Synthesis of *Erythrina* and Related Alkaloids. XXX.[1] Photochemical Approach. (1). Synthesis of Key Intermediates to *Erythrina* Alkaloids by Intermolecular [2+2] Photocycloaddition Followed by 1,3-Shift

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A novel synthetic route to *Erythrina* alkaloids consisting in [2+2] intermolecular photocycloaddition of the isoquinolinodioxopyrroline 4 to 2-trimethylsilyloxybutadienes and the subsequent ring enlargement reaction of the trimethylsilyloxyvinylcyclobutane 5 by thermal or tetrabutylammonium fluoride (TBAF)-induced 1,3-shift was developed. The TBAF method was particularly useful, offering a good yield under mild reaction conditions. Thus, photoannulation of 4 with 1-methoxy-3-trimethylsilyloxybutadiene, followed by hydride reduction, TBAF-induced 1,3-shift, and hydrogenation gave the 7α-hydroxy-2,8-dioxoerythrinan 19 in overall 45% yield, and this product was converted, in 70% yield, into the 1,7-cycloerythrinan 24, a key intermediate for the total synthesis of *Erythrina* alkaloids.

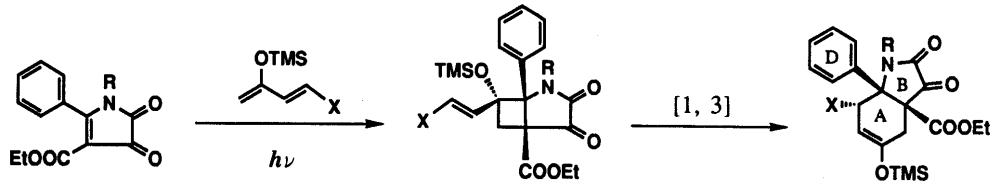
Keywords *Erythrina* alkaloid; isoquinolinodioxopyrroline; photocycloaddition; trimethylsilyloxybutadiene; vinylcyclobutane; oxyvinyl 1,3-shift; tetrabutylammonium fluoride; erythrinan

Recently, we reported[2] a new method of regio-controlled synthesis of hydroindoles (**3**) through 1,3-shift of 7-vinyl-2-azabicyclo[3.2.0]heptane-3,4-dione (**2**), which is readily available by photocycloaddition of 1*H*-pyrrole-2,3-dione (**1**) (dioxopyrroline) to butadienes.[3] Since the products (**3**) have the structure corresponding to rings A, B, and D of the erythrinan skeleton, the above synthesis implies that, when this method is applied to isoquinolinodioxopyrroline **4**, erythrinan derivatives should be obtained, providing a novel synthetic route to natural *Erythrina* alkaloids. This paper describes the results of an investigation of this approach.[4]

Results and Discussion

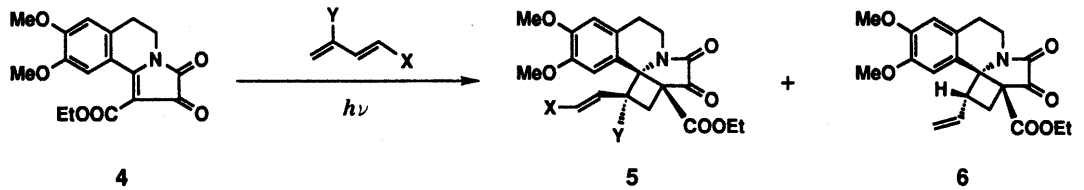
Synthesis of Erythrinan by [2+2] Photocycloaddition Followed by Thermolysis Irradiation of a solution of the isoquinolinodioxopyrroline **4** and butadiene in dimethoxyethane (DME) with >300 nm light afforded two [2+2] cycloadducts, the *exo*-adduct **5a** (16%) and the *endo*-adduct **6** (10%). The structures of **5a** and **6** including the stereochemistry of the vinyl group were elucidated by comparisons of their ^{1}H-nuclear magnetic resonance (NMR) spectra with those of known vinylcyclobutanes.[3]

Similar photoannulation of **4** with silyloxybutadienes proceeded more readily to give adducts in regio- and stereo-selective manners. Thus, 2-trimethylsilyloxybutadiene and 1-methoxy-3-trimethylsilyloxybutadiene afforded the photoadducts **5b** and **5c** in 93% and 64% yields, respectively. Their structures and stereochemistries were deduced from the spectral analogy with the known photoadduct **2** (R=H, X=H)[5] whose structure had been established by X-ray analysis; the vinyl or methoxyvinyl group was in *exo* and the trimethylsilyloxy group was in *endo* configuration.



1 **2** **3**

Chart 1



4 **5** **6**

a : X=Y=H
b : X=H, Y=OTMS
c : X=OMe, Y=OTMS

cyclobuta[1′,2′:2′,3′]pyrrolo[2,1-*a*]isoquinoline

Chart 2

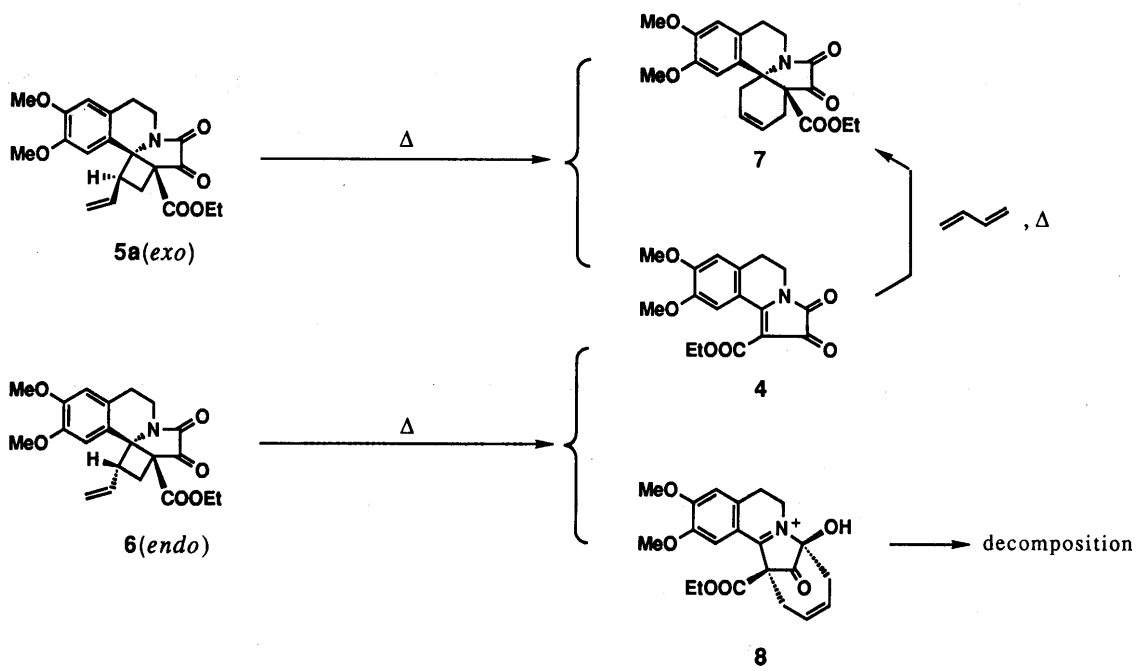


Chart 3

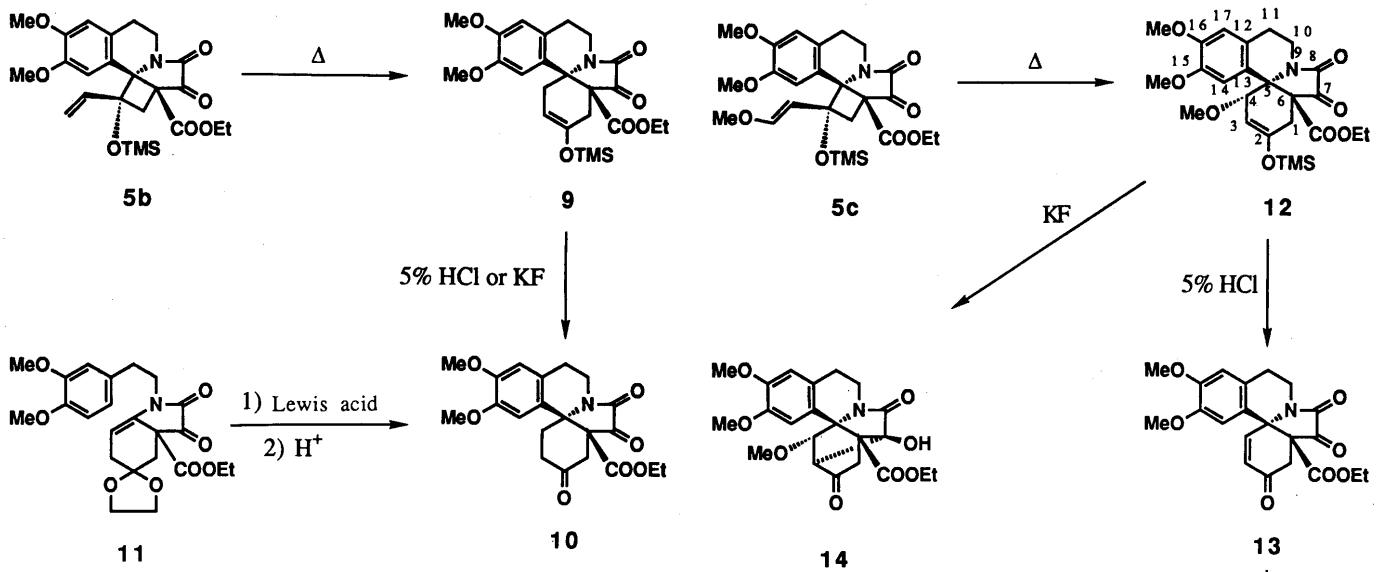


Chart 4

Chart 5

Previously we showed[6] that, on thermolysis of vinylcyclobutanes, *exo*-isomers gave the 1,3-shift products, hydroindoles, while *endo*-isomers gave Cope-type rearrangement products. Thus, heating of the *exo*-adduct **5a** in toluene at 130 °C gave the expected erythrinan **7** in 40% yield together with the cyclo-reversion product, dioxopyrroline **4** (21%). The erythrinan **7** was identical with the Diels–Alder product of **4** and butadiene.[7] In contrast to the *exo*-isomer, on a similar thermolysis of the *endo*-isomer **6**, no characterizable product was isolated except for a low yield of the cyclo-reversion product **4**. This may be due to instability of the expected Cope product **8**, which has a quarternary iminium structure.

The thermal 1,3-shift of the trimethylsilyloxy derivative **5b** occurred more readily, giving the erythrinan **9** in 63% yield under reflux in toluene. Hydrolysis of the silyloxy group in **9** with 5% hydrochloric acid or potassium fluoride gave the ketone **10** (90%), which was identical with the known trioxo-erythrinan **10** obtained from **11** by an intramolecular cyclization method,[8] thus proving the regiochemistry of the silyloxy group in **9**.

Similar thermolysis of the methoxyvinyl derivative **5c** gave the erythrinan **12** and the dioxopyrroline **4** (15%). Although **12** was not isolated in a pure state, the structure was proved by hydrolysis with boiling 5% HCl–tetrahydrofuran (THF) to the conjugated enone **13** (38% from **5c**). Catalytic hydrogenation of **13** over Pd–C gave the saturated ketone, which was identical with **10**. Treatment of **12** with potassium fluoride, however, gave the ketol **14**

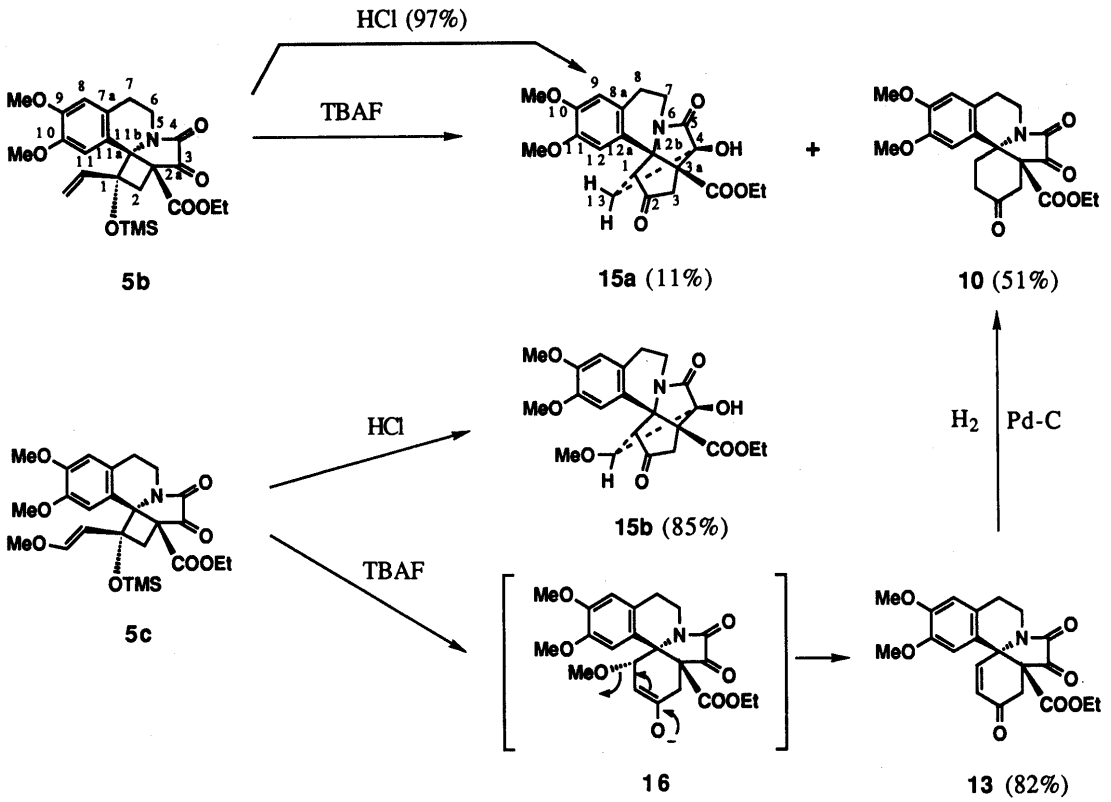


Chart 6

(48% from **5c**). This is the product derived from intramolecular aldol reaction of the intermediate enolate to the C_7 carbonyl group. A similar intramolecular aldol reaction of 2,7,8-trioxoerythrinans to 3,7-cycloerythrinans under Lewis acid catalysis was reported previously.[8a,9]

The above evidence shows that the vinylsilyloxycyclobutanes **5b** and **5c** readily undergo the expected thermal 1,3-shift to yield erythrinans. However, the reaction was always accompanied by the cyclo-reversion product, which lowered the yield of the desired erythrinans. This side reaction was avoided by adopting an anionic 1,3-shift method as described in the next section.

Construction of Erythrinan by Tetrabutylammonium Fluoride Induced Anionic 1,3-Shift of the Photoadduct In a previous paper,[2] we showed that tetrabutylammonium fluoride (TBAF) dramatically accelerated the oxyvinyl 1,3-shift, and the reaction proceeded under extremely mild conditions such as $-30\,°C$. This modified method was successfully applied for construction of the erythrinan skeleton.

Treatment of **5b** with TBAF in THF at $-30\,°C$ for 5 min yielded two products, the expected ketone **10** (51%) and the ketol **15a** (11%). The ketol **15a** was identical with the product obtained by treatment of **5b** with hydrochloric acid. This reaction was discussed in detail in a previous paper[2] and proved to proceed as follows: 1) hydrolysis of the trimethylsilyloxy group to an alcohol, 2) epimerization at C_1, and 3) Prins-type cyclization of the vinyl group to the C_3 carbonyl followed by 1,2-shift of the C_1–C_{11b} bond.

This undesirable side reaction could be suppressed by reducing the electron density at the vinyl terminus which participates in Prins-type cyclization. In accord with our expectation, the methoxyvinyl derivative **5c**, on similar treatment with TBAF, gave exclusively the enone **13** (82%), *i.e.*, the product due to 1,3-shift followed by β-elimination of the methoxy group from the intermediary enolate **16**. On the other hand, when **5c** was treated with 5% HCl–THF, the ketol **15b** was produced in 85% yield.

Another method for preventing this side reaction is prior reduction of the C_3 carbonyl to an alcohol group. Reduction of **5b** and **5c** with sodium borohydride gave the alcohols **17a** (83%) and **17b** (90%), respectively. The configuration of the newly formed alcohol was assigned as *endo* based on the fact that hydride reduction of azabicyclo[3.2.0]heptane-3,4-diones always takes place from the convex face[10] (for this configuration, see below).

The alcohol **17a**, on treatment with TBAF at $-30\,°C$, suffered only desilylation to yield the hydroxyvinyl derivative **18** (81%). But the expected 1,3-shift occurred when the reaction temperature was elevated to $20\,°C$, to give the keto-alcohol **19** in 66% yield. The product **19** was found to be isomeric to the 6β-ethoxycarbonyl-7β-hydroxy-2,8-dioxo-*cis*-erythrinan **20**[8b] and was oxidized with dimethyl sulfoxide (DMSO)–acetic anhydride to give the trioxo derivative **10**, clarifying the structure and the stereochemistry of the C_7-OH group (thus C_3-OH in **17**).

The methoxyvinyl derivative **17b** gave, on a similar treatment, the enone **21** in 81% yield, as a result of β-elimination of the methoxy group from the expected 1,3-shift product **22**. Catalytic hydrogenation of **21** gave the saturated ketone **19** in quantitative yield. Overall yield of **19** from the dioxopyrroline **4** in four steps (photoannulation by 1-methoxy-3-trimethylsilyloxybutadiene, hydride reduction, TBAF-induced 1,3-shift, and hydrogenation) was 45%, so that this method is the most appropriate for the synthesis of erythrinans.

Synthesis of Key Intermediates to *Erythrina* Alkaloids The trioxo derivative **10**, on treatment with ethylene

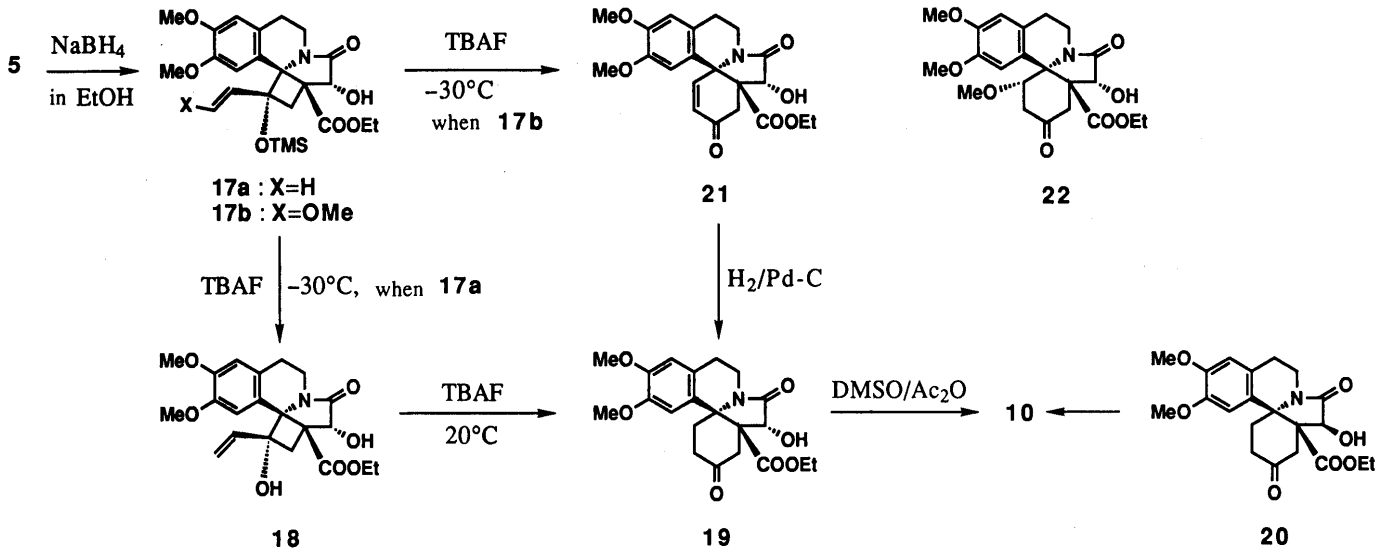


Chart 7

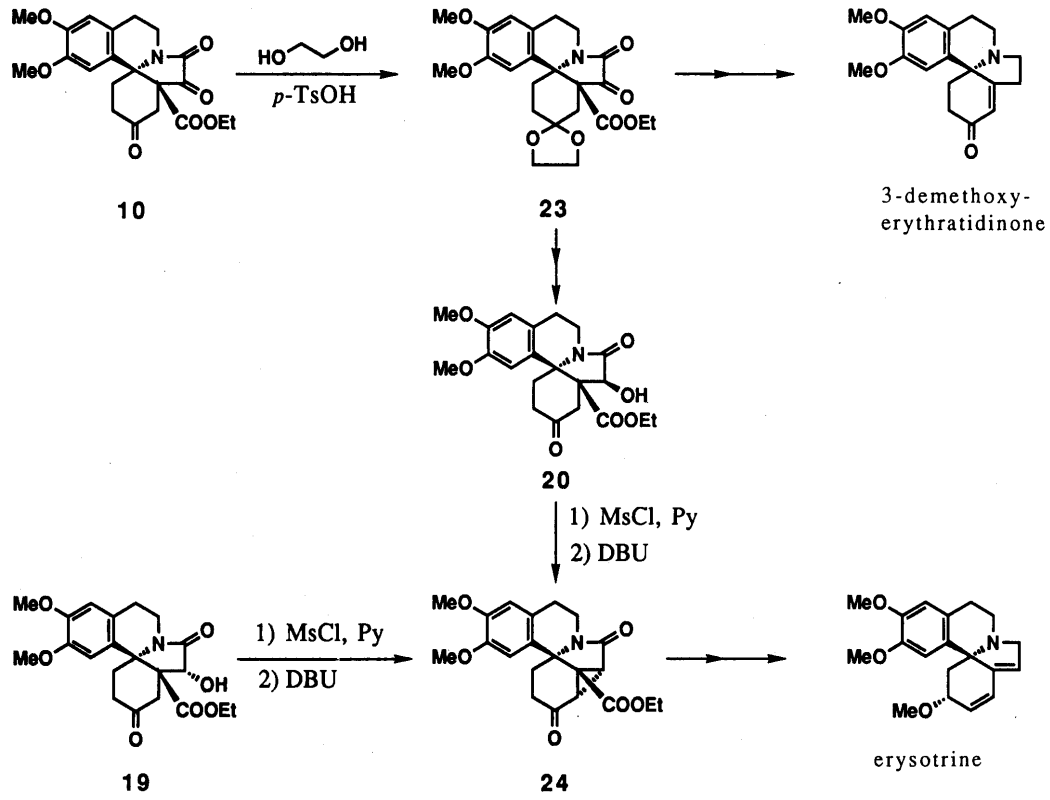


Chart 8

glycol and a catalytic amount of *p*-toluenesulfonic acid, gave the monoethylene acetal **23**. Conversion of **23** into 3-demethoxyerythratidinone, an alkaloid of *Erythrina lithsoperma*, has already been described.[8b,11]

Like the 7β-hydroxy derivative **20**,[12] the 7α-hydroxy isomer **19** smoothly gave, on methanesulfonylation followed by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), the 1,7-cycloerythrinan **24**,[12] which is a key intermediate in synthesis of natural *Erythrina* alkaloids of dienol type such as erysotrine.[13]

Hence, the transformations described in this paper constitute a new method of total synthesis of *Erythrina* alkaloids, in a formal sense.

The results described above demonstrate that the thermal or TBAF-induced 1,3-shift, when coupled with photoannulation of the dioxopyrroline **4** by activated butadienes provides an efficient method of erythrinan synthesis. In particular, the TBAF method offers a good yield under mild reaction conditions. Erythrinans prepared by this photochemical route have different regiochemistry when compared to those obtained by Diels–Alder reaction of **4** with the same substituted butadienes.[7]

Although the erythrinans obtained by this photochemical route are also preparable by the intramolecular cyclization route,[8b] the method can be successfully applied to compounds for which intramolecular cyclization did not

give satisfactory results. Examples of such cases will be presented in a subsequent paper.

Experimental

Unless otherwise noted, the following procedures were adopted. All melting points are uncorrected. Infrared (IR) spectra were measured as Nujol mulls and are given in cm^{-1}. NMR spectra were taken on a JEOL JNM-FX 100 (^{1}H-NMR, 100 MHz; ^{13}C-NMR, 25 MHz) or a JEOL JNM-GX 270 (^{13}C-NMR, 67.5 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard and the chemical shifts are given in δ values. The following abbreviations are used; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. High-resolution mass spectra (HRMS) were determined with a JEOL JMS-D 300 spectrometer at 30 eV by using a direct inlet system. Ultraviolet (UV) spectra were measured in EtOH and are given in λ_{max} nm (ε). Column chromatography was carried out with silica gel (Wakogel C-200). Medium-pressure liquid chromatography (MPLC) was performed on a Kusano CIG prepacked silica gel column. All organic extracts were dried over anhydrous sodium sulfate before concentration. Identities were confirmed by comparisons of thin layer chromatography (TLC) behavior and IR and NMR spectra.

Photocycloaddition of the Isoquinolinodioxopyrroline 4 to Butadienes A solution of **4**[7b] (1.0 g) and butadiene (large excess) in acetone (300 ml) was irradiated under a 300 W high-pressure mercury lamp with a Pyrex filter at 0 °C for 60 min with stirring. After concentration of the solvent *in vacuo*, the residue was filtered through a short column of Al_2O_3 using CH_2Cl_2 as an eluent. The eluate was separated by MPLC (AcOEt : hexane = 1 : 1) to give the *endo*-adduct **6** (110 mg, 10%) and the *exo*-adduct **5a** (191 mg, 16%).

exo-Adduct **5a**: Colorless prisms from ether–acetone, mp 163.5—165 °C. IR: 1760, 1725, 1705, 1665. ^{1}H-NMR: 0.75 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.44 (1H, dd, J = 7,14 Hz, C_2-H), 2.6—3.5 (5H, m), 3.7—4.0 (2H, m, $OC\underline{H}_2CH_3$), 3.82, 3.87 (each 3H, s, OMe), 4.3—4.7 (1H, m, C_6-H), 4.9—5.8 (3H, m, vinylic H), 6.56, 6.63 (each 1H, s, Ar-H). ^{13}C-NMR: 13.6 (q), 25.9 (t), 28.2 (t), 37.0 (t), 52.5 (d), 55.9 (q × 2), 57.5 (s), 58.0 (s), 61.9 (t), 109.6 (d), 111.6 (d), 117.5 (t), 121.3 (s), 126.8 (s), 136.1 (d), 147.2 (s), 148.0 (s), 157.7 (s), 166.2 (s), 195.9 (s). HRMS: m/z (M^+) Calcd for $C_{21}H_{23}NO_6$: 385.1524. Found: 385.1521. *Anal.* Calcd for $C_{21}H_{23}NO_6$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.22; H, 6.07; N, 3.69.

endo-Adduct **6**: Colorless prisms from ether–acetone, mp 145—147 °C. IR: 1760, 1730, 1710, 1610. ^{1}H-NMR: 0.76 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.11 (1H, dd, J = 5, 13 Hz, C_2-H), 2.5—3.7 (5H, m), 3.87 (2H, q, J = 7 Hz, $OC\underline{H}_2CH_3$), 3.87, 3.89 (each 3H, s, OMe), 4.3—4.7 (1H, m, C_6-H), 4.9—5.9 (3H, m, vinylic H), 6.60, 6.77 (each 1H, s, Ar-H). ^{13}C-NMR: 13.6 (q), 25.4 (t), 28.4 (t), 38.6 (t), 50.1 (d), 56.0 (q), 56.1 (q), 57.9 (s), 61.9 (t), 66.5 (s), 108.1 (d), 111.6 (d), 119.5 (t), 125.5 (s), 126.6 (s), 132.9 (d), 148.4 (s), 149.2 (s), 159.0 (s), 166.5 (s), 195.1 (s). HRMS: m/z (M^+) Calcd for $C_{21}H_{23}NO_6$: 385.1524. Found: 385.1513. *Anal.* Calcd for $C_{21}H_{23}NO_6$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.18; H, 6.05; N, 3.71.

Photocycloaddition of the Dioxopyrroline 4 to Activated Butadienes 1) A solution of **4** (1.0 g) and 2-trimethylsilyloxy-1,3-butadiene (2 mol eq) in acetone (300 ml) was irradiated under a 300 W high-pressure mercury lamp with a Pyrex filter at 0 °C for 60 min with stirring. After evaporation of the solvent *in vacuo* below 40 °C, the residue was purified by filtering it through a short column of SiO_2 using bezene as an eluent, followed by crystallization of the product from ether–hexane to give **5b** (1.33 g, 93%) as colorless prisms, mp 122—124 °C. IR: 1770, 1725. ^{1}H-NMR: 0.06 (9H, s, $SiMe_3$), 0.77 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.23, 3.50 (each 1H, d, J = 14 Hz, C_2-H), 2.5—3.4 (3H, m), 3.78, 3.86 (each 3H, s, OMe), 3.8—4.0 (2H, m, $OC\underline{H}_2CH_3$), 4.2—4.6 (1H, m, C_6-H), 5.1—5.6 (3H, m, vinylic H), 6.49, 6.62 (each 1H, s, Ar-H). ^{13}C-NMR: 1.6 (q × 3), 13.7 (q), 27.7 (t), 36.0 (t), 37.8 (t), 55.8 (q × 2), 55.8 (s), 61.9 (t), 71.3 (t), 83.3 (s), 110.2 (d), 111.6 (d), 118.0 (t), 120.6 (s), 127.2 (s), 138.3 (d), 147.0 (s), 148.8 (s), 160.1 (s), 166.3 (s), 194.8 (s). HRMS: m/z (M^+) Calcd for $C_{24}H_{31}NO_7Si$: 473.1868. Found: 473.1865.

2) A solution of **4** (1.0 g) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (12 mol eq) in dimethoxyethane (300 ml) was irradiated at 0 °C for 1 h as described above. The product in CH_2Cl_2 was chromatographed over Florisil to give **5c** (966 mg, 64%) as colorless prisms from ether–hexane, mp 135—136 °C (dec.). IR: 1760, 1730, 1710, 1665. ^{1}H-NMR: 0.06 (9H, s, $SiMe_3$), 0.76 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.28, 3.36 (each 1H, d, J = 13 Hz, C_2-H), 2.5—3.3 (3H, m), 3.33, 3.79, 3.89 (each 3H, s, OMe), 3.5—4.1 (2H, m, $OC\underline{H}_2CH_3$), 4.3—4.6 (1H, m, C_6-H), 4.34, 6.52 (each 1H, d, J = 13 Hz, olefinic H), 6.50, 6.63 (each 1H, s, Ar-H). ^{13}C-NMR: 1.8 (q × 3), 13.7 (q), 27.8 (t), 37.8 (t × 2), 56.0 (q × 2), 56.2 (s), 61.8 (t), 71.4 (t), 81.7 (s), 104.4 (d), 110.5 (d), 111.5 (d), 121.1 (s), 127.3 (s), 147.0 (s), 148.7 (s), 151.0 (d), 162.0 (s), 166.3 (s), 194.9 (s). HRMS: m/z (M^+) Calcd for $C_{25}H_{33}NO_8Si$: 503.1975. Found: 503.1990.

Thermal Rearrangement of the *exo*-Adduct 5a A solution of **5a** (50 mg) in anhydrous toluene (5 ml) was heated at 130 °C for 19 h in a sealed tube with stirring. After concentration of the reaction mixture, the residue was passed through a short column of Al_2O_3 using CH_2Cl_2 as an eluent. The eluate was subjected to MPLC with AcOEt–hexane (1 : 1) to afford **7** (20 mg, 40%) as colorless prisms from MeOH, mp 175—176 °C (lit. 175—176 °C)[7] and **4** (9 mg, 21%).

Thermal Rearrangement of the *endo*-Adduct 6 A solution of **6** (40 mg) in anhydrous toluene (5 ml) was heated at 130 °C for 8 h in a sealed tube with stirring. After concentration of the mixture *in vacuo*, the residue was passed through a short column of Al_2O_3 using CH_2Cl_2 as an eluent. The product showed many spots on TLC. The dioxopyrroline **4** (2 mg, 6%) was isolated from the mixture by chromatography.

Thermal Rearrangement of 5b A solution of **5b** (500 mg) in anhydrous toluene (20 ml) was heated under reflux for 3 h with stirring. After concentration of the mixture to dryness *in vacuo*, the residue was purified by chromatography on SiO_2 with CH_2Cl_2. Crystallizations of the eluate from ether afforded **9** (315 mg, 63%) as colorless prisms, mp 158—160 °C. IR: 1765, 1740, 1705, 1645. ^{1}H-NMR: 0.20 (9H, s, $SiMe_3$), 0.66 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.5—3.9 (7H, m), 3.61 (2H, q, J = 7 Hz, $OC\underline{H}_2CH_3$), 3.86 (6H, s, MeO × 2), 4.5—4.7 (2H, m, C_{10}-H and olefinic H), 6.58, 6.64 (each 1H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{24}H_{31}NO_7Si$: 473.1867. Found: 473.1865.

The Ketone (10) A mixture of **9** (315 mg) and 5% HCl–THF (1 : 1) (20 ml) was stirred at room temperature for 1 h. The reaction mixture was diluted with $CHCl_3$, then washed with water. Crystallizations of the product from $CHCl_3$–MeOH gave **10** (230 mg, 86%) as colorless prisms, mp 283—284 °C (lit. 282—283 °C).[8]

Intramolecular Aldol Condensation Product (14) A solution of **5c** (300 mg) in anhydrous toluene (18 ml) was heated under reflux for 3 h with stirring. Concentration of the mixture *in vacuo* and trituration of the residue with ether precipitated **4** (30 mg, 15%). The filtrate in THF (10 ml) was treated with KF (200 mg) under stirring at room temperature for 1.5 d. The mixture was diluted with CH_2Cl_2, washed with water, and concentrated. Crystallizations of the product from ether–CH_2Cl_2 gave **14** (112 mg, 48%) as colorless prisms, mp 196—198 °C. IR: 3200, 1760, 1710, 1685. ^{1}H-NMR: 0.94 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.6—3.4 (6H, m), 3.24 (3H, s, C_4-OMe), 3.7—4.5 (4H, m), 3.89, 3.91 (each 3H, s, $C_{15,16}$-OMe), 6.68, 6.77 (each 1H, s, Ar-H). ^{13}C-NMR ($CDCl_3$–DMSO-d_6): 13.6 (q), 28.3 (t), 37.3 (t × 2), 55.9 (q), 56.7 (q), 58.6 (q), 60.6 (t), 61.5 (d), 68.4 (s), 70.0 (s), 86.1 (d), 87.7 (s), 109.4 (d), 112.1 (d), 122.1 (s), 128.8 (s), 148.3 (s), 149.1 (s), 167.3 (s), 168.4 (s), 205.3 (s). HRMS: m/z (M^+) Calcd for $C_{22}H_{25}NO_8$: 431.1577. Found: 431.1569. *Anal.* Calcd for $C_{22}H_{25}NO_8$: C, 61.24; H, 5.84; N, 3.25. Found: C, 60.98; H, 5.79; N, 3.23.

The Enone (13) A solution of **5c** (200 mg) in anhydrous toluene (10 ml) was heated under reflux for 3h with stirring. The reaction mixture was concentrated to dryness *in vacuo*. The residue in 5% HCl–THF (1 : 1) (10 ml) was heated under reflux for 1 h. The mixture was extracted with $CHCl_3$ and the extract was washed with water, and concentrated. Crystallization of the product from ether–acetone gave **13** (60 mg, 38%) as colorless prisms, mp 170—172 °C. IR: 1765, 1730, 1710, 1680. ^{1}H-NMR: 0.89 (3H, t, J = 7 Hz, $OCH_2C\underline{H}_3$), 2.6—3.7 (5H, m), 3.81 (2H, q, J = 7 Hz, $OC\underline{H}_2CH_3$), 3.82, 3.88 (each 3H, s, OMe), 4.5—4.8 (1H, m, C_{10}-H), 6.06, 6.80 (each 1H, d, J = 10 Hz, olefinic H), 6.53, 6.67 (each 1H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{21}H_{21}NO_7$: 399.1317. Found: 399.1342. *Anal.* Calcd for $C_{21}H_{21}NO_7$: C, 63.15; H, 5.30; N, 3.51. Found: C, 62.97; H, 5.41; N, 3.53.

Catalytic Hydrogenation of the Enone 13 The enone **13** (50 mg) in acetone (20 ml) was hydrogenated over 5% Pd–C for 2 h to give the saturated ketone (48 mg, 96%), which was identical with compound **10** described above.

TBAF-Induced 1,3-Shift of 5 1) A 1.0 M TBAF solution in THF (1.2 mol eq) was injected into an argon-purged solution of **5b** (100 mg) in anhydrous THF (10 ml) at −30 °C. The mixture was stirred for 5 min at the same temperature, then diluted with CH_2Cl_2, and washed with water. Evaporation of the solvent gave a crystalline residue, which was purified by crystallizations from CH_2Cl_2–MeOH to give **10** (43 mg, 51%) and **15a** (9 mg, 11%) as colorless prisms, mp 212—214 °C (see below).

2) The reaction of **5c** (100 mg) was carried out for 10 min as described above. Chromatography of the product over a short column of SiO_2 with $CHCl_3$ and crystallization of the eluate from AcOEt gave **13** (68 mg, 82%).

Treatment of the Photoadduct 5 with Hydrochloric Acid (General Procedure) A solution of **5** (100 mg) in 5% HCl–THF (1 : 1) (5—10 ml) was stirred at room temperature for 1—3 h. The reaction mixture was extracted with CH_2Cl_2. After evaporation of the solvent, the residue was purified by crystallizations from an appropriate solvent.

d,l-Ethyl(1*R**,3a*R**,4*S**,12b*R**)-4-hydroxy-10,11-dimethoxy-2,5-dioxo-1,2,3,3a,4,5,7,8-octahydro-1,4-methano-6-azapentaleno[6a,1-*a*]isoquinoline-3a-carboxylate **15a**: Yield, 82 mg, 97%. Colorless prisms from ether–MeOH, mp 212—215 °C. IR: 3340, 1750, 1730, 1705. ^{1}H-NMR: 1.01 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 1.89 (1H, d, J=14 Hz, C_{13}-H), 2.41 (1H, dd, J=7, 14 Hz, C_{13}-H), 2.5—4.4 (9H, m), 3.80, 3.87 (each 3H, s, OMe), 6.67, 6.69 (each 1H, s, Ar-H). ^{13}C-NMR (270 MHz, $CDCl_3$–DMSO-d_6): 13.8 (q), 29.4 (t), 36.3 (t), 36.7 (t), 37.1 (t), 55.9 (q × 2), 59.8 (d), 61.4 (t), 67.8 (s), 70.5 (s), 83.1 (s), 108.6 (d), 112.2 (d), 121.6 (s), 129.4 (s), 147.9 (s), 148.8 (s), 168.0 (s), 174.0 (s), 209.6 (s). HRMS: m/z (M^+) Calcd for $C_{21}H_{23}NO_7$: 401.1475. Found: 401.1475. *Anal.* Calcd for $C_{21}H_{23}NO_7$: C, 62.83; H, 5.78; N, 3.49. Found: C, 62.71; H, 5.75; N, 3.52.

d,l-Ethyl(1*R**,3a*R**,4*S**,12b*R**,13*S**)-4-hydroxy-10,11,13-trimethoxy-2,5-dioxo-1,2,3,3a,4,5,7,8-octahydro-1,4-methano-6-azapentaleno[6a,1-*a*]isoquinoline-3a-carboxylate **15b**: Yield, 73 mg, 85%. Colorless prisms from AcOEt–ether, mp 212—213 °C. IR: 3350, 1745, 1725, 1705. ^{1}H-NMR: 1.01 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.5—4.3 (10H, m), 3.47, 3.79, 3.87 (each 3H, s, OMe), 3.75 (1H, s, C_{13}-H), 6.63, 6.67 (each 1H, s, Ar-H). ^{13}C-NMR (270 MHz, $CDCl_3$–DMSO-d_6): 13.8 (q), 29.3 (t) 36.6 (t), 37.8 (t), 55.9 (q × 2), 59.1 (q), 61.5 (t), 65.9 (s), 69.7 (s), 69.9 (s), 85.1 (d), 89.2 (s), 108.6 (d), 112.2 (d), 121.4 (s), 129.5 (s), 147.8 (s), 148.8 (s), 167.5 (s), 169.9 (s), 207.8 (s). HRMS: m/z (M^+) Calcd for $C_{22}H_{25}NO_8$: 431.1578. Found: 431.1560. *Anal.* Calcd for $C_{22}H_{25}NO_8$: C, 61.24; H, 5.84; N, 3.25. Found: C, 61.02; H, 5.77; N, 3.26.

$NaBH_4$ Reduction of the Photoadduct 5 (General Procedure) $NaBH_4$ (5 mol eq) was added to a stirred and ice-cooled solution of **5** in EtOH. After completion of the reaction, the mixture was extracted with CH_2Cl_2. Evaporation of the solvent gave a crude product, which was purified by crystallizations from an appropriate solvent.

17a: The reaction of **5b** (200 mg) was carried out in EtOH (50 ml) for 11 min to give **17a** (167 mg, 83%) as colorless prisms from ether–acetone, mp 163—165 °C (dec.). IR: 3240, 1730, 1680. ^{1}H-NMR: 0.09 (9H, s, $SiMe_3$), 0.99 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.61, 3.27 (each 1H, d, J=14 Hz, C_2-H), 2.5—4.6 (7H, m), 3.76, 3.84 (each 3H, s, OMe), 4.89 (1H, s, C_3-H), 5.2—5.8 (3H, m, olefinic H), 6.52, 6.55 (each 1H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{24}H_{33}NO_7Si$: 475.2025. Found: 475.2045.

17b: The reaction of **5c** (453 mg) was carried out in EtOH (100 ml) for 7 min to give **17b** (377 mg, 90%) as colorless prisms from MeOH, mp 186—188 °C (dec.). IR: 3240, 1730, 1680. ^{1}H-NMR: 0.09 (9H, s, $SiMe_3$), 1.00 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.4—4.5 (7H, m), 2.62, 3.13 (each 1H, d, J=14 Hz, C_2-H), 3.42, 3.76, 3.85 (each 3H, s, OMe), 4.42, 6.66 (each 1H, d, J=13 Hz, olefinic H), 4.87 (1H, s, C_3-H), 6.55 (2H, br s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{25}H_{35}NO_8Si$: 473.1870. Found: 473.1877.

Treatment of 17a with TBAF 1) A 1.0 M solution of TBAF in THF (253 μl, 1.2 mol eq) was injected into an argon-purged and stirred solution of **17a** (100 mg) in anhydrous THF (10 ml) at −30 °C. The mixture was stirred for 1 h at the same temperature and extracted with CH_2Cl_2. After removal of the solvent, the residue was purified by filtration through a short column of SiO_2 using CH_2Cl_2 as an eluent, followed by crystallization of the product from ether–acetone to afford **18** (69 mg, 81%), mp 143—144 °C (dec.), as colorless prisms. IR: 3350, 3240, 1720, 1690. ^{1}H-NMR: 0.90 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.4—4.7 (4H, m), 2.63, 3.26 (each 1H, d, J=14 Hz, C_2-H), 3.81, 3.84 (each 3H, s, OMe), 3.96 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.83 (1H, s, C_3-H), 5.1—5.9 (3H, m, olefinic H), 6.57, 6.64 (each 1H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{21}H_{25}NO_7$: 403.1632. Found: 403.1633. *Anal.* Calcd for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.28; H, 6.26; N, 3.50.

2) A 1.0 M solution of TBAF in THF (253 μl, 1.2 mol eq) was injected into an argon-purged and stirred solution of **17a** (100 mg) in anhydrous THF (10 ml) at −30 °C. The reaction mixture was stirred at room temperature for 8 h and extracted with CH_2Cl_2. Concentration of the extract gave a residue, which was crystallized from ether–acetone to give **19** (56 mg, 66%), mp 236—239 °C, as colorless prisms. IR: 3425, 1730, 1675. ^{1}H-NMR: 0.73 (3H, dt, J=1, 7 Hz, $OCH_2C\underline{H}_3$), 1.9—4.6 (12H, m), 3.84, 3.85 (each 3H, s, OMe), 4.52 (1H, d, J=6 Hz, C_7-H), 5.79 (1H, d, J=6 Hz, O$\underline{H}$), 6.56, 6.61 (each 1H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{21}H_{25}NO_7$: 403.1632. Found: 403.1635. *Anal.* Calcd for $C_{21}H_{25}NO_7$: C, 62.52; H, 6.25; N, 3.47. Found: C, 62.39; H, 6.33; N, 3.61.

Oxidation of 19 with Ac_2O–DMSO A solution of **19** (44 mg) in Ac_2O (102 mg) and anhydrous DMSO (3 ml) was stirred at room temperature for 16 h. The reaction mixture was diluted with water and the resulting precipitates were collected by filtration. Recrystallization from CH_2Cl_2–MeOH gave **10** (32 mg, 73%).

Treatment of the Alcohol 17b with TBAF A 1.0 M solution of TBAF in THF (238 μl, 1.2 mol eq) was injected into an argon-purged and stirred solution of **17b** (100 mg) in anhydrous THF (10 ml), at −30 °C. The resulting mixture was stirred for 1 h at the same temperature and extracted with CH_2Cl_2. Concentration of the extract and crystallization of the product from MeOH gave the enone **21** (64 mg, 81%), mp 283—284 °C, as colorless prisms. IR: 3100, 1730, 1690. ^{1}H-NMR: 0.86 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 2.5—3.6 (5H, m), 3.72 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 3.81, 3.85 (each 3H, s, OMe), 4.34 (1H, d, J=5 Hz, C_7-H), 5.33 (1H, d, J=5 Hz, O$\underline{H}$), 6.10, 6.64 (each 1H, d, J=10 Hz, olefinic H), 6.59 (2H, s, Ar-H). HRMS: m/z (M^+) Calcd for $C_{21}H_{23}NO_7$: 401.1475. Found: 401.1490. *Anal.* Calcd for $C_{21}H_{23}NO_7$: C, 62.83; H, 5.78; N, 3.49. Found: C, 62.75; H, 5.79; N, 3.61.

Catalytic Hydrogenation of 21 The enone **21** (100 mg) in acetone (30 ml) was hydrogenated over 5% Pd–C for 2 h at room temperature and worked up as usual. Crystallization of the product from ether–acetone gave **19** (98 mg, 98%).

The Ethyleneacetal (23) A mixture of compound **10** (100 mg), ethyleneglycol (1 ml), *p*-toluenesulfonic acid (20 mg), and anhydrous Na_2SO_4 (large excess) in benzene (20 ml) was heated under reflux for 3 h with stirring, then filtered. The cooled filtrate was washed with aqueous $NaHCO_3$ and water, dried, and concentrated to give **23** (95 mg, 86%) as colorless needles from ether, mp 184—186 °C (lit. 185—186 °C).[8b]

The 1,7-Cyclo-*cis*-erythrinan (24) A mixture of compound **19** (30 mg) and methanesulfonyl chloride (15 mg) in pyridine (3 ml) was stirred at room temperature for 1 h. The mixture was poured into water and extracted with CH_2Cl_2. The crude mesylate obtained by evaporation of the solvent from the extract was dissolved in toluene (5 ml) and heated with DBU (200 mg) under reflux for 2 h. The mixture was diluted with benzene, washed with 1 N HCl and water, dried, and concentrated to give **24** (20 mg, 70%), as colorless prisms from MeOH, mp 183—184 °C. This product was identical with the 1,7-cycloerythrinan **24** (mp 183—184 °C) obtained from the 7β-hydroxy compound **20**.[12]

References and Notes

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