Studies toward Total Synthesis of Non-aromatic *Erythrina* Alkaloids. (5). Cyclization of Perhydro-2-epoxymethylene-6-oxo-6*H*-pyrido[2,1-*i*]indole-1-acetic Acid: Synthesis of 8-Oxoerythroidans[1)]

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Treatment of the epoxy-acid (7) with acidic reagents produced a variety of products, hydroxy-γ- and δ-lactones (8 and 9), unsaturated δ-lactones (10, 11, and 18), and seco derivatives (15 and 17), depending on the reagents used. Alkaline hydrolysis of the hydroxy-γ-lactone (8) followed by acidification yielded an isomeric δ-lactone 21, which on further contact with acid regenerated the γ-lactone (8). The hydroxy-δ-lactones, 9 and 21, were stereoselectively dehydrated with thionyl chloride–pyridine to the unsaturated lactones, 18 and 10, respectively. Thus, successive treatments of the epoxy-acid (7) with NaOH, acidification, and dehydration of the product with thionyl chloride–pyridine gave 10 in an overall yield of 86%, and 10 was isomerized to the conjugated lactone (22) on treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene. For the above unsaturated δ-lactones, 22, 10, 11, and 18, the names α-, β-, γ-, and δ-erythroidans are proposed, respectively.

Keywords *Erythrina* alkaloid; erythroidine; erythroidine skeleton; erythroidan; stereoselective synthesis; interconversion; hydroxy-lactone; unsaturated δ-lactone

In a previous paper,[2)] we showed that the epoxy-ester having the illustrated stereochemistry **1** gave, on treatment with acids, a mixture of bicyclic γ- and δ-lactones (A and B), which are the products of attack by nucleophiles on *exo*-methylene or spiro carbon of the protonated oxirane ring. On the other hand, treatment of **1** with pyridinium *p*-toluenesulfonate (PPTS) resulted in, together with the product A (**2**), an aldehyde **3** and unsaturated δ-lactones, **4** and **5**, which could be derived from the carbocation intermediate C.

For the application of this cyclization method to the synthesis of natural non-aromatic *Erythrina* alkaloids [such as β-erythroidine (**6**)], it is necessary to prepare the epoxy-ester (or the corresponding acid) of the tricyclic structure. A model compound of established stereochemistry, *rel*-[1*R*,-2*S*,7a*R*,11a*R*]-1,2,3,4,7,7a,8,9,10,11-decahydro-2-epoxymethylene-6-oxo-6*H*-pyrido[2,1-*i*]indole-1-acetic acid (**7**) is now available, which was prepared from D-furano-8-oxoerythrinan in three steps with high overall yield; its structure was definitively established by an X-ray crystallographic analysis.[3)]

This paper deals with cyclization of this acid (**7**) with various reagents and describes syntheses of erythroidine skeletons (erythroidans) of natural (α and β) and unnatural type (γ and δ) as their 8-oxo derivatives.

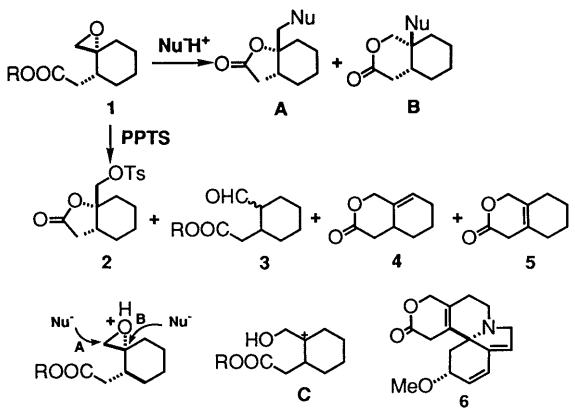

Chart 1

Results and Discussion

Reaction of the Epoxy-Acid (7) with Acidic Reagents As suggested already,[3)] treatment of **7** with MeOH–HCl did not give any unsaturated δ-lactone. Instead, the product was a complex mixture of saturated lactones due to the attack of Cl^-, OMe^-, and OH^-, as anticipated from the model experiment.[2)] Therefore other reagents were examined for the selective cyclization of **7** to unsaturated δ-lactones.

Treatment of **7** with 2% H_2SO_4 produced two isomeric hydroxy-lactones, *cis*-γ-lactone (**8**) and *cis*-δ-lactone (**9**), in yields of 30 and 23%. Although they were inseparable on thin-layer chromatography (TLC), good separation was achieved by recycling high-performance liquid chromatography (HPLC). The major product **8** was a γ-lactone as suggested from the infrared (IR) absorption at 1765 cm^{-1}, and exhibited ABq peaks at δ 3.63 and 3.54 with $J=12$ Hz in the ^{1}H-nuclear magnetic resonance (NMR) spectrum. The other product was assigned as the hydroxy δ-lactone (**9**), since it gave an IR absorption at 1713 cm^{-1}, and ^{1}H-NMR peaks at δ 4.48 and 4.19 as an ABq of $J=13$ Hz, which can be attributed to CH_2OCO. These compounds

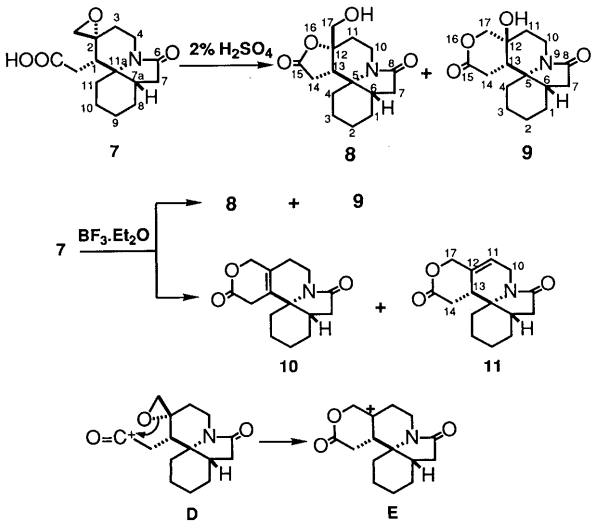

Chart 2

are the products of attack of H_2O at the methylene and the spiro carbon of the oxirane ring, respectively, as expected from the model experiment.[2] The stereochemistry of these compounds is discussed in a later section.

Reaction of **7** with boron trifluoride etherate in methylene chloride produced four compounds: a mixture of saturated lactones (**8** and **9**, 44% yield) and a mixture of unsaturated δ-lactones (**10** and **11**, 32% yield). The hydroxy-lactones are considered to be produced by attack of BF_3 and OH^- (generated from the COOH group) on the oxirane ring, and the unsaturated lactones are considered to be the products formed through the intermediate E. (For the structures of **10** and **11**, see below.)

Heating of **7** with PPTS in benzene at 120 °C produced a complex mixture, from which six compounds (**10**, **11**, **12**, **15**, **17**, and **18**) were isolated by a combination of preparative TLC (PTLC) and recycling HPLC (see Experimental). A major product **11** (26% yield) was proved to be an unsaturated δ-lactone (IR: 1734 cm^{-1}) with the double bond at C11–C12, as follows. In the ^{1}H-NMR spectrum, the olefinic proton appeared at δ 5.76 as a singlet, showing the abscence of coupling with vicinal protons. In accordance with this, two C-10 protons appeared at δ 4.55 and 3.40, both as doublets. Two C-17 protons appeared at δ 4.75 and 4.65 as an ABq of $J=13$ Hz, and the protons at C-14 as two doublet-of-doublets at δ 2.25 and 2.17. Since this compound is considered to be produced through the carbocation intermediate E and since stereochemical inversion at C-13 during the process is not plausible, the stereochemistry of 13-H is assigned as β-configuration. For this compound, we propose the name "γ-erythroidan."

The second unsaturated δ-lactone (**10**, 5% yield) was identical with β-erythroidan previously reported.[3]

The third unsaturated δ-lactone (**18**, 2% yield) exhibited an olefinic proton signal at δ 6.53 as a singlet and showed no CH_2O signal. The protons vicinal to the lactonic carbonyl group appeared as two doublet-of-doublets at δ 2.88 and 2.72. Thus, the enol lactone structure **18** was assigned to this compound, for which we propose the name "δ-erythroidan." δ-Erythroidan (**18**) was probably produced by either of the following processes: from the carbocation intermediate E together with β- and γ-erythroidans or from the *cis*-tosyloxy-δ-lactone (**13**) by direct elimination of tosic acid.[4]

The fourth compound (8% yield) was a γ-lactone **12** carrying a tosyl group, which is also predictable from the model experiment.[2] The γ-lactone absorption at 1786 cm^{-1} in the IR spectrum, CH_2O signals at δ 3.92 (2H, s) and a tosyl group [δ 7.76, 7.38 (each 2H, d) and 2.47 (3H, s)] in the ^{1}H-NMR spectrum suggested the illustrated structure, which was confirmed by tosylation of **8** to **12**, as expected.

The fifth and sixth compounds, **15** and **17** (2% and 4%, respectively), are isomeric to erythroidans in their formulae, but they showed two olefinic protons [δ 5.62 (s) and 4.80 (t) for **15** and 5.75 (s) and 5.62 (s) for **17**] in the ^{1}H-NMR spectra. In addition to the presence of similar olefinic protons (at δ 5.62 in both compounds), similarity of the signals attributable to ring D protons [OCH_2: δ 4.85 and 4.80 for **15** and δ 4.87 and 4.81 for **17**, and CH_2CO: δ 3.05 (br s) for **15** and δ 3.06 (br s) for **17**] suggested that they have a similar structure for this ring.

The H–H and H–C chemical shift correlation spectra (COSY) of **17** revealed that it is a seco derivative, as follows. Compound **17** showed a secondary carbon signal at δ 61.9 (d). The proton (δ 3.70, dd) attached to this carbon is correlated to high field protons at δ 2.42 and 1.07, assignable to H-4, thus revealing the partial structure CH_2–CH–N–CO. The ultraviolet (UV) absorption at 213 nm ($\varepsilon=6900$) and a singlet olefinic proton signal (δ 5.75) in the ^{1}H-NMR spectrum indicated the position of the second double bond to be at C6–C7. These findings are consistent with the seco-erythroidan structure **17** for this compound.

In compound **15**, the second olefinic proton appeared at δ 4.80 as a triplet of $J=4$ Hz. This evidence, together with the similarity of the ring D proton pattern to that of **17**, suggested the seco-erythroidan structure **15** for this compound.

We assume that these compounds were produced from the expected angularly substituted tosylate **13** through the concerted process shown in F. The initially produced

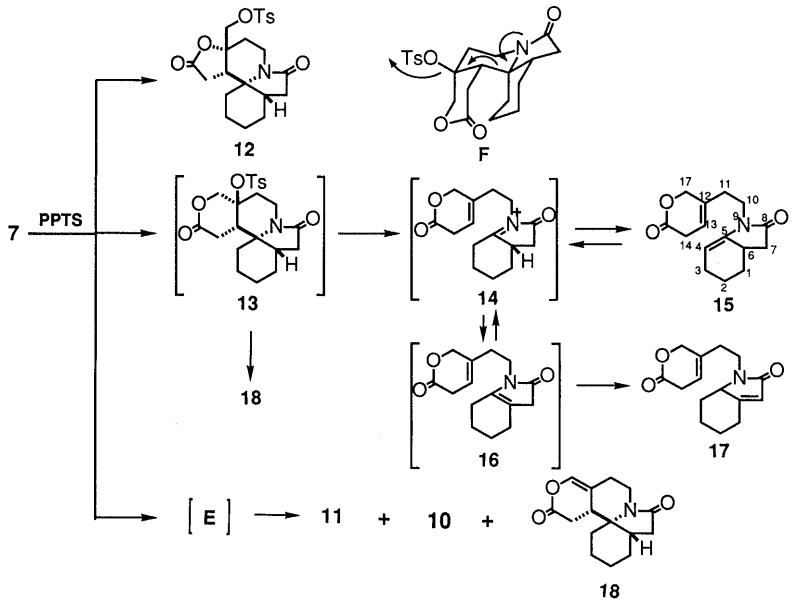

Chart 3

TABLE I. ^{13}C-NMR Spectral Data for 8-Oxoerythroidans (125 MHz in $CDCl_3$)

Carbon No.	22 (α)	10 (β)	11 (γ)	18 (δ)	17
1	19.7 (t)[a]	19.6 (t)[a]	19.8 (t)[a]	19.1 (t)[a]	33.3 (t)
2	20.7 (t)[a]	19.7 (t)[a]	21.3 (t)[a]	20.6 (t)[a]	23.0 (t)[a]
3	26.2 (t)[a]	23.9 (t)[a]	24.3 (t)[a]	24.1 (t)[a]	27.4 (t)[a]
4	26.4 (t)[a]	26.2 (t)[a]	28.5 (t)[a]	28.1 (t)[a]	28.4 (t)[a]
5	62.3 (s)	61.4 (s)	61.6 (s)	65.2 (s)	61.9 (d)
6	31.2 (d)	34.3 (d)	34.5 (d)	28.3 (d)	162.1 (s)
7	34.3 (t)[b]	31.1 (t)	31.3 (t)	29.4 (t)[b]	118.3 (d)[b]
8	164.3 (s)	168.8 (s)	171.7 (s)	166.4 (s)	169.1 (s)
10	35.3 (t)[b]	33.1 (t)	38.2 (t)	33.9 (t)[b]	37.9 (t)
11	32.8 (t)[b]	36.2 (t)	121.0 (d)	36.6 (t)[b]	31.8 (t)
12	35.5 (d)	130.6 (s)	129.0 (s)	113.8 (s)	131.8 (s)
13	160.5 (s)	124.2 (s)	40.1 (d)	43.6 (d)	117.6 (d)[b]
14	114.9 (d)	30.6 (t)	37.1 (t)	38.1 (t)	30.2 (t)
15	171.9 (s)	173.9 (s)	174.4 (s)	174.2 (s)	171.6 (s)
17	70.0 (t)	70.4 (t)	70.1 (t)	135.9 (d)	70.8 (t)

a, b) Assignments may be interchanged in each column.

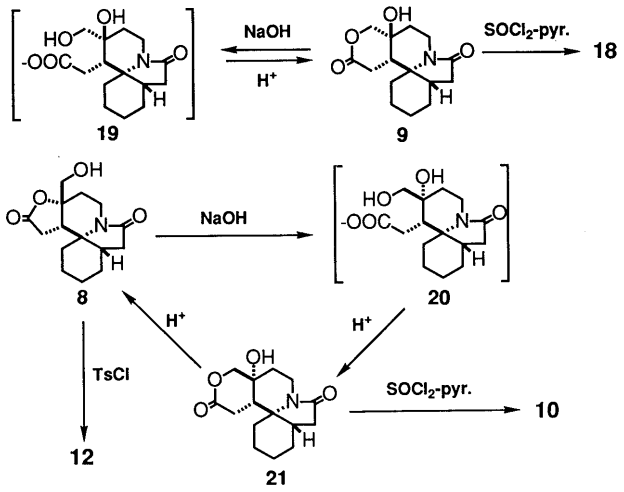

Chart 4

iminium salt (**14**) would have been isomerized to **15** and to **17** through the *endo* cyclic intermediate (**16**).

Stereochemistry and Interconversion of the Hydroxy-Lactones When the hydroxy-γ-lactone (**8**) was hydrolyzed with 10% NaOH and the hydrolysate was carefully acidified, a new lactone (**21**) was produced almost quantitatively. This new lactone was isomeric to **8** and showed IR absorption at 1722 cm^{-1} and CH_2O peaks at δ 4.13 and 4.04 as an ABq in the ^{1}H-NMR spectrum, indicating the hydroxy-δ-lactone structure (**21**). Contact of this compound with 2% H_2SO_4 overnight at room temperature quantitatively regenerated the original γ-lactone (**8**). The above interconversion reactions indicate that the diol acid (**20**) produced by alkaline hydrolysis of **8** rapidly cyclizes to the kinetically controlled product, the δ-lactone (**21**) of *trans* configuration, then slowly isomerizes into the thermodynamically more stable γ-lactone (**8**) of *cis* configuration, thus revealing their stereochemistry. In accord with this stereochemistry, the *trans*-δ-lactone (**21**) was dehydrated with thionyl chloride–pyridine to give exclusively β-erythroidan (**10**).

In contrast to **8**, alkaline hydrolysis of **9** followed by acidification of the hydrolysate regenerated the original δ-

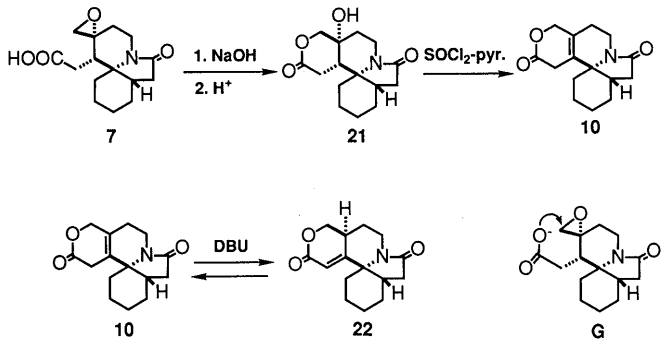

Chart 5

under the plasma drug concentration–time curve (*AUC*) was lactone (**9**). This was stable to a similar acid treatment, indicating that it is the thermodynamically more stable *cis* isomer rather than the corresponding γ-lactone of *trans* stereochemistry. Dehydration of **9** with thionyl chloride in pyridine produced δ-erythroidan (**18**) exclusively, in accord with the assigned stereochemistry, in which 12-OH and 13-H are in *cis* relationship.

Selective Synthesis of α- and β-Erythroidans The above interconversion reactions indicate that, if the diol-acid (**21**) can be produced exclusively, selective synthesis of β-erythroidan (**10**) from the epoxy-acid (**7**) will be achieved effectively. Keeping this idea in mind, the epoxy-acid (**7**) was heated with 10% NaOH at 120 °C, since we thought that the reaction might proceed through an intramolecular attack of the carboxylate ion on the methylene carbon of the oxirane ring (*cf.*, the intermediate G). Careful acidification and extraction of the reaction mixture gave the *trans* hydroxy-δ-lactone (**21**) almost quantitatively, as expected. This was dehydrated with thionyl chloride in pyridine to give β-erythroidan (**10**) in an overall yield of 86% from **7**, thus completing a high yield and selective synthesis of β-erythroidan.

β-Erythroidan (**10**), when heated with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in benzene at 120 °C, isomerized into the conjugated δ-lactone **22** (α-erythroidan), as expected from the model experiment,[2] to give a 2:3 mixture of **10** and **22**. They were separated by recycling HPLC and the structure of **22** was supported by the UV, IR, and NMR spectra. The stereochemistry of 12-H in **22** must be α, since, otherwise, the compound would have severe steric strain.

The above transformation is a most efficient route to β- and α-erythroidans from the epoxy-acid (**7**) and should be applicable to the synthesis of natural α- and β-erythroidines.

Experimental

General Unless otherwise stated, the following procedures were adopted. Melting points were determined on a Yanaco micro hot stage melting point apparatus and are uncorrected. IR spectra were taken in $CHCl_3$ solutions and are given in cm^{-1}. ^{1}H-NMR spectra were taken with a JEOL GSX500 (500 MHz) spectrometer in $CDCl_3$ solution with tetramethylsilane as an internal standard, and the chemical shifts are given in δ values. Mass spectra (MS) and high-resolution MS (HRMS) were taken with a Hitachi M-80 machine and M^+ and/or major peaks are indicated as *m/z* (%). Column chromatography was performed on Wakogel C-200 (silica gel). For PTLC, Merck precoated plates GF_{254} (0.5 mm thick) were used and spots were monitored under UV light (254 nm). Recycling HPLC was performed with a Nihon Bunseki Kogyo LC-908 apparatus on an octadecyl silica (ODS) column (20 × 250 mm) with 50% MeOH–H_2O as a mobile phase, and peaks were collected by monitoring

with both UV and refractive index detectors. All organic extracts were washed with brine and dried over anhydrous sodium sulfate before concentration. Identities were confirmed by mixed melting point determination (for crystalline compounds) and also by comparisons of TLC behavior and ^{1}H-NMR and IR spectra.

Reaction of the Epoxy-Acid (7) with Sulfuric Acid The acid **7** (56 mg) was dissolved in a limited amount of 3% NaOH and the solution was immediately acidified with 2% H_2SO_4 (5 ml). The mixture was stirred at room temperature for 2 d (during which time precipitates dissolved), and then extracted with $CHCl_3$–MeOH. The product obtained from the extract was purified by recycling HPLC to give **8** (17 mg, 30%) and **9** (13 mg, 23%).

cis-Hydroxy-γ-lactone (**8**): Colorless gum. IR: 3390, 1765, 1668. ^{1}H-NMR: 3.70 (1H, dt, J=14, 8 Hz, H-10β), 3.63, 3.54 (each 1H, d, J=12 Hz, H-17), 3.21 (1H, dt, J=14, 6.5 Hz, H-10α), 2.63 (2H, m, H-11), 2.45 (1H, dd, J=17, 8 Hz, H-14), 2.28 (1H, dd, J=17, 7 Hz, H-14), 2.06 (1H, dd, J=8, 7 Hz, H-13). HRMS: Calcd for $C_{15}H_{21}NO_4$: 279.1469. Found: 279.1431.

cis-Hydroxy-δ-lactone (**9**): Colorless prisms from MeOH, mp 217—218 °C. IR (KBr): 3265, 1713, 1658. ^{1}H-NMR (CD_3OD): 4.48 (1H, d, J=13 Hz, H-17), 4.19 (1H, dd, J=13, 1 Hz, H-17), 3.79 (1H, dt, J=14, 6.5 Hz, H-10β), 2.97 (1H, dddd, J=14, 8, 5.5, 1 Hz, H-10α), 2.59 (1H, dd, J=17, 8.5 Hz, H-14), 2.55 (1H, dd, J=17, 6 Hz, H-14), 2.06 (1H, dd, J=8.5, 6 Hz, H-13), 1.89 (1H, ddd, J=15, 6.5, 5.5 Hz, H-11α), 1.62 (1H, ddd, J=15, 8, 6.5 Hz, H-11β). MS: 279 (M^+, 65), 265 (25), 248 (26), 236 (100), 223 (16), 202 (17), 165 (60), 164 (76), 151 (61), 150 (68), 137 (99). *Anal.* Calcd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58; N, 5.01. Found: C, 64.28; H, 7.61; N, 4.96. HRMS: Calcd for M^+: 279.1469. Found: 279.1473.

Reaction of the Acid (7) with Boron Trifluoride Etherate A mixture of **7** (51 mg) and $BF_3 \cdot Et_2O$ (50 mg) in CH_2Cl_2 (5 ml) was heated under reflux for 2 h. The cooled mixture was poured into saturated $NaHCO_3$ solution and extracted with CH_2Cl_2–MeOH. The product obtained by concentration of the extract was firstly separated by chromatography on silica gel to a mixture of hydroxy-lactones (**8** and **9**, 23 mg) and a mixture of unsaturated lactones (**10** and **11**, 16 mg). Each mixture was further separated by recycling HPLC to yield **8** (16 mg, 31%), **9** (3 mg, 6%), **10** (6.5 mg, 13%), and **11** (8 mg, 16%).

Reaction of the Acid (7) with Pyridinium *p*-Toluenesulfonate A mixture of **7** (200 mg) and PPTS (250 mg) in benzene (5 ml) was heated in a sealed tube at 120 °C for 5 h. The mixture was diluted with benzene, washed with 5% HCl and saturated $NaHCO_3$ solution, and concentrated. The residue was separated by PTLC into four zones by monitoring the UV (254 nm) absorption, and each zone was further separated by recycling HPLC. The least mobile zone (UV-positive) gave the seco derivative **17** (7 mg, 4%). The second zone (UV-negative) gave **11** (48 mg, 26%) and **10** (9 mg, 5%). The third zone (UV-positive) gave the tosylate **12** (25 mg, 8%) and δ-erythroidan **18** (4 mg, 2%). The fourth zone (UV-positive) gave the seco derivative **15** (4 mg, 2%).

The Tosylate (**12**): Colorless needles from AcOEt–hexane, mp 170—171 °C. IR: 1786, 1679. ^{1}H-NMR: 7.76, 7.38 (each 2H, d, J=8.3 Hz, ArH), 3.92 (2H, s, H-17), 3.66 (1H, ddd, J=14, 8.5, 7.5 Hz, H-10β), 3.18 (1H, dt, J=14, 6 Hz, H-10α), 2.90 (1H, dd, J=18, 9 Hz, H-14), 2.63 (1H, d, J=18, 4 Hz, H-14), 2.56 (1H, dd, J=9, 4 Hz, H-13), 2.43 (1H, ddd, J=17, 8.5, 6 Hz, H-11β), 2.27 (1H, ddd, J=17, 7.5, 6 Hz, H-11α). MS: 443 (M^+, 72), 390 (42), 278 (40), 262 (68), 248 (93), 218 (100), 190 (29). *Anal.* Calcd for $C_{22}H_{27}NO_6S$: C, 60.96; H, 6.28; N, 3.23. Found: C, 60.77; H, 6.31; N, 3.19. HRMS: Calcd for M^+: 433.1557. Found: 433.1566.

The Seco Derivative (**15**): Colorless gum. ^{1}H-NMR: 5.62 (1H, br s, H-13), 4.85, 4.80 (each 1H, br d, J=15 Hz, H-17), 4.80 (1H, t, J=4 Hz, H-4), 3.73 (1H, dt, J=14, 7.5 Hz, H-10), 3.36 (1H, dt, J=14, 6.5 Hz, H-10), 3.05 (2H, br s, H-14), 2.64 (1H, m, H-6), 2.31 (2H, dd, J=7.5, 6.5 Hz, H-11). MS: 261 (M^+, 21), 217 (8), 216 (7), 202 (11), 188 (7), 167 (24), 151 (22), 150 (100), 149 (63), 122 (59). HRMS: Calcd for $C_{15}H_{19}NO_3$: 261.1362. Found: 261.1400.

The Seco Derivative (**17**): Colorless gum. UV λ_{max}^{EtOH} nm (ε): 213 (6900). IR: 1731, 1668. ^{1}H-NMR: 5.75 (1H, s, H-7), 5.62 (1H, br s, H-13), 4.87, 4.81 (each 1H, br d, J=16 Hz, H-17), 3.75 (1H, dt, J=14, 7.5 Hz, H-10β), 3.70 (1H, dd, J=11.5, 6 Hz, H-5), 3.27 (1H, ddd, J=14, 8, 6 Hz, H-10α), 3.06 (2H, br s, H-14), 2.34 (1H, ddd, J=15, 7.5, 6 Hz, H-11α), 2.29 (1H, ddd, J=15, 8, 7.5 Hz, H-11β). MS: 261 (M^+, 2), 151 (11), 150 (100). HRMS: Calcd for $C_{15}H_{19}NO_3$: 261.1362. Found: 261.1377.

γ-Erythroidan (**11**): Colorless prisms from AcOEt–hexane, mp 123—124 °C. IR (KBr): 1734, 1698, 1678. ^{1}H-NMR: 5.76 (1H, br s, H-11), 4.75, 4.65 (each 1H, d, J=13 Hz, H-17), 4.55 (1H, br d, J=19 Hz, H-10β), 3.40 (1H, br d, J=19 Hz, H-10α), 2.78 (1H, dd, J=19, 8.5 Hz, H-7β), 2.77 (1H, dd, J=8.5, 4 Hz, H-13), 2.53 (1H, dd, J=19, 9.5 Hz, H-7α), 2.52 (1H, dd, J=18, 8.5 Hz, H-14α), 2.18 (1H, m, H-6), 2.17 (1H, dd, J=18, 4 Hz, H-14β). MS: 261 (M^+, 15), 218 (4), 138 (100), 95 (5). *Anal.* Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.88; H, 7.34; N, 5.28. HRMS: Calcd for M^+: 261.1362. Found: 261.1367.

β-Erythroidan (**10**): Colorless prisms from AcOEt, mp 190 °C (dec.). ^{1}H-NMR: 4.71, 4.67 (each 1H, d, J=15 Hz, H-17), 4.22 (1H, dd, J=13.5, 7.5 Hz, H-10β), 3.20 (1H, br d, J=20 Hz, H-14), 3.13 (1H, d of quintet, J=20, 2.5 Hz, H-14), 2.96 (1H, ddd, J=13.5, 11.5, 5.5 Hz, H-10α), 2.41 (1H, td, J=11.5, 5.5 Hz, H-11β), 2.29 (1H, dd, J=11.5, 5.5 Hz, H-11α). MS: 261 (M^+, 54), 232 (5), 219 (15), 218 (100), 205 (13), 190 (39). HRMS: Calcd for $C_{15}H_{19}NO_3$: 261.1362. Found: 261.1359. This was identical with the reported specimen.[3]

δ-Erythroidan (**18**): Colorless gum. IR: 1756, 1734 sh, 1678. ^{1}H-NMR: 6.53 (1H, br s, H-17), 4.22 (1H, ddd, J=13.5, 4.5, 3 Hz, H-10β), 2.88 (1H, dd, J=17.5, 10.5 Hz, H-14α), 2.72 (1H, dd, J=17.5, 2.5 Hz, H-14β), 2.69 (1H, dd, J=13.5, 8 Hz, H-10α), 2.56 (1H, dd, J=19.5, 9.5 Hz, H-7β), 2.48 (1H, dd, J=10.5, 2.5 Hz, H-13), 2.16 (1H, dd, J=14, 3 Hz, H-11α), 2.12 (1H, ddd, J=14, 8, 4.5 Hz, H-11β). MS: 261 (M^+, 35), 217 (12), 216 (9), 202 (11), 188 (9), 151 (33), 150 (100), 138 (39). HRMS: Calcd for $C_{15}H_{19}NO_3$: 261.1362. Found: 261.1363.

Tosylation of 8 A mixture of **8** (2 mg), *p*-toluenesulfonyl chloride (2 mg), and 4-dimethylaminopyridine (1 mg) in pyridine (1 ml) was stirred at room temperature for 4 h, and worked up as usual to yield the tosylate (**12**, 3 mg), which was identical with the tosylate obtained in the reaction with PPTS.

Interconversion between *cis*-Hydroxy-γ-lactone (8) and *trans*-Hydroxy-δ-lactone (21) (1) The γ-lactone **8** (10 mg) was heated with 10% NaOH (2 ml) at 100 °C for 2 h. The cooled mixture was carefully acidified (< 5 °C) with 10% H_2SO_4 to pH 1, stirred at room temperature for 20 min, and then extracted with $CHCl_3$–MeOH. The extract was washed with saturated $NaHCO_3$, and concentrated to give a residue (9 mg), which was a mixture of **21** and **8** in a ratio of *ca.* 8 : 1 as judged from the ^{1}H-NMR spectrum. The *trans*-hydroxy-δ-lactone (**21**) was purified by recycling HPLC as a colorless gum. IR: 3340, 1722, 1665. ^{1}H-NMR (CD_3OD): 4.13, 4.04 (each 1H, d, J=11.5 Hz, H-17), 3.95 (1H, ddd, J=13, 5.5, 2 Hz, H-10β), 3.11 (1H, td, J=13, 2 Hz, H-10α), 2.85 (1H, dd, J=17.5, 13.5 Hz, H-14α), 2.62 (1H, dd, J=17.5, 5.5 Hz, H-14β), 2.06 (1H, dd, J=13.5, 5.5 Hz, H-13), 1.61 (1H, dt, J=13, 2 Hz, H-11β), 1.43 (1H, td, J=13, 5.5 Hz, H-11α). MS: 279 (M^+, 68), 262 (7), 248 (72), 237 (14), 236 (100), 220 (15), 150 (64). HRMS: Calcd for $C_{15}H_{21}NO_4$: 279.1469. Found: 279.1472.

(2) A solution of the *trans*-hydroxy-δ-lactone **21** (10 mg) in tetrahydrofuran (2 ml) and 2% H_2SO_4 (2 ml) was stirred at room temperature for 20 h, and then extracted with $CHCl_3$. The extract was washed with $NaHCO_3$ solution, and concentrated to give the *cis*-γ-lactone **8** (10 mg, 100%).

Attempted Isomerization of *cis*-Hydroxy-δ-lactone (9) The *cis*-δ-lactone **9** (3 mg) was heated with 10% NaOH at 100 °C for 2 h. The cooled mixture was carefully acidified as described for **21**, and extracted with $CHCl_3$–MeOH. Concentration of the extract gave a residue, whose ^{1}H-NMR spectrum in CD_3OD was identical with that of the starting material.

Dehydration of *cis*-Hydroxy-δ-lactone (9) Thionyl chloride (0.1 ml) was added to a solution of **9** (8 mg) in pyridine (2 ml) at 0 °C. The mixture was stirred overnight at room temperature, poured into ice-water, and extracted with AcOEt, then the extract was washed with 10% HCl and brine, and concentrated to give the residue (8 mg). This product was identical with δ-erythroidan (**18**) slightly contaminated with γ-erythroidan (**11**). The ratio was *ca.* 10 : 1 as judged from the ^{1}H-NMR spectrum.

Dehydration of *trans*-Hydroxy-δ-lactone (21) A mixture of the *trans*-δ-lactone **21** (10 mg) and $SOCl_2$ (0.1 ml) in pyridine (2 ml) was treated and worked up as above. The ^{1}H-NMR spectrum of the product (9 mg) was identical with that of β-erythroidan (**10**) slightly contaminated with γ-erythroidan (**11**). The ratio was judged as *ca.* 10 : 1.

Selective Synthesis of β-Erythroidan (10) from the Epoxy-Acid (7) The epoxy-acid **7** (60 mg) was heated with 10% NaOH (4 ml) in a sealed tube at 120 °C for 6 h. The mixture was cooled to 0 °C and carefully acidified with 2% H_2SO_4 to pH 1. After being kept at 10 °C for 10 min, the mixture was extracted with $CHCl_3$–MeOH. Concentration of the dried extract left a gum, whose NMR spectrum (in CD_3OD) was identical with that of the *trans*-hydroxy-δ-lactone (**21**). This gum was dissolved in pyridine (10 ml), dehydrated with $SOCl_2$ (0.5 ml) and worked up as described above. The product was purified by recycling HPLC to give β-erythroidan (**10**, 48 mg, 86%).

α-Erythroidan (22) A mixture of **10** (31 mg) and DBU (60 mg) in

benzene (3 ml) was heated in a sealed tube at 120 °C for 5 h. The mixture was poured into ice-water and extracted with CH_2Cl_2. The extract was washed with 5% HCl and brine, and concentrated. The residue was dissolved in AcOEt and passed through a short silica gel column. The AcOEt eluate was further separated by recycling HPLC to give α-erythroidan (**22**, 18 mg, 58%) and the starting material (**10**, 12 mg, 39%). α-Erythroidan (**22**) was obtained as colorless prisms from AcOEt–ether, mp 123—124 °C. IR: 1709, 1674. UV λ_{max}^{EtOH} nm (ε): 217 (12400). ^{1}H-NMR: 6.07 (1H, d, J=2 Hz, H-14), 4.43 (1H, dd, J=11.5, 6 Hz, H-17α), 4.18 (1H, ddd, J=13.5, 5, 2 Hz, H-10β), 3.94 (1H, t, J=11.5 Hz, H-17β), 2.98 (1H, ttd, J=11.5, 6, 2 Hz, H-12), 2.93 (1H, td, J=13.5, 3 Hz, H-10α), 2.56 (1H, m, H-6), 2.42 (1H, dd, J=17, 8.5 Hz, H-7α), 2.37 (1H, dd, J=17, 11 Hz, H-7β), 1.87 (1H, dddd, J=13.5, 6, 3, 2 Hz, H-11α), 1.24 (1H, tdd, J=13.5, 11.5, 5 Hz, H-11β). HRMS: Calcd for $C_{15}H_{19}NO_3$: 261.1362. Found: 261.1355.

References and Notes

1) Part XXXV of Synthesis of *Erythrina* and Related Alkaloids. Part XXXIV: T. Sano, J. Toda, R. Yamamoto, M. Shoda, K. Isobe, and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 2663 (1992).
2) Y. Tsuda, A. Ishiura, S. Takamura, S. Hosoi, K. Isobe, and K. Mohri, *Chem. Pharm. Bull.*, **39**, 2797 (1991).
3) K. Isobe, K. Mohri, Y. Itoh, Y. Toyokawa, N. Takeda, J. Taga, S. Hosoi, and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 2632 (1992).
4) Compound **18** corresponds to the aldehyde **3** in the model experiment.[2] However, a different mechanism had been proposed for the formation of **3**.[2]