Chiral Synthesis of *Erythrina* Alkaloids. I.[1] Total Synthesis of (+)-Erysotrine *via* Asymmetric Diels–Alder Reaction under High Pressure[2]

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(*S*)-(+)-3,4-Dimethoxyphenylalanine methyl ester (1b) was converted, in 3 steps, into (5*S*)-(−)-8,9-dimethoxy-1,5-dimethoxycarbonyl-2,3-dioxo-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline (2b). Diels–Alder reaction of 2b with 1-methoxy-3-trimethylsilyloxybutadiene under extremely high pressure (10 kbar), followed by desilylation, gave moderate yields of erythrinan derivatives (11), which were converted, in several steps, into (+)-erysotramidine (23b) and (+)-erysotrine (4), thus accomplishing the first total synthesis of natural *Erythrina* alkaloids in chiral forms.

Keywords *Erythrina* alkaloid; chiral synthesis; high pressure; Diels–Alder reaction; dioxopyrroline; erysotrine

The unique physiological activity of erythrinan alkaloids has attracted the interest of many synthetic chemists.[3] Our total syntheses of aromatic erythrinan alkaloids in racemic forms have been achieved by three different routes[4]: (1) Diels–Alder route,[5] (2) intramolecular cyclization route,[6] and (3) [2+2] photocycloaddition route.[7] Each of these methods utilize an arylethylamine (*e.g.*, **1a**) as the common starting material. Thus, if the corresponding amine were available in a chiral form (*e.g.*, **1b**), chiral synthesis of erythrinan alkaloids could be achieved by one of the above methods. In this paper, we describe a chiral synthesis of (+)-erysotrine (**4**) by method (1).

Synthesis of the Chiral Dioxopyrroline (2b) Sano *et al.*[5] reported that Diels–Alder reaction of the dioxopyrroline (**2a**) with 1-methoxy-3-trimethylsilyloxybutadiene at 130 °C under ordinary pressure gave the 1,4-cycloadduct (**3a**), a key intermediate to (±)-erysotrine (**4**), in high yield.

The corresponding chiral dioxopyrroline (**2b**) bearing a methoxycarbonyl group was prepared from (*S*)-(+)-3,4-dimethoxyphenylalanine methyl ester (**1b**).[8] The ester (**1b**) was condensed with methyl chloroformylacetate and the resulting amide (**5**) was heated with polyphosphate ester (PPE) at 100 °C, then treated with oxalyl chloride at room temperature to give the chiral dioxopyrroline (**2b**) in 94% yield from **1b**. An X-ray analysis of **2b** revealed that B-ring is in half-chair conformation and the methoxycarbonyl group at C-5 is axially orientated, so high diastereofacial differentiation in the Diels–Alder reaction is expected.

Diels–Alder Reaction of the Dioxopyrroline (2b) with 1-Methoxy-3-trimethylsilyloxybutadiene When the dioxopyrroline (**2b**) was heated with 1-methoxy-3-trimethylsilyloxybutadiene (5 eq) in CH_2Cl_2 at 130 °C under atmospheric pressure (1 bar) for 1 h, followed by treatment with silica gel, three compounds, A, B, and C, were produced in the yield of 45%, 14%, and 13%, respectively. These products were not the desired ene-adduct[9] but were concluded to be one-adducts[9] (**7**, **8**, and **9**) for the following reasons. Compounds A and B are isomeric (*m/z* 443). They did not show the absorption of a five-membered ring ketone in the IR spectra, and exhibited olefinic protons of (*Z*)-

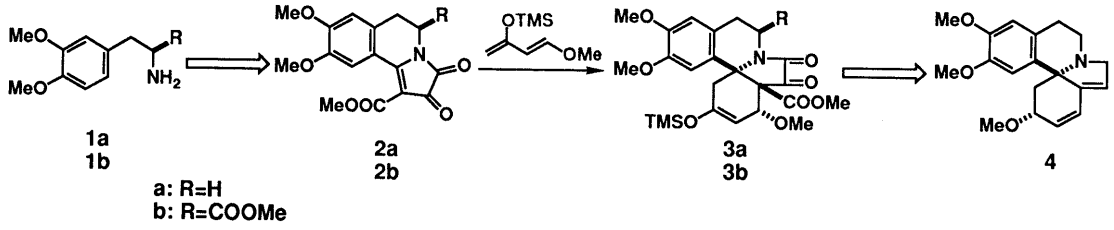

Chart 1. Synthetic Plan for (+)-Erysotrine

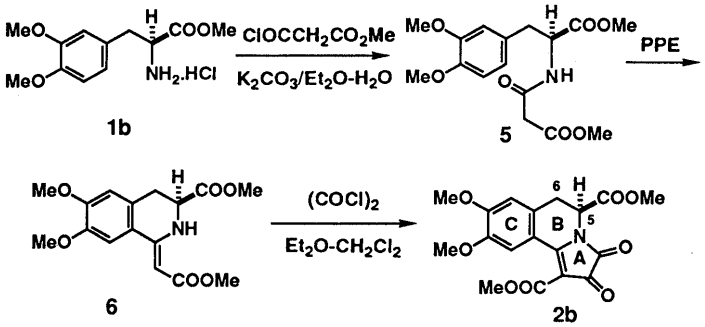

Chart 2. Synthesis of the Chiral Dioxopyrroline (**2b**)

configuration (A: δ 5.44, 7.22, each d, $J=6$ Hz; B: δ 5.44, 7.28, each d, $J=6.5$ Hz) in the ^{1}H-NMR spectra. An X-ray crystallographic analysis of compound B (mp 192—193 °C) proved it to be **8** (Fig. 2). Therefore the structure of compound A is **7**. On the other hand, compound C was presumed to be a stereoisomeric mixture of **9**, since it had no absorption ascribable to a five-membered ring ketone, and exhibited the molecular ion peak at m/z 475 in the mass spectrum and two pairs of five methoxyls in the ^{1}H-NMR spectrum.[10] The reaction in toluene increased the yield of **7**, but did not produce the desired ene-adduct (see Experimental).

The above evidence suggests that cycloaddition of the diene to the dioxopyrroline (**2a**) had occurred from the β-face (the same side as C-5 axial H) of the molecule, probably because of the steric hindrance between C-6 axial H and the trimethylsilyl group in the diene, provided **2a** had the same conformation as that of **2b** (see *A* in Fig. 3),[11] since introduction of a COOMe group at the 5-axial position completely prohibited the cycloaddition to the C=C bond (see *B*).

Extremely high pressure might change the reaction path, because it generally enforces two reactants to take the smallest molecular volume at the transition state.[12] Apparently, the transition state of ene-addition has a smaller molecular volume than that of the one-addition. Therefore the expected cycloaddition to **2b** should occur from the α-face, *i.e.*, the opposite face to the 5β-COOMe group, against the steric repulsion due to the axial H at C-6 (see *C*). Actually, when dioxopyrroline (**2b**) was reacted with 1-methoxy-3-trimethylsilyloxybutadiene (5 eq) in CH_2Cl_2 at room temperature under a 10 kbar pressure (followed by treatment with silica gel as described above), the desired ene-adduct (**11**) was obtained as a major product (51%) together with one-adducts. The structure of **11** was supported by its molecular ion peak at m/z 475 in the mass spectrum and the IR absorption of a five-membered ring ketone at 1770 cm^{-1}. However, it was found to be a mixture of *endo*- and *exo*-isomers (**11a** and **11b**) from the signals of pairs of aromatic protons (δ 6.64, 6.06 and δ 7.25, 6.62) in the ^{1}H-NMR spectrum.[13]

Treatment of **11** with ethylene glycol in the presence of *p*-TsOH gave a mixture of ethylene acetals, which were separated into the stereoisomers (**12a** and **12b**) by silica gel chromatography. The X-ray analysis of the crystalline

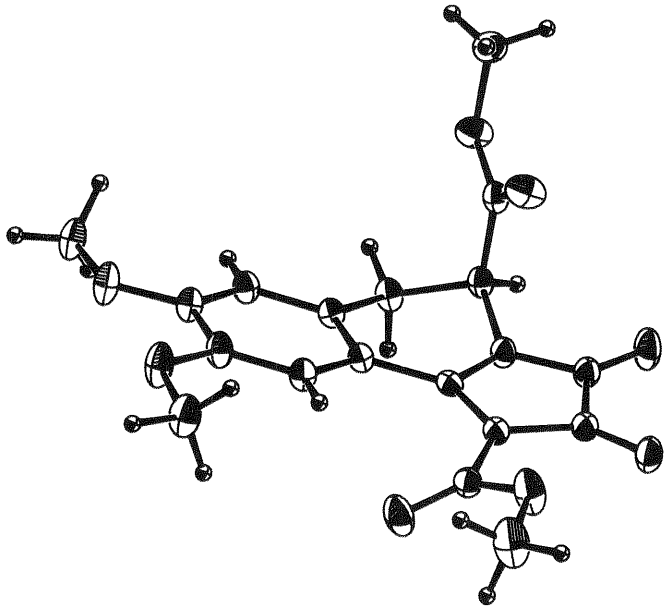

Fig. 1. ORTEP Drawing of Compound **2b**

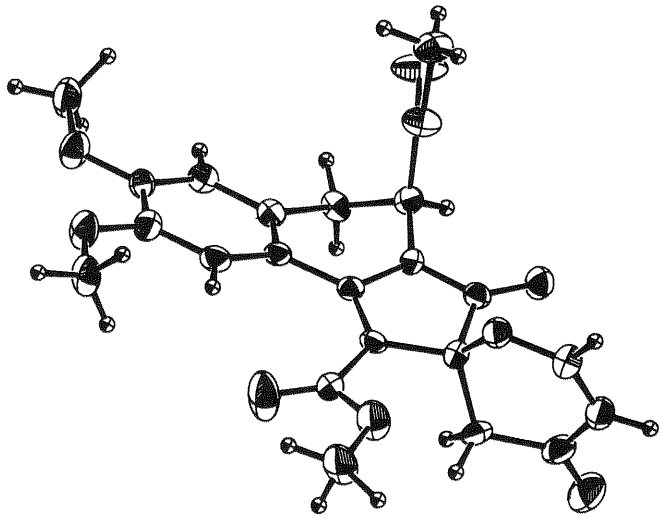

Fig. 2. ORTEP Drawing of Compound **8**

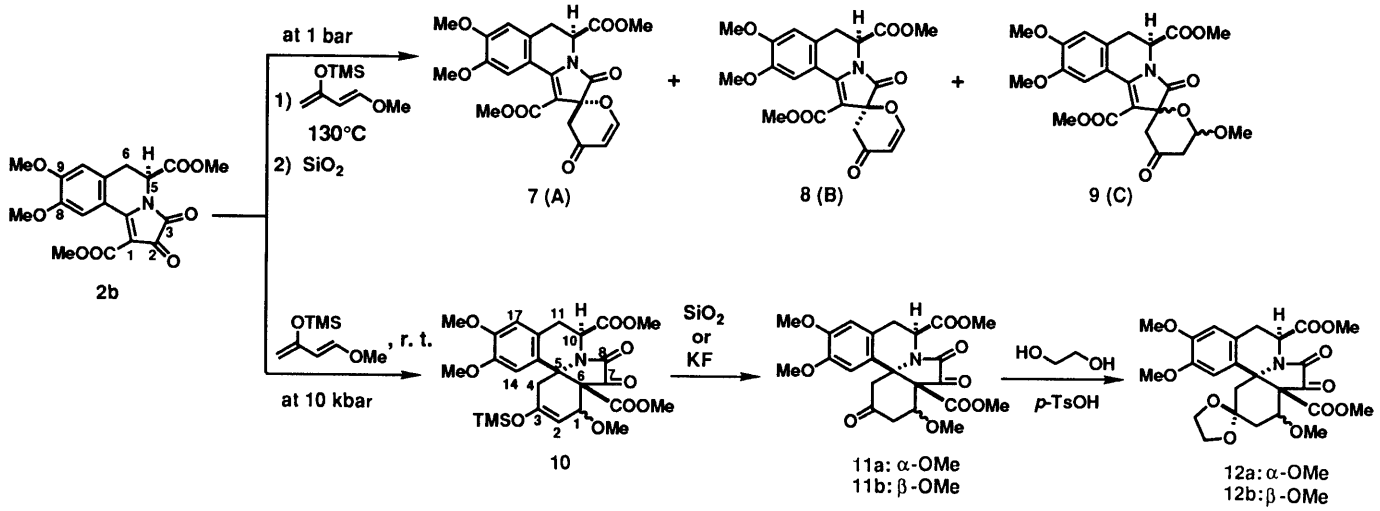

Chart 3. Diels–Alder Reactions at Ordinary Pressure and at Extremely High Pressure

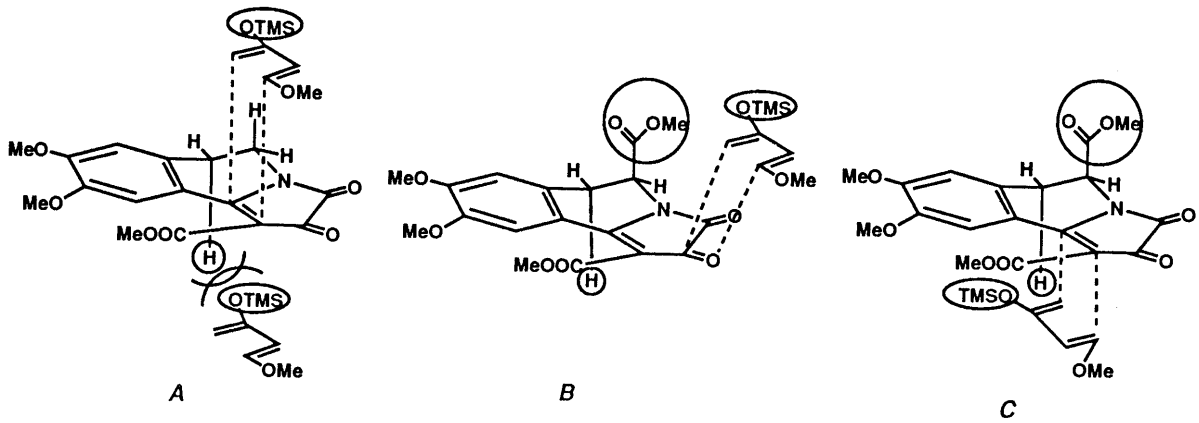

Fig. 3. Approaches of the Diene to **2a** and **2b** at Ordinary Pressure and at Extremely High Pressure (Schematic)

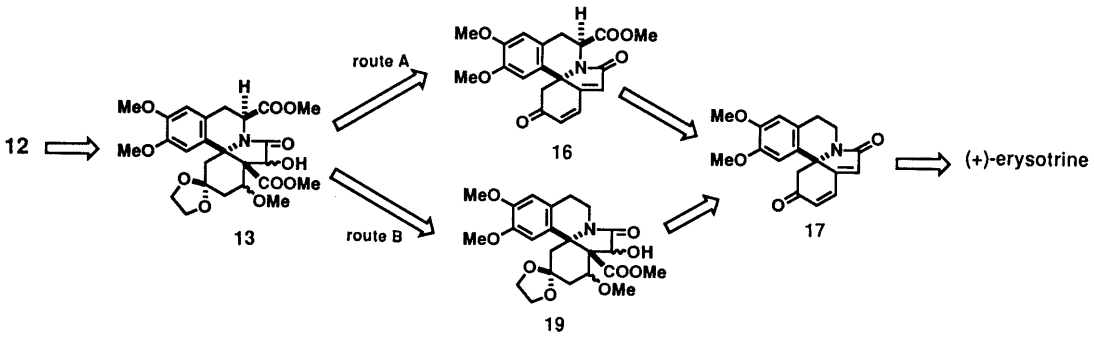

Chart 4. Attempted Synthetic Routes to the Chiral Dienone (**17**)

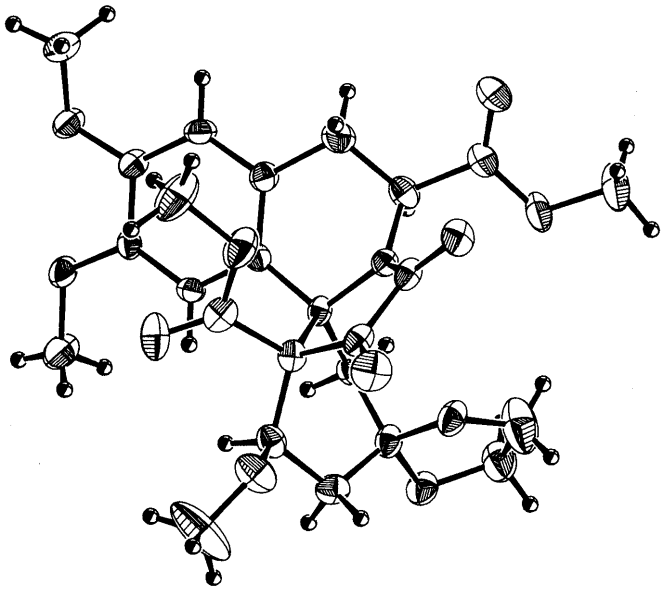

Fig. 4. ORTEP Drawing of Compound **12a**

isomer (Fig. 4) revealed that it is the *endo*-isomer (**12a**) of (5*R*,6*R*)-configuration.

Total Synthesis of (+)-Erysotrine (4) The ethylene acetal (**12**) was converted to the natural alkaloid, (+)-erysotrine, through the intermediate **17**, since transformation of **17** to erysotrine has already been acheived in a racemic form.[5] For this purpose, we examined two routes (routes A and B in Chart 4).

For route A, the *endo*-isomer **12a** was reduced with n-Bu_4NBH_4 in MeOH to afford a single 7β-OH isomer (**13a**), which was converted to the enone (**14a**) by treatment with 5% HCl in 77% yield from **12a**. On the other hand, the *exo*-isomer (**12b**) gave, on similar reduction, a 1:2 mixture of 7β-OH (**13b**) and 7α-OH isomers (**13c**). Reduction of **12b** with $NaBH_4$ gave the same products more stereoselectively (**13b**:**13c**=1:4). Acid hydrolysis of this mixture afforded the enones, **14a** and **14b**, in 18% and 80% yields from **12b**. The minor product was identical with the enone (**14a**) obtained from **12a**.

A mixture of the enones (**14**) was mesylated and the resulting mesylate (**15**) was decarbomethoxylated on heating with $MgCl_2$ in dimethyl sulfoxide (DMSO)[6c] to yield a single dienone (**16**) in 60% yield from **15**. This product was hydrolyzed and the resulting acid was subjected to Barton's decarboxylation.[14] However, the product was a complex mixture, probably because of photo-susceptibility of the dienedione system. Thus this route was abandoned.

As an alternative route B, a mixture of the acetals (**13**) [derived from the ene-adduct **11** (*endo*:*exo*=2:1)] was hydrolyzed with alkali and the resulting acid was decarboxylated by Barton's method.[14] Acid hydrolysis of the product (**19**) gave a mixture of the enone **20** (60% yield from **13**), which was separated into 7α-OH and 7β-OH isomers (**20a** and **20b**) by chromatography. The spectral data of **20b** were identical with those of the racemate reported previously.[5,6c]

Each of these isomers (**20a** and **20b**) was mesylated, then decarbomethoxylated by heating with $CaCl_2$ in DMSO in the presence of *tert*-heptylmercaptan,[6c] to afford the same dienone **17** (91% from **20a** and 98% from **20b**), whose spectral data (^{1}H-NMR, IR) were identical with those of the racemic specimen reported previously.[5,6c]

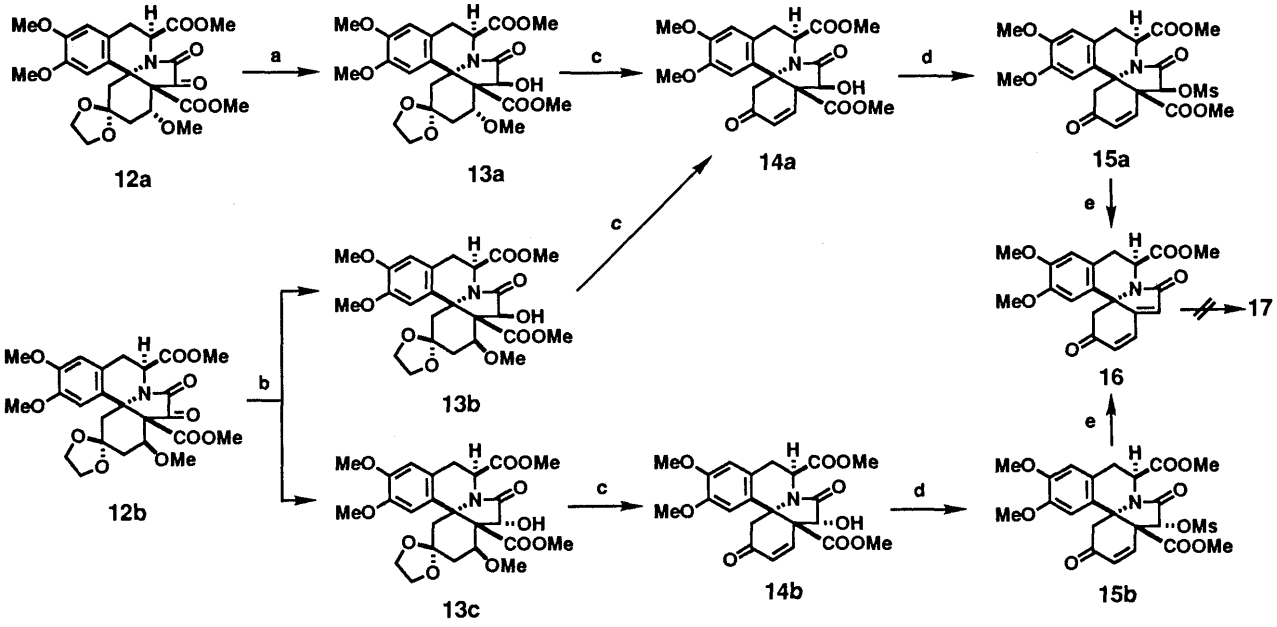

Chart 5. Synthesis of the Chiral Dienone-Ester (**16**) (Route A)

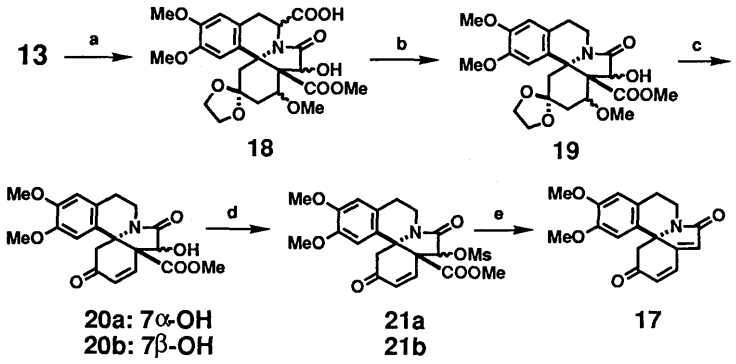

Chart 6. Synthesis of the Chiral Dienone (**17**) (Route B)

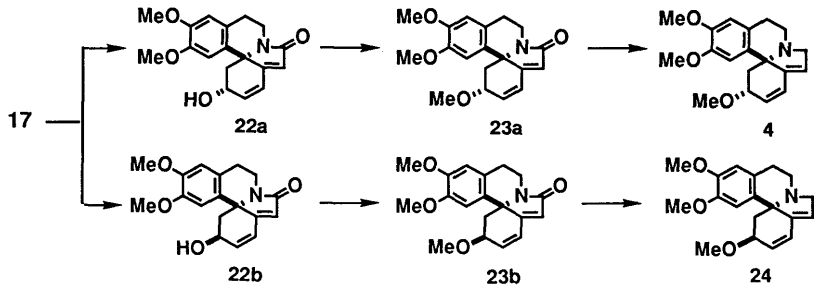

Chart 7. Synthesis of (+)-Erysotramidine (**23a**), (+)-Erysotrine (**4**), (−)-Epierysotramidine (**23b**), and (+)-Epierysotrine (**24**) from the Chiral Dienone (**17**)

Transformation of the dienone **17** to (+)-erysotrine (**4**) was performed as reported for the racemic compound.[5] Reduction of **17** with $NaBH_4$–$CeCl_3$ in MeOH gave the 3α- and 3β-alcohols (**22a** and **22b**) in 87% and 13% yields, respectively. Methylation of **22a** in the presence of phase transfer catalyst (Et_4NBr) gave (+)-erysotramidine (**23a**)[15] in 85% yield. This was further converted to the amine (**4**). Identity of **4** with the natural (+)-erysotrine was confirmed by converting it to the readily characterizable picrate, mp 163—164 °C, $[\alpha]_D^{20}$ +143° (c=0.14, EtOH), whose mp,

$[\alpha]_D$, and the spectral data were identical with those of (+)-erysotrine picrate [mp 162—163 °C, $[\alpha]_D$ +142° (EtOH)].[16] Thus the first total syntheses of *Erythrina* alkaloids, erysotramidine and erysotrine, in optically active forms have been accomplished.

Similarly, the 3β-alcohol (**22b**) was converted into the 3-epi-alkaloids, (−)-3-epierysotramidine (**23b**) and (+)-epierysotrine (**24**).

Experimental

Unless otherwise noted, 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 data are given in cm^{-1}. ^{1}H-NMR spectra were taken with a JEOL GX 400 (400 MHz) or 500 (500 MHz) spectrometer in $CDCl_3$ solutions 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 carried out with silica gel (Wakogel C-200). Recycling high-performance liquid chromatography (HPLC) was performed on a JAIGEL H column and medium-pressure LC (MPLC) on a Merck Lobar column. For thin-layer chromatography (TLC), Merck precoated plates GF_{254} were used and spots were monitored under UV light (254 nm), then developed by spraying 1% $Ce(SO_4)_2$ in 10% H_2SO_4 and heating the plate at 100 °C until coloration took place. Preparative TLC (PTLC) was performed with precoated silica gel plates, Merck 60 F_{254} (0.5 mm thick). 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 IR and NMR spectra.

(5*S*)-(−)-8,9-Dimethoxy-1,5-dimethoxycarbonyl-2,3-dioxo-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline (2b) (1) The Amide (+)-**5**: A solution of methyl chloroformylacetate (828 mg) in Et_2O (10 ml) was added to a stirred mixture of (*S*)-3,4-dimethoxyphenylalanine methyl ester hydrochloride[8] (**1b**, 1.4 g) and potassium carbonate (1.76 g) in water (15 ml) and Et_2O (15 ml) at −15 °C over a period of 10 min and the solution was stirred for a further 30 min, then extracted with $CHCl_3$. Chromatography of the product (AcOEt) gave the amide (+)-**5** (1.65 g, 97%), as colorless needles from Et_2O–CH_2Cl_2, mp 95—95.5 °C, $[\alpha]_D^{20}$ +55° (*c*=0.56, $CHCl_3$). IR: 1735, 1670. ^{1}H-NMR (100 MHz): 7.44 (1H, br d, *J*=6 Hz, NH), 6.84—6.48 (3H, ArH), 4.80 (1H, q, *J*=6 Hz, CHCOOMe), 3.85 (6H), 3.71 (6H) (each s, 4×OMe), 3.31 (2H, s, $COCH_2COOMe$), 3.07 (2H, d, *J*=6 Hz, $ArCH_2$). MS: 339 (M^+), 222 (base peak). *Anal.* Calcd for $C_{16}H_{21}NO_7$: C, 56.63; H, 6.24; N, 4.13. Found: C, 56.65; H, 6.34; N, 4.20.

(2) The Enamino-ester (−)-**6**: The amide (+)-**5** (1.311 g) in a large excess of PPE was heated at 100 °C for 2 h. The mixture was neutralized with saturated K_2CO_3 solution, and extracted with $CHCl_3$. Purification of the extract by Florisil column chromatography (AcOEt) gave (−)-**6** (1.213 g, 98%), as pale yellow prisms from Et_2O–CH_2Cl_2, mp 139—141 °C, $[\alpha]_D^{22}$ −171° (*c*=0.5, $CHCl_3$). IR (KBr): 1737, 1662, 1596, 1566 cm^{-1}. ^{1}H-NMR (100 MHz): 9.32 (1H, br s, NH), 7.11, 6.67 (each 1H, s, ArH), 5.16 (1H, s, =CHCOOMe), 4.20 (1H, m, CHCOOMe), 3.91, 3.89, 3.78, 3.73 (each 3H, s, OMe), 3.08 (2H, m, $ArCH_2$). MS: 321 (M^+), 230 (base peak). *Anal.* Calcd for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 59.50; H, 6.10; N, 4.16.

(3) The Dioxopyrroline (−)-**2b**: A solution of oxalyl chloride (450 mg) in Et_2O (10 ml) was added to a solution of the enamino-ester (−)-**6** (970 mg) in dry Et_2O–CH_2Cl_2 (1:1, 20 ml) at 0 °C over a period of 10 min and the mixture was stirred for 30 min. The precipitated crystals (**2b**, 934 mg) were collected by filtration, and the filtrate was passed through a short silica gel column. Concentration of the eluate gave (−)-**2b** (185 mg), as red-orange prisms from AcOEt–CH_2Cl_2, mp 223—224 °C. Total yield: 1.119 g, 99%, $[\alpha]_D^{24}$ −92° (*c*=1.0, $CHCl_3$). IR (KBr): 1761, 1731, 1706 cm^{-1}. ^{1}H-NMR (100 MHz): 8.27, 6.78 (each 1H, s, ArH), 5.14 (1H, dd, *J*=5, 3 Hz, CHCOOMe), 4.01, 3.64, 3.93, 3.90 (each 3H, s, OMe), 3.41 (2H, m, $ArCH_2$). MS: 375 (M^+), 288 (base peak). *Anal.* Calcd for $C_{18}H_{17}NO_8$: C, 57.60; H, 4.57; N, 3.73. Found: C, 57.40; H, 4.59; N, 3.59. X-Ray analysis: see below.

Diels–Alder Reaction of the Dioxopyrroline (2b) with 1-Methoxy-3-trimethylsilyloxybutadiene (at 1 bar) (1) In Toluene: A mixture of (−)-**2b** (100 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (230 mg, 5 eq) in toluene (1.2 ml) was heated in a sealed tube with stirring at 130 °C for 1 h. The mixture was diluted with $CHCl_3$ (20 ml) and stirred with silica gel (1 g) at room temperature overnight. The silica gel was collected by filtration and washed with $CHCl_3$–MeOH (10:1). The combined filtate and washings were concentrated and the residue was purified by MPLC (benzene : AcOEt = 5:2) to give the one-adducts, **7** (85 mg, 73%), **8** (15 mg, 13%), and **9** (9 mg, 7%).

(2) In CH_2Cl_2: A mixture of (−)-**2b** (100 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (230 mg, 5 eq) in CH_2Cl_2 (1.2 ml) was treated as described above to give **7** (53 mg, 45%), **8** (16 mg, 14%), and **9** (17 mg, 13%).

The Enone **7**: Red oil, $[\alpha]_D^{25}$ −8.5° (*c*=1.1, $CHCl_3$). IR: 1740, 1690, 1679, 1599 cm^{-1}. ^{1}H-NMR (100 MHz): 8.04 (1H, s, ArH), 7.22 (1H, d, *J*=6 Hz, COCH=CH), 6.63 (1H, s, ArH), 5.44 (1H, d, *J*=6 Hz, COCH=CH), 4.98 (1H, dd, *J*=5, 3 Hz, CHCOOMe), 3.86, 3.88, 3.74, 3.53 (each 3H, s, OMe), 3.59, 2.74 (each 1H, d, *J*=17 Hz, CH_2CO). MS: 443 (M^+), 373 (base peak). HRMS: Calcd for $C_{22}H_{21}NO_9$: 443.1216 (M^+). Found: 443.1216.

The Enone **8**: Orange prisms from CH_2Cl_2–Et_2O, mp 192—193 °C, $[\alpha]_D^{24}$ −49° (*c*=0.17, $CHCl_3$). IR: 1740, 1690, 1679, 1600 cm^{-1}. ^{1}H-NMR (100 MHz): 8.45, 6.64 (each 1H, s, ArH), 7.28, 5.44 (each 1H, d, *J*=6.5 Hz, COCH=CH), 4.92 (1H, dd, *J*=5, 2.5 Hz, CHCOOMe), 3.88 (6H, s, 2×OMe), 3.55, 3.72 (each 3H, s, OMe), 3.26, 2.63 (each 1H, ABq, *J*=17 Hz, CH_2CO). MS: 443 (M^+), 373 (base peak). HRMS: Calcd for $C_{22}H_{21}NO_9$: 443.1216 (M^+). Found: 443.1340. X-Ray analysis: see below.

The Methoxyketone **9**: Red oil. IR: 1736, 1695 cm^{-1}. MS: 475 (M^+), 344 (base peak). ^{1}H-NMR (100 MHz) proved that the product is a 10:1 mixture of two stereoisomers. Major isomer: ArH 7.85, 6.69; OMe 3.94, 3.90, 3.76, 3.58, 3.55. Minor isomer: ArH 7.84, 6.68; OMe 3.94, 3.90, 3.81, 3.59, 3.45.

Diels–Alder Reaction of the Dioxopyrroline (2b) with 1-Methoxy-3-trimethylsilyloxybutadiene (at 10 kbar) (1) A solution of (−)-**2b** (100 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (230 mg, 5 eq) in CH_2Cl_2 (4 ml) was stirred at room temperature for 3 h under a pressure of 10 kbar and worked up as described above. Purification of the product by MPLC (benzene : AcOEt = 5:2) gave **11** (*endo* : *exo* = 1 : >20, 65 mg, 51%) and the methoxyketone **9** (25 mg, 20%).

(2) A solution of (−)-**2b** (100 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (92 mg, 2 eq) in CH_2Cl_2 was treated as described above. The mixture was diluted with tetrahydrofuran (THF, 5 ml) and stirred with KF (50 mg) at room temperature for 16 h. The reaction mixture was diluted with CH_2Cl_2 and washed with water. Purification of the CH_2Cl_2 extract by MPLC (benzene : AcOEt = 5:2) gave the ene-adduct **11** (*endo* : *exo* = 1:12, 60 mg, 47%), and a mixture of **7** and **8** (25 mg, 21%). The product **11** was separated into the *endo*-adduct and *exo*-adduct (**11a** and **11b**) by a combination of recycling HPLC ($CHCl_3$) and recrystallizations.

The *endo*-Adduct (−)-**11a**: Colorless needles from benzene–Et_2O, mp 177—179 °C, $[\alpha]_D^{23}$ −147° (*c*=0.24, $CHCl_3$). IR (KBr): 1772, 1748, 1733, 1716 cm^{-1}. ^{1}H-NMR: 6.64, 6.06 (each 1H, s, ArH), 4.64 (1H, t, *J*=3 Hz, H-1), 4.18 (1H, dd, *J*=12, 4 Hz, H-10), 3.87, 3.85, 3.72, 3.08, 3.36 (each 3H, s, OMe), 3.53, 3.13 (each 1H, ABq, *J*=14.5 Hz, H-4), 3.33 (1H, dd, *J*=16, 12 Hz, H-11), 3.16, 3.06 (each 1H, dd, *J*=20, 3 Hz, H-2), 3.02 (1H, dd, *J*=16, 4 Hz, H-11). MS: 475 (M^+), 344 (base peak). *Anal.* Calcd for $C_{23}H_{25}NO_{10}$: C, 58.10; H, 5.30; N, 2.95. Found: C, 58.00; H, 5.28; N, 2.92.

The *exo*-Adduct (−)-**11b**: Colorless needles from benzene–hexane, mp 206—207 °C, $[\alpha]_D^{23}$ −221° (*c*=0.17, $CHCl_3$). IR (KBr): 1773, 1756, 1747, 1710 cm^{-1}. ^{1}H-NMR: 7.25, 6.62 (each 1H, s, ArH), 4.58 (1H, t, *J*=3 Hz, H-1), 4.28 (1H, dd, *J*=12, 4 Hz, H-10), 3.87, 3.85, 3.82, 3.73, 3.11 (each 3H, s, OMe), 3.52, 3.06 (each 1H, ABq, *J*=16 Hz, H-4), 3.28 (1H, dd, *J*=16, 12 Hz, H-11), 3.05 (1H, dd, *J*=16, 4 Hz, H-11), 2.80, 2.25 (each 1H, dd, *J*=20, 3 Hz, H-2). MS: 475 (M^+), 344 (base peak). *Anal.* Calcd for $C_{23}H_{25}NO_{10}$: C, 58.10; H, 5.30; N, 2.95. Found: C, 58.53; H, 5.29; N, 2.83.

Ethyleneacetalization of the Ene-Adducts (11) A mixture of the ene-adducts **11** (14 mg, *endo* : *exo* = 12:5), ethylene glycol (0.5 ml), and a catalytic amount of *p*-TsOH·H_2O in benzene (10 ml) was heated under reflux for 5 h. The mixture was poured into ice-water and washed with saturated K_2CO_3 solution. Purification of the organic extract by PTLC (benzene : AcOEt = 1:1) gave the ethylene acetals, **12a** (9.7 mg, 63%) and **12b** (4 mg, 26%).

The *endo*-Isomer **12a**: Colorless prisms from MeOH–Et_2O, mp 246—247 °C. IR: 1773, 1749, 1719 cm^{-1}. ^{1}H-NMR: 6.82, 6.60 (each 1H, s, ArH), 4.48 (1H, dd, *J*=10, 6.4 Hz, H-1), 4.23 (1H, dd, *J*=10.5, 4 Hz, H-10), 3.93 (4H, m, OCH_2CH_2O), 3.90, 3.86, 3.84, 3.49, 3.21 (each 3H, s, OMe), 3.26 (1H, dd, *J*=16, 10.5 Hz, H-11), 2.99 (1H, dd, *J*=16, 4 Hz,

H-11), 2.64 (1H, dd, J=14.5, 6.4 Hz, H-2), 2.32, 2.27 (each 1H, ABq, J=15 Hz, H-4), 2.10 (1H, dd, J=14.5, 10 Hz, H-2). MS: 519 (M^+), 288 (base peak). *Anal.* Calcd for $C_{25}H_{29}NO_{11}$: C, 57.80; H, 5.63; N, 2.70. Found: C, 57.71; H, 5.60; N, 2.68. X-Ray analysis: see below.

The *exo*-Isomer **12b**: Colorless gum. IR: 1775, 1745, 1718 cm^{-1}. ^{1}H-NMR: 7.52, 6.59 (each 1H, s, ArH), 4.43 (1H, br d, J=5.3 Hz, H-1), 4.39 (1H, dd, J=10, 4.5 Hz, H-10), 3.93 (4H, m, OCH_2CH_2O), 3.86, 3.82, 3.85, 3.61, 3.16 (each 3H, s, OMe), 3.28 (1H, dd, J=16, 10 Hz, H-11), 3.07 (1H, dd, J=16, 4.5 Hz, H-11), 2.57 (1H, d, J=15 Hz, H-4), 2.27 (1H, dd, J=15, 1 Hz, H-4), 2.29 (1H, br d, J=16 Hz, H-2), 2.04 (1H, dd, J=16, 5.3 Hz, H-2). MS: 519 (M^+), 288 (base peak). HRMS: $C_{25}H_{29}NO_{11}$: 519.1739 (M^+). Found: 519.1739.

Reduction of 12 with *n*-Bu_4NBH_4 (1) A solution of the *endo*-isomer **12a** (4 mg) and *n*-Bu_4NBH_4 (2.9 mg) in MeOH (1 ml) was stirred at 0 °C for 10 min. After addition of water, the mixture was extracted with $CHCl_3$ and the product was purified by PTLC (AcOEt) to give the 7β-alcohol **13a** (4 mg, 100%) as a colorless gum. IR: 3500, 1735, 1710 cm^{-1}. ^{1}H-NMR: 7.08, 6.56 (each 1H, s, ArH), 4.90 (1H, s, H-7), 4.68 (1H, dd, J=12, 5.5 Hz, H-1), 4.10 (1H, dd, J=8.5, 5.4 Hz, H-10), 3.92 (3H, m, 3H of OCH_2CH_2O), 3.87, 3.85, 3.78, 3.55, 3.25 (each 3H, s, OMe), 3.65 (1H, q, J=7.5 Hz, 1H of OCH_2CH_2O), 3.09 (1H, dd, J=16, 8.5 Hz, H-11), 2.96 (1H, dd, J=16, 5.4 Hz, H-11), 2.50 (1H, ddd, J=13.5, 5.4, 2.3 Hz, H-2), 2.42 (1H, dd, J=14.2, 2.3 Hz, H-4), 2.17 (1H, s, OH), 2.07 (1H, d, J=14.2 Hz, H-4), 1.97 (1H, dd, J=13.5, 12 Hz, H-2). MS: 521 (M^+). HRMS: Calcd for $C_{25}H_{31}NO_{11}$: 521.1897 (M^+). Found: 521.1886.

(2) A solution of the *exo*-isomer **12b** (4 mg) and *n*-Bu_4NBH_4 (3 mg) in MeOH (1 ml) was stirred at 0 °C for 30 min. The mixture was worked up as described above to give a mixture of the 7β-alcohol **13b** and the 7α-alcohol **13c** (**13b**:**13c**=1:2, 4 mg, 100%). ^{1}H-NMR: for **13b**: 7.59, 6.53 (each 1H, s, ArH), 4.52 (1H, s, H-7); for **13c**: 6.82, 6.54 (each 1H, s, ArH), 4.82 (1H, s, H-7).

$NaBH_4$ Reduction of the *exo*-Isomer (12b) A solution of the *exo*-isomer **12b** (16 mg) and $NaBH_4$ (2.8 mg) in MeOH (1 ml) was stirred at 0 °C for 20 min. Work-up of the mixture gave **13b** and **13c** (16 mg, 100%) in a ratio of 1:4.

Acid Hydrolysis of the Acetal (13) (1) A solution of **13a** (14 mg) in 5% HCl–THF (1:1, 5 ml) was heated with stirring at 80 °C for 40 min. The mixture was poured into water and extracted with $CHCl_3$. The product was purified by flash column chromatography (AcOEt) to give the 7β-OH-enone **14a** (9.2 mg, 77%), as colorless needles from MeOH–Et_2O, mp 212—216 °C. IR: 1745, 1725, 1690 cm^{-1}. ^{1}H-NMR: 7.54 (1H, d, J=10.5 Hz, H-1), 6.61, 6.50 (each 1H, s, ArH), 6.45 (1H, d, J=10.5 Hz, H-2), 4.75 (1H, br s, H-7), 4.19 (1H, dd, J=8.5, 5 Hz, H-10), 3.84, 3.81, 3.69, 3.35 (each 3H, s, OMe), 3.16 (1H, dd, J=16, 8.5 Hz, H-11), 2.99 (1H, dd, J=16, 5 Hz, H-11), 3.14, 2.99 (each 1H, ABq, J=16 Hz, H-4). MS: 445 (M^+), 386 (base peak). *Anal.* Calcd for $C_{22}H_{23}NO_9$: C, 59.32; H, 5.21; N, 3.14. Found: C, 59.28; H, 5.24; N, 3.15.

(2) A mixture of **13b** and **13c** (1:4, 16 mg) was heated with 5% HCl–THF at 80 °C for 4 h, and worked up as described above to give the 7β-OH-enone **14a** (2.5 mg, 18%) and the 7α-OH-enone **14b** (11 mg, 80%), which were separated by chromatography.

14b: Colorless oil. IR: 1740, 1695 cm^{-1}. ^{1}H-NMR: 7.11 (1H, d, J=10.5 Hz, H-1), 6.54, 6.53 (each 1H, s, ArH), 6.43 (1H, d, J=10.5 Hz, H-2), 4.44 (1H, br s, H-7), 4.30 (1H, OH), 4.19 (1H, dd, J=8, 5.8 Hz, H-10), 3.77, 3.71, 3.66, 3.39 (each 3H, s, OMe), 3.22, 2.97 (each 1H, ABq, J=15.2 Hz, H-4), 3.11 (1H, dd, J=16.5, 8 Hz, H-11), 2.97 (1H, dd, J=16.5, 5.8 Hz, H-11). MS: 445 (M^+), 386 (base peak). HRMS: Calcd for $C_{22}H_{23}NO_9$: 445.1371 (M^+). Found: 445.1368.

(5*R*,10*S*)-(+)-15,16-Dimethoxy-10-methoxycarbonyl-3,8-dioxoerythrinan-1,6-diene (16) A mixture of **14a** and **14b** (40 mg) and methanesulfonyl chloride (83 μl) in dry pyridine (1 ml) was stirred at room temperature for 1.5 h, then diluted with CH_2Cl_2 and washed with 1 N HCl. Purification of the product by chromatography (benzene:AcOEt=1:2) gave a mixture of **15a** and **15b** as a gum. This mixture was dissolved in DMSO (2 ml) and heated with $MgCl_2$ (41 mg) at 140 °C for 2.5 h in a sealed tube under stirring. The mixture was diluted with CH_2Cl_2 and washed with water. Concentration of the extract and purification of the residue by PTLC (benzene:AcOEt=1:3) gave the dienone (+)-**16** (20 mg, 60%), as colorless prisms from MeOH–Et_2O, mp 220—221 °C, $[\alpha]_D^{20}$ +122° (c=0.265, $CHCl_3$). IR: 1760, 1695, 1685 cm^{-1}. ^{1}H-NMR: 7.81 (1H, d, J=10 Hz, H-1), 6.73, 6.68 (each 1H, s, ArH), 6.42 (1H, s, H-7), 6.39 (1H, d, J=10 Hz, H-2), 4.55 (1H, t, J=6 Hz, H-10), 3.84, 3.75, 3.67 (each 3H, s, OMe), 3.29, 3.17 (each 1H, dd, J=16, 6 Hz, H-11), 3.22, 2.88 (each 1H, ABq, J=15 Hz, H-4). MS: 369 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.19; N, 3.79. Found: C, 64.98; H, 5.15; N, 3.82.

Conversion of Ene-Adducts (11) to the Enone (20) A mixture of ene-adducts **11** (*endo*:*exo*=2:1, 1.03 g), *p*-TsOH·H_2O (30 mg), and ethylene glycol (15 ml) in benzene (80 ml) was heated under reflux for 8 h with stirring. The mixture was poured into ice-water and the organic layer was washed with saturated $NaHCO_3$ solution and brine, then dried, and concentrated. The residue (**12**) was dissolved in MeOH (30 ml) and reduced with $NaBH_4$ (160 mg) at 0 °C for 20 min. The product (**13**) obtained by a usual work-up was dissolved in MeOH (10 ml) and treated with 4% NaOH–MeOH (13 ml) at room temperature for 50 min. Acidification of the reaction mixture to pH 2 with 10% HCl followed by extraction with AcOEt gave a mixture of the acid (**18**).

N-Methylmorpholine (266 μl) and isobutyl chloroformate (310 μl) were added to a solution of the acid (**18**) in dry THF (15 ml) at −10 °C. After stirring of the mixture for 10 min, *N*-hydroxypyridinethione sodium salt (356 mg) and triethylamine (365 μl) in THF (15 ml) were added successively and stirring was continued at −10 °C for 50 min. The precipitate formed was quickly removed by filtration and the filtrate was irradiated, after addition of *tert*-butylmercaptan (2.7 ml), with a 100 W high-pressure mercury lamp for 20 min under an Ar atmosphere. The resulting mixture was taken up in $CHCl_3$, washed with 1 N HCl, saturated $NaHCO_3$ solution and brine, and concentrated to yield a decarbomethoxylated product **19**.

The product **19** in 5% HCl–THF (1:1, 40 ml) was heated at 80 °C for 3.5 h. After evaporation of the organic solvent, the mixture was extracted with $CHCl_3$, and the product was purified by chromatography (AcOEt) to give a mixture of enones **20** (500 mg, 60% from **11**), which were separated into **20a** and **20b** by PTLC ($CHCl_3$:MeOH=9:1).

(5*R*,6*S*,7*S*)-(+)-15,16-Dimethoxy-6-methoxycarbonyl-7-hydroxy-3,8-dioxoerythrinan-1-ene [(+)-**20a**]: Colorless crystals from MeOH–Et_2O, mp 217—219 °C, $[\alpha]_D^{23}$ +131° (c=0.385, $CHCl_3$). IR (KBr): 3255, 1736, 1690, 1670 cm^{-1}. ^{1}H-NMR: 7.15 (1H, d, J=10.5 Hz, H-1), 6.56, 6.55 (each 1H, s, ArH), 6.56 (1H, d, J=10.5 Hz, H-2), 4.53 (1H, s, H-7), 4.36 (1H, ddd, J=13.5, 6, 1 Hz, H-10), 3.83, 3.70, 3.26 (each 3H, s, OMe), 3.19, 3.09 (each 1H, ABq, J=15.5 Hz, H-4), 3.10 (1H, td, J=13.5, 4 Hz, H-10), 2.83 (1H, ddd, J=16, 13.5, 6 Hz, H-11), 2.67 (1H, ddd, J=16, 4, 1 Hz, H-11). MS: 387 (M^+). *Anal.* Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.88; H, 5.50; N, 3.58.

The (7*R*)-Isomer [(+)-**20b**]: Colorless prisms from MeOH–Et_2O, mp 209.5—211 °C, $[\alpha]_D^{23}$ +73.4° (c=1.4, $CHCl_3$). IR (KBr): 3315, 1730, 1720, 1672. ^{1}H-NMR: 7.57 (1H, d, J=10 Hz, H-1), 6.55, 6.47 (each 1H, s, ArH), 6.46 (1H, d, J=10 Hz, H-2), 4.78 (1H, s, H-7), 4.35 (1H, ddd, J=12.5, 6, 2 Hz, H-10), 3.83, 3.67, 3.29 (each 3H, s, OMe), 3.17, 2.83 (each 1H, ABq, J=15.5 Hz, H-4), 3.11 (1H, td, J=12.5, 3.5 Hz, H-10), 2.89 (1H, ddd, J=16, 12.5, 6 Hz, H-11), 2.67 (1H, ddd, J=16, 3.5, 2 Hz, H-11). MS: 387 (M^+), 328 (base peak). *Anal.* Calcd for $C_{20}H_{21}NO_7 \cdot 1/2H_2O$: C, 60.06; H, 5.50; N, 3.50. Found: C, 59.91; H, 5.54; N, 3.43.

Methanesulfonylation of 20a and 20b (1) A mixture of **20a** (16 mg), methanesulfonyl chloride (16 μl), and 4-dimethylaminopyridine (10 mg) in pyridine (1 ml) was stirred at room temperature for 4.5 h. Work-up of the product as usual gave the *O*-mesylate **21a** (19 mg, 99%), as colorless needles from MeOH–Et_2O, mp 181.5—182 °C, $[\alpha]_D^{23}$ +181° (c=0.1, $CHCl_3$). IR (KBr): 1731, 1698. ^{1}H-NMR: 7.08 (1H, d, J=10.6 Hz, H-1), 6.62 (1H, br d, J=10.6 Hz, H-2), 6.56, 6.50 (each 1H, s, ArH), 5.20 (1H, s, H-7), 4.41 (1H, ddd, J=13, 5.6, 1.3 Hz, H-10), 3.84, 3.70, 3.29 (each 3H, s, OMe), 3.27 (3H, s, SO_2Me), 3.17, 2.91 (each 1H, ABq, J=15.5 Hz, H-4), 3.17 (1H, td, J=12, 4 Hz, H-10), 2.86 (1H, ddd, J=16, 12, 5.6 Hz, H-11), 2.69 (1H, ddd, J=16, 4, 1.3 Hz, H-11). MS: 465 (M^+), 354 (base peak). *Anal.* Calcd for $C_{21}H_{23}NO_9S$: C, 54.19; H, 4.98; N, 3.00. Found: C, 53.98; H, 4.95; N, 3.02.

(2) A mixture of **20b** (23 mg) and methanesulfonyl chloride (25 μl) in dry pyridine was stirred at room temperature for 1.5 h. Purification of the product by PTLC ($CHCl_3$:MeOH=19:1) gave the *O*-mesylate **21b** (27 mg, 98%), as colorless prisms from AcOEt, mp 258—259 °C, $[\alpha]_D^{23}$ +83.6° (c=0.275, $CHCl_3$). IR (KBr): 1725, 1710, 1705 cm^{-1}. ^{1}H-NMR: 7.37 (1H, d, J=11 Hz, H-1), 6.49, 6.36 (each 1H, s, ArH), 6.44 (1H, d, J=11 Hz, H-2), 5.44 (1H, s, H-7), 4.30 (1H, ddd, J=12.5, 6, 1.5 Hz, H-10), 3.76, 3.60, 3.30 (each 3H, s, OMe), 3.25 (3H, s, SO_2Me), 3.14, 2.77 (each 1H, ABq, J=15.6 Hz, H-4), 3.05 (1H, td, J=12.5, 4 Hz, H-10), 2.84 (1H, ddd, J=16, 12.5, 6 Hz, H-11), 2.62 (1H, ddd, J=16, 4, 1.5 Hz, H-11). MS: 465 (M^+), 386 (base peak). *Anal.* Calcd for $C_{21}H_{23}NO_9S$: C, 54.19; H, 4.98; N, 3.00. Found: C, 54.10; H, 4.99; N, 2.99.

(5*R*)-(+)-15,16-Dimethoxy-3,8-dioxoerythrinan-1,6-diene (17) (1) A mixture of **21a** (13 mg), anhydrous $CaCl_2$ (16 mg), and *tert*-heptylmercaptan (1 drop) in DMSO (1 ml) was heated at 140 °C for 2.5 h in a sealed tube with stirring. The mixture was diluted with $CHCl_3$, washed with water, dried, and concentrated. The residue was purified by PTLC (AcOEt)

to give the dienone (+)-**17** (8 mg, 92%), as pale yellow leaflets from acetone–hexane, mp 196—197 °C, $[\alpha]_D^{23}$ +217° (c=0.26, $CHCl_3$). IR (KBr): 1689, 1670. ^{1}H-NMR (270 MHz): 7.75 (1H, dd, J=10, 0.6 Hz, H-1), 6.85, 6.66 (each 1H, s, ArH), 6.42 (1H, d, J=10 Hz, H-2), 6.37 (1H, d, J=0.6 Hz, H-7), 4.22 (1H, ddd, J=14, 6.6, 5 Hz, H-10), 3.84, 3.72 (each 3H, s, OMe), 3.40 (1H, ddd, J=14, 8.5, 5.6 Hz, H-10), 3.27, 2.80 (each 1H, ABq, J=15 Hz, H-4), 3.30 (1H, ddd, J=16, 8.5, 6.6 Hz, H-11), 2.83 (1H, dt, J=16, 5.6 Hz, H-11). MS: 311 (M^+). *Anal.* Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.43; H, 5.53; N, 4.50. The TLC behavior and ^{1}H-NMR spectrum of this compound were identical with those of (±)-**17**.[5,6c]

(2) A mixture of **21b** (15 mg), anhydrous $CaCl_2$ (18 mg), and *tert*-heptylmercaptan (1 drop) in DMSO (1 ml) was heated at 140 °C for 2.5 h in a sealed tube and worked up as described above to give the dienone (+)-**17** (10 mg, 100%), which was identical with the product obtained from (+)-**21a**.

$NaBH_4$–$CeCl_3$ Reduction of the Dienone (17) $NaBH_4$ (16 mg) was added to a stirred solution of (+)-**17** (54 mg) and $CeCl_3 \cdot 7H_2O$ (154 mg) in MeOH (5 ml) at room temperature. Stirring was continued for 10 min, then water was added, and the mixture was extracted with $CHCl_3$ to give a mixture of alcohols **22**, which was separated by PTLC ($CHCl_3$: MeOH = 19 : 1) into (+)-**22a** (47.5 mg, 87%) and (+)-**22b** (7 mg, 13%).

The 3α-Alcohol (+)-**22a**: Colorless needles from AcOEt, mp 87—88 °C, $[\alpha]_D^{23}$ +182.4° (c=0.25, $CHCl_3$). IR (KBr): 3420, 1652 cm^{-1}. ^{1}H-NMR: 6.81 (1H, dd, J=10.3, 3 Hz, H-2), 6.78, 6.70 (each 1H, s, ArH), 6.32 (1H, br d, J=10.3 Hz, H-1), 5.93 (1H, s, H-7), 4.26 (1H, m, H-3), 3.92 (1H, dt, J=13, 7.5 Hz, H-10), 3.85, 3.74 (each 3H, s, OMe), 3.55 (1H, ddd, J=13, 7.5, 5.5 Hz, H-10), 3.05 (1H, dt, J=16, 7.5 Hz, H-11), 2.95 (1H, ddd, J=16, 7.5, 5.5 Hz, H-11), 2.77 (1H, dd, J=11.5, 5.5 Hz, H-4), 1.64 (1H, dd, J=11.5, 10.5 Hz, H-4). MS: 313 (M^+). *Anal.* Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.72; H, 6.14; N, 4.26.

The 3β-Alcohol (+)-**22b**: Colorless needles from AcOEt, mp 82—83 °C, $[\alpha]_D^{23}$ +23.8° (c=0.105, $CHCl_3$). IR (KBr): 3400, 1647, 1626 cm^{-1}. ^{1}H-NMR: 6.97, 6.77 (each 1H, s, ArH), 6.92 (1H, d, J=10.3 Hz, H-1), 6.32 (1H, dd, J=10.3, 5 Hz, H-2), 6.01 (1H, s, H-7), 4.49 (1H, t, J=5 Hz, H-3), 3.87, 3.80 (each 3H, s, OMe), 3.80 (1H, ddd, J=12.5, 10.5, 7 Hz, H-10), 3.66 (1H, ddd, J=12.5, 7.5, 3.5 Hz, H-10), 3.19 (1H, ddd, J=16, 10.5, 7.5 Hz, H-11), 2.97 (1H, ddd, J=16, 7, 3.5 Hz, H-11), 2.68 (1H, d, J=14 Hz, H-4), 2.11 (1H, dd, J=14, 5 Hz, H-4). MS: 313 (M^+). *Anal.* Calcd for $C_{18}H_{19}NO_4$: C, 68.99; H, 6.11; N, 4.47. Found: C, 68.89; H, 6.13; N, 4.45.

(+)-Erysotramidine (23a) A mixture of (+)-**22a** (63 mg), 85% KOH (133 mg), Et_4NBr (127 mg), and CH_3I (3 ml) in THF (5 ml) was stirred at room temperature for 34 h, then poured into ice-water and extracted with $CHCl_3$. The extract was washed with 5% $Na_2S_2O_3$ solution and brine,

TABLE I. Positional Parameters and B_{eq} for **2b**

Atom	x	y	z	B_{eq}
O(1)	−0.5860	0.4213	1.4107	4.42 (7)
O(2)	−0.8012 (4)	0.1235 (4)	1.0457 (6)	5.13 (8)
O(3)	−0.1442 (5)	0.7096 (4)	1.3341 (5)	5.61 (9)
O(4)	−0.2356 (5)	0.6408 (4)	1.5758 (5)	5.72 (8)
O(5)	−0.4542 (5)	−0.0185 (4)	1.0993 (5)	4.91 (8)
O(6)	−0.5617 (5)	−0.1863 (4)	0.7651 (5)	4.41 (7)
O(7)	0.1836 (4)	0.5529 (4)	1.0226 (5)	4.87 (7)
O(8)	0.0606 (4)	0.3365 (4)	0.6531 (5)	4.54 (7)
N(1)	−0.5716 (4)	0.2193 (4)	0.9487 (5)	3.16 (7)
C(1)	−0.4032 (5)	0.3489 (4)	1.0471 (6)	2.72 (7)
C(2)	−0.3842 (5)	0.4526 (4)	1.2349 (6)	3.07 (8)
C(3)	−0.5420 (5)	0.3813 (4)	1.2689 (6)	3.29 (8)
C(4)	−0.6618 (5)	0.2243 (5)	1.0765 (6)	3.52 (8)
C(6)	−0.6125 (5)	0.0672 (4)	0.7888 (6)	3.01 (7)
C(7)	−0.5441 (5)	0.1105 (5)	0.6247 (6)	3.30 (8)
C(8)	−0.3500 (5)	0.2283 (4)	0.7411 (6)	2.89 (7)
C(9)	−0.2849 (5)	0.3456 (4)	0.9425 (6)	2.86 (7)
C(10)	−0.1031 (5)	0.4553 (5)	1.0405 (6)	3.27 (8)
C(11)	0.0077 (5)	0.4499 (5)	0.9415 (6)	3.53 (8)
C(12)	−0.0577 (5)	0.3311 (5)	0.7383 (6)	3.47 (8)
C(13)	−0.2366 (5)	0.2222 (5)	0.6406 (6)	3.24 (8)
C(14)	−0.2407 (5)	0.6121 (4)	1.3817 (6)	3.46 (9)
C(15)	−0.1039 (9)	0.7949 (7)	1.7352 (9)	6.9 (2)
C(16)	−0.5308 (5)	−0.0488 (4)	0.9055 (6)	3.16 (7)
C(17)	−0.5025 (7)	−0.3140 (5)	0.8522 (8)	4.8 (1)
C(18)	0.2503 (6)	0.6827 (6)	1.2188 (8)	5.0 (1)
C(19)	0.0010 (6)	0.2209 (6)	0.4472 (7)	4.5 (1)
H(1)	−0.741 (4)	0.015 (4)	0.714 (5)	2.7 (6)
H(2)	−0.623 (4)	0.172 (4)	0.537 (5)	3.7 (6)
H(3)	−0.556 (4)	0.013 (4)	0.527 (5)	2.7 (5)
H(4)	−0.052 (4)	0.534 (4)	1.175 (5)	2.8 (6)
H(5)	−0.284 (4)	0.144 (3)	0.505 (5)	1.9 (5)
H(6)	0.012 (9)	0.802 (7)	1.739 (9)	9 (1)
H(7)	−0.133 (7)	0.876 (6)	1.650 (8)	7 (1)
H(8)	−0.128 (7)	0.809 (7)	1.85 (1)	8 (1)
H(9)	−0.581 (7)	−0.378 (6)	0.898 (8)	8 (1)
H(10)	−0.479 (6)	−0.371 (6)	0.757 (8)	7 (1)
H(11)	−0.399 (8)	−0.266 (7)	0.99 (1)	8 (1)
H(12)	0.244 (4)	0.635 (4)	1.331 (6)	4.1 (7)
H(13)	0.174 (6)	0.754 (5)	1.194 (7)	6 (1)
H(14)	0.372 (6)	0.748 (6)	1.243 (7)	7 (1)
H(15)	0.096 (5)	0.251 (4)	0.413 (6)	4.3 (7)
H(16)	−0.109 (5)	0.227 (4)	0.355 (6)	3.6 (7)
H(17)	−0.037 (7)	0.103 (7)	0.445 (8)	7 (1)

TABLE II. Positional Parameters and B_{eq} for **8**

Atom	x	y	z	B_{eq}
O(1)	0.217 (1)	0.0967	1.0964 (3)	7.7 (4)
O(2)	−0.1872 (7)	0.2400 (8)	0.9141 (2)	4.1 (2)
O(3)	0.2402 (8)	0.3775 (9)	0.9496 (3)	4.5 (2)
O(4)	0.3949 (8)	0.618 (1)	0.7377 (4)	7.4 (4)
O(5)	0.0820 (8)	0.5176 (9)	0.7515 (3)	4.7 (3)
O(6)	0.0850 (9)	0.0787 (8)	0.4845 (3)	5.3 (3)
O(7)	0.4228 (8)	0.2145 (8)	0.4519 (3)	5.1 (3)
O(8)	−0.092 (1)	−0.039 (1)	0.7277 (4)	9.9 (5)
O(9)	−0.2661 (9)	0.0025 (9)	0.8357 (3)	6.1 (3)
N(1)	0.2659 (8)	0.3083 (9)	0.8195 (3)	3.1 (2)
C(1)	0.119 (1)	0.090 (1)	0.9585 (4)	4.1 (4)
C(2)	0.090 (1)	0.132 (1)	1.0428 (4)	4.6 (4)
C(3)	−0.111 (1)	0.207 (1)	1.0545 (5)	4.6 (4)
C(4)	−0.237 (1)	0.251 (1)	0.9922 (4)	4.5 (4)
C(5)	0.031 (1)	0.188 (1)	0.8964 (4)	3.4 (3)
C(6)	0.190 (1)	0.304 (1)	0.8948 (4)	3.4 (3)
C(7)	0.417 (1)	0.408 (1)	0.7935 (4)	3.5 (3)
C(8)	0.566 (1)	0.349 (1)	0.7341 (4)	3.5 (3)
C(9)	0.429 (1)	0.278 (1)	0.6696 (4)	3.2 (3)
C(10)	0.241 (1)	0.209 (1)	0.6868 (4)	3.0 (3)
C(11)	0.124 (1)	0.144 (1)	0.6248 (4)	3.8 (4)
C(12)	0.192 (1)	0.144 (1)	0.5477 (4)	3.9 (3)
C(13)	0.378 (1)	0.215 (1)	0.5305 (4)	3.4 (3)
C(14)	0.497 (1)	0.280 (1)	0.5913 (5)	3.7 (4)
C(15)	0.167 (1)	0.212 (1)	0.7696 (4)	3.0 (3)
C(16)	0.022 (1)	0.139 (1)	0.8108 (4)	3.1 (3)
C(17)	−0.111 (1)	0.028 (1)	0.7849 (4)	4.3 (4)
C(18)	−0.423 (2)	−0.102 (1)	0.8183 (8)	7.0 (7)
C(19)	−0.097 (2)	−0.001 (1)	0.5001 (6)	5.4 (5)
C(20)	0.595 (2)	0.299 (1)	0.4274 (6)	6.1 (6)
C(21)	0.295 (1)	0.527 (1)	0.7578 (4)	3.2 (3)
C(22)	−0.036 (2)	0.634 (1)	0.7201 (6)	5.1 (5)
H(1)	0.29 (1)	0.068 (6)	0.941 (3)	3 (1)
H(2)	0.034 (8)	0.009 (6)	0.954 (3)	2 (1)
H(3)	−0.15 (1)	0.223 (6)	1.107 (4)	3 (1)
H(4)	−0.411 (9)	0.293 (6)	1.000 (3)	4 (1)
H(5)	0.51 (1)	0.433 (6)	0.838 (3)	3 (1)
H(6)	0.05 (3)	0.69 (2)	0.71 (1)	21 (8)
H(7)	−0.07 (1)	0.621 (8)	0.662 (5)	6 (2)
H(8)	−0.17 (1)	0.63 (1)	0.742 (5)	9 (3)
H(9)	0.66 (1)	0.418 (6)	0.707 (3)	3 (1)
H(10)	0.68 (1)	0.294 (7)	0.760 (3)	4 (2)
H(11)	0.027 (8)	0.092 (5)	0.632 (3)	1 (1)
H(12)	−0.06 (1)	−0.056 (8)	0.546 (5)	7 (3)
H(13)	−0.24 (1)	0.052 (8)	0.518 (4)	7 (2)
H(14)	−0.150 (8)	−0.039 (5)	0.451 (3)	2 (1)
H(15)	0.72 (1)	0.28 (1)	0.460 (5)	8 (3)
H(16)	0.61 (1)	0.274 (7)	0.373 (4)	5 (2)
H(17)	0.55 (1)	0.393 (8)	0.444 (4)	5 (2)

TABLE III. Positional Parameters and B_{eq} for **12a**

Atom	x	y	z	B_{eq}
O(1)	0.6506 (3)	0.4642 (3)	0.0577 (5)	5.6 (2)
O(2)	0.7915 (2)	0.2694 (3)	−0.2251 (4)	4.5 (2)
O(3)	0.6400 (3)	0.2755 (3)	−0.1980 (4)	4.6 (2)
O(4)	0.6459 (3)	0.3526 (3)	0.2779 (4)	6.3 (3)
O(5)	0.5201 (3)	0.2796 (4)	0.2283 (4)	5.8 (3)
O(6)	0.4905 (3)	0.3806 (3)	−0.0208 (4)	5.6 (2)
O(7)	0.4285 (3)	0.1990 (3)	−0.0631 (4)	4.6 (2)
O(8)	0.4332 (3)	−0.0173 (4)	−0.0417 (5)	7.1 (3)
O(9)	0.5110 (3)	0.0492 (3)	−0.1868 (4)	5.1 (2)
O(10)	0.8523 (3)	0.1658 (3)	0.3992 (3)	4.9 (2)
O(11)	0.7417 (2)	0.0516 (3)	0.4948 (3)	4.2 (2)
N(1)	0.5725 (3)	0.1663 (3)	−0.0020 (4)	3.1 (2)
C(1)	0.6929 (4)	0.3796 (4)	0.0422 (5)	3.9 (3)
C(2)	0.7339 (4)	0.3720 (4)	−0.0817 (5)	4.0 (3)
C(3)	0.7238 (4)	0.2808 (4)	−0.1361 (5)	3.7 (3)
C(4)	0.7304 (4)	0.2077 (4)	−0.0432 (5)	3.1 (3)
C(5)	0.6537 (3)	0.2084 (4)	0.0494 (5)	2.9 (3)
C(6)	0.6224 (4)	0.3090 (4)	0.0732 (5)	3.2 (3)
C(7)	0.5338 (4)	0.3149 (4)	0.0043 (5)	3.8 (3)
C(8)	0.5037 (4)	0.2203 (4)	−0.0270 (5)	3.4 (3)
C(10)	0.5640 (4)	0.0685 (4)	0.0084 (6)	4.0 (3)
C(11)	0.5484 (4)	0.0491 (5)	0.1375 (6)	4.9 (4)
C(12)	0.6255 (4)	0.0886 (4)	0.2076 (5)	3.6 (3)
C(13)	0.6789 (3)	0.1576 (4)	0.1627 (5)	3.0 (3)
C(14)	0.7567 (3)	0.1829 (4)	0.2249 (5)	3.0 (3)
C(15)	0.7778 (4)	0.1451 (4)	0.3343 (5)	3.3 (3)
C(16)	0.7195 (4)	0.0815 (4)	0.3838 (5)	3.5 (3)
C(17)	0.6465 (4)	0.0533 (4)	0.3197 (5)	3.8 (3)
C(18)	0.7064 (6)	0.5323 (6)	0.095 (1)	11.9 (7)
C(19)	0.7529 (5)	0.2146 (5)	−0.3152 (6)	6.3 (4)
C(20)	0.6536 (5)	0.2313 (6)	−0.3044 (8)	8.7 (6)
C(21)	0.5989 (5)	0.3189 (4)	0.2043 (6)	4.3 (4)
C(22)	0.4973 (6)	0.2704 (6)	0.3537 (6)	8.3 (5)
C(23)	0.4936 (5)	0.0301 (5)	−0.0738 (7)	4.8 (4)
C(24)	0.4448 (5)	0.0177 (5)	−0.2718 (6)	6.9 (4)
C(25)	0.9155 (6)	0.2228 (7)	0.3461 (7)	11.6 (6)
C(26)	0.6727 (4)	0.0091 (4)	0.5606 (6)	4.5 (3)

dried, and concentrated. The residue was purified by PTLC (AcOEt) to give (+)-**23a** (63 mg, 96%) as a colorless oil, $[\alpha]_D^{23}$ +148.5° (c=1.2, $CHCl_3$) [lit. $[\alpha]_D^{21}$ +121° (c=1.0, $CHCl_3$)].[15] IR: 1670, 1508 cm^{-1}. ^{1}H-NMR: 6.91 (1H, dd, J=10, 2.5 Hz, H-1), 6.81, 6.73 (each 1H, s, ArH), 6.34 (1H, br d, J=10 Hz, H-2), 6.03 (1H, s, H-7), 4.00 (1H, ddd, J=13, 8.5, 7.5 Hz, H-10), 3.86, 3.77, 3.35 (each 3H, s, OMe), 3.86 (1H, m, H-3), 3.62 (1H, ddd, J=13, 7.5, 5.5 Hz, H-10), 3.09 (1H, ddd, J=16, 8.5, 7.5 Hz, H-11), 3.00 (1H, ddd, J=16, 7.5, 5.5 Hz, H-11), 2.81 (1H, dd, J=11, 5.5 Hz, H-4), 1.71 (1H, dd, J=11, 10 Hz, H-4). MS: 327 (M^+). HRMS: Calcd for $C_{19}H_{21}NO_4$: 327.1471 (M^+). Found: 327.1474. This compound was identical with erysotramidine in TLC behavior and ^{1}H-NMR spectrum.[17]

(−)-3-Epierysotramidine (23b) A mixture of (+)-**22b** (19 mg), 85% KOH (40 mg), Et_4NBr (38 mg), and CH_3I (2 ml) in THF (2 ml) was stirred at room temperature for 23 d. The mixture was worked up as described above to give (−)-**25** (14 mg, 71%), with recovery of the starting material (4.7 mg), as pale yellow prisms from acetone–Et_2O, mp 201—203 °C, $[\alpha]_D^{23}$ −10.6° (c=0.635, $CHCl_3$). IR (KBr): 1669 cm^{-1}. ^{1}H-NMR: 7.19 (1H, s, ArH), 6.92 (1H, d, J=10 Hz, H-1), 6.61 (1H, s, ArH), 6.36 (1H, dd, J=10, 5 Hz, H-2), 5.95 (1H, s, H-7), 4.11 (1H, t, J=5 Hz, H-3), 4.09 (1H, dd, J=13.2, 7, 6 Hz, H-10), 3.84, 3.78, 3.18 (each 3H, s, OMe), 3.46 (1H, ddd, J=13.2, 7, 6 Hz, H-10), 3.00 (1H, dt, J=16, 7 Hz, H-11), 2.91 (1H, dt, J=16, 6 Hz, H-11), 2.75 (1H, d, J=14 Hz, H-4), 1.96 (1H, dd, J=14, 5 Hz, H-4). MS: 327 (M^+). HRMS: Calcd for M^+: 327.1469. Found: 327.1467. *Anal.* Calcd for $C_{19}H_{21}NO_4$: C, 69.70; H, 6.47; N, 4.28. Found: C, 69.54; H, 6.51; N, 4.27. The spectral data were identical with those reported for a racemic specimen.[5,17]

(+)-Erysotrine (4) A solution of AlH_3 [prepared from $LiAlH_4$ (40 mg) and $AlCl_3$ (46 mg)] in dry Et_2O (3 ml) was added to a solution of (+)-**23** (30 mg) in THF (2 ml) at 0 °C and the mixture was stirred for 40 min at 0 °C. The reaction mixture was poured into ice-water, basified with 28% NH_4OH, and extracted with Et_2O. The ethereal layer was extracted with 1 N HCl. The HCl layer was basified and extracted with $CHCl_3$. The extract was washed with brine, dried over anhydrous K_2CO_3 and concentrated to dryness *in vacuo* to afford (+)-**4** (27 mg, 94%) as pale yellow crystals, mp 95—100 °C (lit. mp 92—93 °C).[16] IR: 1507 cm^{-1}. ^{1}H-NMR (C_6D_6): 7.05, 6.48 (each 1H, s, ArH), 6.40 (1H, dd, J=10, 2.5 Hz, H-1), 5.99 (1H, br d, J=10 Hz, H-2), 5.46 (1H, br s, H-7), 4.15 (1H, m, H-3), 3.49, 3.46, 3.06 (each 3H, s, OMe), 2.72 (1H, dt, J=16, 5.5 Hz, H-11), 2.68 (1H, dd, J=11, 5.5 Hz, H-4), 2.41 (1H, dt, J=16, 5.5 Hz, H-11), 2.25 (1H, t, J=11 Hz, H-4). MS: 313 (M^+), 282 (base peak). HRMS: Calcd for $C_{19}H_{23}NO_3$: 313.1679 (M^+). Found: 313.1678. The spectral data (in $CDCl_3$) were identical with those reported.[17]

This product was converted to the picrate, yellow prisms from EtOH, mp 163—164 °C, $[\alpha]_D^{23}$ +143.6° (c=0.14, $CHCl_3$) [lit. mp 162—163 °C, $[\alpha]_D^{23}$ +142° (c=0.40, $CHCl_3$)].[16]

(+)-3-Epierysotrine (24) A solution of AlH_3 [prepared from $LiAlH_4$ (8 mg) and $AlCl_3$ (9 mg)] in dry Et_2O (1 ml) was added to a solution of (−)-**23b** (6 mg) in anhydrous THF (1 ml) at 0 °C. The mixture was stirred at the same temperature for 40 min. The mixture was worked up as described above to give (+)-**24** as a colorless oil, $[\alpha]_D^{23}$ +75° (c=0.145, $CHCl_3$). IR: 1505 cm^{-1}. ^{1}H-NMR (C_6D_6): 6.41, 6.18 (each 1H, s, ArH), 6.51 (1H, d, J=10 Hz, H-1), 5.95 (1H, dd, J=10, 4.5 Hz, H-2), 5.54 (1H, s, H-7), 3.69 (1H, dd, J=6.5, 4.5 Hz, H-3), 3.66, 3.46, 2.86 (each 3H, s, OMe), 2.75 (1H, d, J=14 Hz, H-4), 2.24 (1H, dd, J=14, 6.5 Hz, H-4). MS: 313 (M^+), 282 (base peak). HRMS: Calcd for $C_{19}H_{23}NO_3$: 313.1677 (M^+). Found: 313.1711. The spectral data (in $CDCl_3$) were identical with those reported for a racemic specimen.[5,17]

X-Ray Crystallographic Analyses The reflection data were collected on a Rigaku AFC-5R four-circle diffractometer using graphite-monochromated MoK_α radiation in the $\omega-2\theta$ scan mode at a 2θ scan speed of 4°/min for $3° < 2\theta < 55°$. Of the reflections collected, those above the $3\sigma(I)$ level were used for calculation. The structures of **2b**, **8**, and **12a** were solved by the direct method using MITHRIL[18] and refined by the full-matrix least-squares procedure with anisotropic thermal factors for the non-hydrogen atoms and with isotropic ones for hydrogen atoms. For **12a**, some hydrogen atoms were located at calculated positions. The positional parameters are listed in Tables I, II, and III, respectively.

Crystal Data for **2b**: Triclinic, a=8.450 (1) Å, b=8.6892 (9) Å, c=6.9538 (8) Å, α=99.42 (1)°, β=112.760 (9)°, γ=104.17 (1)°, V=437 (1) Å^3, D_c=1.43 g/cm^3, Z=1. Space group, $p\bar{1}$. Reflections observed, 2187; reflections used for calculation, 1719. R=0.034.

Crystal Data for **8**: Monoclinic, a=6.021 (2) Å, b=10.295 (2) Å, c=16.696 (2) Å, β=93.62 (2)°, V=1032.8 (5) Å^3, D_c=1.43 g/cm^3, Z=2. Space group, $p2_1$. Reflections observed, 2808; reflections used for calculation, 1088. R=0.038.

Crystal Data for **12a**: Orthorhombic, a=14.841 (4) Å, b=14.920 (3) Å, c=11.247 (2) Å, V=2490.4 (9) Å^3, D_c=1.03 g/cm^3, Z=4. Space group, $p2_12_12_1$. Reflections observed, 3312; reflections used for calculation, 1330. R=0.039.

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