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A Novel Conversion of Dibenzazecines into Homoerythrina Compounds: Synthesis of *cis*-16,17-Dimethoxyhomoerythrinan-3-one

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Two dibenzazecine derivatives (**8** and **9**) were readily prepared as a mixture by a photochemical reaction of the bromophenolic compound (**6**). Reduction of the mixture (**8** and **9**) with diborane followed by column chromatography on silica gel gave the secondary amine (**11**), which was converted into the diene derivative (**12**) by Birch reduction. Treatment of **12** with 5% hydrochloric acid, followed by *O*-methylation with diazomethane provided the homoerythrina base (**1**) in 21% yield.

On the other hand, the base (**1**) was also prepared *via* Birch reduction of the amide (**9**). The mixture of the amides (**8** and **9**) was reduced directly with sodium in liquid ammonia and subjected to fractional crystallization to yield **13**. On treatment with 5% hydrochloric acid, **13** produced the homoerythrina derivative (**14**), which was methylated with diazomethane to afford **15**. Finally, the homoerythrina base (**1**) was obtained by reduction of the amide group in **15**.

Keywords——homoerythrina base; dibenzazecine base; photochemical reaction; Birch reduction; acid cyclization; *cis*-16,17-dimethoxyhomoerythrinan-3-one

A series of homoerythrina alkaloids has been found[1] in species of the plant genera *Schelhammera* (Liliaceae), *Cephalotaxus* (Cephalotaxaceae), and *Phelline* (Phellinaceae). The homoerythrina alkaloids are proposed[2] to originate from a dibenzazecine alkaloid, 3,12-dihydroxy-2,13-dimethoxy-5,6,7,8,9,10-hexahydrodibenz[*d*,*f*]azecine, through *in vivo* phenolic coupling according to a sequence of transformations analogous to the biosynthesis of the erythrina alkaloids. This dibenzazecine base was also transformed in considerable yield[3] into the homoerythrina alkaloid by oxidation with potassium ferricyanide. Recently, we described[4] the efficient formation of the dibenzazecine skeleton by means of a photochemical reaction of *N*-(6-bromo-3,4-methylenedioxyphenyl)-3-(3-hydroxy-4-methoxyphenethyl)-propionamide, and further achieved the synthesis of the naturally occurring dibenzazecine alkaloid dysazecine, which was isolated from *Dysoxylum lenticellare* (Meliaceae) by Leary *et al.*[5]

We have now found[6,7] a novel synthesis of the homoerythrina compounds *via* Birch reduction of the readily available dibenzazecine derivatives (**9** and **11**), followed by acid treatment of the dienes (**12** and **13**), and we describe here the synthesis of the homoerythrina base *cis*-16,17-dimethoxyhomoerythrinan-3-one (**1**) in detail.

Synthesis

Our synthetic approach to the homoerythrina base (**1**) was initiated by condensation of 3-(3-benzyloxy-4-methoxyphenyl)propylamine (**3**)[8] and 6-bromo-4-methoxyphenylacetic acid (**4**)[9] in decalin, giving the corresponding amide (**5**) in 73% yield. Debenzylation of **5** with a mixture of conc. hydrochloric acid and ethanol afforded the bromophenolic compound (**6**) in 84% yield. Irradiation of **6** in methanol in the presence of sodium hydroxide with a 100 W high-pressure mercury lamp at room temperature for 3 h led to the formation of three

products (**7**, **8**, and **9**), which were chromatographed on silica gel using a mixture of chloroform and acetone (9 : 1) as the eluent. The structures of these substances (**7**, **8**, and **9**) were assigned on the basis of spectral and chemical studies.

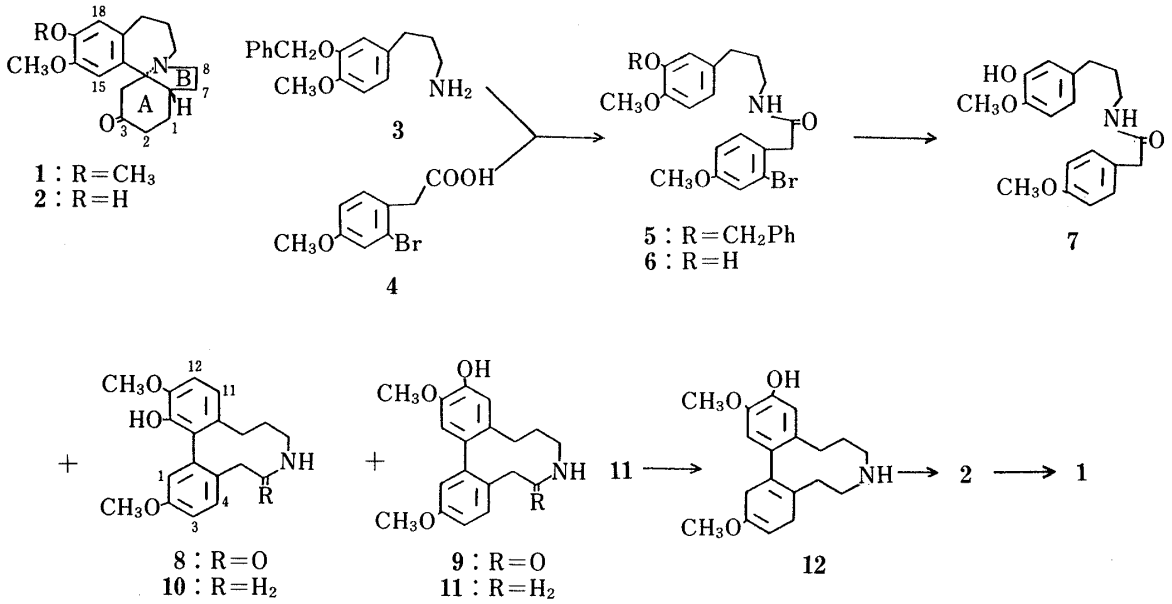
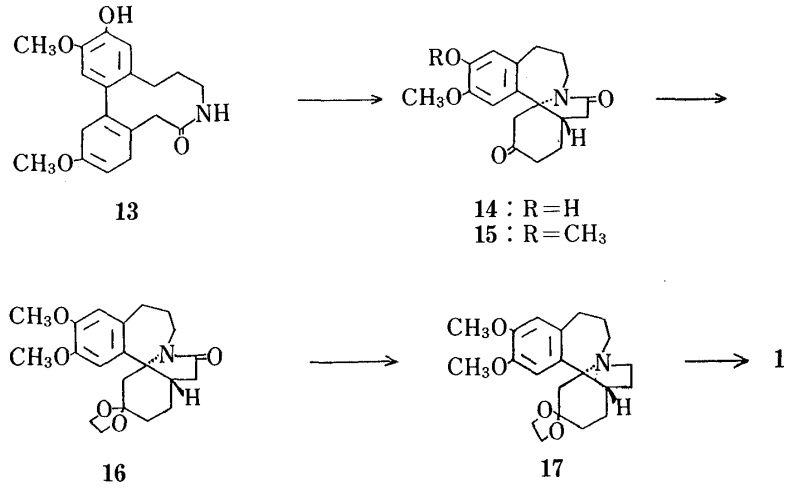


Chart 1

The compound (**7**) obtained from the first eluate, mp 127—128 °C, $C_{19}H_{23}NO_4$, showed the molecular ion peak at *m/z* 329 in the mass spectrum (MS) and the infrared (IR) spectrum revealed the presence of a hydroxyl group (3580 cm^{-1}) and an amide group (3440 and 1660 cm^{-1}). The nuclear magnetic resonance (NMR) spectrum displayed the signals of two methoxyl groups (δ 3.76, 3.80), four methylene groups (δ 1.72, 2.44, 3.16, 3.46) and seven aromatic protons. This product was assigned the structure (**7**), which corresponds to loss of the bromine atom from **6**. A mixture of **8** and **9** (51% yield), obtained from the subsequent eluate, exhibited one spot on thin layer chromatography (TLC) in various solvents. The mixture displayed the molecular ion peak, $C_{19}H_{21}NO_4$, at *m/z* 327 as a base peak in the MS and the IR spectrum revealed the presence of a hydroxyl group (3560 cm^{-1}) and amide groups (3450, 3420, 1670 and 1660 cm^{-1}). The NMR spectrum exhibited the signals of four methoxyl groups (δ 3.85, 3.78, 3.80 ($2 \times OCH_3$)), and ten aromatic protons (complex signals). From these data, the mixture was assumed to consist of the expected photocyclization products (**8** and **9**). In order to confirm the structure of the products, **8** and **9** were subjected to reduction with diborane in tetrahydrofuran (THF), followed by column chromatography on silica gel to afford secondary amines (**10** and **11**). The less polar minor product (**10**), a colorless oil, $C_{19}H_{23}NO_3$, showed the molecular ion peak at *m/z* 313 in the MS and the IR spectrum revealed the absorption of a hydroxyl group (3580 cm^{-1}). The NMR spectrum exhibited signals of two methoxyl groups (δ 3.76, 3.88) and, in the aromatic proton region, the characteristic *ortho* signals of two aromatic protons (δ 6.76, d; 6.90, d, J=9 Hz) along with a typical ABX-type signal (δ 6.58, d, J=3 Hz; 7.24, d, J=8 Hz; 6.94, dd, J=8, 3 Hz). Thus, this compound was concluded to have the structure **10**, and so the photochemical coupling reaction had occurred at the *ortho* position to the hydroxyl group in **6**. The more polar product (**11**), mp 223—225 °C, $C_{19}H_{23}NO_3$, also showed a hydroxyl group absorption (3580 cm^{-1}) in the IR spectrum. The NMR spectrum showed close similarity to that of **10** except for the aromatic proton region. The two aromatic protons appeared as singlet signals at δ 6.42 and 6.68 together with the ABX-type signal (δ 6.60, d, J=3 Hz; 6.86, dd, J=10, 3 Hz;

7.16, d, $J=10$ Hz). This product was assigned the structure **11**, and so the photochemical reaction had occurred at the *para* position to the hydroxyl group in **6**.

Next, our attention was directed to the synthesis of the homoerythrina base (**1**) from the dibenzazecine base (**11**). Treatment of **11** with sodium in liquid ammonia at -70 °C afforded the diene (**12**), which displayed a broad singlet signal due to an olefinic proton at δ 4.62 and a singlet signal of the methoxyl group (δ 3.54) of the enol methyl ether moiety in the NMR spectrum. This compound (**12**) underwent hydrolysis and cyclization upon heating with 5% hydrochloric acid at 60 °C to give **2** in 28% yield. The IR spectrum exhibited a ketone absorption at 1715 cm^{-1} and the NMR spectrum demonstrated the loss of both the olefinic proton and the methoxyl group of the enol methyl ether moiety. The observed singlet signals of two aromatic protons (δ 6.58, 6.68) suggested[10,11] that the A/B ring configuration of **2** is *cis*. Treatment of **2** with an excess of diazomethane afforded the *O*-methylation product, *cis*-16,17-dimethoxyhomoerythrinan-3-one (**1**), in 76% yield.



13 **14** : R=H; **15** : R=CH_3 **16** **17**

Chart 2

Because of the poor yield of **2** in the acid cyclization of **12**, we investigated the cyclization reaction of the amide (**13**). Reduction of the mixture (**8** and **9**) with sodium by the same procedure as described for **12**, followed by fractional recrystallization from acetone gave the desired diene (**13**) in 43% yield. The IR spectrum displayed the hydroxyl absorption (3580 cm^{-1}) and the amide group absorption (3430 and 1650 cm^{-1}), and the NMR spectrum exhibited the olefinic proton signal (δ 4.72) and the methoxyl group signal (δ 3.54) of the enol methyl ether moiety. On acid treatment as described for **2**, the compound (**13**) gave the cyclization product (**14**) in 79% yield. The structure of **14** is supported by the physical properties. The IR spectrum showed a ketone absorption (1720 cm^{-1}) and, based on an analysis[10,11] of the aromatic proton signals in the NMR spectrum, the ring A/B of **14** might be *cis*-fused.

Finally, the cyclization product (**14**) was converted to **1** by the following procedure. Methylation of **14** with diazomethane produced the *O*-methylated compound (**15**) in 79% yield. Treatment of **15** with ethylene glycol in benzene gave a ketal derivative (**16**) in 84% yield. Reduction of **16** with lithium aluminum hydride in tetrahydrofuran produced the amine (**17**), and subsequently the deprotection of **17** with 2% hydrochloric acid gave the desired compound (**1**) in 80% yield. The spectral characteristics of obtained compound (**1**) were found to be superimposable on those of *cis*-16,17-dimethoxyhomoerythrinan-3-one synthesized *via* the acid treatment of the secondary amine (**12**) as described before.

Thus, we achieved a convenient synthesis of the homoerythrina ring system by Birch reduction of dibenzazecine bases, followed by acid treatment.

Experimental

All melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Column chromatography was run on silica gel (Kieselgel, Merck 60, 70—230 mesh) and TLC was carried out by using a 0.25 mm thickness of Merck Silica gel 60F-254. MS were recorded on a Hitachi M-52 spectrometer and high-resolution MS on a JEOL JMS-D-300 spectrometer. IR spectra were obtained on a JASCO IRA-3 spectrophotometer and NMR spectra were recorded on a JEOL JNM-PS-100 nuclear magnetic resonance spectrometer with tetramethylsilane as an internal standard. The following abbreviations are used: s = singlet, d = doublet, dd = doublet-of-doublets, t = triplet, q = quartet, m = multiplet, and br = broad.

***N*-(3-Benzyloxy-4-methoxyphenylpropyl)-2-(2-bromo-4-methoxyphenyl)acetamide (5)**——A mixture of **3**[8] (8.6 g), **4**[9] (8.0 g), and decalin (150 ml) was heated under reflux for 3 h. The mixture was evaporated to dryness and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with dil. hydrochloric acid, 5% NaOH and water, dried over Na_2SO_4, and then evaporated. The crude solid was recrystallized from benzene. Colorless needles. mp 130—132 °C (11.8 g) (73%). *Anal.* Calcd for $C_{26}H_{28}BrNO_4$: C, 62.66; H, 5.66; N, 2.81. Found: C, 62.83; H, 5.65; N, 2.77.

2-(2-Bromo-4-methoxyphenyl)-*N*-(3-hydroxy-4-methoxyphenylpropyl)acetamide (6)——A mixture of **5** (11.3 g), conc. hydrochloric acid (100 ml), and EtOH (100 ml) was heated under reflux for 4 h. The mixture was evaporated and the resulting brown oil was dissolved in $CHCl_3$. The $CHCl_3$ solution was dried over Na_2SO_4 and evaporated to leave a brownish oil, which was chromatographed on a silica gel. Elution with a mixture of $CHCl_3$ and acetone (10 : 1) afforded a solid, which was recrystallized from benzene. Colorless needles. mp 107—109 °C (7.8 g) (84%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570 (OH), 3460 (NHCO), 1665 (NHCO). *Anal.* Calcd for $C_{19}H_{22}BrNO_4$: C, 55.89; H, 5.43; N, 3.43. Found: C, 55.69; H, 5.35; N, 3.30.

Irradiation of 6 (Formation of 7, 8, and 9)——A mixture of (**6**) (500 mg), NaOH (500 mg), and MeOH (300 ml) was irradiated with a 100 W high-pressure mercury lamp under a nitrogen atmosphere for 3 h at room temperature. The mixture was evaporated and neutralized with hydrochloric acid, followed by extraction with $CHCl_3$. The $CHCl_3$ layer was dried over Na_2SO_4 and evaporated to afford an oil, which was chromatographed on a silica gel column and eluted with a mixture of $CHCl_3$ and acetone (9 : 1). A solid obtained from the first fraction was recrystallized from benzene to yield **7**. Colorless needles. mp 127—128 °C (52.4 mg) (13%). TLC (silica gel/$CHCl_3$–acetone (10 : 1), Rf = 0.45). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 3440 (NHCO), 1660 (NHCO). NMR ($CDCl_3$) δ: 1.72 (2H, m, $CH_2CH_2CH_2NH$), 2.44 (2H, t, J = 8 Hz, $CH_2CH_2CH_2NH$), 3.16 (2H, q, J = 6 Hz, $CH_2CH_2CH_2NH$), 3.46 (2H, s, CH_2CO), 3.76, 3.80 (6H, 2 × s, 2 × OCH_3), 5.30 (1H, m, NH), 5.62 (1H, s, OH), 6.48 (1H, dd, J = 9, 2 Hz, arom. H), 6.59 (1H, d, J = 2 Hz, arom. H), 6.66 (1H, d, J = 9 Hz, arom. H), 6.80 (2H, d, J = 8 Hz, 2 × arom. H), 7.06 (2H, d, J = 8 Hz, 2 × arom. H). MS m/z: 329 (M^+), 208 (100%), 179, 164, 137, 121. *Anal.* Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 68.94; H, 6.96; N, 4.14.

The next fraction was evaporated to give a solid (**8** and **9**). Colorless needles. mp 226—233 °C (204 mg) (51%). TLC (silica gel/$CHCl_3$–acetone (10 : 1), Rf = 0.31). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 3450 (NHCO), 3420 (NHCO), 1670 (NHCO), 1660 (NHCO). NMR ($CDCl_3$) δ: 3.85, 3.78 (6H, 2 × s, 2 × OCH_3), 3.80 (6H, s, 2 × OCH_3), 5.84 (4H, s, 2 × CH_2CO), 6.50—7.93 (10H, m, 10 × arom. H). MS m/z: 327 (M^+, 100%), 312, 310, 269, 257, 255, 225, 211.

14-Hydroxy-2,13-dimethoxy-5,6,7,8,9,10-hexahydrodibenz[*d*,*f*]azecine (10) and 12-Hydroxy-2,13-dimethoxy-5,6,7,8,9,10-hexahydrodibenz[*d*,*f*]azecine (11)——BF_3-etherate (1.5 ml) was added dropwise to a cold mixture of **8** and **9** (450 mg), $NaBH_4$ (500 mg), and dry THF (70 ml) under a nitrogen atmosphere with stirring. The mixture was allowed to stand at room temperature for 5 h, then decomposed with EtOH and water, and evaporated to dryness. The resulting oil was dissolved in a mixture of MeOH (20 ml) and conc. hydrochloric acid (1.5 ml) and heated at 60 °C for 1 h. After being cooled, the mixture was evaporated to dryness. The obtained oil was neutralized with NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried over Na_2SO_4, and concentrated to give a brownish oil, which was chromatographed on a silica gel column. The first fraction eluted with a mixture of $CHCl_3$ and MeOH (10 : 1) was evaporated to afford **10**. A colorless oil (79 mg) (18%). TLC (silica gel/$CHCl_3$–MeOH (3 : 1), Rf = 0.47). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH). NMR ($CDCl_3$) δ: 3.76, 3.88 (6H, 2 × s, 2 × OCH_3), 6.58 (1H, d, J = 3 Hz, C_1-H), 6.76 (1H, d, J = 9 Hz, C_{11}-H or C_{12}-H), 6.90 (1H, d, J = 9 Hz, C_{11}-H or C_{12}-H), 6.94 (1H, dd, J = 8, 3 Hz, C_3-H), 7.24 (1H, d, J = 8 Hz, C_4-H). MS m/z: 313 (M^+, 100%), 298, 281, 255. High-resolution MS m/z: 313.1677 Calcd for $C_{19}H_{23}NO_3$ (M^+). Found: m/z 313.1703.

The next fraction was evaporated to yield a solid **11**, which was recrystallized from EtOH. Colorless needles. mp 223—225 °C (317 mg) (74%). TLC (silica gel/$CHCl_3$–MeOH (3 : 1), Rf = 0.31). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH). NMR ($CDCl_3$) δ: 3.74 (6H, s, 2 × OCH_3), 6.42 (1H, s, C_{11}-H or C_{14}-H), 6.60 (1H, d, J = 3 Hz, C_1-H), 6.68 (1H, s, C_{11}-H or C_{14}-H), 6.86 (1H, dd, J = 10, 3 Hz, C_3-H), 7.16 (1H, d, J = 10 Hz, C_4-H). MS m/z: 313 (M^+), 298, 281 (100%), 269, 255. *Anal.* Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.56; H, 7.53; N, 4.33.

Birch Reduction of 11 (Formation of 12)——Sodium (500 mg) was added during 1 h to a stirred mixture of **11** (200 mg), MeOH (4 ml), dry THF (4 ml), and liquid ammonia (30 ml) at −70 °C. After cautious addition of water and NH_4Cl, the ammonia was allowed to evaporate off and the mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried over Na_2SO_4, and evaporated to afford **12**. The residual solid was recrystallized from MeOH. Colorless prisms.[12] mp 228—230 °C (175 mg) (87%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550 (OH). NMR ($CDCl_3$) δ: 3.54 (3H, s, aliphatic OCH_3), 3.79 (3H, s, aromatic OCH_3), 4.62 (1H, br s, olefinic H), 6.40, 6.60 (2H, 2×s, 2×arom. H). MS *m/z*: 315 (M^+, 100%), 314, 300, 284, 269, 255. High-resolution MS *m/z*: 315.1833 Calcd for $C_{19}H_{25}NO_3$ (M^+). Found: *m/z* 315.1845.

***cis*-17-Hydroxy-16-methoxyhomoerythrinan-3-one (2)**——A mixture of **12** (20 mg), dioxane (2 ml) and 5% hydrochloric acid (4 drops) was heated at 60 °C for 1 h with stirring. After cooling, the mixture was evaporated to dryness. A small amount of water was added to the resulting residue and neutralized with NH_4OH. The mixture was extracted with $CHCl_3$, dried over Na_2SO_4, and evaporated to dryness. Purification of the residue by column chromatography on silica gel using a mixture of $CHCl_3$ and acetone (10:1) as the eluent gave an oil (**2**). A colorless oil (5.4 mg) (28%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3570 (OH), 1715 (CO). NMR ($CDCl_3$) δ: 3.80 (3H, s, OCH_3), 6.58, 6.68 (2H, 2×s, 2×arom. H). MS *m/z*: 301 (M^+), 244 (100%), 230, 229, 210, 200. High-resolution MS *m/z*: 301.1676 Calcd for $C_{18}H_{23}NO_3$ (M^+). Found: *m/z* 301.1684.

***cis*-16,17-Dimethoxyhomoerythrinan-3-one (1)**——An ethereal solution of an excess of diazomethane was added to a solution of **2** (10 mg) in MeOH (2 ml), and the mixture was stirred for 4 h. The ether was evaporated off and the resulting oil was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4, and evaporated to give an oil, which was purified by chromatography on a silica gel column and eluted with a mixture of $CHCl_3$ and MeOH (10:1). A colorless oil (8 mg) (76%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1710 (CO). NMR ($CDCl_3$) δ: 3.80 (6H, s, 2×OCH_3), 6.52, 6.70 (2H, 2×s, 2×arom. H). MS *m/z*: 315 (M^+), 313, 258 (100%), 256, 242, 225. High-resolution MS *m/z*: 315.1833 Calcd for $C_{19}H_{25}NO_3$ (M^+). Found: *m/z* 315.1789.

Birch Reduction of 8 and 9 (Formation of 13)——Sodium (450 mg) was added during 1.5 h with stirring to a mixture of **8** and **9** (170 mg), MeOH (4 ml), dry THF (4 ml), and liquid ammonia (30 ml) at −70 °C and then the mixture was treated in a manner similar to that described for **12** to yield a mixture of products as a crude solid. The mixture was first crystallized[13] from acetone to yield a crude product (**13**), which was purified by recrystallization from acetone. Colorless prisms. mp 223—225 °C (73 mg) (43%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 3430 (NHCO), 1650 (NHCO). NMR ($CDCl_3$) δ: 3.54 (3H, s, aliphatic OCH_3), 3.84 (3H, s, aromatic OCH_3), 4.72 (1H, br s, olefinic H), 5.48 (1H, br s, NH), 6.52, 6.78 (2H, 2×s, 2×arom. H). MS *m/z*: 329 (M^+, 100%), 284, 271, 257, 225, 211. *Anal.* Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.29; H, 7.25; N, 4.16.

***cis*-17-Hydroxy-16-methoxyhomoerythrinan-3,8-dione (14)**——A solution of **13** (50 mg) in dioxane (3 ml) and 5% hydrochloric acid (0.5 ml) was treated in the same way as for **2** to provide **14**. The solid was recrystallized from acetone. Colorless needles. mp 261—262 °C (38 mg) (79%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560 (OH), 1720 (CO), 1680 (NCO). NMR ($CDCl_3$) δ: 3.83 (3H, s, OCH_3), 5.86 (1H, br s, OH), 6.58, 6.60 (2H, 2×s, 2×arom. H). MS *m/z*: 315 (M^+), 300, 272, 258 (100%), 245, 244, 226, 216. *Anal.* Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.26; H, 6.79; N, 4.31.

***cis*-16,17-Dimethoxyhomoerythrinan-3,8-dione (15)**——A solution of **14** (100 mg) in MeOH (2 ml) was treated with an ethereal solution of an excess of diazomethane in the same way as for **1** to yield **15**. A colorless oil (82 mg) (79%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CO), 1680 (NCO). NMR ($CDCl_3$) δ: 3.82 (6H, s, 2×OCH_3), 6.50, 6.60 (2H, 2×s, 2×arom. H). MS *m/z*: 329 (M^+), 286, 272 (100%), 259, 258, 240. High-resolution MS *m/z*: 329.1626 Calcd for $C_{19}H_{23}NO_4$ (M^+). Found: *m/z* 329.1616.

***cis*-16,17-Dimethoxyhomoerythrinan-3,8-dione 3-Ethyleneacetal (16)**——A mixture of **15** (20 mg), ethylene glycol (1 ml), TsOH (1 mg), and dry benzene (10 ml) was heated while the resulting water was removed continuously. The mixture was evaporated to dryness and the residual oil was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4, and evaporated to produce **16**. A colorless oil (19 mg) (84%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (CO). NMR ($CDCl_3$) δ: 3.81, 3.84 (6H, 2×s, 2×OCH_3), 3.90 (4H, s, OCH_2CH_2O), 6.46, 6.77 (2H, 2×s, 2×arom. H). MS *m/z*: 373 (M^+, 100%), 330, 328, 311, 286, 272, 271, 259, 240. High-resolution MS *m/z*: 373.1888 Calcd for $C_{21}H_{27}NO_5$ (M^+). Found: *m/z* 373.1885.

***cis*-16,17-Dimethoxyhomoerythrinan-3-one Ethyleneacetal (17)**——A mixture of **16** (15 mg), $LiAlH_4$ (10 mg), and dry THF (3 ml) was heated under reflux for 4 h. After cooling of the mixture, a small amount of water was added under ice cooling. The whole was filtered and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$, and the combined organic layer was washed with water, dried over Na_2SO_4, and evaporated to give **17**. A colorless oil (11 mg) (76%). NMR ($CDCl_3$) δ: 3.83 (6H, s, 2×OCH_3), 6.54, 6.93 (2H, 2×s, 2×arom. H). MS *m/z*: 359 (M^+), 345, 316, 302, 258 (100%), 244. High-resolution MS *m/z*: 359.2095 Calcd for $C_{21}H_{29}NO_4$ (M^+). Found: *m/z* 359.2095.

Formation of 1 from 17——A solution of **17** (10 mg) in 2% hydrochloric acid (1.5 ml) and acetone (1.5 ml) was heated under reflux for 1.5 h. After cooling, the mixture was evaporated. The resulting residue was neutralized with NH_4OH and the mixture was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4, and evaporated to afford **1** as a colorless oil (7 mg) (80%).

Spectral (IR, NMR, and MS) properties of this compound were identical with those of the product prepared from **2**.

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References and Notes

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6) In the previous paper,[7] we reported that Birch reduction of the dibenzazonine base 2,12-dimethoxy-5,6,8,9-tetrahydro-7*H*-dibenz[*d*,*f*]azonin-3-ol, followed by acid treatment gave *cis*-16-hydroxy-15-methoxyerythrinan-3-one.
7) H. Tanaka, M. Shibata, and K. Ito, *Chem. Pharm. Bull.*, **32**, 3271 (1984).
8) S. Kano, T. Yokomatsu, and S. Shibuya, *Chem. Pharm. Bull.*, **25**, 2401 (1977).
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10) In the ^{1}H-NMR spectra of our synthesized compounds (**1**, **2**, **14**, and **15**), the chemical shifts of aromatic proton signals were found at δ 6.50—6.70 and the differences of chemical shifts between the C_{15}-proton and the C_{18}-proton were small (0.1—0.18 ppm). The chemical shifts of the aromatic protons are within the range appropriate for *cis*-homoerythrina compounds as indicated by Mondon and Seidel.[11] Based on molecular models (Dreiding models), the aromatic proton at C-15 in *cis*-homoerythrina derivatives is not affected by the ring A moiety and hence the chemical shift of the aromatic protons will take a normal value. Thus the A/B ring of these compounds (**1**, **2**, **14**, and **15**) might be *cis*-fused.
11) A Mondon and P.-R. Seidel, *Chem. Ber.*, **104**, 2937 (1971).
12) This compound was unstable.
13) The mother liquor contained an inseparable mixture which appeared as a homogeneous spot on silica gel in various solvents.