INVESTIGATIONS IN HETEROCYCLIC CHEMISTRY

XLIV. Comparative Ease of Ring-Closure of Five- and Six-Membered Heterocycles in the Acid Condensation of Arylides of Diarylglycolic Acids*

P. A. Petyunin, A. K. Sukhomlinov, and N. G. Panferova


With the acid condensation of diarylglycolic benzylanilides as an example, it has been shown that the predominant formation of a five-membered ring rather than a six-membered ring takes place even in the case where the internal structure of the anilide permits the simultaneous formation of both rings. It has also been shown that it is possible to determine the size of the ring formed on condensation from the UV and IR spectra, and the presence of hydrogen bonds in the arylamides of diarylglycolic acids and the formation of the lactim form and of the quaternary ammonium salt of the base of 8,8-diphenyloxindole in solutions of sodium ethoxide and concentrated H$_2$SO$_4$, respectively, have been confirmed.

It has been shown previously [1–3] that in the acid condensation of arylides of hydroxy carboxylic acids the rate of ring closure falls in the sequence: 5 > 6 > 7 > 8. It was interesting to determine to what extent this feature is observed in the ease where the internal structure of the arylide permits the formation of rings of different sizes. For arylcarboxylic acids, for example, it is known that six-membered rings are formed more easily than five-membered rings [4].

The present investigation was devoted to a study of the comparative ease of closure of five- and six-membered rings in the arylides of diarylglycolic acids.

As subjects, we used the diarylglycolic N-benzylanilides II–IV, the synthesis of which was effected by the reaction of ethyl N-benzyloxanilate I with Grignard compounds (RMgX, R = C$_6$H$_5$, 4-CH$_2$C$_6$H$_5$, 2-CH$_3$OC$_6$H$_4$) (Table 1). They are crystalline substances soluble in the usual organic solvents; with concentrated H$_2$SO$_4$ they give a coloration which rapidly disappears (halochromism).

The aryldies II–IV contain two nucleophilic radicals (N-phenyl and N-benzyl) and therefore, in the cation of the halochromic salt V, ring closure may lead both to a five-membered (oxindole) ring VI–VIII and to a six-membered (3-oxotetrahydroisoquinoline) ring IX. This possibility also depends on the nature of the radicals present on the carbinal carbon [5].

Experiments showed that, in the acid condensation of the aryldies II–IV, 1-benzyl-3,3-diaryloxindoles VI–VIII are formed (Table 2). The structure of the latter was shown by the independent synthesis of one of them (VI), which was obtained by the benzylation of 3,3-diphenyloxindole X, and also by the UV and IR absorption spectra of VI (curve 3, Fig. 3; $\nu$C=O 1700 cm$^{-1}$). They are crystalline substances with higher melting points than the initial arylides.

In addition, to prove the predominant formation of the five-membered ring rather than the six-membered ring, the acid condensation of N-benzyl-4,4'-dimethoxybenzylanilide (XI) was carried out. This was condensed by means of formic acid without preliminary isolation [6]. According to the literature [3], in XI only the five-membered ring can form, giving 1-benzyl-3,3-di(p-anisyl)oxindole (XII).

An attempt was made to use spectroscopic methods to determine the size of the rings formed. The UV and IR absorption spectra of the benzilic acid aryldies (II, XIII–XVIII) and the products of their acid condensation (X, XIX–XXI) were studied.

The tertiary arylamides XXII are feebly associated (in the crystalline state, XIV gives bands at 3560 and 1621 cm$^{-1}$ of bound HO and CO groups) and, in spite of statements in the literature [7], do not contain intramolecular hydrogen bonds. This is confirmed by the similarity of the UV absorption spectra of II and

*For part XLIII, see [17].
### Table 1

Melting Points, Yields, and Analytical Results for the Diarylglycolic N-Benzylanilides

<table>
<thead>
<tr>
<th>Compound</th>
<th>Name</th>
<th>Mp, °C</th>
<th>Empirical formula</th>
<th>N, %</th>
<th>Yield, %</th>
<th>Coloration with conc H₂SO₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>N-Benzylbenzanilide</td>
<td>88—89</td>
<td>C₂₇H₂₅NO₂</td>
<td>3.62</td>
<td>3.56</td>
<td>85.2 Yellow</td>
</tr>
<tr>
<td>III</td>
<td>N-Benzyl-4,4'-dimethylbenzanilide</td>
<td>126—127</td>
<td>C₂₉H₂₇NO₂</td>
<td>3.13</td>
<td>3.21</td>
<td>93.1 Crimson</td>
</tr>
<tr>
<td>IV</td>
<td>N-Benzyl-2,2'-dimethylbenzanilide</td>
<td>112—113</td>
<td>C₂₉H₂₇NO₂</td>
<td>3.07</td>
<td>3.20</td>
<td>90.5 Green</td>
</tr>
</tbody>
</table>

*Compounds II and IV were crystallized from ethanol and III from glacial acetic acid.*

### Table 2

Melting Points, Yields, and Analytical Results for the Oxindole Derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>Name</th>
<th>Mp, °C (from ethanol)</th>
<th>Empirical formula</th>
<th>N, %</th>
<th>Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>VI</td>
<td>1-Benzyl-3,3-diphenyloxindole</td>
<td>163</td>
<td>C₂₇H₂₁NO</td>
<td>3.68</td>
<td>3.73</td>
</tr>
<tr>
<td>VII</td>
<td>1-Benzyl-3,3-di(p-tolyl)oxindole</td>
<td>154</td>
<td>C₂₉H₂₅NO</td>
<td>3.38</td>
<td>3.47</td>
</tr>
<tr>
<td>VIII</td>
<td>1-Benzyl-3,3-di(o-anisyl)oxindole</td>
<td>191</td>
<td>C₂₉H₂₅NO₂</td>
<td>3.15</td>
<td>3.21</td>
</tr>
</tbody>
</table>

### Table 3

IR Absorption Spectra of the Cyclic Lactams

<table>
<thead>
<tr>
<th>Compound</th>
<th>Position of the absorption maxima in the region of the C=O stretching vibrations, cm⁻¹</th>
<th>Δν, cm⁻¹</th>
<th>Size of the ring</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>1716, 1711</td>
<td>—</td>
<td>5</td>
</tr>
<tr>
<td>XIX</td>
<td>1706, 1711</td>
<td>—</td>
<td>6</td>
</tr>
<tr>
<td>XX</td>
<td>1667</td>
<td>44</td>
<td>6</td>
</tr>
<tr>
<td>XXI</td>
<td>1645</td>
<td>66</td>
<td>7</td>
</tr>
</tbody>
</table>