Total Synthesis of Homoerythrinan Alkaloids, Schelhammericine and 3-Epischelhammericine[1,2]

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Total syntheses of two homoerythrinan alkaloids, schelhammericine and 3-epischelhammericine, are described. Photocycloaddition of a dioxopyrrolobenzazepine to 1-methoxy-3-trimethylsilyloxybutadiene afforded, in a regio- and stereo-specific manner, the cyclobutane derivative, which was converted to a homoerythrinan derivative by utilizing a TBAF-induced 1,3-anionic rearrangement. The product was transformed into the title alkaloids in several steps.

Key words homoerythrinan alkaloid; total synthesis; schelhammericine; 3-epischelhammericine; [2+2]photo-cycloaddition; 1,3-anionic rearrangement

More than 70 ring-C-homo analogs of erythrinan alkaloids are known at present. They occur in plants of genera *Schelhammera* (Liliaceae), *Phelline* (Phellinaceae or Aquifoliaceae), *Cephalotaxus* (Cephalotaxaceae), *Athrotaxis* (Taxodiaceae), and *Dysoxylum* (Meliaceae), indicating a wide distribution in the plant kingdom. Chemically, they are classified into aromatic and non-aromatic alkaloids according to the structure of ring D, as in erythrinan alkaloids. In spite of a number of elegant syntheses of erythrinan alkaloids so far reported,[3] total synthesis of these homoerythrinan alkaloids was elusive until we reported the synthesis of schelhammericine and epischelhammericine.[2c] Since then, syntheses of comosine, dihydroschelhammeridine, schelhammeridine, and 3-*epi*-schelhammeridine have been achieved.[4,5] This paper describes in detail the total synthesis of the title homoerythrinan alkaloids, bearing an aromatic group.

Strategy for Construction of the Homoerythrinan Skeleton Our syntheses of erythrinan alkaloids have involved the following three general methods: (1) intramolecular nucleophilic cyclization of the *N*-acyliminium derived from an *N*-arylethylhydroindole,[6] (2) Diels–Alder cycloaddition of an activated butadiene to a dioxopyrroloisoquinoline,[7] and (3) [2+2] photocycloaddition of an activated butadiene to a dioxopyrroloisoquinoline followed by 1,3-anionic rearrangement.[2b,8] Although all of them were successfully applied to the total synthesis of natural erythrinan alkaloids, application of methods (1) and (2) to homoerythrinan synthesis was disappointing. For example, attempted cyclization of an *N*-3,4-methylenedioxyphenylpropyl derivative **1** proceeded in only 2.7% yield to afford the homoerythrinan derivative **2** with concomitant hydrolysis of the methylenedioxy group.[6b] The corresponding dimethoxy derivative did not give any homoerythrinan derivative.

The Diels–Alder reaction of the dioxopyrrolobenzazepine **3b** (for the synthesis, see below) with 1,3-bis(trimethylsilyloxy)butadiene gave the adduct **5**, in which the diene cycloadded to the carbonyl group (*one*-adduct) as a major product (39.5%), while the formation of desired homoerythrinan **4** (*ene*-adduct) was only 4.5%.[2a] The reaction with 1-methoxy-3-trimethylsilyloxybutadiene gave only the *one*-adducts **5** and **6** in yields of 33 and 23%. This remarkable discrepancy between the cases of the dioxopyrrolobenzazepine **3** and the dioxopyrroloisoquinoline **8**[7] is explained by the conformational difference between two dioxopyrroline dienophiles. The aromatic and dioxopyrroline rings in **8** are almost coplanar (dihedral angle, 24°), while those in **3** are arranged at an angle of 34°. The diene approaches the dienophile from the opposite side to the 7α-hydrogen in this cycloaddition reaction,[9] and this face is sterically hindered by the C5–C6 ethylene bridge and the aromatic ring in this twisted molecule. An analogous steric effect was observed in the Diels–Alder reaction of 2-phenyldioxopyrrolines **9**, in which the *one*-addition predominates over the *ene*-addition, when the *N*-substituent (*R*) is bulkier than an ethyl group.[10]

The reaction of **3b** with the diene in the presence of a Lewis acid ($ZnCl_2$) proceeded very rapidly (3 min), but resulted only in the formation of the *one*-adduct **5** in a high yield. Reaction of **3b** with 1-methoxy-3-trimethylsilyloxybutadiene under KF catalysis again gave the aldol adduct **7**, which, on treatment with $ZnCl_2$, cyclized to **5**.

In contrast to the above two methods, the photocycloaddition of an activated butadiene to dioxopyrrolobenzazepine **3** was found to proceed in a highly stereo- and regio-selective manner to give a [2+2] adduct which, on hydride reduction followed by an anionic 1,3-rearrangement, gave the expected homoerythrinan derivative in an acceptable overall yield (see below). Thus, method (3) was adopted for the following synthesis of homoerythrinan alkaloids.

Synthesis of Dioxopyrrolobenzazepine 3 The dioxopyrrolobenzazepine **3** was prepared by the reaction of oxalyl chloride with the enamino ester **15** of benzazepine type. We initially prepared **15** by Bischler–Napieralski cyclization of the malonamide derivative **17** of 3,4-dimethoxy-(or methylenedioxy)-phenylpropylamine **16**, as in the synthesis of an dioxopyrroloisoquinoline.[7b] However, cyclization yield of **17b** to **15b** did not exceed 15%, though various conditions were examined. Thus, the following alternative route was undertaken for large-scale synthesis of **15**.

Safrole **10a** was converted to 4-(3,4-methylenedioxy-

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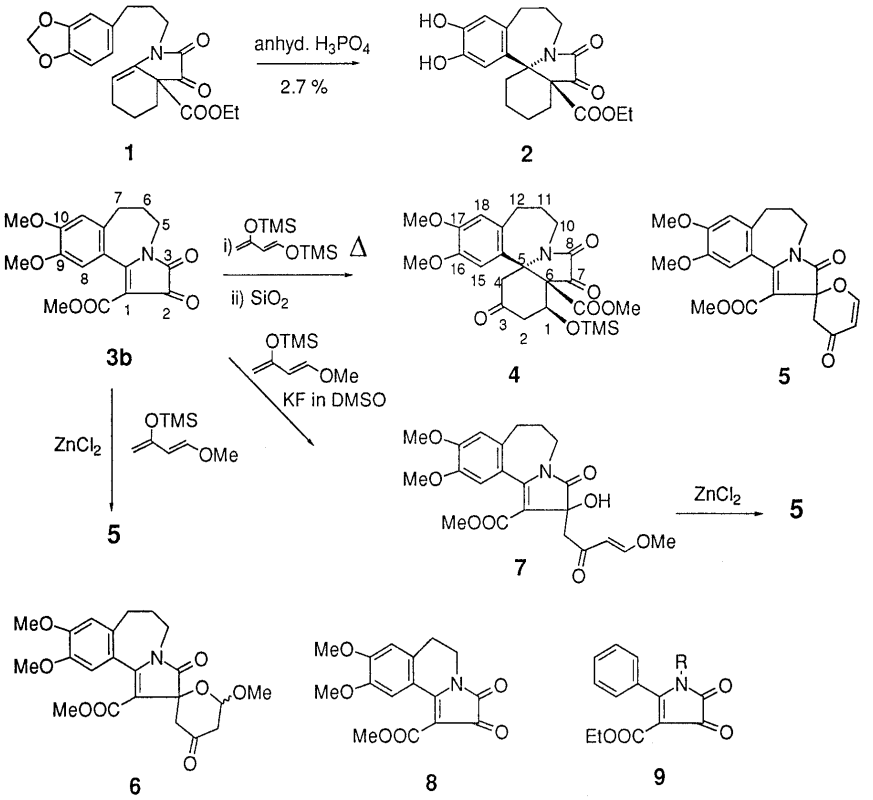


Chart 1

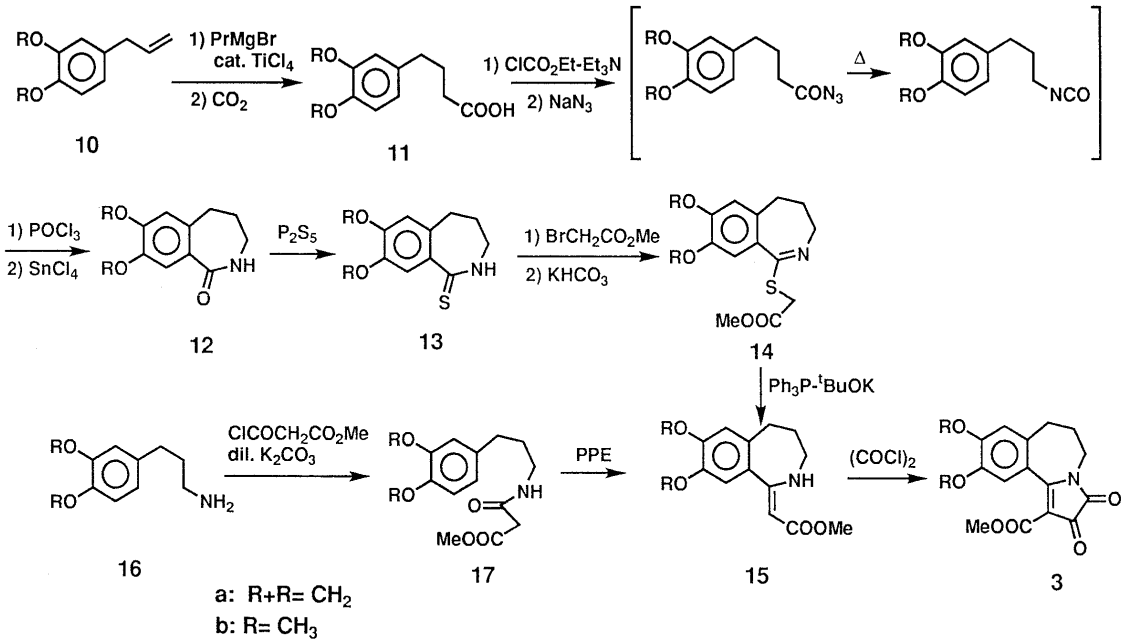


Chart 2

phenyl)butanoic acid **11a** by an application of the titanium(IV)-catalyzed Grignard exchange reaction,[11] and **11a** was converted to the isocyanate by conventional procedures, then cyclized *in situ* by treatment with $POCl_3$ and $SnCl_4$[12] to afford the benzazepinone **12a** in 40% overall yield from **10a**. Treatment of **12a** with P_2S_5 in benzene under reflux gave the thiolactam **13a** (96%). This was subjected to Eschenmoser's alkenylation[13] to give the enamino ester **15a** in 65% yield. This was identical with the compound obtained by the Bischler–Napieralski reaction of **17a** and was proved to be of *Z*-configuration (as in the six-membered analog)[7b] on the basis of the ^{1}H-NMR and IR spectra: the former showed the presence of an olefinic proton and the latter showed an intramolecular hydrogen-bonding of the NH to the methoxycarbonyl group. Reaction of **15a** with oxalyl chloride in ether smoothly gave the dioxopyrrolobenzazepine **3a** as red crystals in an overall yield of 50% from the benzazepinone **12a** (total yield 20% from **10a**). The structure of **3a** was supported by the IR (five-membered-ring ketone) and the UV spectra (λ_{max} 400 nm).

In a similar way, **3b** was prepared in a comparable yield

(20%) starting from methyleugenol **10b**.

[2+2] Photocycloaddition of Dioxopyrrolobenzazepine to Activated Butadienes: Synthesis of the 1,7-Cyclohomoerythrinan 34 When a mixture of the dioxopyrrolobenzazepine **3a** and 2-trimethyl-silyloxybutadiene was irradiated in tetrahydrofuran (THF) with >290 nm light for 15 min, a [2+2] adduct **18** was obtained in 57% yield. The ^{1}H-NMR spectrum of **18** [δ: OTMS 0.05; $-CH=CH_2$ 5.41 (d), 5.55 (t); CH_2 on a cyclobutane ring 2.18 (d), 3.34 (d)] supported the assigned structure. The stereochemistry was assigned as depicted in Chart 3 by analogy with the corresponding photo-adduct in the erythrinan series.[8] The reaction in CH_2Cl_2–MeOH also produced **18** but accompanied with a methoxy derivative **19**. Similarly, irradiation of **3a** with 1-methoxy-3-trimethylsilyloxybutadiene gave the expected photo-cycloadduct **30** in 25% yield in THF and in 79% yield in acetonitrile.

Firstly, thermal rearrangement[14] of **18** was examined. Heating of **18** in toluene at 120 °C for 3 h furnished the pyrrolinedione **3a**, the cycloreversion product, and an enol silylate **20**, the latter of which was characterized, by acid hydrolysis, as the trioxo derivative **21** (overall yield 30%).

Since the yield of the homoerythrinan **21** in thermolysis was low, the 1,3-anionic rearrangement[15] was next examined. Treatment of **18** with tetrabutylammonium fluoride (TBAF) in THF at −30—0 °C gave a single product of mp 255—258 °C, in 74% yield. This product was analyzed as $C_{20}H_{19}NO_7$ and showed absorptions of an OH (3430 cm^{-1}) and a five-membered-ring ketone (1760 cm^{-1}) in the IR spectrum, suggesting the 3,7-cyclohomoerythrinan structure **22**. However, this compound did not show a high-field shift of the COOMe signal in the ^{1}H-NMR spectrum, as was seen in the corresponding erythrinan derivative,[6a] and was not affected by Zn–AcOH treatment, which might reduce **22** to keto-alcohols.[16] Therefore, we considered the structure **23**, which could be produced by desilylation of **18** followed by epimerization and a Prins-type cyclization of the vinyl group to the ketone with a concomitant 1,2-shift. A similar sequence of reactions is already known for erythrinan derivatives,[17] giving the corresponding cage compound in a high yield on treatment with Lewis acid. Treatment of **18** with BF_3–etherate produced the same compound **23** in 64% yield, proving the assigned structure.

This undesirable reaction might be avoided when the ketone group in **18** is reduced to the alcohol prior to rearrangement. This procedure, at the same time, would discriminate the two ketonic groups in the rearrangement product. Thus, reduction of **18** with $NaBH_4$ in MeOH gave an alcohol **24** in 91% yield, whereas the reduction with Bu_4NBH_4 in CH_2Cl_2 gave three products, **24**, a diol **25**, and the cage compound **23**. The stereochemistry of the newly formed alcohol group was assigned as α (*trans* to the COOMe group) on the basis of a similar reduction in the erythrinan series[8] and the following transformations. Treatment of **24** with TBAF at −30 °C gave only the diol **25**, but when the temperature was elevated to room temperature, the expected rearrangement occurred to give the keto-alcohol **26** of homoerythrinan structure in 40% yield. The structure of **26** was supported by its spectral data [IR: 3250 (OH), 1735, 1715, 1680 (CO) cm^{-1}; ^{1}H-NMR: δ 3.27 (shielded COOMe as in erythrinan

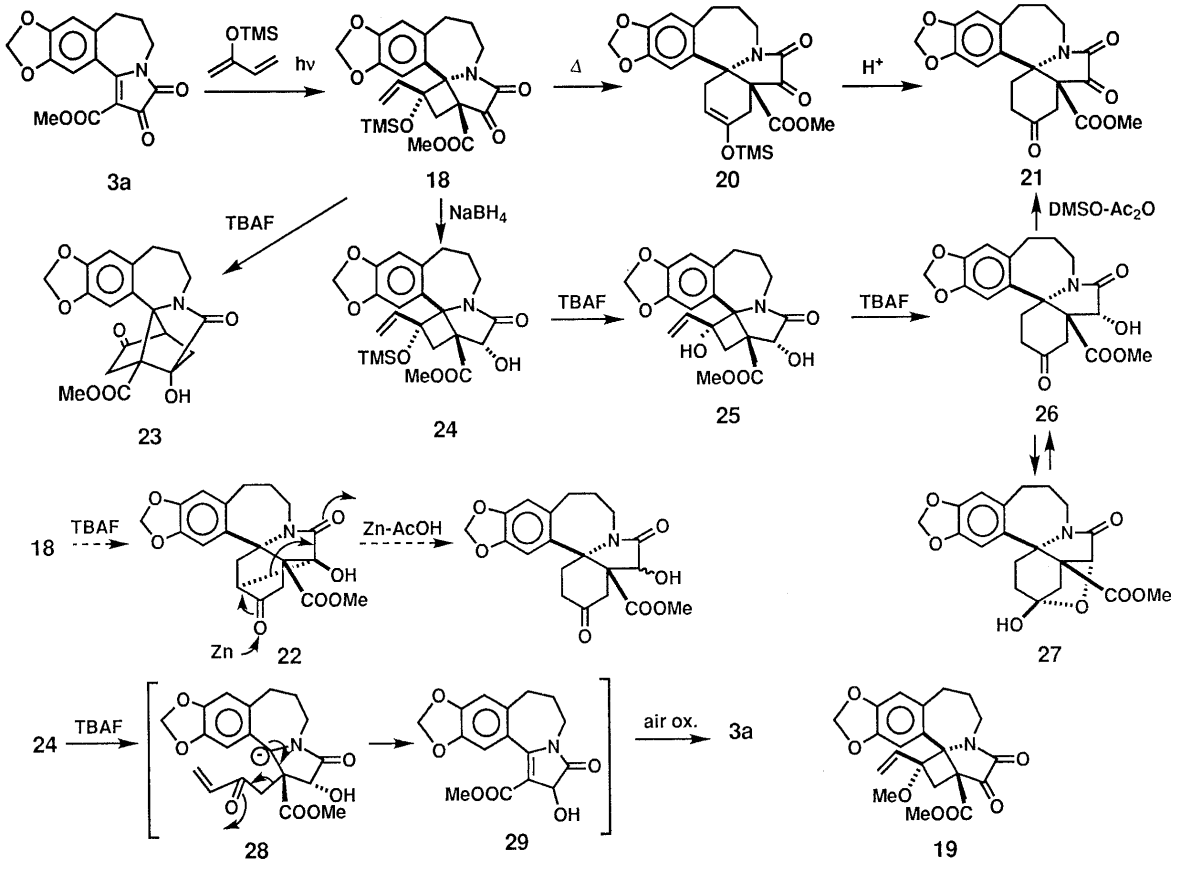


Chart 3

derivatives)[6a)]] and by conversion to the trioxo derivative **21** by DMSO–Ac_2O oxidation. The presence of an intramolecular hemiacetal **27** in solution confirmed the stereochemistry.[18)]

However, the yield of **26** in the above reaction is not satisfactory (40%), probably because of a partial contribution of the fragmentation reaction of the intermediary enone anion **28** to **29**. This was supported by isolation of **3a** after air oxidation of the reaction mixture. We thought that introduction of a methoxy group at the olefin terminus would probably suppress this undesirable fragmentation and, at the same time, accelerate the rearrangement reaction. In fact, treatment of **31**, obtained by hydride reduction of **30**, with TBAF at −30 °C for 45 min smoothly gave the enone **32** in 85% yield. This is the product of methanol elimination from the intermediary enolate anion, and was readily hydrogenated to afford the above-described **26**. Thus, starting from **3a**, we could synthesize **26** in four steps with an overall yield of 59%.

Methanesulfonylation of **26** followed by treatment of the resulting mesylate **33** with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in toluene resulted in the formation of 1,7-cyclohomoerythrinan **34** in 60% yield. The IR spectrum of **34** [1735, 1705, 1690 cm^{-1}] clearly eliminates an alternative five-membered-ring ketone structure (3,7-cyclohomoerythrinan).

Synthesis of (±)-Schelhammericine and (±)-3-Epischelhammericine The 1,7-cyclohomoerythrinan **34** was converted to the ketone **39** (Chart 5) in the manner described for the total synthesis of erythrinan alkaloids.[19)]

Compound **34** was treated with phenylselenenyl chloride in the presence of $BF_3 \cdot Et_2O$ and the resulting phenylselenenylated mixture was treated with mercury(II) perchlorate (MPC) in methanol to afford the dimethoxyketone **35** in 76% yield. This was reduced with $NaBH_4$ to the alcohol **36** as a single product, which was converted into the dithiocarbonate **37** by a conventional method. Treatment of **37** with Bu_3SnH in toluene followed by acid hydrolysis of the resulting olefin gave the conjugated ketone **38**. A by-product in this deoxygenation reaction, sometimes obtained in a small amount, was a seven-membered ketone **40**, whose structure was tentatively assigned on the basis of the spectral data.

Demethoxycarbonylation of **38** was achieved by heating the compound with $CaCl_2$ in DMSO containing *tert*-heptylmercaptan[6b,20)] resulting in the formation of the kinetically controlled product **39** in 62% yield. The by-product in this reaction was the dibenzazecinone **42**,

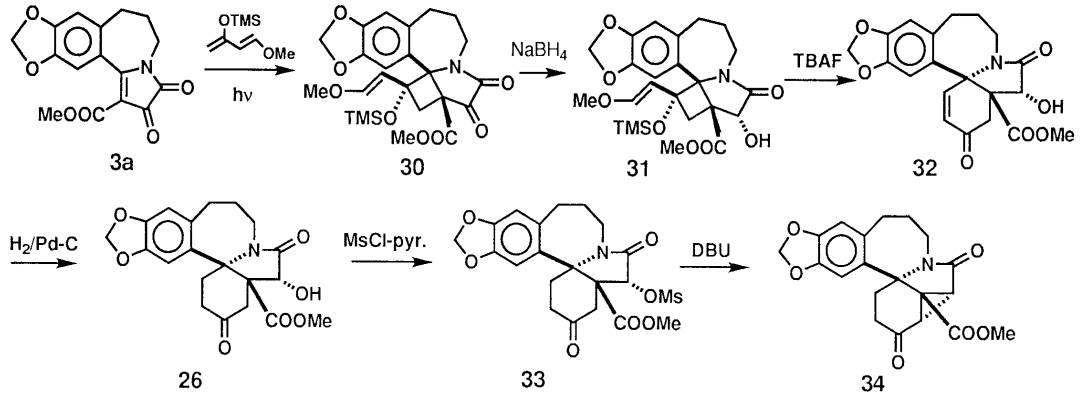


Chart 4

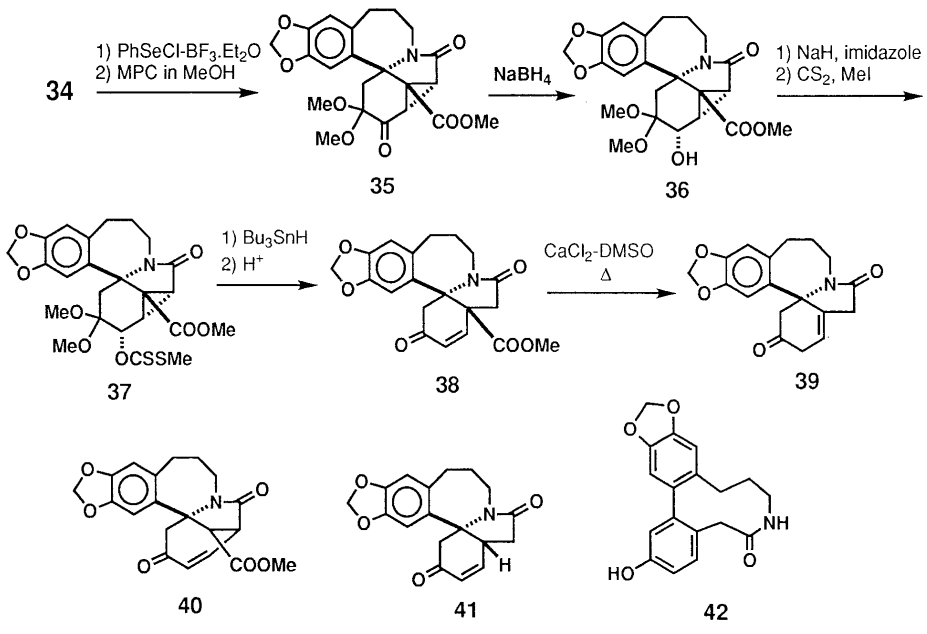
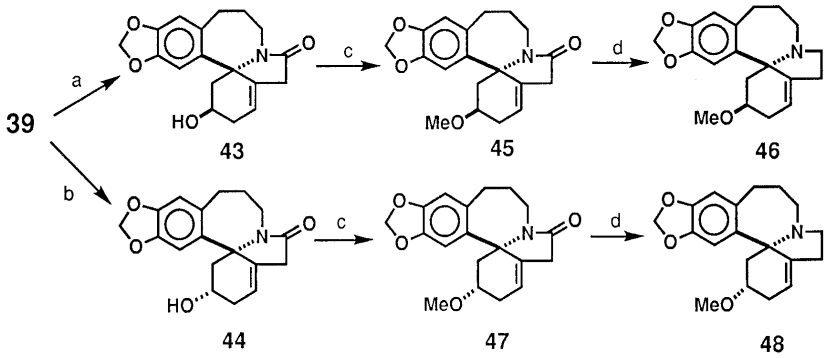


Chart 5



a) Bu_4NBH_4 in MeOH, b) $NaBH_4$-$CeCl_3$ in MeOH, c) NaH/Bu_4NHSO_4-MeI, d) $LiAlH_4$-$AlCl_3$

Chart 6

which should be produced from the isomeric conjugated ketone **41**.[21]

Reduction of **39** with Bu_4NBH_4 in methanol stereoselectively gave the alcohol of axial configuration, **43**. On the other hand, reduction with $NaBH_4$–$CeCl_3$ gave predominantly the equatorial alcohol, **44**. The product ratios of α and β alcohols were 1 : 6 in the former and 5 : 1 in the latter reactions.

Methylation of **43** with iodomethane with the use of imidazole and phase-transfer catalyst gave the methyl ether **45**, which was reduced with AlH_3 (prepared from $LiAlH_4$ and $AlCl_3$)[7b,22] to the amine **46** in 43% yield. Similarly, the epimeric alcohol **44** was methylated to **47**, and then reduced to the amine **48** in 69% yield. These amines were proved to be identical with the homoerythrinan alkaloids, schelhammericine and 3-epischelhammericine, by comparison of the spectral data (^{1}H-NMR and IR) and TLC behavior with those of authentic specimens. Thus, total syntheses of (±)-schelhammericine and (±)-3-epischelhammericine were accomplished.

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 as KBr disks on a Jasco IR-G spectrometer and data are given in cm^{-1}. UV spectra were taken in EtOH and λ_{max} values are given in nm with ε in parentheses. ^{1}H-NMR spectra were taken with a JEOL FX 100 (100 MHz) or GX 400 (400 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 (Wacogel C-200). Medium-pressure liquid chromatography (MPLC) was performed 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.

4-(3,4-Methylenedioxyphenyl)butanoic Acid (11a) 1-Bromopropane (55.67 g) in dry Et_2O (50 ml) was added dropwise to a stirred mixture of magnesium ribbon (11.73 g) in dry Et_2O (80 ml) at room temperature under an Ar atmosphere and the mixture was heated under reflux for 40 min. After cooling, unreacted magnesium was removed by filtration with an aid of glass-wool. The filtrate was diluted with Et_2O–THF (15 : 7, 220 ml) and cooled, then $TiCl_4$ (1 ml) was added at 0 °C. Safrole **10a** (40 g) in THF (100 ml) was added dropwise over a period of 15 min at room temperature and the mixture was stirred for 3 h, then heated under reflux for 9 h, during which time propene evolved and was released through a hood. The resulting mixture was cooled and quenched by addition of dry ice (600 g), and kept overnight. It was again diluted with THF (60 ml), then further dry ice (500 g) was added, and the whole was acidified with 20% H_2SO_4 under cooling. The organic solvents were removed by steam distillation, and the cooled residue was filtered to yield a solid and a filtrate. The filtrate was extracted with AcOEt. The solid and the AcOEt extract were combined and extracted with 28% NH_4OH. The alkaline layer was collected, acidified with HCl, and extracted with AcOEt. Concentration of the organic layer gave **11a** (31.9 g, 64%), as colorless needles from Et_2O–hexane, mp 76—78 °C. This product was identical with an authentic specimen (lit. mp 79—80 °C,[23a] 75—76 °C[23b]).

4-(3,4-Dimethoxyphenyl)butanoic Acid (11b) (1) Methyleugenol (30—40 g) was treated 5 times (total 192 g) as described above to give **11b** (145.8 g, average yield 60%), mp 58—59 °C. The product was identical with the specimen obtained below.

(2) From Veratrole: 3-(3,4-Dimethoxybenzoyl)propanoic acid[24] [obtained from veratrole (20 g) by Friedel–Crafts acylation with succinic anhydride (15.94 g)] was subjected to Clemensen reduction with Zn–amalgam [prepared from mossy Zn (50.8 g), $HgCl_2$ (5.0 g), concentrated HCl (2.5 ml) and water (75 ml) by stirring for 5 min at room temperature], water (40 ml), concentrated HCl (80 ml), toluene (50 ml), and acetic acid (5 ml) for 9 h under reflux to give, on usual work-up, **11b** (15.6 g, 48% from veratrole), mp 58—59 °C.[24]

2,3,4,5-Tetrahydro-7,8-methylenedioxy-1*H*-2-benzazepin-1-one (12a) Triethylamine (3.59 g) in acetone (8 ml) was added to a solution of the acid **11a** (5 g) in acetone (10 ml). The mixture was stirred at 0 °C for 1 h, then ethyl chloroformate (3.9 g) in acetone (8 ml) was added and stirring was continued for a further 30 min. The precipitate was removed by filtration and washed with a small amount of acetone. Sodium azide (2.36 g) in water (7 ml) was added to the combined filtrate and washings, and the mixture was stirred for 1 h at room temperature, poured into ice-water, and extracted with benzene. Concentration of the dried benzene extract gave a gummy residue, which was dissolved in toluene (60 ml) and heated under reflux for 1 h under an Ar atmosphere, then cooled. After addition of $POCl_3$ (37 g, 10 eq), the mixture was stirred for 1 h, then $SnCl_4$ (6.29 g, 1 eq) in toluene (16 ml) was added at 0 °C, and the whole was stirred for a further 17 h at room temperature. Quenching with ice and 28% NH_4OH, followed by stirring for 1 h resulted in precipitates, which were collected by filtration and washed with $CHCl_3$. The filtrate was separated into toluene and water layers, and the water layer was extracted with $CHCl_3$. All organic layers and washings were combined and concentrated to dryness. Chromatography of the residue in $CHCl_3$ gave **12a** (3.1 g, 63 %), which formed colorless needles from CH_2Cl_2–Et_2O, mp 137—138 °C. IR: 1655. ^{1}H-NMR: 7.10 (1H, brs, >NH), 7.02, 6.50 (each 1H, s, ArH), 5.83 (2H, s, OCH_2O), 3.13 (2H, t, J=6 Hz, $>NCH_2$), 2.73 (2H, t, J=6 Hz, $ArCH_2$), 1.93 (2H, quint, J=6 Hz, CH_2). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.12; H, 5.34; N, 6.68.

2,3,4,5-Tetrahydro-7,8-dimethoxy-1*H*-2-benzazepin-1-one (12b) Treatment of **11b** (20 g × 5) as described above gave **12b** (total 172 g,

average yield 49%), as colorless needles from $CHCl_3$–AcOEt, mp 191—193 °C (lit. 192—194 °C).[12b] IR: 1656. ^{1}H-NMR: 7.16, 6.58 (each 1H, s, ArH), 7.10 (1H, br s, >NH), 3.86 (6H, s, OMe×2), 3.10 (2H, q, J=6 Hz, –NHC$\underline{H}_2$–), 2.78 (2H, t, J=7 Hz, ArCH_2), 2.04 (2H, quint, J=6.5 Hz, CH_2). *Anal.* Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 64.75; H, 6.70; N, 6.12.

2,3,4,5-Tetrahydro-7,8-methylenedioxy-1*H*-2-benzazepine-1-thione (13a) A mixture of **12a** (5 g) and P_2S_5 (5.4 g) in benzene (130 ml) was heated under reflux for 1 h under an Ar atmosphere, then separated to afford the precipitate and benzene layer by filtration. The precipitate was heated with MeOH (60 ml) under reflux for 1 h, concentrated, and extracted with hot $CHCl_3$. The combined $CHCl_3$ extract and benzene layer was washed with water, dried, and concentrated to yield **13a** (5.2 g, 96%). Crystallizations from MeOH gave pale yellow needles, mp 188—190 °C. IR: no CO. ^{1}H-NMR: 9.03 (1H, br s, >NH), 7.23, 6.41 (each 1H, s, ArH), 5.81 (2H, s, OCH_2O), 3.14 (2H, q, J=6.5 Hz, –NHC$\underline{H}_2$–), 2.62 (2H, t, J=6 Hz, ArCH_2), 2.03 (2H, quint, J=6.5 Hz, CH_2). *Anal.* Calcd for $C_{11}H_{11}NO_2S$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.58; H, 4.81; N, 6.14.

2,3,4,5-Tetrahydro-7,8-dimethoxy-1*H*-2-benzazepine-1-thione (13b) Treatment of **12b** (500 mg) as described above gave **13b** (478 mg, 89%) as pale yellow needles from MeOH, mp 181—183 °C. IR: no CO. ^{1}H-NMR: 9.03 (1H, br s, >NH), 7.38, 6.51 (each 1H, s, ArH), 3.86 (6H, s, OMe), 3.19 (2H, q, J=6 Hz, –NHC$\underline{H}_2$–), 2.70 (2H, t, J=6 Hz, ArCH_2), 2.10 (2H, quint, J=6.5 Hz, CH_2).

Methyl 2-(2,3,4,5-Tetrahydro-7,8-methylenedioxy-1*H*-2-benzazepin-1-ylidene)acetate (15a) A solution of **13a** (3.0 g) and methyl bromoacetate (2.52 g) in MeCN (150 ml) was stirred at room temperature for 17 h. After removal of the solvent, the residue was dissolved in CH_2Cl_2. This solution was washed three times with saturated $KHCO_3$ solution, dried, and evaporated to give **14a**. IR: 1720. ^{1}H-NMR: 6.92, 6.57 (each 1H, s, ArH), 5.87 (2H, s, OCH_2O), 3.85 (2H, s, SCH_2), 3.68 (3H, s, CO_2Me), 3.27 (2H, t, J=6 Hz, >NCH_2–). This was used for the following reaction without further purification.

A mixture of **14a**, triphenylphosphine (9.01 g), and potassium *tert*-butoxide (60 mg) in DMF (75 ml) was heated at 140 °C for 8 h under an Ar atmosphere. The mixture was concentrated *in vacuo*, 10% HCl was added, and the whole was extracted with benzene. The aqueous layer was basified with solid $KHCO_3$ and extracted with CH_2Cl_2. Purification of the CH_2Cl_2 extract by chromatography in CH_2Cl_2 gave **15a** (2.31 g, 65%) as colorless needles from Et_2O–hexane, mp 163—165 °C. IR: 1650, 1620. ^{1}H-NMR: 8.70 (1H, br s, >NH), 6.77, 6.50 (each 1H, s, ArH), 5.83 (2H, s, OCH_2O), 4.52 (1H, s, =CH–), 3.60 (3H, s, CO_2Me), 3.07 (2H, q, J=6 Hz, –NHC$\underline{H}_2$–), 2.63 (2H, t, J=7 Hz, ArCH_2), 1.92 (2H, quint, J=6.5 Hz, CH_2). *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.76; N, 5.36. Found: C, 64.46; H, 5.87; N, 5.63.

Methyl 2-(2,3,4,5-Tetrahydro-7,8-dimethoxy-1*H*-2-benzazepin-1-ylidene)-acetate (15b) (1) Treatment of **13b** (5 g) as described above gave **14b** and then **15b** (4.9 g, 85%). Average yield of six experiments: 78%. **14b**: Gum. IR: 1734. ^{1}H-NMR: 6.94, 6.59 (each 1H, s, ArH), 3.83 (6H, s, OMe×2), 3.68 (3H, s, CO_2Me), 3.28 (2H, t, J=6 Hz, >NCH_2–), 2.68—1.91 (4H, m, ArC$\underline{H}_2$C$\underline{H}_2$). **15b**: Colorless needles from Et_2O–hexane, mp 109—111 °C. IR: 1640. ^{1}H-NMR: 8.78 (1H, br s, >NH), 6.86, 6.58 (each 1H, s, ArH), 4.59 (1H, s, =CH–), 3.85, 3.81 (each 3H, s, OMe), 3.62 (3H, s, CO_2Me), 3.09 (2H, q, J=6.5 Hz, –NHC$\underline{H}_2$–), 2.70 (2H, t, J=7 Hz, ArCH_2), 1.96 (2H, quint, J=6 Hz, CH_2). *Anal.* Calcd for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.91; H, 6.82; N, 4.90.

(2) From the amine **16b**[25]: 3-(3,4-Dimethoxyphenyl)propylamine (**16b**) was acylated with methyl chloroacetylformate as described in the case of erythrinan synthesis[7b] to give the malonamide **17b**, mp 82—84 °C.

The amide **17b** (1 g) and an excess of polyphosphate ester (PPE) (20 g) were heated at 80 °C for 10 h. Excess PPE was decomposed with ice-water, then the solution was basified with 10% K_2CO_3 and extracted with $CHCl_3$. Concentration of the extract and chromatography of the residue in $CHCl_3$ gave **15b** (0.16 g, 15%), which was identical with the compound obtained above.

Dioxopyrrolobenzazepine 3a Oxalyl chloride (750 mg) was added dropwise to a cooled solution of **15a** (1.15 g) in dry Et_2O (100 ml) and the mixture was stirred for 2 h at 0 °C. The precipitated crystals were collected by filtration and recrystallized from CH_2Cl_2–AcOEt to give **3a** (1.11 g, 80%) as orange needles, mp 283—285 °C. IR: 1755, 1705, 1680. ^{1}H-NMR: 7.20, 6.81 (each 1H, s, ArH), 6.09 (2H, s, OCH_2O), 3.79 (3H, s, CO_2Me). *Anal.* Calcd for $C_{16}H_{13}NO_6$: C, 60.95; H, 4.16; N, 4.44. Found: C, 60.76; H, 4.05; N, 4.64.

Dioxopyrrolobenzazepine 3b Treatment of **15b** (1 g) as described above gave **3b** (1.06 g, 89%) as orange needles from CH_2Cl_2–AcOEt, mp 258—261 °C. In the case of **3b**, hexane (30 ml) was sometimes added if necessary, and the reaction mixture was gently warmed to remove evolved HCl gas, then cooled. UV (dioxane): 257 (11600), 324 (5970), 367 (6300), 432 (7700). IR: 1750, 1730, 1680. ^{1}H-NMR: 7.32, 6.81 (each 1H, s, ArH), 3.99, 3.90 (each 3H, s, OMe), 3.77 (3H, s, CO_2Me), 2.83 (2H, t, J=7 Hz, ArCH_2), 2.11 (2H, quint, J=7 Hz, CH_2). *Anal.* Calcd for $C_{16}H_{13}NO_6$: C, 61.63; H, 5.17; N, 4.23. Found: C, 61.66; H, 5.17; N, 4.26.

Diels–Alder Reaction of Dioxopyrrolobenzazepine 3b with 1,3-Bis(trimethylsilyloxy)butadiene The pyrrolinedione **3b** (105 mg) and 1,3-bis(trimethylsilyloxy)butadiene (350 mg) were heated in a sealed tube at 180 °C for 15 min. The product in benzene–AcOEt (4:1) was chomatographed to give **4** (7 mg, 4.5%) and then **5** (50 mg, 39.5%).

4: Colorless plates, mp 202—204 °C, from acetone–hexane. IR: 1770, 1750, 1725, 1720. UV: 238 (10800), 282 (7100). ^{1}H-NMR: 6.91, 6.56 (each 1H, s, ArH), 4.92 (1H, t, J=3 Hz, C_1-H), 3.87, 3.84 (each 3H, s, OMe), 3.08 (3H, s, CO_2Me), 0.27 (9H, s, TMS). HRMS: Calcd for $C_{24}H_{31}NO_8Si$: 489.1816. Found: 489.1811.

5: Pale orange prisms, mp 191—195 °C, from acetone–hexane. IR: 1735, 1685, 1670. UV: 246 (17400), 288 (10340), 348 (10420). ^{1}H-NMR: 7.32 (1H, d, J=6 Hz, olefin-H), 7.19 (1H, br s, ArH), 6.74 (1H, s, ArH), 5.33 (1H, d, J=6 Hz, olefin-H), 3.95, 3.90 (each 3H, s, OMe), 3.66 (3H, s, CO_2Me). ^{13}C-NMR: see ref. 2*a*. HRMS: Calcd for $C_{21}H_{21}NO_7$: 399.1316. Found: 399.1313.

Diels–Alder Reaction of Dioxopyrrolobenzazepine 3b with 1-Methoxy-3-trimethylsilyloxybutadiene The pyrrolinedione **3b** (100 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (excess) in CH_2Cl_2 (2 ml) were heated in a sealed tube at 180 °C for 15 min. Hexane was added to the cooled mixture and precipitated **3b** was removed by filtration. The filtrate was adsorbed on a silica gel column and kept overnight. The column was then eluted with benzene–EtOAc (6:1) to yield **6** (30 mg, 23%) and then **5** (40 mg, 33%).

6: Colorless prisms, mp 196—198 °C, from MeOH. IR: 1735, 1725, 1685. UV (dioxane): 242 (15500), 285 (6900), 337 (11000). ^{1}H-NMR at 27.5 °C: 7.22 (1H, br s, ArH), 6.73 (1H, s, ArH), 5.41 (1H, t, J=3 Hz, >CH–), 3.94, 3.89, 3.52 (each 3H, s, OMe), 3.65 (3H, s, CO_2Me). At −30 °C: 7.35, 6.96 (C_{15}-H), 6.78, 6.75 (C_{18}-H). This phenomenon is attributed to an atrop-isomerism of the benzazepine ring.[2a] ^{13}C-NMR: see ref. 2*a*. *Anal.* Calcd for $C_{22}H_{25}NO_8$: C, 61.24; H, 5.84; N, 3.25. Found: C, 61.01; H, 5.77; N, 3.07.

Lewis Acid-Catalyzed Condensation of Dioxopyrrolobenzazepine 3b with 1-Methoxy-3-trimethylsilyloxybutadiene (1) In the presence of $ZnCl_2$: A mixture of **3b** (60 mg), 1-methoxy-3-trimethylsilyloxybutadiene (95 mg), and a small amount of anhydrous $ZnCl_2$ (*ca.* 2 eq) in CH_2Cl_2 (3 ml) was stirred for 5 min at room temperature. The solvent was evaporated *in vacuo* and the residue was chromatographed to give **5** (53 mg, 73%).

(2) In the presence of KF: Potassium fluoride (15 mg) was added to a solution of **3b** (50 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (40 mg) in DMSO (2 ml) and the mixture was stirred for 3.5 h at room temperature. It was diluted with water and extracted with AcOEt. Chromatography of the product gave **7** from CH_2Cl_2–AcOEt (1:1) eluate as a gum (49.8 mg, 76%). IR ($CHCl_3$): 1735, 1685, 1665, 1620. ^{1}H-NMR: 7.43 (1H, d, J=12 Hz, olefin-H), 7.03, 6.60 (each 1H, s, ArH), 5.41 (1H, d, J=12 Hz, olefin-H), 3.85, 3.80, 3.57 (each 3H, s, OMe), 3.62 (3H, s, CO_2Me). MS: 431 (M^+).

A mixture of **7** and $ZnCl_2$ (30 mg) in CH_2Cl_2 (2 ml) was stirred for 1.5 h at room temperature. Dilution of the mixture with water, extraction with CH_2Cl_2, and chromatography of the product gave **5** (25 mg, 39%).

Photocycloaddition of Dioxopyrrolobenzazepine 3a to 2-Trimethylsilyloxybutadiene (1) In THF: A solution of **3a** (400 mg) and 2-trimethylsilyloxybutadiene (1.26 g) in THF (350 ml) was irradiated with a 300 W high-pressure mercury lamp equipped with a Pyrex filter at 0 °C for 15 min under an N_2 atmosphere. Precipitated **3a** (33 mg) was filtered off and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography to give **18** (328 mg, 57%, net yield 62%), as colorless plates from Et_2O–hexane, mp 139—142 °C. IR: 1765, 1742, 1710. ^{1}H-NMR: 6.63, 6.45 (each 1H, s, ArH), 5.78 (2H, s, OCH_2O), 5.55 (1H, t, J=7 Hz, –C$\underline{H}$=CH_2), 5.41 (2H, d, J=7 Hz, –CH=C$\underline{H}_2$), 3.34 and 2.18 (each 1H, d, J=13 Hz, $H_2C<$ on cyclobutane), 3.22 (3H, s, CO_2Me), 0.05 (9H, s, TMS). HRMS: Calcd for $C_{23}H_{27}NO_7Si$: 457.1554. Found:

457.1548.

(2) In CH_2Cl_2–MeOH: A solution of **3a** (50 mg) in CH_2Cl_2 (10 ml) containing a few drops of MeOH was irradiated with a pencil-type mercury lamp at 0 °C for 1 h. After evaporation of the solvent in vacuo, the residue was purified by PTLC to give **18** (13.5 mg, 19%) and **19** (10.5 mg, 17%).

19: Gum. IR: 1770, 1740, 1720. ^{1}H-NMR: 6.78, 6.50 (each 1H, s, ArH), 5.84 (2H, s, OCH_2O), 5.60—5.40 (3H, m, –CH=CH_2), 3.10 (3H, s, CO_2Me), 2.95 (3H, s, OMe), 2.36 (1H, d, J=14 Hz, one of H_2C<). MS: 399 (M^+).

Photocycloaddition of Dioxopyrrolobenzazepine 3a to 1-Methoxy-3-trimethylsilyloxybutadiene (1) In MeCN: A solution of **3a** (915 mg) and 1-methoxy-3-trimethylsilyloxybutadine (748 mg) in MeCN (400 ml) was irradiated with a 300 W high-pressure mercury lamp equipped with a Pyrex filter at 0 °C for 15 min under an Ar atmosphere. After removal of the solvent, the residue was purified by chromatography to give **30** (1.12 g, 79%) as colorless prisms from Et_2O–hexane, mp 158—160 °C. IR: 1765, 1740, 1720. ^{1}H-NMR: 6.77, 6.48 (each 1H, s, ArH), 6.43 (1H, d, J=13 Hz, –CH=C<u>H</u>OMe), 5.82 (2H, s, OCH_2O), 4.61 (1H, d, J=13 Hz, –C<u>H</u>=CHOMe), 3.48 (3H, s, CO_2Me), 3.24 (3H, s, OMe), 3.23 and 2.24 (each 1H, d, J=13 Hz, H_2C< on cyclobutane), 0.08 (9H, s, TMS). HRMS: Calcd for $C_{24}H_{29}NO_8Si$: 487.1661. Found: 487.1663.

(2) In THF: A solution of **3a** (410 mg) and 1-methoxy-3-trimethylsilyloxybutadiene (672 mg) was irradiated as described above. After the removal of precipitated **3a** by filtration, the filtrate was worked up as above to give **30** (155 mg, 25%, net yield 43%).

Thermolysis of the Photo-Adduct 18 A solution of **18** (40 mg) in toluene (2.5 ml) was heated in a sealed tube at 120 °C for 3 h. Orange crystals **3a** (7.6 mg, 27%) precipitated by addition of hexane were removed by filtration. The filtrate was concentrated *in vacuo*. The residue in THF–5% HCl (1 : 1, 2.5 ml) was stirred at room temperature for 1 h and extracted with CH_2Cl_2. Crystallization of the product from MeOH gave **21** (10 mg, 30%) as colorless prisms, mp 212—216 °C. IR: 1770, 1745, 1725, 1710. ^{1}H-NMR: 6.63, 6.48 (each 1H, s, ArH), 5.85 (2H, s, OCH_2O), 3.17 (3H, s, CO_2Me). MS: 385 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.22; H, 5.10; N, 3.66.

The Cage Compound 23 (1) A 1 M TBAF solution in THF (0.11 ml) was added to a solution of **18** (50 mg) in dry THF (5 ml) and the mixture was stirred at 0 °C for 15 min. Brine was added and the whole was extracted with benzene. The product was purified by chromatography with benzene–AcOEt (1 : 1) to give **23** (31 mg, 74%) as colorless needles from CH_2Cl_2–MeOH, mp 255—258 °C. IR: 3430, 1760, 1735, 1698. ^{1}H-NMR: 6.57, 6.52 (each 1H, s, ArH), 5.83 (2H, s, OCH_2O), 3.67 (3H, s, COOMe). *Anal.* Calcd for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.25; H, 5.05; N, 3.52.

(2) A mixture of **18** (50 mg) and $BF_3 \cdot Et_2O$ in CH_2Cl_2 (5 ml) was stirred at 0 °C for 3 h. Extraction of the mixture with benzene and work-up of the product as above gave **23** (27 mg, 64%).

Reduction of the Photo-Adduct 18 (1) With $NaBH_4$: The photo-adduct **18** (200 mg) in MeOH (15 ml) was reduced with $NaBH_4$ (16 mg) at 0 °C for 15 min. The precipitated crystals (**24**, 126 mg) were collected by filtration. The filtrate was diluted with CH_2Cl_2, washed with water, and concentrated to dryness to give an additional crop (56 mg) of **24**. Total yield, 182 mg (91%). It crystallized as colorless needles from CH_2Cl_2–hexane, mp 178—180 °C. IR: 3300, 1730, 1675. ^{1}H-NMR: 6.65, 6.37 (each 1H, s, ArH), 5.73 (2H, s, OCH_2O), 5.62—5.17 (3H, m, –CH=CH_2), 3.12 and 2.55 (each 1H, d, J=14 Hz, H_2C< on cyclobutane), 4.88 (1H, br s, >C<u>H</u>OH), 3.30 (3H, s, OMe), 0.27 (9H, s, TMS). HRMS: Calcd for $C_{23}H_{29}NO_7Si$: 459.1712. Found: 459.1719.

(2) With Bu_4NBH_4: A solution of **18** (200 mg) and Bu_4NBH_4 (112 mg) in CH_2Cl_2 (5 ml) was stirred at 0 °C for 20 min. The mixture was diluted with Et_2O, washed with water, and concentrated to dryness. Purification of the residue by chromatography gave **24** (47 mg, 23%) and a mixture of **25** and **23** (71 mg). Crystallizations of the latter mixture from CH_2Cl_2 gave **25** as colorless prisms, mp 165—167 °C. IR: 3400, 1740, 1675. ^{1}H-NMR: 6.72, 6.43 (each 1H, s, ArH), 5.80 (2H, s, OCH_2O), 5.52—5.15 (3H, m, –CH=CH_2), 3.30 (3H, s, CO_2Me), 2.58 (1H, d, J=14 Hz, one of H_2C< on cyclobutane). *Anal.* Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.43; N, 3.62. Found: C, 61.75; H, 5.43; N, 3.46.

Anionic Rearrangement of 24 A solution of **24** (50 mg), triethylamine (5 drops), and 1 M TBAF (0.11 ml) in THF (5 ml) was stirred at −30 °C for 15 min. TLC of the mixture indicated the formation of **25**. After having been stirred at room temperature for 2 h, the mixture was extracted with CH_2Cl_2. Purification of the product by PTLC gave **26** (17 mg, 40%) as colorless prisms from CH_2Cl_2–MeOH, mp 291—293 °C. IR: 3250, 1735, 1715, 1680. ^{1}H-NMR: 6.74, 6.55 (each 1H, s, ArH), 5.94 (2H, s, OCH_2O), 4.92 (1H, br s, >C<u>H</u>OH), 3.27 (3H, s, CO_2Me). *Anal.* Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.82; H, 5.41; N, 3.63.

Another fraction of PTLC gave a pale orange gum, which on standing in air at room temperature changed into the pyrrolinedione **3a**.

Oxidation of 26 with Ac_2O–DMSO A solution of **26** (10 mg) in Ac_2O (1 ml) and DMSO (2 ml) was stirred at room temperature for 65 h. The reaction was quenched with ice and the mixture was stirred for a further 1 h. Extraction with AcOEt and purification of the product by chromatography in $CHCl_3$ gave **21** (4 mg), which was identical with the specimen obtained above.

Reduction of the Photo-Adduct 30 The photo-adduct **30** (981 mg) in MeOH (20 ml) was reduced with $NaBH_4$ (76 mg) under stirring at 0 °C for 15 min. Work-up of the product as described for **24** gave **31** (984 mg, 100%) as colorless needles from CH_2Cl_2–MeOH, mp 152—156 °C. IR: 3275, 1725, 1680, 1640. ^{1}H-NMR: 6.77, 6.42 (each 1H, s, ArH), 6.48 (1H, d, J=12.5 Hz, –CH=C<u>H</u>OMe), 5.77 (2H, s, OCH_2O), 4.80 (1H, s, >C<u>H</u>OH), 4.68 (1H, d, J=12.5 Hz, –C<u>H</u>=CHOMe), 3.50 (3H, s, OMe), 3.30 (3H, s, CO_2Me), 3.00 and 2.53 (each 1H, d, J=13 Hz, H_2C< on cyclobutane), 0.10 (9H, s, TMS). HRMS: Calcd for $C_{24}H_{31}NO_8Si$: 489.1817. Found: 489.1849.

7α-Hydroxy-6β-methoxycarbonyl-16,17-methylenedioxy-2,8-dioxo-Δ^3-homoerythrinan (32) A solution of TBAF (157 mg) in THF (6 ml) was injected into an argon-purged solution of **31** (200 mg) in dry THF (23 ml) at −30 °C. The mixture was stirred for 45 min at the same temperature, then gradually brought to room temperature. The mixture was diluted with CH_2Cl_2, washed with water, and concentrated to give **32** (134 mg, 85%) as colorless prisms from MeOH, mp 289—292 °C. IR: 3450, 1725, 1680, 1675. ^{1}H-NMR: 6.48, 6.45 (each 1H, s, ArH), 6.45 (1H, d, J=10 Hz, –C<u>H</u>=CHCO–), 6.10 (1H, d, J=10 Hz, –CH=C<u>H</u>CO–), 5.83 (2H, s, OCH_2O), 4.60 (1H, br s, >C<u>H</u>OH), 3.27 (3H, s, CO_2Me). *Anal.* Calcd for $C_{20}H_{19}NO_7$: C, 62.33; H, 4.97; N, 3.64. Found: C, 62.54; H, 4.90; N, 3.68.

7α-Hydroxy-6β-methoxycarbonyl-16,17-methylenedioxy-2,8-dioxo-homoerythrinan (26) The enone **32** (50 mg) in acetone (15 ml) was hydrogenated over 5% Pd–C (50 mg) for 6.5 h at room temperature. Removal of the solvent and catalyst gave **26** (44 mg, 88%), which was identical with the specimen obtained from **24**.

Methanesulfonylation of 26 A mixture of **26** (185 mg) and methanesulfonyl chloride (110 mg) in pyridine (3 ml) was stirred at room temperature for 12 h. Work-up of the product as usual gave **33** (216 mg, 97%) as colorless needles from CH_2Cl_2–MeOH, mp 258—261 °C. IR: 1745, 1725, 1690. ^{1}H-NMR: 6.58, 6.42 (each 1H, s, ArH), 5.80 (2H, s, OCH_2O), 5.68 (1H, s, >CHOMs), 3.25, 3.17 (each 3H, s, OMe, OMs). *Anal.* Calcd for $C_{21}H_{23}NO_9S$: C, 54.19; H, 4.98; N, 3.01. Found: C, 54.04; H, 4.96; N, 2.97.

6β-Methoxycarbonyl-16,17-methylenedioxy-2,8-dioxo-1,7-cyclo-homoerythrinan (34) A mixture of **33** (101 mg) and DBU (600 mg) in toluene (10 ml) was heated under reflux for 2 h. The mixture was diluted with benzene, washed with 5% HCl and water, and concentrated to give **34** (50 mg, 62%) as colorless needles from CH_2Cl_2–MeOH, mp 243—245 °C. IR: 1735, 1705, 1690. ^{1}H-NMR: 6.79, 6.47 (each 1H, s, ArH), 5.86 (2H, s, OCH_2O), 3.39 (3H, s, CO_2Me). MS: 369 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.19; N, 3.79. Found: C, 65.12; H, 5.11; N, 3.76.

Dimethoxyketone 35 A mixture of **34** (386 mg), PhSeCl (360 mg, 1.8 eq), and $BF_3 \cdot Et_2O$ (8 drops) in dry THF (40 ml) was heated under reflux for 10.5 h under an Ar atmosphere, then concentrated *in vacuo*. The residue was dissolved in MeOH (80 ml), MPC (3.41 g) was added, and the mixture was stirred for 13 h at room temperature. The precipitates that appeared were removed by filtration and the filtrate was treated with aqueous Na_2S until the solution became faintly alkaline. The resultant black precipitates were removed by filtration with the aid of Celite. The filtrate was diluted with water and extracted with $CHCl_3$, then the extract was washed with water and concentrated. The product was purified by chromatography with benzene–acetone (19 : 1) to give **35** (343 mg, 76%) as colorless prisms from benzene–hexane, mp 227.5—229 °C. IR: 1730, 1720, 1690. ^{1}H-NMR: 6.83, 6.47 (each 1H, s, ArH), 5.87 (2H, s, OCH_2O), 3.45 (3H, s, CO_2Me), 3.22, 3.18 (each 3H, s, OMe). MS: 429 (M^+). *Anal.* Calcd for $C_{22}H_{23}NO_8$: C, 61.53; H, 5.40; N, 3.26. Found: C, 61.39; H, 5.29; N, 3.34.

Dimethoxy-alcohol 36 Compound **35** (334 mg) in MeOH–THF (2 : 1, 57 ml) was reduced with $NaBH_4$ (44 mg) for 45 min at room temperature. The mixture was neutralized with 5% HCl and extracted with CH_2Cl_2. The dried extract was concentrated and the residue was purified by chromatography in benzene–acetone (1 : 1) to give **36** (321 mg, 96%) as colorless prisms from MeOH–AcOEt, mp 285—287 °C. IR: 1725, 1665. ^{1}H-NMR: 6.90, 6.54 (each 1H, s, ArH), 5.94 (2H, s, OCH_2O), 4.52 (1H, br d, J=7 Hz, C_2-H), 3.38 (3H, s, CO_2Me), 3.36, 3.22 (each 3H, s, OMe). *Anal.* Calcd for $C_{22}H_{25}NO_8$: C, 61.24; H, 5.84; N, 3.25. Found: C, 61.22; H, 5.82; N, 3.16.

Dithiocarbonate 37 A mixture of the alcohol **36** (321 mg), NaH (60% oil dispersion, 171 mg), and a catalytic amount of imidazole (15 mg) in THF (40 ml) was heated under reflux for 3 h under an Ar atmosphere. Carbon disulfide (2 ml) and iodomethane (2 ml) were added successively, and the mixture was heated for a further 30 min. The reaction mixture was poured into ice-water, adjusted to pH 7 with AcOH, and extracted with $CHCl_3$. Concentration of the dried extract and chromatography of the residue gave **37** (255 mg, 66%) as a gum from the benzene–acetone (6 : 1) eluate. ^{1}H-NMR: 6.96, 6.52 (each 1H, s, ArH), 6.14 (1H, d, J=8 Hz, C_2-H), 5.92 (2H, s, OCH_2O), 3.42, 3.38 (each 3H, s, OMe), 3.22 (3H, s, CO_2Me), 2.56 (3H, s, SMe). This was used for the following reaction without further purification.

6β-Methoxycarbonyl-16,17-methylenedioxy-2,8-dioxo-Δ^1-homoerythrinan (38) Bu_3SnH (2.2 ml) was added to a hot stirred solution of the above dithiocarbonate **37** (244 mg) and α,α-azobisisobutyronitrile (AIBN, catalytic amount) in toluene (40 ml) under an Ar atmosphere and the mixture was heated under reflux for 5 h. The cooled mixture was poured onto a silica gel column and the column was washed with benzene to remove tin compounds. Elution of the column with benzene–acetone (7 : 1) gave a gum, which was hydrolyzed with 10% HCl–acetone (1 : 1, 20 ml) at 50 °C for 2.5 h to give the conjugated ketone **38** (115 mg, 67%) as colorless plates from AcOEt–hexane, mp 220—222 °C. IR: 1730, 1695, 1685. ^{1}H-NMR: 6.71 (1H, d, J=10 Hz, C_1-H), 6.53, 6.42 (each 1H, s, ArH), 6.24 (1H, d, J=10 Hz, C_2-H), 5.90 (2H, s, OCH_2O), 3.44 (3H, s, CO_2Me). MS: 365 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_6 \cdot 1/2H_2O$: C, 63.50; H, 5.29; N, 3.70. Found: C, 63.59; H, 5.48; N, 3.52.

In some experiments, a by-product **40** (separated from **38** by repeated chromatography) was obtained in up to 8% yield, as colorless needles from EtOAc, mp 230—233 °C. IR: 1740, 1685, 1662. ^{1}H-NMR: 7.02, 6.59 (each 1H, s, ArH), 6.73 (1H, dd, J=12, 8.5 Hz, C_1-H), 6.13 (1H, d, J=12 Hz, C_2-H), 5.96 (2H, s, OCH_2O), 4.37, 3.21 (2H, ABq, J=17 Hz, C_4-H), 3.69 (3H, s, CO_2Me). MS: 365 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.19; N, 3.79. Found: C, 65.11; H, 5.38; N, 3.62.

Demethoxycarbonylation of 38 A mixture of **38** (100 mg), anhydrous $CaCl_2$ (240 mg), and 3-ethylpentane-3-thiol (0.9 ml) in dry DMSO (9 ml) was heated at 140—145 °C for 1 h. The mixture was diluted with water, acidified with HCl, and extracted with CH_2Cl_2. The product was separated by MPLC (benzene–acetone, 6 : 1) to give **39** (52 mg, 62%) and **41** (26 mg, 26%).

39: Pale yellow prisms from AcOEt, mp 192—194 °C. IR: 1710, 1680. ^{1}H-NMR: 6.70, 6.66 (each 1H, s, ArH), 6.04 (1H, br s, C_1-H), 5.92 (2H, s, OCH_2O), 4.53 (1H, m, C_{10}-H), 3.49, 3.77 (each 1H, d, J=14 Hz, C_7-H). HRMS: Calcd for $C_{18}H_{17}NO_4$: 311.1153. Found: 311.1172.

The data for **41** are given in ref. 21.

Reduction of the Enone 39 (1) With Bu_4NBH_4: Bu_4NBH_4 (194 mg) was added to a stirred solution of **39** (47 mg) in MeOH (5 ml) at 0 °C. Stirring was continued for 70 min, then the reaction was quenched with 2% HCl, and the mixture was extracted with CH_2Cl_2 to give a mixture of **43** and **44**, which was separated by MPLC ($CHCl_3$–EtOH, 24 : 1) into the β-alcohol **43** (38 mg, 80%) and the α-alcohol **44** (6 mg, 13%).

(2) With $NaBH_4$–$CeCl_3$: $NaBH_4$ (16 mg) was added to a stirred solution of **38** (48 mg) and $CeCl_3 \cdot 6H_2O$ (159 mg) in MeOH (12 ml) at 0 °C and the mixture was stirred for 1 h at the same temperature. Work-up and purification of the product gave the α-alcohol **44** (37 mg, 81%) and the β-alcohol **43** (8 mg, 16%).

The β-alcohol **43**: Colorless needles from AcOEt, mp 110—114 °C. IR: 1650. ^{1}H-NMR: 6.92 (1H, s, C_{15}-H), 6.64 (1H, s, C_{18}-H), 5.91 (2H, s, OCH_2O), 5.79 (1H, m, C_1-H), 4.41 (1H, m, C_{10}-H), 4.22 (1H, m, C_3-H), 1.89 (1H, dd, J=14, 4 Hz, C_4-H). MS: 313 (M^+). HRMS: Calcd for $C_{18}H_{19}NO_4$: 313.1315. Found: 313.1310.

The α-alcohol **44**: Gum. IR: 1675. ^{1}H-NMR: 6.72 (1H, s, C_{15}-H), 6.63 (1H, s, C_{18}-H), 5.90 (2H, s, OCH_2O), 5.72 (1H, m, C_1-H), 5.37 (1H, m, C_{10}-H), 4.74 (1H, m, C_3-H), 1.68 (1H, t, J=12 Hz, C_4-H). MS: 313 (M^+). HRMS: Calcd for $C_{18}H_{19}NO_4$: 313.1315. Found: 313.1310.

(±)-8-Oxo-schelhammericine (45) A mixture of the β-alcohol **43** (55 mg), NaH (60% oil dispersion, 152 mg), and a catalytic amount of imidazole in dry THF (20 ml) was heated under reflux for 1 h under an Ar atmosphere. Iodomethane (3 ml) and Bu_4NHSO_4 (60 mg) were added to the cooled mixture and the whole was stirred for 14 h at room temperature, then neutralized with 2% HCl, and extracted with $CHCl_3$. Purification of the product by MPLC ($CHCl_3$–acetone, 5 : 1) gave the *O*-methyl derivative **45** (25 mg, 44%) as colorless needles from AcOEt, mp 162—165 °C. IR: 1680. ^{1}H-NMR: 6.84 (1H, s, C_{15}-H), 6.58 (1H, s, C_{18}-H), 5.88 (2H, s, OCH_2O), 5.74 (1H, m, C_1-H), 4.41 (1H, m, C_{10}-H), 3.70 (1H, m, C_3-H), 2.76 (3H, s, OMe), 1.74 (1H, dd, J=14, 3 Hz, C_4-H). MS: 327 (M^+). HRMS: Calcd for $C_{19}H_{21}NO_4$: 327.1471. Found: 327.1459.

(±)-8-Oxo-3-epischelhammericine (47) A mixture of the α-alcohol **44** (40 mg), NaH (60% oil dispersion, 110 mg) and a catalytic amount of imidazole in dry THF (20 ml) was heated under reflux for 1 h under an Ar atmosphere, then methylated with iodomethane (3 ml) and Bu_4NHSO_4 (43 mg) for 5 h at room temperature. The reaction mixture was worked up as above to give the *O*-methyl derivative **47** (35 mg, 73%) as colorless prisms from AcOEt, mp 182—183 °C. IR ($CHCl_3$): 1670. ^{1}H-NMR: 6.72 (1H, s, C_{15}-H), 6.65 (1H, s, C_{18}-H), 5.91 (1H, s, OCH_2O), 5.74 (1H, m, C_1-H), 4.41 (1H, m, C_{10}-H), 1.63 (1H, t, J=12 Hz, C_4-H). MS: 327 (M^+). HRMS: Calcd for $C_{19}H_{21}NO_4$: 327.1471. Found: 327.1487.

(±)-Schelhammericine (46) A solution of AlH_3 [prepared from $LiAlH_4$ (11 mg) and $AlCl_3$ (35 mg) in dry THF–Et_2O (3 : 2, 2 ml)] was added to a solution of **45** (15.4 mg) in dry THF (2 ml), and the mixture was stirred for 1 h at room temperature. It was then basified with 28% NH_4OH and extracted with Et_2O. The organic solution was washed with water, dried over anhydrous K_2CO_3, and concentrated. The residue was purified by chromatography with $CHCl_3$–cyclohexane–Et_3N (5 : 4 : 1) to give **46** (14.5 mg, 98%) as a colorless oil. ^{1}H-NMR: 6.84 (1H, s, C_{15}-H), 6.54 (1H, s, C_{18}-H), 5.85 (2H, s, OCH_2O), 5.25 (1H, m, C_1-H), 2.73 (3H, s, OMe), 1.78 (1H, dd, J=14, 3 Hz, C_4-H). MS: 313 (M^+, 23), 282 (26), 269 (22), 268 (33), 255 (86), 254 (base peak), 178 (64), 146 (28). HRMS: Calcd for $C_{19}H_{23}NO_3$: 313.1679. Found: 313.1650. The ^{1}H-NMR spectrum was superimposable on that of (+)-schelhammericine. The IR spectrum in $CHCl_3$ and the TLC behavior were identical with those of the natural alkaloid.

(±)-3-Epischelhammericine (48) Compound **47** (15.4 mg) was reduced with AlH_3 as described above to give **48** (13.9 mg, 94%), as a solid mass from pentane, mp 91—93 °C. ^{1}H-NMR: 6.73 (1H, s, C_{15}-H), 6.63 (1H, s, C_{18}-H), 5.91 (2H, s, OCH_2O), 5.52 (1H, m, C_1-H), 3.25 (3H, s, OMe), 1.58 (1H, t, J=12 Hz, C_4-H). MS: 313 (M^+, 26), 282 (33), 255 (85), 254 (base peak), 178 (99), 165 (28), 146 (40). HRMS: Calcd for $C_{19}H_{23}NO_3$: 313.1679. Found: 313.1667. The ^{1}H-NMR spectrum was superimposable on that of (+)-3-epischelhammericine. The IR spectrum in $CHCl_3$ and the TLC behavior were identical with those of the natural alkaloid.

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