Studies toward Total Synthesis of Non-aromatic *Erythrina* Alkaloids. (6).[1] Synthesis of 8-Oxo-γ-erythroidine and 8-Oxo-cycloerythroidine, Isomers of the Natural Alkaloids

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A study directed to the total synthesis of β-erythroidine 1, a non-aromatic *Erythrina* alkaloid, was conducted based on a strategy involving construction of D-furanoerythrinan *via* Diels–Alder reaction of furodioxopyrroline and the conversion of the resulting furan to the δ-lactone *via* oxidative fission of the furan ring followed by one-carbon homologation. Oxidation of the furanoerythrinan 17 with *N*-bromoacetamide followed by treatment with Nafion-H gave the enol γ-lactone 27. Alkaline hydrolysis of 27 followed by methylation with diazomethane gave the keto-ester 31. Alkylation of 31a with dimethylsulfoxonium methylide gave 8-oxo-γ-erythrodine (5). One-carbon homologation of 31a by Yamakawa's method using chloromethyl phenyl sulfoxide resulted in the formation of 8-oxocycloerythroidine (6). Compounds 5 and 6 are structural isomers of natural 8-oxo-β-erthroidine (2).

Keywords *Erythrina* alkaloid; non-aromatic *Erythrina* alkaloid; synthesis; dioxopyrroline; D-furanoerythrinan; 8-oxo-γ-erythroidine; 8-oxocycloerythroidine; Diels–Alder reaction; *N*-bromoacetamide; one-carbon homologation

Recently, Isobe *et al.* developed a method for the conversion of furan ring to a β,γ-unsaturated δ-lactone by oxidative cleavage of the furan ring followed by introduction of a C_1-unit, leading to the synthesis of the β-erythroidine skeleton.[2] This paper describes studies directed toward total synthesis of β-erythroidine **1** and/or α-erythroidine **3** based on a strategy involving the following three steps: (i) constructuion of the erythrinan skeleton (B) having a furan ring (D-furanoerythrinan)[3] through Diels–Alder reaction of furodioxopyrroline (A) with an activated butadiene, (ii) conversion of the furan (B) to the keto-ester (C) *via* oxidative fission of the furan ring, and (iii) construction of the unsaturated δ-lactone by one-carbon homologation followed by cyclization (Chart 1). The study, which resulted in the synthesis of 8-oxo-γ-erythroidine **5** and 8-oxo-cycloerythroidine **6**, the unnatural isomers of 8-oxo-β-erythroidine **2** and 8-oxo-α-erythroidine **4**, demonstrates that the construction of a δ-lactone ring *via* a furan ring can be achieved by the methodology described above, although the intermediate (B) has a dienol moiety which is supposed to be vulnerable to oxidation and acid treatment.

Synthesis of D-Furanoerythrinan The furodioxopyrroline **10** was prepared from the β-furylethylamine **7**. Acylation of **7** with methyl chloroformylacetate gave the amide **8** (83%). Bischler–Napieralski cyclization of **8** with phosphorus oxychloride in the presence of potassium carbonate[4] gave the furopyridine **9** in a moderate yield (43%). Condensation of **9** with oxalyl chloride gave the dioxopyrroline **10** in an excellent yield (92%). All these compounds were characterized by ^{1}H-nuclear magnetic resonance (NMR), infrared (IR) and ultraviolet (UV) spectroscopy and elementary analyses.

Construction of the D-furanoerythrinan was effectively achieved by intermolecular Diels–Alder reaction of **10** with an activated butadiene. Thus, heating of **10** with 1,3-bis(trimethylsilyloxy)-1,3-butadiene in dioxane at 130 °C for

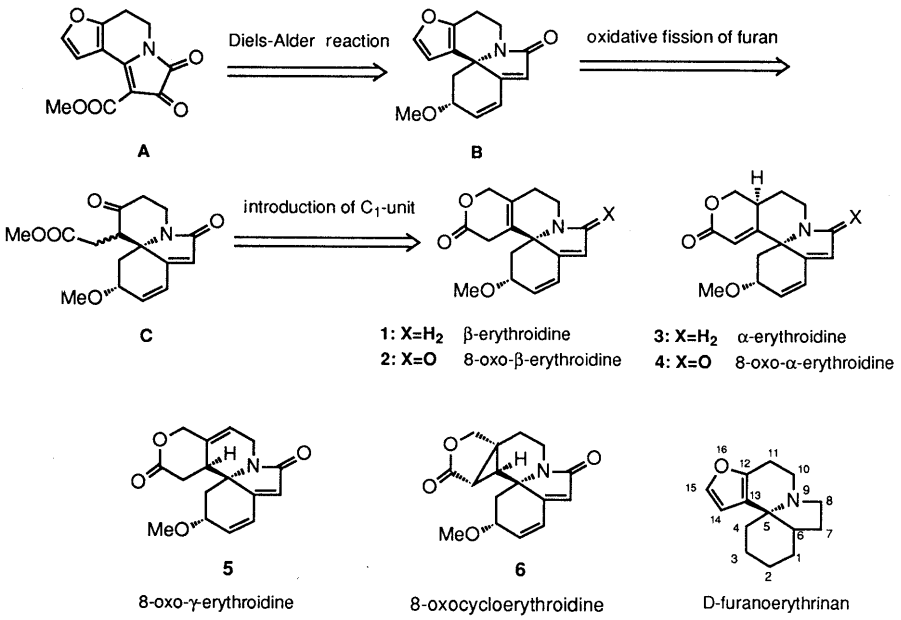


Chart 1

30 min gave the expected ene-adducts **11** [*endo*-**11a** (67%) and *exo*-adduct **11b** (12%)] together with one-adduct **12** (2%). The stereochemistry of the 1-OTMS group of the adducts **11** was assigned on the basis of a comparison of the chemical shift of C_1-H with those of analogous adducts.[5] The structure of **12** was deduced from spectral comparison with the analogous one-adduct obtained from isoquinolinodioxopyrroline.[5]

Reduction of the *endo*-adduct **11a** with lithium borohydride in tetrahydrofuan (THF) followed by treatment of the crude product with 5% hydrochloric acid in THF gave the enone alcohol **13** in 87% yield. Similarly, the *exo*-adduct **11b**, subjected to the same reactions, gave **13** in 83% yield. Compound **13** was mesylated to give the mesylate **14**, which was subjected to the demethoxycarbonylation reaction of vinylogous β-ketoesters under a neutral condition developed by Tsuda *et al.*[6] Thus, heating of **14** in dimethyl sulfoxide (DMSO) at 140 °C in the presence of magnesium chloride caused the expected demethoxycarbonylation with concomitant elimination of the methanesulfonyl group to give the dienone **15** in 94% yield. Reduction of **15** with sodium borohydride–cerous chloride in methanol gave the 3α-alcohol **16a** as a major (55%) and the 3β-alcohol **16b** as a minor (30%) product. Methylation of **16a** and **16b** with methyl iodide in the presence of a phase transfer catalyst (KOH–Et_4NBr) gave the corresponding methyl ethers **17a** and **17b** in quantitative yields, respecively. The stereochemical assignment of the 3-OMe group was achieved by comparison of the ^{1}H-NMR spectra with those of erysotramidine and its 3-epimer.[5]

Conversion of the Furan Ring to γ-Lactones As described in the model experiments,[7] oxidation of **15** with *N*-bromoacetamide (NBA) in methanol at room temperature gave an epimeric mixture of dimethoxydihydrofurans **18a** (42%) and **18b** (29%) with respect to C_{15}-OMe. The stereochemistry of the C_{12}-OMe group was assigned as the thermodynamically more stable α-configuration, as discussed in the preceding paper.[7] Oxidation of **15** with thallium trinitrate (TTN) in methanol at 60 °C also afforded a mixture of **18a** and **18b** in 31% yield and the 11β-methoxyfuran **20** in 7% yield, with recovery of 40%

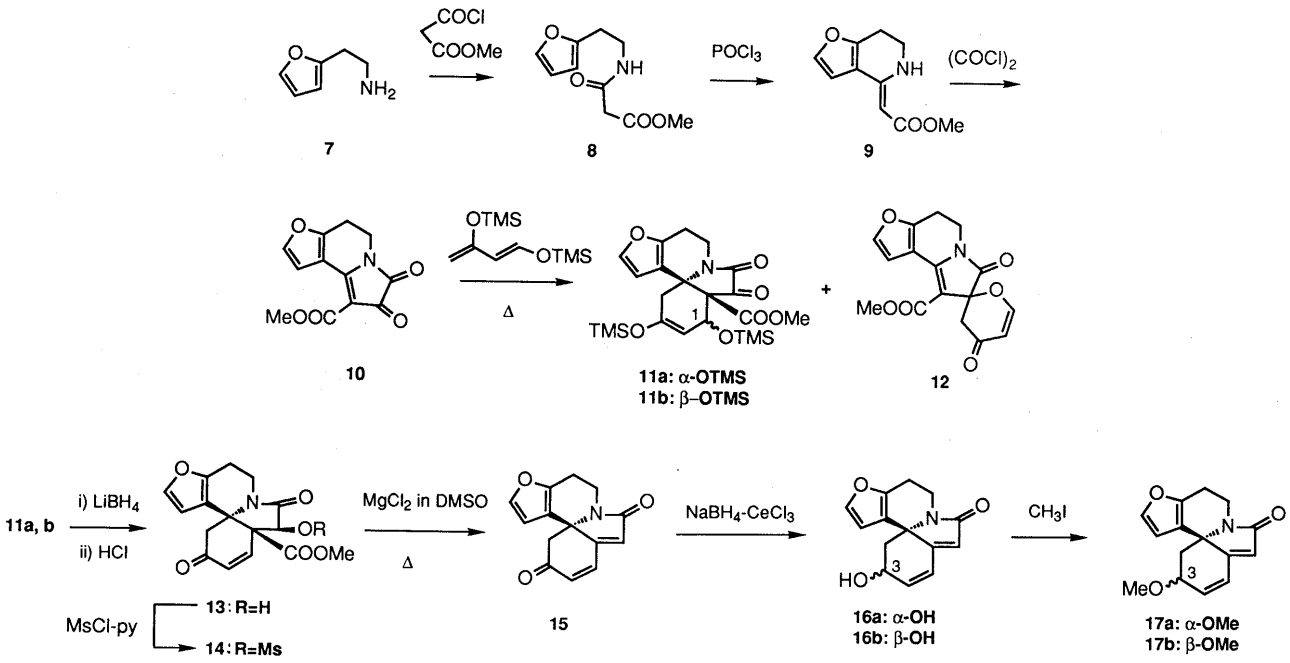
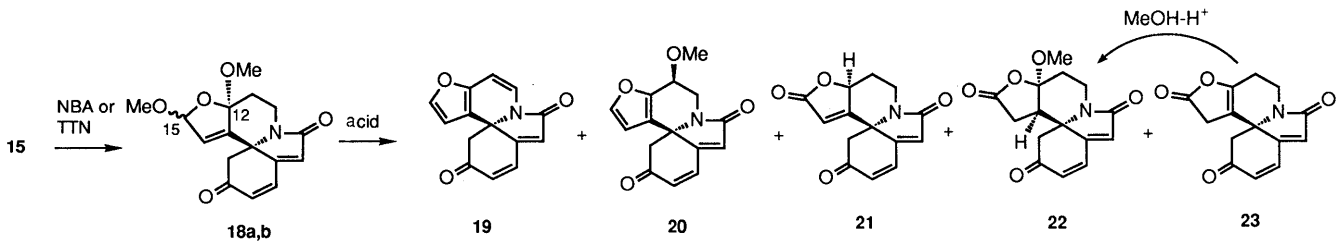


Chart 2



			furans(%)		γ-lactones(%)		
acid	solv.	temp.°C	19	20	21	22	23
TsOH	benzene	80	6	6	18	16	--
Me_3SiI	CH_3CN	25	--	--	12	--	17

Chart 3

of the starting material. Conversion of the dimethoxydihydrofuran (**18**) to γ-lactones required stronger acidic conditions than had been employed in the model experiment.[7] The dimethoxydihydrofuran **18**, on heating in benzene under reflux in the presence of *p*-toluenesulfonic acid (*p*-TsOH), was converted into four products, the α,β-unsaturated γ-lactone **21** (18%), the 12-methoxylactone **22** (16%), the Δ^{10}-furan **19** (6%), and the 11-methoxy derivative **20** (6%). Reaction of **18** with trimethylsilyl iodide, a reagent effectively catalyzing the conversion of a dimethoxydihydrofuran to an unsaturated γ-lactone,[8] proceeded at room temperature to form the γ-lactone **21** (12%) and the enol γ-lactone **23** (17%). It is noteworthy that only the γ-lactone was formed, though the yield was low.

Oxidation of the dienone **15** with NBA in aqueous acetone followed by treatment of the crude products (**24**) with silica gel in methanol at room temperature overnight gave two γ-lactones, **22** (33%) and **23** (11%) as major products, and the furano derivative **20** (7%) as a minor product. Treatment of **24** with *p*-TsOH in benzene under reflux for 30 min gave the desired lactone **23** (52%) as a major and 11β-hydroxyfuran **25** (23%) as a minor product. Reaction of **24** with silica gel in refluxing benzene gave **23** as a single product, though the yield was not satisfactory (56%). On the other hand, treatment of **22** with perfluorinated cation-exchange powder (Nafion-H)[9] in THF at room temperature gave the desired lactone **23** as a sole product in 65% yield. This result presents a sharp contrast to that observed in the same reaction of the model compound, which only produced the undesired 11β-hydroxyfuran derivative.[7] Selective transformation of the furan ring to γ-lactone was thus achieved by site-selective oxidation followed by acidic rearrangement of the resulting products.

The structures and formation mechanisms of these products have already been discussed for the model compounds.[7] Acid treatment (SiO_2 or HCl) of the enol lactone **23** in methanol yielded the 12-methoxy lactone **22** quantitatively. The formation of **22** can be rationalized in terms of lactonization of the keto-acid generated by hydrolysis of **23** (see also below).

Attempted reduction of the 3-ketone of **22** or **23** to the alcohol with several reagents ($NaBH_4$, $NaBH_4$–$CeCl_3$, and Meerwein–Ponndorf reduction) was unsuccessful, merely causing degradation.

Similar oxidation of the dienol 3-*O*-methyl ethers, **17a** and **17b**, with NBA in methanol gave the dimethoxydihydrofuran derivatives, **26a** and **26b** respectively, as a stereoisomeric mixture of the 15-OR group in high yields. However, selective conversion of the dimethoxydihydrofuran ring to γ-lactone without deterioration of the dienol moiety was difficult. For example, treatment of **26a** with trimethylsilyl iodide in acetonitrile gave a 1 : 1 mixture of the enol γ-lactone **27a** and the α,β-unsaturated γ-lactone **28a** in only 25% yield. Other attempts using Nafion-H or *p*-TsOH as a catalyst were unsuccessful.

Finally, conversion of the furan ring into γ-lactones was successfully achieved as follows. Oxidation of **17a** with NBA in aqueous acetone, followed by treatment of the product with Nafion-H in THF at room temperature gave **27a** in 66% yield, though an undesired γ-lactone **28a** was also formed (13%). Similarly, successive treatments of **17b** with NBA followed by Nafion-H also gave the enol γ-lactone **27b** (46%) and then the α,β-unsaturated γ-lactone **28b** (12%).

Hydrolysis of **27a** with potassium hydroxide in aqueous methanol followed by acidification gave the 12-hydroxylactone **30a** (95%), which, on methylation with diazomethane, gave the keto-ester **31a** (73%). Similarly alkaline hydrolysis of the 3β-isomer **27b** gave the 12-hydroxylactone **30b** (93%), which, on methylation with diazomethane, gave the keto-ester **31b** (60%). Since **30** is considered to have the most stable *cis* stereochemistry, 12α-OH and 13α-H,[6] the CH_2COOMe side chain of **31** is assigned β-configuration.[10]

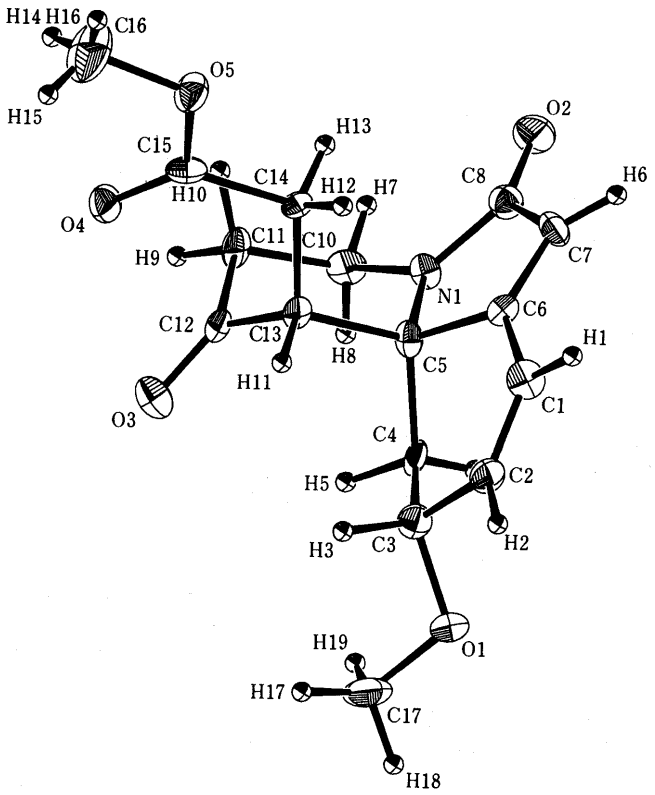
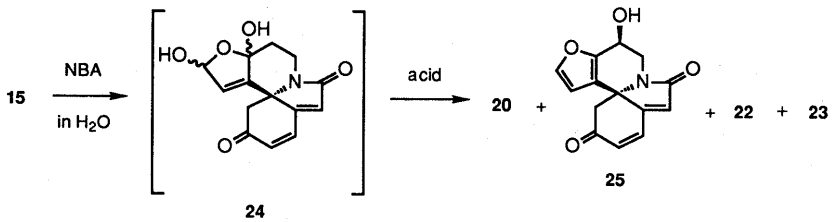


Fig. 1



			furans(%)		γ-lactones(%)	
acid	solv.	temp.°C	20	25	22	23
SiO_2	MeOH	25	7	--	33	11
SiO_2	benzene	80	--	--	--	56
TsOH	benzene	80	--	23	--	52
Nafion-H	THF	25	--	--	--	65

Chart 4

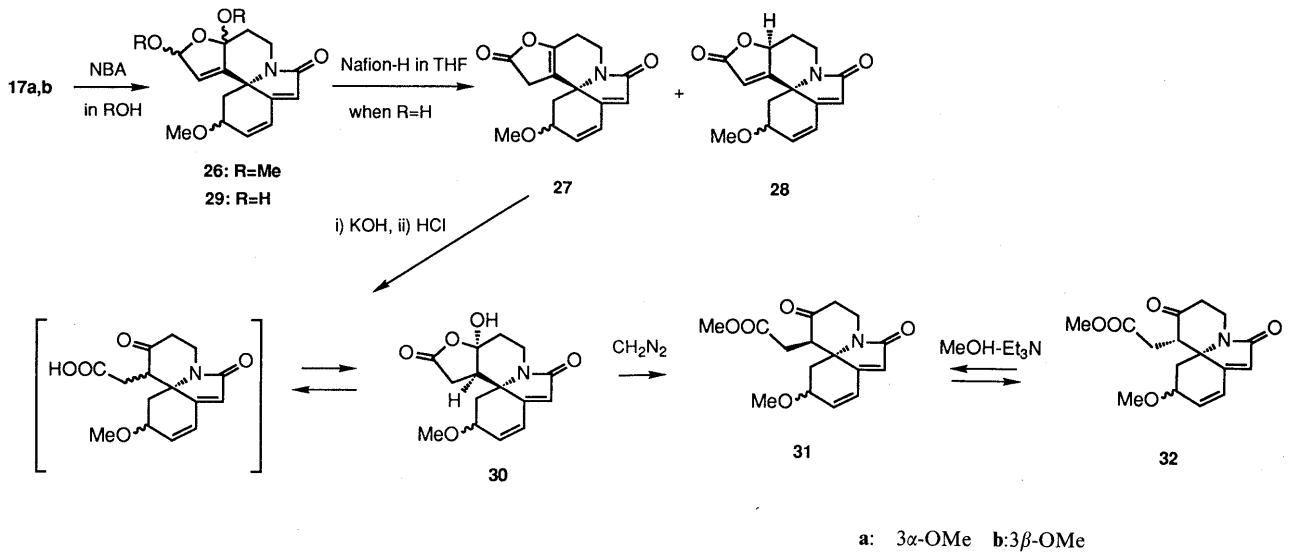


Chart 5

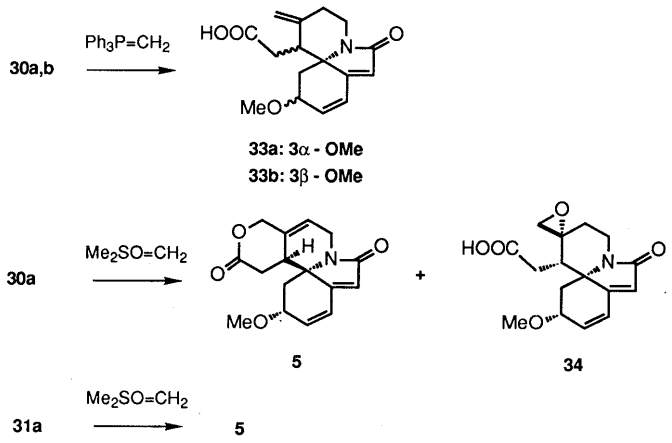


Chart 6

This assignment was proved by an X-ray analysis of **31a**, which unambiguously demonstrated that the side chain is in axial orientation with ring C in chair conformation (Fig. 1). The analysis by high-performance liquid chromatography (HPLC) revealed that, when **31a** was dissolved in methanol, epimerization of the side chain took place slowly at room temperature and rapidly in the presence of triethylamine to give a *ca.* 1 : 1 equilibrium mixture of the axial (**31a**) and equatorial (**32a**) isomers, though an attempt to isolate **32a** was unsuccessful. HPLC analysis also suggested that treatment of **31a** with 0.5 N hydrochloric acid in methanol at room temperature caused not only epimerization but also other reactions such as lactonization.

Introduction of a C_1-Unit Wittig reaction of the 12-hydroxylactone **30a** with triphenylphosphine methylide took place under forcing conditions (heating in toluene at 130 °C in a sealed tube) to give the expected *exo*-methylene acid **33a** as a single product, but the yield was very low (18%). The 3β-isomer **30b** also gave the corresponding *exo*-methylene acid **33b** (8%). Wittig reaction of the keto-ester **31a** with the same reagent gave no characterizable product. Thus, this synthetic route was discarded.

Reaction of the 12-hydroxylactone **30a** with excess dimethylsulfoxonium methylide in DMSO gave the epoxide **34** (19%) as a major and 8-oxo-γ-erythroidine **5** (2%) as a minor product. Application of this reaction to the keto-ester **31a** gave **5** (15%) as a sole characterizable product. The stereochemistry of these products will be discussed later.

Attempted conversion of the epoxide **34** into a δ-lactone under several acidic conditions (Nafion-H or hydrochloric acid) was unsuccessful. These treatments afforded only the starting material or merely caused decomposition of the dienol group.

We then applied Yamakawa's one-carbon homologation method using 1-chloromethyl phenyl sulfoxide carbanion, leading to α,β-unsaturated aldehydes from ketones.[11] Reaction of the keto-ester **31a** with lithium 1-chloromethyl phenyl sulfoxide in dry THF proceeded very rapidly to give, within a few minutes, the chlorohydrin **35** in 67% yield as an inseparable diastereoisomeric mixture, whose ^{1}H-NMR spectrum showed two COOMe signals (with an intensity ratio of 3 : 1). Although this reaction creates three new chiral centers, two chiral carbons and a sulfoxide, the products are assumed to be a mixture of diastereoisomers with respect to the stereochemistry at C_{17} derived from the reagent. The stereochemistry at C_{12} was assigned on the assumption that the reagent was introduced from the sterically less hindered β-side (see also below).

The product **35** was then converted to the α,β-epoxy sulfoxide **36**. Although the isolation of **36** by the reaction of **35** with base (potassium hydroxide in aqueous methanol, triethylamine in chloroform, and potassium *tert*-amyloxide in toluene) failed, the following reactions indicated the intermediary formation of **36**. Treatment of **35** with *tert*-butoxide in the presence of benzenethiol and subsequent reduction of the crude products with sodium borohydride gave two products, the hydroxydithioacetal **38** (31%) and the phenylthio epoxide **39** (11%). Formation of **38** was rationalized in terms of the reduction of a thioacetal sulfoxide **37** which was generated by ring opening of the epoxide **36** by attack of phenylthio anion. Compound **39** was considered to be formed by reduction of the phenylsulfoxide **36** or by elimination of the phenylsulfoxide group from **37** through intramolecular nucleophilic attack of 12-OH.

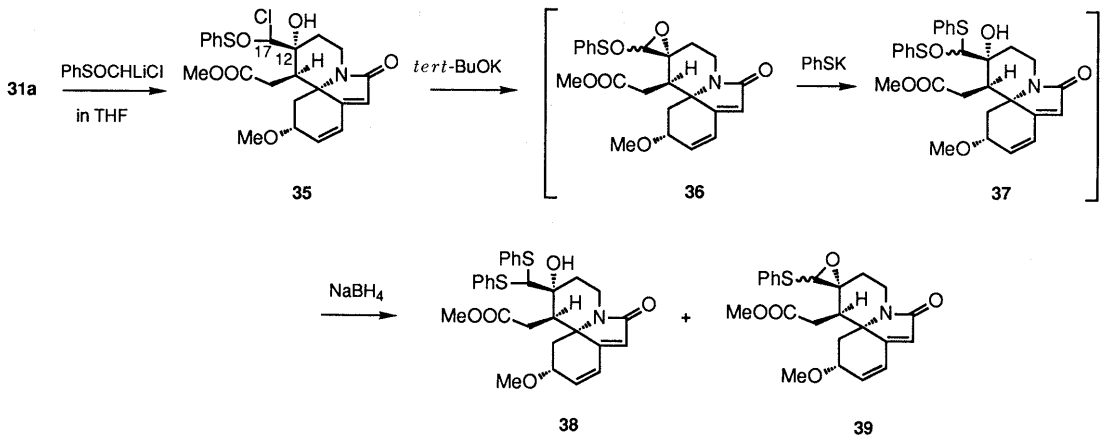


Chart 7

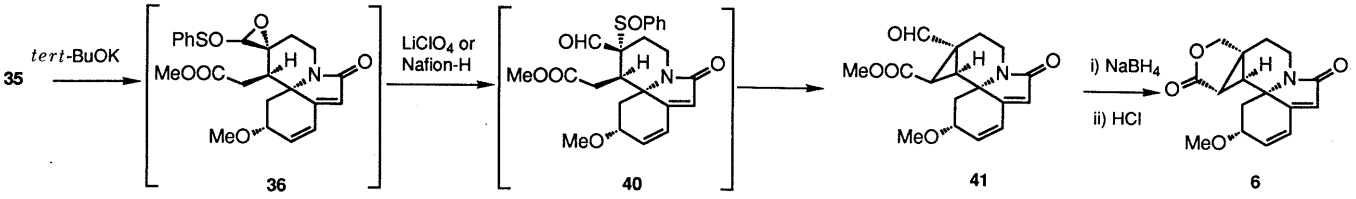


Chart 8

Table I. ^{1}H-NMR Spectral Data for 8-Oxoerythroidines (8-Oxo-E)[a] [Chemical Shifts (δ) and Coupling Constants (Hz) in $CDCl_3$]

H	8-Oxo-α-E (**4**)[12a]	8-Oxo-β-E (**2**)[12a]	8-Oxo-γ-E (**5**)	8-Oxocyclo-E (**6**)
1	6.25 (d, 10)	6.25 (d, 12)	6.22 (d, 10)	6.20 (d, 10)
2	6.74 (dd, 2, 10)	6.77 (dd, 2.5, 10)	6.63 (dd, 2, 10)	6.62 (dd, 2, 10)
3	3.75 (m)	4.08 (m)	4.18 (t, 8)	4.06 (m)
4a	1.62 (q, 10, 12)	1.72 (q, 10, 12)	1.53 (dd, 10, 12)	1.69 (q, 10, 12)
4e	2.78 (q, 6, 12)	2.82 (q, 6, 10)	2.80 (dd, 6, 12)	2.86 (q, 6, 10)
7	6.02 (s)	5.96 (s)	6.02 (s)	5.93 (s)
10a	3.11 (m)	3.22 (dq, 6, 8, 14)	3.64 (d, 19)	3.09 (m)
10e	4.35 (dq, 4, 14)	4.34 (dq, 2, 8, 14)	4.74 (dd, 5, 19)	4.23 (m)
11a	1.45 (dq, 12, 14)	2.02 (dd, 8, 15)	6.06 (d, 5)	2.10 (m)
11e	1.93 (m)	2.40 (m)	—	2.28 (m)
12	3.03 (m)	—	—	—
13	—	—	2.6—2.7 (m)	1.48 (d, 2)
14a	5.83 (d, 2)	3.10 (d)	2.04 (dd, 13, 17)	1.44 (d, 2)
14e	—	3.10 (d)	2.38 (d, 5, 17)	—
17a	3.97 (q, 10, 12)	4.59 (d, 16)	4.70 (d, 12)	4.15 (d, 10)
17e	4.46 (q, 6, 12)	4.73 (d, 16)	4.85 (d, 12)	4.34 (d, 10)
OMe	3.41 (s)	3.42 (s)	3.42 (s)	3.45 (s)

a) H–H and C–H COSY spectra were taken on a JEOL FX 500 (500 MHz) spectrometer.

Table II. ^{13}C-NMR Spectral Data for 8-Oxoerythroidines (8-Oxo-E) (δ in $CDCl_3$)

C	8-Oxo-α-E (**4**)[12b]	8-Oxo-β-E (**2**)[12b]	8-Oxo-γ-E (**5**)	8-Oxocyclo-E (**6**)
1	120.3 (d)	135.9 (d)	135.7 (d)	134.9 (d)
2	115.1 (d)	120.6 (d)	119.8 (d)	118.6 (d)
3	74.2 (d)	73.6 (d)	73.7 (d)	73.9 (d)
4	35.3 (t)	31.7 (t)	36.4 (t)	32.6 (t)
5	66.2 (s)	65.2 (s)	62.2 (s)	61.1 (s)
6	155.2 (s)	155.7 (s)	155.6 (s)	157.7 (s)
7	122.7 (d)	124.2 (d)	123.1 (d)	122.1 (d)
8	163.3 (s)	168.3 (s)	168.6 (s)	170.0 (s)
10	37.7 (t)	33.7 (t)	37.8 (t)	39.2 (t)
11	30.2 (t)	24.7 (t)	121.9 (d)	20.2 (t)
12	31.3 (d)	127.4 (s)	129.6 (s)	29.0 (s)
13	156.1 (s)	127.8 (s)	36.2 (d)	28.6 (d)
14	136.6 (d)	41.7 (t)	36.5 (t)	23.9 (d)
15	168.5 (s)	170.0 (s)	168.8 (s)	174.6 (s)
17	69.6 (t)	69.9 (t)	72.8 (t)	72.3 (t)
OMe	56.5 (q)	56.4 (q)	56.4 (q)	56.4 (q)

The rearrangement of the sulfinyl group of the α-sulfinylated epoxide was achieved by a thermal reaction in the presence of Lewis acid.[11] When the crude product **36** obtained by the reaction of **35** with potassium *tert*-butoxide was immediately heated in toluene at 110 °C in the presence of lithium perchlorate and tributylphosphine oxide, the aldehyde **41** was obtained as an oil. The ^{1}H-NMR spectrum of **41** showed an aldehydic proton signal at δ 9.55 ppm as a singlet. Reduction of **41** with sodium borohydride followed by acid treatment gave a lactone, 8-oxocycloerythroidine **6** (13% yield from **35**) as a single characterizable product. The same compound **6** was obtained in an increased yield (28% from **35**) by heating the crude epoxide **36** at 80 °C in THF with Nafion-H followed by $NaBH_4$ reduction. The cyclopropane ring in **41** should be created by an intramolecular alkylation at the active methylene (C14) by C_{12} with elimination of the phenylsulfinyl group from the α-sulfinyl aldehyde **40** which was formed by 1,2-rearrangement of the sulfinyl group in the epoxide **36**.

Structures of 8-Oxo-γ-erythroidine and 8-Oxocycloerythroidine 8-Oxo-γ-erythroidine **5** and 8-oxocycloerythroidine **6** have the same molecular formula as 8-oxo-β-erythroidine **2**, the target molecule, as revealed by their high-resolution mass spectra (HRMS). The structures were deduced from their ^{1}H- and ^{13}C-NMR spectra. The signal assignment of all protons and carbons (Tables I and II) was readily achieved by the use of H–H and C–H correlation spectroscopy (COSY) and nuclear Overhauser effect spectroscopy (NOESY) spectra and by comparison with the

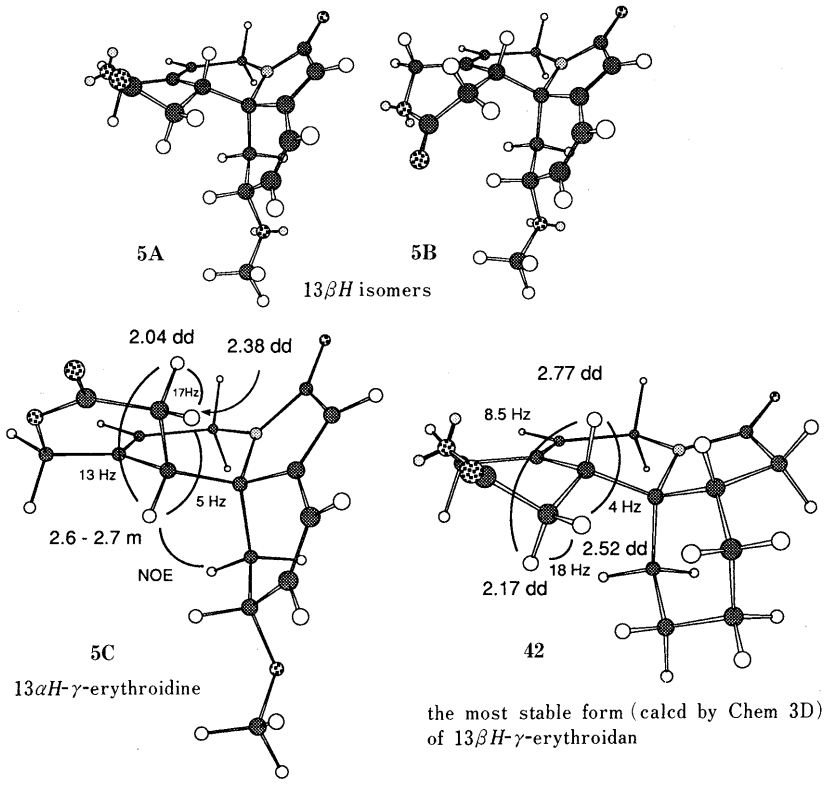


Fig. 2

reported data for 8-oxo-β-erythroidine **2** and 8-oxo-α-erythroidine **4**,[12] revealing that they are isomeric with respect to the structures of rings C and D.

The spectra of 8-oxo-γ-erythroidine **5** showed the presence of a δ-lactone (IR: 1740 cm^{-1}) and a trisubstituted double bound [δ_H 6.06 (1H, d); δ_C 121.9 (d) and 129.2 (s)]. Coupling of the olefinic proton with C_{10}-H proved that the double bond is at C_{11}–C_{12}. The C_{13}-H was deduced to have α-configuration as follows. Calculations of the steric energies by Chem 3D generated three stable stereostructures, two lactone boat forms (**5A** and **5B**) for the 13βH isomer, and a lactone half-chair form (**5C**) for the 13αH isomer (Fig. 2). The coupling constants between the 13-H and 14-methylene protons (5 and 13 Hz) were consistent with the stereostructures **5A** and **5C**, eliminating the stereostructure **5B**. The signal due to one of the 14-methylene protons appeared at an abnormally high field (δ 2.04) despite the fact that it is vicinal to the carbonyl group. This high-field shift can be rationalized in terms of the stereostructure **5C**, where 14β-H projects over ring C and is positioned in the shielding region of the α,β-unsaturated lactam moiety. A similar high-field shift of 14β-H was also observed in the ^{1}H-NMR spectrum of 8-oxocycloerythroidine (see below). The *trans* relationship of this proton to 13-H (J=13 Hz) confirmed that 13-H has α-configuration. An nuclear Overhauser effect (NOE) observed between 13-H and 4β-H in the NOESY spectrum, though it was very weak, supported this assignment, This stereochemistry is different from that of 8-oxo-13β*H*-γ-erythroidan (**42**) reported in a preceding paper.[13] In the latter compound, the proton at C13 (δ 2.77) couples to C14-protons at δ 2.17 and 2.52 with the coupling constants of J=8.5 and 4 Hz, respectively.

The ^{1}H-NMR spectrum of 8-oxocycloerythroidine (**6**) showed no additional olefinic proton signal besides the signals due to the diene protons, but the compound was apparently different from 8-oxo-β-erythroidine **2**. The ^{13}C-NMR spectrum exhibited four saturated carbon signals attributed to ring D at δ 23.9 (d), 28.6 (d), 29.0 (s), 72.3 (t) besides the lactone carbonyl (δ 174.6); these observations together with the lactone carbonyl absorption in the IR spectrum (1760 cm^{-1}) suggest the presence of a γ-lactone ring fused with a cyclopropane ring. In accord with this

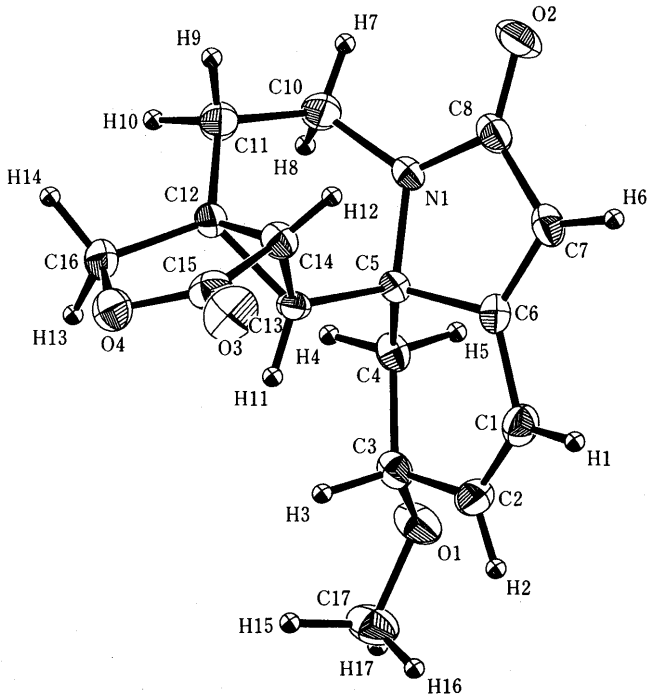


Fig. 3

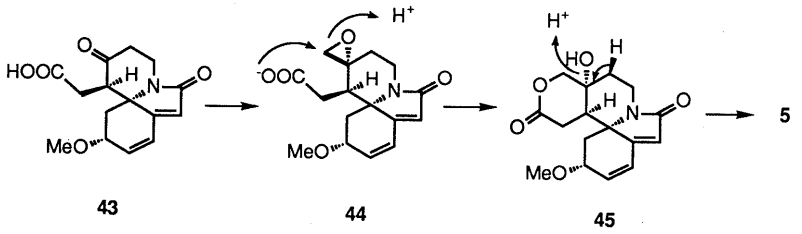


Chart 9

structural assignment, two signals due to the protons on the cyclopropane ring appeared at δ 1.48 and 1.44 (each as a doublet), which are attributable to the protons at C_{13} and C_{14}.

The C_{14}-proton, in spite of its vicinity to the lactone carbonyl group, appeared at abnormally high field (δ 1.44). This abnormal high-field shift is attributable to not only the fact that the proton is on a cyclopropane ring, but also the fact that it projects over ring C, being oriented just above the α,β-unsaturated lactam moiety at ring B, in the shielding region of this group. The observed NOE between 13-H and 3β-H in the NOESY spectrum, together with the results described above, suggests that 13-H has α-configuration. The assigned structure of **6** was finally confirmed by an X-ray crystallographic analysis (Fig. 3).

The stereochemistries clarified for **5** and **6** indicate that these compounds are produced by attack of the anionic reagents from the β-side to the carbonyl group of **31** (or the lactone **30**) with retention of the stereochemistry of the side chain. The reactivity of chloromethylphenylsulfinyl anion with **31** is very high (0 °C, <5 min), so the reaction is completed before epimerization of the side chain to give the product with retained stereochemistry. On the other hand, the reactivity of trimethylsulfinyl anion is relatively low (room temperature),[2h] so the reaction may proceed with equilibration of the stereochemistry of the side chain, as suggested in the model experiment.[2b] Thus, we consider that the epoxy-acid **34** could have the side chain with inverted stereochemistry (see Chart 6). The other epoxide **44**, a possible product derived from the β-face attack of the sulfur ylide on the keto-acid **43** with the side chain of retained stereochemistry (β-configuration), would be converted into **45** by intramolecular nucleophilic attack of carboxylic anion on the epoxide under the reaction conditions. Subsequent dehydration by concerted *trans* elimination is possible only between the 12α-OH and 11β-H, thus site-selectively forming a double bond at C_{11}–C_{12} to give the final product **5**.

Attempted isomerization[14] of 8-oxo-γ-erythroidine **5** and 8-oxocycloerythroidine **6** into 8-oxo-β- or α-erythroidine (**2** or **4**) under acidic or basic conditions (HCl, $AgBF_4$, $BF_3 \cdot Et_2O$, and KOH) and attempted cyclopropane ring cleavage of **6** *via* the enolization of the lactone carbonyl with lithium diisopropylamide, potassium hydroxide, trimethylsilyl chloride, or trimethylsilylated Nafion-H were unsuccessful, merely causing gradual deterioration of the dienol moiety.

Experimental

Unless otherwise noted, the following procedures were adopted. All melting points are uncorrected. IR spectra were measured as Nujol mulls and data are given in cm^{-1}. NMR spectra were taken on a JEOL JNM-FX 100 (^1H, 100 MHz; ^{13}C, 25 MHz) or a JEOL JNM-GX 270 (^1H, 270 MHz; ^{13}C, 68 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard and the chemical shifts are given in δ values. The following abbreviations are used; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. HRMS were determined with a JEOL JMS-D 300 spectrometer at 30 eV using a direct inlet system. UV spectra were measured in EtOH and are given in λ_{max} nm (ε). Preparative thin-layer chromatography (PTLC) was performed with a precoated silica gel plate Merck 60 F_{254} (0.5 mm thick). Column chromatography was carried out with silica gel (Wakogel C-200). Medium pressure liquid chromatography (MPLC) was performed on a Kusano CIG prepacked silica gel column. HPLC analysis was performed on a Tosoh TSK gel 120T column octadecyl silica (ODS), 4.6 × 250 mm) with an appropriate ratio of MeOH–H_2O as a mobile phase (flow rate, 0.6 ml/min), and the peak was detected by measuring UV (254 nm) absorption. The NMR spectral data of **5** and **6** are given in Tables I and II. All organic extracts were washed with brine and dried over anhydrous sodium sulfate before concentration. Identities were confirmed by comparisons of TLC behavior and IR and NMR spectra.

***N*-2-(2′-Furyl)ethylmethoxycarbonylacetamide (8)** A solution of methyl chloroformylacetate (20 g, 0.2 mol) in CH_2Cl_2 (40 ml) was added to a two layer solution of 50% K_2CO_3 aqueous solution (13.6 g, 0.2 mol) and β-furylethylamine **7** (20 g, 0.18 mol) in CH_2Cl_2 (200 ml) at 0 °C under vigorous stirring. The reaction mixture was further stirred for 1 h. After filtration to remove insoluble material, the reaction mixture was separated into the organic and aqueous layers. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was concentrated to dryness *in vacuo*. The residue in CH_2Cl_2 was passed through a short column of SiO_2 to give **8** (32 g, 83%) as colorless leaflets from Et_2O, mp 46—47 °C. IR: 3300, 1740, 1650. ^1H-NMR: 2.87 (2H, t, J = 7 Hz, –C<u>H</u>$_2$CH$_2$–N–), 3.30 (2H, s, –C<u>H</u>$_2$COOMe), 3.57 (2H, q, J = 7 Hz, –CH$_2$C<u>H</u>$_2$–N–), 3.73 (3H, s, COO<u>Me</u>), 6.08 (1H, dd, J = 1, 3 Hz, furan-H), 6.30 (1H, dd, J = 2, 3 Hz, furan-H), 7.33 (1H, dd, J = 1, 2 Hz, furan-H). *Anal.* Calcd for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.68; H, 6.13; N, 6.57.

Bischler–Napieralski Cyclization of 8 A solution of $POCl_3$ (10.92 g, 71 mmol) in CH_3CN (10 ml) was added to a solution of **8** (3 g, 14 mmol) and K_2CO_3 (5.88 g, 42 mmol) in CH_3CN (75 ml) over a period of 30 min under reflux with vigorous stirring. After further refluxing for 30 min, the mixture was cooled and basified by pouring it slowly into 5% NH_4OH solution at 0 °C. The solution was extracted with CH_2Cl_2, and the extract was concentrated to dryness *in vacuo*. The residue in benzene was passed through a short column of Florisil to give (*Z*)-4-methoxycarbonylmethylene-4,5,6,7-tetrahydrofuro[3,2-*c*]pyridine (**9**) (1.2 g, 43%), as colorless needles from Et_2O, mp 69—71 °C. IR: 3325, 1660, 1630. ^1H-NMR: 2.90 (2H, t, J = 7 Hz, –C<u>H</u>$_2$CH$_2$–N–), 3.57 (2H, dt, J = 2, 7 Hz, –CH$_2$C<u>H</u>$_2$–N–), 3.68 (3H, s, COO<u>Me</u>), 4.85 (1H, s, olefinic H), 6.47, 7.30 (each 1H, d, J = 2 Hz, furan-H), 8.11 (1H, br s, N<u>H</u>). ^{13}C-NMR: 23.1 (t), 40.4 (t), 50.2 (q), 79.8 (d), 106.4 (d), 115.2 (s), 142.3 (d), 153.4 (s), 154.1 (s), 170.9 (s). *Anal.* Calcd for $C_{10}H_{11}NO_3$: C, 62.16; H, 5.74; N, 7.25. Found: C, 61.99; H, 5.78; N, 7.17. HRMS *m/z* (M^+): Calcd: 193.0740. Found: 193.0758.

Methyl 4,5,7,8-Tetrahydrofuro[2,3-*g*]indolizine-9-carboxylate (Dioxopyrroline) (10) A solution of oxalyl chloride (7.2 g, 57 mmol) in dry Et_2O (50 ml) was added at 0 °C to a solution of **9** (9 g, 47 mmol) in dry Et_2O (100 ml). The mixture was stirred at room temperature for 10 min and the resulting crystals were collected by filtration. The crystals in $CHCl_3$ were passed through a short column of SiO_2 to give **10** (10.6 g, 92%), as orange needles from Et_2O, mp 196—198 °C. IR: 1750, 1700. UV: 249 (17100), 332 (9000), 405 (6000). ^1H-NMR: 3.23 (2H, t, J = 7 Hz, –C<u>H</u>$_2$CH$_2$–N–), 3.87 (3H, s, COOMe), 4.04 (2H, t, J = 7 Hz, –CH$_2$C<u>H</u>$_2$–N–), 7.54, 7.65 (each 1H, d, J = 2 Hz, furan-H). ^{13}C-NMR: 22.8 (t), 36.8 (t), 51.7 (q), 99.5 (s), 112.1 (s, d), 144.2 (d), 157.6 (s), 161.8 (s), 162.3 (s), 164.6 (s), 177.7 (s). *Anal.* Calcd for $C_{12}H_9NO_5$: C, 58.30; H, 3.67; N, 5.67. Found: C, 58.13; H, 3.55; N, 5.44. HRMS *m/z* (M^+): Calcd: 247.0479. Found: 247.0479.

Diels-Alder Reaction of 10 with 1,3-Bis(trimethylsilyloxy)-1,3-butadiene A solution of **10** (500 mg, 2 mmol) and 1,3-bis(trimethylsilyloxy)-1,3-butadiene[15] (1.4 g, 6 mmol) in dry dioxane (5 ml) was heated in a sealed tube at 130 °C for 30 min under stirring. The reaction mixtures obtained from ten experiments were combined and concentrated to dryness *in vacuo*. The residue was crystallized from hexane to give crude crystals, which were separated by fractional recrystallization from CH_2Cl_2–AcOEt to give (±)-(1*R**,5*R**,6*R**)-6-methoxycarbonyl-7,8-dioxo-1,3-bis(trimethyl-silyloxy)furanoerythrin-2-ene (**11a**) (6.45 g, 67%) and (±)-(1*R**,5*S**,6*S**)-6-methoxycarbonyl-7,8-dioxo-1,3-bis(trimethyl-silyloxy)furanoerythrin-2-ene (**11b**) (1.19 g, 12%).

11a: Colorless prisms, mp 162—164 °C. IR: 1765, 1740, 1720, 1600. ^{1}H-NMR: 0.10, 0.24 (each 9H, s, $OSiMe_3$), 2.53 (1H, d, J=14 Hz, H-4), 2.6—3.5 (3H, m, H-10, 11), 3.08 (1H, dd, J=2, 14 Hz, H-4), 3.25 (3H, s, COOMe), 4.5—4.8 (1H, m, H-10), 5.12 (1H, d, J=6 Hz, H-1), 5.33 (1H, br d, J=6 Hz, H-2), 6.06 (1H, d, J=2 Hz, H-14), 7.22 (1H, d, J=2 Hz, H-15). HRMS m/z (M^+): Calcd for $C_{22}H_{31}NO_7Si_2$: 477.1639. Found: 477.1649.

11b: Colorless prisms, mp 143.5—145.5 °C. IR: 1780, 1760, 1730, 1655. ^{1}H-NMR: 0.15, 0.22 (each 9H, s, $OSiMe_3$), 2.32 (1H, dd, J=1, 16 Hz, H-4), 2.6—3.9 (3H, m, H-10, 11), 3.19 (1H, dd, J=2, 16 Hz, H-4), 3.28 (3H, s, COOMe), 4.5—4.8 (1H, m, H-10), 5.06 (1H, d, J=7 Hz, H-1), 5.20 (1H, br d, J=7 Hz, H-2), 6.29 (1H, d, J=2 Hz, H-14), 7.27 (1H, d, J=2 Hz, H-15). HRMS m/z (M^+): Calcd for $C_{22}H_{31}NO_7Si_2$; 477.1639. Found: 477.1636.

The mother liquor was evaporated under reduced pressure (10 mmHg, 100 °C, 1 h) and the residue was crystallized from CH_2Cl_2–AcOEt to give **12** (102 mg, 2%) as pale yellow leaflets, mp 192—193 °C. IR: 1730, 1700, 1670. ^{1}H-NMR: 2.68, 3.49 (each 1H, d, J=17 Hz), 3.08 (2H, t, J=7 Hz), 3.6—4.1 (2H, m), 3.80 (3H, s, COOMe), 5.50, 7.28 (each 1H, d, J=6 Hz), 7.44, 7.48 (each 1H, d, J=2 Hz). ^{13}C-NMR: 22.1 (t), 36.8 (t), 39.9 (t), 51.1 (q), 82.8 (s), 102.7 (s), 105.8 (d), 111.1 (s), 111.3 (d), 143.0 (d), 147.8 (s), 158.0 (s), 160.2 (d), 162.9 (s), 173.2 (s), 189.5 (s). MS m/z: 315 (M^+), 245 (base peak). HRMS m/z (M^+): Calcd for $C_{16}H_{13}NO_6$: 315.0743. Found: 315.0748.

(±)-(5*R,6*S**,7*S**)-7-Hydroxy-6-methoxycarbonyl-3,8-dioxofurano-erythrin-1-ene (13)** A solution of **11a** (500 mg) in dry THF (20 ml) was stirred with $LiBH_4$ (50 mg) at −60 °C for 2 h under an Ar atmosphere. The reaction mixture was diluted with CH_2Cl_2, washed with brine, dried over $MgSO_4$, and concentrated to dryness *in vacuo*. The residue was dissolved in 5% HCl–THF (1 : 1, 50 ml) and refluxed for 45 min. The reaction mixture was extracted with CH_2Cl_2, and the extract was concentrated to dryness *in vacuo*. The residue was crystallized from CH_2Cl_2–MeOH to give **13** (290 mg, 87%) as colorless prisms, mp 217—218 °C. IR: 3270, 1735, 1690. UV: 210 (16000), 240 (sh, 5000). ^{1}H-NMR: 2.5—3.6 (5H, m, H-4, 10, 11), 3.41 (3H, s, COOMe), 4.76 (1H, br s, H-7), 5.98 (1H, d, J=2 Hz, H-14), 6.39 (1H, d, J=11 Hz, H-2), 7.22 (1H, d, J=2 Hz, H-15), 7.32 (1H, d, J=11 Hz, H-1). *Anal.* Calcd for $C_{16}H_{15}NO_6$: C, 60.56; H, 4.77; N, 4.41. Found: C, 60.32; H, 4.79; N, 4.32. HRMS m/z (M^+): Calcd: 317.0898. Found: 317.0895.

11b (100 mg) was reduced and treated with acid as described above to give **13** (55 mg, 83%).

Mesylation of Enone-alcohol 13 A solution of **13** (1 g, 32 mmol) and methanesulfonyl chloride (500 mg, 44 mmol) in pyridine (8 ml) was stirred at room temperature for 2 h. The mixture was diluted with ice-cooled 5% K_2CO_3 solution and extracted with CH_2Cl_2. Concentration of the extract gave a residue, which was crystallized from AcOEt–Et_2O to give (±)-(5*R**,6*S**,7*S**)-7-methanesulfonyloxy-6-methoxycarbonyl-3,8-di oxofuranoerythrin-1-ene (**14**) (1.16 g, 93%), as colorless prisms, mp 215—217 °C. IR: 1740, 1710, 1680. UV: 210 (4100), 238 (sh, 1200). ^{1}H-NMR: 2.4—3.5 (3H, m, H-10, 11), 2.83 (1H, d, J=17 Hz, H-4), 3.07 (1H, br d, J=17 Hz, H-4), 3.38 (3H, s, $OSO_2\underline{Me}$), 3.44 (3H, s, COOMe), 5.53 (1H, s, H-7), 5.97 (1H, d, J=2 Hz, H-14), 6.44 (1H, d, J=11 Hz, H-2), 7.23 (1H, d, J=2 Hz, H-15), 7.25 (1H, d, J=11 Hz, H-1). ^{13}C-NMR: 22.6 (t, C11), 35.0 (t, C4), 40.0 (q, COOMe), 48.6 (t, C10), 52.6 (q, OSO_2Me), 57.3 (s, C6), 62.5 (s, C5), 80.8 (d, C7), 106.5 (d, C14), 116.5 (s, C13), 129.6 (d, C2), 142.3 (d, C1), 142.4 (d, C15), 148.7 (s, C12), 164.8 (s, C8), 166.9 (s, COOMe), 193.6 (s, C3). HRMS m/z (M^+): Calcd for $C_{17}H_{17}NO_8S$: 395.0675. Found: 395.0663.

(±)-3,8-Dioxofuranoerythrina-1,6-diene (15) A mixture of **14** (100 mg, 0.25 mmol) and $MgCl_2$ (60 mg, 1.25 mmol) in DMSO (5 ml) was heated at 140 °C in a sealed tube for 3h. The combined reaction mixture obtained from the same reaction of **14** (3 g) was diluted with $CHCl_3$. The organic layer was washed with water, and concentrated to dryness *in vacuo*. The residue in $CHCl_3$ was passed through a short column of SiO_2 to give **15** (1.72 g, 94%), as pale yellow prisms from AcOEt–Et_2O, mp 181—182 °C. IR: 1690, 1670. UV: 210 (3500), 267 (3000). ^{1}H-NMR: 2.4—3.5 (3H, m, H-10, 11), 2.76, 3.17 (each 1H, d, J=15 Hz, H-4), 4.3—4.7 (1H, m, H-10), 6.17 (1H, d, J=2 Hz, H-14), 6.26 (1H, s, H-7), 6.39 (1H, d, J=10 Hz, H-2), 7.24 (1H, d, J=2 Hz, H-15), 7.56 (1H, d, J=10 Hz, H-1). ^{13}C-NMR: 23.1 (t, C11), 35.3 (t, C4), 51.3 (t, C10), 66.0 (s, C5), 106.6 (d, C14), 118.7 (s, C13), 123.6 (d, C7), 132.4 (d, C2), 137.0 (d, C1), 142.1 (d, C15), 148.5 (s, C6), 155.1 (s, C12), 170.6 (s, C8), 195.0 (s, C3). *Anal.* Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.59; N, 5.80. Found: C, 69.51; H, 4.82; N, 5.78. HRMS m/z (M^+): Calcd: 241.0736. Found: 241.0716.

Reduction of Dienone 15 with $NaBH_4$–$CeCl_3$ $NaBH_4$ (80 mg, 2.1 mmol) was added to a solution of **15** (500 mg, 2.1 mmol) and $CeCl_3 \cdot 7H_2O$ (510 mg, 0.42 mmol) in MeOH (100 ml) at −60 °C. The mixture was stirred at the same temperature for 30 min. After decomposition of the excess hydride with water, the mixture was extracted with $CHCl_3$ to give the alcohol **16**, which was separated by MPLC (with $CHCl_3$: iso-PrOH (1 : 1)) to give (±)-(3*R**,5*S**)-3-hydroxy-8-oxofuranoerythrina-1,6-diene (**16a**) (278 mg, 55%) and (±)-(3*R**,5*R**)-3-hydroxy-8-oxofuranoerythrina-1,6-diene (**16b**) (148 mg, 30%).

16a: Colorless prisms from CH_2Cl_2–Et_2O, mp 198—200 °C. IR: 3250, 1650. UV: 212 (11000), 248 (14800). ^{1}H-NMR ($CDCl_3$–DMSO-d_6–D_2O): 1.74 (1H, t, J=11 Hz, H-11), 2.2—3.5 (4H, m, H-4, 10, 11), 4.4—4.8 (1H, m, H-3), 4.48 (1H, dd, J=6, 13 Hz, H-10), 4.92 (1H, br s, O$\underline{H}$), 5.18 (1H, s, H-7), 6.21 (1H, d, J=2 Hz, H-14), 6.32 (1H, br d, J=10 Hz, H-1), 6.62 (1H, dd, J=2, 10 Hz, H-2), 7.24 (1H, d, J=2 Hz, H-15). *Anal.* Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.40; H, 5.18; N, 5.54. HRMS m/z (M^+): Calcd: 243.0896. Found: 243.0896.

16b: Colorless prisms from CH_2Cl_2–Et_2O, mp 176—178 °C. IR: 3400, 1660. UV: 215 (12000), 242 (13500). ^{1}H-NMR ($CDCl_3$–DMSO-d_6–D_2O): 1.8—3.5 (5H, m, H-4, 10, 11), 4.3—4.8 (2H, m, H-3, 10), 5.81 (1H, s, H-7), 6.29 (1H, dd, J=5, 10 Hz, H-2), 6.56 (1H, d, J=2 Hz, H-14), 6.70 (1H, d, J=10 Hz, H-1), 7.21 (1H, d, J=2 Hz, H-15). *Anal.* Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.32; H, 5.41; N, 5.65. HRMS m/z (M^+): Calcd: 243.0896. Found: 243.0895.

Methylation of the Dienol 16 with Methyl Iodide A mixture of **16a** (500 mg), KOH (2.5 g), and Et_4NBr (1.3 g) in dry THF (300 ml) was treated with CH_3I (5 g) at room temperature for 18 h under stirring. The mixture was extracted with $CHCl_3$, and the extract was washed with 10% Na_2SO_3, and concentrated to dryness *in vacuo*. The residue was crystallized from Et_2O to give (±)-(3*R**,5*S**)-3-methoxy-8-oxofuranoerythrina-1,6-diene (**17a**) (519 mg, 98%), as colorless prisms, mp 139—142 °C. IR: 1660. UV: 214 (12800), 250 (13600). ^{1}H-NMR: 1.72 (1H, dd, J=10, 11 Hz, H-4), 2.4—3.5 (4H, m, H-4, 10, 11), 3.41 (3H, s, OMe), 4.0—4.5 (1H, m, H-3), 4.0—4.5 (1H, m, H-3), 4.55 (1H, ddd, J=1,6,7 Hz, H-10), 5.86 (1H, s, H-7), 6.20 (1H, d, J=2 Hz, H-14), 6.31 (1H, d, J=10 Hz, H-1), 6.69 (1H, dd, J=2, 10 Hz, H-2), 7.24 (1H, d, J=2 Hz, H-15). ^{13}C-NMR ($CDCl_3$–DMSO-d_6): 22.7 (t, C11), 34.3 (t, C4), 41.2 (t, C10), 56.4 (q, OMe), 64.1 (s, C5), 74.3 (d, C3), 107.7 (d, C14), 117.5 (d, C2), 118.6 (s, C13), 122.5 (d, C7), 136.6 (d, C1), 141.3 (d, C15), 148.2 (s, C6), 158.2 (s, C12), 171.4 (s, C8). *Anal.* Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.22; H, 5.78; N, 5.56. HRMS m/z (M^+): Calcd: 257.1049. Found: 257.1036.

16b (500 mg) was similarly methylated to give (±)-(3*R**,5*R**)-3-methoxy-8-oxofuranoerythrina-1,6-diene (**17b**) (518 mg, 98%), as colorless prisms from Et_2O, mp 173—175 °C. IR: 1670. UV: 215 (13000), 242 (14300). ^{1}H-NMR: 1.93 (1H, dd, J=6, 14 Hz, H-4), 2.3—3.4 (4H, m, H-4, 10, 11), 3.37 (3H, s, OMe), 4.14 (1H, t, J=6 Hz, H-3), 4.49 (1H, ddd, J=1, 6, 13 Hz, H-10), 5.80 (1H, s, H-7), 6.33 (1H, dd, J=4, 10 Hz, H-2), 6.52 (1H, d, J=2 Hz, H-14), 6.70 (1H, d, J=10 Hz, H-1), 7.17 (1H, d, J=2 Hz, H-15). *Anal.* Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.12; H, 5.65; N, 5.32. HRMS m/z (M^+): Calcd: 257.1049. Found: 257.1054.

Oxidation of the Dienone 15 with NBA NBA (25 mg, 1.5 eq) was added to a solution of **15** (30 mg) in MeOH (15 ml) at 0 °C and the mixture was stirred at room temperature for 10 min. The mixture was extracted with CH_2Cl_2 and the extract was washed with 10% Na_2SO_3, and concentrated to dryness *in vacuo*. The residue was purified by column chromatography (with CH_2Cl_2) and then by MPLC (with AcOEt) to give (±)-(5*R**,12*R**,15*R** or 15*S**)-12,15-dimethoxy-3,8-dioxo-12,15-dihydrofuranoerythrina-1,6-diene (**18a**) (16 mg, 42%) from the less polar fractions and (±)-(5*R**,12*R**,15*S** or 15*R**)-12,15-dimethoxy-3,8-dioxo-12,15-dihydrofuranoerythrina-1,6-diene (**18b**) (11 mg, 29%) from the more polar fractions.

18a: Colorless prisms from CH_2Cl_2–Et_2O, mp 182—184 °C. IR: 1700, 1680. UV: 205 (10600), 270 (11300). ^{1}H-NMR: 1.69 (1H, dd, J=5, 13 Hz,

H-11), 2.30 (1H, br d, $J=13$ Hz, H-11), 2.54, 3.48 (each 1H, d, $J=15$ Hz, H-4), 3.0—3.5 (1H, m, H-10), 3.19, 3.46 (each 3H, s, OMe), 4.27 (1H, ddd, $J=2$, 5, 13 Hz, H-10), 5.28 (1H, d, $J=1$ Hz, H-15), 5.57 (1H, d, $J=1$ Hz, H-14), 6.26 (1H, d, $J=10$ Hz, H-2), 6.31 (1H, s, H-7), 7.56 (1H, d, $J=10$ Hz, H-1). *Anal.* Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.16; H, 5.76; N, 4.43. HRMS *m/z* (M^+): Calcd: 303.1105. Found: 303.1105.

18b: Colorless prisms from CH_2Cl_2–Et_2O, mp 208—210 °C. IR: 1700, 1680. UV: 205 (11000), 271 (12800). ^{1}H-NMR: 1.90 (1H, dd, $J=5$, 13 Hz, H-11), 2.43 (1H, br d, $J=13$ Hz, H-11), 2.54, 3.47 (each 1H, d, $J=15$ Hz, H-4), 3.0—3.4 (1H, m, H-10), 3.13, 3.34 (each 3H, s, OMe), 4.1—4.4 (1H, m, H-10), 5.58 (1H, s, H-15), 5.70 (1H, s, H-14), 6.27 (1H, d, $J=10$ Hz, H-2), 6.32 (1H, s, H-7), 7.58 (1H, d, $J=10$ Hz, H-1). *Anal.* Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.22; H, 5.54; N, 4.80. HRMS *m/z* (M^+): Calcd: 303.1105. Found: 303.1109.

Oxidation of the Dienone 15 with TTN A mixture of **15** (10 mg) and TTN (18 mg, 5 eq) in MeOH (5 ml) was heated at 60 °C for 18 h. NaCl (2 mg) was added, and the reaction mixture was heated for a further 30 min. After removal of precipitates by filtration, the filtrate was extracted with CH_2Cl_2 and the extract was washed with 10% Na_2SO_3, and concentrated to dryness *in vacuo*. The residue was purified by column chromatograhy (with CH_2Cl_2) and MPLC (with AcOEt) to give **18** (4 mg, 31%) as a colorless oil (1 : 1 mixture of **18a** and **18b**) from the less polar fractions, the starting material **15** (4 mg, 40%) from the next fractions, and (±)-(5*R**,11*R**)-11-methoxy-3,8-dioxofuranoerythrina-1,6-diene (**20**) (1 mg, 7%) from the most polar fractions as colorless prisms from Et_2O–hexane, mp 233—235 °C. IR ($CHCl_3$): 1680. UV: 207 (15000), 268 (12000). ^{1}H-NMR: 2.71, 3.11 (each 1H, d, $J=15$ Hz, H-4), 3.19 (1H, dd, $J=3$, 15 Hz, H-10), 3.46 (3H, s, OMe), 4.37 (1H, br d, $J=3$ Hz, H-11), 4.75 (1H, br d, $J=15$ Hz, H-10), 6.23 (1H, d, $J=2$ Hz, H-14), 6.34 (1H, s, H-7), 6.40 (1H, d, $J=10$ Hz, H-2), 7.34 (1H, d, $J=2$ Hz, H-15), 7.60 (1H, d, $J=10$ Hz, H-1). HRMS *m/z* (M^+): Calcd for $C_{15}H_{13}NO_4$; 271.0843. Found: 271.0843.

Acidic Rearrangement of the Dimethoxy-dihydrofuran 18 1) A mixture of **18** (20 mg) and *p*-TsOH (4 mg) in benzene (20 ml) was heated under reflux for 1 h. The reaction mixture was diluted with benzene, washed with water, dried and concentrated. The residue was purified by column chromatography (with CH_2Cl_2) and MPLC (with AcOEt) to give (±)-3,8-dioxofuranoerythrina-1,6,10-triene (**19**) (1 mg, 6%), (±)-(5*R**,12*R**)-3,8,15-trioxo-3,8-dioxo-12,15-dihydrofuranoerythrina-1,6-diene (**21**) (3 mg, 18%), **20** (1 mg, 6%), and (±)-(5*R**,12*R**,13*S**)-12-methoxy-3,8,15-trioxo-12,13,14,15-tetrahydrofuranoerythrina-1,6-diene (**22**) (3 mg, 16%).

19: Colorless prisms from CH_2Cl_2–MeOH, mp 152—154 °C. IR ($CHCl_3$): 1700. UV: 209 (11200), 267 (22300), 409 (1600). ^{1}H-NMR: 2.45, 3.28 (each 1H, d, $J=14$ Hz, H-4), 6.16 (1H, d, $J=2$ Hz, H-14), 6.20 (1H, dd, $J=1$,7 Hz, H-10), 6.38 (1H, d, $J=10$ Hz, H-2), 6.40 (1H, s, H-7), 6.88 (1H, d, $J=7$ Hz, H-10), 7.24 (1H, d, $J=2$ Hz, H-15), 7.73 (1H, dd, $J=1$, 10 Hz, H-1). HRMS *m/z* (M^+): Calcd for $C_{14}H_9NO_3$: 239.0582. Found: 239.0597.

21: Colorless oil. IR ($CHCl_3$): 1790, 1700. UV: 212 (10500), 267 (7600). ^{1}H-NMR: 2.2—3.2 (3H, m, H-10, 11), 2.76, 3.23 (each 1H, d, $J=15$ Hz, H-4), 4.3—4.6 (1H, m, H-10), 5.17 (1H, dd, $J=5$, 11 Hz, H-12), 5.66 (1H, br s, H-14), 6.34 (1H, d, $J=10$ Hz, H-2), 6.41 (1H, s, H-7), 7.63 (1H, d, $J=10$ Hz, H-1). HRMS *m/z* (M^+): Calcd for $C_{14}H_{11}NO_4$: 257.0689. Found: 257.0714.

22: Colorless prisms from Et_2O, mp 152—154 °C. IR ($CHCl_3$): 1720, 1680. UV: 210 (8400), 268 (11800). ^{1}H-NMR: 1.9—3.9 (8H, m), 3.63 (3H, s, OMe), 6.21 (1H, d, $J=10$ Hz, H-2), 6.43 (1H, s, H-7), 7.53 (1H, d, $J=10$ Hz, H-1). HRMS *m/z* (M^+): Calcd for $C_{15}H_{15}NO_5$: 289.0951. Found: 289.0983.

2) A mixture of **18** (50 mg) and trimethylsilyl iodide (165 mg, 5eq) in MeCN (60 ml) was stirred at room temperature for 18 h under an Ar atmosphere. The reaction mixture was diluted with Et_2O, washed with 10% Na_2CO_3 and 10% $Na_2S_2O_3$, and concentrated to dryness *in vacuo*. The residue was purified as described above to give (±)-3,8,15-trioxo-14,15-dihydrofuranoerythrina-1,6-diene (**23**) (7 mg, 17%) and **21** (5 mg, 12%).

23: Colorless prisms from AcOEt–Et_2O, mp 177—180 °C. IR: 1810, 1770, 1660. ^{1}H-NMR: 2.0—3.5 (5H, m, H-10, 11, 14), 2.76, 3.17 (each 1H, d, $J=16$ Hz, H-4), 4.51 (1H, ddd, $J=1$, 6, 14 Hz, H-10), 6.32 (1H, s, H-7), 6.33 (1H, d, $J=10$ Hz, H-2), 7.55 (1H, dd, $J=1$, 10 Hz, H-1). ^{13}C-NMR (68 MHz, $CDCl_3$–DMSO-d_6): 22.7 (t, C11), 33.8 (t, C4), 34.8 (t, C14), 50.3 (t, C10), 65.9 (s, C5), 112.1 (d, C13), 124.8 (d, C2), 132.6 (d, C7), 136.6 (d, Cl), 150.8 (s, C12), 153.7 (s, C6), 170.2 (s, C8), 172.7 (s, C15), 194.6 (s, C3). MS *m/z*: 257 (M^+), 239 (base peak). *Anal.* Calcd for $C_{14}H_{11}NO_4$: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.42; H, 4.48; N, 5.23. HRMS *m/z* (M^+): Calcd: 257.0689. Found: 257.0651.

Oxidation of the Dienone 15 with NBA in Aqueous Acetone and Rearrangement of the Product 24 General Method of NBA Oxidation: A solution of **15** and NBA (1.5 mol eq) in acetone–H_2O (9 : 1) was stirred at room temperature for 5 min. After evaporation of the solvent *in vacuo*, the residue (crude **24**) was used for the following reactions.

SiO_2 in MeOH: Compound **24** from **15** (50 mg) in MeOH (5 ml) was treated with SiO_2 (10 mg) at room temperature overnight. After removal of SiO_2 by filtration, the filtrate was concentrated to dryness *in vacuo*. The residue was purified by column chromatography (with CH_2Cl_2) and PTLC (with AcOEt) to give **22** (20 mg, 33%), **20** (4 mg, 7%), and **23** (6 mg, 11%).

SiO_2 in Benzene: A mixture of **24** [from **15** (10 mg)] and SiO_2 (2 mg) in benzene (10 ml) was refluxed for 1 h. The product was purified by MPLC (with AcOEt) to give **23** (6 mg, 56%).

p-TsOH in Benzene: A mixture of **24** [from **13** (100 mg)] and *p*-TsOH (5 mg) in benzene (60 ml) was refluxed for 30 min. The product was purified by MPLC (eluted with AcOEt) to give **23** (36 mg, 52%) and (±)-(5*R**,11*R**)-11-hydroxy-3,8-dioxofuranoerythrina-1,6-diene (**25**) (24 mg, 23%), as colorless prisms from CH_2Cl_2–MeOH, mp 238—240 °C. IR: 3300, 1670. UV: 212 (14000), 268 (9800). ^{1}H-NMR ($CDCl_3$–DMSO-d_6–D_2O): 2.71, 3.10 (each 1H, d, $J=15$ Hz, H-4), 3.34 (1H, dd, $J=3$, 15 Hz, H-10), 4.59 (1H, d, $J=15$ Hz, H-10), 4.80 (1H, d, $J=3$ Hz, H-11), 6.21 (1H, d, $J=2$ Hz, H-14), 6.35 (1H, s, H-7), 6.40 (1H, d, $J=10$ Hz, H-2), 7.34 (1H, d, $J=2$ Hz, H-15), 7.66 (1H, d, $J=10$ Hz, H-1). HRMS *m/z* (M^+): Calcd for $C_{14}H_{11}NO_4$; 257.0689. Found: 257.0700.

Nafion-H in THF: A mixture of **24** [from **15** (200 mg)] and Nafion-H (500 mg, 10—35 mesh, Aldrich Chemical Co.) in THF (40 ml) was stirred at room temperature for 15 min. After removal of Nafion-H by filtration, the filtrate was concentrated *in vacuo* and extracted with CH_2Cl_2. The extract was washed with 10% Na_2SO_3, and concentrated to dryness *in vacuo*. The residue was crystallized from AcOEt–Et_2O to give **23** (135 mg, 65%).

Addition of Methanol to the Enol-Lactone 23 1) A solution of **23** (10 mg) in MeOH (5 ml) was treated with SiO_2 (100 mg) at room temperature overnight. After removal of SiO_2 by filtration, the filtrate was concentrated to dryness *in vacuo* and the residue was crystallized from Et_2O to give **22** (11 mg, 97%).

A solution of **23** (10 mg) in MeOH (5 ml) and concentrated HCl (1 drop) was stirred at room temperature for 1 h, then basified with 10% K_2CO_3 solution, and extracted with CH_2Cl_2. The extract was concentrated to dryness *in vacuo* and the residue was crystallized from Et_2O to give **22** (10 mg, 90%).

Oxidation of the Dienol 17 with NBA in MeOH 1) A mixture of **17a** (200 mg) and NBA (170 mg, 1.5 mol eq) in MeOH (30 ml was stirred at 0 °C for 10 min. The product was purified by MPLC (with benzene : acetone = 4 : 1) to give (±)-(3*R**,5*S**,12*S**,15*R** or 15*S**)-3,12,15-trimethoxy-8-oxo-12,15-dihydrofuranoerythrina-1,6-diene (**26a**-1) (87 mg, 45%) and (±)-(3*R**,5*S**,12*S**,15*S** or 15*R**)-3,12,15-trimethoxy-8-oxo-12,15-dihydrofuranoerythrina-1,6-diene (**26a**-2) (104 mg, 52%).

26a-1: Colorless gum. IR: 1675 cm^{-1}. ^{1}H-NMR: 1.3—4.4 (7H, m), 3.34, 3.42, 3.49 (each 3H, s, OMe), 5.29 (1H, d, $J=1$ Hz, H-15), 5.57 (1H, d, $J=1$ H, H-14), 5.93 (1H, s, H-7), 6.22 (1H, br d, $J=10$ Hz, H-1), 6.66 (1H, dd, $J=2$, 10 Hz, H-2). ^{13}C-NMR: 34.7 (dd, C4), 36.6 (dd, C11), 39.6 (dd, C10), 50.3 (q, OMe), 56.2 (q, OMe), 56.4 (q, OMe), 65.5 (s, C5), 74.9 (d, C3), 105.3 (d, C15), 108.8 (s, C12), 118.5 (d, C2), 121.5 (d, C7), 123.3 (d, C14), 137.3 (d, C1), 140.3 (s, C6), 156.8 (s, C13), 170.0 (s, C8). HRMS *m/z* (M^+): Calcd for $C_{17}H_{21}NO_5$: 319.1418. Found: 319.1412.

26a-2: Colorless prisms, mp 122—124 °C from Et_2O. IR: 3070, 1690. ^{1}H-NMR: 1.2—4.4 (7H, m), 3.27, 3.30, 3.41 (each 3H, s, OMe), 5.58, 5.76, 5.94 (each 1H, s, H-7, 14, 15), 6.21 (1H, br d, $J=10$ Hz, H-1), 6.67 (1H, dd, $J=2$, 10 Hz, H-2). ^{13}C-NMR: 34.7 (t, C4), 36.3 (t, C11), 39.0 (t, C10), 49.6 (q, OMe), 54.4 (q, OMe), 56.3 (q, OMe), 65.3 (s, C5), 74.9 (d, C3), 106.7 (d, C15), 110.7 (s, C12), 118.8 (d, C2), 121.9 (d, C7), 124.0 (d, C14), 136.9 (d, C1), 140.5 (s, C6), 156.5 (s, C13), 170.0 (s, C8).

Anal. Calcd for $C_{17}H_{21}NO_5$: C: 63.93, H: 6.63, N: 4.39. Found: C: 63.78, H: 6.72, N: 4.41. HRMS *m/z* (M^+): Calcd: 319.1418. Found: 319.1442.

2) A solution of **17b** (10 mg) in MeOH (10 ml) was similarly treated with NBA (7 mg) to give (±)-(3*R**,5*R**,12*R**,15*R** and 15*S**)-3,12,15-trimethoxy-8-oxo-12,15-dihydrofuranoerythrina-1,6-diene (**26b**) (12 mg, 97%) as a mixture of stereoisomers, colorless oil. IR (film): 1690. HRMS *m/z* (M^+): Calcd for $C_{17}H_{21}NO_5$; 319.1418. Found: 319.1432.

γ-Lactones 27 and 28 1) A solution of **17a** (300 mg, 1.17 mmol) and

NBA (240 mg, 1.74 mmol) in acetone–H_2O (9 : 1, 50 ml) was treated at 0 °C for 10 min. After removal of the solvent by evaporation *in vacuo*, the residue in dry THF (50 ml) was treated with Nafion-H (250 mg) under stirring at room temperature for 15 min. The product was crystallized from AcOEt–Et_2O to give (±)-(3*R**,5*S**)-3-methoxy-8,15-dioxo-14,15-dihydrofuranoerythrina-1,6-diene (**27a**) (210 mg, 66%) as colorless prisms, mp 202—204 °C. IR: 1800, 1680. ^{1}H-NMR: 1.74 (1H, dd, J=10, 12 Hz, H-4), 1.9—3.5 (6H, m, H-4, 10, 11, 14), 3.43 (3H, s, OMe), 3.9—4.2 (1H, m, H-3), 4.44 (1H, dq, J=1, 7 Hz, H-10), 5.92 (1H, s, H-7), 6.25 (1H, br d, J=10 Hz, H-1), 6.68 (1H, dd, J=2, 10 Hz, H-2). ^{13}C-NMR (68 MHz): 22.6 (t, C11), 34.1 (t, C4), 34.7 (t, C14), 41.1 (t, C10), 56.5 (q, OMe), 64.2 (s, C5), 73.8 (d, C3), 112.5 (s, C13), 119.1 (d, C2), 122.7 (d, C7), 136.2 (d, Cl), 150.8 (s, C12), 156.5 (s, C6), 171.4 (s, C8), 173.6 (s, C15). MS m/z: 273 (M^+), 241 (M^+-32), 175 (base peak). *Anal.* Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.78; H, 5.68; N, 5.24. HRMS m/z (M^+): Calcd: 273.1000. Found: 273.0991.

The mother liquor was purified by MPLC (with AcOEt) to give (±)-(3*R**,5*S**,12*S**)-3-methoxy-8,15-dioxo-12,15-dihydrofuranoerythrina-1,6-diene (**28a**) (40 mg, 13%), as pale yellow prisms from AcOEt–Et_2O, mp 223—225 °C. IR: 1740, 1680. ^{1}H-NMR: 1.0—3.3 (5H, m, H-4, 10, 11), 3.44 (3H, s, OMe), 3.7—4.0 (1H, m, H-3), 4.45 (1H, ddd, J=2, 5, 14 Hz, H-10), 5.19 (1H, ddd, J=2, 6, 12 Hz, H-12), 5.66 (1H, br d, J=1 Hz, H-14), 6.02 (1H, s, H-7), 6.30 (1H, br d, J=10 Hz, H-1), 6.73 (1H, dd, J=2, 10 Hz, H-2). ^{13}C-NMR ($CDCl_3$–DMSO-d_6): 33.6 (t, C4), 35.6 (t, C11), 37.4 (t, C10), 56.4 (q, OMe), 65.4 (s, C5), 73.8 (d, C3), 77.8 (d, C-12), 113.2 (d, C14), 118.7 (d, C2), 121.2 (d, C7), 137.7 (d, C1), 155.3 (s, C6), 166.6 (s, C13), 169.2 (s, C8), 174.3 (s, C15). MS m/z: 273 (M^+), 241 (base peak). HRMS m/z (M^+): Calcd for $C_{15}H_{15}NO_4$; 273.1000. Found; 273.1033.

2) Compound **17b** (500 mg, 1.95 mmol) was oxidized with NBA (400 mg, 2.90 mmol) in acetone–H_2O (9 : 1, 75 ml) and treated with Nafion-H (375 mg) at room temperature for 15 min. The product was purified as described above to give (±)-(3*R**,5*R**)-3-methoxy-8,15-dioxo-14,15-dihydrofuranoerythrina-1,6-diene (**27b**) (245 mg, 46%) and (±)-(3*R**,5*R**,12*R**)-3-methoxy-8,15-dioxo-12,15-dihydrofuranoerythrina-1,6-diene (**28b**) (67 mg, 12%).

27b: Colorless prisms from AcOEt–Et_2O, mp 160—162 °C. IR: 1800, 1690. ^{1}H-NMR: 1.94 (1H, dd, J=6, 14 Hz, H-4), 2.1—3.5 (6H, m, H-4, 10, 11, 14), 3.43 (3H, s, OMe), 4.08 (1H, br t, J=6 Hz, H-3), 4.44 (1H, q, J=6 Hz, H-10), 5.85 (1H, s, H-7), 6.23 (1H, dd, J=4, 10 Hz, H-2), 6.64 (1H, d, J=10 Hz, H-1). ^{13}C-NMR: 22.5 (t, C11), 34.1 (t, C4), 34.9 (t, C14), 37.3 (t, C10), 57.4 (q, OMe), 60.9 (s, C5), 72.7 (d, C3), 114.3 (s, C13), 119.4 (d, C2), 122.8 (d, C7), 133.0 (d, C1), 148.9 (s, C12), 156.4 (s, C6), 171.3 (s, C8), 175.0 (s, C15). MS m/z: 273 (M^+), 241 (base peak). HRMS m/z (M^+): Calcd for $C_{15}H_{15}NO_4$; 273.1000. Found: 273.0980.

28b: Pale yellow prisms from AcOEt–Et_2O, mp 210—212 °C. IR: 1740, 1680. ^{1}H-NMR: 1.1—3.2 (4H, m, H-4, 10, 11) 1.90 (1H, dd, J=5, 14 Hz, H-4), 3.30 (3H, s, OMe), 4.08 (1H, br t, J=5 Hz, H-3), 4.38 (1H, br dd, J=6, 15 Hz, H-10), 5.15 (1H, br dd, J=6, 11 Hz, H-12), 5.59 (1H, d, J=1 Hz, H-14), 5.98 (1H, s, H-7), 6.33 (1H, dd, J=4, 10 Hz, H-2), 6.77 (1H, d, J=10 Hz, H-1). ^{13}C-NMR: 33.5 (t, C4), 35.7 (t, C10 and C11), 57.0 (q, OMe), 62.8 (s, C5), 72.2 (d, C3), 77.8 (d, C12), 113.3 (d, C14), 119.7 (d, C2), 122.6 (d, C7), 133.7 (d, C1), 155.0 (s, C6), 169.0 (s, C8 and C13), 171.7 (s, C15). MS m/z: 273 (M^+), 241 (base peak). HRMS m/z (M^+): Calcd for $C_{15}H_{15}NO_4$; 273.1000. Found: 273.1031.

Alkaline Hydrolysis of the Enol Lactone 27 1) A mixture of **27a** (150 mg) and KOH (500 mg) in H_2O–MeOH (4 : 1, 25 ml) was heated at 80 °C for 1 h. The mixture was acidified with 5% HCl and extracted with $CHCl_3$ and then Et_2O. The combined organic extract was concentrated to dryness *in vacuo* and the residue was crystallized from AcOEt–Et_2O to give (±)-(3*R**,5*R**,12*S**,13*R**)-12-hydroxy-3-methoxy-8,15-dioxo-12,13,14,15-tetrahydrofuranoerythrina-1,6-diene (**30a**) (152 mg, 95%) as colorless prisms, mp 195—197 °C. IR: 3200, 1780, 1670. ^{1}H-NMR ($CDCl_3$–DMSO-d_6): 1.1—4.6 (10H, m), 3.43 (3H, s, OMe), 5.91 (1H, s, H-7), 6.19 (1H, br d, J=10 Hz, H-1), 6.55 (1H, dd, J=2, 10 Hz, H-2). ^{13}C-NMR (68 MHz, $CDCl_3$–DMSO-d_6): 32.6 (t, C4), 33.1 (t, C11), 34.4 (t, C14), 37.4 (t, C10), 45.1 (d, C13), 56.3 (q, OMe), 63.0 (s, C5), 73.5 (d, C3), 106.8 (s, C12), 118.4 (d, C2), 121.3 (d, C7), 136.5 (d, C1), 157.4 (s, C6), 169.8 (s, C8), 171.5 (s, C15). MS m/z: 291 (M^+), 273 (M^+-H_2O), 175 (base peak). *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.77: H, 5.78; N, 4.91. HRMS m/z (M^+): Calcd: 291.1106. Found: 291.1106.

(2) A mixture of **27b** (100 mg) and KOH (400 mg) in H_2O–MeOH (4 : 1, 20 ml) was hydrolyzed as described above to give (±)-(3*R**,5*S**,12*R**,13*S**)-3-hydroxy-3-methoxy-8,15-dioxo-12,13,14,15-tetrahydrofuranoerythrina-1,6-diene (**30b**) (99 mg, 93%), as colorless prisms from AcOEt–Et_2O, mp 150—152 °C. IR: 3375, 1740, 1680. ^{1}H-NMR: 1.2—4.3 (9H, m), 3.48 (3H, s, OMe), 4.11 (1H, br t, J=5 Hz, H-3), 5.93 (1H, s, H-7), 6.22 (1H, dd, J=4, 10 Hz, H-2), 6.53 (1H, d, J=10 Hz, H-1). ^{13}C-NMR: 32.3 (t, C4, 11), 33.2 (t, C4), 34.9 (t, C10), 46.0 (d, C13), 57.2 (q, OMe), 60.4 (s, C5), 73.3 (d, C3), 106.4 (s, C12), 118.9 (d, C2), 121.6 (d, C7), 133.6 (d, C1), 157.3 (s, C6), 170.1 (s, C8), 171.7 (s, C15). MS m/z: 291 (M^+), 273 (M^+-H_2O, base peak). *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.98; H, 5.78; N, 4.56. HRMS m/z (M^+): Calcd: 291.1104. Found: 291.1094.

Methylation of the 12-Hydroxylactone 30 with Diazomethane 1) A solution of **30a** (150 mg) in MeOH (40 ml) was treated with excess diazomethane in Et_2O at room temperature for 30 min. After removal of the solvent by evaporation *in vacuo*, the residue was crystallized from AcOEt–hexane to give **31a** (115 mg, 73%) as colorless prisms, mp 137—138 °C. IR: 1740, 1680. ^{1}H-NMR: 1.1—3.7 (8H, m), 3.42 (3H, s, OMe), 3.61 (3H, s, COOMe), 4.0—4.4 (1H, m, H-3), 4.58 (1H, br dd, J=8, 13 Hz, H-10), 6.03 (1H, s, H-7), 6.18 (1H, br d, J=10 Hz, H-1), 6.51 (1H, dd, J=2, 10 Hz, H-2). ^{13}C-NMR (68 MHz): 33.0 (t, C4), 34.8 (t, C11), 36.0 (t, C14), 37.7 (t, C10), 52.1 (q, COOMe), 52.2 (d, C13), 56.6 (q, OMe), 67.3 (s, C5), 73.4 (d, C3), 120.3 (d, C2), 121.2 (d, C7), 136.3 (d, C1), 154.6 (s, C6), 169.1 (s, C8), 170.4 (s, COOMe), 207. 3 (s, C12). MS m/z: 305 (M^+), 175 (base peak). *Anal.* Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.75; H, 6.25; N, 4.29. HRMS m/z (M^+): Calcd: 305.1264. Found: 305.1270.

(2) Compound **30b** (150 mg) in MeOH (40 ml) was similarly methylated with excess diazomethane to give **31b** (95 mg, 60%) as colorless prisms from AcOEt–hexane, mp 86—89 °C. IR: 1760, 1680. ^{1}H-NMR: 1.4—3.5 (10H, m), 3.46 (3H, s, OMe), 3.53 (3H, s, COOMe), 5.91 (1H, s, H-7), 6.19 (1H, br dd, J=4, 10 Hz, H-2), 6.52 (1H, br d, J=10 Hz, H-1). ^{13}C-NMR: 32.2 (t, C4), 32.9 (t, C11), 34.9 (t, C14), 36.6 (t, C10), 52.0 (q, COOMe), 52.3 (d, C13), 57.1 (q, OMe), 64.9 (s, C5), 72.7 (d, C3), 120.5 (d, C2), 121.2 (d, C7), 133.7 (d, C1), 154.6 (s, C6), 169.1 (s, C8), 170.6 (s, COOMe), 208.1 (s, C12). MS m/z: 305 (M^+), 175 (base peak). *Anal.* Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.85; H, 6.25; N, 4.66. HRMS m/z (M^+): Calcd 305.1264. Found: 305.1274.

Isomerization of 31a 1) A solution of **31a** in 5% Et_3N–MeOH (0.5 mg/100 μl) was allowed to stand at room temperature. The solution (2 μl) was analyzed periodically by HPLC (solvent, 60% MeOH). After 30 min, the mixture showed peaks of **31a** (t_R, 7.39 min), **32a** (t_R; 7.78 min), and an unidentified compound (t_R, 5.26 min) in a ratio of 1 : 1 : 0.2. This ratio was unchanged after the mixture had been kept at room temperature for 2 h.

2) A solution of **31a** in 0.5 N HCl–MeOH (0.5 mg/100 μl) was allowed to stand at room temperature. The solution (2 μl) was analyzed periodically by HPLC (solvent, 50% MeOH). After 1 h, the mixture gave three peaks, an overlapped peak of **31a** and **32a** (t_R, 7.67 min), a peak of **28a** (t_R, 6.35 min) and a peak of **30a** (t_R, 5.18 min) in the ratio of 4 : 1 : 1. This ratio changed to 1 : 2 : 1 after the mixture had been kept at room temperature for 24 h.

Wittig Reaction of the 12-Hydroxylactone 30 1) Methyltriphenylphosphonium iodide (693 mg, 1.76 mmol) was added to a dry toluene solution (1.08 ml) containing *tert*-AmOK (1.72 mmol), and the mixture was heated in a sealed tube at 130 °C for 30 min under stirring. A solution of **30a** (100 mg, 0.343 mmol) in dry toluene (2 ml) was added, and the whole was heated at 130 °C for 6 h under stirring. After cooling, the mixture was poured into 1 N HCl (10 ml) and extracted with $CHCl_3$, and the extract was concentrated to dryness *in vacuo*. The residue was taken up in CH_2Cl_2 and the precipitated reagent was filtered off. The filtrate was diluted with CH_2Cl_2 and extracted with 2% KOH solution. The water layer was acidified with 5% HCl and reextracted with $CHCl_3$ and then Et_2O. The combined organic extract was concentrated to dryness *in vacuo*. The residue was purified by MPLC (with acetone : benzene = 4 : 1) to give **33a** (18 mg, 18%), as colorless prisms from acetone–Et_2O, double mp 128—133 and 213—215 °C. IR: 1700, 1620. ^{1}H-NMR ($CDCl_3$–DMSO-d_6): 2.0—4.4 (10H, m), 3.79 (3H, s, OMe), 4.61, 4.90 (each 1H, s, CH_2=), 6.20 (1H, br s, COOH), 6.73 (1H, d, J=8 Hz, H-1), 6.84 (1H, br s, H-7), 7.30 (1H, d, J=8 Hz, H-2). MS m/z: 289 (base peak, M^+). HRMS m/z (M^+): Calcd for $C_{16}H_{19}NO_4$; 289.1313. Found; 289.1283.

2) Compound **30b** (100 mg, 0.343 mmol) was allowed to react with methyltriphenylphosphonium iodide (693 mg, 1.72 mmol) and *tert*-AmOK (1.72 mmol) in toluene as described above. The product was purified by MPLC (with acetone : benzene = 4 : 1) to give **33b** (8 mg, 8%), as colorless prisms from $CHCl_3$–acetone, double mp 125—129 and 210—212 °C. IR: 1710, 1630. ^{1}H-NMR (acetone-d_6): 2.1—4.4 (10H, m), 3.78 (3H, s, OMe), 4.53, 4.84 (each 1H, br s, CH_2=), 6.50 (1H, br s, COOH), 6.71 (1H, dd,

J=2.8 Hz, H-2), 6.89 (1H, br s, H-7), 7.22 (1H, br d, J=8 Hz, H-1). MS m/z: 289 (M^+), 83 (base peak). MRMS m/z (M^+): Calcd for $C_{16}H_{19}NO_4$: 289.1313. Found: 289.1319.

Methylenation of the 12-Hydroxylactone 30a with Dimethylsulfoxonium Methylide A oil suspension of NaH (55%, 110 mg, 2.46 mmol) was washed with dry heptane. Dry DMSO (10 ml) and dry THF (15 ml) was added to the solid and stirred at toom temperature for 15 min. To this mixture, trimethylsulfoxonium tetrafluoroborate[2b] (443 mg, 2.46 mmol) was added at 0 °C and the whole was stirred for 15 min. Then **30a** (250 mg, 0.82 mmol) was added and the reaction mixture was stirred at 0 °C for 15 min and then at room temperature for 2 h. The reaction mixture was poured into NH_4Cl solution, acidified with 5% HCl, and extracted with $CHCl_3$ to give the product, which was purified by column chromatography on SiO_2 (CC-7, with CH_2Cl_2) to give **34** (50 mg, 19%), as colorless prisms from CH_2Cl_2–Et_2O, mp 195—197 °C. IR: 3400, 1770, 1670. ^{1}H-NMR (CD_3OD): 1.2—4.5 (13H, m), 3.44 (3H, s, OMe), 5.97 (1H, s, H-7), 6.26 (1H, br d, J=10 Hz, H-1), 6.63 (1H, dd, J=2, 10 Hz, H-2). MS m/z: 305 (M^+), 175 (base peak). *Anal.* Calcd for $C_{16}H_{19}NO_5$: C. 62.94; H, 6.27; N, 4.59. Found: C, 62.88; H, 6.35; N, 4.48. HRMS m/z (M^+): Calcd: 305.1264. Found: 305.1269.

The mother liquor was further purified by PTLC (with AcOEt : acetone = 4 : 1) to give 13α*H*-γ-8-oxoerythroidine **5** (5 mg, 2%), as colorless prisms from AcOEt–Et_2O, mp 250—255 °C. IR: 1740, 1680. UV: 249 (12800). MS m/z: 287 (M^+, base peak), 256 (M^+ − OMe). HRMS m/z (M^+): Calcd for $C_{16}H_{17}NO_4$: 287.1156. Found: 287.1118.

Methylenation of the Keto-ester 31a with Dimethylsulfoxonium Methylide Compound **31a** (250 mg) was alkylated with dimethylsulfoxonium methylide as described above. The product was purified by column chromatography on SiO_2 (CC-7, with CH_2Cl_2) to give **5** (35 mg, 15%).

Alkylation of Keto-ester 31a with Chloromethyl Phenyl Sulfoxide Carbanion A solution of chloromethyl phenyl sulfoxide (187 mg, 1.05 mmol) in dry THF was injected into a solution of lithium diisopropylamide (1.2 mmol) in dry THF (20 ml) at −60 °C under an Ar atmosphere, and the mixture was stirred at the same temperature for 15 min. A solution of **31a** (100 mg, 0.33 mmol) in dry THF (3 ml) was added using a syringe (3 min). Immediately, the reaction mixture was poured into a saturated NH_4Cl solution and extracted with $CHCl_3$. The extract was purified by MPLC (with AcOEt) to give the starting material **31a** (9 mg, 9%) and **35** (105 mg, 67%) as colorless prisms, mp 232—237 °C. IR: 3400, 1730, 1670, 1040. ^{1}H-NMR: 3.42, 3.47 (3 : 1, total 3H, s, OMe), 3.53, 3.68 (3 : 1, total 3H, s, COOMe), 4.51, 4.68 (3 : 1, total 1H, s, –C<u>H</u>Cl–), 5.93, 6.00 (3 : 1, total 1H, s, H-7), 6.13 (1H, d, J=10 Hz, H-1), 6.37 (1H, dd, J=2, 10 Hz, H-2), 7.59 (5H, br s, SOPh). MS m/z: 481 and 479 (M^+).

Reaction of the Chlorohydrin 35 with Potassium *tert*-Butoxide A solution of **35** (100 mg, 0.21 mmol) in dry THF (5 ml) was added to a solution of benzenethiol (46 μl, 0.42 mmol) and *tert*-BuOK (67 mg, 0.60 mml) in *tert*-BuOH (25 ml). The mixture was stirred at room temperature overnight under an Ar atmosphere. The mixture was extracted with $CHCl_3$. The product in MeOH (20 ml) was treated with $NaBH_4$ (100 mg) at 0 °C for 3 h under an Ar atmosphere. After decomposition of excess $NaBH_4$ with water, the mixture was concentrated *in vacuo*, and extracted with $CHCl_3$ and then Et_2O. The combined organic layer was concentrated and the residue in $CHCl_3$ was passed through a short column of SiO_2 (CC-7). The eluate was purified by PTLC (with AcOEt) to give **38** (35 mg, 31%) and **39** (10 mg, 11%).

38: Colorless prisms from AcOEt, mp 192—195 °C. IR: 3400, 1740, 1660. ^{1}H-NMR (270 MHz): 1.2—4.5 (9H, m), 3.40 (3H, s, OMe), 3.43 (3H, s, COOMe), 4.01 (1H, dd, J=4, 11 Hz, H-3), 4.44 (1H, s, –CH(SPh)$_2$), 4.71 (1H, br s, O<u>H</u>), 5.92 (1H, s, H-7), 6.12 (1H, br d, J=10 Hz, H-1), 6.32 (1H, dd, J=2, 10 Hz, H-2), 6.6—7.6 (10H, m, 2 × SPh). ^{13}C-NMR (68 MHz): 31.5 (t, C4), 32.6 (t, C11), 33.1 (t, C14), 39.4 (t, C10), 40.9 (d, C13), 51.7 (q, OMe), 56.6 (q, COOMe), 66.9 (s, C5), 74.7 (d, C3), 79.0 (d, –<u>C</u>H(SPh)$_2$), 80.7 (s, C12), 119.6 (d, C2), 122.0 (d, C7), 125.9 (d × 2, Ar), 126.4 (d, Ar), 128.5 (d × 2, Ar), 128.7 (d × 2, Ar), 129.5 (d × 2, Ar), 132.0 (d, Ar), 133.6 (s, Ar), 136.0 (d, C1), 138.1 (s, Ar), 159.4 (s, C6), 169.7 (s, C8), 170.8 (s, <u>C</u>OOMe). CI-MS m/z: 538 (M^+ + 1).

39: Colorless prisms from AcOEt–hexane, mp 180—183 °C. IR: 1730, 1680. ^{1}H-NMR: 1.1—3.8 (8H, m), 3.36 (3H, s, OMe), 3.69 (3H, s, COOMe), 3.82 (1H, s, –C<u>H</u>SPh), 3.8—4.1 (1H, m, H-3), 4.50 (1H, br d, J=6, 14 Hz, H-10), 5.97 (1H, s, H-7), 6.11 (1H, br d, J=10 Hz, H-1), 6.45 (1H, dd, J=2, 10 Hz, H-2), 7.4—7.8 (5H, m, SPh). MS m/z: 428 (M^+ + 1), 148 (base peak).

8-Oxocycloerythroidine 6 1) A solution of **35** (100 mg, 0.22 mmol) in dry THF (10 ml) was added to a solution of *tert*-BuOK (70 mg, 0.60 mmol) in *tert*-BuOH (30 ml). The mixture was stirred at room temperature for 10 min, and extracted with $CHCl_3$. A mixture of the residue, lithium perchlorate ($LiClO_4 \cdot 3H_2O$, 50 mg, 0.3 mmol), and tri-*n*-butylphosphine oxide (*n*-Bu_3PO, 60 mg, 0.3 mmol) in toluene (8 ml) was heated at 120 °C for 2 h under an Ar atmosphere. The mixture was extracted with $CHCl_3$, and washed with saturated NH_4Cl solution. The aqueous layer was further extracted with Et_2O. The product obtained from the combined extract was dissolved in MeOH (20 ml) and treated with $NaBH_4$ (50 mg) at 0 °C for 30 min under an Ar atmosphere. After decomposition of the excess hydride with water, the mixture was concentrated *in vacuo* and extracted with $CHCl_3$. The product was purified by MPLC (with AcOEt) to give **6** (8 mg, 13%), as colorless prisms from AcOEt, mp 240—243 °C. IR: 1760, 1680. UV: 250 (14700). MS m/z: 287 (M^+), 255 (base peak). HRMS m/z (M^+): Calcd for $C_{16}H_{17}NO_4$: 287.1157. Found: 287.1157.

2) A solution of **35** (150 mg) in THF (10 ml) was treated with *tert*-BuOK (100 mg) in *tert*-BuOH (30 ml) as described above. A solution of the product and Nafion-H (250 mg) in dry THF (20 ml) was heated under reflux for 4 h under an Ar atmosphere. After removal of the polymer by filtration, the filtrate was concentrated to dryness *in vacuo*. The residue was reduced with $NaBH_4$ as described above. The product was purified by MPLC (with AcOEt : acetone = 4 : 1) and then PTLC (with AcOEt : acetone = 4 : 1) to give **6** (25 mg, 28%).

X-Ray Crystallographic Analyses The reflection data were collected on a Rigaku AFC-5 four-circle diffractometer using graphite-monochromated MoK_α radiation in the ω-2θ scan mode at a 2θ scan speed of 4°/min for $3° < 2\theta < 55°$. Of the reflections collected, those above the 3d (I) level were used for the calculation. The structure of **31a** was solved by the direct method using MITHRIL[16] and refined by the full-matrix least-squares procedure with anisotropic thermal factors for the non-hydrogen atoms.

TABLE III. Positional Parameters and B_{eq} for the Keto-ester **31a**

Atom	x	y	z	B_{eq}
O(1)	0.5340 (6)	0.4424 (7)	0.6917 (4)	3.8 (3)
O(2)	0.7899 (6)	0.0198 (7)	1.0217 (3)	4.3 (3)
O(3)	0.9187 (6)	0.0991 (7)	0.7115 (3)	4.1 (3)
O(4)	1.1898 (6)	0.2056 (7)	0.8199 (3)	3.8 (3)
O(5)	1.2638 (6)	0.3456 (7)	0.9288 (4)	3.8 (3)
N(1)	0.7853 (6)	0.0974 (8)	0.8957 (4)	2.4 (4)
C(1)	0.7269 (9)	0.514 (1)	0.8810 (6)	3.1 (5)
C(2)	0.6783 (9)	0.540 (1)	0.8059 (6)	3.4 (5)
C(3)	0.6600 (9)	0.415 (1)	0.7444 (5)	3.1 (5)
C(4)	0.6655 (7)	0.250 (1)	0.7790 (5)	2.8 (5)
C(5)	0.7835 (8)	0.240 (1)	0.8516 (5)	2.4 (5)
C(6)	0.7637 (8)	0.360 (1)	0.9104 (5)	2.2 (4)
C(7)	0.7709 (8)	0.291 (1)	0.9792 (5)	3.0 (5)
C(8)	0.7856 (9)	0.122 (1)	0.9718 (5)	3.1 (5)
C(10)	0.813 (1)	−0.053 (1)	0.8623 (5)	3.3 (5)
C(11)	0.9393 (8)	−0.042 (1)	0.8327 (5)	3.1 (5)
C(12)	0.9297 (7)	0.103 (1)	0.7817 (5)	2.7 (5)
C(13)	0.9187 (8)	0.253 (1)	0.8259 (5)	2.3 (4)
C(14)	1.0348 (8)	0.284 (1)	0.8957 (5)	2.5 (4)
C(15)	1.1685 (9)	0.272 (1)	0.8750 (5)	2.6 (4)
C(16)	1.395 (1)	0.334 (1)	0.9150 (6)	7.3 (7)
C(17)	0.5251 (9)	0.377 (1)	0.6156 (6)	5.3 (6)
H(1)	0.7337	0.5968	0.9168	0.8
H(2)	0.6571	0.6442	0.7832	1.3
H(3)	0.7294	0.4473	0.7117	1.4
H(4)	0.5937	0.2388	0.7937	0.3
H(5)	0.6827	0.1754	0.7340	4.3
H(6)	0.7605	0.3347	1.0267	0.3
H(7)	0.8297	−0.1271	0.9068	0.2
H(8)	0.7421	−0.0736	0.8191	8.5
H(9)	0.9584	−0.1248	0.8016	1.1
H(10)	1.0325	−0.0331	0.8760	7.6
H(11)	0.9129	0.3351	0.7914	0.8
H(12)	1.0316	0.4053	0.9170	5.4
H(13)	1.0463	0.2251	0.9422	4.2
H(14)	1.4086	0.2242	0.9062	11.1
H(15)	1.4087	0.3801	0.8735	9.0
H(16)	1.4426	0.4018	0.9408	6.8
H(17)	0.6031	0.4226	0.5924	7.0
H(18)	0.4418	0.4084	0.5815	1.6
H(19)	0.5312	0.2740	0.6263	5.7

TABLE IV. Positional Parameters and B_{eq} for 8-Oxocycloerythroidine **6**

Atom	x	y	z	B_{eq}
O(1)	0.4373 (3)	0.5482 (2)	−0.1349 (1)	4.9 (1)
O(2)	0.1702 (3)	0.1326 (2)	0.1494 (1)	5.4 (1)
O(3)	0.2359 (3)	−0.1250 (2)	−0.2198 (2)	6.2 (1)
O(4)	0.0663 (2)	0.0166 (2)	−0.2832 (1)	4.5 (1)
N(1)	0.1612 (2)	0.2397 (2)	0.0134 (1)	3.3 (1)
C(1)	0.5381 (3)	0.2403 (3)	−0.0446 (2)	4.0 (1)
C(2)	0.5350 (4)	0.3351 (3)	−0.1045 (2)	4.2 (1)
C(3)	0.3992 (3)	0.4152 (3)	−0.1358 (2)	3.5 (1)
C(4)	0.2801 (3)	0.4017 (3)	−0.0757 (2)	3.2 (1)
C(5)	0.2581 (3)	0.2607 (2)	−0.0540 (2)	2.7 (1)
C(6)	0.4061 (3)	0.2092 (2)	−0.0056 (2)	3.1 (1)
C(7)	0.3870 (4)	0.1534 (3)	0.0719 (2)	3.8 (1)
C(8)	0.2307 (3)	0.1695 (3)	0.0861 (2)	3.7 (1)
C(10)	0.0003 (4)	0.2620 (4)	−0.0104 (2)	4.2 (2)
C(11)	−0.0709 (3)	0.1847 (4)	−0.0927 (2)	4.2 (1)
C(12)	0.0357 (3)	0.1446 (2)	−0.1553 (2)	3.0 (1)
C(13)	0.1962 (3)	0.1858 (2)	−0.1406 (2)	2.8 (1)
C(14)	0.1573 (3)	0.0467 (3)	−0.1302 (2)	3.4 (1)
C(15)	0.1617 (3)	−0.0320 (3)	−0.2114 (2)	4.1 (1)
C(16)	−0.0280 (4)	0.1156 (3)	−0.2534 (2)	4.0 (1)
C(17)	0.4817 (6)	0.5930 (4)	−0.2154 (3)	5.5 (2)
H(1)	0.626 (3)	0.192 (3)	−0.022 (2)	5.0 (7)
H(2)	0.626 (3)	0.354 (3)	−0.126 (2)	4.5 (7)
H(3)	0.356 (3)	0.390 (2)	−0.200 (2)	2.8 (5)
H(4)	0.185 (3)	0.439 (3)	−0.106 (2)	4.7 (7)
H(5)	0.312 (3)	0.447 (3)	−0.017 (2)	4.4 (6)
H(6)	0.462 (3)	0.111 (2)	0.116 (2)	4.4 (7)
H(7)	−0.041 (3)	0.250 (3)	0.041 (2)	5.1 (8)
H(8)	−0.012 (4)	0.361 (3)	−0.029 (2)	6.4 (9)
H(9)	−0.119 (4)	0.105 (3)	−0.072 (2)	7 (1)
H(10)	−0.157 (4)	0.239 (3)	−0.131 (2)	7 (1)
H(11)	0.241 (2)	0.209 (2)	−0.190 (1)	2.0 (5)
H(12)	0.178 (3)	0.010 (2)	−0.075 (2)	4.1 (7)
H(13)	−0.023 (3)	0.191 (3)	−0.295 (2)	5.0 (7)
H(14)	−0.135 (3)	0.080 (2)	−0.258 (2)	3.7 (6)
H(15)	0.405 (5)	0.559 (4)	−0.274 (3)	9 (1)
H(16)	0.583 (6)	0.552 (5)	−0.215 (3)	13 (2)
H(17)	0.481 (4)	0.682 (4)	−0.214 (3)	9 (1)

Hydrogen atoms were located at calculated positions. The structure of **6** was solved by the direct method using SIR85[17] and refined by the full-matrix least-squares method with anisotropic thermal factors for non-hydrogen atoms and with isotropic ones for hydrogen atoms. The atomic parameters are listed in Tables III and IV, respectively.

Crystal Data for **31a**: Colorless columns from acetone–Et_2O, mp 148—149 °C. Monoclinic, $a=10.31(2)$ Å, $b=8.587$ (3) Å, $c=17.51(2)$ Å, $\beta=103.4$ (1)°, $V=1508$ (3) Å^3, $D_c=1.35$ g/cm^3, $Z=4$. Space group, $p2_1/c$. Reflections observed, 3626; reflections used for calculation, 646. $R=0.044$.

Crystal Data for **6**: Colorless prisms from acetone–Et_2O, mp 250—251.5 °C. Monoclinic, $a=9.026(2)$ Å, $b=10.473(2)$ Å, $c=14.852(2)$ Å, $\beta=99.68(2)$°, $V=1384(4)$ Å^3, $D_c=1.38$ g/cm^3, $Z=4$. Space group, $p2_1/c$. Reflections observed 3572; reflections used for calculation 1523. $R=0.041$.

References and Notes

1) Synthesis of *Erythrina* and Related Alkaloids. XXXVI. Part XXXV: Y. Tsuda, S. Hosoi, K. Mohri, and K. Isobe, *Chem. Pharm. Bull.*, **40**, 2686 (1992). This paper also constitutes Part LII of Dioxopyrrolines. Part LI: T. Sano, J. Toda, and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 873 (1992).
2) *a*) K. Isobe, K. Mohri, Y. Itoh, Y. Toyokawa, N. Takeda, J. Taga, and Y. Tsuda, *Chem. Pharm. Bull.*, **35**, 2618 (1987); *b*) K. Isobe, K. Mohri, Y. Itoh, Y. Toyokawa, N. Takeda, J. Taga, S. Hosoi, and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 2632 (1992).
3) The numbering system of D-furanoerythrinan and its derivatives follows that of the erythrinan skeleton.
4) H. Ishii, I-S. Chen, S. Ueki, T. Masuda, K. Morita, and T. Ishikawa, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 2415.
5) T. Sano, J. Toda, N. Kashiwaba, T. Ohshima, and Y. Tsuda, *Chem. Pharm. Bull.*, **35**, 479 (1987).
6) *a*) Y. Tsuda and Y. Sakai, *Synthesis*, **1981**, 119; *b*) Y. Tsuda, S. Hosoi, A Nakai, Y. Sakai, T. Abe, Y. Ishii, F. Kiuchi, and T. Sano, *Chem. Pharm. Bull.*, **39**, 1365 (1991).
7) T. Sano, J. Toda, Y. Yamamoto, M. Shoda, K. Isobe, and Y. Tsuda, *Chem. Pharm. Bull.*, **40**, 2663, 1992.
8) B. L. Feringa and W. Dannenberg, *Synth. Commun.*, **13**, 509 (1983).
9) For a review of synthetic applications of Nafion-H, see G. A. Olah, P. S. Iyer, and G. K. S. Prakrash, *Synthesis*, **1986**, 513.
10) Rough MM2 calculations of steric energies for **31a** and **32a** indicated that the axial isomer (**31a**) is preferred over the equatorial isomer (**32a**) ($\Delta E=0.7$ kcal/mol).
11) T. Satoh, M. Itoh, T. Ohara, and K. Yamakawa, *Bull. Chem. Soc. Jpn.*, **60**, 1839 (1987).
12) *a*) A. S. Chawla, A. H. Jackson, and P. Ludgate, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 2903; *b*) A. S. Chawla, S. Chunchatprasert, and A. H. Jackson, *Org. Mag. Reson.*, **21**, 39 (1983).
13) See Part XXXV.
14) *Cf.*, Y. Tsuda, A. Ishiura, S. Takamura, S. Hosoi, K. Isobe, and K. Mohri, *Chem. Pharm. Bull.*, **39**, 2797 (1991).
15) T. Ibuka, Y. Mori, and Y. Inubushi, *Tetrahedron Lett.*, **1976**, 3169.
16) G. J. Gilmore, "MITHRIL: A Computer Program for the Automatic Solution of Crystal Structures for X-Ray Data," University of Glasgow, Scotland, 1983.
17) C. Giaccovazzo, G. L. Cascarano, G. Polidori, R. Spagna, and D. Viterbo, "SIR85, A computer program for automatic analysis of phase problems," *Acta Crystallogr., Sect. A*, **38**, 663 (1982); *idem*, *ibid.*, **43**, 22 (1987).