 (3H, m, ArH), 6.88 (1H, s, benzylic H), 2.55 (3H, s, CH₃) and 2.24 (3H, s, CH₃).

The Attempted Oxidation of 3-(α-acetoxybenzyl)-5-methyl-1,2,4-triazine (540) using Chromic Acid

A solution of the triazine (540) (0.36 g, 0.0015 mol) in 70% v/v aqueous glacial acetic acid (15.0 ml) was treated with solid chromium trioxide (0.72 g) and the mixture was heated at 100° for 1h. The mixture was cooled and evaporated and the dark residue obtained was treated with water. Extraction of the solution with methylene chloride afforded a negligible quantity of green gum.
The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Thiocyanomethylene Compounds

The Preparation of 5-Amino-4-cyano-1H-1,2,3-triazole (570c)

5-Amino-4-cyano-1H-1,2,3-triazole (570c) was prepared as described earlier in Chapter 2 (cf. page 66).

The Preparation of the Diazonium Chlorides (570a) and (570b) and the Diazonium Betaine (571)

4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (570a) and 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (570b) were prepared as described earlier (cf. page 115).

4-Benzencesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (571) was prepared as described on page 121.

Preparation of the Thiocyanomethylene Compounds

(i) Cyanomethylenethiocyanate (572c)

Chloroacetonitrile (3.80 g, 0.05 mol) in 80% v/v aqueous ethanol (25.0 ml) was treated with swirling with a solution of potassium thiocyanate (9.72 g, 0.10 mol) in 80% v/v aqueous ethanol (75.0 ml). After the initial exothermic reaction had subsided the solution was heated under reflux for 0.5 h. The mixture was cooled, concentrated and extracted with methylene chloride to give a red oil (1.80 g) which was purified by distillation to afford cyanomethylenethiocyanate (572c) (0.56 g) (11%) b.p. 100-110°C/0.05 mm. Hg as a yellow oil, νmax. 2250 (C≡N) and 2160 (-SC≡N) cm⁻¹.

Found: C, 36.9; H, 2.2; N, 28.7%; M⁺, 98.

C₃H₂N₂S requires: C, 36.7; H, 2.2; N, 28.6%; M⁺, 98.
Phenacylthiocyanate (572a)
Phenacylthiocyanate (572a) was prepared in 96% yield as described in the literature\(^{254}\) and had m.p. 65-66° (lit.,\(^{254}\) 72-73°).

Acetonylthiocyanate (572b)
Acetonylthiocyanate (572b) was prepared in 93% yield as described in the literature\(^{255}\) and had b.p. 68-75°/1.0 mm.Hg (lit.,\(^{255}\) 70-73°/1.0 mm.Hg).

Ethyl Thiocyanoacetate (572d)
Ethyl thiocyanoacetate (572d) was prepared in 85% yield as described in the literature\(^{256}\) and had b.p. 80-85°/2.0 mm Hg (lit.,\(^{256}\) 115°/10.0 mm. Hg).

Reactions of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (570a) with Thiocyanomethylene Compounds.
A freshly prepared solution of the diazonium salt (570a) (0.004 mol) in ethanol (12.5 ml) and water (12.5 ml) was added dropwise to stirred suspensions of the thiocyanomethylene compounds (572 a-d) (0.004 mol) and anhydrous sodium acetate (0.75 g) in ethanol (6.0 ml) and water (3.0 ml) at 0° (ice-salt bath) over 15 min. Stirring was continued at room temperature for 2h and any precipitated solid was collected. The filtrate was worked up as described for the individual reactions.

(1) 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-\(\Lambda^4\)-1,3,4-thiadiazoline (573a) (100%) formed buff needles m.p. 214-215° (from glacial acetic acid-ethanol), \(\nu_{\text{max.}}\) 3300 (NH) and 1640 (C=O) cm\(^{-1}\).
Found: C, 58.6; H, 3.6; N, 23.4%; M⁺, 348.

C₁₇H₁₂N₆O₅ requires: C, 58.6; H, 3.5; N, 24.1%; M, 348.

(iii) 5-Acetyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-
Δ⁴-1,3,4-thiadiazoline (573e) (61%) formed colourless plates
m.p. 193-194⁰ (from toluene) ν_max. 3320 (NH) and 1690 (C=O)
cm⁻¹, δ[CDC1₃] 7.80-7.28 (7H, m, ArH and NH) and 2.15
(3H, s, CH₃).

Found: C, 50.5; H, 3.6; N, 28.9%; M⁺, 286.

C₁₂H₁₀N₆O₅ requires: C, 50.3; H, 3.5; N, 29.4%; M, 286.

Concentration of the mother liquor and extraction with
methylene chloride gave only a negligible quantity of gum.

Acidification of the aqueous mother liquor with aqueous
2M hydrochloric acid and extraction with methylene chloride
gave no further material.

(iii) Cyanomethylenethiocyanate (572c) gave a solution which was
concentrated and extracted with chloroform to afford a red
oil (0.72 g). This partially solidified and turned black
on standing. Trituration of the resulting dark semi-solid
with ether gave a dark amorphous solid (0.35 g) m.p. 102-123⁰
(decomp.) having an ill-defined i.r. spectrum and shown by
t.l.c. in chloroform over silica to consist of at least four
unresolvable components. Evaporation of the ether mother
liquor afforded a red gum (0.37 g) which was shown by t.l.c.
in ethyl acetate over alumina to be an unresolvable multi-
component mixture.

Acidification of the aqueous mother liquor with aqueous
2M hydrochloric acid and extraction with methylene chloride
gave only a negligible quantity of gum.

(iv) Ethyl thiocyanoacetate (572d) gave a solution which was
concentrated and extracted with methylene chloride to afford a gum (0.65 g). Trituration of the gum with ether yielded an amorphous solid (0.10 g) m.p. 134-146° (decomp.) having an ill-defined i.r. spectrum and shown by t.l.c. in methylene chloride over silica to consist of at least four unresolvable components.

Evaporation of the ether mother liquor afforded a red gum (0.53 g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.

5-Benzoyl-2-imino-3-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573h)

A suspension of 4-benzenesulphonyl-1,2,3-triazole-5-diazonium betaine (571) (0.47 g, 0.002 mol) in ethanol (10.0 ml) and water (5.0 ml) was treated dropwise with stirring at 0° (ice-salt bath) with a solution of phenacylthiocyanate (572a) (0.35 g, 0.002 mol) and anhydrous sodium acetate (0.25 g) in ethanol (10.0 ml) and water (5.0 ml). The mixture was stirred in the melting ice-bath for 2h and the solid which had precipitated was collected to afford 5-benzoyl-2-imino-3-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573h) (0.33 g) (40%) as pale orange plates m.p. 234-235° (from glacial acetic acid-water), \( \nu_{\text{max}} \) 3280 br (NH) and 1640 (C=O) cm\(^{-1}\).

Found: C, 49.0; H, 2.9; N, 19.6%; M\(^+\), 412.

\( \text{C}_{17}\text{H}_{12}\text{N}_{6}\text{O}_{3}\text{S}_{2} \) requires: C, 49.5; H, 2.9; N, 20.4%; M, 412.

Concentration of the aqueous ethanol mother liquor afforded phenacylthiocyanate (572a) (0.14 g) m.p. 66-69° which was identical (m.p. and i.r. spectrum) to an authentic sample.
Extraction of the aqueous mother liquor with methylene chloride gave a yellow gum (0.31 g) which was shown by t.l.c. in methylene chloride over silica to consist of at least four unresolvable components.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride gave only a negligible quantity of gum.

5-Benzoyl-2-imino-3-(4-cyano-1H-1,2,3-triazol-5-yl)-Δ₄-1,3,4-thiadiazoline (573i)

A suspension of 5-amino-4-cyano-1H-1,2,3-triazole (570c) (1.64 g, 0.015 mol) in concentrated aqueous nitric acid (d 1.42, 1.5 ml) and water (3.5 ml) was treated with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (0.9 g) in water (4.0 ml). The solution was stirred at 0°C for 15 min. and then treated at 0°C dropwise with stirring with a solution of phenacylthiocyanate (572a) (2.70 g, 0.015 mol) and anhydrous sodium acetate (1.6 g) in ethanol (20.0 ml) and water (6.0 ml). Stirring was continued in the melting ice-bath for 2h and the solid which had precipitated was collected to afford 5-benzoyl-2-imino-3-(4-cyano-1H-1,2,3-triazol-5-yl)-Δ₄-1,3,4-thiadiazoline (573i) (2.01 g) (45%), ν_max. 3500 br (NH), 2240 (C≡N) and 1640 (C=O) cm⁻¹, which crystallised from glacial acetic acid as pink plates of the acetic acid solvate, m.p. 294-296°C.

Found: C,46.7; H,3.0; N,27.3%; M⁺,297.

C₁₂H₇N₇OS.CH₃CO₂H requires: C,47.1; H,3.1; N,27.5%; M, 297.

Concentration of the mother liquor and extraction with methylene chloride afforded an orange oil (0.52 g) which was
shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid gave an orange oil (0.13 g) which was shown by t.l.c. in methylene chloride over silica to be a multicomponent mixture.

The Reaction of 4-Carbamoyl-1H-1,2,3-triazole-5-diazonium Chloride (570b) with Phenacylthiocyanate (572a)

A suspension of 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (570a) (0.35 g, 0.002 mol) in ethanol (10.0 ml) and water (5.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of phenacylthiocyanate (572a) (0.35 g, 0.002 mol) and anhydrous sodium acetate (0.25 g) in ethanol (10.0 ml) and water (5.0 ml). The mixture was stirred in the melting ice-bath for 2h and then filtered to give a solid which was combined with a second crop obtained by concentrating the aqueous ethanol mother liquor to afford 5-benzoyl-3H-1,2,3-triazolo[4,5-d]-1,3,4-thiadiazolo[2,3-b]pyrimidin-8-one (584) (total 0.49 g) (82%) as buff plates m.p. 279-280°C (from glacial acetic acid), νmax 3270 br (NH) and 1690 and 1640 (C=O) cm⁻¹. Found: C, 48.4; H, 2.0; N, 27.9%; M⁺, 298. C₁₂H₆N₆O₂S requires: C, 48.3; H, 2.0; N, 28.2%; M, 298.

On standing at room temperature the aqueous mother liquor slowly deposited an unidentified solid (D) (0.16 g) which formed cream plates m.p. 237-238°C (from dimethylformamide), νmax 3425 br (NH) and 1690 br (C=O) cm⁻¹. Found: C, 58.9; H, 3.5; N, 21.5%; M⁺, 390. Calculated for C₁₉H₁₄N₆O₂S: C, 58.5; H, 3.6; N, 21.5%; M, 390.
Extraction of the aqueous mother liquor with methylene chloride gave only a negligible quantity of gum.

2-Acetimino-5-benzoyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-\Delta^4-1,3,4-thiadiazoline (573b)

(a) The triazolylthiadiazoline (573a) (0.35 g, 0.001 mol) was heated at 100\(^\circ\)C with acetic anhydride (0.4 ml) until the solid just dissolved (1-2 min.). The resulting solution was cooled and left at room temperature for 20 min. Dilution of the mixture with ether afforded 2-acetimino-5-benzoyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-\Delta^4-1,3,4-thiadiazoline (573b) (0.26 g) (60\%) as colourless plates m.p. 167-169\(^\circ\)C (from toluene-light petroleum), \(\nu_{\text{max}}\) 1780 and 1640 (C=O) cm\(^{-1}\), \(\delta_{[CDCl_3]}\)
8.28-8.12 (2H, m, ArH), 7.66-7.30 (8H, m, ArH), 2.92 (3H, s, CH\(_3\)), and 2.16 (3H, s, CH\(_3\)).

Found: C, 59.3; H, 3.6; N, 17.8\%; M\(^+\), 432.
C\(_{21}\)H\(_{16}\)N\(_6\)O\(_3\)S requires: C, 58.3; H, 3.7; N, 19.4\%; M, 432.

Evaporation of the mother liquor afforded a dark oil (0.21 g) which was shown by t.l.c. in chloroform over silica to consist of at least four unresolvable components.

(b) The thiadiazoline (573a) (0.70 g, 0.002 mol) was heated under reflux in acetic anhydride (5.0 ml) for 3h. The resulting solution was cooled and the precipitated solid was collected and combined with a second crop deposited from the acetic anhydride mother liquor on standing, to give 2-acetimino-5-benzoyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-\Delta^4-1,3,4-thiadiazoline (573b) (total 0.77g) (89\%) m.p. 165-166\(^\circ\)C which was identical (m.p. and i.r. spectrum) to the sample obtained in (a) before.
Evaporation of the mother liquor gave a dark gum (0.21 g), shown by t.l.c. in ethyl acetate over silica to contain at least four unresolvable components.

2-Acetimino-5-benzoyl-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ^4-1,3,4-thiadiazoline (573c)

The diacetyltriazolythiadiazoline (573b) (0.39 g, 0.0009 mol) was heated under reflux in 70% v/v aqueous ethanol (10.0 ml) for 0.5 h. The resulting solution was cooled and the solid was collected and combined with a second crop obtained by concentrating the aqueous ethanol mother liquor and treating the residue with water to afford 2-acetimino-5-benzoyl-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ^4-1,3,4-thiadiazoline (573c) (total 0.31 g) (88%) which crystallised from toluene as colourless needles of the toluene solvate, m.p. 196-198° V_max. 3090 br (NH) and 1645 br (C=O) cm\(^{-1}\), δ([CDCl\(_3\)]) 8.24-8.10 (2H, m, ArH), 7.60-7.14 (8H, m, ArH), and 2.33 (3H, s, CH\(_3\)).

Found: C, 64.4; H, 4.6; N, 17.7%; M, 390
C\(_{19}\)H\(_{14}\)N\(_6\)O\(_2\)S.C\(_7\)H\(_8\) requires: C, 64.7; H, 4.6; N, 17.4%; M, 390.

Extraction of the mother liquor with methylene chloride gave no further material.

The acetylthiadiazoline (573c) (0.35 g, 0.00089 mol) was heated at 100° with acetic anhydride (0.4 ml) until the solid just dissolved (1-2 min.). The solution was diluted with ether to afford 2-acetimino-5-benzoyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-Δ^4-1,3,4-thiadiazoline (573b) (0.36 g) (95%) m.p. 164-166° which was identical (m.p. and i.r. spectrum) to an authentic sample.
2-Acetimino-5-acetyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-1,3,4-thiadiazoline (573f)

The thiadiazoline (573e) (0.29 g, 0.001 mol) was heated at 100\(^\circ\) with acetic anhydride (0.3 ml) until the solid just dissolved (1-2 min.). The solution obtained was cooled and left at room temperature for 20 min. Dilution with ether afforded 2-acetimino-5-acetyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-1,3,4-thiadiazoline (573f) (0.31 g) (84%) as colourless needles m.p. 152-153 \(^\circ\) (from toluene-light petroleum), \(\nu\)\(_{\text{max.}}\) 1780, 1690 and 1640 (C=O) cm\(^{-1}\), \(\delta[(CD_3)_2SO]\) 7.60-7.36 (5H, m, ArH), 2.86 (3H, s, CH\(_3\)), 2.59 (3H, s, CH\(_3\)), and 1.98 (3H, s, CH\(_3\)).

Found: C, 52.2; H, 3.8; N, 22.5%; M\(^+\), 370.

C\(_{16}\)H\(_{14}\)N\(_6\)O\(_3\)S requires: C, 51.9; H, 3.8; N, 22.7%; M, 370.

Evaporation of the ether mother liquor yielded only a negligible quantity of gum.

2-Acetimino-5-Acetyl-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-1,3,4-thiadiazoline (573g)

The diacetyltriazolylthiadiazoline (573f) (0.13 g, 0.00035 mol) was heated under reflux in 70% v/v aqueous ethanol (5.0 ml) for 0.5 h. The solution was cooled and concentrated to afford 2-acetimino-5-acetyl-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-1,3,4-thiadiazoline (573g) (0.10 g) (87%) as colourless plates m.p. 202-203 \(^\circ\) (from toluene), \(\nu\)\(_{\text{max.}}\) 3235 br (NH) and 1690 (C=O) cm\(^{-1}\), \(\delta[CDCl_3]\) 8.14-7.98 (2H, m, ArH), 7.78-7.42 (4H, m, ArH and NH), 2.81 (3H, s, CH\(_3\)), and 1.97 (3H, s, CH\(_3\)).
Found: C, 51.3; H, 3.7; N, 25.2%; M⁺, 328.

C₁₄H₁₂N₆O₂S requires: C, 51.2; H, 3.7; N, 25.6%; M, 328.

Extraction of the aqueous mother liquor with methylene chloride gave no further material.

The Attempted Reaction of the Triazol-5-yl-1,3,4-thiadiazolines (573a) and (573e) with Ethanol

The triazolylthiadiazolines (573a) and (573e) (0.002 mol) were heated under reflux in ethanol (15.0 ml) for 0.5 h. In each case the solution obtained was cooled to afford a solid, which was combined with a second crop obtained by evaporation of the ethanol mother liquor.

(i) 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573a) afforded unreacted starting material (91%) m.p. 210-212°C which was identical (m.p. and i.r. spectrum) to an authentic sample.

(ii) 5-Acetyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573e) gave unchanged starting material (95%) m.p. 190-194°C identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of the Triazol-5-yl-1,3,4-thiadiazolines (573a) and (573e) with Ethanoic Sodium Acetate

The triazolylthiadiazolines (573a) and (573e) (0.002 mol) were heated under reflux with aqueous 2M sodium acetate solution (5.0 ml) in ethanol (10.0 ml) for 1 h. In each case the solution was cooled and concentrated and the solid precipitated collected and washed with water. The filtrate was worked up
as described for the individual reactions.

(i) 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573a) gave unreacted starting material (63%) m.p. 209-213° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride afforded a red gum (0.13 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(ii) 5-Acetyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573e) afforded unreacted starting material (97%) m.p. 189-193° identical (m.p. and i.r. spectrum) to an authentic sample.

The Attempted Reaction of 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ⁴-1,3,4-thiadiazoline (573a) with Acetic Acid

The thiaadiazole (573a) (0.70 g, 0.002 mol) was heated under reflux in glacial acetic acid (15.0 ml) for 0.5 h. The resulting solution was cooled, evaporated and the gum obtained was triturated with ether to afford unchanged starting material (0.35 g) m.p. 211-214° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor gave an oil (0.31g) which was shown by t.l.c. in chloroform over silica to be an unresolvable multicomponent mixture.
The Attempted Reaction of 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-4H-1,3,4-thiadiazoline (573a) with Hydrazine

The thiadiazoline (573a) (0.70 g, 0.002 mol) in methanol (15.0 ml) was heated under reflux with 85% v/v aqueous hydrazine hydrate (0.5 ml) for 1.5 h. The solution was cooled and evaporated and the residue was treated with water. Extraction of the resulting solution with methylene chloride afforded a gum (0.43 g) which was shown by t.l.c. in ethyl acetate over alumina to consist of at least four unresolvable components.

The Attempted Reaction of 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-4H-1,3,4-thiadiazoline (573a) with Hydroxylamine

The thiadiazoline (573a) (0.70 g, 0.002 mol) in methanol (25.0 ml) was heated under reflux for 1 h with a solution of hydroxylamine hydrochloride (0.13 g, 0.002 mol) in water (1.0 ml) which had been neutralised with solid sodium acetate. The mixture was cooled, evaporated and treated with water to afford an amorphous solid (0.78 g) m.p. 66-81° (decomp.). Extraction of the solid (0.78 g) with boiling ethyl acetate afforded an insoluble solid (0.10 g) m.p. > 300° (decomp.) which showed an ill-defined i.r. spectrum. Evaporation of the ethyl acetate mother liquor afforded a dark gum (0.61 g) which was shown by t.l.c. in ethyl acetate over alumina to be a multicomponent mixture.
5-Benzoyl-2-nitrosoimino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-
$\Lambda^4$-1,3,4-thiadiazoline (573d)

The thiadiazoline (573a) (1.40 g, 0.004 mol) in glacial acetic acid (15.0 ml) was treated dropwise with stirring at 0°C (ice-salt bath) with a solution of sodium nitrite (2.0 g) in water (12.0 ml) and stirring was continued at 0°C for 2h. The precipitated solid was collected and washed with water to afford 5-benzoyl-2-nitrosoimino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-$\Lambda^4$-1,3,4-thiadiazoline (573d) (1.09 g) (72%) as orange plates m.p. 148-149°C (from ethanol) $\nu_{\text{max}}$ 3130 br (NH) and 1650 (C=O) cm$^{-1}$.

Found: C, 54.7; H, 3.0; N, 25.9%; M$^+$, 377.
C$_{17}$H$_{11}$N$_7$O$_2$S requires: C, 54.1; H, 2.9; N, 26.0%; M, 377.

Extraction of the mother liquor with methylene chloride afforded only a negligible quantity of gum.

The Reaction of 5-Benzoyl-2-nitrosoimino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-$\Lambda^4$-1,3,4-thiadiazoline (573d) with Acetic Anhydride

The nitrosoiminothiadiazoline (573d) (0.38 g, 0.001 mol) was heated at 100°C in acetic anhydride (0.4 ml) until the solid just dissolved (1-2 min.). The solution was cooled and left at room temperature for 20 min. Trituration of the semi-solid with ether afforded 2-acetimino-5-benzoyl-3-(1-acetyl-4-phenyl-1,2,3-triazol-5-yl)-$\Lambda^4$-1,3,4-thiadiazoline (573b) (0.37 g) (86%) m.p. 164-168°C identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the mother liquor afforded only a negligible quantity of gum.
The Attempted Reduction of 5-Benzoyl-2-nitrosoimino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ4-1,3,4-thiadiazoline (573d) with Sulphur Dioxide

The nitrosoiminothiadiazoline (573d) (0.38 g, 0.001 mol) was added in portions with stirring at 0°C (ice-salt bath) to a solution of ethanol (15.0 ml) which had been saturated with sulphur dioxide. The resulting solution was resaturated with sulphur dioxide left stoppered at room temperature overnight, then evaporated. Trituration of the resulting gum with a little ether gave an unidentified solid (C) (0.32 g) as white plates m.p. 180-182°C (from ethanol-light petroleum) v$_{\text{max}}$ 3200 br and 1640 w cm$^{-1}$.

Found: C, 48.2; H, 3.8; N, 17.6%; M$^+$, 377.

Evaporation of the ether mother liquor afforded a negligible quantity of gum.

The Attempted Reaction of 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-Δ4-1,3,4-thiadiazoline (573a) with Sulphuric Acid

The triazolythiadiazoline (573a) (0.70 g, 0.002 mol) in ethanol (50.0 ml) was heated under reflux with aqueous 2M sulphuric acid (5.0 ml) for 1.5 h. The mixture was cooled and concentrated to remove the ethanol and the solid was collected to afford the sulphate salt of the starting triazolylthiadiazoline (573a) (0.51 g) (64%) as colourless plates m.p. 208-209°C (from glacial acetic acid) v$_{\text{max}}$ 3200 br (NH) and 1640 (C=O) cm$^{-1}$. 
Found: C, 51.5; H, 3.3; N, 21.1%.

\[ \text{C}_{17} \text{H}_{12} \text{N}_5 \text{O}_3 \text{S}_2 \text{H}_2 \text{SO}_4 \text{ requires: C, 51.4; H, 3.3; N, 21.2\%} \]

which on treatment with saturated aqueous sodium hydrogen carbonate liberated the free triazolylthiadiazoline (573a) (0.46 g) m.p. 166-167° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the acidic aqueous mother liquor with methylene chloride gave only a negligible quantity of gum.

The Attempted Reaction of 5-Benzoyl-2-imino-3-(4-phenyl-1H-1,2,3-triazol-5-yl)-A^4-1,3,4-thiadiazoline (573a) with Sodium Hydroxide

The thiadiazoline (573a) (0.70 g, 0.002 mol) was heated under reflux in aqueous 2M sodium hydroxide (10.0 ml) for 0.5 h. The resulting solution was cooled and neutralised with aqueous 2M hydrochloric acid to afford an amorphous solid (0.20 g) m.p. 140-160° with an ill-defined i.r. spectrum, shown by t.l.c. in ethyl acetate over silica to contain at least four unresolvable components.

Extraction of the aqueous mother liquor with methylene chloride gave no material. Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride afforded benzoic acid (0.10 g) (45%) m.p. 119-122° identical (m.p. and i.r. spectrum) to an authentic sample.

The Coupling Reactions of 5-Diazo-1H-1,2,3-triazoles with Naphthols and Phenols
The Preparation of 5-Amino-4-cyano-1H-1,2,3-triazole (590c)

5-Amino-4-cyano-1H-1,2,3-triazole (590c) was prepared as described on page 66.

The Preparation of the Diazonium Chlorides (590a) and (590b) and the Diazonium Betaine (591)

4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (590a) and 4-carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (590b) were prepared as described on page 115.

4-Benzenezesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (591) was prepared as described on page 121.

The Coupling Reactions of the 1,2,3-Triazole-5-diazonium Salts (590a and b) and the 1,2,3-Triazole-5-diazonium Betaine (591) with β-Naphthol

(a) A solution of the diazonium chlorides (590a) or (590b) (0.002 mol) in ethanol (10.0 ml) and water (10.0 ml) was added dropwise with stirring at 0°C (ice-salt bath) to a solution of β-naphthol (0.29 g, 0.002 mol) in aqueous 2M sodium hydroxide (5.0 ml) and ethanol (5.0 ml) and the mixture stirred in the melting ice-bath for 0.5 h. In each case the resulting red solution was concentrated and acidified with aqueous 2M sulphuric acid and the solid obtained collected. The filtrate was worked up as described for the individual reactions.

(i) 4-Phenyl-1H-1,2,3-triazole-5-diazonium chloride (590a) afforded 1-(4-phenyl-1H-1,2,3-triazol-5-ylazo)-2-naphthol (592a) (100%) as red needles m.p. 190-191°C (from ethanol-water), $\nu_{\text{max}}$ 3125 br (NH, OH) cm$^{-1}$, $\delta$[(CD$_3$)$_2$SO] 8.64-8.46 (1H, m, ArH), 8.09 (1H, d, J 10Hz, ArH), 7.98-7.82 (3H, m, ArH),
7.74-7.38 (5H, m, ArH) and 7.20 (1H, d, J 10Hz, ArH).

Found: C, 68.3; H, 4.3; N, 22.5%; M⁺, 315.

C₁₈H₁₃N₅O requires: C, 68.6; H, 4.2; N, 22.3%; M, 315.

(ii) 4-Carbamoyl-1H-1,2,3-triazole-5-diazonium chloride (590b) gave the azo compound (592c) which when crystallised afforded 3-carbamoyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-1,2,4-triazine (593b) (59%) as orange plates m.p. 251-252° (from dimethylformamide-water) \( \nu_{\text{max}} \) 3360 br and 3215 br (NH) and 1660 br (C=O) cm⁻¹.

Found: C, 59.4; H, 3.5; N, 31.5%; M⁺, 264.

C₁₃H₈N₆O requires: C, 59.1; H, 3.0; N, 31.8%; M, 264.

Extraction of the mother liquor with methylene chloride gave a red gum (0.16 g) which was shown by t.l.c. in methylene chloride over silica to consist of at least four unresolvable components.

(b) The aminotriazole (590c) (0.44g, 0.004 mol) in concentrated aqueous nitric acid (d 1.42, 0.4 ml) and water (0.9 ml) was treated with stirring at 0° (ice-salt bath) with a solution of sodium nitrite (0.23 g) in water (2.5 ml). The solution was stirred at 0° for 15 min. and then treated at 0° dropwise with stirring with a solution of \( \beta \)-naphthol (0.58 g, 0.004 mol) in aqueous 2M sodium hydroxide (5.0 ml) and ethanol (5.0 ml). Stirring was continued in the melting ice-bath for 2h and the dark solution was concentrated and acidified with aqueous 2M hydrochloric acid to afford 1-(4-cyano-1H-1,2,3-triazol-5-yl)azo-2-naphthol (592e) (0.98 g) (93%) as orange plates m.p. 223-225° (decomp.) [lit., 209° 200° (decomp.)] from dimethylformamide-water), \( \nu_{\text{max}} \) 3450 br (NH, OH) and 2230 (C=N) cm⁻¹,
δ[(CD₃)₂SO] 8.58-8.42 (1H, m, ArH), 8.04 (1H, d, J 10Hz, ArH),
7.88-7.74 (1H, m, ArH) 7.64-7.44 (2H, m, ArH), and 6.96
(1H, d, J 10Hz, ArH).

Found: C,59.2; H,3.3; N,32.2%; M⁺,264.
C₁₃H₈N₆O requires: C,59.1; H,3.0; N,31.8%; M, 264.

(c) A suspension of the betaine (591) (0.47 g, 0.002 mol)
in ethanol (10.0 ml) and water (10.0 ml) was treated dropwise
with stirring at 0°C (ice-salt bath) with a solution of β-
naphthol (0.29 g, 0.002 mol) in aqueous 2M sodium hydroxide
(5.0 ml) and ethanol (5.0 ml). Stirring was continued in the
melting ice-bath for 2h and the solution was concentrated and
acidified with aqueous 2M hydrochloric acid to afford 1-(4-
benzenesulphonyl-1H-1,2,3-triazol-5-ylazo-2-naphthol (592f)
(0.38 g) (50%) as orange plates m.p. 142-144°C (from dimethyl-
formamide-water) νmax. 3430 br (NH, OH) cm⁻¹, δ[(CD₃)₂SO]
8.68-8.50 (1H, m, ArH), 8.12-7.92 (3H, m, ArH), 7.82- 7.46
(6H, m, ArH), and 6.81 (1H, d, J 10Hz, ArH).

Found: C,56.6; H,4.3; N,18.4%; M⁺,379.
C₁₆H₁₃N₅O₃S requires: C,57.0; H,3.4; N,18.5%; M, 379.

Extraction of the aqueous mother liquor with methylene
chloride gave a red gum (0.14 g) which was shown by t.l.c. in
methylene chloride over silica to consist of at least four
unresolvable components.

The azo compounds (592a), (592c), (592e) and (592f) were
all soluble in aqueous 2M sodium hydroxide and recovered,
unchanged from their alkaline solutions on acidification with
aqueous 2M hydrochloric acid.
The Coupling Reactions of 4-Phenyl-1H-1,2,3-triazole-5-diazonium Chloride (590a) with Phenols

A solution of the diazonium chloride (590a) (2.10 g, 0.01 mol) in ethanol (50.0 ml) and water (50.0 ml) was added dropwise with stirring at 0°C (ice-salt bath) to a solution of the phenols (see below) (0.01 mol) in aqueous 2M sodium hydroxide (5.0 ml) and ethanol (5.0 ml). Stirring was continued in the melting ice-bath for 0.5 h, and then each solution was concentrated and acidified with aqueous 2M hydrochloric acid and any solid deposited was collected. The filtrates were worked up as described for the individual reactions.

(i) Reaction with p-cresol afforded 1-(4-phenyl-1H-1,2,3-triazol-5-yl)azo-2-hydroxy-5-methylbenzene (594a) (96%) as yellow plates m.p. 195-196°C (from glacial acetic acid), ν_max. 3450 br (NH, OH) cm⁻¹, δ[(CD₃)₂SO] 10.30 br (1H, s, OH), 8.26-7.92 (2H, m, ArH), 7.70-7.40 (4H, m, ArH), 7.36-7.26 (1H, m, ArH), 6.97 (1H, d, J 8Hz, ArH) and 2.29 (3H, s, CH₃).

Found: 279.113561 (error < 6 p.p.m.)
C₁₅H₁₃N₅O requires: 279.112004.

The azo compound (594a) was soluble in aqueous 2M sodium hydroxide, and was recovered unchanged from its alkaline solution on acidification with aqueous 2M hydrochloric acid.

(ii) Reaction with 6-methyluracil gave a solution which when extracted with methylene chloride and the gum obtained triturated with benzene afforded 4-phenyl-1H-1,2,3-triazole (596) (69%) m.p. 142-144°C identical (m.p. and i.r. spectrum) to an authentic sample.
(iii) Reaction with p-nitrophenol afforded 4-phenyl-1H-1,2,3-triazole (596) (52%) m.p. 143-145° which was identical (m.p. and i.r. spectrum) to an authentic sample. Extraction of the aqueous mother liquor with chloroform afforded p-nitrophenol (82%) m.p. 110-112° which was identical (m.p. and i.r. spectrum) to an authentic sample.

(iv) Reaction with pyrimidin-4(1H)-one afforded 4-phenyl-1H-1,2,3-triazole (596) (59%) m.p. 141-144° which was identical (m.p. and i.r. spectrum) to an authentic sample.

(v) Reaction with hydroquinone gave a solution which was extracted with chloroform to afford 4-phenyl-1H-1,2,3-triazole (596) (41%) m.p. 140-143° identical to an authentic sample.

The Reactions of the Azo Compounds (592a), (592c) and (594a) with Acetic Anhydride

The azo compounds (592a), (592c) and (594a) (0.001 mol) were heated at 100° with acetic anhydride (1.5 ml) for 10 min. In each case the reaction mixture was allowed to cool and left at room temperature for 20 min. Dilution with water afforded solids which were collected to give the corresponding N-acetyl derivatives.

(i) 1-(1-Acetyl-4-phenyl-1,2,3-triazol-5-yl)azo-2-naphthol (592b) (81%) formed red plates m.p. 164-165° (from glacial acetic acid). \( \nu_{\text{max}} \) 1750 (C=O) cm\(^{-1}\), \( \delta[(\text{CD}_3)_2\text{SO}] \) 8.20-7.40 (1OH, m, ArH), 6.88 (1H, d, J 10Hz, ArH), and 2.84 (3H, s, CH\(_3\)).

Found: C, 67.0; H, 4.2; N, 19.9%; M\(^+\), 357. 

C\(_{20}\)H\(_{15}\)N\(_5\)O\(_2\) requires: C, 67.2; H, 4.2; N, 19.6%; M, 357.
(ii) 1-(1-Acetyl-4-phenyl-1,2,3-triazol-5-yl)azo-2-hydroxy-5-methylbenzene (594b) (83%) formed orange needles m.p. 64-66° (from ethanol-glacial acetic acid), \( \nu_{\text{max}} \) 1765 (C=O) cm\(^{-1}\)
\[ \delta[(\text{CD}_3)_2\text{SO}] 8.14-7.96 (2\text{H}, \text{ m, ArH}), 7.60-7.40 (5\text{H}, \text{ m, ArH}), 6.94 (1\text{H}, \text{ d, J 8Hz, ArH}), 2.52 (3\text{H}, \text{ s, CH}_3) \] and 2.27 (3H, s, CH\(_3\)).

Found: C, 63.3; H, 4.6; N, 21.3%; M\(^+\), 321.

\( \text{C}_{17}\text{H}_{15}\text{N}_5\text{O}_2 \) requires: C, 63.5; H, 4.7; N, 21.8%; M, 321.

(iii) The azo compound (592c) afforded 3-carbamoyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-1,2,4-triazine (593b) (68%) m.p. 244-250° identical (m.p. and i.r. spectrum) to an authentic sample.

The Cyclisation of the Azo Compounds (592a, c, e and f) and (594a) with Acetic Acid

The azo compounds (592a, c, e and f) and (594a) (0.002 mol) were heated under reflux in glacial acetic acid (10.0 ml) for 2h. In each case the solution was cooled and the deposited product collected. The filtrate was worked up as described for the individual reactions.

(i) 3-Phenyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-1,2,4-triazine (593a) (52%) formed purple needles m.p. 242-243° (from dimethylformamide).

Found: C, 72.9; H, 3.9; N, 23.7%; M\(^+\), 297.

\( \text{C}_{18}\text{H}_{11}\text{N}_5 \) requires: C, 72.7; H, 3.7; N, 23.6%; M, 297.

Evaporation of the mother liquor and trituration of the oil with ethanol gave \( \alpha \)-acetoxylbenzynaphtho[2,1-e]-1,2,4-triazine (598a) (46%) m.p. 142-146° identical (m.p. and i.r. spectrum) to a sample obtained later.
(ii) 3-Benzensulphonyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-
1,2,4-triazine (593d) (83%) formed yellow plates m.p. 249-250°
(from dimethylformamide).

Found: C,59.9; H,3.2; N,19.3%; M⁺,361.
C₁₈H₁₁N₅O₂S requires: C,59.8; H,3.1; N,19.4%; M, 361.

(iii) 3-Carbamoyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-1,2,4-
triazone (593b) (86%) had m.p. 249-252° and was identical
(m.p. and i.r. spectrum) to a sample obtained earlier.

(iv) The azo compound (592e) gave unreacted starting
material (19%) m.p. 220-225° identical (m.p. and i.r. spectrum)
to an authentic sample.

Evaporation of the acetic acid mother liquor afforded a
red gum (0.40 g) which was shown by t.l.c. in methylene
chloride over silica to be an unresolvable multicomponent
mixture.

(v) The azo compound (594a) afforded unchanged starting
material (95%) m.p. 193-196° which was identical (m.p. and i.r.
spectrum) to an authentic sample.

The Cyclisation of the Azo Compounds (592a) and (594a) in
Boiling Ethanolic Sodium Acetate

The azo compounds (592a) and (594a) (0.005 mol) in
ethanol (20.0 ml) were heated under reflux with aqueous 4M
sodium acetate solution (10.0 ml) for 1h. In each case the
solution was cooled and the precipitated solid collected.

(i) 3-Phenyl-1,2,3-triazolo[5,1-c]naphtho[2,1-e]-1,2,4-
triazine (593a) (89%) had m.p. 240-243° and was identical
(m.p. and i.r. spectrum) to an authentic sample.
(ii) The azo compound (594a) gave a solid which was combined with a second crop obtained by concentrating the mother liquor to afford unchanged starting material (93%) m.p. 192-195° identical (m.p. and i.r. spectrum) to an authentic sample.

3-α-Acetoxybenzynaphtho[2,1-e]-1,2,4-triazine (598a)

The triazolonaphthotriazine (593a) (1.80 g, 0.006 mol) was heated under reflux in glacial acetic acid (50.0 ml) for 3h. The solution was cooled to afford unchanged starting material (0.48 g) m.p. 240-242° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the mother liquor and trituration of the gummy semi-solid with ethanol afforded α-acetoxybenzynaphtho[2,1-e]-1,2,4-triazine (598a) (1.16 g) (59%) as yellow plates m.p. 145-146° (from ethanol), ν max. 1745 (C=O) cm⁻¹, δ [CDCl₃] 9.48-9.32 (1H, m, ArH), 8.13 (1H, d, J 10Hz, ArH), 7.94-7.62 (6H, m, ArH), 7.42-7.26 (3H, m, ArH), 7.22 (1H, s, benzylic H), and 2.28 (3H, s, CH₃).

Found: C, 72.7; H, 4.4; N, 12.8%; M⁺, 329.
C₂₀H₁₅N₃O₂ requires: C, 72.9; H, 4.6; N, 12.8%; M, 329.

3-α-Hydroxybenzynaphtho[2,1-e]-1,2,4-triazine (598b)

(a) The triazolonaphthotriazine (593a) (0.30 g, 0.001 mol) was heated under reflux with 20% w/v aqueous sulphuric acid (5.0 ml) in glacial acetic acid (12.0 ml) for 1h. The solution was cooled to give unchanged starting material (0.09 g) m.p. 239-242° identical (m.p. and i.r. spectrum) to an authentic sample. The mother liquor was concentrated to afford
3-α-hydroxybenzynaphtho[2,1-e]-1,2,4-triazine (598b) (0.20 g) (69%) as yellow plates m.p. 160-162° (from ethanol-water), ν\text{max.} 3260 br (OH) cm\(^{-1}\), δ[(CD\(_3\)]\(_2\)SO] 9.26-9.18 (1H, m, ArH), 8.40 (1H, d, J 9Hz, ArH), 8.20-8.00 (1H, m, ArH) 7.96-7.78 (2H, m, ArH), 7.84 (1H, d, J 9Hz, ArH), 7.72-7.54 (2H, m, ArH), 7.46-7.22 (3H, m, ArH), and 6.38 (1H, s, benzylic H).

Found: C,74.9; H,4.6; N,13.5%; M\(^+\),287

C\(_{18}\)H\(_{13}\)N\(_3\)O requires: C,75.2; H,4.6; N,14.6%; M, 287.

(b) The acetoxybenzynaphthotriazine (598a) (0.66 g, 0.002 mol) in ethanol (20.0 ml) was heated under reflux with aqueous 0.5 M sodium carbonate solution (5.0 ml) for 0.5 h. The mixture was cooled and the solid obtained was collected and washed with water to afford α-hydroxybenzynaphtho[2,1-e]-1,2,4-triazine (598b) (0.44 g) (77%) m.p. 159-162° identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

3-Benzoylnaphtho[2,1-e]-1,2,4-triazine (599)

The hydroxybenzynaphthotriazine (598b) (0.29 g, 0.001 mol) in 70% v/v aqueous acetic acid (10.0 ml) was heated at 100° with solid chromium trioxide (0.50 g) for 1h. The solid obtained from the cooled solution was combined with a second crop obtained by evaporating the mother liquor and treating the residue with water to afford 3-benzoylnaphtho[2,1-e]-1,2,4-triazine (599) (total 0.20 g) (70%) as pale yellow plates m.p. 147-148° (from acetic acid-water), ν\text{max.} 1680 (C=O) cm\(^{-1}\), δ[(CD\(_3\)]\(_2\)SO] 8.52-8.38 (1H, m, ArH), 7.98 (1H, d, J 10Hz, ArH), 7.85-7.10 (8H, m, ArH), and 6.90 (1H, d, J 10Hz, ArH).

Found: M\(^+\), 285.090493 (error < 2 p.p.m.)

C\(_{18}\)H\(_{11}\)N\(_3\)O requires: M, 285.090207
Scheme 121

\[
\begin{align*}
\text{ArNEN Cl}^- & \quad \rightarrow \quad \text{ArNHNH}_2 + \text{COR} \quad \text{CH}_2 \quad \text{COR} \\
& \quad \downarrow \quad \text{COR} \\
& \quad \text{Ar} \\
\text{N=N=NNX}^+ & \quad \rightarrow \quad \text{N=N=NNNH}_2 \\
& \quad \downarrow \quad \text{(COR)}^2 \\
& \quad \text{R} \quad \text{R}
\end{align*}
\]
3.3 The Reductive Condensation Reactions of 5-Diazo-1H-1,2,3-triazoles with α-Dicarbonyl Compounds

3.3.1 Introduction

As already mentioned in Chapter 1, aryldiazonium salts can be reduced to the corresponding hydrazines, using a variety of reducing agents. Aromatic hydrazines prepared in this way have been shown to condense readily with β-diketones to afford the corresponding pyrazoles, as is illustrated in Scheme 121 [(607) → (608) + (609) → (610)]. Since the reduction of aryldiazonium salts to the corresponding hydrazines is a general reaction, undergone by many diazonium salts (cf. Chapter 1), such reactions should therefore be applicable to 1,2,3-triazolediazonium salts of the type (611), under investigation in the present work. The hydrazines (612) formed from such reactions could then be used to obtain fused heterocycles of the type (613), by condensation with suitable α-dicarbonyl derivatives (Scheme 121). These condensation reactions, if successful, would then serve two purposes. As well as being of synthetic value, the fused triazolotriazines formed by condensation of the 1,2,3-triazolylhydrazines with α-dicarbonyl derivatives, would have the isomeric triazolotriazine structure of those compounds under investigation in the study of the Dimroth rearrangement, described earlier in Chapter 2.2.

The proposed condensation reactions of α-dicarbonyl compounds with 1H-1,2,3-triazolylhydrazines finds analogy in the literature. Partridge and Stevens have reported the
\[
\begin{align*}
\text{Scheme 122}
\end{align*}
\]
Scheme 123
\[
\begin{align*}
\text{(620)} & \quad \begin{array}{c}
N = N \\
\text{HN} \quad \text{H} \\
\text{R}^1 \quad \text{R}^2
\end{array} \\
\text{R}^1 & = \text{R}^2 \\
a) \quad \text{SO}_2\text{Ph} & \quad \text{NH}_2 \\
b) \quad \text{SO}_2\text{Ph} & \quad \text{N}_2\text{NO}_3^- \\
c) \quad \text{CN} & \quad \text{NH}_2 \\
d) \quad \text{CN} & \quad \text{N}_2\text{NO}_3^- \\
e) \quad \text{SO}_2\text{Ph} & \quad \text{H}
\end{align*}
\]

(622)

(623)

(624)
reduction of pyrazole-3-diazonium chloride (614) with ethanolic sulphur dioxide to form the hydrazine (615), followed by condensation with benzil (616a) or methylglyoxal (616b), in situ, to afford the pyrazolotriazines (617a) and (617b) (Scheme 122). In addition, Hogarth\textsuperscript{181} has demonstrated the ready condensation of the hydrazino-1,2,4-triazole (618) with benzaldehyde to afford the benzylidene derivative (619).

The present investigation was carried out in an attempt to synthesise new 1,2,3-triazolo[5,1-c]-1,2,4-triazines by reactions analogous to those described in Schemes 121, 122 and 123.

3.3.2 The Reductive Synthesis of the 1,2,3-Triazolo[5,1-c]-1,2,4-triazine Ring System from 4-Substituted-5-diazo-1H-1,2,3-triazoles

When the diazonium betaine (621) was treated with a saturated solution of aqueous ethanolic sulphur dioxide, followed by heating the resulting solution under reflux with phenylglyoxal the triazolotriazine (622a) was obtained. This compound was identical to that obtained in the coupling reaction of the betaine (621) with phenacyltriphenylphosphonium bromide, described earlier, in Chapter 3.2.4. The alternative structure (622b) is ruled out on this basis and on the expectation that initial condensation of phenylglyoxal with the hydrazine intermediate (625) will occur via the most reactive carbonyl group (i.e. CHO), rather than with the less reactive ketonic group.
Scheme 124
Scheme 125
The proposed mechanism for the formation of the triazolotriazine (622a) is outlined in Scheme 124. The initial step in this mechanism is the formation of the hydrazine (625). Condensation of (625) with phenylglyoxal then occurs [Scheme 124; \((621) \rightarrow (625) \rightarrow (626)\)], followed by cyclisation to the triazolotriazine [Scheme 124; \((627) \rightarrow (628) \rightarrow (622a)\)]. The isomeric triazolo[1,5-b]triazine structure (630) (Scheme 125), derivable by the potential Dimroth rearrangement of either (622a) or the hydrazine intermediate (625), is readily ruled out by consideration of chemical evidence. The intermediate hydrazine (625) can, in principle, rearrange to the diaminotriazole (629) by initial reversible Dimroth rearrangement [Scheme 125; \((625) \rightleftharpoons (629)\)]. However, initial formation of the diaminotriazole (629) is readily excluded by the outcome of the reductive reaction of the betaine (621) with benzaldehyde. When the betaine (621) was treated with aqueous ethanolic sulphur dioxide, followed by heating the resulting solution under reflux with benzaldehyde, the hydrazone (623) was isolated. This product (623) gave the correct elemental analysis and showed the expected i.r., \(^1\)H n.m.r. and mass spectra and, consistent with its assigned structure was soluble in aqueous sodium hydroxide. This result excludes the diaminoo compound (629), which would have reacted to afford a bis-benzylidene derivative (624). Further work up of the reaction mother liquor afforded a solid whose i.r., \(^1\)H n.m.r. and mass spectra are in agreement with its being the deaminated triazole (620e). The presence of the triazole (620e) is readily explained by reference to the
literature, since it is known\textsuperscript{95} that reductive deamination of diazonium salts occurs in ethanol. In addition, reductive deamination of triazole-diazonium salts in ethanol has been observed elsewhere in this thesis (cf. Chapter 3.1 and 3.2).

Further consideration of Scheme 125 illustrates the potential reversible Dimroth rearrangement of the triazolo[5,1-c]triazine (622a) to the triazolo[1,5-b]triazine (630). However, the latter structure is excluded on the basis of the reaction of the triazolo[5,1-c]triazine derivative (622c), with phenylhydrazine (see Chapter 3.2.2). The formation of the corresponding azo compound, which for structural reasons cannot be formed from the corresponding [1,5-b] structure, favours the presence of the [5,1-c] structure (622a). Furthermore synthesis of the triazolotriazine (622a) by an unambiguous route (cf. Chapter 3.2.4) strongly suggests that the product from condensation of phenylglyoxal with the hydrazine (625) exists as the [5,1-c] isomer.

When the betaine (621) was treated with an aqueous ethanolic solution of sulphur dioxide followed by benzil, the triazolotriazine (622d) was obtained. This product gave analytical and spectral data consistent with its assigned structure. Further work up of the reaction mother liquor afforded the triazole (620c), formed by deamination of the betaine (621) (see before).

When the diazonium nitrate (620b) [prepared in situ from the amine (620a)] was treated with sulphur dioxide, followed by benzil, an amorphous solid (which could not be characterised) was obtained, accompanied by unreacted benzil and a small quantity of the deaminated triazole (620e) obtained before.
When the betaine (621) was treated with aqueous ethanolic sulphur dioxide and the resulting solution heated under reflux with methylglyoxal, the triazolotriazine (622e) was obtained, as indicated by its i.r., $^1$H n.m.r. and mass spectra and its combustion analysis. As with the triazolotriazine (622a) before, the isomer (622f) is excluded because initial condensation of methylglyoxal with the corresponding hydrazine intermediate should occur via the most reactive aldehydic carbonyl group.

When the diazonium betaine (621) was treated with aqueous ethanolic sulphur dioxide followed by biacetyl, the corresponding triazolotriazine (622g) was obtained. The properties of this product were again consistent with the assigned structure.

When the betaine (621) was treated with aqueous ethanolic sulphur dioxide, followed by glyoxal, a gum was obtained. This is assigned the triazolotriazine structure (622h) on the basis of its i.r. and $^1$H n.m.r. spectra. In particular its $^1$H n.m.r. spectrum contained two single proton doublets at $\delta$ 9.09 and 9.00 p.p.m., assigned to H(7) and H(6) respectively. The assignment of the H(7) and H(6) protons is based on the enhanced deshielding exerted by a bridgehead nitrogen atom on a proton attached to an adjacent carbon atom. Thus, in the $^1$H n.m.r. spectrum of (622h), it is observed that H(7) absorbs at a lower field than H(6). However, attempts to obtain supporting analytical figures for the triazolotriazine (622h), were unsuccessful, due to difficulties encountered in its purification.
The successful synthesis of the triazolotriazines (622 a,d,e,g and h) prompted an investigation into the analogous reactions of 4-cyano-1H-1,2,3-triazole-5-diazonium nitrate (620d). However, treatment of the diazonium nitrate (620d) [prepared in situ from the corresponding amine (620c)] with sulphur dioxide and subsequent reaction with benzil, using conditions successful for the conversion of the betaine (621) into the triazolotriazines (622 a,d,e,g and f), resulted only in the recovery of unchanged benzil. Similarly, a multi-component gum was obtained when the diazonium nitrate (620d) was treated with sulphur dioxide followed by attempted condensation with phenylglyoxal. Column chromatography of the gum in an attempt to isolate any identifiable material was unsuccessful.

3.3.3 The Reactivity of the 3-Benzenesulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) to Nucleophilic Attack

The successful nucleophilic displacement of the C(6) benzenesulphonyl group of 6-benzenesulphonyl-7-methyl-3-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (631) (see Chapter 3.2), prompted an analogous investigation into the potential displacement of the benzenesulphonyl group at C(3) in the triazolotriazine (622a). The particular triazolotriazine (622a) was chosen for study in preference to other 3-benzenesulphonyltriazolo[5,1-c]-1,2,4-triazines, prepared earlier in Chapter 3.2 by various coupling reactions, because it lacks substituents sensitive to competing nucleophilic attack.
R
a) H
b) Ac
c) Me

(633)

(620a)
Thus, 3-benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) was heated under reflux with ethanolic sodium ethoxide. The acidic product obtained from this reaction gave elemental and mass spectral data consistent with its being 4-benzenesulphonyl-5-(2-ethoxybenzylideneamino)-1H-1,2,3-triazole (632a). In addition, it showed i.r. absorption at 3130 cm\(^{-1}\), consistent with the presence of an NH-group, and a two proton quartet at \(\delta 4.45\) p.p.m. and a three proton triplet at \(\delta 1.42\) p.p.m. in its \(^1\)H n.m.r. spectrum assignable to an ethyl group. Furthermore, the presence of a ten proton multiplet at \(\delta 7.78-7.20\) p.p.m. in the \(^1\)H n.m.r. spectrum of (632a), indicates the presence of two phenyl groups, and suggests that the 3-benzenesulphonyl group is retained in the product. Any doubt as to the exact structure of (632a) is removed by consideration of its reactions with acetic anhydride and methyl iodide. As mentioned earlier in this thesis (cf. Chapter 3.2), the 1H-1,2,3-triazole nucleus is susceptible to acetylation, resulting in the formation of the corresponding N-acetyl derivative, which exhibits characteristic absorption in its i.r. and \(^1\)H n.m.r.spectra. Correspondingly, acetylation of the triazole (632a) was accomplished smoothly in warm acetic anhydride, affording 1-acetyl-4-benzenesulphonyl-5-(2-ethoxybenzylideneamino)-1,2,3-triazole (632b) in good yield. The N-acetyl derivative (632 b) had the correct elemental analysis and mass spectrum and showed a characteristic signal at \(\delta 2.60\) p.p.m. in its \(^1\)H n.m.r. spectrum and a band at 1770 cm\(^{-1}\) in its i.r. spectrum consistent with the presence of a 1,2,3-triazole ring N-acetyl group. When the N-acetyl derivative (632 b) was heated under reflux briefly with aqueous sodium hydroxide, the free triazole
Scheme 126
(632a) was quickly regenerated. Methylation of the triazole (632a) with methyl iodide readily afforded the corresponding N-methyltriazole (632c), as indicated by its elemental analysis and \(^1\)H n.m.r., i.r. and mass spectra. Additional evidence for the triazole structure (632a) is provided by its acid hydrolysis. Thus, when the triazole (632a) was heated under reflux in glacial acetic acid the 5-benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633) was obtained, as indicated by its i.r. and mass spectra and combustion analysis. Hydrolysis of the triazole (632a) in aqueous hydrochloric acid also afforded the benzamidotriazole (633), which under these conditions was accompanied by 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (620a), prepared elsewhere in this work (see Chapter 2). As a proof of structure of (633), its reaction with aqueous sodium hydroxide was investigated. When the benzamidotriazole (633) was heated under reflux with aqueous sodium hydroxide, the 5-amino-1,2,3-triazole (620a), prepared earlier, was obtained.

The question now arises as to the mechanism involved in the formation of the triazole (632a). Consideration of Scheme 126 indicates two plausible routes. Firstly attack by ethoxide ion at C(7) in the triazolotriazine (622a) would afford the intermediate (634). Dimroth rearrangement of this adduct (634) to (635) then follows, and subsequent elimination of hydrogen cyanide gives, on acidification, the observed product [Scheme 126; (634)\(\rightleftharpoons\) (635)\(\rightarrow\) (636)\(\rightarrow\) (632a)]. Alternatively, Dimroth rearrangement of (622a) to its [1,5-b]isomer (630) may occur, prior to attack by ethoxide ion, [Scheme 126; (622a)\(\rightleftharpoons\) (630)\(\rightarrow\) (635)]. Subsequent elimination of hydrogen cyanide then follows as before, to
Scheme 127
Scheme 128
afford (636), which on acidification yields the triazole (632a). Evidence for the mechanism outlined in Scheme 126 is provided by the reaction of the triazolotriazine (622d) with ethanolic sodium ethoxide. When the triazolotriazine (622d) was heated under reflux with ethanolic sodium ethoxide, a solid was isolated whose elemental analysis and mass spectrum are consistent with its being either the adduct (637) or its Dimroth isomer (638). However, lack of time and material prevented further confirmation of structure by $^1\text{H} \text{n.m.r.}$ spectral data, and chemical transformation.

In view of the interesting result obtained in the reaction of the triazolotriazine (622a) with sodium ethoxide, further investigations of the reactions of (622a) with other nucleophilic agents were undertaken. Thus, when the triazolotriazine (622a) was heated under reflux with aqueous sodium hydroxide, the 5-benzamido-4-benzenesulphonyl 1H-1,2,3-triazole (633) obtained before, was isolated.

The formation of this product is readily explained by consideration of the mechanism outlined earlier in Scheme 126. As before, attack of hydroxide ion on (622a) can occur either before or after the attendant Dimroth rearrangement of (622a), so affording the product [Scheme 128; (622a)$\rightarrow$(639) $\rightarrow$(633)].

When the triazolotriazine (622a) was heated under reflux with triethylamine, only unchanged starting material was recovered from the reaction mother liquor. Similarly, unchanged starting material was obtained when the triazolotriazine (622a) was heated under reflux with hydrazine or sodium azide.
It has been shown, by many workers\textsuperscript{156,157,233-238}, that fused 1,2,3-triazole ring systems are susceptible to scission of the triazole ring in acidic media. However, a noteworthy feature of such acid-catalysed scission is the unwillingness of fused triazoles to undergo cleavage with subsequent loss of nitrogen when the substituent at C(3) in the triazole ring is electron withdrawing.\textsuperscript{156,157,233,234} Consistent with these reports, the triazolotriazine (622a) was recovered unchanged, when heated under reflux with glacial acetic acid or aqueous sulphuric acid.
3.3.4 Experimental

(For general experimental procedures, see Appendix).

The Preparation of the 5-Amino-1H-1,2,3-triazoles (620a) and (620c)

5-Amino-4-benzenesulphonyl-1H-1,2,3-triazole (620a) and 5-amino-4-cyano-1H-1,2,3-triazole (620c) were prepared as described previously in Chapter 2 (cf. pages 68 and 66 respectively).

The Preparation of 4-Benzenesulphonyl-1H-1,2,3-triazole-5-diazonium Betaine (621)

4-Benzenesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (621) was prepared as described previously in Chapter 2 (cf. page 121).

3-Benzenesulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazines (622a,d,e,g and h)

4-Benzenesulphonyl-1,2,3-triazole-5-diazonium betaine (621) (0.47 g, 0.002 mol) was added in portions at 0°C (ice-salt bath) to 80% v/v aqueous ethanol (20.0 ml) which had been saturated with sulphur dioxide. The mixture was then re-saturated with sulphur dioxide and left stoppered at room temperature overnight. A solution of each of the α-dicarbonyl compounds (see below) (0.002 mol) in 80% v/v aqueous ethanol (10.0 ml) was then added and the mixture was heated under reflux for 2h. In each case the reaction mixture was cooled and any product deposited was collected. The filtrate was worked up as described for the individual reactions.

(i) Benzil afforded 3-benzenesulphonyl-6,7-diphenyl-1,2,3-
triazolo[5,1-c]-1,2,4-triazine (622d) (27%) as colourless plates m.p. 170-171°C (from ethanol).

Found: C, 63.8; H, 3.7; N, 16.7%; M+, 413.
C_{22}H_{15}N_{5}O_{2}S requires: C, 63.9; H, 3.6; N, 16.9%; M, 413.

Concentration of the mother liquor, extraction with methylene chloride and trituration of the gum with ethyl acetate afforded 4-benzenesulphonyl-1H-1,2,3-triazole (620e) (14%) as buff plates m.p. 164-166°C (from ethanol-water), ν_{max} 3340 br (NH) cm^{-1}, δ[(CD_{3})_{2}SO] 8.59 (1H, s, H-5), 8.00-7.88 (2H, m, ArH), and 7.74-7.56 (3H, m, ArH).

Found: M+, 209.026954 (error < 6 p.p.m.)
C_{8}H_{7}N_{3}O_{2}S requires: M, 209.025895.

Evaporation of ethyl acetate mother liquor afforded benzil (71%) m.p. 92-94°C which was identical (m.p. and i.r. spectrum) to an authentic sample.

(ii) Biacetyl gave 3-benzenesulphonyl-6,7-dimethyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622g) (48%) as cream plates m.p. 145-147°C (from ethanol-light petroleum), δ[(CD_{3})_{2}SO] 8.12-7.92 (2H, m, ArH), 7.74-7.52 (3H, m, ArH), 2.72 (3H, s, CH_{3}), and 2.63 (3H, s, CH_{3}).

Found: C, 49.8; H, 3.7; N, 24.0%; M+, 289.
C_{12}H_{11}N_{5}O_{2}S requires: C, 49.8; H, 3.8; N, 24.2%; M, 289.

(iii) Phenylglyoxal afforded 3-benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) (15%) as pale green plates m.p. 214-215°C (from glacial acetic acid), δ[(CD_{3})_{2}SO] 9.64 (1H, s, H-6) 8.46-8.26 (2H, m, ArH), 8.18-7.98 (2H, m, ArH), and 7.76-7.50 (6H, m, ArH).

Found: C, 56.7; H, 3.3; N, 21.0%; M+, 337.
C_{16}H_{11}N_{5}O_{2}S requires: C, 57.0; H, 3.3; N, 20.8%; M, 337.
Concentration of the mother liquor and extraction with methylene chloride afforded a yellow gum (0.49 g) which was shown by t.l.c. in methylene chloride over silica to be an unresolvable multicomponent mixture.

(iv) Methylglyoxal-dimethylacetal afforded 3-benzenesulphonyl-7-methyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622e) (29%) as buff needles m.p. 216-217° (from glacial acetic acid), δ[(CD₃)₂SO] 9.02 (1H, s, H-6), 8.10-7.96 (2H, m, ArH), 7.76-7.58 (3H, m, ArH), and 2.69 (3H, s, CH₃).

Found: C,48.4; H,3.3; N,25.5%; M⁺,275.

\( \text{C}_{11} \text{H}_{9} \text{N}_{5} \text{O}_{2} \text{S} \) requires: C,48.0; H,3.3; N,25.5%; M,275.

(v) Glyoxal afforded a solution which was concentrated and extracted with methylene chloride to give a gum whose i.r. and \(^1\text{H}\) n.m.r. spectra are consistent with its being 3-benzene-sulphonyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622h) (49%), δ[(CD₃)₂SO] 9.09 (1H, d, J 2Hz, H-7), 9.00 (1H, d, J 2Hz, H-6), 8.14-7.90 (2H, m, ArH), and 7.88-7.52 (3H, m, ArH).

Attempted purification of the gum by distillation resulted in its decomposition to complex mixtures.

The Attempted Reductive Condensation of 4-Benzenesulphonyl-1H-1,2,3-triazole-5-diazonium Nitrate (620b) with Benzil

A suspension of 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (620a) (0.45 g, 0.002 mol) in concentrated aqueous nitric acid (d 1.42, 1.0 ml) and 80% v/v aqueous ethanol (5.0 ml) was treated dropwise with stirring at 0° (ice-salt bath) with a solution of sodium nitrite (0.5 g) in 80% v/v aqueous ethanol (3.0 ml). Stirring was continued at 0° for 15 min. and the solution was then saturated with sulphur dioxide and left stoppered at room temperature overnight.
The mixture was then treated with a solution of benzil (0.42 g, 0.002 mol) in 80% v/v aqueous ethanol (10.0 ml) and heated under reflux for 2h. The mixture was cooled and the precipitated solid was collected and combined with a second crop obtained by concentrating the aqueous-ethanol mother liquor (total 0.71 g). Extraction of the solid with boiling light petroleum left an insoluble amorphous solid (0.36 g) m.p. 230-260° (decomp.) which showed an ill-defined i.r. spectrum and left a residue on burning.

Evaporation of the light petroleum mother liquor afforded benzil (0.29 g) m.p. 90-94° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride and treatment of the resulting residue with water gave 4-benzenesulphonyl-1H-1,2,3-triazole (620e) (0.10 g) (24%) m.p. 162-166° identical (m.p. and i.r. spectrum) to an authentic sample.

Benzaldehyde-(4-benzenesulphonyl-1H-1,2,3-triazol-5-yl) hydrazone (623)

4-Benzenesulphonyl-1H-1,2,3-triazole-5-diazonium betaine (621) (0.47 g, 0.002 mol) was added in portions at 0° (ice-salt bath) to 80% v/v aqueous ethanol (20.0 ml) which had been saturated with sulphur dioxide. The mixture was then re-saturated with sulphur dioxide and left stoppered at room temperature overnight. A solution of freshly distilled benzaldehyde (0.21 g, 0.002 mol) in 80% v/v aqueous ethanol (10.0 ml) was added and the solution was heated under reflux for 2h. The mixture was cooled and the solid was collected to afford benzaldehyde-(4-benzenesulphonyl-1H-1,2,3-triazol-
The Attempted Reductive Condensation of 4-Cyano-1H-1,2,3-
triazole-5-diazonium Nitrate (620d) with α-Dicarbonyl Compounds

A suspension of 5-amino-4-cyano-1H-1,2,3-triazole (620c)
(0.44 g, 0.004 mol) in concentrated aqueous nitric acid
(d 1.42, 2.0 ml) and 80% v/v aqueous ethanol (5.0 ml) was
treated dropwise at 0° (ice-salt bath) with stirring with
a solution of sodium nitrite (0.5 g) in 80% v/v aqueous ethanol (5.0 ml). Stirring was continued at 0° for 15 min. and the resulting solution was then saturated with sulphur dioxide and left at room temperature overnight. A solution of the α-dicarbonyl compound (see below) (0.004 mol) in 80% v/v aqueous ethanol (15.0 ml) was then added and the mixture was heated under reflux for 2h. In each case the solution was cooled and any solid deposited was collected. The filtrate was worked up as described for the individual reactions. (i) Benzil gave a solid which was combined with a second crop obtained by concentrating the ethanol-water mother liquor to afford unreacted benzil (98%) m.p. 90-94° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride afforded only a negligible quantity of gum. Neutralisation of the aqueous mother liquor with solid sodium acetate and extraction with methylene chloride gave no material. Evaporation of the neutral aqueous mother liquor and extraction of the residue with boiling ethyl acetate gave only a small quantity of an unidentified yellow gum (0.02 g).

(ii) Phenylglyoxal gave a solution which when concentrated and extracted with methylene chloride afforded a yellow gum (0.94 g). This was shown by t.l.c. in ethyl acetate over silica to be a multicomponent mixture. Attempted wet column chromatography of the gum over silica was unsuccessful.
4-Benzencesulphonyl-5-(2-ethoxybenzylideneamino)-1H-1,2,3-triazole (632a)

(a) 3-Benzencesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) (1.35 g, 0.004 mol) was heated under reflux with a solution of sodium (0.276 g) in absolute ethanol (50.0 ml) for 0.5 h. The resulting solution was cooled and evaporated, and the residue was treated with water, filtered to remove some dark tarry solid, and washed with methylene chloride. Evaporation of the methylene chloride extract gave no material.

Acidification of the aqueous mother liquor with concentrated aqueous hydrochloric acid afforded 4-benzenesulphonyl-5-(2-ethoxybenzylideneamino)-1H-1,2,3-triazole (632a) (1.21 g) (85%) m.p. 188-189° as colourless plates (from methanol), \( \nu_{\text{max}} \) 3130 (NH) cm\(^{-1}\), \( \delta [(\text{CD}_3)_2\text{SO}] \) 7.78-7.20 (10H, m, ArH), 4.45 (2H, q, J 8Hz, CH\(_2\)) and 1.42 (3H, t, J 8Hz, CH\(_3\)).

Found: C, 57.4; H, 4.5; N, 15.7%; M\(^+\), 356.

C\(_{17}\)H\(_{16}\)N\(_4\)O\(_3\)S requires: C, 57.3; H, 4.5; N, 15.7%; M, 356.

Extraction of the aqueous mother liquor with methylene chloride gave only a negligible quantity of yellow gum.

(b) 1-Acetyl-4-benzenesulphonyl-5-(2-ethoxybenzylideneamino)-1,2,3-triazole (632b) (0.23 g, 0.0006 mol) was heated under reflux in aqueous 2M sodium hydroxide (5.0 ml) for 5 min. The dark solution was cooled, washed with methylene chloride and acidified with aqueous 2M hydrochloric acid to afford 4-benzenesulphonyl-5-(2-ethoxybenzylideneamino)-1H-1,2,3-triazole (632a) (0.17 g) (80%) m.p. 186-188° identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.
1-Acetyl-4-benzenesulphonyl-5-(2-ethoxybenzylidene amino)-1,2,3-triazole (632b)

4-Benzenesulphonyl-5-(2-ethoxybenzylidene amino)-1H-1,2,3-triazole (632a) (0.21 g, 0.0006 mol) was heated at 100° with acetic anhydride (0.4 ml) until the solid just dissolved (1-2 min.). The solution was cooled and left at room temperature for 20 min. then evaporated and the residue triturated with ether to afford 1-acetyl-4-benzenesulphonyl-5-(2-ethoxybenzylidene amino)-1,2,3-triazole (632b) (0.23 g) (96%) m.p. 144-145° as colourless plates (from toluene-light petroleum), ν max. 1770 (C=O) and 1640 br (NH def.) cm⁻¹, δ[(CD₃)₂SO] 7.92-7.22 (10H, m, ArH), 4.42 (2H, q, J 8Hz, CH₂), 2.60 (3H, s, CR₃) and 1.41 (3H, t, J 8Hz, CH₃).

Found: C, 57.5; H, 4.5; N, 14.1%; M⁺, 398.
C₁₉H₁₈N₄O₄S requires: C, 57.3; H, 4.5; N, 14.1%; M, 398.

4-Benzenesulphonyl-5-(2-ethoxybenzylidene amino)-1-methyl-1,2,3-triazole (632c)

The ethoxybenzylideneaminotriazole (632a) (0.42 g, 0.0012 mol), anhydrous potassium carbonate (2.17 g), and methyl iodide (1.75 ml) were heated under reflux in Analar acetone (67.0 ml) for 3h. The mixture was hot filtered to remove inorganic material and evaporated, and the residue was treated with water to afford 4-benzenesulphonyl-5-(2-ethoxybenzylidene amino)-1-methyl-1,2,3-triazole (632c) (0.41 g) (92%) as colourless needles m.p. 173-174° (from ethanol), δ[(CD₃)₂SO] 7.92-7.14 (10H, m, ArH), 4.50 (2H, q, J 7Hz, CH₂), 3.96 (3H, s, CH₃) and 1.46 (3H, t, J 7Hz, CH₃).
5-Benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633)

(a) The ethoxybenzylideneaminotriazole (632a) (0.42 g, 0.0012 mol) was heated under reflux in glacial acetic acid (15.0 ml) for 3h. The solution was cooled and evaporated and the semi-solid obtained was triturated with ether to afford 5-benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633) (0.26 g) (66%) as colourless plates m.p. 240-241 °C (from ethanol-glacial acetic acid), \( \nu_{\text{max}} \) 3380 and 3220 br (NH) and 1680 (C=O) cm\(^{-1}\).

Found: C, 54.9; H, 3.7; N, 16.9%; M\(^+\), 328.

\[ \text{C}_{15}\text{H}_{12}\text{N}_{4}\text{O}_{3}\text{S} \text{ requires: C}, 54.9; \text{H}, 3.7; \text{N}, 17.1%; \text{M}, 328. \]

Evaporation of the ether mother liquor gave only a negligible quantity of yellow gum.

(b) The ethoxybenzylideneaminotriazole (632a) (0.28 g, 0.0008 mol) was heated under reflux with aqueous 2M hydrochloric acid (2.5 ml) in ethanol (5.0 ml) for 1h. The solution was cooled to afford the insoluble 5-benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633) (0.05 g) (19%) m.p. 236-239 °C identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

Concentration of the aqueous ethanol mother liquor afforded 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (620a) (0.13 g) (73%) m.p. 199-201 °C identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride gave no more material.
(c) 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) (0.34 g, 0.001 mol) was heated under reflux with aqueous 2M sodium hydroxide (5.0 ml) in 1,2-dimethoxyethane (5.0 ml) for 0.5h. The solution was cooled and evaporated and the residue obtained was treated with water and extracted with methylene chloride to afford a yellow gum (0.03 g), shown by t.l.c. in methylene chloride over silica to consist of four unresolvable components.

Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid afforded 5-benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633) (0.05 g) (15%) m.p. 237-240° identical (m.p. and i.r. spectrum) to a sample obtained in (a) before.

The Reaction of 5-Benzamido-4-benzenesulphonyl-1H-1,2,3-triazole (633) with Sodium Hydroxide

The triazole derivative (633) (0.33 g, 0.001 mol) was heated under reflux in aqueous 2M sodium hydroxide for 0.5h. The solution was cooled and acidified with concentrated aqueous hydrochloric acid and the solid precipitated was collected to afford 5-amino-4-benzenesulphonyl-1H-1,2,3-triazole (620a) (0.19g) (85%) m.p. 189-196° identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the aqueous mother liquor with methylene chloride afforded only a negligible quantity of gum.
The Attempted Reaction of 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) with Triethylamine

The triazolotriazine (622a) (0.20 g, 0.0006 mol) was heated under reflux with triethylamine (0.3 ml) in ethanol (10.0 ml) for 0.5 h. The solution was cooled to give the starting triazolotriazine (622a) (0.14 g) m.p. 209-213\degree identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ethanol mother liquor afforded only a small quantity of yellow gum (0.03 g).

The Attempted Reaction of 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) with Hydrazine

The triazolotriazine (622a) (0.34 g, 0.001 mol) was heated under reflux with 100% hydrazine hydrate (0.20 g, 0.004 mol) in 1,4-dioxan (20.0 ml) for 0.5 h. The solution was cooled and evaporated and the gummy semi-solid was treated with ether to afford the starting triazolotriazine (622a) (0.25 g) m.p. 210-214\degree identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the ether mother liquor afforded only a negligible quantity of gum.

The Attempted Reaction of 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) with Sodium Azide

3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) (0.44 g, 0.0013 mol) was heated under reflux with sodium azide (0.17 g, 0.0026 mol) in ethanol (8.0 ml) and water (2.0 ml) for 1 h. The mixture was cooled to afford the starting triazolotriazine (622a) (0.36 g) m.p. 209-213\degree which was identical (m.p. and i.r. spectrum) to an authentic sample.
Concentration of the aqueous ethanol mother and extraction with methylene chloride gave no further material.

The Attempted Reaction of 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) with Glacial Acetic Acid

The triazolotriazine (622a) (0.34 g, 0.001 mol) was heated under reflux in glacial acetic acid (10.0 ml) for 3h. The solution was cooled to afford the starting triazolotriazine (622a) (0.15 g) m.p. 212-214° identical (m.p. and i.r. spectrum) to an authentic sample.

Evaporation of the acetic acid mother liquor afforded a dark brown gum (0.11 g) which was shown by t.l.c. in ethyl acetate over silica to be an unresolvable multicomponent mixture.

The Attempted Reaction of 3-Benzenesulphonyl-7-phenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622a) with Sulphuric Acid

The triazolotriazine (622a) (0.34 g, 0.001 mol) was heated under reflux with 20% w/v aqueous sulphuric acid (5.0 ml) in glacial acetic acid (10.0 ml) for 1h. Hot filtration of the mixture afforded unreacted triazolotriazine (622a) which was combined with a second crop deposited on cooling the mother liquor (total 0.30 g) m.p. 211-213° and was identical (m.p. and i.r. spectrum) to an authentic sample.

Extraction of the mother liquor with methylene chloride afforded only a negligible quantity of yellow oil.
The Reaction of 3-Benzenesulphonyl-6,7-diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622d) with Ethanolic Sodium Ethoxide

3-Benzene sulphonyl-6,7-diphenyl-1,2,3-triazolo[5,1-c]-1,2,4-triazine (622d) (0.20 g, 0.0005 mol) was heated under reflux for 0.5h with a solution of sodium (0.04g) in absolute ethanol (12.5 ml). The resulting dark solution was evaporated and the residue obtained was treated with water to afford either 3-benzenesulphonyl-6,7-diphenyl-7-ethoxy-4-hydro-1,2,3-triazolo[5,1-c]-1,2,4-triazine (637) or 3-benzenesulphonyl-5,6-diphenyl-5-ethoxy-4-hydro-1,2,3-triazolo[1,5-b]-1,2,4-triazine (638) (0.08 g) (35%) as colourless plates m.p. 154-156°C (from glacial acetic acid-water).

**Found:** C, 62.3; H, 4.4; N, 15.5%; M⁺, 459.

C₂₄H₂₁N₅O₃S requires: C, 62.7; H, 4.6; N, 15.3%; M, 459.

Extraction of the aqueous mother liquor with methylene chloride gave no material. Acidification of the aqueous mother liquor with aqueous 2M hydrochloric acid and extraction with methylene chloride before or after neutralisation with solid sodium acetate gave no further material.
APPENDIX
General Experimental Procedures

Crude solids obtained from reaction mixtures by filtration were dried in vacuo at room temperature unless otherwise stated.

Infra-red spectra were measured for nujol suspensions or thin films using a Perkin-Elmer 157G spectrophotometer. Bands were either strong or very strong, unless otherwise specified (w) weak or (br) broad, or (sh) shoulder.

Nuclear magnetic resonance (\(^1\)H n.m.r.) spectra were measured at 100 MHz using a Varian HA 100 instrument. Signals are specified as: (s) singlet, (d) doublet, (q) quartet, (t) triplet, (m) multiplet, (dq) double quartet, (dt) double triplet.

Mass spectra were measured at 800 Kv on an A.E.I. MS 902 instrument.

Microanalyses were carried out by Mr. J. Grunbaum, Department of Chemistry, Edinburgh University. Melting point (m.p.) (uncorrected) of all analytical samples were determined on a Kofler block.

Thin layer chromatography (t.l.c.) was carried out in the specified solvent over silica, which was Kieselgel G.F. nach Stahl (Typ 60), or over alumina, which was Aluminium oxid G.F. 254 (Typ 60/E). Column chromatography was carried out over 5% deactivated alumina or Fisons Silica Gel (100-200 mesh).
Solvents were of technical grade, unless otherwise specified, and light petroleum had b.p. 60-80°C.

Chloroform and methylene chloride extracts were dried over anhydrous magnesium sulphate, and evaporated under reduced pressure.
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