Assignment was made by COSY spectrum.

Preparation of 9. For the isolation of **9**, another EtOAc-soluble portion was prepared as described above starting from 50 mg of **1**. To the material in 1% Me_3N/water (6 mL) was added a 5-mL portion of 5% dinitrofluorobenzene in EtOH, and the resultant mixture stirred for 2 h at room temperature. After evaporation of the solvent, the residue was partitioned between 1 N HCl (1 mL) and ether (3 × 1 mL). The ether layer was subjected to the preparative silica gel TLC ($CHCl_3$/AcOH, 98:2) and a major yellow band (R_f 0.4) was obtained. The $CHCl_3$-soluble portion of the resulting yellow material was purified by HPLC [YMC silica gel (5 μm) 2 × 25 cm, $CHCl_3$, detection at 345 nm] to obtain **9** (2.4 mg).

9: ^{1}H NMR ($CDCl_3$) DNP unit δ 9.17 (1 H, d, J = 2.7 Hz), 8.33 (1 H, dd, J = 2.7, 9.6 Hz), 6.79 (1 H, d, J = 9.6 Hz); X5-lactone unit δ 8.80 (1 H, d, J = 7.1 Hz, NH), 7.1-7.25 (5 H, m, aromatic protons), 4.83 (1 H, ddd, J = 3.9, 5.1, 10.1 Hz, H-4), 4.40 (1 H, dddd, J = 3.2, 5.1, 6.9, 7.1 Hz, H-3), 3.04 (1 H, dd, J = 6.9, 17.5 Hz, H-2), 2.70 (1 H, ddd, J = 5.5, 9.5, 14.0 Hz, H-8), 2.64 (1 H, dd, J = 3.2, 17.5 Hz, H-2′), 2.56 (1 H, ddd, J = 6.5, 9.5, 14.0 Hz, H-8′), 1.95 (1 H, ddd, J = 4.5, 10.1, 14.0 Hz, H-5), 1.77 (1 H, m, H-6), 1.67 (2 H, m, H_2-7), 1.43 (1 H, ddd, J = 3.9, 8.7, 14.0 Hz, H-5′), 1.02 (3 H, d, J = 6.5 Hz, 6-CH_3). Qualitative difference NOE experiment: irr δ 8.80, enhanced δ 4.40 (w, weak), 2.64 (m, medium), 1.95 (s, strong), and 1.43 (m); irr δ 4.83, enhanced δ 4.40 (s), 3.04 (w), 1.95 (w), 1.43 (m), and 1.02 (s); irr δ 4.40, enhanced δ 4.83 (s), 3.04 (s), and 2.64 (w).

Preparation of 10. To a solution of **9** (2 mg) in 0.2 mL of MeOH was added a 1-mg portion of K_2CO_3, which was stirred at room temperature for 1 h. After addition of $CHCl_3$ (2 mL), the reaction mixture was applied to a short silica gel column (1.5 × 3 cm) and eluted with $CHCl_3$/MeOH/H_2O (85:15:2) to give 1.8 mg of **10**.

10: FABMS (diethanolamine) m/z 537 (MH + diethanolamine)$^+$; ^{1}H NMR (CD_3OD) δ 9.02 (1 H, d, J = 2.7 Hz), 8.22 (1 H, dd, J = 2.7, 9.6 Hz), 7.20 (1 H, d, J = 9.6 Hz), 7.1-7.3 (5 H, m), 4.05 (2 H, m), 2.61 (4 H, m), 1.2-1.8 (5 H, m), 0.94 (3 H, d, J = 6.0 Hz).

Hoffman-Type Degradation of Theonellamide F with [Bis(trifluoroacetoxy)iodo]benzene (BTI).[38] To a solution of theonellamide F (7 mg) in 50% aqueous MeCN (6 mL) was added BTI (60 mg) and pyridine (100 μL). The mixture was stirred at room temperature for 2 days, evaporated, and partitioned between water and EtOAc. A 500-μg portion of the material was subjected to amino acid analysis and chiral GC-MS analysis.

Preparation of Theonellamide F Methyl Ester. To a solution of theonellamide F (1 mg) in water (0.5 mL) was added ethereal CH_2N_2 (1 mL), and the resultant mixture was left at room temperature for 30 min. After evaporation the product was subjected to FAB mass spectrometry (thioglycerol) which gave the MH$^+$ ion at m/z 1663.

Preparation of Theonellamide F Pentaacetate. Theonellamide F dissolved in a 1:1 mixture of Ac_2O/pyridine (1 mL) was stirred at room temperature overnight. The product was dried and subjected to FAB mass spectrometry (thioglycerol) to give the MH$^+$ ion at m/z 1859.

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Synthesis and Absolute Configuration of the *Aristotelia* Alkaloid Peduncularine

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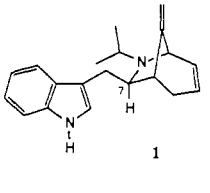
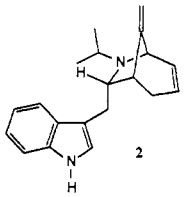
Abstract: The first synthesis of the *Aristotelia* alkaloid peduncularine (**1**) is described. The synthetic sequence commences with (*S*)-malic acid and amounts to 16 steps. Key transformations are (1) the stereoselective transalkylation of the β-hydroxylactam dianion derived from **8**, (2) the formation of the azabicyclo[3.2.1]octanone skeleton **6** via a silicon-assisted *N*-acyliminium ion cyclization of **7**, (3) the introduction of the endocyclic double bond in **5** by flash-vacuum thermolysis of an acetate, and (4) the four-step conversion of lactam **5** into the target molecule **1**. This work conclusively establishes the structure and absolute stereochemistry of natural peduncularine. In addition to **1**, the synthesis also furnishes 7-*epi*-peduncularine (**2**). Contrary to the conclusion in a recent publication, the structures of natural isopeduncularine and 7-*epi*-peduncularine are different.

Peduncularine is the principal alkaloid of the Tasmanian shrub *Aristotelia peduncularis* (Elaeocarpaceae).[1] Bick and co-workers reported the isolation of this natural product in 1971 and initially assigned to it an indole-pyrrolizidine structure on the basis of limited spectroscopic data.[2] Several years later,[3] the revised structure **1** was put forward, containing the unique 6-azabicyclo[3.2.1]-3-octene skeleton with a 3-indolylmethyl substituent. This structure for peduncularine was in complete accordance with



1



2

the results of extensive spectroscopic and degradative work.[3] Recently, a closely related alkaloid was reported to accompany **1** in *A. peduncularis*.[4] This new base, also isolated from *Aristotelia fruticosa*[4] and *Aristotelia serrata*,[5] small trees of New

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(2) Bick, I. R. C.; Bremner, J. B.; Preston, N. W. *J. Chem. Soc., Chem. Commun.* **1971**, 1155.
(3) Ros, H.-P.; Kyburz, R.; Preston, N. W.; Gallagher, R. T.; Bick, I. R. C.; Hesse, M. *Helv. Chim. Acta* **1979**, *62*, 481.
(4) Bick, I. R. C.; Hai, M. A.; Preston, N. W. *Tetrahedron* **1985**, *41*, 3127.

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Zealand, showed very similar spectroscopic data as peduncularine, but some distinctly different physical data. This alkaloid was given structure **2** (7-*epi*-peduncularine) and was called isopeduncularine.[4] The absolute stereochemistry of both alkaloids was unknown prior to the present report. It has been suggested that they biosynthetically arise from tryptophan and a nonrearranged geranyl subunit.[1]

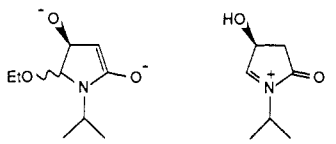
Some years ago, we began a study toward the synthesis of peduncularine and its epimer. These structures caught our attention, because they seemed excellent target molecules to demonstrate the synthetic utility of our novel method for the synthesis of azabicyclic compounds.[6-8] Our synthetic endeavor was further motivated by the desire to conclusively establish structure and absolute configuration of natural peduncularine and isopeduncularine. Finally, these alkaloids are interesting from a pharmacological viewpoint. Plants of the genus *Aristotelia* have been used medicinally by the Maoris in New Zealand and by Indian tribes in South America.[1] Peduncularine appears to display low activity against human breast cancer cells.[1]

In this paper we present the results of our study, which has led to the first syntheses of enantiomerically pure peduncularine and its C-7 epimer, starting from (*S*)-malic acid.[9] Synthetic peduncularine was identical with the natural product, including sign of rotation, so that the structure of this alkaloid has now been proven to be as shown in **1**. On the other hand, synthetic 7-*epi*-peduncularine (**2**) showed spectral data that strongly deviated from those of natural isopeduncularine. Thus, the structural assignment of the latter alkaloid is incorrect.[4]

Results and Discussion

Strategy. Our synthetic approach toward structures **1** and **2** called for the intermediacy of bicyclic skeleton **5**, in order that divergence into the two diastereomeric series occurs late in the synthesis (Scheme I). Introduction of the 3-indolylmethyl moiety was anticipated to be possible by way of Grignard type introduction of the 2-(1,3-dioxanyl)ethyl function coupled with a reduction to give **3** and **4**, and subsequent Fischer indolization.

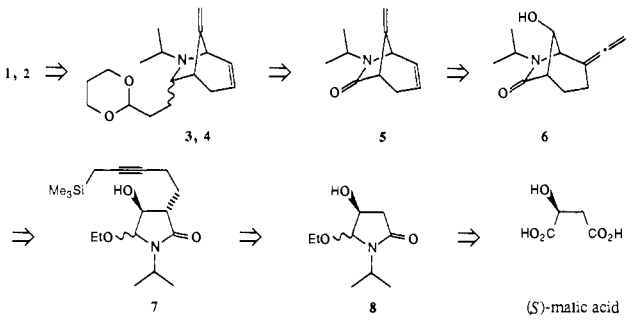
Our plan for the synthesis of **5** from **8** was based on the recently developed methodology to utilize ω-alkoxy lactams as dipolar synthons.[6-8,10,11] Deprotonation of **8** with 2 equiv of LDA leads to the *nucleophilic* dianion **8a** which furnishes **7** after alkylation



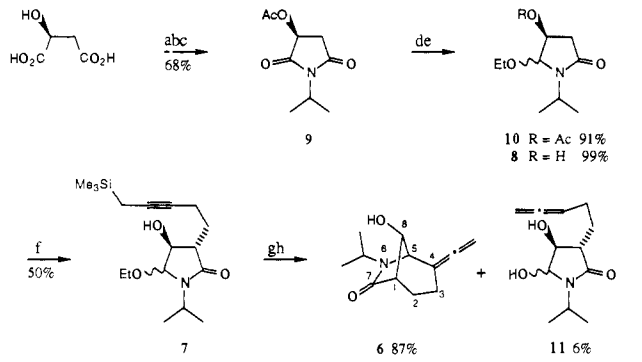
8a **7a**

with the appropriate alkyl halide. Subsequent treatment of **7** with acid then generates the *electrophilic N*-acyliminium cation **7a**, which reacts intramolecularly to give bicyclic **6**.[12] The conversions of the bridge hydroxyl function into an exocyclic double bond and of the allene function into an endocyclic double bond were expected to be more or less standard operations to arrive at **5**. A more direct route from **8** to **5** by employing a vinylsilane cyclization has been shown to fail in a comparable system for stereoelectronic reasons.[13] The synthesis of **8** from malic acid has literature analogy.[14] We began our synthetic venture with inexpensive (*S*)-malic acid, which eventually appeared the correct choice to arrive at the natural stereochemistry.

Scheme I



Scheme II[a]



[a] Conditions: (a) AcCl (7.2 equiv), 1.5 h reflux; (b) *i*-$PrNH_2$ (2.6 equiv), THF, room temperature; (c) AcCl (7.2 equiv), 5 h reflux; (d) 1. $NaBH_4$ (5 equiv), EtOH, 15 min −15 °C; 2 H_2SO_4 (1 M in EtOH), 15 min −25 °C, 1 h room temperature; (e) NaOEt (catalytic), EtOH; (f) LDA (2.1 equiv), THF, −78 °C, then 1 h −25 °C; 2. $ICH_2CH_2C{\equiv}CCH_2SiMe_3$[13] (1.1 equiv), 6 h −117 °C, then 39 h room temperature; (g) HCO_2H, 3 h; (h) NH_3 (50% in MeOH), 18 h.

Synthesis of Bicyclic Lactam 6. Imide **9** (Scheme II) was synthesized by treating (*S*)-malic acid with, successively, acetyl chloride, isopropylamine, and again acetyl chloride.[14] One recrystallization of the crude product gave a sharp-melting crystalline compound [mp 54–55 °C, $[\alpha]^{20}_D$ −31.1° (*c* 2.25, MeOH)], which we assumed to be enantiomerically pure.[15] Regioselective reduction of **9** with $NaBH_4$,[14] immediately followed by ethanolysis, produced ethoxy lactam **10** as an epimeric mixture at C-5. Alcohol **8** was then obtained as an 85:15 mixture of C-5 epimers through ethoxide-catalyzed transesterification in ethanol.

The crucial alkylation reaction of dianion **8a**, obtained from **8** through deprotonation with 2.1 equiv of LDA, with 5-iodo-1-(trimethylsilyl)-2-pentyne[13] proceeded with virtually complete stereoselectivity[16] to give the 3,4-trans lactam **7** as a 85:15 mixture of C-5 epimers. The optimum yield (50%) was obtained when the reaction was carried out at −117 °C. Higher temperatures gave lower alkylation yields, probably due to more serious competition of hydrogen iodide elimination from the alkylating agent.

(5) Anderson, B. F.; Robertson, G. B.; Avey, H. P.; Donovan, W. F.; Bick, I. R. C.; Bremner, J. B.; Finney, A. J. T.; Preston, N. W.; Gallagher, R. T.; Russell, G. B. *J. Chem. Soc., Chem. Commun.* **1975**, 511.

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(8) Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron* **1988**, *44*, 6729.

(9) For successful syntheses of other *Aristotelia* alkaloids, see: Mirand, C.; Massiot, G.; Lévy, J. *J. Org. Chem.* **1982**, *47*, 4169. Stevens, R. V.; Kenney, P. M. *J. Chem. Soc., Chem. Commun.* **1983**, 384. Darbre, T.; Nussbaumer, C.; Borschberg, H.-J. *Helv. Chim. Acta* **1984**, *67*, 1040. Gribble, G. W.; Barden, T. C. *J. Org. Chem.* **1985**, *50*, 5900.

(10) Preliminary communication: Klaver, W. J.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron Lett.* **1987**, *28*, 1581.

(11) For alternative, racemic syntheses of the 6-azabicyclo[3.2.1]-3-octene skeleton, see: Krow, G. R.; Shaw, D. A.; Jovais, C. S.; Ramjit, H. G. *Synth. Commun.* **1983**, *13*, 575. Kvita, V.; Sauter, H.; Rihs, G. *Helv. Chim. Acta* **1983**, *66*, 2769. Snyder, H. R.; Hasbrouck, R. B.; Richardson, J. F. *J. Am. Chem. Soc.* **1939**, *61*, 3558.

(12) For a review on intramolecular *N*-acyliminium ion reactions, see: Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, *41*, 4367.

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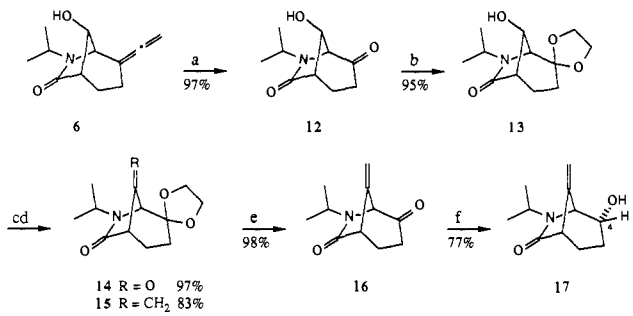
(15) This assumption was not contradicted in subsequent experiments.

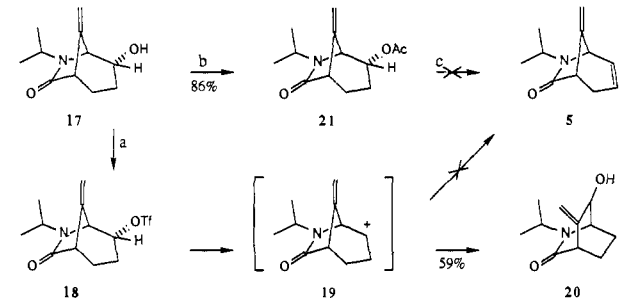
(16) For similar results in the case of β-hydroxy lactone dianions: Shieh, H.-M.; Prestwich, G. D. *J. Org. Chem.* **1981**, *46*, 4319. Chamberlin, A. R.; Dezube, M. *Tetrahedron Lett.* **1982**, *23*, 3055. Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Lawson, K.; Sutter, M. A.; Thaisrivongs, S.; Zimmerman, J. *J. Am. Chem. Soc.* **1985**, *107*, 5292.

Scheme III[a]



[a] Conditions: (a) 1. O_3, CH_2Cl_2, −78 °C; 2. Me_2S; (b) $HOCH_2C$-H_2OH (3 equiv), *p*-TsOH, benzene, 18 h reflux; (c) 1. $(ClCO)_2$ (1.7 equiv), DMSO (3.3 equiv), CH_2Cl_2, −60 °C; 2. Et_3N (7.5 equiv), 18 h room temperature; (d) Ph_3PMeBr (1.6 equiv), *n*-BuLi (1.5 equiv), THF, 20 h reflux; (e) 30% aqueous H_2SO_4/acetone 1:1, 94 h; (f) $NaBH_4$ (2 equiv), EtOH, 30 min.

Scheme IV[a]



[a] Conditions: (a) triflic anhydride (3 equiv), pyridine, 67 h; (b) acetic anhydride (1 equiv), DMAP (catalytic), pyridine, 20 h; (c) FVT, 500–600 °C, 0.05 mmHg.

When **7** was dissolved in formic acid, smooth *N*-acyliminium ion cyclization took place. The crude product was treated with methanolic ammonia to convert formate esters back to the free hydroxy compounds. In this manner, a high yield of the desired bicyclic lactam **6** was obtained. The small amount of byproduct **11** resulted from protodesilylation. The relative stereochemistry of **6** was proved by using the ^1H NMR NOE difference technique. Irradiation of H-8, adjacent to the hydroxyl group, led to a clear intensity enhancement of the signal of the axial H-2. Thus, **6** was obtained as a nicely crystalline solid [mp 147–149 °C, $[\alpha]^{20}_D$ +258° (*c* 5.04, $CHCl_3$)] in five steps and 27% overall yield from (*S*)-malic acid.

Introduction of the Olefinic Double Bonds. The vinylidene substituent in **6** was easily transformed into a carbonyl group by treatment with ozone and reductive workup to furnish keto alcohol **12** (Scheme III). After protection of the ketone as dioxolane, alcohol **13** was subjected to a Swern oxidation[17] to give **14**. The exocyclic double bond was introduced by a Wittig reaction producing the desired olefin **15**. Acidic hydrolysis regenerated the ketone to give **16**, which on reduction with $NaBH_4$ was transformed into a 93:7 mixture of equatorial alcohol **17** and its readily separable axial isomer, respectively.

Our next task was the introduction of the endocyclic double bond. Base-induced E2 elimination of a derivative of alcohol **17** was not feasible because of the equatorial position of the hydroxyl function in a conformationally locked chair cyclohexane ring.[13] Extensive efforts to directly convert the ketone function in **16**, or comparable model systems, into an endocyclic double bond, without going through the alcohol stage, met with failure. The problem was now the instability of the ketone enolate anion, which most likely underwent a fast retro Michael process before it could be trapped in a useful manner. We then directed our attention

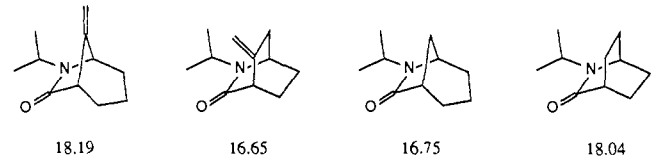
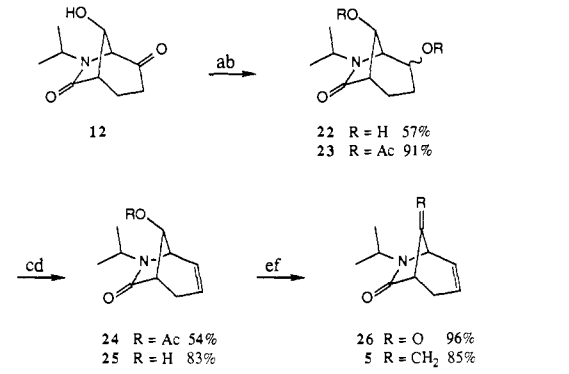


Figure 1. MODEL MM2 energies (in kcal) of some azabicyclic octanones (the program MODEL KS2.92 was used, provided by the Dutch CAOS/CAMM center).

Scheme V[a]



[a] Conditions: (a) $NaBH_4$ (1 equiv), EtOH; (b) acetic anhydride (3 equiv), DMAP (catalytic), pyridine, 19 h; (c) FVT, 600 °C, 0.05 mmHg; (d) NaOEt (catalytic), EtOH; (e) 1. $(ClCO)_2$ (1.7 equiv), DMSO (3.3 equiv), CH_2Cl_2, −60 °C; 2. Et_3N (7.5 equiv), 18 h room temperature; (f) Ph_3PMeBr (1.6 equiv), *n*-BuLi (1.5 equiv), THF, 16 h reflux.

to an E1 elimination reaction. To this end (Scheme IV), alcohol **17** was treated with triflic anhydride in pyridine to generate, via triflate **18**, the cation **19**, which was supposed to give **5** after proton abstraction. However, instead of formation of a double bond, a skeletal rearrangement took place to the azabicyclo[2.2.2]octanone **20**, which was obtained as the sole product after aqueous workup. The skeletal change was very obvious from the IR carbonyl frequencies, i.e., 1690 cm^{-1} in **17** and 1640 cm^{-1} in **20**. This rearrangement was somewhat surprising in view of the results with the saturated analogue of **17**, which show a preference for the azabicyclo[3.2.1]octanone system.[18] Apparently, the presence of the extra sp^2 center, which enhances the strain in **17**, renders the [2.2.2]octane skeleton **20** more favorable. This observation was nicely confirmed by MM2 calculations (Figure 1).

Having experienced the failure of anionic and cationic elimination procedures, we turned our attention to a neutral pericyclic process, i.e., the pyrolytic elimination of acetic acid from acetate **21** (Scheme IV).[19] However, flash-vacuum thermolysis (FVT) of this compound at various temperatures between 400 and 600 °C gave either starting material or complete decomposition. This failure must be ascribed to the homolytic weakness of the (bis)allylic N–C-5 bond in either the starting material **21** or, more likely, in the desired product **5**. To alleviate this problem, we went back in the synthetic sequence and applied the FVT technique to diacetate **23** (Scheme V). This compound or its elimination product should be less sensitive to homolytic cleavage, and only the C-4 acetate substituent was expected to eliminate. Diacetate **23** was easily prepared in two steps from keto alcohol **12**. FVT of **23** was successful at 600 °C to produce an acceptable yield of monoacetate **24**. The remaining steps toward **5**, i.e., regeneration of the hydroxyl function, oxidation to the ketone, and Wittig olefination, proceeded in high yield. Thus, diolefin **5** was obtained as a crystalline solid [mp 59–60 °C, $[\alpha]^{20}_D$ −2.8° (*c* 1.02, $CHCl_3$)] in seven steps and 18% overall yield from **6**.

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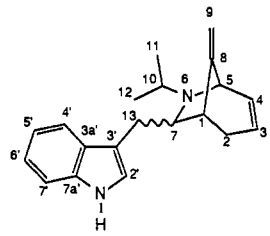
Table I. Comparison of the ^{13}C NMR Chemical Shifts[a] of the Natural and Synthetic Products



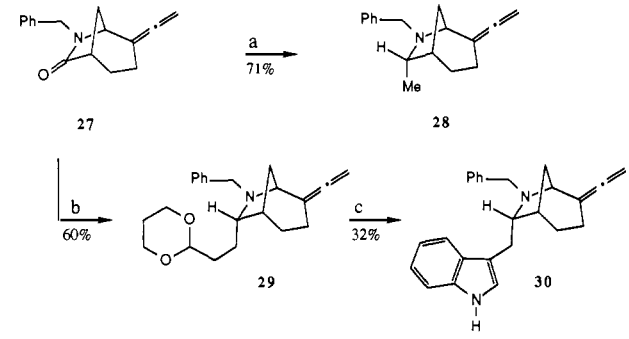
	natural peduncularine[b]	synthetic peduncularine	natural isopeduncularine[c]	synthetic 7-*epi*-peduncularine
C-1	45.9	46.0	46.2	43.2
C-2	34.2	34.3	34.2	29.6
C-3,4	128.4, 130.4	128.3, 130.8	128.5, 130.9	127.4, 134.5
C-5	69.9	69.8	70.1	64.7
C-7	60.4	60.5	60.7	58.3
C-8	149.8	150.2	149.7	152.1
C-9	101.3	101.2	101.2	99.4
C-10	50.9	50.9	51.0	53.8
C-11,12	22.7, 23.6	22.8, 23.7	22.7, 23.6	20.2, 22.1
C-13	40.1	40.2	40.3	32.2
C-2′	121.8	122.0	122.1	122.1
C-3′	114.8	115.3	114.8	114.5
C-3a′	127.7	128.0	127.7	127.6
C-4′,6′	119.0, 119.1	119.1, 119.3	119.2, 119.5	119.0, 119.3
C-5′	121.3	121.1	121.5	121.2
C-7′	110.9	111.0	111.1	111.0
C-7a′	136.1	136.4	136.2	136.1

[a] In ppm, solvent $CDCl_3$. [b] According to ref 2. [c] According to ref 4.

Introduction of the 3-Indolylmethyl Substituent and Completion of the Synthesis. Only limited literature precedent is available on the reaction of lactams with organometallic reagents, followed by reduction of the intermediate carbinol amine.[20] We, therefore, performed some test reactions on the model lactam **27**[13] (Scheme VI). Treatment of **27** with methyllithium in ether and subsequent reduction with $LiAlH_4$ or with $NaBH_3CN$ gave an intractable mixture of products, probably caused by ring opening of the intermediate carbinol amine. Reaction of **27** with excess methylmagnesium chloride followed by acidic reduction with $NaBH_3CN$[21] proceeded satisfactorily to furnish amine **28** as a single stereoisomer. Amine **29** was obtained in a similar fashion by using the Grignard reagent derived from 2-(2-bromoethyl)-1,3-dioxane.[22] The stereochemistry of the alkyl substituent was assigned endo on the basis of the vicinal coupling constant of 4 Hz between H-1 and H-7 in both products. This stereochemistry is very reasonable, because endo hydride attack is clearly sterically hindered by the axial hydrogen at C-3. When **29** was refluxed overnight in 4% aqueous sulfuric acid in the presence of phenylhydrazine,[23] the desired indole **30** was formed. Thus, we have developed a simple two-step procedure to convert a lactam into a cyclic amine with an α-(3-indolylmethyl) substituent.

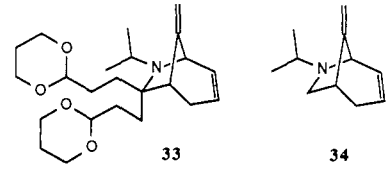
Application of the above methodology to lactam **5** was thwarted by the inertness of **5** to reaction with the Grignard reagent. We reasoned that because of the steric hindrance of the *N*-isopropyl group a greater reactivity at C-7 in **5** was required. Thus, lactam **5** was converted into (methylthio)methyleniminium salt **32**[24] via the corresponding thiolactam **31**[25] in high yield (Scheme VII).

Scheme VI[a]



[a] Conditions: (a) 1. MeMgCl (3 equiv), Et_2O, THF, 18 h; 2. $NaBH_3CN$ (4 equiv), AcOH; (b) 1. [3,3-(trimethylenedioxy)propyl]magnesium bromide[22] (3 equiv), THF, 18 h; 2. $NaBH_3CN$ (4 equiv), AcOH; (c) $PhNHNH_2$ (1 equiv), 4% aqueous H_2SO_4, reflux, 16 h.

Iminium salt **32** appeared to be very reactive toward Grignard reagents.[26] Treatment of a suspension of salt **32** in THF with 2 equiv of the Grignard reagent of 2-(2-bromoethyl)-1,3-dioxane for 68 h at room temperature gave a mixture of dialkylated product **33** (32%) and thiolactam **31** (20%). Shorter reaction times and



lower temperatures always led to mixtures of **31**, **33**, monoalkylated products **3** and **4**, and probably, reduction product **34**. Because the formation of unwanted products was presumably caused by the low solubility of salt **32** in THF we changed the reaction medium. When the Grignard reagent in THF was added to a solution of salt **32** in dichloromethane at −78 °C, and the

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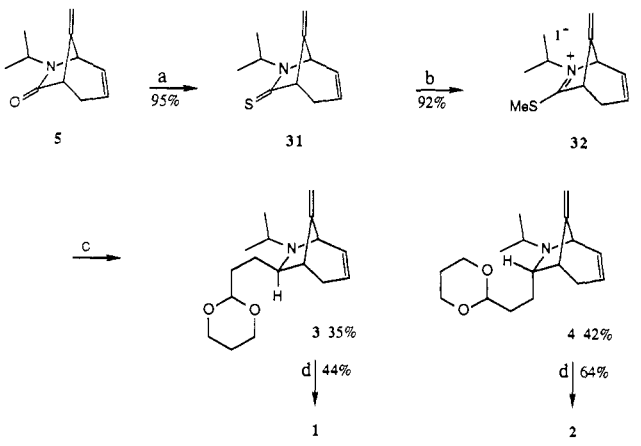
(23) Robinson, B. *Chem. Rev.* **1969**, *69*, 227. Morrison, G. C.; Waite, R. O.; Caro, A. N.; Shavel, J., Jr. *J. Org. Chem.* **1967**, *32*, 3691.

(24) For a review on the synthesis and reactions of (alkylthio)methyleniminium salts, see: Kantlehner, W. In *Iminium Salts in Organic Chemistry*; Böhme, H., Viehe, H. G., Eds.; Wiley: New York, 1979; Part 2, p 279.

(25) Thomsen, I.; Clausen, K.; Scheibye, S.; Lawesson, S.-O. *Org. Synth.* **1984**, *62*, 158.

(26) Yamaguchi, T.; Shimizu, Y.; Suzuki, T. *Chem. Ind.* **1972**, 380. Takahata, H.; Yamazaki, T. *Heterocycles* **1988**, *27*, 1953.

Scheme VII[a]



[a] Conditions: (a) Lawesson's reagent[25] (0.6 equiv), toluene, reflux, 5 h; (b) MeI (17 equiv), Et_2O, 18 h; (c) I. [3,3-(trimethylenedioxy)-propyl]magnesium bromide[22] (1.4 equiv), CH_2Cl_2, THF, −78 °C → 0 °C (40 min) then 0 °C → 20 °C (90 min); 2. $NaBH_3CN$ (2.0 equiv), AcOH; (d) $PhNHNH_2$ (1.6 equiv), 4% aqueous H_2SO_4, reflux, 17 h.

temperature was then allowed to slowly rise to room temperature, dialkylation could be entirely suppressed. In this manner, the desired products **3** and **4** were obtained in a 45:55 ratio, respectively, in 77% yield. The low stereoselectivity, which is fortunate for the synthesis of both target molecules, can be ascribed to the absence of the axial C-3 substituent, if one compares the stereochemical details of formation of **3** and **4** with **29** (vide supra). The isomers **3** and **4** could be separated by flash chromatography. The individual isomers were subjected to the Fischer indole synthesis,[23] which provided the target structures peduncularine (**1**) and 7-*epi*-peduncularine (**2**).

Synthetic peduncularine (**1**) was identical with the natural material by comparison of IR, ^1H NMR, and ^{13}C NMR (Table I) spectral data[3] and melting point [mp 150–158 °C (lit.[3] mp 155–157 °C)]. An authentic sample of the alkaloid, provided by Professor I. R. C. Bick, showed the same ^1H NMR signals and TLC mobility. The specific rotation of our synthetic material [$[\alpha]^{20}_D$ −68° (*c* 0.315, $CHCl_3$)] was within range of the value of the natural product [$[\alpha]^{20}_D$ −76° (*c* 2.33, $CHCl_3$)]. Thus, the structure of natural peduncularine has now been conclusively established to be as shown in **1** with configuration 1*S*,5*R*,7*R*.

Synthetic 7-*epi*-peduncularine (**2**) deviated strongly from natural isopeduncularine with respect to ^1H NMR and ^{13}C NMR (Table I) spectral data,[4] melting point [mp 118–125 °C (lit.[4] mp 113–114 °C)], TLC mobility, and specific rotation [$[\alpha]^{20}_D$ +4.1° (*c* 0.435, $CHCl_3$) (lit.[4] $[\alpha]^{19}_D$ −40° (*c* 4.12, $CHCl_3$))]. An authentic sample of the alkaloid, provided by Professor I. R. C. Bick, showed ^1H NMR signals that were clearly different from those of our synthetic sample. Thus, natural isopeduncularine cannot have a structure **2**. It was reported[4] that the ^1H and ^{13}C NMR spectra of peduncularine and isopeduncularine are very similar. This is difficult to understand, if these compounds are C-7 epimers. Our ^{13}C NMR data (Table I) show considerable differences between **1** and **2**, in particular for C-2 and C-13. This is quite reasonable, because the γ-gauche effect causes upfield shifts[27] for these carbon atoms in the endo isomer **2** in comparison with the exo isomer **1**. Particularly diagnostic in the ^1H NMR spectra are the vicinal coupling constants between H-1 and H-7. To obtain unequivocal information, 600-MHz ^1H NMR spectra of our synthetic products were measured. It was confirmed, that *J*(H-1, H-7) is close to 0 Hz in peduncularine.[3] The epi compound showed a considerable *J*(H-1, H-7) of 5.7 Hz, which is in accord with the expected value from models of the endo isomer showing a dihedral angle of ~35°. The great similarity of the spectra of natural isopeduncularine and peduncularine, as well as the identical R_f values of authentic samples of the alkaloids, inclines us to believe that the structures of these compounds are the same. The differences in solubility, rotation values, and melting points[4] could be the result of inadvertent quaternary ammonium salt formation.

(27) See, e.g.: Wehrli, F. W.; Wirthlin, T. *Interpretation of Carbon-13 NMR Spectra*; Heyden: London, 1976; p 28.

Conclusions

We have achieved the first syntheses of peduncularine (**1**) and 7-*epi*-peduncularine (**2**) in 16 steps from (*S*)-malic acid in overall yields of 0.7% and 1.2%, respectively. Our study demonstrates the utility of the silicon-assisted *N*-acyliminium ion cyclization reaction in alkaloid synthesis.[28] The structure and absolute stereochemistry of natural peduncularine have now been conclusively established. The structure of natural isopeduncularine is clearly different from 7-*epi*-peduncularine.

Experimental Section

General Information. Infrared (IR) spectra were obtained from $CHCl_3$ solutions with a Perkin-Elmer 298 spectrophotometer and are reported in cm^{-1}. Proton nuclear magnetic resonance (^1H NMR) spectra were determined in $CDCl_3$ as solvent with a Varian XL-100 (100 MHz), a Bruker AC 200 (200 MHz), a Bruker WM 250 (250 MHz), or a Bruker AM 600 (600 MHz) instrument. The Bruker AC 200 and WM 250 instruments were also used for the ^{13}C NMR spectra (50 or 63 MHz) in $CDCl_3$ solution. Chemical shifts are given (in ppm) downfield from tetramethylsilane. Exact mass measurements were carried out with a Varian MAT 711 or a VG Micromass ZAB-2HF instrument. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. The elemental analyses were performed by TNO, Utrecht (G. J. Rotscheid). R_f values were obtained by using thin-layer chromatography (TLC) on silica gel coated plastic sheets (Merck silica gel 60 F_{254}) with the indicated solvent (mixture). Chromatographic purification refers to flash chromatography[29] using the same solvent as for TLC and Merck silica gel 60 (230–400 mesh). Melting and boiling points are uncorrected.

(*S*)-Acetoxy-1-isopropylsuccinimide (9). A mixture of (*S*)-malic acid (23.81 g, 177.6 mmol) and acetyl chloride (90 mL, 1.27 mol) was refluxed for 1.5 h and then concentrated in vacuo. The crude anhydride was dissolved in THF (120 mL), and isopropylamine (40 mL, 470 mmol) was added slowly. After the solution was stirred for 2 h, it was concentrated in vacuo, and the residue was refluxed with acetyl chloride (90 mL, 1.27 mol) for another 5 h. After concentration of the reaction mixture in vacuo, the residue was purified by using flash chromatography. Recrystallization of the product from EtOH gave **9** (24.22 g, 121.6 mmol, 68%) as white needles: mp 54–55 °C; $[\alpha]^{20}_D$ −31.1° (*c* 2.25, MeOH); R_f 0.32 (EtOAc/hexanes 2:3); IR 1780 and 1710 (imide CO), 1745 (CO); ^1H NMR (100 MHz) 1.41 (d, *J* = 7 Hz, 6 H, $CH(CH_3)_2$), 2.17 (s, 3 H, $COCH_3$), 2.60 (dd, *J* = 5, 18 Hz, 1 H), 3.12 (dd, *J* = 9, 18 Hz, 1 H), 4.41 (septet, *J* = 7 Hz, 1 H, $CH(CH_3)_2$), 5.36 (dd, *J* = 5, 9 Hz, 1 H, OCH); ^{13}C NMR (50.3 MHz) 18.8 (q), 19.0 (q), 20.3 (q), 35.4 (t, CH_2), 44.0 (d, NCH), 67.2 (d, OCH), 169.7 (s, $COCH_3$), 173.0 (s), 173.3 (s); exact mass found 199.0870, calcd for $C_9H_{13}NO_4$ 199.0845. Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.28; H, 6.58; N, 7.23.

(4*S*,5*R*)-4-Acetoxy-5-ethoxy-1-isopropyl-2-pyrrolidinone and (4*S*,5*S*) Epimer (10). To a solution of **9** (670 mg, 3.36 mmol) in EtOH (35 mL) at −15 °C was added $NaBH_4$ (636 mg, 16.8 mmol). After the reaction mixture was stirred for 15 min at −15 °C, it was cooled to −50 °C, and a 1 M solution of H_2SO_4 in EtOH (ca. 15 mL) was added over 15 min (the temperature of the reaction mixture was maintained below −25 °C). After the reaction mixture was stirred for an additional hour at room temperature, it was poured into saturated aqueous $NaHCO_3$ (150 mL). Extraction with CH_2Cl_2 (4 × 30 mL), followed by drying ($MgSO_4$), concentration of the combined organic layers in vacuo, and chromatography gave **10** (705 mg, 3.07 mmol, 91%) as a colorless oil (87:13 mixture of epimers), R_f 0.39 (major isomer) and 0.30 (minor isomer) (EtOAc/hexanes 3:1). Major isomer: IR 1735 (CO, ester), 1690 (CO, lactam); ^1H NMR (100 MHz) 1.22 (d, *J* = 7 Hz, 3 H, $CH(CH_3)_2$), 1.24 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 1.24 (t, *J* = 7 Hz, 3 H, OCH_2CH_3), 2.09 (s, 3 H, $COCH_3$), 2.27 (d, *J* = 18 Hz, 1 H), 2.90 (dd, *J* = 6, 18 Hz, 1 H), 3.66 (m, 2 H, OCH_2CH_3), 4.22 (septet, *J* = 7 Hz, 1 H, $CH(CH_3)_2$), 4.76 (s, 1 H, CHOEt), 5.05 (d, *J* = 6 Hz, 1 H, OCH); ^{13}C NMR (50.3 MHz) 15.0 (q, OCH_2CH_3), 19.6 (q, $CHCH_3$), 20.6 (q, $COCH_3$), 21.2 (q, $CHCH_3$), 35.8 (t, CH_2CO), 43.4 (d, $CH(CH_3)_2$), 62.8 (t, OCH_2CH_3), 70.2 (d, OCH), 91.2 (d, CHOEt), 169.9 (s, $COCH_3$), 171.9 (s, NCO). Minor isomer: ^1H NMR (100 MHz) 1.10–1.40 (m, 9 H, $CH(CH_3)_2$ and

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OCH_2CH_3), 2.16 (s, 3 H, $COCH_3$), 2.64 (m, 2 H), 3.59 (m, 2 H, OCH_2CH_3), 4.22 (septet, J = 7 Hz, 1 H, $CH(CH_3)_2$), 5.10 (m, 1 H, OCH), 5.11 (s, 1 H, CHOEt); ^{13}C NMR (50.3 MHz) 15.3 (q, OCH_2CH_3), 19.8 (q, $CHCH_3$), 20.5 (q, $COCH_3$), 21.1 (q, $CHCH_3$), 34.7 (t, CH_2CO), 43.6 (d, $CH(CH_3)_2$, 64.0 (t, OCH_2CH_3), 68.1 (d, OCH), 86.3 (d, CHOEt), 170.3 (s, $COCH_3$), 170.3 (s, NCO).

(4*S*,5*R*)-5-Ethoxy-4-hydroxy-1-isopropyl-2-pyrrolidinone and (4*S*,5*S*) Epimer (8). To a solution of the epimeric mixture **10** (8.60 g, 37.5 mmol) in EtOH (10 mL) was added under nitrogen a 0.087 M solution of NaOEt in EtOH (25 mL). After the solution was stirred for 1.5 h at room temperature, it was poured into saturated aqueous NH_4Cl(100 mL). Extraction with CH_2Cl_2 (3 × 25 mL), followed by drying ($MgSO_4$) and concentration of the combined organic layers in vacuo, gave after chromatography **8** (6.93 g, 37.0 mmol, 99 %) as a yellowish oil (82:18 mixture of epimers), R_f 0.32 (acetone/CH_2Cl_2 1:1). Major isomer: IR 3380 (br, OH), 1685 (CO); ^1H NMR (200 MHz) 1.20 (d, J = 6.8 Hz, 6 H, $CH(CH_3)_2$), 1.22 (t, J = 6.5 Hz, 3 H, OCH_2CH_3), 2.20 (d, J = 17.5 Hz, 1 H), 2.82 (dd, J = 5.8, 17.5 Hz, 1 H), 3.56 (m, 2 H, OCH_2CH_3), 3.68 (br s, 1 H, OH), 4.16 (septet, J = 6.8 Hz, 1 H, $CH(CH_3)_2$), 4.16 (d, J = 5.4 Hz, 1 H, CHOH), 4.73 (s, 1 H, CHOEt); ^{13}C NMR (50.3 MHz) 15.2 (q, OCH_2CH_3), 19.6 (q, $CHCH_3$), 21.3 (q, $CHCH_3$), 39.3 (t, CH_2CO), 43.6 (d, $CH(CH_3)_2$), 62.5 (t, OCH_2CH_3), 68.1 (d, CHOH), 94.5 (d, CHOEt), 173.9 (s, CO); exact mass found 187.1195, calcd for $C_9H_{17}NO_3$ 187.1208. Minor isomer: ^1H NMR (200 MHz) 2.33 (dd, J = 8, 17 Hz, 1 H), 2.46 (dd, J = 8, 17 Hz, 1 H), 4.75 (d, J = 5.3 Hz, 1 H, CHOEt); ^{13}C NMR (50.3 MHz) 15.3 (q, OCH_2CH_3), 19.7 (q, $CHCH_3$), 21.3 (q, $CHCH_3$), 38.2 (t, CH_2CO), 43.5 (d, $CH(CH_3)_2$), 65.2 (t, OCH_2CH_3), 66.3 (d, CHOH), 88.3 (d, CHOEt), 173.8 (s, CO).

(3*S*,4*S*,5*R*)-5-Ethoxy-4-hydroxy-1-isopropyl-3-[5-(trimethylsilyl)-3-pentynyl]-2-pyrrolidinone and (3*S*,4*S*,5*S*) Epimer (7). To a mechanically stirred solution of diisopropylamine (8.56 mL, 61.1 mmol) in THF (75 mL) was added under nitrogen at −78 °C a 1.6 M solution of *n*-BuLi in hexane (38.2 mL, 61.1 mmol). After the mixture was stirred for 15 min, a solution of the epimeric mixture **8** (5.45 g, 29.1 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 1 h at −25 to −20 °C and then cooled to −117 °C. A solution of 5-iodo-1-(trimethylsilyl)-2-pentyne[13] (8.39 g, 31.5 mmol) in THF (5 mL) was added. The reaction mixture was stirred for 6 h at −117 °C, allowed to slowly warm, stirred for 40 h at room temperature, and then poured into saturated aqueous NH_4Cl. The aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **7** (4.70 g, 14.4 mmol, 50%) as a yellowish oil (83:17 mixture of epimers), R_f 0.54 (minor isomer) and 0.44 (major isomer) (EtOAc/hexanes 2:1). Major isomer: IR 3400 (br, OH), 2210 (w, C≡C), 1675 (CO), 1245 and 850 (Si—C); ^1H NMR (200 MHz) 0.07 (s, 9 H, $Si(CH_3)_3$), 1.12–1.28 (m, 9 H, $CH(CH_3)_2$ and OCH_2CH_3), 1.40 (t, J = 2.5 Hz, 2 H, CH_2Si), 1.64 (m, 1 H), 2.03 (m, 1 H), 2.33 (m, 3 H), 3.20 (br, 1 H, OH), 3.61 (m, 2 H, OCH_2CH_3), 3.96 (m, 1 H, CHOH), 4.12 (septet, J = 7 Hz 1 H, $CH(CH_3)_2$), 4.67 (d, J = 1.5 Hz, 1 H, CHOEt); ^{13}C NMR (50.3 MHz) −2.2 (q, $Si(CH_3)_3$), 6.9 (t, CH_2Si), 15.3 (q, OCH_2CH_3), 17.3 (t, $COCHCH_2$), 19.3 (q, $CHCH_3$), 21.6 (q, $CHCH_3$), 29.9 (t, $CH_2C{\equiv}C$), 43.8 (d, $CH(CH_3)_2$), 51.0 (d, COCH), 62.8 (t, OCH_2CH_3), 74.8 (d, CHOH), 77.9 (s, C≡C), 78.5 (s, C≡C), 94.0 (d, CHOEt), 174.6 (s, CO); exact mass found 325.2073, calcd for $C_{17}H_{31}NO_3Si$ 325.2073. Minor isomer: IR 3470 (br, OH), 2210 (w, C≡C), 1685 (CO), 1245 and 850 (Si—C); ^1H NMR (250 MHz) 0.07 (s, 9 H, $Si(CH_3)_3$), 1.20 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.22 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.24 (t, J = 7 Hz, 3 H, OCH_2CH_3), 1.40 (t, J = 2.5 Hz, 2 H, CH_2Si), 2.05 (m, 1 H), 2.36–2.58 (m, 4 H), 3.72 (m, 2 H, OCH_2CH_3), 3.88 (m, 1 H, CHOH), 4.12 (septet, J = 7 Hz, 1 H, $CH(CH_3)_2$), 4.71 (d, J = 5.5 Hz, 1 H, CHOEt); ^{13}C NMR (50.3 MHz) −2.3 (q, $Si(CH_3)_3$), 6.7 (t, CH_2Si) 15.3 (q, OCH_2CH_3), 16.6 (t, $COCHCH_2$), 19.8 (q, $CHCH_3$), 21.2 (q, $CHCH_3$), 28.7 (t, $CH_2C{\equiv}C$), 43.3 (d, $CH(CH(CH_3)_2)_2$), 46.3 (d, COCH), 65.3 (t, OCH_2CH_3), 73.2 (d, CHOH), 77.9 (s, C≡C), 78.0 (s, C≡C), 86.4 (d, CHOEt), 173.5 (s, CO); exact mass found 325.2067, calcd for $C_{17}H_{31}NO_3Si$ 325.2073.

(1*S*,5*R*,8*S*)-8-Hydroxy-6-isopropyl-4-vinylidene-6-azabicyclo[3.2.1]-octan-7-one (6). A solution of the epimeric mixture **7** (4.54 g, 13.9 mmol) in HCO_2H (50 mL) was stirred at room temperature for 3 h and then concentrated in vacuo. The residue was dissolved in a 50% methanolic NH_3 solution (10 mL). After this solution was stirred for 18 h at room temperature, it was concentrated in vacuo. The residue was recrystallized from EtOAc to give **6** (2.26 g, 10.9 mmol, 78%). The mother liquor was concentrated in vacuo, and the residue was chromatographed to yield an additional amount of **6** (261. mg, 1.26 mmol, 9%) and **11** (179 mg, 0.796 mmol, 6%). **6**: white needles from EtOAc; mp 148–149 °C; $[\alpha]^{20}_D$ +259° (c 5.04, $CHCl_3$); R_f 0.22 (EtOAc); IR 3370 (br, OH), 1965 (C=C=C), 1680 (CO); ^1H NMR (200 MHz) 1.15 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.18 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.68 (m, 1 H), 1.99 (m, 1 H), 2.20 (m, 2 H), 2.53 (m, 1 H, COCH), 3.10 (br, 1 H, OH), 3.89 (s, 1 H, CHOH), 4.11 (s, 1 H, NCH), 4.34 (septet, J = 7 Hz, 1 H, $CH(CH_3)_2$), 4.72 (m, 2 H, $C{=}CH_2$); ^{13}C NMR (50.3 MHz) 20.0 (q, $CHCH_3$), 20.2 (q, $CHCH_3$), 22.5 (t), 23.8 (t), 43.1 (d, $CH(CH_3)_2$), 49.3 (d, COCH), 63.6 (d, NCH), 75.7 (t, $C{=}CH_2$), 77.9 (d, CHOH), 98.5 (s, $C{=}C{=}CH_2$), 174.1 (s, CO), 202.5 (s, $C{=}CH_2$); exact mass found 207.1258, calcd for $C_{12}H_{17}NO_2$ 207.1259. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.54; H, 8.25; N, 6.87. **11**: yellow oil; R_f 0.40 and 0.50 (EtOAc); IR 3400 (br, OH), 1955 (C=C=C), 1680 (CO); ^1H NMR (250 MHz) 0.91–1.33 (m, 6 H, $CH(CH_3)_2$), 1.45–2.85 (m, 5 H), 3.50–4.50 (br, 2 H, OH (2×)), 3.80 (m, 1 H, CHOH), 4.08 (m, 1 H, $CH(CH_3)_2$), 4.51–4.76 (m, 2 H, $C{=}CH_2$), 4.91–5.13 (m, 2 H, HC=C and NCH).

(1*S*,5*S*,8*S*)-8-Hydroxy-6-isopropyl-6-azabicyclo[3.2.1]octane-4,7-dione (12). A solution of **6** (902 mg, 4.35 mmol) in CH_2Cl_2 (25 mL) was treated with ozone (5% in oxygen) at −78 °C until a blue color appeared. The mixture was then flushed with nitrogen to remove excess ozone, treated with 1 mL of dimethyl sulfide, allowed to warm to room temperature, and concentrated in vacuo. The residue was dissolved in 10 mL of dimethyl sulfide and left at room temperature for 17 h. Crystallized **12** was collected by filtration. The filtrate was concentrated in vacuo and chromatographed to give a total of 830 mg (4.21 mmol, 97%) of **12** as a white crystalline solid: mp 168–171 °C (EtOAc), $[\alpha]^{20}_D$ +301° (c 0.770, $CHCl_3$); R_f 0.42 (EtOAc/acetone 1:1); IR 3370 (br, OH), 1730 and 1685 (CO); ^1H NMR (200 MHz) 1.02 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.14 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.76 (m, 1 H), 2.15 (m, 1 H), 2.28 (dd, J = 7, 16.5 Hz, 1 H), 2.58 (ddd, J = 10, 11, 16.5 Hz, 1 H), 2.71 (m, 1 H, COCH), 3.89 (s, 1 H, CHOH), 3.99 (s, 1 H, NCH), 4.32 (br, 1 H, OH), 4.35 (septet, J = 7 Hz, 1 H, $CH(CH_3)_2$); ^{13}C NMR (50.3 MHz) 19.9 (q, $CHCH_3$), 20.6 (q, $CHCH_3$), 20.9 (t), 33.3 (t, CH_2CO), 43.3 (d, $CH(CH_3)_2$), 48.8 (d, COCH), 70.0 (d, NCH), 76.1 (d, CHOH), 174.1 (s, NCO), 207.4 (s, CO); exact mass found 197.1049, calcd for $C_{10}H_{15}NO_3$ 197.1052.

(1*S*,4*R*,5*R*,8*S*)-4,8-Diacetoxy-6-isopropyl-6-azabicyclo[3.2.1]octan-7-one and (1*S*,4*S*,5*R*,8*S*) Epimer (23). To a solution of **12** (3.46 g, 17.5 mmol) in EtOH (50 mL) was added at 0 °C $NaBH_4$ (664 mg, 17.6 mmol). After the reaction mixture was stirred for 1 h at room temperature, it was neutralized with an aqueous 2 M HCl solution and poured into saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was first extracted with CH_2Cl_2 (4 × 20 mL) and then continuously extracted with $CHCl_3$ for 18 h. The organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed to give **22** (2.00 g, 10.0 mmol, 57%), R_f 0.17 and 0.07 (acetone/CH_2Cl_2 2:1). To a solution of **22** (1.95 g, 9.81 mmol) in pyridine (20 mL) was added acetic anhydride (2.78 mL, 29.5 mmol) and a catalytic amount of 4-(dimethylamino)pyridine. After the reaction mixture was stirred for 19 h at room temperature, it was concentrated in vacuo, and the residue was chromatographed to give **23** (2.52 g, 8.89 mmol, 91%, predominantly one isomer) as a viscous yellowish oil: R_f 0.43 (EtOAc); IR 1735 and 1680 (CO); ^1H NMR (200 MHz) 1.13 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.21 (d, J = 6.8 Hz, 3 H, $CHCH_3$), 1.42–2.18 (m, 4 H), 2.01 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.52 (m, 1 H, COCH), 3.90 (s, 1 H, NCH), 4.18 (septet, J = 6.8 Hz, 1 H, $CH(CH_3)_2$), 4.65 (s, 1 H, OCH), 4.85 (dd, J = 6.5, 8.7 Hz, 1 H, OCH); ^{13}C NMR (50 MHz) 19.7 (q), 20.2 (t), 20.8 (q), 20.9 (q), 21.4 (q), 23.4 (t), 44.3 (d, $CH(CH_3)_2$), 46.1 (d, COCH), 61.3 (d, NCH), 70.2 (d, OCH), 78.0 (d, OCH), 169.6 (s, $COCH_3$), 170.1 (s, $COCH_3$), 173.6 (s, NCO).

(1*S*,5*R*,8*S*)-8-Acetoxy-6-isopropyl-6-azabicyclo[3.2.1]oct-3-en-7-one (24). The above mixture of diacetates **23** (2.52 g, 8.89 mmol) was subjected to flash-vacuum thermolysis[19] (600 °C, 0.05 mmHg). The crude product was chromatographed to give **24** (1.06 g, 4.77 mmol, 54%) as a yellow oil which was crystallized from EtOAc/hexane (1:1) to give a white crystalline solid: mp 60–63 °C; $[\alpha]^{20}_D$ −108° (c 1.01, $CHCl_3$); R_f 0.36 (EtOAc); IR 1730 and 1675 (CO); ^1H NMR (200 MHz) 1.08 (d, J = 7 Hz, 3 H, $CHCH_3$), 1.11 (d, J = 7 Hz, 3 H, $CHCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.49 (m, 2 H), 2.71 (m, 1 H, COCH), 3.77 (d, J = 5.4 Hz, 1 H, NCH), 4.31 (septet, J = 7 Hz, 1 H, $CH(CH_3)_2$), 5.04 (s, 1 H, OCH), 5.66 (dm, J_d = 9.3 Hz, 1 H, NCHCH=CH), 6.11 (ddm, J_d = 5.8, 9.2 Hz, 1 H, NCHCH=CH); ^{13}C NMR (50 MHz) 20.2 (q, $CHCH_3$), 20.9 (q, $COCH_3$), 21.9 (q, $CHCH_3$), 28.1 (t), 42.3 (d, $CH(CH_3)_2$), 45.1 (d, COCH), 53.4 (d, NCH), 76.9 (d, OCH), 128.3 (d, HC=CH), 130.5 (d, HC=CH), 170.6 (s, CO), 173.2 (s, CO); exact mass found 223.1214, calcd for $C_{12}H_{17}NO_3$ 223.1208.

(1*S*,5*R*,8*S*)-8-Hydroxy-6-isopropyl-6-azabicyclo[3.2.1]oct-3-en-7-one (25). To a solution of **24** (0.967 g, 4.33 mmol) in EtOH (5 mL) was added at room temperature under nitrogen a 0.40 M solution of NaOEt in EtOH (1.1 mL, 0.44 mmol). After the reaction mixture was stirred for 45 min, it was poured into saturated aqueous NH_4Cl(10 mL). The aqueous layer was extracted with CH_2Cl_2 (4 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated in vacuo, and the residue was chromatographed to give **25** (653 mg, 3.60 mmol, 83%) as a white

crystalline solid: mp 85–88 °C (EtOAc/hexanes 1:1); $[\alpha]^{20}_D$ −126° (*c* 1.02, $CHCl_3$); R_f 0.26 (EtOAc/acetone 1:1); IR 3350 (br, OH), 1660 (CO); ^{1}H NMR (200 MHz) 1.14 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 1.16 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 2.37 (br, 1 H, OH), 2.45 (m, 2 H), 2.65 (m, 1 H, COCH), 3.64 (d, *J* = 5.5 Hz, 1 H, NCH), 4.22 (s, 1 H, CHOH), 4.31 (septet, *J* = 7 Hz, 1 H, $CH(CH_3)_2$), 5.61 (dm, J_d = 9 Hz, 1 H, NCHCH=CH), 6.11 (ddm, J_d = 5.5, 9 Hz, 1 H, NCHCH=CH).

(1*S*,5*R*)-6-Isopropyl-6-azabicyclo[3.2.1]oct-3-ene-7,8-dione (26). To a solution of oxalyl chloride (0.53 mL, 6.1 mmol) in CH_2Cl_2 (10 mL), under a nitrogen atmosphere at −60 °C, was added DMSO (0.84 mL, 12 mmol). After the reaction mixture was stirred for 5 min, a solution of **25** (648 mg, 3.57 mmol) in CH_2Cl_2 (3 mL) was added, and the reaction mixture was stirred for 1 h at −60 °C. Then Et_3N (3.73 mL, 26.8 mmol) was added, and the reaction mixture was allowed to warm to room temperature, stirred for 20 h, and poured into water (10 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **26** (614 mg, 3.42 mmol, 96%) as a white crystalline solid: mp 67–69 °C (EtOAc/hexanes 1:1); $[\alpha]^{20}_D$ +153° (*c* 1.38, $CHCl_3$); R_f 0.35 (EtOAc); IR 1780 and 1685 (CO); ^{1}H NMR (200 MHz) 1.15 (d, *J* = 6.8 Hz, 3 H, $CHCH_3$), 1.23 (d, *J* = 6.8 Hz, 3 H, $CHCH_3$), 2.93 (m, 2 H), 2.94 (m, 1 H, COCH), 3.80 (d, *J* = 5.6 Hz, 1 H, NCH), 4.55 (septet, *J* = 6.8 Hz, 1 H, $CH(CH_3)_2$), 5.84 (dm, J_d = 9.2 Hz, 1 H, NCHCH=CH), 6.23 (ddm, J_d = 5.6, 9.2 Hz, 1 H, NCHCH=CH); ^{13}C NMR (50 MHz) 20.3 (q, $CHCH_3$), 22.3 (q, $CHCH_3$), 33.9 (t), 42.9 (d, $CH(CH_3)_2$), 50.9 (d, COCH), 56.5 (d, NCH), 130.9 (d, HC=CH), 132.5 (d, HC=CH), 170.2 (s, NCO), 204.0 (s, CO); exact mass found 179.0922, calcd for $C_{10}H_{13}NO_2$ 179.0946.

(1*S*,5*R*)-6-Isopropyl-8-methylene-6-azabicyclo[3.2.1]oct-3-en-7-one (5). To a solution of methyltriphenylphosphonium bromide (1.97 g, 5.39 mmol) in THF (20 mL) was added under a nitrogen atmosphere at 0 °C a 1.6 M solution of *n*-BuLi in hexane (3.26 mL, 5.22 mmol). After the yellow solution was stirred for 25 min at room temperature, a solution of **26** (604 mg, 3.37 mmol) in THF (3 mL) was added. The reaction mixture was refluxed for 16 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (4 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **5** (508 mg, 2.87 mmol, 85%) as a white crystalline solid: mp 59–60 °C (hexane), $[\alpha]^{20}_D$ −2.8°, $[\alpha]^{20}_{436}$ +43°, $[\alpha]^{20}_{365}$ +178° (*c* 1.02, $CHCl_3$); R_f 0.49 (EtOAc); IR 1660 (CO); ^{1}H NMR (200 MHz) 1.13 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 1.16 (d, *J* = 7 Hz, 3 H, $CHCH_3$), 2.53 (m, 2 H), 3.06 (d, *J* = 4.3 Hz, 1 H, COCH), 4.00 (d, *J* = 5.2 Hz, 1 H, NCH), 4.32 (septet, *J* = 7 Hz, 1 H, $CH(CH_3)_2$), 4.72 (s, 1 H, C=CHH), 4.78 (s, 1 H, C=CHH), 5.60 (dm, J_d = 9.3 Hz, 1 H, NCHCH=CH), 6.21 (ddm, J_d = 5.3, 9.2 Hz, 1 H, NCHCH=CH); ^{13}C NMR (50 MHz) 20.5 (q, $CHCH_3$), 22.1 (q, $CHCH_3$), 31.9 (t), 42.7 (d, $CH(CH_3)_2$), 47.6 (d, COCH), 54.9 (d, NCH), 99.0 (t, C=CH_2), 128.1 (d, HC=CH), 133.6 (d, HC=CH), 147.9 (s, C=CH_2), 174.4 (s, CO). Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.40; H, 8.37; N, 8.01.

***endo*-6-Benzyl-7-methyl-4-vinylidene-6-azabicyclo[3.2.1]octane (28).** To a solution of **27**[13] (80.5 mg, 0.336 mmol) in Et_2O (5 mL) was added under nitrogen at 0 °C a 3 M solution of MeMgCl in THF (0.336 mL, 1.01 mmol). The reaction mixture was stirred for 15 min at 0 °C and for 18 h at room temperature. Then $NaBH_3CN$ (84.5 mg, 1.34 mmol) was added at 0 °C, and after addition of acetic acid (15 mL), the reaction mixture was stirred for 1 h at 0 °C and for 2 h at room temperature. Then a 20% aqueous solution of NaOH (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **28** (57.1 mg, 0.239 mmol, 71%) as a colorless oil: R_f 0.31 (EtOAc/hexanes 1:8); IR 1960 (C=C=C); ^{1}H NMR (200 MHz) 1.14 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.44–2.03 (m, 4 H), 2.18 (m, 2 H), 2.73 (m, 1 H, NCHCH), 3.02 (dq, J_d = 4 Hz, J_q = 6.5 Hz, 1 H, $CHCH_3$), 3.52 (d, *J* = 6 Hz, 1 H, NCH), 3.82 (d, *J* = 14.5 Hz, 1 H, CHPh), 3.94 (d, *J* = 14.5 Hz, 1 H, CHPh), 4.49 (d, *J* = 5 Hz, 2 H, C=CH_2), 7.33 (m, 5 H, Ph); ^{13}C NMR (50.3 MHz) 15.0 (q, CH_3), 25.0 (t), 25.9 (t), 37.6 (t), 39.8 (d, NCHCH), 59.1 (t, CH_2Ph), 63.5 (d, NCH), 64.7 (d, NCH), 73.7 (t, C=CH_2), 104.3 (s, C=C=CH_2), 126.5 (d, Ph), 127.9 (d, Ph), 128.4 (d, Ph), 140.7 (s, Ph), 202.5 (s, C=CH_2); exact mass found 239.1681, calcd for $C_{17}H_{21}N$ 239.1674.

***endo*-6-Benzyl-7-[3,3-(trimethylenedioxy)propyl]-4-vinylidene-6-azabicyclo[3.2.1]octane (29).** To a solution of **27**[13] (209 mg, 0.873 mmol) in THF (3 mL) was added under nitrogen at 0 °C a 0.94 M solution of [3,3-(trimethylenedioxy)propyl]magnesium bromide[22] in THF (2.79 mL, 2.62 mmol). The reaction mixture was stirred for 30 min at 0 °C and for 18 h at room temperature. Then $NaBH_3CN$ (219.4 mg, 3.49 mmol) was added at 0 °C, and after addition of acetic acid (4 mL), the reaction mixture was stirred for 1.5 h at room temperature. Then a 10% aqueous solution of NaOH (30 mL) was added. After addition of CH_2Cl_2 (20 mL), the mixture was filtered over Celite and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **29** (178 mg, 0.525 mmol, 60%) as a colorless oil: R_f 0.40 (EtOAc/hexanes 1:2); IR 1960 (C=C=C), 1140 (CO); ^{1}H NMR (200 MHz) 1.17–2.34 (m, 12 H), 2.72 (m, 1 H, NCHCH), 2.83 (m, 1 H, $NCHCH_2CH_2$), 3.45 (d, *J* = 5.5 Hz, 1 H, NCH), 3.64–3.88 (m, 2 H, OCH_2), 3.74 (d, *J* = 14.5 Hz, 1 H, CHPh), 3.95 (d, *J* = 14.5 Hz, 1 H, CHPh), 4.01–4.19 (m, 2 H, OCH_2), 4.43 (d, *J* = 5 Hz, 2 H, C=CH_2), 4.51 (t, *J* = 4.5 Hz, 1 H, OCHO), 7.32 (m, 5 H, Ph); ^{13}C NMR (50.3 MHz) 24.2 (t), 25.1 (t), 25.5 (t), 25.8 (t), 33.0 (t), 37.1 (d, NCHCH), 37.2 (t), 59.3 (t, CH_2Ph), 64.3 (d, NCH), 66.8 (2 t, OCH_2), 68.7 (d, NCH), 73.7 (t, C=CH_2), 102.4 (d, OCHO), 104.0 (s, C=C=CH_2), 126.4 (d, Ph), 127.9 (d, Ph), 128.2 (d, Ph), 140.7 (s, Ph), 200.4 (s, C=CH_2); exact mass found 339.2200, calcd for $C_{22}H_{29}NO_2$ 339.2198.

***endo*-6-Benzyl-7-(3′-indolylmethyl)-4-vinylidene-6-azabicyclo[3.2.1]octane (30).** To a solution of **29** (116.5 mg, 0.343 mmol) and 0.30 mL of 95% H_2SO_4 in 7 mL of water was added phenylhydrazine (33.8 μL, 0.344 mmol). The reaction mixture was refluxed for 16 h and then poured into 40% aqueous NaOH (30 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL), and the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed to give **30** (38.5 mg, 0.109 mmol, 32%) as a yellowish oil: R_f 0.46 (EtOAc/hexanes 1:2); IR 3480 (NH), 1960 (C=C=C); ^{1}H NMR (200 MHz) 1.54 (d, *J* = 11.1 Hz, 1 H), 1.63 (m, 1 H), 1.83–2.43 (m, 4 H), 2.83–3.12 (m, 2 H, CHH-indolyl and NCHCH), 3.13 (dd, *J* = 6, 15 Hz, 1 H, CHH-indolyl), 3.34 (m, 1 H, NCHCH), 3.54 (d, *J* = 5.6 Hz, 1 H, NCH), 3.80 (d, *J* = 14.5 Hz, 1 H, CHPh), 3.95 (d, *J* = 14.5 Hz, 1 H, CHPh), 4.51 (d, *J* = 5.1 Hz, 2 H, C=CH_2), 7.03 (d, *J* = 1.7 Hz, 1 H, C=CHN), 7.09–7.84 (m, 8 H), 7.63 (d, *J* = 7.4 Hz, 1 H), 7.92 (br, 1 H, NH); ^{13}C NMR (50.3 MHz) 25.2 (t), 25.9 (2 t), 37.3 (t, CH_2-indolyl), 37.8 (d, NCHCH), 60.1 (t, CH_2Ph), 64.9 (d, NCH), 69.0 (d, NCH), 73.8 (t, C=CH_2), 104.2 (s, C=C=CH_2), 111.1 (d), 114.5 (s), 119.0 (d), 119.1 (d), 121.8 (d), 121.9 (d), 126.5 (d, Ph), 127.6 (s), 127.9 (d, Ph), 128.3 (d, Ph), 136.2 (s), 140.9 (s, Ph), 200.5 (s, C=CH_2).

(1*S*,5*R*)-6-Isopropyl-8-methylene-6-azabicyclo[3.2.1]-3-octene-7-thione (31). A solution of **5** (184 mg, 1.04 mmol) and Lawesson's reagent[25] (251 mg, 0.622 mmol) in toluene (10 mL) was refluxed under a dry atmosphere for 5 h and then concentrated in vacuo. The residue was chromatographed to yield **31** (190 mg, 0.984 mmol, 95%) as a colorless oil: $[\alpha]^{20}_D$ −151° (*c* 1.10, $CHCl_3$); R_f 0.60 (CH_2Cl_2/hexanes 1:1); IR 1690, 1455; ^{1}H NMR (200 MHz) 1.20 (d, *J* = 6.8 Hz, 3 H, $CHCH_3$), 1.24 (d, *J* = 6.8 Hz, 3 H, $CHCH_3$), 2.62 (m, 2 H), 3.55 (m, 1 H, CSCH), 4.23 (d, *J* = 5.5 Hz, 1 H, NCH), 4.80 (s, 1 H, C=CHH), 4.83 (s, 1 H, C=CHH), 5.04 (septet, *J* = 6.8 Hz, 1 H, $CH(CH_3)_2$), 5.65 (dm, J_d = 9.2 Hz, 1 H, NCHCH=CH), 6.14 (ddm, J_d = 5.5, 9.2 Hz, 1 H, NCHCH=CH). ^{13}C NMR (63 MHz) 19.6 (q, $CHCH_3$), 21.0 (q, $CHCH_3$), 33.7 (t), 47.8 (d, $CH(CH_3)_2$), 58.3 and 59.0 (2 d, CSCH and NCH), 100.0 (t, C=CH_2), 129.5 (d, HC=CH), 131.0 (d, HC=CH), 147.8 (s, C=CH_2), 201.7 (s, CS).

(1*S*,5*R*)-6-Isopropyl-8-methylene-7-(methylthio)-6-azabicyclo[3.2.1]-octa-3,6-dienium Iodide (32). To a solution of **31** (182 mg, 0.943 mmol) in Et_2O (2 mL) was added under a nitrogen atmosphere MeI (1.0 mL, 16 mmol). After the reaction mixture was stirred for 18 h, the solvent was decanted. The remaining crystalline solid was washed with Et_2O (3 × 3 mL) and dried in vacuo to give **32** (292 mg, 0.870 mmol, 92%) as a white crystalline solid: mp 148–149 °C; IR 2940 (CH), 1540 (CN); ^{1}H NMR (200 MHz) 1.48 (d, *J* = 6.6 Hz, 6 H, $CH(CH_3)_2$), 2.61 (br d, *J* = 19.2 Hz, 1 H, HC=CHCHH), 3.04 (dm, J_d = 19.2 Hz, 1 H, HC=CHCHH), 3.16 (s, 3 H, SCH_3), 4.33 (septet, *J* = 6.6 Hz, 1 H, $CH(CH_3)_2$), 4.89 (d, *J* = 5.5 Hz, 1 H, CSCH), 5.00 (d, *J* = 5.7 Hz, 1 H, NCH), 5.23 (s, 1 H, C=CHH), 5.41 (s, 1 H, C=CHH), 5.81 (dm, J_d = 9.2 Hz, 1 H, NCHCH=CH), 6.30 (m, 1 H, NCHCH=CH).

(1*S*,5*R*,7*R*)-6-Isopropyl-8-methylene-7-[3,3-(trimethylenedioxy)-propyl]-6-azabicyclo[3.2.1]-3-octene (3) and the C-7 Epimer (4). To a solution of **32** (30.0 mg, 0.0899 mmol) in CH_2Cl_2 (1 mL) was added under nitrogen at −78 °C a 0.91 M solution of [3,3-(trimethylenedioxy)propyl]magnesium bromide[22] in THF (0.14 mL, 0.13 mmol). The reaction mixture was allowed to warm to 0 °C over a 40-min period. After the solution was stirred for 30 min at 0 °C, the cooling bath was removed and the reaction mixture was stirred for 1 h. Then $NaBH_3CN$ (11 mg, 0.18 mmol) was added, and after addition of acetic acid (0.5 mL), the reaction mixture was stirred for 1.5 h. Then a 10% aqueous solution of NaOH was added until pH 10. The aqueous layer was extracted with CH_2Cl_2 (4 × 15 mL), and the combined organic extracts were dried (K_2CO_3) and concentrated in vacuo. The residue was chromatographed to give a 45:55 mixture of **3** and **4** (19.2 mg, 0.0692 mmol,

77%). A larger scale experiment (using 96.3 mg, 0.287 mmol of **32**) under otherwise identical conditions also gave a 45:55 mixture, which was chromatographically separated to yield **3** (14.7 mg, 0.0530 mmol, 18%), **4** (13.0 mg, 0.0469 mmol, 16%), and a 25:75 mixture of **3** and **4** (11.5 mg, 0.0415 mmol, 14%) as colorless oils. **3**: $[\alpha]^{20}_D$ −41.5° (*c* 0.735, $CHCl_3$); R_f 0.15 (EtOAc/acetone/Et_3N 100:100:1); IR 2960, 2930 and 2860 (CH), 1685 (C=C), 1145 (CO); ^1H NMR (200 MHz) 1.08 (d, J = 6.1 Hz, 3 H, $CHCH_3$), 1.09 (d, J = 6.4 Hz, 3 H, $CHCH_3$), 1.20–1.75 (m, 4 H), 2.05 (m, 2 H), 2.20 (dm, J_d = 17.6 Hz, 1 H, HC=CHCHH), 2.38 (m, 2 H, NCHCH and NCHCH), 2.56 (dm, J_d = 17.6 Hz, 1 H, HC=CHCHH), 2.85 (septet, J = 6.3 Hz, 1 H, $CH(CH_3)_2$), 3.64–3.84 (m, 3 H, OCH_2 and NCH), 4.08 (m, 2 H, OCH_2), 4.48 (t, J = 4.8 Hz, 1 H, OCHO), 4.77 (s, 1 H, C=CHH), 4.87 (s, 1 H, C=CHH), 5.69 (dm, J_d = 9.2 Hz, 1 H, NCHCH=CH), 5.90 (ddm, J_d = 5.2, 9.3 Hz, 1 H, NCHCH=CH). **4**: $[\alpha]^{20}_D$ +8.6° (*c* 0.43, $CHCl_3$); R_f 0.04 (EtOAc/acetone/Et_3N 100:100:1); IR 2960, 2930 and 2860 (CH), 1675 (C=C), 1145 (CO); ^1H NMR (200 MHz) 0.99 (d, J = 6.2 Hz, 3 H, $CHCH_3$), 1.07 (d, J = 6.4 Hz, 3 H, $CHCH_3$), 1.22–2.20 (m, 6 H), 2.35 (m, 2 H, HC=CHCH), 2.66 (septet, J = 6.4 Hz, 1 H, $CH(CH_3)_2$), 2.70 (br s, 1 H, NCHCH), 2.85 (m, 1 H, NCHCH), 3.43 (d, J = 6.0 Hz, 1 H, NCH), 3.74 (m, 2 H, OCH_2), 4.09 (m, 2 H, OCH_2), 4.50 (t, J = 5 Hz, 1 H, OCHO), 4.65 (s, 1 H, C=CHH), 4.77 (s, 1 H, C=CHH), 5.57 (dm, J_d = 9.1 Hz, 1 H, NCHCH=CH), 6.04 (ddm, J_d = 6.6, 9.0 Hz, 1 H, NCHCH=CH).

(1*S*,5*R*,7*R*)-7-(3′-Indolylmethyl)-6-isopropyl-8-methylene-6-azabicyclo[3.2.1]-3-octene (Peduncularine, 1). To a solution of **3** (13.9 mg, 0.0501 mmol) and 0.10 mL of 95% H_2SO_4 in 2.3 mL of water was added phenylhydrazine (8.0 μL, 0.081 mmol). The reaction mixture was refluxed for 17 h and then poured into 20% aqueous NaOH (5 mL). The aqueous layer was extracted with Et_2O (4 × 15 mL), and the combined organic extracts were dried (K_2CO_3) and concentrated in vacuo. The residue was chromatographed to give **1** (6.3 mg, 0.022 mmol, 44 %) as a yellow oil that crystallized upon standing as white needles, which were washed with $CHCl_3$: mp 148–158 °C, $[\alpha]^{20}_D$ −68°; $[\alpha]^{20}_{546}$ −83° (*c* 0.315, $CHCl_3$), $[\alpha]^{20}_D$ −67°, $[\alpha]^{20}_{546}$ −80° (*c* 0.315, MeOH); R_f 0.30 (EtOAc/acetone/Et_3N 100:100:1); IR 3480 (NH), 1685 (C=C), 1620 (C=CH_2), 1485, 1450 (Ar), 890 (C=CH_2); ^1H NMR [600 MHz, 40% NaOD in D_2O (15 μL) was added to the $CDCl_3$ solution to remove traces of DCl (for numbering see Table I)] 1.15 (d, J = 6.2 Hz, 3 H, H-11), 1.30 (d, J = 6.4 Hz, 3 H, H-12), 2.06 (ddt, J_d = 3.6, 17.6 Hz, J_t = 1.8 Hz, 1 H, H-2(endo)), 2.44 (ddt, J_d = 4.8, 17.6 Hz, J_t = 2.5 Hz, 1 H, H-2(exo)), 2.49 (br d, J = 4.7 Hz, 1 H, H-1), 2.69 (dd, J = 11.3, 14.9 Hz, 1 H, H-13), 2.87 (dd, J = 2.8, 11.3 Hz, 1 H, H-7), 2.93 (dd, J = 2.9, 15.0 Hz, 1 H, H-13), 2.99 (septet, J = 6.3 Hz, 1 H, H-10), 3.83 (d, J = 5.2 Hz, 1 H, H-5), 4.80 (s, 1 H, H-9), 4.94 (s, 1 H, H-9), 5.67 (dt, J_d = 9.3 Hz, J_t = 3.2 Hz, 1 H, H-3), 5.94 (ddt, J_d = 5.2, 9.3 Hz, J_t = 2.0 Hz, 1 H, H-4), 6.96 (s, 1 H, H-2′), 7.10 and 7.18 (2 t, J = 7.5 Hz, 1 H, H-5′ and H-6′), 7.34 (d, J = 8.1 Hz, 1 H, H-7′), 7.59 (d, J = 7.9 Hz, 1 H, H-4′); for ^{13}C NMR see Table I; exact mass found 292.1914, calcd for $C_{20}H_{24}N_2$ 292.1939).

(1*S*,5*R*,7*S*)-7-(3′-Indolylmethyl)-6-isopropyl-8-methylene-6-azabicyclo[3.2.1]-3-octene (7-*epi*-Peduncularine, 2). In the same manner as above, **4** (13.0 mg, 0.0469 mmol) was transformed into **2** (8.7 mg, 0.030 mmol, 64%) as a yellow oil that solidified upon standing: mp 118–125 °C; $[\alpha]^{20}_D$ +4.1°, $[\alpha]^{20}_{546}$ +6.2° (*c* 0.435, $CHCl_3$), $[\alpha]^{20}_D$ −13°, $[\alpha]^{20}_{546}$ −15° (*c* 0.425, MeOH); R_f 0.21 (EtOAc/acetone/Et_3N 100:100:1); IR 3480 (NH), 1675 (C=C), 1615 (C=CH_2), 1485, 1450 (Ar), 890 (C=CH_2); ^1H NMR [600 MHz, 40% NaOD in D_2O (15 μL) was added to the $CDCl_3$ solution to remove traces of DCl (for numbering see Table I)] 1.05 (d, J = 6.3 Hz, 3 H, H-11), 1.39 (d, J = 6.5 Hz, 3 H, H-12), 2.27 (ddt, J_d = 4.6, 18.1 Hz, J_t = 2.4 Hz, 1 H, H-2(exo)), 2.45 (ddt, J_d = 3.9, 18.1 Hz, J_t = 2.0 Hz, 1 H, H-2(endo)), 2.71 (br t, J = 5.2 Hz, 1 H, H-1), 2.74 (septet, J = 6.4 Hz, 1 H, H-10), 2.97 (dd, J = 11.6, 15.4 Hz, 1 H, H-13), 3.10 (dd, J = 4.1, 15.4 Hz, 1 H, H-13), 3.42 (ddd, J = 4.3, 5.7, 11.5 Hz, 1 H, H-7), 3.49 (d, J = 6.5 Hz, 1 H, H-5), 4.64 (s, 1 H, H-9), 4.71 (s, 1 H, H-9), 5.63 (dt, J_d = 9.1 Hz, J_t = 3.2 Hz, 1 H, H-3), 6.11 (ddt, J_d = 6.9, 8.6 Hz, J_t = 1.9 Hz, 1 H, H-4), 7.00 (s, 1 H, H-2′), 7.10 and 7.18 (2 t, J = 7.5 Hz, 1 H, H-5′ and H-6′), 7.34 (d, J = 8.1 Hz, 1 H, H-7′), 7.61 (d, J = 7.9 Hz, 1 H, H-4′); For ^{13}C NMR see Table I; exact mass found 292.1948, calcd for $C_{20}H_{24}N_2$ 292.1939.

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Supplementary Material Available: Experimental details, including spectral and analytical data, for the preparation of compounds **13–17**, **20**, **21**, and **33** (3 pages). Ordering information is given on any current masthead page.