SYNTHESIS OF THE CLAVINE SKELETONS
BY PHOTOCYCLISATION OF N-METHACRYLNNAPHTHALIDES

Ichisa Ninomiya*, Toshiko Kiguchi, and Takeaki Naito

Kobe Women's College of Pharmacy
Motoyamakita, Higashinada, Kobe, Japan

Photocyclisation of N-methacrylnaphthalides (Ia-d, and VIII), prepared from various 2-naphthylamines and 4-aminonaphthostyril, afforded the benzo[f]quinolones (IIa-d) and indolo[4,3-f,g]quinoline-5,8-dione (IX), providing a route for the preparation of the clavine alkaloids.

Unsaturated acylanilides are known to undergo facile photocyclisation to afford the quinoline skeletons\(^1,2\). This reaction is particularly useful for the preparation of quinolines and phenanthridines.\(^3\) As an extension of this photocyclisation, we now report facile photocyclisation of N-methacrylnaphthalides which would offer an useful route for the preparation of the skeleton of the clavine alkaloids.
N-Methacrylnaphthalides (Ia–d), which were prepared from various 2-naphthylamines and methacryloyl chloride, were readily photocyclised in a benzene solution by irradiation of a low pressure mercury lamp at room temperature to afford the corresponding benzo[f]quinolones (IIa–d) in good yields as summarised in the scheme. Since examples of introduction of a nitro group into the peri position (7) to a carboxyl group were known, we attempted nitration of the photocyclised product (IId). However, the nitro group was introduced not into the desired position but 8- and 10-positions (IIla,b,c). Therefore, in order to prepare the compound having the skeletal structure of clavines, the mono-nitro derivative (IIla) was employed for further transformation, that is, reduction with Raney-nickel and hydrazine converted (IIla) into the 10-aminobenzof[f]quinolone (IV) which was then acetylated. Nitration of the acetamido derivative (V) afforded the mono-nitro product (VI) which was then transformed by reduction with Raney-nickel and hydrazine into the corresponding indolo[4,3-f,g]quinoline-5,8-dione (VII), m.p. > 300°, which exhibited i.r. absorptions at 3300-3100 (NHx2) and 1690-1640 (NCOx3) and n.m.r. peaks at 7.87 (1H, s, 6-H), 7.25 and 6.91 (2H, each d, J 7Hz, 2- and 3-H), 3.43 (3H, s, NMe), 2.10 (3H, s, COMe), and 1.18 (3H, d, J 6.5Hz, CMe), thus proving the position of a nitro group as shown.

However, the above result, which seemed not so useful as a preparative method for the clavine structures though its basic skeleton was prepared, pushed us to investigate photocyclisation of N-methacrylamide (VIII), which was prepared by acylation of 4-aminonaphthostyril with methacryloyl chloride in good yield.
Irradiation Yield

<table>
<thead>
<tr>
<th>R_1</th>
<th>R_2</th>
<th>Time(hr)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>46</td>
<td>59</td>
</tr>
<tr>
<td>Me</td>
<td>H</td>
<td>17</td>
<td>50</td>
</tr>
<tr>
<td>H</td>
<td>CO_2Me</td>
<td>96</td>
<td>42.5</td>
</tr>
<tr>
<td>Me</td>
<td>CO_2Me</td>
<td>26</td>
<td>48</td>
</tr>
</tbody>
</table>

Nitration Yield (%)

<table>
<thead>
<tr>
<th>R_1</th>
<th>R_2</th>
<th>90%</th>
<th>60%</th>
<th>70%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNO_3 HNO_3 HNO_3-AC_2O</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>NO_2</td>
<td>27</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>NO_2 H</td>
<td>35</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO_2 NO_2</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- (II) R_1 R_2
- (III) R_1 R_2
- (IV)
- (V)
- (VI)
- (VII)
- (VIII)
- (IX)
- (X)
Irradiation of the naphthalide (VIII) in a benzene solution in the presence of acetic acid (15:1) over 96 hrs. afforded the corresponding photocyclised product (IX) in 42% yield, which exhibited i.r. absorptions at 3400 (NH), 1710 (NCO), and 1655 (NCO) and n.m.r. peaks at δ 10.63 (1H, br s, NH), 7.82 (1H, s, 6-H), 7.63 (1H, d-d, J 9 and 2Hzs, 3-H), 7.50 (1H, d-d, J 9 and 6Hzs, 2-H), 6.90 (1H, d-d, J 6 and 2Hzs, 1-H), 3.45 (3H, s, NMe), and 1.25 (3H, d, J 7Hz, CMe). Lithium aluminium hydride reduction of (IX) followed by acetylation afforded the compound (X) in good yield, which has the structure of clavines.

REFERENCES
1 N.m.r. spectra were measured in DMSO-d₆ solution.

Received, 18th February, 1976