A SIMPLE PHOTOSYNTHESIS OF PYRROLOINDOLOQUINONES

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Abstract --- The improved photoreaction of pyrrolidino-1,4-benzoquinones having the active methylene groups afforded a simple and preparative route to the synthesis of pyrroloindoloquinones, which were the mother framework of mitomycins.

The pyrroloindoloquinones have the basic structure of mitomycins and very important for their biological activities. Recently we have reported that the photolysis of amino-1,4-naphthoquinones having the active methylene groups at the 2-position provided a preparative route to the heterocyclic quinones. In this paper we wish to describe the improvement and application of this photo-induced reaction to newly prepared pyrrolidinobenzoquinones for the simple synthesis of pyrroloindoloquinones.

The synthetic process can be represented as shown in Scheme I. The benzoquinone was prepared easily from the substitution reaction of the dibromoquinone with ethyl sodium malonate. However, were not obtained from the corresponding quinones under the same condition. Since it is possible for the active methylene anion to react with at three positions (C_2, C_3, and C_5 or C_6) or four positions (C_2, C_3, C_5 or C_6, and methyl group), the reaction resulted in an intractable mixture. Using the thallium malonates, the regioselective Michael addition of these to followed by oxidation gave the corresponding quinones in moderate yields. On treatment with equimolar amounts of pyrrolidine in chloroform, afforded the corresponding aminoquinones in good yields, respectively. The structures of and , oily products, were confirmed by the analytical and spectroscopic data (IR, NMR, and MS).

The photo-induced reaction of pyrrolidinoquinones was carried out as follows. A solution of in ethanol was irradiated with a high pressure mercury lamp.
through Pyrex glass. After allowing the irradiated solution \( \text{3a-c} \) to stand for more than 3 days at room temperature, the pyrroloindoloquinones \( \text{8a-c} \) were obtained in 47-51% yields (Method A). Secondly, an attempt to increase the yield of \( \text{8} \) was examined under the mild condition. The irradiated solution of \( \text{3a-c} \) in ethanol was retained on a silica gel column for a few days, and then eluted with ethyl acetate to give \( \text{8a-c} \) in 60-68% yields (Method B). The similar photolysis of \( \text{3d} \) afforded the stereoisomers, \( \text{8d-(i)} \) and \( \text{8d-(ii)} \), due to the different substituents in a ratio of 5 : 4 after chromatography on silica gel. The stereochemistry of these isomers has not been clarified yet. The structural assignments for \( \text{8a-d} \) were based on their analytical and spectral properties, which were in good agreement with their formulations. The results are summarized in Table I.

![Scheme I](image-url)
Table I. Photoreaction of Pyrrolidinoquinones 3

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mp (°C)</th>
<th>Yield (%)</th>
<th>IR (\text{cm}^{-1})</th>
<th>NMR (\delta (CDCl_3)) ppm</th>
<th>Mass (M^+ (m/z))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Method A</td>
<td>Method B</td>
<td>ester C=O</td>
<td>bridgehead CH</td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>137</td>
<td>49</td>
<td>65</td>
<td>1740, 1715</td>
<td>4.81</td>
</tr>
<tr>
<td>b</td>
<td>86-88</td>
<td>47</td>
<td>60</td>
<td>1745, 1730</td>
<td>4.80</td>
</tr>
<tr>
<td>c</td>
<td>90-91</td>
<td>51</td>
<td>68</td>
<td>1740, 1718</td>
<td>4.70</td>
</tr>
<tr>
<td>d-(i)</td>
<td>109</td>
<td>--</td>
<td>34</td>
<td>1740, 1717</td>
<td>4.71</td>
</tr>
<tr>
<td>d-(ii)</td>
<td>oil</td>
<td>--</td>
<td>27</td>
<td>1740, 1718</td>
<td>4.72</td>
</tr>
</tbody>
</table>

a  Recrystallized from hexane
b  1H, double doublet

this photoreaction may proceed through the following sequence: photo-insertion, ring degradation, intramolecular cyclization, and oxidation (4, 5, 6, 7, and 8) as reported previously. Silica gel in this reaction sequence may be considered to act as acid and make promotion of 4 to dissociate to 5 and 6. Although the closure of 5 to 7 is "5-endo-trig", it also involves a fully conjugated 6π electron system and this can also be viewed as a thermally allowed disrotatory electrocyclization of the Woodward-Hoffmann classification \(\pi 6s \rightarrow \pi 4s + 62s\).

The compounds, 8c and 8d, will be a key intermediate of the mitosene synthesis. Therefore, these conversion to mitosene are being carried out and will be reported elsewhere.

ACKNOWLEDGEMENTS
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REFERENCES AND NOTES
1. For a recent review: T. Kametani and K. Takahashi, Heterocycles, 1978, 9, 293.

5. It has been reported that the addition of active methylene compounds to the methyl group probably involved the methylene tautomer as shown in equation (I).

\[ \text{CH}_3 \text{O} \text{CH}_3 \quad \text{CH}_3 \text{O} \text{CH}_2 \text{CH}_3 \]


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