DDQ OXIDATION OF SOME ERYTHRINAN ENONES AND DIENONES:
SYNTHESES OF (+)-ERYTHARBINE AND (−)-CRYSTAMIDINE

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Abstract—DDQ oxidation of 3,8-dioxoerythrinan-1(6)-ene 1 in
dioxane gave the ring C/D oxidized product, the dienone 2, while
that of 3,8-dioxoerythrinan-1-ene 4 gave the ring B dehydrogenated
product 5. The either product was convertible to the same trienone
3 on further oxidation in different solvents. The trienone 3a and
3b were transformed by a conventional procedure to the highly
dehydrogenated oxo-erythrinan alkaloids, erytharbine 8a and
cristamidine 8b, respectively.

During our synthetic work on erythrinan alkaloids,1 we have observed interesting
solvent and structure dependence on DDQ oxidation of some erythrinan enones and
dienones.

The enone-a 1a1, when heated with an excess of DDQ (7 eq.) in dioxane at 110°C
for 5 h, gave the dienone 2a2, mp 193-195°C, in 29% yield. On the other hand,
it gave the trienone 3a, gum3, as a major product together with minute amount of
the dienone 2a on a similar oxidation in benzene (130°C, 3 h). In the latter
solvent, it was difficult to isolate the dienone 2a, since the trienone 3a was
always formed predominantly even when the starting material remained in the
reaction mixture.

In contrast, the isomeric enone-b 4a1, on a similar treatment with DDQ either in
dioxane or benzene (110°C, 1.5 h), suffered the oxidation at different position
to give the isomeric dienone 5a3, mp 243-247°C, in 59% yield with recovery of
the starting material (23%). However, oxidation of 4a in t-BuOH (110°C, 2 h) directly produced the trienone 3a, though the yield was not satisfactory (ca. 5%).

Based on the above evidence the diene 2b was oxidized in benzene with 10 eq. of DDQ (130°C, 12 h) to yield the trienone 3b, mp 192-193°C, as expected (28%). Other solvents such as methanol, dioxane, and dichloromethane did not give a satisfactory result.

\[
\text{DDQ in benzene} \\
\begin{align*}
\text{RO} & \text{RO} \\
\text{N} & \text{FO} \\
\text{2} & \text{10} \text{8} \\
\text{DDQ} & \text{DDQ} \\
\text{11} & \text{12} \text{17} \\
\text{in dioxane} & \text{in benzene} \\
\text{RO} & \text{RO} \\
\text{N} & \text{FO} \\
\text{3} & \text{3} \\
\text{DDQ in t-BuOH} \\
\text{RO} & \text{RO} \\
\text{N} & \text{FO} \\
\text{5} & \text{4} \\
\text{DDQ} & \text{DDQ} \\
\text{in dioxane or benzene} \\
\end{align*}
\]

\[a: R=\text{CH}_3 \quad b: R-R=\text{-CH}_2-\]

Chart 1

The trienones 3a and 3b were converted to the highly dehydrogenated oxo-erythrinan alkaloids, erytharine 8a and crystamidine 8b, which were isolated from leaves of *Erythrina arborescens* Roxb. and *Erythrina crystagalli* L., respectively.

Meerwein-Ponndorf reduction of the trienone (3a or 3b) with alumin isopropoxide in isopropanol (reflux, 4-5 h) afforded the 3α-ol (6a or 6b) and the epimeric 3β-ol (7a or 7b) in a ratio of ca. 7:3-6:4, respectively, which were separated by preparative TLC. Methylation of each product with CH₃I/KOH/Et₄NBr in tetrahydrofuran (r.t., 20-40 h) gave the corresponding methyl-ether 8a, 8b, 9a, and 9b, respectively.

The methyl-ethers 8a and 8b were identical in their spectral behaviors (IR, UV, and ¹H-NMR) with the authentic samples of (+)-erytharine and (+)-crystamidine, respectively, provided by Prof. Ito and Dr. Haruna, thus accomplishing the first
Table I. $^1$H-NMR Chemical Shifts of The Aromatic and Olefinic Protons

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Ar-H</th>
<th>C$_1$-H</th>
<th>C$_2$-H</th>
<th>C$_7$-H$^a$</th>
<th>C$_{10}$-H$^b$</th>
<th>C$_{11}$-H$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>6.30, 6.56</td>
<td>6.06 (m)</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>4a</td>
<td>6.58, 6.64</td>
<td>7.04 (dd 10,5)</td>
<td>6.29 (dd 10,2)</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>2a</td>
<td>6.64, 6.84</td>
<td>7.75 (dd 10,1)</td>
<td>6.40 (d 10)</td>
<td>6.35</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>2b</td>
<td>6.65, 6.77</td>
<td>7.76 (dd 10,1)</td>
<td>6.37 (d 10)</td>
<td>6.39</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>3a</td>
<td>6.60, 6.74</td>
<td>7.85 (dd 10,1)</td>
<td>6.37 (d 10)</td>
<td>6.46</td>
<td>6.90</td>
<td>6.16</td>
</tr>
<tr>
<td>3b</td>
<td>6.66, 6.71</td>
<td>7.83 (dd 10,1)</td>
<td>6.36 (d 10)</td>
<td>6.46</td>
<td>6.90</td>
<td>6.13</td>
</tr>
<tr>
<td>5a</td>
<td>6.62, 6.66</td>
<td>7.20 (dd 10,5)</td>
<td>6.29 (d 10)</td>
<td>-----</td>
<td>6.85</td>
<td>6.02</td>
</tr>
<tr>
<td>6a</td>
<td>6.67, 6.76</td>
<td>6.32 (d 10)</td>
<td>6.98 (dd 10,2)</td>
<td>6.09</td>
<td>6.91</td>
<td>6.16</td>
</tr>
<tr>
<td>6b</td>
<td>6.68, 6.71</td>
<td>6.29 (d 10)</td>
<td>6.91 (dd 10,2)</td>
<td>6.07</td>
<td>6.88</td>
<td>6.10</td>
</tr>
<tr>
<td>7a</td>
<td>6.77, 6.88</td>
<td>6.97 (d 10)</td>
<td>6.32 (dd 10,5)</td>
<td>6.04</td>
<td>6.88</td>
<td>6.13</td>
</tr>
<tr>
<td>7b</td>
<td>6.72, 6.88</td>
<td>6.93 (d 10)</td>
<td>6.28 (dd 10,5)</td>
<td>6.02</td>
<td>6.85</td>
<td>6.08</td>
</tr>
<tr>
<td>8a</td>
<td>6.66, 6.75</td>
<td>6.32 (d 10)</td>
<td>6.95 (dd 10,2)</td>
<td>6.07</td>
<td>6.90</td>
<td>6.14</td>
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<tr>
<td>8b</td>
<td>6.69, 6.72</td>
<td>6.31 (d 10)</td>
<td>6.91 (dd 10,2)</td>
<td>6.06</td>
<td>6.89</td>
<td>6.10</td>
</tr>
<tr>
<td>9a</td>
<td>6.65, 6.87</td>
<td>6.95 (d 10)</td>
<td>6.30 (dd 10,5)</td>
<td>6.00</td>
<td>6.82</td>
<td>6.09</td>
</tr>
<tr>
<td>9b</td>
<td>6.64, 6.87</td>
<td>6.94 (d 10)</td>
<td>6.28 (dd 10,5)</td>
<td>6.01</td>
<td>6.82</td>
<td>6.07</td>
</tr>
</tbody>
</table>

a): singlet.  b): doublet, J=7 Hz.
total syntheses of these natural alkaloids.

ACKNOWLEDGEMENT

The authors thank Prof. Ito and Dr. Haruna, Meijo University, for providing the spectral data of the natural alkaloids.

REFERENCES AND NOTES


3. Unless otherwise stated, IR spectra were taken in CHCl₃ (cm⁻¹), UV in EtOH (λmax nm (log ε)), and NMR in CDCl₃ (δ).

   3a: 309 (M⁺); IR: 1710, 1690; UV: 246 (4.13), 277 (4.15).

   3b: IR (Nujol): 1700, 1670; UV: 246 (4.28), 276 (4.31), 418 (3.22).

   5a: 311 (M⁺); IR (KBr): 1710, 1690; UV: 230 (4.39), 319 (4.04).

   6a: mp 257-259°C; IR: 1690; UV: 267 (4.47), 360 (3.34).

   6b: mp 219-220°C; IR (Nujol): 1650; UV: 228 (4.35), 265 (4.38), 360 (3.44).

   7a: gum; IR: 1690. 7b: gum; IR: 1680.

   8a: gum; IR: 1685; UV: 225 (4.32), 266 (4.32), 355 (3.25).

   8b: gum; IR: 1680; UV: 228 (4.28), 264 (4.29), 357 (3.35).

   9a: gum; IR: 1690; UV: 230 (4.27), 255 (4.11), 370 (2.98).

   9b: gum; IR: 1690; UV: 225 (4.37), 255 (4.24), 368 (3.28).


   b) Idem, ibid., 1973, 93, 1617.


Received, 25th June, 1984