Some Aspects of Azido-Tetrazolo Isomerization

M. TISLER

Department of Chemistry, University of Ljubljana, 61001 Ljubljana, Yugoslavia

A survey of azido-tetrazolo isomerizations of tetrazoloazines is presented. Included are:
- general aspects of azido-tetrazolo isomerizations and particular heterocyclic systems involved in these processes;
- transformations involving the tetrazole or azide part or the non-tetrazolic part of the molecules,
- transformations based on decomposition of tetrazoloazines.

Azido-tetrazolo isomerizations are dealt with only sparingly in existing review articles on azides and tetrazoles\(^1\textsuperscript{--}^4\). During the last decade, the chemistry of compounds capable of such isomerizations has developed significantly. Thus, it was felt that a survey on azido-tetrazolo isomerizations would be desirable.

Among the most common methods of generating an azido group attached to a heterocyclic ring are the nitrosation of a hydrazino group and the nucleophilic displacement of a halogen atom (usually chlorine) by means of sodium azide or hydrogen azide. If the generated azido group is attached to the C-atom adjacent to an annular nitrogen (1) it may spontaneously cyclize to give a fused tetrazolo ring (2) or, at least, an equilibrium mixture of both forms.

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{C-X} & \quad \text{C-N}_3 \\
& \quad \text{C-N} \quad \text{N}_2 \\
X & = \text{-NH-NO}_2, \text{ Hal}
\end{align*}
\]

Although the possibility of generating both forms has been discovered early, the use of highly sensitive spectrometric methods has only recently made possible a detailed and reliable investigation of such isomerizations.

1. General Aspects of Azido-Tetrazolo Isomerizations

The transformation of a heterocyclic azide into the tetrazolo isomer has been defined or interpreted as a case of tautomerism, as an azidoazomethine-tetrazolo (imideamide-tetrazole) equilibrium, as a 1,5-dipolar cyclization\(^5\textsuperscript{--}^6\), and as a valence isomerization. Although the last three definitions are in agreement with the description of the process, these interconversions are in our opinion best interpreted as azido-tetrazolo isomerizations and this term is used throughout this review\(^7\).

In their ground state, azido compounds possess a linear arrangement of the three N-atoms (3a), but according to MO calculations, the energy difference between the linear and the bent arrangement (3b) of the N-atoms in the azido group is not large. For the first excited state, MO calculations predict the bent form to be the more stable.

Interconversions are possible with systems of the general types 4 and 5, where Y is a C-unit or a substituted or unsubstituted hetero atom which may or may not, together with R, be part of a cyclic system.

\[ R-C^Y_N-N \quad R-N-N-Y \]

From the chemistry of the open-chain analogs of 4 it is evident that, in the first approximation, the nature of the atom or group Y is responsible for the existence of the particular form. Thus, the character of Y \([Y = O, S, N-R, C(R')_2, etc.]\), possibly in combination with effects of functional groups R, exerts a stabilizing or destabilizing effect on the azido or tetrazole form. For example, acyl azides \((Y = O)\) are known to exist only in the azide form in contrast to the sulfur analogs which exist as 1,2,3,4-thiatriazoles. There are several more examples of definitely open-chain azido compounds and monocyclic tetrazoles.

In azolazines, the azine part of the molecule is responsible for the magnitude of the charge on the N-atom common to both rings. If the negative charge can be further delocalized on other N-atoms in the m-position of the azine ring, this enhances the stability of the azido form. An extreme case is that of the azido-1,3,5-triazines which exist entirely in the azido form. In this connection it should be pointed out that an aromatic azido group is a strongly electron-donating group; its electronegativity lies between those of the methoxy and methyl groups.

The conversion of the tetrazole form into an azido form is an endothermic process (see Table 2). Similar observations are reported with some monocyclic tetrazoles which are by 10–12 kcal/mol more stable than the isomeric azido compounds.

Several attempts to prepare ring systems with two tetrazole rings fused to a single N-heteroaromatic ring have been reported, but so far there is no reliable proof for the azinobistetrazole structure of these compounds. However, there is evidence from mass spectra that the molecular ions of some of these compounds have the ditetrazole structure. The first step of the fragmentation, common to tetrazolazines, is the loss of \(N_2\), but with 6-azidotetrazolo[1,5-b]pyridazines and related 6-azidopyridotetrazolo[1,5-b]pyridazines, the prevalent fragmentation is the loss of six N-atoms, thus implying the intermediary of a bis-tetrazolo structure.

2. Azido-Tetrazolo Isomerizations of Particular Azolazines

Several heterocyclic systems having an azido group adjacent to the annular N-atom have been investigated with regard to cyclization to condensed tetrazoles in order to establish their structures and equilibria. Systems for which structural analyses have not been carried out are not dealt with in this review. It should be mentioned that chemical methods used to assign a particular structure are not always reliable.

In the most cases, azido-tetrazole equilibria were observed in solutions; in some cases, however, this phenomenon has also been observed in the melt. As already mentioned, azido-tetrazolo isomerizations are controlled by the electron-donating capacity of the heterocycle to which the tetrazole ring is fused. The smaller this capacity, the weaker is the \(N-N\) bond and the less stable is the tetrazole form. This electron-donor property can be reduced by introduction of electron-withdrawing groups into the azine part of the molecule or by protonating the heterocycle. Other factors which influence the isomerization are the polarity of the solvent (in polar solvents, the equilibrium is shifted towards the side of tetrazole and in less polar solvents, towards the side of the azido form) and temperature (with raising temperature, the azido form is formed at the expense of the tetrazole form). On the other hand, it is possible to stabilize the azido form and thus completely convert a fused tetrazole ring into an azido group by forming another condensed ring (see Section 3.2.). Heats of isomerizations for some systems are presented in Table 2.

---

5 The term ‘valence isomerization’, and in particular ‘valence tautomerism’, is in general used to characterize fast, usually concerted rearrangements accompanied by reorganizations of electrons.
### Table 1. Equilibrium Constants, $K_T$ (ratio azido/tetrazolo form)

<table>
<thead>
<tr>
<th>Compounds in Equilibrium</th>
<th>$K_T$</th>
<th>Solvent</th>
<th>Concentration (%) (w/v)</th>
<th>Temperature</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Diagram" /></td>
<td>2.51</td>
<td>DMSO-d$_6$</td>
<td>7</td>
<td>25º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image2" alt="Diagram" /></td>
<td>4.32</td>
<td>DMSO-d$_6$</td>
<td>7</td>
<td>57º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image3" alt="Diagram" /></td>
<td>6.37</td>
<td>DMSO-d$_6$</td>
<td>7</td>
<td>80º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image4" alt="Diagram" /></td>
<td>0.83</td>
<td>CDCl$_3$</td>
<td>5</td>
<td>23º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image5" alt="Diagram" /></td>
<td>1.04</td>
<td>CDCl$_3$</td>
<td>5</td>
<td>40º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image6" alt="Diagram" /></td>
<td>1.15</td>
<td>CDCl$_3$</td>
<td>5</td>
<td>60º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image7" alt="Diagram" /></td>
<td>3.84</td>
<td>TFA*</td>
<td>5</td>
<td>23º</td>
<td>30</td>
</tr>
<tr>
<td><img src="image8" alt="Diagram" /></td>
<td>0.07</td>
<td>DMSO-d$_6$</td>
<td>32</td>
<td>37–38º</td>
<td>40</td>
</tr>
<tr>
<td><img src="image9" alt="Diagram" /></td>
<td>0.37</td>
<td>acetone-d$_6$</td>
<td>&lt;5</td>
<td>37–38º</td>
<td>40</td>
</tr>
<tr>
<td><img src="image10" alt="Diagram" /></td>
<td>0.14</td>
<td>pyridine-d$_3$</td>
<td>5</td>
<td>37–38º</td>
<td>40, 43</td>
</tr>
<tr>
<td><img src="image11" alt="Diagram" /></td>
<td>0.36</td>
<td>CDCl$_3$</td>
<td>7</td>
<td>37–38º</td>
<td>40, 43</td>
</tr>
<tr>
<td><img src="image12" alt="Diagram" /></td>
<td>0.08</td>
<td>acetone-d$_6$</td>
<td>5</td>
<td>37–38º</td>
<td>40, 43</td>
</tr>
<tr>
<td><img src="image13" alt="Diagram" /></td>
<td>0.12</td>
<td>CD$_3$OD</td>
<td>4</td>
<td>37–38º</td>
<td>40</td>
</tr>
<tr>
<td><img src="image14" alt="Diagram" /></td>
<td>~0</td>
<td>DMSO-d$_6$</td>
<td>20</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image15" alt="Diagram" /></td>
<td>∞</td>
<td>TFA</td>
<td>10</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image16" alt="Diagram" /></td>
<td>3.3</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image17" alt="Diagram" /></td>
<td>0.94</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image18" alt="Diagram" /></td>
<td>3.1</td>
<td>acetone-d$_6$</td>
<td>&lt;3</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image19" alt="Diagram" /></td>
<td>2.7</td>
<td>pyridine-d$_3$</td>
<td>6.7</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image20" alt="Diagram" /></td>
<td>1.6</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>38º</td>
<td>41</td>
</tr>
<tr>
<td><img src="image21" alt="Diagram" /></td>
<td>0.33</td>
<td>CD$_3$COOD</td>
<td>&lt;5</td>
<td>34º</td>
<td>60</td>
</tr>
<tr>
<td><img src="image22" alt="Diagram" /></td>
<td>0.37</td>
<td>DMSO-d$_6$–TFA*</td>
<td>(1:1, v/v)</td>
<td>34º</td>
<td>60, 62</td>
</tr>
<tr>
<td><img src="image23" alt="Diagram" /></td>
<td>0.20</td>
<td>DMSO-d$_6$–TFA*</td>
<td>(1:1, v/v)</td>
<td>34º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image24" alt="Diagram" /></td>
<td>4.9</td>
<td>TFA</td>
<td>10</td>
<td>34º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image25" alt="Diagram" /></td>
<td>0.41</td>
<td>DMSO-d$_6$–TFA*</td>
<td>(1:1, v/v)</td>
<td>34º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image26" alt="Diagram" /></td>
<td>0.44*</td>
<td>DMSO-d$_6$</td>
<td>5</td>
<td>34º</td>
<td>60, 62</td>
</tr>
<tr>
<td><img src="image27" alt="Diagram" /></td>
<td>3.5*</td>
<td>DMSO-d$_6$</td>
<td>5</td>
<td>34º</td>
<td>60, 62</td>
</tr>
<tr>
<td><img src="image28" alt="Diagram" /></td>
<td>2.0*</td>
<td>DMSO-d$_6$–TFA*</td>
<td>(2:1, v/v)</td>
<td>34º</td>
<td>60</td>
</tr>
<tr>
<td><img src="image29" alt="Diagram" /></td>
<td>2.7*</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>34º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image30" alt="Diagram" /></td>
<td>1.1*</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>34º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image31" alt="Diagram" /></td>
<td>4.6*</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>92º</td>
<td>62</td>
</tr>
<tr>
<td><img src="image32" alt="Diagram" /></td>
<td>2.9*</td>
<td>DMSO-d$_6$</td>
<td>10</td>
<td>92º</td>
<td>62</td>
</tr>
</tbody>
</table>

* Ratio B:A.  
* Ratio B:C.  
*TFA = trifluoroacetic acid.
Table 2. Heats of Isomerization of Tetrazoloazines

<table>
<thead>
<tr>
<th>Compounds</th>
<th>$\Delta H$ (kcal/mol)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="" /></td>
<td>3.4</td>
<td>30</td>
</tr>
<tr>
<td><img src="image2" alt="" /></td>
<td>4.2</td>
<td>30</td>
</tr>
<tr>
<td><img src="image3" alt="" /></td>
<td>5.1</td>
<td>24</td>
</tr>
<tr>
<td><img src="image4" alt="" /></td>
<td>6.8</td>
<td>40</td>
</tr>
<tr>
<td><img src="image5" alt="" /></td>
<td>4.7</td>
<td>60</td>
</tr>
<tr>
<td><img src="image6" alt="" /></td>
<td>2.7</td>
<td>60</td>
</tr>
<tr>
<td><img src="image7" alt="" /></td>
<td>-5.9</td>
<td>39</td>
</tr>
<tr>
<td><img src="image8" alt="" /></td>
<td>-1.3</td>
<td>69</td>
</tr>
<tr>
<td><img src="image9" alt="" /></td>
<td>-2.2</td>
<td>69</td>
</tr>
</tbody>
</table>

2.2. Tetrazolo[1,5-b]pyridazines (7)

Several derivatives of this system have been prepared. From their I.R. spectra it follows that no azido forms are present. In general, tetrazoloazines are transformed (partially or completely) into the isomeric azido compounds when dissolved in trifluoroacetic acid. As an exception, the tetrazolo[1,5-b]pyridazines (7) usually remain in the tetrazole form\(^\text{32}\), although in a few cases azido compounds may be formed\(^\text{33}\) to some extent.

Nitrosation of 6-hydrazino-3-nitropyridazine 1-oxide gives exclusively the corresponding azido compound; the isomeric tetrazole is not formed\(^\text{34}\). The fused tetrazole ring is similarly destabilized as in the case of 3-azidopyridazine 1-oxide\(^\text{35, 36}\).

Theoretically, the 6-azidotetrazolo[1,5-b]pyridazines can exist in the following forms (8–11).

![Diagrams](image10)

Pyridazinobistetrazoles (10) and bis-[azido]-pyridazines (9) have so far not been isolated or detected. All compounds investigated showed strong azide absorptions in the I.R. spectra; they exist as azidotetrazolopyridazines\(^\text{32, 35, 37, 38, 39}\).

2.3. Tetrazolo[1,5-a]pyrimidines

The parent compound (12) exists as the tetrazole in the solid state and as an equilibrium mixture of azido and tetrazole forms in most solutions; in chloroform solution, the azido form is exclusively present. A comparison of tetrazolo[1,5-a]pyrimidine (a "stabilized" form of 2-azidopyrimidine) with tetrazolo[1,5-c]pyrimidine (isomeric with 4-azidopyrimidine) reveals that in the first case the tetrazole form is somewhat more stable than in the second case\(^\text{40, 41}\).

A similar observation was made with the tetrazoles derived from 2- and 4-azidoquinazoline\(^\text{42}\).

---

18 R. Huisgen, Angew. Chem. 72, 359 (1960).
In the case of the tetrazolo[1,5-α]pyrimidines, electron-donating groups in positions 5 and 7 (methyl) stabilize the tetrazole form as a result of their inductive effect. On the other hand, an electron-withdrawing group in position 5 (chlorine) favors the isomeric azido form. Equilibrium constants for some compounds are given in Table 1 and heats of isomerization in Table 2.

In the case of compound 13, one azido and two tetrazole forms are possible.

Earlier reports on the structure of 13 were inconsistent. A recent detailed investigation revealed that in the solid state the anticipated tetrazole isomer 13a is present whereas in solution an equilibrium mixture of both tetrazole forms (13a and 13c) exists.

The formation of the second tetrazole isomer is precluded in 14. Here, the effect of the N-methyl group on the stabilization of the tetrazole form is quite strong; thus, in trifluoroacetic acid, in which most tetrazolazines are transformed into the isomeric azido compounds, the azido isomer is present to an extent of only 10⁻⁶.

The effect of substituents on the stabilization or destabilization of the tetrazole forms in tetrazolo[1,5-α]pyrimidines is opposite to that observed in the isomeric [1,5-α]-series. Thus, the azido form is stabilized by electron-donating groups in positions 5 and 7 of the tetrazolo[1,5-α]pyrimidine. The azido-2,6-dimethoxy pyrimidine shows no tendency to isomerize into the tetrazole form whereas their presence in position 8 should stabilize the tetrazole isomer (for equilibrium constants, see Table 1).

Contradictory observations have been reported in the latter case: some 8-amino- and N-substituted 8-amino derivatives have been found to exist in the tetrazole form in the solid state and in solution, whereas in the case of other derivatives having electron-donating groups in position 8 the azido and tetrazole forms were found in the solid state and only the azido isomer in solution. These findings might possibly be rationalized in terms of steric effects or of the ionization constants of the compounds in question.

---

26 In the literature, different nomenclature for particular azoloxazines is encountered. In this review, the nomenclature of the Ring Index has been used.
The 2,4-diazidopyrimidines (18b) are somewhat more complicated since two different cyclic isomers are possible. Although the diazido form has been postulated by several authors\textsuperscript{37,50,51,52} it could be shown that in the solid state the monotetrazolo form 18c together with 10\% of the isomer 18a is present\textsuperscript{24}.

\[ \begin{array}{c}
\text{N} \\
\text{N}_3 \\
\text{N} \\
\text{N}_3 \\
\end{array} \quad \leftrightarrow \quad 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\text{N} \\
\text{N}_3 \\
\end{array} 
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\text{N} \\
\text{N}_3 \\
\end{array}
\]

18a 18b 18c

Examination of some 4,6-diazidopyrimidines (19a) revealed, however, that the diazido form is favored over the tetrazolo form 19b in solution and that 4,6-diazido-5-trifluoroacetamidopyrimidine exists as such in the solid state\textsuperscript{41}.

\[ \begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} \quad \leftrightarrow \quad 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} 
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array}
\]

19a 19b

2.5. Tetrazolo[1,5-\( \alpha \)]pyrazines

There is no evidence for the presence of the azido form in the solid parent compound\textsuperscript{53} (20); in solution, however, the azido isomer was found to be present\textsuperscript{24}.

\[ \begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} \quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} 
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array}
\]

20

In the case of the 5,6-diphenyl derivative of 20, N.M.R. analysis revealed the presence of the azido isomer in solution\textsuperscript{52}. (In chloroform, the tetrazolo and azido isomers are present in the ratio 10:3.)

2.6. Azido-1,3,5-triazines

The destabilization of the tetrazolo form of azido-1,3,5-triazines is so strong that these compounds generally exist in the azido form. Thus, it has been found that 2,4,6-triazido-1,3,5-triazine exists entirely in the triazido form\textsuperscript{54,55,56} and investigations of other monooazido or diazido-1,3,5-triazines revealed the absence of a fused tetrazole ring in the solid state and in solution\textsuperscript{57}.

2.7. Tetrazolo[1,5-\( \beta \)-1,2,4-triazines

Detailed investigations have been performed only with the 5,6-diphenyl derivative (21). In the solid state and in dimethyl sulfoxide solution, compound 21 exists in the tetrazolo form, whereas in other solvents weak azide absorption bands have been observed in the I.R. spectrum\textsuperscript{52}.

\[ \text{C}_6\text{H}_5-N\equiv\text{N} \quad 21 \]

2.8. Tetrazolo[1,5-\( \beta \)-1,2,4,5-tetrazines

Only aryl derivatives of the system 22 have hitherto been investigated\textsuperscript{58}.

\[ \begin{array}{c}
\text{N} \\
\text{N} \\
\end{array} \quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N} \\
\end{array}
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N} \\
\end{array}
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N} \\
\end{array}
\]

22

From the U.V. and I.R. spectra is was concluded that the phenyl derivative exists in the azido form in the solid state and in pentane solution, whereas both forms are present in other solvents in different proportions (in polar solvents, more tetrazolo isomer is present). For example, the equilibrium mixture obtained in dimethylformamide after 8 hr contains ~80\% of the tetrazolo form.

2.9. Tetrazolo[5,1-\( \gamma \)]purines

Tetrazolo[5,1-\( \gamma \)]purines (parent compound: 23a) may tautomerize to 6-azidopurines (23b). Although previous investigations on this system\textsuperscript{51,59} led to the assumption that only the tetrazolo form is present in the solid state it was later found\textsuperscript{60} that the isomeric azido form is also present to some extent\textsuperscript{60}.

\[ \begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} \quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array} 
\quad \leftrightarrow 
\begin{array}{c}
\text{N} \\
\text{N}_3 \\
\end{array}
\]

23a 23b

Also in various other solvents, the tetrazolo form is the predominant one, except for 2-chloro-6-azido-purine. In this case, the effect of the substituent on the stabilization of the azido form is quite remarkable and this form is present in the solid state as well as in solution\textsuperscript{61,62}. For equilibrium constants and heats of isomerization, see Tables 1 and 2.

\textsuperscript{54} W. H. Bragg, Nature 134, 138 (1934).
2.10. Tetrazolo[1,5-\alpha]- (24a) and 
Tetrazolo[5,1-b]purines (24c)

Both systems can be regarded as the cyclic forms of 
the corresponding 2-azidopurines (24b).

\[
\text{24a} \xrightarrow{\text{N}} \text{24b} \xrightarrow{\text{N}} \text{24c}
\]

In the solid state and in acidic solution, the parent 
compound exists in the azido form\(^{51.60}\), but in 
dimethyl sulfoxide the presence of all three forms in 
the ratio 6 : 3 : 1 was revealed by N.M.R.\(^{50}\). With 
increasing temperature, the formation of the azido 
form is favored, however only at the expense of one 
tetrazole form (24a). On the other hand, an amino 
substituent in position 6 of the azidopurine changes 
the ratio of both tetrazole forms in the opposite sense 
(ratio 1 : 2.7 : 2.6) and 24c predominates\(^{62}\). For 
equilibrium constants, see Table 1.

A still more complicated relationship exists in the case 
of the diazid- and triazidopurines. Although for 
derivatives of 2,6-, 6,8-diazido-, and 2,6,8-triazido- 
purine the azido structure has been proposed\(^{61}\), a 
detailed investigation of the 2,6-diazidopurine system 
where five isomers (24a, 24b, 24c, \(R = N_3\); 25a and 
25b) are possible, revealed that no more than three 
isomers are present\(^{62}\).

\[
\text{25a} \quad \uparrow \quad \text{24a} \xrightarrow{\text{N}} \text{24b} \xrightarrow{\text{N}} \text{24c}
\]

In the presence of acids, only compound 24b is 
found, but in dimethyl sulfoxide two tetrazole forms 
are present (probably 24a and 25a).

2.11. Tetrazoloquinazolines

Whereas tetrazolo[1,5-\alpha]quinazolines (26) exist as 
solids or in solution entirely as tetrazoles, with some 
tetrazolo[1,5-c]quinazolines (27) isomerization has 
been observed and in solution the presence of the 
azido isomer was detected\(^{42}\).

\[
\text{26} \quad \text{27}
\]

It is concluded that an azido group in position 4 of 
the quinazoline nucleus is more stable than in 
position 2.

2.12. Tetrazolo[1,5-\alpha]-1,8-naphthyridines

Normally, these compounds exist in the tetrazolo 
form unless a second "azido group" is present in the 
position adjacent to the nitrogen atom in the other 
ring of the naphthyridine system. These compounds 
show azido-tetrazole isomerizations and do not 
exist as ditetrazoles\(^{63-67}\). With asymmetrically 
substituted compounds such as 28a, 28b, two isomeric 
forms are possible. One form is exclusively present 
in the solid state; the structural assignment, however, 
has so far not been made. In solution, both forms 
are present in most cases as is evidenced by the 
fact that a mixture of substitution products (29a, 
29b) is obtained from the reaction of 28 with various 
nucleophiles. The composition of the product 
mixture (Table 3) indicates that the positions of 
substituents present (which may exhibit a stabilizing 

effect on a particular form) and the particular 
nucleophile (or the catalytic reduction) control the 
ratio of products 29a and 29b.

\[
\text{28a} \xrightarrow{\text{R}} \text{28b} \quad \downarrow \quad \text{28a} \xrightarrow{\text{R}} \text{28b} \quad \text{29a} \xrightarrow{\text{R}} \text{29b}
\]

Table 3. Products obtained from the Reaction of Substituted Azidotetrazolo[1,5-a]-1,8-naphthyridines with Nucleophiles (or by Hydrogenation)

<table>
<thead>
<tr>
<th>R1</th>
<th>R2</th>
<th>Ratio 29a:29b</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH3</td>
<td>OC2H5</td>
<td>1:4</td>
<td>64</td>
</tr>
<tr>
<td>CH3</td>
<td>OH</td>
<td>1:1</td>
<td>64</td>
</tr>
<tr>
<td>CH3</td>
<td>NH2</td>
<td>0:1</td>
<td>64</td>
</tr>
<tr>
<td>CH3</td>
<td>NH2</td>
<td>0:1</td>
<td>65</td>
</tr>
<tr>
<td>CH3</td>
<td>NH2</td>
<td>0:1</td>
<td>65</td>
</tr>
<tr>
<td>CH3</td>
<td>NH2</td>
<td>0:1</td>
<td>65</td>
</tr>
<tr>
<td>OC2H5</td>
<td>OC2H5</td>
<td>10:1</td>
<td>67</td>
</tr>
<tr>
<td>OC2H5</td>
<td>NH2</td>
<td>10:0</td>
<td>67</td>
</tr>
<tr>
<td>OC2H5</td>
<td>OH</td>
<td>1:10</td>
<td>67</td>
</tr>
<tr>
<td>C6H5</td>
<td>OC2H5</td>
<td>1:10</td>
<td>66,67</td>
</tr>
<tr>
<td>C6H5</td>
<td>NH2</td>
<td>1:7</td>
<td>66,67</td>
</tr>
<tr>
<td>C6H5</td>
<td>OH</td>
<td>2:3</td>
<td>66,67</td>
</tr>
</tbody>
</table>

The predominant form is 29a.

2.13. Pyridotetrazolo[5,1-b]pyridazines

The isomeric pyrido[3,2-d]- (30) and pyrido[2,3-d]-tetrazolo[5,1-b]pyridazines (31) exist as tetraroles.

![30](image)
![31](image)

The isomeric 6-azidopyridotetrazolo[1,5-b]pyridazines 32 and 33 have been synthesized and isolated.

![32](image)
![33](image)

Compound 32 is converted into the thermodynamically more stable isomer 33 upon crystallization from ethanol. In dimethyl sulfoxide at 70°, an equilibrium mixture of 32 (~33%) and 33 (67%) is obtained. Similarly, compounds 34 and 35 form an equilibrium mixture (42 and 58%, respectively) in solution.

The heats of isomerization and the activation energies are given in Table 2.

6-Azidopyrido[4,3-d]tetrazolo[1,5-b]pyridazine (33)

Method A: A solution of 6-hydropyridopyrido[4,3-d]tetrazolo[1,5-b]pyridazine (0.2 g) in 2 N hydrochloric acid (4 ml) was cooled in ice and treated dropwise with a cold solution of sodium nitrite (80 mg) in water (1 ml). The resultant product (0.16 g) was dissolved in the minimum amount of ethanol at 40°, a small quantity of charcoal was added, and the mixture stirred at 40° for a few minutes. It was then filtered, the filtrate cooled to ~20°, and the precipitated product isolated by filtration; m.p. 146–147°.

I.R. (KBr): νN= 2155 cm⁻¹.

1H-N.M.R. (DMSO-d₆): δ = 9.46 (s, 7-H), 9.37 (d, 9-H), 8.53 (d, 10-H) ppm; J₉,₁₀ = 5.9 Hz.

Method B: A suspension of 1,4-dichloropyrido[3,4-d]pyridazine (1 g) and sodium azide (0.65 g) in ethanol (20 ml) was heated under reflux for 1 hr and then evaporated to half of its original volume. The residue was poured onto ice (10 g) and the separated product (0.81 g) was collected. For analysis, the compound was recrystallized from ethanol as described under Method A. The compound was identical in all respects with the product obtained as described under Method A.

6-Azidopyrido[3,4-d]tetrazolo[1,5-b]pyridazine (32)

This compound was prepared from 6-hydropyridopyrido[3,4-d]tetrazolo[1,5-b]pyridazine in a manner analogous to the preparation of 33 (Method A); yield: 83%; m.p. 163° (from ethanol, as in Method A). Attempted recrystallization of 32 from boiling ethanol gave compound 33. Compound 33 was likewise obtained upon melting of 32 (resolidification occurred).

I.R. (KBr): νN= 2151 cm⁻¹.

1H-N.M.R. (DMSO-d₆): δ = 8.06 (d, 7-H), 9.20 (d, 8-H), 9.93 (s, 10-H) ppm; J₉,₁₀ = 5.7 Hz.

2.14. Other Systems

Azido-tetrazole isomerizations have also been studied with other polycyclic systems. The isomeric dihydrobenzo[b]tetrazolophthalazines of the helicene (36) and steroid (37) types exist as tetraroles. Of the four possible forms of the azido derivative 38 only the thermodynamically most stable form shown below is found.

![36](image)
![37](image)
![38](image)

Cases in which an azido group in a position suited for cyclization to give a fused tetrazole ring does not cyclize are found but are rare. One such example is 4-azidobenzo-1,2,3-triazine which, according to N.M.R. spectral data, exists only in the azido form in the solid state and in solution. The same is true for 4-azidoimidazo[4,5-d]-1,2,3-triazine (40).

In general, the tendency for the formation of tetrazoles fused with a five-membered heterocyclic ring is low. Thus, 2-azido-1,3-thiazole exists predominantly in the open-chain form, not as 1,3-thiazolo[2,3-ε]-tetrazole (41). Tetrazolo[5,1-b]benzothiazoles (parent compound: 42) have the tetrazole structure in the solid state, except for certain substitution products which exhibit characteristic azide absorptions in the i.r. spectrum; however, in solution the azido form is in all cases the predominant form. A similar behavior was observed with the related naphtho-1,3-thiazoles.

On the other hand, 3-azidobenzo-1,2-thiazole 1,1-dioxide (43) exists only in the azido form in the solid state and in solution. 2-Azidobenzimidazole, 2-azidobenzo-1,3-oxazole, and 2-azidobenzo-1,3-thiazole-1,1-dioxide behave similarly.

3. Transformations

Most tetrazoloazines exhibit remarkable stability. Nevertheless, many reactions in which the intermediacy of reactive azido forms can be postulated have been successfully performed. Thus, tetrazolo[1,5-α]pyridine can be catalytically hydrogenated in the presence of ammonia to give a moderate yield of 2-aminopyridine (41). (The same compound is stable in sulfuric acid at 120° and catalytical hydrogenation in the presence of acid affects only the pyridine part of the molecule.) Hydrogen/deuterium exchange has been reported for tetrazolo[1,5-b]pyridazine (7); the reaction proceeds only under base-catalysis, thus indicating that the most reactive sites of the molecule are the 6- and 8-positions.

Attempts to extend some reactions of simple tetrazoles to tetrazoloazines failed. Thus, tetrazolo[1,5-α]pyridine (6) does not react with several organometallic compounds or with sodium cyanide (the reaction of tetrazoles with sodium cyanide yields cyanotriazenes).

Conversions exclusively involving substituents are not dealt with in this review.

3.1. Reactions involving the Non-tetrazolic Part of Tetrazoloazines

There are only few reports on ring-opening reactions involving exclusively the azine part of tetrazoloazines. 5,7-Dimethyltetrazolo[1,5-α]pyrimidine (44) can take part in two equilibria, i.e. in an azidotetrazole isomerization and in a pH-dependent equilibrium in alkaline solution. The sodium salt 45 can be isolated and the tetrazolopyrimidine regenerated by acidification.

Similar observations have been made with the tetrazolo[1,5-c]pyrimidines (16b). Thus, attempted nitration in the cold of the corresponding 4-hydrizinopyrimidines led to formation of the isolable open-chain compounds 46 via the intermediary of a hydrated species.

The analogous reaction has been observed with tetrazolo[1,5-c]quinazolines (parent compound: 27). In this case, the open-chain N-acyl derivative 48 could be recycled to the isolable hydrated species 47.
Apparently the same phenomenon is operative in the tetrazo[1.5-c]pyrimidine series. Here, compound 49 was isolated from the reaction between 4-amino-6-chloro-5-nitropyrimidine and sodium azide in the presence of hydrochloric acid.

Neither the tricyclic compound 50 nor its isomeric azido form are stable in the solid state or in solution. Instead, the isomeric diazonium betaine 51 is found.

The same probably applies to the debenzylated compound.

Another transformation in which the tetrazolyl ring remains unchanged is the ring cleavage of tetrazo[1.5-c]pyridines under the influence of a base. The pyridine ring is cleaved exclusively and the initially formed cis,cis-diene (52) is subsequently isomerized to the cis,trans- (53) and/or to the trans,trans-form (54).

3.2. Apparent Migration of Substituents as a Result of Azido-Tetrazole Isomerization and Conversions to Other Ring Systems

It has already been mentioned that the introduction of certain substituents into tetrazo[1.5-c]azines may effect a considerable shift of the azido-tetrazole equilibrium toward the side of one isomer. However, there are many examples in which such changes produce exclusively one isomer, which may be regarded as the “stabilized form”. Most of these conversions have been observed with tetrazo[1.5-c]azines. In some cases (e.g. 55 and 56), both isomers can be prepared at low temperature and the thermodynamically less stable isomer (e.g. 55) converted into the more stable one (e.g. 56) by melting or by heating in solution.

An intermediate diazido or bis-tetrazolo structure may be postulated; however, no such intermediate could be detected and the conversion proceeds most probably via a concerted mechanism.

6-Azido-7-methyltetrazo[1.5-c]pyridazine (55): 6-Hydrazino-7-methyltetrazolo[1.5-c]pyridazine (0.33 g) was dissolved in 5N hydrochloric acid (6 ml) and the solution cooled in ice. To the stirred solution, a solution of sodium nitrite (0.15 g) in water (2 ml) was added dropwise. After the addition was complete, the mixture was left to stand on ice for 30 min. The crude product was separated, dried, and crystallized from 50% ethanol; yield: 0.29 g (82%); m.p. 113-114°. (The melt of compound 55 solidifies on cooling to give impure 56; m.p. 87-92°). I.R. (Nujol): v_max = 2132 cm^{-1}.

1H-N.M.R. (CF3COOH): δ = 8.43 (d, 8-H), 2.58 (d, 7-CH3); J = 1.2 Hz (8-H, 7-CH3).
1H-N.M.R. (acetone-d6 at −30°): δ = 8.47 (d, 8-H), 2.40 (d, 7-CH3) ppm.

6-Azido-8-methyltetrazolo[1.5-c]pyridazine (56): The compound was prepared from 6-hydrazino-8-methyltetrazolo[1.5-c]pyridazine (0.495 g) using the procedure described for the preparation of 55; yield: 0.38 g (72%). The product was recrystallized from 50% ethanol; m.p. 95°.
I.R. (Nujol): v_max = 2169 cm^{-1}.
1H-N.M.R. (CF3COOH): δ = 7.19 (d, 7-H), 2.85 (d, 8-CH3); J = 1.2 Hz (7-H, 8-CH3).
1H-N.M.R. (acetone-d6 at −30°): δ = 7.33 (d, 7-H), 2.77 (d, 8-CH3) ppm.

Isomerization of 55 to 56: Azido compound 55 (0.176 g) was heated in toluene (2.5 ml) under reflux for 15 min. The product was precipitated by the addition of hexane (10 ml) to the cold reaction mixture; yield: nearly quantitative. A sample was recrystallized from 50% ethanol; m.p. 93°. The mixture m.p. of pure 56 and 56 from the above preparation showed no depression. The I.R. and N.M.R. spectra were identical.

The N-oxide function in 3-azidopyridazine N-oxides (57, 58) precludes cyclization to the condensed tetrazole. However, when compounds 57 and 58 are deoxygenated, cyclization to 59 takes place immediately. The reverse reaction, i.e. N-oxidation of 59, regenerates azido compound 57.

---

Regeneration of the azido group from a tetrazole ring (e.g. to give compounds 60–66) is also observed when another heterocyclic ring is condensed to the azine part of the tetrazoloazine molecule, e.g. from an amino, hydrazino, or alkylthio function. A similar reaction leading to a derivative of 68 has been performed to prove the structure of a compound presumed to be a pyridazino[3,4-c]pyridazine derivative.

Finally, transformations of the above type were successfully applied to the conversion of polycyclic compounds of the helicene type (69) into those of the steroid type (70). The azido group generated in these conversions can subsequently be subjected to nucleophilic substitution reactions or reduced to an amino group.

3.3. Cycloaddition Reactions involving the Azido Group

1,3-Dipolar cycloaddition reactions have been performed with tetrazoloazines that exist in a stabilized azido or tetrazole form as well as with equilibrium mixtures of both forms. Thus, tetrazolo[1,5-a]pyrimidines, tetrazolo[1,5-a]pyridines, 6-azidotetrazolo[1,5-b]pyridazine, and 7,8-diphenyltetrazolo[1,5-a]pyrazine have been subjected to thermal cycloaddition reactions with various acetylenic compounds to give 1,2,3-triazoles (71).

A conversion of the same type is the formation of 7-azido-3-methyl-4-oxo[6,1-c]-1,2,4-triazine (68) from the tetrazolopyridazine 67 in polyphosphoric acid; compound 67 can be regenerated by treatment of 68 with 20% hydrochloric acid.

1,3-Dipolar Cycloaddition of Tetrazolo[1,5-a]pyridines (Type 6) and Dimethyl Acetylenedicarboxylate; General Procedure:

A mixture of the tetrazolo[1,5-a]pyridine (0.01 mol) and dimethyl acetylenedicarboxylate (0.012 mol) is heated in an oil bath. After cooling, the mixture is worked up by filtration, evaporation, and chromatography of the residue on silica gel (chloroform as eluent).

In the manner described above, dimethyl 1-(2-pyridyl)-1,2,3-triazole-3,4-dicarboxylate was obtained from tetrazolo[1,5-a]pyridine by heating the reactants at 150°C for 7 hr; yield: 46%; m.p. 120–121°C.
Similarly, the thermal cycloaddition of tetrazolooazines and 1-morpholinocyclohexene\textsuperscript{92} (or other enamines) gave compounds of the type 72.

The cycloadducts obtained from these reactions as well as from the cycloaddition with norbornene\textsuperscript{91} indicate the participation of the isomeric azido form.

With other ethylenic compounds, 1,3-dipolar cycloadditions were carried out at temperatures at which the resultant \(\Delta^1\)-1,2,3-triazolines decompose\textsuperscript{91}. In the addition reaction of 6-azidotetrazolo[1,5-\(a\)]pyridazine with alkyl acrylates\textsuperscript{94}, the initially formed triazolines presumably decompose in the same manner as is described for the addition product of phenyl azide and ethyl acrylate\textsuperscript{93}, yielding the 1:2 adducts 73 as final products.

3.4. Products resulting from the Decomposition of Tetrazolooazines

There are many examples of the decomposition of tetrazolooazines with elimination of nitrogen and stabilization of the fragmentation product by cycloaddition, addition of hydrogen or other reaction components, C–H insertion reactions, or rearrangement reactions. Although in many cases nitrenes have been postulated as intermediates, this interpretation of the reaction mechanism has only to be accepted with reserve\textsuperscript{95} since in most cases the intervention of nitrenes is not proven.

3.4.1. C–H-Insertion Reactions and Addition of Hydrogen

In contrast to the reaction with acrylic esters, 6-azidotetrazolo[1,5-\(a\)]pyridazine reacts with methyl acrylate to afford an insertion product (74)\textsuperscript{94}. The product has the \textit{cis}-configuration with respect to the H and CH\(_3\) group. In a similar manner, tetrazolo[1,5-\(a\)]pyridine reacts with esters of fumaric or maleic acid to give the bicyclic system 75 via the intermediate enamine.

The intermediates formed from tetrazolooazines by elimination of nitrogen can also be stabilized by abstraction of hydrogen from the solvent. In addition, insertion reactions may take place. Thus, decomposition of 5,6-dimethyltetrazolo[1,5-\(a\)]pyrimidine in the presence of olefinic compounds or cyclohexane yields the corresponding 2-aminopyrimidine as the main product together with the insertion product (e.g. 76)\textsuperscript{96, 97}. In the case of tetrazolo[1,5-\(a\)]pyridine, only 2-aminopyridine was obtained in low yield upon thermal decomposition in cyclohexane\textsuperscript{96, 97}, whereas decomposition in the presence of aniline gave 2-aminopyridine as the main product and azobenzene as a minor product in low yield\textsuperscript{90}.

Neither aryl azides nor simple tetrazoles undergo copper-catalyzed decomposition and phenyl azide does not give substitution products when decomposed in aromatic solvents. However, both of these reactions proceed with some tetrazolooazines. It was found that the decomposition temperature of tetrazolo[1,5-\(a\)]pyridines and tetrazolo[1,5-\(a\)]pyrimidines is lowered in the presence of copper-containing catalysts\textsuperscript{96}. Moreover, hydrogen abstraction from arenes and formation of substitution products was also observed with tetrazolooazines\textsuperscript{97}. In this respect, tetrazolooazines seem to resemble the sulfonyl azides\textsuperscript{98}.

Decomposition of an azido group with formation of an amino group was observed in the attempted preparation of 6-azido-7(or 8)-methyltetrazolo[1,5-\(b\)]pyridazine from 3,6-dichloro-4-methylpyridazine. The isolated product, 6-amino-8-methyltetrazolo[1,5-\(b\)]pyridazine, indicates the intermediacy of either 77 or 78 (the isomer 78 is thermodynamically more stable) since both are transformed into 79 when heated in high-boiling solvents\textsuperscript{39}.

The intermediacy of a nitrone is assumed in the photolytic decomposition of 6-azidoazolopyridazines. The isolated products result either from hydrogen abstraction from the solvent or from dimerization reactions. The photolytic decomposition of 6-azidotetrazolo[1,5-h]pyridazine affords the 6-amino compound (80) as the main product together with ~3% of the corresponding azo compound (81)\(^9\).

3.4.2. Cycloaddition Reactions

The thermal decomposition of 5,7-dimethyltetrazolo[1,5-\(a\)]pyrimidine in the presence of \textit{trans}-stilbene yields a mixture of \textit{trans} (82) and \textit{cis}-2,3-diphenylaziridines (83), the \textit{trans}-isomer being the predominant product.

\[
\begin{array}{c}
\text{82} \\
\text{83}
\end{array}
\]

The reaction is regarded as a 2+1 cycloaddition\(^9\). 3+2 Cycloadditions have been observed to take place with nitriles and with alkynes. Thus, the thermal decomposition of tetrazolo[1,5-\(a\)]pyridine in the presence of benzonitrile yields 2-phenyl-1,2,4-triazolo[1,5-\(a\)]pyridine (84) and a small amount of 85. In the presence of alkynes, the copper-catalyzed decomposition of the same substrate gives rise to imidazolo[1,2-\(a\)]pyridines of the type 86\(^9\).

\[
\begin{array}{c}
\text{84} \\
\text{85} \\
\text{86}
\end{array}
\]

3.4.3. Rearrangement Reactions

The intermediacy of nitrenes has been postulated to explain certain thermal conversions of tetrazoloazines. It was shown that at high temperatures (~500 °C in vacuo) thermal interconversion of 2-pyridylcarbene and phenylnitrene takes place\(^10\). Moreover, with labelled 2-pyridylnitrene, generated from tetrazolo[1,5-\(a\)]pyridine, exchange of the two nitrogens could be observed, thus verifying the equilibrium 87\(^10\).

\[
\begin{array}{c}
\text{87}
\end{array}
\]

No definite mechanism of the ring contraction reactions of tetrazoloazines has yet been established. The first step of the reaction, however, certainly is the isomerization to the azido form which is favored at elevated temperatures. The azido compound is then decomposed to give an intermediate nitrene or biradical.

Gas-phase pyrolysis of tetrazolo[1,5-\(a\)]pyridines affords 2-cyanopyrroles\(^10\). Tetrazolo[1,5-\(a\)]pyrimidines are converted into 1-cyanopyrazoles and 2-aminopyridines under these conditions\(^10\), whereas gas-phase pyrolysis of tetrazolo[1,5-\(c\)]pyrimidines and tetrazolo[1,5-\(a\)]pyrazine gives l-cyanimidazoles\(^10\) in high yield, without formation of the aminoazines.

\[
\begin{array}{c}
\text{88}
\end{array}
\]

Gas-phase pyrolysis of tetrazolo[1,5-\(h\)]pyridazine affords a mixture of open-chain products such as cyanoallene (89), tetrolonitrile (90), 3-butynonitrile (91), and 2-cyanocyclopropene (92)\(^10\).

\[
\begin{array}{c}
\text{89} \\
\text{90} \\
\text{91} \\
\text{92}
\end{array}
\]

The 2-quinolylnitrene formed in the gas-phase pyrolysis of tetrazolo[1,5-\(a\)]quinoline rearranges to 1-isoquinolylnitrene (also directly formed from tetrazolo[5,1-\(a\)]isoquinoline) which in turn rearranges to \textit{o}-cyanophenylacetonitrile (93) and 4-cyanoindole (94)\(^10\).
Identical products are also obtained from the pyrolysis of tetrazolo[1,5-a]quinazoline and tetrazolo[1,5-c]quinazoline: 1-cyano benzimidazole (95) and N-cyanoanthranilonitrile (96), the latter resulting from ring opening of the intermediate nitrene\(^{10,5}\).

It was recently reported that ring-contraction reactions of tetr azo loazines with elimination of nitrogen can also be carried out under less drastic conditions. Thus, 5,6-diphenyltetrazolo[1,5-a]pyrazine may be converted into 4,5-diphenylimidazole (97) by simple heating in boiling acetic acid\(^{12}\); minor amounts of the N-acetyl derivative of 97 are obtained as a by-product.

Photochemical decomposition of the same tetr az olo pyrazine gives 97 and its N-acetyl derivative together with minor amounts of benzoic acid\(^{32}\).

A different type of reaction is observed with 4-azido-benzo-1,2,3-triazine; irradiation of this compound, which exists exclusively in the azido form, leads to the formation of the pentacyclic system 98\(^{7,3}\).

Tetrazolopyridines having a nitro group in position 8 may undergo conversion to pyrido[2,3-c]furoxans (e.g. [1,2,3]oxadiazolo[3,4-b]pyridine 3-oxides, 99) at elevated temperatures\(^{29,80,107}\). The reaction parallels the formation of benzofuroxans\(^{106}\) upon decomposition of 2-azidonitrobenzenes.

Analogous reactions have been observed in the tetrazolo[1,5-c]pyrimidine series. In an attempt to prepare 4- amino-6-azido-5-nitropyrimidine (or the corresponding tetrazolopyrimidine) from 4-amino-6-chloro-5-nitropyrimidine and sodium azide, 7-amino-[1,2,3]oxadiazolo[3,4-d]pyrimidine 1-oxide (100, R = H) was obtained\(^{88}\), not the expected azido compound.

The reaction has also been carried out with other azidopyrimidines\(^{88}\).

Received: December 8, 1971

---

94. B. Stanovnik, J. Heterocyclic Chem. 8, 1055 (1971).