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SYNTHESIS OF SAFRAMYCINS. V. SELENIUM OXIDE OXIDATION OF HEXAHYDRO-1,5-IMINO-3-BENZAZOCIN-7,10-DIONE; A USEFUL METHOD FOR CONSTRUCTING SAFRAMYCINS C AND D FROM SAFRAMYCIN B.[1)]

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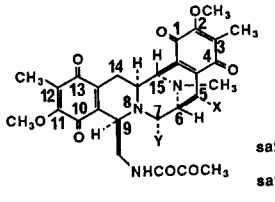
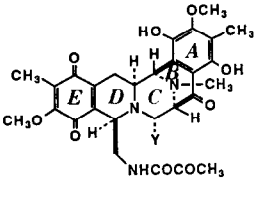
Abstract: (±)-Saframycins C (**3**) and D (**4**) have been synthesized for the first time by the regiospecific and stereoselective oxidation of (±)-saframycin B (**2**) with selenium oxide.

The saframycins (**1-6, Chart I**) are a class of antibiotics with activity against gram-positive bacteria and also against several kinds of tumor.[2)] Over the last several years other saframycin derivatives (**7-16, Chart II**)[3)] have been independently isolated from bacterial sources and marine sponges. The structure of saframycin D (**4**) was elucidated by comparing its spectroscopic data with those of saframycin C (**3**), the structure of which was determined by X-ray crystallographic analysis. We recently reported the total synthesis of (±)-saframycin B (**2**).[4)] To extend the scope of the synthetic route to saframycins, we have focused our attention on the synthesis of saframycins C (**3**) and D (**4**). Our original plan aimed at the extensive model studies on the chemistry of introduction of a hydroxy group into the C-5 position[5)] of the hexahydro-1,5-imino-3-benzazocin-7,10-dione. We now detail these investigations and their applications to the first successful transformation of (±)-saframycin B (**2**) to (±)-saframycins C (**3**) and D (**4**).

Chart I





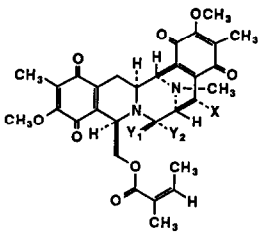
saframycin A (1): X = H, Y = CN
saframycin B (2): X = Y = H
saframycin C (3): X = OCH_3, Y = H
saframycin G (6): X = OH, Y = CN

saframycin D (4): Y = H
saframycin F (5): Y = CN

Results and Discussion

The challenge addressed was the introduction of a hydroxy group into the C-5 position of the hexahydro-1,5-imino-3-benzazocine skeleton (**Scheme I**). As a model compound we selected the phenol **18a** which was prepared in 72% yield by the partial demethylation of the readily available tricyclic lactam **17**[6)] with boron tribromide. Formation of benzyl alcohols by the direct chemical oxidation of benzylic methylene groups is not of

Chart II



renieramycin A (7): X = OH, $Y_1 = Y_2 = H$

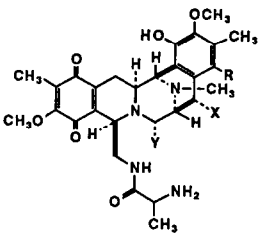
renieramycin B (8): X = OC_2H_5, $Y_1 = Y_2 = H$

renieramycin C (9): X = OH, Y_1, Y_2 = O

renieramycin D (10): X = OC_2H_5, Y_1, Y_2 = O

renieramycin E (11): X = Y_1 = H, Y_2 = OH

renieramycin F (12): X = OCH_3, Y_1 = H, Y_2 = OH



safracin A (13): R = X = Y = H

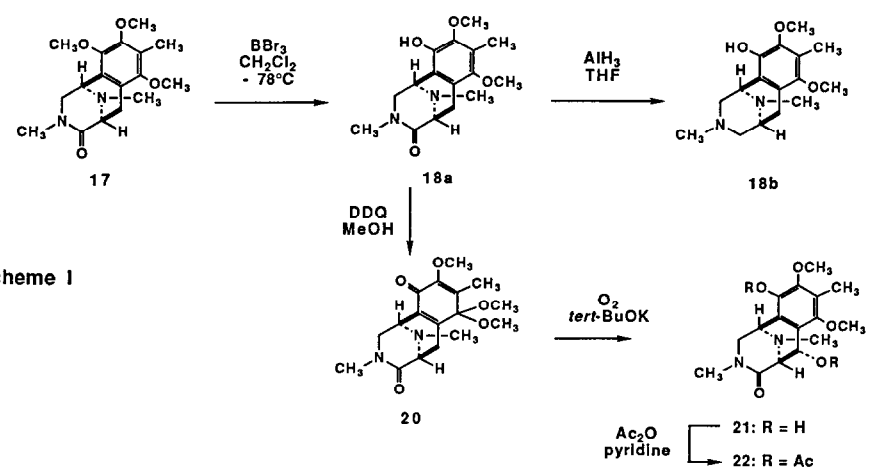
safracin B (14): R = X = H, Y = OH

saframycin Mx 1 (15): R = Y = OH, X = OCH_3

saframycin Mx 2 (16): R = OH, X = OCH_3, Y = H

general preparative value, since the alcohols so formed are susceptible to oxidation.[7] It is well known that a hydrogen atom in an allylic position of a phenol can be replaced by one of an acetoxy group on treatment with lead tetraacetate.[8] However, treatment of **18a** with lead tetraacetate in dichloromethane gave the *p*-quinone **19a** (51% yield) and the *p*-quinone acetal **20** (43% yield), the latter of which was identical in all respects with **20** prepared by DDQ oxidation at **18a** in methanol[9] in 87% yield. Homolytic bromination of **18a** with bromine in carbon tetrachloride followed by solvolysis[10] also failed. On the other hand, exposure of the quinone acetal **20** to molecular oxygen in a dimethyl sulfoxide-*tert*-butyl alcohol (4:1) solution containing potassium *tert*-butoxide[11] gave the phenol **21** in only 13% yield along with **19a** and **20** in 7.7% and 27.7% yields, respectively. Acetylation of **21** with acetic anhydride in pyridine afforded **22** in 68% yield, whose ^{1}H NMR spectrum indicated a low-field shift of the singlet of H-5 proton at δ 6.05.

Scheme I



17 18a 18b 20

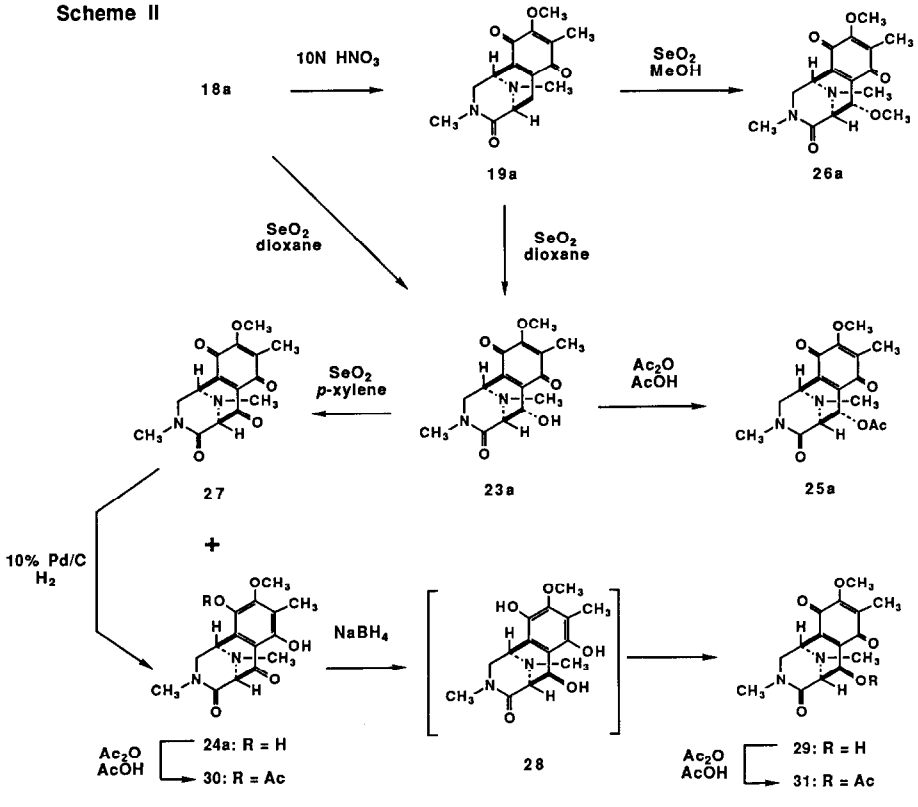
These observations indicated that the introduction of a hydroxy group required a different approach (**Scheme II**). In the chemistry of tetrasubstituted *p*-benzoquinones, duroquinone and 2,3-dimethyl-1,4-

naphthoquinone are known to react with a variety of nucleophiles such as enolates or amines to give side-chain oxidation products.[12] Thus, this problem was solved by using *p*-quinone **19a** with selenium oxide oxidation because C-5 was at an allylic position. Treating **19a** which was prepared from **18a** with 10N HNO_3 in 87% yield with selenium oxide (1.1 equiv) in dioxane afforded the allylic alcohol **23a** in 80% yield. Furthermore, oxidation of the phenol **18a** with selenium oxide in dioxane afforded **23a** in 71% yield. The ^1H NMR spectrum of **23a** displayed H-5 as a doublet at δ 4.80 (J = 1 Hz). Acetylation of **23a** with acetic anhydride in acetic acid afforded **25a** in 91% yield, whose ^1H NMR spectrum indicated a low-field shift of the signal of the H-5 proton (δ 5.96, J = 1.7 Hz). Experiments now in progress are directed to introduction of the methoxy group at C-5 position. Treating **19a** with selenium oxide in methanol under reflux for 30 h gave **26a** in 60.5% yield.

We then investigated the conversion of **23a** into the hydroquinone **24a**. Treatment of **23a** with selenium oxide in *p*-xylene afforded the unstable ketone **27** (7.3%) and the hydroquinone **24a** (29.6%). The intramolecular redox reaction of **23a** produced **24a**.[14, 15] Hydrogenation of **27** with 10% palladium on carbon in ethyl acetate gave **24a** in 98% yield. The structure of **24a** is supported by the ^{13}C NMR spectrum, which shows a peak at δ 196.4 assigned to the carbonyl carbon at C-5 position. The ^1H NMR spectrum also shows two D_2O exchangeable singlets at δ 5.58 and 11.52 assigned to the hydroxy peaks.

The next stage of the investigation established a method of synthesizing the alcohol **29** with the

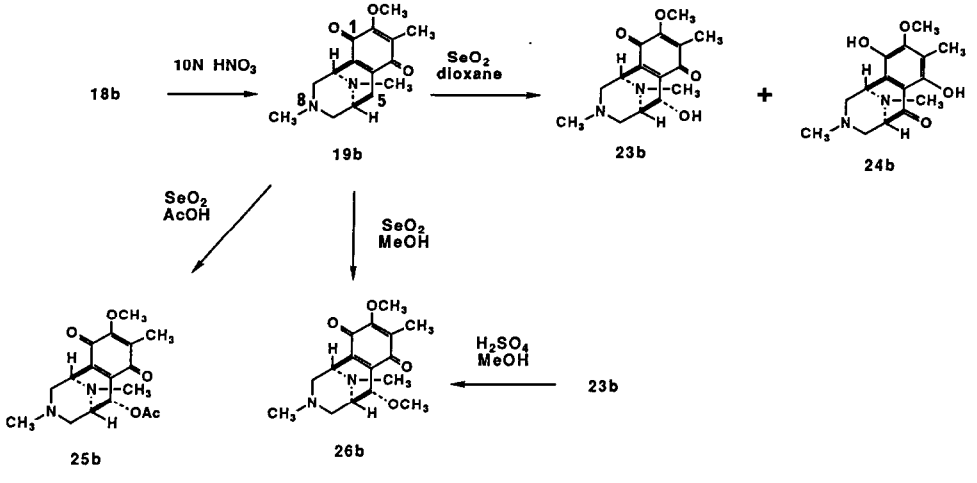
Scheme II



stereochemistry of the C-5 position epimeric to that of **23a**. Reduction of **24a** with sodium borohydride in ethanol at room temperature for 10 min accompanied by auto-oxidation through **28** gave **29** in 81% yield. The stereochemistry of the C-5 position in **29** is supported by the ^{1}H NMR spectrum, which displays H-5 as a doublet at δ 5.10 (J = 6.8 Hz), whereas the ^{1}H NMR spectrum of **23a** shows the H-5 as a doublet at δ 4.80 (J = 1.0 Hz). Acetylation of **29** with acetic anhydride in acetic acid at 100°C for 1 h afforded **30** (75.5%) and **31** (5.4%). ^{1}H NMR spectrum of **30** indicated a low-field shift of the signal of the H-5 proton at δ 6.07 (d, J = 7.3 Hz). Treatment of **29** with selenium oxide in dioxane under reflux for 3 h afforded **27** (57.4%) and **24a** (7.5%). The oxidation was especially rapid for the axial alcohol **29** because the steric strain was relieved in going from the reactant to the product.

Before continuing with the syntheses of saframycins C (**3**) and D (**4**) the reaction of the quinone **19b** as the N-8 amine model with selenium oxide was explored. Oxidative demethylation of **18b** with 10N HNO_3 afforded the *p*-quinone **19b** in 98.7% yield. Disappointingly, subjecting **19b** to selenium oxide in dioxane under reflux led to the rapid consumption of the starting material and the production of an unidentifiable product.[16] The prehibition of undesired reactions would probably best be accomplished with a method which utilizes room temperature. This was accomplished as outlined in **Scheme III**.

Scheme III



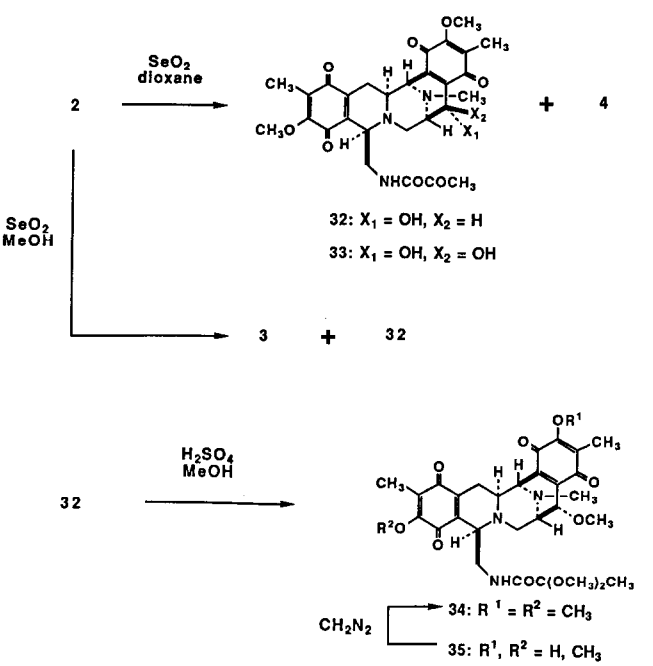
The reaction run at room temperature gave the desired alcohol **23b** in 74.8% yield along with **24b** in 11.8% yield. Structure of the alcohol **23b** was supported by comparison of ^{1}H NMR spectral data with that of alcohols **23a** and **29**. Most telling was the signal of the C-5 methine proton of **23b** at δ 4.39 compared to a doublet at δ 4.80 (J = 1.0 Hz) for **23a** and a doublet at δ 5.10 (J = 6.8 Hz) for **29**. Treatment of **19b** with selenium oxide in acetic acid at room temperature for 48 h afforded **25b** (77.5%) and **23b** (20.4%). The ^{1}H NMR spectrum of **25b** showed the H-5 as a singlet at δ 5.56. Finally, Treatment of **19b** with selenium oxide in methanol at room temperature for 9 days afforded **26b** in only 11.1% yield along with **23b** in 30.8% yield

(**19b**; 26.2% recovery). In studying the conversion of **24b** to **26b**, however, the replacement of a hydroxy group of **23b** using methanol and concentrated H_2SO_4 at room temperature for 70 h provided a 9.4% yield of **26b** in addition to recovery of 77.1% of the starting material.

Thus, we efficiently synthesized the quinones **26a** and **26b** and the hydroquinones **24a** and **24b**, embodying all of the skeletal features of the "right half" of saframycins C and D.

Encouraged by the results of these model studies, we successfully applied the syntheses of saframycins C (**3**) and D (**4**) (**Scheme IV**). Unlike the ABC model, the saframycin system has the potential to form isomers (at C-5 and/or C-14 position), thereby creating a regiochemical problem in the oxidation step. We were , however, able to anticipate that this oxidation might be highly selective by the steric environment of the two methylene groups. Treating (±)-saframycin B (**2**) with selenium oxide (2 equiv) in dioxane at room temperature for 72 h afforded (±)-saframycin D (**4**) in 15.6% yield (10.9% yield of **2** was recovered) along with the 5-hydroxy compounds **32** and **33** in 40.0% and 4.5% yields, respectively. The hydroxy stereochemistry of **32** was assigned on the basis of a 0.5 Hz coupling between H-5 (δ 4.36) and H-6 (δ 3.21). The H-5 (δ 5.04) and H-6 (δ 3.21) coupling for the C-5 isomer **33** was 6.8 Hz. Furthermore, treating (±)-saframycin B (**2**) with selenium oxide in methanol at room temperature for 88 h afforded (±)-saframycin C (**3**) and **32** in 44.7% and 19.1% yields, respectively. The synthetic saframycins C and D were identical with the natural one when data of spectroscopic ^1H NMR, ^{13}C NMR, IR, UV, MS, and TLC data were compared.

Scheme IV



Finally, we turned our attention to the conversion of the alcohol **32** to saframycin C (**3**). Several common methods of effecting alcohol alkylation were eliminated as being inappropriate to meet our need. Indeed, numerous attempts at this conversion under basic conditions were totally unsuccessful because of the

labile nature of the quinones. Fly's procedure[17] using Meerwein's trimethyloxonium tetrafluoborate salts and Ohno's procedure[18] using diazomethane catalyzed by silica gel failed, and only starting material was recovered. Alternatively, the replacement of a hydroxy group of **32** using methanol and concentrated H_2SO_4 at 60°C for 24 h gave a 1:1 ratio of **34** and **35**, which was subsequently treated with diazomethane to provide **34** in 47.8% yield. The structure proposed for the ketal **34** was supported by the ^{13}C NMR spectrum, which showed a peak at δ 100.3 assigned to the new ketal carbon. In addition, the ^{1}H NMR spectrum showed five methoxy methyl peaks at δ 2.82, 3.00, 3.54, 4.02, and 4.08. However, attempts at hydrolysis of the ketal **34** under acidic conditions were unsuccessful.[19]

In summary, we have achieved a one step conversion of saframycin B (**2**) to saframycins C (**3**) and D (**4**) using regiospecific and stereoselective selenium oxide oxidation. Efforts to apply this transformation to the syntheses of saframycins F and G and renieramycins are continuing in our laboratory.

Experimental Section

All melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. UV spectra were determined in methanol with a Hitachi 340 spectrometer. IR spectra were obtained with a Hitachi 260-10 spectrophotometer and ^{1}H-NMR spectra were recorded at 400MHz with a JEOL GX 400 spectrometer. ^{13}C-NMR were recorded at 100MHz (multiplicity determined from off-resonance decoupled or INEPT spectra). NMR spectra were measured in $CDCl_3$, and chemical shifts were recorded in δ_H values relative to internal $(CH_3)_4Si$ standard. Mass spectra were recorded on a JMS-DX 302 mass spectrometer. Elemental analyses were obtained by 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, and removal of the solvent was done with a rotary evaporator and, finally, under high vacuum. Column chromatography was performed with E. Merck silica gel 60 (70-230 mesh).

10-Hydroxy-7,9,-dimethoxy-3,8,11-trimethyl-4-oxo-1,2,3,4,5,6-hexahydro-1,5-imino-3-benzazocine (18a). To a stirred solution of **17** (960 mg, 3 mmol) in dichloromethane (60 mL) at -78°C was added a dichloromethane solution of boron tribromide (1.0 M, 6 mL, 6 mmol). After being kept at the same temperature for 1 h, and then at 0°C for 1 h, the reaction mixture was poured onto ice-water (20 g) and the phase was separated. The aqueous layer was extracted with dichloromethane (50 mL x 3). The combined extracts were washed with brine (50 mL), dried, and concentrated in vacuo to give the residue (46 mg). The acidic aqueous layer was made alkaline with 5% $NaHCO_3$ solution and extracted with chloroform (50 mL x 3). The combined extracts were washed with water (50 mL), dried, and concentrated in vacuo to give a solid (845 mg), recrystallization of which from acetone gave **18a** (663.1 mg, 72.2 %) as colorless prisms: mp 199-201°C; IR (KBr) 3500-3100, 1645 cm^{-1}; UV λ_{max} (log ε) 224sh (3.95), 276sh (3.30), 282 (3.37) nm; ^{1}H NMR δ 2.16 (3H, s, Ar CH_3), 2.46 (3H, s, amine NCH_3), 2.84 (1H, dd, J = 17.1, 1.2 Hz, H-6β), 2.86 (3H, s, amide NCH_3), 2.91 (1H, dd, J = 17.1, 6.4 Hz, H-6α), 3.11 (1H, dd, J = 11.1, 0.7 Hz, H-2α), 3.69 (1H, ddd, J = 6.4, 1.2, 0.5 Hz, H-5), 3.79 and 3.84 (each 3H, s, OCH_3), 3.94 (1H, dd, J = 11.1, 5.1 Hz, H-2β), 4.11 (1H, ddd, J = 5.1, 0.7, 0.5 Hz, H-1), 5.82 (1H, br s, OH); ^{13}C NMR δ 9.0 (q), 22.7 (t, C^6), 34.1 (q),

39.9 (q), 51.1 (d, C^1), 54.1 (t, C^2), 58.7 (d, C^5), 60.1 (q), 60.4 (q), 115.2 (s), 118.2 (s), 125.0 (s), 143.3 (s), 148.3 (s), 149.7 (s), 170.7 (s, CO); MS, *m/z* (relative intensity) 306 (M^+, 17), 235 (19), 234 (100), 220 (7), 219 (13), 204 (9). Anal. Calcd for $C_{16}H_{22}N_2O_4$: C, 62.72; H, 7.24; N, 9.14. Found: C, 62.69; H, 7.41; N, 9.03.

1,2,3,4,5,6,7,10-Octahydro-9-methoxy-3.8.11-trimethyl-4,7,10-trioxo-1.5-imino-3-benzazocine (19a). A solution of **18a** (122.4 mg, 0.4 mmol) in 10 N HNO_3 (5 mL) was stirred at room temperature for 1 h. The reaction mixture was diluted with water (20 mL) and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give **19a** (133.9 mg) as a pare yellow solid, which was recrystallized from ethyl acetate-ether to give pure **19a** (100.9 mg, 87 %) as pale yellow prisms: mp 150-152°C; IR (KBr) 1650, 1630 cm^{-1}; UV λ_{max} (log ε) 268 (4.12), 370 (2.82) nm; ^1H NMR δ 1.96 (3H, s, quinone CH_3), 2.45 (3H, s, amine NCH_3), 2.75 (1H, dd, *J* = 20.5, 1.7 Hz, H-6β), 2.76 (1H, dd, *J* = 20.5, 6.1 Hz, H-6α), 2.89 (3H, s, amide CH_3), 3.04 (1H, dd, *J* = 12.0, 0.5 Hz, H-2α), 3.49 (1H, ddd, *J* = 6.1, 1.7, 0.5 Hz, H-5), 3.90 (1H, dd, *J* = 12.0, 5.4 Hz, H-2β), 3.96 (1H, ddd, *J* = 5.4, 0.5, 0.5 Hz, H-1), 4.01 (3H, s, OCH_3); ^{13}C NMR δ 8.7 (q), 24.0 (t, C^6), 33.8 (q), 39.8 (q), 49.7 (d, C^1), 51.1 (t, C^2), 58.2 (d, C^5), 60.9 (q), 129.4 (s), 137.4 (s), 140.9 (s), 155.4 (s), 169.2 (s, CO), 182.3 (s, quinone CO), 186.6 (s, quinone CO), MS, *m/z* (relative intensity) 290 (M^+, 100), 235 (22), 231 (27), 220 (22), 219 (27), 218 (65), 205 (13), 204 (56), 202 (16), 201 (21), 190 (26), 176 (32), 131 (10). Anal. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25; N, 9.65. Found: C, 61.88; H, 6.26; N, 9.54.

Oxidation of 18a with Lead Tetraacetate. To a stirred solution of **18a** (122.4 mg, 0.4 mmol) in dichloromethane (10 mL) was added lead tetraacetate (193.2 mg, 0.436 mmol) in one portion at room temperature and stirring was continued at the same temperature for 30 min. The reaction mixture was poured into water (20 mL) and the phase was separated. The aqueous layer was extracted with dichloromethane (20 mL x 2). The combined extracts were washed with 5% $NaHCO_3$ solution (20 mL), dried, and concentrated in vacuo to give the residue (193.8 mg). Chromatography on a silica gel (10 g) column with dichloromethane-acetone (3:1) afforded **19a** (59.6 mg, 51.4 %), as a pale yellow solid. Recrystallization of which from ethyl acetate-ether afforded pure **19a** as pale yellow prisms, mp 150-152°C, whose spectra were identical with those of an authentic sample as above. Further elution with dichloromethane-acetone (1:1 - 1:3) gave **20** (57.2 mg, 42.6 %) a colorless solid. Recrystallization of which from ethyl acetate-ether afforded pure **20** as colorless prisms: mp 166-168°C; IR (KBr) 1655, 1635, 1615 cm^{-1}; UV λ_{max} (log ε): 239 (4.14), 306 (3.51) nm; ^1H NMR δ 1.85 (3H, s, C=C-CH_3), 2.42 (3H, s, amine NCH_3), 2.71 (2H, d like, H_2-6), 2.92 (3H, s, amide NCH_3), 3.13 and 3.24 (each 3H, s, OCH_3), 3.36 (1H, dd, *J* = 12.2, 0.7 Hz, H-2α), 3.62 (1H, t like, H-5), 3.68 (1H, ddd, *J* = 4.9, 0.7, 0.5 Hz, H-1), 3.82 (1H, dd, *J* = 12.2, 4.9 Hz, H-2β), 4.17 (3H, s, OCH_3); ^{13}C NMR δ 7.9 (q), 23.3 (t, C^6), 33.7 (q), 39.8 (q), 50.7 (d, C^1), 51.3 (q), 51.3 (q), 51.9 (t, C^2), 58.6 (d, C^5), 58.8 (q), 98.7 (s), 120.9 (s), 136.4 (s), 140.4 (s), 160.3 (s), 169.9 (s, CO), 184.6 (s, CO); MS, *m/z* (relative intensity) 336 (M^+, 16), 321 (23), 305 (100), 289 (13), 264 (13), 262 (15), 234 (47), 219 (16), 218 (26), 204 (13). Anal. Calcd for $C_{17}H_{24}N_2O_5$: C, 60.70; H, 7.19; N, 8.33. Found: C, 60.57; H, 7.31; N, 8.24.

Reaction of 18a with DDQ. To a stirred solution of **18a** (306 mg, 1 mmol) in dry methanol (10 mL) was successive by added dichlorodicyano-*p*-benzoquinone (DDQ, 98 %, 242.1 mg, 1.05 mmol) and finely powdered anhydrous $KHCO_3$ (105 mg, 1.05 mmol). The reaction mixture was stirred at room temperature for

1.5 h, and then concentrated. The residue was added to water (50 mL), and extracted with dichloromethane (50 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (50 mL), dried, and concentrated in vacuo to give a solid (352.8 mg). Recrystallization of which from ethyl acetate-ether gave **20** (293 mg, 87.2 %) as colorless prisms, mp 166-168°C, which were identical in all respects with an authentic sample obtained earlier.

Oxidation of 20 by Triplet Oxygen. A solution of **20** (150.4 mg, 0.448 mmol) in dimethyl sulfoxide-*tert*-butyl alcohol (4:1, 20 mL) was stirred in atmosphere of oxygen at room temperature for 10 min. To the equilbrated solution was added potassium *tert*-butoxide (75 mg, 1.5 molar equiv.) and the solution was stirred at room temperature for 1 h. The reaction mixture was poured into water (20 mL) and neutralized by addition of acetic acid. The solution was extracted with chloroform (20 mL x 3). The combined extracts were washed with brine (30 mL), dried, and concentrated in vacuo to give the residue (110.8 mg). Chromatography on a silica gel (10 g) column with dichloromethane-methanol (80:1) afforded **19a** (10.0 mg, 7.7 %), with dichloromethane-methanol (40:1) afforded **20** (41.6 mg, 27.7 %), and with dichloromethane-methanol (20:1) afforded **21** (19.1 mg, 13.3 %) as a colorless solid. An analytical sample of **21** was obtained by crystallization from methanol: mp 203-205°C; IR (KBr) 3430, 3350, 1645 cm^{-1}: UV λmax (log ε) 224 (3.89), 276sh (3.26), 284 (3.40) nm; ^1H NMR δ (CD_3OD) 2.13 (3H, s, Ar CH_3), 2.65 (3H, s, amine NCH_3), 2.83 (3H, s, amide NCH_3), 3.07 (1H, d, J = 12.7 Hz, H-2α), 3.50 (1H, dd, J = 1.7, 0.5 Hz, H-5), 3.79 and 3.84 (each 3H, s, OCH_3), 4.06 (1H, dd, J = 12.7, 4.9 Hz, H-2β), 4.20 (1H, dd, J = 4.9, 0.5 Hz, H-1), 4.82 (1H, d, J = 1.7 Hz, H-6); ^{13}C NMR δ (CD_3OD) 7.2 (q), 32.7 (q), 39.6 (q), 49.0 (t, C^2), 50.2 (d, C^1), 58.6 (q), 59.0 (q), 64.4 (d, C^5), 66.7 (d, C^6), 116.4 (s), 118.2 (s), 126.3 (s), 141.3 (s), 149.6 (s), 150.7 (s), 168.0 (s, CO); MS, *m/z* (relative intensity) 322 (M^+, 45), 305 (17), 304 (14), 289 (19), 273 (13), 251 (15), 250 (100), 235 (24), 234 (50), 219 (12), 218 (21). Anal. Calcd for $C_{16}H_{22}N_2O_5 \cdot 1/4H_2O$: C, 58.79; H, 6.94; N, 8.57. Found: C, 58.67; H, 7.03; N, 8.44.

Acetylation of 21. To a solution of **21** (14.5 mg, 0.045 mmol) in dry pyridine (0.5 mL) was added acetic anhydride (0.2 mL), and the mixture was kept at room temperature for 2 h. After dilution with water (10 mL), the mixture was extracted with chloroform (10 mL x 3). The combined extracts were washed with water (10 mL), dried, and concentrated in vacuo. The residue (17.4 mg) was subjected to chromatography (silica gel, 8 g, elution with dichloromethane-methanol 50:1) to give **22** (12.5 mg, 68.4 %) as a solid, which was recrystallized from ethyl acetate-ether to give pure **22** as colorless needles: mp 208-209°C; IR (KBr) 1765, 1735, 1655 cm^{-1}; UV λ_{max} (log ε) 224 (3.97), 270sh (2.53), 276 (2.60) nm; ^1H NMR δ 2.03 (3H, s, $COCH_3$), 2.10 (3H, s, Ar CH_3), 2.24 (3H, s, $COCH_3$), 2.65 (3H, s, amine NCH_3), 2.85 (3H, s, amide NCH_3), 3.02 (1H, d, J = 12.7 Hz, H-2α), 3.53 (1H, dd, J = 1.7, 0.5 Hz, H-5), 3.83 and 3.92 (each 3H, s, OCH_3), 4.00 (1H, dd, J = 12.7, 4.9 Hz, H-2β), 4.28 (1H, dd, J = 4.9, 0.5 Hz, H-1), 6.05 (1H, d, J = 1.7 Hz, H-6); MS, *m/z* (relative intensity) 406 (M^+, 37), 363 (12), 347 (33), 335 (21), 334 (100), 292 (28), 289 (15), 277 (18), 276 (99), 250 (25), 234 (28), 219 (15), 218 (40), 204 (11). Anal. Calcd for $C_{20}H_{26}N_2O_7$: C, 59.10; H, 6.45; N, 6.89. Found: C, 58.73; H, 6.62; N, 6.66.

6-Hydroxy-9-methoxy-3,8,11-trimethyl-4,7,10-trioxo-(1α,5α,6β)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (23a). From 19a. A solution of **19a** (39.1 mg, 0.135 mmol) and selenium oxide (15 mg, 0.149 mmol) in dioxane (3 mL) was heated at reflux for 4 h. The reaction mixture

was filtered and then washed with chloroform (50 mL). After the combined filtrates were concentrated to dryness, the residue was diluted with water (20 mL) and extracted with chloroform (20 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (30 mL), dried, and concentrated in vacuo to give the residue (126 mg). Chromatography on a silica gel (8 g) column with dichloromethane-methanol (100:1 - 40:1) afforded **23a** (33.0 mg, 80.0 %) as a solid. **From 18a**. A solution of **18a** (229.5 mg, 0.75 mmol) and selenium oxide (88.8 mg, 0.80 mmol) in dioxane (10 mL) was heated at reflux for 5 h. The following the standard workup (vide supra) to give the residue (277.4 mg). Chromatography on a silica gel (15 g) column with dichloromethane-methanol (100:1) afforded a pale yellow solid (44.6 mg), which showed two major spots on TLC (R_f 0.33 and 0.20, solvent 4:5 acetone-dichloromethane). This material was subjected to chromatography on preparative layer silica gel plates (Merck, 5715, solvent 4:5 acetone-dichloromethane) to afford **24a** (18.2 mg, 7.9 %) and **27** (14.1 mg, 6.5 %). Further elution with dichloromethane-methanol (75:1 - 40:1) gave **23a** (161.9 mg, 70.5 %) as a solid.

Compound 23a: pale yellow prisms from ethyl acetate-ether, mp 175.5-178°C; IR (KBr) 3410, 1675, 1655, 1650, 1615 cm^{-1}; UV λ_{max} (log ε) 262 (3.92), 378 (2.69) nm; ^1H NMR δ 1.98 (3H, s, quinone CH_3), 2.66 (3H, s, amine NCH_3), 2.88 (3H, s, amide NCH_3), 2.98 (1H, d, J = 12.9 Hz, H-2α), 3.11 (1H, br s, OH), 3.60 (1H, dd, J = 1.0, 0.5 Hz, H-5), 3.98 (1H, dd, J = 12.9, 5.4 Hz, H-2β), 4.01 (3H, s, OCH_3), 4.03 (1H, dd, J = 5.4, 0.5 Hz, H-1), 4.80 (1H, d, J = 1.0 Hz, H-6); ^{13}C NMR δ 8.7 (q), 34.1 (q), 40.8 (q), 47.5 (d, C^1), 49.9 (t, C^2), 61.0 (q), 64.1 (d, C^5), 66.0 (d, C^6), 129.7 (s), 138.9 (s), 139.4 (s), 155.5 (s), 166.5 (s, CO), 182.5 (s, quinone CO), 186.9 (s, quinone CO); MS, *m/z* (relative intensity) 306 (M^+, 100), 291 (13), 290 (10), 277 (18), 275 (13), 263 (14), 236 (18), 235 (22), 234 (29), 220 (19), 219 (23), 218 (91), 206 (29), 204 (12), 177 (15), 101 (12). Anal. Calcd for $C_{15}H_{18}N_2O_5 \cdot 1/4H_2O$: C, 57.96; H, 6.00; N, 9.01. Found: C, 57.84; H, 5.93; N, 8.85.

Compound 24a: pale yellow needles from acetone, mp 232.5-234°C dec; IR (KBr) 3300-2500, 1710, 1690, 1670, 1625 cm^{-1}; UV λ_{max} (log ε) 241 (3.93), 283 (3.95), 374 (3.71), and λmin (log ε) 231 (3.90), 259 (3.57), 316 (2.88) nm; ^1H NMR δ 2.20 (3H, s, Ar CH_3), 2.55 (3H, s, amine NCH_3), 2.92 (3H, s, amide NCH_3), 3.30 (1H, dd, J = 12.2, 1.2 Hz, H-2α), 3.89 (3H, s, OCH_3), 3.92 (1H, d, J = 1.2 Hz, H-5), 4.04 (1H, dd, J = 12.2, 5.2 Hz, H-2β),4.38 (1H, dd, J = 5.2, 1.2 Hz, H-1), 5.58 (1H, br s, OH), 11.52 (1H, br s, OH); ^{13}C NMR δ 8.8 (q), 34.5 (q), 40.7 (q), 51.5 (d, C^1), 52.7 (t, C^2), 61.1 (q), 71.8 (d, C^5), 109.3 (s), 118.5 (s), 120.7 (s), 137.8 (s), 153.4 (s), 155.5 (s), 163.1 (s, CO), 196.4 (C^6, CO); MS, *m/z* (relative intensity) 306 (M^+, 100), 289 (6), 249 (14), 236 (26), 235 (66), 234 (17), 220 (25), 217 (13), 206 (11), 204 (16), 192 (11). Anal. Calcd for $C_{15}H_{18}N_2O_5$: C, 58.81; H, 5.92; N, 9.15. Found: C, 58.70; H, 5.96; N, 9.10.

6-Acetoxy-9-methoxy-3,8,11-trimethyl-4,7,10-trioxo-(1α,5α,6β)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazo-cine (25a). To a solution of **23a** (306 mg, 1 mmol) in acetic acid (10 mL) was added acetic anhydride (2 mL), and the mixture was heated at 100°C for 1 h. After dilution with water (40 mL), the mixture was extracted with chloroform (20 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (20 mL), dried, and concentrated in vacuo to give a red solid (343.6 mg), recrystallization of which from ethyl acetate gave **25a** (317 mg, 91.1 %) as pale yellow prisms: mp 183-185°C; IR (KBr) 1735, 1665, 1655, 1625, 1605 cm^{-1}; UV λmax (log ε) 262 (4.05), 378 (2.91) nm; ^1H NMR δ 1.97 (3H, s, quinone

CH_3), 2.10 (3H, s, $COCH_3$), 2.63 (3H, s, amine NCH_3), 2.89 (3H, s, amide NCH_3), 2.99 (1H, d, J = 13.2 Hz, H-2α), 3.57 (1H, dd, J = 1.7, 0.5 Hz, H-5), 3.97 (1H, dd, J = 13.2, 5.4 Hz, H-2β), 4.01 (3H, s, OCH_3), 4.12 (1H, dd, J = 5.4, 0.5 Hz, H-1), 5.96 (1H, d, J = 1.7 Hz, H-6); MS, *m/z* (relative intensity) 348 (M^+, 70), 306 (23), 290 (17), 289 (39), 235 (11), 234 (16), 219 (20), 218 (100), 204 (10). Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.51; H, 5.85; N, 7.99.

6,9-Dimethoxy-3,8,11-trimethyl-4,7,10-trioxo-(1α,5α,6β)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (26a). A solution of **19a** (130.1 mg, 0.449 mmol) and selenium oxide (99.6 mg, 0.898 mmol) in methanol (6 mL) was heated at reflux for 30 h. After dilution with water (20 mL) and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (30 mL), dried, and concentrated in vacuo to give the residue (134.7 mg). Chromatography on a silica gel (15 g) column with dichloromethane-methanol (100:1 - 80:1) afforded **26a** (86.9 mg, 60.5 %) as a solid, recrystallization of which from acetone-ether afforded pure **26a** as pale yellow prisms. Further elution with dichloromethane-methanol (20:1) gave the starting material **19a** (15.0 mg, 11.5 % recovery) as pale yellow prisms.

Compound 26a: mp 158-159°C; IR 1655, 1640, 1615 cm^{-1}; UV λ_{max} (log ε) 262 (4.00), 376 (2.86) nm; ^1H NMR δ 1.99 (3H, s, quinone CH_3), 2.64 (3H, s, amine NCH_3), 2.87 (3H, s, amide NCH_3), 2.95 (1H, d, J = 13.2 Hz, H-2α), 3.58 (1H, dd, J = 1.2, 0.5 Hz, H-5), 3.60 (3H, s, OCH_3), 3.96 (1H, dd, J = 13.2, 5.4 Hz, H-2β), 3.98 (3H, s, OCH_3), 4.05 (1H, dd, J = 5.4, 0.5 Hz, H-1), 4.26 (1H, d, J = 1.5 Hz, H-6); MS, *m/z* (relative intensity) 320 (M^+, 75), 289 (18), 248 (10), 219 (18), 218 (100). Anal. Calcd for $C_{16}H_{20}N_2O_5$: C, 59.99; H, 6.29; N, 8.75. Found: C, 60.03; H, 6.36; N, 8.76.

Oxidation of 23a with Selenium Oxide. A solution of **23a** (91.8 mg, 0.3 mmol) and selenium oxide (66.6 mg, 0.6 mmol) in *p*-xylene (5 mL) was heated at reflux for 3 h. The reaction mixture was filtered and then washed with chloroform (50 mL). After the combined filtrates were concentrated to dryness, the residue was diluted with water (20 mL) and extracted with chloroform (20 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (30 mL), dried, and concentrated in vacuo to give the residue (57.3 mg). Chromatography on a silica gel (8 g) column with dichloromethane-methanol (150:1) afforded **27** (6.7 mg, 7.3 %), with dichloromethane-methanol (100:1) afforded **24a** (27.2 mg, 29.6 %), and with dichloromethane-methanol (40:1) afforded the starting material **23a** (4.4 mg, 4.8 % recovery).

9-Methoxy-3,8,11-trimethyl-4,6,7,10-tetraoxo-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (27). This is a red solid, which is recrystallized from ethyl acetate to give green prisms: mp 230-235°C dec; IR (KBr) 1725, 1665, 1655, 1605 cm^{-1}; UV λ_{max} (log ε) 226 (4.12), 264sh (3.89), 380 (2.99), and λ_{min} (log ε) 210 (4.04), 256 (3.92), 318 (2.78) nm; ^1H NMR δ 1.98 (3H, s, quinone CH_3), 2.59 (3H, s, amine NCH_3), 2.95 (3H, s, amide NCH_3), 3.20 (1H, dd, J = 12.8, 0.9 Hz, H-2α), 3.82 (1H, d, J = 1.2 Hz, H-5), 4.03 (3H, s, OCH_3), 4.13 (1H, dd, J = 12.8, 5.8 Hz, H-2β), 4.21 (1H, ddd, J = 5.8, 1.2, 0.9 Hz, H-1); ^{13}C NMR δ 8.9 (q), 34.5 (q), 40.4 (q), 50.3 (t, C^2), 51.6 (d, C^1), 60.9 (q), 72.3 (d, C^5), 125.1 (s), 130.5 (s), 145.2 (s), 155.0 (s), 183.7 (s, quinone CO), 184.5 (s, C^6 CO), 188.8 (s, quinone CO); MS, *m/z* (relative intensity) 306 (M^+ + 2, 50), 304 (M^+, 100), 262 (14), 261 (84), 247 (13), 236 (20), 235 (69), 234 (51), 233 (20), 232 (14), 220 (34), 219 (13), 218 (43), 217 (18), 206 (28), 205 (29), 204 (26), 192 (22), 191 (11), 190 (29), 176 (18), 162 (13), 134 (10), 108 (11). Anal. Calcd for $C_{15}H_{16}N_2O_5$: C, 59.20; H, 5.30; N, 9.21. Found: C, 59.20; H, 5.39; N, 9.08.

7,10-Dihydroxy-9-methoxy-3,8,11-trimethyl-6-oxo-1,2,3,4,5,6-hexahydro-1,5-imino-3-benzazocine (24a). A solution of **27** (28.3 mg, 0.093 mmol) in ethyl acetate (4 mL) was hydrogenated over 10% palladium on carbon (10 mg) at 1 atm for 20 min. The catalyst was removed by filtration and washed with ethyl acetate (50 mL). The combined filtrates were concentrated in vacuo to give a solid. Recrystallization of which from acetone afforded pure **24a** (28.0 mg, 98 %) as pale yellow needles, mp 232.5-234°C, whose spectra were identical with those of an authentic sample obtained as above.

6-Hydroxy-9-methoxy-3,8,11-trimethyl-4,7,10-trioxo-(1α,5α,6α)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (29). Sodium borohydride (9 mg, 0.24 mmol) was added to a stirred solution of **24a** (28.0 mg, 0.0915 mmol) in methanol (2 ml), and the mixture was stirred for 10 min at room temperature. The reaction mixture was poured into water (10 mL) and extracted with chloroform (10 mL x 3). The combined extracts were washed with water (10 mL), dried, and concentrated in vacuo to give a solid, recrystallization of which from ethyl acetate-ether afforded pure **29** (22.7 mg, 81.0 %) as pale yellow prisms: mp 157-159°C; IR (KBr) 3450, 1670, 1655, 1615 cm^{-1}; UV λ_{max} (log ε) 264 (4.01), 372 (2.87) nm; ^1H NMR δ 1.97 (3H, s, quinone CH_3), 2.56 (3H, s, amine NCH_3), 2.96 (3H, s, amide NCH_3), 3.07 (1H, dd, *J* = 14.9, 2.9 Hz, H-2α), 3.68 (1H, dd, *J* = 6.8, 1.0 Hz, H-5), 3.94 (1H, s, OH), 3.94 (1H, ddd, *J* = 5.4, 2.9, 1.0 Hz, H-1), 3.95 (1H, dd, *J* = 14.9, 5.4 Hz, H-2β), 4.01 (3H, s, OCH_3), 5.10 (1H, d, *J* = 6.8 Hz, H-6); ^{13}C NMR δ 8.7 (q), 34.2 (q), 40.7 (q), 48.0 (d, C^1), 50.5 (t, C^2), 61.0 (q), 61.6 (d, C^6), 64.6 (d, C^5), 130.1 (s), 138.9 (s), 141.2 (s), 155.3 (s), 166.8 (s, CO), 182.2 (s, quinone CO), 187.8 (s, quinone CO), MS, *m/z* (relative intensity) 306 (M^+, 100), 291 (17), 275 (10), 263 (13), 259 (11), 236 (27), 235 (20), 234 (16), 220 (26), 219 (15), 218 (45), 206 (24), 205 (10), 204 (11), 177 (13), 101 (11), 42 (18). Anal. Calcd for $C_{15}H_{18}N_2O_5$: C, 58.81; H, 5.92; N, 9.15. Found: C, 58.58; H, 5.99; N, 9.14.

10-Acetoxy-7-hydroxy-9-methoxy-3,8,11-trimethyl-6-oxo-1,2,3,4,5,6-hexahydro-1,5-imino-3-benzazocine (30). From 24a. To a solution of **24a** (20.6 mg, 0.0673 mmol) in acetic acid (1 mL) was added acetic anhydride (0.2 mL), and the mixture was heated at 100°C for 1 h. After dilution with water (10 mL), the mixture was extracted with chloroform (10 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (10 mL), dried, and concentrated in vacuo to give the residue (31.0 mg). Chromatography on a silica gel (5 g) column with dichloromethane-methanol (200:1) afforded **30** (18.0 mg, 76.8 %) as a solid, recrystallization of which from ethyl acetate-ether gave pure **30** as pale yellow needles. **From 29.** Acetylation of **29** (16.3 mg, 0.0533 mmol) as described above afforded the residue (20.0 mg). This material was subjected to chromatography on preparative layer silica gel plates (Merck 5715, solvent 1:4 benzene-ethyl acetate) to afford **30** (14.0 mg, 75.5 %) as pale yellow needles which were identical in all respects with prepared from **24a** and **31** (1.0 mg, 5.4 %) as a solid: mp 183-185°C; ^1H NMR δ 1.98 (3H, s, quinone CH_3), 2.08 (3H, s, $COCH_3$), 2.55 (3H, s, amine NCH_3), 2.92 (3H, s, amide NCH_3), 3.10 (1H, d, *J* = 12.2 Hz, H-2α), 3.85 (1H, dd, *J* = 7.3, 1.5 Hz, H-5), 3.93 (1H, dd, *J* = 12.2, 5.6 Hz, H-2β), 3.96 (1H, dd, *J* = 5.6, 1.5 Hz, H-1), 4.00 (3H, s, OCH_3), 6.07 (1H, d, *J* = 7.3 Hz, H-6).

Compound 30: mp 176-177.5°C; IR (KBr) 3600-3400, 1775, 1765, 1670, 1625 cm^{-1}; UV λ_{max} (log ε) 216 (4.22), 278 (3.96), 340 (3.64), and λmin (log ε) 245 (3.47), 308 (3.30) nm; ^1H NMR δ 2.18 (3H, s, Ar CH_3), 2.37 (3H, s, $COCH_3$), 2.53 (3H, s, amine NCH_3), 2.90 (3H, s, amide NCH_3), 3.17 (1H, dd, *J* = 11.9, 0.7 Hz, H-2α), 3.82 (3H, s, OCH_3), 3.93 (1H, d, *J* = 1.0 Hz, H-5), 4.01 (1H, dd, *J* = 11.9, 5.9 Hz,

H-2β), 4.10 (1H, ddd, J = 5.9, 1.0, 0.7 Hz, H-1), 11.89 (1H, s, OH); MS, *m/z* (relative intensity) 348 (M^+, 56), 306 (28), 305 (15), 289 (23), 277 (12), 247 (14), 236 (36), 235 (100), 234 (53), 220 (16). Anal. Calcd for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.51; H, 5.88; N, 7.87.

Oxidation of 29 with Selenium Oxide. A solution of **29** (22.8 mg, 0.0745 mmol) and selenium oxide (16.5 mg, 0.149 mmol) in dioxane (4 mL) was heated at reflux for 3 h. The reaction mixture was filtered and then washed with chloroform (30 mL). After the combined filtrates were concentrated to dryness, the residue was diluted with water (10 mL) and extracted with chloroform (20 mL x 3). The combined extracts were washed with 5% $NaHCO_3$ solution (20 mL), dried, and concentrated in vacuo to give the residue (23.7 mg). Chromatography on a silica gel (6 g) column with dichloromethane-methanol (200:1) afforded **27** (13.0 mg, 57.4 %) as a solid. Further elution with dichloromethane-methanol (100:1) gave **24a** (1.7 mg, 7.5 %).

10-Hydroxy-7,9-dimethoxy-3,8,11-trimethyl-1,2,3,4,5,6-hexahydro-1,5-imino-3-benzazocine (18b). A stirred solution of **18a** (918 mg, 3 mmol) in dry THF (30 mL) was cooled with ice-water, a THF solution of aluminium hydride (0.5 M, 36 mL, 18 mmol) was added dropwise over 10 min, and then stirred was continued at 0°C for 1 h. After being quenched by addition of methanol (2 mL), the reaction mixture was concentrated in vacuo. The residue (1.05 g) was subjected to chromatography (silica gel, 50 g; 20:1 dichloromethane-methanol) to give a solid, recrystallization of which from ethyl acetate-ether gave **18b** (653.0 mg, 74.5 %) as colorless needles: mp 140.5-142°C; IR (KBr) 3170, 1610, 1590 cm^{-1}: UV λ_{max} (log ε) 204 (4.57), 226sh (3.91), 276sh (3.21), 282 (3.28) nm; ^1H NMR δ 1.72 (3H, s, Ar CH_3), 2.23 and 2.31 (each 3H, s, NCH_3), 2.51 (1H, dd, J = 10.7, 2.9 Hz, H-2α), 2.52 (1H, dd, J = 10.7, 2.9 Hz, H-4α), 2.73 (1H, d, J = 17.8 Hz, H-6β), 2.86 (1H, dd, J = 17.8, 7.6 Hz, H-6α), 2.86 (1H, ddd, J = 10.7, 2.9, 1.5 Hz, H-2β), 2.94 (1H, dd, J = 10.7, 2.9 Hz, H-4β), 3.17 (1H, br d, H-5), 3.74 and 3.81 (each 3H, s, OCH_3), 3.99 (1H, ddd, J = 2.9, 2.9, 0.5 Hz, H-1), 6.63 (1H, br s, OH); MS, *m/z* (relative intensity) 292 (M^+, 21), 235 (17), 234 (100). Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.72; H, 8.27; N, 9.58. Found: C, 65.62; H, 8.52; N, 9.48.

1,2,3,4,5,6,7,10-Octahydro-9-methoxy-3.8.11-trimethyl-7,10-dioxo-1,5-imino-3-benzazocine (19b). A solution of **18b** (730 mg, 2.5 mmol) in 10 N HNO_3 (20 mL) was stirred at room temperature for 1 h. The reaction mixture was diluted with water (50 mL) and extracted with chloroform (40 mL x 3). The combined extracts were washed with water (40 mL), dried, and concentrated in vacuo to give **19b** (855 mg) as a pare yellow solid, which was recrystallized from ether to give pure **19b** (681.2 mg, 98.7 %) as pale yellow prisms: mp 106.5-107°C (lit.[6a] 108-110°C); IR (KBr) 1650, 1630, 1610 cm^{-1}; UV λ_{max} (log ε) 271 (4.10), 362 (2.53) nm; ^1H NMR δ 1.94 (3H, s, quinone CH_3), 2.16 (3H, s, NCH_3), 2.21 (1H, d, J = 20.7 Hz, H-6β), 2.29 (3H, s, NCH_3), 2.37 (1H, dd, J = 10.7, 3.2 Hz, H-4α), 2.41 (1H, ddd, J = 10.7, 1.9, 1.0 Hz, H-4β), 2.41 (1H, dd, J = 11.9, 2.9 Hz, H-2α), 2.64 (1H, ddd, J = 11.9, 1.0, 1.0 Hz, H-2β), 2.72 (1H, dd, J = 20.7, 7.5 Hz, H-6α), 3.09 (1H, br d, H-5), 3.80 (1H, br s, H-1), 3.99 (3H, s, OCH_3); ^{13}C NMR δ 8.7 (q), 22.4 (t, C^6), 40.9 (q), 45.8 (q), 51.9 (d, C^1), 52.3 (d, C^5), 57.2 (t, C^2), 60.8 (q), 61.8 (t, C^4), 128.9 (s), 138.0 (s), 142.3 (s), 155.3 (s), 182.7 (s, quinone CO), 187.3 (s, quinone CO); MS, *m/z* (relative intensity) 276 (M^+, 18), 218 (20), 58 (100). Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.19; H, 7.30; N, 10.14. Found: C, 65.08; H, 7.42; N, 10.04.

Oxidation of 19b with Selenium Oxide. A solution of **19b** (690 mg, 2.5 mmol) and selenium oxide (555 mg, 5 mmol) in dioxane (50 mL) was stirred for 44 h at room temperature. The reaction mixture was

made alkaline with diluted NH_4OH and extracted with chloroform (50 mL x 3). The combined extracts were washed with water (50 mL), dried, and concentrated in vacuo to give the residue (745 mg). Chromatography on a silica gel (50 g) column with dichloromethane-methanol (100:1) afforded **24b** (86 mg, 11.8 %) as a solid. Further elution with dichloromethane-methanol (80:1 - 50:1) afforded **23b** (546 mg, 74.8 %) as a solid.

Compound 24b: pale yellow needles from acetone, mp 202.5-204°C; IR (KBr) 3400-2500, 1640, 1630 cm^{-1}; UV λ_{max} (log ε) 237 (4.00), 280 (4.00), 368 (3.75), and λ_{min} (log ε) 228 (3.98), 258 (3.65), 314 (3.39) nm; ^1H NMR δ 2.17 (3H, s, Ar CH_3), 2.18 and 2.42 (each 3H, s, OCH_3), 2.52 (1H, dd, *J* = 10.8, 3.5 Hz, H-4α), 2.57 (1H, dd, *J* = 10.8, 3.2 Hz, H-2α), 2.85 (1H, ddd, *J* = 10.8, 1.3, 0.5 Hz, H-2β), 2.99 (1H, ddd, *J* = 10.8, 1.3, 0.5 Hz, H-4β), 3.52 (1H, ddd, *J* = 3.5, 1.3, 0.5 Hz, H-5), 3.86 (3H, s, OCH_3), 4.23 (1H, ddd, *J* = 3.2, 1.3, 0.5 Hz, H-1), 5.45 (1H, s, OH), 11.85 (1H, s, OH); ^{13}C NMR δ 8.8 (q), 42.0 (q), 45.9 (s), 53.7 (d, C^1), 57.4 (t, C^2), 57.6 (t, C^4), 60.9 (q), 65.5 (d, C^5), 112.8 (s), 117.2 (s), 122.3 (s), 137.8 (s), 152.8 (s), 154.5 (s), 204.0 (s, CO); MS, *m/z* (relative intensity) 292 (M^+, 25), 236 (15), 235 (100), 234 (13), 220 (23), 192 (14), 58 (44), 57 (24), 42 (16). Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.63; H, 6.90; N, 9.58. Found: C, 61.52; H, 7.02; N, 9.54.

Compound 23b: pale yellow prisms from ethyl acetate-ether, mp 130-132°C; IR (KBr) 3280, 1650, 1615 cm^{-1}; UV λ_{max} (log ε) 268 (4.07), 406 (2.89) nm; ^1H NMR δ 1.96 (3H, s, quinone CH_3), 2.12 (3H, s, NCH_3), 2.34 (1H, dd, *J* = 11.1, 3.2 Hz, H-2α), 2.35 (1H, dd, *J* = 11.1, 1.9 Hz, H-4α), 2.47 (3H, s, NCH_3), 2.51 (1H, ddd, *J* = 11.1, 2.5, 0.5 Hz, H-2β), 2.69 (1H, ddd, *J* = 11.1, 1.2, 0.5 Hz, H-4β), 3.11 (1H, ddd, *J* = 1.9, 1.2, 0.5 Hz, H-5), 3.34 (1H, br s, OH), 3.85 (1H, ddd, *J* = 3.2, 2.5, 0.5 Hz, H-1), 4.03 (3H, s, OCH_3), 4.39 (1H, s, H-6); ^{13}C NMR δ 8.5 (q), 41.7 (q), 45.9 (q), 52.8 (d, C^1), 55.5 (t, C^2), 58.3 (t, C^4), 60.3 (d, C^5), 60.9 (q), 64.2 (d, C^6), 128.8 (s), 138.7 (s), 140.8 (s), 155.6 (s), 183.0 (s, quinone CO), 189.0 (s, quinone CO); MS, *m/z* (relative intensity) 292 (M^+, 12), 218 (7), 58 (100), 42 (11). Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.63; H, 6.90; N, 9.58. Found: C, 61.61; H, 7.04; N, 9.47.

6-Acetoxy-9-methoxy-3,8,11-trimethyl-7,10-dioxo-(1α,5α,6β)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (25b). A solution of **19b** (110.4 mg, 0.4 mmol) and selenium oxide (91.6 mg, 0.826 mmol) in acetic acid (8 mL) was stirred for 48 h at room temperature. The reaction mixture was diluted with water (10 mL), made alkaline with diluted NH_4OH, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give the residue (161.2 mg). Chromatography on a silica gel (8 g) column with dichloromethane-methanol (200:1) afforded **25b** (103.6 mg, 77.5 %) as an oil. Further elution with dicloromethane-methanol (80:1 - 50:1) afforded **23b** (23.8 mg, 20.4 %) as a solid.

Compound 25b (not crystallizable): IR ($CHCl_3$): 1730, 1655, 1610 cm^{-1}: UV λ_{max} (log ε) 268 (4.12), 368 (3.33) nm; ^1H NMR δ 1.97 (3H, s, quinone CH_3), 2.06 (3H, s, $COCH_3$), 2.11 (3H, s, NCH_3), 2.33 (1H, dd, *J* = 11.4, 3.2 Hz, H-4α), 2.36 (1H, dd, *J* = 11.4, 3.2 Hz, H-2α), 2.46 (3H, s, NCH_3), 2.47 (1H, dd, *J* = 11.4, 1.9 Hz, H-2β), 2.82 (1H, dd, *J* = 11.4, 1.0 Hz, H-4β), 3.00 (1H, ddd, *J* = 3.2, 1.0, 0.5 Hz, H-5), 3.86 (1H, ddd, *J* = 3.2, 1.9, 0.5 Hz, H-1), 4.00 (3H, s, OCH_3), 5.56 (1H, s, H-6); ^{13}C NMR δ 8.8 (q), 21.0 (q), 41.6 (q), 45.6 (q), 52.4 (d, C^1), 55.1 (t, C^2), 56.9 (t, C^4), 59.7 (d, C^5), 60.8 (q), 64.0 (d, C^6), 129.7 (s), 138.2 (s), 155.3 (s), 169.9 (s), 182.5 (s, quinone CO), 185.6 (s, quinone CO), 196.1 (s, CO), MS, *m/z*

(relative intensity) 334 (M^+, 42), 231 (22), 219 (17), 218 (100), 116 (30), 58 (32), 57 (10); high-resolution MS calcd for $C_{17}H_{22}N_2O_5$ 334.1528, found 334.1544.

6,9-Dimethoxy-3,8,11-trimethyl-7,10-dioxo-(1α,5α,6β)-1,2,3,4,5,6,7,10-octahydro-1,5-imino-3-benzazocine (26b). From 19b. A solution of **19b** (69.0 mg, 0.25 mmol) and selenium oxide (55.5 mg, 0.5 mmol) in methanol (4 mL) was stirred for 9 days at room temperature. The reaction mixture was diluted with water (10 mL), made alkaline with diluted NH_4OH, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give the residue (75.3 mg). Chromatography on a silica gel (8 g) column with dichloromethane-methanol (200:1) afforded **26b** (8.5 mg, 11.1 %) as an oil, with dichloromethane-methanol (100:1 - 50:1) afforded 54.2 mg of solid, which showed two major spots on TLC (R_f 0.25 and 0.21, 19:1 chloroform-methanol), was subjected to chromatography on preparative layer silica gel (Merck 5715, solvent 19:1 chloroform-methanol) to afford **23b** (22.5 mg, 30.8 %) and **19b** (18.1 mg, 26.2 % recovery). **From 23b.** Concentrated H_2SO_4 (0.3 mL) was added to a solution of **23b** (58.4 mg, 0.2 mmol) in methanol (6 mL), and the resulting solution was stirred for 70 h at room temperature. The reaction mixture was diluted with water (10 mL), made alkaline with $NaHCO_3$, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give the residue (54.4 mg). Chromatography on a silica gel (7 g) column with dichloromethane-methanol (200:1) afforded **26b** (5.5 mg, 9.4 %) as pale yellow oil. Further elution with dichloromethane-methanol (50:1) afforded the starting material **23b** (45 mg, 77.1 % recovery) as a solid.
Compound 26b (not crystallizable): IR ($CHCl_3$) 1650, 1615 cm^{-1}; UV λmax (log ε) 267 (4.03), 384 (2.94) nm; ^1H NMR d 1.98 (3H, s, quinone CH_3), 2.09 (3H, s, NCH_3), 2.32 (1H, dd, J = 11.1, 3.2 Hz, H-2α), 2.39 (1H, dd, J = 11.1, 3.5 Hz, H-4α), 2.42 (1H, ddd, J = 11.1, 2.2, 0.5 Hz, H-2β), 2.49 (3H, s, NCH_3), 2.60 (1H, ddd, J = 11.1, 1.0, 0.5 Hz, H-4β), 3.15 (1H, ddd, J = 3.5, 1.0, 0.5 Hz, H-5), 3.52 (3H, s, OCH_3), 3.86 (1H, s, H-6), 3.86 (1H, ddd, J = 3.2, 2.2, 0.5 Hz, H-1), 3.97 (3H, s, OCH_3); ^{13}C NMR δ 8.8 (q), 41.9 (q), 45.8 (q), 52.4 (d, C^1), 54.9 (t, C^2), 57.5 (d, C^5), 57.6 (t, C^4), 58.9 (q), 60.8 (q), 72.2 (d, C^6), 129.8 (s), 138.9 (s), 140.4 (s), 155.1 (s), 183.0 (s, quinone CO), 186.7 (s, quinone CO); MS, *m/z* (relative intensity) 306 (M^+, 58), 291 (11), 248 (26), 232 (11), 220 (10), 219 (15), 218 (81), 131 (15), 88 (20), 58 (100), 57 (22), 42 (19); high-resolution MS calcd for $C_{16}H_{22}N_2O_4$ 306.1579, found 306.1608.

Oxidation of (±)-Saframycin B (2) with Selenium Oxide in Dioxane. A solution of (±)-**2** (134.3 mg, 0.25 mmol) and selenium oxide (55.5 mg, 0.5 mmol) in dioxane (10 mL) was stirred for 72 h at room temperature. The reaction mixture was diluted with water (20 mL), made alkaline with $NaHCO_3$, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give the residue (147 mg). Chromatography on a silica gel (20 g) column with benzene-ethyl acetate (1:1) afforded **(±)-saframycin D (4)** (21.6 mg, 15.6 %) as a solid, with benzene-ethyl acetate (1:2) - ethyl acetate afforded 109.2 mg of solid, which showed three major spots on TLC (R_f 0.45, 0.37 and 0.28, 19:1 chloroform-methanol), was subjected to chromatography on preparative layer silica gel (Merck 5715, solvent 19:1 chloroform-methanol) to afford **33** (6.2 mg, 4.5 %), **2** (14.7 mg, 10.9 % recovery), and **32** (55.3 mg, 40.0 %).

***N*-[(1,4-Dihydroxy-2,11-dimethoxy-3,12,16-trimethyl-5,10,13-trioxo-6α,9α,14aα,15α-6,7,9,10,13,14,14a,15-octa-hydro-6,15-imino-5H-isoquino[3,2-*b*][3]benzazocin-9-yl)-**

methyl]-2-oxo-propanamide (Saframycin D, 4). pale yellow needles from acetone, mp 228-232°C dec; IR (KBr) 3400, 3300-2800, 1720, 1690, 1655, 1630, 1610 cm^{-1}; UV λ_{max} (log ε) 241 (4.08), 273 (4.19), 366 (3.73), and λ_{min} (log ε) 229 (4.00), 252 (3.99), 315 (3.23) nm; ^1H NMR δ 1.57 (1H, ddd, *J* = 17.8, 10.5, 2.7 Hz, H-14β), 1.89 (3H, s, quinone CH_3), 2.15 (3H, s, Ar CH_3), 2.26 (3H, s, $COCH_3$), 2.42 (3H, s, NCH_3), 2.92 (1H, dd, J = 10.5, 2.7 Hz, H-7α), 2.93 (1H, ddd, *J* = 10.5, 2.7, 2.0 Hz, H-14a), 2.97 (1H, dd, *J* = 17.8, 2.0 Hz, H-14α), 3.06 (1H, ddd, *J* = 14.1, 3.7, 3.7 Hz, C*H*NH), 3.27 (1H, ddd, *J* = 2.7, 2.7, 0.5 Hz, H-6), 3.28 (1H, dd, *J* = 10.5, 2.7 Hz, H-7β), 3.67 (1H, ddd, *J* = 3.7, 2.7, 1.4 Hz, H-9), 3.70 (1H, ddd, *J* = 14.1, 9.7, 1.4 Hz, C*H*NH), 3.94 and 4.02 (each 3H, s, OCH_3), 4.35 (1H, *J* = 2.7, 0.5 Hz, H-15), 5.53 (1H, s, OH), 6.28 (1H, dd, *J* = 9.7, 3.7 Hz, NH), 11.88 (1H, s, OH); ^{13}C NMR δ 8.6 (q), 8.9 (q), 24.2 (s, CO*C*H3), 24.5 (t, C^{14}), 40.8 (t, CH_2NH), 42.3 (q), 54.7 (t, C^7), 56.9 (d, C^{14a}), 57.4 (d, C^{15}), 57.6 (d, C^9), 60.9 (q), 61.1 (q), 65.5 (d, C^6), 112.2 (s, C^{15a}), 118.3 (s, C^{4a}), 118.6 (s, C^3), 127.5 (s, C^{12}), 136.6 (s, C^{9a}), 139.3 (s, C^1), 141.7 (s, C^{13a}), 153.3 (C^4), 154.8 (s, C^2), 156.3 (s, C^{11}), 160.3 (s, CO), 181.2 (s, C^{10}), 186.1 (s, C^{13}), 195.8 (s, CO), 203.7 (s, C^5); MS, *m/z* (relative intensity) 553 (M^+, 1), 455 (11), 453 (4), 319 (41), 237 (14), 236 (100), 235 (9), 234 (6), 221 (13), 220 (12), 218 (10). Anal. Calcd for $C_{28}H_{31}N_3O_9 \cdot H_2O$: C, 58.83; H, 5.82; N, 7.35. Found: C, 59.14; H, 5.54; N, 7.28.

***N*-[(5-Hydroxy-2,11-dimethoxy-3,12,16-trimethyl-1,4,10,13-tetraoxo-5β,6α,9α,14aα,15α-1,5,6,7,9,10,13,14,14a,15-decahydro-6,15-imino-4H-isoquino[3,2-*b*][3]benzazocin-9-yl)methyl]-2-oxo-propanamide (32)**. pale yellow prisms from ethyl acetate-ether, mp 163-166°C dec; IR (KBr) 3590, 3400, 1720, 1680, 1660, 1620 cm^{-1}; UV λ_{max} (log ε) 267 (4.31), 368 (3.22) nm; ^1H NMR δ 1.20 (1H, ddd, *J* = 17.6, 11.1, 2.9 Hz, H-14β), 1.89 and 2.02 (each 3H, s, quinone CH_3), 2.25 (3H, s, $COCH_3$), 2.45 (3H, s, NCH_3), 2.68 (1H, ddd, *J* = 11.1, 2.9, 2.9 Hz, H-14a), 2.75 (1H, dd, *J* = 17.6, 2.9 Hz, H-14α), 2.77 (1H, dd, *J* = 10.8, 2.9 Hz, H-7α), 3.09 (1H, dd, *J* = 10.8, 2.5 Hz, H-7β), 3.19 (1H, ddd, *J* = 14.0, 3.5, 2.8 Hz, C*H*NH), 3.21 (1H, dddd, *J* = 2.9, 2.5, 1.3, 0.5 Hz, H-6), 3.41 (1H, d, *J* = 2.2 Hz, OH), 3.63 (1H, ddd, *J* = 3.5, 2.9, 1.3 Hz, H-9), 3.74 (1H, ddd, *J* = 14.0, 9.8, 1.3 Hz, C*H*NH), 4.01 and 4.04 (each 3H, s, OCH_3), 4.09 (1H, dd, *J* = 2.9, 1.3 Hz, H-15), 4.36 (1H, dd, *J* = 2.2, 0.5 Hz, H-5), 6.80 (1H, dd, *J* = 9.8, 2.8 Hz, NH); ^{13}C NMR δ 8.5 (q), 8.6 (q), 24.2 (s, CO*C*H3), 25.6 (t, C^{14}), 40.5 (t, CH_2NH), 42.1 (q), 55.7 (d, C^{15}), 56.1 (d, C^{14a}), 56.1 (t, C^7), 57.8 (d, C^9), 60.2 (d, C^6), 60.9 (q), 61.0 (q), 63.8 (d, C^5), 127.9 (s), 129.2 (s), 136.6 (s), 136.6 (s), 141.5 (s), 141.5 (s), 156.1 (s), 156.1 (s), 160.1 (s, CO), 181.3, 183.2, 185.6, and 188.8 (each s, quinone CO), 196.7 (s, CO); MS, *m/z* (relative intensity) 553 (M^+, 28), 537 (23), 455 (31), 454 (22), 453 (66), 439 (28), 437 (100), 320 (12), 319 (53), 250 (23), 237 (13), 236 (89), 235 (19), 234 (35), 232 (19), 222 (11), 221 (21), 220 (88), 219 (37), 218 (73), 206 (15), 204 (23), 203 (12), 190 (13), 176 (13), 43 (17). Anal. Calcd for $C_{28}H_{31}N_3O_9$: C, 60.75; H, 5.65; N, 7.59. Found: C, 60.74; H, 5.64; N, 7.65.

***N*-[(5-Hydroxy-2,11-dimethoxy-3,12,16-trimethyl-1,4,10,13-tetraoxo-5α,6α,9α,14aα,15α-1,5,6,7,9,10,13,14,14a,15-decahydro-6,15-imino-4H-isoquino[3,2-*b*][3]benzazocin-9-yl)methyl]-2-oxo-propanamide (33)**. pale yellow prisms from ethyl acetate-ether (unstable), mp 170-172°C; IR (KBr) 3700-3200, 1715, 1685, 1665, 1645, 1625 cm^{-1}; UV λ_{max} (log ε) 268 (4.27), 372 (3.16) nm; ^1H NMR δ 1.14 (1H, ddd, *J* = 17.8, 11.3, 3.2 Hz, H-14β), 1.89 and 2.03 (each 3H, s, quinone CH_3), 2.23 (3H, s, $COCH_3$), 2.46 (3H, s, NCH_3), 2.60 (1H, dd, *J* = 11.0, 2.9 Hz, H-7α), 2.69 (1H, ddd, *J* =

17.8, 2.9, 1.0 Hz, H-14α), 2.86 (1H, ddd, *J* = 11.3, 2.9, 2.9 Hz, H-14a), 3.21 (1H, dddd, *J* = 6.8, 2.9, 2.6, 0.5 Hz, H-6), 3.36 (1H, ddd, *J* = 13.6, 4.2, 2.9 Hz, C*H*NH), 3.55 (1H, dd, *J* = 11.0, 2.6 Hz, H-7β), 3.64 (1H, dddd, *J* = 4.2, 3.2, 1.3, 1.0 Hz, H-9), 3.75 (1H, d, *J* = 1.3 Hz, OH), 3.82 (1H, ddd, *J* = 13.6, 10.0, 1.3 Hz, C*H*NH), 3.94 (1H, dd, *J* = 2.9, 0.5 Hz, H-15), 3.99 and 4.04 (each 3H, s, OCH_3), 5.04 (1H, dd, *J* = 6.8, 1.3 Hz, H-5), 7.28 (1H, dd, *J* = 10.0, 2.9 Hz, NH); MS, *m/z* (relative intensity) 553 (M^+, 10), 537 (4), 453 (70), 437 (22), 319 (49), 251 (11), 250 (73), 248 (11), 237 (15), 236 (100), 235 (12), 234 (14), 232 (14), 222 (23), 221 (19), 220 (40), 219 (50), 218 (72), 206 (17), 205 (15), 204 (21), 43 (26); high-resolution MS calcd for $C_{28}H_{31}N_3O_9$ 553.2060, found 553.2050.

Oxidation of (±)-Saframycin B (2) with Selenium Oxide in Methanol. A solution of (±)-**2** (21.4 mg, 0.04 mmol) and selenium oxide (10.0 mg, 0.09 mmol) in methanol (4 mL) was stirred for 88 h at room temperature. The reaction mixture was diluted with water (20 mL), made alkaline with $NaHCO_3$, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo. The residue (23 mg) was subjected to chromatography on preparative layer silica gel plates (Merck 5715, solvent 1:5 benzene-ethyl acetate) to afford **(±)-saframycin C (3)** (10.1 mg, 44.7 %), alcohol (**32**) (4.2 mg, 19.1 %), and **saframycin B (2)** (0.2 mg, 1.0 % recovery).

***N*-[(2,5,11-Trimethoxy-3,12,16-trimethyl-1,4,10,13-tetraoxo-5β,6α,9α,14aα,15α-1,5,6,7,9,10,13,14,14a,15-decahydro-6,15-imino-4H-isoquino[3,2-*b*][3]benzazocin-9-yl)-methyl]-2-oxo-propanamide (Saframycin C, 3).** pale yellow prisms from ethyl acetate-ether, mp 168-171°C dec; IR (KBr) 3430, 1725, 1695, 1665, 1640, 1620 cm^{-1}; UV λ_{max} (log ε) 265 (4.30), 366 (3.29) nm; ^1H NMR δ 1.18 (1H, ddd, *J* = 17.8, 11.5, 2.9 Hz, H-14β), 1.89 and 2.09 (each 3H, s, quinone CH_3), 2.24 (3H, s, $COCH_3$), 2.48 (3H, s, NCH_3), 2.66 (1H, ddd, *J* = 11.5, 2.9, 2.9 Hz, H-14a), 2.73 (1H, dd, *J* = 17.8, 1.7 Hz, H-14α), 2.82 (1H, dd, *J* = 11.0, 3.2 Hz, H-7α), 3.02 (1H, dd, *J* = 11.0, 2.2 Hz, H-7β), 3.19 (1H, ddd, *J* = 13.9, 3.9, 1.0 Hz, C*H*NH), 3.25 (1H, ddd, *J* = 3.2, 2.2, 1.0 Hz, H-6), 3.53 (3H, s, OCH_3), 3.62 (1H, ddd, *J* = 3.9, 2.9, 1.2 Hz, H-9), 3.74 (1H, ddd, *J* = 13.9, 9.8, 1.2 Hz, C*H*NH), 3.83 (1H, s, H-5), 3.99 and 4.01 (each 3H, s, OCH_3), 4.09 (1H, dd, *J* = 2.9, 1.0 Hz, H-15), 6.71 (1H, dd, J = 9.8, 1.0 Hz, NH); ^{13}C NMR δ 8.6 (q), 8.8 (q), 24.2 (q), 25.4 (t, C^{14}), 40.6 (t, CH_2NH), 42.2 (q), 55.1 (d, C^{15}), 55.6 (d, C^{14a}), 55.7 (t, C^7), 57.5 (d, C^6), 57.9 (d, C^9), 59.3 (q), 60.8 (q), 61.0 (q), 71.9 (d, C^5), 127.9 (s), 130.6 (s), 136.5 (s), 136.6 (s), 141.5 (s), 141.6 (s), 155.4 (s), 156.2 (s), 160.2 (s, CO), 181.3, 183.2, 185.6, and 186.6 (each s, quinone CO), 196.5 (s, CO); MS, *m/z* (relative intensity) 567 (M^+, 25), 537 (17), 471 (10), 470 (21), 469 (71), 468 (21), 467 (64), 439 (25), 438 (23), 437 (75), 435 (19), 368 (14), 319 (12), 259 (11), 250 (20), 235 (11), 234 (23), 232 (17), 221 (18), 220 (70), 219 (42), 218 (100), 205 (18), 204 (21), 203 (11). Anal. Calcd for $C_{29}H_{33}N_3O_9$: C, 61.36; H, 5.86; N, 7.40. Found: C, 61.10; H, 5.90; N, 7.29.

Conversion of 32 to (±)-Saframycin C Ketal (34). Concentrated H_2SO_4 (0.2 mL) was added to a solution of **32** (20.4 mg, 0.037 mmol) in methanol (4 mL), and the resulting solution was stirred for 24 h at 60°C. The reaction mixture was diluted with water (10 mL), made alkaline with $NaHCO_3$, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo. The residue (20.8 mg) showed two major spots on TLC (R_f 0.49 and 0.28, 4:5 acetone:chloroform), the respective molar ratios of which were determined by 400MHz ^1H NMR. Ethreral diazomethane solution (1 mL) was added dropwise to a cooled solution of this material in dry dichloromethane (1 mL), and the reaction mixture

was kept at the same temperature for 1 h. After quenched with acetic acid, the reaction mixture was diluted with water (20 mL), made alkaline with $NaHCO_3$, and extracted with chloroform (20 mL x 3). The combined extracts were washed with water (20 mL), dried, and concentrated in vacuo to give the residue (15.4 mg, R_f 0.49, 4:5 acetone:chloroform). This material was subjected to chromatopraphy on preparative layer silica gel plates (Merck 5715, solvent 4:5 acetone:chloroform) to afford **34** (10.8 mg, 47.8 %) as a solid, which was recrystallized from ethyl acetate-ether to give pale yellow prisms: mp 180-182°C dec; IR (KBr) 3430, 1690, 1655, 1615 cm^{-1}; UV λ_{max} (log ε) 266 (4.26), 365 (3.28) nm; ^1H NMR δ 1.14 (3H, s, CCH_3), 1.18 (1H, ddd, *J* = 17.8, 11.4, 3.2 Hz, H-14β), 1.83 and 2.01 (each 3H, s, quinone CH_3), 2.47 (3H, s, NCH_3), 2.62 (1H, ddd, *J* = 11.4, 2.9, 2.2 Hz, H-14a), 2.74 (1H, ddd, *J* = 17.8, 2.2, 0.5 Hz, H-14α), 2.78 (1H, dd, *J* = 10.8, 3.2 Hz, H-7α), 2.82 and 3.00 (each 3H, s, OCH_3), 3.00 (1H, ddd, *J* = 13.6, 2.9, 2.2 Hz, C*H*NH), 3.05 (1H, dd, *J* = 10.8, 2.2 Hz, H-7β), 3.27 (1H, ddd, *J* = 3.2, 2.2, 1.0 Hz, H-6), 3.54 (3H, s, OCH_3), 3.56 (1H, dddd, *J* = 3.2, 3.2, 2.2, 1.6 Hz, H-9), 3.86 (1H, s, H-5), 3.94 (1H, ddd, *J* = 13.6, 10.2, 1.6 Hz, C*H*NH), 4.02 (3H, s, OCH_3), 4.06 (1H, dd, *J* = 2.9, 1.0 Hz, H-15), 4.08 (3H, s, OCH_3), 6.50 (1H, dd, *J* = 10.2, 2.2 Hz, NH); ^{13}C NMR δ 8.3 (q), 8.9 (q), 21.1 (q), 25.7 (t, C^{14}), 40.3 (t, CH_2NH), 42.1 (q), 49.2 (q), 49.5 (q), 55.0 (d, C^{15}), 55.7 (d, C^{14a}), 55.9 (t, C^7), 57.5 (d, C^6), 59.2 (d, C^9), 59.3 (q), 60.9 (q), 61.0 (q), 71.9 (d, C^5), 100.3 (s, $C(OCH_3)_2$), 126.5 (s), 129.2 (s), 136.5 (s), 137.4 (s), 140.7 (s), 141.7 (s), 155.2 (s), 156.9 (s), 170.1 (s, CO), 181.3, 182.9, 185.6, and 186.4 (each s, quinone CO); MS, *m/z* (relative intensity) 613 (M^+, 22), 583 (11), 470 (14), 469 (49), 468 (54), 467 (100), 439 (11), 438 (26), 437 (57), 435 (19), 250 (15), 234 (15), 232 (14), 220 (47), 219 (36), 218 (90), 205 (10), 204 (13), 89 (85). Anal. Calcd for $C_{31}H_{39}N_3O_{10}\cdot 1/4H_2O$: C, 60.23; H, 6.44; N, 6.80. Found: C, 60.20; H, 6.66; N, 6.50.

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