Synthesis of Saframycins. VIII.[1] Synthesis of the ABC Ring of Safracins

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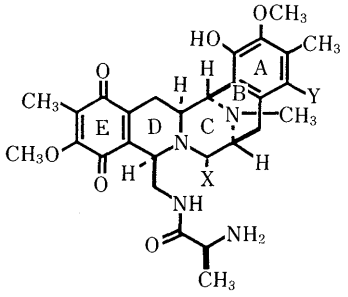
An efficient synthesis of the 1,5-imino-3-benzazocine derivative (18) from 1,4-diacetyl-2,5-piperazinedione (7) and 4-methoxy-3-methylbenzaldehyde (8) is described. The tricyclic lactam (18) is shown to be a useful intermediate for preparation of a phenol (5), which has the structure of the ABC ring system of safracins and ecteinascidins. This conversion is a promising route to total synthesis of (±)-safracin A (1a).

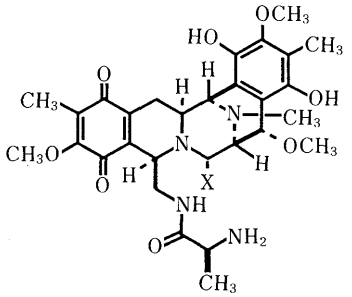
Keywords synthesis; safracin; ecteinascidin; 1,5-imino-3-benzazocine; biogenetic intermediate

Safracins A (**1a**) and B (**1b**) were first isolated by the Yoshitomi Laboratories group from *Pseudomonas fluorescens* A2-2 in 1983. The Squibb Laboratories group independently isolated **1b** from *Pseudomonas fluorescens* SC 12695 in the same year.[2] Both safracins were active against mouse tumors, L1210 and P388 leukemias and B16 melanoma. The toxic and effective doses of **1b** were much lower than those of **1a**.[3] The structure of the safracins with the absolute configuration was elucidated by X-ray crystallography of the 4-brominated derivative of safracin A (**1c**).[4,5] The safracin structure is similar to that of saframycins (**3**); however, the pyruvamide side chain and one of the *p*-quinone parts of the saframycins are substituted, respectively, by an alaninamide chain and a monophenol ring in safracins. Ecteinascidins (**4**) with potent *in vivo* antitumor activity were independently isolated from the colonial tunicate *Ecteinascidia turbinata* by Rinehart *et al.*[6a,b] and Wright *et al.*[6c] in 1990, and the structures assigned to them were similar to those of safracins. Saframycin Mxs-1 (**2a**) and -2 (**2b**) were isolated from *Myxococcus xanthus* Mx x 48 in 1988.[7]

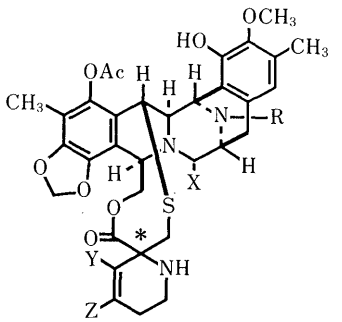
It is interesting that these monoquinone-type antibiotics, such as saframycins D (**3d**) and F (**3e**), safracins A (**1a**) and B (**1b**), and saframycin Mxs-1 (**2a**) and -2 (**2b**), have a quinone moiety at ring E and a highly substituted benzene ring A with a variety of oxidation levels. The possible biosynthetic pathway shown in Fig. 2 involves initial oxidation of a type I compound (such as safracins) to form a type II compound (such as saframycins A and B), into which a hydroxy group could be introduced at the C-5 position to give a type III compound, which in turn would be oxidized and reduced (redox process) to form a type IV compound (such as saframycins D and F). On the other hand, introduction of a methoxy group at the C-5 position of a type II compound would give a type V compound (such as saframycin C), which could then be reduced to a type VI compound (such as saframycin Mxs). We reported the total synthesis of (±)-saframycin B (**3b**),[8a] the trans-



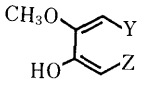
safracin A (**1a**) : X=Y=H
safracin B (**1b**) : X=OH, Y=H
1c : X=H, Y=Br

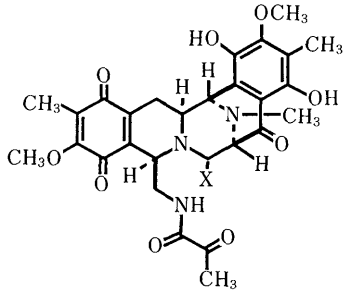


saframycin Mx-1 (**2a**) : X=OH
saframycin Mx-2 (**2b**) : X=H

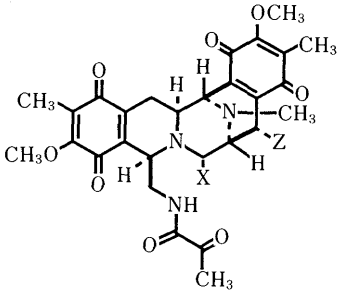


ecteinascidins
*S-form
Et 729 (**4a**) : X=OH, R=H
Et 743 (**4b**) : X=OH, R=CH$_3$
Et 745 (**4c**) : X=H, R=CH$_3$
Et 759A (**4d**) and Et 759B (**4e**) : Et 743 *N*-oxide





saframycin D (**3d**) : X=H
saframycin F (**3e**) : X=CN



saframycin A (**3a**) : X=CN, Z=H
saframycin B (**3b**) : X=Z=H
saframycin C (**3c**) : X=H, Z=OCH$_3$

*stereochemistry not determined
Et 722 (**4f**) : X=OH, R=CH$_3$
Et 736 (**4g**) : X=OH, R=H

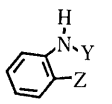


Fig. 1

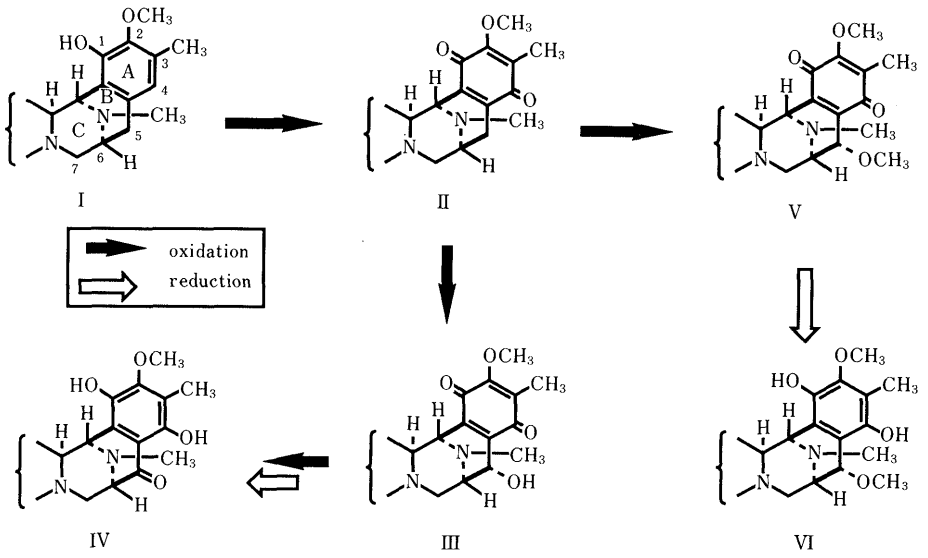


Fig. 2

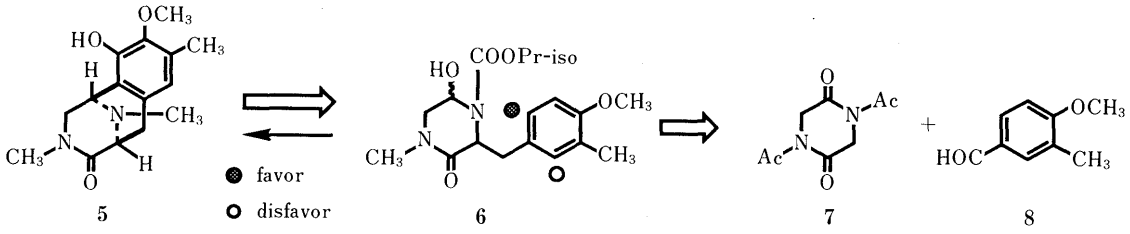


Chart 1

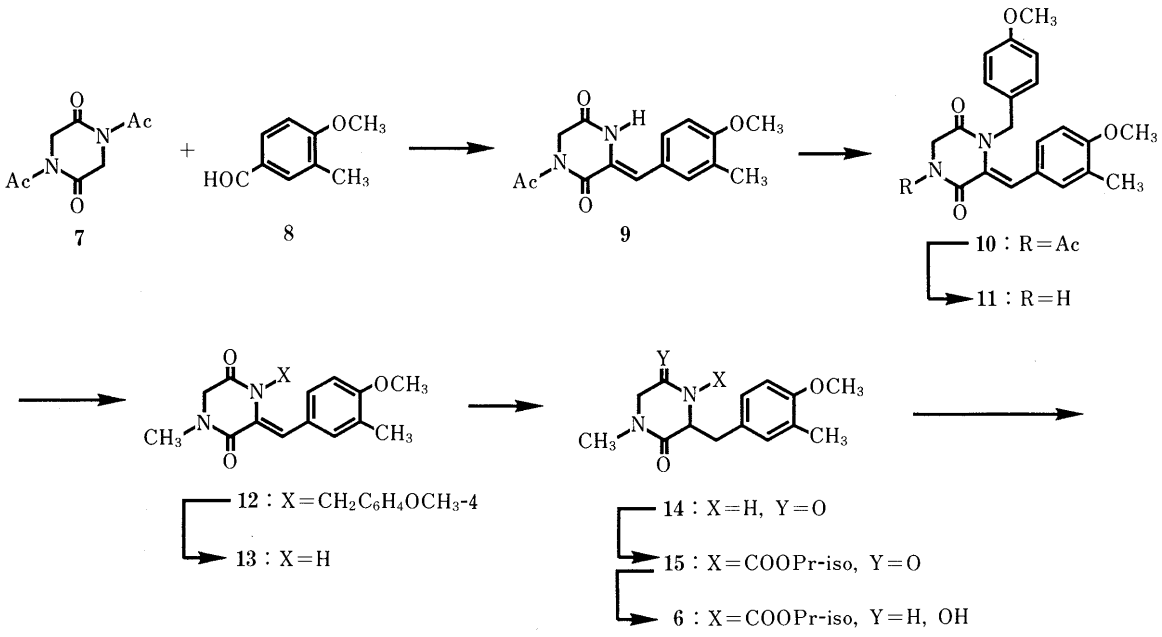
formation of (±)-saframycin B (**3b**) (type II) to (±)-saframycins C (**3c**) (type V) and D (**3d**) (type IV),[8b] and recently the transformation of (−)-saframycin A (**3a**) (type II) to a (−)-saframycin Mx type compound (type VI) *via* the 5-methoxybisquinone (type V).[8c] We became interested in safracins as attractive synthetic targets because they were plausible and important biogenetic intermediates of saframycins and saframycin Mxs. We report here the first synthesis of the ABC ring system of safracins and ecteinascidins using the methods described in connection with our total synthesis of the ABC ring system of saframycins.[9]

Our initial strategy for the synthesis of the ABC ring model compound (**5**) was based on the retrosynthetic analysis outlined in Chart 1. To prevent the formation of any unwanted tetrahydroisoquinoline isomer from **6**, it was decided to introduce the hydroxy group at a late stage.

A mixture of commercially available 4-methoxy-3-methylbenzaldehyde (**8**) and 1,4-diacetyl-2,5-piperazinedione (**7**) in dimethylformamide (DMF) was treated with potassium *tert*-butoxide in *tert*-butyl alcohol at room temperature for 15 h to afford 3-arylidene-2,5-piperazinedione (**9**) in 74% yield (Chart 2). 4-Methoxybenzylation of **9** with 4-methoxybenzyl chloride in the presence of sodium hydride in DMF at room temperature for 1 h furnished **10** in quantitative yield, and successive treatment with hydrazine hydrate afforded **11** in 70% yield. Methylation of **11** with methyl iodide in the presence of sodium hydride in DMF at room temperature for 1 h furnished **12** in quantitative yield. Deprotection of **12** with trifluoroacetic acid (TFA) and concentrated H_2SO_4 at room temperature for 14 h gave **13** in 92% yield. Catalytic hydrogenation of **13** with hydrogen (3.5 atm) over 20% palladium on carbon in ethanol at 80 °C for 14 h furnished **14** in 76% yield. The piperazine ring of **14** was activated by introduction of an isopropoxycarbonyl group to give **15** in 78% yield. The chemoselective reduction of **15** with an excess of lithium tri-*tert*-butoxyaluminohydride in tetrahydrofuran (THF) afforded a diastereomeric mixture of the alcohol (**6**), which on treatment with formic acid afforded the desired cyclization product (**16**) in 85% overall yield.[10,11] The structure of **16** is supported by the proton nuclear magnetic resonance (^{1}H-NMR) spectrum, which displays the signals of H-1 as a singlet at δ 6.59 and H-4 as a singlet at δ 6.87. Deprotection of **16** with TFA and H_2SO_4 gave the secondary amine (**17**) in 81% yield. Methylation of **17** with formaldehyde and formic acid at 70 °C for 1 h gave **18** in 74% yield.

The next stage of the investigation required establishing a method to introduce a hydroxy group at the C-1 position of compound **18** (Chart 3). Treatment of **18** with boron tribromide at −20 °C for 1 h afforded the phenol (**19**) in 75% yield,[12] but numerous efforts to convert **19** to the *o*-quinone **20** using potassium nitrosodisulfonate (Fremy's salt),[13a] lead tetraacetate,[13b] and benzeneseleninic anhydride[13c] were all unsuccessful.[14]

These results indicated that the introduction of a hydroxy group required a different approach. Nitration of **18** with HNO_3–H_2SO_4 at 0 °C for 2 h afforded **21** in 80% yield.[15] Hydrogenation of **21** with 10% palladium on carbon in ethanol gave **22** in 85% yield. Finally, the reaction of **22** with sodium nitrite in H_2SO_4 and water for 1 h gave the



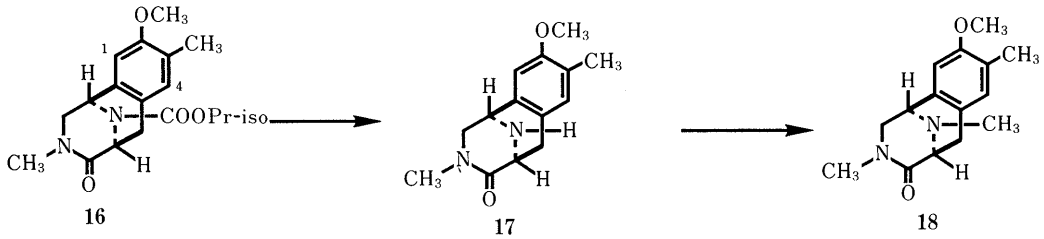


Chart 2

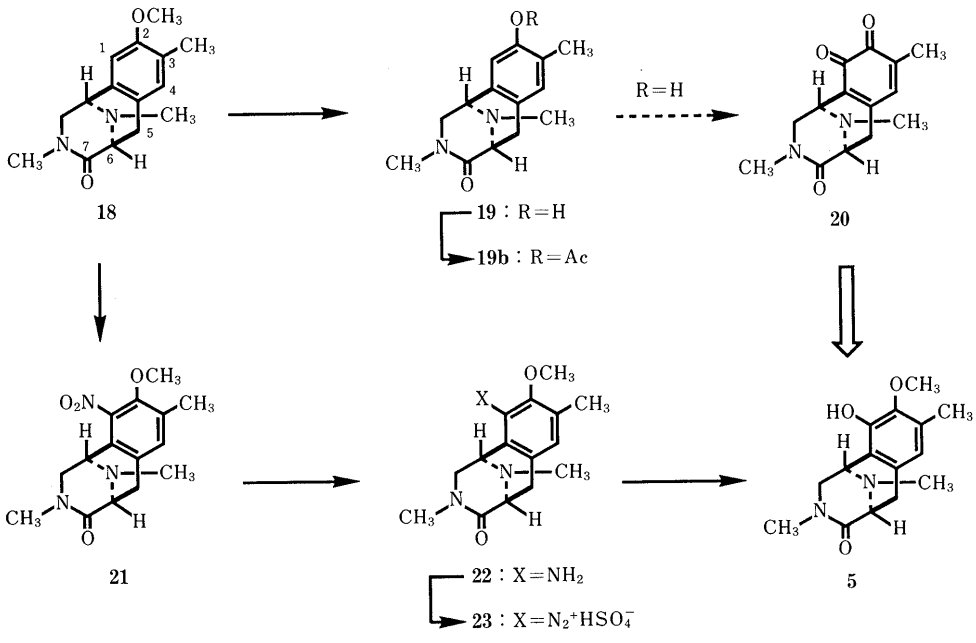


Chart 3

diazonium salt (**23**), which was subsequently treated with 20% H_2SO_4 at 140 °C for 5 min to provide the desired phenol (**5**) in 5% yield. The major products were the reduction products **18** and **19**, obtained in 22% and 16% yields, respectively.[16,17] Assignment of **5** was made by ^{1}H-NMR analysis. When H-4 (δ 6.49) was irradiated, nuclear Overhauser enhancement (10%) of the methyl protons at δ 2.26 was observed.

In summary, we have succeeded in synthesizing the ABC ring system of safracins and ecteinascidins. The results described herein are being applied to the total synthesis of (±)-safracin A (**1a**) which is currently under way in our

laboratories.

Experimental

All melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. MS (electron impact (EI)) were obtained on a JEOL JMS-DX 302 spectrometer. IR spectra were recorded on Hitachi 260-10 and 270-30 spectrophotometers. UV spectra were determined in methanol with a Hitachi 340 spectrophotometer. ^{1}H-NMR spectra were obtained at 270 MHz with a JEOL EX 270 spectrometer. ^{13}C-NMR spectra were measured at 67.5 MHz with a JEOL EX 270 spectrometer (multiplicity determined from off-resonance decoupled or insensitive nuclei enhanced by polarization transfer (INEPT) spectra). NMR spectra were taken in $CDCl_3$ and chemical shifts are reported in δ values in parts per million relative to tetramethylsilane as an internal standard. Column chromatography was performed with E. Merck Silica gel 60 (70—230 mesh). Elemental analyses were obtained by using a Perkin-Elmer Model 240B elemental analyzer. All reactions were conducted under an argon atmosphere. Dry solvents and reagents were obtained using standard procedures. Anhydrous sodium sulfate was used for drying organic solvent extracts; removal of the solvent was done with a rotary evaporator and finally, under high vacuum.

(*Z*)-1-Acetyl-3-(4-methoxy-3-methylphenylmethylene)-2,5-piperazinedione (9) A solution of potassium *tert*-butoxide (31.42 g, 0.28 mol) in *tert*-butyl alcohol (580 ml) was added to a stirred solution of 4-methoxy-3-methylbenzaldehyde **8** (42.0 g, 0.28 mol) and 1,4-diacetyl-2,5-piperazinedione **7** (55.5 g, 0.28 mol) in dry DMF (560 ml). After being stirred for 15 h at room temperature, the reaction mixture was poured into brine (2 l) and extracted with ethyl acetate (500 ml × 3). The combined extracts were washed with water (500 ml), dried, and concentrated *in vacuo* to give the residue as a pale yellow solid, recrystallization of which from ethyl acetate gave **9** (59.4 g, 74%) as pale yellow prisms, mp 201.5—204.5 °C. *Anal.* Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.40; H, 5.56; N, 9.65. MS *m/z* (%): 288 (M^+, 100), 247 (12), 246 (75), 231 (10), 161 (17), 147 (21). IR (KBr): 3240, 1710, 1695, 1638, 1615 cm^{-1}. UV λ_{max} nm (log ε): 237 (4.17), 338 (4.31). ^{1}H-NMR δ: 2.24 (3H, s, $ArCH_3$), 2.65 (3H, s, $COCH_3$), 3.88 (3H, s, OCH_3), 4.52 (2H, s, 6-H_2), 6.88 (1H, d, J=8.6 Hz, 5′-H), 7.12 (1H, s, C=CH), 7.20 (1H, d, J=2.0 Hz, 2′-H), 7.25 (1H, dd, J=8.6, 2.0 Hz, 6′-H), 7.93 (1H, s, NH).

(*Z*)-3-(4-Methoxy-3-methylphenylmethylene)-4-(4-methoxyphenylmethyl)-2,5-piperazinedione (11) Sodium hydride (60% oil dispersion, washed with dry hexane three times, 1.62 g, 67.5 mmol) was added to a stirred solution of **9** (14.4 g, 50 mmol) in dry DMF (250 ml) under ice-cooling, and stirring was continued for 1 h at 0 °C. 4-Methoxybenzyl chloride (10.45 g, 66.7 mmol) in dry DMF (100 ml) was added during 10 min, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with water (100 ml) and extracted with benzene (100 ml × 3). The combined extracts were washed with water (100 ml), dried, and concentrated *in vacuo* to furnish **10** (20.4 g, 100%) as a pale yellow oil, which was used for the next step without further purification. An analytical sample was obtained by crystallization from ether to give pure **10** as pale yellow prisms, mp 155—156 °C. *Anal.* Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.51; H, 5.95; N, 6.84. MS *m/z* (%): 408 (M^+, 19), 122 (9), 121 (100). IR (KBr): 1715, 1690, 1625, 1610 cm^{-1}. UV λ_{max} nm (log ε): 229 (4.36), 248 sh (4.07), 278 sh (3.83), 284 sh (3.87), 333 (4.29). ^{1}H-NMR δ: 2.26 (3H, s, $ArCH_3$), 2.51 (3H, s, $COCH_3$), 3.75, 3.90 (each 3H, s, OCH_3), 4.50 (2H, s, 6-H_2), 4.65 (2H, s, NCH_2), 6.73 (2H, d, J=8.6 Hz, 2 × ArH), 6.87 (2H, d, J=8.6 Hz, 2 × ArH), 6.89 (1H, d, J=8.6 Hz, 5′-H), 7.20 (1H, s, C=CH), 7.22 (1H, d, J=2.3 Hz, 2′-H), 7.29 (1H, dd, J=8.6, 2.3 Hz, 6′-H).

Hydrazine monohydrate (20 ml) was added to a stirred solution of the crude **10** (20.4 g) in dry DMF (250 ml), and the resulting solution was stirred for 1 h at room temperature. The reaction mixture was poured into water (500 ml), and extracted with chloroform (300 ml × 3). The combined extracts were washed with brine (300 ml), dried, and concentrated *in vacuo* to give a solid, recrystallization of which from ethyl acetate–ether gave **11** (12.81 g, 70% from **9**) as pale yellow prisms, mp 174—177 °C. *Anal.* Calcd for $C_{21}H_{22}N_2O_4 \cdot 1/4H_2O$: C, 68.26; H, 6.11; N, 7.55. Found: C, 68.26; H, 6.15; N, 7.51. MS *m/z* (%): 366 (M^+, 28), 160 (4), 122 (10), 121 (100). IR (KBr); 3200, 1690, 1675, 1625, 1605 cm^{-1}. UV λ_{max} nm (log ε): 227 (4.35), 314 (4.29). ^{1}H-NMR δ: 2.24 (3H, s, $ArCH_3$), 3.73, 3.88 (each 3H, s, OCH_3), 4.05 (2H, d, J=2.0 Hz, 6-H_2), 4.61 (2H, s, NCH_2), 6.71 (2H, d, J=8.6 Hz, 2 × ArH), 6.86 (1H, d, J=8.6 Hz, 5′-H), 6.89 (2H, d, J=8.6 Hz, 2 × ArH), 7.13 (1H, s, C=CH), 7.16 (1H, d, J=2.3 Hz, 2′-H), 7.22 (1H, dd, J=8.6, 2.3 Hz, 6′-H), 7.54 (1H, br s, NH).

(*Z*)-1-Methyl-3-(4-methoxy-3-methylphenylmethylene)-2,5-piperazinedione (13) Sodium hydride (60% oil dispersion, washed with dry hexane three times, 864 mg, 26.0 mmol) was added to a stirred solution of **11** (10.98 g, 30 mmol) in dry DMF (80 ml) under ice-cooling, and stirring was continued for 30 min at 0 °C. Methyl iodide (2.24 ml, 36.0 mmol) in dry DMF (20 ml) was added during 30 min, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with water (100 ml) and extracted with benzene (100 ml × 3). The combined extracts were washed with water (100 ml), dried, and concentrated *in vacuo* to furnish **12** (11.4 g, 100%) as a pale yellow oil, which was used for the next step without further purification. An analytical sample was obtained by crystallization from ether to give pure **12** as pale yellow prisms, mp 73—75 °C. MS *m/z* (%): 380 (M^+, 41), 122 (9), 121 (100). High-resolution MS Calcd for $C_{22}H_{24}N_2O_4$: 380.1736. Found: 380.1749. IR (KBr): 1670, 1650, 1610 cm^{-1}. UV λ_{max} nm (log ε): 229 (4.27), 284 sh (3.99), 314 (4.20). ^{1}H-NMR δ: 2.24 (3H, s, $ArCH_3$), 3.01 (3H, s, NCH_3), 3.73, 3.88 (each 3H, s, OCH_3), 4.05 (2H, s, 6-H_2), 4.64 (2H, s, NCH_2), 6.72 (2H, d, J=8.9 Hz, 2 × ArH), 6.85 (1H, d, J=8.6 Hz, 5′-H), 6.89 (2H, d, J=8.9 Hz, 2 × ArH), 7.13 (1H, s, C=CH), 7.15 (1H, d, J=2.3 Hz, 2′-H), 7.21 (1H, dd, J=8.6, 2.3 Hz, 6′-H).

Concentrated H_2SO_4 (1.5 ml) was added to a stirred solution of the crude **12** (11.4 g) in TFA (50 ml), and stirring was continued for 14 h at room temperature. The reaction mixture was poured into brine (500 ml) and extracted with chloroform (200 ml × 3). The combined extracts were washed with 10% aqueous NH_3 (200 ml), dried, and concentrated *in vacuo* to give a solid, recrystallization of which from methanol afforded pure **13** (7.145 g, 92% from **11**) as pale yellow needles, mp 192.5—194 °C. MS *m/z* (%): 262 (M^+, 11), 135 (100). High-resolution MS Calcd for $C_{14}H_{16}N_2O_3$: 260.1161. Found: 260.1180. IR (KBr): 3600—3100, 1670, 1615, 1595 cm^{-1}. UV λ_{max} nm (log ε): 230 (4.16), 316 (4.21). ^{1}H-NMR δ: 2.23 (3H, s, $ArCH_3$), 3.09 (3H, s, NCH_3), 3.86 (3H, s, OCH_3), 4.16 (2H, s, 6-H_2), 6.86 (1H, d, J=8.3 Hz, 5′-H), 6.99 (1H, s, C=CH), 7.12 (1H, br s, 2′-H), 7.21 (1H, br d, J=8.3 Hz, 6′-H), 7.99 (1H, br s, NH).

3-(4-Methoxy-3-methylphenylmethyl)-1-methyl-2,5-piperazinedione (14) A solution of **13** (6.50 g, 25 mmol) in ethanol (50 ml) was shaken for 14 h at 80 °C under 3.5 atm of hydrogen in the presence of 20% palladium on carbon (1.2 g). The catalyst was removed by filtration and washed with ethanol (450 ml). The combined filtrates were evaporated and the residue was diluted with water (200 ml), and extracted with chloroform (200 ml × 3). The combined extracts were washed with 5% $NaHCO_3$, dried, and concentrated *in vacuo* to give a solid, recrystallization of which from acetone afforded pure **14** (4.978 g, 76%) as colorless needles, mp 169—170.5 °C. *Anal.* Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 63.97; H, 7.00; N, 10.62. MS *m/z* (%): 262 (M^+, 11), 135 (100). IR (KBr): 3250, 1685, 1655 cm^{-1}. UV λ_{max} nm (log ε): 231 (3.94), 277 (3.19), 284 (3.05). ^{1}H-NMR δ: 2.19 (3H, s, $ArCH_3$), 2.85 (3H, s, NCH_3), 3.01 (1H, dd, J=13.9, 6.6 Hz, ArCH), 3.08 (1H, dd, J=13.9, 4.3 Hz, ArCH), 3.10 (1H, d, J=17.5 Hz, 6-H), 3.61 (1H, d, J=17.5 Hz, 6-H), 3.82 (3H, s, OCH_3), 4.21 (1H, m, 3-H), 6.14 (1H, br s, NH), 6.76 (1H, d, J=7.9 Hz, 5′-H), 6.95 (1H, d, J=2.0 Hz, 2′-H), 6.96 (1H, dd, J=7.9, 2.0 Hz, 6′-H).

3-(4-Methoxy-3-methylphenylmethyl)-1-methyl-4-isopropoxycarbonyl-2,5-piperazinedione (15) A solution of **14** (3.93 g, 15 mmol), triethylamine (4.18 ml, 30 mmol), and 4-dimethylaminopyridine (3.665 g, 30 mmol) in dry dichloromethane (200 ml) was cooled with ice-water, and isopropyl chloroformate (6.81 ml, 60 mmol) was added dropwise over 10 min. The solution was stirred for 1 h at room temperature. The organic layer was washed with 1 N HCl (50 ml), and then water (50 ml), dried, and concentrated *in vacuo* to give the residue (9.57 g). Chromatography on a silica gel (120 g) column with hexane–ethyl acetate (1 : 1) as the eluent gave **15** (4.08 g, 78%) as a colorless amorphous powder. MS *m/z* (%): 348 (M^+, 17), 136 (10), 135 (100). High-resolution MS Calcd for $C_{18}H_{24}N_2O_5$: 348.1685. Found: 348.1673. IR ($CHCl_3$): 1775, 1725, 1625 cm^{-1}. UV λ_{max} nm (log ε): 228 (4.01), 277 (3.27), 284 (3.19). ^{1}H-NMR δ: 1.36, 1.39 (each 3H, d, J=6.6 Hz, $CHC\underline{H}_3$), 2.17 (3H, s, $ArCH_3$), 2.31 (1H, d, J=18.2 Hz, 6-H), 2.76 (3H, s, NCH_3), 3.12 (1H, dd, J=14.2, 4.6 Hz, ArCH), 3.27 (1H, dd, J=14.2, 3.6 Hz, ArCH), 3.40 (1H, d, J=18.2 Hz, 6-H), 3.81 (3H, s, OCH_3), 4.95 (1H, dd, J=4.6, 3.6 Hz, 3-H), 5.15 (1H, sept, J=6.6 Hz, OCH), 6.72 (1H, d, J=8.9 Hz, 5′-H), 6.95 (1H, d, J=2.0 Hz, 2′-H), 6.96 (1H, dd, J=7.9, 2.0 Hz, 6′-H). ^{13}C-NMR δ: 15.9 (q, $ArCH_3$), 21.7 (q, $CH\underline{C}H_3$), 21.7 (q, $CH\underline{C}H_3$), 32.8 (q, NCH_3), 38.4 (t, $ArCH_2$), 52.6 (t, 6-C), 55.3 (d, 3-C), 60.2 (q, OCH_3), 72.2 (d, OCH), 109.8 (d,), 125.9 (s), 127.2 (s), 128.7 (d), 132.2 (d), 151.1 (s, COO), 157.6 (s), 164.4 (s, CO), 166.0 (s, CO).

1,2,3,4,5,6-Hexahydro-1,5-imino-9-methoxy-3,8-dimethyl-4-oxo-3-

benzazocine-11-carboxylic Acid Isopropyl Ester (16) A stirred solution of **15** (972 mg, 2.79 mmol) in dry THF (60 ml) was cooled with ice-water, and lithium tri-*tert*-butoxyaluminohydride (2.841 g, 11.2 mmol) was added over 15 min. After continued stirring at the same temperature for 1 h, the reaction mixture was quenched by addition of water (10 ml). The reaction mixture was filtered through a Celite pad, and filtrates were concentrated *in vacuo*. The unstable diastereomeric mixture of the alcohols **6** (1.05 g) obtained was used for the next step without isolation. A solution of **6** in formic acid (40 ml) was heated at 70 °C for 40 min. The reaction mixture was diluted with water (100 ml) and extracted with chloroform (50 ml × 3). The combined extracts were washed with 5% $NaHCO_3$ (50 ml), dried, and concentrated *in vacuo* to give the residue (1.226 g). Chromatography on a silica gel (100 g) column with dichloromethane–methanol (100 : 1) as the eluent afforded a solid, recrystallization of which from ethyl acetate–ether gave **16** (787.0 mg, 85%) as colorless needles, mp 200.5—202 °C. *Anal.* Calcd for $C_{18}H_{24}N_2O_4$: C, 65.04; H, 7.28; N, 8.43. Found: C, 64.76; H, 7.25; N, 8.34. MS *m/z* (%): 332 (M^+, 100), 260 (28), 247 (11), 246 (48), 245 (37), 219 (42), 218 (53), 175 (14), 43 (10). IR (KBr): 1710, 1690, 1640 cm^{-1}. UV λ_{max} nm (log ε): 226 (3.83), 234 sh (3.54), 280 (3.45), 288 (3.41). ^{1}H-NMR δ: 1.23, 1.27 (each 3H, d, J=6.6 Hz, $CHC\underline{H}_3$), 2.16 (3H, s, $ArCH_3$), 2.85 (3H, s, NCH_3), 2.99 (1H, d, J=16.5 Hz, 6-Hβ), 3.12 (1H, dd, J=16.5, 5.6 Hz, 6-Hα), 3.23 (1H, d, J=11.6 Hz, 2-Hβ), 3.81 (3H, s, OCH_3), 3.95 (1H, dd, J=11.6, 4.3 Hz, 2-Hα), 4.92—5.01 (2H, m, 5-H and OCH), 5.38 (1H, br d, 1-H), 6.59 (1H, s, 10-H), 6.87 (1H, br s, 7-H). ^{13}C-NMR δ: 15.8 (q, $ArCH_3$), 22.1 (q, $CH\underline{C}H_3$), 22.1 (q, $CH\underline{C}H_3$), 31.1 (t, 6-C), 34.2 (q, NCH_3), 48.8 (d, 1-C), 53.3 (d, 5-C), 55.3 (q, OCH_3), 56.3 (t, 2-C), 69.4 (d, OCH), 107.5 (d, 10-C), 124.1 (s), 126.7 (s), 131.1 (d, 7-C), 132.6 (s), 153.5 (s, COO), 156.4 (s), 168.3 (s, 4-CO).

1,2,3,4,5,6-Hexahydro-1,5-imino-9-methoxy-3,8-dimethyl-4-oxo-3-benzazocine (17) Concentrated H_2SO_4 (1.0 ml) was added to a stirred solution of **16** (1.04 g, 3.13 mmol) in TFA (20 ml), and stirring was continued for 15 h at room temperature. The reaction mixture was poured into water (100 ml), and extracted with chloroform (50 ml × 3). The combined extracts were washed with 10% aqueous NH_3 (100 ml), dried, and concentrated *in vacuo* to give a solid, recrystallization of which from ethyl acetate–ether afforded pure **17** (877.2 mg, 81%) as colorless prisms, mp 160—161 °C. *Anal.* Calcd for $C_{14}H_{18}N_2O_2 \cdot 1/3H_2O$: C, 66.64; H, 7.46; N, 11.10. Found: C, 66.66; H, 7.31; N, 10.87. MS *m/z* (%): 246 (M^+, 30), 175 (18), 174 (100). IR (KBr); 3295, 1640, 1625 cm^{-1}. UV λ_{max} nm (log ε): 226 (3.83), 234 sh (3.53), 282 (3.42), 288 (3.39). ^{1}H-NMR δ: 2.17 (3H, s, $ArCH_3$), 2.36 (1H, s, NH), 2.85 (3H, s, NCH_3), 2.95 (1H, dd, J=16.8, 1.3 Hz, 6-Hβ), 3.11 (1H, dd, J=16.8, 5.9 Hz, 6-Hα), 3.22 (1H, dd, J=11.6, 1.0 Hz, 2-Hβ), 3.81 (3H, s, OCH_3), 3.91 (1H, ddd, J=5.9, 1.3, 1.0 Hz, 5-H), 3.98 (1H, dd, J=11.6, 4.6 Hz, 2-Hα), 4.23 (1H, dd, J=4.6, 1.0 Hz, 1-H), 6.53 (1H, s, 10-H), 6.86 (1H, s, 7-H). ^{13}C-NMR δ: 15.9 (q, $ArCH_3$), 32.1 (t, 6-C), 34.1 (q, NCH_3), 50.2 (d, 1-C), 53.6 (d, 5-C), 55.4 (q, OCH_3), 57.6 (t, 2-C), 107.5 (d, 10-C), 124.6 (s), 126.4 (s), 131.2 (d, 7-C), 134.3 (s), 156.2 (s), 170.2 (s, 4-CO).

1,2,3,4,5,6-Hexahydro-1,5-imino-9-methoxy-3,8,11-trimethyl-4-oxo-3-benzazocine (18) Formaldehyde (37% solution in water, 14.3 ml) was added to a stirred solution of **17** (492 mg, 2.0 mmol) in formic acid (16.6 ml) at 60 °C. After being stirred at 70 °C for 1 h, the reaction mixture was poured into water (80 ml) and extracted with chloroform (40 ml × 3). The combined extracts were washed with 5% $NaHCO_3$ (50 ml), dried, and concentrated *in vacuo* to give a solid, recrystallization of which from ethyl acetate gave **18** (386.7 mg, 74%) as colorless prisms, mp 149—150 °C. *Anal.* Calcd for $C_{15}H_{20}N_2O_4 \cdot 1/4H_2O$: C, 68.03; H, 7.80; N, 10.58. Found: C, 68.06; H, 7.69; N, 10.33. MS *m/z* (%): 260 (M^+, 27), 189 (18), 188 (100). IR (KBr): 1630 cm^{-1}. UV λ_{max} nm (log ε): 224 (3.81), 280 (3.37), 288 (3.33). ^{1}H-NMR δ: 2.17 (3H, s, $ArCH_3$), 2.50 (3H, s, NCH_3), 2.80 (1H, d, J=17.2 Hz, 6-Hβ), 2.84 (3H, s, NCH_3), 3.13 (1H, d, J=11.6 Hz, 2-Hβ), 3.15 (1H, dd, J=17.2, 6.6 Hz, 6-Hα), 3.66 (1H, d, J=6.6 Hz, 5-H), 3.81 (3H, s, OCH_3), 3.86 (1H, d, J=5.0 Hz, 1-H), 3.99 (1H, dd, J=11.6, 5.0 Hz, 2-Hα), 6.52 (1H, s, 10-H), 6.86 (1H, s, 7-H). ^{13}C-NMR δ: 15.9 (q, $ArCH_3$), 26.8 (t, 6-C), 33.9 (q, NCH_3), 39.9 (q, NCH_3), 55.2 (t, 2-C), 55.3 (q, OCH_3), 56.4 (d, 1-C), 59.7 (d, 5-C), 108.3 (d, 10-C), 123.9 (s), 126.3 (s), 130.9 (d, 7-C), 132.5 (s), 156.4 (s), 170.2 (s, 4-CO).

1,2,3,4,5,6-Hexahydro-9-hydroxy-1,5-imino-3,8,11-trimethyl-4-oxo-3-benzazocine (19) A dichloromethane solution of boron tribromide (1.0 M, 10 ml, 10 mmol) was added to a stirred solution of **18** (520.0 mg, 2.0 mmol) in dry dichloromethane (60 ml) at −20 °C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into ice-water (200 ml) and the phases were separated. The aqueous layer was brought to pH 7 with 10% Na_2CO_3, and extracted with dichloromethane (100 ml × 3). The combined extracts were washed with water (100 ml), dried, and concentrated *in vacuo* to give the residue (456.2 mg). Chromatography of the residue on a silica gel (60 g) column with chloroform–methanol (20 : 1) as the eluent afforded a solid, recrystallization of which from acetone–methanol gave **19** (371.2 mg, 75%) as colorless prisms, mp 249—250 °C. *Anal.* Calcd for $C_{14}H_{18}N_2O_2 \cdot 1/5H_2O$: C, 67.28; H, 7.42; N, 11.20. Found: C, 67.21; H, 7.25; N, 11.30. MS *m/z* (%): 246 (M^+, 28), 175 (18), 174 (100). IR (KBr): 1660, 1645, 1620 cm^{-1}. UV λ_{max} nm (log ε): 222 (3.81), 282 (3.43), 288 (3.42). ^{1}H-NMR δ: 2.18 (3H, s, $ArCH_3$), 2.47 (3H, s, NCH_3), 2.76 (1H, d, J=17.2 Hz, 6-Hβ), 2.83 (3H, s, NCH_3), 3.06 (1H, d, J=11.7 Hz, 2-Hβ), 3.15 (1H, dd, J=17.2, 6.6 Hz, 6-Hα), 3.62 (1H, d, J=6.6 Hz, 5-H), 3.78 (1H, d, J=5.0 Hz, 1-H), 3.94 (1H, dd, J=11.7, 5.0 Hz, 2-Hα), 6.50 (1H, s, 10-H), 6.82 (1H, s, 7-H). ^{13}C-NMR δ: 15.8 (q, $ArCH_3$), 27.1 (t, 6-C), 34.1 (q, NCH_3), 39.8 (q, NCH_3), 55.0 (t, 2-C), 55.9 (d, 1-C), 59.6 (d, 5-C), 113.0 (d, 10-C), 123.1 (s), 124.6 (s), 131.1 (d, 7-C), 132.6 (s), 153.5 (s), 170.9 (s, 4-CO).

9-Acetoxy-1,2,3,4,5,6-hexahydro-1,5-imino-3,8,11-trimethyl-4-oxo-3-benzazocine (19b) Acetic anhydride (0.5 ml) was added to a solution of **19** (49.2 mg, 0.2 mmol) in dry pyridine (2.0 ml) and the mixture was kept at room temperature for 1 h. After dilution with water (10 ml), the mixture was extracted with chloroform (10 ml × 3). The combined extracts were washed with 5% $NaHCO_3$, dried, and concentrated *in vacuo*. The residue (71.5 mg) was subjected to chromatography (silica gel, 8 g, methanol : dichloromethane = 1 : 50) to give a solid, recrystallization of which from ethyl acetate–methanol gave **19b** (30.3 mg, 68%) as colorless prisms, mp 129—131 °C. *Anal.* Calcd for $C_{16}H_{20}N_2O_3$: C, 66.64; H, 6.99; N, 9.72. Found: C, 66.61; H, 6.98; N, 9.71. MS *m/z* (%): 288 (M^+, 28), 217 (23), 216 (100), 174 (47). IR (KBr): 1760, 1650 cm^{-1}. UV λ_{max} nm (log ε): 216 (4.00), 272 (2.79), 278 (2.73). ^{1}H-NMR δ: 2.14 (3H, s, $ArCH_3$), 2.31 (3H, s, $COCH_3$), 2.49 (3H, s, NCH_3), 2.84 (3H, s, NCH_3), 2.86 (1H, d, J=17.5 Hz, 6-Hβ), 3.09 (1H, dd, J=11.6, 1.0 Hz, 2-Hβ), 3.19 (1H, dd, J=17.5, 6.6 Hz, 6-Hα), 3.66 (1H, d, J=6.6 Hz, 5-H), 3.87 (1H, d, J=4.8 Hz, 1-H), 3.95 (1H, dd, J=11.6, 4.8 Hz, 2-Hα), 6.79 (1H, s, 10-H), 6.98 (1H, s, 7-H). ^{13}C-NMR δ: 15.9 (q, $ArCH_3$), 20.8 (q, $CO\underline{C}H_3$), 27.3 (t, 6-C), 33.9 (q, NCH_3), 39.9 (q, NCH_3), 55.1 (t, 2-C), 55.9 (d, 1-C), 59.5 (d, 5-C), 120.3 (d, 10-C), 129.4 (s), 130.4 (s), 131.5 (d, 7-C), 133.5 (s), 147.8 (s), 169.3 (CO), 170.1 (s, 4-CO).

11-Formyl-1,2,3,4,5,6-hexahydro-1,5-imino-9-methoxy-3,8-dimethyl-4-oxo-3-benzazocine (18a) Acetic anhydride (2.1 ml) was added to a stirred solution of **17** (492 mg, 2 mmol) in formic acid (6.3 ml) and the mixture was stirred for 1 h at room temperature. Removal of the solvent *in vacuo* afforded the residue, which was partitioned between chloroform and 5% $NaHCO_3$ solution. The organic phase was washed with water, dried, and concentrated *in vacuo* to give a solid, recrystallization of which from methanol gave **18a** (505.7 mg, 92.3%) as colorless needles, mp 267—270 °C. This product was a mixture of two rotational isomers (ratio, 2 : 1). *Anal.* Calcd for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.59; H, 6.60; N, 10.18. MS *m/z* (%): 274 (M^+, 68), 231 (42), 204 (12), 203 (93), 202 (100), 174 (50), 159 (10), 131 (13), 130 (10). IR (KBr): 1650, 1640 cm^{-1}. UV λ_{max} nm (log ε): 222 (4.03), 280 (3.40), 288 (3.38). ^{1}H-NMR δ: 2.17 (3H, s, $ArCH_3$, both isomers), 2.86 (2/3 × 3H, s, NCH_3, main isomer), 2.87 (1/3 × 3H, s, NCH_3), 3.08—3.20 (2H, br, 6-H_2, both isomers), 3.24 (2/3H, d, J=11.6 Hz, 2-Hβ, main isomer), 3.34 (1/3H, d, J=11.6 Hz, 2-Hβ, minor isomer), 3.82 (3H, s, OCH_3, both isomers), 3.92 (2/3H, dd, J=11.6, 4.6 Hz, 2-Hα, main isomer), 3.93 (1/3H, dd, J=11.6, 4.6 Hz, 2-Hα, minor isomer), 4.50 (2/3H, d, J=6.3 Hz, 5-H, main isomer), 4.84 (1/3H, d, J=4.6 Hz, 1-H, minor isomer), 5.22 (1/3H, d, J=6.3 Hz, 5-H, minor isomer), 5.61 (2/3H, d, J=4.6 Hz, 1-H, main isomer), 6.56 (1/3H, s, 10-H, minor isomer), 6.59 (2/3H, s, 10-H, main isomer), 6.88 (2/3H, s, 7-H, main isomer), 6.90 (1/3H, s, 10-H, minor isomer), 8.15 (2/3H, s, CHO, main isomer), 8.24 (1/3H, s, CHO, minor isomer).

11-Formyl-1,2,3,4,5,6-hexahydro-9-hydroxy-1,5-imino-3,8-dimethyl-4-oxo-3-benzazocine (19a) By the same procedure as used to prepare **19**, *O*-demethylation of **18a** (274 mg, 1 mmol) with a dichloromethane solution of boron tribromide (1.0 M, 5 ml, 5 mmol) in dry dichloromethane (30 ml) afforded **19a** (200.7 mg, 77%) as colorless needles, mp 147—152 °C (chloroform–acetone). This product was a mixture of two rotational isomers (ratio, 5 : 2). *Anal.* Calcd for $C_{14}H_{16}N_2O_3 \cdot 2H_2O$: C, 57.53; H, 5.52; N, 9.59. Found: C, 57.74; H, 5.60; N, 9.25. MS *m/z* (%): 260 (M^+, 82), 218 (11), 217 (76), 190 (12), 189 (90), 188 (100), 160 (64), 159 (10), 131 (13), 130 (10). IR (KBr): 3200, 1665, 1650, 1630, 1610 cm^{-1}. UV λ_{max} nm (log ε): 220 (3.98), 284 (3.38). ^{1}H-NMR δ: 2.18 (2/7 × 3H, s, $ArCH_3$, minor isomer), 2.21 (5/7 × 3H, s, $ArCH_3$, main isomer), 2.85 (5/7 × 3H, s, NCH_3, main isomer), 2.86 (2/7 × 3H, s, NCH_3, minor isomer), 2.87 (1/3 × 3H, s, NCH_3, both isomers), 3.01—3.15 (2H, br, 6-H_2, both isomers), 3.19 (5/7H, d, J=11.9 Hz, 2-Hβ, main isomer), 3.31 (2/7H, d, J=11.6 Hz,

2-Hβ, minor isomer), 3.88 (2/7H, dd, J=11.9, 4.6 Hz, 2-Hα, main isomer), 3.91 (1/3H, dd, J=11.6, 4.6 Hz, 2-Hα, minor isomer), 4.50 (5/7H, d, J=5.9 Hz, 5-H, main isomer), 4.80 (2/7H, d, J=4.6 Hz, 1-H, minor isomer), 5.22 (2/7H, d, J=5.9 Hz, 5-H, minor isomer), 5.56 (5/7H, d, J=4.6 Hz, 1-H, main isomer), 6.60 (2/7H, s, 10-H, minor isomer), 6.62 (5/7H, s, 10-H, main isomer), 6.88 (5/7H, s, 7-H, main isomer), 6.89 (2/7H, s, 10-H, minor isomer), 8.15 (5/7H, s, CHO, main isomer), 8.23 (2/7H, s, CHO, minor isomer). ^{13}C-NMR δ ($CDCl_3$–CD_3OD): main peaks; 15.4 (q, $ArCH_3$), 32.7 (t, 6-C), 34.0 (q, NCH_3), 45.7 (d, 1-C), 54.6 (d, 5-C), 55.9 (t, 2-C), 111.9 (d, 10-C), 121.9 (s), 125.4 (s), 130.9 (d, 7-C), 131.3 (s), 154.0 (s), 159.3 (s, CHO), 167.8 (s, CO), minor peaks; 15.4 (q, $ArCH_3$), 30.8 (t, 6-C), 34.0 (q, NCH_3), 49.8 (d, 5-C), 51.1 (d, 1-C), 57.4 (t, 2-C), 111.4 (d, 10-C), 122.6 (s), 125.5 (s), 130.8 (d, 7-C), 131.2 (s), 153.8 (s), 159.1 (s, CHO), 167.7 (s, CO).

1,2,3,4,5,6-Hexahydro-1,5-imino-9-methoxy-3,8,11-trimethyl-10-nitro-4-oxo-3-benzazocine (21) The amine **18** (300.0 mg, 1.154 mmol) was added to a mixture of H_2SO_4–HNO_3 (1 : 1, 2.0 ml) and the whole was stirred for 2 h under ice-cooling. The reaction mixture was diluted with water (50 ml), made alkaline with diluted aqueous NH_3, and extracted with chloroform (30 ml × 3). The combined extracts were washed with water (30 ml), dried, and concentrated *in vacuo* to give the residue (360 mg). Chromatography of the residue on a silica gel (90 g) column with dichloromethane–methanol (50 : 1) as the eluent gave a solid, recrystallization of which from ethyl acetate–ether gave **21** (280.6 mg, 80%) as colorless prisms, mp 151—153 °C. *Anal.* Calcd for $C_{15}H_{19}N_3O_4$: C, 59.00; H, 6.27; N, 13.76. Found: C, 58.91; H, 6.28; N, 13.63. MS m/z (%): 305 (M^+, 26), 234 (24), 233 (100), 186 (12). IR (KBr): 1660, 1530, 1400, 1380 cm^{-1}. UV λ_{max} nm (log ε): 216 (4.09), 272 (3.04), 306 (2.68). ^{1}H-NMR δ: 2.32 (3H, s, $ArCH_3$), 2.46 (3H, s, NCH_3), 2.87 (3H, s, NCH_3), 2.88 (1H, d, J=17.2 Hz, 6-Hβ), 3.17 (1H, dd, J=17.2, 6.6 Hz, 6-Hα), 3.23 (1H, d, J=12.2 Hz, 2-Hβ), 3.65 (1H, d, J=6.6 Hz, 5-H), 3.84 (3H, s, OCH_3), 3.88 (1H, d, J=12.2 Hz, 2-Hα), 3.88 (1H, s, 1-H), 7.09 (1H, s, 7-H). ^{13}C-NMR δ: 15.9 (q, $ArCH_3$), 27.0 (t, 6-C), 33.8 (q, NCH_3), 40.0 (q, NCH_3), 51.9 (d, 1-C), 53.7 (t, 2-C), 58.5 (d, 5-C), 62.4 (q, OCH_3), 124.6 (s), 129.5 (s), 132.4 (s), 133.5 (d, 7-C), 145.3 (s), 148.4 (s), 169.5 (s, CO).

10-Amino-1,2,3,4,5,6-hexahydro-1,5-imino-9-methoxy-3,8,11-trimethyl-4-oxo-3-benzazocine (22) A solution of **21** (244.0 mg, 0.8 mmol) in ethanol (20 ml) was shaken for 7 h at room temperature under 1 atm of hydrogen in the presence of 10% palladium on carbon (70 mg). The catalyst was removed by filtration and washed with ethanol (100 ml). The combined filtrates were evaporated and the residue was diluted with water (50 ml), and extracted with chloroform (30 ml × 3). The combined extracts were washed with water (20 ml), dried, and concentrated *in vacuo* to give the residue (322.8 mg). Chromatography of the residue on a silica gel (20 g) column with dichloromethane–methanol (15 : 1) as the eluent gave a solid, recrystallization of which from ethyl acetate gave **22** (187.1 mg, 85%) as colorless prisms, mp 197—199 °C. *Anal.* Calcd for $C_{15}H_{21}N_3O_2 \cdot 1/6H_2O$: C, 64.72; H, 7.71; N, 15.10. Found: C, 64.71; H, 7.66; N, 15.15. MS m/z(%): 275 (M^+, 28), 204 (28), 203 (100), 188 (21). IR (KBr): 3350, 1620 cm^{-1}. UV λ_{max} nm (log ε): 222 (4.05), 272 (3.75), 288 (3.27). ^{1}H-NMR δ: 2.29 (3H, s, $ArCH_3$), 2.50 (3H, s, NCH_3), 2.79 (1H, d, J=17.2 Hz, 6-Hβ), 2.86 (3H, s, NCH_3), 3.15 (1H, dd, J=17.2, 6.6 Hz, 6-Hα), 3.19 (1H, d, J=10.9 Hz, 2-Hβ), 3.61 (1H, d, J=6.6 Hz, 5-H), 3.73 (3H, s, OCH_3), 3.88 (1H, d, J=5.0 Hz, 1-H), 3.91 (1H, dd, J=10.9, 5.0 Hz, 2-Hα), 6.39 (1H, s, 7-H). ^{13}C-NMR δ: 15.8 (q, $ArCH_3$), 27.6 (t, 6-C), 34.0 (q, NCH_3), 40.2 (q, NCH_3), 51.7 (t, 2-C), 52.0 (d, 1-C), 59.2 (d, 5-C), 59.4 (q, OCH_3), 117.9 (s), 120.7 (d, 7-C), 128.2 (s), 129.7 (s), 136.2 (s), 144.2 (s), 170.2 (s, CO).

1,2,3,4,5,6-Hexahydro-10-hydroxy-1,5-imino-9-methoxy-3,8,11-trimethyl-4-oxo-3-benzazocine (5) The amine **22** (55.0 mg, 0.2 mmol) was dissolved in concentrated H_2SO_4 (0.2 ml) and water (0.2 ml) and then cooled to below 5 °C. A solution of sodium nitrite (15.2 mg) in water (0.02 ml) was added dropwise under the surface of the ice-cooled solution with stirring at such a rate as to maintain the temperature at 0—5 °C. The solution was stirred for an additional 60 min. A solution of diazonium salt was added in portions to 20% H_2SO_4 (2 ml) at 140 °C over 5 min and after evolution of nitrogen gas ceased, the reaction mixture was diluted with water (10 ml), made alkaline with 5% $NaHCO_3$, and extracted with chloroform (20 ml × 3). The combined extracts were washed with water (20 ml), dried, and concentrated *in vacuo* to give the residue (51.3 mg). Chromatography of the residue on a silica gel (6 g) column with dichloromethane–methanol (30 : 1—10 : 1) as the eluent gave the residue (28.0 mg), which showed three major spots on TLC (dichloromethane–methanol (20 : 1)). This residues was subjected to chromatography on preparative layer silica gel plates (Merck 5715, solvent dichloromethane–methanol (200 : 15)) to afford **18** (11.1 mg, 22%), **19** (7.9 mg, 16%), and **5** (3.0 mg, 5%).

Compound **5**: Colorless prisms from ethyl acetate, mp 217—218.5 °C. MS m/z (%): 276 (M^+, 24), 204 (100), 189 (15). High-resolution MS Calcd for $C_{15}H_{20}N_2O_3$: 276.1474. Found: 276.1473. Calcd for $C_{12}H_{14}NO_2$: 204.1025. Found: 204.1011. IR (KBr): 3500—3050, 1645 cm^{-1}. UV λ_{max} nm (log ε): 226 (3.91), 272 (3.23), 278 (3.24). ^{1}H-NMR δ: 2.26 (3H, s, $ArCH_3$), 2.51 (3H, s, NCH_3), 2.85 (1H, d, J=16.2 Hz, 6-Hβ), 2.86 (3H, s, NCH_3), 3.16 (1H, dd, J=16.2, 6.6 Hz, 6-Hα), 3.20 (1H, d, J=11.9 Hz, 2-Hβ), 3.65 (1H, d, J=6.6 Hz, 5-H), 3.78 (3H, s, OCH_3), 3.96 (1H, dd, J=11.9, 4.6 Hz, 2-Hα), 4.22 (1H, d, J=4.6 Hz, 1-H), 5.93 (1H, br s, OH), 6.49 (1H, s, 7-H). ^{13}C-NMR δ: 15.8 (q, $ArCH_3$), 27.3 (t, 6-C), 34.0 (q, NCH_3), 39.9 (q, NCH_3), 50.9 (q, 1-C), 52.6 (t, 2-C), 59.2 (d, 5-C), 60.8 (q, OCH_3), 118.8 (s, 10a-C), 122.0 (d, 7-C), 128.7 (s, 8-C), 129.5 (s, 6a-C), 143.4 (s, 9-C), 145.5 (s, 10-C), 169.8 (s, CO).

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References and Notes

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steps (Chart 4). Oxidation of **19a** with the above reagents was unsuccessful and afforded only a polar polymeric material.

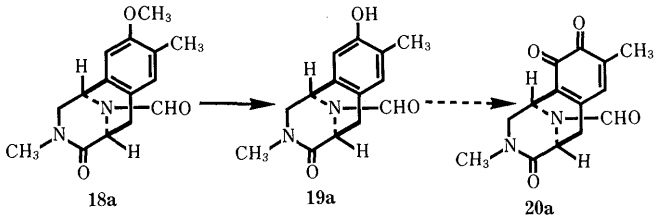

Chart 4

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