SYNTHESIS AND CYCLOADDITION REACTIONS OF DI- AND
TRI-SUBSTITUTED 1,3-OXAZEPINE DERIVATIVES

Takashi Toda, Takeo Takeg, and Yoshio Mukai
Department of Chemistry, Faculty of Science, Tohoku University
Aoba, Aramaki, Sendai 980, Japan
Yoshizo Suzuki
Department of Chemistry, Faculty of Education, Iwate University
Ueda-Sanchome, Morioka 020, Japan

The reactions of pyrylium salts and sodium azide are proven to be a general synthetic method for di- to pentaphenyl-1,3-oxazepines. Cycloadditions of mono-, di-, and triphenyl-1,3-oxazepines with cyclopentadienone and triazoline derivatives were also investigated.

Because of simplicity of the procedure and ready availability of the starting materials, we have interested conversion of pyrylium salts to 1,3-oxazepines which was originally discovered by Le Roux et al. It has been reported that this method as well as the photolysis of aromatic amine oxides are very useful for the synthesis of polysubstituted derivatives of 1,3-oxazepine. Since our discovery of an effective synthesis of the least substituted derivative, 2-aryl-1,3-oxazepines, synthesis of more substituted derivatives have remained unexplored. Herein, the details of the investigation of 1,3-oxaze-
pine by Le Roux's method are reported.

Substituted pyrylium fluoroborates (1-5) were treated with an excess of sodium azide in absolute dioxane to give corresponding 1,3-oxazepine derivatives (6-10) in satisfactory yields as shown in the Table I. Although disubstituted 1,3-oxazepines (6 & 7) are fairly stable after purification, strictly anhydrous conditions are required during the reaction and purification since the pyrylium salts (1 & 2) and/or the 1,3-oxazepines can be hydrolyzed to the corresponding diketones and unidentified products. On the other hand, poly-substituted pyrylium fluoroborates (3-5) are stable to hydrolysis and give good results. All unsymmetrical tetra-substituted pyrylium salts (3-5) afforded sterically less hindered 1,3-oxazepines.

The structures of the 1,3-oxazepines were deduced from their elemental analyses and spectral properties which are consistent with those of reported 1,3-oxazepines. Our results together with Le Roux's provide a general synthetic procedure of aryl and aralkyl substituted 1,3-oxazepines; the procedure is especially for 2,7-diphenyl- and 2,5,7-trisubstituted derivatives.
As a part of our studies on 1,3-oxazepines, we also investigated the cycloadditions of these 1,3-oxazepines with 2,5-dimethyl-3,4-diphenylcyclopentadiene (11) and N-phenyltriazolin-3,5-dione (12). Treatment of diphenyl- (6) and triphenyl- (7) derivatives with 11 in refluxing benzene or xylene resulted in complete recovery of the starting substances. At an elevated temperature, i.e. in boiling o-dichlorobenzene, reactions of 7 with 11 afforded only 2,4-diphenylpyrrole which is a thermal rearrangement product of 7. As 2-phenyl-1,3-oxazepine (13) gave a normal [2+4] addition product, it must be concluded that the steric hindrance due to the substituents in 1,3-oxazepines plays an important role in the reaction with 11.
Table II

<table>
<thead>
<tr>
<th></th>
<th>14</th>
<th>15</th>
<th>16: R=Ph</th>
<th>17: R=Me</th>
</tr>
</thead>
<tbody>
<tr>
<td>mp °C</td>
<td>220-222</td>
<td>212-213</td>
<td>205</td>
<td>132-134</td>
</tr>
<tr>
<td>Yield %</td>
<td>57</td>
<td>60</td>
<td>33</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>3460</td>
<td>1790</td>
<td>1780</td>
<td>1780</td>
</tr>
<tr>
<td></td>
<td>3340</td>
<td>1735</td>
<td>1740</td>
<td>1735</td>
</tr>
<tr>
<td>$\sqrt{\text{KBr}}$ cm$^{-1}$</td>
<td>1780</td>
<td>1680-</td>
<td>1680-</td>
<td>1680-</td>
</tr>
<tr>
<td></td>
<td>1720</td>
<td>1700</td>
<td>1700</td>
<td>1700</td>
</tr>
<tr>
<td></td>
<td>1680-</td>
<td>1700</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PMR (CDCl$_3$) ppm (J=Hz)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_4$</td>
<td>5.74 (d; 3.5)</td>
<td>5.22 (d; 4.0)</td>
<td>5.20 (s)</td>
<td>5.20 (s)</td>
</tr>
<tr>
<td>H$_5$</td>
<td>6.23 (d,d; 9.5 &amp; 9.5)</td>
<td>5.40 (d,d; 9.0 &amp; 9.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_6$</td>
<td>6.03 (d,d; 9.5 &amp; 4.0)</td>
<td>6.78 (d; 9.0 &amp; 4.0)</td>
<td>5.30 (s)</td>
<td>5.30 (s)</td>
</tr>
<tr>
<td>H$_7$</td>
<td>6.54 (d,d; 8.0 &amp; 4.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OH's H</td>
<td>9.19 (d; 8.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In contrary, oxazepines (13, 6, and 7) reacted with N-phenyltriazolin-3,5-dione (12) readily at room temperature to yield the corresponding addition products (14-16). Addition of N-methyltriazolin-3,5-dione with 7 also gave the adduct (17). It appeared that the cycloadducts were formed in excellent yields but were hydrolyzed readily during purification to hydroxyamide derivatives; one of which, 14, was isolated in the pure state. This seems to be reason why products were isolated in moderate yields.

The structures of the adducts were deduced from their elemental analyses and spectral data. All of them shows strong bands at 1720-1735 cm\(^{-1}\) and 1780-1790 cm\(^{-1}\) for the carboxyls and also a characteristic absorption at 1675-1700 cm\(^{-1}\). Additionally, 14 shows the NH and/or OH streching bands at 3340 and 3460 cm\(^{-1}\) and the amide band at 1675-1700 cm\(^{-1}\). The PMR chemical shifts and coupling patterns of these products as shown in the Table II are consistent with those of the proposed structures. Thus, the addition has taken place at the C\(_4\) and C\(_7\) positions of the 1,3-oxazepines, i.e. a [4+2] type cycloaddition; the isolation of such products has not been reported previously. Tetra- and pentaphenyl-1,3-oxazepines upon treating with 12 under the same conditions resulted in complete recovery of the starting substances.

The authors are indebted to Dr. Y. Yamashita and Mr. T. Abe and T. Maruyama for their experimental assistance.

References and Notes
1. Dedicated to Professor Tetsuo Nozoe on the occasion of his 77th birthday.

---335--
   M. Ishikawa and C. Kaneko, Kagaku no Ryoiki (J. Japanese Chemistry),
   Nankodo, Tokyo, 1970, supplement Issue, 92, p 149.
   1873. M. Ishikawa, C. Kaneko, I. Yokoe, and S. Yamada, Tetrahedron,
   1969, 25, 295.
9. All pyrylium fluoroborates were prepared by the modified method of
10. All new compounds gave satisfactory elemental analyses.
    423.

Received, 5th September, 1978