and chromatographed (solvent d, 3/2) to afford **54**: 0.83 g (76%); mp 115–117 °C; NMR δ 1.28 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 2.71 (m, 2 H, CH_2CH, CCHN), 3.58 (m, 4 H, cH_2 Ar, CH_2N), 4.10 (q, 2 H, CH_2CH_3, J = 7.1), 4.81 (s, 1 H, C=CH), 7.32 (m, 5 H, Ar H); IR 3400, 3160, 3030, 2985, 1720, 1620, 1260 cm^{-1}; $[\alpha]^{23}_D$ +2.1° (c 0.014, CH_3OH). Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.7; H, 7.0; N, 10.8. Found: C, 69.6; H, 7.0; N, 10.7.

Ethyl (1*S*,2*S*,5*R*)- and (1*S*,2*R*,5*R*)-6-Benzyl-3,6-diazabicyclo[3.1.0]hexane-2-acetate (55). To a solution of **54** (125 mg, 0.48 mmol) in ethanol (10 mL), containing a trace of bromocresol green was added sodium cyanoborohydride (150 mg, 2.39 mmol), and glacial acetic acid was added dropwise over the course of 4 h to maintain an acidic pH as indicated by the yellow color of the bromocresol green. The reaction mixture was diluted with dichloromethane (50 mL) and washed with 10% $NaHCO_3$ (20 mL), the aqueous phase was extracted with dichloromethane (20 mL), and the combined organic extracts were dried, filtered, and evaporated to an oil. Chromatography (solvent e, 95/5) afforded **55** as a colorless oil: 112 mg, 89%, mixture of diastereomers: NMR δ 1.21 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 2.07 (br s, 1 H, NH), 2.29–2.62 (m, 4 H), 2.74 (dd, 1 H, NHCHH, J = 1.6, 12.3 Hz), 3.09 (d, 1 H, NHCHH, J = 12.3 Hz), 3.29 (m, 2 H), 3.61 (m, 1 H), 4.08 (m, 2 H, CH_2CH_3), 7.35 (m, 5 H, Ar H).

Quinones 56. To a stirred solution of **55** (110 mg, 0.42 mmol) in benzene (15 mL) were added dibromoquinone **27** (159 mg, 0.51 mmol) and potassium carbonate (120 mg, 0.87 mmol). After 65 h in the dark, the mixture was filtered and evaporated. Chromatography, eluting with benzene, gave recovered dibromoquinone **27**, and, eluting with solvent d (2/3), gave **56** as a purple oil: 192 mg (93%); R_f (solvent c, 7/3) 0.57; NMR δ 1.17 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 1.87 (s, 3 H, CH_3), 2.53 (m, 2 H), 2.85 (m, 1 H), 3.28 (d, 1 H, J = 13.3 Hz), 3.43 (dd, 1 H), 3.62 (d, 1 H, J = 13.3 Hz), 3.75–4.03 (m, 3 H), 4.04 (s, 3 H, OCH_3), 4.68 (d, 1 H, J = 13.2 Hz), 5.22 (br m, 1 H), 7.39 (m, 5 H). Anal. Calcd for $C_{23}H_{25}N_2O_5Br$: C, 56.5; H, 5.1; N, 5.7. Found: C, 57.0; H, 5.1; N, 5.7.

Ethyl (1*R*,2*R*)-1,2-(*N*-Benzylaziridino)-7-methoxy-6-methyl-2,3,5,8-tetrahydro-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]-indole-9-carboxylate (59). A solution of **56** (29 mg, 0.059 mmol) in methanol was degassed with argon and irradiated in an argon atmosphere for 2 h with a visible lamp (Pyrex filtered). The solvent was then evaporated and the residue dissolved in ethyl acetate and stirred in the dark, open to the air, with 10% Pd/C (15 mg). After 21 h the mixture was filtered, the catalyst was washed with ethyl acetate, and the combined filtrate and washings were evaporated to an oil. Chromatography (solvent c, 2/3) afforded **58** (17.5 mg, 61%) as a purple oil: R_f (solvent c, 7/3) 0.42; NMR δ 1.21 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 1.97 (s, 3 H, CH_3), 2.71 (m, 1 H), 3.38–3.61 (m, 2 H), 3.91–4.20 (m, 8 H), 4.59 (d, 1 H, J = 16.7 Hz), 7.40 (m, 5 H, Ar H); mass spectrum, m/e (relative intensity) 490, 488 (29, 40, M + 2 with ^{81}Br, M + 2 with ^{79}Br), 486 (7, M+, ^{79}Br), 397 (50), 395 (28), 334 (35); mass spectrum, calcd for $C_{23}H_{23}N_2O_5$ ^{79}Br m/e 486.0788, found m/e 486.0789. The intermediate **58** (17.5 mg, 35.8 μmol) was dissolved in acetonitrile (2 mL), and the solution was added to $Pd(OAc)_2$ (2 mg, 8.9 mmol) in acetonitrile (1 mL) with stirring. TEA (20 μL, 0.144 mmol) was added, and the mixture was stirred for 12 h and then partitioned between water (15 mL) and dichloromethane (15 mL). The aqueous layer was extracted with dichloromethane (15 mL), and the combined organic extracts were dried, evaporated, and chromatographed (solvent c, 3/2; then solvent e, 98/2) to give **59** as a yellow solid: 14 mg (96%); mp 187–190 °C; NMR δ 1.23 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 1.92 (s, 3 H, CH_3), 3.17 (br t, 1 H, CH_2CHN, J = 4.3 Hz), 3.45 (d, 1 H, CCHN, J = 4.9 Hz), 3.67 (dd, 2 H, CH_2 Ar, J = 13.7, 24.5 Hz), 4.06 (s, 3 H, OCH_3), 4.17–4.36 (m, 3 H, CH_2CH_3, NCHH), 4.45 (d, 1 H, NCHH, J = 14.0 Hz), 7.33 (m, 5 H, Ar H); $[\alpha]^{23}_D$ −66° (c 0.013, $CHCl_3$. Anal. Calcd for $C_{23}H_{22}N_2O_5$: C, 68.0; H, 5.5; N, 6.9. Found: C, 67.7; H, 5.3; N, 6.7.

Ethyl (1*R*,2*R*)-1,2-(*N*-Benzylaziridino)-6-methoxy-7-methyl-2,3,5,8-tetrahydro-5,8-dioxo-1*H*-pyrrolo[1,2-*a*]-indole-9-carboxylate (60). To a stirred solution of dibromoquinone **27** (61.3 mg, 0.198 mmol) and unsaturated pyrrolidine **54** (34 mg, 0.132 mmol) in acetonitrile (3 mL) were added K_2CO_3 (91 mg, 0.66 mmol) and $CuBr_2$ (3.5 mg, 0.016 mmol). After 16 h at 50 °C, the mixture was cooled, poured into water (20 mL), and extracted with $CHCl_3$ (3 × 25 mL). The combined organic extracts were dried and evaporated, and the residue was chromatographed (solvent e, 97/3) to afford a mixture of **59** and **60** as a yellow solid: 50 mg (93%); mp 187–191 °C dec; NMR (analysis of the methyl ether resonances of **59** and **60**, 4.06 and 3.94 ppm, respectively, showed a ratio of 5/95) δ 1.25 (t, 3 H, CH_2CH_3, J = 7.1 Hz), 2.00 (s, 3 H, CH_3), 3.18 (br t, 1 H, CH_2CHN, J = 4.3 Hz), 3.48 (d, 1 H, CCHN, J = 4.9 Hz), 3.67 (s, 2 H, CH_2 Ar), 3.94 (s, 3 H, OCH_3), 4.19–4.36 (m, 3 H, CH_2CH_3, NCHH), 4.45 (d, 1 H, NCHH, J = 13.9 Hz), 7.33 (m, 5 H, Ar H); HPLC (59/60, 5/95 column D; solvent f, 2/3; 2 mL/min) **60**, t_R 21.2 min, **59**, t_R 25.6 min. Anal. Calcd for $C_{23}H_{22}N_2O_5$: C, 68.0; H, 5.4; N, 6.9. Found: C, 67.6; H, 5.4; N, 6.8.

Acknowledgment. The assistance of Jeff Roberts, Bruce Watkins, and A. Afzali-Ardakani in studies on the stereochemistry of vinylglycine epoxidation is gratefully acknowledged.

[3,3] Sigmatropic Rearrangements of Benzyl Vinyl Ethers. Model Studies Directed toward the Total Synthesis of Cephalotaxine[1]

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Received March 22, 1985

Model studies directed toward the synthesis of cephalotaxine are described. Thermolysis of 11 gave 14 rather than 12.

Cephalotaxine (1), the major alkaloid of the genus *Cephalotaxus*, has attracted considerable interest both due to its unique structure and because of the promising antitumor activity of several ester derivatives of 1.[3]

We have recently been exploring a new approach for the synthesis of cephalotaxine. The key step in this approach involves the [3,3] sigmatropic rearrangement of a benzyl vinyl ether[4] such as **2** to give **3**. Elaboration of **3** to 1 would

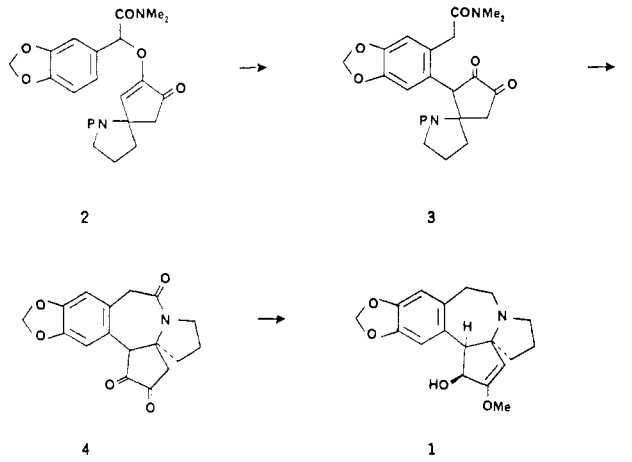
(1) Synthesis Via Sigmatropic Rearrangements. 8. For previous papers in this series see: Raucher, S.; Lawrence, R. F. *Tetrahedron* **1983**, *39*, 3731.

(2) (a) Fellow of the Alfred P. Sloan Foundation (1980–1984). Recipient of an NIH Research Career Development Award (1983–1988). (b) Department of Biological Structure.

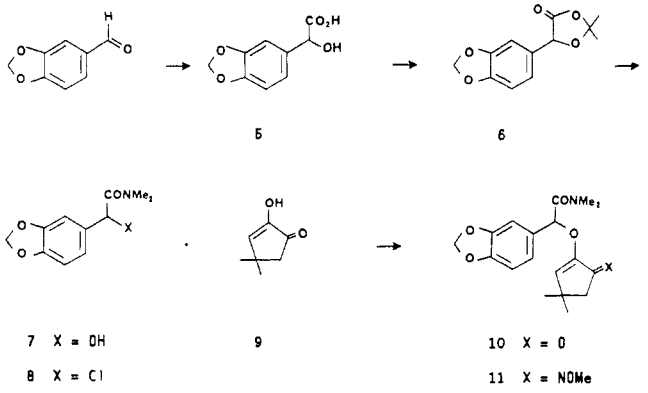
(3) Reviews: (a) Weinreb, S. M.; Semmelhack, M. F. *Acc. Chem. Res.* **1975**, *8*, 158. (b) Smith, C. R., Jr.; Mirolajczak, K. L.; Powell, R. G. In: "Antitumor Agents Based on Natural Product Models"; Academic Press: New York, 1980; Chapter 11. For an extensive list of references concerning *Cephalotaxus* alkaloids see the footnotes in: (c) Hiranuma, S.; Shibata, M.; Hudlicky, T. *J. Org. Chem.* **1983**, *48*, 5321.

0022-3263/85/1950-4523$01.50/0

Scheme I



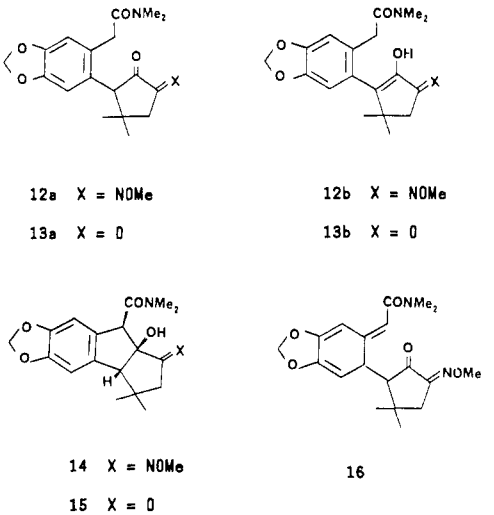
Scheme II



then require deprotection of the nitrogen and cyclization to **4**, followed by appropriate modification of functionality (Scheme I). This synthetic strategy is attractive since we have demonstrated that the [3,3] sigmatropic rearrangement of benzyl vinyl ethers is facilitated by a carbonyl group at the benzylic position;[4] the dimethyl amide group would function in this capacity in the transformation of **2** to **3**. Furthermore, the [3,3] sigmatropic rearrangement of allyl vinyl ethers derived from either cyclic α-diketones (the diosphenol Claisen rearrangement[5]) or the corresponding "donor imine derivatives"[5d] has been shown to occur readily.

Prior to embarking on the efforts directed toward the total synthesis of **1**, we decided to examine studies involving the [3,3] sigmatropic rearrangement of the model benzyl vinyl ether **10**. The preparation of **10** is outlined in Scheme II. Piperonal was converted to 3,4-(methylenedioxy)mandelic acid (**5**) by treatment with $CHBr_3$ and KOH in 1:1 dioxane/H_2O utilizing the method of Compere.[6] Reaction of **5** with 2,2-dimethoxypropane to form the acetonide **6** followed by treatment with dimethylamine gave *N,N*-dimethyl-3,4-(methylenedioxy)mandelamide (**7**), which was converted to the corresponding α-chloro amide **8** by reaction with methanesulfonyl chloride. Acyloin condensation of dimethyl 3,3-dimethylglutarate in the presence of trimethylsilyl chloride,[7] followed by oxidation with Br_2, provided 4,4-dimethylcyclopentane-1,2-dione (**9**).[8] Reaction of **8** with **9** in acetone containing K_2CO_3 gave the benzyl vinyl ether **10**.

Thermolysis of a dilute solution of **10** in *o*-dichlorobenzene at 240 °C for 24 h led only to the recovery of unreacted starting material. Since Ponaras had reported substantial rate enhancements for the rearrangement of "donor-imine derivatives" of diosphenol allyl ethers,[5d] we next examined the thermolysis of **11**, prepared by treatment of **10** with $MeONH_3Cl$ in pyridine. When a 2×10^{-2} M solution of **11** in *o*-dichlorobenzene was heated at 230 °C in a sealed tube for 24 h, a new oxime *O*-methyl ether, which was shown to be isomeric with **11** by mass spectral analysis, was obtained in 36% yield. The same compound was obtained in 91% yield when 2×10^{-2} M solution of **11** in toluene containing 4 equiv of *O,N*-bis(trimethylsilyl)acetamide was heated at 190–220 °C in a sealed tube. The ^1H NMR spectrum of this new compound did not appear to correspond to the expected rearrangement product **12a** or its tautomer **12b**. In particular, the anticipated AB doublet of doublet for the benzylic methylene protons was absent. Instead, the ^1H NMR showed one-proton singlets at δ 3.30 and 4.62 and an exchangeable one-proton singlet at δ 5.33. In addition, the ^{13}C NMR showed no resonances for sp^2-hybridized carbons other than those assigned to the aromatic ring (δ 104.6, 106.7, 133.5, 135.6, 147.4, 147.5), the carbonyl carbons of the oxime (δ 165.8), and the amide (δ 173.1). Furthermore, the 11 other carbons present in the new compound were accounted for by signals for sp^3-hybridized carbons. Also, the IR clearly showed that the new compound contained a hydroxyl group. The new oxime *O*-methyl ether was hydrolyzed to the corresponding ketone, and again the spectral features of the new ketone did not appear to correspond to **13a** or **13b**. The anticipated AB doublet



of doublets for the benzylic methylene protons was absent, and one-proton singlets at δ 3.47 and 4.35 and an exchangeable one-proton singlet at δ 5.23 were present. In addition, the ^{13}C NMR showed no resonances for sp^2-hybridized carbons other than those assigned to the aromatic ring (δ 104.4, 107.6, 133.3, 136.0, 148.6, 148.7), the carbonyl carbons of the ketone (δ 217.0), and the amide (δ 175.2).

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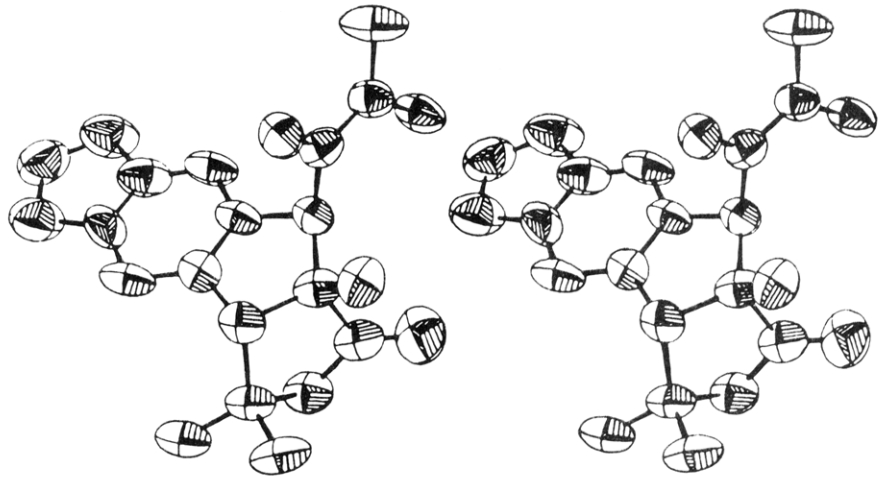

Figure 1. ORTEP stereoview of **15**.

The ten other carbons were accounted for by signals for sp^3-hybridized carbons. The IR showed a hydroxyl group. The structures for the new oxime and new ketone which fit these data best appeared to be **14** and **15**, respectively.

A single-crystal X-ray structure determination performed on the ketone confirmed that it is indeed **15**. A stereoview ORTEP drawing indicating the relative stereochemistry is presented in Figure 1.

At present, it is not known whether formation of **14** occurs by cyclization of **12** or directly from **16**, the putative intermediate[4a] of the [3,3] sigmatropic rearrangement. We are currently investigating the factors responsible for this unusual cyclization, the possibility of effecting retroaldol reaction of **15** to **13**, and the application of this strategy to the synthesis of cephalotaxine.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Canadian Microanalytical Services, Ltd., Vancouver, BC. IR spectra were obtained on a Beckman Acculab 4 and are reported in cm^{-1}. ^1H NMR spectra were recorded on a Varian EM-360 (60 MHz), a Varian CFT-20 (80 MHz), or a Bruker WM-500 (500 MHz). ^{13}C NMR spectra were recorded on a Bruker WM-500 (125 MHz) or a Bruker CX-200 (50 MHz) instrument. Chemical shifts are reported in ppm downfield (δ) from tetramethylsilane. Mass spectra were determined on a VG 7070 GC/MS and associated VG 2035 F/B data system. New compounds gave satisfactory elemental or high-resolution mass spectral analyses. Solvents and reagents were generally distilled or recrystallized prior to use. Flash chromatography was conducted by the method of Still.[9]

3,4-(Methylenedioxy)mandelic Acid (5). To a mixture of piperonal (12.01 g, 80 mmol), KOH (17.95 g, 320 mmol), and LiCl (6.78 g, 160 mmol) in 1,4-dioxane (64 mL) and H_2O (64 mL) cooled to 5 to 10 °C was added $CHBr_3$ (20.22 g, 80 mmol), and the mixture was stirred at 5 to 10 °C for 30 h and then at 25 °C for 65 h. The mixture was cooled to 5 °C, acidified with concentrated HCl (5 mL), and extracted with EtOAc (2 × 100 mL). The combined EtOAc layers were extracted with 10% NaOH (150 mL) and H_2O (100 mL). The combined aqueous layers were acidified with concentrated HCl and extracted with EtOAc (2 × 100 mL). The combined EtOAc layers were evaporated in vacuo to give a brown residue which was crystallized from hexane/EtOAc to afford **5** (8.22 g, 41.9 mmol) as an off-white solid in 52% yield: mp 158–159 °C, [Lit[10] mp 160–162 °C]; IR (KBr) 3660–2350, 1730 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 4.93 (s, 1 H), 6.02 (s, 2 H), 6.95 (m, 3 H).

***N,N*-Dimethyl-3,4-(methylenedioxy)mandelamide (7).** A solution of **6** (2.00 g, 10.2 mmol), 2,2-dimethoxypropane (10.62 g, 102 mmol), and *p*-toluenesulfonic acid monohydrate (38 mg, 0.2 mmol) in CH_2Cl_2 (20 mL) under argon was stirred at 25 °C for 18 h, K_2CO_3 (2.0 g) was added, and the mixture was stirred for 15 min, filtered, and concentrated under reduced pressure to give **6** as a viscous brown oil (2.54 g) ^1H NMR ($CDCl_3$) δ 1.64 (s, 3 H), 1.69 (s, 3 H) 5.25 (s, 1 H), 5.95 (s, 2 H), 6.84 (m, 3 H). The crude acetonide **6** (2.54 g) was dissolved in THF (14 mL), 40% aqueous dimethylamine (11.5 mL) was added, and the mixture was stirred under argon at 25 °C for 69 h. The THF was removed in vacuo, and the resulting white solid (1.76 g) was crystallized from $CHCl_3$/hexane to give **7** (1.55 g, 6.95 mmol) as colorless needles in 68% yield: mp 159–161 °C; IR (KBr) 3300, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.78 (s, 3 H), 3.02 (s, 3 H), 4.67 (d, 1 H), 5.10 (d, 1 H), 5.96 (s, 2 H), 6.84 (m, 3 H). Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.27. Found: C, 58.87; H, 5.62; N, 6.10.

***N,N*-Dimethyl-2-chloro-2-[3,4-(methylenedioxy)phenyl]-acetamide (8).** To a solution of **7** (1.00 g, 4.48 mmol) and Et_3N (1.58 g, 15.6 mmol) in CH_2Cl_2 (25 mL) cooled to 0 °C under argon was added dropwise over 2 min methanesulfonyl chloride (1.19 g, 10.38 mmol). The mixture was stirred at 0 °C for 1 h and washed sequentially with H_2O (20 mL), 5% HCl (20 mL), and saturated Na_2CO_3 (20 mL). The CH_2Cl_2 layer was dried (K_2CO_3), filtered, and evaporated in vacuo to give crude **8** (1.03 g, 4.27 mmol) as an amber oil which was used without further purification: IR (KBr) 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.02 (s, 6 H), 5.65 (s, 1 H), 6.00 (s, 2 H), 6.78–7.34 (m, 3 H); HRMS calcd for $C_{11}H_{12}NO_3Cl$, 241.0501; found, 241.0499. A sample purified by chromatography crystallized on standing in the freezer. Recrystallization from Et_2O gave white crystals, mp 53.5–55 °C.

4,4-Dimethyl-1,2-cyclopentanedione (9).[8a] To a mixture of 1:5 Na/K alloy[11] (2.5 mL) and benzene (57 mL) under argon in a 100-mL flask maintained at 25 °C by a water bath was added with magnetic stirring Me_3SiCl (4.38 g, 40.4 mmol), and then dimethyl 3,3-dimethylglutarate (1.07 g, 5.7 mmol). The mixture was stirred rapidly for 21 h and filtered through a plug of Celite with positive argon pressure, and the benzene and excess Me_3SiCl were removed by rotary evaporation to give a colorless liquid (1.76 g) which was dissolved in CH_2Cl_2 (25 mL) and cooled to −78 °C under argon. Br_2 (888 mg, 5.5 mmol) was added dropwise to this solution over 5 min. The reaction solution was allowed to warm to 25 °C, the CH_2Cl_2 was removed in vacuo, and the resulting yellow liquid (0.93 g) was purified by flash chromatography on silica gel (5% Et_2O/CH_2Cl_2) to give **9** (0.56 g, 4.4 mmol) as a colorless liquid in 76% yield: IR (neat) 3350, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (s, 6 H), 2.32 (s, 2 H), 6.22 (bs, 1 H), 6.41 (s, 1 H); HRMS calcd for $C_7H_{10}O_2$, 126.0681; found, 126.0656.

4,4-Dimethyl-2-[[α-(*N,N*-dimethylcarbamoyl)-3,4-(methylenedioxy)benzyl]oxy]-2-cyclopentenone (10). A mixture of **8** (316 mg, 1.31 mmol), **9** (138 mg, 1.09 mmol), and anhydrous

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K_2CO_3 (388 mg, 2.18 mmol) in acetone (6.5 mL) was heated at 45 °C under argon with stirring for 15 h and then at reflux for 2.5 h. The mixture was cooled and partitioned between pH 7 buffer solution (10 mL) and CH_2Cl_2 (2 × 10 mL). The CH_2Cl_2 layers were combined, dried ($MgSO_4$), filtered, and evaporated in vacuo to give a yellow oil (438 mg) which was purified by flash chromatography on silica gel (20% Et_2O/CH_2Cl_2) to afford a colorless oil which crystallized from hexane/$CHCl_3$ to give **10** as white clusters (235 mg, 0.71 mmol) in 65% yield: mp 135–145 °C; IR (KBr) 1725, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (s, 6 H), 2.28 (s, 2 H), 2.93 (s, 6 H), 5.71 (s, 1 H), 5.95 (s, 2 H), 6.41 (s, 1 H), 6.70–7.09 (m, 3 H); HRMS calcd for $C_{18}H_{21}NO_5$, 331.1420; found, 331.1412.

Oxime *O*-Methyl Ether 11. To a solution of **10** (200 mg, 0.60 mmol) in pyridine (3 mL) under argon was added NH_2OMe·HCl (55 mg, 0.70 mmol), and the mixture was stirred for 24 h at 25 °C. Most of the pyridine was evaporated in vacuo, and the residue was partitioned between CH_2Cl_2 (10 mL) and 5% HCl (10 mL). The CH_2Cl_2 layer was washed with sat Na_2CO_3, dried ($MgSO_4$), filtered, and evaporated in vacuo to afford a white gummy solid (209 mg) which was crystallized from hexane/CH_2Cl_2 to give **11** (176 mg, 0.49 mmol) as white flakes in 81% yield: mp 154–155 °C; IR (KBr) 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (s, 6 H), 2.42 (s, 2 H), 2.94 (s, 3 H), 2.98 (s, 3 H), 3.89 (s, 3 H), 5.38 (s, 1 H), 5.66 (s, 1 H), 5.95 (s, 2 H), 6.68–7.12 (m, 3 H). Anal. Calcd for $C_{19}H_{24}N_2O_5$: C, 63.32; H, 6.71; N, 7.77. Found: C, 63.28; H, 6.65; N, 7.75.

Thermolysis of 11. An oven-dried sealed tube containing a solution of **11** (111 mg, 0.31 mmol) and bis(trimethylsilyl)acetamide (252 mg, 1.24 mmol) in toluene (15.5 mL) was immersed in a preheated (210 °C) vertical tube oven. The temperature equilibrated to about 190 °C over 17 h and was then raised to 220 °C over 4 h and maintained at 220 °C for 20 h. The oven was turned off, and the tube was allowed to cool to 25 °C. The toluene was evaporated in vacuo, and the residue was dissolved in a solution of MeOH (3 mL), H_2O (0.25 mL), and citric acid (12.6 mg, 0.06 mmol) and stirred at 25 °C for 18 h. The MeOH was evaporated in vacuo, and the residue was purified by flash chromatography (hexane/EtOAc) to give **14** (101 mg, 0.28 mmol) as a yellow foam in 91% yield: IR (CCl_4) 3340, 1645, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (s, 3 H), 1.32 (s, 3 H), 2.33 (d, J = 18, 1 H), 2.62 (d, J = 18, 1 H), 3.04 (s, 3 H), 3.32 (s, 3 H), 3.39 (s, 1 H), 3.90 (s, 3 H), 4.62 (s, 1 H), 5.33 (s, 1 H), 5.91 (s, 1 H), 5.95 (s, 1 H), 6.50 (s, 1 H), 6.75 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 26.2, 30.2, 36.0, 38.3, 39.5, 42.3, 54.0, 62.0, 67.6, 90.0, 101.2, 104.6, 106.7, 133.5, 135.6, 147.4, 147.5, 165.8, 173.1; HRMS calcd for $C_{19}H_{24}N_2O_5$, 360.1685; found, 360.1655.

Hydrolysis of 14 to 15. A solution of **14** (101 mg, 0.28 mmol), 37% aqueous CH_2O (0.28 mL), 1 M HCl (0.28 mL), and HOAc (0.56 mL) was stirred at 25 °C for 17 h, and the solution was partitioned between H_2O (10 mL) and CH_2Cl_2 (2 × 10 mL). The CH_2Cl_2 layers were combined, dried ($MgSO_4$), filtered, and evaporated in vacuo to afford a yellow oil which was purified by flash chromatography on silica gel (30% Et_2O/CH_2Cl_2) and crystallized from Et_2O to give **15** (89 mg, 0.27 mmol) in 96% yield. Recrystallization from hexane/$CHCl_3$ gave white needles: mp 177.5–178; IR (KBr) 3320, 1755, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.03 (s, 3 H), 1.37 (s, 3 H), 1.20 (d, J = 16, 1 H), 1.45 (d, J = 16, 1 H), 3.03 (s, 3 H), 3.27 (s, 3 H), 3.47 (s, 1 H), 4.35 (s, 1 H), 5.23 (s, 1 H), 5.94 (s, 1 H), 5.97 (s, 1 H), 6.49 (s, 1 H), 6.78 (s, 1 H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.1, 30.5, 36.4, 36.9, 38.6, 51.1, 52.2, 65.2, 89.0, 101.6, 104.4, 107.6, 133.3, 136.0, 148.6, 148.7, 175.2, 217.0; UV (EtOH) λmax (logϵ) 296 (4.28). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 64.84; H, 6.19; N, 4.17.

Single-Crystal X-ray Structure Determination of 15. Monoclinic crystals suitable for X-ray diffraction were grown from hexane/chloroform. Precession photos showed the space group to be $P2_1/c$ ($0k0$ present for $k = 2n$, $h0l$ present for $l = 2n$), $Z = 4$. X-ray intensity measurements were obtained from a single crystal (0.05 × 0.05 × 0.2 mm) with a computer-controlled, four-circle diffractometer. Unit cell constants obtained from 18 centered reflections were a = 6.944 (5) Å, b = 21.59 (1) Å, c = 12.04 (2) Å, β = 67.27 (10)°. Data were collected in the ω–2θ mode, scan width 1.4 × 0.35 tan θ°, scan rate 2°/min, λ = 1.5418 Å (Cu Kα radiation), maximum 2θ = 100° with 10-s backgrounds measured on both sides of each reflection. Four reflections measured periodically indicated no deterioration of the crystal during data collection. An empirical adsorption correction[12] was applied (maximum correction 1.21). The structure was solved using MULTAN80[13] and was refined and analyzed by using the XRAY76 system of programs.[14] All the hydrogen atoms were located in difference electron density maps. The final cycles of refinement against F with $1/\sigma$ weights included positional and anisotropic temperature factors for C, O, N atoms and positional and isotropic temperature factors for H atoms (except the temperature factor of H(173)). The least-squares refinement converged to an R ($=\sum||F_o| - |F_c||/\sum|F_o|$) of 0.082 for 901 reflections with $F_o > 4\sigma(F_o)$, and 801 reflections had $F_o < 4\sigma(F_o)$. The weighted R was 0.083, the goodness of fit was 2.04, and the maximum shift/error in the last cycle was 0.63. The bond lengths between the nonhydrogen atoms do not indicate any unusual characteristics within the molecule.

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Supplementary Material Available: Tables of bond lengths, bond angles, atomic positional parameters, atomic thermal parameters, and structure factors for **15** (8 pages). Ordering information is given on any current masthead page.

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