COMPounds related to acridine. xi.\(^1\)

reaction of 1,3-di(9-acridinyl)propane

with \(p\)-nitroso-N,N-dimethylaniline

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Although 9-propylacridine (II) did not react with \(p\)-nitroso-N,N-dimethylaniline (I) under various conditions, 1,3-di(9-acridinyl)propane (III) reacted with I under the influence of HCl to give the mono-nitrone compound (IV) and cleaved products V-VII, whose relative yields were greatly affected by the reaction conditions.

Previously,\(^2\) we have reported that hydrochloric acid (HCl) is an extremely effective catalyst for the condensation of acridine having an active methyl group with \(p\)-substituted nitrosobenzenes, and that the total yield of nitrone and anil as condensation products is fairly good compared with that in the presence of a basic catalyst which is usually employed in the Ehrlich-Sachs re-
Moreover, even 9-ethylacridine and 9-ethynylacridine react with two moles of p-nitroso-N,N-dialkylaniline under the influence of HCl to yield a mixture of 1-(9-acridinyl)-1,2-bis(p-N,N-dialkylanaminophenylimino)ethane and its N\(^1\)-oxide, and N\(^1\),N\(^2\)-dioxide, respectively, as depicted below.

\[
\begin{align*}
\text{Ar: } & p-N,N\text{-dialkylaminophenyl} \\
\text{Ar-NO} & \quad \text{Ar-N=CH} \\
& \quad \text{C=N-Ar} \\
& \quad \text{C=CH} \\
& \quad \text{C=N-Ar}
\end{align*}
\]

Therefore, it appeared of interest to investigate further the scope of the above reaction. In this communication we wish to report the reaction of the 9-propylacridine system with p-nitroso-N,N-dimethylaniline (I). In view of the result of reaction of 9-ethylacridine with I, 9-propylacridine (II) might be expected to react with three moles of I. Contrary to expectation, the reaction of II with I did not take place in the presence of HCl as well as of a basic catalyst under various conditions. However, we found that 1,3-di(9-acridinyl)-propane (III) having methylene groups activated by two acridinyl groups, reacted with three moles of I under the influence of HCl to afford several products: whose relative yields depended on the reaction conditions as shown in Table I.

In the reaction in refluxing ethanol, products, N-V, were formed together with tarry materials, and the yield of IV increased with the decrease in the amount

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of HCl. At lower reaction temperatures, the compound N was the predominant product.

The molecular formula of \( \text{N}[C_{37}H_{30}N_4O, \text{mp } 225^\circ \text{C dec., orange prisms}] \) was consistent with that of a mono-nitrone compound, and the nmr spectrum in CF₃COOH displayed signals at \( \delta 3.3 \) (6H, s, NCH₃), 3.5 (4H, m, CH₂CH₂), and 7.1-9.0 ppm (20H, aromatic protons). Although 1,3-di(9-acridinyl)-1-(p-N,N-dimethylaminophenylimino)propane N-oxide and its 2-isomer are possible for the structure of mono-nitrone compound, the mass spectrum supports strongly that \( \text{N} \) is 1-isomer \([m/e 546 (M^+), 530 (M^+ - O), 528 (530^+ - H_2), 324 (9-acridinyl-C=O-C_6H_4NMe_2, base peak)].\)

By the identification with authentic samples, the structures of other products obtained as all red prisms were confirmed to be 1-(9-acridinyl)-1,2-

\[
\begin{align*}
\text{II} & \quad + \quad (\text{CH}_3)\text{NNO} \quad \rightarrow \quad \# \quad \rightarrow \quad \text{no reaction} \\
\text{III} & \quad + \quad \text{I} \quad \rightarrow \quad \text{N}
\end{align*}
\]

\( \text{Ar}: \ p-N,N\text{-dimethylaminophenyl} \)
bis(p-N,N-dimethylaminophenylimino)ethane N\(^1\)-oxide (V) [mp 265\(^\circ\)C dec.],\(^4\) (9-acridinyl)methylene)-p-N,N-dimethylaminoaniline (M) [mp 248\(^\circ\)C],\(^2\) and its N-oxide (W) [mp 243\(^\circ\)C dec.],\(^2\) respectively.

<table>
<thead>
<tr>
<th>Reaction conditions(^a)</th>
<th>Product, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V</td>
</tr>
<tr>
<td>Time, h</td>
<td>Temp. (^\circ)C</td>
</tr>
<tr>
<td>4</td>
<td>reflux</td>
</tr>
<tr>
<td>1.5</td>
<td>reflux</td>
</tr>
<tr>
<td>1.5</td>
<td>reflux</td>
</tr>
<tr>
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<td>50</td>
</tr>
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<td>15</td>
<td>60</td>
</tr>
<tr>
<td>15</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^a\) A mixture of I (1.1 g), III (1.0 g), and the specified amount of HCl (d\(^2\) 1.1748) in ethanol (20 ml) was heated under the reaction conditions described in the Table. \(^b\) A sign, +, means a trace amount.

It is known that anil and nitrone compounds are difficult to separate. The yields shown in Table 1 are those of pure products obtained by several recrystallizations of the respective reaction mixture. As shown in Table 1, no 1:2 and 1:3 condensation products of III and I were formed, and the cleaved products, V—VII, were obtained under forcing conditions.

Attempts to obtain 1,3-di(9-acridinyl)-1-(p-N,N-dimethylaminophenylimino)-propane (VIII) by deoxygenation of IV with triethylphosphite were unsuccessful; IV (1.0 g) was heated with triethylphosphite (10 ml) under reflux for 5 h, giving 0.31 g (52%) of the anil VI along with resinous materials. This fact suggests that the mono-anil VIII undergoes thermal decomposition to form VI and 9-vinylacridine which polymerizes to resinous material. The reaction of the
mono-nitrone IV with two or three moles of I in the presence of HCl did not give 1:2 and 1:3 condensation products, but the cleaved products, V and VII, were obtained in small quantities, besides the recovery of IV. For example, when a mixture of IV (1.0 g) and I (0.82 g) in ethanol (20 ml) was heated with HCl (0.04 ml) at 70°C for 15 h, V (22 mg, 2.5%) and VII (26 mg, 4%) were obtained together with recovery of IV (57.5%).

\[
\begin{align*}
&\text{IV} \xrightarrow{\text{P(OEt)}_3} \text{[Ar'-CH=CH} \text{CH}_2 \text{CH} = \text{Ar'}] \rightarrow \text{Ar'-CH=N-Ar} + \text{Ar'-CH=CH}_2 \\
&\text{IV} \xrightarrow{\text{I}} 1:2 \text{ and } 1:3 \text{ condensation products} \rightarrow V + VII
\end{align*}
\]

\[\text{Ar: p-N,N-dimethylaminophenyl; Ar': 9-acridinyl}\]

Kröhne and his co-workers suggested the mechanism via the aldol-type intermediate for the formation of the anil VI and nitrone VII in the reaction of 9-methylacridine (Ar'-CH₃) with I (ArNO) under the influence of a basic catalyst:

\[
\begin{align*}
\text{Ar'-CH₃} + \text{ArNO} \rightarrow \text{Ar'-CH=CH-N-Ar} \xrightarrow{- \text{H}_2\text{O}} \text{Ar'-CH=N-Ar} \quad \text{(VI)} \\
\text{Ar'-CH₃} + \text{ArNO} \rightarrow \text{Ar'-CH=CH-N-Ar} \xrightarrow{- \text{H}_2} \text{Ar'-CH=CH-N-Ar} \quad \text{(VII)}
\end{align*}
\]

Although the exact pathway for the formation of products in the reaction of III with I is not clear, we viewed the following pathway on the basis of above considerations. The compound III reacts with one mole of I to give the aldol-type intermediate A, followed by dehydrogenation or dehydration to form the nitrone IV or anil VIII. As described above, the anil VIII undergoes thermal decomposition to give VI and 9-vinylacridine. Since the nitrone IV is stable under the reaction conditions, a further reaction of IV with two moles of I takes place under forcing conditions, forming the aldol-type intermediate B.
I + III $\rightarrow \begin{pmatrix} \text{HO-N-Ar} \\ \text{Ar'-CH-CH}_2\text{CH}_2\text{-Ar'} \end{pmatrix}$

$\xrightarrow{-\text{H}_2\text{O}}$ $\begin{pmatrix} \text{N-Ar} \\ \text{Ar'}\text{-C-CH}_2\text{CH}_2\text{-Ar'} \end{pmatrix}$

$\xleftarrow{-\text{H}_2}$ $\begin{pmatrix} \text{O+H-N-Ar} \\ \text{Ar'-C-CH}_2\text{CH}_2\text{-Ar'} \end{pmatrix}$

$\xrightarrow{\text{V}}$

$\begin{pmatrix} \text{O+H-N-Ar} \\ \text{Ar'-C-CH=CH=O} \end{pmatrix}$

$\xleftarrow{-\text{H}_2\text{O}}$

$\begin{pmatrix} \text{OH} \\ \text{Ar'-C-CH=N-Ar} \end{pmatrix}$

\[ \xrightarrow{-\text{C}} \]

$\begin{pmatrix} \text{OH} \\ \text{Ar'-C-CH=N-Ar} \end{pmatrix}$

$\xrightarrow{-\text{C}}$

$\begin{pmatrix} \text{OH} \\ \text{Ar'-C-CH=N-Ar} \end{pmatrix}$

The intermediate B decomposes into V and diol C, which gives VII by dehydration.

References

6. O. Tsuge and A. Torii, ibid., 1972, 45, 3187.

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