A TRANSFORMATION OF 7-AZAPTERIDINES INTO 6-AZAPURINES
(IMIDAZO[4,5-e]-AS-TRIAZINES)

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Treatment of 6-substituted 3-methyl-7-azalumazines and 6-
substituted 1,3-dimethyl-7-azalumazines (fervenulins) with
alcoholic sodium hydroxide caused a benzylic acid type
rearrangement followed by decarboxylation and oxidation by
air to give the respective 5-methyl- and 5,7-dimethyl-5H-
imidazo[4,5-e]-as-triazine-6(7H)-ones.

The reaction of 7-azapteridine 5-oxides with acetic anhydride
or alcoholic sodium hydroxide caused a ring contraction to give the
corresponding 6-azapurines (imidazo[4,5-e]-as-triazines)¹ which are
interesting from the chemical and potentially biological point of
view. We now wish to report a further new synthetic approach to
6-azapurines which involves a benzylic acid type rearrangement of
7-azapteridines.
The key intermediates, 7-azapteridine derivatives were prepared by the following methods. It is known that the treatment of 6-benzylidenehydrazino-3-methyluracil in acetic acid with saturated aqueous sodium nitrite gives 6-benzylidenehydrazino-3-methyl-5-nitrosouracil (Ia).\(^2\) By this method, 6-(4-chlorobenzylidenehydrazino)- (Ib) (mp 224°, 89%), 6-(3,4-dichlorobenzylidenehydrazino)- (Ic) (mp 230°, 83%), 6-(4-methoxybenzylidenehydrazino)- (Id) (mp 245°, 75%), 6-(3,4-methyleneoxybenzylidenehydrazino)- (Ie) (mp 233°, 75%), and 6-(4-dimethylaminobenzylidenehydrazino)-3-methyl-5-nitrosouracil (If) (mp 220°, 68%) were obtained from the corresponding 6-benzylidenehydrazino-3-methyluracils.\(^3\) Refluxing of these 5-nitroso derivatives (Ia-f) in acetic anhydride for 1 hr caused dehydrative cyclization to give the respective 6-substituted 3-methyl-7-azalumazines (IIa-f) in 40-60% yields, which were identical with authentic samples\(^4\) prepared by the demethylation of toxoflavins. 6-Substituted 1,3-dimethyl-7-azalumazines (fervenulins) (IIg-1) were obtained by the condensation of 6-amino-1,3-dimethyl-5-nitrosouracil with aldehyde hydrazones according to the procedure
described previously.\textsuperscript{5}

Treatment of the 3-methyl- (IIa-f) and 1,3-dimethyl-7-azalumazines (IIg-1) thus obtained with 10% alcoholic sodium hydroxide under the conditions described in Table, followed by acidification\textsuperscript{6} with acetic acid, precipitated the respective 3-substituted 5-methyl-(IIIa-f) and 3-substituted 5,7-dimethyl-5H-imidazo[4,5-e]az-

\begin{center}
\begin{tabular}{lll}
\hline
II & \hspace{1cm} & III \\
\hline
a; & R\textsuperscript{1} = H, & R\textsuperscript{2} = C\textsubscript{6}H\textsubscript{5} \\
b; & R\textsuperscript{1} = H, & R\textsuperscript{2} = 4-Cl-C\textsubscript{6}H\textsubscript{4} \\
c; & R\textsuperscript{1} = H, & R\textsuperscript{2} = 3,4-Cl\textsubscript{2}-C\textsubscript{6}H\textsubscript{3} \\
d; & R\textsuperscript{1} = H, & R\textsuperscript{2} = 3-CH\textsubscript{3}O-C\textsubscript{6}H\textsubscript{4} \\
e; & R\textsuperscript{1} = H, & R\textsuperscript{2} = 3,4-CH\textsubscript{2}O\textsubscript{2}-C\textsubscript{6}H\textsubscript{3} \\
f; & R\textsuperscript{1} = H, & R\textsuperscript{2} = 4-(CH\textsubscript{3})\textsubscript{2}N-C\textsubscript{6}H\textsubscript{4} \\
g; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = C\textsubscript{6}H\textsubscript{5} \\
h; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = 4-Cl-C\textsubscript{6}H\textsubscript{4} \\
i; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = 3,4-Cl\textsubscript{2}-C\textsubscript{6}H\textsubscript{3} \\
j; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = 4-CH\textsubscript{3}O-C\textsubscript{6}H\textsubscript{4} \\
k; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = 3,4-CH\textsubscript{2}O\textsubscript{2}-C\textsubscript{6}H\textsubscript{3} \\
l; & R\textsuperscript{1} = CH\textsubscript{3}, & R\textsuperscript{2} = 4-(CH\textsubscript{3})\textsubscript{2}N-C\textsubscript{6}H\textsubscript{4} \\
\hline
\end{tabular}
\end{center}

triazine-6(7H)-ones (IIIg-1)\textsuperscript{1} (see Table). The structures of compounds (IIIa-l) were derived on the basis of elemental analysis,
molecular weight determination and fragmentation study by mass spectrometry, IR (the presence of a carbonyl band at 1760 cm\(^{-1}\)) and NMR data, and by consideration of its probable mode of formation (Scheme). Furthermore, compounds (IIIa-f) were converted into the 5,7-dimethyl derivatives (IIIg-l) by methylation with methyl iodide and potassium carbonate in dimethylformamide for identification purpose.

Table 6-Azapurines Formation by Reaction of 7-Azapteridines with Alcoholic Sodium Hydroxide

<table>
<thead>
<tr>
<th>Starting material</th>
<th>Reaction condition</th>
<th>Product</th>
<th>(\text{Mp (°C)}^a)</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>reflux, 1 hr</td>
<td>IIIa</td>
<td>283</td>
<td>61</td>
</tr>
<tr>
<td>IIb</td>
<td>reflux, 1 hr</td>
<td>IIIb</td>
<td>266</td>
<td>49</td>
</tr>
<tr>
<td>IIc</td>
<td>reflux, 1 hr</td>
<td>IIIc</td>
<td>284</td>
<td>52</td>
</tr>
<tr>
<td>IID</td>
<td>reflux, 1 hr</td>
<td>IIId</td>
<td>292</td>
<td>37</td>
</tr>
<tr>
<td>IIe</td>
<td>reflux, 2 hr</td>
<td>IIIe</td>
<td>324</td>
<td>35</td>
</tr>
<tr>
<td>IIf</td>
<td>reflux, 2 hr</td>
<td>IIIf</td>
<td>281</td>
<td>50</td>
</tr>
<tr>
<td>IIg</td>
<td>60°, 10 min</td>
<td>IIIg</td>
<td>203</td>
<td>71</td>
</tr>
<tr>
<td>IIh</td>
<td>60°, 10 min</td>
<td>IIIh</td>
<td>251</td>
<td>65</td>
</tr>
<tr>
<td>IIIi</td>
<td>60°, 10 min</td>
<td>IIIi</td>
<td>247</td>
<td>55</td>
</tr>
<tr>
<td>IIIj</td>
<td>60°, 30 min</td>
<td>IIIj</td>
<td>255</td>
<td>58</td>
</tr>
<tr>
<td>IIIk</td>
<td>60°, 30 min</td>
<td>IIIk</td>
<td>330</td>
<td>51</td>
</tr>
<tr>
<td>IIIl</td>
<td>60°, 30 min</td>
<td>IIIl</td>
<td>290</td>
<td>87</td>
</tr>
</tbody>
</table>

a) These compounds were recrystallized from ethanol.
We suggest that these 6-azapurines are formed from 7-aza-pteridines by a benzylic acid type rearrangement, followed by decarboxylation and oxidation by air, as depicted in the following Scheme.

Scheme
REFERENCES AND NOTES


6. Evolution of carbon dioxide was observed here.

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