General Method for Synthesis of Erythrinan and Homoerythrinan Alkaloids (1): Synthesis of a Cycloerythrinan, as a Key Intermediate to *Erythrina* Alkaloids, by Pummerer-Type Reaction[1)]

Jun TODA,[a] Yoshihiro NIIMURA,[a] Kaoru TAKEDA,[a] Takehiro SANO,*[,a] and Yoshisuke TSUDA[b]

Showa College of Pharmaceutical Sciences,[a] 3–3165 Higashi-tamagawagakuen, Machida, Tokyo 194–8543, Japan and Faculty of Pharmaceutical Sciences,[b] Kanazawa University, 13–1 Takara-machi, Kanazawa 920–0923, Japan.
Received November 19, 1997; accepted January 26, 1998

A new synthetic route to *Erythrina* alkaloids by formation of ring C utilizing a Pummerer-type intramolecular cyclization was developed. The *N*-(2-phenylthioethyl)-dioxopyrroline (3) was converted to 13 in five steps with satisfactory overall yield (69%) by means of [2+2] photocycloaddition followed by 1,3-anionic rearrangement as crucial reactions. Treatment of the sulfoxide (13) with trifluoroacetic anhydride gave the cyclization product, 11-phenylthioerythrinan (15), in 87% yield. This was converted to the cycloerythrinan (22) by reductive elimination of the PhS group, thus constituting a formal total synthesis of (±)-erysotrine.

Key words *Erythrina* alkaloid; (±)-erysotrine; cycloerythrinan; total synthesis; Pummerer reaction; dioxopyrroline

Total synthesis of erythrinan alkaloids has been achieved by several efficient routes,[2–5)] of which routes 1—3 in Chart 1 are representative. However, only route 2 proved to be applicable to the synthesis of homoerythrinan alkaloids.[6)] Here, we wish to present a different approach which constitutes a general method for constructing erythrinan and homoerythrinan skeletons. Cyclization of compound (A) possessing a C2-unit at the nitrogen atom would lead to erythrinans and that of compound (A) possessing a C3-unit would give homoerythrinans. For this purpose, we adopted an electrophilic cyclization reaction (Pummerer reaction)[7)] of the phenyl sulfoxides (A). Since the products (B) of this reaction bear a phenylthio group at the C-11 position, it may be readily convertible by simple chemical modifications into the 11-non-oxygenated or oxygenated congeners.

In this paper, we describe the synthesis of a cycloerythrinan, as a key synthetic intermediate to *Erythrina* alkaloids, by means of the above strategy.

Results and Discussion

For construction of a functionalized hydroindole ring system (A) we adopted the [2+2] photoannulation route,[5a)] since this route is applicable to dioxopyrrolines with bulky *N*-substituents.[4b,6,8)]

N-(2-Phenylthioethyl)dioxopyrroline **3** was synthesized by amination of methyl 3,4-dimethoxybenzoylacetate (**1**) with 2-phenylthioethylamine[9)] followed by condensation of the resulting enamine **2** with oxalyl chloride in 81% overall yield. The [2+2] photocycloaddition of **3** to 2-trimethylsilyloxybutadiene smoothly proceeded at 0 °C in a regio- and stereoselective manner to afford the vinylcyclobutane **4** as a sole product in 79% yield. The stereochemistry of the product **4** was deduced from the

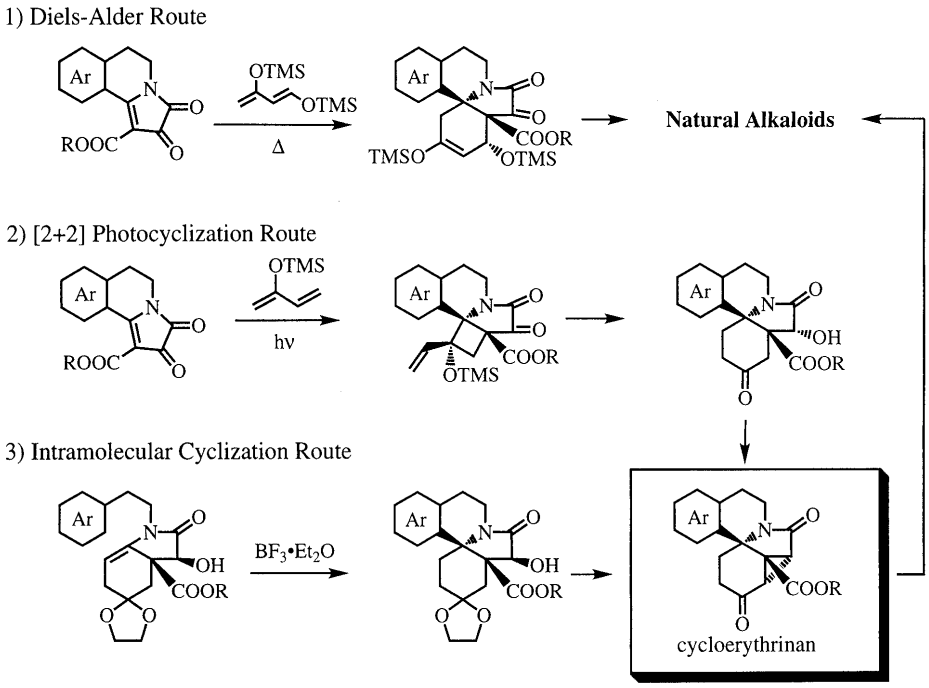
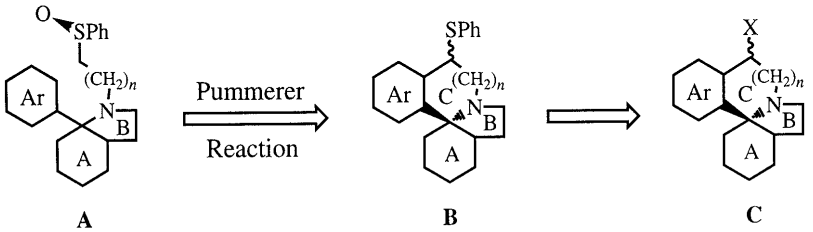
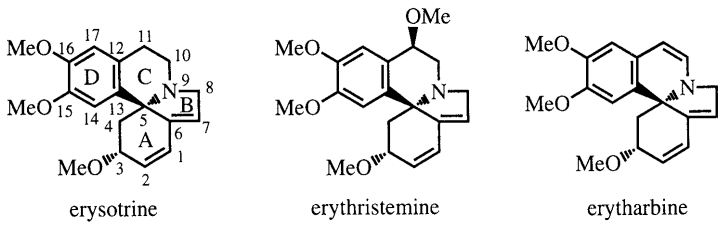


Chart 1

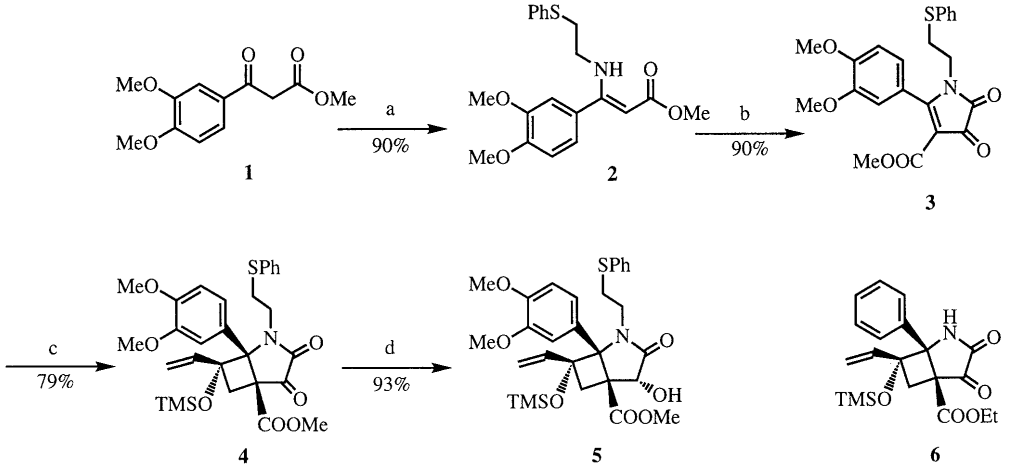
* To whom correspondence should be addressed.





Natural Alkaloids

Chart 2



a) $PhS(CH_2)_2NH_2$-AcOH, Δ b) $(COCl)_2$ c) 2-OTMS-butadiene, hv, 0°C d) $NaBH_4$

Chart 3

spectral analogy with the analogous photoadduct **6**, whose structure has been established by X-ray analysis[10]; the vinyl group being in *exo* and the trimethylsilyloxy group in *endo* configuration.

Heating of **4** in toluene at 150 °C for 8 h caused a 1,3-shift to give the hydroindole **7** as a trimethylsilyl enol ether, which, however, gave the expected acetal **8** in only 6% yield on BF_3-mediated acetalization. The major product was a tricyclic hydroindole **9** (20%). This undesired intramolecular aldol condensation between C-6 active methylene and C-3 ketone has already been noted in erythrinan ring systems.[11] In order to avoid this side reaction, the C-4 ketone in **4** was firstly reduced with $NaBH_4$ (93% yield),[12] then the resulting alcohol **5** was subjected to 1,3-anionic rearrangement.[4b] Treatment of **5** with tetrabutylammonium fluoride (TBAF) in CH_2Cl_2 at −30 °C to room temperature smoothly gave the hydroindole **10** in 99% yield. This was converted to the mesylate **11**, which was then treated with diazabicyclo[5.4.0]undecene (DBU) to yield the cyclohydroindole **12**. However, the yield of **12** was variable (6—60% yield) in different runs. Therefore, the mesylate **11** was converted to the sulfoxide **13**, a substrate of the Pummerer reaction, by oxidation with $NaIO_4$ in 99% yield. In contrast, oxidation of **11** with metachloroperbenzoic acid (*m*-CPBA) gave the sulfone **14**, an over-oxidation product, in a quantitative yield.

The sulfoxide **13**, when treated with trifluoroacetic anhydride (TFAA) in CH_2Cl_2 at room temperature, gave the expected cyclization product, 11α-phenylthioerythrinan **15** (87%) together with a minute amount of the β-phenylthio isomer **16** (1%). The stereochemistry of **15** and **16** was readily clarified from the ^{1}H-NMR signals of their C-11 protons. The product **15** exhibited the signal at δ 4.36 as a double-doublet with large *J* values of 6 and 11 Hz, while the isomer **16** gave the signal at δ 4.23 as a doublet with a small *J* value of 3 Hz (the other coupling constant with an adjacent hydrogen is zero). These patterns are in good agreement with those previously established[13] for 11α-methoxy- and 11β-methoxyerythrinan derivatives

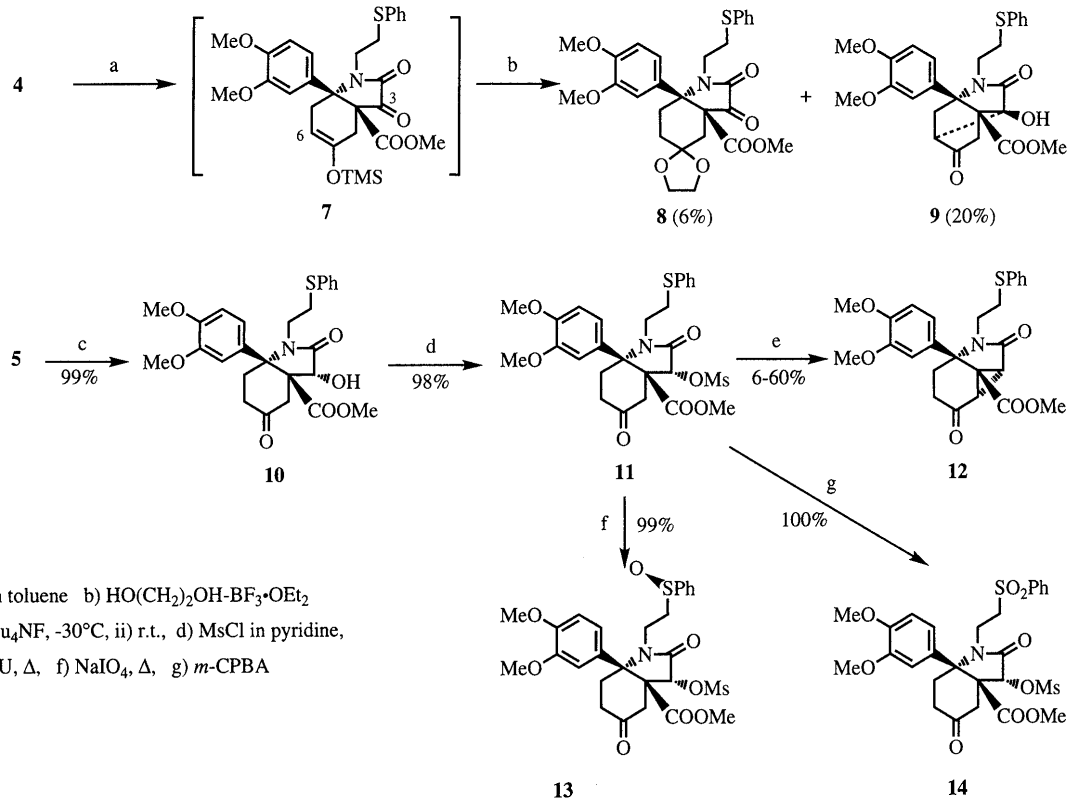


Chart 4

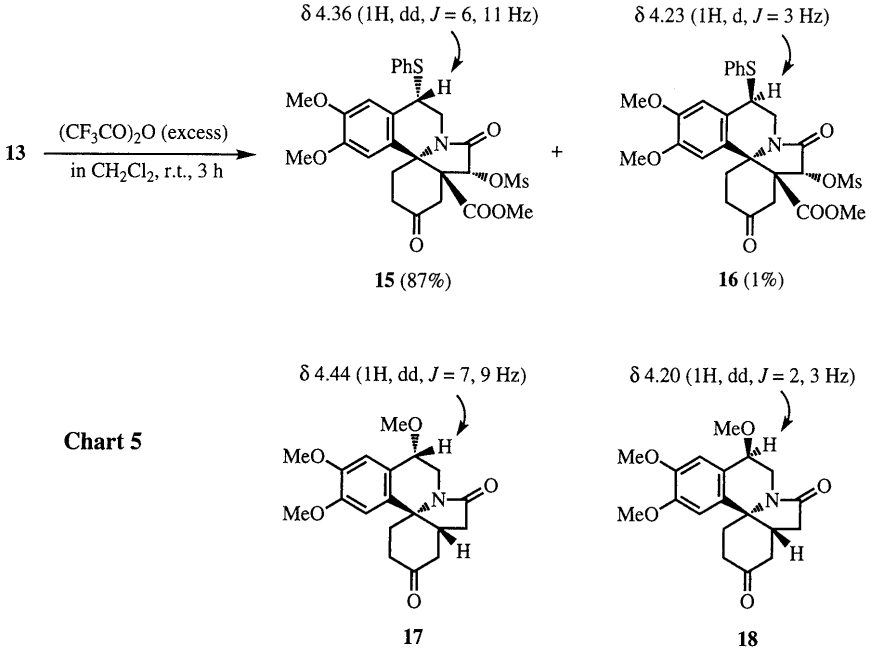


Chart 5

(**17**, **18**), respectively. Thus, assuming that ring C has a half-chair form, the stereochemistry of C_{11}-SPh is equatorial (α) in **15** and axial (β) in **16**.

The high stereoselectivity observed in this C–C bond formation reaction may be rationalized in terms of stereoelectronic control, as depicted in Fig 1. Two transition states are possible for maximum overlap between the orbitals of the nucleophilic aromatic ring and the electrophilic sulfenium cation. The transition state D should lead to **15**, while the transition state E, to **16**. In the transition state E the C_6-COOMe and C_{11}-SPh groups are situated very close together, producing a severe steric interaction, while in the transition state D such a steric repulsion is not present, so that the product **15** is formed almost exclusively.

The conversion of **15** into the cycloerythrinan **22** was achieved as follows. Treatment of **15** with DBU in boiling toluene caused an intramolecular alkylation without

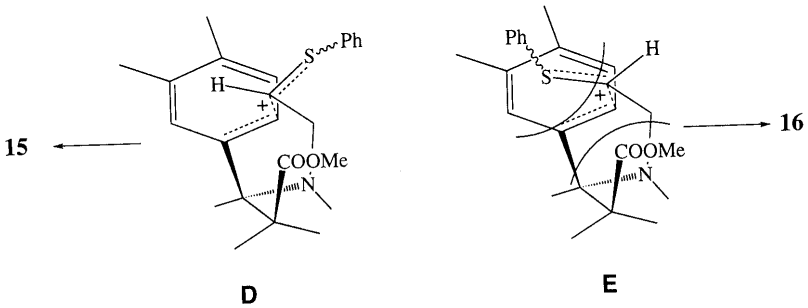
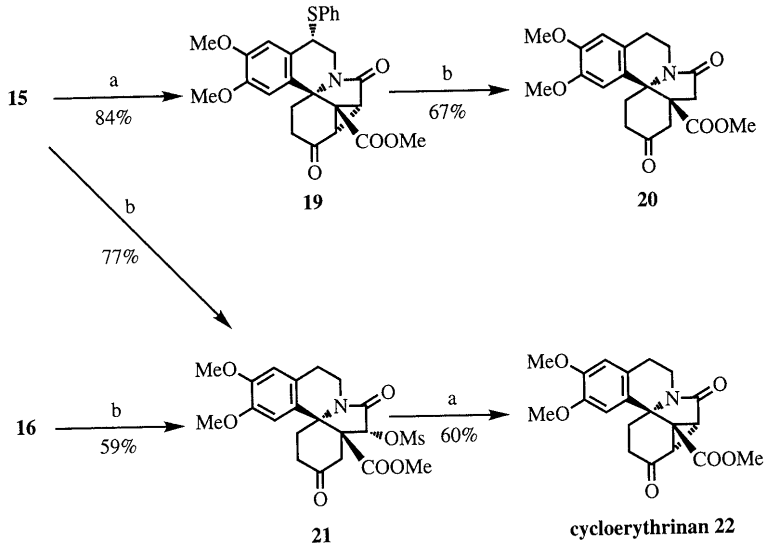


Fig. 1

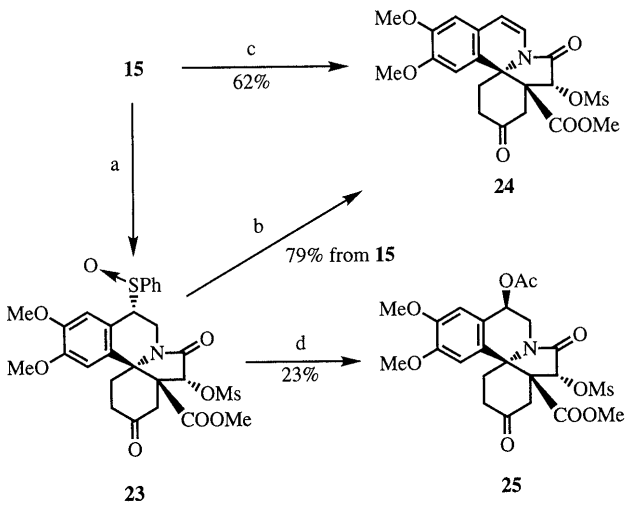


a) DBU in toluene, Δ, b) Bu_3SnH-AIBN in toluene, Δ

Chart 6

change of the SPh group, giving rise to 11α-phenylthiocycloerythrinan **19** in 84% yield. Reductive desulfurization of **19** with Raney Ni, contrary to our expectation, yielded a complex mixture. The reductive elimination of SPh by a radical reaction with tributyltin hydride (TBTH) catalyzed by azobisisobutyronitrile (AIBN) proceeded effectively, however, accompanied with cleavage of the cyclopropane to give the product **20** in 67% yield. Finally, the radical reduction of **15** caused selective elimination of SPh to give the erythrinan **21** in 77% yield, and this was converted with DBU to the cycloerythrinan **22** in 60% yield. The 11β-isomer **16**, on similar radical reduction, gave **21** in 59% yield. The cycloerythrinan **22** was identical with the sample reported by Tsuda *et al.*[14] Since compound **22** has been converted to (±)-erysotrine,[15] the above transformation represents a formal total synthesis of the alkaloid.

Further synthetic usefulness of the C_{11}-SPh group in the intermediates was indicated by the following transformations. Oxidation of **15** with $NaIO_4$ followed by the thermal elimination of the sulfoxide **23** gave the Δ^{10}-erythrinan (erytharbine type) **24** in 79% yield. The same compound **24** was obtained in 62% yield simply by heating **15** in trifluoroacetic acid (TFA)–CH_2Cl_2 at 85 °C for 5 d. On the other hand, when the sulfoxide **23** was treated with a mixed reagent of Ac_2O–TFAA, 11β-



a) $NaIO_4$, r.t., b) Δ, in toluene, c) CF_3COOH, Δ, d) Ac_2O-TFAA

Chart 7

acetoxyerythrinan (erythrinine type) **25** was produced in a low yield (23%), instead of the expected Pummerer rearrangement product, the 11-oxoerythrinan. The stereochemistry of C_{11}-OAc in **25** was proved to be β by the ^{1}H-NMR spectrum (H-11: δ 5.78, t, J=2 Hz), indicating that the acetoxy group had been introduced *via* an *SN2*

reaction. Further manipulations of these products at rings A and B through the 1,2-carbonyl transposition reaction developed by Tsuda *et al.*[15] should lead to ring C functionalized alkaloids such as erytharbine and erythristemine.

In conclusion, the cycloerythrinan **22**, a key intermediate to *Erythrina* alkaloids, was synthesized in 8 steps from the dioxopyrroline **3** in 35% overall yield with high regio- and stereo-control by utilizing sulfoxide-mediated intramolecular electrophilic cyclization as a crucial step. An application of this strategy to the synthesis of homoerythrinan alkaloids will be described in a forthcoming paper.

Experimental

Unless otherwise stated, the following procedure were adopted. Melting points (mp) were determined with Yanaco MP-S1 melting point apparatus and are uncorrected. Infrared (IR) spectra were measured with a JASCO FT/IR-5000 Fourier transform spectrometer using KBr disks and values are given in cm^{-1}. Ultraviolet (UV) spectra were recorded on a Hitachi U-3200 spectrophotometer and values are given in nm (ε). ^{1}H-NMR and ^{13}C-NMR spectra were obtained with a JEOL JNM-EX90 (^{1}H; 90 MHz, ^{13}C; 22.5 MHz), JNM-GX270 (^{1}H; 270 MHz, ^{13}C; 67.5 MHz), or JNM-A500 (^{1}H; 500 MHz, ^{13}C; 125 MHz) instrument in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shifts are given in δ ppm. High-resolution (HR-MS) and low-resolution mass spectra (LR-MS) were obtained with a JEOL JMS-D300 or JMS-HX110A spectrometer at 30 or 70 eV by using a direct inlet system. Photoirradiation was carried out with a 300W high-pressure mercury lamp equipped with a Pyrex filter (>300 nm). All organic extracts were washed with water or brine, and dried over Na_2SO_4 or $MgSO_4$ before concentration. Preparative thin layer chromatography (PTLC) was performed with 20×20 cm precoated Silica gel 60 F_{254} glass plates (0.5 mm thickness/Merck) and spots were detected by irradiation with UV (254 nm) light. Column chromatography and flash chromatography were carried out with Wakogel C-200 (Wako Pure Chemical Industry Ltd.).

Methyl 3,4-Dimethoxybenzoylacetate (1) Na metal (7.4 g, 3 mol eq) was carefully added in several portions to a solution of methyl acetoacetate (37.6 g, 3 mol eq) in ether (200 ml). The mixture was stirred for 1 h at room temperature to give the sodium salt of methyl acetoacetate.

A mixture of veratric acid (20 g), benzene (60 ml), thionyl chloride (27 g, 2 mol eq) and pyridine (2 drops) was heated under reflux for 30 min. The mixture was concentrated, and benzene was added to the residue, then the resulting solution was concentrated. This procedure was repeated in order to remove an excess of thionyl chloride, affording crude veratryl chloride.

A solution of the chloride prepared above in ether (200 ml) was added dropwise to sodium methyl acetoacetate over a period of 30 min at room temperature. The resulting mixture was refluxed for an additional 3 h with stirring. After cooling, the mixture was filtered. The remaining cake was washed with ether, then dissolved in a solution of NH_4Cl (10 g) and 28% NH_4OH (2 ml) in H_2O (30 ml). The solution was heated at 100 °C on a steam bath. After having been cooled to room temperature, the reaction mixture was acidified with 10% HCl, then the whole was extracted with CH_2Cl_2. The organic layer was separated and concentrated *in vacuo* to give a crude product, which was purified by column chromatography (hexane : AcOEt = 1 : 2) followed by crystallizations from ether–AcOEt to afford methyl 3,4-dimethoxybenzoylacetate (**1**) (22.5 g, 86%) as pale yellow needles from ether–AcOEt, mp 51.5—53 °C. IR: 1676, 1744. UV: 276 (27800), 307 (23700). ^{1}H-NMR: 3.75, 3.93, 3.96 (each 3H, s, OMe), 3.97 (2H, s, $-CH_2-$), 6.9—7.6 (3H, m, ArH). ^{13}C-NMR: 45.2 (t), 52,2 (q), 55.8 (q), 55.9 (q), 110.0 (d), 110.2 (d), 123.4 (d), 129.0 (d), 149.1 (s), 153.7 (s), 167.9 (s), 190.7 (s). *Anal.* Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.29; H, 5.90. LR-MS *m/z*: 238 (M^+), 165 (base peak).

2-Phenylthioethylamine[11] Thiophenol (11 g) was added to a solution of KOH (12.9 g, 2.3 mol eq) in EtOH (200 ml) at room temperature under an argon atmosphere. The mixture was stirred for an additional 10 min to afford sodium thiophenolate. A solution of 2-bromoethylamine hydrobromide (20.5 g, 1 mol eq) in EtOH (100 ml) was added dropwise to the solution of PhSK over a period of 5 min, then the whole was heated under reflux for 1.5 h with stirring. After cooling, the precipitate was filtered off and the filtrate was concentrated to dryness. The residue was dissolved in benzene, then washed with water. After removal of the solvent, the residue was purified by chromatography (CH_2Cl_2) to give 2-phenylthioethylamine (13.5 g, 88%) as a pale yellow oil, bp 103—105 °C (3 mmHg). IR: 3346. ^{1}H-NMR: 2.8—3.1 (4H, m, $-CH_2-$), 7.2—7.4 (5H, m, SPh). LR-MS *m/z*: 153 (M^+), 124 (base peak).

Enamine (2) A solution of **1** (4.4 g), 2-phenylthioethylamine (5.7 g, 2 mol eq) and acetic acid (2.2 g, 2 mol eq) in MeOH (70 ml) was refluxed for 27 h with stirring. After concentration of the mixture *in vacuo*, the residue was chromatographed over SiO_2 (hexane : AcOEt = 6 : 1) to give methyl (*Z*)-3-(2-phenylthioethylamino)-3,4-dimethoxycinnamate (**2**) (6.18 g, 90%) as pale yellow needles from ether–hexane, mp 48—50 °C. IR: 1719, 2948. UV: 257 (13700), 296 (17600). ^{1}H-NMR: 2.8—3.4, 3.2—3.4 (each 2H, m, $-CH_2-$), 3.69, 3.83, 3.91 (each 3H, s, OMe), 4.66 (1H, s, $=CH-$), 6.8—6.9 (3H, m, ArH), 7.17 (5H, s, SPh), 8.67 (1H, br s, NH). ^{13}C-NMR: 35.4 (t), 43.4 (t), 50.1 (q), 55.7 (q), 55.8 (q), 85.9 (d), 110.8 (d), 110.9 (d), 120.4 (d), 126.1 (d), 128.0 (s), 128.7 (d×2), 129.4 (d×2), 134.8 (s), 148.7 (s), 149.8 (s), 164.0 (s), 170.3 (s). *Anal.* Calcd for $C_{20}H_{23}NO_4S$: C, 64.32; H, 6.21; N, 3.75. Found: C, 64.10; H, 6.23; N, 3.73. LR-MS *m/z*: 373 (M^+), 237 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{20}H_{23}NO_4S$: 373.1383. Found: 373.1348.

Synthesis of the Dioxopyrroline 3 A solution of oxalyl chloride (3.4 g, 1 mol eq) in dry ether (59 ml) was added dropwise to a solution of **2** (10 g) in dry ether (150 ml) at 0 °C over a period of 30 min. After addition of dioxane (100 ml) to the mixture, ether was removed by distillation at 80 °C. The reaction mixture was crystallized by addition of dry benzene to give 5-(3,4-dimethoxyphenyl)-4-methoxycarbonyl-2,3-dioxo-1-(2-phenylthioethyl)-2,3-dihydro-1*H*-pyrrole (**3**) (10.3 g, 90%) as yellow plates from benzene–ether, mp 132—135 °C. IR: 1684, 1748, 1767. UV: 253 (16400), 378 (4100). ^{1}H-NMR: 2.92 (2H, dd, J=6, 8 Hz, $-CH_2-$), 3.1—3.4, 3.9—4.0 (each 1H, m, $-CH_2-$), 3.70, 3.85, 3.97 (each 3H, s, OMe), 6.9—7.4 (8H, m, ArH, SPh). ^{13}C-NMR: 31.5 (t), 41.1 (t), 51.6 (q), 56.1 (q), 56.2 (q), 103.8 (s), 110.9 (d), 111.2 (d), 118.9 (d), 122.0 (s), 126.8 (d), 129.0 (d×2), 129.5 (d×2), 134.0 (s), 149.1 (s), 152.4 (s), 158.2 (s), 161.4 (s), 177.4 (s), 178.0 (s). LR-MS *m/z*: 427 (M^+), 124 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{22}H_{21}NO_6S$: 427.1087. Found: 427.1069. *Anal.* Calcd for $C_{22}H_{21}NO_6S$: C, 61.82; H, 4.95; N, 3.28. Found: C, 62.00; H, 4.98; N, 3.32.

Photocycloaddition of 3 with 2-Trimethylsilyloxy-1,3-butadiene A solution of **3** (5 g) and 2-trimethylsilyloxy-1,3-butadiene (2 g, 2 mol eq) in 1,2-dimethoxyethane (DME) (400 ml) was irradiated at 0 °C for 3 h with stirring. After removal of the solvent, the residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 2) to give *dl*-(1*R**, 5*S**,7*R**)-1-(3,4-dimethoxyphenyl)-5-methoxycarbonyl-3,4-dioxo-2-(2-phenylthioethyl)-7-trimethylsilyloxy-7-vinyl-2-azabicyclo[3.2.0]heptane (**4**) (5.242 g, 79%) as pale yellow prisms from ether–hexane, mp 123—129 °C. IR: 1717, 1744, 1771. UV: 245 (12600), 279 (6100). ^{1}H-NMR: 0.11 (9H, s, OTMS), 2.37, 3.21 (each 1H, d, J=13 Hz, $-CH_2-$), 2.9—4.0 (4H, m, $-CH_2-$), 3.55, 3.74, 3.88 (each 3H, s, OMe), 5.41 (1H, dd, J=1, 10 Hz, vinyl), 5.48 (1H, dd, J=1, 17 Hz, vinyl), 6.27 (1H, dd, J=10, 17 Hz, vinyl), 6.7—7.6 (8H, m, ArH, SPh). ^{13}C-NMR: 1.7 (q×3), 29.0 (t), 35.2 (t), 44.9 (t), 52.8 (q), 55.1 (s), 55.7 (q), 55.8 (q), 75.2 (s), 80.7 (s), 110.6 (d), 111.7 (d), 115.7 (t), 121.5 (d), 124.7 (s), 126.1 (d), 128.8 (d×2), 129.0 (d×2), 134.5 (s), 139.9 (s), 148.5 (s), 149.2 (s), 161.1 (s), 166.6 (s), 193.4 (s). LR-MS *m/z*: 569 (M^+), 276 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{29}H_{35}NO_7SSi$: 569.1903. Found: 569.1904.

Thermal [1,3] Rearrangement of 4 A solution of **4** (200 mg) in toluene (15 ml) was heated in a sealed tube at 150 °C under stirring for 8 h. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (10 ml) and stirred with ethylene glycol (5 ml) and BF_3–Et_2O (200 mg, 5 mol eq) at room temperature for 5 h. The mixture was neutralized with saturated $NaHCO_3$, and extracted with CH_2Cl_2, and the extract was evaporated *in vacuo*. The product was purified by flash chromatography over Al_2O_3 (AcOEt) and chromatography over SiO_2 (benzene : acetone = 10 : 1) to afford *dl*-(3a*R**,7a*S**)-7a-(3,4-dimethoxyphenyl)-5,5-ethylenedioxy-3a-methoxycarbonyl-2,3-dioxo-1-(2-phenylthioethyl)-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indole (**8**) (11 mg, 6%) and *dl*-(1*R**,4*S**,6*R**,9*R**)-4-(3,4-dimethoxyphenyl)-1-hydroxy-9-methoxycarbonyl-2,7-dioxo-3-(2-phenylthioethyl)-3-azatricyclo[4.3.0.0^{4,9}]nonane (**9**) (35 mg, 20%).

8: Colorless gum. IR: 1715, 1775. UV: 243 (13600). ^{1}H-NMR: 1.8—4.0 (12H, m, $-CH_2-$), 2.39, 2.56 (each 1H, d, J=14 Hz, $-CH_2-$), 3.08, 3.82, 3.89 (each 3H, s, OMe), 6.6—6.8 (3 H, m, ArH), 7.2—7.4 (5H, m, SPh).

^{13}C-NMR: 27.3 (t), 29.0 (t), 30.9 (t), 37.7 (t), 43.2 (t), 52.4 (q), 55.9 (s), 56.1 (q), 59.6 (s), 64.0 (t), 64.6 (t), 66.6 (s), 106.0 (s), 110.5 (d), 110.6 (d), 120.0 (t), 126.2 (d), 128.5 (d × 2), 129.1 (d × 2), 130.7 (s), 134.6 (s), 148.6 (s), 149.3 (s), 160.8 (s), 168.1 (s), 195.3 (s). LR-MS *m/z*: 541 (M^+), 405 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{28}H_{31}NO_8S$: 541.1768. Found: 541.1746.

9: Colorless gum. IR: 1710, 1725, 1767. UV: 240 (13600), 280 (4200). ^{1}H-NMR: 2.2—4.2 (9H, m, –CH_2–), 3.74, 3.80, 3.93 (each 3H, s, OMe), 6.7—7.2 (8H, m, ArH, SPh). ^{13}C-NMR: 31.0 (t), 34.9 (t), 35.2 (t), 40.9 (t), 52.5 (q), 53.1 (d), 55.9 (q), 56.0 (s), 67.7 (s), 72.7 (s), 87.4 (s), 110.8 (d), 111.1 (d), 120.9 (d), 123.2 (s), 126.1 (d), 128.7 (d × 2), 128.9 (d × 2), 134.7 (s), 149.3 (s), 150.3 (s), 169.3 (s), 173.2 (s), 206.8 (s). LR-MS *m/z*: 497 (M^+), 361 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{26}H_{27}NO_7S$: 497.1506. Found: 497.1490.

$NaBH_4$ Reduction of 4 $NaBH_4$ (239 mg, 3 mol eq) was slowly added to a solution of **4** (1.2 g) in MeOH (20 ml) at −30 °C under stirring. The mixture was treated at the same temperature for 15 min and then at room temperature for an additional 5 min. After decomposition of excess hydride by addition of H_2O, the mixture was extracted with CH_2Cl_2. After removal of the solvent from the organic layer, the residue was purified by chromatography (hexane : AcOEt = 1 : 1) and crystallizations from ether–hexane–CH_2Cl_2 to afford *dl*-(1*R**,4*R**,5*S**,7*R**)-1-(3,4-dimethoxy)phenyl-4-hydroxy-5-methoxycarbonyl-3-oxo-2-(2-phenylthio)ethyl-7-trimethylsilyloxy-7-vinyl-2-azabicyclo[3.2.0]heptane (**5**) (1.119 g, 93%), mp 60—65 °C, as colorless prisms. IR: 1682, 1731. UV: 241 (12300), 278 (4000). ^{1}H-NMR: 0.16 (9H, s, OTMS), 2.7—4.2 (6H, m, –CH_2–), 3.68, 3.72, 3.86 (each 3H, s, OMe), 5.24 (1H, br s, C<u>H</u>–OH), 5.29 (1H, dd, *J* = 2, 11 Hz, vinyl), 5.35 (1H, dd, *J* = 2, 17 Hz, vinyl), 6.61 (1H, dd, *J* = 11, 17 Hz, vinyl), 6.7—7.2 (8H, m, ArH, SPh). ^{13}C-NMR: 1.7 (q × 3), 29.2 (t), 35.8 (t), 43.5 (t), 52.8 (q), 53.3 (s), 55.7 (q × 2), 73.1 (d), 76.4 (s), 80.0 (s), 110.6 (d), 112.1 (d), 112.1 (t), 121.3 (d), 125.9 (d), 128.4 (s), 128.7 (d × 2), 128.9 (d × 2), 135.0 (s), 142.2 (s), 148.4 (s), 148.8 (s), 171.6 (s), 172.3 (s). LR-MS *m/z*: 571 (M^+), 397 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{29}H_{37}NO_7SSi$: 571.2060. Found: 571.2062.

[1,3] Rearrangement of 5 with TBAF A 1.0 M tetrahydrofuran (THF) solution of TBAF (1051 μl, 1.2 mol eq) was injected at −30 °C into a solution of **5** (500 mg) in THF (20 ml) under an argon atmosphere. The mixture was stirred for 20 min, and then heated under reflux for 1.5 h. The mixture was extracted with CH_2Cl_2, and the extract was washed with brine and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane : AcOEt = 2 : 3) to afford *dl*-(3*R**,3a*S**,7a*R**)-7a-(3,4-dimethoxyphenyl)-3-hydroxy-3a-methoxycarbonyl-2,5-dioxo-1-(2-phenylthioethyl)-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indole (**10**) (432 mg, 99%) as a colorless gum. IR: 1702, 1718, 1726. UV: 239 (11900), 278 (3900). ^{1}H-NMR: 2.2—3.9 (8H, m, –CH_2–), 2.78 (2H, d, *J* = 2 Hz, –CH_2–), 3.34, 3.84, 3.88 (each 3H, s, OMe), 5.14 (1H, br s, C<u>H</u>–OH), 6.6—6.9 (3H, m, ArH), 7.2—7.3 (5H, m, SPh). ^{13}C-NMR: 29.8 (t), 30.2 (t), 35.5 (t), 39.5 (t), 41.9 (t), 52.6 (q), 55.8 (q), 56.1 (q), 59.7 (s), 67.4 (s), 71.1 (d), 110.2 (d), 110.8 (d), 119.4 (d), 126.3 (d), 128.7 (d × 2), 129.0 (d × 2), 135.0 (s), 134.6 (s), 148.9 (s), 149.4 (s), 170.9 (s), 174.5 (s), 206.9 (s). LR-MS *m/z*: 499 (M^+), 363 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{26}H_{29}NO_7S$: 499.1662. Found: 499.1655.

Methanesulfonylation of 10 A mixture of **10** (795 mg) and methanesulfonyl chloride (MsCl) (1.46 g, 8 mol eq) in pyridine (30 ml) was stirred at room temperature for 1.5 h. The mixture was extracted with CH_2Cl_2, and the extract was washed with H_2O, 5% HCl, and brine, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 1) to afford *dl*-(3*R**,3a*S**,7a*R**)-7a-(3,4-dimethoxyphenyl)-3-methanesulfonyloxy-3a-methoxycarbonyl-2,5-dioxo-1-(2-phenylthioethyl)-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indole (**11**) (900 mg, 98%) as a brown gum. IR: 1702, 1718, 1726. UV: 239 (11900), 278 (3900). ^{1}H-NMR: 2.4—3.3 (8H, m, –CH_2–), 2.64, 2.94 (each 2H, d *J* = 15 Hz, –CH_2–), 3.35 (6H, s, OMe, OMs), 3.85, 3.89 (each 3H, s, OMe), 6.04 (1H, s, C<u>H</u>–OMs), 6.6—6.9 (3H, m, ArH), 7.25 (5H, s, SPh). ^{13}C-NMR: 29.5 (t), 30.1 (t), 35.2 (t), 39.9 (q), 40.0 (t), 42.2 (t), 52.9 (q), 55.8 (q), 56.1 (q), 58.5 (s), 67.5 (s), 77.5 (d), 110.0 (d), 111.8 (d), 119.2 (t), 126.4 (d), 128.8 (d × 2), 129.0 (d × 2), 129.6 (s), 134.4 (s), 149.0 (s), 149.6 (s), 169.0 (s), 169.5 (s), 205.0 (s). LR-MS *m/z* : 577 (M^+), 441 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{27}H_{31}NO_9S_2$: 577.1438. Found: 577.1437.

Treatment of 11 with DBU A solution of **11** (100 mg) and DBU (264 mg, 10 mol eq) in toluene (5 ml) was heated at 100 °C for 5 h in a sealed tube under stirring. The mixture was extracted with CH_2Cl_2, and the extract was washed with 5% HCl, and evaporated *in vacuo*. The residue was chromatographed over SiO_2 (AcOEt) to afford *dl*-(1*R**,2*S**,6*S**,9*R**)-6-(3,4-dimethoxyphenyl)-1-ethoxycarbonyl-3,8-dioxo-7-(2-phenylthioethyl)-7-azatricyclo[4.3.0.0^{2,9}]nonane (**12**) (50 mg, 60%) as a yellow gum. IR: 1688, 1702, 1736. UV: 240 (13000), 281 (4000). ^{1}H-NMR: 2.2—3.9 (8H, m, –CH_2–), 2.27, 3.17 (each 1H, d, *J* = 10 Hz, H-2, 9), 3.36, 3.87, 3.93 (each 3H, s, OMe), 6.8—7.3 (8 H, m, ArH, SPh). ^{13}C-NMR: 29.6 (t), 29.7 (t), 33.6 (d), 33.9 (d), 34.9 (t), 40.7 (t), 44.5 (s), 52.6 (q), 56.1 (q), 56.3 (q), 63.9 (s), 109.8 (d), 111.3 (d), 119.5 (d), 126.1 (d), 128.3 (d × 2), 129.1 (d × 2), 131.6 (s), 135.0 (s), 149.7 (s × 2), 167.5 (s), 168.7 (s), 200.6 (s). LR-MS *m/z*: 481 (M^+), 345 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{26}H_{27}NO_6S$: 481.1557. Found: 481.1509.

***m*-CPBA Oxidation of 11** A solution of **11** (300 mg) and *m*-CPBA (180 mg, 2 mol eq) in CH_2Cl_2 (50 ml) was stirred for 30 min at room temperature. The reaction mixture was washed with 5% $NaHSO_3$, 5% $NaHCO_3$, and then brine. After removal of the solvent, the residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 2) to afford *dl*-(3*R**,3a*S**,7a*R**)-7a-(3,4-dimethoxyphenyl)-3-methanesulfonyloxy-3a-methoxycarbonyl-2,5-dioxo-1-(2-phenylsulfonylethyl)-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indole (**14**) (372 mg, 100%) as a colorless gum. IR: 1309, 1734. UV: 239 (9100), 281 (3400). ^{1}H-NMR: 2.3—3.6 (10H, m, –CH_2–), 3.28, 3.34, 3.85, 3.90 (each 3H, s, OMe, OMs), 6.00 (1H, s, C<u>H</u>–OMs), 6.5—6.9 (3 H, m, ArH), 7.6—7.9 (5H, m, SPh). ^{13}C-NMR: 29.5 (t), 35.5 (t), 36.2 (t), 40.1 (t), 40.1 (q), 53.0 (t), 53.3 (q), 56.1 (q), 56.4 (q), 58.8 (s), 68.2 (s), 77.3 (d), 110.1 (d), 111.5 (d), 119.3 (t), 128.1 (d × 2), 129.3 (s), 129.8 (d × 2), 134.5 (s), 138.7 (s), 149.5 (s), 150.0 (s), 169.4 (s), 170.0 (s), 205.3 (s). LR-MS *m/z*: 609 (M^+, base peak). HR-MS *m/z* (M^+): Calcd for $C_{27}H_{31}NO_{11}S_2$: 609.1339. Found: 609.1370.

$NaIO_4$ Oxidation of 11 A solution of $NaIO_4$ (861 mg, 1.5 mol eq) in H_2O (10 ml) was added in one portion to a solution of **11** (1.547 g) in MeOH (50 ml)–CH_2Cl_2 (5 ml) at 0 °C under stirring. After refluxing of the mixture for 2.5 h, it was extracted with CH_2Cl_2 and the extract was concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 1) to afford *dl*-(3*R**,3a*S**,7a*R**)-7a-(3,4-dimethoxyphenyl)-3-methanesulfonyloxy-3a-methoxycarbonyl-2,5-dioxo-1-(2-phenylsulfinylethyl)-2,3,3a,4,5,6,7,7a-octahydro-1*H*-indole (**13**) (1.571 g, 99%) as a colorless gum. IR: 1100, 1734. UV: 240 (13600), 279 (4100). ^{1}H-NMR: 2.3—3.9 (total 10H, m, –CH_2–), 3.30, 3.35, 3.80, 3.87, 3.90 (total 12H, s, OMe, OMs), 6.00, 6.03 (total 1H, s, C<u>H</u>–OMs), 6.5—6.9 (total 3H, m, ArH), 7.52, 7.55 (total 5H, s, SPh). ^{13}C-NMR: 29.5 , 29.6 (t), 35.7 (t), 36.6 (t), 40.2 (q), 52.6 (t), 53.3 (q), 53.7 (t), 56.2 (q), 56.4, 56.4 (q), 58.9 (s), 68.3, 68.3 (s), 77.5, 77.6 (d), 110.2, 110.2 (d), 111.4 (d), 119.3, 119.4 (t), 124.0 (d × 2), 129.5 (s), 129.6, 129.7 (d × 2), 131.5, 131.6 (d), 142.5, 142.9 (s), 149.5, 149.6 (s), 149.9, 150.1 (s), 169.7 (s), 170.0 (s), 205.3 , 205.4 (s). LR-MS *m/z*: 593 (M^+), 312 (base peak).

Intramolecular Pummerer Reaction of 13 A solution of **13** (1.034 g) and TFAA (5 ml, large excess) in CH_2Cl_2 (10 ml) was stirred at room temperature for 3 h. After removal of the solvent *in vacuo*, the residue was chromatographed over SiO_2 (benzene : acetone = 3 : 1) to afford *dl*-(5*R**,6*S**,7*R**,11*S**)-7-methanesulfonyloxy-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxo-11-phenylthioerythrinan (**15**) (847 mg, 87%) and *dl*-(5*R**,6*S**,7*R**,11*R**)-7-methanesulfonyloxy-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxo-11-phenylthioerythrinan (**16**) (19 mg, 1%).

15: Colorless prisms from ether–AcOEt, mp 224—226 °C. IR: 1711, 1723, 1746. UV: 283 (4800). ^{1}H-NMR (500 MHz): 2.2—2.4 (4H, m, –CH_2–), 2.94, 3.22 (each 1H, d, *J* = 18 Hz, –CH_2–), 3.16 (1H, dd, *J* = 11, 13 Hz, –CH_2–), 3.17, 3.18, 3.88, 3.91 (each 3H, s, OMe, OMs), 4.36 (1H, dd, *J* = 6, 11 Hz, C<u>H</u>–SPh), 4.58 (1H, dd, *J* = 6, 13 Hz, –CH_2–), 6.54 (1H, s, C<u>H</u>–OMs), 7.32 (1H, s, ArH), 7.3—7.5 (6H, m, ArH, SPh). ^{13}C-NMR: 33.2 (t), 34.6 (t), 39.0 (q), 40.9 (t), 41.7 (t), 43.9 (d), 52.9 (q), 54.9 (s), 56.0 (q), 56.1 (q), 66.2 (s), 78.9 (d), 108.4 (d), 111.2 (d), 126.7 (s), 128.2 (d), 129.4 (d × 2), 129.9 (s), 132.2 (s), 132.3 (d × 2), 148.1 (s), 148.6 (s), 165.6 (s), 170.1 (s), 205.6 (s). LR-MS *m/z*: 575 (M^+), 370 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{27}H_{29}NO_9S_2$: 575.1330. Found: 575.1307. *Anal.* Calcd for $C_{27}H_{29}NO_9S_2$: C, 56.34; H, 5.08; N, 2.43. Found: C, 56.04; H, 5.09; N, 2.34.

16: Colorless gum. IR: 1723, 1781. UV: 244 (11500), 283 (4400). ^{1}H-NMR (500 MHz): 2.2—2.4 (4H, m, –CH_2–), 3.01, 3.27 (each 1H, d, *J* = 18 Hz, –CH_2–), 3.25, 3.26, 3.89, 3.91 (each 3H, s, OMe, OMs), 3.33 (1H, dd, *J* = 3, 14 Hz, –CH_2–), 4.23 (1H, d, *J* = 3 Hz, C<u>H</u>–SPh), 4.48 (1H, d, *J* = 14 Hz, –CH_2–), 5.55 (1H, s, C<u>H</u>–OMs), 6.53, 6.85 (each 1H, s, ArH), 7.4—7.8 (5H, m, SPh). ^{13}C-NMR: 33.4 (t), 34.6 (t), 39.1 (q), 39.3 (t), 41.3 (t), 48.9 (d), 52.9 (q), 54.3 (s), 56.1 (q × 2), 66.1 (s), 78.9 (d), 108.2 (d), 112.9 (d), 125.1 (s), 128.8 (d), 129.4 (d × 2), 129.8 (s), 133.9 (s), 134.7 (d × 2), 148.7 (s × 2), 166.9 (s), 170.2 (s), 205.9 (s).

Treatment of 15 with DBU A solution of **15** (50 mg) and DBU (66 mg, 5 mol eq) in toluene (20 ml) was heated under reflux for 3.5 h under an argon atmosphere. After cooling, the mixture was extracted with CH_2Cl_2, and the extract was washed with 5% HCl, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 8) to afford *dl*-(1*R**,5*S**,6*S**,7*S**,11*R**)-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxo-11-phenylthio-1,7-cycloerythrinan (**19**) (35 mg, 84%) as a colorless gum. IR: 1711, 1734. UV: 284 (4400). ^{1}H-NMR: 2.0—3.0 (5H, m, $-CH_2-$), 2.39 (1H, br d, J = 10 Hz, H-1 or 7), 2.69 (1H, d, J = 10 Hz, H-7 or 1), 3.50, 3.88, 3.92 (each 3H, s, OMe), 4.4—4.6 (2H, m, $-CH_2-$), 6.81 (1H, s, ArH), 7.2—7.5 (6H, m, ArH, SPh). ^{13}C-NMR: 33.4 (d), 34.7 (d), 35.1 (t), 36.3 (t), 41.1 (t), 44.5 (s), 46.2 (d), 53.1 (q), 56.2 (q × 2), 62.1 (s), 108.2 (d), 112.3 (d), 127.0 (s), 128.2 (d), 128.6 (s), 129.5 (d × 2), 132.3 (q × 2), 132.9 (s), 148.4 (s), 148.8 (s), 166.9 (s), 167.8 (s), 200.5 (s). LR-MS m/z : 479 (M^+), 370 (base peak). HR-MS m/z (M^+): Calcd for $C_{26}H_{25}NO_6S$: 479.1400. Found: 479.1400.

Desulfurization of 19 with TBTH A solution of TBTH (337 μl, 3.0 mol eq) and AIBN (14 mg, 0.2 mol eq) in toluene (5 ml) was injected into a stirred solution of **19** (200 mg) in toluene (6 ml) over a period of 30 min at 90 °C under an argon atmosphere. The mixture was further heated for 1.5 h. After removal of the solvent, the residue was chromatographed over SiO_2 (hexane : CH_2Cl_2 = 10 : 1 and hexane : AcOEt = 1 : 1) to afford *dl*-(5*R**,6*R**)-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxoerythrinan (**20**) (105 mg, 67%) as a colorless gum. IR: 1688, 1723. UV: 286 (2900). ^{1}H-NMR: 2.2—4.4 (12H, m, $-CH_2-$), 3.11 (3H, s, OMe), 3.86 (6H, s, OMe), 6.59 (2H, s, ArH). ^{13}C-NMR: 28.5 (t), 34.7 (t), 35.2 (t), 35.6 (t), 42.1 (t), 45.3 (t), 50.9 (s), 52.2 (q), 56.1 (q), 56.4 (q), 66.2 (s), 109.0 (d), 111.7 (d), 127.4 (s), 129.9 (s), 147.6 (s), 148.4 (s), 170.8 (s), 172.8 (s), 208.9 (s). LR-MS m/z: 373 (M^+, base peak). HR-MS m/z (M^+): Calcd for $C_{20}H_{23}NO_6$: 373.1522. Found: 373.1512.

Desulfurization of 15 with TBTH A solution of TBTH (140 μl, 3.0 mol eq) and AIBN (6 mg, 0.2 mol eq) in toluene (10 ml) was injected into a stirred solution of **15** (100 mg) in toluene (3 ml) over a period of 30 min at 90 °C under an argon atmosphere and the mixture was further heated for 3.5 h. The product was chromatographed over SiO_2 (hexane : AcOEt = 1 : 1) to give *dl*-(5*R**,6*S**,7*R**)-7-methanesulfonyloxy-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxoerythrinan (**21**) (62 mg, 77%) as colorless prisms from hexane–CH_2Cl_2, mp 260—264 °C. IR: 1711, 1721. UV: 212 (15700), 285 (3700). ^{1}H-NMR: 2.3—4.4 (10H, m, $-CH_2-$), 3.16, 3.21 (each 3H, s, OMe, OMs), 3.86 (6H, s, OMe), 5.31 (1H, s, ArH), 6.56, 6.58 (each 1H, s, ArH). ^{13}C-NMR: 28.6 (t), 34.0 (t), 34.9 (t), 36.5 (t), 39.2 (q), 41.0 (t), 45.3 (t), 52.9 (q), 54.9 (s), 56.1 (q), 56.4 (q), 66.4 (s), 79.3 (d), 109.3 (d), 111.8 (d), 126.8 (s), 128.8 (s), 147.8 (s), 148.7 (s), 166.2 (s), 170.4 (s), 206.1 (s). LR-MS m/z: 467 (M^+), 316 (base peak). HR-MS m/z (M^+): Calcd for $C_{21}H_{25}NO_9S$: 467.1247. Found: 467.1219. *Anal.* Calcd for $C_{21}H_{25}O_9S$: C, 53.96; H, 5.39; N, 3.00. Found: C, 53.82; H, 5.50; N, 2.98.

Desulfurization of 16 with TBTH A solution of TBTH (77 μl, 3.0 mol eq) and AIBN (3 mg, 0.2 mol eq) in toluene (10 ml) was injected into a stirred solution of **16** (50 mg) in toluene (3 ml) over a period of 30 min at 90 °C under an argon atmosphere, and the mixture was further heated for 8 h. The product was chromatographed over SiO_2 (hexane : AcOEt = 1 : 1) to afford **21** (24 mg, 59%).

Conversion of 21 into the Cycloerythrinan 22 A solution of **21** (50 mg) and DBU (82 mg, 5 mol eq) in toluene (20 ml) was heated at 110 °C for 6.5 h under an argon atmosphere, and the mixture was further heated at 120 °C for 2.5 h. After cooling, the mixture was extracted with CH_2Cl_2, and the extract was washed with 5% HCl, then concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane : AcOEt = 1 : 2) to afford *dl*-(1*R**,5*S**,6*S**,7*S**)-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxo-1, 7-cycloerythrinan (**22**) (23 mg, 60%) as a colorless gum.[14]

Introduction of a Double Bond into Ring C of Erythrinan 1) A solution of $NaIO_4$ (186 mg, 5 mol eq) in H_2O (2 ml) was added to a solution of **15** (100 mg) in MeOH (5 ml)–CH_2Cl_2 (2 ml) at room temperature and the mixture was stirred for 30 h and extracted with CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo* at low temperature to give the crude sulfoxide **23**. This was dissolved in toluene (10 ml) and heated at 100 °C for 8 h under an argon atmosphere. After removal of the solvent *in vacuo*, the residue was chromatographed over SiO_2 (hexane : AcOEt = 2 : 1) to give *dl*-(5*R**,6*S**,7*R**)-7-methanesulfonyloxy-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxo-Δ^{10}-erythrinan (**24**) (64 mg, 79%) as a colorless gum. IR: 1719. UV: 238 (12800), 250 (12900). ^{1}H-NMR: 2.33 (4H, br s, $-CH_2-$), 3.06, 3.47 (each 1H, d, J = 18 Hz, $-CH_2-$), 3.26, 3.47, 3.86, 3.89 (each 3H, s, OMe, OMs), 5.24 (1H, s, C<u>H</u>–OMs), 6.09, 6.87 (each 1H, d, J = 8 Hz, $-C\underline{H}=C\underline{H}-$), 6.66, 6.68 (each 1H, s, ArH). ^{13}C-NMR: 34.1 (t), 34.9 (t), 39.3 (q), 41.2 (t), 53.6 (q), 54.9 (s), 55.9 (q), 56.2 (q), 65.9 (s), 79.4 (d), 107.7 (d), 110.0 (d), 113.8 (d), 118.4 (d), 122.6 (s), 126.3 (s), 148.4 (s), 148.7 (s), 164.5 (s), 170.4 (s), 205.7 (s). LR-MS m/z: 465 (M^+), 314 (base peak). HR-MS m/z (M^+): Calcd for $C_{21}H_{23}NO_9S$: 465.1091. Found: 465.1070.

2) A solution of **15** (30 mg) and TFA (1 ml) in CH_2Cl_2 (3 ml) was heated in a sealed tube at 85 °C for 5 d under stirring. After removal of the solvent, the residue was chromatographed over SiO_2 (hexane : AcOEt = 2 : 1) to give **24** (15 mg, 62%).

Introduction of an Acetoxy Group into the C_{11} Position of Erythrinan A mixture of acetic anhydride (5 ml) and TFAA (0.1 ml) was stirred at room temperature for 5 h prior to use. Then, a solution of **23** in CH_2Cl_2 (2 ml) prepared from **15** (100 mg) was added to the mixture of acetic anhydride and TFAA. The reaction mixture was stirred at room temperature for 2 h. After evaporation of the solvent, the residue was chromatographed over SiO_2 (hexane : AcOEt : CH_2Cl_2 = 4 : 4 : 1) to give *dl*-(5*R**,6*S**,7*R**,11*R**)-11-acetoxy-7-methanesulfonyloxy-15,16-dimethoxy-6-methoxycarbonyl-2,8-dioxoerythrinan (**25**) (21 mg, 23%) as a colorless gum. IR: 1719. ^{1}H-NMR (500 MHz): 2.07 (3H, s, $COCH_3$), 2.2—2.5 (4H, m, $-CH_2-$), 3.1—3.5 (1H, m, $-CH_2-$), 2.99, 3.28 (each 1H, d, J = 18 Hz, $-CH_2-$), 3.16, 3.22 (each 3H, s, OMe, OMs), 3.31 (1H, dd, J = 2, 14 Hz, $-CH_2-$), 3.88, 3.90 (each 3H, s, OMe), 4.65 (1H, dd, J = 2, 14 Hz, $-CH_2-$), 5.38 (1H, s, C<u>H</u>–OMs), 5.78 (1H, t, J = 2 Hz, C<u>H</u>–$OCOCH_3$), 6.59, 6.79 (each 1H, s, ArH). ^{13}C-NMR: 21.2 (q), 32.6 (t), 34.6 (t), 39.0 (q), 40.5 (t), 40.9 (t), 52.7 (q), 54.6 (s), 56.1 (q), 56.2 (q), 66.1 (s), 67.3 (d), 78.6 (d), 108.4 (d), 112.7 (d), 123.5 (s), 130.7 (s), 148.7 (s), 149.5 (s), 167.1 (s), 169.9 (s), 170.7 (s), 205.7 (s). LR-MS m/z: 525 (M^+), 314 (base peak).

References and Notes

1) Part XLVII of Synthesis of *Erythrina* and Related Alkaloids. Part XLVI: Hosoi S., Sato M., Nagao M., Tsuda Y., *Chem. Pharm. Bull.*, **44**, 2342—2343 (1996). This paper also constitutes Part LXII of Dioxopyrrolines. Part LXI: Horiguchi Y., Sano T., Kiuchi F., Tsuda Y., *ibid.*, **44**, 681—689 (1996).
2) Tsuda Y., Sano T., "The Alkaloids," Vol. 48, ed. by Cordell G. A., Academic Press Inc., San Diego, 1996, pp. 249—337.
3) Sano T., Toda J., Kashiwaba N., Tsuda Y., Iitaka Y., *Heterocycles*, **16**, 1151—1156 (1981).
4) *a*) Sano T., Toda J., Horiguchi Y., Imafuku K., Tsuda Y., *Heterocycles*, **16**, 1463—1468 (1981); *b*) Sano T., Toda J., Ohshima T., Tsuda Y., *Chem. Pharm. Bull.*, **40**, 873—878 (1992).
5) Tsuda Y., Sakai Y., Kaneko M., Ishiguro Y., Isobe K., Taga J., Sano T., *Heterocycles*, **15**, 431—436 (1981); Tsuda Y., Sakai Y., Nakai A., Kaneko M., Ishiguro Y., Isobe K., Taga J., Sano T., *Chem. Pharm. Bull.*, **38**, 1462—1472 (1990).
6) Tsuda Y., Ohshima T., Hosoi S., Kaneuchi S., Kiuchi F., Toda J., Sano T., *Chem. Pharm. Bull.*, **44**, 500—508 (1996); Tsuda Y., Murata M., Hosoi S., Ikeda M., Sano T., *ibid.*, **44**, 515—524 (1996).
7) The Pummerer reaction has been described as being efficient for isoquinoline synthesis. [Takano S., Iida H., Inomata K., Ogasawara K., *Heterocycles*, **35**, 47—52 (1993); Shinohara T., Toda J., Sano T., *Chem. Pharm. Bull.*, **45**, 813—819 (1997)].
8) Sano T., Toda J., Tsuda Y., *Chem. Pharm. Bull.*, **31**, 356—359 (1983).
9) Brighton K., Reid E. E., *J. Am. Chem. Soc.*, **65**, 458—459 (1943).
10) Sano T., Toda J., Tsuda Y., Yamaguchi K., Sakai S., *Chem. Pharm. Bull.*, **32**, 3255—3258 (1984).
11) Tsuda Y., Sakai Y., Sano T., Toda J., *Chem. Pharm. Bull.*, **39**, 1402—1406 (1991).
12) The configuration of the newly formed C_7-OH group was elucidated as a based on the results of a similar reduction of an analogous compound (ref. 4*b*).
13) Isobe K., Mohri K., Takeda N., Suzuki K., Hosoi S., Tsuda Y., *Chem. Pharm. Bull.*, **42**, 197—203 (1994).
14) Tsuda Y., Sakai Y., Nakai A., Ohshima T., Hosoi S., Isobe K., Sano T., *Chem. Pharm. Bull.*, **38**, 2136—2142 (1990).
15) Tsuda Y., Hosoi S., Nakai A., Sakai Y., Abe T., Ishi Y., Kiuchi F., Sano T., *Chem. Pharm. Bull.*, **39**, 1365—1373 (1991).