DDQ OXIDATION OF SOME ERYTHRINAN ENONES AND DIENONES: SYNTHESES OF (±)-ERYTHARBINE AND (±)-CRYSTAMIDINE[1]

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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 crystamidine **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 **1a**[1], when heated with an excess of DDQ (7 eq.) in dioxane at 110°C for 5 h, gave the dienone **2a**[2], mp 193-195°C, in 29% yield. On the other hand, it gave the trienone **3a**, gum[3], 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 **4a**[1], 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 **5a**[3], 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 dienone **2b**[2] was oxidized in benzene with 10 eq. of DDQ (130°C, 12 h) to yield the trienone **3b**[3], mp 192-193°C, as expected (28%). Other solvents such as methanol, dioxane, and dichloromethane did not give a satisfactory result.

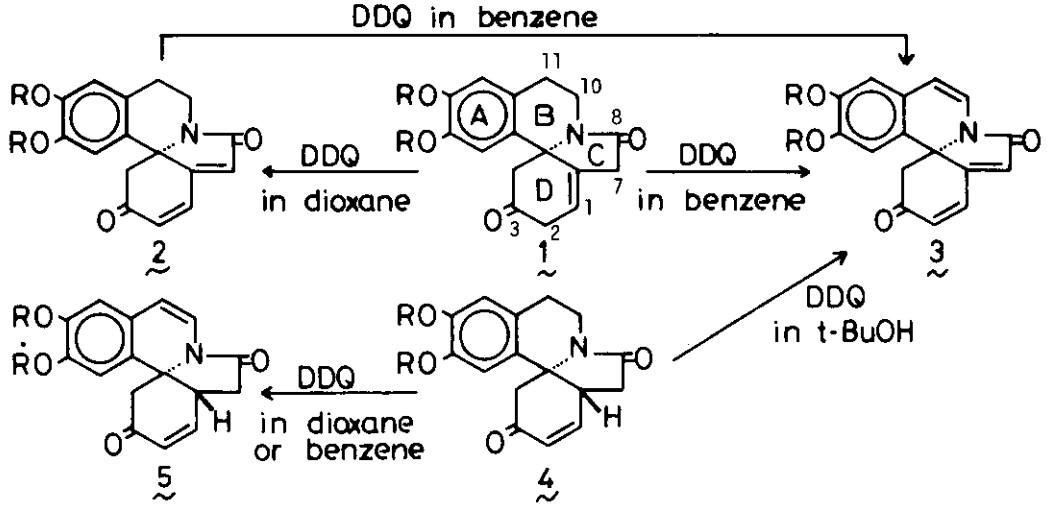

Chart 1

The trienones **3a** and **3b** were converted to the highly dehydrogenated oxo-erythrinan alkaloids, erytharbine **8a**[4] and crystamidine **8b**[5], which were isolated from leaves of Erythrina arborescens Roxb. and Erythrina crysta-galli L., respectively.

Meerwein-Ponndorf reduction of the trienone (**3a** or **3b**) with alminum isopropoxide in isopropanol (reflux, 4-5 h) afforded the 3α-ol (**6a** or **6b**)[3] and the epimeric 3β-ol (**7a** or **7b**)[3] in a ratio of ca. 7:3—6:4, respectively, which were separated by preparative TLC. Methylation of each product with CH_3I/KOH/Et_4NBr in tetrahydrofuran[2] (r.t., 20-40 h) gave the corresponding methyl-ether **8a**[3], **8b**[3], **9a**[3], and **9b**[3], respectively.

The methyl-ethers **8a** and **8b** were identical in their spectral behaviors (IR, UV, and ^{1}H-NMR) with the authentic samples of (+)-erytharbine and (+)-crystamidine, respectively, provided by Prof. Ito and Dr. Haruna, thus accomplishing the first

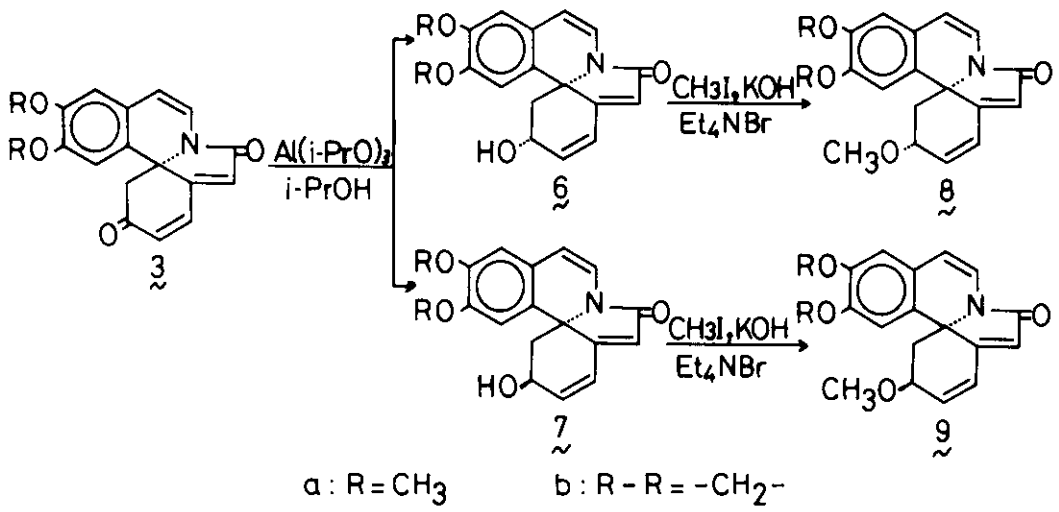

Chart 2

Table I. ^{1}H-NMR Chemical Shifts of The Aromatic and Olefinic Protons

Compd.	Ar-H	C_1-H	C_2-H	C_7-H[a]	C_{10}-H[b]	C_{11}-H[b]
1a	6.30, 6.56	6.06 (m)	----	----	----	----
4a	6.58, 6.64	7.04 (dd 10,5)	6.29 (dd 10,2)	----	----	----
2a	6.64, 6.84	7.75 (dd 10,1)	6.40 (d 10)	6.35	----	----
2b	6.65, 6.77	7.76 (dd 10,1)	6.37 (d 10)	6.39	----	----
3a	6.60, 6.74	7.85 (dd 10,1)	6.37 (d 10)	6.46	6.90	6.16
3b	6.66, 6.71	7.83 (dd 10,1)	6.36 (d 10)	6.46	6.90	6.13
5a	6.62, 6.66	7.20 (dd 10,5)	6.29 (d 10)	----	6.85	6.02
6a	6.67, 6.76	6.32 (d 10)	6.98 (dd 10,2)	6.09	6.91	6.16
6b	6.68, 6.71	6.29 (d 10)	6.91 (dd 10,2)	6.07	6.88	6.10
7a	6.77, 6.88	6.97 (d 10)	6.32 (dd 10,5)	6.04	6.88	6.13
7b	6.72, 6.88	6.93 (d 10)	6.28 (dd 10,5)	6.02	6.85	6.08
8a	6.66, 6.75	6.32 (d 10)	6.95 (dd 10,2)	6.07	6.90	6.14
8b	6.69, 6.72	6.31 (d 10)	6.91 (dd 10,2)	6.06	6.89	6.10
9a	6.65, 6.87	6.95 (d 10)	6.30 (dd 10,5)	6.00	6.82	6.09
9b	6.64, 6.87	6.94 (d 10)	6.28 (dd 10,5)	6.01	6.82	6.07

a): singlet. b): doublet, J=7 Hz.

total syntheses of these natural alkaloids.

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3. Unless otherwise stated, IR spectra were taken in $CHCl_3$ (cm^{-1}), UV in EtOH [λmax nm(log ε)], and NMR in $CDCl_3$ (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(2.90).
   9b: gum; IR: 1690; UV: 225(4.37), 255(4.24), 368(3.28).
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